2021

Analysis of HbA1c, Medication Compliance, Income Subsidies, and Comorbidity in Medicare Type 2 Diabetics

Robert E. Lazarchik
Walden University

Walden University

College of Health Professions

This is to certify that the doctoral dissertation by

Robert Lazarchik

has been found to be complete and satisfactory in all respects,
and that any and all revisions required by
the review committee have been made.

Review Committee
Dr. David Segal, Committee Chairperson, Health Services Faculty
Dr. Mountasser Kadrie, Committee Member, Health Services Faculty
Dr. James Rohrer, University Reviewer, Health Services Faculty

Chief Academic Officer and Provost
Sue Subocz, Ph.D.

Walden University
2021

Abstract

Analysis of HbA1c, Medication Compliance, Income Subsidies, and Comorbidity in Medicare Type 2 Diabetics

by

Robert Lazarchik

MPhil, Waldon University, 2019

MHA, St. Joseph's College, 2015

BS, University of Florida, 1977

Design Plan Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Health Services

Walden University

September 2021

Abstract

Diabetes is one of America's leading chronic diseases with comorbidities contributing to lower health statuses and increased health care costs. While it is known that lowering HbA1c reduces the deleterious effects of diabetes, the capability to identify people with diabetes at risk for uncontrolled HbA1c levels or developing comorbidities based on the compliance rates for different oral antihyperglycemic medication classes (OAMCs) and financial assistance programs does not yet exist. These quantitative longitudinal retrospective studies examined the association between medication compliance, using Proportion of Days Covered (PDC), by OAMC and Medicare financial aid programs, on predicting HbA1c levels and comorbidities in type 2 diabetics. Jaam's medication compliance framework guided sample selection from the 2019 claims database of a large Managed Care Organization with limited eligibility of only 60% of the population which had an HbA1c level checked in the past 12 months. Multiple regression analyses revealed that as compliance rates improve, different OAMC combinations are associated with significant and variable reductions in A1c levels but with minimal effect strengths not allowing the linear regression model to be used as a predictive tool. Financial assistance programs have a small, but statistically significant effect on reducing HbA1c levels, comorbidities, or improving compliance rates. These studies are the first to investigate the association between PDC compliance rates for OAMCs on HbA1c and comorbidities. These findings contribute to positive social change by demonstrating that variable patient compliance rates for different OAMC medication classes and HbA1c testing should be considered when prescribing diabetic therapeutic regimens to achieve optimal HbA1c control and improved health status.

Analysis of HbA1c, Medication Compliance, Income Subsidies, and Comorbidity in Medicare Type 2 Diabetics

by

Robert Lazarchik

MPhil, Waldon University, 2019

MHA, St. Joseph's College, 2015

BS, University of Florida, 1977

Design Plan Submitted in Partial Fulfillment

Of the Requirements for the Degree of

Doctor of Philosophy

Health Services

Walden University

September 2021

Dedication

This dissertation is dedicated to my wife and my parents. I inherited my inquisitive nature and logical thinking from my father, an electrical engineer. From my mother, I inherited my personality, which has allowed me not to take things (or myself) too seriously and gives me confidence that I can do what I set to accomplish and to both of you my love and since thanks.

Finally, and not last by any stretch of the imagination, is my indebtedness to my wife, Debbie. She put up with my coming home from work and disappearing in my office to study without complaint. My weekends of hiding and studying, showing up for a cup of coffee every now and then, or looking for dinner, then hiding again did not faze her. She silently took out the garbage, kept the house going, and never complained once about my obsession with school and the neglect she endured. I will never be able to repay her for all of her silent help during my journey to my Ph.D. because, without her understanding, I would not have endured.

Acknowledgments

These studies would not have been possible without the cooperation of a number of individuals, including Angel Ballew and James Greenough, who helped me with the administrative tasks involved in securing the data. Additionally, I want to acknowledge Asia Lowe and Blessing Ekanem who spent numerous hours identifying available data and providing the final data for these studies.

Table of Contents

List of Tables

List of Figures

Part 1: Overview

Introduction

Purpose for Study

Diabetes ranks seventh in the cause of death in the US, with 122 million Americans actively diagnosed with diabetes or prediabetes; almost one-third of the US population. Diabetes cases surged between 2008 and 2018 with the incidence highest in Native Americans and Alaskan Indians. One third of people with diabetes have chronic kidney disease and fewer than 25% are aware they suffer from this comorbidity. Currently rates in those aged 10-19 have increased significantly. Only 50% of diabetics have their HbA1c levels under control at less than 7% (Centers for Disease Control and Prevention, 2020). One out of every four dollars spent on healthcare in the US is related to diabetes (Riddle & Herman, 2018). Additionally, diabetes comorbidities, including Myocardial infarction, End-Stage Renal Disease, Blindness, and Urinary Tract Infections create additional financial burdens through reduced health statuses. Medication compliance is a crucial part of any diabetes treatment plan, yet people with diabetes remain non-compliant in taking their medications. Diabetes is the most expensive chronic disease to treat, primarily due to the high comorbidity rates and complications.

In 2008, Medicare (CMS) implemented a quality rating system for many healthcare providers, called the Star Score Ratings, ranging from one to five with one being a poor rating and five being the highest rating possible. This ranking system provides consumers a way to compare the quality of care provided by different healthcare

providers (Cotton et al., 2016). In 2017, state Medicaid programs adopted a quality rating system called the Medicaid Health Plan Rating System, or HPR, created by the National Center for Quality Assurance (NCQA) (National Center for Quality Assurance, 2018b). Under Medicare, Managed Care Organizations (MCO) face a 9% loss in payments low quality ratings and a 9% bonus payment for a high quality rating with payment in the form of bonuses and rebates.

NCQA diabetes measures are part of the Healthcare Effectiveness Data and Information Set, better known as the HEDIS system, based on six domains of care (National Center for Quality Assurance, 2018a). Diabetes falls under the chronic conditions domain and includes measures of HbA1c control, annual retinopathy and nephropathy screening compliance, and controlled blood pressure. Because of the financial risk that healthcare organizations face if they do not meet their CMS or HPR HEDIS standards for people with diabetes, there is a need for analytic tools to help these organizations identify those at risk for high HbA1c levels and minimize the comorbidities of diabetes.

Theoretical and Practical Relevance

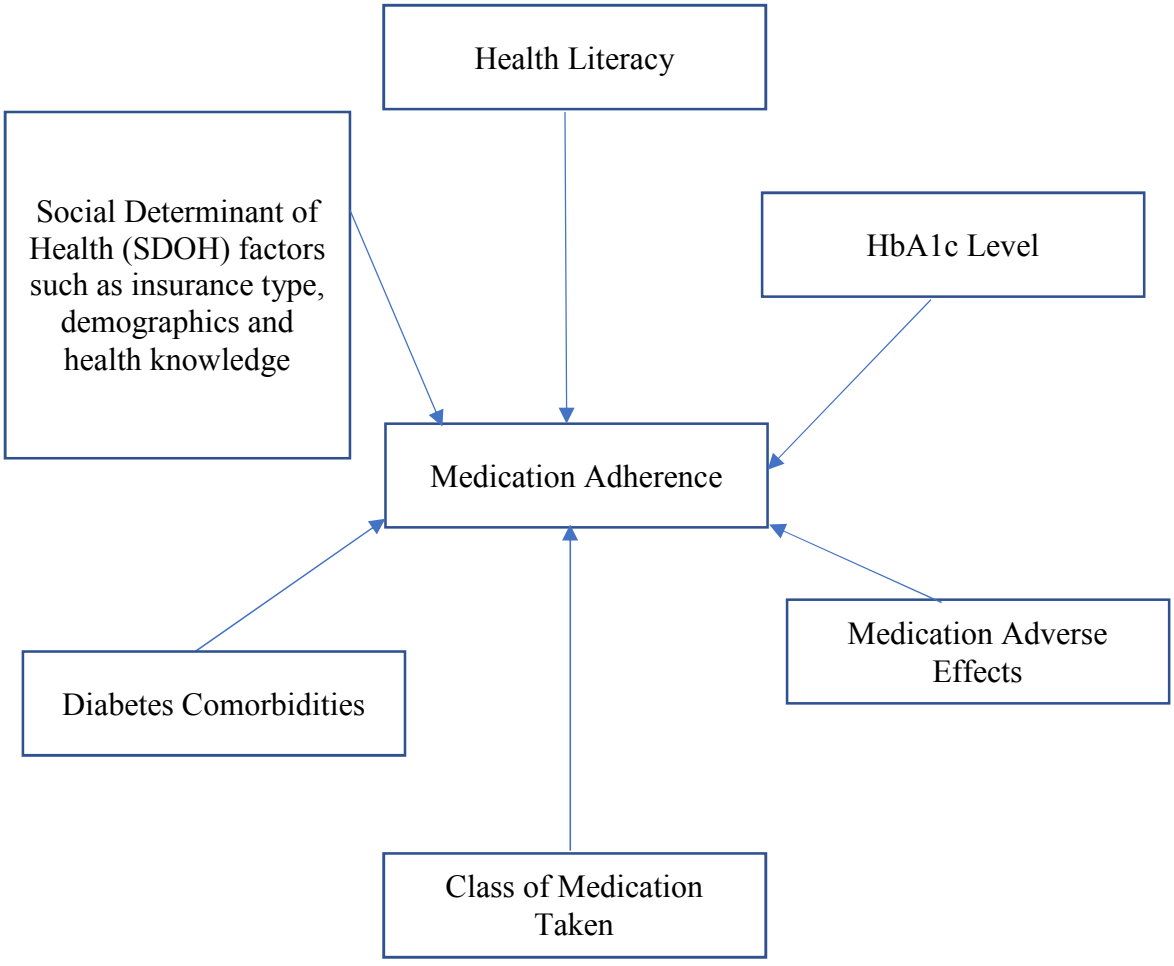
Jaam's Diabetes Medication Compliance Framework

With over forty years of studies on medication compliance, current frameworks are still fragmented (Allemann et al., 2016). In 2018, Jaam et al., developed a framework defining the relationship between the HEDIS CDC diabetes measure and medication compliance, the core objectives of the studies presented in this dissertation. Clinical

predictors included are type of diabetes, HbA1c level, comorbidities, glucose control, duration of diabetes, diabetes-related factors, and classes of blood sugar control medications taken. The Social Determinants of Health (SDOH) factors such as insurance type, demographics and health literacy, are included as predictors in the studies presented here. All these predictors are part of Jaam's framework shown in Figure 1.

Figure 1

Medication Compliance Framework



Taken from Jaam's Medication Compliance Framework Jaam et al. (2018)

Current Scientific Understanding

In 2015, diabetes was the seventh leading cause of death in the US. Approximately 117 million Americans have either diabetes or prediabetes, constituting almost one-third of the US population. Other disturbing factors related to diabetes include only one in four people with diabetes know they have the disease, in 2015 there were 1.5 million new diagnoses in those over 18, more men are diagnosed as prediabetic than women, and diabetes contributes to other diseases such as cardiovascular, stroke, neuropathies, and kidney disease (Center for Disease Control, 2017).

Healthcare organizations are interested in diabetes because of the financial challenges presented by quality measures introduced by Medicare. The NCQA HEDIS measures are used to evaluate the quality of care for 190 million individuals, or 60% of the US population (National Committee for Quality Assurance, 2018a). HEDIS measure compliance is part of the calculation of base financial rewards or penalties based on how well providers perform against NCQA standards. Penalties for Medicare Advantage plans not meeting quality goals can see reduced payment rates and bonus money loss. Penalties for Medicaid MCO's are set by individual states using the HPR system established by the NCQA. Penalties for not meeting quality standards include payment holdbacks, changes in the way individuals are assigned to MCO's, and monetary chargebacks (Rowan et al., 2021).

With one-third of the US population having some form of diabetes and the financial penalties for MCO's not reaching set quality scores, MCO's need help identifying those at risk for uncontrolled HbA1c levels, high rates of medication non-compliance, and for not meeting HEDIS quality standards. The studies in this dissertation focus on developing and validating methods to help MCO's identify people with diabetes that may contribute to low-quality scores, examine the effectiveness of two Medicare financial subsidy programs, and examine the relationship between medication compliance and medication class and four of the comorbidities of diabetes.

Scope and Delimitations

The goal of these studies is to show that the Proportion of Days Covered (PDC), a medication adherence measurement methodology, for individual antihyperglycemic medications class being taken, and participation in financial assistance programs, can be used in multiple regressions as a method to identify at-risk individuals for uncontrolled HbA1c levels and those at risk for the comorbidities of diabetes. If these proposed analysis are found valid, they give organizations a quick and proactive way to improve their HEDIS diabetes compliance rates and reduce their financial risks. While there are studies in the literature discussing the HEDIS PDC measure, there are none on its use combined with a class of antihyperglycemic medication as a predictor for HbA1c levels. This study presents an opportunity to fill a gap in the literature that, to date, has not been studied and could be of significance to health care providers and organizations.

Participants for these studies were selected using secondary claims data provided by a large MCO.

Problem Statement

Healthcare organizations that must comply with the HEDIS standards face both financial and human issues. First, there are financial penalties for not meeting the quality standards set by Medicare and Medicaid. Second, MCO's face additional medical costs created by their members who do not comply with quality standards. The first manuscript establishes a relationship between medication compliance and six of the nine classes of oral antihyperglycemic medications and HbA1c levels. The second study establishes the statistical significance of the relationship between the two Medicare financial subsidy programs, Low Income Subsidy (LIS) and Dually Eligible Special Needs Program (DSNP) on HbA1c levels and medication compliance in any of the six classes of oral antihyperglycemic medications, there is not any significant strength of effect.. The third manuscript identifies some statistically significant factors for those at risk for four of the comorbidities of diabetes, blindness, end-stage renal disease, myocardial infarction, or urinary tract infection based on medication compliance, the class of antihyperglycemic medication taken, and HbA1c levels.

Health care systems have a vested interest in maintaining a high health status for all members because of the shift to value and quality-based contracting. Essentially, the healthier an MCO can keep its members, the higher the financial rewards available from Medicare or Medicaid. Regressions are tools available for finding those at risk for not

paying attention to their health. Many health care systems face high costs from people with type 2 diabetes, primarily due to the disease's complications (Dall et al., 2014). Medication compliance plays a vital role in diabetes management with low medication compliance rates and reduced health status leading to suboptimal therapeutic outcomes in people with diabetes that plays a role in their reduced health statuses (Huang et al., 2018; Polonsky & Henry, 2016).

Research question/hypothesis for each manuscript

The first two manuscripts examine how medication compliance in six of the classes of antihyperglycemic medications and Medicare financial subsidy programs and various covariates such as age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure (Feingold, 2019). Manuscript three looks at the relationship between HbA1c levels, antihyperglycemic medication class, and medication compliance on blindness, urinary tract infections, end-stage renal disease, and myocardial infarction. The relationships presented in the first two studies provide evidence for practitioners treating this diabetes. Study three established that the PDC, HbA1c levels are a predictors four of the comorbidities of diabetes.

In the first manuscript, we investigate the PDC for participants only taking one of the antihyperglycemic medication classes during the year. Because we only have a single HbA1c level during the year, we cannot correlate taking several different medication

classes to a change in a single HbA1c level. The outcome variable, HbA1c levels, is continuous, and therefore, multiple regression analyses were performed on this data. This manuscript's title is "Medication Compliance by Drug Class as a Predictor of HbA1c Values in Medicare Type 2 Diabetics". The research questions for this manuscript are:

RQ1: What is the relationship between the PDC and the antihyperglycemic class of medication on HbA1c in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure?

$H_0$1: There is no statistically significant relationship between the PDC and the Biguanides class of medications on HbA1c in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure?

$H_1$1: There is a statistically significant relationship between the PDC and the Biguanides class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$2: There is no statistically significant relationship between the PDC and the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$2: There is no statistically significant relationship between the PDC and the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$2: There is a statistically significant relationship between the PDC and the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$2: There is no statistically significant relationship between the PDC and the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of

hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$3: There is no statistically significant relationship between the PDC and the Thiazolidinedione class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$3: There is a statistically significant relationship between the PDC and the Thiazolidinedione class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$4: There is no statistically significant relationship between the PDC and the Sulfonylureas class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$4: There is a statistically significant relationship between the PDC and the Sulfonylureas class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$5: There is no statistically significant relationship between the PDC and the Meglitinide Analogues class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$5: There is a statistically significant relationship between the PDC and the individual Meglitinide Analogues class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$6: There is no statistically significant relationship between the PDC and the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex,

deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$6: There is a statistically significant relationship between the PDC and the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

RQ2: What is the relationship between PDC and combinations of antihyperglycemic class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure?

$H_0$7: There is no statistically significant relationship between the PDC and the Meglitinide-Biguanide Combinations class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal

screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$7: There is a statistically significant relationship between the PDC and the Meglitinide-Biguanide Combinations class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$8: There is no statistically significant relationship between the PDC and the SGLT2 Inhibitor - DPP-4 Inhibitor Combinations class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$8: There is a statistically significant relationship between the PDC and the SGLT2 Inhibitor - DPP-4 Inhibitor Combinations class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial

infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$9: There is no statistically significant relationship between the PDC and the Sodium-Glucose Co-Transporter 2 Inhibitor-Biguanide class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$9: There is a statistically significant relationship between the PDC and the Sodium-Glucose Co-Transporter 2 Inhibitor-Biguanide class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$10: There is no statistically significant relationship between the PDC and the Sulfonylurea-Biguanide class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a

diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$10: There is a statistically significant relationship between the PDC and the Sulfonylurea-Biguanide class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$11: There is no statistically significant relationship between the PDC and the Dipeptidyl Peptidase-4 Inhibitor-Biguanide class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$11: There is a statistically significant relationship between the PDC and the Dipeptidyl Peptidase-4 Inhibitor-Biguanide class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI,

end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$12: There is no statistically significant relationship between the PDC and the Sulfonylurea-Thiazolidinedione class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$12: There is a statistically significant relationship between the PDC and the Sulfonylurea-Thiazolidinedione class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

Manuscript two examines participation in Medicare financial assistance programs as an indicator of income and assets and oral antihyperglycemic medication PDC, while controlling for covariates, to see if they can successfully predict HbA1c levels. Medicare sets income levels for participation in the LIS and DSNP programs, and these programs are mutually exclusive in that an individual can only be in one at a time. Participants are those not in a subsidy program, those in a LIS program, and those in a DSNP program. Only participants taking one class of antihyperglycemic medication during the year met

selection criteria. Linear regression analysis were used to develop our model with HbA1c as a continuous outcome variable. This manuscript's title is "Dually Eligible, Low-Income Subsidy Enrollment, and Medication Compliance as Predictors of HbA1c in Type 2 Diabetics". The research questions for this manuscript are:

RQ3: What is the relationship between enrollment in a LIS program, DSNP enrollment, oral antihyperglycemic medication class, PDC, and HbA1c levels in Managed Care enrollees with type 2 diabetes while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County?

$H_0$13: There is no statistically significant relationship between enrollment in a LIS program, oral antihyperglycemic medication class, PDC, and HbA1c levels in Managed Care enrollees with type 2 diabetes while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_1$13: There is a statistically significant relationship between enrollment in a LIS program, oral antihyperglycemic medication class, PDC, and HbA1c levels in Managed Care enrollees with type 2 diabetes while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_0$14: There is no statistically significant relationship between enrollment in DSNP program, oral antihyperglycemic medication class, PDC, and HbA1c levels in Medicare type 2 enrollees with diabetes while controlling for age, sex, diabetes

diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_1$14: There is a statistically significant relationship between enrollment in a DSNP program, oral antihyperglycemic medication class, PDC, and HbA1c levels in Medicare type 2 enrollees with diabetes while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_0$15: There is no statistically significant relationship between enrollment in LIS and DSNP programs, oral antihyperglycemic medication class, PDC, and the and HbA1c levels in Managed Care enrollees with type 2 diabetes while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_1$15: There is a statistically significant relationship between enrollment in LIS and DSNP programs, oral antihyperglycemic medication class, PDC, and the and HbA1c levels in Managed Care enrollees with type 2 diabetes while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

Manuscript three analyzes oral antihyperglycemic medication class compliance in the six classes of antihyperglycemic medications, HbA1c levels, and whether they can be used to predict any of the comorbidities or combinations of comorbidities Managed Care enrollees with type 2 diabetes. Selection criteria limited participants to those taking only

one class of antihyperglycemic medication during the year. The data as analyzed using logistic regression because our outcome variables, comorbidity, or sets of comorbidities, are binary. This manuscript's title is "Medication Compliance, HbA1c Predicting Comorbidities in Medicare Type 2 Diabetics". The research questions for this manuscript are:

RQ4: What is the relationship between the PDC calculated for individual antihyperglycemic class of medications and HbA1c values and the top four type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections, both individually and in combination, in Medicare enrollees with type 2 diabetes while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County as defined by the Census Bureau.

$H_0$16: There is no statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$16: There is a statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness,

End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$17: There is no statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$17: There is a statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$18: There is no statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while

controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$18: There is a statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$19: There is no statistically significant relationship between the PDC index calculated for the Sulfonylureas class of medications and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections and HbA1c values while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$19: There is a statistically significant relationship between the PDC index calculated for the Sulfonylureas class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$20: There is no statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$20: There is a statistically significant relationship between the PDC index calculated for the individual Meglitinide Analogues class of medications and HbA1c values and the top Medicare four type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$21: There is no statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$21: There is a statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$22: There is no statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Myocardial Infarction and HbA1c while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$22: There is a statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Myocardial Infarction while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$23: There is no statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Myocardial Infarction while controlling for age, sex, diabetes diagnosis time, length of time in

MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$23: There is a statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Myocardial Infarction while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$24: There is no statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Myocardial Infarction while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$24: There is a statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Myocardial Infarction while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$25: There is no statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and HbA1c values and the comorbidity of Myocardial Infarction in Medicare type 2 diabetics while

controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$25: There is a statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and the comorbidity of Myocardial Infarction and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$26: There is no statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the comorbidity of Myocardial Infarction in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$26: There is a statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the comorbidity of Myocardial Infarction in type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$27: There is no statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the comorbidity of Myocardial Infarction in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time,

length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$27: There is a statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the comorbidity of Myocardial Infarction in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$28: There is no statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$28: There is a statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$29: There is no statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness

while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$29: There is a statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$30: There is no statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$30: There is a statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$31: There is no statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and HbA1c values and the

Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$31: There is a statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$32: There is no statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$32: There is a statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the comorbidity of Blindness in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$33: There is no statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the comorbidity of Blindness in Medicare

type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$33: There is a statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the comorbidity of Blindness in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$34: There is no statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$34: There is a statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$35: There is no statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications

and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$35: There is a statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$36: There is no statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$36: There is a statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$37: There is no statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$37: There is a statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$38: There is no statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$38: There is a statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the comorbidity of End-Stage Renal Disease in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$39: There is no statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the comorbidity of End-Stage Renal Disease in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$39: There is a statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the comorbidity of End-Stage Renal Disease in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$40: There is no statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$40: There is a statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while

controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$41: There is no statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$41: There is a statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$42: There is no statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$42: There is a statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and

the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$43: There is no statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$44: There is a statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$45: There is no statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$45: There is a statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the comorbidity of Urinary Tract Infections in Medicare type 2 diabetics

while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$46: There is no statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the comorbidity of Urinary Tract Infections in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$46: There is a statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the comorbidity of Urinary Tract Infections in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

Outline of Dissertation

Introduction

With the introduction of quality standards for health care organizations and the financial penalties associated with not attaining established levels of quality, the need for appropriate regression analysis for MCO's has increased. The first study determines the appropriateness of using the Medicare PDC, as for individual antihyperglycemic

medications, in identifying those at risk for high HbA1c levels. Having regression analysis available helps healthcare organizations proactively work with people with diabetes who are a risk for high HbA1c levels. The second study in this dissertation establishes that the PDC, calculated for individual antihyperglycemic medications, and participation in Medicare financial assistance programs can be used to identify individuals at risk for high HbA1c levels. The third study in this dissertation uses logistic regression analysis with diabetes comorbidities as outcome variables and individual HbA1c levels, PDC medication compliance rates, antihyperglycemic medication classes, and various covariates as predictors.

Social change

Diabetes is a chronic disease that impacts more than one-third of Americans (American Diabetes Association, 2018d). Medication compliance in people with diabetes is essential for keeping HbA1c levels under control, and many people with diabetes have issues with compliance (Kennedy-Martin et al., 2017). Medicare created several financial subsidy programs covering medication copays and deductibles with one goal of improving medication compliance. Diabetes comorbidities further complicate dealing with these individuals. Quality standards for diabetes that many healthcare organizations must meet complicate the already tricky scenario of managing diabetes. Using the Medicare PDC calculated for individual antihyperglycemic medications as a predictor of HbA1c levels, predicting comorbidities of diabetes, and evaluating the effectiveness that financial subsidy programs have to health care organizations.

Background

Diabetes

Review of Diabetes

Diabetes refers to a group of diseases related to a defect in the body's ability to utilize glucose properly. In the US, 35 million people have been diagnosed with diabetics, 7 million have undiagnosed diabetes, while another 88 million have prediabetes (Centers for Disease Control and Prevention, 2020). Many people are undiagnosed and unaware that they are at risk for developing diabetes (National Institute of Diabetes and Digestive and Kidney Diseases, 2017). Diabetes-related health expenditures increased from $245 billion in 2012 to $345 billion in 2017, one dollar out of every four spent on healthcare in the US (Riddle & Herman, 2018).

Diabetes can lead to multiple complications, including heart disease, stroke, nephropathies, retinopathies, dental problems, and neuropathies (National Institute of Diabetes and Digestive and Kidney Diseases, 2018). In 2013, diabetes was the seventh leading cause of death in the US, a total that could be underreported. Twenty percent of all healthcare expenditures are for the treatment of diabetes or any one of its complications (National Center for Chronic Disease Prevention, 2016).

The American Diabetes Association established a Professional Practices Committee that developed and annually updates a "Standards of Medical Care in Diabetes." The group comprises physicians, educators, dieticians, and others with expertise in a range of areas related to diabetes (American Diabetes Association, 2018c).

The standards' recommendations are evidence-based, developed through collaboration, aligned with the Chronic Care Model, and support improvements in quality of care through quality improvement strategies. These standards address the Social Determinants of Health and their role in diabetes (American Diabetes Association, 2018c).

For many years, the standard test for determining a diagnosis of diabetes was a glucose tolerance test. However, in 2006, the World Health Organization recommended using the HbA1c, a glycosylated form of hemoglobin, with a measure that indicates glucose levels for several months. Reported studies use the continuous HbA1c value, including self-efficacy, medication compliance and health literacy, and a longitudinal study in the UK that looked at estimating future HbA1c levels (Huang et al., 2018; Sheppard et al., 2017). In 2011, the ADA recommended an HbA1c value of greater than 6.5% for a diagnosis of Diabetes and have included it as part of their standards (Malkani & Mordes, 2011; World Health Organization, 2006).

Type 2 diabetes is the most expensive of all the chronic diseases for many healthcare systems, primarily due to the disease's high rate of complications (Dall et al., 2014). This cost burden is continuing to grow (Seuring et al., 2015)**.** To complicate this issue, only 50% of individuals on medications for diabetes fail to achieve adequate blood sugar control or attain an HbA1c level of less than 7% (Centers for Disease Control and Prevention, 2020; Polonsky & Henry, 2016).

Types of Diabetes

There are several types of diabetes. Chronic diabetes includes type one, or insulin-dependent, and type two, generally treated with oral medications. There are other types of diabetes, including gestational, that occurs during pregnancy, cystic fibrosis-related diabetes, and monogenic or genetically related diabetes. A blood test diagnoses diabetes, looking at fasting glucose levels greater than 120 mg/dl or HbA1c levels greater than 6.5% in all of these forms of diabetes.

Type one diabetes, generally diagnosed in children and young adults, is also known as juvenile diabetes but can present at any age. It occurs in approximately five percent of the population and has no regard for body size, ethnicity, or age. In type one diabetes, the body does not produce any insulin and, as a result, has no way to get glucose from the blood into the cells (American Diabetes Association, 2019).

Type two diabetes is the most common form and comes from the body's inability to utilize insulin properly. It appears at any age, but most often in adults (National Institute of Diabetes and Digestive and Kidney Diseases, 2016b). Type two diabetes forms slowly, and its onset can be delayed by lifestyle changes such as weight loss or diet change. In diabetes early stages, the body secretes additional amounts of insulin to make up for its inability to use it, a condition called insulin resistance. Over time, the pancreas cannot produce enough insulin and either oral medication or insulin is instituted. The health status of people with type two diabetes generally worsens over time. The symptoms of type two diabetes include thirst, frequent urination, feeling hungry or tired, blurry eyesight, slow healing, and losing weight without trying (Medline Plus, 2016):

Prediabetes Implications

Individuals with a fasting glucose level above 110 mg/dl to 125 mg/dl and a two-hour glucose tolerance test level of 140 – 200 mg/dl are at risk of developing type 2 diabetes, a condition known as prediabetes. The American Diabetes Association further refined the definition of prediabetes to include an HbA1c level between 5.7% – 6.4% (Bansal, 2015). However, there is some controversy about the value of using HbA1c levels to make a diagnosis of prediabetes, with the best diagnostic tool being a two-hour fasting glucose tolerance test (Maki, 2017). Approximately 10% of prediabetics convert to diabetics each year (Knowler et al., 2002). Prediabetes puts patients at risk for type 2 diabetes, heart disease, and stroke. Predictors of prediabetes include being overweight, older than 45, have a parent or sibling with type 2 diabetes, low physical activity, a previous diagnosis of gestational diabetes, or are African American, Native American, Latino, or Asian American.

Just because an individual is diagnosed with prediabetes does not mean that they will transition to diabetes. Changing dietary habits, increasing physical activity, and reducing stress are all shown to delay or prevent a diagnosis of prediabetes (Centers for Disease Control and Prevention, 2018b).

The association between prediabetes and macrovascular disease is well established (H. Hu et al., 2018). Prediabetes in adolescents leads to obesity, high cholesterol levels, low levels of HDL cholesterol, and elevated liver transaminase (Casagrande et al., 2018). The risk in people with diabetes for atherosclerotic

cardiovascular disease (ASCVD) is twice that in prediabetics, and elevated lipoprotein(a) is more common in prediabetic Caucasians than in African Americans (Saeed et al., 2019).

Microvascular risks from prediabetics include renal, retinal, and peripheral problems. The exact mechanism of these complications is unknown, but the metabolic changes associated with diabetes cause oxidative stresses, inflammation, and vascular occlusion (Safi et al., 2014). However, these injuries take years to develop with uncontrolled glucose levels. Therefore, active efforts to change diet and lifestyle can eliminate or delay the onset of these complications (Brannick et al., 2016).

Prediabetes presents with the same cardiovascular (macrovascular), renal, retinal, and peripheral nerve (microvascular) damage potential as in people with diabetes, just at a lower rate. When a patient is diagnosed with prediabetes, it does not necessarily foretell future diabetes. Diabetes can be stalled or prevented by making lifestyle and dietary changes. Patients who avoid the progression of prediabetes to diabetes can reduce their overall healthcare costs, improve their health status and quality of life (Carris et al., 2019).

Measurement

Blood glucose monitoring is the foundation of diabetes and prediabetes treatment. Blood glucose level was the traditional method for diagnosing diabetes before accepting the HbA1c level as a viable measure. Any level over 99 mg/dl is considered pre-diabetes. Once the blood glucose exceeds 120 mg/dl, a diagnosis of diabetes can be made

(National Institute of Diabetes and Digestive and Kidney Diseases, 2016a). In 2011, the ADA endorsed the use of the HbA1c level (Malkani & Mordes, 2011). The advantage of HbA1c is that it indicates how high the blood sugar level reached over the last two to three months, based on the lifetime of the red blood cell holding the glucose (Medline Plus, 2018).

HbA1c was first identified in 1958 and identified as a glycoprotein in 1968. In 1969 elevated HbA1c levels were found in diabetics and was first proposed in 1976 as an identifier of diabetes (Bookchin & Gallop, 1968; Huisman et al., 1958; Koenig et al., 1976; Rahbar et al., 1969). Clinically accepted normal levels of HbA1c are below 5.7%, prediabetes levels are between 5.7% and 6.4%, and diabetes is diagnosed at levels above 6.5% (American Diabetes Association, n.d.).

Blood sugar measurement falls into several categories, invasive and non-invasive and intermittent and continuous. Invasive techniques are those where a sensor is implanted into the body and has some means for transmitting glucose levels to an external monitoring system. Finger prick systems are considered an invasive method and are the most common measuring method in use. Non-invasive systems are those where there is no body implantation of sensors to determine glucose levels. Continuous systems can consistently monitor glucose levels over time, and with intermittent systems, HbA1c levels are determined at various points in time.

The most common invasive method of monitoring glucose levels is using a glucometer, an electronic device that measures glucose levels in a blood sample. In

invasive methods, a drop of blood is applied to a test strip inserted into a device displaying the amount of glucose present in the sample. These electronic devices must be recalibrated with each new packet of measurement sticks. Failure to do so can introduce errors of up to 50 mg/dl. Low health literacy may affect these measurements' accuracy due to numeracy issues (Ginsberg, 2009; Jun, 2019). Continuous monitoring is generally reserved for those with type 1 diabetes.

Complications of Diabetes

Primary complications of diabetes come from the micro and macrovascular co-morbidities associated with diabetes. The complications include diabetic retinopathy, nephropathies, neuropathies, and atherosclerosis. Diabetes is a predictor of stroke and cardiovascular disease (Fowler, 2008). Approximately one-third of the 285 million diabetics worldwide suffer from diabetic retinopathy, which is the leading cause of vision loss in adults 20 – 74 years old (Yau et al., 2012). Diabetic retinopathy contributes to other diabetes complications, including nephropathy, cardiovascular events, and peripheral neuropathies.

Diabetic neuropathies can be asymptomatic and are not exclusively related to diabetes. Because the nerve damage from diabetic neuropathies cannot be reversed, the best plan is prevention (Bourne et al., 2013; Pop-Busui et al., 2017). Diabetic neuropathies can be non-painful, making patient recognition difficult if they do not perform regular body checks (Hägg et al., 2013; He et al., 2013; Mottl et al., 2014). The macro and microvascular effects of diabetes are severe enough that the American

Diabetic Association recommends the use of low-density lipoprotein (LDL) and cholesterol-reducing statins for diabetic patients along with lifestyle change (American Diabetes Association, 2018a).

Cardiovascular comorbidities from type 2 diabetes include myocardial infarction (MI), atrial fibrillation, and heart failure, with an increased incidence over time (Larsson et al., 2018). It is now an accepted standard of practice in mitigating comorbidity effects for physicians to place diabetic patients on a statin. The American Diabetes Association recommends a target LDL cholesterol of <100 mg/dl, and the HEDIS CDC measures have a quality standard for those with diabetes, assuring they are on a statin medication (American Diabetes Association, 2009; National Center for Quality Assurance, 2018c). While there are studies that examined the relationship between Medication compliance and some of the comorbidities of diabetes, there are none found that have looked at six of the classes of diabetes medications, medication compliance with the PDC, and the comorbidities of diabetes (Giugliano et al., 2018; Shih et al., 2016).

Urinary tract infections (UTI) in people with diabetes are generally attributed to the kidneys' inability to handle elevated blood sugar values resulting in glucose in the urine. Spilled glucose is a food source for bacteria present and can lead to overgrowth and infection. In addition to this, people with diabetes may have immune system compromises, emptying problems due to neuropathy, and UTI’s in people with diabetes are generally more severe, last longer, have worse outcomes, and have more cases of resistant bacteria causing these infections (Nitzan et al., 2015).

Because diabetes is a complex disease, individuals face self-management decisions multiple times daily. Some of these decisions can be complex and are directly related to individual outcomes (Brunisholz et al., 2014). Problem-solving is a difficult concept to teach and is a daily issue for those with diabetes. Because it is such an important part of self-management, the American Association of Diabetes Educators hosted a Problem-Solving Symposium that developed 11 key factors in educating people with diabetes in dealing with their disease. Several of the key points from that symposium include problem-solving is a skill set that can be taught, is impacted by the physician's problem-solving style, it aligns itself with Continuous Quality Improvement principles, interventions must address the patient's highest priority goals, and recommendations must be practical (Stetson et al., 2010).

Prediabetes is defined as having a blood sugar not high enough to diagnose diabetes (Centers for Disease Control and Prevention, 2018a). There are no recognized prediabetes symptoms, which presents problems for those who are not visiting a doctor regularly. The risk factors for prediabetes include increased BMI, being over 40, having a relative with diabetes, participating in physical activity less than three times weekly, ever having been diagnosed with gestational diabetes, and being African American, Latino, Asian American, or Native American (Centers for Disease Control and Prevention, 2018b).

Among the silent complications common to diabetes are retinopathy and nephropathy (Esen et al., 2018). Diabetic retinopathy is the number one cause of

blindness in the US. Because of its insidiousness, people with diabetes may not recognize that they have diabetic retinopathy until it is in its advanced stages (Center for Disease Control, n.d.-a). Thus, the need for annual screenings. Vascular changes in the retina characterize diabetic retinopathy. These changes all contribute to the development of macular edema from the leaky vasculature of the retina. Of interest is that in people with type one diabetes, retinopathy does not usually appear until an individual has diabetes for three to five years. However, in twenty-one percent of people with type two diabetes, retinopathy has already developed before diagnosis, perhaps due to macular edema and capillary nonperfusion (Fong et al., 2004).

Diabetic nephropathy is defined by increased albumin secretion in the urine. It occurs in fifteen to forty percent of people with type one diabetes but less frequently in type two diabetics (Gross et al., 2005). Forty-four percent of end-stage renal disease comes from patients with diabetic nephropathy. Nephropathy of any origin may also lead to an increased chance of stroke (Center for Disease Control, n.d.-b). Smoking may be an additional risk factor for diabetes developing nephropathy (Jiang et al., 2017).

Socioeconomic status and other SDOH are related to participation in retinal and renal screenings in diabetics (Fathy et al., 2016; Lee, 2018). Retinal screenings in people with diabetes can reduce the incidence of severe vision loss by 94% (Schoenfeld et al., 2001). However, many recently published diabetic retinopathy studies use old data and show varying vision impairment rates (Leasher et al., 2016; Ting et al., 2016). An area

that needs further research is examining improved medications that could contribute to lower retinopathy rates.

Medication Adherence in Diabetics

Of the risk factors that people with diabetes face, medication adherence is the easiest way to limit risks. While losing weight, reducing sugar intake, and exercising are all techniques that a person with diabetes should use to reduce their risks from diabetes, medication adherence should be the easiest and is one of the most significant ways to help them keep their A1C levels under control. In newly diagnosed diabetics on Metformin with reasonable adherence rates in the first year, HbA1c levels dropped by 0.75% (Nichols et al., 2016). Proper medication adherence leads to fewer Emergency Department visits, better sugar control, fewer hospitalizations, and decreased overall medical costs (Capoccia et al., 2015).

Because of the complications of diabetes, polypharmacy is common. However, the need for multiple medications treating co-morbidities leads to lower levels of medication adherence. The incidence of low adherence related to medication costs is 16% to 19%, with medications costs the second most common factor in non-compliance in people with diabetes following depression. (Kang et al., 2018). Improving health literacy levels and numeracy skills are other ways to improve medication compliance in people with diabetes (Nandyala et al., 2018).

Summary of Diabetes

Diabetes is a disease of glucose metabolism. There are over 110 million diabetic or pre-diabetic individuals in the US (National Institute of Diabetes and Digestive and Kidney Diseases, 2017). The complications of diabetes include retinopathy, cardiovascular complications, UTIs, and nephropathy, and multiple comorbidities. The cost of treatment of diabetes in the US exceeded $80 billion in 2017, or $228 for every citizen (American Diabetes Association, 2018b). While there are several proven therapeutic modalities available to physicians for the treatment of diabetes, medication compliance limits treatment effectiveness (Huang et al., 2018a). Even with the implementation of Medicare Part D covering prescription drug costs, many people with diabetes report that they are unable to afford copays and deductibles and are skipping doses to compensate (Choi et al., 2017).

Medication Compliance

Introduction

Many people report substantial medication costs, particularly in chronic diseases (Kesselheim et al., 2016). A recent Kaiser Foundation study found that one in four US senior citizens found it difficult to pay for their prescriptions. Of interest, those participating in that study said that prescription drugs made their lives better, but at an unreasonable cost. Three in ten of the participants in this study said they are skipping their medications because of cost (Kaiser Family Foundation, 2019). From 2010 to 2015, prescription drug spending in the US increased from $8.7 billion to $32.8 billion.

Specialty drugs account for 1% of prescriptions but 30% of spending (Anderson-Cook et al., 2019).

What is Medication Compliance

There are five broad factors related to medication adherence or compliance, including patient factors of medication knowledge and beliefs and the SDOH. Medication issues such as how they are packaged, how complex it is to take or administer, cost directly affect medication compliance. Factors related to a patient's physician, such as poor communication skills, lack of trust or dissatisfaction, and system-based factors related to the patient's lack of follow-up, are pertinent to the compliance discussion. Finally, other factors such as caregiver issues, no caregiver, or lack of perceived health status improvement also contribute to adherence to medication therapy (Yap et al., 2016).

An estimated 20% of the population has to deal with medication compliance's financial stresses (McHorney & Spain, 2011). When individuals are struggling to pay their rent or provide food for themselves or their family, taking their medications takes a back seat. They adopt new strategies such as skipping a month, reducing their daily dosage such as only taking it once rather than twice a day, or taking a dose every other day (Ippolito et al., 2017). These strategies may lead to poorer health outcomes and statuses. One MCO has gone so far as to implement a Community Help Line to assist individuals with food, rent, transportation, and utility payments because these are serious issues for their population (Pruitt et al., 2018).

Medication packaging plays a role in compliance. Efforts such as packaging each dose individually in bubble packs, packaging all medications together that should be taken at a prescribed time, and electronically controlled dispensers connected to smartphones are all strategies that are being considered to help improve medication adherence. Individual blister packs with medications taken by the time of day are one attempt at improving compliance through packaging changes. Risks presented by similar products such as pillboxes and pharmacist-provided multi-dose packaging have not been thoroughly studied. These other methods do not overcome features such as ease of opening the package or bottle and remembering to take the medication. A recent study of different packaging systems found no compliance differences (Gilmartin-Thomas et al., 2017).

Poor communication skills on the part of those prescribing medications are another issue. This lack of communication by providers is of importance for those with low health literacy. Because of their lack of understanding, low health literacy individuals are notoriously non-compliant with their medications (Shiyanbola et al., 2018). The use of the teach-back method is one way of overcoming compliance issues in patients, especially those with low health literacy (Bussell et al., 2017; Dinh et al., 2016).

Lack of trust or dissatisfaction with providers contributes to low rates of medication adherence. A study of individuals with hypertension looked at physician trust and medication adherence. The authors found a positive relationship between physician trust and medication adherence (Jneid et al., 2018). In a Mexican-American immigrant

study, the authors found that improved trust in providers improved compliance after educational programs (Baghikar et al., 2019). Brown et al. (2016) found that trust in the health system is another factor in medication adherence.

System-based factors influence the follow-up of patients on their treatment regimen. In Osteoporosis, patients with multiple physicians and physicians with poor communication skills contributed to these patients' poor medication compliance (Yeam et al., 2018). In a study of diabetics, the authors found that medication benefits and access to care (among other factors) are system-based factors related to medication adherence (Brown et al., 2016). In a meta-review of medication adherence in diabetes, hypertension, and dyslipidemia, the authors found that only 59% of those studied were compliant with their medication (Polonsky & Henry, 2016a). Other factors such as caregiver issues, no caregiver, or perceived health status improvement contribute to poor medication adherence.

Medication Adherence Importance

In clinical trials, researchers' assumption that participants are going to adhere to their medication regimens may lead to incorrect results. The Vaginal and Oral Interventions to Control the Epidemic study had to be halted when the researchers discovered that 30% of biologic samples collected had no study medication present (Marrazzo et al., 2015). In diabetes, adherence to medications is necessary for keeping glucose and HbA1c within normal limits. Comorbidity risk is reduced with controlled sugar levels, health statuses are improved, and costs are reduced.

Adherence and persistence are both critical for people with diabetes to maintain glucose control. However, there is conflicting evidence on the contribution of adherence and persistence to care costs for diabetics. Chandran et al. (2015) found significant overall healthcare costs in insulin pen compliance. Stuart et al. (2015), found that although better medication adherence improved glucose control, savings may be offset by increased medication costs. Finally, Busyman et al. (2015) found no change in costs when looking at adherence and persistence.

Measurement Tools

Because medication adherence is an essential topic with health status and cost implications, measurement is just as important. There are several tools for measuring medication compliance. Among them is the Morisky Medication Adherence Scale, Medication Possession Ratio (MPR), Proportion of Days Covered (PDC), and SEAMS. These tests have been developed as improvements over previous methods or as tests for particular conditions.

There are three different Morisky scales, the Morisky Medication Adherence Scale-4 (MMAS-4, or the Medication Adherence Questionnaire (MAQ)), Morisky Medication Adherence Scale-8 (MMAS-8), and the Morisky Green Levine scale (MLGS). The MMAS-4 was the first medication-adherence test developed by David Morisky and has yes/no answers. While it was the first test of its type, it has a low Cronbach's alpha of 0.61 (Morisky et al., 1986). To create a better tool, Morisky developed the MMAS-8 test in 2008. This test consists of seven dichotomous responses

and a single Likert scale question. The new test has a Cronbach's alpha of 0.83 (Morisky et al., 2008). The MMAS-8 is a widely used tool for measuring medication compliance and is cited in 1985 studies when doing a Google Scholar search. The MLGS test comprises four questions with yes/no answers, and the lower the score, the higher adherence.

The MPR tests the relationship between the number of days covered and the number of days in the measurement period, first mentioned in the literature in 1993 in a study of diltiazem, a calcium channel antagonist (Skaer et al., 1993). In other words, it is the days' medication a person had on hand divided by the number of days being measured. An issue with the MPR is that it can exceed 100% when a patient refills the medication earlier than needed, and this surplus is counted in the days measured. It is a widely used medication adherence measurement tool used to determine adherence in comparing different medication delivery systems, hypertension, and medication regimen complexity (Ho et al., 2017; Na et al., 2018). However, researchers have some dissension on precisely what the MPR is and what it is measuring. In 2017, Sperber, Samarasinghe, and Lomax suggested that the MPR should not be used as a static measure of medication adherence but should be used only to examine adherence trends. They cited evidence of its inability for direct use in studies and to compare values across studies. They suggested that using the MRP with upper and lower bounds and not removing patients with limited refills would make it a more valuable tool.

With the MPR, it is possible to have values higher than 100%, and the PDC addresses this issue. For example, if two medications are available to an individual for 180 days during a calendar 365-day period, their PDC value is 0.49. In this example, an individual can possess 480 days of medication for 365 days, and their MPR value would be 1.3. A value of 1.3 is neither reasonable nor possible (Patel, 2018).

The SEAMS test is 13 questions on a 3-point Likert-type scale, medication compliance assessment tool. The original was a 21-question survey. This tool has been validated for use; however, scoring this tool can be challenging (Lavsa et al., 2011). Additionally, the length of time it takes to administer is an issue (Lam & Fresco, 2015). SEAMS was developed in 2004 by a group of nurses looking for a medication adherence tool that took into account health literacy (Risser et al., 2007). The SEAMS method has been widely cited over the last 15 years.

In 2015, the CDC adopted the PDC measurement as their guide for researchers examining medication adherence. The PDC measurement is supported by the Pharmacy Quality Alliance and CMS and is the leading method for determining medication adherence in large populations (Center for Disease Control, 2015). The PDC is a measure of the proportion of doses that should have been taken compared to doses taken while the MPR looks at the medications an individual had on hand.

Self-Assessment and Compliance

When researchers examine medication adherence based on self-assessment, participants are aware of the goals of the research. For instance, in studying AIDS

patients and their compliance with retroviral therapy, researchers found a discrepancy between participant medication self-assessment and the drug's blood levels (Simoni et al., 2014). While the AIDs study found discrepancies, a diabetes study comparing medication self-assessment using the Medication Event Monitoring System (MEMS) and HbA1c levels, researchers found validity and reliability of the evaluation tool based on HbA1c levels suggesting that the type of disease may also be a factor in medication compliance (Gonzalez et al., 2013). Over time, studies have found a significant relationship between medication self-assessment and HbA1c levels in people with diabetes (Tandon et al., 2015). However, others purport to show that self-assessment tools are not valid as they do not correlate well with HbA1c levels (Cohen et al., 2010).

How Medication Adherence is Measured

There are two ways to measure medication adherence, direct and indirect methods. Direct methods include examining levels of the drug in the bloodstream, directly observing dosing, and looking for markers applied to the drug in biological samples. Indirect methods include electronic methods counting bottle-opening, pillboxes, and self-reporting. These indirect methods are less than ideal because of time requirements, cost, or impracticability (McRae-Clark et al., 2015).

There are issues with the direct methods of measurement. For example, spot blood levels only reflect dosage at a point in time, but not longitudinally. Direct oversight, while helpful, means that someone must witness every dose taken; if not impossible to do, it could be prohibitively expensive. Pill counts at a researcher’s office require that

participants bring in all their medications, which cannot be verified. This method cannot determine if the medication was taken as prescribed. For example, a medication is ordered three times daily; there is no way to determine if the participant took the medication three times daily or all at once in the morning. Researchers only know that all the medication was taken by count (McRae-Clark et al., 2015).

Indirect methods, such as electronic methods that automatically record when a medication bottle is opened, may be accurate. However, they are expensive and can be impractical (Gonzalez & Schneider, 2011). Pillboxes have the same issue. One can see that medication is gone from its compartment, but it is impossible to know for sure that the medication was consumed. Self-reporting mechanisms for medication adherence depend entirely on the honesty of the one completing the form. It has been found that participants in self-assessment tools tend to overstate their compliance. Other methods commonly used in assessing compliance are based on pharmacy claims data. However, this method has the same potential for error as the others do. Just because a person gets a prescription filled, it does not mean that they will take it (McRae-Clark et al., 2015).

The NCQA has adopted the CDC PDC methodology as its way to determine medication compliance. The PDC method suffers from the same problems as other compliance methods, but Medicare and Medicaid have adopted it for help in determining the financial rewards of those under the HEDIS quality mandates.

Current Medication Compliance Tools

There are several different research tools for determining medication compliance. The most common of these is the Morisky Self-Assessment tool. A Google Scholar search of Morisky AND MMAS revealed 2340 studies citing this medication compliance measuring method since 2016. Ideally, any medication compliance study would be by some biological method that measures the quantity of drug in the blood. If measuring the drug is not feasible, measuring a metabolic by-product or biological indicator such as HbA1c would be ideal. Unfortunately, these are neither practical nor financially viable. For now, the best method we have is either the PDC, MMAS-4, or MMAS-8 method. Those covered under the HEDIS quality measures are going to have to use the PDC measure.

Health System Quality Overview

Ernest Codman and Robert Dickinson were early 20th century surgeons who first attempted to apply formalized, scientific-based quality to health care. Dr. Codman developed an "End Result System" for hospitals to improve surgery centers' low quality (Wrege, 1980). Frank Gilbreth, an efficiency expert, was added to the group to formalize their ideas into measurable outcomes. The End Result system was a measuring stick of the accepted level of outcomes used to measure patients' surgical outcomes.

Skipping ahead, in 2001, the Institute of Medicine developed the STEEP model of quality (National Institute of Medicine, 2001). This model has been a driving force for current models of quality adopted in the US. STEEEP or Safety, Timely care, Effective care, Efficient care, Equitable care, and Patient-centered care represent the six domains of

health care quality and are the framework for what is now known as the HEDIS measures. One purpose of the HEDIS measures is to help make quality more transparent and easier for health care consumers to understand (Agency for Healthcare Research and Quality, 2018). However, little attention has been paid to patients in developing these standards, nor were patients involved in creating the six domains of health.

Quality improvement systems currently in use include Plan, Do, Study, Act (PDSA), Smart (SMART), Achievable, Relevant, and Time-bound and Continuous Quality Improvement (CQI). Edward Deming developed the PDSA methods centered on learning from actions taken. Deming worked in Japan during the post-war period and was instrumental in improving the quality of Japanese products. PDSA is a rapid cycle model where results feedback to actions, leading to study, then improvement. George Doran first referenced the SMART system in 1980 (Doran, 1981). The SMART system is a way to help clarify goals and ideas and is a way to get to those goals in an efficient and timely manner. The CQI process encompasses many different techniques for improving quality. The concept behind CQI is that it is a model for reducing or eliminating waste, improving efficiency, and is an ongoing process to improve an organization's process.

NCQA HEDIS quality rating system

The Healthcare Effectiveness Data and Information Set or HEDIS are the most used performance improvement measures in the US. Over 190 million people are enrolled in MCO's and other healthcare systems covered by the HEDIS measure quality requirements (National Committee for Quality Assurance, 2019b). These quality

measures cover six domains of health and 90 different measures. The six domains include (National Committee for Quality Assurance, 2018a):

- Effectiveness of Care.
- Access/Availability of Care.
- Experience of Care.
- Utilization and Risk-Adjusted Utilization.
- Health Plan Descriptive Information.
- Measures Collected Using Electronic Clinical Data Systems

A weakness of these measures is that they do not sufficiently account for the Social Determinants of Health. There is evidence showing that disparities in health and socioeconomic factors contribute to clinical outcomes (Kind et al., 2014). While there have been some adjustments in specific measures for Dually Eligible Medicare Members (DSNP's are eligible for Medicare and Medicaid) using the Categorical Adjustment Index, there are still not adjusted. Evidence shows that adjustment of all socioeconomic factors measures has value (J. Hu et al., 2018).

The HEDIS measures are the most widely used quality measurement tools for healthcare providers and organizations in the US. They are being used to determine financial rewards, which MCO's get favored treatment in Medicaid state plans, and help the public determine which MCO's they want to belong to. The failure of the NCQA to adjust the measures for socioeconomic status continues to present problems for MCO's. Others believe that board adjustments would contribute to reduced quality for the disadvantaged. However, evidence disputes this claim.

HEDIS Comprehensive Diabetes Control (CDC)

One of the HEDIS measures is the CDC measure, which has multiple components, including HbA1c levels, eye care, and kidney monitoring. It is defined by:

1. Hemoglobin A1c (HbA1c) testing.
2. HbA1c poor control (>9.0%).
3. Annual Eye exam (retinal) performed.
4. Annual Renal exam for Nephropathy.
5. Blood Pressure Control (<140/90 mm Hg, diastolic and systolic values must be met to be compliant)

There have been some positive results from implementing this measure in Medicare managed care programs. In comparing Medicare 2012 and 2017, retinopathy rates improved by 5.1%, nephropathy rates improved 5.6%, the number of patients with a completed HbA1c increased by 2.3%, and those with HbA1c levels less than 9% reduced by 15.1% (National Committee for Quality Assurance, 2019a).

Proportion of Days Covered (PDC)

While the PDC is not a HEDIS measure specifically, it is used to determine medication compliance in some HEDIS measures. The first reference to the PDC in the literature was 2002 (Benner et al., 2002). Since then, there have been several different recommendations for calculating the PDC with the current method, developed by the Pharmacy Quality Alliance, having been validated by several sources. The PDC is calculated by determining the number of days the medication should have been taken. Then the number of doses actually taken by the number that should have been taken. For patients on multiple medications, then only count the days when all meds are available. Medicare considers a PDC value higher than 80% as a compliant rate.

The PDC method is used in determining medication adherence in the HEDIS measures and includes these medication classes, Renin-Angiotensin System Antagonists (RASA), all classes of diabetes drugs, some psychotropics, and statins. The HEDIS measures use the CDC version of the PDC in determining how well healthcare organizations are doing at monitoring their members' medication adherence and should be used in interventions for improving compliance. The Medicare CDC measure is calculated based on all medications taken during the measurement year. For the studies presented here, the PDC is calculated on an individual antihyperglycemic mediation basis.

HEDIS Summary

The HEDIS metrics are the current step in the development of healthcare quality. They cover 90 different aspects of healthcare quality and are used by Medicare, Medicaid, and Commercial payers in determining quality ratings, bonus or penalty payments, and are promoted to the public as a tool to help them determine which MA plan they want to join. The NCQA reviews every health care provider under the HEDIS measurements annually. The NCQA collects HEDIS results, and a substantial set of information for researchers and others is in this data store. The NCQA uses this data in identifying aspects of health that might lend themselves to quality measures. A National Institutes of Medicine workshop examined if it is time to create health literacy measures or if health literacy should be incorporated into existing measures (National Academies

of Sciences Engineering Medicine, 2018). The jury is still out on the results of this workgroup.

Star and HPR rating systems

Medicare Star Score Rating System

CMS uses the Medicare Star Score system to rate the performance of and determine bonus payments for Medicare Advantage (MA) plans and other health care providers. The rating system incorporates different quality measures taken from different surveys done during the year. The surveys are the HEDIS measure, the Health Outcomes Survey (HOS), and the Consumer Assessment of Healthcare Providers and Systems (CAHPS). Each of these surveys measures different areas of compliance. Medicare requires that all MCO's submit these surveys on an annual basis. The Star Score rating scale ranges from one to five in whole number increments.

The HEDIS quality measures look at the clinical aspects of care, including clinical outcomes, participation in preventive screenings, and medication adherence. Outcome evaluations in the HEDIS quality measures include diabetes measures that look at how well blood glucose levels are controlled, whether statins are appropriately prescribed, rates of depression, and how compliant individuals are with their medications. The measures are updated annually, with changes announced in the release of a set of technical notes. These notes identify precisely how each measure is calculated and what changed in the calculation. Sometimes, new measures are promoted from a study status

or retired from active status. Body Mass Index measurement is an example of this and is being retired in the calendar year 2020.

Star Score Financial Awards and Penalties

Medicare wants to link MCO payments with quality. The 2012 Affordable Care Act (ACA) included provisions that tied MCO payments to quality measures (Patient Protection and Affordable Care Act, 2010). There are billions of dollars available to MCO's for improving their quality in both insurance and prescription drug plans. Between 2012 and 2014, CMS paid out $10.9 billion in quality bonus payments (L&M Policy Research, 2016).

The star ranking system provides penalties for MCO's that do not reach a 3-star rating. Payment penalties are in the form of lost bonuses and rebate payments. If a plan is rated at one star, there is a loss of 9% of the contracted payment rate. For two stars, there is a loss of 4.5% of contracted payment amounts. A three-star rating is neutral, and four-star programs receive a 4.5% bonus, and 5-star programs receive a 5% bonus in addition to rebates. Four and 5-star programs get an additional benefit in that they can enroll members at times other than the Medicare Annual Election Period. However, MCO's cannot keep all of the bonus payments. Some of it must be returned to its members in improved benefits (Elisver, n.d.). Having extra money to improve benefits makes higher-quality plans more attractive to the public.

Medicaid Health Plan Rating System

The Medicaid Health Plan Rating system (HPR) is based on HEDIS results, CAHPS, and NCQA Accreditation standards scores (National Committee for Quality Assurance, 2019c). The purpose of this rating system is to help states better choose the MCO they contract with. The HPR rating scale ranges from one to five. The HPR system follows the NCQA quality rankings ranging from 0 to 5, but unlike the Medicare Star ranking system, the HPR system is ranked in 0.5 intervals.

A plan's overall NCQA rankings are determined by a complicated set of rules based on having a set amount of data to analyze, length of time the organization has been established. Additionally, measures can be weighted from one to three, where process measures have a value of one, and clinical measures are weighted at three. (National Committee for Quality Assurance, 2018b). Any plan that submits HEDIS and CAHPS surveys is eligible for ranking.

Health Plan Rating Financial Awards and Penalties

State Medicaid programs reward MCO's in several ways. There is withhold money that is returned at the end of the year. New members may be auto-assigned based on a plan based on HPR ratings, with more members going to better plans, and finally, liquidated damages. Medicaid Plans participating in a capitated payment program receive withholds from payments until quality rankings are determined at the end of each year. Plans receive back an amount of their withhold money based on their quality scores. Some states choose to carve-out certain functions that their contracted MCO's provide,

such as pharmacy or dental benefits, and handle them within the state system rather than the MCO.

Those who qualify for Medicaid are given a chance to choose the plan they want to join. However, if they fail to do so, they are auto-assigned to a plan. Auto-assign is a methodology that state Medicaid plans use to determine which participants are assigned to which plans. These auto-assignment methodologies do vary from state to state (Smith et al., 2015). Since 2015, 19 state Medicaid MCO's contracts include quality requirements and have withhold systems included in their contracts (Smith et al., 2019). These withhold programs can include substantial amounts of money, reaching the $10's of millions in some states.

Medicare Low Income Subsidy (LIS) and Dually Eligible Special Needs (DSNP) Programs

Individuals with a monthly income of less than $1650 for individuals and $2,175 for couples and limited assets are eligible for a Medicare Part D subsidy known as the LIS program administered by Medicare under the Extra Help program. The program helps pay for prescription costs, premiums, deductibles, and coinsurance $8.95 (Centers for Medicare & Medicaid Services, n.d.). The program was established under the Medicare Modernization Act, with 4.7 million enrolled in the LIS program in 2018 (Centers for Medicare & Medicaid Services, 2020a). LIS programs are only available for those enrolled in a Medicare Advantage and Prescription Drug plans or Prescription Drug Plan only, not traditional Medicare. Additionally, the LIS program eliminates the Donut

Hole in Part D Medication coverage. The Donut Hole is a range of costs for medications that are not covered by MA plans, generally between $3,000 and $4,500, where members pay all of their prescription costs. The program's purpose is to take advantage of the associated lower medical costs related to improved compliance (Kirkman et al., 2015).

While the LIS program attempts to address some health problems around income inequality, it has some problems. The LIS program offers lower copays and premiums, but the deductibles may be higher than before being on the LIS program, and the MA formularies limit some medications. Both copays and deductibles are related to health inequalities and medication adherence. One of the studies presented looks at how the LIS program and medication compliance for individual antihyperglycemic medications control HbA1c levels.

DSNP programs are designed for those below the poverty level and include those in Medicare Part A and Part B and getting full Medicaid benefits, including Medicare premium assistance. In the DSNP program, Medicare is the primary payor, and Medicaid is the secondary payor. Medicaid also covers items and services not covered by Medicare but covered by the state Medicaid program. States control the income limits, but it is generally a requirement that the enrollee's income is below the poverty level, currently set between $12,760 and $44,120, depending on the number of individuals in the household (U.S. Department of Health and Human Services, 2020). There are also asset limitations for enrollment in the DSNP program. There are eight different participation levels within the DSNP program (Centers for Medicare & Medicaid Services, 2020b).

For the studies presented here, DSNP and LIS participation are used to measure income and education levels or Social Determinants' indicators. A 2018 Health and Human Services documented the relationship between DSNP enrollment and Social Determinants issues (Sorbero et al., 2018). DSNP enrollees have an income at or below the poverty level. LIS enrollees cannot be over 300% of the poverty level. Finally, we have the other participants of this study who are not in either of these programs and will be assumed to be not eligible for either of these programs. Therefore, we have a categorical variable of income with non-participation at the highest level of income, LIS at the middle level of income, 300% to 100% of the poverty level, and DSNP enrollees the lower level of income either at or below the poverty level. Having actual income levels would be a better approach, but the MCO does not collect that information, so we use the data available in the best way we can.

Other Considerations in Analysis

The data used in these studies came from a large MCO and were analyzed as secondary data. The individual variables used across these studies are:

Table 1

Predictor Variables, their type, and possible values

Variable Name	Variable Type	Possible Values
Unique member identifier.	Nominal	Format TBD by MCO
Age	Continuous	21-100
Sex	Categorical	0=male,1=female
HBA1c level	Continuous	actual level
Regional area of US	Categorical	N, E, S, W
Deductible	Continuous	actual level
Medication Class	Ordinal	1-35
Number of Hospital Visits	Ordinal	In days

Mean Adjusted Medication PDC	Continuous	0-1
Had Retinopathy Screening	Nominal	0=no, 1=yes.
Had Nephropathy Screening	Nominal	0=no, 1=yes.
Diabetes diagnosis time	Ordinal	In days
Length of time in the plan	Ordinal	In days
Plan type	Categorical	1=PDP, 2=MA + PDP
Seeing an Endocrinologist	Nominal	0=no, 1=yes.
Had Myocardial Infraction	Nominal	0=no, 1=yes.
Is Blind	Nominal	0=no, 1=yes.
Has End-Stage Renal Disease	Nominal	0=no, 1=yes.
Had Urinary Tract infections	Nominal	0=no, 1=yes.
LIS enrollment	Categorical	0=no, 1=yes
Dual enrollment	Categorical	0=no, 1=yes

The generally accepted demarcation between an Urban and Rural area is a population of more than 50,000. However, in 1910, the Census Bureau modified that definition to include Urban Clusters as an area where the population threshold is between 2,500 and 50,000. For example, a small city located in a rural part of the country with 3,000 is considered an Urban Cluster. Those living outside of the city limits would be considered living in a rural area (U.S. Census Department, n.d.).

There are nine diabetes medication classes used in treating type 2 diabetes based on their mechanism of action (Feingold, 2019). Injectable medications are not included because the PDC methodology cannot be used for injectables. For this study, we are only looking at six of the nine classes included in the MCO formulary which include Biguanides, Dipeptidyl Peptidase-4 (DPP-4) Inhibitors, Thiazolidinediones, Sulfonylureas, Meglitinide Analogues, Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors. Additionally, the six classes of commercially available combinations of medications included in the MCO formulary used to treat type 2 diabetes are considered.

These six combination classes are Meglitinide-Biguanide, SGLT2 Inhibitor - DPP-4 Inhibitor, Sodium-Glucose Co-Transporter 2 Inhibitor-Biguanide, Sulfonylurea-Biguanide, Dipeptidyl Peptidase-4 Inhibitor-Biguanide, Sulfonylurea-Thiazolidinedione.

The final issue to address in these dissertation studies is what four comorbidities to use in the analysis. The EQ-5D score is a questionnaire that scores chronic conditions in the United States and the United Kingdom with data taken from the Medical Expenditure Panel Survey. This questionnaire is used for both cost-effectiveness studies and public health modeling. Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract Infections (UTI) are the four diabetes comorbidities that will be used in these studies, and the following ICD-10 diagnosis codes for type 2 diabetes are being used E11.40, E11.51, E11.29, E11.36, E11.21, E11.319, E11.65, E11.311, E11.39, E11.9 (Sullivan & Ghushchyan, 2016).

Predictive Analytics

Predictive Analytics is the use of statistics, data, and in some cases, machine intelligence to predict future outcomes. Even though predictive analytics is a hot topic in many fields, the concept has been around since the late 1700's when Lloyds of London used predictive analytics in determining risks around insuring goods or assets. We live in a world of predictive analytics that includes foretelling our future purchase activities, what we want to watch on TV, and how marketing efforts can influence voting (Bradlow et al., 2017; Maca et al., 2016; Udanor et al., 2016). Predictive analytics in healthcare

has grown in importance, particularly in predicting clinical and intervention outcomes (Harris et al., 2016; Lin et al., 2017).

Healthcare big data and Electronic Health Records (EHR) are two areas where predictive analytics are used extensively within healthcare. Big Data is defined as voluminous and complex data beyond the ability of traditional data analytic systems. The term is evolving to include predictive analytics or behavior analysis (Ongsulee et al., 2018). Healthcare systems collect massive amounts of data on their members. MCO's have extensive claims data on their members, and government data sources are even more significant. All these transactional data can be applied to predictive analytics to help improve outcomes and health statuses.

Predictive analytics foretells outcomes and future needs for people with diabetes. One study looking at readmission of people with diabetes used predictor variables such as labs, number of medications, admission time, number of inpatient visits and found that they are all predictive of future hospital admissions (Srinivasan, 2018). Having this kind of data gives MCO's tools for reducing future diabetic readmissions and reducing costs. In an international study of flu vaccination rates in people with diabetes, predictive analytics showed that it is necessary to account for country-specific behaviors when creating flu vaccination interventions for people with diabetes (Liska et al., 2018). Predictive analytics have been used to find future diabetics. It was found that oversampling and the use of 16 predictors worked well in predicting both short and long-term patients at risk for diabetes (Talaei-Khoei & Wilson, 2018).

While predictive analytics is mainstream in healthcare, caution must be exercised in conclusions. With many free software applications for predictive analytics available, analysis is as easy as downloading the application, plugging in the data, and looking at the results. However, potential harm from these analytics is there and must be considered. Determining clinical procedures based on analytics can be problematic at an individual level. "The potential of prediction to influence decision making also implies the potential for harm, through the dissemination of misinformation at the point of care. This potential for harm from insufficiently validated models in a profit-driven market suggests the need for oversight (Kent et al., 2018, p. 2)."

Studies one and two examine the association between HbA1c levels OAMC and PDC and not whether HbA1c is controlled to PDC levels, and how financial assistance programs impact PDC and HbA1c levels. For these studies using HbA1c as a continuous variable is appropriate because the continuous variable gives much better granularity. Also, for these two studies, examining HbA1c as a categorical variable would give too large of variation in values and what would be meaningful value ranges? Finally, determining proper and clinical appropriate ranges for a categorical HbA1c would be difficult.

Variance Inflation Factors (VIF)

VIF is a statistical analysis that looks for collinearity. Collinearity is an effect where two or more predictors are correlated or express the dependent variable's same

effect. Collinearity may cause increased variance in predictors, produce models where a sizeable R^2 value is present even though no predictors are statistically significant, confuses the direction of effect, and produce a model where small predictor changes produce significant variances in the outcome (O'Brien, 2007).

A generally accepted value for VIF that expresses collinearity or multicollinearity is 10. However, using this rule of thumb must include cautions. As related to these studies, we must use caution in interpreting the VIF. One factor to consider is that some of the medication classes are a combination of the single medication classes, which could induce collinearity. Another factor to consider is that even if the regression predictors show collinearity, we will only use one of the medication class predictors at a time. For example, our regressions are designed for use when an individual is on one medication, and we are attempting to predict their HbA1c level when they are changed to another medication. In using the equation, all the other medications classes are removed from the prediction because their value in the equation is 0, eliminating the potential for interaction between medications.

Summary

Diabetes is one of the fastest-growing chronic diseases health care providers face, and the comorbidities of diabetes are numerous and severe. Most of the blindness in the country is related to diabetes, as is end-stage renal disease. Both impact individuals' lives, their families and, in the case of renal disease, create substantial financial burdens.

Medication adherence is a serious issue. Medical treatments have their foundation in the use of medications. When prescribed and medications are not taken as directed, not only do individuals face failed treatment plans, but physicians are generally not aware that their patients are non-compliant and may misdiagnose problems. Determining adherence is a tricky proposition as people tend not to be honest when completing medication compliance surveys, furthering the difficulty of assessing adherence. The best currently available tool for measuring medication adherence is the PDC.

While the current literature discusses medication compliance in people with type 2 diabetes, there are no studies to date that examine the relationship between the classes of medications, compliance with those medications, and HbA1c levels. Additionally, no studies have looked at this same relationship and the comorbidities of type 2 diabetes. Finally, Medicare created financial supplement programs that lower deductibles and copays. There are no studies to date examining the effectiveness of these programs in lowering HbA1c levels. These are the gaps that these studies look to close.

MCO's face financial penalties for not attaining set quality goals for diabetes and medication adherence. Additionally, Medicaid MCO's face populations with lower health literacy levels, high rates of chronic conditions, and lower health statuses. Putting all this together, we have the toxic mix of chronic diseases that are not understood by those that have them, in part, due to low health literacy. We have diseases that require medication adherence for successful treatment, people who tend to be non-compliant, and insurers facing financial penalties if they do not show successful clinical outcomes in these

people. The study's purpose is to provide tools for healthcare organizations to identify those at risk for higher HbA1c levels and at risk for the comorbidities of diabetes.

Overview of the Manuscripts

Manuscript 1 short description

This manuscript's title is "Medication Compliance by Drug Class as a Predictor of HbA1c Values in Medicare Type 2 Diabetics." Participants have type 2 diabetes and were enrolled in a Medicare Advantage plan in 2018**.** The PDC is the medication adherence methodology Medicare and Medicaid MCO use in measuring medication compliance in members. The PDC is a ratio of the number of doses of a medication that should have been taken over a measurement period of at least six months and calculated from claims data readily available to MCO's (Centers for Medicare & Medicaid Services, 2015). In diabetics, longer-term glucose values are measured by the HbA1c test. The advantage of using the HbA1c level is that it correlates with the glucose levels over the last several months. HbA1c has been the accepted method for monitoring glucose levels since 2011 (Malkani & Mordes, 2011). This study's medications are six of the nine classes of medications used in treating type 2 diabetes (Feingold, 2019). This study provides a predictive tool to assist MCO in identifying members at risk for future uncontrolled HbA1c levels based on their PDC. Linear regression analysis is appropriate here because the outcome variable in this study, HbA1c level, is a continuous variable expressed as a percentage.

Studies show an association between PDC and HbA1c levels (Nichols et al., 2016). One study showed that HbA1c levels are reduced by 0.6% in newly diagnosed diabetics with a PDC greater than 80%, and in those with a PDC less than 80%, the reduction was only 0.4% (Nichols et al., 2016). While other research has looked at individual medication compliance using the PDC, none have made a comparison of the six antihyperglycemic class medications and HbA1c and attempted to develop predictive modeling around these classes of medications. Statistical analysis was used to determine whether individual antihyperglycemic medication classes and the PDC can be used to predict future HbA1c levels. Other medication compliance measures, MPR, and the Morisky scores, have been used and have shown that medication compliance in diabetics leads to lower levels of HbA1c (Capoccia et al., 2015). This study uses the PDC, the current CMS, and CDC-recommended medication compliance method (Centers for Medicare & Medicaid Services, 2015).

Manuscript 2 short description

Manuscript two examines the relationship between participation in Medicare LIS and DSNP financial assistance programs and the PDC for the six classes of antihyperglycemic medications on HbA1c levels. We only chose those who had taken just one of the classes of antihyperglycemic medication classes during the year because we are not able to relate HbA1c levels to a single medication if they took more than one during the year. Medicare sets maximun income and asset levels for participation in these mutually exclusive programs. One of the goals of these programs is to improve

compliance and thereby reduce HbA1c levels. Study participants are in one of three categories, those not in a subsidy program, those in a LIS program, and those in a DSNP program. Linear regressions analyze the data to determine the effectiveness of these programs in improving PDC rates and lowering HbA1c. As of this writing, there are no peer-reviewed studies found that examine the effect of Medicare subsidy programs on HbA1c levels in MA type 2 individuals with diabetics using the PDC methodology and antihyperglycemic medication classes. The title for this manuscript is "Dually Eligible, Low-Income Subsidy Enrollment, and Medication Compliance as Predictors of HbA1c in Type 2 Diabetics."

Manuscript 3 short description

In manuscript three, we are analyzing medication compliance in the six classes of antihyperglycemic medications, HbA1c levels, and examining whether they can be used to predict four of the comorbidities, or combinations of comorbidities, of type 2 diabetes. Diabetes is a chronic disease that produces a number of comorbidities so being able to relate compliance with oral antihyperglycemic medciations or HbA1c to chances of developing a comorbidity would be helpful to practitioners (Luo et al., 2017). To date, there have been no peer-reviewed studies found looking at this topic. This study has significance to the medical community in that it may find that certain classes, along with the compliance of those medications, may do a better job at reducing the incidence of comorbidities. We are only selecting participants taking one class of antihyperglycemic medication during the year. The data will be analyzed using logistic regression because

our outcome variables, comorbidity, or sets of comorbidities, are binary. This manuscript's title is "Medication Compliance, HbA1c Predicting Comorbidities in Medicare Type 2 Diabetics."

Significance

There are implications that can have tens of millions of dollars in penalties associated with failure to meet Medicare quality goals. Of even more significance are the medical costs associated with patients or members who do not comply with the HEDIS standards of care. Third, there are the societal penalties of poorer health statuses associated with individuals who are non-compliant with HEDIS diabetes measures.

These studies look at topics of clinical significance for the treatment of MCO individuals with type 2 diabetes. There is a well-documented relationship between individual medication compliance and HbA1c using the PDC. The first study looks to see if there is a relationship between medication compliance and the different antihyperglycemic medication classes and individual HbA1c levels. We examine medication classes combined with compliance rates based on the PDC and determine if this is an effective way of determining new medications when attempting to lower HbA1c levels. We look to answer whether one medication with a lower compliance rate more effectively reduces HbA1c levels than another medication with a higher compliance rate. This study could be of significance given the medication compliance issues present in those with diabetes.

The second study looks at Medicare financial subsidy programs and the relationship between these and HbA1c levels, which has little discussion in the literature. One purpose of these programs is to help individuals make their copays and deductibles for their prescription medications. In those with type 2 diabetes, this assistance has an aim at improving medication compliance. In people with diabetes, medication compliance equals better HbA1c control. This study looks to validate that premise.

Study three will examine the relationship between medication compliance, HbA1c levels, and the incidence of four of the common comorbidities of diabetes, Blindness, Urinary Tract Infections, Myocardial Infarctions, and End-Stage Renal disease. This study's significance is to see if the combined relationship between HbA1c levels, medication class, and compliance has different comorbid complications rates. Suppose we find that even though there is a lower compliance rate for a class of medications, there is a lower rate of comorbidities. In that case, this is a clinically significant finding for future medication therapies showing that not only is a particular medication choice important but that medication compliance should also be part of the clinical decision process.

Summary

The HEDIS CDC measure has four subcategories: HbA1c under control (< 8%), completing an HbA1c during the calendar year, controlled blood pressure (under 140/90), and were there renal and retinal screening performed in the calendar year. MCO's face many barriers in getting their diabetic members to comply with these standards.

However, controlling blood sugar and HbA1c levels is entirely up to individual healthcare organization members.

Medicare and Medicaid adopted the HEDIS quality measures to determine the financial rewards for healthcare organizations. These rewards can be significant, and MCO's struggle to get their members compliant with quality measures. The studies presented establish relationships between medication compliance, oral antihyperglycemic medication class, financial programs, and diabetes comorbidities. MCO's can use this evidence to helps improve individual health statuses and assist organizations earn or recoup financial rewards to meet the HEDIS CDC measure requirements.

Part 2: Manuscripts

Medication Compliance by Drug Class as a Predictor of HbA1c Values in Medicare Type 2 Diabetics

Robert Lazarchik

Walden University

Outlet for Manuscript

This article will be submitted to the journal Diabetes Care, a peer-reviewed journal dedicated to diabetes and diabetes research. The size limit is 5000 words or 20 double spaced pages. The journal requires discussion of hypothesis testing, proper controls, correct statistical analysis, clear conclusions, and discussion supported by results. Submissions are judged on uniqueness and importance. Titles must be less than 40 words, and the abstract is limited to 250 words and contain no references. The journal provides an Endnote library format for their citation requirements, and there is a charge of $50 per page.

The article must name a 'guarantor' of the data used in the study; the data must be available to other researchers following guidelines from *Nature Research's* Policy (go.nature.com/2bf4vqn). Data access must be defined in a section called "Data and Resource Availability" under the Research Design and Methods section. There is a formal manuscript submission form attached in Appendix A. The journal accepts the ICMJE's "**Uniform Disclosure Form for Potential Conflicts of Interest"** attached in the Appendix.

Manuscripts must use the following layout.

- title page
- abstract
- introduction (no heading necessary)
- Research Design and Methods
- Results
- Discussion
- Acknowledgments (including Author Contributions, Guarantor Statement, Conflict of Interest statement, funding, and Prior Presentation information),

- References
- tables (each including a title and legend)
- figure legends

This manuscript has been adjusted from the supplied template to this format. The URL for other details is at https://diabetes.diabetesjournals.org/content/instructions-for-authors

Abstract

Medication therapy is a crucial component in managing diabetes, yet compliance rates only approach 50% after the first year of diagnosis. Managed Care Organizations (MCO) face considerable financial stress with rewards and penalties reaching millions of dollars for achieving set standards of care, including several diabetes measures. The Centers for Disease Control (CDC) accepts the Proportion of Days Covered (PDC) as the current research method for establishing medication compliance. The association between medication compliance using the PDC and oral antihyperglycemic medication (OAMC) and HbA1c levels has not been studied. This study aimed to determine the association between medication compliance, as determined by the PDC, and six of the OAMCs. This is the first study establishing the association between medication compliance, measured by the PDC, and one of six OAMC and by not specific medications. Sample selection included those over 21 years of age, took only one of six OAMCs, having an HbA1c level completed, diagnosed with type 2 diabetes selected from the 2019 claims database of a large MCO yielded 23,000 participants. Multiple regression analysis shows that as PDC rates improve, Sulfonylurea Biguanides have 27 times more impact on HbA1c control, and the DPP-Biguanide and Thiazolidinediones classes are ten times more effective when compared to the Dipeptidyl Peptidase-4 (DPP-4) medication class. These findings may help providers promote positive social change by establishing the importance of considering patient compliance when making medication selection in treating people with type 2 diabetes.

Introduction

U.S. individual medication non-adherence costs for people with type 2 diabetes are approximately $28,824 per year (Kennedy-Martin et al., 2017). There are several methods for measuring medication compliance, but the most commonly used are the Medication Possession Ratio (MPR) and the Proportion of Days Covered (PDC) (Cutler et al., 2018). Both use algorithms that consider the proportion of prescribed medication doses that should have been taken to the number taken. (Center for Disease Control, 2015). The Pharmacy Quality Alliance (PQA) created the current version of the PDC, and the CDC has since endorsed it as acceptable for research purposes (Nau, 2012).

The use of dispensing data has been validated by the PQA and has been used in the literature for the last twenty years (Martin et al., 2009). Having compliance methodologies utilizing dispensing data, such as MPR or PDC, that can be extracted from MCO claims data to measure compliance provides convenience and usability when resources are limited. The first of these is the MPR. The MPR medication adherence measurement tool is used to determine compliance in comparing different medication delivery systems, hypertension, and medication regimen complexity (Ho et al., 2017; Na et al., 2018). An issue with the MPR is that it may overstate compliance due to its methodology. The PDC evolved from an effort to improve this weakness in the MPR and in 2015, the CDC adopted the PDC measurement as their accepted methodology for researchers examining medication compliance. The PDC's advantage over other methods is that it looks at how many doses of medication an individual should have taken during a

measurement period and not, as with the MPR, what they possessed. The PDC measurement is now the leading method for determining medication adherence in large populations (Center for Disease Control, 2015).

The National Committee for Quality Assurance (NCAQ) developed Healthcare Effectiveness Data and Information Set (HEDIS), a set of quality measures affecting 190 million Americans, and is used by Medicare and State Medicaid programs in their quality initiatives (National Committee for Quality Assurance, 2018a). Several of the HEDIS quality measures use the PDC to measure medication compliance: D10 Medication Adherence for Diabetes Medications, D11 Medication Adherence for Hypertension (RAS antagonists), D12 Medication Adherence for Cholesterol (Statins), D14 Statin Use in Persons with Diabetes (SUPD) (Center for Disease Control, 2019). Medicare set PDC level greater than 80% as an acceptable rate of compliance. Regression analysis were performed on a mean adjusted PDC index for each of six classes, or the combination of any of six classes of diabetes medications, Biguanides, Dipeptidyl Peptidase-4 (DPP-4) Inhibitors, Sulfonylureas, Thiazolidinediones, Meglitinide Analogues, and Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors (these are the classes with enough participants).

There are numerous studies in the literature establishing relationships between medication adherence and HbA1c levels. One study used a modified PDC called the Biologic Response Based Proportion of Days Covered (BRB-PDC) and found that obtaining optimal PDC values in glycemic lowering medications during therapy initiation

is related to lower HbA1c levels (Nichols et al., 2016). A 2016 meta-study found a relationship between medication adherence in diabetics and HbA1c levels (Capoccia et al., 2016). Other studies have established the association between the PDC measurement and HbA1c levels (Polonsky & Henry, 2016; Ramos et al., 2018). However, no studies to date have established the relationships between the PDC and antihyperglycemic medication class. The purpose of this study is to determine what association exists between the PDC and the individual classes of antihyperglycemic medications and HbA1c levels.

Research Design and Methods

Creswell (2017) said that a quantitative approach is appropriate when a researcher tries to establish relationships between dependent and independent variables. This is a longitudinal retrospective study looking at 2019 MCO secondary data. Since the purpose of this study is to determine the quantitative relationship between the PDC for the six different classes of antihyperglycemic medications, individually and in combination (independent variables), and HbA1c levels (dependent variable), the quantitative approach is appropriate.

Research Questions:

RQ1: What is the relationship between the PDC and the antihyperglycemic class of medication on HbA1c in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and

retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure?

$H_0$1: There is no statistically significant relationship between the PDC and the Biguanides class of medications on HbA1c in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure?

$H_1$1: There is a statistically significant relationship between the PDC and the Biguanides class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$2: There is no statistically significant relationship between the PDC and the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$2: There is no statistically significant relationship between the PDC and the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$2: There is a statistically significant relationship between the PDC and the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$2: There is no statistically significant relationship between the PDC and the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$3: There is no statistically significant relationship between the PDC and the Thiazolidinedione class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$3: There is a statistically significant relationship between the PDC and the Thiazolidinedione class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$4: There is no statistically significant relationship between the PDC and the Sulfonylureas class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$4: There is a statistically significant relationship between the PDC and the Sulfonylureas class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits,

seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$5: There is no statistically significant relationship between the PDC and the Meglitinide Analogues class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$5: There is a statistically significant relationship between the PDC and the individual Meglitinide Analogues class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$6: There is no statistically significant relationship between the PDC and the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial

infarction, UTI, or end stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$6: There is a statistically significant relationship between the PDC and the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

RQ2: What is the relationship between PDC and combinations of antihyperglycemic classes of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure?

$H_0$7: There is no statistically significant relationship between the PDC and the Meglitinide-Biguanide Combinations class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-

stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$7: There is a statistically significant relationship between the PDC and the Meglitinide-Biguanide Combinations class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$8: There is no statistically significant relationship between the PDC and the SGLT2 Inhibitor - DPP-4 Inhibitor Combinations class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$8: There is a statistically significant relationship between the PDC and the SGLT2 Inhibitor - DPP-4 Inhibitor Combinations class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial

infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$9: There is no statistically significant relationship between the PDC and the Sodium-Glucose Co-Transporter 2 Inhibitor-Biguanide class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$9: There is a statistically significant relationship between the PDC and the Sodium-Glucose Co-Transporter 2 Inhibitor-Biguanide class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$10: There is no statistically significant relationship between the PDC and the Sulfonylurea-Biguanide class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a

diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$10: There is a statistically significant relationship between the PDC and the Sulfonylurea-Biguanide class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$11: There is no statistically significant relationship between the PDC and the Dipeptidyl Peptidase-4 Inhibitor-Biguanide class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$11: There is a statistically significant relationship between the PDC and the Dipeptidyl Peptidase-4 Inhibitor-Biguanide class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or

end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_0$12: There is no statistically significant relationship between the PDC and the Sulfonylurea-Thiazolidinedione class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

$H_1$12: There is a statistically significant relationship between the PDC and the Sulfonylurea-Thiazolidinedione class of medications and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, deductible, number of hospital visits, seeing an endocrinologist, participation in renal and retinal screenings, having a diagnosis of blindness, myocardial infarction, UTI, or end-stage renal disease, LIS enrollment, DSNP enrollment, and controlled blood pressure.

Population and Study Sample

In longitudinal studies, participants are followed over long periods. Retrospective study designs look at past events related to the subject of study (Caruana et al., 2015). Longitudinal retrospective studies last over time while examining selected events at different points during the study period. In this study, we will be looking at the

relationship between various predictor variables and HbA1c levels. Participants were selected based on enrollment in an MCO, having a type 2 diabetes diagnosis, over 21 years of age, taking only one class or combination class of antihyperglycemic medications during the past 2019 year.

To calculate the minimum sample size needed for each of the research questions G*Power, version 3.1.9.4, was used with an effect size of 0.15, an alpha error probability of 0.05, a power of 0.95, to yield a recommended sample size of 89. The effect size was determined based on findings from a meta-analysis of medication compliance studies with different diseases, which found that studies with more than 85 participants and effect sizes of 0.17 to 0.18 had high statistical power with $P < 0.0001$ (Foot et al., 2016). G* Power's effect size is a method to quantify the differences between the test and control groups and is based on Cohen's effect size or the explained variance and error variance (Cunningham & McCrum-Gardner, 2007). We chose a small effect size, which means the difference between the two variances is not important, because the large sample size of 56,000 provides more than sufficient participants to achieve statistical power (Cohen, 2013).

Our sample includes individuals enrolled in a Medicare Advantage plan (MA) with a type 2 diabetes diagnosis based on 2019 claims data. Participants are over twenty-one and took only one of the six classes or a combination of antihyperglycemic medications during 2019. Those who took more than one of the antihyperglycemic medications classes in 2019 were removed from this study. Diagnoses were coded

according to the ICD-10 World Health Organization International Statistical Classification of Diseases and Related Health Problems. Cases were selected using the ICD-10 diabetes diagnosis code of E11.9, claim data from pharmacy dispensing records at outpatient pharmacies. The PDC measurement does not include those on insulin, so we did not include members on insulin. MCO members were included in the study until disenrollment, death, or the end of the study period. All the data provided by the MCO was deidentified with a unique serial number that is with the released data.

We divided the sample group into two groups using a data-splitting technique consisting of a learning group and a holdout group (Picard & Berk, 1990). We split our samples into our learning group and holdout group, 70% into the learning used for analysis, and 30% holdout used to test our analysis, based on Pang, H., & Jung, S. (2013). We conducted our data analysis using SPSS version 27 using the standard p-value of < 0.05 to indicate statistical significance. Multiple linear regression analysis was used to determine the effect each of the predictors has on the outcome variable, the continuous HbA1c value, and determining which of the predictor variables has a statistically significant effect on the outcome (Warner, 2013).

The American Diabetic Association established that any HbA1c value higher than 6.5% is considered diagnostic for diabetes (American Diabetes Association, 2018c). Categorical variables were dummy coded for inclusion in these analyses. There are four regressions in this study, first, medication compliance and the PDC, second,

comorbidities, third, the PDC alone, and fourth, all of the items in Table 2 to determine the regression equations for each of our research questions.

Table 2

Predictor Variables, their type, and possible values

Variable Name	Variable Type	Possible Values
Unique member identifier.	Nominal	Format TBD by MCO
Age	Continuous	21-103
Sex	Categorical	0=male, 1=female
HBA1c level	Continuous	actual level
Regional area of US	Categorical	N, E, S, W
Medication Class	Categorical	1-35
Medication PDC (mean adj)	Continuous	0-1
Diabetes diagnosis time	Ordinal	In days
Deductible	Ordinal	
Number of Hospital visits	Ordinal	In days
Seeing Endocrinologist	Categorical	0=no, 1=yes
Had Renal Screening	Categorical	0=no, 1=yes
Had Retinal Screening	Categorical	0=no, 1=yes
Had Myocardial Infraction	Categorical	0=no, 1=yes.
Is Blind	Categorical	0=no, 1=yes.
Has End-Stage Renal Disease	Categorical	0=no, 1=yes.
Has Urinary Tract infections	Categorical	0=no, 1=yes.
LIS enrollment	Categorical	0=no, 1=yes
Dual enrollment	Categorical	0=no, 1=yes
Controlled Blood Pressure[1]	Categorical	0=no, 1=yes

[1] Blood pressure under 140 systolic and 90 diastolic

Statistical Analysis

Regression results were validated using the HO1 group. The final regression equation analysis includes looking at the individual predictor variables, checking correlations between the outcome and predictor variables, and the R^2 value. We will use a Chi-Square test to compare predicted HbA1c values to actual HbA1c values in the HO1 group.

Pearson's correlation values tell us the direction and strength of the linear relationship between two variables (Warner, 2013). Pearson's correlation values of greater than 0.5 show significant levels of correlation between the variables. Values down to 0.3 and above have small correlations but still significant enough to consider in the final equation. Any predictor variable must have a p-value of less than 0.05 (Warner, 2013). Pearson's correlations can give us some insight into the R^2 value produced by regression analysis and are obtained by selecting a correlation from the SPSS interface and adding all of the variables in the analysis.

R^2 is a statistical value created by a regression analysis indicating how well the predictor variables match the regression line (Warner, 2013). In human research, an R^2 value greater than 0.2 is considered adequate. This value is somewhat lower than in other kinds of research, but because of the effect of human behavior in the analysis, this lower number is acceptable (Hair et al., 2011). HbA1c level, the outcome variable in this analysis, is controlled by human behavior in medication compliance, following a recommended diet, and quantity of exercise.

Collinearity, a type of regression interference defined as the potential for correlations between a predictor variable, must be determined when doing regression analysis. Multicollinearity is the condition where multiple predictors interfere with the regression results. One assumption of regression is that all the predictor variables are independent of each other, and each predictor has unique information about the outcome variable. When one or more variables display collinearity, they may significantly impact

the regression results and must be considered. Collinearity can cause issues where standard errors appear high, or a Beta weight can have a direction that makes no sense (Belsley, 1984). The method chosen for determining collinearity in this study is the Variance Inflation Factor (VIF). VIF is a measure of the degree of standard error inflation, where a VIF factor greater than 10 is indicative of collinearity (Weisberg, 2005, p. 217). Our analysis checks VIF values using the SPSS collinearity diagnostics when running the regression analysis. One method of addressing collinearity issues is to remove a redundant variable (multiple variables predicting the same thing). Another method of dealing with collinearity is to aggregate redundant variables into a single variable (O'Brien, 2007). We used the Variance Inflation Factor to determine collinearity or multicollinearity to determine which variables to remove from the analysis.

The equation for each regression analysis is the same as the fundamental equation for a straight line, y = mx + b, where y is the predicted HbA1c value, b is the y-axis intercept, and m is the coefficient for the statistically significant predictor variable. The final equation will take the final form of y = b + coeff1*predictor1 value + coeff2*predictor2 value + coeff3*predictor3 value + coeffN*predictorN value where each of the predictors have a significance of less than 0.05. These final equations define the different models from the research questions for predicting HbA1c values.

The data that support the findings of this study are available from the corresponding author, but restrictions apply to the availability of these data used under license for the current study, and so are not publicly available. Data are available from the

corresponding author upon reasonable request and with permission of the MCO that provided the data.

Results

The purpose of this quantitative research was to determine if there is an association between medication compliance, as calculated by the PDC, oral antihyperglycemic medication class, and HbA1c levels in Medicare individuals with type 2 diabetes while controlling for covariates such as age, sex, financial subsidy type, comorbidities, hospital visits, and if they are seeing an endocrinologist. On September 29, 2020, a large, nationwide MCO agreed to provide the use of their client data for this study. Approval for this study was received by the Walden University IRB, number 10-30-20-0721525, on October 30, 2020. Two MCO Business Analysts produced secondary, de-identified data compliant with HIPAA regulations using the enrollment criteria for the study.

Data Collection and Cleaning

The initial data pull included members enrolled in a Medicare Advantage plan for 2019, over 21, diagnosed with type 2 diabetes, and took one or a combination of the six antihyperglycemic medications classes. The initial data pull included 76,586 MCO members. After eliminating those who had not had an HbA1c level completed during the 2019 calendar year and those who had taken more than one of the medication classes either as a single class or a combination class during the year, the final count dropped to 22,638. This list was further divided into a learning group consisting of 70%, or 15,846

members, and a test group of 30%, or 6,792 members. There was an error in the methodology used to determine participation in the Low -Subsidy (LIS) program by the MCO. There were members listed in both the LIS and DSNP programs simultaneously, a situation that is not possible. To correct this problem a new variable in SPSS reflecting the correct value for anyone in the LIS program sample was created for an adjusted LIS variable where a member who showed in both a DSNP and LIS program was coded as in a DSNP program while individuals showing in a LIS plan only were coded as in a LIS program. We created dummy variables for the following categorical variables, region, sex, and medication class.

Finally, PDC values were mean-centered providing better understanding of the PDC value. In our new variables, a value of 0 indicates a real PDC value of 0.8581. This centering technique allowed us to better see those who were above and below the mean of each medication (Hayes, 2009, pp. 466-467).

Comparing Samples

The differences between the sample chosen for the study and the population not selected were examined to find any differences that might explain the lack of HbA1c levels. Of our total 2019 population, 76586, only 32307 had an HbA1c completed during the year, with a compliance rate of 42%. We examined the two groups to try to find evidence on why individuals did not have an HbA1c level during the year when HbA1c levels are an integral part of a treatment plan.

The independent samples T test from SPSS compares continuous predictors and the Crosstabs function for comparing categorical predictors. The independent samples T test is the correct test because we want to compare the means between those we included in our analysis and those we did not. Additionally, one group's selection did not influence the other group's selection (Peck et al., 2012).

We analyzed the continuous variables age, number of visits to an Endocrinologist, the PDC value, and the number of hospital visits. Table 4 shows that PDC, Hospital visits, and Endocrinologist visits all have a Levene's Test for Equality of Variances significance level of less than 0.001 with equal variances not assumed. We can reject the null hypothesis that these predictors' means are equal and accept the alternate hypothesis that there are statistically significant differences in the two groups. The categorical HbA1c value is the grouping variable using a value 0 for no test and 1 for having an HbA1c level done during the measurement year, 2019. In Table 3 the Levene's test for age has a significance of 0.240; thus, we accept the null hypothesis that there are no statistical differences between the groups ages. However, when we examine the T-Test significance values for all the predictors in their appropriate row, we see that the p values are all less than 0.05 and therefore, we can conclude that there are statistically significant differences between the two groups.

To compare the categorical predictor values in the two groups, the crosstabs chi-square function of SPSS is the appropriate test. The HbA1c is used as a categorical value in this analysis. A medication in the Thiazolidinediones or DPP class and having a

Myocardial Infarction or blindness diagnosis showed no statistically significant differences between the no HbA1c level done and had an HbA1c level done groups. While there are statistically significant differences between the predictor values, there are too many of them, and we did not have the correct data set to determine which ones might contribute to better identify what differences, if any, contributed to not having an HbA1c level completed during the year. And this examination is beyond the scope of this discussion. Table 5 is a list of the predictors that show a statistically significant difference between the two groups.

Table 3

Independent Samples Test

		Levene's Test for Equality of Variances					
		F	Sig.	df[1]	Sig. (2-tailed)	95% Confidence Interval of the Difference	
						Lower	Upper
PDC	EVA	141.12	0	36122	0	-0.042	-0.031
	EVNA			4417	0	-0.043	-0.0301
Age	EVA	1.38	0.24	36607	0	-2.075	-1.47
	EVNA			4809	0	-2.08	-1.466
Hospital Visits	EVA	12.95	0	36607	0.003	-0.448	-0.093
	EVNA			5093	0.001	-0.433	-0.107
Seeing Endocrinologist	EVA	33.35	0	36607	0.003	0.013	0.066
	EVNA			4456	0.015	0.008	0.072

1 rounded to an integer
EVA - Equal variances assumed
EVNA - Equal variances not assumed

Table 4

Categorical Predictors vs. HbA1c level completed

Predictor	No A1c	Had A1c	Pearson's Chi-Square	p-value	Cramer's V
Taking Biguanide	2732	25277	88.6	0.000	0.049
Taking Thiazolidinediones	66	559	0.001	0.978	0
Taking DPP	171	1297	1.957	0.162	0.007
Taking Sulfonylureas	631	4187	36.72	0.000	0.032
Taking DPP Biguanide	135	749	20.936	0.000	0.024
Taking Sulfonylurea Biguanide	100	415	42948	0.000	0.034
Seeing Endocrinologist	186	1348	3.968	0.046	0.01
Retinopathy screening	417	3748	2.228	0.000	0.008
Nephropathy screening	723	7064	14.862	0.000	0.02
BP Control	1137	11459	49.261	0.000	0.061
End Stage Renal Disease	2693	20324	80.219	0.000	0.047
Myocardial Infraction	257	1984	1.93	0.165	0.007
UTI	554	5153	5.559	0.018	0.012
Blindness	63	435	2.257	0.133	0.008
DSNP Program	797	8939	81.13	0.000	0.047
LIS Program	960	7319	11.354	0.001	0.018
No Financial Subsidy	2121	16473	26.428	0.000	0.027

Table 5

Statistically different predictors HbA1c group vs. No HbA1c group

Predictor	Sig ($p<0.05$)
PDC	0.0001
Hospital Visits	0.0001
Seeing an Endocrinologist	0.0001
Biguanide	0.0001
Sulfonylureas	0.0001
DPP Biguanide	0.0001
Sulfonylurea Biguanide	0.0001
Seeing Endocrinologist	0.046

Retinopathy screening	0.0001
Nephropathy screening	0.0001
BP Control	0.0001
End-Stage Renal Disease	0.0001
UTI	0.018
DSNP Program	0.0001
LIS Program	0.001
No Financial Subsidy	0.0001

Descriptive Statistics

We ran a set of descriptive statistics for each of the medication classes and found that combination classes did not have a sufficient number of members to provide statistical power for analysis. Table 6 is a count of members taking each class of medication.

Table 6

Count for each of the Classes and Combination of Classes

Medication Class	Count
Biguanides	11713
Dipeptidyl Peptidase-4 (DPP-4) Inhibitors	601
Thiazolidinediones	214
Sulfonylureas	2554
Meglitinide Analogues	35
Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors	71
Meglitinide-Biguanide Combination	0
SGLT2 Inhibitor - DPP-4 Inhibitor Combinations	2
Sodium-Glucose Co-Transporter 2 Inhibitor-Biguanide Combination	41
Sulfonylurea-Biguanide Combinations	260
Dipeptidyl Peptidase-4 Inhibitor-Biguanide Combination	353
Sulfonylurea-Thiazolidinedione Combination	0
Thiazolidinedione-Biguanide Combination	1
DPP-4 Inhibitor-Thiazolidinedione Combination	0

Using G*Power, we calculated the need for a population of at least 89 members for statistical power in calculations. Meglitinide Analogues, SGLT2 inhibitors, Meglitinide-Biguanide Combinations, SGLT2 Inhibitor - DPP-4 Inhibitor Combinations, Sulfonylurea-Thiazolidinedione Combinations, Thiazolidinedione-Biguanide Combinations, and DPP-4 Inhibitor-Thiazolidinedione Combinations were eliminated due to insufficient counts. Medication classes, their corresponding mean-centered PDC value, the region of the country in which the member lives, and sex were dummy coded. Tables 7 and 8 show the descriptive statistics for the group that did and the group that did not have an HbA1c level taken during the 2019 calendar year.

Table 7

Descriptive Statistics for Members with an HbA1c level

	Min	Max	Mean	Std. Deviation
Biguanide	0	1	.75	.435
DPP	0	1	.04	.194
Thiazolidinediones	0	1	.01	.114
Sulfonylurea	0	1	.16	.369
Sulfonylurea Biguanide	0	1	.02	.125
DPP Biguanide	0	1	.02	.146
Male	0	1	.41	.492
Age	22	101	71.1	9.38
DSNP	0	1	.32	.466
LIS	0	1	.22	.413
South	0	1	.85	.354
NE	0	1	.09	.293
NW	0	1	.02	.134
W	0	1	.02	.123
Deductible	0	415	168	196

HbA1c Level	4.10	15.50	6.59	0.98
Hospital Visits	0	91	2.78	5.42
Seeing Endocrinologist	0	1	.04	.193
Retinopathy Screening	0	1	.10	.306
Nephropathy Screening	0	1	.21	.408
Blood Pressure Controlled	0	1	.94	0.2253
End Stage Renal Disease	0	1	.49	.500
Blindness diagnosis	0	1	.01	.112
Myocardial Infarction diagnosis	0	1	.06	.244
UTI diagnosis	0	1	.15	.358
Mean Adj PDC	-.77	.14	.0006	.178
PDC Value	0.094	1.000	0.8587	0.178
Biguanide Mean PDC	-.77	.14	.0007	.152
DPP Mean PDC	-.73	.14	-.0016	.043
Thiazolidinediones Mean PDC	-.68	.14	.0003	.0192
Sulfonylurea Mean PDC	-.76	.14	.0018	.0707
Sulfonylurea Biguanide Mean PDC	-.73	.14	.0004	.0202
DPP Biguanide Mean PDC	-.70	.14	-.0008	.0292

Count for all items is 15713
PDC values are mean adjusted with 0. 8587 as mean value.

Table 8

Descriptive Statistics Members with no HbA1c level in 2019

	Min	Max	Mean	Std. Deviation
Male	0	1	.40	.490
Age	22	103	70.41	9.927
DSNP	0	1	.30	.459
LIS	0	1	.27	.443
South	0	1	.62	.484
NE	0	1	.28	.449
West	0	1	.04	.187
NW	0	1	.04	.201
Deductible	0	415	181	196

Number of Hospital Visits	0	253	5.3	8.5
Seeing an Endocrinologist	0	1	.04	.194
Retinopathy Screening	0	1	.06	.233
Nephropathy Screening	0	1	.07	.250
End Stage renal disease diagnosis	0	1	.47	.499
Blindness diagnosis	0	1	.02	.124
Myocardial Infarction	0	1	.07	.254
UTI	0	1	.14	.347
Blood Press Controlled	0	1	.16	.368
Biguanides	0	1	.74	.436
DPP	0	1	.05	.215
Thiazolidinediones	0	1	.01	.117
Sulfonylurea	0	1	.14	.348
Sulfonylurea Biguanide	0	1	.01	.104
DPP Biguanide	0	1	.03	.165
Mean Adjusted PDC	-.7957	.1727	-.0009	.2086
Biguanide Mean Adj PDC	-.7957	.1727	.0010	.1762
DPP Mean Adj PDC	-.7461	.1727	-.0016	.0535
Thiazolidinediones Mean Adj PDC	-.6792	.1727	.0001	.0231
Sulfonylurea Mean Adj PDC	-.7403	.1727	.0014	.0784
Sulfonylurea Biguanide Mean Adj PDC	-.7382	.1727	.0001	.0192
DPP Biguanide Mean Adj PDC	-.7775	.1727	-.0011	.0399
PDC Value	.0315	1.0000	.8263	.2086

Count for all items is 23331
PDC values are mean adjusted with 0.8263 as mean value
Max PDC value of 0.1727 equals a PDC of 100% or full compliance

Regression Equations

The requirements for using multilinear regressions are a continuous outcome variable, categorical or continuous predictors, normally distributed residuals, no multicollinearity, and homoscedasticity must be present (Osborne & Waters, 2002). Our outcome variable, HbA1c level, is measured as a continuous variable. PDC, deductible, age, and hospital visits are all continuous. Sulfonylurea, Blindness, Retinopathy

Screening, BP Controlled, Myocardial Infarction, LIS, DSNP, Thiazolidinediones, UTI, DPP Biguanide, End-Stage Renal Disease, Male, DPP, Nephropathy Screening, seeing an endocrinologist, and Sulfonylurea Biguanide are all categorical variables. We did find multicollinearity with the regional variable and eliminated that predictor from our analysis. Figure 2 shows normally distributed residuals in our data. Figure 3 verifies that we have homoscedasticity in our data.

Figure 2

HbA1c Histogram

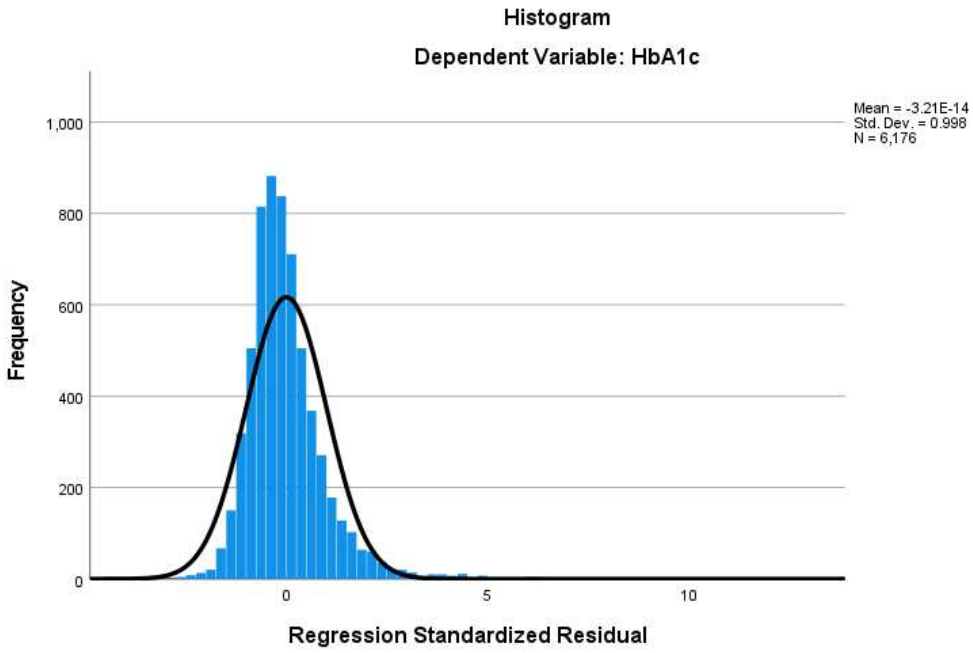
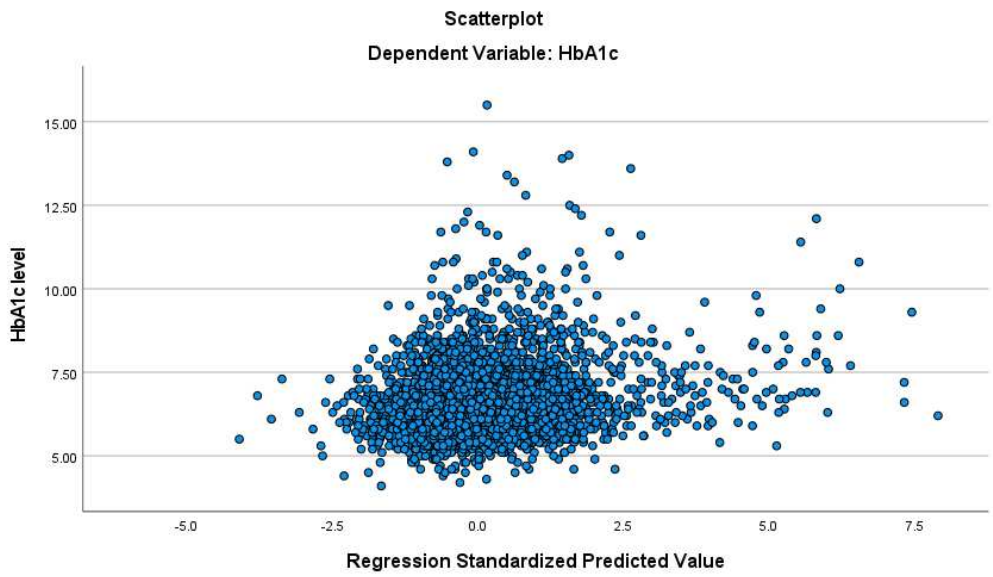


Figure 3

HbA1c Scatterplot



Each of the six medication classes were recoded into binary variables. There was sufficient sample size to include in our analysis the following medication classes, Biguanide, DPP, Sulfonylurea Biguanide combination, Thiazolidinediones, Sulfonylurea, and DPP Biguanide combination. From these regression analyses, we developed predictive model equations for each of these medication classes. We included all regression values, even if they are not statistically significant because even if a predictor is not statistically significant, it has clinical significance (Schober et al., 2018). These equations give us a model that predicts HbA1c values when switching from one medication class to another. Use of the equation requires user input of the new medication class wanted, the PDC for that class, and values for each covariate. The result of the calculation is a predicted HbA1c value.

In our first run of this analysis, we found multicollinearity among those living in the country's south and NE regions based on the Variance of Inflation Factor (VIF) values. Using a value of ten as the value to indicate a collinearity problem, the four regional covariates Northeast, Northwest, South, and West were removed from our regression analysis because of the collinearity problem.

Table 9

Multicollinearity values for South and NE region variables.

	B	Sig.	Lower Bound	Upper Bound	Tolerance	VIF
South	0.15	0.439	-0.23	0.529	0.04	25.156
NE	0.308	0.118	-0.078	0.694	0.042	23.789

Table 10

Biguanide Medication Class as Reference Variable

Model Summary [b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.206[a]	0.043	0.039	0.88371

a. Predictors: (Constant), Sulfonylurea, Thiazolidinediones Mean PDC, Blindness, DPP Biguanide Mean PDC, DPP Mean PDC, Seeing Endocrinologist, Retinopathy Screening, Sulfonylurea Biguanide Mean PDC, BP Controlled, Myocardial Infarction, LIS, Thiazolidinediones, UTI, DPP Biguanide, Sulfonylurea Mean PDC, End-Stage Renal Disease, Male, IsDPP2, Hospital Visits, Nephropathy Screening, Age, Deductible, Sulfonylurea Biguanide, DSNP
b. Dependent Variable: HbA1c level

Table 11

Coefficients with DPP as Reference

	B	Sig	Lower Bound [1]	Upper Bound [1]	VIF
(Constant)	7.031	0	6.829	7.232	
DPP	0.057	0.334	-0.059	0.173	1.076
DPP Mean PDC	0.169	0.542	-0.375	0.713	1.035
DPP Biguanide	0.191	0.021	0.029	0.353	1.024
DPP Biguanide Mean PDC	-1.231	0.006	-2.114	-0.35	1.014
Sulfonylurea Biguanide	0.925	0	0.727	1.123	1.346
Sulfonylurea Biguanide Mean PDC	-1.797	0.039	-3.501	-0.09	1.343
Thiazolidinedione	-0.09	0.375	-0.29	0.109	1.011
Thiazolidinedione Mean PDC	-0.814	0.183	-2.013	0.385	1.003
Sulfonylurea	0.274	0	0.212	0.336	1.084
Sulfonylurea Mean PDC	-0.27	0.112	-0.603	0.063	1.024
Male	0.088	0	0.042	0.134	1.059
Age	-0.004	0.001	-0.007	-0	1.108
DSNP	-0.272	0	-0.393	-0.15	7.032
LIS	-0.092	0.004	-0.155	-0.03	1.228
Deductible	0	0.003	0	0.001	6.62
Hospital Visits	-0.007	0.001	-0.012	-0	1.081
Seeing Endocrinologist	-0.071	0.208	-0.18	0.039	1.034
Retinopathy Screening	0.045	0.189	-0.022	0.111	1.08
Nephropathy Screening	0.005	0.832	-0.042	0.052	1.081
End Stage Renal Disease	-0.04	0.094	-0.087	0.007	1.121
Blindness	0.168	0.078	-0.019	0.354	1.004
Myocardial Infarction	-0.031	0.504	-0.123	0.06	1.032
UTI	-0.035	0.27	-0.097	0.027	1.054
BP Controlled	-0.207	0	-0.306	-0.11	1.017

[1] 95% CI

Table 12

DPP Reference Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate

.212[a]	0.045	0.041	0.88287

a. Predictors: (Constant), Sulfonylurea, Thiazolidinediones Mean PDC, Blindness, DPP Biguanide Mean PDC, Biguanide Mean PDC, Seeing Endocrinologist, Retinopathy Screening, Sulfonylurea Biguanide Mean PDC, BP Controlled, Myocardial Infarction, LIS, Thiazolidinediones, UTI, DPP Biguanide, Sulfonylurea Mean PDC, End-Stage Renal Disease, Male, Biguanide, Hospital Visits, Nephropathy Screening, Age, Deductible, Sulfonylurea Biguanide, DSNP

Table 13

Coefficients with DPP as Reference

	B	Sig	Lower Bound[1]	Upper Bound[1]	VIF
(Constant)	7.076	0	6.837	7.315	
Biguanide	-0.05	0.389	-0.165	0.064	5.064
Biguanide Mean PDC	-0.055	0.489	-0.211	0.101	1.02
Thiazolidinediones	-0.142	0.22	-0.368	0.085	1.298
Thiazolidinediones Mean PDC	-0.814	0.183	-2.013	0.385	1.003
Sulfonylurea	0.223	0	0.099	0.347	4.281
Sulfonylurea Mean PDC	-0.27	0.112	-0.603	0.063	1.024
Sulfonylurea Biguanide	0.874	0	0.648	1.099	1.75
Sulfonylurea Biguanide Mean PDC	-1.798	0.039	-3.502	-0.094	1.343
DPP Biguanide	0.14	0.158	-0.055	0.335	1.473
DPP Biguanide Mean PDC	-1.232	0.006	-2.116	-0.349	1.014
Male	0.088	0	0.042	0.134	1.059
Age	-0.004	0.001	-0.007	-0.002	1.109
DSNP	-0.268	0	-0.39	-0.146	7.03
LIS	-0.092	0.004	-0.155	-0.029	1.226
Deductible	0	0.004	0	0.001	6.639
Hospital Visits	-0.008	0.001	-0.012	-0.003	1.08
Seeing Endocrinologist	-0.07	0.21	-0.18	0.04	1.034
Retinopathy Screening	0.044	0.19	-0.022	0.111	1.08
Nephropathy Screening	0.006	0.797	-0.041	0.053	1.085

End Stage Renal Disease	-0.039	0.1	-0.086	0.008	1.121
Blindness	0.168	0.077	-0.018	0.354	1.004
Myocardial Infarction	-0.031	0.505	-0.122	0.06	1.032
UTI	-0.035	0.263	-0.097	0.027	1.054
BP Controlled	-0.205	0	-0.304	-0.107	1.019

[1] 95% CI

Table 14

Sulfonylurea Biguanide Reference Model Summary [b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.212[a]	0.045	0.041	0.88287

a. Predictors: (Constant), Sulfonylurea, Thiazolidinediones Mean PDC, Blindness, DPP Biguanide Mean PDC, Biguanide Mean PDC, Seeing Endocrinologist, Retinopathy Screening, DPP Mean PDC, BP Controlled, Myocardial Infarction, LIS, Thiazolidinediones, UTI, DPP Biguanide, Sulfonylurea Mean PDC, End-Stage Renal Disease, Male, Biguanide, Hospital Visits, Nephropathy Screening, Age, Deductible, DPP, DSNP, LIS

b. Dependent Variable: HbA1c continuous value

Table 15

Coefficients Sulfonylurea Biguanide Reference

	B	Sig	Lower Bound	Upper Bound	VIF
(Constant)	7.847	0	7.581	8.113	
Biguanide	-0.819	0	-0.991	-0.648	11.358
Biguanide Mean PDC	-0.055	0.491	-0.211	0.101	1.02
DPP	-0.763	0	-0.966	-0.559	3.31
DPP Mean PDC	0.17	0.541	-0.374	0.714	1.035
Thiazolidinediones	-0.911	0	-1.171	-0.65	1.719
Thiazolidinediones Mean PDC	-0.814	0.184	-2.013	0.386	1.003
Sulfonylurea	-0.546	0	-0.724	-0.368	8.88

Sulfonylurea Mean PDC	-0.271	0.111	-0.604	0.062	1.024
DPP Biguanide	-0.629	0	-0.862	-0.396	2.114
DPP Biguanide Mean PDC	-1.232	0.006	-2.115	-0.348	1.014
Male	0.088	0	0.042	0.135	1.059
Age	-0.004	0.001	-0.007	-0.002	1.11
DSNP	-0.275	0	-0.397	-0.153	7.033
LIS	-0.095	0.003	-0.158	-0.032	1.228
Deductible	0	0.003	0	0.001	6.629
Hospital Visits	-0.007	0.001	-0.012	-0.003	1.081
Seeing Endocrinologist	-0.072	0.198	-0.182	0.038	1.034
Retinopathy Screening	0.046	0.172	-0.02	0.113	1.079
Nephropathy Screening	0.007	0.765	-0.04	0.054	1.084
End Stage Renal Disease	-0.04	0.09	-0.087	0.006	1.121
Blindness	0.167	0.08	-0.02	0.353	1.004
Myocardial Infarction	-0.031	0.503	-0.123	0.06	1.032
UTI	-0.035	0.266	-0.097	0.027	1.054
BP Controlled	-0.205	0	-0.303	-0.106	1.019

Table 16

Model Summary [b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.212[a]	0.045	0.041	0.88287

a. Predictors: (Constant), Sulfonylurea Biguanide Mean PDC, DPP Biguanide Mean PDC, DPP Mean PDC, Sulfonylurea Mean PDC, Biguanide Mean PDC, BP Controlled, Myocardial Infarction, LIS, Thiazolidinediones, UTI, Seeing Endocrinologist, DSNP, LIS, DPP Biguanide, Age, Male, DPP, Sulfonylurea, Hospital Visits, Deductible, Sulfonylurea Biguanide, Biguanide, Mean PDC
b. Dependent Variable: HbA1c level

Table 17

Coefficients Thiazolidinediones as Reference [a]

	B	t	Sig	Lower Bound	Upper Bound	VIF

(Constant)	6.929	47.12	0	6.641	7.218	
DPP	0.154	1.326	0.185	-0.073	0.381	4.117
DPP Mean PDC	0.169	0.609	0.543	-0.375	0.713	1.035
DPP Biguanide	0.288	2.215	0.027	0.033	0.542	2.52
DPP Biguanide Mean PDC	-1.231	-2.73	0.006	-2.114	-0.347	1.014
Sulfonylurea Biguanide	1.021	7.184	0	0.742	1.299	2.668
Sulfonylurea Biguanide Mean PDC	-1.797	-2.067	0.039	-3.501	-0.093	1.343
Sulfonylurea	0.37	3.535	0	0.165	0.576	11.77
Sulfonylurea Mean PDC	-0.27	-1.592	0.111	-0.603	0.063	1.024
Biguanide	0.097	0.954	0.34	-0.102	0.297	15.41
Biguanide Mean PDC	-0.055	-0.691	0.49	-0.211	0.101	1.02
Male	0.089	3.775	0	0.043	0.135	1.059
Age	-0.004	-3.321	0.001	-0.007	-0.002	1.11
DSNP	-0.271	-4.354	0	-0.393	-0.149	7.042
LIS	-0.093	-2.911	0.004	-0.156	-0.031	1.229
Deductible	0	2.951	0.003	0	0.001	6.64
Hospital Visits	-0.008	-3.37	0.001	-0.012	-0.003	1.081
Seeing Endocrinologist	-0.07	-1.241	0.215	-0.179	0.04	1.034
Retinopathy Screening	0.044	1.303	0.193	-0.022	0.111	1.08
Nephropathy Screening	0.006	0.249	0.803	-0.041	0.053	1.085
End Stage Renal Disease	-0.04	-1.664	0.096	-0.086	0.007	1.121
Blindness	0.168	1.772	0.076	-0.018	0.355	1.004
Myocardial Infarction	-0.032	-0.686	0.493	-0.123	0.059	1.032
UTI	-0.035	-1.113	0.266	-0.097	0.027	1.054
BP Controlled	-0.206	-4.085	0	-0.305	-0.107	1.019

Table 18

Sulfonylurea Model Summary [b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.212[a]	0.045	0.041	0.88287

a. Predictors: (Constant), Sulfonylurea Biguanide Mean PDC, DPP Biguanide Mean PDC, DPP Mean PDC, Thiazolidinediones Mean PDC, Biguanide Mean PDC, BP Controlled, Myocardial Infarction, LIS, Thiazolidinediones, UTI, Seeing Endocrinologist, DSNP, LIS, DPP Biguanide, Age, Male, DPP, Hospital Visits, Deductible, Sulfonylurea Biguanide, Biguanide, Mean PDC
b. Dependent Variable: HbA1c level

Table 19

Coefficients Sulfonylurea as Reference [a]

	B	t	Sig	Lower Bound	Upper Bound	VIF
(Constant)	7.293	66.184	0	7.077	7.509	
DPP	-0.21	-3.298	0.001	-0.336	-0.085	1.25
DPP Mean PDC	0.169	0.608	0.543	-0.375	0.713	1.035
DPP Biguanide	-0.08	-0.875	0.381	-0.246	0.094	1.125
DPP Biguanide Mean PDC	-1.23	-2.732	0.006	-2.115	-0.348	1.014
Sulfonylurea Biguanide	0.658	6.323	0	0.454	0.862	1.43
Sulfonylurea Biguanide Mean PDC	-1.8	-2.069	0.039	-3.503	-0.094	1.343
Biguanide	-0.27	-8.446	0	-0.328	-0.204	1.478
Biguanide Mean PDC	-0.05	-0.682	0.495	-0.21	0.102	1.02
Thiazolidinedione	-0.36	-3.416	0.001	-0.563	-0.152	1.068
Thiazolidinedione Mean PDC	-0.82	-1.331	0.183	-2.014	0.385	1.003
Male	0.088	3.729	0	0.042	0.134	1.058
Age	-0	-3.329	0.001	-0.007	-0.002	1.11
DSNP	-0.27	-4.339	0	-0.392	-0.148	7.044
LIS	-0.09	-2.865	0.004	-0.155	-0.029	1.228
Deductible	0	2.949	0.003	0	0.001	6.64
Hospital Visits	-0.01	-3.293	0.001	-0.012	-0.003	1.079
Seeing Endocrinologist	-0.07	-1.244	0.213	-0.18	0.04	1.034
Retinopathy Screening	0.045	1.312	0.19	-0.022	0.111	1.08
Nephropathy Screening	0.005	0.217	0.828	-0.042	0.052	1.084
End Stage Renal Disease	-0.04	-1.656	0.098	-0.086	0.007	1.121

Blindness	0.167	1.757	0.079	-0.019	0.353	1.004
Myocardial Infarction	-0.03	-0.672	0.502	-0.123	0.06	1.032
UTI	-0.04	-1.11	0.267	-0.097	0.027	1.054
BP Controlled	-0.21	-4.091	0	-0.305	-0.107	1.019

Table 20

DPP Biguanide Model Summary [b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.212[a]	0.045	0.041	0.88287

a. Predictors: (Constant), Sulfonylurea Biguanide Mean PDC, Sulfonylurea Mean PDC, DPP Mean PDC, Thiazolidinediones Mean PDC, Biguanide Mean PDC, BP Controlled, Myocardial Infarction, LIS, Thiazolidinediones, UTI, Seeing Endocrinologist, DSNP, LIS, Sulfonylurea, Age, Male, DPP, Hospital Visits, Deductible, Sulfonylurea Biguanide, Biguanide, Mean PDC

b. Dependent Variable: HbA1c level

DPP Biguanide Model Summary [b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.212a	0.045	0.041	0.88287

a. Predictors: (Constant), Sulfonylurea Biguanide Mean PDC, Sulfonylurea Mean PDC, DPP Mean PDC, Thiazolidinediones Mean PDC, Biguanide Mean PDC, BP Controlled, Myocardial Infarction, LIS, Thiazolidinediones, UTI, Seeing Endocrinologist, DSNP, LIS, Sulfonylurea, Age, Male, DPP, Hospital Visits, Deductible, Sulfonylurea Biguanide, Biguanide, Mean PDC

b. Dependent Variable: HbA1c level

Table 21

Coefficients DPP Biguanide as Reference [a]

	Beta	t	Sig	Lower Bound	Upper Bound	VIF
(Constant)		55.155	0	6.99	7.505	
IsDPP2	-0.034	-1.578	0.115	-0.352	0.038	3.036
DPP Mean PDC	0.008	0.616	0.538	-0.373	0.715	1.035
Sulfonylurea Biguanide	0.102	5.502	0	0.457	0.962	2.195
Sulfonylurea Biguanide Mean PDC	-0.03	-2.067	0.039	-3.503	-0.093	1.343
Biguanide Mean PDC	-0.009	-0.685	0.493	-0.211	0.101	1.02
Biguanide	-0.103	-2.6	0.009	-0.376	-0.053	10.085
Thiazolidinediones	-0.038	-2.351	0.019	-0.559	-0.051	1.637
Thiazolidinediones Mean PDC	-0.017	-1.327	0.184	-2.012	0.388	1.003
Sulfonylurea	0.024	0.683	0.495	-0.111	0.229	8.021
Sulfonylurea Mean PDC	-0.02	-1.592	0.111	-0.604	0.063	1.024
Male	0.048	3.772	0	0.043	0.135	1.059
Age	-0.044	-3.342	0.001	-0.007	-0.002	1.11
DSNP	-0.146	-4.396	0	-0.396	-0.152	7.04
LIS	-0.041	-2.953	0.003	-0.158	-0.032	1.228
Deductible	0.095	2.954	0.003	0	0.001	6.641
Hospital Visits	-0.044	-3.374	0.001	-0.012	-0.003	1.081
Seeing Endocrinologist	-0.016	-1.256	0.209	-0.18	0.039	1.034
Retinopathy Screening	0.017	1.289	0.197	-0.023	0.11	1.08
Nephropathy Screening	0.003	0.205	0.837	-0.042	0.052	1.085
End Stage Renal Disease	-0.022	-1.689	0.091	-0.087	0.006	1.121
Blindness	0.022	1.771	0.077	-0.018	0.355	1.004
Myocardial Infarction	-0.009	-0.685	0.493	-0.123	0.059	1.032
UTI	-0.014	-1.104	0.269	-0.097	0.027	1.054
BP Controlled	-0.052	-4.138	0	-0.308	-0.11	1.019

Using these regression results to create equations for each medication class, one of the medication classes as a reference variable and left out of the analysis. Running the DPP to Biguanide regression to determine how well the equation predicted biguanide levels there were 1925 members from the test list on a biguanide medication used as our base group. Both sets of data showed normal distributions—however, significant differences in minimum and maximum values as seen in figures 4 and 5.

Figure 4

HbA1c Distribution

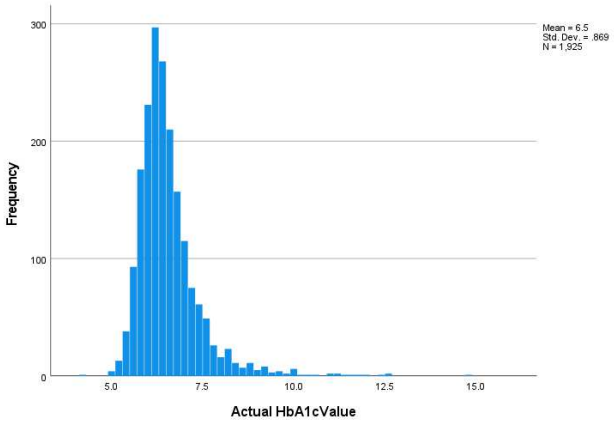
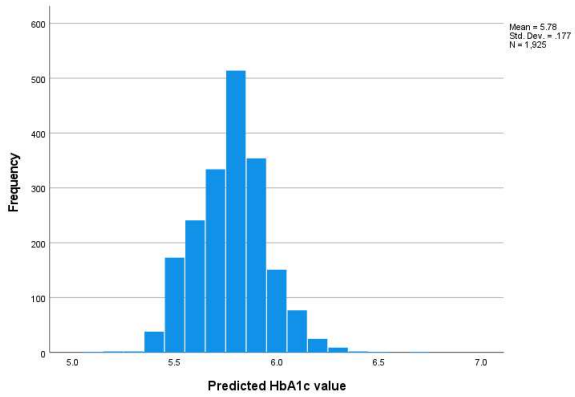


Figure 5

Predicted HbA1c distribution



There were statistically significant differences between the actual and predicted HbA1c levels, as demonstrated in Table 22. Kurtosis analysis shows that the predicted values have a different distribution of values at the distribution tails, and we see this in the predictive values. The ends of the distribution are much lower values than those in the actual data. Table 23 shows the SPSS interclass correlation function results with the two-way mixed model and absolute agreement selected. The two-way mixed model is appropriate for this analysis because there is a randomly selected sample, the values are fixed, and we selected absolute agreement because we want to see how well the regression can predict an HbA1c values. There is very little correlation between either single or average measure tests. Finally, there is no statistically significant correlations as the p-value for the average measurements was 0.088.

Table 22

HbA1c Actual vs. Predicated

		HbA1cValue	Predicted
N	Valid	1925	1925

Missing	0	0
Mean	6.502	5.776
Median	6.300	5.800
Std. Deviation	0.8686	0.1767
Skewness	2.587	0.167
Std. Error of Skewness	0.056	0.056
Kurtosis	12.480	0.551
Std. Error of Kurtosis	0.112	0.112
Minimum	4.2	5.1
Maximum	14.7	6.7

Table 23

Intraclass Correlation Coefficient

		95% Confidence Interval		F Test with True Value 0			
	Intraclass Correlation [b]	Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	.031[a]	-0.014	0.075	1.064	1924	1924	0.088
Average Measures	.060[c]	-0.028	0.140	1.064	1924	1924	0.088

Two-way mixed-effects model where people effects are random and measures effects are fixed.

a. The estimator is the same, whether the interaction effect is present or not.

b. Type C intraclass correlation coefficients using a consistency definition. The between-measure variance is excluded from the denominator variance.

c. This estimate is computed assuming the interaction effect is absent because it is not estimable otherwise.

Discussion

Data analysis answered both research questions in the affirmative, that in making medication change decisions for oral antihyperglycemics, considering both the new

medication and patient compliance rate is important. Research question one asks if there is a relationship between PDC calculated for individual antihyperglycemic class of medications and HbA1c values in Medicare MCO members with type 2 diabetes while controlling for age, sex, LIS enrollment, DSNP enrollment, and seeing an endocrinologist? Research question two asks if there is a relationship between PDC index calculated for individual, commercially available combination, antihyperglycemic class of medications and HbA1c values in Medicare MCO members with type 2 diabetes while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, and DSNP enrollment? Figure 6 is a simple slopes graph looking at the relationship between the reported HbA1c level and the mean adjusted PDC (the zero value is a PDC of 85%) for each of the medication classes with a sufficient sample population to analyze.

Figure 6

HbA1c Simple Slopes

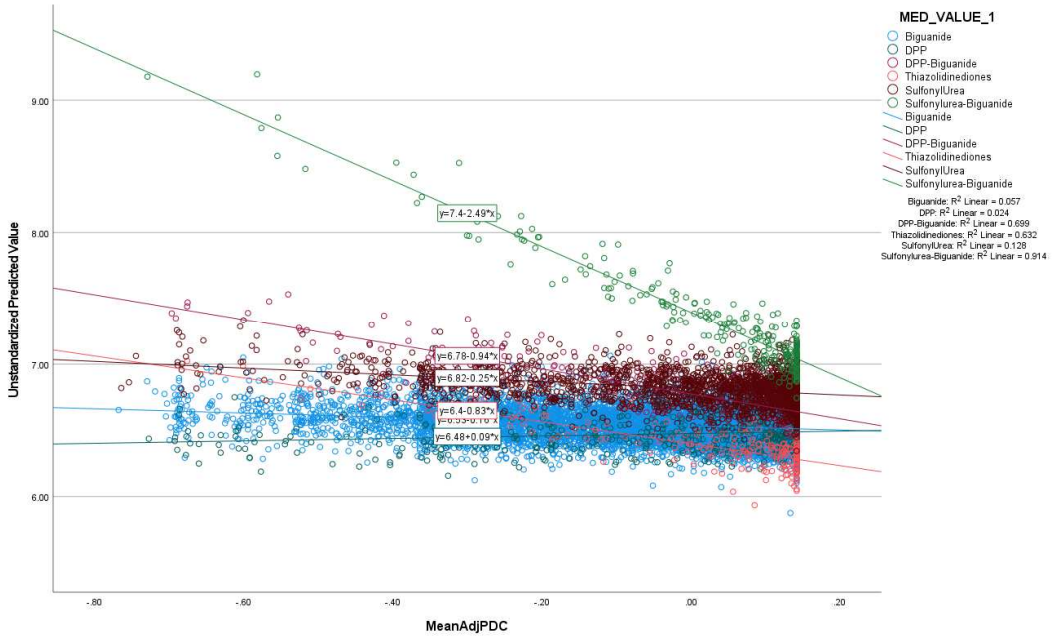


Table 24

Simple slope Equation and R^2

Medication Class	Equation	R^2 Value
Biguanide	y = 6.53 - 0.16*x	0.057
DPP	y = 6.48 – 0.09*x	0.024
DPP-Biguanide	y = 6.78 - 0.94*x	0.699
Thiazolidinediones	y = 6.4 - 0.83*x	0.632
Sulfonylurea	y = 6.82 - 0.25*x	0.128
Sulfonylurea-Biguanide	y = 7.4 - 2.49*x	0.914

X=mean centered PDC value

R^2 values are given as a percent, range from 0% to 100%, and indicate the degree of correlation between the predicted HbA1c value and the actual HbA1c value. Generally, the higher the value of R^2, the better the correlation between the PDC, medication class,

and the predicted HbA1c values. Low R^2 values, less than 0.25, indicate low effect size, less than 0.255 indicate medium effect size, and above 0.75 are related to a high effect size (Hair et al., 2011). Figure 6 demonstrates that at high levels of compliance, above 85%, there is not a significant difference in HbA1c values. However, as compliance rates drop, there is a difference in medication effectiveness on HbA1c levels. Three of the medication classes showed poor predictive value based on the data, Biguanide, DPP, and Sulfonylurea, all with R^2 values less than 0.25. Showing mean to high predictive value were DPP-Biguanide, Thiazolidinediones, and the Sulfonylurea Biguanide combinations. The Sulfonylurea Biguanide combination showed the highest R^2 value at 0.914.

An analysis of the regression equations showed that they did not fit well. The DPP to Biguanide and Thiazolidine to DPP Biguanide regressions were performed using the reliability analysis function of SPSS. Neither of the predicted values was close to the actual HbA1c values with p values = 0.088. One explanation for this failure to predict HbA1c levels accurately is due to the inability to correlate the HbA1c level and medication compliance.

Clinical Indications of this Study

This preliminary study examines the potential association between the PDC and medication class and its effect on HbA1c levels. The results support the hypothesis that a provider must consider medication compliance rates when selecting an oral antihyperglycemic medication. For example, figure 6 demonstrates that for patients who are non-compliant with their medications, the Sulfonylurea Biguanide combination may

not be the best therapeutic route considering the higher HbA1c levels at lower compliance rates compared to the other medications. The DPP class of medications shows consistent HbA1c control across all PDC values with a slope of only 0.09 (this means that for each unit increase in compliance, HbA1c drops by 0.09). Assuming no effect from medication side effects, the DPP class may be best for controlling HbA1c as it is not as affected by PDC as the other medication classes. However, these conclusions can only be used to show that a relationship exists between medication compliance, the class of medication taken, and medication compliance. A detailed study of this is needed because the precisely relationship between the HbA1c level was completed compared to when the medication was taken cannot be established.

While this study showed little statisticaly significance with low R^2 values, it does demonstrate clinically significant differences in the associations between OAMC, PDC and HbA1c levels. Schober et al., (2018), discusses differences in core temps post-surgery. The authors said:

> "Researchers need to define and to support what they consider a minimal clinically important effect, and journal editors, reviewers, and readers need to assess whether this seems reasonable. Note that an important effect does not necessarily have to be large. For example, a small effect on mortality can make a huge difference not only for individual patients but also for society if a large percentage of patients is affected by the condition."

Finally, in coversations with my my personal physician and Justin Zaghi, Medical Director for Heal and Board Certified Internist, about what they consider clinically significant changes in HbA1c. Both told me that a 0.5% decrease from

medication would be considered significant by them (J. Zaghi, S. Hartl, personal communication, January 2021).

Limitations of the Study

Several biases arise with this study. Because we only had data on Medicare Advantage individuals, the results are limited to people with type 2 diabetes and in a Medicare Advantage plan. Because we had a large group that did not have an HbA1c level completed, our results might be biased towards those who are overall more compliant, i.e., if they had an HbA1c level done then they could be more compliant towards their medication consumption. These results are of interest because both groups showed average medication compliance rates of over 80%. These findings are different from previously published studies indicating that people with diabetes are around 50% compliant with the medications (Wang et al., 2013). Second, we are not able to directly relate medication compliance with exact HbA1c draw dates. Therefore, we have to interpret the data with caution; however, what is shown by the data is that our hypothesis that providers must consider both the medication and compliance rate when making therapeutic decisions is valid. Finally, because we could not relate the HbA1c level to particular medications, we had to remove those who took more than one antihyperglycemic medication during the year. This data is preliminary, and our results should be considered with caution. Better controlled studies where HbA1c levels can definitively be associated with medication compliance are needed. Additionally, this

study only looks at those on single medication therapy. Many people with diabetes take multiple medications, and these should be examined.

References

American Diabetes Association. (2018). Standards of Medical Care in Diabetes. Retrieved August 11, 2018, from http://www.diabetes.org/newsroom/press-releases/2009/cpr-2010-a1c-diagnostic-tool.html

Belsley, D. A. (1984). Collinearity and forecasting. *Journal of Forecasting, 3*(2), 183-196.

Capoccia, K., Odegard, P. S., & Letassy, N. (2016). Medication adherence with diabetes medication: A systematic review of the literature. *The Diabetes Educator, 42*(1), 34-71.

Caruana, E. J., Roman, M., Hernández-Sánchez, J., & Solli, P. (2015). Longitudinal studies. *Journal of thoracic disease, 7*(11), E537-E540. https://doi.org/10.3978/j.issn.2072-1439.2015.10.63

Center for Disease Control. (2015). Calculating the Proportion of Days Covered (Pdc) for Antihypertensive Andantidiabetic Medications: An Evaluation Guide for Grantees. Retrieved May 12, 2019, from https://www.cdc.gov/dhdsp/docs/med-adherence-evaluation-tool.pdf

Center for Disease Control. (2019). 2019 Medicare-Medicaid Plan Performance Data Technical Notes. Retrieved August 12, 2019, from https://www.cms.gov/Medicare-Medicaid-Coordination/Medicare-and-Medicaid-Coordination/Medicare-Medicaid-Coordination-Office/FinancialAlignmentInitiative/Downloads/MMPPerformanceDataTechNotes.pdf

Cohen, J. (2013). *Statistical Power Analysis for the Behavioral Sciences*. Academic Press.

Creswell, J. W., & Creswell, J. D. (2017). *Research Design: Qualitative, Quantitative, and Mixed Methods Approaches*. Sage publications.

Cunningham, J. B., & McCrum-Gardner, E. (2007). Power, effect and sample size using Gpower: Practical issues for researchers and members of research ethics Committees. *Evidence-Based Midwifery, 5*(4), 132-137.

Cutler, R. L., Fernandez-Llimos, F., Frommer, M., Benrimoj, C., & Garcia-Cardenas, V. (2018). Economic impact of medication non-adherence by disease groups: A systematic review. *BMJ open, 8*(1). https://doi.org/10.1136/bmjopen-2017-016982

Foot, H., La Caze, A., Gujral, G., & Cottrell, N. (2016). The Necessity–concerns framework predicts adherence to medication in multiple illness conditions: A meta-analysis. *Patient Education and Counseling, 99*(5), 706-717.

Hair, J. F., Ringle, C. M., & Sarstedt, M. (2011, Spring2011). Pls-Sem: Indeed a Silver Bullet [Article]. *Journal of Marketing Theory & Practice, 19*(2), 139-152. https://doi.org/10.2753/MTP1069-6679190202

Hayes, A. F. (2009). *Statistical Methods for Communication Science*. Routledge.

Ho, C., Yeh, J., Wen, S., & Lee, T. J. (2017). Associations among medication regimen complexity, medical specialty, and medication possession ratio in newly diagnosed hypertensive patients: A population-based study. *Medicine, 96*(45), 8. https://doi.org/10.1097/MD.0000000000008497

Kennedy-Martin, T., Boye, K. S., & Peng, X. (2017). Cost of medication adherence and persistence in type 2 diabetes mellitus: A literature review. *Patient Preference and Adherence, 11*, 1103-1117. https://doi.org/10.2147/PPA.S136639

Martin, B. C., Wiley-Exley, E. K., Richards, S., Domino, M. E., Carey, T. S., & Sleath, B. L. (2009). Contrasting measures of adherence with simple drug use, medication switching, and therapeutic duplication. *Annals of Pharmacotherapy, 43*(1), 36-44.

Na, K., Yoo, C., Park, J. J., & Kim, Y. Y. (2018, 04/01/April 2018). Eye drop dispenser type and medication ospsession ratio in patients with glaucoma: Single-Use containers versus multiple-use bottles. *American Journal of Ophthalmology, 188*, 9-18. https://doi.org/10.1016/j.ajo.2018.01.011

National Committee for Quality Assurance. (2018a). Hedis® & Performance Measurement. Retrieved June 11, 2018, from https://www.ncqa.org/about-ncqa

Nau, D. P. (2012). Proportion of Days Covered (PDC) as a Preferred Method of Measuring Medication Adherence. Retrieved May 18, 2019, from http://www.pqaalliance.org/files/PDCvsMPRfinal.pdf

Nichols, G. A., Rosales, A. G., Kimes, T. M., Tunceli, K., Kurtyka, K., & Mavros, P. (2016). The Change in Hba1c associated with initial adherence and subsequent change in adherence among diabetes patients newly initiating metformin therapy. *Journal of Diabetes Research*, 1-5. https://doi.org/10.1155/2016/9687815

O'Brien, R. M. (2007). A caution regarding rules of thumb for variance inflation Factors. *Quality & Quantity, 41*(5), 673-690.

Osborne, J. W., & Waters, E. (2002). Four assumptions of multiple regression that researchers should always test. *Practical Assessment, Research, and Eevaluation, 8*(1), 2.

Peck, R., Olsen, C., & Devore, J. L. (2012). *Introduction to Statistics and Data Analysis*. Cengage Learning.

Picard, R. R., & Berk, K. N. (1990, 5/1/1990). Data splitting. *The American Statistician, 44*(2), 140-147. https://doi.org/10.1080/00031305.1990.10475704

Polonsky, W. H., & Henry, R. R. (2016a). Poor medication adherence in type 2 diabetes: Recognizing the scope of the problem and its key contributors. *Patient Preference and Adherence, 10*, 1299.

Ramos, M., Foos, V., Ferrufino, C., Yu-Isenberg, K., & Lamotte, M. (2018). The Relationship between poor adherence and Hba1c and weight changes in patients

with type 2 diabetes. *Values in Health, 21*, S138-S138. https://doi.org/10.1016/j.jval.2018.09.821

Schober, P., Bossers, S. M., & Schwarte, L. A. (2018). Statistical significance versus clinical importance of observed effect sizes: What do P values and confidence intervals really represent? *Anesthesia and Analgesia, 126*(3), 1068.

Wang, L., Wei, W., Miao, R., Xie, L., & Baser, O. (2013). Real-World outcomes of US employees with type 2 diabetes mellitus treated with Insulin Glargine or Neutral Protamine Hagedorn Insulin: A comparative retrospective database study. *BMJ Open, 3*(4), e002348.

Warner, R. M. (2013). *Applied Statistics from Bivariate Throught Multivariate Techniques* (2nd ed.). Sage Publications, Inc.

Weisberg, S. (2005). *Applied Linear Regression* (Vol. 528). John Wiley & Sons.

Dually Eligible and Low-Income Subsidy Participation, Medication Compliance and HbA1c Values in Medicare Type 2 Diabetics

Robert Lazarchik

Walden University

Outlet for Manuscript

This article will be submitted to the Journal Managed Care, a peer-reviewed journal, an independently published journal. This journal accepts manuscripts related to research relating to clinical, economic, and policy aspects of financing and delivering healthcare. This journal's audience is HMO/PPO/IHOs, hospitals, long-term care, Pharmacy Benefit Managers, VA/government, and employers.

The journal requires each author to submit the journal's copyright transfer agreement and requires disclosure of any financial, consultant, institutional, and other relationships that might lead to bias or a conflict of interest. Conflicts should be disclosed. If there are no conflicts, then the author should state so. Submissions are submitted to https://mc.manuscriptcentral.com/ajmc.

Original articles should be less than 3000 words using the AMA style with superscripted references, double spaced with 1-inch margins, and judicious use of graphic elements (i.e., tables and figures) is encouraged, and no more than 50 references. The authors' names should be submitted on a separate page to keep anonymity for peer reviewers. All authors must have had substantial contributions to the study and can have no more than ten authors. All authors must complete the Author's Disclosure form on this website, http://www.ajmc.com/authorshipforms. The title is limited to 10 words, abstract to 250 words, and submission should include takeaway points of less than 100 words. There should be a summary of the author's credentials, title, affiliation, city and

state, and current roles and accountabilities and must include an IRB approval. Citations should generally be less than five years old.

Abstract

Individual medication nonadherence costs for each type 2 diabetic are approximately $28,000 per year. Costs are the second most common reason for individual type 2 diabetic medication nonadherence, with one in four Americans having difficulty paying for their medications. As a result, Medicare instituted the Low-Income Subsidy (LIS) program and a Dually Eligible Special Need Program (DSNP) to improve medication compliance through reduced financial burden. The purpose of this study is to determine whether financial assistance programs improve medication compliance, as calculated by the Proportion of Days Covered (PDC), or HbA1c levels in people with type 2 diabetes. This is a longitudinal retrospective study utilizing secondary claims data from a large nationwide Managed Care Organization with a sample size of 23,000. Linear regression analysis identified the effects of Low-Income Subsidy (LIS) and Dually Eligible Special Needs Program (DSNP) programs combined with medication compliance on lowering HbA1c levels. While both LIS and DSNP programs have statistically significant effects on HbA1c levels and medication compliance, their overall effect is minimal, with R^2 values below 1%, indicating that their goal of improving health status has not been met. These findings indicate that a review of the LIS and DSNP program's goal of improving medication compliance should be further studied.

Introduction

Diabetes is the seventh leading cause of death in the US, affecting 34 million diagnosed people with diabetes and another 88 million with prediabetes (Centers for Disease Control and Prevention, 2020). Additionally, some individuals do not know that they have diabetes, and many physicians are unsure of what indicates prediabetes (National Institute of Diabetes and Digestive and Kidney Diseases, 2017; Tseng et al., 2017). One out of four dollars spent on healthcare in the US is spent on diabetes or any of the comorbidities associated with diabetes, including heart disease, stroke, nephropathies, and retinopathies (National Institute of Diabetes and Digestive and Kidney Diseases, 2018; Riddle & Herman, 2018).

Medication compliance in individuals with diabetes is an important part of their therapeutic regimen (Huang et al., 2018). One issue that faces those with diabetes is the cost of antihyperglycemic medications (Kang et al., 2018; Kennedy-Martin et al., 2017). Lower compliance rates in those with diabetes result in lower health statuses and increase morbidity and mortality. People with diabetes are notoriously non-compliant, and in their first year after diagnosis, almost half missed 80% of their doses (Cramer, 2004). Medication compliance is a complex issue requiring patients to purchase and take their medications on a prescribed dosing schedule.

Individuals with diabetes and lower socioeconomic statuses have higher medication non-compliance (Nam et al., 2011). One way to increase compliance is to reduce copays and deductibles for those with a financial need. Reducing copays by 36%

reduces the number of non-compliant patients by 30%, which can be offset by reducing medical costs such as hospitalizations (Zeng et al., 2010). Income and asset-based subsidy programs are a tool for improving medication compliance, reducing overall medical costs, and improving health statuses. There are two subsidy programs that Medicare implemented intending to improve medication compliance. Low-Income Subsidy (LIS) programs are for those in Medicare Part D programs and Dually Eligible Special Needs Programs are for those who qualify for both Medicare and Medicaid. Both programs are administered by Managed Care Organizations (MCO) and are not available with traditional Medicare.

The 2018 Medicare Modernization Act created the LIS program and covered 4.7 million enrollees. This program subsidized Part D for prescription costs, premiums, deductibles, and coinsurance (Centers for Medicare & Medicaid Services, n.d.). The program is part of the Medicare Extra Help initiative, where those participating must have a monthly income of less than $1650 for individuals and $2,175 for couples, and they must have limited assets. The LIS program is only available to those in a Medicare Advantage plan and is not available to traditional Medicare patients. The LIS program eliminates Part D's donut hole provision, a gap in coverage lying between initial coverage limits and the catastrophic-coverage threshold as determined by the MCO. The purpose of the LIS program is to reap the benefits of lower overall medical costs through improved medication compliance (Kirkman et al., 2015).

Both copays and deductibles add to health inequalities and lower medication adherence rates. While the LIS program attempted to address some of the issues around health inequalities, there are still problems. While the program subsidizes lower copays and premiums, deductibles may be higher, and there may be limited medication coverage depending on the MCO formulary.

The DSNP program is a set of special needs programs implemented by Congress in 2003 based on Medicaid enrollment, income, and asset levels, with the first DSNP program started in 2006. In 2013, the Affordable Care Act (ACA) modified DSNP programs to require that MCO's have a contract with State Medicaid plans to improve the integration of Medicare and Medicaid benefits. The ACA set up a list of eight elements state Medicaid programs must include to maintain DSNP participation eligibility (Archibald et al., 2019).

Medicare is considered the primary payor, and Medicaid is the secondary payor for DSNP programs. Additionally, services not covered by Medicare may be covered by Medicaid for DSNP enrollees. Individual states set the income and asset limits, but it is generally a requirement that the enrollee's income is below the poverty level, currently set between $12,760 and $44,120, depending on the number of individuals in the household (U.S. Department of Health and Human Services, 2020). Asset limitations also apply.

A 2018 Health and Human Services report documented the relationship between DSNP enrollment and Social Determinants of Health (SDOH) issues with income levels

being a part of the SDOH (Sorbero et al., 2018). DSNP programs set income requirements at or below the poverty level, and LIS programs are generally from the poverty level to 300% of the poverty level. Therefore, we have three sets of income levels, and we treat these as a categorical variable in this study. The categorical income variable comprises those not participating in an assistance program at the first level of income, LIS at the second with a value of 100% to 300% of the poverty level, and DSNP enrollees being at the third level of income, either at or below the poverty level. Having actual income levels would have been a better approach, but the MCO does not collect income data.

Research Design and Methods

According to Creswell and Creswell, 2017, a quantitative approach is used when a researcher tries to establish relationships between variables. The purpose of this study is to examine the relationship between enrollment in a financial assistance program and medication compliance in one of six classes of antihyperglycemic medications and HbA1c levels. Ideally, an individual with diabetes should have an HbA1c level below 6.5%, the threshold for a diagnosis of diabetes (American Diabetes Association, 2018). Covariates for this study include age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural counties. The research questions for this manuscript are:

RQ3: Is there a relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for one of the six classes of individual

antihyperglycemic medications on HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County?

$H_0$13: There is no statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Biguanide class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_1$13: There is a statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Biguanide class of medications, both individually and in combination, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_0$14: There is no statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications, both individually and in combination, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_1$14: There is a statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_0$15: There is no statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Thiazolidinedione class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_1$15: There is a statistically significant relationship the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Thiazolidinedione class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_0$16: There is no statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_1$16: There is a statistically significant relationship the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_0$17: There is no statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Sulfonylureas class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_1$17: There is a statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Sulfonylureas class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_0$18: There is no statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Meglitinide Analogues class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_1$18: There is a statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Meglitinide Analogues class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

RQ 4: Is there a relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for one of the six classes of combined antihyperglycemic medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County?

$H_0$19: There is no statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Meglitinide-Biguanide Combinations class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_1$19: There is a statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Meglitinide-Biguanide Combinations class of medications, both individually and in combination, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_0$20: There is no statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the SGLT2 Inhibitor - DPP-4 Inhibitor Combinations class of medications, both individually and in combination, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_1$20: There is a statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the SGLT2 Inhibitor - DPP-4 Inhibitor Combinations class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_0$21: There is no statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Sodium-Glucose Co-Transporter 2 Inhibitor-Biguanide class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_1$21: There is a statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Sodium-Glucose Co-Transporter 2 Inhibitor-Biguanide class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes

diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_0$22: There is no statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Sulfonylurea-Biguanide class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_1$22: There is a statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Sulfonylurea-Biguanide class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_0$23: There is no statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Dipeptidyl Peptidase-4 Inhibitor-Biguanide class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_1$23: There is a statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Dipeptidyl Peptidase-4 Inhibitor-Biguanide class of medications, and HbA1c

levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_0$24: There is no statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Sulfonylurea-Thiazolidinedione class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

$H_1$24: There is a statistically significant relationship between the type of subsidy plan enrollment (LIS or DSNP), PDC Medication Compliance rate for the Sulfonylurea-Thiazolidinedione class of medications, and HbA1c levels in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, and living in Urban or Rural County.

Longitudinal studies are done over time, with data collection done at different times during the study period, while retrospective studies look at past events. The sample was taken from 2019 claims data of those enrolled in a large nationwide MCO in this study with a size of 23,000 participants. Using G*Power, version 3.1.9.4, an effect size of 0.15, an alpha error probability of 0.05, a power of 0.95, the recommended sample size is 89. In a meta-analysis of medication compliance studies with different diseases, including diabetes, the authors found that studies with more than 85 participants had high statistical power. The authors also found that effect sizes in the studies reviewed was 0.17 to 0.18

with $p < 0.0001$. Based on this meta-study, a value of 0.15 was used (Foot et al., 2016). G* Power's effect size quantifies the differences between the test and control groups (Cunningham & McCrum-Gardner, 2007). We selected participants who have taken only one of the six classes of antihyperglycemic medications during 2019 and who have had an HbA1c level done during the year. We excluded individuals who may have taken more than one medication class because we cannot associate an HbA1c level draw times when multiple medications are taken.

The study population was selected from a large nationwide MCO claims database and include members of the MCO who are:

1. Over 21
2. Have type 2 diabetes
3. Enrolled in either a Medicare Advantage (MA) or Prescription Drug Plan (PDP) in 2019
4. Took only one of the six classes of antihyperglycemic medications or a combination of classes.

All the data provided by the MCO were deidentified before release to the researcher. Each member was assigned a unique serial number that is part of the released data. After analysis, if the MCO wants to do further studies, the research data can be mapped back to individual members with an assigned serial number.

Type 2 diabetes diagnoses were coded according to the ICD-10 World Health Organization International Statistical Classification of Diseases and Related Health using E11.8. Claim data will be chosen from pharmacy dispensing records, and the medication start date is the date of the first antihyperglycemic medication dispensing. The PDC measure excludes those on insulin, so these patients are not included.

Linear regressions were performed on each research question. We split our sample into a learning group consisting of 70% of our total sample and a testing group consisting of 30% of the total sample using a split-sample validation technique (Pang & Jung, 2013). The learning group, L1, is the sample we used to develop the model, and the test group, HO1, is the one we used to test the model. We analyzed the predicted HbA1c values with the actual HbA1c values using a Chi-Square test.

One potential interference with regression analysis is collinearity. In regressions, each predictor must identify a unique effect on the outcome variable. In this study, we address the issue of collinearity in two different ways. Using the SPSS linear regression analysis, an absolute value greater than 0.8 indicates collinearity between predictors.

In the SPSS regression we utilized the Collinearity diagnostics function to provide a Variance Inflation Factor (VIF). VIF is a measure of the degree of standard error inflation, where a VIF factor greater than 10 is indicative of collinearity (Weisberg, 2005, p. 217). For this study, the unit of analysis is the member.

Table 25 is a listing of the data variables and data types used in the analysis.

Table 25

Predictor Variables, their type, and possible values

Variable Name	Variable Type	Possible Values
Unique member identifier.	Nominal	Format TBD by MCO
Age	Continuous	21-100
Sex	Categorical	0=male,1=female
HBA1c level	Continuous	actual level
Deductible	Continuous	0 - 410
Medication Class	Ordinal	1-35
Medication PDC	Continuous	0-1
In DSNP Program	Nominal	0=no, 1=yes

In LIS program	Nominal	0=no, 1=yes
Plan type	Categorical	1=PDP, 2=MA + PDP
Had Myocardial Infraction	Nominal	0=no, 1=yes.
Is Blind	Nominal	0=no, 1=yes.
Has End-Stage Renal Disease	Nominal	0=no, 1=yes.
Has Urinary Tract infections	Nominal	0=no, 1=yes.
Income Indicator	Categorical	0=DSNP, 1=LIS, 3=Neither

The predictive model equation will be determined by picking the predictors with a p-value is < 0.05. The equations for each of the research questions will be created by using the fundamental equation for a straight line, y = mx + b, where y is the HbA1c value, b is the y-axis intercept, and m is the coefficient for a statistically significant predictor variable. The final equation will take the final form of y = b + coeff1*predictor1 value + coeff2*predictor2 value + coeff3*predictor3 value + coeffN*predictorN value. The direction and strength of a linear relationship between two variables can be determined by Pearson's correlation (Warner, 2013). Values greater than 0.5 show significant levels of correlation between the variables. Values approaching 0.3 have small correlations but still significant enough to consider in the final equation. Any predictor variable used must have a p-value of less than 0.05. Pearson's correlations can give us some insight into the R^2 value produced by regression analysis because it gives us a feeling for the strength of effect (Hair et al., 2011). Pearson's correlation values are obtained by selecting a correlation from the SPSS interface and adding in all of the variables in the analysis.

R^2 is a statistical value created by a regression analysis indicating how well the predictor variables match the regression line (Warner, 2013). The models' R^2 value

indicates the quality of the fit of the data to the line created by the regression. In human research, an R^2 value greater than 0.2 is considered adequate. This value is somewhat lower than in other kinds of research, but because human behavior is included in the analysis, this lower number is acceptable (Hair et al., 2011). Plots of the data are necessary to determine bias in the data. If the data is evenly dispersed around the regression line, then linear regression is appropriate. If the data is not evenly dispersed, then a non-linear approach is better (Warner, 2013).

Results

The purpose of this quantitative research was to determine the effect of Medicare DSNP or LIS programs on medication compliance or HbA1c levels in people with type 2 diabetes while controlling for covariates such as age, sex, comorbidities, hospital visits, and if they are seeing an endocrinologist. On September 29, 2020, a large, nationwide MCO provided, and corporate compliance approved the use of their data. Approval for this study was received from the Walden University IRB, number 10-30-20-0721525, on October 30, 2020. Two MCO Business Analysts produced de-identified, secondary claims data.

Sample Selection

Our analysis included a total population of 15,713. Of that population, 4995 are in a DSNP program, and 3434 are in a LIS program. The study group included members over 21, have only taken 1 of the oral antihyperglycemic medication classes in 2019, and have had an HbA1c level taken during the calendar year. In reviewing the data, we found

an issue in the MCO data on how LIS and DSNP program participation was determined. When members went from a LIS program to a DSNP program, the system did not remove them from the LIS program, so our data showed them in both programs. To correct this, we created a new adjusted LIS variable where members who were in both programs were shown as in the DSNP program only.

A mean centering technique was used to better understand the PDC values (Hayes, 2009, pp. 466-467). A mean adjusted PDC was created by taking the individual PDC value and subtracting the overall mean PDC of 0.8583. A not in a subsidy program dummy variable was used as the reference variable for the in a LIS, DSNP, or no financial aid predictor.

Because of insufficient members taking the Meglitinide Analogues, SGLT2 inhibitors, Meglitinide-Biguanide Combinations, SGLT2 Inhibitor - DPP-4 Inhibitor Combinations, Sulfonylurea-Thiazolidinedione Combinations, Thiazolidinedione-Biguanide Combinations, and DPP-4 Inhibitor-Thiazolidinedione Combinations, we eliminated these medication classes from our data. Table 26 is a count of the members taking each of the classes used in the study.

Table 26

Count for each of the Classes and Combination of Classes

Medication Class	Count
Biguanides	11743
Dipeptidyl Peptidase-4 (DPP-4) Inhibitors	615
Thiazolidinediones	208
Sulfonylureas	2559
Sulfonylurea-Biguanide Combinations	248

Two multiple regressions were run on the data. The first one looked at the effect of being in a LIS or DSNP program on HbA1c levels. The second one looked at the effect of being in either program on the interaction between PDC and medication class. Our first two regressions indicated that LIS and DSNP programs have a statistically significant effect on HbA1c levels and PDC. However, the R^2 values were minimal and insignificant, 0.3% for HbA1c levels and 0.5% for overall PDC. Our final regression analysis for each medication class's mean adjusted PDC values again showed statistical significance but insignificant R^2 values. Tables 27 and 28 are the HbA1c regression analysis results, and Table 29 is the individual mean adjusted PDC regressions R^2 values and regression results. We did not include any of the covariates in our analysis because of the low R^2 values we found when running regressions on the programs alone. Only the DPP Biguanide medication class showed an R^2 value of any significance at 5%. Additional covariates would only give us the covariates' effect and not by HbA1c or PDC, our predictors of concern. No collinearity was present with a VIF value of 1.150 for all of the regressions performed.

Table 27

HbA1c Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate

1	.055[a]	0.003	0.003	0.99438

a. Predictors: (Constant), Adj LIS, DSNP_INDICATOR

Table 28

HbA1c Analysis Coefficients [a]

	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
Model	B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound
Constant	6.650	0.010		682.504	0.000	6.631	6.670
DSNP	-0.126	0.015	-0.059	-8.313	0.000	-0.156	-0.097
LIS	-0.050	0.017	-0.021	-2.916	0.004	-0.084	-0.016

a. Dependent Variable: HbA1c level

Table 29

Regression Analysis for Each of the Medication Classes PDC Values.

				95.0% Confidence Interval for B		
Medication class	Adjusted R2 value	Unstandardized B	Sig	Lower	Upper	VIF
Biguanides	0.008					
DSNP		-0.030	0.000	-0.036	-0.024	1.150
LIS		-0.033	0.000	-0.040	-0.026	1.150
DPP	0.071					
DSNP		0.148	0.000	0.112	0.184	1.150
LIS		0.124	0.000	0.084	0.163	1.150
Thiazolidinediones	0.001					
DSNP		-0.14	0.564	-0.06	0.033	1.150
LIS		0.009	0.722	-0.58	0.04	1.150

Sulfonylureas	0.007					
DSNP		-0.033	0.000	-0.047	-0.200	1.150
LIS		-0.023	0.002	-0.038	-0.009	1.150
Sulfonylurea-Biguanide	0.001					
DSNP		-0.028	0.165	-0.069	0.012	1.150
LIS		-0.024	0.261	-0.066	0.018	1.150
DPP Biguanide	0.050					
DSNP		0.107	0.000	0.065	0.149	1.150
LIS		0.105	0.000	0.055	0.154	1.150

Discussion

Our analysis indicates that while the DSNP and LIS financial subsidy programs have statistically significant effects on HbA1c and medication compliance measured by the PDC, they have a minimal overall effect on these measures with R^2 values below 1%. Our analysis demonstrates that both research questions' null hypothesis can be accepted and that there is no significant relationship between these subsidy programs and either PDC or HbA1c levels. Our results are the same as those of a 2012 study in that we found little difference in medication compliance based on MPR, whether an individual was in a LIS subsidy program or not, and even where there were differences, those differences were of little clinical significance (Stuart et al., 2012).

CMS implemented these plans to help participants by reducing their financial burden from deductibles and copays, particularly the LIS program which is designed solely for this purpose. The DSNP program covers more than just medication costs. Our primary findings indicate that participation in either a LIS or DSNP program does not significantly affect either medication compliance, measured by the PDC, or HbA1c

levels. However, caution should be used in interpreting these results. Because of our large sample size, one would expect to see statistical significance in the predictors. However, there is little clinical significance in these programs, as demonstrated by the minimal R^2 values.

Limitations of the Study

The results of this analysis of financial subsidy programs can only be applied to people with diabetes and not to other chronic conditions. Additionally, there are difficulties in relating PDC values to someone actually consuming a medication as directed. In this study we have to assumed that purchased medications are equal to consumed medications. Smaller sample size research that closely monitors HbA1c levels and PDC are needed to examine the effects of these subsidy programs on other morbidities. It was beyond the scope of this study to examine whether increased subsidies would positively impact compliance and reduce HbA1c levels, and further research is needed to clarify these issues. Finally, because we examined only members who took one of the medication classes, there may be positive effects for those taking more than one class of these medications.

References

American Diabetes Association. (2018). Standards of Medical Care in Diabetes. Retrieved August 11, 2018, from http://www.diabetes.org/newsroom/press-releases/2009/cpr-2010-a1c-diagnostic-tool.html

Archibald, N., Soper, M., Smith, L., Kruse, A., & Wiener, J. (2019). Integrating care through Dual Eligible Special Needs Plans (D-SNPS): Opportunities and challenges. Retrieved June 13, 2020, from https://aspe.hhs.gov/basic-report/integrating-care-through-dual-eligible-special-needs-plans-d-snps-opportunities-and-challenges#overview

Centers for Disease Control and Prevention. (2020). National Diabetes Statistics Report 2020 Estimates of Diabetes and Its Burden in the United States. Retrieved September 26, 2020, from https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf

Centers for Medicare & Medicaid Services. (n.d.). Lower Prescription Costs. Retrieved April 12, 2020, from https://www.medicare.gov/your-medicare-costs/get-help-paying-costs/lower-prescription-costs

Cramer, J. A. (2004). A systematic review of adherence with medications for diabetes. *Diabetes Care, 27*(5), 1218-1224.

Cunningham, J. B., & McCrum-Gardner, E. (2007). Power, effect and sample size using Gpower: Practical issues for researchers and members of research ethics committees. *Evidence-Based Midwifery, 5*(4), 132-137.

Foot, H., La Caze, A., Gujral, G., & Cottrell, N. (2016). The necessity–concerns framework predicts adherence to medication in multiple illness conditions: A meta-analysis. *Patient Education and Counseling, 99*(5), 706-717.

Hair, J. F., Ringle, C. M., & Sarstedt, M. (2011, Spring2011). Pls-Sem: Indeed a silver bullet. *Journal of Marketing Theory & Practice, 19*(2), 139-152. https://doi.org/10.2753/MTP1069-6679190202

Hayes, A. F. (2009). *Statistical Methods for Communication Science*. Routledge.

Huang, Y., Shiyanbola, O. O., & Smith, P. D. (2018). Association of health literacy and medication self-efficacy with medication adherence and diabetes control. *Patient Preference and Adherence, 12*, 793.

Kang, H., Lobo, J. M., Kim, S. H., & Sohn, M. (2018). Cost-Related medication non-adherence among US adults with diabetes. *Diabetes Research and Clinical Practice, 143*, 24-33. https://doi.org/10.1016/j.diabres.2018.06.016

Kennedy-Martin, T., Boye, K. S., & Peng, X. (2017). Cost of medication adherence and persistence in type 2 diabetes mellitus: A literature review. *Patient Preference and Adherence, 11*, 1103-1117. https://doi.org/10.2147/PPA.S136639

Kirkman, M. S., Rowan-Martin, M. T., Levin, R., Fonseca, V. A., Schmittdiel, J. A., Herman, W. H., & Aubert, R. E. (2015, 01/08 09/03/received 12/08/accepted). Determinants of adherence to diabetes medications: Findings from a large pharmacy claims database. *Diabetes Care, 38*(4), 604-609. https://doi.org/10.2337/dc14-2098

Nam, S., Chesla, C., Stotts, N. A., Kroon, L., & Janson, S. L. (2011). Barriers to diabetes management: Patient and provider factors. *Diabetes Research and Clinical Practice, 93*(1), 1-9.

National Institute of Diabetes and Digestive and Kidney Diseases. (2017). Diabetes Statistics. Retrieved https://www.niddk.nih.gov/health-information/health-statistics/diabetes-statistics

National Institute of Diabetes and Digestive and Kidney Diseases. (2018). Diabetes Complications Retrieved September 8, 2018, from https://medlineplus.gov/diabetescomplications.html

Pang, H., & Jung, S. (2013). Sample size considerations of prediction-validation methods in high-dimensional data for survival outcomes. *Genetic Epidemiology, 37*(3), 276-282. https://doi.org/10.1002/gepi.21721

Riddle, M. C., & Herman, W. H. (2018). The cost of diabetes care—an elephant in the room. *Diabetes Care, 41*(5), 929-932.

Sorbero, M. E., Kranz, A. M., Bouskill, K. E., Ross, R., Palimaru, A. I., & Meye A. (2018). *Addressing Social Determinants of Health Needs of Dually Enrolled Beneficiaries in Medicare Advantage Plan*. https://aspe.hhs.gov/system/files/pdf/259896/MAStudy_Phase2_RR2634-final.pdf

Stuart, B., Yin, X., Davidoff, A., Simoni-Wastila, L., Zuckerman, I., Shoemaker, J. S., & Doshi, J. (2012). Impact of Part D low-income subsidies on medication patterns for medicare beneficiaries with diabetes. *Medical Care, 50*(11), 913-919.

Tseng, E., Greer, R. C., O'Rourke, P., Yeh, H., McGuire, M. M., Clark, J. M., & Maruthur, N. M. (2017, 2017/11/01). Survey of primary care providers' knowledge of screening for, diagnosing and managing prediabetes. *Journal of General Internal Medicine, 32*(11), 1172-1178. https://doi.org/10.1007/s11606-017-4103-1

U.S. Department of Health and Human Services. (2020). Poverty Guidelines. Retrieved May 3, 2020, from https://aspe.hhs.gov/poverty-guidelines

Warner, R. M. (2013). *Applied Statistics from Bivariate Throught Multivariate Techniques* (2nd ed.). Sage Publications, Inc.

Weisberg, S. (2005). *Applied Linear Regression* (Vol. 528). John Wiley & Sons.

Zeng, F., An, J., Scully, R., Barrington, C., Patel, B. V., & Nichol, M. B. (2010). The impact of value□based benefit design on adherence to diabetes medications: A propensity score□weighted difference in difference evaluation. *Value in Health, 13*(6), 846-852.

Medication Compliance, Oral Antihyperglycemic Medications, and HbA1c in Predicting Comorbidities in Medicare Type 2 Diabetics

Robert Lazarchik

Walden University

Outlet for Manuscript

This article will be submitted to the journal Diabetes Care, a peer-reviewed journal dedicated to diabetes and diabetes research. The size limit is 5000 words or 20 double spaced pages. The journal requires discussion of hypothesis testing, proper controls, correct statistical analysis, clear conclusions, and discussion supported by results. Submissions are judged on uniqueness and importance. Titles must be less than 40 words, and the abstract is limited to 250 words and contain no references. The journal provides an Endnote library format for their citation requirements, and there is a charge of $50 per page.

The article must name a 'guarantor' of the data used in the study; the data must be available to other researchers following guidelines from *Nature Research's* Policy (go.nature.com/2bf4vqn). Data access must be defined in a section called "Data and Resource Availability" under the Research Design and Methods section. There is a formal manuscript submission form attached in the Appendix. The journal accepts the ICMJE's "**Uniform Disclosure Form for Potential Conflicts of Interest"** attached in the Appendix.

Manuscripts must use the following layout.

- title page
- abstract
- introduction (no heading necessary)
- Research Design and Methods
- Results
- Discussion

- Acknowledgments (including Author Contributions, Guarantor Statement, Conflict of Interest statement, funding, and Prior Presentation information),
- References
- tables (each including a title and legend)
- figure legends

This manuscript has been adjusted from the supplied template to this format. The URL for other details is at https://diabetes.diabetesjournals.org/content/instructions-for-authors

Abstract

Cardiovascular disease is the number one killer of Americans, and one-third of blindness worldwide is related to diabetes. However, less than one-third of people with diabetes are compliant with their antibiotic therapy treating a UTI, and diabetes is the most common cause of end-stage renal disease in the US. Medication is a primary therapeutic modality in the treatment of diabetes that reduces the incidence of these comorbidities, yet compliance rates are as low as 50%. The Proportion of Days Covered (PDC) is the accepted method for determining medication compliance. The purpose of this study is to determine the associations between antihyperglycemic medication class PDC rates and HbA1c levels and four of the diabetes comorbidities, vision impairment, renal disease, myocardial infarction, and urinary tract infections. A sample of 22,000 adults over 21 years of age, who took only one of six oral antihyperglycemic medication classes, had an HbA1c reported during the year, and diagnosed with type 2 diabetes were selected from the 2019 claims database of a large MCO. There are statistically significant relationships between HbA1c, compliance, and comorbidities but, the highest strength of effect found was 0.5%. It may indicate a need to look at different predictors such as those related to the Social Determinants of Health, none of which were included. These results are similar to other studies using different methods of measuring medication compliance.

Introduction

Thirty-four million Americans are diagnosed with diabetes, and another 88 million have pre-diabetes. Many pre-diabetic individuals do not know they have the disease (Centers for Disease Control and Prevention, 2020; National Institute of Diabetes and Digestive and Kidney Diseases, 2017). The Center for Disease Control (CDC) has undertaken programs to address the issue of prediabetes diagnosis by Primary Care Providers (PCP) (Li et al., 2013). In 2017, Tseng et al. found that only six percent of PCP's recognized all the risk factors that should initiate a prediabetes screening, and only 17% correctly identified the laboratory parameters for diagnosing prediabetes. Twenty percent of all U.S. healthcare costs can be related to the treatment of diabetes and its complications, and diabetes is the seventh leading cause of death in the US (National Center for Chronic Disease Prevention, 2016).

Effective management of people with type 2 diabetes includes supporting efforts that improve medication compliance. The comorbidities of diabetes result from micro and macrovascular changes leading to reduced health statuses. Macrovascular complications include congestive heart failure, myocardial infarction, stroke, and coronary artery disease. Microvascular complications include neuropathy, retinopathy, and nephropathy. One person dies every 37 seconds from cardiovascular disease which is the leading killer in the United States. (Heron, 2017). Hyperglycemia induces the formation of glycated end products, the production of oxygenated free radicals, and increased rates of glomerular filtration, all leading to comorbidities of diabetes (Vlassara, 1992). Long-term

comorbidity risks in people with diabetes increase as HbA1c levels increase, so consistent control of HbA1c levels is imperative for comorbidity control (Luo et al., 2017).

Diabetic retinopathy is the most common microvascular complication of diabetes (Antonetti et al., 2012). Across the world, one-third of people with diabetes are affected by retinopathy, a leading cause of vision loss in 20 to 74-year-olds. Risk factors for retinopathy include duration of diabetes, HbA1c levels, and blood pressure control (Solomon et al., 2017; Yau et al., 2012). Progression of retinopathies at four to six years post-diagnosis range from 24.1% to 38.9% and increase to 64.1% and 83.1 % in 16-year and 25-year follow-ups (Lee et al., 2015).

Diabetes is the most common cause of end-stage renal disease (ESRD) in the US. Due to the increased longevity in people with diabetes, comorbidity rates are increasing, and those diagnosed with ESRD are accepted in treatment centers where they have not been in the past (Molitch et al., 2004). Twenty to forty percent of all people with diabetes develop some nephropathy, yet it rarely develops in people with type 1 diabetes within the first ten years of diagnosis (Gall et al., 1991). Annual albuminuria screenings are recommended for all people with diabetes.

The risk of Urinary Tract Infections increases with age, poor HbA1 control, immune system compromise, and poor bladder emptying due to neuropathies. Those who have diabetes have a higher incidence of UTI's and the infections they get are more severe than those who do not have diabetes (de Lastours & Foxman, 2014). In some

cases, UTIs can lead to death due to pyelonephritis (Saleem & Daniel, 2011). UTI's have been traced to the neuropathies associated with diabetes (Brown et al., 2005). Less than 35% of those with diabetes and a UTI are compliant with their antibiotic therapies and UTIs can increase total health care costs by 53% (Davis-Ajami et al., 2019).

Medication compliance in those with diabetes is an essential part of their therapy. However, in those diagnosed with diabetes, compliance rates fall around 50% (Wang et al., 2013). Forty-five percent of diabetics fail to achieve adequate HbA1c or blood sugar control (Polonsky & Henry, 2016)**.** Medication compliance is the best way to reduce the risks of diabetes complications (Nichols et al., 2016). Because of the multiple complications of diabetes, polypharmacy is common and presents additional problems for providers. The incidence of noncompliance related to medication cost is 16% and is the second most common reason for non-compliance in people with diabetes. The Social Determinants of Health, medication packaging, poor communication skills, low health literacy levels, a lack of trust in providers, and belief that the medications they are prescribed do not help their diabetes all contribute to poor HbA1c and glucose level control (Gilmartin-Thomas et al., 2017; Pruitt et al., 2018; Shiyanbola et al., 2018).

The currently accepted method of calculating medication compliance is using the Proportion of Days Covered (PDC). The CDC adopted the PDC as the recommended medication compliance methodology for researchers in 2015 with the PDC supported by the Pharmacy Quality Alliance and CMS and is the leading method for determining medication adherence in large populations (Center for Disease Control, 2015). The

NCQA has accepted the PDC method of measuring medication compliance in their HEDIS measures. Medications used in treating type 2 diabetes are separated into nine classes based on their mechanism of action (Feingold, 2019). Only six of these classes, both as individual classes and commercially available combinations of classes are analyzed in this study To date, there is little in the literature studying the relationship between classes of antihyperglycemic medications, HbA1c levels, and comorbidities. One purpose of this study is to examine relationships between various classes of antihyperglycemic medications, compliance with these medications, and the comorbidities of diabetes.

Research Design and Methods

When a researcher wants to establish the relationships between variables, a quantitative approach is appropriate (Creswell & Creswell, 2017). The purpose of this study is to examine the relationships between antihyperglycemic medications, HbA1c levels, the PDC and the comorbidities of diabetes, Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections and a set of covariates including age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County as defined by the Census Bureau. The research questions for this manuscript are:

RQ5: Is there a relationship between the PDC calculated for individual antihyperglycemic class of medications and HbA1c values on the top four type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary

Tract infections, both individually and in combination, in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County as defined by the Census Bureau.

$H_0$25: There is no statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$25: There is a statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$26: There is no statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in

MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$26: There is a statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$27: There is no statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$27: There is a statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$28: There is no statistically significant relationship between the PDC index calculated for the Sulfonylureas class of medications and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections and HbA1c values while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$28: There is a statistically significant relationship between the PDC index calculated for the Sulfonylureas class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$29: There is no statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$29: There is a statistically significant relationship between the PDC index calculated for the individual Meglitinide Analogues class of medications and HbA1c values and the top Medicare four type 2 diabetes comorbidities of

Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$30: There is no statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$30: There is a statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the top four Medicare type 2 diabetes comorbidities of Myocardial Infarction, Blindness, End-Stage Renal Disease, and Urinary Tract infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$31: There is no statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Myocardial Infarction and HbA1c while

controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$31: There is a statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Myocardial Infarction while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$32: There is no statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Myocardial Infarction while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$32: There is a statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Myocardial Infarction while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$33: There is no statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and

the Medicare type 2 diabetes comorbidity of Myocardial Infarction while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$33: There is a statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Myocardial Infarction while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$34: There is no statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and HbA1c values and the comorbidity of Myocardial Infarction in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$34: There is a statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and the comorbidity of Myocardial Infarction and HbA1c values in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$35: There is no statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the comorbidity of Myocardial Infarction in Medicare type 2 diabetics while

controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$35: There is a statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the comorbidity of Myocardial Infarction in type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$36: There is no statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the comorbidity of Myocardial Infarction in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$36: There is a statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the comorbidity of Myocardial Infarction in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$37: There is no statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the

Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$37: There is a statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$38: There is no statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$38: There is a statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$39: There is no statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$39: There is a statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$40: There is no statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$40: There is a statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$41: There is no statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Blindness while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$41: There is a statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the comorbidity of Blindness in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$42: There is no statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the comorbidity of Blindness in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$42: There is a statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the comorbidity of Blindness in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of

time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$43: There is no statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$43: There is a statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$44: There is no statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$44: There is a statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage

Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$45: There is no statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$45: There is a statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$46: There is no statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$46: There is a statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while

controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$47: There is no statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of End-Stage Renal Disease while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$47: There is a statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the comorbidity of End-Stage Renal Disease in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$48: There is no statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the comorbidity of End-Stage Renal Disease in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$48: There is a statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of

medications and HbA1c values and the comorbidity of End-Stage Renal Disease in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$49: There is no statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$49: There is a statistically significant relationship between the PDC index calculated for the Biguanides class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$50: There is no statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$50: There is a statistically significant relationship between the PDC index calculated for the Dipeptidyl Peptidase-4 (DPP-4) Inhibitors class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$51: There is no statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$51: There is a statistically significant relationship between the PDC index calculated for the Thiazolidinedione class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$52: There is no statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$52: There is a statistically significant relationship between the PDC index calculated for the Sulfonylurea class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$53: There is no statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the Medicare type 2 diabetes comorbidity of Urinary Tract Infections while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$53: There is a statistically significant relationship between the PDC index calculated for the Meglitinide Analogues class of medications and HbA1c values and the comorbidity of Urinary Tract Infections in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_0$54: There is no statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the comorbidity of Urinary Tract Infections in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time,

length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

$H_1$54: There is a statistically significant relationship between the PDC index calculated for the Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors class of medications and HbA1c values and the comorbidity of Urinary Tract Infections in Medicare type 2 diabetics while controlling for age, sex, diabetes diagnosis time, length of time in MCO, Plan type, LIS enrollment, DSNP enrollment, and living in Urban or Rural County.

This is a quantitative longitudinal retrospective study using 2019 secondary claims data from a large nationwide MCO. According to Creswell (2017), a longitudinal study is appropriate when a researcher is looking for relationships between predictor and outcome variables. This longitudinal retrospective study examines the relationships between the comorbidities of diabetes, medication compliance with antihyperglycemic medications, and HbA1c levels as predictors, along with multiple covariates. The study population is approximately 23,000 are over 21, currently diagnosed with type 2 diabetes, enrolled in either a Medicare Advantage (MA) plan during the 2019 calendar year, had an HbA1c level done during 2019, and took only one of the six classes of antihyperglycemic medications or a combination of classes.

All the data provided by the MCO were deidentified before release to the researcher. Each member is assigned a unique serial number that was included with the released data. After analysis, if the MCO wants to do further studies, the research data

can be mapped back to individual members using the serial number assigned. Using G*Power, version 3.1.9.4, an effect size of 0.15, an alpha error probability of 0.05, a power of 0.95, the recommended sample size is 89. In a meta-analysis of medication compliance studies with different diseases, the authors found that studies with more than 85 participants had high statistical power. The authors also found that effect sizes in the studies reviewed was 0.17 to 0.18 with $P < 0.0001$. Based on this meta-study, we chose a value of 0.15 (Foot et al., 2016). G* Power's effect size is a method to quantify the differences between the test and control groups and is based on Cohen's effect size or the explained variance and error variance (Cunningham & McCrum-Gardner, 2007). With 23,000 participants, this study has more than sufficient participants to achieve statistical power. The entire sample population will be used for each research question. We excluded individuals who may have taken more than one medication class because we cannot associate an HbA1c level with multiple medications.

The ICD-10 World Health Organization International Statistical Classification of Diseases and Related Health Problems is used to determine a diagnosis of diabetes. We will use the ICD-10 code of E11.9 for this data pull. Pharmacy records were pulled from claims data, and demographic data came from other in-house databases. The medication start date will be the date of the first dispensing of an antihyperglycemic medication. Members are split between a learning group, L1, and a holdout group, HO1, which is those in the plan during 2019 following a data-splitting technique (Picard & Berk, 1990).

Income and asset levels are implied from participation in either a Low-Income Subsidy (LIS) or a Dually Eligible Special Needs Program (DSNP) program. The eligibility requirements for DSNP plans are that income levels be less than the poverty level. For enrollment in a LIS program, income levels must be between the poverty level and 300% of the poverty level. We created a categorical variable with three items indicating the three different income levels of our participants. The third level is those not in one of these programs with an income above 300% of the poverty level.

Analysis of the data was conducted using SPSS version 27 with a standard p-value of < 0.05 to indicate statistical significance. Logistic regression analysis was used to determine the effect each of the predictors on the outcome variable, and we can us statistical significance to determine which of the variables are predictive of an outcome (Warner, 2013). Logistic regressions are used to explain relationships between a binary outcome variable, in this case, comorbidities of diabetes, and ordinal, nominal, or ratio predictor variables (Wagner, 2016). For logistic regression, the outcome variable must be binary, so we used binary variables in defining the comorbidities of interest.

The sample was split into learning groups and testing groups for each of the research questions. The sample was split with 70% to the learning group and 30% to the testing group (Pang & Jung, 2013). Predictions will be made on each testing group model and then run a Chi-Square test on the actual comorbidities' incidence and the predicted comorbidities incidence to determine our predictive model's validity.

In running regressions, caution is necessary, and collinearity must be examined. In regression analysis, each predictor variable must represent a unique effect on the outcome variable. When two or more predictors conflict and have the same effect on the outcome variable, collinearity is present. We addressed collinearity using the SPSS bivariate correlation function where a positive collinearity absolute value greater than 0.8 indicates collinearity. Additionally, we included the collinearity diagnostics in the regression analysis using a VIF value greater than 10 to indicate a collinearity problem.

Table 30

Predictor Variables, their type, and possible values

Variable Name	Variable Type	Possible Values
Unique member identifier.	Nominal	Format TBD by MCO
Age	Continuous	21-100
Sex	Categorical	0=male, 1=female
HBA1c level	Continuous	actual level
Seeing an Endocrinologist	Categorical	0=no, 1=yes
Medication Class	Ordinal	1-35
Medication PDC	Continuous	0-1
Deductible	Continuous	$0 - $415
Had Myocardial Infraction	Nominal	0=no, 1=yes.
Is Blind	Nominal	0=no, 1=yes.
Has End-Stage Renal Disease	Nominal	0=no, 1=yes.
Has Urinary Tract infections	Nominal	0=no, 1=yes.
LIS enrollment	Continuous	0=no, 1=yes
Dual enrollment	Continuous	0=no, 1=yes

Each of these predictive model equations was determined by picking the predictors where their p-value is < 0.05. The equations for each of the research questions will be created using the fundamental equation for a straight line, $y = mx + b$, where y is

the HbA1c value, b is the y-axis intercept, and m is the coefficient for a statistically significant predictor variable. The final equation will take the final form of y = b + coeff1*predictor1 value + coeff2*predictor2 value + coeff3*predictor3 value + coeffN*predictorN value. This final equation will define the model for predicting either renal or retinal screening participation. The direction and strength of a linear relationship between two variables can be determined by Pearson's correlation (Warner, 2013). Values greater than 0.5 show significant levels of correlation between the variables. Values approaching 0.3 have small correlations but still significant enough to consider in the final equation. Any predictor variable used must have a p-value of less than 0.05. Pearson's correlations can give us some insight into the R^2 value produced by regression analysis because it gives us a feeling for the strength of effect (Warner, 2013). Pearson's correlation values are obtained by selecting a correlation from the SPSS interface and adding all of the analysis variables.

R^2 is a statistical value created by a regression analysis indicating how well the predictor variables match the regression line (Warner, 2013). The models' R^2 value indicates the quality of the data's fit to the line created by the regression. In human research, an R^2 value greater than 0.2 is considered adequate. This value is somewhat lower than in other kinds of research, but because human behavior is included in the analysis, this lower number is acceptable (Hair et al., 2011). Plots of the data are necessary to determine bias in the data. If the data is evenly dispersed around the regression line, then a regression is appropriate. If the data is not evenly dispersed, then a

non-linear approach is better (Warner, 2013). An analysis of Pearson's and the R^2 value will be conducted in the same manner as for the learning group.

Results

The purpose of this study is to determine what relationships exist between four of the comorbidities of type 2 diabetes, myocardial infarction, renal disease, blindness, and urinary tract infections, and HbA1c, medication class, and the PDC value. Our original sample size was 37,363. We removed those who did not have an HbA1c level reported for 2019, leaving a final sample size of 22,638. We then split this into a learning group of 15,845 and a testing group of 6,793. Table 31 is a list of predictors available in the data and the count for each. Because the regression analysis requires that each predictor entered have a value, many of our regressions either had no cases or too few for statistical power.

Table 31

Predictor variable Counts

Predictor	Count
Biguanide	11743
DPP	597
Thiazolidinedione	206
Sulfonylurea	2574
Sulfonylurea Biguanide	228
DPP Biguanide	367
Male	6482
Female	9363
DSNP Plan	5151
LIS Plan	3432
No Subsidy	7262
Seeing Endocrinologist	623

Retinopathy screening	1639
Nephropathy screening	3346
Controlled Blood Pressure	5896

We ran individual binary logistic regressions, using SPSS version 27, with end-stage renal disease, blindness, myocardial infarction, and UTI as the outcome variables, and each of the medication class PDC's as the predictor variables. Table 32 shows the outcome of those regressions for each of the comorbidities and each of the means adjusted medication class PDC values. We then removed the models that did not show any statistical significance and where we had case counts less than 89, as number derived by G*Power.

For many of the regressions that included all of our predictors, we could not get enough cases to complete a regression analysis. Table 32 show the results of running additional regressions where we could get enough cases.

Table 32

Binary Regression of Comorbidity and Medication PDC values

Outcome Variable	PDC Predictor	Chi Square Model Sig	Count (1)	Sig	Exp(B)
Renal Disease	Total PDC	0.000	3681	0.000	1.556
	Biguanide	0.001	2113	0.001	1.592
	DPP	0.460	260	0.460	0.745
	Thiazolidinediones	0.942	80	0.942	1.060
	Sulfonylurea	0.018	1048	0.019	1.728
	Sulfonylurea Biguanide	0.141	44	0.170	6.381
	DPP Biguanide	0.094	58	0.109	3.554

Blindness	Total PDC	0.565	207	0.569	1.259
	Biguanide	0.583	140	0.858	1.312
	DPP	0.020	11	0.014	0.059
	Thiazolidinediones	0.536	6	0.514	0.278
	Sulfonylurea	0.007	39	0.025	30.346
	Sulfonylurea Biguanide	0.538	5	0.581	9.064
	DPP Biguanide	0.346	2	0.454	126.53
Myocardial Infarction	Total PDC	0.009	1007	0.008	0.631
	Biguanide	0.114	648	0.110	0.703
	DPP	0.004	59	0.003	0.180
	Thiazolidinediones	0.266	11	0.239	0.186
	Sulfonylurea	0.776	248	0.775	0.898
	Sulfonylurea Biguanide	0.645	12	0.633	0.433
	DPP Biguanide	0.427	17	0.446	2.849
UTI	Total PDC	0.778	2460	0.778	0.968
	Biguanide	0.909	1735	0.909	0.983
	DPP	0.453	128	0.449	0.700
	Thiazolidinediones	0.412	35	0.402	0.444
	Sulfonylurea	0.874	460	0.875	1.048
	Sulfonylurea Biguanide	0.065	28	0.107	23.059
	DPP Biguanide	0.267	48	0.258	0.445

Table 33

Binary Regression of Comorbidity and Significant Medication PDC Values with Covariates

Outcome Variable	PDC Predictor	Chi Square Model Sig	Count	Coeff	Sig	Exp (B)
Renal Disease	Total PDC	0.000	3529	0.183	0.109	1.201
	Age			0.059	0.000	1.060
	Deductible			-0.002	0.000	0.998

	LIS			0.026	0.623	1.027
	DSNP			0.628	0.000	1.874
	HbA1c Level			-0.200	0.332	0.980
	Seeing Endocrinologist			0.043	0.116	1.044
	Hospital Visits			0.055	0.116	1.056
	Retinopathy Screening			-0.161	0.183	0.851
	Nephropathy Screening			0.111	0.187	1.118
	Gender (F reference)			0.226	0.000	1.254
	Biguanide PDC	0.000	2103	0.163	0.271	1.117
	Age			0.052	0.000	1.053
	Deductible			-0.002	0.000	0.998
	LIS			0.004	0.955	1.004
	DSNP			0.599	0.000	1.820
	Gender (F reference)			0.136	0.007	1.146
	HbA1c Level			-0.029	0.318	0.971
	Seeing Endocrinologist			0.086	0.005	1.089
	Hospital Visits			0.027	0.000	1.027
	Retinopathy Screening			0.109	0.176	1.115
	Nephropathy Screening			0.511	0.000	1.667
	Constant			-5.269	0.000	0.005
	Sulfonylurea PDC	0.000	677	0.405	0.000	0.030
	Age			0.490	0.000	1.051
	Deductible			-0.002	0.000	0.998
	LIS			-0.030	0.795	0.971
	DSNP			0.590	0.005	1.804
	HbA1c Level			-0.111	0.003	0.895
	Seeing Endocrinologist			-0.026	0.533	0.974
	Hospital Visits			0.041	0.000	1.042
	Retinopathy Screening			0.091	0.543	1.095
	Nephropathy Screening			0.371	0.001	1.449
	Gender (F reference)			0.344	0.000	1.410
Myocardial Infarction	Total PDC	0.000	1003	-0.479	0.008	0.620
	Age			0.024	0.000	1.025
	Deductible			-0.001	0.100	0.999
	LIS			0.067	0.458	1.069
	DSNP			0.232	0.141	1.261

Gender (F reference)	0.698	0.000	2.009
Seeing Endocrinologist	0.043	0.116	1.044
Hospital Visits	0.055	0.116	1.056
Retinopathy Screening	-0.161	0.183	0.851
Nephropathy Screening	0.111	0.187	1.118
HbA1c Level	0.006	0.849	1.006
Constant	-4.9360	0.000	0.007

Discussion

HbA1c levels consistently show no statistical significance related to the four comorbidities examined here, UTI, MI, blindness, and renal disease. These findings are not what we expected, nor what has been published in the literature (Luo et al., 2017). The discrepancy could be related to our lack of understanding of the relationship between comorbid diagnosis date and when HbA1c levels were drawn, and when the comorbid diagnosis was made. Additionally, we do not have HbA1c levels over time.

The analysis showed that being in a DSNP program doubles the chances of renal disease compared to those not in a financial subsidy program while controlling for covariates. However, this is not surprising, as ESRD is one of the diagnoses needed for eligibility into a DSNP program. We also found that males have a two times greater chance of having an MI than females when controlling for the other covariates, matching the literature, where women generally have heart attacks 7 to 10 years later than males (Liakos & Parikh, 2018; Maas & Appelman, 2010). However, we did not see any differences in mean age by gender as demonstrated in Table 34, but we have 30% more

females in the study than males who may have contributed to females having a greater risk of MI than males in our data.

Table 34

Mean Age by Gender

Gender	Mean	N	Composition	Std. Deviation
Female	71.30	9363	59%	9.470
Male	70.59	6482	41%	9.414
Total	71.01	15845		9.453

Our analysis did not uncover any significant relationships other than what has been found in previously published studies (however, these studies were not looking at specific comorbidities of diabetes). We did not have enough members with comorbidity and covariates to do as complete an analysis as we wanted, nor were we able to develop any predictive models for the same reason. We did have enough members to find the R^2 values to be so low as to render our models insignificant.

Limitations and Future Areas for Study

There are several limitations to this study related to the comorbidities of type 2 diabetes. Our data did not give the length of time since any of the comorbidities were diagnosed. Our data did not provide when HbA1c levels were completed, which may have affected our results. Additionally, we are not able to relate HbA1c levels to comorbidities.

The insignificance of our R^2 values, where we could get one, indicates that we are looking at the wrong covariates. The SDOH are gaining popularity in the literature so an

area of future study would be to look at how the SDOH impact the four comorbidities examine here. There is evidence for the relationship between the SDOH and diabetes (McBrien et al., 2017).

References

Antonetti, D. A., Klein, R., & Gardner, T. W. (2012). Diabetic retinopathy. *New England Journal of Medicine, 366*(13), 1227-1239. https://ezp.waldenulibrary.org/login?url=https://search.ebscohost.com/login.aspx?direct=true&db=rzh&AN=104545236&site=eds-live&scope=site

Brown, J. S., Wessells, H., Chancellor, M. B., Howards, S. S., Stamm, W. E., Stapleton, A. E., Steers, W. D., Van Den Eeden, S. K., & McVary, K. T. (2005). Urologic complications of diabetes. *Diabetes Care, 28*(1), 177-185.

Center for Disease Control. (2015). Calculating the Proportion of Days Covered (PDC) for antihypertensive andantidiabetic medications: An evaluation guide for grantees. Retrieved May 12, 2019, from https://www.cdc.gov/dhdsp/docs/med-adherence-evaluation-tool.pdf

Centers for Disease Control and Prevention. (2020). National Diabetes Statistics Report 2020 Estimates of Diabetes and Its Burden in the United States. Retrieved September 26, 2020, from https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf

Creswell, J. W., & Creswell, J. D. (2017). *Research Design: Qualitative, Quantitative, and Mixed Methods Approaches*. Sage publications.

Cunningham, J. B., & McCrum-Gardner, E. (2007). Power, effect and sample size Using Gpower: Practical issues for researchers and members of research ethics Committees. *Evidence-Based Midwifery, 5*(4), 132-137.

Davis-Ajami, M. L., Pakyz, A., Wu, J., & Baernholdt, M. (2019). A payer perspective of the costs of urinary tract and skin and soft tissue infections in adults with diabetes and the relationship to oral antidiabetic medication nonadherence. *Journal of Managed Care & Specialty Pharmacy, 25*(12), 1409-1419.

de Lastours, V., & Foxman, B. (2014). Urinary tract infection in diabetes: epidemiologic considerations. *Current Infectious Disease Reports, 16*(1), 389.

Feingold, K. R. (2019). Oral and Injectable (Non-Insulin) Pharmacological Agents for Type 2 Diabetes. In F. K.R., B. Anawalt, & A. Boyce (Eds.), *Endotext [Internet]*. MDText. com, Inc. https://www.ncbi.nlm.nih.gov/books/NBK279141/

Foot, H., La Caze, A., Gujral, G., & Cottrell, N. (2016). The necessity–concerns framework predicts adherence to medication in multiple illness conditions: A meta-analysis. *Patient Education and Counseling, 99*(5), 706-717.

Gall, M.-A., Rossing, P., Skøtt, P., Damsbo, P., Vaag, A., Bech, K., Dejgaard, A., Lauritzen, M., Lauritzen, E., & Hougaard, P. (1991). Prevalence of micro-and macroalbuminuria, arterial hypertension, retinopathy and large vessel disease in european type 2 (Non-Insulin-Dependent) Diabetic Patients. *Diabetologia, 34*(9), 655-661.

Gilmartin-Thomas, J. F., Smith, F., Wolfe, R., & Jani, Y. (2017). A comparison of medication administration errors from original medication packaging and multi-compartment compliance aids in care homes: A prospective observational study. *International Journal of Nursing Studies, 72*, 15-23.

Hair, J. F., Ringle, C. M., & Sarstedt, M. (2011, Spring2011). Pls-Sem: Indeed a silver bullet. *Journal of Marketing Theory & Practice, 19*(2), 139-152. https://doi.org/10.2753/MTP1069-6679190202

Heron, M. P. (2017). *Deaths: Leading Causes for 2017*. C. f. D. C. a. Prevention. https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_06-508.pdf

Lee, R., Wong, T. Y., & Sabanayagam, C. (2015). Epidemiology of diabetic retinopathy, diabetic macular ddema and related vision loss. *Eye and Vision, 2*, 17-17. https://doi.org/10.1186/s40662-015-0026-2

Li, Y., Geiss, L. S., Burrows, N. R., Rolka, D. B., & Albright, A. (2013). Awareness of prediabetes—United States, 2005–2010. *Morbidity and Mortality Weekly Report, 62*(11), 209.

Liakos, M., & Parikh, P. B. (2018, 2018/06/16). Gender disparities in presentation, management, and outcomes of acute myocardial infarction. *Current Cardiology Reports, 20*(8), 64. https://doi.org/10.1007/s11886-018-1006-7

Luo, M., Lim, W. Y., Tan, C. S., Ning, Y., Chia, K. S., van Dam, R. M., Tang, W. E., Tan, N. C., Chen, R., & Tai, E. S. (2017). Longitudinal trends in Hba1c and associations with comorbidity and all-cause mortality in Asian patients with type 2 diabetes: A cohort study. *Diabetes Research and Clinical Practice, 133*, 69-77.

Maas, A. H. E. M., & Appelman, Y. E. A. (2010). Gender differences in coronary heart disease. *Netherlands Heart Journal, 18*(12), 598-602. https://doi.org/10.1007/s12471-010-0841-y

McBrien, K. A., Naugler, C., Ivers, N., Weaver, R. G., Campbell, D., Desveaux, L., Hemmelgarn, B. R., Edwards, A. L., Saad, N., & Nicholas, D. (2017). Barriers to care in patients with diabetes and poor glycemic control—a cross-sectional survey. *PloS One, 12*(5), e0176135.

Molitch, M. E., DeFronzo, R. A., Franz, M. J., & Keane, W. F. (2004). Nephropathy in diabetes. *Diabetes Care, 27*, S79.

National Center for Chronic Disease Prevention. (2016). Diabetes. Retrieved October 2, 2018, from https://www.cdc.gov/chronicdisease/resources/publications/aag/diabetes.htm

National Institute of Diabetes and Digestive and Kidney Diseases. (2017). Diabetes Statistics. Retrieved https://www.niddk.nih.gov/health-information/health-statistics/diabetes-statistics

Nichols, G. A., Rosales, A. G., Kimes, T. M., Tunceli, K., Kurtyka, K., & Mavros, P. (2016). The change in Hba1c associated with initial adherence and subsequent change in adherence among diabetes patients newly initiating metformin therapy. *Journal of Diabetes Research*, 1-5. https://doi.org/10.1155/2016/9687815

Pang, H., & Jung, S. (2013). Sample size considerations of prediction-validation methods in high-dimensional data for survival outcomes. *Genetic Epidemiology, 37*(3), 276-282. https://doi.org/10.1002/gepi.21721

Picard, R. R., & Berk, K. N. (1990, 5/1/1990). Data splitting. *The American Statistician, 44*(2), 140-147. https://doi.org/10.1080/00031305.1990.10475704

Polonsky, W. H., & Henry, R. R. (2016a). Poor medication adherence in type 2 diabetes: Recognizing the scope of the problem and its key contributors. *Patient Preference and Adherence, 10*, 1299.

Pruitt, Z., Lyons Taylor, P., & Bryant, K. M. (2018). A managed care organization's call center–based social support role. *The American Journal of Accountable Care, 6*(1), e16-e22. https://www.ajmc.com/journals/ajac/2018/2018-vol6-n1/a-managed-care-organizations-call-center-based-social-support-role

Saleem, M., & Daniel, B. (2011). Prevalence of urinary tract infection among patients with diabetes in Bangalore City. *International Journal of Emerging Sciences, 1*(2), 133.

Shiyanbola, O. O., Unni, E., Huang, Y., & Lanier, C. (2018). The association of health literacy with illness perceptions, medication beliefs, and medication adherence among individuals with type 2 diabetes. *Research in Social and Administrative Pharmacy, 14*(9), 824-830. https://doi.org/10.1016/j.sapharm.2017.12.005

Solomon, S. D., Chew, E., Duh, E. J., Sobrin, L., Sun, J. K., VanderBeek, B. L., Wykoff, C. C., & Gardner, T. W. (2017). Diabetic retinopathy: A position statement by the American Diabetes Association. *Diabetes Care, 40*(3), 412-418.

Tseng, E., Greer, R. C., O'Rourke, P., Yeh, H., McGuire, M. M., Clark, J. M., & Maruthur, N. M. (2017, 2017/11/01). Survey of primary care providers' nkowledge of screening for, diagnosing and managing prediabetes. *Journal of General Internal Medicine, 32*(11), 1172-1178. https://doi.org/10.1007/s11606-017-4103-1

Vlassara, H. (1992). Receptor-Mediated interactions of advanced glycosylation end products with cellular components within diabetict. *Diabetes, 41*(Supplement 2), 52-56.

Wagner, W. E. (2016). *Using Ibm® Spss® Statistics for Research Methods and Social Science Statistics*. Sage Publications.

Wang, L., Wei, W., Miao, R., Xie, L., & Baser, O. (2013). Real-World outcomes of US employees with type 2 diabetes mellitus treated with insulin glargine or neutral protamine hagedorn insulin: A comparative retrospective database study. *BMJ Open, 3*(4), e002348.

Warner, R. M. (2013). *Applied Statistics from Bivariate Throught Multivariate Techniques* (2nd ed.). Sage Publications, Inc.

Yau, J. W., Rogers, S. L., Kawasaki, R., Lamoureux, E. L., Kowalski, J. W., Bek, T., Chen, S., Dekker, J. M., Fletcher, A., & Grauslund, J. (2012). Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care*, DC_111909. https://doi.org/https://doi.org/10.2337/dc11-1909

Part 3 : Summary

Introduction

The first of the three studies presented here examined the relationship between medication compliance in six of the antihyperglycemic medication classes and HbA1c levels in people with type 2 diabetes. The second study examined the effectiveness of financial subsidies on medication compliance and HbA1c levels in people with type 2 diabetes. The third study examined the relationship between the comorbidities of type 2 diabetes and medication compliance. The individuals in all these studies came from a large, nationwide MCO, have a diagnosis of type 2 diabetes, were taking one of six medication classes of antihyperglycemic medications, or a combination of them, took only one of these during the year, and had at least one HbA1c level done during the year. Participants were chosen from the claims database of a large, national MCO from 2019. Of the original 56,000 potential MCO members for this study, final counts varied from 22,000 to 15,000, depending on the study. All studies have sufficient members to achieve statistical power.

The study results demonstrate clinically significant findings in the relationship between medication compliance and the medication a person with diabetes consumes. It shows that practitioners should consider how compliant their patient is when considering a medication regimen. In part, Medicare created the LIS and DSNP programs to improve medication compliance by reducing copays and deductibles. Study two demonstrated that this is not the case. Additionally, these programs do not appear to affect HbA1c

levels, the ultimate goal of therapy. Finally, the third study was unable to establish any relationships between four of the comorbidities of diabetes and medication compliance in people with type 2 diabetes.

Summary of Findings

Study one demonstrated that medication compliance should be a factor when providers decide which medications they are going to use to treat their patients. We found that the Sulfonylurea-Biguanide combination, slope[1] = -2.49, is most sensitive to compliance, demonstrating that the Sulfonylurea-Biguanide class of medications should be avoided in patients providers feel, or will be, non-compliant. However, the DPP class of medications, slope = -0.09, Biguanide class, slope = -0.16, and Sulfonylurea class, slope = -0.25, are the least affected by medication compliance. Thiazolidinediones, slope = -0.83, and DPP-Biguanides, slope = -0.94, are moderately affected by medication compliance compared to the other classes discussed here. Finally, we demonstrate that with compliance rates above 85%, each of these medication classes' effectiveness is similar.

In part, Medicare instituted the LIS and DSNP programs that reduce copays and deductibles to improve medication compliance and in people with diabetes, thereby reducing HbA1c levels. While we had statistically significant findings that these programs affect compliance and HbA1c levels, the R2 values were all less than 1%,

[1] Slope is for each unit increase in PCD, HbA1c changes by slope value units. Slopes are all negative showing that as compliance increases HbA1c levels fall.

indicating that their effect is insignificant. Our findings are similar to another study conducted in 2012 that used the MPR compliance method and not the PDC method for calculating compliance as used in this study.

Our third study examined the relationship between HbA1c levels and four of the comorbidities of diabetes, UTIs, MI's, ESRD, and blindness. Our findings conflict with the published literature, but our evidence is conflicting. For example, those in a DSNP program showed double the chance of having renal disease when compared to those not getting financial assistance. However, having an ESRD diagnosis is one of the predicates of being in a DSNP program, and we did not have diagnosis dates to include in our analysis. We did find that males had two times greater chance than females of having an MI, and we did not find any differences when examing age.

Interpretation of Findings

In our study of the relationship between HbA1c and medication compliance, we found a statistically significant relationship. This study's findings reveal that during the clinical medication therapy decision-making process for people with type 2 diabetes, providers should consider how compliant their patients are in taking their medications and considering the medication class to prescribe. Most significantly, we found that the Sulfonylurea-Biguanide combination should be reserved for patients who will be more than 85% compliant to maintain acceptable HbA1c levels. We also found that the DPP, Sulfonylurea, and Biguanide classes of medication are not affected much by compliance,

so these would be good therapy choices for patients that providers feel will be non-compliance in taking their medications.

In examining the LIS and DSNP program's effects on medication compliance and HbA1c levels, we found that while there is a statistically significant relationship, these relationships' strength is minimal at best ($R^2 < 1\%$). The purpose of these programs is to help reduce the financial burdens that may lead to medication non-compliance. However, the evidence does not support this.

Our final study found little evidence establishing a relationship between UTIs, MI's, blindness, or ESRD. Our findings in this study were unexpected as it is not consistent with past studies on the comorbidities of diabetes. However, these studies did not look specifically at medication compliance and these comorbidities. There could be several explanations for this discrepancy. First, this is not a long-term study, there are other factors than what we looked at that contribute to the comorbidities, and we only had a single HbA1c level taken during one year.

Limitations of Study

We identified several limitations for all these studies. We could not associate the date an HbA1 level was obtained and medication compliance rates, possibly skewing our results. We found statistically significant relationships that the R2 values were low with values less than 5%. We did not have access to the social determinant of health data at a member level. We tried a multilevel analysis at a zip code level but did not get any statistical significance. Because we found relatively low R^2 values throughout our

studies, further studies need to examine how the social determinant of health fit into the relationships between medication compliance and HbA1c and the comorbidities of diabetes. While we found indications of strong relationships between medication class and HbA1c levels, smaller studies are needed where compliance and medication class can be more closely associated with HbA1c levels. Finally, we only looked at people with diabetes who took a single medication during 2019. People with diabetes are also on multiple medications during the year or switched from one medication to another. These cases are also deserving of closer scrutiny with more closely controlled studies

Individual

Eighty-five million Americans have been diagnosed with diabetes, and another 30 million have been diagnosed with pre-diabetes, constituting one-third of the country's population. Diabetes costs the US hundreds of billions of dollars in medical costs each year and is one of the most prominent US's chronic diseases. Medication therapy is a crucial component for a person with diabetes, and compliance with their medications is the primary component of that regimen. These studies provide new evidence for practitioners when making therapy decisions showing them that not only is the class of medication selected essential but that the compliance level of their patient must be just as important a factor in medication selection. Additionally, the studies show that the Medicare financial incentive program aimed at improving compliance is not having the desired impact and the need for future studies of the LIS and DSNP (pharmacy part) programs.

Clinical

Primarily related to practitioners is study one. This study provides evidence on the importance of compliance when instituting a medication therapy plan. We showed that the ability of different medications to control HbA1c levels is statistically related to how compliant their patient will be. We showed that some medication classes are susceptible to compliance, and others a not affected much by compliance rates. We showed that for compliant patients (over 80% of the time), there is not much difference in the effect of compliance on HbA1c control. Provider medication decisions are essential in finding ways to control their patients' blood sugar levels. Controlled blood sugars result in lower societal medication costs, better health statuses, and lowered diabetes complications for people who have diabetes.

Societal

The societal costs from diabetes are significant including financial, burdens on the healthcare system and the effects of poor health statuses of people with diabetes. The financial costs are borne by insurers, payors, and those without insurance individuals. Lost work productivity contributes to the financial costs of diabetes, and for those without sick, benefits may add to lowered health statuses.

We found that Medicare's financial programs aimed at improving compliance rates are not having the desired effect. We demonstrated that a reevaluation of these programs should be considered, and new approaches are needed. These financial programs do not

contribute to improved compliance or lowered HbA1c levels as designed, and there should be consideration for allocating these resources differently.

Implications for Social Change

Individual

Eighty-five million Americans have been diagnosed with diabetes, and another 30 million have been diagnosed with pre-diabetes constituting one-third of the country's population. Diabetes costs the US hundreds of billions of dollars in medical costs each year and is one of the most prominent US chronic diseases. Medication therapy is a crucial component for a person with diabetes, and compliance with their medications is the primary component of that regimen. These studies provide new evidence for practitioners when making therapy decisions showing them that not only is the class of medication selected essential but that the compliance level of their patient must be just as important a factor in medication selection. Additionally, the studies show that the Medicare financial incentive program aimed at improving compliance is not having the desired impact and the need for future studies of the LIS and DSNP (pharmacy part) programs.

Clinical

Primarily related to practitioners is study one. This study provides evidence on the importance of compliance when instituting a medication therapy plan. We showed that different medications' ability to control HbA1c levels is statistically related to how compliant their patient will be. We showed that some medication classes are susceptible

to compliance, and others a not affected much by compliance rates. We also showed that across patients compliant with their medications (over 80% of the time), there is not much difference in HbA1c control based on different medications. These decisions are essential in provider's efforts in finding ways to control their patients' blood sugar levels. Controlled blood sugars result in lower societal medication costs, better health statuses, and lowered diabetes complications for people who have diabetes.

Societal

The societal costs from diabetes are significant including financial, burdens on the healthcare system and the effects of poor health statuses of people with diabetes. Financial costs fall on insurers, payors, and those individuals without insurance. Lost work productivity contributes to the financial costs of diabetes, and for those without sick, benefits may add to lowered health statuses.

We found that Medicare's financial programs aimed at improving compliance rates are not having the desired effect. We demonstrated that a reevaluation of these programs should be considered, and new approaches are needed. These financial programs do not contribute to improved compliance or lowered HbA1c levels as designed, and there should be a reconsideration to allocating these resources differently.

References

Agency for Healthcare Research and Quality. (2018). Six Domains of Health Care Quality. Retrieved May 13, 2019, from https://www.ahrq.gov/talkingquality/measures/six-domains.html

Allemann, S., Nieuwlaat, R., van den Bemt, B., Hersberger, K., & Arnet, I. (2016, 2016-November-14). Matching adherence interventions to patient determinants using the theoretical domains framework. *Frontiers in Pharmacology, 7*(429). https://doi.org/10.3389/fphar.2016.00429

American Diabetes Association. (2009). American Diabetes Association Indications for Statins in Diabetes. Retrieved June 8, 2020, from https://care.diabetesjournals.org/content/32/suppl_2/S384

American Diabetes Association. (2018a). Cardiovascular disease and risk management: standards of medical care in diabetes — 2018. *Diabetes Care, 41*(Supplement 1), S86-S104.

American Diabetes Association. (2018b). The cost of diabetes. Retrieved September 22, 2018, from http://www.diabetes.org/advocacy/news-events/cost-of-diabetes.html

American Diabetes Association. (2018c). Standards of medical care in diabetes. Retrieved August 11, 2018, from http://www.diabetes.org/newsroom/press-releases/2009/cpr-2010-a1c-diagnostic-tool.html

American Diabetes Association. (2018d). Statistics about diabetes. Retrieved August 11, 2018, from http://www.diabetes.org/diabetes-basics/statistics/

American Diabetes Association. (2019). Type 1 diabetes. Retrieved April 20, 2019, from http://www.diabetes.org/diabetes-basics/type-1/

American Diabetes Association. (n.d.). Understanding diabetes diagnosis. Retrieved May 15, 2021, from https://www.diabetes.org/a1c/diagnosis

Anderson-Cook, A., Maeda, J., & Nelson, L. A. (2019). *Prices for and Spending on Specialty Drugs in Medicare Part D and Medicaid: An Iin-Depth Analysis: Working Paper 2019-02*. https://www.cbo.gov/system/files?file=2019-03/54964-Specialty_Drugs.pdf

Antonetti, D. A., Klein, R., & Gardner, T. W. (2012). Diabetic retinopathy. *New England Journal of Medicine, 366*(13), 1227-1239. https://ezp.waldenulibrary.org/login?url=https://search.ebscohost.com/login.aspx?direct=true&db=rzh&AN=104545236&site=eds-live&scope=site

Archibald, N., Soper, M., Smith, L., Kruse, A., & Wiener, J. (2019). Integrating care through Dual Eligible Special Needs Plans (D-SNPS): Opportunities and challenges. Retrieved June 13, 2020, from https://aspe.hhs.gov/basic-report/integrating-care-through-dual-eligible-special-needs-plans-d-snps-opportunities-and-challenges#overview

Baghikar, S., Benitez, A., Piñeros, P. F., Gao, Y., & Baig, A. A. (2019). Factors impacting adherence to diabetes medication among urban, low income Mexican-Americans with diabetes. *Journal of Immigrant and Minority Health*, 1-8.

Bansal, N. (2015). Prediabetes diagnosis and treatment: A review. *World Journal Of Diabetes, 6*(2), 296-303. https://doi.org/10.4239/wjd.v6.i2.296

Belsley, D. A. (1984). Collinearity and forecasting. *Journal of Forecasting, 3*(2), 183-196.

Benner, J. S., Glynn, R. J., Mogun, H., Neumann, P. J., Weinstein, M. C., & Avorn, J. (2002). Long-Term persistence in use of statin therapy in elderly patients. *Journal of the American Medical Association, 288*(4), 455-461.

Bookchin, R. M., & Gallop, P. M. (1968). Structure of Hemoglobin A1c: Nature of the N-Terminal B Chain Blocking Group. *Biochemical and Biophysical Research Communications, 32*(1), 86-93.

Bourne, R. R., Stevens, G. A., White, R. A., Smith, J. L., Flaxman, S. R., Price, H., Jonas, J. B., Keeffe, J., Leasher, J., & Naidoo, K. (2013). Causes of vision loss worldwide, 1990–2010 : A Systematic Analysis. *The Lancet Global Health, 1*(6), e339-e349.

Bradlow, E. T., Gangwar, M., Kopalle, P., & Voleti, S. (2017). The role of big data and predictive analytics in retailing. *Journal of Retailing, 93*(1), 79-95.

Brannick, B., Wynn, A., & Dagogo-Jack, S. (2016). Prediabetes as a toxic environment for the initiation of microvascular and macrovascular complications. *Experimental Biology and Medicine, 241*(12), 1323-1331. https://doi.org/10.1177/1535370216654227

Brown, J. S., Wessells, H., Chancellor, M. B., Howards, S. S., Stamm, W. E., Stapleton, A. E., Steers, W. D., Van Den Eeden, S. K., & McVary, K. T. (2005). Urologic complications of diabetes. *Diabetes Care, 28*(1), 177-185.

Brown, M. T., Bussell, J. K., Dutta, S., Davis, K., Strong, S., & Mathew, S. (2016). Medication adherence: Truth and Consequences. *The American Journal of the Medical Sciences, 351*(4), 387-399.

Brunisholz, K. D., Briot, P., Hamilton, S., Joy, E. A., Lomax, M., Barton, N., Cunningham, R., Savitz, L. A., & Cannon, W. (2014). Diabetes self-management education improves quality of care and clinical outcomes determined by a diabetes bundle measure. *Journal of Multidisciplinary Healthcare, 7*, 533.

Bussell, J. K., Cha, E., Grant, Y. E., Schwartz, D. D., & Young, L. A. (2017). Ways health care providers can promote better medication adherence. *Clinical Diabetes, 35*(3), 171-177.

Buysman, E. K., Liu, F., Hammer, M., & Langer, J. (2015). Impact of medication adherence and persistence on clinical and economic outcomes in patients with type 2 diabetes treated with Liraglutide: A retrospective cohort study. *Advances in Therapy, 32*(4), 341-355.

Capoccia, K., Odegard, P. S., & Letassy, N. (2015, 2016/02/01). Medication adherence with diabetes medication: A systematic review of the literature. *The Diabetes Educator, 42*(1), 34-71. https://doi.org/10.1177/0145721715619038

Capoccia, K., Odegard, P. S., & Letassy, N. (2016). Medication adherence with diabetes medication: A systematic review of the literature. *The Diabetes Educator, 42*(1), 34-71.

Carris, N. W., Magness, R. R., & Labovitz, A. J. (2019, 02/01/February 2019). Prevention of diabetes mellitus in patients with prediabetes. *The American Journal of Cardiology, 123*(3), 507-512. https://doi.org/10.1016/j.amjcard.2018.10.032

Caruana, E. J., Roman, M., Hernández-Sánchez, J., & Solli, P. (2015). Longitudinal studies. *Journal of Thoracic Disease, 7*(11), E537-E540. https://doi.org/10.3978/j.issn.2072-1439.2015.10.63

Casagrande, S. S., Menke, A., Linder, B., Osganian, S. K., & Cowie, C. C. (2018). Cardiovascular risk factors in adolescents with prediabetes. *Diabetic Medicine, 35*(9), 1202-1209.

Center for Disease Control. (2015). Calculating the Proportion of Days Covered (PDC) for antihypertensive andantidiabetic medications: An evaluation guide for grantees. Retrieved May 12, 2019, from https://www.cdc.gov/dhdsp/docs/med-adherence-evaluation-tool.pdf

Center for Disease Control. (2017). New CDC report: More than 100 million Americans have diabetes or prediabetes. Retrieved April 19, 2019, from https://www.cdc.gov/media/releases/2017/p0718-diabetes-report.html

Center for Disease Control. (2019). 2019 Medicare-Medicaid Plan Performance Data Technical Notes. Retrieved August 12, 2019, from https://www.cms.gov/Medicare-Medicaid-Coordination/Medicare-and-Medicaid-Coordination/Medicare-Medicaid-Coordination-Office/FinancialAlignmentInitiative/Downloads/MMPPerformanceDataTechNotes.pdf

Center for Disease Control. (n.d.-a). Diabetic Retinopathy. Retrieved May 5, 2019, from https://www.cdc.gov/visionhealth/pdf/factsheet.pdf

Center for Disease Control. (n.d.-b). National Chronic Kidney Disease Fact Sheet, 2017 Retrieved May 5, 2019, from National Chronic Kidney Disease Fact Sheet, 2017

Centers for Disease Control and Prevention. (2018a, June 11, 2018). About Prediabetes & Type 2 Diabetes. Retrieved Janurary 26, 2019, from https://www.cdc.gov/diabetes/prevention/prediabetes-type2/index.html

Centers for Disease Control and Prevention. (2018b). The Surprising Truth About Prediabetes. Retrieved January 26, 2018, from https://www.cdc.gov/features/diabetesprevention/index.html

Centers for Disease Control and Prevention. (2020). National Diabetes Statistics Report 2020 Estimates of Diabetes and Its Burden in the United States. Retrieved September 26, 2020, from https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf

Centers for Medicare & Medicaid Services. (2015). *Calculating Proportion of Days Covered (PDC) for Antihypertensive and Antidiabetic Medications: An Evaluation Guide for Grantees*. https://www.cdc.gov/dhdsp/docs/med-adherence-evaluation-tool.pdf

Centers for Medicare & Medicaid Services. (2020a). 2018 Low Income Subsidy Contract Enrollment by County Retrieved April 12, 2020, from https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/MCRAdvPartDEnrolData/LIS-Contract-Enrollment-by-County-Items/2018-Low-Income-Subsidy-Contract-Enrollment-by-County

Centers for Medicare & Medicaid Services. (2020b). Dually Eligible Beneficiaries under Medicare and Medicaid. Retrieved May 3, 2020, from https://www.cms.gov/outreach-and-education/medicare-learning-network-mln/mlnproducts/downloads/medicare_beneficiaries_dual_eligibles_at_a_glance.pdf

Centers for Medicare & Medicaid Services. (n.d.). Lower Prescription Costs. Retrieved April 12, 2020, from https://www.medicare.gov/your-medicare-costs/get-help-paying-costs/lower-prescription-costs

Chandran, A., Bonafede, M. K., Nigam, S., Saltiel-Berzin, R., Hirsch, L. J., & Lahue, B. J. (2015). Adherence to insulin pen therapy is associated with reduction in healthcare costs among patients with type 2 diabetes mellitus. *American Health & Drug Benefits, 8*(3), 148.

Choi, Y. J., Jia, H., Gross, T., Weinger, K., Stone, P. W., & Smaldone, A. M. (2017). The impact of Medicare Part D on the proportion of out-of-pocket prescription drug costs among older adults with diabetes. *Diabetes Care, 40*(4), 502-508.

Cohen, H. W., Shmukler, C., Ullman, R., Rivera, C. M., & Walker, E. A. (2010). Measurements of medication adherence in diabetic patients with poorly controlled Hba1c. *Diabetic Medicine, 27*(2), 210-216.

Cohen, J. (2013). *Statistical Power Analysis for the Behavioral Sciences*. Academic Press.

Cotton, P., Newhouse, J. P., Volpp, K. G., Fendrick, A. M., Oesterle, S. L., Oungpasuk, P., Aggarwal, R., Wilensky, G., & Sebelius, K. (2016). Medicare advantage: Issues, insights, and implications for thef. *Population Health Management, 19*(S3), S1-S8. https://doi.org/10.1089/pop.2016.29013.pc

Cramer, J. A. (2004). A systematic review of adherence with medications for diabetes. *Diabetes Care, 27*(5), 1218-1224.

Creswell, J. W., & Creswell, J. D. (2017). *Research Design: Qualitative, Quantitative, and Mixed Methods Approaches*. Sage publications.

Cunningham, J. B., & McCrum-Gardner, E. (2007). Power, effect and sample size using Gpower: Practical issues for researchers and members of research ethics committees. *Evidence-Based Midwifery, 5*(4), 132-137.

Cutler, R. L., Fernandez-Llimos, F., Frommer, M., Benrimoj, C., & Garcia-Cardenas, V. (2018). Economic impact of medication non-adherence by disease groups: A systematic review. *BMJ Open, 8*(1). https://doi.org/10.1136/bmjopen-2017-016982

Dall, T. M., Yang, W., Halder, P., Pang, B., Massoudi, M., Wintfeld, N., Semilla, A. P., Franz, J., & Hogan, P. F. (2014). The economic burden of elevated blood glucose levels in 2012 : Diagnosed and undiagnosed diabetes, gestational diabetes mellitus, and prediabetes. *Diabetes Care, 37*(12), 3172-3179.

Davis-Ajami, M. L., Pakyz, A., Wu, J., & Baernholdt, M. (2019). A payer perspective of the costs of urinary tract and skin and soft tissue infections in adults with diabetes and the relationship to oral antidiabetic medication nonadherence. *Journal of Managed Care & Specialty Pharmacy, 25*(12), 1409-1419.

de Lastours, V., & Foxman, B. (2014). Urinary Tract Infection in Diabetes: Epidemiologic Considerations. *Current infectious disease reports, 16*(1), 389.

Dinh, T. T., Bonner, A., Clark, R., Ramsbotham, J., & Hines, S. (2016). The Effectiveness of the Teach-Back Method on Adherence and Self-Management in Health Education for People with Chronic Disease: A Systematic Review. *JBI database of systematic reviews and implementation reports, 14*(1), 210-247.

Doran, G. T. (1981). There's a S.M.A.R.T. Way to Write Managements's Goals and Objectives [Article]. *Management Review, 70*(11), 35. https://ezp.waldenulibrary.org/login?url=https://search.ebscohost.com/login.aspx?direct=true&db=bth&AN=6043491&site=eds-live&scope=site

Elisver. (n.d.). *CMS Star Ratings and Their Impact on Health Insurers, Pcms, and Retail Pharamcy* https://www.elsevier.com/__data/assets/pdf_file/0007/246958/EL-Star-Ratings-White-Paper-PDF-Download.pdf

Esen, İ., Demirci, H., Güçlü, M., Esen, S. A., & Şimşek, E. E. (2018). The relationship between health literacy, diabetic control, and disease-specific complications in patients with type 1 diabetes mellitus. *Southern Clinics of Istanbul Eurasia, 29*(3).

Fathy, C., Patel, S., Sternberg, P., Jr., & Kohanim, S. (2016). Disparities in adherence to screening guidelines for diabetic retinopathy in the United States: A comprehensive review and guide for future directions. *Seminars in Ophthamology, 31*(4), 364-377. https://doi.org/10.3109/08820538.2016.1154170

Feingold, K. R. (2019). Oral and Injectable (Non-Insulin) Pharmacological agents for type 2 diabetes. In F. K.R., B. Anawalt, & A. Boyce (Eds.), *Endotext [Internet]*. MDText. com, Inc. https://www.ncbi.nlm.nih.gov/books/NBK279141/

Fong, D. S., Aiello, L., Gardner, T. W., King, G. L., Blankenship, G., Cavallerano, J. D., Ferris III, F. L., & R., K. (2004). Retinopathy in diabetes. Retrieved April 28, 2019, from http://care.diabetesjournals.org/content/27/suppl_1/s84.short

Foot, H., La Caze, A., Gujral, G., & Cottrell, N. (2016). The necessity–concerns framework predicts Adherence to medication in multiple illness conditions: A meta-analysis. *Patient Education and Counseling, 99*(5), 706-717.

Fowler, M. J. (2008). Microvascular and macrovascular complications of diabetes. *Clinical Diabetes, 26*(2), 77-82. https://doi.org/10.2337/diaclin.26.2.77

Gall, M.-A., Rossing, P., Skøtt, P., Damsbo, P., Vaag, A., Bech, K., Dejgaard, A., Lauritzen, M., Lauritzen, E., & Hougaard, P. (1991). Prevalence of micro-and macroalbuminuria, arterial hypertension, retinopathy and large vessel disease in european type 2 (non-insulin-dependent) diabetic patients. *Diabetologia, 34*(9), 655-661.

Gilmartin-Thomas, J. F., Smith, F., Wolfe, R., & Jani, Y. (2017). A comparison of medication administration errors from original medication packaging and multi-compartment compliance aids in Care Homes: A prospective observational study. *International Journal of Nursing Studies, 72*, 15-23.

Ginsberg, B. H. (2009, 07/). Factors affecting blood glucose monitoring: Sources of errors in measurement. *Journal of Diabetes Science and Technology, 3*(4), 903-913. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2769960/

Giugliano, D., Maiorino, M., Bellastella, G., & Esposito, K. (2018, 2018/07/01). Glycemic control in type 2 diabetes: From medication nonadherence to residual vascular risk. *Endocrine, 61*(1), 23-27. https://doi.org/10.1007/s12020-017-1517-9

Gonzalez, J. S., & Schneider, H. E. (2011). Methodological issues in the assessment of diabetes treatment adherence. *Current Diabetes Reports, 11*(6), 472.

Gonzalez, J. S., Schneider, H. E., Wexler, D. J., Psaros, C., Delahanty, L. M., Cagliero, E., & Safren, S. A. (2013). Validity of medication adherence self-reports in adults with type 2 diabetes. *Diabetes Care, 36*(4), 831-837. https://doi.org/10.2337/dc12-0410

Gross, J. L., De Azevedo, M. J., Silveiro, S. P., Canani, L. H., Caramori, M. L., & Zelmanovitz, T. (2005). Diabetic nephropathy: Diagnosis, prevention, and treatment. *Diabetes Care, 28*(1), 164-176.

Hägg, S., Thorn, L. M., Putaala, J., Liebkind, R., Harjutsalo, V., Forsblom, C. M., Gordin, D., Tatlisumak, T., Groop, P., & Group, F. S. (2013). Incidence of stroke according to presence of diabetic nephropathy and severe diabetic retinopathy in patients with type 1 diabetes. *Diabetes Care*, DC_130669. https://doi.org/https://doi.org/10.2337/dc13-0669

Hair, J. F., Ringle, C. M., & Sarstedt, M. (2011, Spring2011). Pls-Sem: Indeed a silver bullet. *Journal of Marketing Theory & Practice, 19*(2), 139-152. https://doi.org/10.2753/MTP1069-6679190202

Harris, S. L., May, J. H., & Vargas, L. G. (2016). Predictive analytics model for healthcare planning and scheduling. *European Journal of Operational Research, 253*(1), 121-131.

Hayes, A. F. (2009). *Statistical Methods for Communication Science*. Routledge.

He, F., Xia, X., Wu, X., Yu, X., & Huang, F. (2013). Diabetic retinopathy in predicting diabetic nephropathy in patients with type 2 diabetes and renal disease : A meta-analysis. *Diabetologia, 56*(2), 457–466.

Heron, M. P. (2019). Deaths: leading causes for 2017. https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_06-508.pdf

Ho, C., Yeh, J., Wen, S., & Lee, T. J. (2017). Associations among medication regimen complexity, medical specialty, and medication possession ratio in newly diagnosed hypertensive patients: A population-based study. *Medicine, 96*(45), 8. https://doi.org/10.1097/MD.0000000000008497

Hu, H., Mizoue, T., Sasaki, N., Ogasawara, T., Tomita, K., Nagahama, S., Hori, A., Nishihara, A., Imai, T., & Yamamoto, M. (2018). Prediabetes and cardiovascular disease risk: A nested case-control study. *Atherosclerosis, 278*, 1-6.

Hu, J., Schreiber, M., Jordan, J., George, D. L., & Nerenz, D. (2018). Associations between community sociodemographics and performance in HEDIS quality measures: A study of 22 medical Centers in a Primary Care Network. *American Journal of Medical Quality*(1), 5.

Huang, Y., Shiyanbola, O. O., & Smith, P. D. (2018). Association of health literacy and medication self-efficacy with medication adherence and diabetes Control. *Patient Preference and Adherence, 12*, 793-802. https://doi.org/10.2147/PPA.S153312

Huisman, T., Martis, E., & Dozy, A. (1958). Chromatography of hemoglobin types on carboxymethylcellulose. *The Journal of Laboratory and Clinical Medicine, 52*(2), 312-327.

Ippolito, M. M., Lyles, C. R., Prendergast, K., Marshall, M. B., Waxman, E., & Seligman, H. K. (2017). Food insecurity and diabetes self-management among food pantry clients. *Public Health Nutrition, 20*(1), 183-189.

Jaam, M., Awaisu, A., Ibrahim, M., & Kheir, N. (2018). A holistic conceptual framework model to describe medication adherence in and guide interventions in diabetes mellitus. *Research in Social and Administrative Pharmacy 14*, 391-397. https://doi.org/10.1016/j.sapharm.2017.05.003

Jiang, N., Huang, F. X., & Zhang, X. (2017). Smoking and the risk of diabetic nephropathy in patients with type 1 and type 2 diabetes: A meta-analysis of observational studies. *Oncotarget, 8*(54), 93209.

Jneid, S., Jabbour, H., Hajj, A., Sarkis, A., Licha, H., Hallit, S., & Khabbaz, L. R. (2018). Quality of life and its association with treatment satisfaction, adherence to medication, and trust in physician among patients with hypertension: A cross-sectional designed study. *Journal of Cardiovascular Pharmacology and Therapeutics, 23*(6), 532-542.

Jun, W. (2019). Quality control circle improves self-monitoring of blood glucose in type 2 diabetic patients. *Australian Journal of Advanced Nursing, 36*(3), 22-28.

Kaiser Family Foundation. (2019). KFF Health Tracking Poll – February 2019: Prescription Drugs. Retrieved May 11, 2019, from KFF Health Tracking Poll – February 2019: Prescription Drugs

Kang, H., Lobo, J. M., Kim, S. H., & Sohn, M. (2018). Cost-Related medication non-adherence among US adults with Diabetes. *Diabetes Research and Clinical practice, 143*, 24-33. https://doi.org/10.1016/j.diabres.2018.06.016

Kennedy-Martin, T., Boye, K. S., & Peng, X. (2017). Cost of medication adherence and persistence in type 2 diabetes mellitus: A literature review. *Patient Preference and Adherence, 11*, 1103-1117. https://doi.org/10.2147/PPA.S136639

Kent, D. M., Steyerberg, E. W., & Shah, N. D. (2018). Big data and predictive analytics recalibrating expectations. *Journal of the American Medical Association*.

Kesselheim, A. S., Avorn, J., & Sarpatwari, A. (2016). The high cost of prescription drugs in the United States : Origins and prospects for reform *Journal of the American Medical Association, 316*(8), 858-871. https://doi.org/10.1001/jama.2016.11237

Kind, A. J. H., Jencks, S., Brock, J., Yu, M., Bartels, C., Ehlenbach, W., Greenberg, C., & Smith, M. (2014). Neighborhood socioeconomic disadvantage and 30-Day Rehospitalization: A retrospective cohort Study. *Annals of Internal Medicine, 161*(11), 765-774.

Kirkman, M. S., Rowan-Martin, M. T., Levin, R., Fonseca, V. A., Schmittdiel, J. A., Herman, W. H., & Aubert, R. E. (2015, 01/08 09/03/received 12/08/accepted). Determinants of Adherence to Diabetes Medications: Findings from a Large Pharmacy Claims Database. *Diabetes Care, 38*(4), 604-609. https://doi.org/10.2337/dc14-2098

Knowler, W. C., Barrett-Connor, E., Fowler, S. E., Hamman, R. F., Lachin, J. M., Walker, E. A., & Nathan, D. M. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *The New England Journal of Medicine, 346*(6), 393-403.

Koenig, R. J., Peterson, C. M., Jones, R. L., Saudek, C., Lehrman, M., & Cerami, A. (1976). Correlation of glucose regulation and hemoglobin A1c in diabetes mellitus. *New England Journal of Medicine, 295*(8), 417-420.

L&M Policy Research. (2016). Evaluation of the medicare quality bonus payment demonstration. Retrieved May 18, 2019, from Evaluation of the Medicare Quality Bonus Payment Demonstration

Lam, W. Y., & Fresco, P. (2015). Medication adherence measures: An overview. *BioMed Research International, 2015*.

Larsson, S. C., Wallin, A., Håkansson, N., Stackelberg, O., Bäck, M., & Wolk, A. (2018). Type 1 and type 2 diabetes mellitus and incidence of seven cardiovascular diseases. *International Journal of Cardiology, 262*, 66-70.

Lavsa, S. M., Holzworth, A., & Ansani, N. T. (2011). Selection of a validated scale for measuring medication adherence. *Journal of the American Pharmacists Association, 51*(1), 90-94.

Leasher, J. L., Bourne, R. R. A., Flaxman, S. R., Jonas, J. B., Keeffe, J., Naidoo, K., Pesudovs, K., Price, H., White, R. A., & Wong, T. Y. (2016). Global estimates on the number of people blind or visually impaired by diabetic retinopathy: A meta-analysis from 1990 to 2010. *Diabetes Care, 39*(9), 1643-1649.

Lee, R., Wong, T. Y., & Sabanayagam, C. (2015). Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. *Eye and Vision, 2*, 17-17. https://doi.org/10.1186/s40662-015-0026-2

Lee, Y. S. (2018). Socioeconomic Differences among Community-Dwelling Diabetic Adults Screened for Diabetic Retinopathy and Nephropathy : The 2015 Korean

Community Health Survey [Report]. *PloS One*(1). https://doi.org/10.1371/journal.pone.0191496

Li, Y., Geiss, L. S., Burrows, N. R., Rolka, D. B., & Albright, A. (2013). Awareness of prediabetes—United States, 2005–2010. *Morbidity and Mortality Weekly Report, 62*(11), 209.

Liakos, M., & Parikh, P. B. (2018, 2018/06/16). Gender disparities in presentation, management, and outcomes of acute myocardial infarction. *Current Cardiology Reports, 20*(8), 64. https://doi.org/10.1007/s11886-018-1006-7

Lin, Y., Chen, H., Brown, R. A., Li, S., & Yang, H. (2017). Healthcare predictive analytics for risk profiling in chronic care: A bayesian multitask learning approach. *MIS Quarterly, 41*(2).

Liska, J., Gupta, A., Thomson, A., Samson, S. I., Mills, H. G., Greenberg, M. E., Kamkolkar, M., Beal, A. C., & Beaudin, M. (2018). Using Google cloud and predictive analytics to promote influenza vaccination among people with diabetes. *Diabetes* Jul 2018, 67 (Supplement 1) 1595-P; DOI**:** 10.2337/db18-1595-P

Luo, M., Lim, W. Y., Tan, C. S., Ning, Y., Chia, K. S., van Dam, R. M., Tang, W. E., Tan, N. C., Chen, R., & Tai, E. S. (2017). Longitudinal trends in Hba1c and associations with comorbidity and all-cause mortality in Asian patients with type 2 diabetes: A cohort study. *Diabetes Research and Clinical Practice, 133*, 69-77.

Maas, A. H. E. M., & Appelman, Y. E. A. (2010). Gender differences in coronary heart disease. *Netherlands Heart Journal, 18*(12), 598-602. https://doi.org/10.1007/s12471-010-0841-y

Maca, V. M., Diaz, V. G., Espada, J. P., & Semwal, V. B. (2016). Measurement of Viewer Sentiment to Improve the Quality of Television and Interactive Content Using Adaptive Content. 2016 International Conference on Electrical, Electronics, and Optimization Techniques Chennai, India.

Maki, D. G. (2017). HbA1c has low accuracy for prediabetes; lifestyle programs and metformin reduce progression to T2DM. *Annals of Internal Medicine*, *166*(8), JC41-JC41.

Malkani, S., & Mordes, J. P. (2011). The implications of using hemoglobin A1c for diagnosing diabetes mellitus. *The American Journal of Medicine, 124*(5), 395-401. https://doi.org/10.1016/j.amjmed.2010.11.025

Marrazzo, J. M., Ramjee, G., Richardson, B. A., Gomez, K., Mgodi, N., Nair, G., Palanee, T., Nakabiito, C., Van Der Straten, A., & Noguchi, L. (2015). Tenofovir-based preexposure prophylaxis for HIV infection among African women. *New England Journal of Medicine, 372*(6), 509-518.

Martin, B. C., Wiley-Exley, E. K., Richards, S., Domino, M. E., Carey, T. S., & Sleath, B. L. (2009). Contrasting measures of adherence with simple drug use, medication switching, and therapeutic duplication. *Annals of Pharmacotherapy, 43*(1), 36-44.

McBrien, K. A., Naugler, C., Ivers, N., Weaver, R. G., Campbell, D., Desveaux, L., Hemmelgarn, B. R., Edwards, A. L., Saad, N., & Nicholas, D. (2017). Barriers to care in patients with diabetes and poor glycemic control—a cross-sectional survey. *PloS One, 12*(5), e0176135.

McHorney, C. A., & Spain, C. V. (2011). Frequency of and reasons for medication non□ fulfillment and non□persistence among American adults with chronic disease in 2008. *Health Expectations, 14*(3), 307-320.

McRae-Clark, A. L., Baker, N. L., Sonne, S. C., DeVane, C. L., Wagner, A., & Norton, J. M. (2015). Concordance of direct and indirect measures of medication adherence in a treatment trial for cannabis dependence. *Journal of Substance Abuse Treatment, 57*, 70-74. https://doi.org/10.1016/j.jsat.2015.05.002

Medline Plus. (2016). Diabetes Type 2 Retrieved April 20, 2019, from https://medlineplus.gov/diabetestype2.html

Medline Plus. (2018). Hemoglobin A1c (Hba1c) Test. Retrieved April 27, 2019, from https://medlineplus.gov/lab-tests/hemoglobin-a1c-hba1c-test/

Molitch, M. E., DeFronzo, R. A., Franz, M. J., & Keane, W. F. (2004). Nephropathy in diabetes. *Diabetes Care, 27*, S79.

Morisky, D. E., Ang, A., Krousel□Wood, M., & Ward, H. J. (2008). Predictive validity of a medication adherence measure in an outpatient setting. *The Journal of Clinical Hypertension, 10*(5), 348-354.

Morisky, D. E., Green, L. W., & Levine, D. M. (1986). Concurrent and predictive validity of a self-reported measure of medication adherence. *Medical Care, 24*(1), 67-74.

Mottl, A. K., Pajewski, N., Fonseca, V. A., Ismail-Beigi, F., Chew, E., Ambrosius, W. T., Greven, C., Schubart, U., & Buse, J. (2014). The degree of retinopathy is equally predictive for renal and macrovascular outcomes in the accord trial. *Journal of Diabetes and its Complications, 28*(6), 874-879.

Na, K., Yoo, C., Park, J. J., & Kim, Y. Y. (2018, 04/01/April 2018). Eye drop dispenser type and medication possession ratio in patients with glaucoma: Single-Use containers versus multiple-use bottles. *American Journal of Ophthalmology, 188*, 9-18. https://doi.org/10.1016/j.ajo.2018.01.011

Nam, S., Chesla, C., Stotts, N. A., Kroon, L., & Janson, S. L. (2011). Barriers to diabetes management: Patient and provider factors. *Diabetes Research and Clinical Practice, 93*(1), 1-9.

Nandyala, A. S., Nelson, L. A., Lagotte, A. E., & Osborn, C. Y. (2018). An analysis of whether health literacy and numeracy are associated with diabetes medication adherence. *Health Literacy Research and Practice, 2*(1), e15-e20.

National Academies of Sciences Engineering Medicine. (2018). *A Proposed Framework for Integration of Quality Performance Measures for Health Literacy, Cultural*

Competence, and Language Access Services: Proceedings of a Workshop. National Academies Press.

National Center for Chronic Disease Prevention. (2016). Diabetes. Retrieved October 2, 2018, from https://www.cdc.gov/chronicdisease/resources/publications/aag/diabetes.htm

National Center for Quality Assurance. (2018a). Hedis and Performance Measurement. Retrieved January 29, 2018, from https://www.ncqa.org/hedis/

National Center for Quality Assurance. (2018b). Ncqa's Health Insurance Plan Ratings 2018-2019. Retrieved January 29, 2019, from https://www.ncqa.org/hedis/reports-and-research/ratings-methodology-and-guidelines/

National Center for Quality Assurance. (2018c). Statin Therapy for Patients with Cardiovascular Disease and Diabetes (Spc/Spd). Retrieved December 18, 2018, from https://www.ncqa.org/hedis/measures/statin-therapy-for-patients-with-cardiovascular-disease-and-diabetes/

National Committee for Quality Assurance. (2018a). Hedis® & Performance Measurement. Retrieved June 11, 2018, from https://www.ncqa.org/about-ncqa

National Committee for Quality Assurance. (2018b). Ncqa Health Insurance Plan Ratings Methodology July 2018. Retrieved May 19, 2019, from https://www.ncqa.org/wp-content/uploads/2018/09/201808013_Health_Plan_Ratings_Methodology.pdf

National Committee for Quality Assurance. (2019a). Comprehensive Diabetes Care (Cdc). Retrieved 2019, May 18, from https://www.ncqa.org/hedis/measures/comprehensive-diabetes-care/

National Committee for Quality Assurance. (2019b). Hedis Measures and Technical Resource. Retrieved May 18, 2019, from https://www.ncqa.org/hedis/measures/

National Committee for Quality Assurance. (2019c). Ncqa's Health Insurance Plan Ratings 2019-2020. Retrieved May 18, 2019, from https://www.ncqa.org/hedis/reports-and-research/ratings-methodology-and-guidelines/

National Institute of Diabetes and Digestive and Kidney Diseases. (2016a). Diabetes Tests & Diagnosis. Retrieved April 27, 2019, from https://www.niddk.nih.gov/health-information/diabetes/overview/tests-diagnosis

National Institute of Diabetes and Digestive and Kidney Diseases. (2016b). What Is Diabetes? Retrieved April 20, 2019, from https://www.niddk.nih.gov/health-information/diabetes/overview/what-is-diabetes

National Institute of Diabetes and Digestive and Kidney Diseases. (2017). Diabetes Statistics. Retrieved https://www.niddk.nih.gov/health-information/health-statistics/diabetes-statistics

National Institute of Diabetes and Digestive and Kidney Diseases. (2018). Diabetes Complications Retrieved September 8, 2018, from https://medlineplus.gov/diabetescomplications.html

National Institute of Medicine. (2001). *Crossing the Quality Chasm : A New Health System for the 21st Century* [Bibliographies Non-fiction Electronic document]. National Academy Press,. https://ezp.waldenulibrary.org/login?url=https://search.ebscohost.com/login.aspx?direct=true&db=cat06423a&AN=wal.EBC3375215&site=eds-live&scope=site

http://ebookcentral.proquest.com/lib/waldenu/detail.action?docID=3375215

Nau, D. P. (2012). Proportion of Days Covered (Pdc) as a Preferred Method of Measuring Medication Adherence. Retrieved May 18, 2019, from http://www.pqaalliance.org/files/PDCvsMPRfinal.pdf

Nichols, G. A., Rosales, A. G., Kimes, T. M., Tunceli, K., Kurtyka, K., & Mavros, P. (2016). The change in Hba1c associated with initial adherence and subsequent Change in Adherence among Diabetes Patients Newly Initiating Metformin therapy. *Journal of Diabetes Research*, 1-5. https://doi.org/10.1155/2016/9687815

Nitzan, O., Elias, M., Chazan, B., & Saliba, W. (2015). Urinary tract infections in patients with type 2 diabetes mellitus: Review of prevalence, diagnosis, and management. *Diabetes, Metabolic Syndrome and Obesity : Targets and Therapy, 8*, 129-136. https://doi.org/10.2147/DMSO.S51792

O'Brien, R. M. (2007). A caution regarding rules of thumb for variance inflation factors. *Quality & Quantity, 41*(41), 673-690. https://doi.org/10.1007/s11135-006-9018-6

O'Brien, R. M. (2007). A caution regarding rules of thumb for variance inflation factors. *Quality & Quantity, 41*(5), 673-690.

Ongsulee, P., Chotchaung, V., Bamrungsi, E., & Rodcheewit, T. (2018). *Big Data, Predictive Analytics and Machine Learning* [Conference](978-1-5386-7159-7 2157-099X). (16th International Conference on ICT and Knowledge Engineering Issue. https://ezp.waldenulibrary.org/login?url=https://search.ebscohost.com/login.aspx?direct=true&db=edseee&AN=edseee.8612393&site=eds-live&scope=site

Osborne, J. W., & Waters, E. (2002). Four assumptions of multiple regression that researchers should always test. *Practical Assessment, Research, and Evaluation, 8*(1), 2.

Pang, H., & Jung, S. (2013). Sample size considerations of prediction-validation methods in high-dimensional data for survival outcomes. *Genetic Epidemiology, 37*(3), 276-282. https://doi.org/10.1002/gepi.21721

Patel, N. (2018). The Difference between Primary Measures of Medication Adherence: PDC and MPR Retrieved May 12, 2019, from https://www.usciences.edu/blog/noteworthy/posts/the-difference-between-primary-measures-of-medication-adherence-pdc-and-mpr.html

Patient Protection and Affordable Care Act (2010). Patient protection and affordable care act. Public law. Washington, DC., Government Printing Office. 111**:** 759-762

Peck, R., Olsen, C., & Devore, J. L. (2012). *Introduction to Statistics and Data Analysis*. Cengage Learning.

Picard, R. R., & Berk, K. N. (1990, 5/1/1990). Data splitting. *The American Statistician, 44*(2), 140-147. https://doi.org/10.1080/00031305.1990.10475704

Polonsky, W. H., & Henry, R. R. (2016). Poor medication adherence in type 2 diabetes: Recognizing the scope of the problem and its key contributors. *Patient Preference and Adherence, 2016*(Issue 1), 1299. https://ezp.waldenulibrary.org/login?url=https://search.ebscohost.com/login.aspx?direct=true&db=edsdoj&AN=edsdoj.028463f3e84f4b5bb13041b5398bc9d5&site=eds-live&scope=site

Pop-Busui, R., Boulton, A. J. M., Feldman, E. L., Bril, V., Freeman, R., Malik, R. A., Sosenko, J. M., & Ziegler, D. (2017). Diabetic neuropathy : A position statement by the American Diabetes Association. *Diabetes Care, 40*(1), 136-154.

Pruitt, Z., Lyons Taylor, P., & Bryant, K. M. (2018). A Managed Care Organization's Call Center–Based Social Support Role. *The American Journal of Accountable Care, 6*(1), e16-e22. https://www.ajmc.com/journals/ajac/2018/2018-vol6-n1/a-managed-care-organizations-call-center-based-social-support-role

Rahbar, S., Blumenfeld, O., & Ranney, H. M. (1969). Studies of an unusual hemoglobin in patients with diabetes mellitus. *Biochemical and Biophysical Research Communications, 36*(5), 838-843.

Ramos, M., Foos, V., Ferrufino, C., Yu-Isenberg, K., & Lamotte, M. (2018). The relationship between poor adherence and Hba1c and weight changes in patients with type 2 diabetes. *Values in Health, 21*, S138-S138. https://doi.org/10.1016/j.jval.2018.09.821

Riddle, M. C., & Herman, W. H. (2018). The cost of diabetes care—an elephant in the room. *Diabetes Care, 41*(5), 929-932.

Risser, J., Jacobson, T. A., & Kripalani, S. (2007). Development and psychometric evaluation of the self-efficacy for appropriate medication use scale (Seams) in low-literacy patients with chronic disease. *Journal of Nursing Measurement, 15*(3), 203.

Rowan, P., Hsu, R., Masaoay, T., & Parver, S. (2021). *Quality Rating Systems in Medicaid Managed Care*. M. P. Research.

Saeed, A., Sun, W., Agarwala, A., Virani, S. S., Nambi, V., Coresh, J., Selvin, E., Boerwinkle, E., Jones, P. H., & Ballantyne, C. M. (2019). Lipoprotein (a) levels and risk of cardiovascular disease events in individuals with diabetes mellitus or prediabetes: The atherosclerosis risk in communities study. *Atherosclerosis, 282*, 52-56.

Safi, S. Z., Qvist, R., Kumar, S., Batumalaie, K., & Ismail, I. S. B. (2014). Molecular mechanisms of diabetic retinopathy, general preventive strategies, and novel therapeutic targets. *BioMed Research International, 2014*, 801269-801269. https://doi.org/10.1155/2014/801269

Saleem, M., & Daniel, B. (2011). Prevalence of urinary tract infection among patients with diabetes in Bangalore City. *International Journal of Emerging Sciences, 1*(2), 133.

Schober, P., Bossers, S. M., & Schwarte, L. A. (2018). Statistical significance versus clinical importance of observed effect sizes: What do p values and confidence intervals really represent? *Anesthesia and Analgesia, 126*(3), 1068.

Schoenfeld, E. R., Greene, J. M., Wu, S. Y., & Leske, M. C. (2001). Patterns of adherence to diabetes vision care guidelines: Baseline findings from the diabetic retinopathy awareness program. *Ophthalmology, 108*(3), 563-571.

Seuring, T., Archangelidi, O., & Suhrcke, M. (2015). The economic costs of type 2 diabetes: A global systematic review. *Pharmacoeconomics, 33*(8), 811-831.

Sheppard, T., Tamblyn, R., Abrahamowicz, M., Lunt, M., Sperrin, M., & Dixon, W. G. (2017). A comparison of methods for estimating the temporal change in a continuous variable: Example of Hba1c in patients with diabetes. *Pharmacoepidemiology and Drug Safety, 26*(12), 1474-1482.

Shih, C., Chen, H., Kuo, S., Ou, S., & Chen, Y. (2016). Cardiovascular outcomes of Dipeptidyl Peptidase-4 Inhibitors in elderly patients with type 2 diabetes: A nationwides. *Journal of the American Medical Directors Association, 17*(1), 59-64.

Shiyanbola, O. O., Unni, E., Huang, Y., & Lanier, C. (2018). The association of health literacy with illness perceptions, medication beliefs, and medication adherence among individuals with type 2 diabetes. *Research in Social and Administrative Pharmacy, 14*(9), 824-830. https://doi.org/10.1016/j.sapharm.2017.12.005

Simoni, J. M., Huh, D., Wang, Y., Wilson, I. B., Reynolds, N. R., Remien, R. H., Goggin, K., Gross, R., Rosen, M. I., Schneiderman, N., Arnsten, J., Golin, C. E., Erlen, J. A., Bangsberg, D. R., & Liu, H. (2014). The validity of self-reported medication adherence as an outcome in clinical trials of adherence-promotion interventions: Findings from the Mach14 Study. *AIDS and Behavior, 18*(12), 2285-2290. https://doi.org/10.1007/s10461-014-0905-x

Skaer, T. L., Sclar, D. A., Robison, L. M., Markowski, D. J., & Won, J. K. (1993). Effect of pharmaceutical formulation for Diltiazem on health care expenditures for hypertension. *Clinical Therapeutics, 15*(5), 905-911.

Smith, V., Gifford, K., Ellis, E., Rudowitz, R., Snyder, L., & Hinton, E. (2015). *Medicaid Reforms to Expand Coverage Control, Costs, and Improve Care: Results from a 50-State Medicaid Budget Survey for State Fiscal Years 2015 and 2016*. K. F. Foundation. https://www.kff.org/medicaid/report/medicaid-reforms-to-expand-

coverage-control-costs-and-improve-care-results-from-a-50-state-medicaid-budget-survey-for-state-fiscal-years-2015-and-2016/

Smith, V., Gifford, K., Ellis, E., Rudowitz, R., Snyder, L., & Hinton, E. (2019). Medicaid Reforms to Expand Coverage, Control Costs and Improve Care: Results from a 50-State Medicaid Budget Survey for State Fiscal Years 2015 and 2016. Retrieved May 18, 2019, from https://www.kff.org/report-section/medicaid-reforms-to-expand-coverage-control-costs-and-improve-care-managed-care-reforms/

Solomon, S. D., Chew, E., Duh, E. J., Sobrin, L., Sun, J. K., VanderBeek, B. L., Wykoff, C. C., & Gardner, T. W. (2017). Diabetic retinopathy: A position statement by the American Diabetes Association. *Diabetes Care, 40*(3), 412-418.

Sorbero, M. E., Kranz, A. M., Bouskill, K. E., Ross, R., Palimaru, A. I., & Meye A. (2018). *Addressing Social Determinants of Health Needs of Dually Enrolled Beneficiaries in Medicare Advantage Plan*. https://aspe.hhs.gov/system/files/pdf/259896/MAStudy_Phase2_RR2634-final.pdf

Srinivasan, A. T. S. M. (2018). A predictive analytics system to predicti re-admission to hospital for diabetes treatment. *Journal Current Science, 19*(12).

Stetson, B., Boren, S., Leventhal, H., Schlundt, D., Glasgow, R. E., Fisher, E., Iannotti, R., Randal, D., Kent, D., & Lumber, T. (2010). Embracing the evidence on problem solving in diabetes self-management education and support. *Self Care Journal, 1*(3), 83-99

Stuart, B., Yin, X., Davidoff, A., Simoni-Wastila, L., Zuckerman, I., Shoemaker, J. S., & Doshi, J. (2012). Impact of Part D low-income subsidies on medication patterns for medicare beneficiaries with diabetes. *Medical Care, 50*(11), 913-919.

Stuart, B. C., Dai, M., Xu, J., E Loh, F., & S Dougherty, J. (2015). Does good medication adherence really save payers money? *Medical Care, 53*(6), 517-523.

Sullivan, P. W., & Ghushchyan, V. H. (2016). Eq-5d scores for diabetes-related comorbidities. *Value in Health, 19*(8), 1002-1008.

Talaei-Khoei, A., & Wilson, J. M. (2018). Identifying people at risk of developing type 2 diabetes: A comparison of predictive analytics techniques and predictor variables. *International Journal of Medical Informatics, 119*, 22-38.

Tandon, S., Chew, M., Eklu-Gadegbeku, C. K., Shermock, K. M., & Morisky, D. E. (2015). Validation and psychometric properties of the 8-Item Morisky Medication Adherence Scale (Mmas-8) in type 2 diabetes patients in Sub-Saharan Africa. *Diabetes Research and Clinical Practice, 110*(2), 129-136.

Ting, D. S. W., Cheung, G. C. M., & Wong, T. Y. (2016). Diabetic Retinopathy: Global prevalence, major risk factors, screening practices and public health challenges: A review. *Clinical & Experimental Ophthalmology, 44*(4), 260-277.

Tseng, E., Greer, R. C., O'Rourke, P., Yeh, H., McGuire, M. M., Clark, J. M., & Maruthur, N. M. (2017, 2017/11/01). Survey of primary care providers' knowledge of screening for, diagnosing and managing prediabetes. *Journal of General Internal Medicine, 32*(11), 1172-1178. https://doi.org/10.1007/s11606-017-4103-1

U.S. Census Department. (n.d.). How Does the Us Census Bureau Define Rural? Retrieved April 26, 2020, from https://gis-portal.data.census.gov/arcgis/apps/MapSeries/index.html?appid=7a41374f6b03456e9d138cb014711e01

U.S. Department of Health and Human Services. (2020). Poverty Guidelines. Retrieved May 3, 2020, from https://aspe.hhs.gov/poverty-guidelines

Udanor, C., Aneke, S., & Ogbuokiri, B. O. (2016). Determining social media impact on the politics of developing countries using social network analytics. *Program, 50*(4), 481-507.

Vlassara, H. (1992). Receptor-mediated interactions of advanced glycosylation end products with cellular components within diabetic tissues. *Diabetes, 41*(Supplement 2), 52-56.

Wagner, W. E. (2016). *Using Ibm® Spss® Statistics for Research Methods and Social Science Statistics*. Sage Publications.

Wang, L., Wei, W., Miao, R., Xie, L., & Baser, O. (2013). Real-world outcomes of US employees with type 2 diabetes mellitus treated with Insulin Glargine or Neutral Protamine Hagedorn insulin: A comparative retrospective database study. *BMJ Open, 3*(4), e002348.

Warner, R. M. (2013). *Applied Statistics from Bivariate Throught Multivariate Techniques* (2nd ed.). Sage Publications, Inc.

Weisberg, S. (2005). *Applied Linear Regression* (Vol. 528). John Wiley & Sons.

World Health Organization. (2006). *Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycemia*. W. H. Organization. http://apps.who.int/iris/bitstream/handle/10665/43588/9241594934_eng.pdf?sequence=1

Wrege, C. D. (1980). The Efficient Management of Hospitals: Pioneer Work of Ernest Codman, Robert Dickinson, and Frank Gilbreth; 1910-1918. *Academy of Management Proceedings*, 114. https://ezp.waldenulibrary.org/login?url=https://search.ebscohost.com/login.aspx?direct=true&db=edb&AN=4976161&site=eds-live&scope=site

Yap, A. F., Thirumoorthy, T., & Kwan, Y. H. (2016). Systematic review of the barriers affecting medication adherence in older adults. *Geriatrics & gerontology International, 16*(10), 1093-1101.

Yau, J. W., Rogers, S. L., Kawasaki, R., Lamoureux, E. L., Kowalski, J. W., Bek, T., Chen, S., Dekker, J. M., Fletcher, A., & Grauslund, J. (2012). Global prevalence

and major risk factors of diabetic retinopathy. *Diabetes Care*, DC_111909. https://doi.org/https://doi.org/10.2337/dc11-1909

Yeam, C. T., Chia, S., Tan, H. C. C., Kwan, Y. H., Fong, W., & Seng, J. J. B. (2018). A systematic review of factors affecting medication adherence among patients with osteoporosis. *Osteoporosis International, 29*(12), 2623-2637.

Zeng, F., An, J., Scully, R., Barrington, C., Patel, B. V., & Nichol, M. B. (2010). The impact of value□based benefit design on adherence to diabetes aedications: A propensity score□weighted difference in difference evaluation. *Value in Health, 13*(6), 846-852.

Appendix A : ADA Manuscript Submission Form

American Diabetes Association | Manuscript Submission Form

Please complete this form and upload it with your submission. Questions regarding this form or its contents should be sent to the Editorial Office at EditorialOffice@diabetes.org.

Journal:

Manuscript #:

Title:

Author List:

1. Statement of Originality and Authorship

We have read and understand the policies and procedures outlined in the journal's online instructions for authors. We approve the submission of this manuscript to the American Diabetes Association (ADA) for publication and have taken due care to ensure the integrity of this work.

We attest that each author has made an important scientific contribution to the study and has assisted with the drafting or revising of the manuscript, in accordance with the definition of an author as stated by the International Committee of Medical Journal Editors (ICMJE) at http://www.icmje.org/recommendations/. The contributions of each individual Author are described in the manuscript.

We confirm that neither the manuscript nor any part of it has been published or is under consideration for publication elsewhere (abstracts excluded). Any reference to or use of previously published material protected by copyright is explicitly acknowledged in the manuscript. Posting of submitted material on a Web site may be considered prior publication and should be noted in the comments to the editor upon submission.

2. Potential Conflict of Interest Disclosure

We confirm that potential conflicts of interest for all Authors, or acknowledgment that no conflicts exist, are included in the manuscript's Acknowledgments section. Disclosures include relationships with a company whose products or services are related to the subject matter of the manuscript. Company is defined as a for-profit concern engaged in the development, manufacture, or sale of pharmaceutical or biomedical devices or supplies. Please refer to the "Publications Policies and Procedures" document on the journal's online instructions for authors for examples of relevant duality of interest.

3. Copyright Assignment Agreement (select one)

We hereby assign all rights, including but not limited to the copyright, for this manuscript to ADA upon its acceptance for publication. The rights assigned include, but are not limited to, the sole and exclusive rights to license, sell, subsequently assign, derive, distribute, display, and reproduce this manuscript, in whole or in part, in any format, electronic or otherwise, including formats not in existence at the time this agreement was signed. The Authors hereby warrant that they have not granted or assigned, and shall not grant or assign, the aforementioned rights to any other person, firm, organization, or other entity.

Reuse. Authors are permitted to reuse portions of their ADA-copyrighted work, including tables and figures, in their own work, and to reuse portions or all of their ADA-copyrighted work for educational purposes, provided that the proper citation and copyright information is given.

Post-prints. Authors are permitted to submit the final, *accepted version of their manuscript* to their funding body, such as NIH, or institution for inclusion in their funding body or institution's database, archive, or repository, or to post the final, accepted version on their personal Web site. These manuscripts may be made freely accessible to the public upon acceptance. See the journal's online instructions for authors for more information.

Work Made for Hire

Authorized Representative:

This work was produced for an employer as a "work made for hire." An authorized representative of that employer must sign here to indicate copyright assignment on behalf of the authors. The employer of the author(s) is permitted to transmit the work on an internal, secure network for use by its employees only, provided that such use is for the promotion of its business enterprise and does not imply endorsement by ADA.

Government Employee

This work was produced by an employee of the United States Government as part of his/her official duties. No copyright exists, and therefore it cannot be transferred.

The Authors agree to the terms outlined in this document and have provided consent to authorize the Corresponding Author to act on behalf of all Authors and enter into this agreement.

Electronically signed for and on behalf of the Authors:

Date:

Appendix B: ICMJY Conflict of Interest Disclosure

ICMJE INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

SAVE

ICMJE Form for Disclosure of Potential Conflicts of Interest

Instructions

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form is designed to be completed electronically and stored electronically. It contains programming that allows appropriate data display. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in six parts.

1. Identifying information.

2. The work under consideration for publication.

This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking "No" means that you did the work without receiving any financial support from any third party – that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check "Yes".

3. Relevant financial activities outside the submitted work.

This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer.

Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work's sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed. For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Intellectual Property.

This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

5. Relationships not covered above.

Use this section to report other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work.

Definitions.

Entity: government agency, foundation, commercial sponsor, academic institution, etc.
Grant: A grant from an entity, generally [but not always] paid to your organization
Personal Fees: Monies paid to you for services rendered, generally honoraria, royalties, or fees for consulting, lectures, speakers bureaus, expert testimony, employment, or other affiliations
Non-Financial Support: Examples include drugs/equipment supplied by the entity, travel paid by the entity, writing assistance, administrative support, etc.
Other: Anything not covered under the previous three boxes
Pending: The patent has been filed but not issued
Issued: The patent has been issued by the agency
Licensed: The patent has been licensed to an entity, whether earning royalties or not
Royalties: Funds are coming in to you or your institution due to your patent

Appendix C: National Association for Healthcare Quality Conflict Form

NATIONAL ASSOCIATION FOR HEALTHCARE QUALITY

Conflict of Interest Disclosure Form

*NAME:*_____

I affirm that the following are all my (including anyone with whom I directly share income) material business, financial and organizational interests and affiliations which are or could be construed to be reasonably related to the interests, activities and programs of NAHQ or healthcare quality:

(Please answer the following questions or provide substantially the same information in some other form (e.g. by attaching a vita). If you have no information to list, answer "None.")

1. Business Interests

a. Any employment or consulting arrangements that are current, proposed, or occurred within the previous three (3) years, that reasonably involve the interests of NAHQ.

_____

_____

b. Any honoraria or payments received for presentations, speeches or appearances that are current, proposed, or occurred within the previous three (3) years, that reasonably involve the interests of NAHQ and are or were more than $5,000.00 per year or $10,000.00 over a three-year period.

_____

_____

2. Financial Interests

a. Any material ownership interests in a commercial entity that reasonably may be anticipated to conflict with the interests of NAHQ. Do not report dollar amounts or percentages.

_____

_____

b. Any research funding that you are about to receive or have received within the past three (3) years and that you know has been received, or is about to be received, by others at your institution(s), which reasonably may be anticipated to conflict with the interests of NAHQ.

_____

_____

c. Any travel grants you have received within the past year.

_____

_____