The Thesis committee for Kristin Anne Hanson

Certifies that this is the approved version of the following thesis:

Evaluation of a Pharmacist-led Medication Management Program in High-risk Diabetic Patients: Impact on Clinical Outcomes, Medication Adherence, and Pharmacy Costs

APPROVED BY

SUPERVISING COMMITTEE:

_____

Co-Supervisor: James P. Wilson

_____

Co-Supervisor: Karen L. Rascati

_____

Paul J. Godley

_____

Barry A. Browne

Evaluation of a Pharmacist-led Medication Management Program in High-risk Diabetic Patients: Impact on Clinical Outcomes, Medication Adherence, and Pharmacy Costs

by

Kristin Anne Hanson, Pharm.D.

Thesis

Presented to the Faculty of the Graduate School of

The University of Texas at Austin

in Partial Fulfillment

of the Requirements

for the Degree of

Master of Science in Pharmacy

The University of Texas at Austin

December 2009

I dedicate this thesis to my mother,

Lila Hanson

For her unconditional love and support,

For encouraging me to reach for my dreams,

And for giving me the strength to persevere.

Acknowledgements

I would like to thank Dr. Paul Godley, Dr. Barry Browne, Dr. Jim Wilson, and Dr. Karen Rascati for their guidance and support throughout my fellowship and for serving on my thesis committee.

I would also like to thank Dr. Tricia Tabor and Dr. Joyce Juan for leading the creation and implementation of the medication management program. In addition, I thank all of the clinical pharmacists providing care to the patients in the program, for, without the time and effort of each of these individuals, this project would not have been possible.

A special thanks as well goes to Dr. Cat Bui, Dr. Yoona Kim, and Mrs. Sheree Thomas and her data analytics team for their efforts and assistance in screening patients, verifying continuous enrollment, and providing clinical laboratory data for analysis.

Finally, I would like to thank all those who have championed and nurtured the health economics and outcomes research fellowship at Scott & White, The University of Texas at Austin, and Novartis Pharmaceuticals Corporation.

Evaluation of a Pharmacist-led Medication Management Program in High-risk Diabetic Patients: Impact on Clinical Outcomes and Medication Adherence

by

Kristin Anne Hanson, M.S.Phr.

The University of Texas at Austin, 2009

Supervisors: James P. Wilson and Karen L. Rascati

Diabetes mellitus is a group of metabolic disorders caused by a relative or absolute lack of insulin. Currently, 23.6 million Americans have diabetes. Diabetes can lead to serious microvascular and macrovascular complications, such as cardiovascular disease, blindness, kidney disease, lower-limb amputations, and premature death. Due to the potential cardiovascular complications and the high prevalence of co-morbid hypertension and/or hyperlipidemia in patients with diabetes, diabetes management should include close monitoring of blood glucose, blood pressure, and cholesterol levels.

Medical management of diabetic patients is costly; approximately 1 in every 10 health care dollars is currently spent treating diabetes. Studies have shown that in chronic conditions such as diabetes, increased medication use results in demonstrable

improvements in health outcomes, reduced hospitalization rates, and decreased direct health care costs. To date no studies have evaluated the impact of a pharmacist-led intervention on diabetic medication adherence.

The purpose of this investigation was to analyze the impact of a pharmacist-led medication management program on medication adherence and pharmacy costs and to evaluate clinical measures of diabetes, hypertension, and hyperlipidemia. This study was a quasi-experimental, longitudinal, pre-post study, with a control group. Scott & White Health Plan (SWHP) patients with diabetes (type 1 or type 2), poor glycemic control (most recent A1C >7.5%), and living within 30 miles of participating pharmacies were invited to participate in the intervention which consisted of monthly appointments with a clinical pharmacist and a co-payment waiver for all diabetes medications and testing supplies. A total of 118 patients met study inclusion criteria and were enrolled in the intervention between August 2006 and July 2008. Intervention patients were matched on sex and age to SWHP patients with poor diabetes control living more than 30 miles from a participating pharmacy. To measure the impact of the intervention, medical and pharmacy data were evaluated for one year before and after the study enrollment date.

A significant difference was seen in the percentage of patients with type 1 diabetes in the intervention group (14) and the control group (3). The medication management program significantly improved A1C levels in intervention patients relative to controls (-1.1% vs. 0.6%) and was more effective in lowering A1Cs in type 2 diabetics than type 1 patients. Although the generalized linear model did not show that the intervention significantly improved the percentage of patients achieving the ADA goal

A1C of <7% compared to controls, the multivariate logistic regression, which controlled for factors such as diabetes type, showed that patients participating in the intervention were 8.7 times more likely to achieve the A1C goal. Persistence with diabetic medications and the number of medications taken significantly increased in the intervention group; however, adherence rates, as measured by medication possession ratio (MPR), did not significantly improve relative to controls. The expenditure on diabetic medications and testing supplies increased substantially more in the intervention group than in the control group.

The percentage of patients adherent with antihypertensive medications (MPR ≥80%) increased from 76% to 91% in the intervention group and decreased from 68% to 63% in the control group ($P<0.05$); no significant difference in blood pressure control was observed. For hyperlipidemia medications, adherence and persistence increased and pharmacy costs decreased in both groups, likely due to the introduction of the first generic HMG-CoA reductase inhibitor into the market during the study period. Future research is needed on the impact of the intervention on medical resource utilization and costs.

Table of Contents

List of Tables

List of Figures

CHAPTER ONE: INTRODUCTION

Epidemiology of Diabetes Mellitus

Diabetes mellitus is a group of metabolic disorders caused by a relative or absolute lack of insulin, a hormone that is needed to convert sugar, starches, and other food into energy needed for daily life.[1,2] In response to an increase in blood sugar (for example, after ingestion of food), insulin stimulates muscle and fat cells to remove glucose from the blood and stimulates the liver to metabolize glucose, causing blood sugar to return to normal levels.[3] Without adequate insulin, diabetics experience chronic hyperglycemia, which is associated with long-term damage, dysfunction, and failure of multiple organs.[4] Insulin deficiency may result from a defect in insulin secretion, insulin sensitivity, or both.[5]

Currently, 23.6 million Americans have diabetes, a total which is 8% of the U.S. population. While most diabetics are aware of their condition, about 5.7 million are unaware that they have the disease, and therefore, are not receiving proper medical treatment. Even more alarming is the fact that an additional 57 million Americans are currently pre-diabetic, meaning that if significant lifestyle modifications are not made, those individuals will also become diabetic in the future.[2] Current projections suggest that by 2050, the prevalence of diabetes in the U.S. will increase to 39 million people.[6]

Diabetes is classified as type 1, type 2, gestational, or "other," based on the underlying cause of the disorder. Gestational diabetes occurs in approximately 4% of pregnancies. As the name suggests, gestational diabetes is a glucose intolerance that

begins or is first recognized during pregnancy. In most cases, glucose regulation returns to normal after delivery, but approximately 5-10% of women with gestational diabetes are found to have type 2 diabetes after pregnancy.[2,4] A recent meta-analysis by Bellamy et al. (2009) reported that women with gestational diabetes have a seven-fold increased risk of subsequent development of type 2 diabetes compared to those who maintained normal glycemic levels during pregnancy.[7] "Other" types of diabetes are rare and include cases that arise from the mutation of a single gene.[4] As the vast majority of diabetic patients have type 1 or type 2 diabetes, this thesis will focus solely on the treatment of these two forms of the disorder.

Type 1 Diabetes

Type 1 diabetes results from autoimmune destruction of the pancreatic β-cells and accounts for 5-10% of cases.[1] The rate of β-cell destruction varies between individuals but is commonly rapid in infants and children and slower in adults.[4] Patients with type 1 diabetes generally present with moderate to severe polyuria, polydipsia, polyphagia, fatigue, weight loss, and sometimes blurred vision. At the time of presentation, patients generally have little or no pancreatic reserve, are prone to develop ketoacidosis, and require exogenous insulin to sustain life.[1]

While type 1 diabetes develops most often in children, the disease can occur at any age, is equally likely to affect males and females, and is more common in whites than in nonwhites.[4] A genetic predisposition associated with type 1 diabetes is seen, and these patients are prone to other autoimmune disorders, such as Graves' disease, Hashimoto's

thyroiditis, Addison's disease, vitiligo, and pernicious anemia.[4] In addition, type 1 diabetes is thought to be related to environmental factors that are still poorly defined.

Type 2 Diabetes

Type 2 diabetes accounts for about 90% of cases and is characterized by increased hepatic glucose production, resistance to insulin action, obesity, and β-cell dysfunction.[1] A strong genetic predisposition is associated with this type of diabetes, which is more significant than that seen with type 1 diabetes. Minority populations, such as Hispanics, African Americans, and Native Americans, have a higher prevalence of diabetes and experience a higher rate of diabetic complications than white counterparts.[8] Individuals who develop type 2 diabetes commonly have a history of gestational diabetes, hypertension, and/or dyslipidemia. The risk of developing type 2 diabetes increases with age, weight, and lack of physical activity.[4]

Type 2 diabetes generally develops slowly and commonly goes undiagnosed for many years, because early stages of the disorder are often not severe enough for the patient to notice or recognize the classic signs of hyperglycemia, such as polydipsia, polyuria, and fatigue.[4] Many patients are asymptomatic at the time of diagnosis; however, some present with advanced complications, particularly neuropathy.[5]

The prevalence of type 2 diabetes is growing worldwide, largely as a consequence of a sedentary lifestyle, increased consumption of energy-dense foods, increased obesity, and an aging population.[9,10] The World Health Organization predicts that the number of diabetics worldwide will increase from 143 million in 1997 to 300 million in 2025.[10]

Previous studies have shown that the risk of diabetes is directly related to body weight, with each kilogram increase in weight increasing the risk of diabetes by an estimated 4.5-9%.[8,11] Conversely, intentional weight loss by overweight men and women has been shown to decrease the risk of developing type 2 diabetes; for every 20 pounds lost, the rate of diabetes decreases by 11% and 17% for men and women, respectively.[12]

Burden of Illness

Diabetes can lead to serious microvascular and macrovascular complications, such as cardiovascular disease, blindness, kidney disease, lower-limb amputations, and premature death. According to the CDC, diabetes was the seventh leading cause of death listed on U.S. death certificates in 2006. However, studies have found that only about 35-40% of decedents with diabetes have diabetes noted on the death certificate, therefore, the death rate due to diabetes is likely underreported.[13] Overall, the risk of death for diabetics is approximately twice that of individuals of similar age without diabetes.[13]

Diabetic patients have a 2-4 fold increased risk of heart disease and stroke, and about two-thirds of diabetics have hypertension and some degree of nervous system damage. Diabetes is the leading cause of adult blindness and end-stage renal disease and is responsible for more than half of all lower limb amputations. Abnormalities of lipoprotein metabolism and periodontal disease are also common in diabetics. The physical and emotional impact of diabetes and the demands of therapy may cause significant stress in patients.[2]

Medical management of diabetic patients is costly. In 2007, total direct and indirect costs of diabetes treatment were estimated to be $174 billion per year in the United States. Approximately two-thirds was due to direct medical costs, while $58 billion was attributed to indirect costs such as increased absenteeism, reduced productivity, disease-related unemployment disability, and productivity loss due to early mortality. The $174 billion is an underestimate of the actual cost of diabetes, however, because the total omits the cost of intangibles such as pain and suffering, care provided by non-paid caregivers, and excess medical costs associated with undiagnosed diabetes.[2]

The annual per capita cost of health care for diabetic patients in 2007 in the U.S. was $11,744, with more than half of the money spent directly on diabetes care. On average, the cost of treating a patient with diabetes is 2.3 times greater than the cost of treating a non-diabetic patient. Given the high prevalence of diabetes in the United States, approximately 1 in every 10 health care dollars is currently spent treating diabetes.[2] Therefore, any intervention saving even a small amount of money on a per capita basis for diabetic patients could potentially have a major impact on national health care spending.

Diabetes Treatment Guidelines

The American Diabetes Association (ADA) publishes evidence-based standard of care guidelines as a resource for healthcare professionals treating diabetic patients. Diabetes management encompasses more than blood glucose control, as two out of three patients with diabetes die from heart disease or stroke.[2] Therefore, blood pressure and

cholesterol should also be carefully monitored in diabetic patients. With the care of the patient as a whole in mind, the ADA guidelines provide information that encompasses all aspects of care, from diagnosing patients to treatment of diabetes-related complications and third-party reimbursement. Although specific patient characteristics, such as patient age, co-morbid conditions, and past medical history, may require modification of treatment goals, the ADA guidelines provide target measures that most diabetic patients should strive to achieve. A brief summary of the clinical treatment guidelines relevant to this study is provided below.

Diabetes Care

Diabetic patients should receive collaborative medical care from a health care team which may include physicians, nurse practitioners, physician assistants, nurses, dieticians, and/or pharmacists. A comprehensive diabetes evaluation should be performed at the first medical encounter in order to understand the patient's current health status and formulate a plan to ensure optimal management of the patient (Table 1.1).

The health care team and the patient should create a management plan that is individualized for the patient, taking into consideration their physical, emotional, and social situation. Each management plan should include diabetes self-management education (DSME), as patients must take an active role in their care. Patients should clearly understand treatment goals, and these goals should be obtainable given each patient's unique circumstances.

Table 1.1 Components of the Comprehensive Diabetes Evaluation

Medical History

- Age and characteristics of onset of diabetes (e.g., DKA, asymptomatic laboratory finding)
- Eating patterns, physical activity habits, nutritional status, and weight history; growth and development in children and adolescents
- Diabetes education history
- Review of previous treatment regimens and response to therapy (A1C records)
- DKA frequency, severity, and cause
- Hypoglycemic episodes
    - Hypoglycemic awareness
    - Any severe hypoglycemia: frequency and cause
- History of diabetes-related complications
    - Microvascular: retinopathy, nephropathy, neuropathy (sensory, including history of foot lesions; autonomic, including sexual dysfunction and gastroparesis)
    - Macrovascular: CHD, cerebrovascular disease, PAD
    - Other: psychosocial problems,* dental disease*

Physical Examination

- Height, weight, body mass index
- Blood pressure determination, including orthostatic measurements when indicated
- Fundoscopic examination*
- Thyroid palpation
- Skin examination (for acanthosis nigricans and insulin injection sites)
- Comprehensive foot examination:
    - Inspection
    - Palpation of dorsalis pedis and posterior tibial pulses
    - Presence/absence of patellar and Achilles reflexes
    - Determination of proprioception, vibration, and monofilament sensation

Laboratory Evaluation

- A1C, if results not available within past 2-3 months

If not performed/available within past year:

- Fasting lipid profile, including total, LDL- and HDL-cholesterol and triglycerides
- Liver function tests
- Test for urine albumin excretion with spot urine albumin/creatinine ratio
- Serum creatinine and calculated glomerular filtration rate (GFR)
- Thyroid-stimulating hormone in type 1 diabetes, dyslipidemia or women over age 50

Referrals

- Annual dilated eye exam
- Family planning for women of reproductive age
- Registered dietitian for medical nutrition therapy (MNT)
- Diabetes self-management education
- Dental examination
- Mental health professional, if needed

*See appropriate referrals for these categories.
Source: American Diabetes Association. Standards of Medical Care in Diabetes – 2009[14]
DKA = diabetic ketoacidosis; CHD = coronary heart disease; PAD = peripheral arterial disease

Glycemic control is a key component of diabetic treatment. Glycemic control can be measured using two methods: self-monitoring of blood glucose (SMBG) or a test of glycosylated hemoglobin A1C.

The frequency and timing of SMBG depends on the individual. Most insulin-using patients should test their blood glucose three or more times daily to reach A1C goals safely without hypoglycemic episodes, whereas the utility of frequent SMBG in non-insulin patients is less certain. All patients should have their SMBG technique evaluated, both initially and at regular intervals thereafter. In addition, patients must be taught how to use the SMBG data to appropriately adjust food intake, exercise, or pharmacological therapy to achieve specific glycemic goals. The ability to correctly obtain and use SMBG data should be reevaluated periodically.

The glycosylated hemoglobin (A1C) assay, a time-weighted average of the mean daily blood glucose over the previous three to four months, is the most widely used and reliable means of assessing chronic glycemia in order to make treatment modifications.[15,16] The correlation between A1C and mean blood glucose is presented in Table 1.2.

Table 1.2. Correlation of A1C with Mean Blood Glucose

A1C (%)	Mean Blood Glucose (mg/dL)
6	126
7	154
8	183
9	212
10	240
11	269
12	298

Source: ADA treatment guidelines (2009)[14]

All patients should have A1C testing performed routinely. The frequency of the A1C test depends on the clinical control of the patient, the treatment regimen used, and the judgment of the clinician. In patients who have stable glycemic control and are meeting treatment goals, the A1C test should be performed a minimum of two times a year, whereas, patients not achieving treatment goals and/or whose therapy has changed should have the A1C test quarterly.

The A1C goal for most adults is <7%. This goal is based on studies which show that lowering A1C to below or around 7% reduces microvascular, macrovascular, and neuropathic complications in type 1 and type 2 diabetes. However, less stringent A1C goals may be appropriate for patients with any of the following:

- History of severe hypoglycemia
- Limited life expectancy
- Advanced microvascular or macrovascular complications
- Extensive co-morbid conditions
- Inability to attain A1C <7% despite DSME, appropriate glucose monitoring, and effective doses of multiple glucose-lowering agents, including insulin

The self-monitored blood glucose goal should be a preprandial blood glucose of 70-130 mg/dL and peak postprandial blood glucose <180 mg/dL; both values should be measured 1-2 hours after the beginning of a meal.[14]

Blood Pressure Control

Hypertension is a common co-morbid condition in patients with diabetes. Blood pressure increases when arteries are narrowed and blood flow is restricted. Arterial narrowing may be caused by atherosclerosis, the accumulation of cholesterol, or chronically elevated blood glucose levels. Proper blood pressure control in diabetic patients decreases cardiovascular disease by 33% to 50% and microvascular disease by approximately 33%. Research has shown that for each 10 mmHg reduction in systolic blood pressure, the risk for any complication related to diabetes is reduced by 12%.[13]

For most adults, normal blood pressure is defined as <120/80 mmHg and individuals with a blood pressure ≥140/90 mmHg on two or more consecutive occasions are diagnosed with hypertension. The clinical categories and measurement values for hypertension established by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) are presented in Table 1.3.

Table 1.3. Classification of Blood Pressure for Adults Aged ≥18 Years

Blood Pressure Classification[†]	**SBP (mmHg)**	**DBP (mmHg)**
Normal	<120	<80
Prehypertension	120-139	80-89
Stage 1 hypertension	140-159	90-99
Stage 2 hypertension	≥160	≥100

Source: Chobanian (2003)[17]
SBP = systolic blood pressure; DBP = diastolic blood pressure
[†]If SBP and DBP numbers are not in the same category, the patient is classified as the more severe category.

Due to the synergistic risks of hypertension and diabetes, the diagnostic cutoff for hypertension is 10 mmHg lower for patients with diabetes than non-diabetics (≥130/80 vs. ≥140/90, respectively). Similarly, blood pressure goals are 10 mmHg lower for

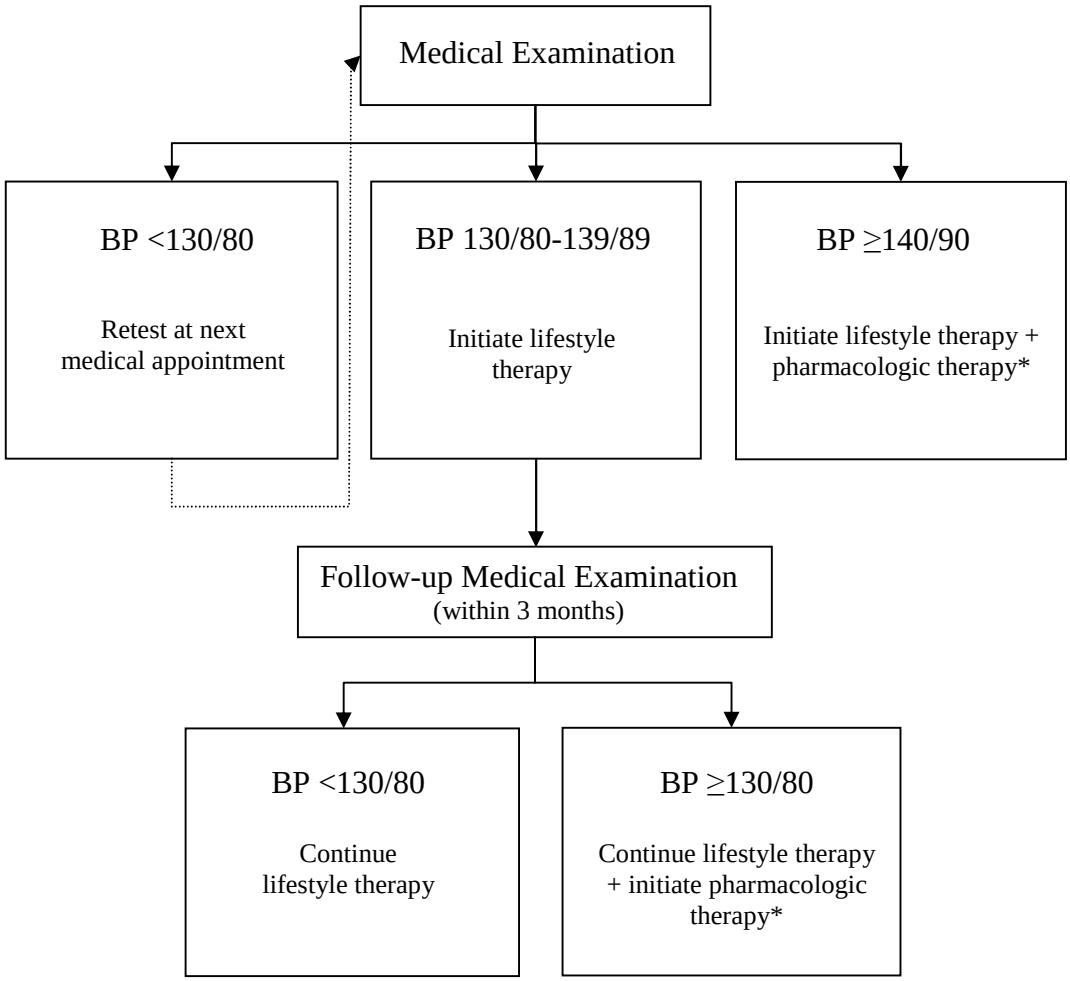
people with diabetes or chronic kidney disease, who have a BP goal of <130/80 vs. <140/90 for non-diabetic adults.[14]

The ADA recommends that most adults with diabetes who have risk factors for CAD, PVD, hypertension, or heart attack should take an 81 mg dose of aspirin daily. In addition, several lifestyle behaviors are recommended in order to treat and prevent hypertension including:[17]

- Maintaining a healthy body weight
- Exercising regularly
- Eating a healthy diet, low in saturated fat, total fat, cholesterol, and sodium and rich in vegetables, fruit, and nonfat dairy, commonly referred to as the DASH (Dietary Approaches to Stop Hypertension) diet
- Quitting smoking
- Keeping alcohol intake at a moderate level
- Practicing good stress management

According to the ADA diabetes treatment guidelines, patients with blood pressures >140/90 should initiate pharmacologic therapy in addition to lifestyle therapy. Most hypertensive patients will require more than one antihypertensive medication to achieve their target blood pressure.[17] Patients with mildly elevated blood pressures (130-139/80-89) should initiate lifestyle therapy. If blood pressures remain elevated (>130/80) after three months of lifestyle therapy, pharmacologic therapy should be initiated (Figure 1.1).

Figure 1.1. Algorithm for Treatment of Blood Pressure in Diabetic Patients



*The pharmacologic therapy regimen should include an angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB). A diuretic may be added to achieve blood pressure targets; use a thiazide diuretic in patients with an estimated GFR ≥30 mL/min per 1.73 m^2 and a loop diuretic in patients with an estimated GFR <30 mL/min per 1.73 m^2.

Source: ADA treatment guidelines (2009)[14]

Blood pressure control is critical because hypertension increases the risk of macrovascular and microvascular complications in diabetic patients. Insulin resistance is a common underlying mechanism for both hypertension and diabetes.[18] In addition, diabetic patients have lower threshold levels for hypertension diagnosis. Therefore, it is not surprising that hypertension is more common in diabetics than among the general population. According to the Centers for Disease Control and Prevention, 75% of adults with self-reported diabetes in 2003-2004 had a blood pressure greater than or equal to the recommended 130/80 mmHg or used prescription medication for hypertension, while the National Health And Nutrition Examination Survey (NHANES) reported a prevalence of hypertension of 29.6% among all adults during that same year.[13,19]

Lipid Management

According to the ADA treatment guidelines, most diabetic patients should have cholesterol measured annually, whereas adults with known low-risk lipid values (LDL cholesterol <100 mg/dL, HDL cholesterol >50 mg/dL, and TG <150 mg/dL) may be tested every 2 years.[14] The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III [ATP III]) has established clinical practice guidelines for cholesterol treatment. The recommended cholesterol levels in these guidelines are represented in Table 1.4.[20]

Table 1.4. ATP III Cholesterol Goal Levels

Cholesterol Type	Cholesterol Goal (mg/dL)
Total cholesterol	<200
LDL cholesterol	<100[†]
HDL cholesterol	≥60
Triglycerides	<150

Source: NCEP ATP III Guidelines (2002)[20]
[†]LDL <100 mg/dL is the goal for patients with coronary heart disease (CHD) or a CHD risk equivalent (i.e. diabetes)

The ADA recommends a LDL cholesterol goal level of <100 mg/dL for most patients with diabetes. However, recent clinical trials have shown that high-risk patients, such as those with acute coronary syndromes or previous cardiovascular events, have a significant reduction in further events when more aggressive therapy, aimed to achieve a LDL cholesterol of <70 mg/dL, is implemented. Therefore, the ADA supports an optional goal of <70 mg/dL in very high-risk diabetic patients with overt CVD.[14]

While high HDL cholesterol levels (≥60 mg/dL) are ideal in that they are considered a "negative risk factor," patients with diabetes are likely to have lower than normal HDL levels and LDL cholesterol control is the source of primary concern in diabetic patients.[20] Therefore, the ADA recommends a lower HDL cholesterol goal level of >40 mg/dL for males and >50 mg/dL for females with diabetes.[14]

Similar to the treatment and prevention of high blood pressure, lifestyle recommendations for hyperlipidemia include: exercise, weight loss (if indicated), smoking cessation, and a healthy diet low in saturated fat, trans unsaturated fat, and cholesterol.[14] Unlike treatment of hypertension, however, pharmacologic treatment is recommended in certain diabetic patients, regardless of patient cholesterol serum concentrations. The ADA recommends HMG-CoA reductase inhibitor ("statin") therapy

in addition to lifestyle change for all diabetic patients with overt CVD and for diabetic patients without CVD who are over the age of 40 and have one or more CVD risk factors.[14]

Medication Adherence

Adherence, compliance, and persistence are three commonly used terms for describing medication-taking behavior. Adherence is defined by the World Health Organization[21] as "the extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes corresponds with agreed recommendations from a health care provider." The terms "adherence" and "compliance" are nearly synonymous. The term "compliance" has fallen into disfavor in recent years, however, because the term suggests a patient is passively and submissively following a physician's orders. The more-positive connotation of "adherence" suggests the patient has a collaborative partnership with the healthcare provider and is actively involved in treatment.[22] "Persistence" is defined as the ability of a patient to take medication for the intended course of therapy, or operationally as the duration of time from initiation to discontinuation of therapy.[23,24] For patients with chronic conditions such as diabetes, the intended course of therapy is often the person's lifetime.

Medication adherence and persistence rates are generally higher among patients with acute compared to chronic conditions. While most patients will complete a course of therapy for acute conditions, several studies have shown that persistence with

medications for chronic conditions drops dramatically after the first six months of therapy.[25,26]

Medication nonadherence is a significant problem worldwide. According to a recent report by the World Health Organization, adherence to long-term therapy for chronic illnesses averages only around 50% in developed countries and is even lower in developing countries. A growing body of adherence research evidence suggests that since the problem of nonadherence is widespread and can have such detrimental effects on patient health and quality of life, more health benefits would result from improving adherence to existing treatments than would result from developing new therapies.[21]

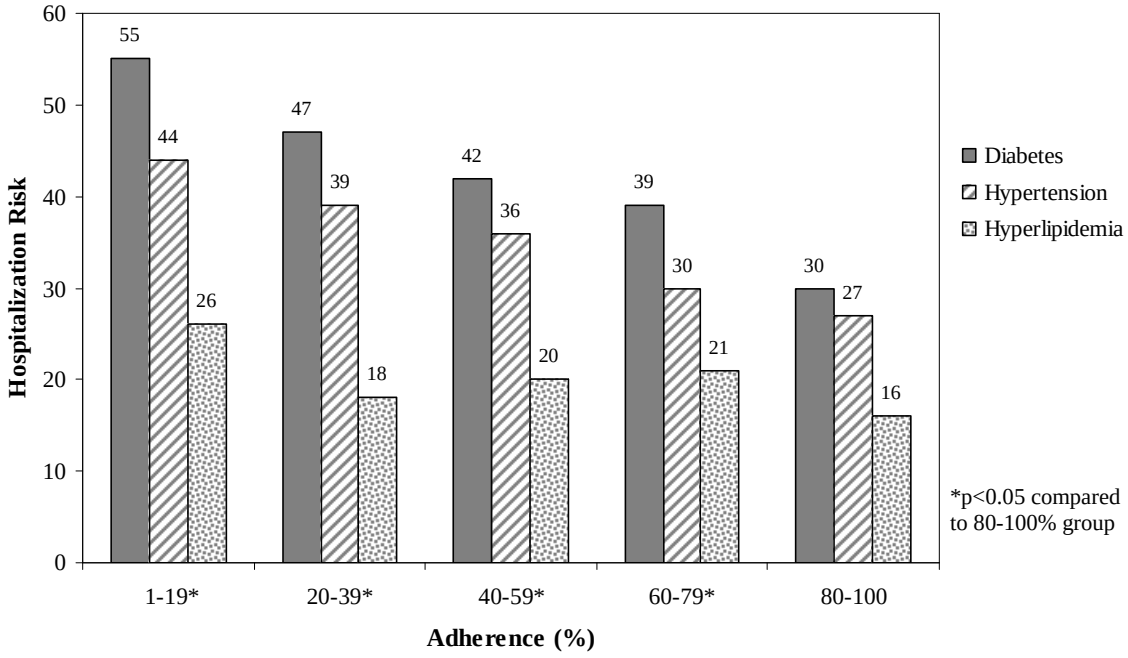
Consequences of Nonadherence

Several studies have demonstrated that nonadherence with medication results in increased use of medical resources, such as physician visits, laboratory tests, emergency department visits, and hospital admissions.[27,28] A retrospective cohort analysis by Sokol et al. (2005) of U.S. adults with hypertension, diabetes, or hyperlipidemia showed an inverse relationship between medication adherence and risk of disease-related hospital admissions; for all three conditions, a significantly decreased risk of hospitalization was observed in patients with high levels of adherence (80-100%) compared with less-adherent patients (Figure 1.2).[29] Similarly, Ho et al. (2006) found medication nonadherence to be associated with a 58% increased risk of all-cause hospitalization and an 81% increased risk of all-cause mortality in patients with type 2 diabetes.[30]

An estimated 125,000 deaths occur each year in the U.S. due to nonadherence with cardiovascular medications alone.[31] Considering all health conditions,

nonadherence is estimated to be responsible for 33-69% of all medication-related hospital admissions and to cost the U.S. health care system $100 billion annually.[25,27]

Figure 1.2 Relationship Between Medication Adherence and Hospitalization Risk



Source: Sokol (2005)[29]

Note: Adherence defined as the percentage of days during the 12-month analysis period that patients had a supply of one or more maintenance medications for the condition (based on "days' supply" in the patients' prescription claim records)

Factors Related to Adherence

Nearly 200 unique doctor-, patient-, and encounter-related variables have been studied to date to evaluate the complex phenomenon of medication-taking behavior and to identify and address barriers. However, none have been found to fully explain or predict medication adherence.[22] Ingersoll and Cohen (2008) recently published a review article of medication adherence in multiple chronic conditions, including asthma,

diabetes, HIV, chronic pain, mental disorders, and cardiovascular disease, and found that although the quantity and strength of evidence in the literature varied among the conditions, overall, patients tended to have better adherence when medication regimens were simplified (e.g., once-daily dosing vs. twice-daily dosing) and when patients clearly understood how and when to properly take medications.[32] Other common reasons for medication nonadherence found in the literature are provided in Table 1.5.

Table 1.5 Predictors of Medication Nonadherence

- Low literacy/limited English language proficiency
- Homelessnesss
- Substance abuse
- Psychiatric disease (e.g. depression, anxiety)
- Lower cognitive function or cognitive impairment
- Forgetfulness
- Lack of insight into illness
- Lack of belief in benefit of treatment
- Belief medications are not important or are harmful
- Inconvenience of medication regimen
- Side effects or fear of medication side effects
- Cost of medication, copayment, or both
- Barriers to medical care or medications
- Inadequate follow-up or discharge planning
- Missed appointments

Source: Osterberg (2005)[25], Kreuger (2005)[33], Borzecki (2005)[34]

Grant et al. (2003) conducted a study evaluating adherence with diabetes-related medications (including medications for hypertension and hyperlipidemia) in patients with type 2 diabetes. Overall, patients self-reported high adherence to prescribed medication regimens; among the patients who were classified as poorly adherent, most were highly adherent to all but one medication in their regimen. Telephone interviews with patients found two significant predictors of medication nonadherence: medication adverse effects

and a lack of patient confidence in the ability of the medication to improve current or future health.[35]

Prescription drug cost sharing has been shown to have a negative impact on medication adherence and treatment duration in multiple chronic conditions. Drug cost sharing is intended to offset increasing pharmaceutical costs by reducing "discretionary" pharmaceutical use or steering patients to less-expensive alternatives. However, studies have shown that cost-sharing techniques, such as co-payments, tiering, pharmacy benefit "caps", and formulary restrictions, increase medical services and consequently treatment costs in diabetic patients.[36-38]

Alternatively, reducing or removing co-payments has shown positive effects on medication adherence and health services utilization. Three years after a Pitney Bowes pharmacy benefit design change – which reduced the cost share of brand name diabetic medications (25-50% co-payment) to the same 10% co-payment as generic medications – patients demonstrated significant improvements in medication adherence to both oral antidiabetic agents and insulin. A 7% decrease in total pharmacy costs was seen, emergency room visits decreased by 26%, and short-term disability days were reduced by approximately 50%.[37]

Another reason for nonadherence in type 2 diabetics is "psychological insulin resistance," or the reluctance or refusal of patients to start insulin therapy once insulin is prescribed. Recent studies suggest that approximately 1 in 4 patients prescribed insulin therapy initially refuse the treatment, and the remainder express some degree of unwillingness to initiate insulin therapy.[39,40]

Many believe patients are solely responsible for taking their medication and overlook other important factors which affect one's behavior and ability to adhere to treatment. The World Health Organization has categorized the many factors related to adherence into the following five "dimensions":

1) Patient-related factors
   - Resources, knowledge, attitudes, beliefs, perceptions, and expectations of the patient
2) Condition-related factors
   - Severity of disease, rate of disease progression, co-morbid conditions
3) Therapy-related factors
   - Regimen complexity, duration of treatment, adverse effects
4) Health care team and system-related factors
   - Patient-provider relationship, health insurance reimbursement, knowledge and training of health care providers
5) Social/economic factors
   - Socioeconomic status, literacy, education level, social support network, cultural beliefs about illness and treatment

Measuring Medication Adherence

Although medication adherence research is not a new concept, lack of a standard valid method to measure adherence has been an obstacle in this field of study. Multiple methods are available to measure patient medication-taking behavior (Table 1.6).

Table 1.6. Methods of Measuring Adherence

Test	Advantages	Disadvantages
Direct Methods		
Directly observed therapy	Most accurate	Patients can hide pills in the mouth and then discard them; impractical for routine use
Measurement of the level of medicine or metabolite in blood	Objective	Variations in metabolism and "white-coat adherence" can give a false impression of adherence; expensive
Measurement of the biologic marker in blood	Objective; in clinical trials, can also be used to measure placebo	Requires expensive quantitative assays and collection of bodily fluids
Indirect Methods		
Patient questionnaires or patient self-reports	Simple; inexpensive; the most useful method in the clinical setting	Susceptible to error with increases in time between visits; results are easily distorted by the patient
Pill counts	Objective, quantifiable, and easy to perform	Data easily altered by the patient (e.g. pill dumping)
Rates of prescription refills	Objective; easy to obtain data	A prescription refill is not equivalent to ingestion of medication; requires a closed pharmacy system
Assessment of the patient's clinical response	Simple; generally easy to perform	Factors other than medication adherence can affect clinical response
Electronic medication monitors	Precise; results are easily quantified; tracks patterns of taking medication	Expensive; requires return visits and downloading data from medication vials
Measurement of physiologic markers (e.g. heart rate in patients using beta-blockers)	Often easy to perform	Marker may be absent for other reasons (e.g. increased metabolism, poor absorption, lack of response)
Patient diaries	Help to correct for poor recall	Easily altered by patient
When the patient is a child, questionnaire for caregiver or teacher	Simple; objective	Susceptible to distortion

Source: Osterberg (2005)[25]

Direct measurement methods, which include direct observation therapy (DOT) and blood draws, are difficult (if not impossible) to implement, particularly when attempting to study adherence in a “real world” setting. Indirect measurement methods,

which include tablet counts, interviews, diaries, medication event monitoring systems (MEMS), and review of pharmacy administrative claims, are less accurate, but are more commonly used for practical reasons. Pharmacy claims are the most frequently used because such claims are convenient, noninvasive, objective, and inexpensive to obtain.[41]

Multiple methods of calculating adherence are available using pharmacy claims; however, the large number methods lead to further complexity in this field of research. In 2006, Hess et al. published a study on use of pharmacy claims to measure medication adherence. This study found that between the years 1990 and 2006, eleven different methods were used to calculate adherence in the literature: continuous measure of medication adherence (CMA), continuous measure of medication gaps (CMG), continuous multiple interval measure of oversupply (CMOS), compliance ratio (CR), continuous, single interval measure of medication acquisition (CSA), days between fills adherence rate (DBR), medication possession ratio (MPR), medication possession ratio, modified (MPRm), medication refill adherence (MRA), proportion of days covered (PDC), and refill compliance rate (RCR).[41]

The Hess study used data from the LOSE weight (Long-term Outcomes of Sibutramine Effectiveness on Weight) study to compare these eleven methods and found that four methods – CMA, CMOS, MPR, and MRA – produced the same results; patients were 63.5% adherent with their medications (Table 1.7). CMG and PDC methods produced nearly identical results, showing that patients were 63.0% adherent.[41]

Table 1.7 Measures to Calculate Adherence Using Pharmacy Claims

Measure	Formula	Value	Result (SD)
CMA	$\frac{\text{cumulative days' supply of medication obtained}}{\text{total days to next fill or to end of observation period}}$	adherence value for cumulative time period	0.635 (0.29)
CMG	$\frac{\text{total days of treatment gaps}}{\text{total days to next fill or end of observation period}}$	nonadherence value for cumulative period, winsorized at zero	0.630 (0.28)
CMOS	$\frac{\text{total days of treatment gaps (+) or surplus}^{a}\text{ (-)}}{\text{total days in observation period}}$	nonadherence value for cumulative period, allowing for surplus	0.635 (0.29)
CR	$\left(\frac{\text{total days supplied - last days' supply}}{\text{last claim date - first claim date}}\right) \times 100$	adherence value for period between fills	84.4% (0.22)[b]
CSA	$\frac{\text{days' supply obtained at beginning of interval}}{\text{days in interval}}$	adherence value for interval of study participation	1.097 (1.73)
DBR	$\left(\frac{\text{last claim date - first claim date - total days' supply}}{\text{last claim date - first claim date}}\right) \times 100$	overall adherence percentage	104.8% (38.6)
MPR	days' supply : days in period	ratio of medication available	0.635:1 (0.29)
MPRm	$\left(\frac{\text{total days' supply}}{\text{last claim date - first claim date + last days' supply}}\right) \times 100$	adherence percentage, adjusted to include final refill period	86.6% (16.6)
MRA	$\left(\frac{\text{total days' supply}}{\text{total number of days evaluated}}\right) \times 100$	overall adherence percentage	63.5% (29.1)
PDC	$\left(\frac{\text{total days' supply}}{\text{total number of days evaluated}}\right)^{c} \times 100$	percentage of days with medication available	63.0% (28.3)
RCR	$\frac{\text{(sum of quantity dispensed over interval / quantity to be taken per day) x 100}}{\text{number of days in interval between first and last refill}}$	overall adherence percentage	104.8% (38.6)

Source: Hess (2006)[41]

CMA = continuous measure of medication adherence; CMG = continuous measure of medication gaps; CMOS = continuous multiple interval measur e of oversupply; CR = compliance ratio; CSA = continuous, single interval measure of medication acquisition; DBR = days between fills adherence rate; MPR = medication possession ratio; MPRm = medication possession ratio, modified; MRA = medication refill adherence; PDC = proportion of days covered; RCR = refill compliance rate

[a]Surplus due to early refill or overfill, resulting in excess medication for the time period evaluated

[b]Single refills accounted for 12 records that were not included in this analysis

[c]Capped at 1.0

Improving Medication Adherence

In chronic conditions such as diabetes, increasing medication use has resulted in demonstrable improvements in health outcomes, reduced hospitalization rates, and decreased direct health care costs.[42-44] However, considering multiple causes of nonadherence exist, it is not surprising no "one size fits all" solution is available to improve medication adherence in all patients.

Even in the earliest stages of medication adherence research Sczupak and Conrad (1977) and Hawkins et al. (1979) demonstrated improved medication adherence, decreased symptoms, improved kept appointment rates, lower dropout rates, and decreased hospital admissions when a pharmacist provided care to diabetic patients.[45,46] More recently, Roter et al. (1998) conducted a meta-analysis of interventions to improve medication adherence for all disease states and found that multi-focused interventions which include cognitive, behavioral, and affective components demonstrate better outcomes than interventions which focus only on one construct.[47]

A recently published Cochrane review included 21 studies evaluating interventions to improve type 2 diabetics' adherence to treatment recommendations (excluding diet and exercise recommendations) in outpatient, community, hospital, and primary care settings.[22] Multiple intervention types were evaluated, including diabetes education, home aids, and nurse-led and pharmacist-led interventions. Although the majority of interventions showed some improvement in A1Cs, mixed results were seen among the studies. For example, in one pharmacist-led intervention study, both the intervention and control groups had a significant improvement in A1C, and the

intervention group demonstrated significant decreases in body weight and systolic blood pressure.[48] In a second pharmacist-led study, both the intervention and control groups demonstrated a small increase in self-reported medication adherence, but neither group had a significant change in A1C.[49] The authors concluded that the effectiveness of medication adherence interventions remains uncertain, as the review of the literature did not show the interventions to be particularly beneficial or harmful.[22]

Lu et al. (2008) conducted a more-recent review of the literature specifically evaluating medication adherence interventions in a managed care setting (N = 51) and concluded that the following interventions were effective: one-to-one academic detailing, computerized alerts and reminders, pharmaceutical collaborative care, and multifaceted disease management. The study also found formulary changes and increases in co-payments were associated with reduced medication use.[50]

Diabetes Management Methods

Treatment of diabetes with medication and lifestyle modification is documented to reduce the risks of diabetic complications. In 2000, the UK Prospective Diabetes Study (UKPDS) showed that for every 1-point improvement in hemoglobin A1C in type 2 diabetics, the risk of microvascular complications is reduced by 37%, the risk of myocardial infarction decreases 14%, and the risk of premature death decreases by 21%.[51] Similarly, the Diabetes Control and Complications Trial (DCCT) showed that maintaining blood glucose serum concentrations as close to normal physiologic values as

possible substantially slowed the onset and progression of eye, nerve, kidney, and heart disease in Type 1 diabetics.[52]

Therapeutic Lifestyle Changes

Lifestyle changes are an important first step in treating patients with type 2 diabetes in order to reduce the risk of microvascular and macrovascular complications. When signs and symptoms are mild, diet and exercise alone can correct glucose intolerance. Patients with A1C ≤7% at the time of diagnosis are generally initiated on therapeutic lifestyle changes alone.[5] Therapeutic lifestyle changes have been shown to improve A1C measures by 1-2%.[53]

Obesity (>120% ideal body weight) is associated with insulin resistance; therefore, overweight or obese type 2 diabetics are strongly encouraged to lose weight. A moderate 5% reduction in body weight has been shown to decrease insulin resistance, improve fasting blood glucose levels, improve serum lipid concentrations, and reduce blood pressure.[54] The combination of a reduced-calorie diet, physical activity, and behavior therapy aimed at developing skills to change problematic eating and activity patterns has the greatest potential for helping individuals achieve and maintain long-term weight goals.[1,54]

The ADA recommends a minimum of 150 minutes per week of moderate-intensity physical activity, defined as 50-70% of maximum heart rate, for people with both type 1 and type 2 diabetes.[14] Nutritionally, trans unsaturated fat should be minimized, saturated fat should comprise <7% of total calories, alcohol consumption

should be limited to a moderate amount (maximum of 1 drink per day for women and 2 drinks per day for men), and carbohydrates should be carefully monitored via carbohydrate counting, exchanges, or experience-based estimation.[14]

Pharmacologic Treatment

Some patients with type 2 diabetes can control and maintain glycemic control with a healthy diet, exercise, and weight loss, while others may also need oral prescription medications and/or insulin. Whether or not prescription antidiabetic medications are needed depends on the individual patient, and this need often changes over the course of the disease. The severity of metabolic abnormality in a patient can progress, regress, or remain stable over time.[4] However, most patients will require more than one medication to achieve and maintain glycemic control as the disease progresses.[53] In contrast, all patients with type 1 diabetes have an absolute insulin deficiency and require exogenous insulin to survive.

According to the CDC, 16% of all diabetic adults manage blood glucose with diet and exercise only, 57% use oral medications only, 13% use oral medications and insulin, and 14% use insulin only.[13] An overview of prescription antidiabetic medication classes is presented in Table 1.8.

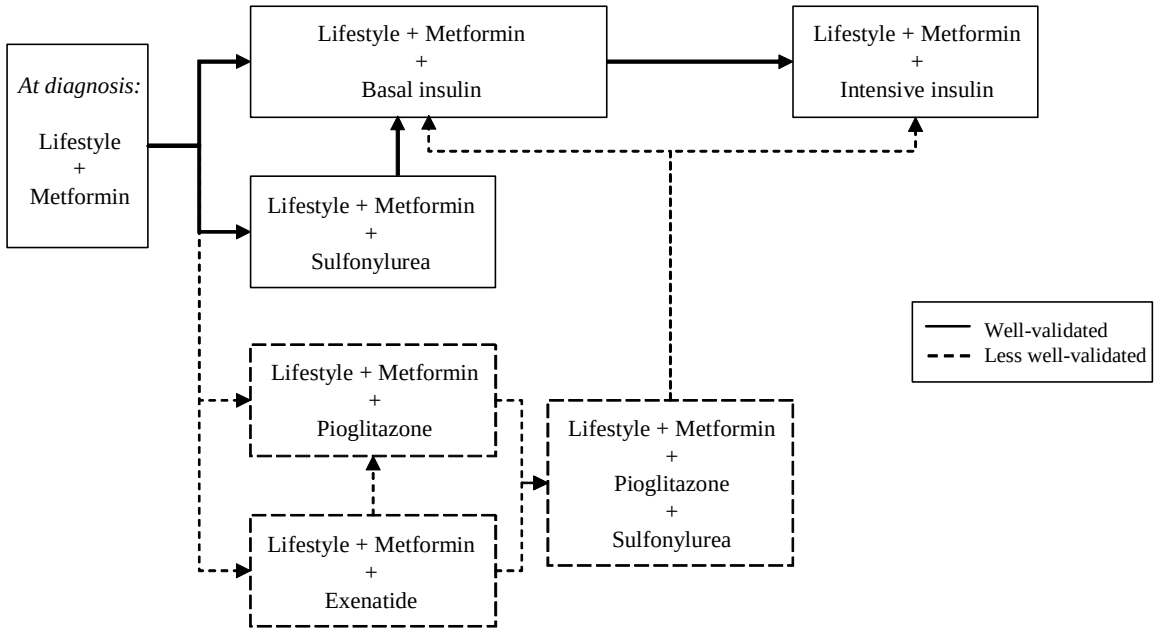
Table 1.8 Comparative Pharmacology of Antidiabetic Agents

Drug Class	Mechanism of Action	Generic Names	Efficacy	Adverse Effects	Comments
α-Glycosidase inhibitors	Slows absorption of complex carbohydrates	Acarbose, Miglitol	↓ A1C 0.5-1.0% ↓ FPG 20-30 mg/dL ↓ PPG 25-50 mg/dL	Flatulence, diarrhea. LFT elevation seen with acarbose – monitor LFTs	Titrate dose slowly to minimize GI effects. No hypoglycemia or weight gain. Sucrose inhibits absorption. Use glycose tablets to treat hypoglycemic episodes.
Amylin agonists	Inhibits glucoagon in a glucose-dependent manner	Pramlintide	↓ A1C 0.5-1.0%	Nausea, vomiting, diarrhea	May worsen insulin-induced hypoglycemia.
Biguanides	Enhances insulin sensitivity. Decreases hepatic glucose output and increases peripheral glucose uptake	Metformin	↓ A1C 1.5-1.7% ↓ FPG 50-70 mg/dL ↓ PPG 83 mg/dL ↓ TG 10-20% ↓ TC 5-10% ↑ HDL (slight)	Cramping, diarrhea. Rare: lactic acidosis	Titrate dose slowly to minimize GI effects. No hypoglycemia or weight gain; weight loss possible. Do not use in patients with renal or hepatic function or CHF requiring treatment.
Dipeptidyl peptidase-IV inhibitors	Stimulates insulin secretion	Sitagliptin	↓ A1C 0.6-0.85%	Generally well tolerated. Weight neutral.	Low risk of hypoglycemia. Serious allergic reactions have been reported during post-marketing surveillance.
Incretin mimetic	Stimulates insulin secretion	Exenatide	↓ A1C 0.8-1.0%	Weight loss, nausea, vomiting, diarrhea.	Low risk of hypoglycemia and favorable effect on weight.
Insulin	Replaces or augments endogenous insulin	Lispro, Aspart, Regular, NPH, Lente, Ultralente, Glargine	↓ A1C 4% ↓ FPG ↓ PPG ↓ TG	Hypoglycemia, weight gain, lipodystrophy, local skin reactions	Offers flexible dosing to match lifestyle and glucose concentrations. Rapid onset. Safe in pregnancy, renal failure, and liver dysfunction. Drug of choice when patients do not respond to oral agents.
Nonsulfonylurea secretagogues (meglitinides)	Stimulates insulin secretion	Repaglinide, Netaglinide	↓ A1C 1.7% ↓ FPG 61 mg/dL ↓ PPG 48 mg/dL	Hypoglycemia, weight gain	Take only with meals. If a meal is skipped, skip a dose. Flexible dosing with lifestyle. Safe in renal and liver failure. Rapid onset.
Sulfonylureas	Stimulates insulin secretion. May decrease hepatic glucose output and enhance peripheral glucose utilization	Glipizide, Glyburide, Glimepiride, Tolbutamine, Chlorpropamide, Tolazamide, Acetohexamide	↓ A1C 1.5-1.7% ↓ FPG 50-70 mg/dL ↓ PPG 92 mg/dL	Hypoglycemia, especially long-acting agents; weight gain (4-22 lb). Rare: rash, hepatotoxicity, alcohol intolerance, and hyponatremia	Hyperinsulinemia, which leads to hypoglycemia and weight gain. Some can be dosed once daily. Rapid onset of effect (1 week).
Thiazolidine-diones	Enhances insulin sensitivity. Decreases insulin resistance in muscle and liver, enhancing glucose utilization and decreasing hepatic glucose control	Pioglitizone, Rosiglitazone	↓ A1C 0.7-1.2% ↓ FPG 40-55 mg/dL	Weight gain. Rare: hepatotoxicity	Monitoring of liver function tests is recommended at baseline, every 2 months for the first year of therapy, and periodically thereafter.

Source: Koda-Kimble (2005)[1], Nathan (2009)[53], Doupis (2008)[55], Bosi (2008)[56], VanDeKoppel (2008)[57], Bartels (2007)[58]
A1C = glycosylated hemoglobin A1C; FPG = fasting plasma glucose; PPG = postprandial glucose; LFT = liver function test; TID = three times daily; GI = gastrointestinal; TG = tryglyceride; TC = total cholesterol; HDL = high-density lipoprotein cholesterol; CHF = chronic heart failure

To date, insufficient data are available to support a recommendation of one class of antidiabetic agent, or combination of agents, over others with regard to long-term effects and resulting complications.[53] The risk of complications appears to be better predicted by the level of glycemic control achieved rather than any specific medication(s) used. Therefore, ADA and European Association for the Study of Diabetes (EASD) consensus guidelines recommend agents primarily based on ability to decrease and maintain A1C levels; safety, tolerability, ease of use, and cost should also be considered.[53] The treatment algorithm based on this data is presented in Figure 1.3.

Figure 1.3 Diabetes Treatment Algorithm for Type 2 Diabetic Patients



Source: Nathan (2009)[53]

Well-validated therapies are those that are the best established, most effective, and most cost-effective therapies for achieving target glycemic goals. This is the preferred route of therapy for most patients. Less well-validated therapies may be preferred in certain circumstances, such as when hypoglycemia is a major concern or weight loss is a desired outcome.

Advancement from one step to the next in the treatment algorithm should be based on glycemic control. Patients should have A1C tested every three months until the individual A1C goal is reached (<7% for most patients), at which time the A1C should be rechecked at least every six months. The current therapy should be changed (i.e. dose increased or another agent added) if the A1C is higher than the specific individual goal.

The ADA has the following recommendations for insulin therapy in patients with type 1 diabetes:[14]

- Intensive insulin therapy, either via an insulin pump or 3-4 injections per day of basal and prandial insulin
- Dosing prandial insulin based on premeal blood glucose, carbohydrate intake, and anticipated activity
- Use of insulin analogs, particularly in patients who commonly experience hypoglycemia

Disease Management Programs

A growing body of evidence exists indicating that diabetes care provided by a pharmacist is effective in lowering patient A1C levels to goal.[59] The first well-known study of this type, The Asheville Project, began in 1997 and involved pharmacists who provided patient education and monitoring in community pharmacies in Asheville, North Carolina. This intervention showed demonstrable reductions in A1C, the percent of patients with A1C >9%, mean LDL cholesterol, and the percent of patients with LDL <100 mg/dL.[60] Five years after the study began, the Asheville program showed the

ability to maintain patients at lower A1C levels and decrease direct medical costs by 58%.[61] The significant clinical and economic outcomes demonstrated in this study generated a new health care model for patients with diabetes and other chronic conditions. For example, the American Pharmacists Association (APhA) Foundation's Patient Self-Management Program for Diabetes, sometime referred to as the Diabetes Ten City Challenge, implemented similar pharmacist services in multiple geographic locations and demonstrated the following outcomes: decrease in mean A1C (7.9% to 7.1%), decrease in mean LDL cholesterol (113.4 mg/dL to 104.5 mg/dL), decrease in mean systolic blood pressure (136.2 mmHg to 131.4 mmHg), increased annual influenza vaccinations (52% to 77%), increased annual eye examinations (46% to 82%), and increased annual foot examinations (38% to 80%), improved satisfaction with overall diabetes care, and decreased mean health care costs.[62] A major limitation of both studies, however, is that there was no control group for comparison. Therefore, additional studies were needed to show that the results could be duplicated.

In April 2008, Wubben and Vivian published a review article on the effects of pharmacist outpatient interventions on adults with diabetes. The review included all randomized control trials, controlled clinical trials, and cohort studies published through August 2007; the studies all included a control group and measured outcomes before and after implementation of the intervention.[63] The authors searched multiple databases, using the following MeSH terms: diabetes mellitus, pharmacy services, pharmacist(s), NIDDM, and IDDM. A total of 21 articles met the inclusion criteria for the review. A similar search was conducted for this study using the same search terms to find any

additional published articles between September 2007 and April 2009. One additional study met the inclusion and exclusion criteria for the review, providing a total of 22 separate trials.

Twenty of the 22 studies evaluating the impact of pharmacist activities in an outpatient diabetes setting used A1C as the primary outcome, with A1C change levels ranging from an increase of 0.2% to a decrease of 2.1%.[63] Interventions which allowed pharmacists to make medication adjustments reported greater improvements in A1C than interventions in which pharmacists provided only drug review and disease education.[63] Twelve studies measured blood pressure as a secondary outcome, and eleven evaluations measured cholesterol serum concentrations. Most studies found decreases in blood pressure and cholesterol serum concentrations in the intervention patients but did not find significant differences between the intervention and control groups for these variables.[63]

Purpose

Although multiple medication adherence studies have been performed in diabetic patients using pharmacy claims data, to date no studies were found to have evaluated the impact of a pharmacist intervention on diabetic medication adherence. Therefore, the aim of this investigation was to analyze the impact of a pharmacist-led medication management program on medication adherence and pharmacy costs and to evaluate clinical measures of diabetes, hypertension, and hyperlipidemia.

CHAPTER TWO: METHODOLOGY

Objectives

1) To evaluate the impact of a pharmacist-led medication management program on adherence to and persistence with medications for diabetes, hypertension, and hyperlipidemia using pharmacy claims data
2) To assess the clinical impact of the intervention on measurements of A1C, blood pressure, and cholesterol
3) To determine the cost of medications for diabetes, hypertension, and hyperlipidemia for the patient and health plan
4) To compare adherence to medications for diabetes (co-payment waiver) vs. adherence to medications for hypertension and hyperlipidemia (no co-payment waiver)

Hypotheses

The following hypotheses were tested in the null form:

$H_0$1: There is no relationship between the change in A1C from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.

$H_0$2: There is no relationship between the change in the percentage of patients achieving goal A1C (<7%) from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.

$H_0$3: There is no relationship between the change in the percentage of patients with poor glycemic control (A1C >9%) from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.

$H_0$4: There is no relationship between the change in the percentage of patients achieving goal blood pressure (BP <130/80) from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.

$H_0$5: There is no relationship between the change in the percentage of patients achieving all goal cholesterol levels (LDL <100, HDL >40 for males, HDL >50 for females, total cholesterol <200, triglycerides <150) from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.

$H_0$6: There is no relationship between the change in adherence to medications for diabetes from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.

$H_0$7: There is no relationship between the change in adherence to medications for hypertension from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.

$H_0$8: There is no relationship between the change in adherence to medications for hyperlipidemia from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.

$H_0$9: There is no relationship between the change in patient pharmacy costs for diabetes/hypertension/hyperlipidemia/other medications and testing supplies for patients participating in the medication management program and patients receiving usual care.

$H_0$10: There is no relationship between the change in health plan pharmacy costs for diabetes/hypertension/hyperlipidemia/other medications and testing supplies for patients participating in the medication management program and patients receiving usual care.

$H_0$11: There is no relationship between the ability of patients to achieve goal A1C (<7%) and study group, sex, age, diabetes type, improvement in medication adherence, improvement in medication persistence, initiation of insulin therapy, increased number of antidiabetic agents, or increased use of diabetic testing supplies.

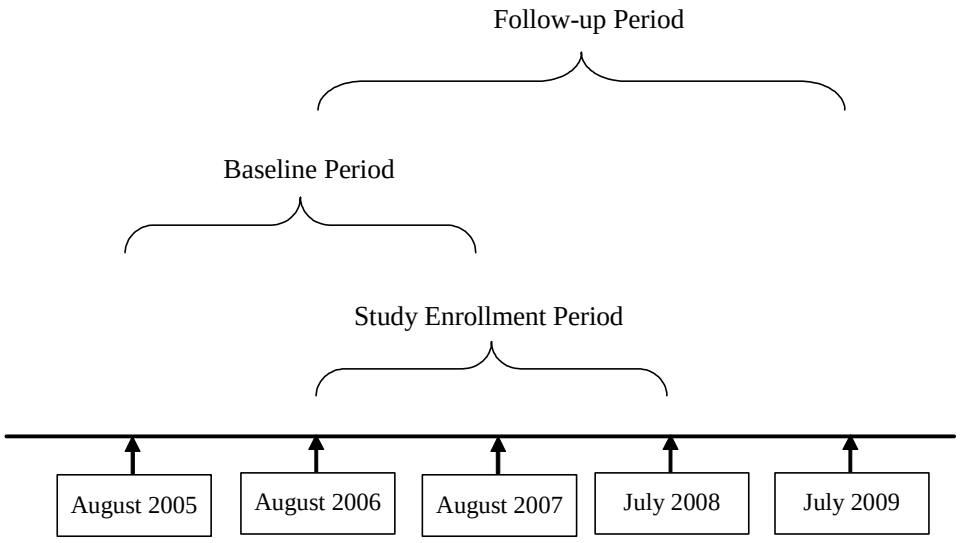
Study Design

This study was a quasi-experimental, longitudinal, pre-post study, with a control group. Patients were drawn from the Scott and White Health Plan (SWHP) membership database. SWHP is a staff-model, non-profit, managed care organization with over 200,000 members and includes 4 hospitals, 7 retail pharmacies, and more than 20 local and regional clinics in central Texas. The pharmacist intervention took place in four of the retail pharmacies. Patients who met the inclusion criteria and lived "nearby" (within 30 miles of the four participating pharmacies) were invited to

participate in the intervention, while those who were not defined as living "nearby" served as control patients.

A "rolling" enrollment period from August 2006-July 2008 was utilized. Data for one year prior to study enrollment were collected to determine subject baseline, and each subject was followed for one year after study enrollment. Therefore, data were collected from August 2005-July 2009 (Figure 2.1). The "study enrollment date" for control patients was based on the enrollment date of that subject's matched intervention counterpart.

Figure 2.1. Study Time Frame



Patients were analyzed on an intent-to-treat basis. Resources used to identify and follow patients included the SWHP membership database, clinic and hospital electronic medical records, and SWHP prescription and medical claims.

Patient Selection

The intervention group was identified prospectively, while the control group was identified at the time of analysis. Intervention and control patients were matched on age and sex.

Inclusion Criteria

Potential subjects were members of SWHP and were identified from SWHP claims data. To be included in the study, subjects must have been between the ages of 18 and 63 at the time of study enrollment and continuously enrolled in SWHP for the two-year data collection period. Subjects must have had a formal diagnosis of diabetes, as specified by HEDIS, which includes the ICD-9 codes 250.xx, 357.2x, 362.0x, and 366.41. To target patients at high risk for poor outcomes, the most recent A1C measurement for each subject must have been > 7.5%. The control patients were required to meet the same inclusion criteria but were not invited to participate in the program due to the geographic constraints noted above.

Exclusion Criteria

Patients were not enrolled in the study if their physician declined to enroll the patient in the program, if the patient declined to give informed consent, or if the patient had impaired ability to comprehend or converse in English (i.e. mentally disabled, advanced dementia, non-English speaking). In addition, subjects were excluded if they currently or formerly participated in the institution's medication management clinic

(MMC), a similar pharmacist-led medication management program for poorly controlled diabetic patients, during the previous 90 days. Two main differences existed between the medication management program studied in this evaluation and the MMC. The first difference was that patients in the MMC were referred by their physicians because those patients were difficult to control, whereas patients in the medication management program were invited to the program based on most recent A1C levels and geographic location. The second difference between the programs was that patients in the medication management program spent approximately 20 minutes during each pharmacy visit learning about a predetermined diabetes-related topic; this formal education was not provided in the MMC.

Recruitment Procedure

SWHP medical claims, medical records, and enrollment data were screened for patients meeting the aforementioned inclusion and exclusion criteria. An introductory letter with a list of patients meeting criteria for participation in the medication management program was sent to the prescribing physician in charge of their diabetes care (Appendix I). The physician was asked to indicate appropriateness for program participation for each patient and to return the list to the SWHP pharmacy. The letter to the physician also indicated that patients enrolled in the program would be eligible to participate in the study protocol.

All patients identified as potential intervention group participants and approved by their physician were contacted by mail with an introductory letter explaining the

program and study protocol (Appendices II and III). The mailing informed patients that they would be contacted within 10 days to discuss possible participation in the program and the research study. The mailing included a self-addressed, stamped envelope and a card on which to indicate willingness to participate in the program. Patients returning the card declining participation in the program were not contacted. Pharmacy telephone numbers were provided in the introductory letter to provide patients who had questions access to information.

Study participants were asked to sign an Authorization for Use and Disclosure of Health Information for Research Purposes that was blended with the Consent Form prior to participating in the research study (Appendix IV). Written informed consent was obtained in person for each participant prior to the initial pharmacy appointment.

SWHP medical claims, medical records, and enrollment data were collected and analyzed retrospectively for patients in the control group. A waiver of informed consent was granted for control patients because information for those individuals was already collected for non-research purposes, as the data came from documentation of their usual care. Institutional Review Board approval for the study was obtained from Scott & White Health System and The University of Texas at Austin.

Matching Procedure

To match intervention and control patients, random numbers were assigned to each potential control patient. The control patient with the lowest number matching an intervention patient on sex and age was selected as the intervention patient's matched

control. In the event no control patient was found that matched an intervention patient for sex and age, the control patient of the same sex whose date of birth was closest to the intervention patient's date of birth was included.

Intervention

Patients in the intervention group met monthly with a SWHP pharmacist in a private patient counseling office in one of the four participating SWHP retail pharmacies. At the initial 60-minute appointment, the pharmacist evaluated the patient therapy needs and developed a patient care plan, with the goal of achieving an A1C <7%, unless otherwise specified, per ADA recommendations. During each 30-minute follow-up appointment, the pharmacist spent approximately 20 minutes teaching the patient about different diabetes-related topics, such as appropriate use of a glucometer, the importance of foot care, how to read nutrition labels, and the importance of exercise (Table 2.1). A complete list of educational topics discussed and the sources from which those topics were derived is available in Appendix V.

In addition, the pharmacist monitored the patient as recommended by the ADA, evaluated home blood glucose journals, and made medication adjustments when necessary as allowed under a collaborative practice agreement with physicians (Appendix VI). While flexibility existed in the program to address specific areas of concern for each patient at each visit, a general listing of all scheduled procedures for each appointment is presented in Table 2.2.

Table 2.1 Schedule of Intervention Educational Topics

Visit #	Educational Topic
1	Overview and goals of therapy
2	Self-monitoring blood glucose / how to use a glucometer
3	Acute complications
4	Medication timing and administration
5	Nutrition requirements / reading nutrition labels
6	Carbohydrate counting
7	Exercise
8	Medication education and adherence
9	Chronic complications
10	Foot care
11	Psychosocial issues
12	Stress management

Table 2.2. Scheduled Procedures at Each Medication Management Program Visit

	Visit Number											
Scheduled Procedures	1	2	3	4	5	6	7	8	9	10	11	12
Patient history (medical, social, family)	X											
Medications	X	X	X	X	X	X	X	X	X	X	X	X
Self-monitored blood glucose (SMBG) readings	X	X	X	X	X	X	X	X	X	X	X	X
Diet and exercise	X	X	X	X	X	X	X	X	X	X	X	X
Preventative health	X											
Physical assessment*	X	X	X	X	X	X	X	X	X	X	X	X
Labs												
Hemoglobin A1C	X			X			X			X		X
Glucose	X						X					X
Lipids	X						X					X
Liver function tests	X						X					X
Thyroid stimulationg hormone (TSH)	X											X
Potassium	X											X
Creatinine	X											X
Blood urea nitrogen (BUN)	X											X
Urine microalbumin	X											X

*includes weight, blood pressure, pulse, and visual foot exam; a comprehensive foot exam with monofilament test will be performed if one has not been documented in the medical record within the previous 12 months

In addition to the monthly care provided by a pharmacist, diabetic medications and testing supplies were provided free to patients participating in the intervention. Patients were provided with, and asked to sign, a SWHP insurance contract waiver specifying the terms under which prescription co-payments were to be waived as well as the list of approved medication and supplies at the first medication management program appointment (Appendix VII).

Outcome Measures

Clinical Measures: A1C, Blood Pressure, Cholesterol

The clinical measures in this analysis were the absolute change in A1C, blood pressure, total cholesterol (TC), LDL cholesterol (LDL-C), HDL cholesterol (HDL-C), and triglycerides (TG). The percentage of patients achieving goal levels for diabetes (A1C <7%), hypertension (BP <130/80), and hyperlipidemia (TC <200, LDL-C <100, HDL-C ≥60, TG <150) at baseline and follow-up were calculated. In addition, the percentage of patients with an uncontrolled A1C, defined by HEDIS as A1C >9%, was calculated and compared between intervention and control groups.[64]

Data were obtained from the electronic medical record. The most recent measurement prior to study enrollment and the one-year follow-up appointment was used for baseline and follow-up measures, respectively. To attain the most accurate baseline and follow-up measurements, in the event a recent clinical measurement was not available prior to the study enrollment and follow-up dates, a measurement obtained within a 30 day grace period of these dates was used in place of the older measurement.

One exception to this rule occurred in the determination of baseline glycemic control. Since the A1C test is a time-weighted average of mean daily blood glucose which places the greatest weight on current glucose levels, a 10-day grace period was established for baseline A1C measurements.

Adherence Measures: Medication Adherence and Persistence

This evaluation applied the most commonly used method to estimate patient adherence using retrospective databases – the medication possession ratio (MPR). With this method, medication adherence rates for individual patients are reported as the percentage of the prescribed doses of the medication taken by the patient over a specified period. The formula to calculate MPR was as follows:

$$\frac{\text{Total Days' Supply of Medication within the Refill Interval}}{\text{Number of Days in the Refill Interval}}$$

where the refill interval was defined as:

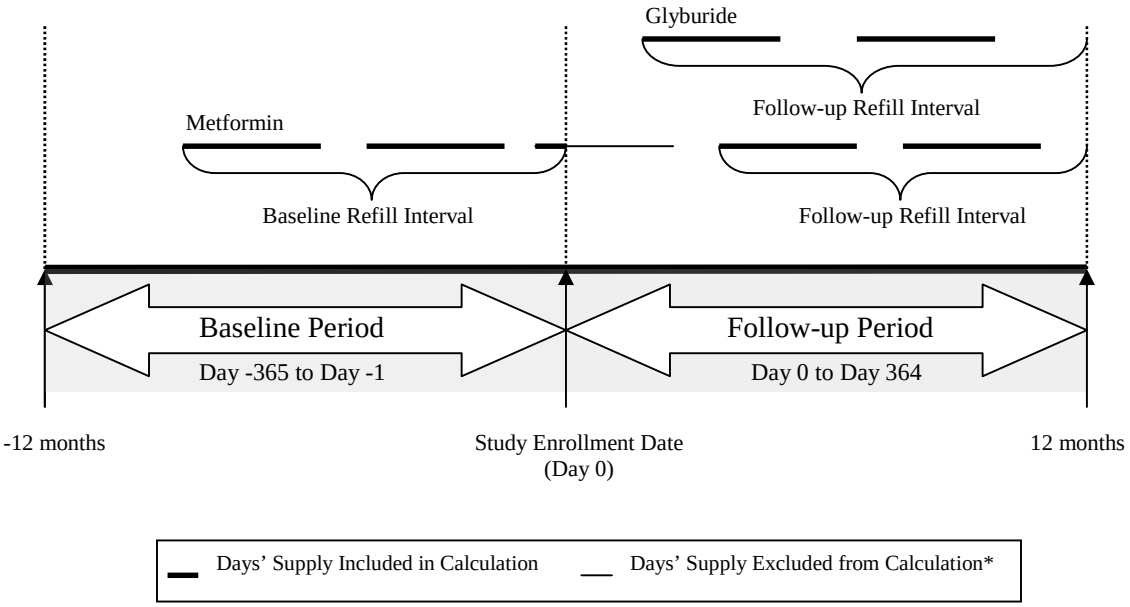
- days between index date (first fill in the baseline period), and baseline end (study enrollment date -1), for the baseline MPR
- days between index date (first fill in the follow-up period) and study end (study enrollment date +364), for the follow-up MPR

and the total days' supply of medication was defined as:

- the sum of days' supply for all prescriptions filled within the refill interval

If the date of the last refill in the refill interval extended by the days' supply of the last refill was greater than the baseline/study end date, the days' supply was truncated at the baseline/study end date. An example of the MPR calculation is presented in Figure 2.2.

Figure 2.2. Illustration of Medication Possession Ratio Calculation Terms



*The days' supply was excluded from the follow-up MPR calculation because this medication was filled during the baseline period. Similarly, the days' supply for any medication filled prior to the baseline period would not be included in the baseline MPR calculation.

Medication names, days' supply of medication, and medication fill dates were obtained from SWHP pharmacy claims. MPRs were calculated for each unique medication class filled by a patient at least twice during the baseline/follow-up period. Two medication fills were required to help ensure adherence calculations included only medications that were well tolerated by the patient and that were to be continued indefinitely.

For patients taking more than one medication class for a particular condition (i.e. a beta blocker and diuretic for hypertension), or combination products (i.e. valsartan/ hydrochlorothiazide), MPRs for each unique medication class were calculated; the medication class MPRs were averaged to generate one overall MPR for that condition. Therefore, up to three distinct MPRs were calculated for each individual subject in order to determine (1) adherence to medications for diabetes (oral medications and exenatide), (2) adherence to medications for hypertension, and (3) adherence to medications for hyperlipidemia. A complete list of all medications used in the MPR calculations and the classification of each medication is presented in Appendix VIII.

Adherence to insulin was not calculated as it is difficult to ascertain whether patients were taking doses as prescribed, particularly since insulin doses may be prescribed on a sliding scale and because insulin should be discarded 28 days after a vial is opened. On the other hand, adherence to the injection medication exenatide was included in adherence calculations since this agent has a fixed-dose, twice-daily administration schedule.

Medication possession ratios can range from 0% to 100%. In this study, MPRs ranged from 17% to 100%. Patients were considered adherent if their MPR was greater than or equal to 80%.

Medication persistence was calculated as the number of days that a patient remained on therapy during the baseline and follow-up periods. Up to three medication regimens were identified for each patient, to measure persistence with medications for (1) diabetes, (2) hypertension, and (3) hyperlipidemia. The medication regimens consisted of

all medications first filled within the first 120 days of the baseline or follow-up periods. Only one fill of a medication was required to be included in the persistence calculation, as the purpose of calculating persistence is to determine the length of time a patient remains on a prescribed medication regimen.

A medication was considered discontinued if the agent was not refilled within 30 days of the last fill date extended by the days' supply of the last fill. As with the MPR calculations, persistence calculations could include more than one medication and/or combination medications for a particular condition, and insulin therapy was not included in the calculations. The formula to calculate days of persistence was as follows:

Date of Discontinuation – Date of First Medication Fill

where the date of discontinuation was defined as:

- the date prior to a 30-day gap in therapy

and date of first medication fill was defined as:

- the first date a medication was filled

If patients took more than one medication and/or combination medications for a particular condition, the date of first medication fill was defined as the last first fill date of a medication in the combination regimen, and the date of discontinuation was defined as the first date of discontinuation of any agent in the combination regimen (Figures 2.3-2.4). In addition, the percentage of patients remaining on therapy at 6 months was calculated for medications for diabetes, hypertension, and hyperlipidemia.

Figure 2.3. Baseline Persistence Measurement Example

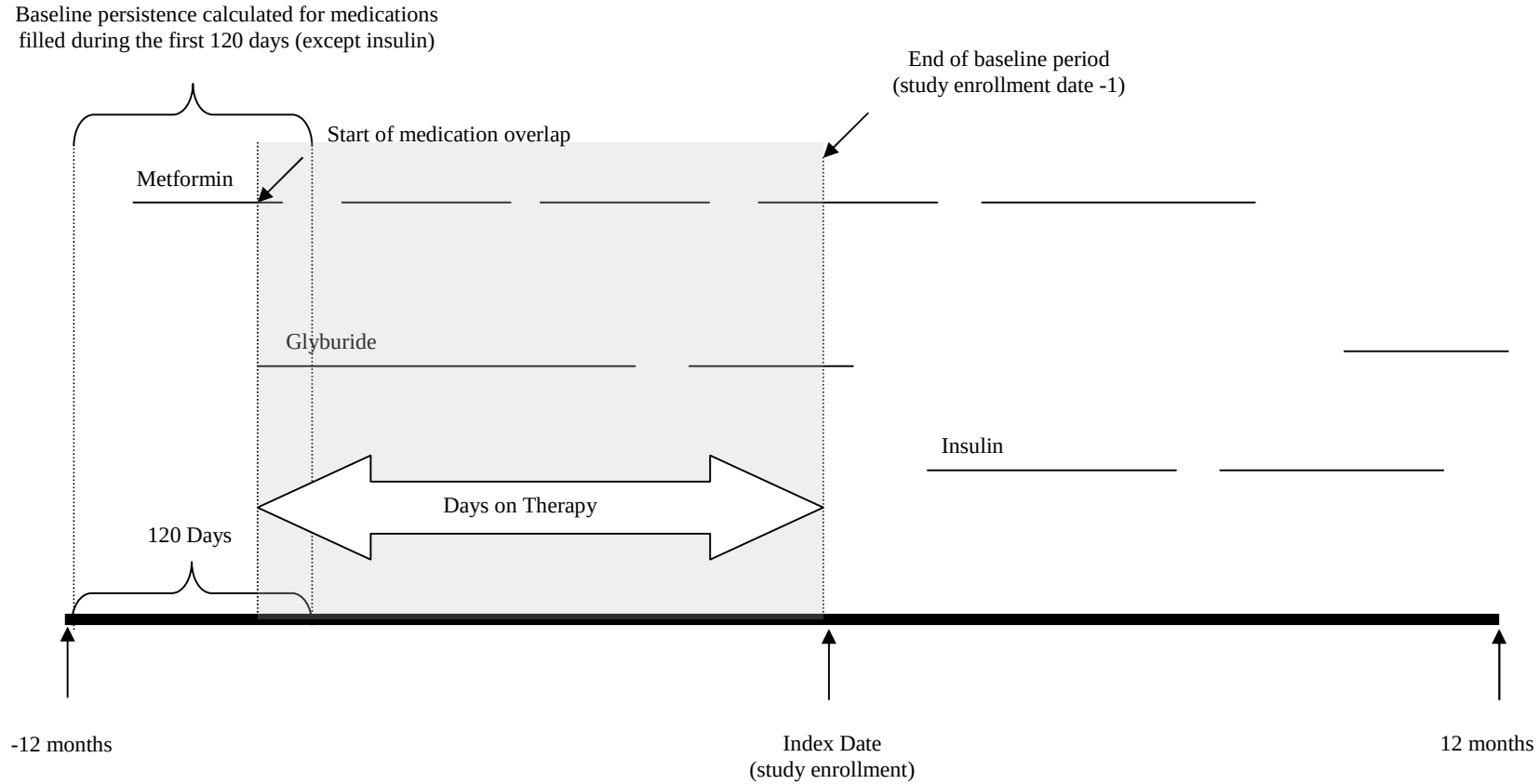
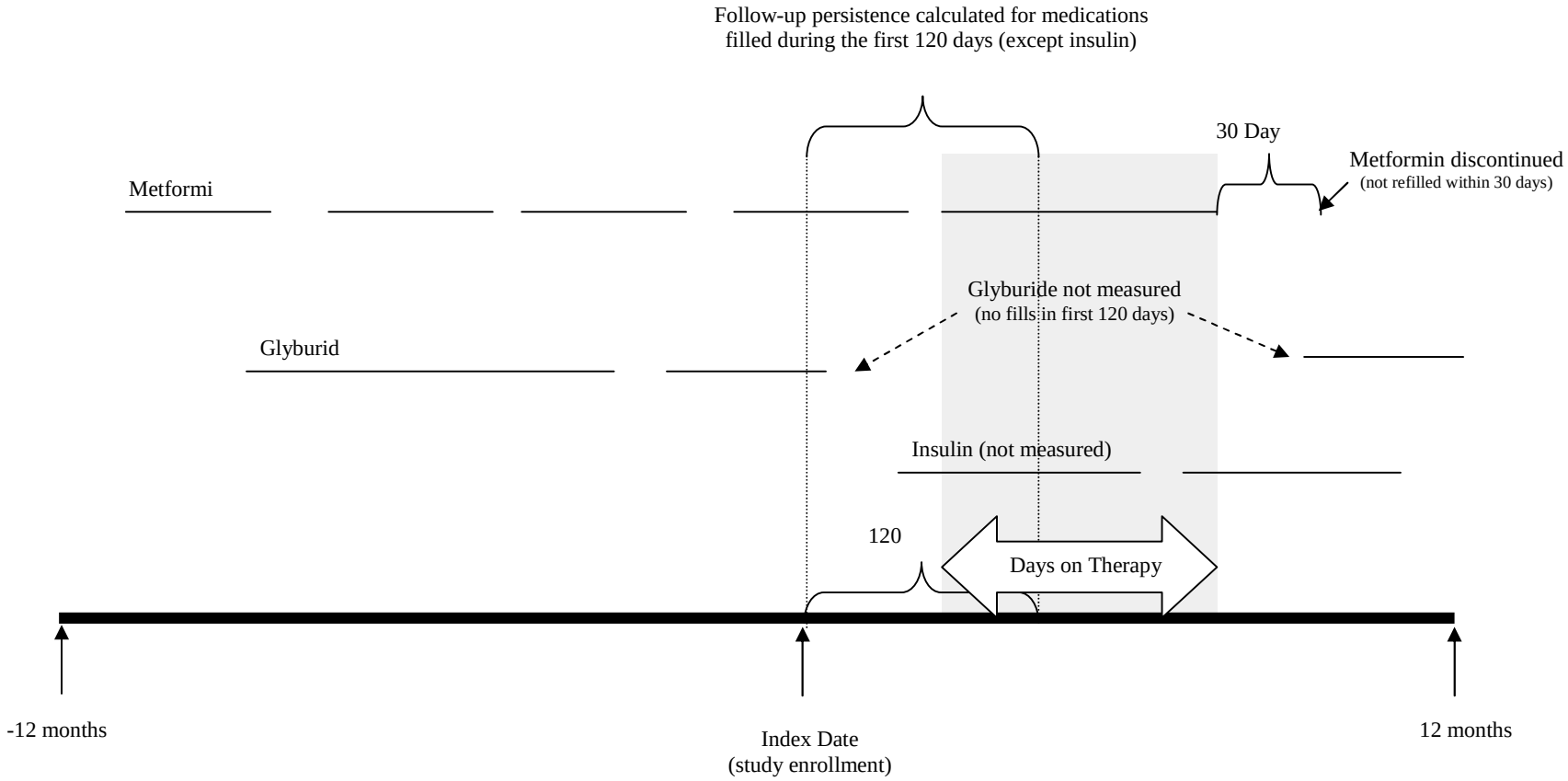


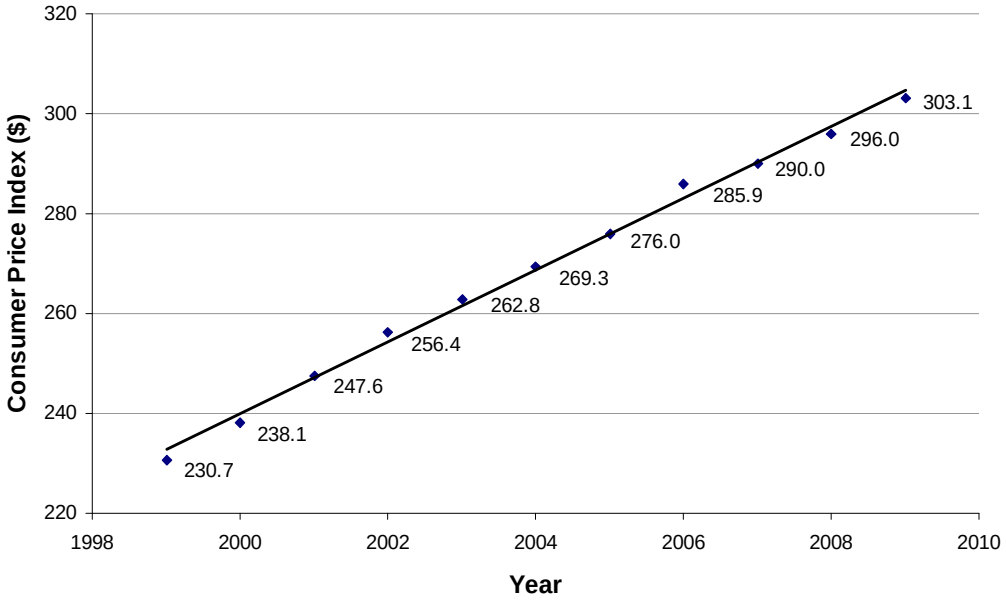
Figure 2.4. Follow-up Persistence Measurement Example



Economic Measures: Patient and Health Plan Pharmacy Costs

Pharmacy costs for both the patient and health plan were obtained from SWHP pharmacy claims data. Costs were divided into the following categories: medications and testing supplies for diabetes, medications for hypertension, medications for hyperlipidemia, and total medication and testing supply costs. Patient medication costs included both deductibles and co-payments for each medication. Pharmacy costs were adjusted to 2009 dollars using the consumer price index for medical commodities.

Figure 2.5. Consumer Price Index for Medical Commodities: 1999-2009



Source: United States Department of Labor: Bureau of Labor Statistics[65]

Note: 2009 CPI estimated from 1999-2008 trendline.

Data Analysis

Descriptive statistics were used to report clinical measures, medication adherence, and pharmacy costs. Means and standard deviations were reported for continuous variables, and frequencies and percents were reported for categorical variables. In addition, medians were reported for pharmacy costs as the cost data were not normally distributed.

Chi-square tests were used to analyze baseline co-morbidities in the two groups. Two-sample paired student's t-tests were used to analyze the change in A1C, MPR, days to discontinuation, and pharmacy costs between the groups. Generalized linear modeling was used to determine if a difference was seen between the groups in the percentage of patients achieving blood pressure control, cholesterol control, the percentage of patients adherent (MPR $\geq$80%) with medications for diabetes, hypertension, and hyperlipidemia, the percentage of patients with uncontrolled A1C (>9%), and the percentage of patients remaining on therapy at 6 months. McNemar's test was used to determine if a difference was seen in the percentage of patients achieving glycemic control (A1C<7%) instead of generalized linear modeling because no patients had glycemic control at baseline per the study inclusion criteria. A multivariate logistic regression was conducted to determine factors related to the achievement of glycemic control (A1C <7%). An a priori level of significance was set at 0.05. Data were analyzed using SPSS 16.0 (SPSS Inc., Chicago, IL) and SAS 9.1 (SAS Institute, Cary, NC).

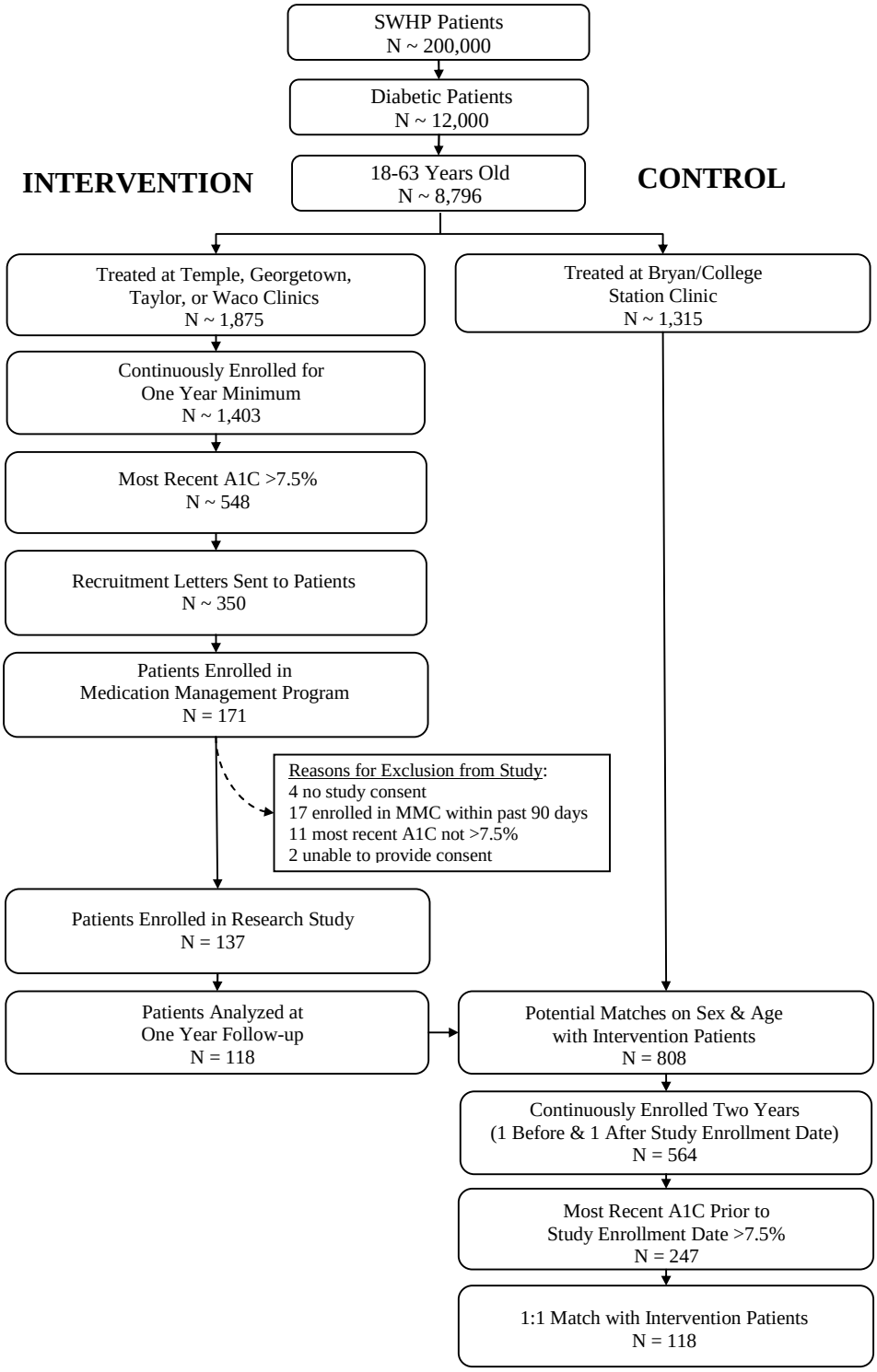
CHAPTER THREE: RESULTS

Patient Population

Approximately 12,000 diabetic patients receiving health care from SWHP were screened for participation in the medication management program. A complete overview of the patient screening, study enrollment, and matching process for both intervention and control patients is provided in Figure 3.1. Between August 2006 and July 2008, 171 patients enrolled in the medication management program. Of these, 137 patients enrolled in the research study evaluating the program. Reasons for participating in the medication management program but not the research study included unwillingness or inability to provide informed consent, participation in the Medication Management Clinic (MMC) within 90 days of program enrollment, and a most recent A1C prior to program enrollment ≤7.5%. Although patients had been screened for an A1C >7.5% prior to being invited to participate in the medication management program, some patients had an additional A1C test result between the time of screening and program enrollment which was ≤7.5%, therefore, making the patient ineligible for the research study.

Nearly 86% of patients (N = 118) remained in the program for at least one year and were analyzed in this evaluation. Of the 19 patients who did not remain in the program, 13 were not continuously enrolled in SWHP, 1 died (chronic heart failure), 4 patients requested to leave the program, and 1 patient was dismissed for not attending the required monthly appointments with the pharmacist.

Figure 3.1. Population Schematic



Note: Most numbers are approximations as there was a rolling enrollment process. Inclusion/exclusion criteria variables, such as age, length of continuous enrollment, and most-recent A1C test results changed over time for each patient. Therefore, the total number of patients that were eligible/ineligible for the study varied across the duration of the study.

As intervention and control patients were matched on sex and age, both groups were 55% female, ranged in age from 28-62 years, and had a mean age of 51.3 years (intervention group SD = 7.9 years, control group SD = 7.7 years). Although all patients were required to have diabetes, type of diabetes was not matched. Fourteen patients in the intervention group and 3 patients in the control group were type 1 diabetics, respectively. This difference was statistically significant ($P<0.05$).

Co-morbidities of primary interest included hypertension and hyperlipidemia. In both groups, 80-84% of patients had hypertension and/or hyperlipidemia. A low prevalence of diabetes-related complications was seen in both groups; complications included nephropathy, neuropathy, and retinopathy (Table 3.1). No significant difference between the groups was seen in the prevalence of co-morbid conditions.

Table 3.1. Prevalence of Diabetes-Related Chronic Conditions in Intervention and Control Patients at Baseline

Condition	**Intervention**	**Control**	**P-value**
Type 1 Diabetes	14 (11.9%)	3 (2.5%)	<0.05
Type 2 Diabetes	104 (88.1%)	115 (97.5%)	<0.05
Hypertension	99 (83.9%)	98 (83.0%)	1.000
Hyperlipidemia	99 (83.9%)	95 (80.5%)	0.610
Retinopathy	15 (12.7%)	11 (9.3%)	0.679
Nephropathy	6 (5.1%)	3 (2.5%)	0.499
Neuropathy	2 (1.7%)	2 (1.7%)	1.000

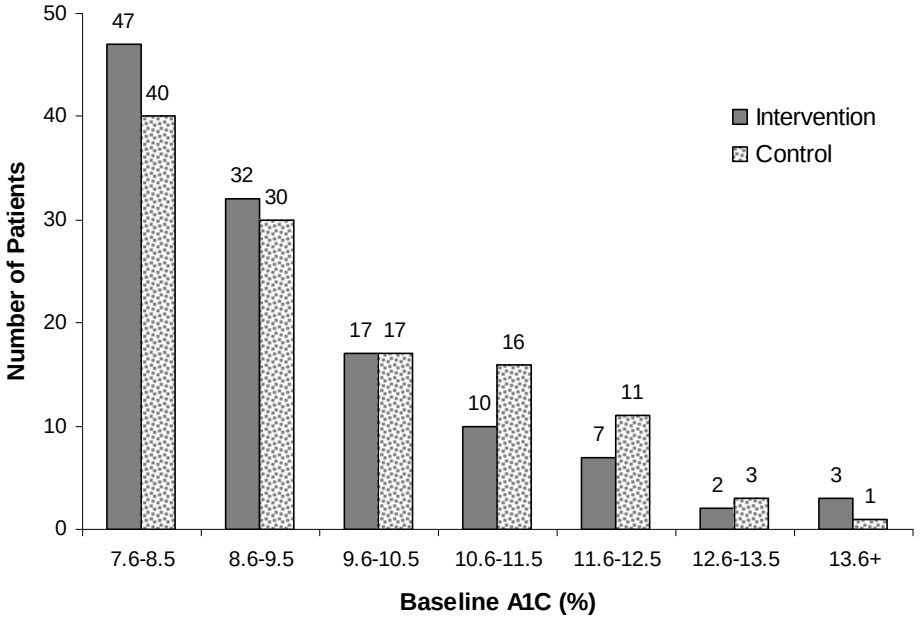
Source: Medical chart review for diabetes, hypertension, and hyperlipidemia; ICD-9 codes for other conditions
Analysis method: X^2 test

Clinical Measures

Glycemic Control

Patients in the intervention and control groups had similar baseline A1C measurements (Figure 3.2). At baseline, 45% and 55% of patients in the intervention and control groups, respectively, had poor glycemic control, as defined by HEDIS guidelines (A1C >9%).

Figure 3.2. Baseline A1C Measurements in Intervention and Control Patients



P=0.297 for paired t-test

Table 3.2 displays the mean baseline and follow-up A1C measurements for both groups. The mean change in A1C from baseline to follow-up in the intervention group was -1.1 ± 1.6, whereas the mean change in the control group was -0.6 ± 1.1. The difference in A1C change between the groups was statistically significant (P<0.05).

Table 3.2. Glycemic Control at Baseline and Follow-up in Intervention and Control Patients

	INTERVENTION GROUP N = 118	**CONTROL GROUP** N = 118	
Mean ± SD A1C			**Significance Level**
Baseline	9.3 ± 1.5	9.5 ± 1.5	
Follow-up	8.2 ± 1.4	9.0 ± 1.9	P<0.05[a]
Difference	*-1.1 ± 1.6*	*-0.6 ± 1.1*	
N (%) Patients with Glycemic Control, Defined as A1C <7%			
Baseline	0 (0%)	0 (0%)	P=0.345[b]
Follow-up	19 (16.1%)	13 (11.0%)	
N (%) Patients with Uncontrolled Hyperglycemia, Defined as A1C >9%			
Baseline	53 (44.9%)	65 (55.1%)	P=0.163[c]
Follow-up	31 (26.3%)	54 (45.8%)	

Note: 11 control patients did not have a follow-up A1C test during the one-year study period.
Analysis method:
a. Paired t-test
b. McNemar's test
c. Generalized linear model

Table 3.2 also shows the number and percentage of patients in each group who achieved the ADA recommended goal of A1C <7% during the one year follow-up. The difference between the groups in the percentage of patients achieving the A1C goal was not statistically significant (P=0.345).

The HEDIS definition of poor glycemic control (A1C >9%) was also used to evaluate the impact of the intervention on glycemic control. Although a greater reduction in the percentage of patients with poor glycemic control was seen in the intervention

group (45% at baseline to 26% at follow-up) than the control group (55% at baseline to 46% at follow-up), the difference was not statistically significant (P=0.163).

It should be noted that while all intervention patients had a baseline A1C measurement and at least one follow-up measurement available to evaluate the change in A1C over time, 11 control patients did not have a second A1C test result recorded in the electronic medical record during the one-year follow-up period. In the aforementioned analyses, the value of the baseline A1C measurement was used for both the baseline and follow-up in patients without a follow-up measurement.

A second evaluation of glycemic control was performed which excluded patients (and their individual matched pair) who did not have a follow-up A1C measurement. The purpose was to ensure that the 11 control patients with no change in A1C from baseline to follow-up, due to lack of a follow-up measurement, were not adversely affecting the study results. The results of these analyses, displayed in Table 3.3, support the prior claims. A significant difference in the absolute reduction of A1C was seen between the groups, but no significant differences were observed in the percentage of patients achieving A1C goal of <7% or in the reduction of the percentage of patients with poor glycemic control.

Table 3.3. Glycemic Control in Intervention and Control Patients with Both Baseline and Follow-up A1C Results

	INTERVENTION GROUP N = 107	**CONTROL GROUP** N = 107	
Mean ± SD A1C			**Significance Level**
Baseline	9.3 ± 1.5	9.5 ± 1.5	
Follow-up	8.2 ± 1.3	8.9 ± 1.9	P<0.05[a]
Difference	*-1.1 ± 1.5*	*-0.6 ± 1.8*	
N (%) Patients with Glycemic Control, Defined as A1C <7%			
Baseline	0 (0%)	0 (0%)	P=0.689[b]
Follow-up	16 (15.0%)	13 (12.1%)	
N (%) Patients with Uncontrolled Hyperglycemia, Defined as A1C >9%			
Baseline	48 (44.9%)	59 (55.1%)	P=0.232[c]
Follow-up	28 (26.2%)	48 (44.9%)	

Analysis method:
a. Paired t-test
b. McNemar's test
c. Generalized linear model

Interestingly, none of the fourteen intervention patients with type 1 diabetes achieved glycemic control at the follow-up, and only one of the three control patients with type 1 diabetes achieved the goal A1C. Based on this finding, an additional analysis of type 2 diabetics only was conducted (Table 3.4). Similar to the previous results, a greater decline in A1C was observed in the intervention group compared to the control group, -1.2% vs. -0.5%, respectively; the difference was statistically significant (P<0.05). More type 2 diabetics in the intervention group than in the control group achieved goal

A1C, but the difference was not statistically significant (P=0.522). Also, no significant difference was seen between the groups in the reduction of patients with poor glycemic control (P=0.293).

Table 3.4. Glycemic Control in Type 2 Diabetic Intervention and Control Patients

	INTERVENTION GROUP N = 102	**CONTROL GROUP** N = 102	
Mean ± SD A1C			**Significance Level**
Baseline	9.4 ± 1.6	9.4 ± 1.5	
Follow-up	8.2 ± 1.3	9.0 ± 1.8	P<0.05[a]
Difference	*-1.2 ± 1.6*	*-0.5 ± 1.8*	
N (%) Patients with Glycemic Control, Defined as A1C <7%			
Baseline	0 (0%)	0 (0%)	P=0.522[b]
Follow-up	15 (14.7%)	11 (10.8%)	
N (%) Patients with Uncontrolled Hyperglycemia, Defined as A1C >9%			
Baseline	34 (33.3%)	42 (41.2%)	P=0.293[c]
Follow-up	20 (19.6%)	37 (36.3%)	

Analysis method:
a. Paired t-test
b. McNemar's test
c. Generalized linear model

Blood Pressure Control

Table 3.5 displays mean systolic and diastolic blood pressures for intervention and control patients at baseline and follow-up. Patients were further stratified by a diagnosis of hypertension, based on manual review of the electronic medical record.

Table 3.5. Mean Blood Pressure and Percentage of Patients at BP Goal <130/80 mmHg at Baseline and Follow-up By Group and Hypertension Diagnosis

	INTERVENTION GROUP			CONTROL GROUP		
	HTN Dx N = 99	**No HTN Dx** N = 19	**All Patients** N = 118	**HTN Dx** N = 98	**No HTN Dx** N = 20	**All Patients** N = 118
Systolic Blood Pressure						
Mean ± SD (mmHg)						
Baseline	132.0 ± 15.3	120.5 ± 13.4	130.1 ± 15.6	134.9 ± 18.4	128.8 ± 16.7	133.9 ± 18.2
Follow-up	130.3 ± 15.4	120.7 ± 11.9	128.7 ± 15.3	136.0 ± 18.3	126.7 ± 13.4	134.4 ± 17.8
Difference	*-1.7 ± 18.2*	*0.2 ± 13.7*	*-1.4 ± 17.5*	*1.1 ± 19.2*	*-2.1 ± 18.8*	*0.6 ± 19.1*
Diastolic Blood Pressure						
Mean ± SD (mmHg)						
Baseline	74.4 ± 10.8	70.8 ± 8.8	73.8 ± 10.5	73.1 ± 9.2	71.9 ± 9.4	72.9 ± 9.2
Follow-up	73.9 ± 10.1	71.1 ± 9.7	73.5 ± 10.0	73.1 ± 10.5	72.3 ± 10.0	72.9 ± 10.4
Difference	*-0.5 ± 11.2*	*0.3 ± 9.9*	*-0.3 ± 10.9*	*-0.1 ± 9.0*	*0.4 ± 10.7*	*0.0 ± 9.3*
N (%) Patients with Blood Pressure at Goal, Defined as BP <130/80 mmHg[a]						
Baseline	41 (34.7%)	13 (68.4%)	54 (45.8%)	31 (31.6%)	9 (45.0%)	40 (33.9%)
Follow-up	42 (35.6%)	13 (68.4%)	55 (46.6%)	28 (28.6%)	10 (50.0%)	38 (32.2%)
N (%) Patients with Systolic BP at Goal, Defined as SBP <130 mmHg						
Baseline	45 (38.1%)	14 (73.7%)	59 (50.0%)	36 (36.7%)	10 (50.0%)	46 (39.0%)
Follow-up	48 (40.7%)	13 (68.4%)	61 (51.7%)	30 (30.6%)	12 (60.0%)	42 (35.6%)
N (%) Patients with Diastolic BP at Goal, Defined as DBP <80 mmHg						
Baseline	67 (56.8%)	17 (89.5%)	84 (71.2%)	73 (74.4%)	16 (80.0%)	89 (75.4%)
Follow-up	71 (60.2%)	16 (84.2%)	87 (73.7%)	75 (76.5%)	16 (80.0%)	91 (77.1%)

HTN = hypertension, Dx = diagnosis, BP = blood pressure, SBP = systolic blood pressure, DBP = diastolic blood pressure

a. Significance test by generalized linear model: P=0.737

In both the intervention and control group, mean blood pressures of patients without a diagnosis of hypertension tended to be slightly lower than those with a chart-documented hypertension diagnosis. Mean systolic and diastolic blood pressures remained relatively unchanged between baseline and follow-up in both groups, regardless of whether or not patients had a diagnosis of hypertension.

The percentage of patients meeting the ADA blood pressure goal of BP <130/80 mmHg remained stable over time in both groups, with approximately 46% patients in the intervention group and 33% of patients in the control group achieving that goal. A generalized linear model indicated no significant improvement in blood pressure control in the intervention group compared to the control group (P=0.737).

Further analysis of the systolic and diastolic blood pressures indicated that uncontrolled systolic blood pressure was largely responsible for the inability of patients to achieve the overall blood pressure goal of <130/80 mmHg, as the majority (71-77%) of patients met the diastolic BP goal of <80 mmHg. As with the overall blood pressure goal results, fewer patients in the control group had controlled systolic blood pressures compared to the intervention group.

Cholesterol Control

Table 3.6 displays mean HDL cholesterol, LDL cholesterol, total cholesterol, and triglyceride levels for intervention and control patients at baseline and follow-up. Similar to the blood pressure analysis, patients were further stratified by a diagnosis of hyperlipidemia, based on manual review of the electronic medical record. With the

Table 3.6. Change in Mean Cholesterol Levels From Baseline to One-Year Follow-up in Intervention and Control Patients

	INTERVENTION GROUP			CONTROL GROUP		
Cholesterol Test	**HLP Dx** N = 99	**No HLP Dx** N = 19	**All Patients** N = 118	**HLP Dx** N = 94	**No HLP Dx** N = 20	**All Patients** N = 114
HDL Cholesterol						
Mean ± SD (mg/dL)						
Baseline	41.0 ± 11.5	49.2 ± 18.3	42.3 ± 13.1	42.8 ± 12.1	42.6 ± 10.0	42.7 ± 11.7
Follow-up	40.0 ± 11.1	47.8 ± 20.4	41.3 ± 13.2	42.9 ± 12.0	43.6 ± 9.9	43.0 ± 11.6
Difference	*-1.0 ± 6.3*	*-1.4 ± 7.3*	*-1.0 ± 6.5*	*0.0 ± 6.6*	*1.1 ± 5.3*	*0.2 ± 6.4*
LDL Cholesterol						
Mean ± SD (mg/dL)						
Baseline[a]	90.1 ± 36.1	97.4 ± 19.2	91.4 ± 33.9	100.9 ± 40.3	106.5 ± 27.9	102.0 ± 38.1
Follow-up[b]	83.1 ± 33.4	94.2 ± 25.5	84.9 ± 32.4	96.1 ± 38.6	105.4 ± 34.7	97.9 ± 37.9
Difference	*-6.0 ± 29.2*	*-4.6 ± 21.8*	*-5.7 ± 28.0*	*-5.0 ± 37.6*	*-1.1 ± 33.9*	*-4.2 ± 36.7*
Total Cholesterol						
Mean ± SD (mg/dL)						
Baseline	168.4 ± 45.5	177.3 ± 20.0	169.8 ± 42.5	185.4 ± 52.8	175.2 ± 32.0	183.6 ± 49.8
Follow-up	161.7 ± 47.6	165.9 ± 32.5	162.4 ± 45.4	176.7 ± 51.0	174.0 ± 41.2	176.2 ± 49.2
Difference	*-6.8 ± 34.9*	*-11.3 ± 27.9*	*-7.7 ± 33.8*	*-9.2 ± 45.2*	*-1.2 ± 35.9*	*-7.8 ± 43.7*
Triglycerides						
Mean ± SD (mg/dL)						
Baseline	194.5 ± 143.2	154.0 ± 78.6	188.0 ± 135.5	232.1 ± 187.6	131.2 ± 42.9	214.4 ± 175.4
Follow-up	184.8 ± 110.0	131.6 ± 102.3	176.2 ± 110.1	203.0 ± 192.0	125.1 ± 50.3	189.3 ± 177.9
Difference	*-9.7 ± 103.4*	*-22.4 ± 69.6*	*-11.7 ± 98.6*	*-29.1 ± 162.3*	*-6.1 ± 43.0*	*-25.1 ± 148.5*

HLP = hyperlipidemia, Dx = diagnosis

Note: 19 control and 8 intervention patients had no lipid tests during the one-year follow-up.

a. Due to excessively high TG levels, 7 intervention and 13 control patients with a HLP dx had no baseline LDL value.

b. Due to excessively high TG levels, 6 intervention and 8 control patients with a HLP dx had no follow-up LDL value.

exception of HDL cholesterol in the intervention group, some improvement in all cholesterol types was seen at the one-year follow-up compared to baseline in both groups, regardless of whether or not patients carried a hyperlipidemia diagnosis.

Table 3.7 shows the percentage of intervention and control patients who met the recommended cholesterol levels of HDL cholesterol >40 mg/dL (males), HDL cholesterol >50 mg/dL (females), LDL cholesterol <100 mg/dL, total cholesterol <200 mg/dL, and triglycerides <150 mg/dL individually, as well as the percentage of patients who met all four goals at baseline and follow-up. In the intervention group, the percentage of patients meeting all cholesterol goals stayed relatively unchanged from baseline (11%) to follow-up (12%), whereas a slightly greater improvement was seen in the control group (7% to 12%). However, a generalized linear model showed that the difference was not significant (P=0.268).

Since the primary goal of lipid treatment in diabetic patients is to control LDL cholesterol levels, a generalized linear model was used to assess the change in LDL cholesterol control between the intervention and control groups. Both intervention and control groups showed some improvement in LDL cholesterol control, and no significant difference was seen between the groups (P=0.925). However, it should be noted that it was difficult to accurately assess LDL cholesterol control, because LDL levels could not be calculated for 20 patients at baseline and 14 patients at follow-up due to excessively high triglyceride levels.

Table 3.7. Number and Percentage of Intervention and Control Patients Meeting ADA Cholesterol Guidelines at Baseline and Follow-up

		HDL Cholesterol		LDL Cholesterol		Total Cholesterol		Triglycerides		All Lipid Tests	
		N (%) Patients at Goal >40 mg/dL (males) Goal >50 mg/dL (females)		N (%) Patients at Goal <100 mg/dL		N (%) Patients at Goal <200 mg/dL		N (%) Patients at Goal <200 mg/dL		N (%) Patients Meeting All Goal Values[a]	
	N	Baseline	Follow-up	Baseline[b]	Follow-up[c]	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
INTERVENTION											
HLP Diagnosis	99	27 (27.3%)	24 (24.2%)	60 (65.2%)	72 (77.4%)	74 (74.4%)	87 (87.9%)	44 (44.4%)	36 (36.4%)	11 (11.1%)	11 (11.1%)
No HLP Diagnosis	19	8 (42.1%)	7 (36.8%)	9 (47.4%)	10 (52.6%)	16 (84.2%)	15 (78.9%)	10 (52.6%)	15 (78.9%)	2 (10.5%)	3 (15.8%)
All Patients	118	35 (29.7%)	31 (26.3%)	69 (62.2%)	82 (73.2%)	90 (76.3%)	102 (86.4%)	54 (45.8%)	51 (43.2%)	13 (11.0%)	14 (11.9%)
CONTROL											
HLP Diagnosis	94	30 (31.9%)	30 (31.9%)	40 (49.4%)	52 (64.2%)	61 (64.9%)	64 (68.1%)	37 (39.4%)	42 (44.7%)	5 (5.3%)	11 (11.7%)
No HLP Diagnosis	20	6 (30.0%)	8 (40.0%)	11 (55.0%)	11 (55.0%)	15 (75.0%)	15 (75.0%)	13 (65.0%)	16 (80.0%)	3 (15.0%)	3 (15.0%)
All Patients	114	36 (31.6%)	38 (33.3%)	51 (45.9%)	63 (56.8%)	76 (66.7%)	79 (69.3%)	50 (43.9%)	58 (50.9%)	8 (7.0%)	14 (12.3%)

HLP = hyperlipidemia

Note: 19 control and 8 intervention patients had no lipid tests during the one-year follow-up.

a. Significance test by generalized linear model: P=0.268

b. Due to excessively high TG levels, 7 intervention and 13 control patients with a HLP dx had no baseline LDL value.

c. Due to excessively high TG levels, 6 intervention and 8 control patients with a HLP dx had no follow-up LDL value.

Among the four lipid types, patients in both the intervention and control groups were least likely to achieve the HDL cholesterol goal, with only approximately one-third of patients meeting this goal at both baseline and follow-up. Since goal HDL cholesterol levels are different for males and females, mean HDL cholesterol and HDL cholesterol control were further assessed by sex (Table 3.8). As expected, mean HDL cholesterol levels were slightly higher in females than males. Although mean HDL cholesterol levels were very similar between the intervention and control group, HDL cholesterol control rates were slightly higher in females in the control group than the intervention group.

Table 3.8. Mean HDL Cholesterol and HDL Cholesterol Control at Baseline and Follow-up By Group, Sex, and Diagnosis of Hyperlipidemia

	INTERVENTION GROUP			CONTROL GROUP		
	HLP Dx	**No HLP Dx**	**All Patients**	**HLP Dx**	**No HLP Dx**	**All Patients**
MALES						
	N = 48	N = 5	N = 53	N = 47	N = 5	N = 52
HDL Cholesterol Levels						
Mean ± SD (mg/dL)						
Baseline	37.7 ± 7.3	33.6 ± 6.8	37.3 ± 7.3	37.1 ± 8.3	38.2 ± 6.1	37.2 ± 8.0
Follow-up	38.1 ± 7.0	31.6 ± 4.0	37.5 ± 7.0	38.0 ± 9.0	40.6 ± 6.5	38.3 ± 8.7
Difference	*0.4 ± 4.6*	*-2.0 ± 3.7*	*0.2 ± 4.6*	*0.9 ± 6.6*	*2.4 ± 5.3*	*1.1 ± 6.5*
HDL Cholesterol Control						
N (%) Patients at Goal, HDL >40%						
Baseline	16 (33.3%)	1 (20.0%)	17 (32.1%)	11 (23.4%)	2 (40.0%)	13 (25.0%)
Follow-up	15 (31.3%)	0 (0.0%)	15 (28.3%)	13 (27.7%)	3 (60.0%)	16 (30.8%)
FEMALES						
	N = 51	N = 14	N = 65	N = 47	N = 15	N = 62
HDL Cholesterol Levels						
Mean ± SD (mg/dL)						
Baseline	44.2 ± 13.8	54.7 ± 18.0	46.5 ± 15.3	48.4 ± 12.7	44.0 ± 10.8	47.4 ± 12.3
Follow-up	41.9 ± 13.8	53.6 ± 20.8	44.5 ± 16.2	47.6 ± 12.8	44.6 ± 10.8	46.9 ± 12.3
Difference	*-2.2 ± 7.4*	*-1.1 ± 8.4*	*-2.0 ± 7.6*	*-0.9 ± 6.5*	*0.6* ± 5.5	*-0.5 ± 6.2*
HDL Cholesterol Control						
N (%) Patients at Goal, HDL >50%						
Baseline	11 (21.6%)	7 (50.0%)	18 (27.7%)	19 (40.4%)	4 (26.7%)	23 (37.1%)
Follow-up	9 (17.6%)	7 (50.0%)	16 (24.6%)	17 (36.2%)	5 (33.3%)	22 (35.5%)

HLP = hyperlipidemia, Dx = diagnosis

Note: 19 control and 8 intervention patients had no lipid tests during the one-year follow-up.

Adherence Measures

Medication Adherence

Tables 3.9 shows that for diabetes medications, a greater increase in medication adherence was observed in the control group than the intervention group, as measured by both the medication possession ratio (MPR) and the percentage of patients with an MPR ≥80%; both measures approached statistical significance with P=0.059 and P=0.066, respectively.

Evaluation of the number of unique medication classes that contributed to the MPR calculations indicates that while patients in the control group maintained a consistent 1.9 medications during the baseline and follow-up periods, patients in the intervention were more likely to have additional medications added during the intervention (2.3 medications at follow-up compared to 1.9 at baseline). The change in number of medications was statistically significant (P<0.05).

Although adherence to insulin was not calculated, adherence to oral antidiabetic medications may appear to decrease over time if patients switch from oral medications to insulin therapy. Therefore, an assessment of the number and percentage of type 2 diabetic patients initiating insulin therapy during the follow-up period was conducted (Table 3.10). No significant difference was seen in the percentage of patients initiating insulin during the follow-up period (P=0.389).

Table 3.9. Medication Adherence with Antidiabetic Agents and Mean Number of Medications Used

	INTERVENTION GROUP N = 79	**CONTROL GROUP** N = 85	
Medication Possession Ratio *Mean ± SD (%)*			**Significance Level**
Baseline	83.3 ± 0.2	75.8 ± 0.2	
Follow-up	84.8 ± 0.2	83.8 ± 0.2	P=0.059[a]
Difference	*1.6 ± 0.2*	*8.0 ± 0.2*	
Patients with MPR ≥ 80% *Number (%)*			
Baseline	54 (68.4%)	44 (51.8%)	P=0.066[b]
Follow-up	53 (67.1%)	59 (69.4%)	
Number of Medications *Mean ± SD*			
Baseline	1.9 ± 0.8	1.9 ± 0.7	
Follow-up	2.2 ± 0.9	1.9 ± 0.7	P<0.05[a]
Difference	*0.3 ± 0.7*	*0.0 ± 0.6*	

Note: Calculations include oral antidiabetic medication and exenatide.
Analysis method:
a. Paired t-test, N = 57
b. Generalized linear model

Table 3.10. Insulin Use in Type 2 Diabetics at Baseline and Follow-up in Intervention and Control Groups

	INTERVENTION GROUP N = 104	**CONTROL GROUP** N = 115	
Patients Using Insulin *Number (%)*			**Significance Level**
Baseline	72 (69.2%)	59 (51.3%)	
Follow-up	76 (73.1%	64 (55.7%)	P=0.389[a]
Difference	*4 (3.9%)*	*5 (4.4%)*	

a. Analysis method: generalized linear model

Table 3.11 shows that for antihypertensive medications, a greater increase in mean MPR was seen in the intervention group compared to the control group; the difference was not statistically significant (P=0.212). However, the increase in percentage of patients with an MPR ≥80% increased from 75.8% to 90.5% in the intervention group, while the percentage decreased from 67.9% to 63.1% in the control group. This difference was statistically significant (P=<0.05). Unlike the antidiabetic medications, a similar change in the number of antihypertensive medications used from baseline to follow-up was seen in both groups (P=1.000).

Table 3.11. Medication Adherence with Antihypertensive Agents and Mean Number of Medications Used

	INTERVENTION GROUP N = 95	**CONTROL GROUP** N = 84	
Medication Possession Ratio *Mean ± SD (%)*			**Significance Level**
Baseline	86.1 ± 0.2	82.3 ± 0.2	
Follow-up	91.2 ± 0.1	83.2 ± 0.2	P=0.212[a]
Difference	*5.1 ± 0.1*	*1.2 ± 0.2*	
Patients with MPR ≥ 80% *Number (%)*			
Baseline	72 (75.8%)	57 (67.9%)	P<0.05[b]
Follow-up	86 (90.5%)	53 (63.1%)	
Number of Medications *Mean ± SD*			
Baseline	2.2 ± 1.2	2.1 ± 1.1	
Follow-up	2.3 ± 1.3	2.3 ± 1.3	P=1.000[a]
Difference	*0.2 ± 0.5*	*0.2 ± 0.6*	

Analysis method:
a. Paired t-test, N = 67
b. Generalized linear model

Table 3.12 indicates that for antihyperlipidemic medications, no significant difference was seen between the intervention and control groups in the increase in MPR (P=0.329), the increase in the percentage of patients with an MPR ≥80% (P=0.845), or the change in number of medications used (P=0.660) from baseline to follow-up.

Table 3.12. Medication Adherence with Antihyperlipidemic Agents and Mean Number of Medications Used

	INTERVENTION GROUP N = 71	**CONTROL GROUP** N = 61	
Medication Possession Ratio *Mean ± SD (%)*			**Significance Level**
Baseline	84.8 ± 0.2	76.2 ± 83.7	
Follow-up	88.2 ± 0.1	83.7 ± 0.2	P=0.329[a]
Difference	*3.3 ± 0.2*	*7.4 ± 0.2*	
Patients with MPR ≥ 80% *Number (%)*			
Baseline	48 (67.6%)	34 (55.7%)	P=0.845[b]
Follow-up	55 (77.5%)	39 (63.9%)	
Number of Medications *Mean ± SD*			
Baseline	1.4 ± 0.6	1.2 ± 0.4	
Follow-up	1.4 ± 0.5	1.3 ± 0.5	P=0.660[a]
Difference	*0.0 ± 0.4*	*0.1 ± 0.4*	

Analysis method:
a. Paired t-test, N = 42
b. Generalized linear model

Medication Persistence

Table 3.13 provides persistence with medications for diabetes, hypertension, and hyperlipidemia, as measured by the mean days to discontinuation with medications started within the first 120 days of the baseline and follow-up time periods. For all three medication types, the days to discontinuation improved in the intervention group compared to the control group; however, the differences were not statistically significant.

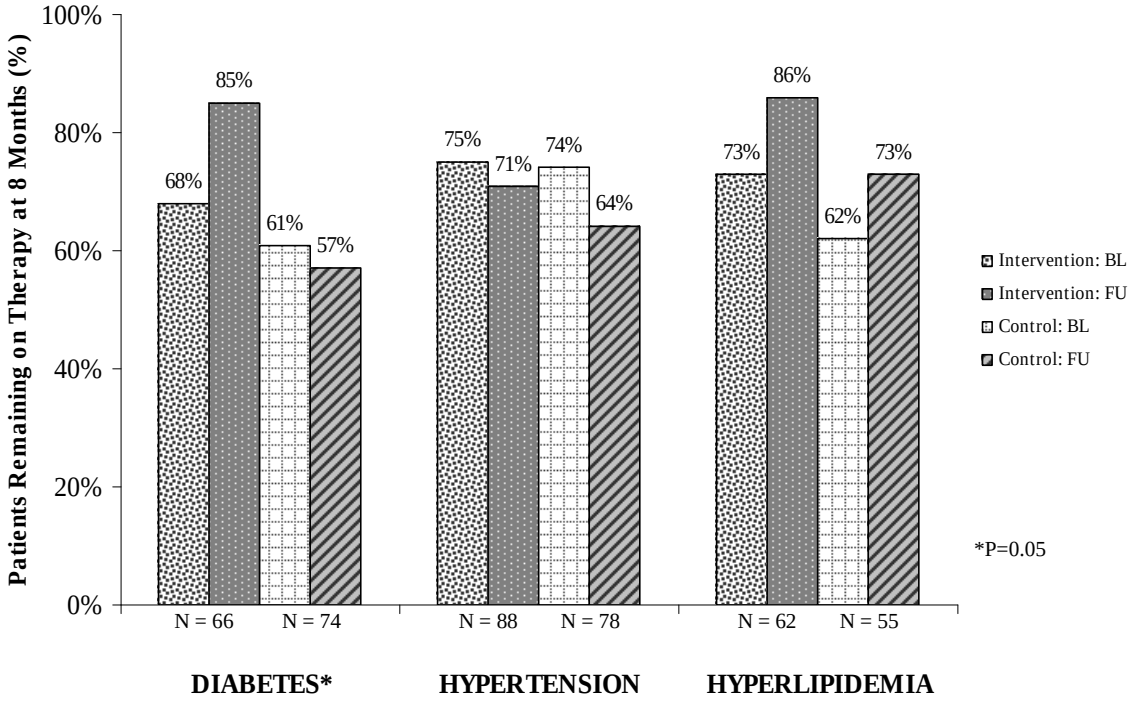
Table 3.13. Mean Days to Discontinuation with Medications for Diabetes, Hypertension, and Hyperlipidemia

	INTERVENTION GROUP	**CONTROL GROUP**	
		Diabetes	
Days to Discontinuation			**Significance Level**
Mean ± SD	N = 66	N = 74	
Baseline	239.1 ± 99.4	228.8 ± 102.5	
Follow-up	259.2 ± 94.6	210.1 ± 106.4	P=0.226[a]
Difference	*20.0 ± 131.2*	*-18.7 ± 125.0*	
		Hypertension	
	N = 88	N = 78	
Baseline	248.1 ± 91.3	242.6 ± 96.0	
Follow-up	241.7 ± 102.5	230.5 ± 103.4	P=0.926[b]
Difference	*-6.4 ± 114.9*	*-12.1 ± 123.8*	
		Hyperlipidemia	
	N = 62	N = 55	
Baseline	249.6 ± 93.0	222.8 ± 104.3	
Follow-up	267.6 ± 82.4	238.6 ± 104.4	P=0.391[c]
Difference	*18.0 ± 113.0*	*15.8 ± 109.4*	

Note: Diabetes calculation includes oral antidiabetic medications and exenatide.
a. Paired t-test, N = 42
b. Paired t-test, N = 56
c. Paired t-test, N = 29

The percentage of patients remaining on therapy at 6 months is presented in Figure 3.3. For diabetes medications, the percentage of patients remaining on therapy increased from 68% to 85% in the intervention group, while it decreased from 61% to 57% in the control group. This difference approached statistical significance (P=0.050).

Figure 3.3. Persistence with Medications for Diabetes, Hypertension, and Hyperlipidemia



BL=baseline, FU=follow-up
Statistical testing method: generalized linear model
Diabetes: P=0.050, Hypertension: P=0.546, Hyperlipidemia: P=0.594

For hypertension medications, the percentage of patients remaining on therapy decreased in both the intervention and control groups. Although the decrease was less in the intervention than the control group, the difference was not statistically significant (P=0.546). For hyperlipidemia medications, the percentage of patients remaining on

therapy increased in both the intervention and control groups. The difference between the groups was not statistically significant (P=0.594).

Economic Measures

Patient Pharmacy Costs

Table 3.14 displays the total pharmacy costs, including both co-payments and deductibles, paid by SWHP members, among patients who had a pharmacy cost in the baseline or follow-up periods. Costs are categorized as those related to diabetes, hypertension, hyperlipidemia, and "other". As expected with the co-payment waiver for diabetes medications and supplies in the intervention group, a significant difference in the change in all diabetes-related member costs from baseline to follow-up was seen between the intervention and control groups (P<0.05). No significant difference was seen in the change in member costs for other medication types. Overall, a 37.2% reduction in patient pharmacy costs in the intervention group and a 6.5% increase in patient pharmacy costs in the control group was seen between baseline and follow-up.

Health Plan Pharmacy Costs

Table 3.15 presents the total health plan costs, categorized as those related to diabetes, hypertension, hyperlipidemia, and other, for patients who had a pharmacy cost in the baseline or follow-up periods. Similar to member costs, a significant difference was observed in the change in all diabetes-related health plan costs from baseline to follow-up between the intervention and control groups (P<0.05). In addition, the change

Table 3.14. Member Costs at Baseline and Follow-up among Patients with a Pharmacy Claim, by Group and Medication Type

INTERVENTION GROUP

		Baseline		Follow-up		Difference	
	N	Median	Mean [SD]	Median	Mean [SD]	Median	Mean [SD]
DIABETES							
Insulin	76	$234.51	$276.14 [$271.70]	$0.00	$9.03 [$21.14]	-$234.51	-$267.11 [$272.39]*
Other DM Medications[a]	94	$73.84	$148.36 [$185.38]	$0.00	$14.46 [$59.98]	-$73.57	-$133.90 [$192.97]*
Diabetic Supplies[b]	118	$101.04	$107.53 [$159.78]	$0.00	$7.95 [$20.58]	-$98.68	-$99.57 [$157.79]*
DIABETES TOTAL	118	$295.42	$403.57 [$351.56]	$0.00	$25.29 [$63.54]	-$288.40	-$378.28 [$356.79]*
HYPERTENSION							
All HTN Medications	112	$98.09	$139.33 [$155.49]	$120.14	$153.57 [$139.03]	$11.36	$14.24 [$74.19]
HYPERLIPIDEMIA							
All HLP Medications	96	$96.92	$140.44 [$188.68]	$90.38	$145.21 [$193.02]	-$2.16	$4.77 [$102.39]
OTHER							
All Other Medications	115	$187.02	$267.97 [$314.01]	$221.56	$290.59 [$324.48]	$1.80	$22.63 [$162.59]

CONTROL GROUP

		Baseline		Follow-up		Difference	
	N	Median	Mean [SD]	Median	Mean [SD]	Median	Mean [SD]
DIABETES							
Insulin	64	$188.10	$190.41 [$136.40]	$202.37	$240.66 [$225.29]	$6.53	$50.25 [$221.55]*
Other DM Medications[a]	104	$71.94	$151.29 [$204.56]	$91.42	$140.54 [$183.32]	-$0.83	-$10.76 [$141.36]*
Diabetic Supplies[b]	94	$59.55	$70.23 [$91.28]	$60.08	$81.54 [$96.77]	$2.62	$11.31 [$69.56]*
DIABETES TOTAL	118	$192.50	$292.56 [$296.29]	$203.86	$319.35 [$318.51]	$5.74	$26.78 [$210.24]*
HYPERTENSION							
All HTN Medications	104	$89.81	$117.07 [$106.63]	$106.20	$117.57 [$105.56]	-$0.11	$0.51 [$76.32]
HYPERLIPIDEMIA							
All HLP Medications	91	$86.68	$112.99 [$130.36]	$66.66	$119.91 [$164.52]	-$0.90	$6.92 [$106.81]
OTHER							
All Other Medications	113	$136.71	$206.42 [$253.00]	$151.20	$218.88 [$269.07]	$3.09	$12.45 [$188.24]

DM = diabetes, HTN = hypertension, HLP = hyperlipidemia
a. Includes all oral prescription antidiabetic medications and exenatide.
b. Includes blood glucose monitors, test strips, lancets, and insulin syringes.
*P<0.05; paired t-test

Table 3.15. Health Plan Costs at Baseline and Follow-up among Patients with a Pharmacy Claim, by Group and Medication Type

INTERVENTION GROUP

		Baseline		Follow-up		Difference	
	N	Median	Mean [SD]	Median	Mean [SD]	Median	Mean [SD]
DIABETES							
Insulin	76	$1,054.00	$1231.27 [$1093.17]	$1,921.12	$2431.70 [$1847.69]	$863.04	$1200.44 [$1397.90]*
Other DM Medications[a]	94	$215.72	$416.36 [$562.43]	$407.67	$1062.13 [$1162.93]	$152.98	$645.77 [$896.17]*
Diabetic Supplies[b]	118	$163.84	$213.71 [$344.46]	$853.96	$794.18 [$564.01]	$520.34	$580.47 [$436.31]*
DIABETES TOTAL	118	$1,031.61	$1338.41 [$1246.67]	2745.35	$3206.47 [$2290.98]	$1,468.57	$1868.06 [$1590.73]*
HYPERTENSION							
All HTN Medications	112	$108.92	$217.84 [$276.43]	$104.34	$247.16 [$312.69]	$3.71	$29.31 [$149.35]
HYPERLIPIDEMIA							
All HLP Medications	96	$316.05	$378.45 [$389.30]	$231.21	$299.02 [$340.61]	-$20.80	-$79.43 [$351.25]
OTHER							
All Other Medications	115	$215.90	$1168.57 [$3717.75]	$423.25	$1372.45 [$4300.01]	$45.45	$202.88 [$854.28]*

CONTROL GROUP

		Baseline		Follow-up		Difference	
	N	Median	Mean [SD]	Median	Mean [SD]	Median	Mean [SD]
DIABETES							
Insulin	64	$923.26	$1011.91 [$987.38]	$1,178.80	$1292.43 [$1229.17]	$151.76	$280.52 [$683.81]*
Other DM Medications[a]	104	$169.14	$486.52 [$775.80]	$222.77	$462.66 [$764.49]	$0.00	-$23.85 [$407.38]*
Diabetic Supplies[b]	94	$152.23	$206.27 [$290.39]	$213.70	$263.01 [$362.62]	$1.14	$56.74 [$201.38]*
DIABETES TOTAL	118	$598.63	$1141.95 [$1356.60]	$709.14	$1318.27 [$1548.23]	$66.04	$176.33 [$686.64]*
HYPERTENSION							
All HTN Medications	104	$84.73	$216.00 [$290.80]	$92.90	$233.76 [$338.25]	$4.19	$17.76 [$181.78]
HYPERLIPIDEMIA							
All HLP Medications	91	$327.75	$401.38 [$433.50]	$122.46	$247.46 [$311.47]	-$25.91	-$153.91 [$378.84]
OTHER							
All Other Medications	113	$175.42	$440.47 [$901.84]	$216.23	$430.06 [$858.79]	$0.84	-$10.41 [$264.01]*

DM = diabetes, HTN = hypertension, HLP = hyperlipidemia

a. Includes all oral prescription antidiabetic medications and exenatide.

b. Includes blood glucose monitors, test strips, lancets, and insulin syringes.

*P<0.05; paired t-test

from baseline to follow-up in the cost of other medications was significantly different between the intervention group ($202.88 ± $854.28) and the control groups (-$10.41 ± $264.01; P<0.05). No significant difference was seen between the two groups in the change in health plan costs for antihypertensive medications (P=0.552) or antihyperlipidemic medications (P=0.416).

Table 3.16 shows the total health plan pharmacy costs for the entire study population, categorized by group and medication type. While pharmacy costs increased 3.1% in the control group, costs increased 67.8% in the intervention group overall. Diabetes-related costs and other medications were primarily responsible for the difference in overall costs between the groups. Among the diabetes-related costs, the largest increase in cost in the intervention group was in diabetic testing supplies (271.6%), followed by non-insulin diabetic medications (155.1%), and insulin (97.5%).

Table 3.16. Total Health Plan Costs at Baseline and Follow-up for all Patients, by Group and Medication Type

	INTERVENTION GROUP (N=118)				CONTROL GROUP (N=118)			
	Baseline	**Follow-up**	**Difference**	**% Change**	**Baseline**	**Follow-up**	**Difference**	**% Change**
DIABETES								
Insulin	$93,576.30	$184,809.48	$91,233.18	97.5%	$64,762.26	$82,715.79	$17,953.53	27.7%
Other DM Medications[a]	$39,138.14	$99,840.25	$60,702.11	155.1%	$50,597.83	$48,117.10	-$2,480.73	-4.9%
Diabetic Supplies[b]	$25,217.84	$93,713.29	$68,495.45	271.6%	$19,389.76	$24,723.38	$5,333.62	27.5%
DIABETES TOTAL	$157,932.28	$378,363.02	$220,430.74	139.57%	$134,749.85	$155,556.27	$20,806.42	15.4%
HYPERTENSION								
All HTN Medications	$24,398.45	$27,681.68	$3,283.23	13.5%	$22,464.17	$24,311.05	$1,846.88	8.2%
HYPERLIPIDEMIA								
All HLP Medications	$36,331.02	$28,705.47	-$7,625.55	-21.0%	$36,525.16	$22,519.19	-$14,005.97	-38.3%
OTHER								
All Other Medications	$134,385.87	$157,716.96	$23,331.09	17.4%	$49,773.52	$48,596.68	-$1,176.84	-2.4%
TOTAL								
All Medications	$353,047.62	$592,467.13	$239,419.51	67.8%	$243,512.70	$250,983.19	$7,470.49	3.1%

HTN = hypertension, HLP = hyperlipidemia

a. Includes all oral prescription antidiabetic medications and exenatide.

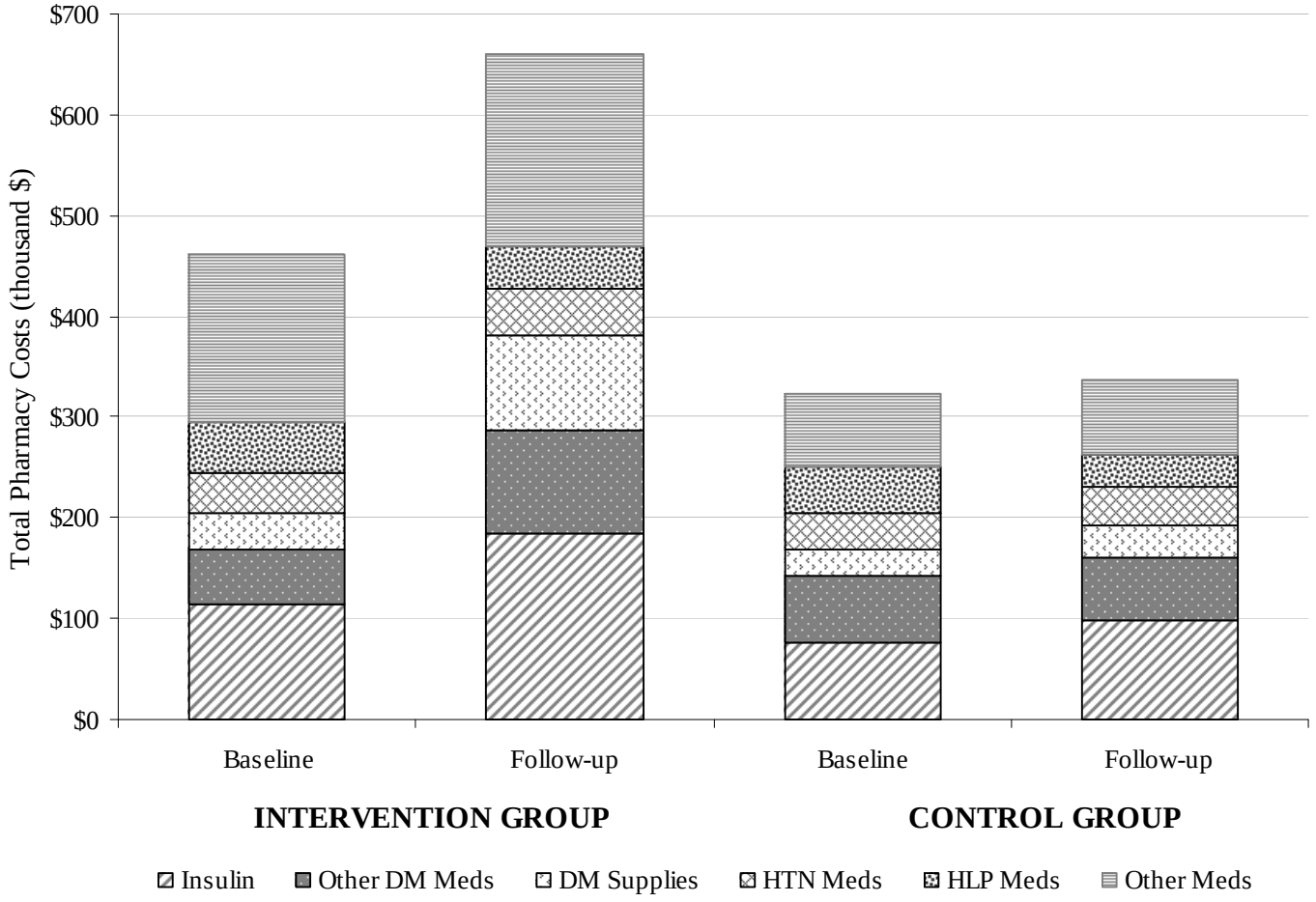
b. Includes blood glucose monitors, test strips, lancets, and insulin syringes.

Total Pharmacy Costs

Total pharmacy costs, which include both member and health plan costs, are presented in Figure 3.4. In the control group, costs remained relatively stable between baseline and follow-up, but expenditures for insulin increased 28%, while those for antihypertensive medications increased 25%. The amount paid for medications for hyperlipidemia decreased by 29%.

In the intervention group, a substantial increase in expenditures for insulin (62%), non-insulin diabetic medications (91%), and diabetic testing supplies (150%) was observed. Also, increased expenditure was seen on other medications during the follow-up period (16%). Similar to the control group, the expenditure on antihypertensive medications increased slightly (12%), while a slight decrease in the amount paid for antihyperlipidemic medications (-14%) was observed. Overall, total pharmacy costs increased 43.3% in the intervention group and increased 3.9% in the control group from baseline to follow-up.

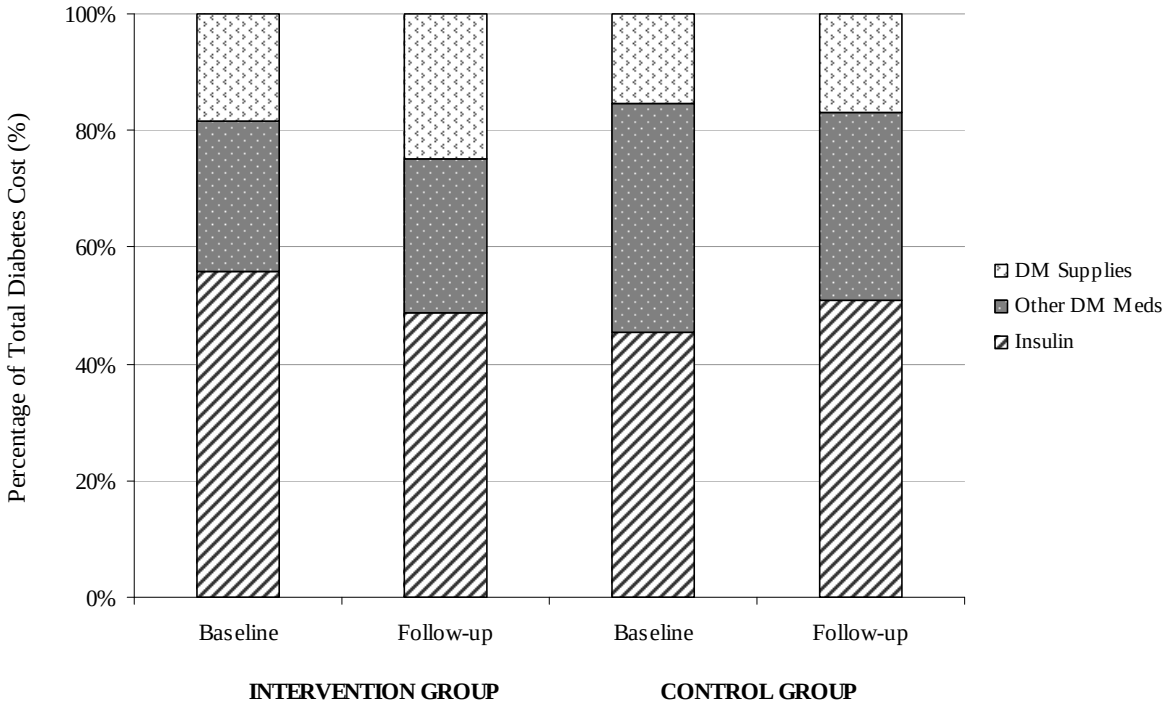
Figure 3.4. Total Pharmacy Costs at Baseline and Follow-up, by Group and Medication Type



Diabetes-related Pharmacy Costs

Figure 3.5 compares each component of the diabetes-related costs (insulin, other diabetic medications, and diabetic testing supplies) at baseline and follow-up in the intervention and control groups. Although expenditure increased for all three components in the intervention group, the greatest increase in expenditure was for diabetic testing supplies, while the largest relative increase in expenditure in the control group was for insulin.

Figure 3.5. Relative Change in Diabetes-related Pharmacy Costs in Intervention and Control Patients



Factors Related to Achieving Glycemic Control

A multivariate logistic regression was conducted to determine factors related to the achievement of goal A1C (<7%) at the end of the follow-up period (Table 3.17). Covariates in the regression included study group, sex, age, diabetes type, improvement in adherence with non-insulin diabetes medications, improvement in persistence with non-insulin diabetes medications, start of insulin therapy, increased number of oral diabetes medications, and increased use of diabetic testing supplies. Results of the regression indicated that patients in the intervention group were approximately 8.7 times more likely to achieve the A1C goal than control patients (P<0.05). All other variables were not statistically significant.

Table 3.17. Logistic Regression of Achievement of Goal A1C at Follow-up

Variable	Odds Ratio	Sig.	95% CI
Adherence	0.86	0.791	0.27-2.67
Age: 35-44 years	1.30	0.748	0.27-6.34
Age: 45-54 years	0.67	0.515	0.20-2.22
Group	8.69	0.035	1.17-64.64
Insulin	3.04	0.434	0.19-49.23
Number of Medications	0.32	0.324	0.04-3.04
Persistence	0.75	0.622	0.24-2.33
Sex	0.65	0.464	0.20-2.07
Testing Supplies	0.22	0.156	0.03-1.78

Reference groups: Adherence= follow-up MPR ≤ baseline MPR; Age=25-34 years at study enrollment; DM type=type 1 diabetes; Group=control; Insulin=no insulin initiated during follow-up period; Number of medications=follow-up diabetes medication number ≤ baseline diabetes medication number; Persistence=follow-up days to discontinuation ≤ baseline days to discontinuation; Sex=male; Testing supplies=cost of follow-up diabetes testing supplies ≤ cost of baseline diabetes testing supplies
Note: DM type and Age 55-64 covariates removed from model due to redundancy.

Summary of Results

Tables 3.18-3.20 provide a review of the hypotheses tested and the study results.

Table 3.18. Summary of Hypotheses for Clinical Outcomes

Hypothesis	Description	Result	Explanation
$H_0$1	There is no relationship between the change in A1C from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.	Rejected	A paired t-test showed a significantly greater decrease in mean A1C in intervention patients (-1.1% ± 1.5%) than control patients (-0.6% ± 1.8%; P<0.05).
$H_0$2	There is no relationship between the change in the percentage of patients achieving goal A1C (<7%) from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.	Accepted	McNemar's test showed no significant difference in the percentage of patients achieving A1C goal at follow-up in the intervention group (16.1%) and the control group (11.0%; P=0.345).
$H_0$3	There is no relationship between the change in the percentage of patients with poor glycemic control (A1C >9%) from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.	Accepted	A generalized linear model showed that although a greater reduction in the percentage of patients with poor glycemic control was seen in the intervention group (45% at BL to 26% at FU) than the control group (55% at BL to 46% at FU), the difference was not statistically significant (P=0.163).
$H_0$4	There is no relationship between the change in the percentage of patients achieving goal blood pressure (BP <130/80) from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.	Accepted	A generalized linear model indicated no significant difference between the groups in change in the percentage of patients achieving in blood pressure control in the intervention group (45.8% at BL to 46.6% at FU) compared to the control group (45.0% at BL to 50.0% at FU; P=0.737).
$H_0$5	There is no relationship between the change in the percentage of patients achieving all goal cholesterol levels (LDL <100, HDL >40 for males, HDL >50 for females, total cholesterol <200, triglycerides <150) from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.	Accepted	A generalized linear model indicated no significant difference between the groups in change in the percentage of patients achieving in cholesterol control in the intervention group (11.0% at BL to 11.9% at FU) compared to the control group (7.0% at BL to 12.3% at FU; P=0.268).

BL=baseline; FU=follow-up

Table 3.19. Summary of Hypotheses for Medication Adherence

Hypothesis	Description	Result	Explanation
$H_0$6	There is no relationship between the change in adherence to medications for diabetes from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.	Accepted*	1) A paired t-test showed no significant difference in the change in MPR in the intervention group (1.6 ± 0.2) and the control group (8.0 ± 0.2; P=0.059).
		Accepted*	2) A generalized linear model showed no significant difference in the change in the percentage of patients achieving MPR ≥80% in the intervention group (68.4% at BL to 67.1% at FU) compared to the control group (51.8% at BL to 69.4% at FU; P=0.066).
		Accepted*	3) A paired t-test showed no significant difference in the change in days to discontinuation in the intervention group (20.0 ± 131.2) and the control group (-18.7 ± 125.0; P=0.226).
		Accepted*	4) A generalized linear model showed no significant difference in the change in the percentage of patients remaining on therapy at 6 months in the intervention group (68% at BL to 85% at FU) compared to the control group (61% at BL to 57% at FU; P=0.050).
$H_0$7	There is no relationship between the change in adherence to medications for hypertension from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.	Accepted	1) A paired t-test showed no significant difference in the change in MPR in the intervention group (5.1 ± 0.1) and the control group (1.2 ± 0.2; P=0.212).
		Rejected	2) A generalized linear model showed a significant difference in the change in the percentage of patients achieving MPR ≥80% in the intervention group (75.8% at BL to 90.5% at FU) compared to the control group (67.9% at BL to 63.1% at FU; P<0.05).
		Accepted	3) A paired t-test showed no significant difference in the change in days to discontinuation in the intervention group (-6.4 ± 114.9) and the control group (-12.1 ± 123.8; P=0.926).
		Accepted	4) A generalized linear model showed no significant difference in the change in the percentage of patients remaining on therapy at 6 months in the intervention group (75% at BL to 71% at FU) compared to the control group (74% at BL to 64% at FU; P=0.546).
$H_0$8	There is no relationship between the change in adherence to medications for hyperlipidemia from baseline to follow-up for patients participating in the medication management program and patients receiving usual care.	Accepted	1) A paired t-test showed no significant difference in the change in MPR in the intervention group (3.3 ± 0.2) and the control group (7.4 ± 0.2; P=0.3.9).
		Accepted	2) A generalized linear model showed a significant difference in the change in the percentage of patients achieving MPR ≥80% in the intervention group (67.6% at BL to 77.5% at FU) compared to the control group (55.7% at BL to 63.9% at FU; P=0.845).
		Accepted	3) A paired t-test showed no significant difference in the change in days to discontinuation in the intervention group (18.0 ± 113.0) and the control group (15.8 ± 109.4; P=0.391).
		Accepted	4) A generalized linear model showed no significant difference in the change in the percentage of patients remaining on therapy at 6 months in the intervention group (75% at BL to 71% at FU) compared to the control group (74% at BL to 64% at FU; P=0.546).

BL=baseline; FU=follow-up

*A significant increase in the number of medications used at FU compared to BL was observed in the intervention group.

Note: 4 methods were used to analyze adherence for each medication type.

Table 3.20. Summary of Hypotheses for Pharmacy Costs and Achievement of Goal A1C

Hypothesis	Description	Result	Explanation
$H_0$9	There is no relationship between the change in patient pharmacy costs for diabetes/hypertension/hyperlipidemia/other medications and testing supplies for patients participating in the medication management program and patients receiving usual care.	Rejected	Paired t-tests showed no significant difference between the groups in the change in patient pharmacy costs for hypertension medications, hyperlipidemia medications, and other medications; however, a significant difference was seen between the groups in the change in patient pharmacy costs for insulin, other diabetes medications, and diabetic testing supplies.
$H_0$10	There is no relationship between the change in health plan pharmacy costs for diabetes/hypertension/hyperlipidemia/other medications and testing supplies for patients participating in the medication management program and patients receiving usual care.	Rejected	Paired t-tests showed no significant difference between the groups in the change in health plan pharmacy costs for hypertension medications and hyperlipidemia medications; however, a significant difference was seen between the groups in the change in health plan pharmacy costs for insulin, other diabetes medications, diabetic testing supplies, and other medications.
$H_0$11	There is no relationship between the ability of patients to achieve goal A1C (<7%) and study group, sex, age, diabetes type, improvement in medication adherence, improvement in medication persistence, initiation of insulin therapy, increased number of antidiabetic agents, or increased use of diabetic testing supplies.	Rejected	A multivariate logistic regression revealed that, controlling for factors such as sex, age, and diabetes type, patients in the intervention group were approximately 8.7 times more likely to achieve goal A1C than patients in the control group.

CHAPTER FOUR: CONCLUSION

Discussion

Patient Population

In the general population, estimates indicate that 5-10% of diabetic patients have type 1 diabetes.[1] In this study population, however, nearly 12% of patients in the intervention group and only 2.5% of the control group were type 1 diabetics. This difference in the prevalence of type 1 diabetes between the two groups was statistically significant ($P<0.05$).

The reason for the observed difference between the groups is difficult to ascertain. While all patients were SWHP members, patients in the intervention were invited to participate in the program and signed a consent form for study enrollment, while patients in the control group were not aware of the research study, were randomly selected from a similar population (that only knowingly differed from the intervention population in that those subjects were treated at a different clinic location), and were matched to intervention patients based on sex and age.

Since random selection of a control group yielded a significantly lower percentage of type 1 diabetics than in the intervention group, this observation suggests one or more of the following may be true:

1) The two patient populations differ in the prevalence of type 1 diabetes

2) Type 1 diabetics were more likely to participate in the intervention than type 2 diabetics (due to patient willingness, physician recommendation, and/or early screening and recruitment of type 1 diabetics)
3) Type 2 diabetics in the control group were more likely to have poorly controlled A1Cs (>7.5%)
4) Type 1 diabetics in the control group were more likely to have well-controlled A1Cs (≤7.5%)
5) Type 1 diabetics in the control group were less likely to be continuously enrolled for two years than type 2 diabetics

Additionally, although a review of ICD-9 codes showed relatively similar co-morbidities in the two groups, the intervention group generally had greater pharmacy costs at baseline than the control group, particularly for insulin (as expected by the greater proportion of type 1 diabetic patients) and "other medications." This suggests patients in the intervention group may have been slightly sicker or more likely to use medications than control patients.

Clinical Measures

The mean A1C significantly improved in the intervention population compared to the controls (-1.1% ± 1.6% vs. -0.6% ± 1.1%; $P<0.05$). The difference of 0.5% is similar to, but slightly less than, two similar retrospective cohort studies evaluating pharmacist interventions in type 1 and type 2 diabetic patients; those studies showed an average difference of 0.75% and 1.0% in A1C improvement between intervention and control

groups.[63] In this study, the percentage of patients achieving goal A1C (<7%) and the percentage of patients with uncontrolled A1C (>9%), although improved, were not significantly better in the intervention group than the control group. These outcome measures have not been reported in other studies.

Interestingly, no type 1 diabetic patients in the intervention achieved goal A1C. The mean change in A1C for type 1 diabetic patients was -0.1%, whereas it was -1.1% for the entire intervention group. This finding suggests that the program may not be as effective in type 1 diabetic patients as in type 2 patients. Type 1 diabetics tend to be diagnosed at a younger age; therefore, the educational component of this program may not have been as useful for them, since those patients had been treated for a number of years and may not have had as much to learn. Also, many of the educational materials provided in the program were directed specifically toward type 2 diabetic patients. In addition, a greater risk of a hypoglycemic episode exists with insulin – which all type 1 diabetics use – compared to oral antidiabetic medications. Therefore, type 1 diabetics may strive to keep their A1C near the upper end of the recommended level to prevent hypoglycemia.

Blood pressure measures remained relatively unchanged in both intervention and control patients, with intervention patients achieving a 0.8 mmHg greater reduction in systolic blood pressure and 0.3 mmHg greater reduction in diastolic blood pressure. A similar study by Martin et al. (2004), which evaluated an intervention in which poorly controlled diabetic patients (A1C >7%) met with a pharmacist for medication adjustments every 6 weeks for a year, found a 4 mmHg greater reduction in systolic

blood pressure and a 2 mmHg greater reduction in diastolic blood pressure.[66] In this study, change in the percentage of patients achieving goal blood pressure of <130/80 at follow-up compared to baseline was not significant (P=0.737). This outcome measure has not been reported in similar studies.

In this study, no significant difference was seen in the change in percentage of patients achieving complete cholesterol control between the groups (P=0.268). This outcome measure has not been evaluated in similar studies. The study by Martin et al. (2004) found the mean LDL cholesterol decreased 9 mg/dL more in the intervention than in the control group.[66] In this study, the mean LDL cholesterol decreased 1.5 mg/dL more in the intervention group than in the control group.

Adherence and Economic Measures

In general, this population was highly adherent with medications. It was expected that the co-payment waiver for diabetic medications and testing supplies would increase adherence to diabetic medications. Only two studies have evaluated adherence with diabetic medications after a similar pharmacist-led intervention was implemented; both found no significant improvement in adherence in the intervention group compared to control patients.[63] However, one major limitation of both studies was that patient reporting was used to measure adherence. This methodology is not ideal since it is subjective and may be limited by patient recall.

This study used pharmacy claims to evaluate medication adherence and generated somewhat mixed results for adherence with diabetic medications; no significant

improvement was seen in medication adherence in the intervention group compared to the control group, as measured by the MPR (P=0.059). On the other hand, a significant increase was seen in the number of medications taken in the follow-up period in the intervention group compared to the control group. This finding suggests that patients in the intervention group were more likely to be prescribed additional medications during the intervention and/or patients in the intervention were more likely to fill and/or refill medications due to the co-payment waiver.

As medication adherence has been shown to decrease with increased pill burden, this observation may help explain why the improvement in MPR in the intervention group was less than expected.[67] Another possible explanation involves the design of the program, in which patients were required to meet with a pharmacist each month to receive a 30-day supply of medication(s). Studies have shown that patients who receive 90-day medication supplies generally have higher adherence rates than patients who receive 30-day supplies.[68] Assuming some patients participating in the intervention previously received 90-day medication supplies, the change to a 30-day supply, along with the necessity to attend an appointment with a pharmacist, may have contributed to the less-than-expected increase in medication adherence for diabetic medications.

Medication persistence was evaluated as the percentage of patients remaining on therapy at 6 months. In this study, the increase from 68% to 85% in the intervention group was significantly different from the decrease from 61% to 57% in the control group ($P<0.05$).

For antihypertensive medications, improvement in MPR, the percentage of patients with MPR ≥80%, days to discontinuation, and percentage of patients remaining on therapy at 6 months was seen in the intervention group relative to controls. However, the difference in the percentage of patients adherent with antihypertensive medications (MPR ≥80%) was the only finding that was statistically significant ($P<0.05$). Both groups used an average of 0.2 additional medications during the follow-up period. Patient co-payment data support the theory that patients in the intervention are more willing to pay for other medications, since those individuals have diabetic medication co-payment waivers. However, the change in co-payment for antihypertensive medications was not significantly different between the groups ($14.24 ± $74.19 vs. $0.51 ± $76.32; $P=0.167$).

Adherence to medications for hyperlipidemia increased from baseline to follow-up in both the intervention and control groups, as measured by the MPR, percentage of patients adherent (MPR ≥80%), days to discontinuation, and percentage of patients remaining on therapy at 6 months. No significant differences were observed between the groups in the change from baseline to follow-up in any of the aforementioned measures, or in the number of antihyperlipidemic medications taken. Patient co-payments and health plan costs decreased for antihyperlipidemic medications during the follow-up period, likely due to the introduction of the first generic HMG-CoA reductase inhibitor into the market and the subsequent placement of the generic product onto the formulary in late 2006-early 2007.

The average annual increase in pharmacy costs during the time of this study was approximately 7-8%.[69,70] The data from this study generally reflect this trend, with a few exceptions. The economic analysis showed a substantial increase in diabetes medications and testing supplies in the intervention group, as would be expected with the medication co-payment waiver and increased medication monitoring via monthly follow-up visits. Additionally, the decrease in cost of antihyperlipidemic medications was likely due to increased use of generic products.

Relative to the control group, the intervention group had a greater increase in antihypertensive and other medication costs and a smaller decrease in cost of antihyperlipidemic medications. Possible explanations for this finding are that the medication co-payment waiver for diabetes medications may have made patients more willing to fill other medications, the educational sessions may have made patients more aware of the importance of adhering to medications, and/or the intervention patients may have been a sicker population.

In an effort to evaluate the effectiveness of the medication management program and control for confounding factors, a multivariate logistic regression was performed. The results of the analysis showed that the intervention itself was the only factor which significantly improved the likelihood of patients achieving glycemic control.

Limitations

- Patients were not matched on diabetes type. Significantly more type 1 diabetic patients were enrolled in the intervention group than the control group.

- The study methodology assumed the A1C goal for all patients was <7%. However, some patients may have had a less-stringent A1C goal.
- The small sample size made it impossible to conduct some sub-analyses of interest (i.e. type 1 diabetics vs. type 2 diabetics, patients taking medication vs. not taking medication, etc.) and may be responsible for some of the non-significant results due to insufficient power.
- Pharmacy and medical claims databases are generated for the purpose of collecting payment for medications and medical services. When using pharmacy and medical claims data for research purposes, many assumptions are made. For example, if a patient fills a prescription for a medication, the assumption is that the patient will take the medication. Similarly, it is assumed that a patient has the disease that a medical service is billed under, although the visit may have actually been to rule out the diagnosis.
- In this study, ICD-9 codes collected from the baseline year did not fully identify co-morbid conditions in the population. For example, although it was known that all intervention and control patients had a diagnosis of diabetes, only 11 of 17 patients had an ICD-9 code for type 1 diabetes and 59 of 219 patients had an ICD-9 code for type 2 diabetes. Therefore, a manual search of the electronic medical record was conducted to determine diabetes type, as well as record of a hypertension or hyperlipidemia diagnosis, as these were the co-morbidities of greatest interest in this study. Other co-morbidities are likely highly underreported in the study results.

- Change in clinical measurements may not be completely accurate due to the timing and limited availability of the baseline and follow-up tests. For example, in the intervention group, nearly all patients had a blood pressure measurement recorded on the date of study enrollment, whereas baseline blood pressure measurements for control patients came from the clinic visit nearest in date (generally within a month) of the study enrollment date. Much greater variation was seen in the timing of A1C measurements. Many baseline A1C tests were conducted greater than 3 months before study enrollment in both the intervention and control groups. Thus, the tests may not accurately reflect the patient's glycemic control at the time of enrollment. Fewer follow-up A1C and cholesterol tests were conducted in the control population compared to the intervention group. In addition, an LDL cholesterol level was not able to be calculated for many patients due to excessively high triglyceride levels.
- Patients may have seen physicians outside the SWHP network for treatment, and thus medical record and laboratory information may not have been complete. For example, for patients with missing A1C or cholesterol tests, a search of the electronic medical record was conducted. Notes from outside physicians provided laboratory values for four of these patients.
- Physician instructions for medication use were not available. Since this study evaluated chronic conditions, it was assumed that once a patient initiated a medication, those subjects would remain on the agent indefinitely. However, patients may have been instructed to discontinue a medication.

- It was assumed that all antihypertensive medications were used for hypertension and should have been continued indefinitely. However, many antihypertensives are used for other diagnoses, or in the case of some diuretics, may be prescribed as needed.
- The number of hospitalizations, office visits, and emergency department visits and cost data were not available for analysis, but are necessary to truly measure the cost-effectiveness of the intervention. Each patient's ethnicity, duration of diabetes, knowledge about diabetes, as well as the frequency of pharmacist-initiated medication changes and incidence of adverse effects (i.e. hypoglycemia) would also be useful and should be evaluated to determine if the study intervention is superior to usual diabetes care.
- Patients who met the study inclusion criteria were invited to participate in the medication management program. As this program required substantial commitment with monthly appointments and also provided a potentially large monetary incentive with the co-payment waiver, selection bias may have occurred.
- This study was conducted in high risk type 1 and type 2 diabetic patients (most recent A1C >7.5%) within a managed care organization in central Texas. Results of this study may not be generalizeable to other populations.
- Pharmacy and/or medical cost savings may not been seen during the first year of the intervention as cost savings are expected to result from a relative reduction in the utilization of medical resources in the long-run due to a slowed progression of diabetes and/or a decrease in diabetes-related complications.

Conclusion

The pharmacist-led medication management program significantly improved A1C levels in intervention patients relative to controls. The intervention was more effective in lowering A1Cs in type 2 diabetics than type 1 patients. Although the generalized linear model showed that the intervention did not significantly improve the percentage of patients achieving the ADA goal A1C of <7% compared to controls, the multivariate logistic regression, which controlled for factors such as diabetes type, showed that patients participating in the intervention were 8.7 times more likely to achieve the A1C goal.

Persistence with diabetic medications and the number of medications taken significantly increased in the intervention group; however, adherence rates, as measured by MPR, did not significantly improve relative to controls. The expenditure on diabetic medications and testing supplies increased substantially more in the intervention group than in the control group. Whether or not the increased pharmacy cost was offset by decreased medical costs is unknown.

Patients participating in the intervention were significantly more likely to become adherent with their antihypertensive medications; however, this finding did not translate into significantly better blood pressure control. For patients taking medications for hyperlipidemia, adherence and persistence increased in both groups, while pharmacy costs decreased in both groups. The introduction of the first generic HMG-CoA reductase inhibitor during the study was likely responsible for this finding.

CHAPTER FIVE: APPENDICES

APPENDIX I: Physician Letter and Patient List

(Insert Date)

Dear Dr. (Insert Last Name):

We are currently recruiting patients with diabetes to participate in a member benefit medication management program. Enrollees in the program will also be eligible to participate in a protocol which has received approval from the Scott & White Institutional Review Board.

The Scott and White Health Plan in conjunction with the CDM Pharmacy will be providing patients with information about diabetes and diabetes medications as well as provide monitoring to help improve treatment of the disease. The program is designed to improve medication and glycemic monitoring compliance as well as improve patients' self monitoring skills. Participants in the program will have selected medication and supply co-payments waived for the duration of their participation in the program. Patients who meet the eligibility criteria will continue to qualify for these copay waivers, for up to two years, as long as they continue to participate in the program.

Patients will be invited to participate via letter (see Appendices II and III). All patients will be given a phone number to call if they have any questions regarding the service and therefore should not need to contact your office.

After providing written agreement with the terms of the program, patients enrolling in the medication management program will meet with a pharmacist monthly to review medications and self-monitoring results as well as receive written and verbal educational materials.

Enclosed is a list of your patients meeting the program criteria as identified by SWHP claims databases. Screening criteria included the patient being 18 – 63 years of age, utilizing more than $1200 per year of medications based on 2005 claims, and taking an antidiabetic medication.

If you are not the physician provider for a patient, please check the column, "*not my patient*". In addition, if you know the patient's physician provider, please list the provider name in the appropriate column. If you identify additional patient names you feel would qualify for the program, please submit their name and MRN or date of birth.

If you are aware of special circumstances such that this program and study would **not be beneficial to a particular patient, please circle the patient's name on the enclosed**

sheet and fax the sheet to (254)215-9106 **by _____.** You may also reply by emailing ttabor@swmail.sw.org or jjuan@swmail.sw.org. Feel free to contact Tricia Tabor, Pharm.D. or Joyce Juan, Pharm.D. by telephone at 254-215-9117 (or T1 extension 219117) or pager 254-762-1067 (Tabor) or 254-762-3308 (Juan).

Thank you for your time in reviewing this list and also for your support of this new program
and important research project.

The following is a list of your patients who are identified as possible candidates for the medication management program and study. **Please circle the name of any patient who would not benefit from the program or the study**. Again, thank yoSu for your involvement.

Patient Name	**MRN**	**Not my patient**	**If not your patient, please list primary care provider if known**

Please return by fax to 254-215-9106 or email (ttabor@swmail.sw.org or jjuan@swmail.sw.org).

APPENDIX II: Medication Management Program Research Study Patient Letter

(Insert date)

Dear (insert patient name):

A research study is being done at Scott & White to look at the care of people with diabetes. This study will look at a way to provide care and educate patients with diabetes. This study will also look at how having diabetes affects the way people feel about their health and well-being.

The study will last 2 years, and about 450 other people will be participating. This study will evaluate the outcomes from involvement in the Medication Management Program. The program is described in the attached letter from Scott & White Health Plan. The people participating in the study will have the medical information that has been collected during the course of the program evaluated and compared to medical information from people who do not participate in a Medication Management Program. You may choose not to be in the study, and your decision will not affect your care in any way. Being in the study will not change the medical care you receive or the medications you take.

Please indicate on the enclosed card if you are or are not interested in participating in the study and mail the card back in the enclosed self-addressed, stamped envelope. If you indicate on the card that you are interested in participating (or if you don't return the card), you will be contacted by telephone by one of the individuals conducting the study within 10 days. The purpose of the phone call is to answer any questions you might have and to discuss your possible participation.

Please feel free to contact the Scott & White number 1-254-215-9117 and leave a message with any questions you may have. The pharmacist will then call you back to answer your questions.

Sincerely,

APPENDIX III: Medication Management Program Patient Letter

Dear Scott & White Health Plan Member:

The Scott & White Health Plan is announcing a Member Benefit Medication Management Program at the CDM Outpatient Pharmacy. We would like to invite you to participate in this program. This program involves monthly meetings with the pharmacist to help you better manage your diabetes. By participating in this program, you would also receive your diabetes medications and testing supplies free of charge.

At the first appointment, the pharmacist would ask information from you about your diabetes, medications, and lifestyle. Then you would meet with the pharmacist every month to receive diabetes monitoring and education. The pharmacist would adjust the doses of your diabetes medicines as needed as well as recommend diet and exercise changes. The pharmacist would also monitor your blood pressure and cholesterol. This type of pharmacist-led diabetes management service has been used in other areas of the country and has been shown to improve patients' health.

Although the main goal of this program is to improve your diabetes control, another benefit of this program is that the co-pays for your diabetes medications would be waived. You would receive your diabetes medications and testing supplies free of charge if you follow the requirements of the program, which include the monthly appointments with the pharmacist, laboratory tests, and regular visits to your primary care doctor. This program requires a commitment from you to attend these appointments, but in return we hope you will see improvement in your diabetes control.

Please indicate on the enclosed card if you are or are not interested in participating in the program and mail the card back in the enclosed self-addressed, stamped envelope. If you would like more information about this program or you would like to participate, you may also contact the Scott & White Pharmacy at 254-215-9117.

If you indicate on the card that you are interested in participating (or if you don't return the card), you will be contacted by telephone by one of the pharmacists within 10 days to answer any questions you might have and to discuss your possible participation in the program.

Sincerely,

Craig Clanton, M.D.

APPENDIX IV: Authorization for Use and Disclosure of Health Information for Research Purposes and Consent Form

CONSENT FORM and
AUTHORIZATION FOR USE AND DISCLOSURE
OF HEALTH INFORMATION for Research Purposes

Diabetes Outcomes Evaluation

SCOTT & WHITE CLINIC
SCOTT AND WHITE MEMORIAL HOSPITAL AND
SCOTT, SHERWOOD AND BRINDLEY FOUNDATION
TEMPLE, TEXAS 76508

You are being offered an opportunity to participate in a research study to evaluate the effects of pharmacist counseling and education on the health and health care costs of patients with diabetes. This is a non-funded research project. Neither the investigator nor Scott & White will receive payment from an outside source for the costs related to the conduct of this study.

Before you agree to volunteer to take part in this research study, it is very important that you understand the purpose of the study and how health information about you may be used or given to others during the study and after the study is finished.

Purpose and Background
The purpose of this research study is to test a method for improving control of diabetes. You will be one of approximately 450 subjects in this research study. The method to be evaluated is the Medication Management Program at Scott & White.

Procedures
You are eligible to participate in this study because you are eligible to participate in the Medication Management Program. If you agree to participate in the study, the information obtained during the Medication Management Program will be evaluated and compared to the same information from patients who do not participate in the Medication Management Program. This information will be gathered from your answers to questionnaires, your answers to questions from the pharmacist, weight, height and blood pressure measurements at the pharmacist visits, information from your Scott & White medical record as well as information from your Scott & White health care claims. There are no additional visits, tests, or medications needed by the research study.

Length of Study and Number of Visits
The study will last two years.

Exclusions

You should not participate in this study if any of the following apply to you:

- you are unable to fill out the study surveys or communicate with the pharmacist
- you meet with the Medication Management Clinic currently or have met with the clinic in the past 90 days.

Discomfort and Risks

The possible risk of this study is thought to be minimal. A breach of confidentiality of your medical information could occur. For the purposes of the study, you will not be identified by name, picture or any other personally identifying manner. The research team will not release any data collected as part of this research that includes your name, social security number, address, telephone number, health plan beneficiary information or any other direct personal identifier, unless you have given permission for Scott & White to do so.

Benefits

It is not anticipated that you would obtain direct benefit from the research study. The possible benefits of this study are to show the benefits of the Medication Management Program. These benefits could include improved control of diabetes, improved satisfaction with care and treatment, and decreased health care costs.

Alternative Therapies

You have the alternative of not participating in this study. If that is the case you can continue the routine care of your diabetes with your doctor. You also are able to continue participation in the Medication Management Program.

Cost and Compensation

The research study does not require any additional visits with the pharmacist, laboratory tests, or medications. There is no compensation for the research study.

New Findings

Any new findings developed during the course of your participation in the study, which may be related to your willingness to participate, will be provided to you.

Termination of Subject Participation

Your participation may be terminated at any time by your physician and/or the investigators without your consent. You may choose to leave the study at any time without penalty or loss of benefits to which you are otherwise entitled.

Confidentiality

Study records that identify you will be kept confidential as required by law. The health information that may be used and/or disclosed to conduct the study includes medical records and information created or collected during your participation in the Medication Management Program.

Health information that identifies you will be used for medical, statistical and regulatory purposes related to research. By agreeing to participate in this research, you are giving authorization for the research team to use and report the results of treatments, tests and examinations conducted for the Medication Management Program and for matters related to study oversight and data analysis to:

- the Scott & White Institutional Review Board (IRB – a group of people who strive to protect the rights of subjects)
- the Scott & White Research Compliance Office or Privacy Office.
- Scott & White employees involved in this study.
- local, state and federal agencies (such as the Office for Human Research Protections and the U.S. Food and Drug Administration) when required by law.

Once health information about you has been disclosed to a sponsor or anyone outside of this study, the information may no longer be protected by the federal privacy regulation.

The research team will not release any data collected as part of this research that includes your name, social security number, address, telephone number, health plan beneficiary information or any other direct personal identifier, unless you have given permission for Scott & White to do so. You will not be identified by name, picture or any other personally identifying manner if information from this study is presented publicly or published in a medical journal.

Right to Withdraw Consent and Authorization

Participation in this study is voluntary. You may withdraw from participation and/or revoke your authorization for the use of private information at any time during the study. Your decision to withdraw and/or revoke your authorization will not result in any penalty or loss of benefits to which you are entitled. Your decision will not affect the medical care you receive at Scott & White.

You have a right to revoke your authorization. A request to revoke an authorization must be submitted in writing to Tricia Tabor, Pharm.D., Scott & White Pharmacy, 1605 S. 31st Street, Suite 19, Temple, Texas, 76508. Revoking your authorization only affects uses and sharing of information collected after your written request has been received. Information collected prior to revoking the authorization may continue to be used and disclosed for research integrity and reporting purposes only.

Right to Access

You have a right to access your private health information, including health information that is collected for the research. However, in order to protect the integrity of the study, your right to access your research records may be suspended during the conduct of the study. After the study is over (meaning the end of the whole study, not just your own participation), you will be given access to these records upon your request.

This Authorization does not have an expiration date.

Whom to Contact for Questions or Emergencies

If you have additional questions during the course of this study about your rights as a research subject, you may address them to the IRB Office at (254) 724-4072. If you have any questions about the research, please contact Tricia Tabor, Pharm.D., at (254)215-9117.

If you have not already received a copy of the Notice of Privacy Practices, you may request one. If you have any questions or concerns about your privacy rights, you should contact the Scott & White Privacy Office at Ph: 254-724-7600.

Participation

Participation in this study is voluntary and refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled. If you decide not to sign the Authorization, you will not be allowed to participate in the research study.

Statement of Consent and Authorization

The research study has been explained to me and I have had an opportunity to read this consent form/authorization and have all of my questions answered. I have been informed that I may leave the study at any time without affecting my medical care and the Sponsor or my doctor may withdraw me from the study without my consent. I freely agree to take part in this research and authorize the research team to create, obtain, use or disclose personally identifiable information in connection with this study. A signed copy of this consent form/authorization will be given to me.

_____	_____	_____
Printed Name of Subject	Signature	Date

Statement of Person Obtaining Consent

I have carefully explained to the subject the nature of the study. I hereby certify that to the best of my knowledge the subject signing this consent form/authorization understands clearly the nature, demands, risks and benefits involved in participating in this study. A medical problem or language or educational barrier has not prevented a clear understanding of the subject's involvement in this study.

_____	_____	_____
Printed Name of Person Obtaining Consent	Signature	Date

APPENDIX V: Diabetes Patient Education Materials

Scott and White Health Plan Member Benefit Medication Management Program
Diabetes Patient Education Pieces

Education topics:

Visit 1: Diabetes overview and goals
- "What is Diabetes?" (TDC)
- "Getting the Very Best Care for Your Diabetes"(ADA)
- "Taking Care of Type 2 Diabetes" (ADA)
- "Why Worry About Diabetes?" (NDEP)
- Lab dates/results forms (NDEP)

Visit 2: Using glucometer/self-monitoring of blood glucose (SMBG)
- "All About Blood Glucose for People with Type 2 Diabetes" (ADA)
- "General Procedure for Self Blood Glucose Monitoring" (TDC)
- When to call health care provider (TDC)
- Blood glucose log (TDC)

Visit 3: Acute complications
- Hypoglycemia and hyperglycemia picture charts (TDC)
- "Examples of Treatments for Hypoglycemia" (NDEP)

Visit 4: Medication timing and administration
- "Managing Your Medicines" (ADA)
- "Insulin" timing and administering (TDC)

Visit 5: Nutrition, reading labels
- "Basic Nutrition Guidelines for People with Diabetes" (TDC)
- Food Pyramid (TDC)
- MyPyramid.gov – individualized food pyramids (USDA)
- Food labels, portion sizes (TDC)
- "Food and Activity Tracker" (ADA)

Visit 6: Carbohydrate counting
- "All About Carbohydrate Counting" (ADA)

Visit 7: Exercise
- ADA – "All About Physical Activity for People with Diabetes"
- NDEP – "Getting More Active – for People with Diabetes"
- TDC – "Blood Sugar Limits for Exercise"
- TDC – "How to Take Your Pulse"
- TDC – "Leg Exercises for People with Diabetes"

Visit 8: Medications (mechanism of action/side effects/adherence)
- "Oral Medicines" (TDC)

Visit 9: Chronic complications
- "Complications of Diabetes" chart (TDC)
- "Taking Care of Your Heart" (ADA)
- "The SIMPLE Method for Preventing Diabetes Complications" (NDEP)

"Warning Signs for Complications" (NDEP)

Visit 10: Foot care

"Foot Care for People with Diabetes" (TDC)
"Foot Care Tips" (TDC)
"Foot Care Checklist" (NDEP)
"Diabetic Food and Skin Care" (NDEP)
"Preventing Foot Injuries on the Job" (NDEP)
"Shoe Fitting Recommendations" (NDEP)
LEAP Program & monofilament (BPHC)

Visit 11: Psychosocial issues

"Learning How to Change Habits" (ADA)
"Changing Behavior" (TDC)
"Coping with Diabetes" (TDC)
"Lift Your Spirits" (NDEP)
"Facts about Depression" slides (NDEP)
"Recommended Readings for Coping with Diabetes and Depression" (NDEP)

Visit 12: Stress management

"Diabetes and Stress Management" (TDC)
"Stress" slides (signs, coping, management) (NDEP)
Stress test (NDEP)

Sources:

ADA = American Diabetes Association
BPHC = Bureau of Primary Health Care
NDEP = National Diabetes Education Program
USDA = United States Department of Agriculture
TDC = Texas Diabetes Council

Note: This is a general outline of educational topics to be discussed at each visit, when applicable. For example, patients with type 1 diabetes will not receive educational materials such as "All About Blood Glucose for People with Type 2 Diabetes," rather, they would learn about the importance and timing of measuring blood glucose as a type 1 diabetic.

APPENDIX VI: Collaborative Practice Agreement

Scott & White Health Plan
Member Benefit Medication Management Program
Drug Therapy Management Protocol

This drug therapy management protocol is done to comply with the pharmacy and medical practice acts regarding drug therapy management (DTM) by a pharmacist under written protocol of a physician. The procedures, protocols, practices, and other items contained within this document are intended to be helpful reminders for the pharmacists and physicians of this institution. In no instance should the contents of this document be considered as standards of professional practice or as rules of conduct or for the benefit of any third party. This document is a guideline only and allows for professional discretion and deviation where the individual healthcare provider deems variation to be appropriate as allowed by law.

A. The individual physicians authorized to prescribe drugs and responsible for the delegation of DTM are _____ of Community Internal Medicine (CIM) at Scott & White Memorial Hospital.

B. The clinical pharmacist authorized to adjust or titrate medications under the protocol and who will care out the DTM as delegated, is _____, Pharm.D.

C. Upon receipt of written consent from the patient and notification to the patient's primary care physician, and in accordance with the specified treatment guidelines, the clinical pharmacist may provide pharmaceutical care in Scott & White Health Plan pharmacies for enrolled patients under the protocol to include:

    1. Assesses of patients' therapeutic needs for disease states/ailments, which include but are not limited to diabetes mellitus, hypertension, hyperlipidemia, smoking cessation, and obesity.
    2. Evaluates pharmacological and non-pharmacological treatment regimens.
    3. Orders, interprets, and conducts all pertinent laboratory studies.
    4. Adjusts medications in accordance with attached pharmacological privileges (page 3).
    5. The clinical pharmacist will not initiate or discontinue medications without authorization from the physician.
    6. Provides patient education regarding their disease state(s), pharmacological, and non-pharmacological therapy, and medication adherence.
    7. Performs pertinent physical assessments as a component of disease state monitoring.
    8. Documents patient visits, patient care, and treatment decisions in the medical record. The patient's primary care physician will have access to such medical records.

9. Consults with patient's primary care physician and other members of the health care team, as appropriate, to include ancillary services (podiatry, dietary, social work) and ophthalmology.
10. Obtains authorization from the physician for deviations from the protocol.
11. This protocol does not delegate diagnosis to the clinical pharmacist.
12. The clinical pharmacist will utilize the most current version of treatment guidelines for pharmaceutical care. These treatment guidelines include the American Diabetes Association Clinical Practice Recommendations, the Texas Diabetes Council Treatment Algorithm, American College of Cardiology/American Heart Association Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult, the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC), the National Cholesterol Education Program (NCEP), National Asthma Education and Prevention Program (NAEPP) – written by the National Heart Lung and Blood Institute (NHLBI); and the Global Initiative on Asthma (GINA) and Global Initiative for Chronic Obstructive Lung Disease (GOLD) – written by the NHLBI and the World Health Organization (WHO).

Clinical Pharmacist Drug Therapy Management Protocol:
Pharmacologic Privileges for _____, Pharm.D.

Level of Privileges:

A. Independent – no routine MD consultation required.
B. MD consultation required for initiating therapy.
Independent for renewing and adjusting.
C. Independent for renewal only.
D. MD consultation required.
NR. Not requested

A list of medications in each pharmacologic category may be found in the SWHP Formulary

LEVEL	DRUG CATEGORY	LEVEL	DRUG CATEGORY
D	ACNE PRODUCTS	C	ALZHEIMER'S MEDICATIONS
D	ANAL/RECTAL PRODUCTS	B	ANALGESICS – NON-OPIOID
NR	ANALGESICS – OPIOD	NR	ANTIARRHYTHMICS
NR	ANTIMALARIALS	D	ANTIFUNGALS
NR	ANTIVIRALS	D	ANTIMYCOBACTERIALS
C	ANTIDEPRESSANTS	D	ANTIBIOTICS
B	ANTIHYPERTENSIVES	C	ANTICONVULSANTS
B	ANTIINFLAMMATORY/ANTIRHEUMATIC	C	ANTIHISTAMINES, NONSEDATING
NR	ANTIPSYCHOTICS	NR	ANTINEOPLASTICS
NR	ASSORTED CLASSES	B	ASTHMA-INHALTERS/NEBULIZERS
B	ASTHMA – ORAL MEDICATIONS	C	BLOOD MODIFIERS
B	CHOLESTEROL LOWERING AGENTS	C	CONTRACEPTIVES
B	CORTICOSTEROIDS – ORAL	NR	CORTICOSTEROIDS – TOPICAL
C	COUGH/COLD/ALLERGY PRODUCTS	C	DERMATOLOGICALS – ECZEMA/PSORIASIS
C	DERMATOLOGICALS – MISC	B	DIABETIC AGENTS – MISC
B	DIABETIC ORAL AGENTS	B	DIABETIC ORAL AGENTS – TZD
A	DIABETIC SUPPLIES	C	ENDOCRINE – MISC
B	GASTROINTESTINAL – LAXATIVES	D	GASTROINTESTINAL – ANTIEMETICS
C	GASTROINTESTINAL – HEARTBURN/ULCER	C	GASTROINTESTINAL – INFLAM. BOWEL
C	GASTROINTESTINAL – MISC	NR	GASTROINTESTINAL – DIGESTIVE ENZ.
C	GOUT PRODUCTS	B	HEART/ANGINA MEDICATIONS
C	HEMATOLOGICAL AGENTS	NR	HORMONES – ANDROGENS
C	HORMONES – FEMALE	NR	IMMUNOSUPPRESIVE AGENTS
NR	IMPOTENCE MEDICATIONS	B	INSULINS
A	MEDICAL DEVICES	C	MIGRAINE PRODUCTS
D	MOUTH & THROAT TOPICAL PRODUCTS	NR	MUSCLE RELAXANTS
A	MULTIVITAMINS	B	NASAL PRODUCTS
NR	NEUROMUSCULAR DRUGS – MISC.	A	NUTRITIONAL – PRESCRIPTION VITAMINS
B	NUTRITIONAL – MINERALS & ELECTROLYTES	D	OPHTHALMIC AGENTS
D	OTIC AGENTS	C	OSTEOPOROSIS DRUGS
B	PROSTATE MEDICATIONS	C	PARKINSON'S DRUGS
NR	SEDATIVE/HYPNOTICS/ANTIANXIETY	NR	PSYCHOTHERAPEUTIC AGENTS – MISC
B	THYROID MEDICATIONS	NR	STIMULANTS
C	URINARY AGENTS – ANTISPASMOTICS	D	URINARY AGENTS – ANTIINFECTIVES
A	VACCINES	C	URINARY AGENTS – MISC
A	OTCs (ANY CLASS)	C	VAGINAL PRODUCTS

_____ _____
Requesting Practitioner / Date CIM Clinic Supervising Physician / Date

APPENDIX VII: SWHP Insurance Contract Waiver

Scott & White Health Plan Medication Management Program – Diabetes

Scott & White Health Plan Insurance Contract Waiver

Name:	DOB:
Address:	PCP:
Home phone:	Work/cell phone:
E-mail address:	

I agree to voluntarily participate in the Scott & White Health Plan Member Benefit Medication Management Program for Diabetes. I understand that I will be required to comply with proposed elements of this program, which are guided by the Texas Diabetes Council and American Diabetes Association guidelines which include but are not limited to: 12 visits with a pharmacist at the CDM Outpatient Pharmacy prior to beginning of the program and at one month intervals; regular visits to my primary care physician (PCP) as deemed necessary; laboratory tests and life style modifications.

I understand that for my participation, the prescription drugs and supplies listed in Appendix A of this document will be available to me free at a $0 copayment. These prescription drugs and supplies will be dispensed in 30-day supply quantities and must be obtained at the Scott & White CDM or South Loop pharmacies in order to receive this benefit of participation. Prescription drugs and supplies not listed in Appendix A or used for the treatment of other conditions besides diabetes are not included in this program.

I understand that failure to keep appointments with my PCP or pharmacist, to comply with recommendations for laboratory tests, or to pick up my prescription drugs will result in dismissal from this program. Dismissal from the program will occur 30 days after written notification, which will be sent to my home address by certified mail, unless the identified compliance failure is corrected and appropriate visit(s) are rescheduled to occur within 15 days of the original appointment date. Dismissal will occur upon absence from one unexcused appointment without prior notification as described above. Once dismissed, the co-payments for the prescription drugs listed in Appendix A will revert back to my contractually defined co-payments according to the guidelines and limitations of my current Evidence of Coverage (EOC). Exceptions will be made to this dismissal policy if extenuating circumstances occur which include personal medical emergencies and unexpected hospitalizations at the time of my appointment.

Scott & White Health Plan reserves the right to cancel this program at any time with 30 days notice to all participants. This program is available only to those who are current members of Scott & White Health Plan and will not be continued if your eligibility ceases.

I give permission to Scott & White personnel to access my medical and prescription records at Scott & White for the purposes of this program.

Signature _____ Date _____

Scott & White Health Plan Medication Management Program – Diabetes

Scott & White Health Plan Insurance Contract Waiver

Diabetic Medications:
Actos®
Avandamet®
Avandia®
Byetta®
chlorpropamide
glimepiride
glipizide
glipizide XL
Glucagon®
glyburide
glyburide micronized
glyburide-metformin
metformin
metformin XR
Precose®
Starlix®
tolazamide
tolbutamide

Diabetic Syringes & Testing Supplies:
ACCU-CHEK
- Glucometer
- Testing strips
- Lancets

B-D Syringes
B-D Pen Needles
Sure-Comfort Syringes

Insulins:
HUMALOG
HUMULIN Insulins
LANTUS
NOVOLIN INSULIN
NOVOLOG
NOVOLOG MIX

APPENDIX VIII: Classification of Medications Used to Measure Medication Adherence and Persistence: Medications for Diabetes, Hypertension, and Hyperlipidemia

DIABETES MEDICATIONS

Medication Class	Generic Name	Study Classification
α-Glucosidase Inhibitor	Acarbose	α-Glucosidase Inhibitor
Biguanide	Metformin	Biguanide
Dipeptidyl Peptidase IV Inhibitor (DPP4)	Sitagliptin	DPP4
Incretin Mimetic	Exenatide	Incretin Mimetic
Sulfonylurea (SFU)	Glimepiride Glipizide Glyburide	SFU
Thiazolidinedione (TZD)	Pioglitazone Rosiglitazone	TZD
Combination Products	Metformin/Sitagliptin Metformin/Glipizide Metformin/Glyburide Metformin/Pioglitazone Metformin/Rosiglitazone	Biguanide + DPP4 Biguanide + SFU Biguanide + SFU Biguanide + TZD Biguanide + TZD

HYPERTENSION MEDICATIONS

Medication Class	Generic Name	Study Classification
Alpha Blocker	Doxazosin Terazosin	Alpha Blocker Alpha Blocker
Alpha-Beta Blocker	Carvedilol Labetalol	Alpha Blocker + BB Alpha Blocker + BB
Angiotensin Converting Enzyme Inhibitor (ACEi)	Benazepril Enalapril Fosinopril Lisinopril Quinapril Ramipril	ACEi ACEi ACEi ACEi ACEi ACEi

HYPERTENSION MEDICATIONS (continued)

Medication Class	Generic Name	Study Classification
Angiotensin Receptor Blocker (ARB)	Candesartan	ARB
	Losartan	ARB
	Olmesartan	ARB
	Valsartan	ARB
Beta Blocker (BB)	Acebutolol	BB
	Atenolol	BB
	Metoprolol	BB
	Nadolol	BB
	Nibivolol	BB
	Propranolol	BB
Calcium Channel Blocker (CCB)	Amlodipine	CCB
	Diltiazem	CCB
	Felodipine	CCB
	Nifedipine	CCB
	Verapamil	CCB
Direct Renin Inhibitor (DRI)	Aliskiren	DRI
Diuretic: Thiazide-like (TLD)	Chlorthalidone	TLD
	Hydrochlorothiazide	TLD
	Metolazone	TLD
Duretic: Loop (LD)	Ethacrynic Acid	LD
	Furosemide	LD
	Torsemide	LD
Diuretic: Potassium-sparing (PSD)	Spironolactone	PSD
Vasodilator	Hydralazine	Vasodilator
Adrenolytic	Clonidine	Adrenolytic
Combination Products	Benazepril/Amlodipine	ACEi + CCB
	Lisinopril/Hydrochlorothiazide	ACEi + TLD
	Losartan/Hydrochlorothiazide	ARB + TLD
	Olmesartan/Hydrochlorothiazide	ARB + TLD
	Valsartan/Hydrochlorothiazide	ARB + TLD
	Bisoprolol/Hydrochlorothiazide	BB + TLD
	Metoprolol/Hydrochlorothiazide	BB + TLD
	Propranolol/Hydrochlorothiazide	BB + TLD
	Amiloride/Hydrochlorothiazide	PSD + TLD
	Spironolactone/Hydrochlorothiazide	PSD + TLD
	Triamterene/Hydrochlorothiazide	PSD + TLD
	Hydralazine/Isosorbide Dinitrate	Vasodilator + Other

HYPERLIPIDEMIA MEDICATIONS

Medication Class	Generic Name	Study Classification
Choleterol Absorption Inhibitor (CAI)	Ezetimibe	CAI
Fibrate	Fenofibrate	Fibrate
	Fenofibric acid	Fibrate
	Gemfibrozil	Fibrate
HMG-CoA Reductase Inhibitor (Statin)	Atorvastatin	Statin
	Fluvastatin	Statin
	Lovastatin	Statin
	Pravastatin	Statin
	Rosuvastatin	Statin
	Simvastatin	Statin
Nicotinic Acid (NA)	Niacin	NA
Omega-3 Fatty Acid	Omega-3 Acid Ethyl Esters	Omega-3 Fatty Acid
Resin	Cholestyramine	Resin
	Colestipol	Resin
Combination Products	Ezetimibe/Simvastatin	CAI + Statin

APPENDIX IX: ICD-9 Codes Used to Identify Diabetes and Diabetes-related Co-morbidities

ICD-9 Codes	Condition
250.xx, 357.2x, 362.0x, 366.41	Diabetes
401.xx - 404.xx	Hypertension
272.xx	Hyperlipidemia
585.9	Nephropathy
257.2	Neuropathy
362.02, 362.07	Retinopathy

BIBLIOGRAPHY

1. Koda-Kimble MA, Young LY, Kradjan WA, Guglielmo BJ, Alldredge BK, Corelli RL. *Applied Therapeutics: The Clinical Use of Drugs.* Baltimore: Lippincott Williams & Wilkins, 2005.
2. American Diabetes Association. All about diabetes. Available at: http://www.diabetes.org/about-diabetes.jsp. Accessed June 6, 2009.
3. National Institutes of Health. The genetic landscape of diabetes. Available at: http://www.ncbi.nlm.nih.gov/books/bv.fcgi?call=bv.View..ShowTOC&rid=diabetes.TOC&depth=1. Accessed June 6, 2009.
4. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2003 Jan;26 Suppl 1:S5-S20.
5. Wells BG, Depiro JT, Schwinghammer TL, Hamilton CW. *Pharmacotherapy Handbook.* 5th ed. New York: The McGraw-Hill Companies, Inc., 2003.
6. Fera T, Bluml BM, Ellis WM, Schaller CW, Garrett DG. The Diabetes Ten City Challenge: interim clinical and humanistic outcomes of a multisite community pharmacy diabetes care program. *J Am Pharm Assoc*. 2008 March/April;48(2):181-90.
7. Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. The *Lancet.* 23 May 2009; 373(9677):1773-9.

8. Mokdad AH, Ford ES, Bowman BA, Nelson DE, Engelgau MM, Vinicor F, Marks JS. Diabetes trends in the U.S.: 1990-1998. *Diabetes Care*. 2000;23(9):1278-83.
9. Amos A, McCarthy D, Zimmet PZ. The rising global burden of diabetes and its complications: estimates and projections to the year 2010. *Diabet Med.* 1997;14 Suppl:S1-85.
10. Seidell JC. Obesity, insulin resistance and diabetes – a worldwide epidemic. *Br J Nutr*. 2000 Mar;83 Suppl 1:S5-8.
11. Ford ES, Williamson DF, Liu S. Weight change and diabetes incidence: Findings from a national cohort of US adults. *Am J Epidemol*. 1 Aug 1997;146(3):214-22.
12. Will JC, Williamson DF, Ford ES, Calle EE, Thun MJ. Intentional weight loss and 13-year diabetes incidence in overweight adults. *Am J Public Health*. 2002 Aug;92(8):1245-8.
13. Centers for Disease Control. National diabetes fact sheet, 2007. Available at: http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2007.pdf. Accessed June 27, 2009.
14. American Diabetes Association. Standards of medical care in diabetes – 2009. *Diabetes Care*. 2009 Jan;32:S13-61.
15. Saudek CD, Derr RL, Kalyani RR. Assessing glycemia in diabetes using self-monitoring blood glucose and hemoglobin A1C. *JAMA*. 2006;295(14):1688-97.
16. Treviño G. On the weighted-average relationship between plasma glucose and HbA1c. *Diabetes Care*. 2006 Feb;29(2):466.
17. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ; National Heart, Lung, and

Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA.* 2003;289:2560-72.

18. Ferrannini E, Natali A, Capaldo B, Lehtovirta M, Jacob S, Yki-Järvinen H. Insulin resistance, hyperinsulinemia, and blood pressure: role of age and obesity. *Hypertension*. 1997;30:1144-9.
19. Ong KL, Cheung BM, Man YB, Lau CP, Lam KS. Prevalence, awareness, treatment, and control of hypertension among United States adults 1999-2004. *Hypertension*. 2007;49:69-75.
20. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report. *Circulation*. 2002 Dec 17;106(25):3143-421.
21. World Health Organization. Adherence to long-term therapies: Evidence for action. Geneva, Switzerland: WHO, 2003.
22. Vermeire EIJJ, Wens J, Van Royen P, Biot Y, Hearnshaw H, Lindenmeyer A. Interventions for improving adherence to treatment recommendations in people

with type 2 diabetes mellitus. *Cochrane Database of Systematic Reviews* 2005, Issue 2. Art. No.:CD003638. doi:10.1002/14651858.CD003638.pub2.

23. American Society on Aging and American Society of Consultant Pharmacists Foundation. Adult meducation: Improving medication adherence in older adults. 2006. Available at: http://www.AdultMeducation.com. Accessed July 24, 2009.
24. Cramer JA, Roy A, Burrell A, Fairchild CJ, Fuldeore MJ, Ollendorf DA, Wong PK. Medication compliance and persistence: terminology and definitions. *Value Health*. 2008;11(1): 44-7.
25. Osterberg L, Blasche T. Adherence to medication. *N Eng J Med*. 2005;353:487-97.
26. Benner JS, Glynn RJ, Mogun H, Neumann PJ, Weinstein MC, Avorn J. Long-term persistence in use of statin tharapy in elderly patients. *JAMA*. 2002;299:455-61.
27. Vermeire E, Hearnshaw H, Van Royen P, Denekens J. Patient adherence to treatment: three decades of research. A comprehensive review. *J Clin Pharm Ther*. 2001:26:331-42.
28. Col N, Fanale JE, Kromholm P. The role of medication noncompliance and adverse drug reactions in hospitalizations of the elderly. *Arch Intern Med*. 1990;150:841-5.
29. Sokol MC, McGuigan KA, Verbrugge, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care*. 2005;43(6):521-30.
30. Ho PM, Rumsfeld JS, Masoudi FA. Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. *Arch Intern Med*. 2006;166:1836-41.
31. McCarthy R. The price you pay for the drug not taken. *Bus Health*. 1998;16:27-33.

32. Ingersoll KS, Cohen J. The impact of medication regimen factors on adherence to chronic treatment: a review of the literature. *J Behav Med*. 2008;31:213-24.
33. Kreuger KP, Berger BA, Felkey B. Improving use of prescription medications: a national action plan. National Quality Forum, 2005:D1-D41.
34. Borzecki AM, Oliveria SA, Berlowitz DR. Barriers to hypertension control. *Am Heart J*. 2005;149:784-94.
35. Grant RW, Devita NG, Singer DE, Meigs JB. Polypharmacy and medication adherence in patients with type 2 diabetes. *Diabetes Care*. 2003;26(5):1408-12.
36. Goldman DP, Joyce GF, Zheng Y. Prescription drug cost sharing: associations with medication and medical utilization and spending and health. *JAMA*. 2007;298(1):61-9.
37. Mahoney JJ. Reducing patient drug acquisition costs can lower diabetes health claims. *Am J Manag Care*. 2005;11(5):S170-6.
38. Colombi AM, Yu-Isenberg K, Priest J. The effects of health plan copayments on adherence to oral diabetes medication and health resource utilization. *JOEM*. 2008;50(5):535-41.
39. Polonsky WH, Fisher L, Guzman S, Villa-Caballero L, Edelman SV. Psychological insulin resistance in patients with type 2 diabetes: the scope of the problem. *Diabetes Care*. 2005;28:2543-5.
40. Okazaki K, Goto M, YamamotoT. Barriers and facilitators in relation to starting insulin therapy in type 2 diabetes (Abstract). *Diabetes*. 1999;48(1):A319.

41. Hess LM, Raebel MA, Conner DA, Malone DC. Measurement of adherence in pharmacy administrative databases: a proposal for standard definitions and preferred measures. *Ann Pharmacother*. 2006 July/August;40:1280-8.
42. Stephens JM, Botteman MF, Hay JW. Economic impact of antidiabetic medications and glycemic control on managed care organizations: a review of the literature. *J Manag Care Pharm*. 2006;12(2):130-42.
43. Peters AL, Davidson MB, Ossorio RC. Management of patients with diabetes by nurses with support of subspecialists. *HMO Pract*. 1995;9:8-13.
44. Haynes RB, McKibbon KA, Kanani R. Systematic review of randomized trials of interventions to assist patients to follow prescriptions for medications. *Lancet*. 1996;348:383-6.
45. Sczupak CA, Conrad WF. Relationship between patient-oriented pharmaceutical services and therapeutic outcomes of ambulatory patients with diabetes mellitus. *Am J Hosp Pharm*. 1977;34:1238-42.
46. Hawkins DW, Fiedler FP, Douglas HL, Eschbach RC. Evaluation of a clinical pharmacist in caring for hypertensive and diabetic patients. *Am J Hosp Pharm*. 1979;36:1321-5.
47. Roter DL, Hall JA, Merisca R, Nordstrom B, Cretin D, Svarstad B. Effectiveness of interventions to improve patient compliance: a meta-analysis. *Med Care*. 1998;36(8):1138-61.
48. Krier BP, Parker RD, Grayson D, Byrd G. Effect of diabetes education on glucose control. *The Journal of the Louisiana State Medical Society*. 1999;151:86-92.

49. Jiang YD, Chuang LM, Wu HP, Shiau SJ, Wang CH, Lee YJ, Juang JH, Lin BJ, Tai TY. Assessment of the function and effect of diabetes education programs in Taiwan. *Diabetes Research and Clinical Practice*. 1999;46:177-82.
50. Lu CY, Ross-Degnan D, Soumerai SB, Pearson SA. Interventions designed to improve the quality and efficacy of medication use in managed care: a critical review of the literature – 2001-2007. *BMC Health Services Research*. 2008;8:75-86.
51. Stratton IM, Adlet AI, Neil HA, Matthews DR, Manley SE, Cull CA, Hadden D, Turner RC, Holman RR. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *Br Med J.* 2000;321:405-12.
52. National Institutes of Health. Type 1 diabetes fact sheet. Available at: http://diabetes.niddk.nih.gov/dm/pubs/control/#cardio. Accessed April 25, 2008.
53. Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, Zinman B. Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy. A consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2009;32(1):193-203.
54. Klein S, Sheard NF, Pi-Sunyer X, Daly A, Wylie-Rosett J, Kulkarni K, Clark NG. Weight management through lifestyle modification for the prevention and management of type 2 diabetes: rationale and strategies. A statement of the American Diabetes Association, the North American Association for the Study of

Obesity, and the American Society for Clinical Nutrition. *Am J Clin Nutr*. 2004;80:257-63.

55. Doupis J. DPP4 inhibitors: a new approach in diabetes treatment. *Adv Ther*. 2008;25(7):627-43.
56. Bosi E, Lucotti P, Setola E, Monti L, Piatti PM. Incretin-based therapies in type 2 diabetes: a review of clinical results. *Diabetes Research and Clinical Practice*. 2008;82:S102-7.
57. VanDeKoppel S, Choe HM, Sweet BV. Managed care perspective on three new agents for type 2 diabetes. *J Man Care Pharm*. 2008;14(4):363-80.
58. Bartels DW, Davison MH, Gong WC. Type 2 diabetes and cardiovascular disease: reducing the risk. *J Man Care Pharm*. 2007;13(2) Suppl:S2-15.
59. Machado M, Bajcar J, Guzzo GC, Einarson TR. Sensitivity of patient outcomes to pharmacist interventions. Part I: Systematic review and meta-analysis in diabetes management. *Ann Pharmacother*. 2007;41:1569-82.
60. Cranor CW, Christensen DB. The Asheville project: short-term outcomes of a community pharmacy diabetes care program. *J Am Pharm Assoc*. 2003;43:149-59.
61. Cranor CW, Bunting BA, Christensen DB. The Asheville Project: long-term clinical and economic outcomes of a community pharmacy diabetes care program. *J Am Pharm Assoc.* 2003 March/April;43(2):173-84.
62. Garrett DG, Bluml BM. Patient self-management program for diabetes: first-year clinical, humanistic, and economic outcomes. *J Am Pharm Assoc*. 2005;45:130-7.

63. Wubben DP, Vivian EM. Effects of pharmacist outpatient interventions on adults with diabetes mellitus: a systematic review. *Pharmacotherapy*. 2008;28(4):421-36.

64. National Committee for Quality Assurance: 2009 HEDIS Performance Measures. Available at http://www.ncqa.org/tabid/855/Default.aspx. Accessed September 18, 2009.

65. United States Department of Labor, Bureau of Labor Statistics: Consumer Price Index Detailed Report Tables Annual Average 2000-2008. Available at http://stats.bls.gov/cpi/tables.htm. Accessed September 8, 2009.

66. Martin OJ, Wu WC, Schleinitz MD, Taveira TH, Anderson ML, Patel PM, Donofrio G, Sharma S. Effectiveness of pharmacist-coordinated care to reduce cardiovascular risk factors in patients with diabetes mellitus [online exclusive abstract]. *Circulation*. 2004;109:e121. Available at http://circ.ahajournals.org/cgi/reprint/109/7/e71.pdf. Accessed September 28, 2009.

67. Vanderpoel DR, Hussein MA, Watson-Heidarai T, Perry A. Adherence to a fixed-dose combination of rosiglitazone maleate/metformin hydrochloride in subjects with type 2 diabetes mellitus: a retrospective database analysis. *Clin Ther*. 2004;26(12):2066-75.

68. Liberman JN, Wang Y, Hutchins D. Adherence to maintenance medication by election of days' supply. Poster presented at the ISPOR 14th Annual International Meeting, May 16-20, 2009, Orlando, FL.

69. Lundy J. Kaiser Family Foundation: Prescription drug trends. Sept 2008. Available at http://www.kff.org/rxdrugs/upload/3057_07.pdf. Accesssed September 28, 2009.

70. Emigh R. The Novartis Pharmacy Benefit Report: 2008/2009 Facts, Figures, & Forecasts. 16th edition. Novartis Pharmaceuticals Corporation; East Hanover, NJ: 2008.

VITA

Kristin Anne Hanson was born in Dallas, Texas on November 9, 1979, the daughter of Lila Grafton Hanson and Ronald Manley Hanson. After completing her work at Highland Park High School in Dallas, Texas in 1998, she entered Duke University in Durham, North Carolina. She received the degree of Bachelor of Science from Duke in May, 2002. Kristy attended pharmacy school at the University of California, San Francisco, where she specialized in Health Policy and Management; she was awarded the degree of Doctor of Pharmacy in May, 2007. In July 2009, Kristy completed a two-year fellowship with Novartis Pharmaceuticals Corporation, Scott & White Health Plan, and The University of Texas at Austin.

Permanent Address: 4319 Lorraine Avenue
Dallas, Texas 75205

This thesis was typed by the author.