Implementation and Evaluation of a Pharmacist-managed Diabetes Service

by Charlie Kelly and Philip T. Rodgers

In 1992, diabetics made up only 4.5% of the U.S. population, but accounted for more than 14.6% of total health care expenditures, or approximately $105 billion.1 The major costs are attributed to the significant morbidity and mortality intrinsic to this disease. For instance, diabetes has been implicated as the major cause of microvascular complications, causing 12% of all new cases of blindness, almost half of nontraumatic lower-extremity amputations, and over one-third of new cases of end-stage renal disease.2 In addition, macrovascular complications lead to substantial morbidity and mortality. Diabetics are two to four times more likely to die from heart disease or suffer a disabling stroke than nondiabetics.3

Micro- and macrovascular diseases associated with diabetes can be prevented by correcting glucose, blood pressure, and lipids with proper screening and monitoring, even in type 2 diabetics.5 Several studies have documented a positive impact for clinical pharmacists on improving outcomes in diabetic patients.6 Furthermore, other studies have shown positive effects of pharmacy services on costs and outcomes associated with the management of other diseases.7

We sought to implement a pharmacist-managed diabetes service aimed at preventing diabetic complications through appropriate disease management.2 The objective of our study was to evaluate the impact of this service on changes in critical endpoints known to cause significant morbidity and mortality in diabetic patients.

**Methods**

A computer database search of pharmacy claims identified diabetic patients taking oral diabetic agents or insulin from January 1998–July 1998. Patients were sorted by ten physician providers. Each primary care provider received this list of patients for review, along with instructions to select patients from the list for enrollment in the clinical pharmacy service; all of the providers believed that their patients would benefit from comprehensive pharmacological treatment review and titration and diabetes self-management training provided by clinical pharmacists. The clinic site included one full-time clinical pharmacist/faculty member, one pharmacy resident, and fourth-year Doctor of Pharmacy students from the local School of Pharmacy.8

**Study Subjects**

Patients selected from the referral pool were included for study...
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if they had a documented glycosylated hemoglobin (HbA1c) value that was higher than 8%, a documented elevated systolic (over 130 mm Hg) or diastolic blood (over 85 mm Hg) pressure, or a low-density lipoprotein (LDL) cholesterol level that was 120% of goal or more.

Baseline values for HbA1c, blood pressure, and LDL were collected at the initial visit, if they had not been obtained within the previous three months. Otherwise, an HbA1c value documented within a prior three-month period or an LDL collected within a prior year’s period was allowed to qualify as the baseline value. Patients without a follow-up consultation with a pharmacist were excluded from the study.

Interventions

During the initial visit the pharmacist provided one-on-one assessments and consultations regarding diabetes self-management. A complete medical history and appropriate laboratory values (HbA1c, fasting lipid profile, urinalysis, and thyroid function tests) were obtained if indicated. The patient and pharmacist worked together to design a management plan to establish short- and long-term goals, assess medication issues (including dosage adjustments in collaboration with the providers), and individualize nutrition recommendations, lifestyle changes (diet, exercise, smoking cessation), and blood-glucose monitoring instructions. Annual dilated-eye exams, consultation for podiatry services, agreement on continuing support from the clinical pharmacist, follow-up, and instructions on how to contact the physician or pharmacist in the case of an acute problem were also discussed.

Follow-up was scheduled based on the degree of monitoring required, usually monthly. In addition, patients received continuing education on self-management topics including appropriate diet, weight control, daily foot care, medication compliance, and self monitoring of blood glucose (SMBG). Pharmacists implemented a diabetes continuing-care monitoring sheet to track the delivery of appropriate care, such as referrals for dilated-eye exams and foot care, and timely acquisition of fasting lipoprotein analysis, urinalysis, and HbA1c levels. We used the 1997 American Diabetes Association’s clinical practice recommendations regarding goals of therapy. Interventions were customized based on the patient’s individual goals.

Surveillance and Follow-up

Patients were monitored according to the 1997 American Diabetes Association’s clinical practice recommendations as described above. Planned contact frequency was weekly for the initiation of insulin or a change in insulin regimen, biweekly for initiation of oral glucose-lowering agents or change in an oral regimen, biweekly for patients who were not meeting goals, and every two to three months for well-controlled patients.

Laboratory evaluation of HbA1c was obtained quarterly if treatment had changed or the patient was not meeting goals, or every six months if the patient remained stable. A fasting lipid profile, a urinalysis for protein, and a comprehensive dilated eye and visual exam were planned on an annual basis.

Self-management plan evaluation at each visit included review of the patient’s short- and long-term goals, medications, frequency and severity of hypoglycemia, SMBG results, control of lipids, blood pressure, and weight. Also reviewed and discussed were the patient’s medical nutrition therapy (MNT), exercise regimen, follow-up for referrals, and psychosocial adjustment.

Goals of treatment, unless contraindicated, included achievement of near normoglycemia (fasting blood glucose 80-140 mg/dL, bedtime blood glucose 100–140 mg/dL; HbA1c lower than 7%), lowering of blood pressure to less than 130/85 mm Hg or to below 125/75 mm Hg for patients with proteinuria of greater than 1 gm/24 hours; and LDL less than 130 mg/dL for patients with two or more cardiovascular risk factors, or 100 mg/dL or less for patients with established cardiovascular, cerebrovascular, or peripheral vascular disease.15 The LDL goal for all intervention patients was adjusted to 100 mg/dL or less based on the changes made by the 1999 American Diabetes Association’s Clinical Practice Recommendations released at the time of this study.16

HbA1c values and blood pressures were measured at baseline and at the end of the study period seven months later, then compared to values collected from historical controls over an equivalent period. Lipids were assessed at baseline and compared nine months later, then compared to values collected from historical controls over an equivalent period. A collection period of nine months was used to increase the number of lipid values available for analysis. The 1997 American Diabetes Association’s Clinical Practice Recommendations suggest an annual assessment of lipids for most patients. Within-group analysis for smoking status was assessed at the end of the seven-month period. Intention-to-treat analysis used the last available laboratory parameter carried forward.

Historical Controls

Sixteen historical controls (100% type 2 diabetics) were randomly selected from the referral list and studied retrospectively over an equivalent nine-month period, but one year prior to initiation of the clinical service. These patients were matched for baseline age, BMI, HbA1c, SBP, DBP, LDL, HDL, and TG levels (see Table 1, page 490). There were no type 1 diabetes in the historical control group because of the relative infrequency of this type of diabetic in clinical practice compared to type 2 diabetes, making identification of this subset difficult.

Statistical Analysis

For HbA1c, a sample size of seven patients in each arm would have 80% power (p=0.05) to detect a difference in HbA1c of two absolute percentage points between the intervention group and the historical control group if the standard deviation was 1.3%
TABLE 1  Baseline Characteristics of the Subjects

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Historical Controls (N=16)</th>
<th>Intervention Group (N=32)</th>
<th>P Values*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50.2 ±8.9</td>
<td>47.7 ±13.2</td>
<td>0.50</td>
</tr>
<tr>
<td>Female sex (%)</td>
<td>43.8</td>
<td>59.4</td>
<td>0.20</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>56.3</td>
<td>40.6</td>
<td>0.22</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>33.5 ±7.3</td>
<td>34.0 ±8.6</td>
<td>0.85</td>
</tr>
<tr>
<td>Type 1 DM (%)</td>
<td>0.0</td>
<td>18.8</td>
<td>0.05</td>
</tr>
<tr>
<td>Type 2 DM (%)</td>
<td>100.0</td>
<td>81.3</td>
<td>0.05</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>9.0 ±0.74</td>
<td>9.0 ±1.3</td>
<td>0.84</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>144.4 ±14.1</td>
<td>144.9 ±22.9</td>
<td>0.94</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>87.3 ±9.8</td>
<td>87.5 ±12.5</td>
<td>0.94</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>129.7 ±34.7</td>
<td>123.6 ±39.8</td>
<td>0.64</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>40.4 ±12.4</td>
<td>43.0 ±12.6</td>
<td>0.55</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>220.8 ±153.1</td>
<td>193.4 ±135.3</td>
<td>0.57</td>
</tr>
<tr>
<td>Smokers (%)</td>
<td>18.8</td>
<td>25.0</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Note: Plus-minus values are means ± SD. Percentages do not all sum to 100 because of rounding.

*A chi-square test was used for comparisons of categorical variables, and a two-tailed student's t-test was used for comparisons of continuous data.

TABLE 2  Comparison of Endpoints Analyzed by Group Analysis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Historical Controls</th>
<th>Intervention Group</th>
<th>P Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%)</td>
<td>8.5 ±1.4 (7.86–9.20)</td>
<td>7.5 ±1.2 (7.05–7.98)</td>
<td>0.02</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>140.1 ±14.9 (132.8–147.4)</td>
<td>133.5 ±17.9 (127.2–139.9)</td>
<td>0.22</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>82.6 ±13.1 (76.2–89.0)</td>
<td>80.6 ±10.7 (76.9–84.4)</td>
<td>0.58</td>
</tr>
</tbody>
</table>

Note: Plus-minus values are means ± SD (95% confidence intervals). Percentages do not all sum to 100 because of rounding.

for both groups. For SBP, a sample size of 12 patients in each arm would have 80% power (p=0.05) to detect a difference in SBP of 26 mm Hg between the intervention group and the historical control group if the standard deviation was 22.9 mm Hg for both groups. For DBP, a sample size of nine patients in each arm would have 80% power (p=0.05) to detect a difference in DBP of 17 mm Hg between the intervention group and the historical control group if the standard deviation was 12.5 mm Hg for both groups. For LDL, a sample size of 28 in each arm would have 80% power (p=0.05) to detect a difference in LDL of 30 mg/dL between the intervention group and the historical control group if the standard deviation was 39.8 mg/dL for both groups.

For analysis, 32 intervention patients were available, and 16 for the historical control sample, which was half the size of the intervention group; this fact led to the understanding that we might not be able to detect a difference in LDL between the two groups. Results are based on within-group analyses for changes in LDL and smoking cessation rates and between-group analyses for changes.
in HbA\textsubscript{1c}, SBP, and DBP. A paired student's t-test was used to compare baseline continuous values in the intervention group to the follow-up values within the same group. An unpaired student's t-test was used for comparisons of continuous data between the intervention group and the historical controls. Chi-square analysis was used to compare proportions. A two-tailed p-value of less than 0.05 was considered statistically significant.

### Results

Baseline characteristics of the intervention group are presented in Table 1 (see page 490). Of the 32 intervention patients available for study, 27 had available HbA\textsubscript{1c} values for analysis at the end of the seven-month period. Five patients in the intervention group were lost to follow-up; one patient changed insurance plans and the remaining four did not keep appointments. The mean ± SD HbA\textsubscript{1c} at baseline was 9.0 ± 1.3\% for the intervention group and 9.0 ± 0.74\% for the control group; p = 0.84. The mean ± SD HbA\textsubscript{1c} at the end of the study was 7.5 ± 1.2\% (95% CI, 7.05–7.98\%) for the intervention group and 8.5 ± 1.4\% (95% CI, 7.86–9.20\%) for the historical control group; p = 0.02 (see Table 2, page 490). Thirty-one percent (10/32) of the intervention group and 6.3\% (1/16) of the control group had HbA\textsubscript{1c} values less than 7\% at the end of the study period; p = 0.03. By intention-to-treat analysis, the follow-up mean ± SD HbA\textsubscript{1c} was 7.9 ± 1.4\% (95% CI, 7.36–8.35\%) for the intervention group and 8.5 ± 1.4\% (95% CI, 7.86–9.20\%) for the control group; p = 0.12. This difference was not significant but there was a trend toward a lower mean HbA\textsubscript{1c} in the intervention group.

No statistical difference was found for SBP and DBP between the two groups (Table 2), although the proportion of patients with SBP lower than 130 mm Hg was higher in the intervention group, with 43.8\% (14/32) for the intervention group and 12.5\% (2/16) for the historical control group; p = 0.05. The proportion of patients with DBP lower than 85 mm Hg was higher in the intervention group, with 65.6\% (21/32) for the intervention group and 62.5\% (10/16) for the historical control group; p = 0.78 (see Figure 1, right). There was no difference between baseline (mean ± SD LDL 123.6 ± 39.8 mg/dL; 95% CI, 108.3–138.9 mg/dL) and follow-up LDL (mean ± SD LDL 121.2 ± 30.6 mg/dL; 95% CI, 102.2–140.2 mg/dL) by within group analysis, p = 0.82. By intention-to-treat analysis, the follow-up mean ± SD LDL was 117.1 ± 34.8 (95% CI, 95.5–138.6 mg/dL) by within-group analysis for the intervention group; p = 0.21. None of the eight smokers in the intervention group successfully quit smoking despite intervention; p = 1.0.

### Discussion

With the pharmacist-managed diabetes service in this employed physicians group, we were able to demonstrate a significant improvement in the HbA\textsubscript{1c}, which is recognized as an important short-term parameter associated with long-term outcomes.\textsuperscript{17,18} We were able to demonstrate this difference in the relatively short period of seven months. The absolute difference reduction of HbA\textsubscript{1c} of 1.5\% in our study is similar to that found in other trials to benefit microvascular complications.\textsuperscript{19} If the service could be continued, we would strive to maintain glycemic control, attract more diabetic patients, and measure more health-resource use parameters, but the short duration of this initial study did not allow for these analyses.

Although we did not find significant differences in SBP and DBP between the intervention group and the historical control group, a trend toward lower blood pressures was observed in the intervention group, especially in SBP (Table 2). The small number of subjects may have made it impossible to detect the small differences in blood pressures found. For SBP, a sample size of 98 in each arm would have been necessary to detect significance. Similarly, for DBP, a sample size of 561 in each arm.
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would have been necessary. If more subjects had been employed, we might have been able to demonstrate a difference in blood pressure.

Comparisons of LDL between the intervention group and the historical control group were not possible, given the revisions made during the time of this study for the management of dyslipidemia in adults. LDL-cholesterol goals for diabetic patients without preexisting CHD were revised to reflect an LDL goal of 100 mg/dL or lower compared to a less stringent LDL goal that reflected the number of coronary heart disease risk factors present. Because the intervention-group LDL goal was now different from the LDL goal for the historical control group and because our interventions were goal-driven, we chose to compare baseline LDL to follow-up LDL within the intervention group and not utilize the historical control group for comparison of this parameter between groups.

Although no statistical difference (p=0.82) between baseline LDL and follow-up LDL was revealed by within-group analysis, a small trend in LDL reduction was observed (baseline mean ±SD LDL 123.6 ±39.8 mg/dL and follow-up mean ±SD LDL 121.2 ±30.6 mg/dL). With only ten LDL levels available at the end of the study, we may not have had the power to detect such a small difference. The number of evaluable LDL levels is low because we utilized a relatively short period for lipids, to avoid increasing the number of laboratory evaluations of lipids beyond the recommended yearly fasting lipid collection recommended in the 1997 American Diabetes Clinical Practice Recommendations. Clearly, a longer study period would have captured more lipid values, and perhaps we may have reached statistical significance.

By intention-to-treat analysis, the follow-up mean ±SD LDL was 117.1 ±34.8 (95% CI, 95.5–138.6 mg/dL) compared to baseline (mean ±SD LDL 123.6 ±39.8 mg/dL; 95% CI, 108.3–138.9 mg/dL), p=0.21. When utilizing the last evaluable LDL level carried forward, we see a stronger trend but still without statistical significance.

We were surprised to find aspirin use so low in our study (9.4% at baseline). This was not an a priori endpoint in our study and therefore the mechanisms utilized to detect aspirin use at baseline and follow-up were not optimal, although some interpretation of these results can be made. ADA guidelines advise aspirin use in all diabetic patients without contraindications. We were pleased to find an improvement in the number of patients taking aspirin over the course of the study. HMG CoA reductase inhibitor use did increase as a result of our study but did not result in a significant reduction in follow-up LDL levels. This may again be a result of the low number of evaluable LDL levels available at follow-up.

Certain critical parameters should be focused on and optimized in the diabetic population. Large clinical studies have established the benefits of tight control of glucose in reducing the risk of microvascular complications in diabetic patients. The Diabetes Control and Complications Trial (DCCT) demonstrated that tight glycemic control in type 1 diabetics significantly prevents the onset or development of retinopathy, nephropathy, and neuropathy. Evidence also supports the benefits of tight control in type 2 diabetics. Results from the United Kingdom Prospective Diabetes Study-33 (UKPDS 33) revealed a 25% risk reduction in microvascular endpoints, mostly due to a reduction in retinopathy, in tightly controlled patients with type 2 diabetes mellitus.

Controlling blood pressure is also critical in diabetic patients. Hypertension increases the risk of cardiovascular disease, microalumubinuria, and retinopathy in type 2 diabetics. Lowering of blood pressure benefits both type 1 and type 2 diabetics. Lower blood pressure reduces albuminuria both in type 1 and in type 2 diabetics and slows the deterioration of renal function in type 1 diabetics. An analysis from the UKPDS 38 trial of type 2 diabetic patients with hypertension utilizing either captopril or atenolol as the main treatment revealed a 24%, 32%, 44%, 56%, and 37% risk reduction in diabetes related endpoints, deaths related to diabetes, strokes, heart failure, and microvascular endpoints, respectively, over a median follow-up of 8.4 years with tight control (144/82 mm Hg) compared to less tight control (154/87 mm Hg). The Hypertension Optimal Treatment (HOT) study demonstrated a 31% reduction in major cardiovascular events in the group with target diastolic blood pressure 80 mm Hg or lower compared with 90 mm Hg or lower in patients with diabetes.

Subgroup analyses of diabetic patients in clinical studies have also demonstrated substantial benefit of LDL lowering in diabetic patients with coronary artery disease. Recently, results from UKPDS 33 revealed a 25% risk reduction in microvascular endpoints over ten years in 3,867 newly diagnosed type 2 diabetics who received treatment with either a sulphonylurea or insulin versus patients who received conventional treatment with diet. An 11% reduction in HbA1c (7.0% in the intensive group compared with 7.9% in the conventional group) was noted, compared to an 11.8% reduction in HbA1c (7.5% in the intervention group compared with 8.5% in the historical control group) found in our study (Table 2). A similar reduction in microvascular endpoints over ten years might be expected in our study population if this reduction persisted, given continued pharmacy services.

Two similar studies utilizing pharmacists to deliver education, medication counseling and adjustment, and monitoring have shown significant improvements in glycemic control in type 2 diabetic patients. Although only one study utilized a control group, both studies were able to reduce HbA1c values by greater than two absolute percentage points with both studies reaching statistical significance as well. These two studies corroborate the results from our study, showing the positive effects of a pharmacist-managed programs on outcomes in diabetic patients.
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Conclusions
A pharmacist-managed continuing care service is effective in reducing HbA1c values and increasing the proportion of patients who have HbA1c values at goal. The service was not effective in smoking cessation. This study supports the role of clinical pharmacists in the ambulatory care environment, in collaboration with primary care physicians, in reaching therapeutic goals in diabetic patients.

References