RESEARCH

Randomized Controlled Trial of Clinical Pharmacy Management of Patients with Type 2 Diabetes in an Outpatient Diabetes Clinic in Jordan

Anan Sadeq Jarab, PhD; Salam Ghazi Alqudah, BSc;
Tareq Lewis Mukattash, PhD; Ghassan Shattat, PhD; and Tariq Al-Qirim, PhD

ABSTRACT

BACKGROUND: Glycemic goals (hemoglobin A1c <7%) are often not achieved in patients with type 2 diabetes despite the availability of many effective treatments and the documented benefits of glycemic control in the reduction of long-term microvascular and macrovascular complications. Several studies have established the important positive effects of pharmacist-led management on achieving glycemic control and other clinical outcomes in patients with diabetes. Diabetes prevalence and mortality are increasing rapidly in Jordan. Nevertheless, clinical pharmacists in Jordan do not typically provide pharmaceutical care; instead, the principal responsibilities of pharmacists in Jordan are dispensing and marketing of medical products to physicians.

OBJECTIVE: To assess the primary clinical outcome of glycemic control (A1c) and secondary outcomes, including blood pressure, lipid values, self-reported medication adherence, and self-care activities for patients with type 2 diabetes in an outpatient diabetes clinic randomly assigned to either usual care or a pharmacist-led pharmaceutical care intervention program.

METHODS: Patients with type 2 diabetes attending an outpatient diabetes clinic of a large teaching hospital were recruited over a 4-month period from January through April 2011 and randomly assigned to intervention and usual care groups using the Minim software technique. The intervention group at baseline received face-to-face objective-directed education from a clinical pharmacist about type 2 diabetes, prescription medications, and necessary lifestyle changes, followed by 8 weekly telephone follow-up calls to discuss and review the prescribed treatment plan and to resolve any patient concerns. The primary outcome measure was glycemic control (A1c), and secondary measures included systolic and diastolic blood pressure, complete lipid profile (i.e., total cholesterol, low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C], serum triglycerides), and self-reported medication adherence (4-item Morisky Scale) and self-care activities (Summary of Diabetes Self-Care Activities questionnaire). Data were collected at baseline and at 6 months follow-up. Changes from baseline to follow-up were calculated for biomarker values, and between-group differences in the change amounts were tested using the *t* test for independent samples. A *P* value of <0.05 was considered statistically significant.

RESULTS: A total of 77 of 85 patients (90.6%) randomly assigned to the intervention group and 79 of 86 patients (91.9%) assigned to usual care had baseline and 6-month follow-up values. Compared with baseline values, patients in the intervention group had a mean reduction of 0.8% in A1c versus a mean increase of 0.1% from baseline in the usual care group ($P=0.019$). The intervention group compared with the usual care group had small but statistically significant improvements in the secondary measures of fasting blood glucose, systolic and diastolic blood pressure, total cholesterol, LDL-C, serum triglycerides, self-reported medication adherence, and self-care activities. Between-group differences in changes in the secondary measures of HDL-C and body mass index were not significant.

CONCLUSIONS: Patients with type 2 diabetes who received pharmacist-led pharmaceutical care in an outpatient diabetes clinic experienced reduction in A1c at 6 months compared with essentially no change in the usual care group. Six of 8 secondary biomarkers were improved in the intervention group compared with usual care.

J Manag Care Pharm. 2012;18(7):516-26

What is already known about this subject

- Improving glycemic control is the key to reducing microvascular and macrovascular complications associated with type 2 diabetes mellitus. Epidemiological analysis of the United Kingdom Prospective Diabetes Study (UKPDS) showed that for each 1% reduction in hemoglobin A1C, there was a corresponding 21% reduction in any endpoint related to diabetes, with a 14% reduction for myocardial infarction, 12% reduction in stroke, and a 37% reduction for microvascular complications (Stratton et al., 2000).
- Randomized controlled trials (RCTs) of pharmacist interventions in disease management of type 2 diabetes have shown significant reductions in A1c compared with control group patients in usual care. Al Mazroui et al. (2009) found that 117 patients who received clinical pharmacist interventions had a significant reduction in mean A1c values from 8.5% to 6.9% compared with 117 control group patients who had approximately constant mean A1c values at baseline and 12-month assessments (8.4% and 8.3%, respectively). An RCT by Choe et al. (2005) reported a reduction in mean A1c values from 10.1% to 8.0% in 41 intervention patients who received clinical pharmacy services compared with 39 control group patients who showed a reduction in A1c values from 10.2% to 9.3% ($P=0.03$).
- Self-care activities that help to control blood glucose levels and avoid diabetes-related complications are vital in diabetes treatment. Doucette et al. (2009) indicated in an RCT that a pharmacist-provided diabetes care service led to significant improvement in dietary self-management and other self-care activities in patients with diabetes.

What this study adds

- In this RCT, a comprehensive clinical pharmacy service consisting of patient education on type 2 diabetes, prescription therapy, and medication adherence over a 6-month intervention period was significantly associated with improved glycemic control and other cardiovascular risk factors, including systolic and diastolic blood pressure (BP) and lipid values. After 6 months follow-up, mean [95% CI] reductions were significantly greater in pharmaceutical care patients (n = 77) than usual care patients (n = 79) for A1c (-0.8% [-1.6 to 0.1] vs. +0.1 [-0.4 to 0.7]); fasting blood glucose (-2.3 millimoles per litre [mmol/L] [-5.7 to 1.1] vs. +0.9 [-0.8 to 2.8]); systolic BP (-5.8 millimeters of mercury [mm Hg] [-8.2 to -3.2] vs. +1.1 [0.1 to 2.4]); diastolic BP (-7.1 mm Hg [-9.8 to -4.2] vs. +1.8 [-1.1 to 4.8]); total cholesterol (-0.7 mmol/L [-1.7 to 0.3] vs. +0.1 [-3.1 to 3.8]); LDL-C (-0.6 mmol/L [-1.7 to 0.6] vs. 0.0 [-0.4 to 0.4]); and serum triglycerides (-0.5 mmol/L [-2.8 to 2.1] vs. +0.2 [-0.7 to 1.1]). This study also indicated statistically significant differences in favor of the intervention group compared with the control group in the proportion of patients who achieved therapeutic goals for A1c (23.4% vs. 15.2%, $P = 0.031$); BP (80.5% vs. 46.8%, $P = 0.012$); and LDL-C (45.5% vs. 30.4%, $P = 0.018$) over the 6-month study period.
- Compared with the usual care group, intervention patients who received the clinical pharmacy service showed significant improvement in self-reported medication adherence and lifestyle changes that represent the cornerstone in the management of type 2 diabetes.
- The current study is the first RCT to evaluate the effects of clinical pharmacy service on biomarker values and health behavior in patients with type 2 diabetes in Jordan. Improved biomarkers and patient-reported outcomes in the current study provide evidence about the importance of clinical pharmacist involvement in the care for patients with diabetes in Jordan.

Type 2 diabetes results from a progressive insulin secretory defect with reduced sensitivity to the effects of existing insulin.[1] The disease is characterized by fasting and post-prandial hyperglycemia and relative insulin insufficiency. If left untreated, poor control of blood glucose may cause long-term microvascular and macrovascular complications, such as nephropathy, neuropathy, retinopathy, and cardiovascular disease (CVD).[2] Type 2 diabetes is an epidemic disease, and its prevalence is growing at an alarming rate in both developed and developing countries.[3] The prevalence of type 2 diabetes worldwide has increased 5-fold during the last 15 years.[4] It has been estimated that 200 million people had type 2 diabetes in 2010, and the number is expected to reach 300 million by the year 2025.[4]

The prevalence of diabetes in Jordan is among the highest in the world, making it a particularly alarming health problem there.[5] Among Jordanian adults, diabetes prevalence increased from 6.3% in 2002 to 7.4% in 2004.[6] A cross-sectional study of a random sample of 1,121 Jordanians aged 25 years or older in 2008 revealed an "age-standardized prevalence" of 17.1%, a 31.5% increase in the prevalence of diabetes compared with a similar survey conducted in 1994.[7] Furthermore, World Health Organization (WHO) data indicates that the proportion of deaths attributable to diabetes in Jordan increased from 1% in 2002[8] to 7% in 2010.[9] Beside diabetes prevalence, the lack of knowledge of diabetes and of its management in the general population is rapidly becoming one of the most challenging health problems worldwide, particularly in developing countries such as Jordan.[7]

Management of type 2 diabetes is complex and requires continuing medical care and ongoing patient self-management education and support to prevent acute complications and to reduce the risk of long-term complications.[1,10] Several observational studies have shown that intensive glycemic control leads to improved cardiovascular and microvascular outcomes.[11-13] Results from randomized controlled trials (RCTs) have demonstrated that tight glycemic control—hemoglobin A1c less than 7%—correlates with a reduction in the risk of microvascular complications in patients with type 2 diabetes.[14,15] The evidence that tight glycemic control leads to significant reduction in CVD outcomes is controversial. However, long-term follow-up of the United Kingdom Prospective Diabetes Study (UKPDS) suggests that treatment to an A1c target of less than 7% soon after the diagnosis of diabetes is associated with long-term reduction in risk of macrovascular diseases.[11] These findings led the American Diabetes Association (ADA) to recommend an A1c level of less than 7% as a goal of optimal blood glucose control for patients with diabetes.[16] However, these glycemic goals are often not achieved despite the availability of many effective treatments and the documented benefits of blood glucose control.[17,18]

Clinical pharmacists can play a vital role in improving diabetes management by providing pharmaceutical care programs and prudent pharmacological therapy,[19] with an emphasis on the importance of adherence to treatment recommendations,[20] taking into account the importance of patients' participation in designing, implementing, and monitoring therapeutic plans to produce optimal therapeutic outomes.[20,21]

Several RCTs have reported that clinical pharmacist-led management programs improved glycemic control and various other clinical outcomes in patients with diabetes.[22-29] For example, Scott et al. (2006) reported that patients with type 2 diabetes who received pharmacist-managed diabetes care (n = 76) demonstrated improved glycosylated A1c values, systolic blood pressure, and low-density lipoprotein cholesterol (LDL-C) levels and met treatment goals more often than patients receiving standard care (n = 73).[27]

Study Objective

The objective of the present study was to evaluate the impact of a clinical pharmacist-led pharmaceutical care program on different clinical outcomes and self-management behavior in outpatients with type 2 diabetes in Jordan. It was important to study pharmaceutical care in Jordan because of the increasing prevalence and mortality of diabetes and the extremely limited application of effective clinical pharmacy services for patients with diabetes in Jordan.

Methods

Study Design, Setting, and Subjects

The effectiveness of the pharmaceutical care intervention was assessed in an RCT with a 6-month follow-up of patients with type 2 diabetes who visited an outpatient diabetes clinic at the 762-bed Royal Medical Services (RMS) Hospital, one of the largest hospitals in Jordan. The diabetes clinic at the RMS Hospital provides usual care services to more than 100 patients daily with regular follow-up clinic visits every 3 or 6 months, depending on the glycemic control for each patient. Patients were included in the study if they were aged 18 years or older, treated at RMS Hospital and diagnosed with type 2 diabetes at least 1 year previously, took at least 1 prescribed medication for diabetes, and had an A1c level exceeding 7.5%. Patients were excluded from the study if they were diagnosed with convulsive disorder, diabetic proliferative retinopathy, or diabetic neuropathy as reported in their medical files.

Patient Recruitment and Randomization

During an outpatient diabetes clinic visit, those patients who met the inclusion criteria and had their A1c, blood pressure, lipid measures (total cholesterol, LDL-C, HDL-C, and triglycerides), and other laboratory tests measured were informed verbally about the study by the research pharmacist (Alqudah) and were provided with an information sheet. The patients were asked to sign a consent form if they were willing to participate in the study. Study participants were randomly assigned to intervention and control groups via a minimization technique using Minim software (available for free download).[30] The patients were recruited over a period of 4 months from January through April 2011, and the last follow-up was performed on October 27, 2011. The study received approval from the Institutional Review Board, King Hussein Hospital, Royal Medical Services, Jordan.

Description of Pharmacist Intervention Versus Usual Care

Following randomization and the baseline assessment, the clinical pharmacist ensured that intervention patients were receiving evidence-based antidiabetic therapy and adjunct therapy, including treatment for dyslipidemia and hypertension. Clinical pharmacist recommendations, such as simplification of dosage regimens or more intensive management of blood glucose and blood pressure, were discussed with the physician when necessary.

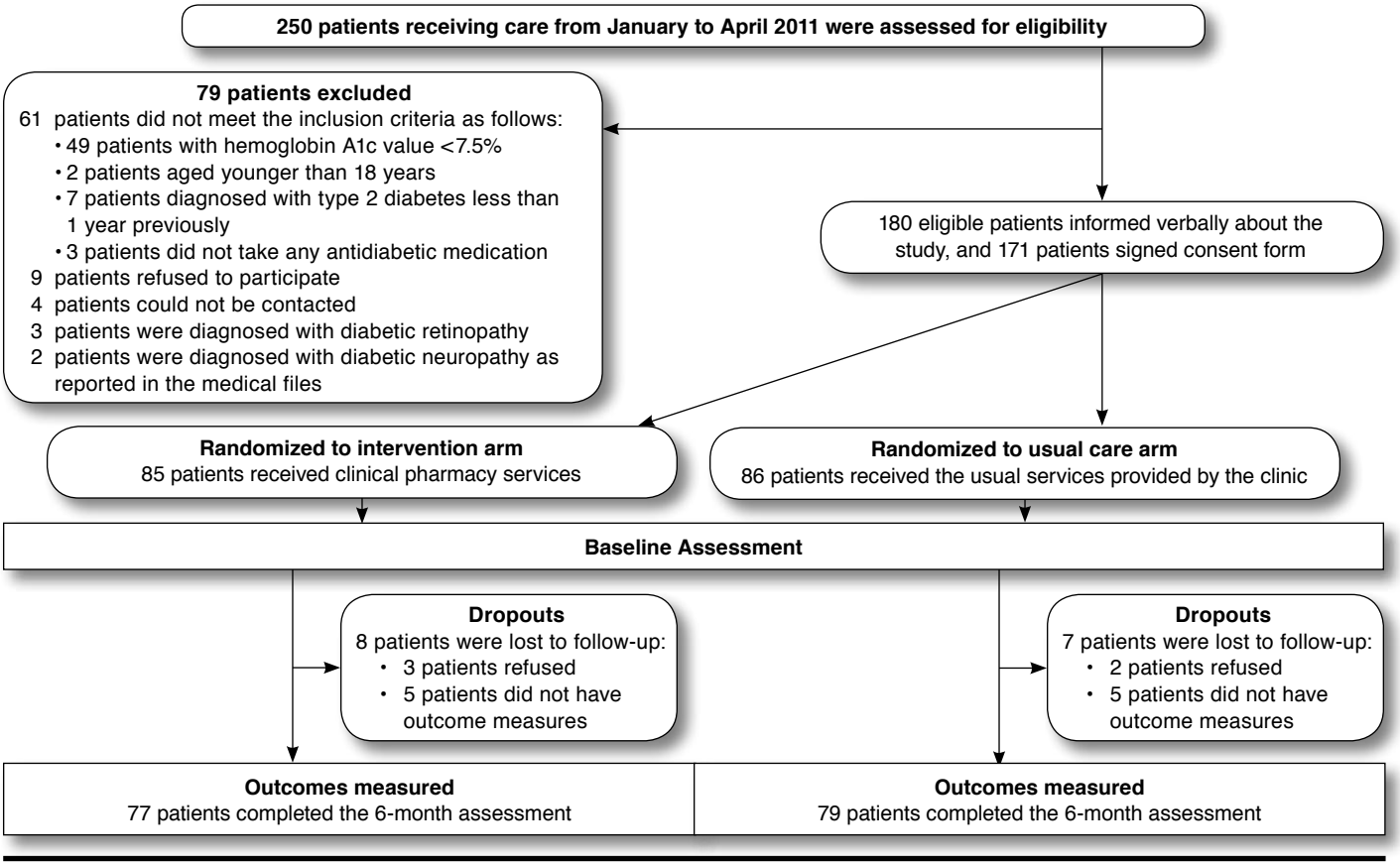
After the patient meeting with the physician, the clinical pharmacist provided, in a separate room at the outpatient clinic, a structured patient education and discussion about type 2 diabetes, risks for and types of complications from diabetes, prescribed drug therapy, proper dosage, possible side effects, and the importance of medication adherence. The clinical pharmacist also emphasized lifestyle management as follows: patients were encouraged to (a) change unhealthy dietary habits that adversely influence blood glucose, blood pressure, and lipid levels; (b) perform regular physical activity that fits with their daily schedule; and (c) monitor and record their blood glucose levels. Using a motivational interviewing technique, advice was provided to patients with a positive smoking history, and patients were referred to a special smoking cessation program run within the hospital when necessary. Diabetes-specific biomarker targets (e.g., A1c < 7%, blood pressure < 130/80 millimeters of mercury [mm Hg], and LDL < 2.6 millimoles per liter [mmol/L],[31] were specified for each intervention patient. A special booklet on diabetes medications and necessary lifestyle changes (e.g., physical activity and meal planning) was prepared to assist in the educational session, and patients were given a copy to take home. Finally, 8 weekly telephone calls were made by the clinical pharmacist to each intervention patient to discuss and review the prescribed therapy, to emphasize the importance of adherence to treatment plan, and to answer patient questions or address patient concerns. The average length of each call was 20 minutes.

Patients in the usual care group did not receive clinical pharmacist intervention or education on disease, medications, or necessary self-care activities and did not receive the 8 weekly telephone follow-up calls from the clinical pharmacist. These patients did not usually receive telephonic or mailed reminders for their upcoming appointments. Patients in the usual care group did, however, receive the usual care provided by the medical and nursing staff, which included patient assessment, a 3- or 6-month review at which blood glucose and blood pressure were measured, advice on self-monitoring of blood glucose (SMBG), and nutrition counseling.

Study Instruments

Self-Reported Medication Adherence (Morisky Scale). This simple, validated 4-question survey assessed the likelihood that patients take their medications as prescribed.[32] The questions were as follows: Do you forget to take your medications? Are you careless about time of taking your medications? Do you stop taking your medications when you feel better? Do you stop taking your medications when you feel worse? To score the questionnaire, each "yes" response is given a score of 1, and each "no" response is given a score of 0 (range 0 to 4). According to the Morisky classification, adherence is divided

FIGURE 1 Study Design Flowchart



into 3 groups: high for those scoring 0, medium for those scoring 1 or 2, and low for those scoring 3 or 4, when scoring one point for each "yes" answer. For the purpose of the present analysis, the patients were divided into 2 groups: those scoring 0 were considered adherent, and those scoring 1-4 were deemed nonadherent.

Summary of Diabetes Self-Care Activities (SDSCA) Questionnaire. The SDSCA is a comprehensive, well-validated, self-report measure of self-care behaviors in patients with diabetes.[33] This instrument is multidimensional, and each of its domains was assessed and scored separately. The instrument asks patients to recall their self-care behaviors during the previous 7 days for 5 domains: diet (4 questions, e.g., How many of the last 7 days have you followed a healthful eating plan?); exercise (2 questions, e.g., On how many of the last 7 days did you participate in at least 30 minutes of physical activity?); SMBG (2 questions, e.g., On how many of the last 7 days did you test your blood sugar the number of times recommended by your health care provider?); foot care (2 questions, e.g., On how many of the last 7 days did you check your feet?); and smoking (1 question, Have you smoked a cigarette, even 1 puff, during the last 7 days?).

The English versions of the Morisky Scale for medication adherence[32] and the SDSCA[33] questionnaire for self-care activities used in the present study were translated into Arabic as follows: a forward translation of the original questionnaire from English into Arabic was performed by 2 qualified independent, native linguistic expert translators. A backward translation from Arabic into English was carried out by 2 different translators. Finally, both translations were compared and found to match the original English copy of the questionnaire. Furthermore, a panel of 4 experts (2 clinical pharmacists and 2 diabetes medicine specialists) examined the research instrument for face and content validity. Pilot work was performed, and questions were adjusted as appropriate before moving to the main study.

Sample Size

The primary outcome measure was a reduction in A1c (intervention vs. control) at the end of the 6-month study period.

A sample size calculation, based on published data on the variability (standard deviation [SD] = 2.2%) of A1c in patients with type 2 diabetes,[34] indicated that to detect an absolute difference of more than 1% in A1c, with $\alpha = 0.05$ and a power of 90%, a sample size of 104 patients in each of the control and intervention groups was required.

Baseline Assessments

After randomization, baseline data for each patient were collected by the researcher pharmacist using a custom-designed questionnaire, medical charts, and hospital computers. The collected data included demographic measures, disease characteristics, prescribed and nonprescribed medications, and medication regimen details. The patients also completed the Morisky Scale[32] and the SDSCA questionnaire.[33]

Follow-Up Assessments

Except for demographic data, baseline data collection measures, including all laboratory and questionnaire data, were repeated by the research pharmacist (Alqudah) with the assistance of Jarab during scheduled diabetes clinic visits 6 months after the initial visit for each patient (e.g., a patient recruited in April 2011 was followed up in October 2011). The pharmacist (Alqudah) called each patient in the intervention group 1 week prior to each upcoming appointment to remind and confirm the scheduled visit. The primary outcome measure was A1c. All other data collected, including systolic and diastolic blood pressure, serum lipid values (total cholesterol, LDL-C, HDL-C, and serum triglycerides), body mass index (BMI), medication adherence, and levels of self-care activities, formed secondary outcome measures.

Data Analysis

Data collected at baseline and at the 6-month assessments were coded and entered into SPSS software, version 17 (IBM SPSS, Armonk, NY) for statistical analysis. Data were examined using Pearson chi-square analysis for categorical variables. For continuous variables, normality of data was tested first using the Kolmogorov-Smirnov and the Shapiro-Wilk statistical tests. Significance in those tests indicated that the continuous variable was not normally distributed. The Mann-Whitney *U* test was performed for the non-normally distributed variables, which were represented as median values. The *t* test for independent samples was performed for the normally distributed variables, which were represented as mean values. A *P* value of < 0.05 was considered statistically significant.

Results

A total of 171 type 2 diabetes patients (85 intervention; 86 usual care) attending an outpatient diabetes clinic were recruited into the study. During the study period, 8 patients from the intervention group and 7 patients from the usual care group dropped out from the study (Figure 1). Therefore, a total of 156 patients (77 intervention; 79 usual care) completed the 6-month study period.

TABLE 1 Baseline Characteristics of the Study Participants

Characteristics	Intervention (n = 85)	Usual Care n = (86)	*P* Value
Age in years, mean [SD]	63.4 [10.1]	65.3 [9.2]	0.215[a]
Female % (n)	42.4 (36)	44.2 (38)	0.832[b]
Duration of diabetes (years), mean [SD]	9.7 [7.4]	10.1 [7.7]	0.717[a]
Education % (n)			0.627[b]
University	24.7 (21)	26.7 (23)	
Secondary/high school	75.3 (64)	73.3 (63)	
Marital status % (n)			0.481[b]
Married	78.8 (67)	74.4 (64)	
Single, divorced, or separated	21.2 (18)	25.6 (22)	
Monthly income % (n)			0.092[b]
Less than 500 JD	69.4 (59)	60.5 (52)	
500-1,000 JD	21.2 (18)	22.1 (19)	
More than 1,000 JD	9.4 (8)	17.4 (15)	

[a]P value from t test for independent samples.
[b]P value from Pearson chi-square test.
JD = Jordanian dinar (approximately $1.41 U.S.); SD = standard deviation.

Patients' Characteristics at Baseline

The age, gender, duration of diabetes, marital status, educational level, and monthly income attained by the 2 groups are represented in Table 1. Statistical analyses indicated no significant differences between the 2 groups on these measures.

Biomedical Outcomes

A1c (Primary Outcome Measure). At the baseline assessment, the A1c values were similar for the intervention and usual care groups. Intervention patients who received clinical pharmacy services showed a mean reduction in A1c of 0.8% over 6 months, while the usual care group had a mean increase of 0.1% in A1c compared with baseline ($P = 0.019$; Table 2). The proportion of patients who achieved the ADA recommendation of A1c less than 7%[1] was significantly higher in the intervention group (23.4%) compared with the usual care group (15.2%) at the 6-month assessment ($P = 0.031$). Compared with baseline values, the intervention patients showed a mean reduction of 2.3 mmol/L, while usual care patients had a mean increase of 0.9 mmol/L in fasting blood glucose (FBG) at the 6-month assessment ($P = 0.014$; Table 2).

Systolic and Diastolic Blood Pressure. Statistically significant differences in mean reduction of both systolic ($P = 0.035$) and diastolic ($P = 0.026$) blood pressure were found between the 2 groups at the end of the study (Table 2). The proportion of patients who achieved target systolic and diastolic blood

TABLE 2 Key Biomarker Values at Baseline and 6 Months for Intervention Versus Usual Care

Outcome	Intervention (n=77)		Usual Care (n=79)		*P* Value (Baseline)[c]	*P* Value (Change)[d]
	Baseline[a]	Change at 6 Months[b]	Baseline[a]	Change at 6 Months[b]		
% A1c	8.5 (6.9 to 10.3)	–0.8 (–1.6 to 0.1)	8.4 (6.6 to 10.2)	+0.1 (–0.4 to 0.7)	0.838	0.019
FBG (mmol/L)	12.5 (9.6 to 14.7)	–2.3 (–5.7 to 1.1)	11.7 (6.5 to 16.1)	+0.9 (–0.8 to 2.8)	0.324	0.014
Systolic BP (mm Hg)	132 (123 to 144)	–5.8 (–8.2 to –3.2)	134 (125 to 144)	+1.1 (0.1 to 2.4)	0.611	0.035
Diastolic BP (mm Hg)	85 (74 to 96)	–7.1 (–9.8 to –4.2)	85 (81 to 89)	+1.8 (–1.1 to 4.8)	0.962	0.026
Serum cholesterol (mmol/L)	4.7 (3.4 to 5.4)	–0.7 (–1.7 to 0.3)	4.7 (3.9 to 5.7)	+0.1 (–3.1 to 3.8)	0.748	0.040
LDL-C (mmol/L)	2.1 (0.9 to 3.0)	–0.6 (–1.7 to 0.6)	2.2 (1.0 to 3.2)	0.0 (–0.4 to 0.4)	0.567	0.031
HDL-C (mmol/L)	1.3 (0.5 to 2.0)	–0.15 (–2.0 to 1.8)	1.3 (0.9 to 1.6)	0.0 (–0.7 to 0.9)	0.893	0.728
Serum triglycerides (mmol/L)	1.9 (0.4 to 3.1)	–0.5 (–2.8 to 2.1)	2.0 (0.8 to 3.3)	+0.2 (–0.7 to 1.1)	0.651	0.017
Body mass index (kg per m^2)	32.4 (21.2 to 39.6)	–0.5 (–1.9 to 2.0)	32.8 (27.7 to 38.4)	+0.4 (–0.7 to 1.9)	0.794	0.189

[a]*Baseline values are presented as median (IQR).*

[b]*Changes over 6 months are shown as the mean difference (95% confidence interval).*

[c]*P values from Mann-Whitney U test for the between-group comparisons of baseline values.*

[d]*P values from t test for independent samples for the between-group comparisons of baseline to follow-up change amounts.*

A1c = glycosylated hemoglobin; BP = blood pressure; FBG = fasting blood glucose; HDL-C = high-density lipoprotein cholesterol; IQR = interquartile range; kg per m^2 = kilograms per squared meter; LDL-C = low-density lipoprotein cholesterol; mm Hg = millimeters of mercury; mmol/L = millimoles per liter.

pressure values (< 130/80 mm Hg)[31,35] was significantly higher in the intervention group (80.5%) compared with the usual care group (46.8%) at the 6-month assessment ($P = 0.012$; Table 3).

Lipid Values. Compared with baseline values, the intervention patients showed a mean reduction of 0.7, 0.6, and 0.5 mmol/L in total cholesterol, LDL-C, and triglycerides levels, respectively, while usual care patients had a constant LDL-C and a mean increase of 0.1 mmol/L in total cholesterol and 0.2 mmol/L in triglycerides levels at the 6-month assessment ($P = 0.040$, 0.031, and 0.17 for total cholesterol, LDL-C, and triglycerides changes, respectively). Results indicated no significant improvement in HDL-C levels (intervention vs. usual care) over the 6-month study period ($P = 0.728$). Furthermore, a significantly greater proportion of intervention patients (53.2%) than usual care patients (30.4%) achieved the LDL-C target (< 2.6 mmol/L)[31,36] at the 6-month assessment ($P = 0.018$; Table 3).

Body Mass Index. Although intervention patients illustrated a reduction in BMI while usual care patients showed an increase in BMI values over the 6-month study period, this difference (intervention vs. usual care) did not reach statistical significance ($P = 0.189$; Table 2).

Self-Reported Adherence with the Prescribed Medications. Except for the significant increase in statin prescriptions in the intervention group patients at the 6-month assessment ($P = 0.038$), results indicated no significant differences between the intervention group and the usual care group in the usage of key medications at baseline and 6-month assessments (Table 3). Furthermore, the Mann-Whitney *U* test revealed no significant differences in the total number of prescribed medications between the 2 groups. Pearson chi-square analysis revealed a significantly lower proportion of nonadherent patients in the intervention group (28.6%) compared with the usual care group (64.6%) at the 6-month assessment ($P = 0.003$; Table 3).

Summary of Diabetes Self-Care Activities Questionnaire. Except for the foot care and smoking domains, the intervention group patients reported significantly better self-care activities, including diet ($P = 0.041$), exercise ($P = 0.025$), and SMBG ($P = 0.007$), compared with the usual care group at 6 months follow-up (Table 3). Each score included in the table is the mean value of the answer to the questions included in each domain (e.g., the diet domain score was calculated as the sum of scores on questions about diet, divided by 4 because there were 4 questions for that domain).

Discussion

Besides being the first study to assess the impact of a clinical pharmacy service on patients with type 2 diabetes in Jordan, this study intervention utilized the positive features of published single-interventional approaches and combined them into a structured diabetes care program. Although the benefits of clinical pharmacy services in the present study cannot be assessed in relation to the individual contributions of these intervention elements, they reflect strategies that have been used successfully in other contexts.[22,37]

The role of clinical pharmacists in Jordan has been expanding very slowly during the last 10 years to include more clinically oriented responsibilities. The slow progression of pharmaceutical care in Jordan may be attributed to several barriers to this concept; examples of these barriers include physicians' negative attitudes toward expanding the pharmacist's role in

TABLE 3 Baseline and Follow-Up Assessments of Study Outcomes for Intervention Versus Usual Care

Outcome	Baseline					6 Months Follow-up				
	Intervention n = 85		Usual Care n = 86		*P* Value[a]	Intervention n = 77		Usual Care n = 79		*P* Value[a]
Number of medications[b]	8	(7-9)	8	(7-10)	0.615	7	(6-8)	8	(6-10)	0.375
Number of antidiabetic medications[b]	2	(1-3)	2	(1-3)	0.591	2	(1-4)	2	(1-3)	0.213
Patients on insulin therapy[c]	65.9%	(56)	69.8%	(60)	0.475	79.2%	(61)	78.5%	(62)	0.881
Patients taking antihypertensive therapy[c]	82.4%	(70)	82.6%	(69)	0.814	89.6%	(69)	87.3%	(69)	0.782
Patients taking statin therapy[c]	62.4%	(53)	64.0%	(55)	0.364	81.8%	(63)	67.1%	(53)	0.038
Patients who achieved target A1c < 7%[c]	0.0		0.0		1.0	23.4%		15.2%		0.031
Patients who achieved target BP < 130/80 mm Hg[c]	45.9%	(39)	48.8%	(42)	0.743	80.5%	(62)	46.8%	(37)	0.012
Patients who achieved LDL-C target < 2.6 mmol/L[c]	29.4%	(25)	27.9%	(24)	0.562	54.5%	(42)	30.4%	(24)	0.018
Patients who self-reported medication nonadherence[c]	74.1%	(63)	70.9%	(61)	0.724	28.6%	(22)	64.6%	(51)	0.003
Domains of the SDSCA questionnaire										
Total diet score[b]	4.2	(1.8-6.4)	4.0	(3.1-5.0)	0.682	4.7	(2.5-7.1)	3.8	(2.8-4.8)	0.041
Physical activity score[b]	2.3	(1.1-4.1)	2.5	(0.5-4.7)	0.725	3.7	(3.0-4.5)	2.7	(0.9-3.9)	0.025
SMBG score[b]	4.5	(3.6-5.4)	4.8	(3.6-5.2)	0.647	5.3	(2.2-7.6)	4.0	(0.5-7.9)	0.007
Foot care score[b]	3.0	(2.2-4.0)	3.0	(2.0-4.0)	0.916	3.5	(1.8-5.5)	3.0	(1.0-5.2)	0.172
Current smokers	54.1%	(46)	45.3%	(39)	0.162	53.2%	(41)	46.8%	(37)	0.331

[a]*P values from Pearson chi-square test for categorical variables and Mann-Whitney U test for continuous variables.*
[b]*Values expressed as median (interquartile range).*
[c]*Values expressed as % (n).*
A1c = glycosylated hemoglobin; BP = blood pressure; LDL-C = low-density lipoprotein cholesterol; mm Hg = millimeters of mercury; mmol/L = millimoles per liter; SDSCA = Summary of Diabetes Self-Care Activities; SMBG = self-monitoring of blood glucose.

the patient care process[38] and the lack of effective pharmaceutical care training.[39] With all of the existing barriers, our study demonstrated the importance of the clinical pharmacist's role in improving clinical outcomes in patients with type 2 diabetes in Jordan.

A clinical pharmacist intervention that consisted of optimizing pharmacotherapy, individualized self-management education, adherence support, and regular telephone follow-up resulted in significant improvement in A1c, the primary outcome measure in this study.

A community-based RCT by Clifford et al. (2005) with an intervention strategy similar to that used in the present study (i.e., individualized education on a patient-specific medication profile along with regular telephone follow-up) for patients with type 2 diabetes indicated that A1c was decreased by a mean of 0.5% in the intervention group, whereas there was no change in the control group over a 12-month follow-up period.[22] An RCT by Choe et al. (2005) reported a reduction in mean A1c values from 10.1% to 8.0% in 41 intervention patients with type 2 diabetes who received a clinical pharmacy intervention similar to the one used in the present study (i.e., modification of pharmacotherapy and self-management diabetes education along with telephone follow-up) compared with 39 control group patients who showed a reduction in A1c values from 10.2% to 9.3% (*P* value for between-group difference in change amount = 0.03).[24] Krass et al. (2007) found in a pharmacy-randomized RCT that patients with type 2 diabetes who received education on diabetes management along with adherence support showed significantly greater reduction in mean A1c compared with patients who did not receive the service.[23] In an RCT conducted in patients aged 18 years or older with A1c exceeding 9.0%, Jameson and Baty (2010) found that a pharmacist collaborative practice program led to a significantly higher proportion of patients in the intervention group improving their A1c values by at least 1% relative to the control group (67.3% vs. 41.2%).[29]

An important finding in the present study was that significantly more patients in the intervention group (23.4%) than in the control group (15.2%) achieved the ADA target goal for A1c of less than 7% at the 6-month assessment. Corresponding data from the RCT by Al Mazroui et al. (2009) indicated that 45.4% of patients in the intervention group and 30.3% in the control group achieved the ADA target at a 12-month follow-up assessment ($P < 0.021$).[28]

Taken together with the results of the present study, it is clear that pharmaceutical care can result in significant improvements in glycemic control in multiple settings. Epidemiological analysis (UKPDS) links a 1% A1c reduction to an estimated 14% reduction in the risk of myocardial infarction and an estimated 12% reduction in the risk of stroke.[11] The intervention group in the present study experienced a 0.8% mean reduction in A1c.

The improvements in A1c in the present study may be due to the integrated clinical pharmacist intervention with regard

to optimizing the prescribed pharmacotherapy, providing individualized education on various self-care activities, improving adherence to prescribed medication, and regular telephone follow-up.

The present study indicated significant improvement in FBG values in patients who received pharmaceutical care when compared with usual care patients over the 6-month study period. This finding is consistent with findings from Al Mazroui et al.[28] who reported a significant decrease in FBG in patients who received pharmaceutical care intervention at the end of a 12-month follow-up period. The Fremantle Diabetes Study (FDS) also showed a greater reduction in FBG in intervention patients than in control patients over a 12-month study period.[22]

Consistent with earlier studies, the clinical pharmacy service in the present study yielded significant improvement in both systolic and diastolic blood pressure.[22,28,40] Improvement in blood pressure was also demonstrated by the significantly higher proportion of intervention patients who achieved target systolic and diastolic blood pressure values (< 130/80 mm Hg) compared with the control group at the end of the study. Since patients in both groups were prescribed similar antihypertensive medications, this finding may be due to comprehensive education of patients and the associated improvements in lifestyle behaviors and medication adherence observed in the intervention group. Epidemiological studies suggest that the risk of cardiovascular events increases by 20% with every 10 mm Hg increase in systolic blood pressure.[41] Although the decline in systolic blood pressure in the intervention patients in the present study was less than 10 mm Hg, it may still have a positive impact on cardiovascular risk.[22,42]

The present study found significant between-group differences in measures of lipid control and in the proportion of patients who achieved target LDL-C values (< 2.6 mmol/L). Consistent with findings from the current study, earlier studies found that a pharmacist-based management program for patients with type 2 diabetes was associated with significant improvements in serum triglycerides,[28,43-46] total cholesterol,[25,28] and LDL-C levels.[24,27,28,47] Analysis of UKPDS data by Turner et al. (1998) indicated that the risk of either angina pectoris or myocardial infarction increases by 1.57 for every 1 mmol/L increase in LDL-C level, and patients with LDL-C levels higher than 3.9 mmol/L were 2.3 times as likely to develop coronary artery disease than those with LDL-C levels less than 3 mmol/L.[48]

The significant improvement in LDL-C, triglycerides, and total serum cholesterol levels observed in the present study could be due to the clinical pharmacist input and the significant increase in the number of intervention patients who were prescribed statin therapy when compared with the control group patients at the 6-month assessment. The improved adherence to medication and lifestyle advice may have contributed to improving the lipid profile. The present study did not find significant improvement in HDL-C levels or BMI. However, only 1 study of which we are aware demonstrated a favorable increase in HDL-C, and 1 study showed a significant reduction in BMI levels as a result of pharmacist-provided diabetes management.[22,43]

Although medication adherence was assessed by an instrument that has not been validated for use in our setting, especially in the format that uses fewer items (e.g., the 4-item instead of 8-item version of the Morisky scale), this instrument has been validated and was found to be reliable and widely used in a variety of medication adherence studies.[49-53] Furthermore, Kripilani et al. (2009) used the Morisky Scale as a "gold standard" against which to test a new adherence measurement instrument.[54] Research has indicated that adherence to medication in type 2 diabetes is poor and is considered as one of the main barriers to the benefit of optimal diabetes care and a major cause of unnecessary hospitalization.[55,56] Consistent with findings from earlier research,[28] patients who received the clinical pharmacy service in the present study demonstrated significantly better self-reported medication adherence compared with the control group patients.

The significant improvement in dietary habits in intervention patients at the end of the present study is consistent with findings from earlier research. Doucette et al. (2009) reported in an RCT that pharmacists were effective at increasing the number of days per week that patients spent engaging in healthy diet and diabetes self-care activities.[57] On the other hand, patients who received the clinical pharmacy service in the present study had significantly better self-reported physical activity than did patients in usual care. Evidence of the beneficial effects of exercise on blood glucose control in patients with type 2 diabetes exists in the literature.[58,59] The significant improvement in dietary and physical activity behaviors seen in the intervention patients in this study is likely due to the robust content of the educational material that determined types and proportions of healthy diet and encouraged the patients to perform regular, individualized physical activity. The reported significant improvement in SMBG in the intervention patients was not surprising and could be attributed to the provision by the clinical pharmacist of high-quality information about the blood glucose values indicative of hyperglycemia and hypoglycemia and about how to respond appropriately to these results. Foot care was not significantly improved in the intervention patients at the end of the study. Similar findings were reported by Sadur et al. (1999).[60] Therefore, foot care is an area where considerable scope for further improvements is required. The present study also did not show significant improvement in smoking behavior; this may be a result of the minimal cessation counseling offered by our intervention and the lack of

focus on this area. Therefore, more intensive smoking intervention that utilizes the transtheoretical model of change and assesses patient readiness to stop smoking may lead to better results in smoking cessation behavior.

Limitations

First, this study used a patient-reported measure of medical adherence, and the results may be affected by social desirability and recall bias. Second, although the study outcomes were statistically more favorable in the intervention group compared with usual care, the study was underpowered because the trial enrolled a small number of patients due to limited availability of a single investigator. Third, our study assessed outcomes after only 6 months, and longer follow-up is necessary to determine if the short-term outcomes are sustained from the clinical pharmacist interventions in this hospital-based diabetes clinic. Fourth, this study assessed only intermediate clinical outcomes and did not examine either humanistic-service outcomes or program costs for the clinical pharmacy interventions.

Conclusions

The present study found that, compared with usual care, a clinical pharmacy service for patients with type 2 diabetes may improve biomarker values, including A1c, blood pressure, and lipid profile, in addition to self-reported medication adherence and self-care activities. Future research with a larger sample size, conducted over a period of follow-up longer than 6 months, is needed to confirm the effects of this clinical pharmacy service and to identify the most effective elements of the service model.

Authors

ANAN SADEQ JARAB, PhD, is Assistant Professor; GHASSAN SHATTAT, PhD, is Associate Professor; and TARIQ AL-QIRIM, PhD, is Associate Professor, AIZaytoonah University of Jordan, Amman, Jordan. SALAM GHAZI ALQUDAH, BSc, is Captain Pharmacist, Jordanian Royal Medical Services Hospital, Amman, Jordan. TAREQ LEWIS MUKATTASH, PhD, is Assistant Professor, Jordan University of Science and Technology, Irbid, Jordan.

AUTHOR CORRESPONDENCE: Anan Sadeq Jarab, PhD, AIZaytoonah University of Jordan, Pharmacy, P.O. Box 130, Amman, Jordan 11733. Tel.: 00962776337513; E-mail: anansalam10@yahoo.com.

DISCLOSURES

All authors certify that there was no external funding for this research article and report no financial or other potential conflicts of interest related to the subject of this article.

Concept and design were performed primarily by Jarab with the assistance of Mukattash. The data were collected primarily by Alqudah and Jarab and interpreted primarily by Jarab and Shattat. The manuscript was written primarily by Jarab and Mukattash and revised primarily by Jarab and Al-Qirim.

ACKNOWLEDGMENTS

The authors thank Maher Khdour, PhD; Firas AlHajji, PhD; Fares Haddad, MD, JMB; and Luay AlEssa, MD, PhD, for reviewing the study survey instrument for validity.

REFERENCES

1. American Diabetes Association. Standards of medical care in diabetes—2012. *Diabetes Care*. 2012;35(Suppl 1):S11-S63. Available at: http://care.diabetesjournals.org/content/35/Supplement_1/S11.full.pdf+htm. Accessed August 19, 2012.

2. Kelly C, Rodgers P. Implementation and evaluation of a pharmacist-managed diabetes service. *J Manag Care Pharm*. 2000;6(6):488-93. Available at: http://www.amcp.org/data/jmcp/research_v6_488-493.pdf.

3. Wild S, Roglic G, Green A, et al. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004;27(5):1047-53. Available at: http://www.who.int/diabetes/facts/en/diabcare0504.pdf. Accessed August 19, 2012.

4. Waly MI, Essa MM, Ali A, Al-Shuaibi YM, Al-Farsi YM. The global burden of Type 2 diabetes: a review. *Int J Biol Med Res*. 2010;1(4):326-29. Available at: http://www.biomedscidirect.com/journalfiles/IJBMRF201046/the_global_burden_of_type_2_diabetes_a_review.pdf. Accessed August 19, 2012.

5. Ajlouni K, Jaddou H, Batieha A. Diabetes and impaired glucose tolerance in Jordan: prevalence and associated risk factors. *J Intern Med*. 1998;244(4):317-23. Available at: http://onlinelibrary.wiley.com/doi/10.1046/j.1365-2796.1998.00369.x/pdf. Accessed August 19, 2012.

6. Centers for Disease Control and Prevention (CDC). Assessing risk factors for chronic disease—Jordan, 2004. *MMWR Morb Mortal Wkly Rep*. 2006;55(23):653-55. Available at: http://www.cdc.gov/mmwR/preview/mmwrhtml/mm5523a3.htm. Accessed August 19, 2012.

7. Ajlouni K, Khader YS, Batieha A, Ajlouni H, El-Khateeb M. An increase in prevalence of diabetes mellitus in Jordan over 10 years. *J Diabetes Complications*. 2008;22(5):317-24.

8. World Health Organization. Facing the facts: the impact of chronic disease in Jordan. Available at: http://www.who.int/chp/chronic_disease_report/media/impact/jordan.pdf. Accessed August 19, 2012.

9. World Health Organization. Noncommunicable diseases: country profiles 2011. Available at: http://www.who.int/nmh/publications/ncd_profiles_report.pdf. Accessed August 19, 2012.

10. Norris SL, Lau J, Smith SJ. Self-management educations for adults with type 2 diabetes: a meta-analysis of the effect on glycaemic control. *Diabetes Care*. 2002;25(7):1159-71. Available at: http://care.diabetesjournals.org/content/25/7/1159.full.pdf+html. Accessed August 19, 2012.

11. Stratton IM, Alder 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(7258):405-12. Available at: http://www.bmj.com/content/321/7258/405.pdf%2Bhtml. Accessed August 19, 2012.

12. Khaw KT, Wareham N, Luben R, et al. Glycated haemoglobin, diabetes, and mortality in men in Norfolk cohort of European Prospective Investigation of Cancer and Nutrition (EPIC-Norfolk). *BMJ*. 2001;322:15-18. Available at: http://www.bmj.com/content/322/7277/15.pdf%2Bhtml. Accessed August 19, 2012.

13. Standl E, Balletshofer B, Dahl B, et al. Predictors of 10-year macrovascular and overall mortality in patients with NIDDM: the Munich General Practitioner Project. *Diabetologia*. 1996;39(12):1540-45.

14. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet*. 1998;352(9131):837-53.

15. Patel A, MacMahon S, Chalmers J, et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Engl J Med*. 2008;358(24):2560-72. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa0802987. Accessed August 19, 2012.

16. Genuth S, Eastman R, Kahn R, Klein R, Lachin J; American Diabetes Association. Implications of the United Kingdom Prospective Diabetes Study. *Diabetes Care*. 2003;26(Suppl 1):S28-S32. Available at: http://care.diabetesjournals.org/content/26/suppl_1/s28.full.pdf+html. Accessed August 19, 2012.

17. American Diabetes Association. Standards of medical care in diabetes. *Diabetes Care*. 2004;27(Suppl 1):S15-S35. Available at: http://care.diabetesjournals.org/content/27/suppl_1/s15.full.pdf+html. Accessed August 19, 2012.

18. Saydah SH, Fradkin J, Cowie CC. Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. *JAMA*. 2004;291(3):335-42. Available at: http://jama.jamanetwork.com/article.aspx?articleid=198035. Accessed August 19, 2012.

19. McClean MT, McElnay JC, Andrews J. The importance of patient education and patient involvement in the treatment of diabetes. *Pharm J*. 2000;265:108-10.

20. Rubin RR. Adherence to pharmacologic therapy in patients with type 2 diabetes mellitus. *Am J Med*. 2005;118(Suppl 5A):S27-S34.

21. Armour CL, Taylor SJ, Hourihan F. Implementation and evaluation of Australian pharmacists' diabetes care services. *J Am Pharm Assoc (2003)*. 2004;44(4):455-66.

22. Clifford RM, Davis WA, Batty KT, Davis TM. Effect of a pharmaceutical care program on vascular risk factors in type 2 diabetes: the Fremantle Diabetes Study. *Diabetes Care*. 2005;28(4):771-76. Available at: http://care.diabetesjournals.org/content/28/4/771.full.pdf+html. Accessed August 19, 2012.

23. Krass I, Armour CL, Mitchell B, et al. The Pharmacy Diabetes Care Program: assessment of a community pharmacy diabetes service model in Australia. *Diabet Med*. 2007;24(6):677-83.

24. Choe HM, Mitrovich S, Dubay D, Hayward RA, Krein SL, Vijan S. 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(4):253-60. Available at: http://www.ajmc.com/publications/issue/2005/2005-04-vol11-n4/Apr05-2017p0253-0260/. Accessed August 19, 2012.

25. Fornos JA, Andrés NF, Andrés JC, Guerra MM, Egea B. A pharmacotherapy follow-up program in patients with type-2 diabetes in community pharmacies in Spain. *Pharm World Sci*. 2006;28(2):65-72.

26. Odegard PS, Goo A, Hummel J, Williams KL, Gray SL. Caring for poorly controlled diabetes mellitus: a randomized pharmacist intervention. *Ann Pharmacother.* 2005;39(3):433-40.

27. Scott DM, Boyd ST, Stephan M, Augustine SC, Reardon TP. Outcomes of pharmacist-managed diabetes care services in a community health center. *Am J Health Syst Pharm*. 2006;63(21):2116-22.

28. Al Mazroui NR, Kamal MM, Ghabash NM, Yacout TA, Kole PL, McElnay JC. Influence of pharmaceutical care on health outcomes in patients with Type 2 diabetes mellitus. *Br J Clin Pharmacol*. 2009;67(5):547-57. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2686072/pdf/bcp0067-0547.pdf. Accessed August 19, 2012.

29. Jameson JP, Baty PJ. Pharmacist collaborative management of poorly controlled diabetes mellitus: a randomized controlled trial. *Am J Manag Care*. 2010;16(4):250-55. Available at: http://www.ajmc.com/publications/issue/2010/2010-04-vol16-n04/AJMC_10apr_Jameson_250to255/3. Accessed August 19, 2012.

30. Evans S, Royston P, Day S. Minim: allocation by minimisation in clinical trials. 2004. Available from: http://www-users.york.ac.uk/~mb55/guide/minim.htm. Accessed August 19, 2012.

31. American Diabetes Association. Standards of medical care in diabetes—2010. *Diabetes Care*. 2010;33(Suppl 1):S11-S61. Available at: http://care.diabetesjournals.org/content/33/Supplement_1/S11.full.pdf+html. Accessed August 19, 2012.

32. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care*. 1986;24(1):67-74.

33. Toobert DJ, Hampson SE, Glasgow RE. The summary of diabetes self-care activities measure: results from 7 studies and a revised scale. *Diabetes Care*. 2000;23(7):943-50. Available at: http://care.diabetesjournals.org/content/23/7/943.full.pdf+html. Accessed August 19, 2012.

34. Kinmonth AL, Woodcock A, Griffin S, Spiegal N, Campbell MJ. Randomised controlled trial of patient-centred care of diabetes in general practice: impact on current wellbeing and future disease risk. The Diabetes Care from Diagnosis Research Team. *BMJ*. 1998;317(7167):1202-08. Available at: www.bmj.com/highwire/filestream/382276/field_highwire_article_pdf/0.pdf. Accessed August 19, 2012.

35. Chobanian AV, Bakris GL, Black HR, et al.; the National High Blood Pressure Education Program Coordinating Committee. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42(6):1206-52. Available at: http://hyper.ahajournals.org/content/42/6/1206.full.pdf+html. Accessed August 19, 2012.

36. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. 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;106(25):3143-21. Available at: http://circ.ahajournals.org/content/106/25/3143.full.pdf. Accessed August 19, 2012.

37. Kennie NR, Schuster BG, Einarson TR. Critical analysis of the pharmaceutical care research literature. *Ann Pharmacother.* 1998;32(1):17-26.

38. AbuRuz SM, Al-Ghazawi MA, Bulatova N, Jarab AS, Alawwa IA, Al-Saleh A. Expectations and experiences of physicians regarding pharmaceutical care and the expanding role of pharmacists in Jordan. *JJPS*. 2012;5(1):74-86. Available at: http://journals.ju.edu.jo/JJPS/article/viewFile/2768/2462. Accessed August 19, 2012.

39. Aburuz S, Al-Ghazawi M, Snyder A. Pharmaceutical care in a community-based practice setting in Jordan: where are we now with our attitudes and perceived barriers? *Int J Pharm Pract*. 2012;20(2):71-79.

40. Pei-Xi Zhao, Chao Wang, Li Qin, et al. Effect of clinical pharmacist's pharmaceutical care intervention to control hypertensive outpatients in China. *Afr J Pharm Pharmacol*. 2012;6(1):48-56. Available at: http://www.academicjournals.org/ajpp/PDF/pdf2012/8%20Jan/Zhao%20et%20al.pdf. Accessed August 19, 2012.

41. Gerstein HC, Malmberg K, Capes S, Yusuf S. Cardiovascular diseases. In: Gerstein HC, Haynes RB, eds. *Evidence-Based Diabetes Care*. Hamilton, Ontario: BC Decker; 2001:488-514.

42. Adler AI, Stratton IM, Neil HA. Association of systolic blood pressure with macrovascular and microvascular complications of type 2 diabetes (UKPDS 36): prospective observational study. *BMJ*. 2000;321(7258):412-19. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC27455/pdf/412.pdf. Accessed August 19, 2012.

43. Johnson CL, Nicholas A, Divine H, Perrier DG, Blumenschein K, Steinke DT. Outcomes from DiabetesCARE: a pharmacist-provided diabetes management service. *J Am Pharm Assoc (2003).* 2008;48(6):722-30.

44. Leal S, Glover JJ, Herrier RN, Felix A. Improving quality of care in diabetes through a comprehensive pharmacist-based disease management program. *Diabetes Care.* 2004;27(12):2983-84. Available at: http://care.diabetesjournals.org/content/27/12/2983.full.pdf+html. Accessed August 19, 2012.

45. McCord AD. Clinical impact of a pharmacist-managed diabetes mellitus drug therapy management service. *Pharmacotherapy.* 2006;26(2):248-53.

46. Morello CM, Zadvorny EB, Cording MA, Suemoto RT, Skog J, Harari A. Development and clinical outcomes of pharmacist-managed diabetes care clinics. *Am J Health Syst Pharm.* 2006;63(14):1325-31.

47. Nau DP, Ponte CD. Effects of a community pharmacist-based diabetes patient management program on intermediate clinical outcome measures. *J Manag Care Pharm.* 2002;8(1):48-53. Available at: http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=6505.

48. Turner RC, Millns H, Neil HA. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS: 23). *BMJ.* 1998;316(7134):823-28. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC28484. Accessed August 19, 2012.

49. Krapek K, King K, Warren SS, et al. Medication adherence and associated hemoglobin A1c in type 2 diabetes. *Ann Pharmacother.* 2004;38(9):1357-62.

50. Venturini F, Nichol MB, Sung JC, Bailey KL, Cody M, McCombs JS. Compliance with sulfonylureas in a health maintenance organization: a pharmacy record-based study. *Ann Pharmacother.* 1999;33(3):281-88.

51. George CF, Peveler RC, Heiliger S, Thompson C. Compliance with tricyclic antidepressants: the value of four different methods of assessment. *Br J Clin Pharmacol.* 2000;50(2):166-71. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2014396/pdf/bcp0050-0166.pdf. Accessed August 19, 2012.

52. Patel RP, Taylor SD. Factors affecting medication adherence in hypertensive patients. *Ann Pharmacother.* 2002;36(1):40-45.

53. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res.* 1999;47(6):555-67.

54. Kripalani S, Risser J, Gatti ME, Jacobson TA. Development and evaluation of the Adherence to Refills and Medications Scale (ARMS) among low-literacy patients with chronic disease. *Value Health.* 2009;12(1):118-23.

55. McDonald HP, Garg AX, Haynes RB. Interventions to enhance patient adherence to medication prescriptions: scientific review. *JAMA.* 2002;288(22):2868-79. Available at: http://www.safetynetinstitute.org/content/Upload/AssetMgmt/Site/resources/chroniccare/InterventionsPatientAdherence.pdf. Accessed August 19, 2012.

56. Irons BK, Lenz RJ, Anderson SL, Wharton BL, Habeger B, Anderson HG. A retrospective cohort analysis of the clinical effectiveness of a physician-pharmacist collaborative drug therapy management diabetes clinic. *Pharmacotherapy.* 2002;22(10):1294-1300.

57. Doucette WR, Witry MJ, Farris KB, McDonough RP. Community pharmacist-provided extended diabetes care. *Ann Pharmacother.* 2009;43(5):882-89.

58. Deakin T, McShane CE, Cade JE, Williams RD. Group based training for self-management strategies in people with type 2 diabetes mellitus. *Cochrane Database Syst Rev.* 2005;(2)CD003417.

59. Pedersen BK, Saltin B. Evidence for prescribing exercise as therapy in chronic disease. *Scand J Med Sci Sports.* 2006;16(Suppl 1):S3-S63.

60. Sadur CN, Moline N, Costa M, et al. Diabetes management in a health maintenance organization: efficacy of care management using cluster visits. *Diabetes Care.* 1999;22(12):2011-17. Available at: http://care.diabetesjournals.org/content/22/12/2011.long. Accessed August 19, 2012.