

Impact of Pharmacist Intervention on Diabetes Patients in an Ambulatory Setting

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Diabetes is the seventh-leading cause of death in the United States, according to the National Center for Health Statistics at the Centers for Disease Control and Prevention.¹ More than 20 million people in the United States have diabetes, and of those > 60 years of age, one in five has the disease.¹

Sixty-five percent of patients with diabetes die from heart disease or stroke. Thirty percent of those > 40 years of age have impaired sensation in their feet; 60% of all nontraumatic amputations are attributed to diabetes.¹ Diabetes is also the leading cause of kidney failure, accounting for 44% of all new cases in 2002.¹

To help prevent long-term complications and deaths related to diabetes, the American Diabetes Association (ADA) publishes an annual position statement titled Standards of Medical Care in Diabetes to provide up-to-date guidelines for the management of diabetes.² The care of diabetes patients is multifaceted and often requires special attention to achieve optimum results. A1C testing is considered the gold standard measurement for diabetes control.

Previous studies have measured A1C values in patients before and after seeing a pharmacist.³⁻⁷ The current study assessed A1C changes resulting from seeing a pharmacist and then compared them to changes that result from usual care to find out whether pharmacist care results in any additional benefit.

METHODS

This study investigated the clinical pharmacist's impact on type 2 diabetes patients as measured by the

change in A1C over a 2-year period in an outpatient clinic at a Veterans Administration institution. Diabetes care for the treatment group included the pharmacist, dietitian, and primary care provider (Team), with patients managed by the primary care provider and dietitian serving as controls (Control). For Team patients, a clinical pharmacist met with patients every 3 months or as needed to help meet ADA goals for therapy.⁸

This retrospective medical record review included four groups. The first two groups were composed of newly diagnosed type 2 diabetic patients receiving their first oral hypoglycemic medication. One group (Team; $n = 33$) included patients monitored by the clinical pharmacist to review blood glucose readings and A1C values, optimize medication dosing, provide diabetes education, and follow up on laboratory testing in addition to visits with their primary care provider and dietitian. The other group (Control; $n = 50$) were patients monitored and having clinical follow-up by their primary care provider and dietitian without the involvement of a pharmacist. The final two groups included type 2 diabetic patients started on insulin therapy (complex patients) seen by the pharmacist in addition to the primary care provider and dietitian (Team Complex; $n = 33$) compared to the primary care provider and dietitian without a pharmacist (Control Complex; $n = 44$). The monitoring parameter compared between the two groups was the change in A1C between the Team and the Control and between the Team Complex and the Control

Complex groups. The review of chart information for each patient covered a 2-year time span from receiving the new prescription.

Pharmacist visits included 30–60 minutes of education, medication counseling, monitoring, and management based on the ADA guidelines for diabetes patients.⁸ At these visits, assessments of blood pressure, weight, A1C, serum creatinine, blood urea nitrogen, lipids, microalbumin, foot care, eye care, and diet and exercise adherence and review of home glucose readings and any changes in health status or medications that might affect blood glucose were performed under protocol by the pharmacist. Referrals to eye, foot care, or kidney specialists could be made if problems were noted. Follow-up labs were ordered, and medications changes were made by the pharmacist under protocol. Changes in drug therapy were done based on glycemic control, while considering potential drug-drug interactions, adverse drug effects, drug-disease state interactions, and patient adherence issues. There were no restrictions on the number of medications that could be used to bring down A1C throughout the 2-year follow-up, so as many as three oral agents were used in some of the Team and Control patients. Clinical pharmacists at this site have a doctor of pharmacy degree and have completed either a general residency or cardiovascular fellowship.

Inclusion and Exclusion Criteria

Patient selection for newly diagnosed patients was procured by identifying electronically patients who were newly diagnosed and had a new

Table 1. Baseline Characteristics: Patients on Oral Medication

	Team ^a			Control ^b			P value
	n	mean (SD)	Median	n	mean (SD)	median	
Age (years)	33	67.76 (10.19)	70.00	50	69.20 (10.08)	70.00	0.589
A1C ^c (%)	33	7.08 (1.46)	6.60	50	6.66 (0.69)	6.70	0.520
Blood pressure							
Systolic (mmHg)	33	123.55 (13.80)	121.00	49	137.53 (19.20)	136.00	<0.001
Diastolic (mmHg)	33	69.27 (8.45)	70.00	50	72.06 (11.52)	72.00	0.236
LDL (mg/dl)	32	91.03 (26.04)	90.00	48	89.69 (24.61)	85.00	0.816
HDL (mg/dl)	33	36.94 (6.23)	36.00	48	39.27 (8.93)	38.50	0.198
Triglycerides (mg/dl)	33	202.67 (105.10)	167.00	48	196.81 (88.87)	181.00	0.878
	n	n (%)		n	n (%)		
Hypertension	33	29 (87.9)		50	45 (90.0)		1.000
Hyperlipidemia	33	27 (81.8)		50	34 (68.0)		0.208
CAD ^d	33	13 (39.4)		50	15 (30.0)		0.478
CVD ^e	33	5 (15.2)		50	4 (8.0)		0.472
Smoker	33	9 (27.3)		50	6 (12.0)		0.089
Endocrinologist	33	1 (3.0)		50	1 (2.0)		1.000

CAD, coronary artery disease; CVD, cerebral vascular disease.

^aPharmacist, primary care provider, and dietitian involved in diabetes care. ^bPrimary care provider and dietitian involved in diabetes care. ^cRange: Team = 6.50 (5.10–11.60); Control = 3.20 (5.30–8.50). ^dDocumented myocardial infarction, coronary stent placement, coronary artery bypass surgery. ^eDocumented cerebral vascular incident, transient ischemic attack, carotid stent placement.

prescription for an oral diabetes medication from 1 January 2002 to 1 January 2004. Patients on more than one diabetes medication were excluded. The remaining patients were separated into two groups: those who had a visit with the clinical pharmacist regarding treatment for diabetes within the 2-year study period and those who did not. Those not seen by the clinical pharmacist became the control group.

Complex patients were identified from electronic medical records with a new insulin prescription from 1 January 2002 to 1 January 2004. Patients could also be taking oral medications. Patients changing from one insulin product to another were excluded. However, patients who had initial prescriptions for two insulin products concurrently, such as regular and NPH, and were previously insulin naïve were included. The final list was separated into two

groups. Those who had a visit with the clinical pharmacist regarding treatment for diabetes made up the Team Complex group of patients. Those who did not meet with a clinical pharmacist became the Control Complex group.

Any patients who had not had at least three A1C measurements in the 2-year study period were excluded from all four groups. Patients taking prednisone, cyclosporine, morphine, phenytoin, pentamidine, or pyriminil were excluded from all four groups. Patients with two missed (no-show) visits with the physician or pharmacist in the 2-year study period were excluded from all four groups.

There were some limitations to this selection process. Patients are typically referred to the clinical pharmacist by the primary care provider. Sometimes the patients who are referred have personalities that are more difficult or behaviors sugges-

tive of medication adherence issues. In addition, some providers tend to refer more often than others. The patients seen by the clinical pharmacists had visits every 3 months during the 2-year study period for most patients, but some patients were seen more frequently if medication changes were being made. All of these factors may have added some variables to the results.

Data Collection and Analysis

To assess the effectiveness of the team approach, two factorial analyses of covariance (ANCOVAs), controlling for the baseline A1C measurement, were conducted separately for newly diagnosed patients starting oral medication and for more complex patients starting on insulin therapy.

A1C data were collected at four equally spaced time points (baseline and at three follow-up time points)

throughout the 2-year study period. Two separate factorial ANCOVAs were employed to assess for group differences in A1C over the three follow-up time points, controlling for baseline. The first analysis compared Team to Control, and the second compared Team Complex to Control Complex.

A factorial analysis will produce three separate statistical tests: two main effects and an interaction effect. The first main effect will assess for an overall difference in A1C between the two groups (i.e., between-groups main effect), whereas the second main effect provides an overall test of change in A1C over the three time points (i.e., within-groups main effect). Finally, the interaction effect will compare whether A1C for the two groups responded differently over the three follow-up measurement times. For both analyses (Team vs. Control and Team Complex vs. Control Complex), the interaction effect is of primary interest (i.e., did A1C for the two groups respond differently over the three follow-up time points?). A computer simulation indicated a power of 0.60 to detect an interaction effect for patients receiving oral medication and 0.57 to detect an interaction effect for patients on insulin therapy.⁹⁻¹⁵

Baseline characteristics within both groups (i.e., Team vs. Control) of oral medication and insulin patients were compared using bivariate analyses. Continuous variables were presented as mean, standard deviation (SD), and median and analyzed employing independent-samples *t*-tests or, where distributional assumptions were violated, Mann-Whitney tests. Categorical variables were presented as frequency and percent and analyzed with Fisher's exact tests. All analyses were performed using PASW Statistics v. 17.0.2 (SPSS Inc., Chicago, Ill.).

RESULTS

A statistically significant result indicated an overall difference in A1C between Team Complex and Control Complex patients initiating insulin therapy ($F_{1, 74} = 5.24; P = 0.025$), with pharmacist team patients,

on average, displaying lower A1C values compared to patients managed without the pharmacist (mean A1C = 7.15 and 7.67%, respectively). Although the Team patients receiving oral medication were trending favorably, decreases in A1C were not statistically different in comparison to Control patients.

Patients on Oral Medication

Table 1 contains baseline characteristics of the Team and Control patients. Control patients had significantly higher systolic blood pressure levels compared to the Team patients. All other baseline characteristics were comparable.

A factorial ANCOVA was employed to assess whether A1C for the two groups of patients (i.e., Team vs. Control) responded differently over the three follow-up time points, after controlling for the baseline

A1C measurement. Six outliers (one Team; five Control) were identified and deleted. After removal, no assumptions were violated.

The Huynh-Feldt correction was applied to all *F* tests to adjust for sphericity violation. Results indicated no statistically significant interaction effect, indicating A1C responded similarly over the three follow-up time points for Team and Control patients, after controlling for baseline A1C. Further, neither main effect was statistically significant. This indicated there was no overall difference in A1C between the two groups and, on average, A1C values remained stable over the three follow-up time points. Adjusted means, standard errors (SEs), and 95% CIs for each group are presented in Table 2. Adjusted means are plotted in Figure 1.

Table 2. Adjusted Means by Treatment Group for Patients on Oral Therapy^a

	Team ^b (n = 33)		Control ^c (n = 50)	
	Mean (SE)	95% CI	Mean (SE)	95% CI
A1C: Time 1 (%)	6.77 (0.16)	6.44–7.09	6.77 (0.13)	6.50–7.03
A1C: Time 2 (%)	6.64 (0.15)	6.34–6.94	6.81 (0.12)	6.57–7.05
A1C: Time 3 (%)	6.55 (0.17)	6.22–6.88	6.88 (0.14)	6.61–7.15

^aMeans adjusted for baseline A1C value of 6.83%

^bPharmacist, primary care provider, and dietitian involved in diabetes care

^cPrimary care provider and dietitian involved in diabetes care

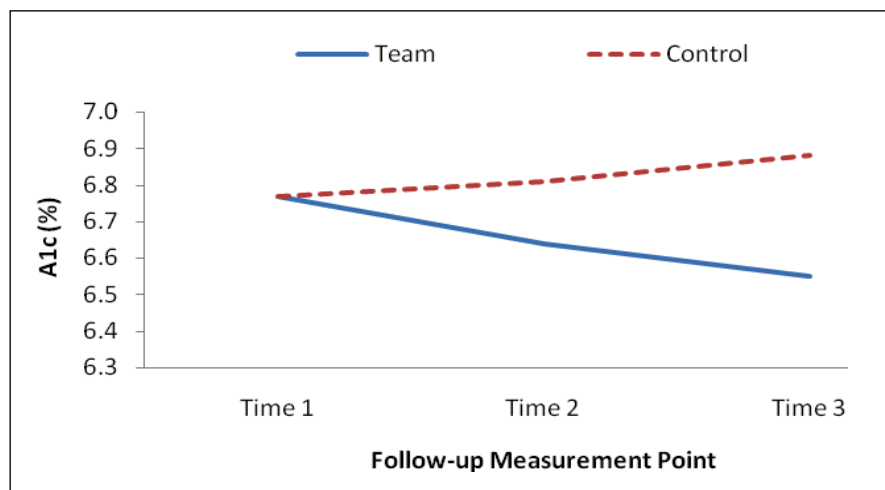


Figure 1. Adjusted means: treatment group by measurement time—oral. Means adjusted for baseline A1C value of 6.83%.

Insulin Patients

Table 3 contains baseline data for the Team Complex and Control Complex patients. Team Complex patients had a significantly higher frequency of hyperlipidemia than Control Complex patients. All other baseline data were comparable.

Factorial ANCOVA was employed. Two outliers (one from each group) were deleted. After removal, no assumption violations were indicated.

No violation of sphericity was indicated. Results of the factorial ANCOVA indicated no statistically significant interaction after adjusting for the baseline A1C measurement. This indicated A1C for the two groups responded similarly over the three follow-up time points. However, there was a statistically significant between-groups main effect after

adjusting for all other effects, including the covariate (F1, 74 = 5.24; P = 0.025; partial η^2 = 0.07 with 95% confidence limits¹⁶ from 0.00 to 0.19). This indicated an overall difference in A1C between the two groups, with Team Complex patients displaying lower A1C values (mean = 7.15; SE = 0.17; 95% CI 6.82–7.49) compared to Control Complex patients (mean = 7.67; SE = 0.15; 95% CI 7.38–7.96). Finally, the within-groups main effect was not statistically significant, indicating, on average, A1C remained stable over the three follow-up time points. Adjusted means, SEs, and 95% CIs for each group are presented in Table 4, and adjusted means are plotted in Figure 2.

DISCUSSION

One of the questions often asked of a pharmacist is, “Are you provid-

ing added benefits to the care of patients?” This study suggests that, in complex diabetic patients, there is indeed added benefit, as is shown with objective evidence provided by group differences in A1C. Why is this so important? In 2000, the U.K. Prospective Diabetes Study (UKPDS) observational study of 3,642 diabetic patients showed that for each 1% reduction in A1C, there was a corresponding 21% reduction in any endpoint related to diabetes, with a 14% reduction for myocardial infarction and a 37% reduction for microvascular complications.⁹

Is there other evidence that pharmacists have a positive impact on patient care in the area of diabetes management? A prospective study published in 2004 by Cioffi et al.⁴ showed a reduction in A1C from 10.3 to 6.9% in 70 patients

Table 3. Baseline Characteristics: Patients on Insulin

	Team Complex ^a			Control Complex ^b			P value
	n	mean (SD)	median	n	mean (SD)	median	
Age (years)	33	66.27 (9.83)	68.00	44	65.30 (12.27)	70.00	0.861
A1C ^c (%)	33	7.82 (1.44)	7.70	44	7.26 (1.07)	7.05	0.061
Blood pressure							
Systolic (mmHg)	31	139.42 (20.12)	134.00	43	133.72 (19.53)	132.00	0.232
Diastolic (mmHg)	32	72.19 (12.90)	69.50	44	72.82 (12.13)	72.00	0.577
LDL (mg/dl)	30	83.33 (33.66)	79.00	38	95.76 (30.55)	89.00	0.115
HDL (mg/dl)	33	36.46 (8.21)	34.00	43	41.47 (23.68)	36.00	0.721
Triglycerides (mg/dl)	33	285.94 (262.78)	235.00	43	259.79 (304.07)	178.00	0.393
	<i>n</i>	<i>n</i> (%)		<i>n</i>	<i>n</i> (%)		
Hypertension	33	32 (97.0)		44	38 (86.4)		0.228
Hyperlipidemia	33	27 (81.8)		44	24 (54.5)		0.015
CAD ^d	33	9 (27.3)		44	12 (27.3)		1.000
CVD ^e	33	2 (6.1)		44	4 (9.1)		0.695
Smoker	33	7 (21.2)		44	9 (20.5)		1.000
Endocrinologist	33	3 (9.1)		44	3 (6.8)		1.000

CAD, coronary artery disease; CVD, cerebral vascular disease; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol.

^aPharmacist, primary care provider, and dietitian involved in diabetes care. ^bPrimary care provider and dietitian involved in diabetes care. ^cRange: Team = 6.30 (5.50–11.80); Control = 5.10 (5.10–10.20). ^dDocumented myocardial infarction, coronary stent placement, coronary artery bypass surgery. ^eDocumented cerebral vascular incident, transient ischemic attack, carotid stent placement.

Table 4. Adjusted Means by Treatment Group for Patients on Insulin Therapy^a

	Team Complex ^b (n = 33)		Control Complex ^c (n = 44)	
	Mean (SE)	95% CI	Mean (SE)	95% CI
A1C: Time 1 (%)	7.22 (0.17)	6.87–7.57	7.71 (0.15)	7.41–8.01
A1C: Time 2 (%)	7.19 (0.22)	6.76–7.63	7.53 (0.19)	7.15–7.91
A1C: Time 3 (%)	7.05 (0.22)	6.61–7.48	7.77 (0.19)	7.40–8.15

^aMeans adjusted for mean baseline A1C value of 6.83%. ^bPharmacist, primary care provider, and dietitian involved in diabetes care. ^cPrimary care provider and dietitian involved in diabetes care.

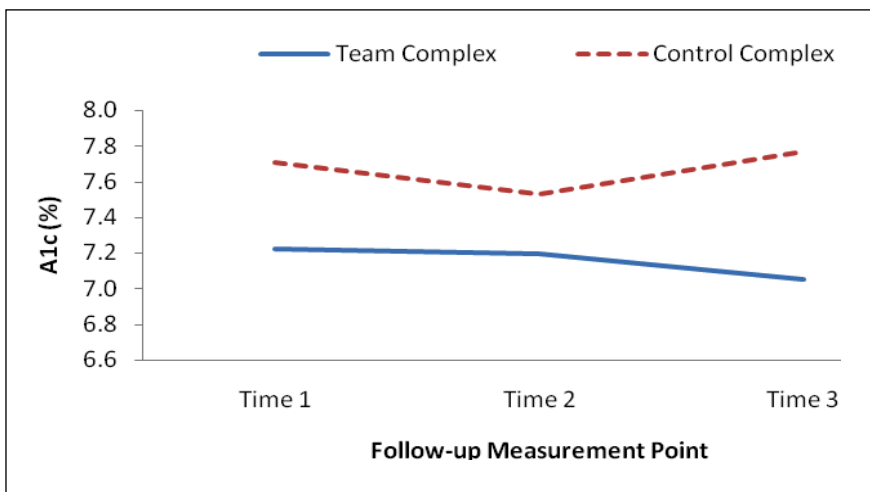


Figure 2. Adjusted means: treatment group by measurement time—insulin. Means adjusted for baseline A1C value of 7.50%.

in a time span of 9–12 months. In this study, patients met with a clinical pharmacist every 6–8 weeks, receiving 30 minutes of education, medication counseling, monitoring, and management. Initial therapy consisted of glyburide or metformin. If glycemic control was not achieved, then a combination of these two were used. Acarbose was added if postprandial blood glucose values were not controlled. Rosiglitazone was also added if another oral agent was needed or intermediate-acting insulin if it was deemed that adequate control would not be achieved with another oral agent. Changes in the regimen were made based on drug-drug interactions, adverse drug effects, drug-disease state interactions, patient adherence issues, and glycemic control. The addition of new medications was discussed with

the primary care provider and carried out by the pharmacist.

In another study by Irons et al.,⁵ a retrospective cohort analysis of 87 diabetic patients managed by pharmacists, the study patients were more successful on achieving an A1C \leq 7% compared to the 85 similar patients in the control group who did not have clinical pharmacists involved. Another group⁶ assessed the impact of a pharmacist-run diabetes management program involving direct teaching, follow-up phone calls, and medication algorithms in 159 patients followed for 6 months. A total of 139 patients completed the study, which showed a decrease in mean A1C of 1.9% in the 6-month time period. McCord³ performed a retrospective chart review of 316 patients who had pharmacist intervention and showed a mean A1C reduction of 1.4% ($P < 0.001$). The

number of patients reaching a goal A1C $< 7\%$ increased from 14.8 to 43.2% ($P < 0.001$).

One concern that administrators state consistently is the cost associated with the care of diabetic patients. The worry is that, by adding pharmacists to the care team for all diabetic patients, the overall cost of care will increase. However, Gerber et al.⁷ performed a data analysis on the total cost to a health maintenance organization (Kaiser Permanente) when a pharmacist provided consultation to diabetic patients and found that overall costs including hospitalization costs, office visits, and medication costs were significantly less compared to the cost of care for those who did not receive consultations for their diabetes. This study not only shows no increase in costs to the system as a whole, but also actual savings.

Our study shows that pharmacist involvement in the care of diabetic patients in the outpatient setting may provide additional benefit to the patients above that of a primary care provider and dietitian. It contributes to the body of evidence that suggests that having multiple health care professionals, including pharmacists, improves diabetic patients' adherence to ADA guidelines for preventive care and reduces A1C values, which the UKPDS suggests may reduce the incidence of myocardial infarction, stroke, and microvascular complications.⁹

CONCLUSION

A1C values $> 7\%$ have been associated with a higher incidence of long-term cardiovascular and peripheral vascular disease, greater incidence of patients requiring dialysis, and numerous microvascular complications, including problems with vision.^{10,17,18} The direct and indirect costs of these complications have been estimated at \$132 billion, which has an enormous impact on health care in the United States.¹ The UKPDS suggests that a 1% reduction in A1C results in a 21% reduction of macrovascular complications, including myocardial infarction, stroke, and amputation (peripheral vascular disease).⁹ The present study suggests that using a clinical pharmacist in

addition to a primary care provider and dietitian to monitor, manage, and provide education to diabetic patients starting insulin therapy will significantly improve A1C values with a mean reduction in A1C from 7.6 to 7.1%.

Acknowledgments

This study was presented as a poster at the American College of Clinical Pharmacist's annual meeting in October 2007. It was supported through an internal research grant from Creighton University.

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