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Impact of Pharmacist Insulin Management on Hemoglobin A_{1c} in Outpatient Hospital Clinic Setting

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Abstract: To assess the efficacy of pharmacist lead insulin management in improvement of HbA_{1c}. Patients were referred to the LMHS (Licking Memorial Health Systems) Outpatient Medication Therapy Insulin Clinic by their physician during the time periods of July 2012 through March 2013 and August 2014 through December 2014. Physician authorization permitted pharmacists to provide clinical monitoring in order to evaluate and adjust insulin, GLP-1 agonist and amylin mimetic doses by adhering to approved dosing guidelines and policy and procedures. Hemoglobin A_{1c} values were obtained from the patients electronic medical records. Patients achieved an average decrease in HbA_{1c} of 0.8 percentage points over a mean of 83 days. Pharmacist insulin management is an innovative pharmacy service through which clinical pharmacists can have an impact on patients' HbA_{1c}.

Key words: Pharmacist, diabetes, insulin management.

1. Introduction

According to the ADA (American diabetes association) 2014 guidelines, diabetes is diagnosed by one of the following: HbA_{1c} (hemoglobin A_{1c}) of 6.5% or greater, fasting plasma glucose of 126 mg/dL or greater, two hour post oral glucose tolerance test plasma glucose of 200 mg/dL or greater, or in a patient with a random glucose of 200mg/dL or greater presenting with symptoms of hyperglycemia or hyperglycemic crisis. The goal HbA_{1c} in diabetic patients is less than 7% per ADA guidelines [1]. Initiation of an oral diabetic medication will provide a decrease in HbA_{1c} of 1–1.25% over the first 3-6 months [2].

Uncontrolled diabetes can lead to long-term complications of the microvascular and macrovascular system. Microvascular complications include diabetic nephropathy, neuropathy and retinopathy. Diabetic nephropathy is the leading cause of chronic kidney disease in patients starting dialysis [3]. Diabetic retinopathy is one of the most common microvascular complications associated with diabetes [4]. Macrovascular complications include coronary artery disease, peripheral artery disease and stroke. It has been shown that reducing HbA_{1c} by 0.8% can reduce the risk of cardiovascular death by 45% [5]. It is evident that glycemic control in diabetics is very important for each patient. Several studies have demonstrated the benefit of glycemic control through pharmacist intervention [6-10]. This study originated as a way to justify pharmacist involvement with diabetes management. Due to the broad nature of the disease state, it was collectively decided to narrow the focus to insulin and other injectable agents and not include adjusting oral diabetic medications. The idea was to collect information to hopefully demonstrate positive results that could be used for future promotion of Clinic services.

The primary outcome was to evaluate glycemic control in patients requiring insulin therapy through close monitoring and routine follow up with pharmacists. This was measured by assessing the average change in HbA_{1c} following pharmacist intervention. The secondary outcomes were to measure the change in: weight over first follow-up period,

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HbA_{1c} over the second follow-up period, HbA_{1c} prior to initial Clinic visit, and HbA_{1c} with physician management compared to pharmacist management.

2. Methods

2.1 Clinic Description

LMHS (licking memorial health systems) is a not-for-profit healthcare organization dedicated to the mission of improving the health of the community. The Health Systems includes a 227-bed inpatient facility in addition to a professional corporation including a group of 100-plus physicians in various practices throughout Licking County. Over 5,000 patients within LMHS have been diagnosed with diabetes, which is nearly 15% of the patients of the LMHS patient population.

An LMHS primary care physician requested that diabetes management be incorporated into the established MTC (medication therapy clinic) where pharmacists provide medication management for anticoagulation therapy and patients with anemia and heart failure. Diabetes management was initially designed to help reduce hospital re-admissions, improve communication during transitions of care and provide more frequent monitoring of glucose readings by pharmacists. An endocrinologist accepted the role of medical director and created clearly defined guidelines and algorithms for dosing insulin, GLP-1 (glucagon-like peptide-1) agonist, and amylin mimetics utilizing ADA guidelines [1]. These guidelines (Fig. 1) and all Clinic policies and procedures were approved by the P&T (pharmacy and therapeutics) and medical executive committees [1]. Clinic pharmacists underwent specialized training and obtained diabetes management certification. Signed physician referral forms received via EMR (electronic medical record) or fax included orders for pharmacist management based on these established guidelines. The referral forms included authorization to evaluate the need for CGM (continuous glucose monitors), basic laboratory standing orders, and referrals for DSMT (diabetes self-management training) or MNT (medical nutrition therapy). Referrals to the Clinic were limited to patients on insulin therapy, GLP-1 agonist or amylin mimetics. The goal was to achieve HbA_{1c} reductions through closer monitoring allowing more frequent opportunities for dose adjustments following approved guidelines and algorithms. In order to evaluate the effectiveness of this model, HbA_{1c} results were tracked during the course of treatment.

2.2 Intervention

Clinic visits were given designated time frames of 60 minutes for initial Clinic visits and 30 minutes for follow-up visits. The Clinic was staffed with a nurse and pharmacist. At each Clinic visit, physical assessments were performed which included weight and vital signs (blood pressure and pulse). Patients were interviewed at every visit and asked about their diet, physical activity, signs and symptoms of low blood sugar, if experienced, and how the patient treated their low blood sugar levels. Patients were educated on use of insulin, how and where to inject insulin and possible side effects. Patients were instructed to bring SMBG (self-monitoring blood glucose) logs or their blood glucose meter to each Clinic appointment for review. Pharmacists assessed glucose logs or readings from the patient's meter and made appropriate insulin dosing changes based on the approved guidelines. Pharmacists were approved to make dose adjustments to patients' injectable diabetes medications per signed Clinic referral forms. All orders and insulin dosage adjustments were written according to the Insulin Management Policy and Procedure Dosing Guidelines, documented in the EMR (electronic medical record) and then reviewed and signed by the supervising physician. A pharmacist and each patient worked together in setting individualized goals for follow-up appointments. Follow-up appointments were scheduled approximately every 4-6 weeks depending on the patient's response to and adherence with treatment. In between Clinic visits, patients were asked to submit

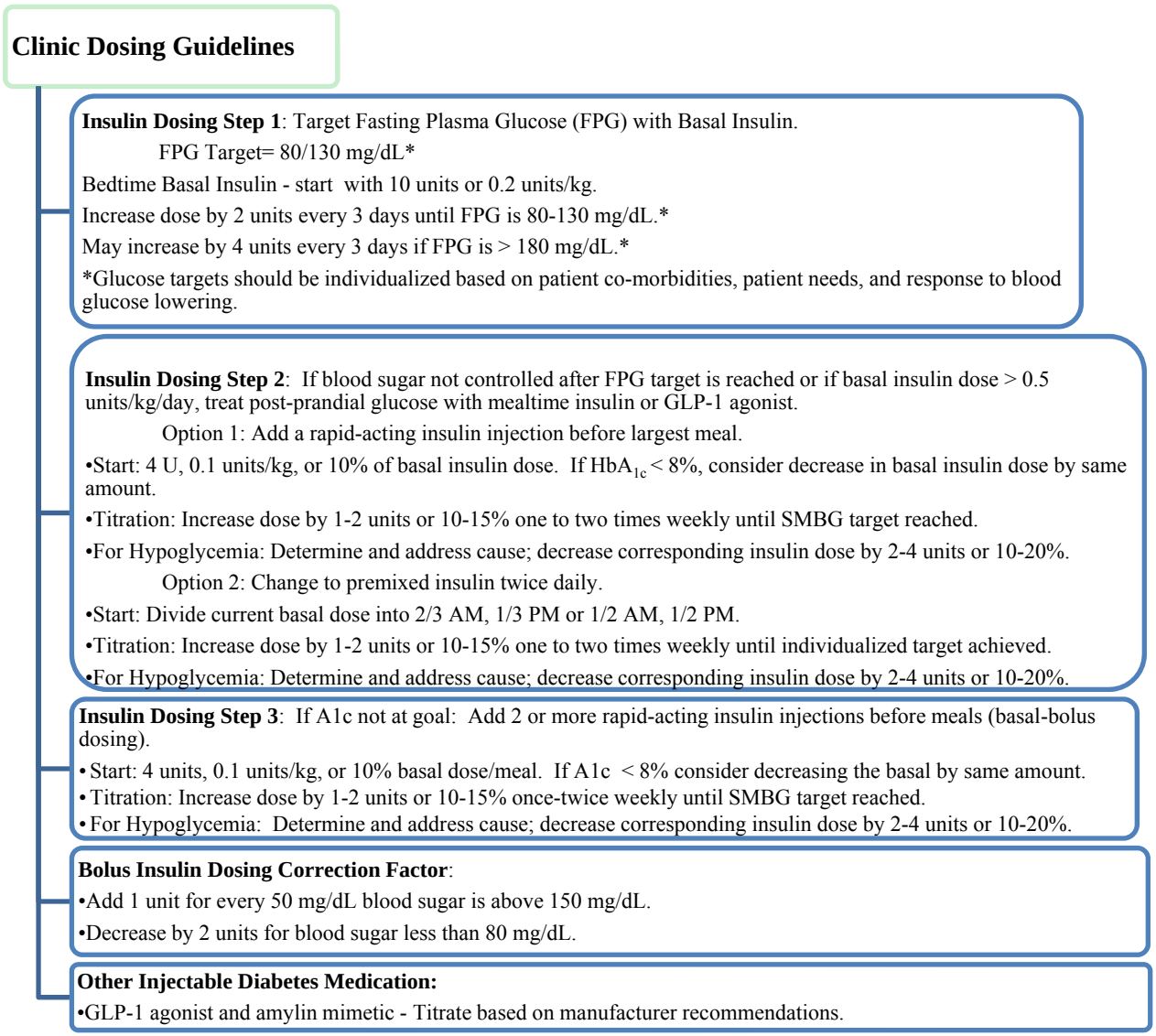

Fig. 1 Clinic Dosing Guidelines: Approved by P&T and medical executive committees [1].

glucose logs every 2-4 weeks for evaluation by the pharmacists. Patients were contacted by telephone to discuss glucose logs and given dosing instructions over the phone. Phone visits also were documented in the EMR and routed to the supervising clinician for signature. Hypoglycemia is a significant risk factor when adjusting insulin therapy. Institutional ED (emergency department) visits and inpatient admissions were monitored and tracked for hypoglycemic events through the EMR.

2.3 Patient Selection

This retrospective chart review was completed for a total of 49 patients who were referred for an initial Clinic visit at the LMHS MTC by their endocrinologist (n = 36) or primary care physician (n = 13) during the designated time periods of the study: July 2012 to March 2013 and August 2014 to December 2014. Several factors attributed to retrospectively reviewing two discontinuous time periods. The initial period served as a pilot period allowing staff training and

education while working closely with an endocrinologist in the office. The gap in-between study periods was used to set up services within the Clinic setting. This time period also included Clinic relocation and staffing changes which were not conducive to initiating additional Clinic services. During the first time period of the study, pharmacists managed patients in the endocrinology office to pilot the program. Once the Clinic relocation was complete and the billing process was set up, the pharmacists began managing patients within the Clinic during the second time period. Follow-up data collection after conclusion of the study was extended through April 2015. Approval for chart review was obtained from the P&T (Pharmacy and Therapeutics) committee. This study was not submitted for Institutional Review Board approval. A pharmacy student provided comprehensive chart review and collection of all data for the study. Patients were excluded from the study if they did not attend the initial Clinic visit or a second follow-up visit. Patients were included in the study if their baseline HbA_{1c} was within 12 weeks before or 4 weeks after their initial Clinic visit and the first follow-up HbA_{1c} was drawn within 4-20 weeks following their initial Clinic visit. HbA_{1c} tests were ordered by the referring physician and results reviewed from the EMR.

For the second follow-up change in HbA_{1c} patients were excluded if they did not have a HbA_{1c} that fell within 12-20 weeks after previous HbA_{1c} from first follow-up visit. Patients were excluded from the assessment of change HbA_{1c} prior to initial Clinic visit if their HbA_{1c} was not drawn within 20 weeks prior to the initial Clinic visit. Those who had a HbA_{1c} within 20 weeks prior to the initial Clinic visit were then compared to their first follow-up change in HbA_{1c}.

2.4 Statistical Analysis

Statistical analyses were conducted using the paired t-test for the primary outcome and the secondary outcomes of mean change in weight at the first follow-up and HbA_{1c} at second follow-up. A non-paired t-test was used to evaluate the secondary outcome that assessed the change in HbA_{1c} of insulin management by the Clinic pharmacists compared to physician managed prior to Clinic. Statistical significance was concluded with a p-value less than 0.05.

3. Results

A total of 49 patients were referred to the Insulin Clinic during the designated time period of the study. Of the 49 patients referred, 35 met the inclusion criteria for the primary outcome as shown in Fig. 2. The baseline demographics of the 35 patients are provided in Table 1 and their diabetic treatment regimens are shown in Table 2.

The primary outcome was the change in HbA_{1c} from baseline at initial Clinic visit to the first follow-up visit. The baseline HbA_{1c} average for the 35 Clinic patients was 9.5%. The average time period between initial Clinic visit and first follow-up HbA_{1c} was 83 (28 to 140) days. During the first follow-up period, the change in HbA_{1c} ranged from a 5.7% decrease to a 1.8% increase. The average HbA_{1c} at first follow-up was 8.7%, resulting in an average reduction of 0.8% ($p = 0.015$). Of the 35 patients, 24 of them had a decrease in HbA_{1c}.

The 35 Clinic patients included in the primary outcome of the study had an average increase in weight of two pounds ($p = 0.279$) over the 83 day average during the first follow-up period.

After assessment of first follow-up, a second follow-up HbA_{1c} was evaluated. Only 17 of the 35 patients had a HbA_{1c} that was 12-20 weeks after the previous HbA_{1c} from the first follow-up. Amongst the 17 patients included in the second follow-up, nine patients had a decrease in HbA_{1c}. Overall, the average change in HbA_{1c} was 0% ($p = 0.967$). The results ranged from a 2.5% decrease to a 2.2% increase for the second follow-up in HbA_{1c}.

To assess the change in HbA_{1c} prior to initial Clinic visit a HbA_{1c} within 20 weeks prior to initial Clinic visit was used. Of the 35 patients included in the study,

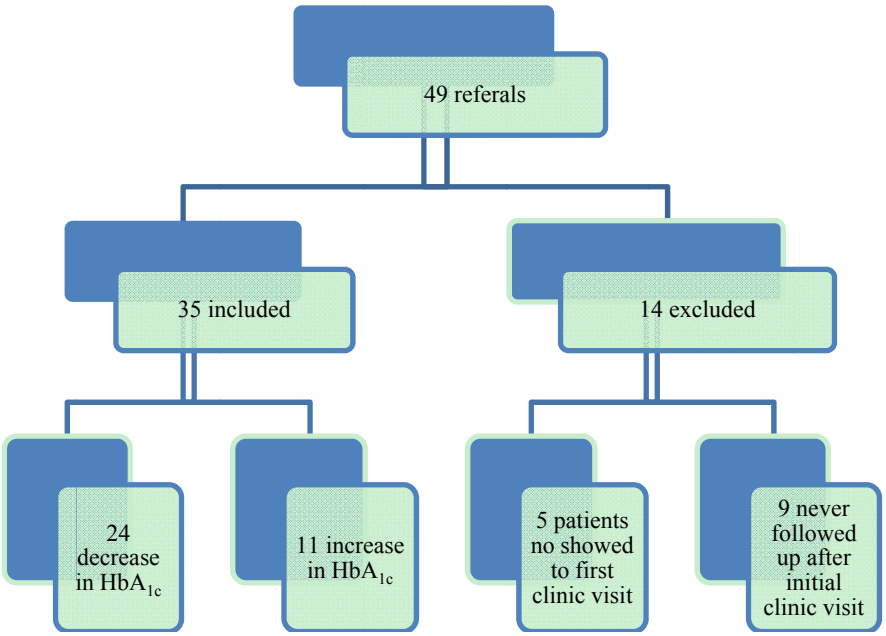

Fig. 2 Inclusion and exclusion criteria.

Table 1 Baseline Demographics (n = 35).

Males (n)	14 (40%)
Females (n)	21 (60%)
Average Age (years)	57 (35-84)
Average Baseline HbA_{1c} (%)	9.5 (6.6-14.2)
Baseline $HbA_{1c} \leq 7.5\%$ (n)	7 (20%)
Average BMI (kg/m^2)	40.1 (20-61)
Type 1 Diabetic (n)	3 (9%)
Type 2 Diabetic (n)	32 (91%)
Referred by Endocrinologist (n)	26 (74%)
Referred by PCP (n)	9 (26%)

Table 2 Diabetic treatment regimens.

Basal Insulin (n)	4 (11%)
Basal-Bolus (n)	28 (80%)
Mix (n)	2 (6%)
U-500 Insulin (n)	1 (3%)
GLP-1 Agonist (n)	4 (11%)
Symlin (n)	2 (6%)
Oral Antidiabetics (n)	20 (57%)

30 of them had a HbA_{1c} that was within 20 weeks prior to initial Clinic visit. Over an average of 99 (34-133) days prior to initial Clinic visit, the 30 patients had an average increase of 0.1% ($p = 0.798$), which ranged from 2.7% decrease to 2.7% increase, under diabetes management with their PCP or endocrinologist.

Lastly, the change in HbA_{1c} prior to the initial Clinic visit was compared to the first follow-up change in HbA_{1c} in order to evaluate diabetes management by the pharmacists versus the management by the PCP or endocrinologist prior to coming to the Clinic. This comparison included the 30 patients who had a HbA_{1c} within 20 weeks prior to their initial Clinic visit. The average change in HbA_{1c} of diabetes management by the PCP or endocrinologist was 0.1% increase. These 30 patients had a change in HbA_{1c} of 0.7% decrease at the first follow-up through pharmacist management.

Patient ED and inpatient admissions were monitored and evaluated for hypoglycemic events. During the designated time frame pharmacists made 134 dose adjustments and only 1 patient had an identified ED admission for hypoglycemia. This patient was treated and released without being admitted and no additional inpatient admissions were identified during post analysis chart review.

4. Discussion

The results of the 35 patients included in the study for management of injectable diabetes medications were evaluated to determine the impact of pharmacists on diabetic care. This study demonstrated that closely

Table 3 Statistical results of study outcomes.

OUTCOMES	RESULTS	P-VALUE (95% CI)
Change in HbA_{1c} at first follow-up (n = 35)	-0.8%	0.015 (0.160-1.388)
Change in weight in first follow-up period (n = 35)	2 pounds	0.279 (-5.53-1.65)
Change in HbA_{1c} at second follow-up (n = 17)	0%	0.967 (-0.587-0.563)
Change in HbA_{1c} prior to initial Clinic visit (n = 30)	0.1%	0.798 (-0.506-0.932)
Endocrinologist/PCP versus Pharmacist Clinic (n = 30)	0.1% vs-0.7%	0.068 (-0.056-1.509)

monitored patient care provided by a pharmacist directly resulted in a statistically significant 0.8 percentage point reduction in HbA_{1c} over an average 83 day period. All patients in the study had diabetes care provided by their PCP or endocrinologist prior to their referral to the Clinic. Achieving significant HbA_{1c} reductions in this group of previously managed patients only strengthens the primary outcome of this study. The introduction of new medication therapy often has the greatest impact on improving disease state management. This holds true with diabetes, as the initiation of an oral agent provides an important HbA_{1c} reduction within the first 3-6 months of beginning treatment. This study produced nearly the same reduction in HbA_{1c} in a shorter time period only by improving current therapy as opposed to adding new therapy. Upon presentation to initial Clinic visit, 20% of patients had a baseline HbA_{1c} less than or equal to 7.5% which showed that maintaining glycemic control was just as important as decreasing HbA_{1c}. At first follow-up, 69% of the 35 patients had a reduction in HbA_{1c}.

Secondary outcomes also were evaluated and the results were not statistically significant. A small increase in weight was identified in the first follow-up period. Weight gain is a common adverse effect of insulin therapy which was an anticipated outcome. Results from a second follow-up were obtained to determine if a further reduction in HbA_{1c} were achieved and no change in HbA_{1c} was noted after an additional 12-20 week time period. The lack of difference between results demonstrates stability with extended pharmacist management beyond the first follow-up period. Unfortunately, less than half of the patients had results reported within the designated time period. Also, HbA_{1c} readings within 20 weeks prior to the initial baseline HbA_{1c} were evaluated. It was confirmed that patients were stable and mostly unchanged prior to initial Clinic referral as a slight increase was noted during this time of physician management. The HbA_{1c} changes between physician and pharmacist time periods were compared and the pharmacist's reduction further demonstrated the clinical importance of the results obtained in this study.

Numerous studies have shown the benefit of having pharmacists as a part of the healthcare team in relation to treating patients with diabetes. In these studies, pharmacists were able to help manage diabetes regardless of the patient's medication profile. Pharmacists were able to serve a more active role in the management of diabetic medications through initiating and adjusting both oral and injectable medications in these studies.[6-10] This study demonstrates the impact that pharmacists can have through management of only injectable diabetic medications. HbA_{1c} reductions were obtained through close monitoring and follow-up of glucose readings, conservative dosing guidelines and protocols, and direct pharmacist to patient interactions.

Limitations were identified in this study. First off, patients were encouraged to document glucose readings, insulin dosing, as well as basic dietary information and report these details to the Clinic. This was done in a variety of ways and often was inconsistent in limiting the ability to make appropriate therapy modifications. With future studies, a more consistent approach utilizing electronic technology to download current glucometer results would be beneficial. Also, having complete autonomy with

HbA_{1c} orders would narrow the timeframe between tests, allowing for more comparable results. Using a point-of-care device in conjunction with appointments would efficiently allow for quicker results and could contribute to improved visit compliance. Weights were recorded using different scales as some results were obtained by a combination of chart review and Clinic visits. This made it difficult to have a true measurement of weight change. Reviewing hypoglycemic events was limited to one health system. However, LMHS includes the only hospital and ED in the remote area as well as two urgent care facilities. It is reasonable that patients could have elected to have care provided outside of LMHS as two patients lived outside of the county.

5. Conclusion

Diabetes is a prevalent disease state that can lead to many devastating complications in patients with uncontrolled diabetes. Glycemic control can decrease the rates of cardiovascular disease and macrovascular and microvascular complications. Therefore, the importance of managing and controlling diabetes cannot be understated. Pharmacists play a vital role in improving the management of insulin and should be utilized routinely in patient-centered diabetes care.

References

[1] American Diabetes Association. 2014. "Executive Summary: Standards of Medical Care in Dabetes 2014." *Diabetes Care* 37 Suppl 1: S5-13.

[2] Sherifali, D., Nerenberg, K., Pullenayegum, E., et al. 2010. "The Effect of Oral Antidiabetic Agents on A1c Levels: A Systematic Review and Meta-analysis." *Diabetes Care* 33 (8): 1859-64.

[3] Gross, J. L., de Azevedo, M. J., Silveiro, S. P., et al 2005. "Diabetic Nephropathy: Diagnosis, Prevention, and Treatment." *Diabetes Care* 28 (1): 164-76.

[4] Fowler, M. 2008. "Microvascular and Macrovascular Complications of Diabetes." *Clinical Diabetes* 26 (2): 77-82.

[5] Diabetes in Control [Internet]. 2012. "ADA: Reducing A1c a Little Less than 1 Point Reduces CV Risk by 45Percent." *Cardiovascular Health* 631. Accessed January 14, 2016. http://www.diabetesincontrol.com/ada-reducing-a1c-a-little-less-than-1-point-reduces-cv-risk-by-45-percent.

[6] Jacobs, M., Sherry, P. S., Taylor, L. M., et al. 2012. "Pharmacist Assisted Medication Program Enhancing the Regulation of Diabetes (PAMPERED) Study." *J. Am. Pharm. Assoc.* 52 (5): 613-21.

[7] Wallgren, S., Berry-Cabán, C. S., and Bowers, L. 2012. "Impact of Clinical Pharmacist Intervention on Diabetes-Related Outcomes in a Military Treatment Facility." *Ann Pharmacother* 46 (3): 353-7.

[8] Cranor, C. W., Bunting, B. A., and Christensen, D. B. 2013. "The Asheville Project: Long-Term Clinical and Economic Outcomes of a Community Pharmacy Diabetes Care Program." *J. Am. Pharm. Assoc*. 43 (2): 173-84.

[9] Hassali, M. A., Nazir, S. U., Saleem, F., et al. 2015. "Literature Review: Pharmacists' Interventions to Improve Control and Management in Type 2 Diabetes Mellitus." *Altern. Ther. Health Med*. 21 (1): 28-35.

[10] Collier, I. A., and Baker, D. M. 2014. "Implementation of a Pharmacist-Supervised Outpatient Diabetes Treatment Clinic." *Am. J. Health Syst. Pharm*. 71 (1): 27-36.