Original Work

Implementation of a System-wide, Telephonic, Pharmacist-led Population Health Program: Metformin Dose Optimization

by Meaghan A. McMurray, PharmD, BCPS, Bradley J. Schermetzler, PharmD, BCACP, Marisa K. Goninen, PharmD, BCACP

Abstract

Objective: To implement a metformin dose optimization program for risk contract patients with poorly controlled Type 2 diabetes taking suboptimal doses of metformin, which used an evidence-based protocol, embraced coordinated care, and provided an additional approach to enhance clinical outcomes and service quality.

Methods: Patients in a risk contract with Type 2 diabetes (HbA1c 7-10%) who were prescribed metformin (≤ 1500 mg/day) were included. Patients were excluded if they were prescribed additional diabetes medication(s) or had safety concerns, such as renal impairment. These criteria were used to build a report that proactively identified patients experiencing clinical inertia. With an evidence-based collaborative practice agreement and protocol in place, centralized pharmacists led targeted interventions for patients across Wisconsin. They performed telephonic outreach to enroll patients, with follow-up every 2-4 weeks during the 12-week program. In addition to titrating the metformin dose, pharmacists also provided patient monitoring, education, and adherence support. Provider engagement was determined based on the percentage of providers that co-signed the referral order request that was sent through the EHR by the pharmacist. Patient engagement was determined based on the percentage of patients that agreed to participate in the program during the initial pharmacist contact.

Results: Patients who completed the Metformin Dose Optimization Program had an average HbA1c improvement of -0.6% (from 7.7% to 7.1%), with sustained control after program completion. Provider engagement was measured 93% and patient engagement was 63%.

Conclusions: Telephonic health initiatives in a centralized location can have a broad reach, all while enhancing coordinated, team-based care. Pharmacist disease management programs that utilize a collaborative practice agreement can efficiently improve a wide variety of quality measures as healthcare reimbursement transitions to value-based payment models.

Healthcare spending in the United States is known to be significantly higher than other developed countries, without advancements in measures such as life expectancy or infant mortality rate.[1] "In 2016, the United States spent 17.8% of its GDP on healthcare (range of the other countries, 9.6%-12.4%; mean of all 11 countries, 11.5%) and had almost double the health spending per capita (mean, $9,403) compared with the other countries (range, $3,377-$6,808; mean of all 11 countries, $5,419)."[1] Life expectancy was the lowest in the United States, at 78.8 years, and infant mortality was the highest, at 5.8 deaths per 1,000 live births.[1] It has become clear that our population is not achieving maximum value in healthcare compared to other high-income nations.

The "Triple Aim" was developed to address the discrepancy between costs and outcomes. The three components of the Triple Aim include: patient care experience, health of a population, and per capita cost.[2] A crucial concept of the Triple Aim is the interdependency of these three components; succeeding in cost savings but sacrificing patient care experience or health of a population does not amount to overall success.[2] Striking a balance between the interdependent components can enable healthcare systems to attain value.

Burnout of healthcare providers and their team members has led to the proposed "Quadruple Aim."[3] "Burnout is associated with lower patient satisfaction, reduced health outcomes, and it may increase costs. Burnout thus imperils the Triple Aim."[3] In order to make strides in patient care experience, health of a population, and per capita cost, it is essential to consider how burnout can be lessened for the patient's care team. As healthcare reimbursement models transition from fee-for-service to value-based payments, pharmacists have an opportunity to engage in disease management activities that improve the health of the population and reduce the burden on providers.

Advocate Aurora Health enters into risk-based contracts with commercial and

public payers, assuming responsibility for the quality and cost of care provided. Pharmacist-led disease management programs are tools that can enhance and support the care of risk contract patients with chronic diseases, increasing the value of care. One such chronic disease with many attributed quality measures is diabetes mellitus. For this reason, pharmacists at Advocate Aurora Health have initially worked to improve diabetes control for its risk contract population by focusing on a cornerstone of therapy, metformin.

Metformin, along with lifestyle modifications, is the gold standard initial treatment of Type 2 diabetes as recommended by the American Diabetes Association in the Standards of Medical Care in Diabetes-2019.[4] It is highly efficacious with 1.5% HbA1c reduction on average.[5] It has been proven safe in extensive studies, with lack of hypoglycemia and potential ability to provide cardiovascular benefit.[4,5] At an approximate average wholesale price (AWP) as low as $4 per month, metformin is much less expensive than some other treatments for Type 2 diabetes that may have an AWP of hundreds of dollars per month.[4] With its efficacy, safety, and low cost, metformin is a valuable treatment for patients with Type 2 diabetes.

As of 2014, the lifetime cost to treat diabetes was estimated at $124,600 for a patient diagnosed at age 40; it is likely even more expensive now.[6] Delaying expensive brand-name treatments may reduce costs in the long-term. Considering the advantages of metformin and lifetime cost to treat diabetes, maximizing the potential benefit of metformin is imperative to cost savings. In maximizing this inexpensive treatment, it is the hope that the patient's diabetes can be controlled with just one affordable, effective, and safe medication for as long as possible.

Titration to the maximum tolerated dose of metformin allows the patient to obtain maximum potential benefit. The maximum total daily dose is 2,550 mg per day of immediate-release metformin, and up to 2,000 mg per day of extended-release metformin.[7] As long as a patient is not experiencing intolerable adverse effects, they will receive the most benefit from the maximum tolerated dose.[8,9] The longer a patient can delay additional diabetes medications, the more potential there is for cost savings and adverse event avoidance.

Metformin is often initiated at a low dose and intended to be incrementally titrated upwards, as frequently as every two weeks (ranging from five days to one month), to reduce potential adverse effects.[7,10,11] In studying the time to treatment intensification, Khunti et al. found that it could take up to 3 years before medication adjustment after an increased HbA1c result.[12] "The term 'clinical inertia' in most instances has been used in relation to failure to advance therapy when appropriate to do so."[13] If medication adjustments are made at provider office visits every 3-6 months, there is likely a prolonged titration to the maximum tolerated dose. Providers may delegate metformin titration and monitoring of safety and efficacy to another healthcare team member such as a pharmacist to decrease workload, enhance between-visit care, and ultimately achieve improved health outcomes for patients.

Pharmacists at Advocate Aurora Health identified an opportunity to improve the benefit patients receive from metformin therapy. Extensive internal data retrieval and analysis showed that some patients were in a state of clinical inertia, where they could be receiving a higher dose of metformin but instead remained on the same, smaller dose of the drug as their HbA1c slowly rose over time. By collaborating with physician leaders, population health pharmacists implemented a program that would optimize metformin dose based on evidence, embrace coordinated care, and provide an additional approach to enhance clinical outcomes and service quality for risk contract patients.

BOX 1. Inclusion and Exclusion Criteria

Inclusion Criteria	*Exclusion Criteria*
• Risk contract patient based on current insurance • Type 2 diabetes mellitus • Age 18-75 years old • HbA1c 7-10% • Current metformin dose ≤ 1500 mg/day	• Currently prescribed additional diabetes medication(s) • Pregnancy • Renal impairment (eGFR < 45 mL/min) • Clinically significant liver disease (ALT, AST > 2.5x ULN, and/or evidence of cirrhosis) • Unstable or acute heart failure • History of acute or chronic metabolic acidosis (including diabetic ketoacidosis)

eGFR=estimated glomerular filtration rate; ALT=alanine aminotransferase; AST=aspartate aminotransferase; ULN=upper limit of normal

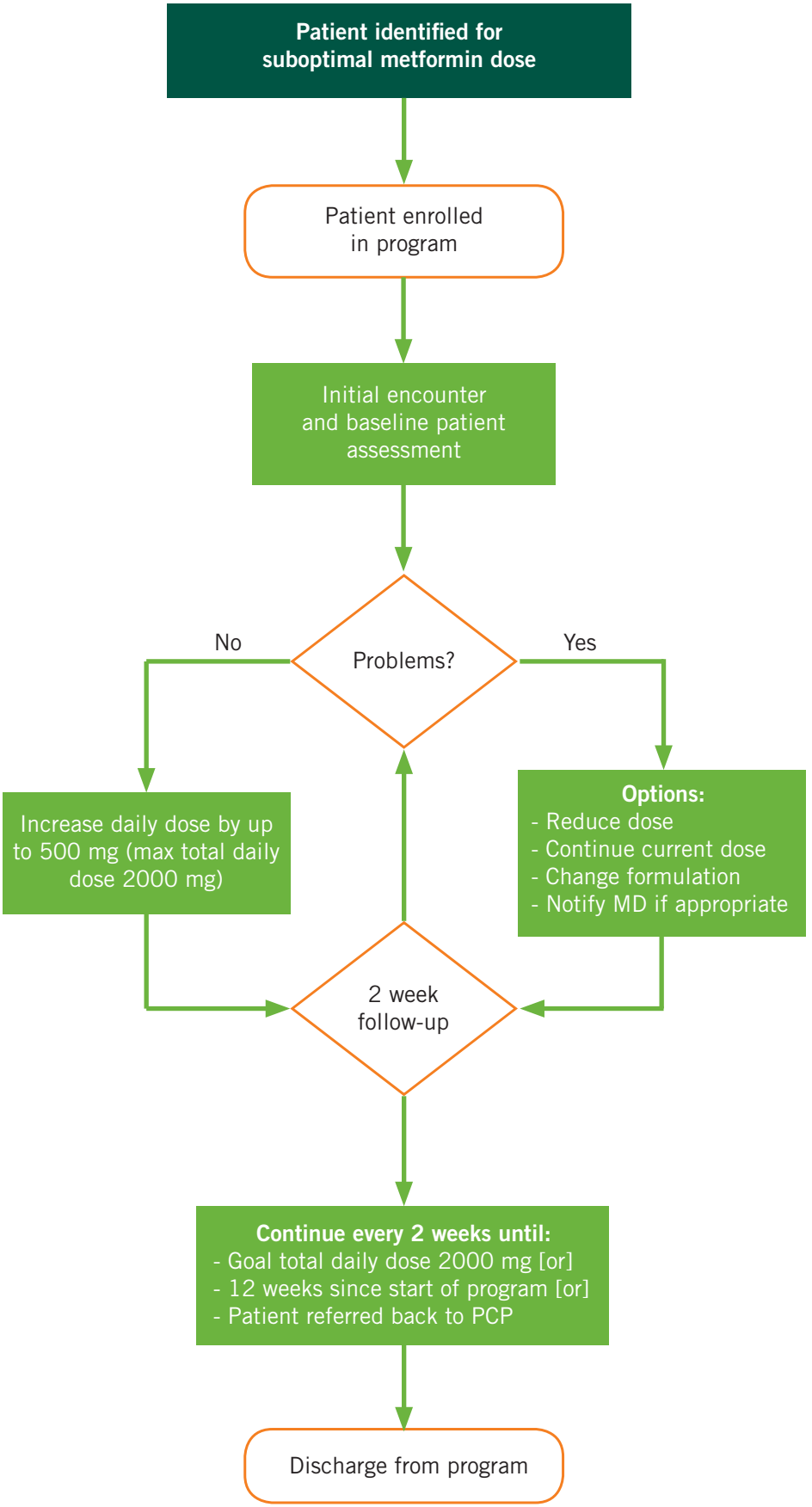
Methods

The Metformin Dose Optimization Program took a population health approach to risk contract adult patients with poorly controlled Type 2 diabetes taking suboptimal doses of metformin. Involvement from primary care physician leaders was sought to obtain support and install a collaborative practice agreement to enable pharmacist-led targeted interventions using an evidence-based protocol. Medical directors provided a review of the proposed protocol prior to signing the collaborative practice agreement. A strategic communication plan was developed that involved both organization-level primary care physician leaders as well as local physician leaders in each region. The goal of this communication plan was to foster collaboration and cultivate program acceptance by delivering a clear message to all involved parties.

The program was conducted telephonically by a centralized group of pharmacists with patients spread throughout the Advocate Aurora Health Wisconsin footprint. The data collection period was from October 2017 to December 2018, during which the program was being expanded to all Wisconsin regions.

Risk contract adult patients with Type 2 diabetes mellitus were included if they had a HbA1c of 7-10%, taking metformin ≤ 1,500 mg per day. Patients were excluded

FIGURE 1. Program Workflow



if they were prescribed additional diabetes medication(s) or had safety concerns, such as renal impairment. Box 1 contains the full list of inclusion and exclusion criteria. These criteria as well as patient qualifiers were leveraged to build a report that proactively identified patients experiencing clinical inertia. Pharmacists sent referral orders to providers within the electronic health record (EHR), giving providers autonomy to approve or deny pharmacist management for each patient. Pharmacists performed telephonic outreach to enroll patients, with follow-up every 2-4 weeks during the 12-week program. Under the collaborative practice agreement, they were able to adjust the metformin dose and change the formulation if needed. In addition, pharmacists also provided patient monitoring, education, and adherence support for metformin (Figure 1). All pharmacist encounters were visibly documented in the EHR, and a summary was sent to the patient's provider at program completion. Documentation tools with discrete elements were built in the EHR to enable efficient, consistent documentation and effortless data retrieval.

The primary clinical endpoint was

TABLE 1. Baseline Characteristics

Characteristic	*n=241*
Male	102 (42%)
Female	139 (58%)
Age ≤ 19	0 (0%)
Age 20-29	1 (0%)
Age 30-39	7 (3%)
Age 40-49	17 (7%)
Age 50-59	47 (19%)
Age 60-69	100 (41%)
Age 70-75	69 (29%)
HbA1c 7.0-7.9%	177 (73%)
HbA1c 8.0-8.9%	52 (22%)
HbA1c 9.0-9.9%	10 (4%)
HbA1c 10.0%	2 (1%)

mean change in HbA1c. Secondary findings included the change in total daily metformin dose and program engagement. Program engagement was measured for both providers and patients. Provider engagement was determined based on the percentage of providers that co-signed the referral order request that was sent through the EHR by the pharmacist. Patient engagement was determined based on the percentage of patients that agreed to participate in the program during the initial pharmacist contact.

Results

Most patients enrolled in the program were female between the ages of 60-69 years, with baseline HbA1c of 7.0-7.9%. Table 1 summarizes the baseline demographics of patients who were candidates for program enrollment (n=241).

Of 241 potential candidates, 210 were enrolled in the program (Figure 2). Thirty-one patients were not enrolled, for reasons including but not limited to: patient did not meet inclusion criteria or met exclusion criteria. Of the 210 patients enrolled in the program, 133 patients successfully completed the program and 77 patients either refused program participation or were lost to follow-up.

Primary Findings

The overall mean change in in HbA1c was -0.6% (from 7.7% to 7.1%; n=98) in patients who successfully completed the 12-week program and had a post-program HbA1c value available (Figure 3). Some patients who successfully completed the program have since had a second HbA1c completed. In this group, initial change in HbA1c was -0.4% (from 7.7% to 7.3%; n=38), with sustained and continued improvement to 7.2% on average at the second HbA1c measurement. HbA1c results were also evaluated for patients that were lost to follow-up and did not successfully complete the program. Patients were considered lost to follow-up after three failed outreach attempts and were lost 6.47 weeks on average after program enrollment. Of this group of patients with a post-program HbA1c value available, a mean change in HbA1c of -0.3% (from 7.7% to 7.4%; n=57) was observed.

FIGURE 2. Program Enrollment

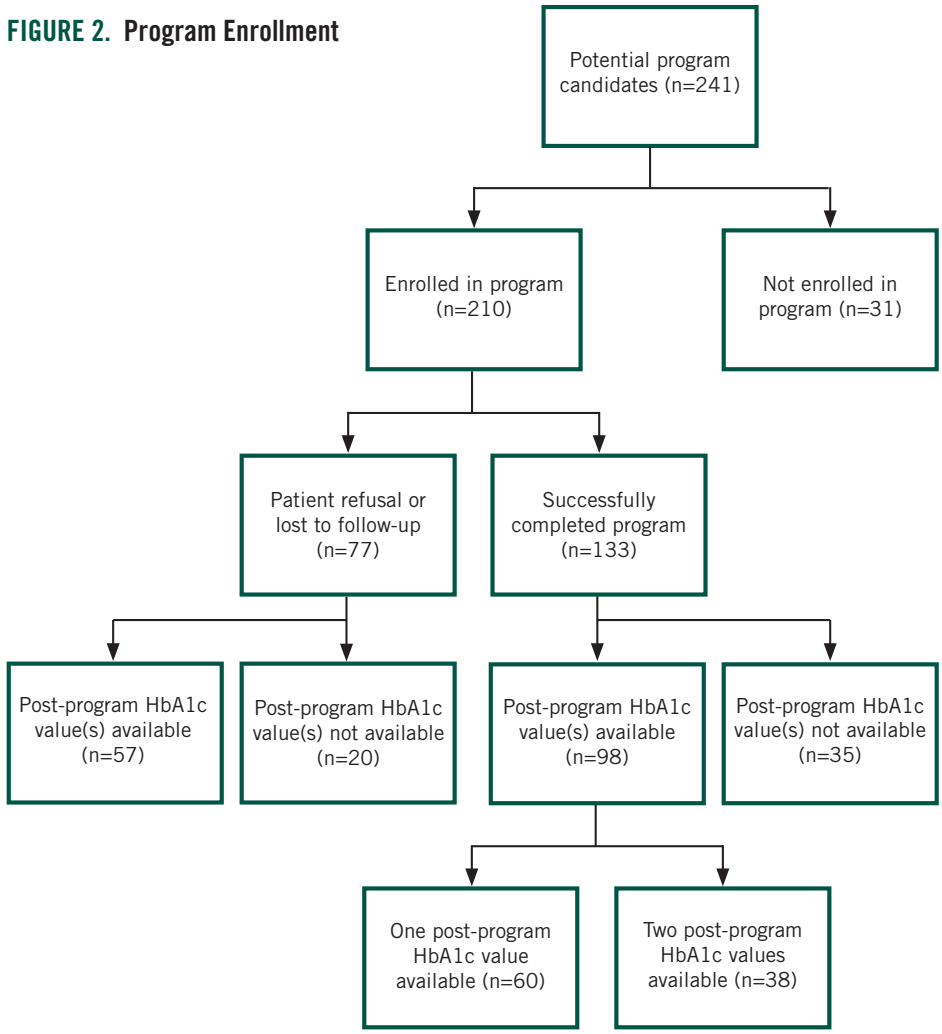


FIGURE 3. HbA_{1c} Progression

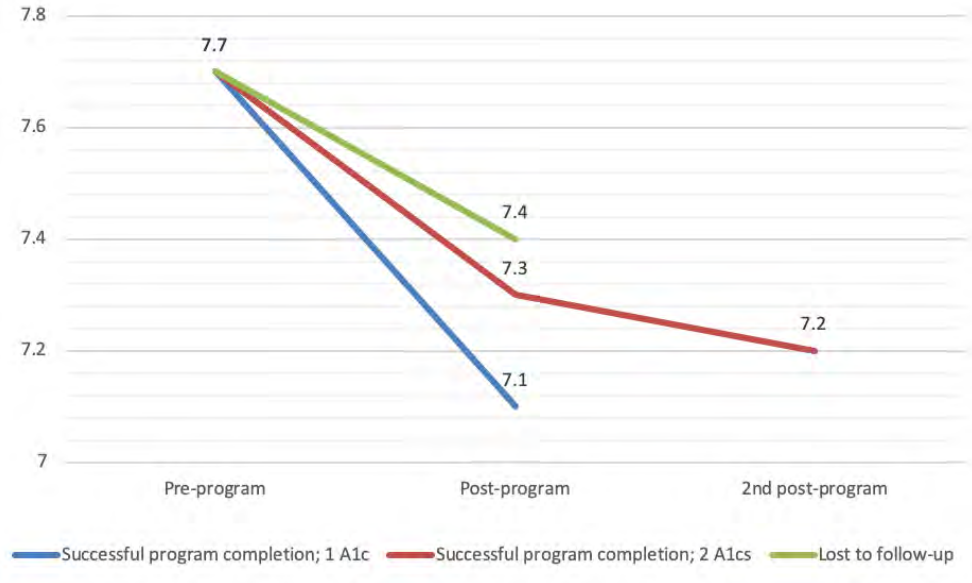
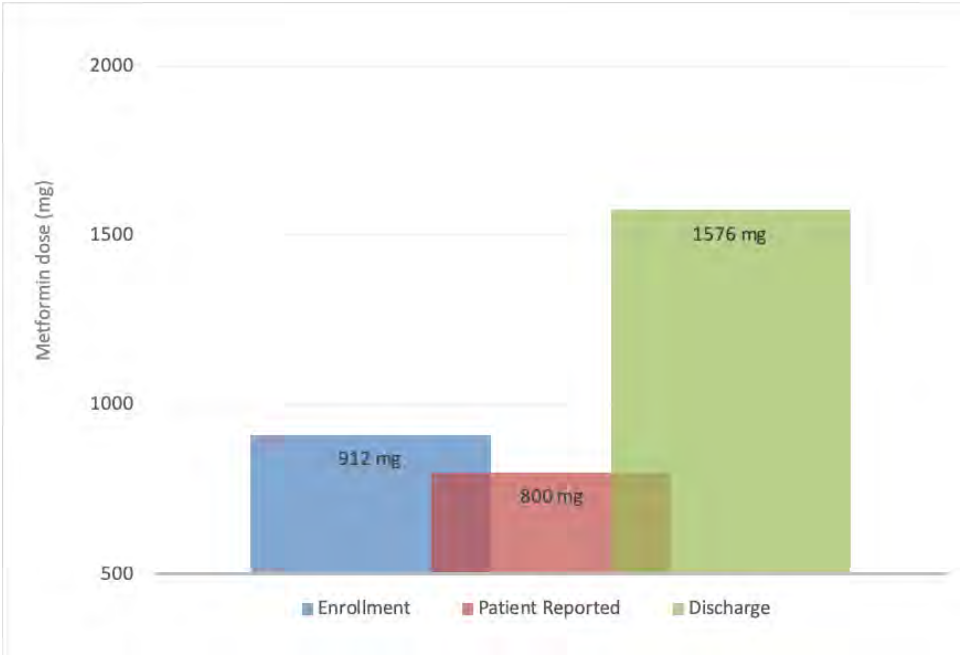


FIGURE 4. Average Metformin Total Daily Dose



Secondary Findings

Upon enrollment, the average total daily metformin dose was 912 mg, per prescription orders entered in the EHR, but it was 800 mg on average as reported by patients (Figure 4). At time of discharge from the program, whether the patient successfully completed it or was lost to follow-up, the average total daily dose of metformin was 1,576 mg per prescription orders entered in the EHR and patient assessment at the final pharmacist contact. Of the 133 patients who successfully completed the program, 73.7% underwent a dose increase (n=98).

Provider engagement, those who agreed to metformin optimization by a pharmacist, was measured at 93%. Patient engagement, those who agreed to participate in the program, was 63%. The remaining patients either refused enrollment or were not able to be reached after three pharmacist outreach attempts.

Discussion

The improvement in HbA1c measurements demonstrated a positive pharmacist impact on diabetes control for risk contract patients at Advocate Aurora Health. Personalized pharmacist support allowed these patients to receive more benefit from metformin and achieve improved diabetes control. Therefore, the pharmacist-led Metformin Dose Optimization Program was successful and fulfilled its purpose.

The transition from fee-for-service to value-based payment models necessitates a population health approach to care, one in which pharmacists can take an active role. Collaborating with healthcare providers in population health efforts can enable top-of-license pharmacist practice, which can improve healthcare quality while reducing cost and improving value. In this specific case, pharmacists were able to assist providers by enhancing diabetes care for their patients, and diabetes control was improved with the hopes of delaying additional, expensive diabetes treatment and diabetic complications. Optimizing patients' use of metformin can help defer additional health care costs associated with diabetes. According to the American Diabetes Association, inpatient hospitalizations (30%) and medications to treat diabetic complications (30%) make up a significant portion of the costs associated with diabetes.[14] Reducing the costs of care in the diabetic population has allowed Advocate Aurora Health to expand its pharmacist-led disease management programs.

Limitations

There were several notable limitations of this program. First, the program is only available to patients whose health insurance plan has a risk-based contract with Advocate Aurora Health. These patients represent only a subset of all patients cared for by Advocate Aurora Health, and therefore many patients are not able to benefit from the program. It would be ideal to offer the program to all patients.

A second limitation was the telephonic method of outreach. The pharmacists were able to reach patients across a broad geographic footprint, but some patients were not able to be reached. Anecdotally, many of the patients that were not enrolled were unable to be reached, versus patient denial to participate. This limitation reduced the number of patients that were able to receive personalized pharmacist support for their diabetes control.

Pharmacist resources were a third limitation to this program. There were many more candidates eligible for pharmacist outreach than there was pharmacist time available to complete the outreach. Positive results have since led to expansion of pharmacist full-time equivalents and therefore the number of patients enrolled.

Lastly, this program has the potential to be more impactful with additional diabetes medications included in the protocol. Pharmacists were limited to optimization of metformin only and could not prescribe additional medications according to evidence-based guidelines, even if patients continued to experience elevated blood glucose levels after reaching the maximum tolerated dose of metformin. There is opportunity for additional impact in the future if pharmacists can continue intensification of diabetes treatment when clinically appropriate.

Conclusion

Utilization of a collaborative practice agreement and protocol to perform centralized, telephonic pharmacy services to a broad patient population enhanced the quality and coordination of care. The positive results from the Metformin Dose Optimization Program indicate a promising future to pharmacist advancement in population health initiatives. In addition to program expansion across Advocate Aurora Health's Illinois footprint, focus may be

placed on medication adherence to excel in Medicare star ratings and development of new chronic disease management programs. Endless possibilities lie ahead for increased collaboration in health care systems leading to an enhanced patient experience, improved health outcomes, and better cost containment.

Meaghan McMurray is the Manager of Population Health Pharmacy Programs at Advocate Aurora Health in Milwaukee, WI. Bradley Schermetzler is the Pharmacy Clinical Coordinator of Informatics & Population Health Pharmacy Programs at Advocate Aurora Health in Milwaukee, WI . Marisa Goninen is the Pharmacy Clinical Coordinator of Population Health Pharmacy Programs at Advocate Aurora Health in Milwaukee, WI.

PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

Disclosures: The authors declare no real or potential conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria.

Bradley J. Schermetzler, PharmD, BCACP: The author declares no real or potential conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employments, gifts, and honoraria. The author declares that he had full access to the original data and takes responsibility for the integrity of the data and the accuracy of the data analysis.

References

1. Papanicolas I, Woskie LR, Jha AK. Health care spending in the United States and other high-income countries. *JAMA*. 2018;319(10):1024-1039.
2. Berwick DM, Nolan TW, Whittington J. The triple aim: care, health, and cost. *Health Aff.* 2008;27(3):759-769.
3. Bodenheimer T, Sinsky C. From triple to quadruple aim: care of the patient requires care of the provider. *Ann Fam Med.* 2014;12(6):573-576.
4. American Diabetes Association. Standards of Medical Care in Diabetes-2019. *Diabetes Care.* 2019;42(Suppl 1);S1-S193.
5. DeFronzo RA, Goodman AM. Efficacy of metformin in patients with non-insulin-dependent diabetes mellitus. *N Engl J Med.* 2002;333(9):541-549.
6. Zhuo X, Zhang P, Barker L, Albright A, Thompson TJ, Gregg E. The lifetime cost of diabetes and its implications for diabetes prevention. *Diabetes Care.* 2014;37(9):2557-2564.
7. Glucophage, Glucophage XR [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2018.
8. Garber AJ, Duncan TG, Goodman AM, Mills DJ, Rohlf JL. Efficacy of metformin in type II diabetes: results of a double-blind, placebo-controlled, dose-response trial. *Am J Med.* 1997;103(6):491-497.
9. Hirst JA, Farmer AJ, Ali R, Roberts NW, Stevens RJ. Quantifying the effect of metformin treatment and dose on glycemic control. *Diabetes Care.* 2012;35(2):446-454.
10. Glumetza [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC. 1995.
11. Riomet [package insert]. Jacksonville, FL: Sun Pharmaceutical Industries Limited. 2017.
12. Khunti K, Wolden ML, Thorsted BL, Andersen M, Davies MJ. Clinical inertia in people with type 2 diabetes: a retrospective cohort study of more than 80,000 people. *Diabetes Care*. 2013;36(11):3411-3417.
13. Khunti K, Seidu S. Therapeutic inertia and the legacy of dysglycemia on the microvascular and macrovascular complications of diabetes. *Diabetes Care*. 2019;42(3):349-351.
14. American Diabetes Association. Economic costs of diabetes in the U.S. in 2017. *Diabetes Care.* 2018;41(5):917-928.