CLINICAL REPORT

Enhancing diabetes care by adding a pharmacist to the primary care team

ERIC J. IP, BIJAL M. SHAH, JUNHUA YU, JAMES CHAN, LYNDA T. NGUYEN, AND DEEMPAL C. BHATT

An audio interview that supplements the information in this article is available on *AJHP*'s website at www.ajhp.org/site/misc/podcasts.xhtml.

Purpose. The impact of pharmacist interventions on short-term clinical markers and long-term cardiovascular risk in patients with type 2 diabetes is investigated.

Methods. Selected health outcomes were retrospectively analyzed in 147 adults with type 2 diabetes whose care was managed by a team of providers including a pharmacist (the enhanced care group) and a matched sample of patients (n = 147) managed by a primary care physician only (the control group). All patients received services through the same health maintenance organization (HMO). The primary study endpoints were (1) the changes from baseline to 12-month follow-up in glycosylated hemoglobin (HbA_{1c}), low-density lipoprotein cholesterol (LDL-C), and blood pressure (BP) values, (2) rates of attainment of HbA_{1c}, LDL-C and BP goals, and (3) changes from baseline in predicted 10-year risks of coronary heart disease (CHD) and stroke.

Results. During the 12-month study period, the mean HbA_{1c} value was decreased from 9.5% to 6.9% in the enhanced care group and from 9.3% to 8.4% in the control group ($p < 0.001$); patients in the enhanced care group were significantly more likely to attain goals for HbA_{1c} (odds ratio [OR], 3.9), LDL-C (OR, 2.0), and BP reduction (OR, 2.0) and three times more likely to attain all three goals (OR, 3.2). The estimated 10-year risk of CHD was decreased from 16.4% to 9.3% with enhanced care versus a reduction from 17.4% to 14.8% with usual care ($p < 0.001$).

Conclusion. The addition of a pharmacist to an HMO primary care team improved short-term surrogate markers as well as long-term cardiovascular risk in adult patients with type 2 diabetes.

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Diabetes mellitus affects 25.8 million Americans, or 8.3% of the U.S. population.[1] The prevalence of diabetes continues to rise, threatening a nationwide epidemic. Providing adequate care poses a challenge due to the multifaceted nature of diabetes-related interventions and clinical goals, especially in an era when primary care physicians (PCPs) are limited in the time they are able to spend with patients.[2] To compound the matter, the number of diabetes patients continues to grow in the face of current and future PCP shortages in the United States.[3]

Nonphysician health care professionals, including nurses and pharmacists, have become contributors to primary care in the face of PCP shortages.[4-6] In particular, pharmacists have stepped outside their traditional dispensing role and are increasingly involved in the management of patients with diabetes in various settings across the country.[6-8] Kaiser Permanente (KP) Northern California, a large health maintenance organization (HMO) with an integrated health care model, uses the skills of pharmacists (as providers) in the management of various chronic conditions, including diabetes.

The objectives of the study described below were to determine

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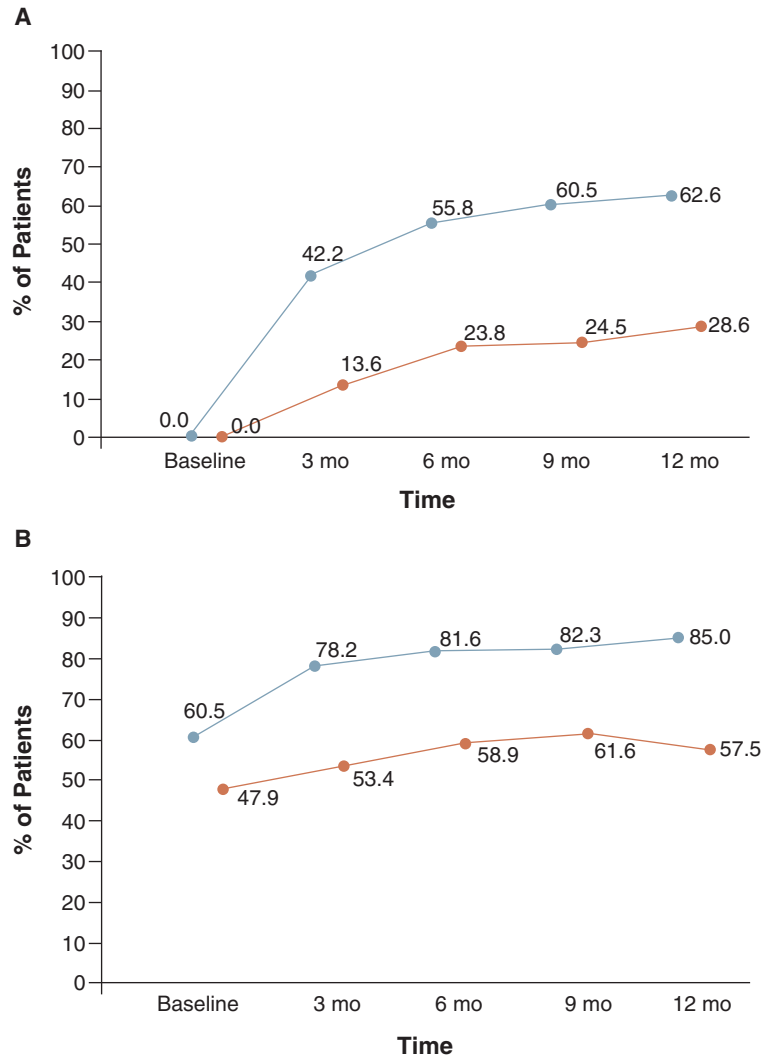
the effects of a clinical pharmacist's involvement on a primary care team on short-term (i.e., 12-month) outcomes and projected long-term cardiovascular disease (CVD) risk in patients with diabetes. This was accomplished by retrospectively evaluating selected clinical measures in a group of adult patients with type 2 diabetes mellitus whose care was managed by a team of clinicians including a pharmacist (the enhanced care group) and a comparable group of patients receiving care from a PCP only (the control group).

The primary study endpoints were (1) the changes from baseline in short-term surrogate markers of cardiovascular risk (glycosylated hemoglobin [HbA_{1c}], low-density lipoprotein cholesterol [LDL-C], and blood pressure [BP] levels), (2) rates of attainment of HbA_{1c}, LDL-C, and BP goals set forth by the American Diabetes Association (ADA),[9] and (3) changes from baseline in predicted long-term clinical outcomes (projected 10-year risks of coronary heart disease [CHD], fatal CHD, stroke, and fatal stroke), as estimated by the United Kingdom Prospective Diabetes Study (UKPDS) risk engine at 12-month follow-up.[10] The UKPDS risk engine uses data on glycemic control (e.g., HbA_{1c} values) and duration of diabetes, in addition to information on total cholesterol, high-density lipoprotein cholesterol, BP, and other factors, to estimate the 10-year risks of CHD and stroke in patients with type 2 diabetes.[10-12]

Figure 1. Trend lines showing change from baseline in the proportions of patients in the enhanced care group (blue) and the usual care group (red) who had attained the study goals at the three-month study time points. The goals were a glycosylated hemoglobin value of <7% (panel A), a low-density lipoprotein cholesterol goal of <100 mg/dL (panel B), a blood pressure of <130/80 mm Hg (panel C), and the simultaneous attainment of all three goals (panel D).



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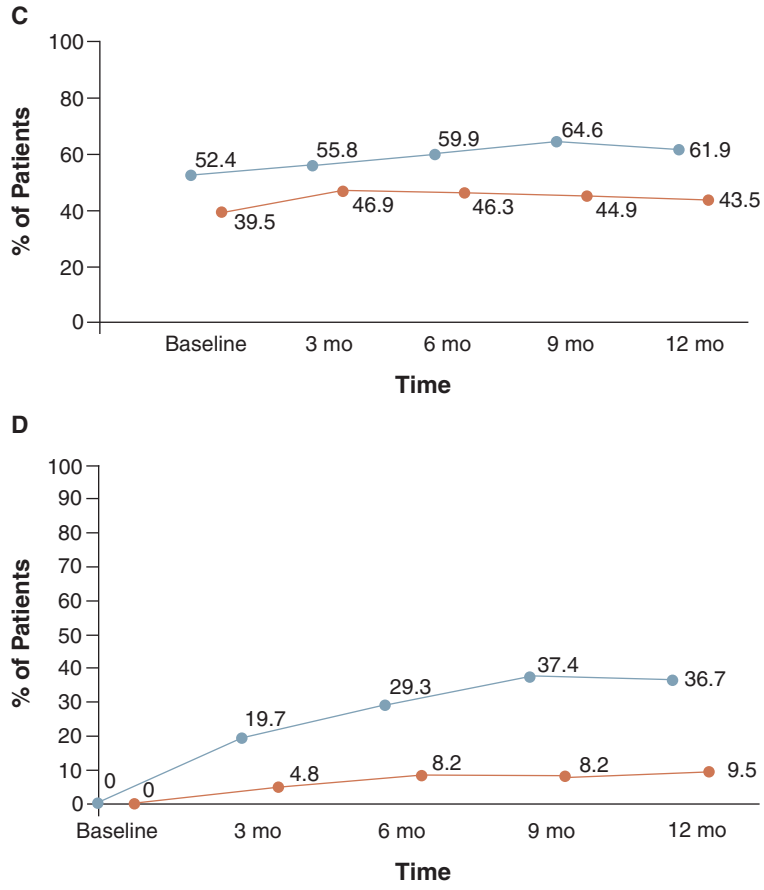
Methods

Study design. A dual-center retrospective study was performed to compare selected diabetes care outcomes in patients under the care of a clinical pharmacist serving on a primary care team at KP Mountain View Medical Clinics (MVMC) and patients under the usual care of PCPs, without pharmacist intervention, at KP Santa Clara Medical Center.

The two-site study design was used to address the concern that control groups in studies of chronic disease state management may be subject to outside health care influences (in this case, possible pharmacist involvement in care), thus biasing the study findings.[6] The two-site design was also intended to eliminate the potential for "learning effects" that can occur in single-site studies (in this case, the possibility that physicians might learn from the pharmacist's recommendations and apply them to the care of patients prior to pharmacist intervention), which can also introduce bias.[13] Moreover, because both of the study sites used the same KP-published clinical practice guidelines as the standard of care,[14] potential confounding influ-

Figure 1 (*continued*)



ences due to differing site-specific diabetes management and clinical goals were eliminated.

Pharmacist interventions. At MVMC, a team of 16 PCPs in the internal medicine department referred their diabetes patients with poor glycemic control (as indicated by an HbA_{1c} value of ≥7%) to a single clinical pharmacist for more stringent control and medical follow-up. The pharmacist managing patients in this study was credentialed as a certified diabetes educator and pharmacotherapy specialist. During an initial 45-minute face-to-face patient visit, the pharmacist evaluated the patient's diabetes status and cardiovascular comorbidities. As permitted by a collaborative practice agreement, the pharmacist performed interventions including pharmacotherapy modifications (i.e., prescribing medications and dosage adjustments), laboratory monitoring, dietary and physical activity recommendations, and the provision of diabetes self-care education. Other activities included performing physical assessments, providing immunizations, and initiating specialist referrals (i.e., podiatry, ophthalmology) when deemed appropriate.

The pharmacist had full access to and routinely documented every clinical encounter in the patients' electronic medical record. Patients were then followed up for further care by the pharmacist via telephone or face-to-face visits. Once patients met their therapeutic goals or were deemed stable by the pharmacist, they were referred back to their PCP for ongoing management.

Patient selection. Patients with type 2 diabetes who were older than 18 years of age, had a baseline HbA_{1c} of ≥7%, and had been under the pharmacist's care for at least two months were included in the enhanced care group. A random sample of patients who met the study criteria and had never received additional care from a diabetes care manager (a clinical pharmacist or a nurse practitioner) served as the control group. Patients with type 1 diabetes or HbA_{1c} values of <7%, as well as patients who disenrolled from KP health insurance during the study time frame, were excluded.

Data collection. Electronic patient charts from the period June 2007–February 2010 were reviewed, and the following data were collected: age, gender, ethnicity, smoking status, height and weight, duration of diabetes, number of clinical visits, laboratory values (HbA_{1c}, LDL-C, and BP at baseline and at 3, 6, 9, and 12 months), comorbid conditions, and medications. Comorbidities were assessed with the Charlson Comorbidity Index (CCI)[15]; because diabetes (1 of 22 conditions included in the CCI) was the index condition under study, it was excluded from the list of evaluated comorbid conditions.[16]

Matched sample selection. To control for patient characteristics that could influence the study outcomes, patients in the enhanced care group (n = 204) were matched 1:1 to patients in the control group (n = 407). Patient matching was based on age, gender, HbA_{1c} levels, and CCI score; the matching methodology permitted an age difference of up to eight years, a difference in HbA_{1c} values of up to 0.7%, and a difference in CCI score of up to four points. None of these differences were statistically significant between the two groups.

Statistical analysis. Baseline characteristics (matched and unmatched) were compared to determine if there

were differences between the two matched groups. Means and 95% confidence intervals (CIs) were reported for continuous variables. For nominal variables, the number and percent of individuals in each category were reported. Independent *t* tests and chi-square tests were used for continuous and categorical variables, respectively, to determine if a difference existed in each individual patient characteristic between the two groups. Raw comparisons were made in terms of the short-term clinical outcomes without adjusting for the other nonmatched characteristics between the two matched groups. Scatterplots were used to illustrate the trend of outcomes over time, as measured by the mean ± S.D. and 95% CI. The independent *t* test was used to examine the difference of the outcomes at each follow-up time point. Taking into account the correlation of repeated outcome measures over time and other potential covariates, a generalized linear mixed-effects model was used to estimate the adjusted effects of enhanced care on the above measures observed at 3, 6, 9, and 12 months.

The primary terms included in the regression models were the binary indicator of the enhanced care group, times at baseline and follow-up, and the interaction terms between the indicator for the enhanced care group and the time indicator. To control for the possible impact of matched or unmatched characteristics on the outcomes, all baseline characteristics and medication treatment during the follow-up period were included in the model. Covariate factors included in the model were age, ethnicity, years of diabetes duration, smoking status (scored as follows: 0 = never smoked, 1 = past smoker, and 2 = current smoker), baseline HbA_{1c} value, systolic BP (SBP), diastolic BP (DBP), total cholesterol, documented diagnosis of hypertension or hyperlipidemia, and the use of certain medications (antihypertensives, statins, aspirin, and thiazolidinediones). For patients whose clinical values were not available in the later follow-up period, the last observation carried forward (LOCF) was used to impute the missing values. The Toeplitz covariance structure was selected according to the Akaike's Information Criterion in the regression model[17]; this structure suggested an autoregressive structure of the repeated measures, with less association between follow-up when the measurements were not adjacent.

Similarly, a generalized linear mixed-effects model with logit link function was used to estimate an adjusted odds ratio (OR) for achieving each of the three goals (HbA_{1c} of <7%, LDL-C of <100 mg/dL, SBP/DBP of <130/80 mm Hg) with enhanced versus usual care. The same

Figure 2. Trends in the change from baseline in the mean glycosylated hemoglobin (HbA_{1c}) value (panel A), mean low-density lipoprotein cholesterol (LDL-C) level, and mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) values (panels C and D, respectively) with enhanced care (blue line) versus usual care (red line). The respective ranges of documented values are indicated at each time point.

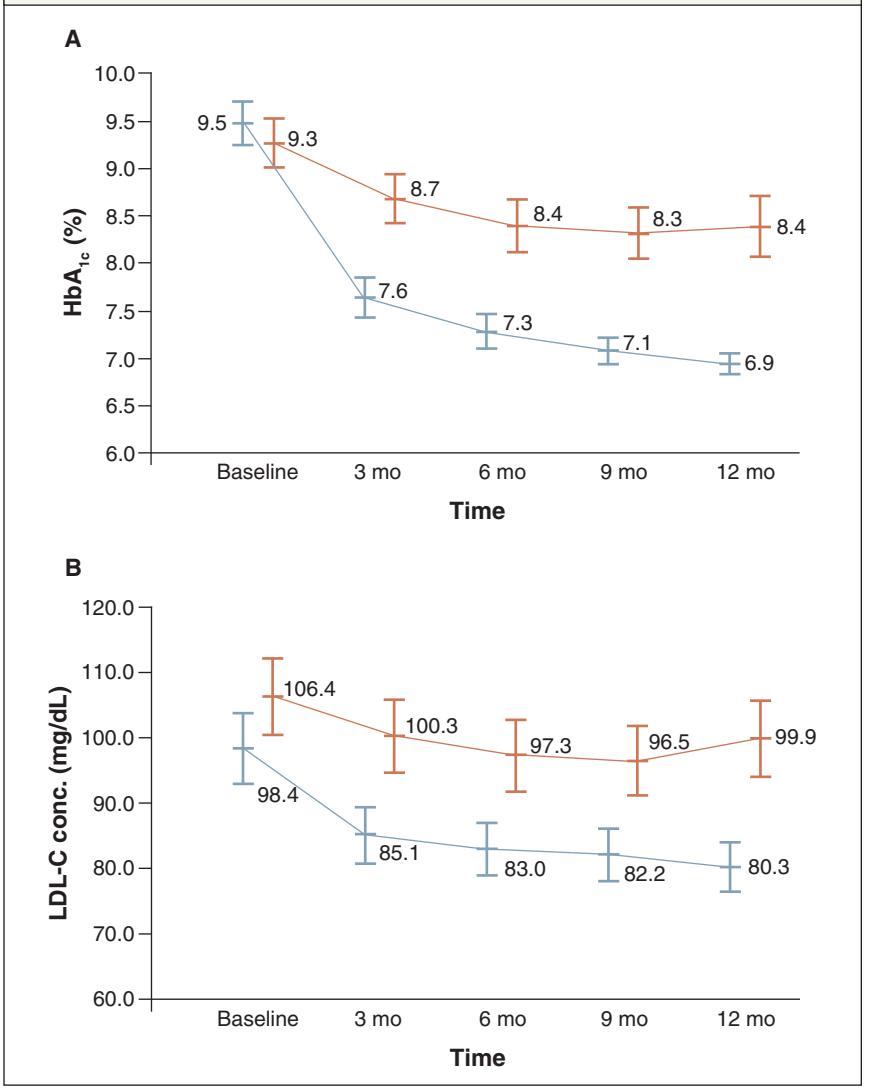


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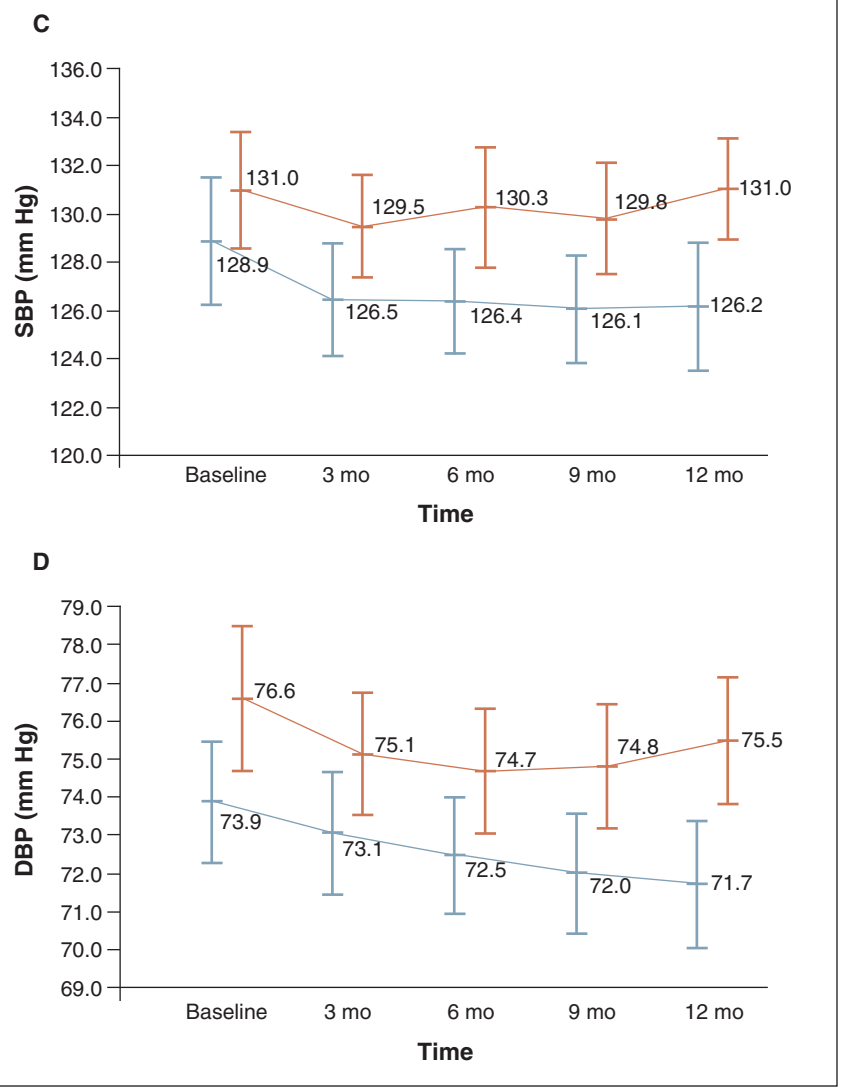
Figure 2 (*continued*)



set of independent variables used in the regression model was used in this analysis, with the exception of the interactions of treatment and time effects, none of which were significant when included.

The final outcome examined was long-term CVD risk, as estimated by the UKPDS risk engine. The 10-year risks of CHD (including fatal CHD) and stroke (including fatal stroke) for each group and relative risk reduction (RRR) values were calculated from baseline and month-12 clinical data. Independent *t* tests were used to ascertain whether baseline CVD risk differed between the two groups, and the difference-in-difference test was used to examine if the reduction of 10-year CVD risk from baseline between the two groups differed. The *p* values associated with the two tests were reported. A *p* value of <0.05 was considered statistically significant.

Results

Baseline characteristics. The study sample consisted of 147 patients in the enhanced care group and 147 in the control group. The baseline characteristics of the enhanced care group and the control group are summarized in Tables 1 and 2. Mean ± S.D. baseline HbA_{1c} levels in the enhanced care and control groups were 9.5% ± 1.4% and 9.3% ± 1.5%, respectively ($p = 0.115$). As shown in Figure 1, at baseline no patients in either group had an HbA_{1c} value of <7% (thus, the number of patients meeting all three clinical goals was also 0); 89 patients (60.5%) in the enhanced care group versus 70 patients (47.9%) in the control group had an LDL-C value of <100 mg/dL, and 77 (52.4%) versus 58 (39.5%) had a BP of <130/80 mm Hg. Differences were seen in ethnicity and mean length of diabetes history between the two groups; more patients in the intervention group were Caucasian (65 [44.2%] versus 46 [31.3%] of controls, $p = 0.001$), and the mean duration of diabetes was about two years longer in the intervention group (6.1 years versus 4.3 years in the control group, $p = 0.033$).

Unadjusted comparisons of short-term clinical outcomes. Comparisons of changes in clinical endpoints between the two matched groups are illustrated in Figure 2. Mean HbA_{1c}, LDL-C, SBP, and DBP levels decreased significantly from baseline to the 3-, 6-, 9-, and 12-month follow-up points in the enhanced care group. Over 12 months, the mean HbA_{1c} value decreased from 9.5% to 6.9% in the enhanced care group, compared with a decrease from 9.3% to 8.4% in the control group—a relative improvement of 1.7 percentage points ($p < 0.001$) favoring patients receiving enhanced care. The enhanced care group also outperformed the control group with regard to improvements in LDL-C, SBP, and DBP levels during the follow-up period.

The percentages of patients reaching the ADA clinical goals are shown in Figure 1. At 3, 6, 9, and 12 months,

Table 1.
Baseline Patient Characteristics[a,b]

Characteristic	Enhanced Care Group (n = 147)	Control Group (n = 147)	p
Age, yr	55.5 ± 11.2 (53.6–57.3)	57.2 ± 11.7 (55.3–59.1)	0.113
Body mass index (kg/m^2)	33.0 ± 8.3 (31.3–34.3)	31.4 ± 6.5 (30.3–32.4)	0.095
History of diabetes, yr	6.1 ± 4.6 (5.4–6.9)	5.0 ± 4.4 (4.3–5.8)	0.033
Charlson Comorbidity Index score	7.0 ± 1.4 (6.8–7.2)	7.0 ± 1.1 (6.8–7.1)	0.913
HbA_{1c} concentration, %	9.5 ± 1.4 (9.2–9.7)	9.3 ± 1.5 (9.0–9.5)	0.115
Lipid panel results, mg/dL			
Total cholesterol	179.4 ± 41.7 (172.6–186.2)	189.6 ± 45.2 (182.2–196.9)	0.055
HDL-C	44.6 ± 10.2 (42.9–46.2)	43.4 ± 9.4 (41.9–45.0)	0.475
LDL-C	98.4 ± 33.2 (93.0–103.8)	106.4 ± 35.9 (100.5–112.3)	0.059
Blood pressure, mm Hg			
Systolic	128.9 ± 16.2 (126.3–131.6)	131.0 ± 14.8 (128.6–133.4)	0.184
Diastolic	73.9 ± 9.8 (72.3–75.5)	76.6 ± 11.6 (74.7–78.5)	0.072

[a]HbA_{1c} = glycosylated hemoglobin, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol.
[b]All data presented as mean ± S.D. (95% confidence interval)

Table 2.
Additional Baseline Patient Characteristics[a]

Characteristic	Enhanced Care Group (n = 147)	Control Group (n = 147)	p
Gender			0.999
Male	88 (59.9)	88 (59.9)	
Ethnicity			0.001
Caucasian	65 (44.2)	46 (31.3)	
Hispanic	38 (25.9)	47 (32.0)	
African American	8 (5.4)	5 (3.4)	
Asian	35 (23.8)	35 (23.8)	
Native America	1 (0.7)	0	
Other	0	14 (9.5)	
Smoking status			0.275
Never	104 (70.7)	92 (62.6)	
Past	33 (22.4)	45 (30.6)	
Current	10 (6.8)	10 (6.8)	
History of hyperlipidemia	105 (71.4)	118 (80.3)	0.077
History of hypertension	107 (72.8)	103 (70.1)	0.606
Use of thiazolidinediones	28 (19)	18 (12.2)	0.108
Mean ± S.D. diabetes-related encounters			
Clinic visit	1.2 ± 0.6	2.3 ± 1.3	<0.001
Phone or e-mail contact	9.5 ± 0.6	0.3 ± 1.0	<0.001
Any encounter	10.7 ± 6.7	2.5 ± 1.5	<0.001

[a]All data are no. (%) unless otherwise indicated.

more patients in the enhanced care group than in the control group reached ADA goals for HbA_{1c}, LDL-C, and BP levels ($p < 0.001$ for each). In addition, relatively more patients in the enhanced care group were able to obtain all three clinical goals simultaneously at 3, 6, 9, and 12 months. At 12 months, 92 (62.6%), 125 (85.0%), and 91 (61.9%) patients in the enhanced care group had achieved the HbA_{1c}, LDL-C, and BP goals, respectively; 54 (36.7%) had achieved all three goals combined. A comparison of those values with the control-group data suggests that enhanced care increased the chances of achieving the HbA_{1c}, LDL-C, and BP goals 2.2-, 1.5-, and 1.4-fold, respectively; the likelihood of attaining all three goals was 3.9-fold higher.

Adjusted comparisons of short-term clinical outcomes. Table 3 displays the results from the mixed-effects model that adjusted for the potential confounding factors. During the 12-month study period, there was a statistically significant decrease in the average HbA_{1c} level in the enhanced care group (mean change, –0.9%; 95% CI, –1.2% to –0.5%; $p < 0.0001$). In addition, the interaction term between the indicator for the enhanced care group and indicators for the points of time follow-up suggests that the effects of pharmacists' intervention on HbA_{1c} levels were modified by the time effect. Taking into consideration the time effects, the reductions from baseline mean HbA_{1c} values in the enhanced care and control groups, respectively, were 3.9 and 1.8 percentage points at 3 months, 4.6 and 2.4 percentage points at 6 months, 5.0 and 2.7 percentage points at 9 months,

and 5.1 and 2.5 percentage points at 12 months. Therefore, the time-adjusted between-group differences in mean HbA_{1c} reductions favoring enhanced versus usual care were 1.1 percentage points at 3 months, 2.2 percentage point at 6 months, 2.3 percentage points at 9 months, and 2.5 percentage points at 12 months; these changes are similar to the unadjusted differences of 1.1, 1.1, 1.2, and 1.5 percentage points at months 3, 6, 9, and 12, respectively, shown in Figure 2A.

Taking into consideration the modifying effects of time on the enhanced care group as suggested by the interaction term, the mean LDL-C reductions at each time point were larger in the enhanced care group than in the control group: 27.6 versus 15.8 mg/dL at month 3, 32.3 versus 21.4 mg/dL at month 6, 34.0 versus 23.0 mg/dL at month 9, and 35.1 versus 18.7 mg/dL at month 12, respectively. Compared to the unadjusted difference in mean LDL-C as shown in Figure 2B, the adjusted improvement due to enhanced care was relatively larger (enhanced care group versus control group: 11.8 versus 6.1 mg/dL at month 3, 10.9 versus 9.1 mg/dL at month 6, 11.0 versus 9.9 mg/dL at month 9, and 16.4 versus 6.5 mg/dL at month 12).

The enhanced care group had a statistically significant ($p = 0.0356$) improvement from baseline in the mean SBP value (mean decrease, 3.0 mm Hg) at month 12, which is similar to the unadjusted decrease at month 12 shown in Figure 2C. There was no significant adjusted group effect on the mean DBP value, but both groups showed improvement over time starting at month 6.

Table 4 shows the relative likelihood of attainment of the clinical goals in the enhanced care group, as measured by ORs, using a mixed-effects model adjusting for potential confounding factors. Compared with the control group, the enhanced care group had increased probabilities of

Table 3.
Comparison of Clinical Endpoints Using Mixed-Effects Modeling[a,b]

Type of Effect	HbA_{1c} Mean (95% CI) Change, % Points	*p*	LDL-C Mean (95% CI) Change, mg/dL	*p*	SBP Mean (95% CI) Change, mm Hg	*p*	DBP Mean (95% CI) Change, mm Hg	*p*
Adjusted group effect	−0.9 (−1.2 to −0.5)	<.0001[c]	−4.6 (−10.3 to 1.0)	0.1065	−3.0 (−5.8 to −0.2)	0.0356[c]	−1.1 (−2.9 to 0.8)	0.2526
Time effect relative to baseline								
3 mo	−1.2 (−1.5 to −1.0)	<.0001[c]	−9.7 (−14.3 to −5.1)	<.0001[c]	−2.1 (−3.8 to −0.3)	0.1337	−1.2 (−2.8 to 0.4)	0.2322
6 mo	−1.5 (−1.8 to −1.3)	<.0001[c]	−12.3 (−17.1 to −7.4)	<.0001[c]	−1.7 (−3.5 to 0.1)	0.3562	−1.7 (−3.4 to −0.1)	0.036[c]
9 mo	−1.7 (−1.9 to −1.4)	<.0001[c]	−13.1 (−18.1 to −8.1)	<.0001[c]	−2.1 (−3.9 to −0.2)	0.1698	−1.9 (−3.5 to −0.2)	0.0175[c]
12 mo	−1.7 (−1.9 to −1.5)	<.0001[c]	−12.3 (−16.2 to −8.3)	<.0001[c]	−1.4 (−2.8 to 0.1)	0.3743	−1.7 (−3.0 to −0.3)	0.0073[c]
Interaction effects of group and time								
Enhanced care group								
3 mo	−1.8 (−2.3 to −1.4)	<.0001[c]	−13.3 (−20.9 to −5.7)	<.0001[c]	−2.4 (−4.9 to 0)	0.6261	−0.8 (−3.4 to 1.7)	0.9918
6 mo	−2.2 (−2.6 to −1.7)	<.0001[c]	−15.4 (−23.4 to −7.4)	<.0001[c]	−2.5 (−5.0 to 0.1)	0.6641	−1.4 (−4.1 to 1.3)	0.82
9 mo	−2.4 (−2.8 to −1.9)	<.0001[c]	−16.3 (−24.4 to −8.1)	<.0001[c]	−2.8 (−5.4 to −0.2)	0.5015	−1.9 (−4.6 to 0.8)	0.4675
12 mo	−2.5 (−2.9 to −2.2)	<.0001[c]	−18.2 (−24.6 to −11.7)	<.0001[c]	−2.7 (−4.8 to −0.6)	0.2479	−2.2 (−4.4 to 0)	0.0592
Control group								
3 mo	−0.6 (−1.0 to −0.2)	<0.0004[c]	−6.1 (−13.8 to 1.5)	0.2464	−1.7 (−4.1 to 0.8)	0.9425	−1.6 (−4.1 to 1.0)	0.6547
6 mo	−0.9 (−1.3 to −0.4)	<.0001[c]	−9.1 (−17.2 to −1.0)	0.0132	−0.9 (−3.5 to 1.7)	0.9996	−2.0 (−4.7 to 0.7)	0.3443
9 mo	−1. (−1.4 to −0.5)	<.0001[c]	−9.9 (−18.1 to −1.7)	0.0053	−1.4 (−4.0 to 1.3)	0.9912	−1.9 (−4.6 to 0.9)	0.4682
12 mo	−0.9 (−1.3 to −0.5)	<.0001[c]	−6.4 (−12.9 to 0.1)	0.0552	0 (−2.1 to 2.1)	1.0	−1.1 (−3.4 to 1.1)	0.8303

[a]HbA_{1c} = glycosylated hemoglobin, LDL-C = low-density lipoprotein cholesterol, SBP = systolic blood pressure, DBP = diastolic blood pressure.

[b]All *p* values adjusted for the following characteristics: age, ethnicity, diabetes duration, smoking status; baseline HbA_{1c}, SBP, DBP, and total cholesterol values; comorbid diagnosis of hypertension and/or hyperlipidemia; use of thiazolidinediones; time effects; and interaction between time and group effects.

[c]For each group, the total reductions in the measurements at different time points are calculated by summing the reductions due to time effects and the interaction of time and group effects. For example, the total mean reduction of LDL-C in the enhanced care group at 3 mo is calculated as 27.6 mg/dL (the sum of the values 4.6, 9.7 and 13.3 mg/dL), and the total mean reduction of LDL-C in the control group is calculated as 15.8 mg/dL (the sum of the values 9.7 and 6.1 mg/dL). Therefore, the difference in mean LDL-C reductions between the two groups at 3 mo is calculated as 11.8 mg/dL.

Table 4.
Odds Ratios (ORs) for Attainment of Clinical Goals in Enhanced Care Group Relative to Control Group[a,b]

Type of Effect	HbA_{1c} <7%		LDL-C <100 mg/dL		SBP/DBP <130/80 mm Hg		All 3 Goals	
	OR	*p*	OR	*p*	OR	*p*	OR	*p*
Adjusted net group effect over 12 mo	3.9	<0.0001	2.0	0.0152	2.0	0.0016	3.2	0.0004
Time effect								
3 mo	…[c]	…	2.2	0.0003	1.3	0.1293	…	…
6 mo	2.0	0.9573	3.2	<0.0001	1.5	0.0467	1.8	0.9631
9 mo	2.4	0.9570	3.6	<0.0001	1.6	0.0139	2.4	0.9624
12 mo	2.7	0.9566	3.4	<0.0001	1.4	0.0582	2.4	0.9624

[a] HbA_{1c} = glycosylated hemoglobin, LDL-C = low-density lipoprotein cholesterol, SBP = systolic blood pressure, DBP = diastolic blood pressure.
[b] All *p* values adjusted for multiple potential confounding factors.
[c] As no patients in either group had at-goal values at baseline, regression analysis not possible; analysis of multigoal attainment also precluded.

achieving an HbA_{1c} value of <7% (OR, 3.9; $p < 0.0001$), an LDL-C value of <100 mg/dL (OR, 2.0; $p = 0.0152$), a BP of <130/80 mm Hg (OR, 2.0; $p = 0.0016$), and all three goals simultaneously (OR, 3.2; $p = 0.0004$).

Adjusted comparisons of predicted long-term cardiovascular risk. Table 5 presents comparative data on the mean estimated 10-year risks of CHD, fatal CHD, stroke, and fatal stroke in the enhanced care group and the control group. In none of the four categories of 10-year risk were mean values significantly different at baseline in the two groups. However, at 12 months, differences favoring the enhanced care group were notable with regard to CHD, fatal CHD, and stroke. Specifically, at the 12-month assessment, 10-year CHD risk was calculated to have been reduced from the baseline value of 16.4% to 9.3% in the enhanced care group and from 17.4% to 14.8% in the control group ($p < 0.001$), a difference of 4.5 percentage points between groups; the RRR was 43.7% in the enhanced care group versus 14.7% in the control group. At the 12-month follow-up, the 10-year risk of fatal CHD had been decreased from 11.3% to 5.7% in the enhanced care group, compared with a decrease from 11.9% to 10.3% in the control group ($p < 0.001$), indicating a RRR of 49.5% in the enhanced care group versus 13.5% in the control group. From baseline to 12-month follow-up, the estimated 10-year stroke risk was decreased from 7.6% to 6.8% in the enhanced care group but was unchanged (8.3% at both time points) in the control group ($p = 0.001$), indicating a RRR of 10.1% in the enhanced care group versus 0.3% in the control group. Despite the lack of a significant between-group difference in reduction of the estimated 10-year risk of fatal stroke at the 12-month follow-up, partly due to the relatively small magnitude of fatal stroke risk, the RRR for the enhanced care group was 14.8%, compared with 0.3% in the control group.

Discussion

The study evaluated the addition of a clinical pharmacist to the diabetes care team in an HMO primary care setting. According to the UKPDS findings, a 1% decrease in HbA_{1c} is associated with a 37% reduction in microvascular complications.[18] The degree of HbA_{1c} reduction observed in the enhanced care group (unadjusted and adjusted decreases of 2.6% and 5.1%, respectively, after 12 months) would potentially translate into a 96% decrease in microvascular complications. It is worth noting that the difference in LDL-C reductions between the study groups via unadjusted comparisons was similar in magnitude to the difference after adjusting for potential confounding factors. The fact that the improvements in HbA_{1c}, LDL-C, and SBP outcomes observed in the two matched groups were similar in magnitude to those estimated through the mixed-effects regression model reinforces the strength of the study design in balancing the two groups' characteristics.

At 12 months, a greater percentage of patients in the enhanced care group than in the control group had achieved ADA goals. In the enhanced care group, the probability of reaching an HbA_{1c} of <7% was increased nearly threefold, and the probability of attaining a BP of <130/80 mm Hg was increased by 100%, relative to the control group. At baseline, no subjects in the enhanced care or control groups had attained all three goals simultaneously. After 12 months, the percentage of patients in the enhanced care group who met all three goals (36.7%) was higher than the national average of 12.2%.[19] As confirmed by the changes in HbA_{1c}, LDL-C, and BP values, as well as attainment of the ADA clinical goals, enhanced care was more effective than usual

Table 5.
Estimated 10-Year Risk of Cardiovascular Disease Outcomes, as Calculated by UKPDS Risk Engine[a]

Outcome	Mean (95% CI) Estimated Risk at Baseline			Mean (95% CI) Estimated Risk at 12-Mo Follow-up		
	Enhanced Care Group[b]	Control Group[b]	p[c]	Enhanced Care Group[d]	Control Group[d]	p[e]
Coronary heart disease (CHD)	16.4 (12.0–22.0)	17.4 (12.6–23.4)	0.1764	9.3 (6.9–12.4)	14.8 (10.6–20.0)	<0.0001
Fatal CHD	11.3 (8.0–15.7)	11.9 (8.3–16.6)	0.2332	5.7 (4.1–7.9)	10.3 (7.2–14.3)	<0.0001
Stroke	7.6 (4.7–11.6)	8.3 (5.3–12.0)	0.2430	6.8 (4.2–10.5)	8.3 (5.3–12.0)	0.0007
Fatal stroke	1.0 (0.6–1.9)	1.1 (0.7–1.9)	0.1787	0.9 (0.5–1.6)	1.1 (0.6–1.9)	0.0645

[a]UKPDS = United Kingdom Prospective Diabetes Study, CI = confidence interval.
[b]n = 147.
[c]Calculated using t test for hypothesis of no between-group difference in baseline risk.
[d]Variable n (range, 139–143).
[e]Calculated using difference-in-difference regression model for hypothesis of no between-group difference in reduction of 10-year risk.

care in improving short-term clinical markers.

In addition to improved attainment of short-term clinical goals, the services provided by a pharmacist in the enhanced care group resulted in a reduction in estimated long-term cardiovascular risk. Few studies to date have analyzed the impact of pharmacist care on long-term CHD risk in patients with diabetes. Al Mazroui and colleagues[20] showed that interventions by clinical pharmacists decreased the mean 10-year risk of CHD in patients with type 2 diabetes, as calculated using the Framingham equation, from 10.6% to 7.7% ($p < 0.001$); however, the reliability of using the Framingham equation to calculate CHD risk in diabetes patient populations has been questioned due to the small proportion of patients with diabetes in the Framingham study.[11] Ladhani and colleagues[21] used the UKPDS risk engine, which is considered a more reliable method of measuring cardiovascular risk in type 2 diabetes. They demonstrated that compared with standard care, adding pharmacists to the primary care team resulted in a median absolute reduction in the UKPDS risk score of 1.0% after 1 year.[22] The study described in this article also used the UKPDS risk engine but demonstrated even greater (i.e., up to 4.5-fold) reductions in the estimated 10-year risks of CHD, fatal CHD, and stroke with pharmacist-enhanced versus usual care; this might be attributed to the fact that the pharmacist had prescribing authority.[6]

The use of pharmacists in the provision of direct care to outpatients with disease states such as diabetes is not a new phenomenon and has been shown to improve patient care.[5-7,23-31] Institutions incorporating pharmacists into the care process in such a manner typically have collaborative practice agreements that allow pharmacists to provide direct medication therapy management services.[6] However, the extent to which pharmacists are able to manage medication therapy varies greatly. On one end of the spectrum, medication management may involve assessing the patient and providing pharmacotherapy recommendations to the physician for implementation; on the other end, the pharmacist has a high level of autonomy and is a prescriber of medications, immunizations, and laboratory work. The study results presented here support the notion that adding a pharmacist to the primary care team is more effective than usual care in improving both short-term clinical markers and long-term cardiovascular risk in an HMO primary care setting. Future studies to evaluate the cost-effectiveness and economic impact of adding a pharmacist to the primary care team in managing patients with diabetes would be beneficial.

Among other limitations, the study reported here was a retrospective cohort analysis involving 147 patients in both study groups and was performed at two medical facilities using a quasiexperimental study design. A similar but randomized and controlled study including a greater number of patients, involving more than one pharmacist provider, and incorporating multiple medical facilities is needed to confirm the apparent benefits of pharmacist intervention observed in our study.

Also, the study did not control for the difference in the mean number of diabetes-related clinic visits between groups. The patients in the enhanced care group averaged more visits than those in the control group, and this may have been a contributing factor in the former group's more favorable results.

Moreover, at baseline, patients in the enhanced care group had a longer history of diabetes than those in the control group. Although this might be expected to bias the results in favor of the control group, the enhanced care group still exhibited better overall clinical outcomes, suggesting that if both groups had been more closely matched for duration of diabetes, the demonstrated benefits

of enhanced versus usual care might have been even greater.

In another notable study limitation, LOCF values were used when clinical markers (e.g., HbA_{1c}, LDL-C, and BP values) were not available for each follow-up time point. However, in clinical practice, laboratory monitoring is often extended beyond a patient's attainment of clinical goals, so we believe that the findings presented here represent those typically seen in actual clinical practice.

Conclusion

The addition of a pharmacist to an HMO primary care team improved short-term surrogate markers as well as long-term cardiovascular risk in adult patients with type 2 diabetes.

References

1. Centers for Disease Control and Prevention. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011. Atlanta: Department of Health and Human Services; 2011.
2. Kane GC, Grever MR, Kennedy JI et al. The anticipated physician shortage: meeting the nation's need for physician services. *Am J Med.* 2009; 122:1156-62.
3. Lakhan SE, Laird C. Addressing the primary care physician shortage in an evolving medical workforce. *Int Arch Med.* 2009; 2:14.
4. Schmittdiel JA, Uratsu CS, Fireman BH et al. The effectiveness of diabetes care management in managed care. *Am J Manag Care.* 2009; 15:295-301.
5. Davidson MB. The effectiveness of nurse- and pharmacist-directed care in diabetes disease management: a narrative review. *Curr Diabetes Rev.* 2007; 3:280-6.
6. Wubben DP, Vivian EM. Effects of pharmacist outpatient interventions on adults with diabetes mellitus: a systematic review. *Pharmacotherapy.* 2008; 28:421-36.
7. 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; 43:173-84.
8. Fera T, Bluml BM, Ellis WM. Diabetes Ten City Challenge: final economic and clinical results. *J Am Pharm Assoc.* 2009; 49:383-91.
9. American Diabetes Association. Standards of medical care in diabetes—2011. *Diabetes Care.* 2011; 34(suppl 1):S11-61.
10. Stevens RJ, Kothari V, Adler AI et al., for the United Kingdom Prospective Diabetes Study (UKPDS) Group. The UKPDS risk engine: a model for the risk of coronary heart disease in type II diabetes (UKPDS 56). *Clin Sci (Lond).* 2001; 101:671-9. [Erratum, *Clin Sci (Lond).* 2002; 102:679.]
11. Coleman RL, Stevens RJ, Retnakaran R et al. Framingham, SCORE, and DECODE risk equations do not provide reliable cardiovascular risk estimates in type 2 diabetes. *Diabetes Care.* 2007; 30:1292-3.
12. Kothari V, Stevens RJ, Adler AI et al. UKPDS 60: risk of stroke in type 2 diabetes estimated by the UK Prospective Diabetes Study risk engine. *Stroke.* 2002; 33:1776-81.
13. De Rijdt T, Willems L, Simoens S. Economic effects of clinical pharmacy interventions: a literature review. *Am J Health-Syst Pharm.* 2008; 65:1161-72.
14. Kaiser Permanente Care Management Institute. Adult diabetes clinical practice guidelines, January 2006. www.guidelinecentral.com/guideline-library/summaries/ngc-7460-type-2-diabetes-management-type-2-diabe (accessed 2013 Feb 8).
15. Charlson M, Szatrowski TP, Peterson J et al. Validation of a combined comorbidity index. *J Clin Epidemiol.* 1994; 47:1245-51.
16. Shah BM, Gupchup GV, Borrego ME et al. Depressive symptoms in patients with type 2 diabetes in the ambulatory care setting: opportunities to improve outcomes in the course of routine care. *J Am Pharm Assoc.* 2008; 48:737-43.
17. Moser EB. Repeated measures modeling with PROC MIXED. Proceedings of the 29th SAS Users Group International Conference, Montreal, Quebec, Canada. Cary, NC: SAS Institute; 2004.
18. Stratton IM, Adler AI, Neil HA et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ.* 2000; 321:405-12.
19. Cheung BM, Ong KL, Cherny SS et al. Diabetes prevalence and therapeutic target achievement in the United States, 1999 to 2006. *Am J Med.* 2009; 122:443-53.
20. Al Mazroui NR, Kamal MM, Ghabash NM et al. Influence of pharmaceutical care on health outcomes in patients with type 2 diabetes mellitus. *Br J Clin Pharmacol.* 2009; 67:547-57.
21. Ladhani NN, Majumdar SR, Johnson JA et al. Adding pharmacists to primary care teams reduces predicted long-term risk of cardiovascular events in type 2 diabetic patients without established cardiovascular disease: results from a randomized trial. *Diabet Med.* 2012; 29:1433-9.
22. Taveira TH, Pirraglia PA, Cohen LB et al. Efficacy of a pharmacist-led cardiovascular risk reduction clinic for diabetic patients with and without mental health conditions. *Prev Cardiol.* 2008; 11:195-200.
23. Choe HM, Mitrovich S, Dubay D et al. Proactive case management of high-risk patients with type 2 diabetes mellitus by a clinical pharmacist: a randomized controlled trial. *Am J Manag Care.* 2005; 11:253-60.
24. Rothman RL, Malone R, Bryant B et al. A randomized trial of a primary care-based disease management program to improve cardiovascular risk factors and glycated hemoglobin levels in patients with diabetes. *Am J Med.* 2005; 118:276-84.
25. Vivian EM. Improving blood pressure control in a pharmacist-managed hypertension clinic. *Pharmacotherapy.* 2002; 22:1533-40.
26. Davidson MB, Karlan VJ, Hair TL. Effect of a pharmacist-managed diabetes care program in a free medical clinic. *Am J Med Qual.* 2000; 15:137-42.
27. Gong C, Hasson NK, Lum BL. Impact of a diabetes disease management clinic on the total glycosylated hemoglobin of patients with type 2 diabetes mellitus. *J Manag Care Pharm.* 1999; 5:511-5.
28. Irons BK, Lenz RJ, Anderson SL et al. A retrospective cohort analysis of the clinical effectiveness of a physician-pharmacist collaborative drug therapy management diabetes clinic. *Pharmacotherapy.* 2002; 22:1294-1300.
29. Kelly C, Rodgers P. Implementation and evaluation of a pharmacist-managed diabetes service. *J Manag Care Pharm.* 2000; 6:488-93.
30. Martin OJ, Wu WC, Taveira TH et al. Multidisciplinary group behavioral and pharmacologic intervention for cardiac risk reduction in diabetes: a pilot study. *Diabetes Educ.* 2007; 33:118-27.
31. Giberson S, Yoder S, Lee MP, for the Office of the Chief Pharmacist, Public Health Service. Improving patient and health system outcomes through advanced pharmacy practice. A report to the U.S. Surgeon General 2011. www.usphs.gov/corpslinks/pharmacy/documents/2011AdvancedPharmacyPracticeReporttotheUSSG.pdf (accessed 2013 Jan 31).