Effect of Pharmacist-Driven Professional Continuous Glucose Monitoring in Adults with Uncontrolled Diabetes

By: Christina H. Sherrill, Christopher T. Houpt, Elisabeth M. Dixon, & Scott J. Richter

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Abstract:

Background: Diabetes requires close monitoring to achieve optimal outcomes and avoid adverse effects. Continuous glucose monitoring (CGM) is one approach to measuring glycemia and has become more widespread with recent advances in technology; however, ideal implementation of CGM into clinical practice is unknown. CGM can be categorized as personal CGM, which can be for at-home use to replace self-monitoring of blood glucose, or professional CGM (proCGM), which is used intermittently under the direction of a health care professional. The expanding role of the clinical pharmacist allows pharmacists to be at the forefront of implementing proCGM technology, but literature on the effect of pharmacist-driven proCGM is lacking. Pharmacists and physicians within 1 physician-owned clinic used proCGM technology differently. Pharmacists conducted 1 or 2 office visits to interpret data and make interventions, while physicians interpreted data 1 time and relayed interventions via phone.

Objectives: To (a) compare the change in hemoglobin A1c from baseline to 6 months between the different methods of proCGM implementation, and (b) describe and compare the clinical interventions made as a result of the different methods of proCGM implementation.

Methods: In this retrospective cohort study, adults identified in the electronic medical record via Current Procedural Terminology code 95250 or 95251 undergoing proCGM with CGM data interpreted and baseline A1c ≥ 7% were included. Patients with additional CGM use within the 6-month follow-up period were excluded. Data collection included demographics, A1c at baseline and during the 6-month follow-up period, and CGM-associated interventions. Patients were categorized as undergoing 1 pharmacist-driven encounter (RPh1), 2 pharmacist-driven encounters (RPh2), or 1 physician-driven encounter (MD1) for proCGM implementation. Combined RPh1 and RPh2 (cRPh) data were also used for analysis. The primary outcome was change in A1c from baseline to 6 months, which was evaluated by analysis of covariance.

Results: Of 378 patient charts reviewed, 315 instances of proCGM implementation met inclusion criteria (58 RPh1, 35 RPh2, 222 MD1), and 253 had post-implementation A1c data for analysis of the primary outcome (52 RPh1, 30 RPh2, 171 MD1). Baseline A1c was 8.4%, 8.8%, and 9.1% with mean reduction from baseline to 6 months of 1.0%, 1.3%, and 0.6%, respectively. cRPh patients experienced a greater mean reduction in A1c compared with MD1 ($P = 0.002$). RPh2 patients had a statistically significant reduction compared with MD1 ($P = 0.005$), but RPh1 patients did not ($P = 0.054$). The number of CGM-associated pharmacological interventions was 1.33 for RPh1 patients, 1.63 for RPh2 at the first encounter and 1.34 at the second, and 1.17 for MD1.

Conclusions: Pharmacist-driven implementation of proCGM was associated with greater A1c reductions and more pharmacological interventions versus physician-driven implementation. This study demonstrated improved clinical outcomes with pharmacists providing direct patient care through implementation of new diabetes technology.

Keywords: Diabetes mellitus | continuous glucose monitoring | diabetes management | physician-driven implementation

Article:

Diabetes mellitus affects more than 30 million Americans and cost the U.S. health care system $327 billion in 2017.[1] Diabetes is a complex chronic disease state that often requires close monitoring and frequent interventions to achieve optimal therapeutic control and avoid adverse effects. While hemoglobin A1c and self-monitoring of blood glucose (SMBG) have long been standards for measuring glycemic control, recent advances in technology for continuous glucose monitoring (CGM) have made this method of glycemic measurement more widespread and accessible. Furthermore, as of 2019, American Diabetes Association's *Standards of Medical Care in Diabetes* includes a new chapter dedicated to diabetes technology in which CGM and its place in therapy are discussed.[2]

CGM devices measure glucose through minimally invasive sensors in the interstitial fluid for 3 to 14 days. Sensors report interstitial glucose every 5 to 15 minutes, which has been found to correlate with capillary blood glucose.[3] CGM devices may be divided into 2 types: real-time CGM and intermittently scanning, or "flash," CGM. Real-time CGM continuously reports glucose levels, while intermittently scanning CGM provides glucose data only when the user scans the device.[2]

CGM can also be categorized as personal use, where the patient uses CGM technology at home to supplement or replace SMBG with results available on demand, or professional use, where results are often blinded to the patient and only viewable in the health care setting.[4] Personal CGM (per CGM) equipment is provided by a pharmacy or durable medical equipment provider and may cost the patient hundreds of dollars per month.[5] Professional CGM (pro CGM) is used intermittently under the direction of a health care professional and can be con-ducted during a regular office visit using Current Procedural Terminology (CPT) codes.

Various studies have demonstrated the benefit of per CGM, showing A1c reductions of 1.0% with per CGM plus SMBG versus 0.5% with SMBG alone, as well as reduction in hypoglycemia (43 minutes vs. 80 minutes in the control).[6,7] Another study showed per CGM users to have a significantly lower number of severe hypoglycemic events (14 compared with 34 without per CGM).[8] Furthermore, the amount of time spent in euglycemia can be increased to 73.7% with per CGM compared with 68.3% in the control.[9]

While these positive outcomes have been demonstrated with per CGM, literature describing the role of pro CGM systems and their effects on diabetes management is more limited. Studies have found modest A1c decreases between 0.4% and 0.7% from baseline A1c. The greatest benefit has been seen in patients using multiple daily insulin injections or continuous subcutaneous insulin infusions.[10,11]

Additionally, literature on pharmacist implementation of this technology is particularly scarce, despite evidence that pharmacists' contributions in general diabetes team-based care can have a significant effect with an average A1c reduction of1.1% compared with usual care.12 A small study found that pharmacist implementation of proCGM resulted in an A1creduction from

9.0% to 8.3% after 6 months.13 There remains a critical need to investigate the role of the clinical pharmacist in proCGM implementation. Determining optimal use of this technology will help improve diabetes patient care and optimize use of resources. In this study, the use of a pro CGM system capable of recording glucose data for 14 days was analyzed. Pharmacists and physicians within 1 physician-owned clinic used this technology differently. Pharmacists conducted 1 or 2 office visits to interpret data and make interventions, while physicians interpreted data 1 time with interventions typically relayed via phone.

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The purpose of this study was to determine which proCGM implementation method (1 interpretation encounter with a pharmacist, 2 interpretation encounters with a pharmacist, or1 interpretation encounter with a physician) was most effective at improving diabetes outcomes and optimizing pharmacological interventions. The study objectives were to (a) compare the change in A1c from baseline to 6 months between the different methods of proCGM implementation, and (b) describe and compare the clinical interventions made as a result of the different methods of proCGM implementation.

Methods

Device

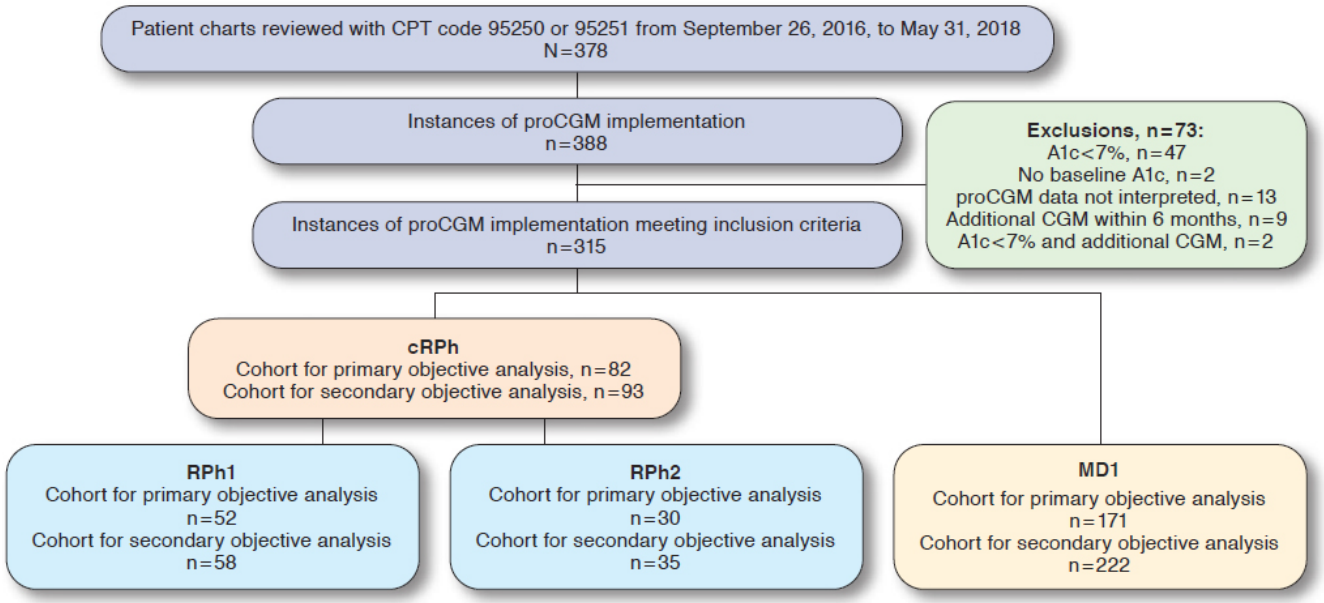
In this study, the FreeStyle Libre Pro (Abbott Diabetes Care, Alameda, CA) was used, which is a proCGM system approved by the U.S. Food and Drug Administration in September 2016.The FreeStyle Libre Pro system consists of single-user sensors and multiuser readers and was the first to not require calibration via glucometer readings. A sensor is placed on the back ofa patient's upper arm with a filament inserted into the interstitial fluid to record glucose every 15 minutes for up to 14 days. Data can be retrieved multiple times during the sensor's 14-day duration of use by scanning the sensor with the reader.

Setting and Clinical Procedures

Patient care was conducted at a physician-owned primary care office with endocrinology, internal medicine, and clinical pharmacy services. Pharmacists in this setting worked under a collaborative practice agreement and could manage diabetes (including medication changes) after a referral from a physician within the practice. Referrals for diabetes management typically came from the internal medicine physicians, and patients were generally not seen by both a pharmacist and endocrinologist for diabetes care. Procedures for pharmacist use of proCGM technology at this facility have been reported elsewhere.14 In brief, clinical pharmacists could see patients for a set of 3 clinic visits per proCGM implementation. The first visit would include placing and activating the CGM sensor, while the second and third visits would involve scanning the sensor, analyzing the data, and making clinical interventions based on data from the single sensor. With the device's capability of collecting glucose data over a period of 14 days, the second visit would occur approximately 1 week after sensor placement with the third visit approximately 2 weeks after placement. Patients following this procedure with 2 pharmacist-driven encounters for CGM data interpretation were categorized as "RPh2" for the study.

While the intent of pharmacist-driven proCGM implementation was to follow the above procedures, some patients only had 1 encounter with the pharmacist for CGM data analysis for various reasons, such as time constraints, sensor loss, or patient loss to follow-up. Patients with 1 pharmacist-driven clinic visit for CGM data interpretation were categorized as"RPh1" for study procedures.

Figure 1. Inclusion Flowchart



Note: All instances of proCGM implementation meeting inclusion criteria (n=315) were included in the secondary objective analysis (clinical interventions). Only those instances with A1c values available during the 6-month follow-up period (n=253) were included in the primary objective analyses (A1c change).

A1c=hemoglobin A1c; CGM=continuous glucose monitoring; CPT=Current Procedural Terminology; cRPh=combined RPh1 and RPh2; MD1=patients with 1 physician-driven encounter; proCGM=professional continuous glucose monitoring; RPh1/2=patients with 1 or 2 pharmacist-driven encounters.

Physician-driven proCGM implementation typically consisted of an in-office encounter to place the CGM device, followed by the patient presenting to the office approximately 1 week latert o have the CGM sensor scanned by a certified medical assistant. CGM data would then be shared with the physician, who would analyze the data and determine appropriate interventions. Results and interventions were communicated to the patient, usually via phone (95% of patients), rather than an office visit. Patients with 1 physician-driven encounter for CGM data interpretation were categorized as "MD1" for study procedures.

Study Design

This single-center retrospective study evaluated A1c and clinical interventions resulting from pharmacist-driven and physician-driven proCGM implementation. Electronic medical records were queried for patients who had a CPT code 95250 or 95251 (CGM-specific billing codes) billed between September26, 2016, and May 31, 2018, followed by a manual review to identify patients who were 18 years of age or older, had a base-line A1c of at least 7%, and had proCGM implemented by a pharmacist or physician with data available for interpretation.

Patients with additional CGM use (whether personal or professional) within the 6-month follow-up period were excluded in an attempt to isolate the effects of a single CGM implementation method during the study period. Data collection included demographics, baseline A1c, CGM-associated interventions, and A1c and clinical encounters during the 6-month follow-

up period. Baseline medications were considered those that the patient was taking before the CGM placement visit. CGM-associated interventions were those documented in the note corresponding to the proCGM data interpretation encounter. Patients were categorized as undergoing 1 pharmacist-driven encounter (RPh1), 2 pharmacist-driven encounters (RPh2), or 1 physician-driven encounter (MD1) for CGM data interpretation from a single sensor, as noted above. Combined RPh1 andRPh2 (cRPh) data were also used for analysis.

Study data were collected and managed using Research Electronic Data Capture (REDCap), a secure, web-based application hosted at High Point University. [15] Investigators reviewed the first 50 patient charts individually and compared findings to ensure consistency in data collection. Data were also reviewed for consistency and accuracy at the conclusion of data collection through the reporting feature in REDCap. This study was approved by the local institutional review board.

Outcomes

The primary outcome was change in A1c from baseline to 6 months. Secondarily, clinical interventions documented for a proCGM interpretation encounter were recorded and categorized as pharmacological or nonpharmacological. Pharmacological interventions consisted of initiating, discontinuing, and changing medication therapy, including switch-ing from 1 formulation to another (e.g., changing metformin immediate release to extended release) or shifting the timing of dosing (e.g., changing the timing of insulin glargine from bedtime to morning). Pharmacological interventions were also classified as increasing medication use (i.e., initiating a new medication or increasing the dose of an existing medication) or decreasing medication use. Patients could have multiple pharmacological interventions per encounter. Recorded non-pharmacological interventions included lifestyle interventions (diet, exercise, and weight loss) and patient education (hypo-glycemia management, medication administration, and medication adherence).

Data Analysis

Data were de-identified before analysis. Bonferroni-adjusted95% confidence intervals were used to compare baseline characteristics between groups for patients with post-implementation A1c. Least squares regression was used to fit an analysis of covariance model to estimate and generate t-tests to compare mean reductions in A1c from baseline. The last A1c measurement within the 6-month follow-up period was the dependent variable. The independent variables were implementation type (cRPh, RPh1, RPh2, or MD1) and baseline A1c. Secondary analyses added insulin treatment (treated or not treated at baseline) along with baseline A1c measurement as covariates. Body mass index, type of diabetes, and total daily insulin dose were considered as additional covariates, but they were not associated with change in A1c and removed from the model. Statistical significance was defined as a P value < 0.05. All analyses were implemented using R statistical software (R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 315 instances of proCGM implementation were included, consisting of 308 individual patients, 7 of whom had an additional proCGM implementation more than 6 months after the initial proCGM implementation (Figure 1). Of the 315 included instances of proCGM implementation, 253 had A1cmeasurements during the follow-up period for analysis of the primary outcome. Of all included patients, most were female and white with diagnoses of type 2

diabetes mellitus, hyper-tension, and hyperlipidemia (Table 1). The mean age was 62.6years with mean body mass index of 34.0 kg per m 2 and baseline A1c of 9.0%. Most patients were treated with metformin and insulin. Of those with documented doses of insulin, the mean total daily dose was 91.4 units. Bonferroni-adjusted 95%confidence intervals showed no difference between groups, except for body mass index for patients in the RPh2 and MD groups. While all patients had baseline A1c of at least 7%, hypoglycemia or intent of deprescribing was a documented indication for proCGM use in 12.1% of RPh1 patients, 17.1% ofRPh2, and 34.7% of MD1.

Change in A1c

Change in A1c was analyzed for the 253 instances of proCGM implementation that had A1c data within 6 months of proCGM placement. The average time from the proCGM placement visit to the A1c value used for analysis was 112 days for the RPh1cohort, 123 days for RPh2, and 124 days for MD1. Unadjusted mean A1c reductions from baseline to 6 months were 1.1%,1.0%, 1.3%, and 0.6% for the cRPh, RPh1, RPh2, and MD1cohorts, respectively, which were all statistically significant with $P < 0.001$ (Table 2). Compared with MD1, patients in cRPh and RPh2 both experienced a greater mean reduction in A1c($P = 0.002$ and $P = 0.005$, respectively).

When adjusted for insulin treatment at baseline and stratified by treated versus not treated, statistically significant reductions in A1c from baseline to 6 months were seen across all groups (Table 2). When comparing between groups, adjusted results for all patients with post-implementation A1c showed statistical significance for cRPh to MD1, RPh1 to MD, and RPh2to MD1 ($P = 0.002$, $P = 0.045$, and $P = 0.004$, respectively). Of note, 5 patients were included in the "not treated" cohort who were started on insulin therapy at their CGM placement visit (1 RPh2, 4 MD1). A total of 10 "not treated" patients were started on insulin by the end of the 6-month follow-up period (2 RPh1, 3 RPh2, 5 MD1).

Comparing groups separately under the different insulin categories revealed no statistically significant differences between groups for patients not treated with insulin therapy (Table 2). Analyses for patients treated with insulin, however, did reveal statistically significant A1c reductions for cRPh versus MD1, RPh2 versus MD1, and RPh2 versus RPh1 ($P = 0.002$, $P < 0.001$, and $P = 0.034$, respectively). Overall, patients who were not undergoing insulin treatment at baseline had a 0.5%greater A1c reduction, on average, than patients undergoing insulin treatment ($P = 0.010$), regardless of the classification of proCGM implementation.

The percentage of patients with A1c less than 7% by the end of the 6-month follow-up period was 42.3% for RPh1, 30.0%for RPh2, and 12.9% for MD1.

Clinical Interventions

Table 1. Baseline Characteristics

	Overall Cohort (n= 315)			**Patients with Post-implementation A1c (n= 253)**		
	RPh1 (n= 58)	RPh2 (n = 35)	MDI (n= 222)	RPh1 (n=52)	RPh2 (n=30)	MDI (n= 171)
Age, mean years (SD)	64.1 (12.7)	65.8 (9.5)	61.7 (12.0)	63.4 (12.4)	66.6 (8.4)	62.8 (11.5)
Female, n (%)	32 (55.2)	19 (54.3)	153 (68.9)	28 (53.8)	16 (53.3)	122 (71.3)
Race, n (%)						

Asian	1 (1.7)	0 (0.0)	4 (1.8)	1 (1.9)	0 (0.0)	3 (1.8)
African American	18 (31.0)	6 (17.1)	71 (32.0)	15 (28.8)	6 (20.0)	60 (35.1)
White	38 (65.5)	25 (71.4)	137 (61.7)	35 (67.3)	20 (66.7)	102 (59.6)
Hispanic	1 (1.7)	0 (0.0)	3 (1.4)	1 (1.9)	0 (0.0)	2 (1.2)
Other	0 (0.0)	4 (11.4)	7 (3.2)	0 (0.0)	4 (13.3)	4 (2.3)
Unknown	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.6)
Ethnicity, n (%)						
Hispanic or Latino	1 (1.7)	1 (2.9)	3 (1.4)	1 (1.9)	0 (0.))	3 (1.8)
Not Hispanic or Latino	57 (98.3)	33 (94.3)	214 (96.4)	51 (98.1)	28 (93.3)	166 (97.1)
Unknown	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.6)
A1c, mean % (SD)	8.4 (1.5)	9.0 (1.8)	9.2 (1.6)	8.4 (1.4)	8.8 (1.6)	9.1 (1.6)
Body mass index, mean kg/m^2 (SD)[a]	34.7 (6.7)	30.9 (5.9)	34.3 (7.8)	34.7 (6.9)	30.3 (5.6)	34.6 (7.7)
Medical conditions, n (%)						
Type 1 diabetes mellitus	2 (3.4)	3 (8.6)	37 (16.7)	2 (3.8)	2 (6.7)	25 (14.6)
Type 2 diabetes mellitus	56 (96.6)	31 (88.6)	185 (83.3)	50 (96.2)	27 (90.0)	146 (85.4)
Unspecified diabetes	0 (0.0)	1 (2.9)	0 (0.0)	0 (0.0)	1 (3.3)	0 (0.0)
Hypertension	52 (89.7)	29 (82.9)	198 (89.2)	46 (88.5)	24 (80.0)	155 (90.6)
Hyperlipidemia	51 (87.9)	30 (85.7)	185 (83.3)	46 (88.5)	25 (83.3)	145 (84.8)
Coronary artery disease	8 (13.8)	6 (17.1)	14 (6.3)	7 (13.5)	6 (20.0)	10 (5.8)
Myocardial infarction	5 (8.6)	2 (5.7)	0 (0.0)	5 (9.6)	2 (6.7)	0 (0.0)
Cerebrovascular accident	5 (8.6)	1 (2.9)	1 (0.5)	3 (5.8)	0 (0.0)	0 (0.0)
Neuropathy	8 (13.8)	4 (11.4)	81 (36.5)	7 (13.5)	4 (13.3)	54 (31.6)
Nephropathy	20 (34.5)	10 (28.6)	81 (36.5)	16 (30.8)	8 (26.7)	60 (35.1)
Retinopathy	1 (1.7)	2 (5.7)	27 (12.2)	1 (1.9)	1 (3.3)	19 (11.1)
Medications, n (%)						
Biguanide	35 (60.3)	20 (57.1)	89 (40.1)	33 (63.5)	19 (63.3)	76 (44.4)
Sulfonylurea	13 (22.4)	6 (17.1)	24 (10.8)	13 (25.0)	5 (16.7)	19 (11.1)
SGLT2 inhibitor	8 (13.8)	6 (17.1)	19 (8.6)	8 (15.4)	6 (20.0)	15 (8.8)
DPP-IV inhibitor	16 (27.6)	4 (11.4)	28 (12.6)	13 (25.0)	4 (13.3)	24 (14.0)
Thiazolidinedione	1 (1.7)	3 (8.6)	1 (0.5)	1 (1.9)	3 (10.0)	1 (0.6)
GLP-1 receptor agonist	9 (15.5)	7 (20.0)	11 (5.0)	9 (17.3)	6 (20.0)	11 (6.4)
Long-acting insulin	23 (39.7)	20 (57.1)	95 (42.8)	21 (40.4)	18 (60.0)	72 (42.1)
Immediate-acting insulin	1 (1.7)	0 (0.0)	35 (15.8)	1 (1.9)	0 (0.0)	26 (15.2)

Short-acting insulin	0 (0.0)	0 (0.0)	18 (8.1)	0 (0.0)	0 (0.0)	15 (8.8)
Rapid-acting insulin	11 (19.0)	11 (31.4)	90 (40.5)	10 (19.2)	10 (33.3)	65 (38.0)
Mixed insulin	3 (5.2)	1 (2.9)	62 (27.9)	3 (5.8)	1 (3.3)	47 (27.5)
Insulin pump	0 (0.0)	2 (5.7)	11 (5.0)	0 (0.0)	1 (3.3)	9 (5.3)
Any insulin therapy, n (%)	26 (44.8)	24 (68.6)	205 (92.3)	24 (46.2)	20 (66.7)	155 (90.6)
Daily dose of basal insulin, mean units (SD)	50.4 (49.6)	43.7 (25.0)	63.4 (45.0)	50.7 (50.9)	45.3 (26.5)	63.6 (44.8)
Daily dose of bolus insulin, mean units (SD)	30.4 (19.4)	40.2 (24.7)	38.0 (30.4)	30.0 (20.2)	40.4 (26.6)	40.7 (32.3)
Total daily insulin dose, mean units (SD)	68.2 (58.0)	65.3 (43.0)	97.7 (68.2)	68.4 (60.5)	69.7 (45.0)	99.9 (68.4)

[a] *Bonferroni-adjusted 95% confidence intervals did not overlap for body mass index for patients with post-implementation A1c groups RPh2 (27.7, 33.0) and MD (33.2, 36.1).A1c = hemoglobin A1c; DPP-IV = dipeptidyl peptidase 4; GLP-1 = glucagon-like peptide-1; MD1 = patients with 1 physician-driven encounter; RPh1/2 = patients with 1 or 2pharmacist-driven encounters; SD = standard deviation; SGLT2 = sodium-glucose cotransporter 2.*

The number of pharmacological interventions made during proCGM interpretation encounters was 1.33 for RPh1 patients,1.63 for RPh2 patients at the first encounter and 1.34 at the second encounter, and 1.17 for MD1 (Figure 2). Insulin was the medication class most commonly changed, diet was the most common lifestyle intervention, and hypoglycemia management was the most common patient education provided (Table 3). Further information can be found in Appendix A (available in online article). The percentage of patients experiencing any intervention was 93.1%, 100%, and 94.1% for RPh1,RPh2 (combined for both encounters), and MD1, respectively (Appendix B, available in online article). The percentage with pharmacological interventions was 70.7%, 97.1%, and 89.6%, respectively, most of which represented increases in medication use.

Table 2. Mean Decrease in Post-Implementation Hemoglobin A1c (n = 253)

	Baseline A1c, Mean % (SD)	**Post-implementation A1c, Mean % (SD)**	**Mean % Decrease in A1c (95% CI)**	**t-Statistic (df)**	***P* value**
Unadjusted analysis					
Baseline comparison by group					
cRPh (n = 82)	8.5 (1.5)	7.5 (1.2)	1.1 (0.8-1.4)	7.35 (250)	<0.001
RPh1 (n= 52)	8.4 (1.4)	7.4 (1.3)	1.0 (0.6-1.3)	5.17 (250)	<0.001
RPh2 (n=30)	8.8 (1.6)	7.5 (1.1)	1.3 (0.8-1.8)	5.30 (250)	<0.001
MDI (n= 171)	9.1 (1.6)	8.5 (1.7)	0.6 (0.4-0.8)	5.39 (250)	<0.001
Comparison between groups					
cRPH-MDI			0.6 (0.2-0.9)	3.13 (250)	0.002

RPH2-MDI	0.8 (0.2-1.3)	2.81 (250)	0.005
RPh1-MDI	0.4 (0.0-0.8)	1.93 (250)	0.054
RPh2-RPh1	0.3 (-0.3-0.9	1.09 (250)	0.277
Adjusted for and stratified by insulin use			
Baseline comparison by group			
All patients with post-implementation A1c (n= 253)			
cRPh (n= 82)	1.3 (1.0-1.6)	9.10 (248)	<0.001
RPh1 (n=52)	1.1 (0.8-1.3)	6.68 (248)	<0.001
RPh2 (n=30)	1.4 (1.0-1.9)	6.32 (248)	<0.001
MDI (n= 171)	0.7 (0.5-1.0)	5.63 (248)	<0.001
Patients treated with insulin therapy (n = 199)			
cRPh (n = 44)	1.2 (0.8-1.6)	5.84 (246)	<0.001
RPh1 (n= 24)	0.8 (0.3-1.3)	3.12 (246)	0.002
RPh2 (n =20)	1.6 (1.0-2.1)	5.75 (246)	<0.001
MDI (n =155)	0.4 (0.2-0.6)	4.17 (246)	<0.001
Patients not treated with insulin therapy (n= 54)			
cRPh (n=38)	1.2 (0.8-1.5_	5.29 (246)	<0.001
RPh1 (n= 28)	1.5 (1.0-2.0)	6.46 (246)	<0.001
RPh2 (n=10)	0.9 (0.1-1.7)	2.34 (246)	0.020
MDI (n=16)	0.4 (0.2-0.6)	4.39 (246)	<0.001
Comparison between groups			
All patients with post-implementation A1c (n = 253)			
cRPh-MDI	0.6 (0.2-0.9)	3.14 (248)	0.002
RPh2-MDI	0.7 (0.2-1.2)	2.90 (248)	0.004
RPh1-MDI	0.4 (0.0-0.9)	2.02 (248)	0.045
RPh2-RPh1	0.3 (-0.03-0.8)	0.99 (248)	0.323
Patients treated with insulin therapy (n = 199)			
cRPh-MDI	0.7 (0.3-1.1)	3.08 (246)	0.002
RPh2-MDI	1.1 (0.6-1.7)	4.00 (246)	<0.001
RPh1-MDI	0.4 (-0.2-0.9)	1.37 (246)	0.171
RPh2-RPh1	0.8 (0.1-1.5)	2.14 (246)	0.034
Patients not treated with insulin therapy (n = 54)			
cRPh-MDI	-0.1 (-0.9-0.6)	-0.34 (246)	0.732
RPh2-MDI	-0.4 (-1.4-0.5)	0.87 (246)	0.383
RPh1-MDI	0.2 (-0.6-0.9)	0.44 (246)	0.660
RPh2-RPh1	-0.6 (-1.5-0.3)	-1.34 (246)	0.182
Insulin use			
Not treated-treated	0.5 (0.1-1.0)	2.49 (248)	0.010

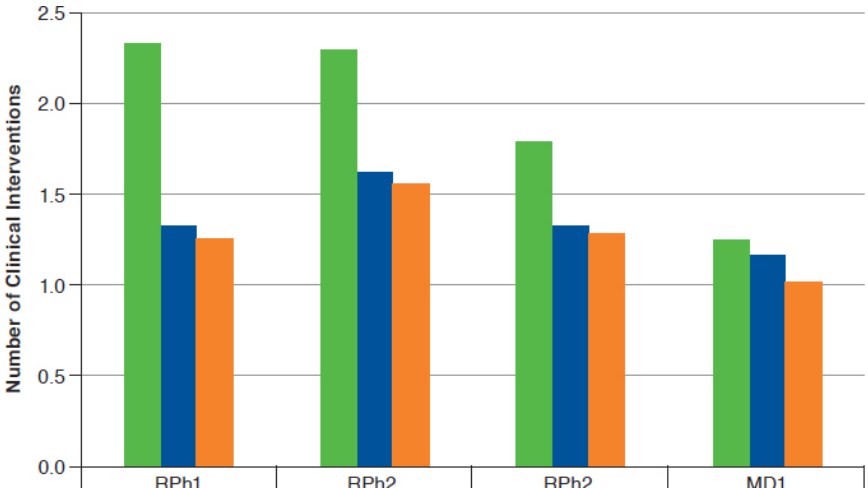
A1c = hemoglobin A1c; CI = confidence interval; cRPh = combined RPh1 and RPh2; df = degrees of freedom; MD1 = patients with 1 physician-driven encounter;RPh1/2 = patients with 1 or 2 pharmacist-driven encounters; SD = standard deviation.

Discussion

In this retrospective cohort study, patients undergoing pharmacist-driven and physician-driven proCGM implementation experienced A1c reductions from baseline that were both clinically and statistically significant. Additionally, both unadjusted and adjusted analyses yielded statistically significantly greater reductions in the cRPh and RPh2 cohorts compared with physician-driven proCGM implementation. As the MD1 cohort typically had results and interventions relayed via phone, results of this study raise the question of whether improved outcomes were because of the difference in the health care practitioner providing this service or the communication method. Furthermore, 34.7% of MD1 patients had hypoglycemia or intent of deprescribing documented as an indication for proCGM use compared with 12.1% for the RPh1 cohort and 17.1% for RPh2, which could have impacted the resultantA1c changes seen between groups. Lastly, the average number of diabetes-related encounters per patient after proCGM implementation during the 6-month follow-up period was 2.6for RPh1 patients, 2.5 for RPh2, and 1.8 for MD1, suggesting that additional encounters and clinical interventions varied between groups and could have affected results.

While the cRPh and RPh2 cohorts had greater A1c reduction compared with MD1 in both unadjusted and adjusted analyses, the reduction seen in the RPh1 cohort was only statistically significantly better than MD1 when adjusted for insulin therapy at baseline. The lack of difference in the unadjusted analysis may be interpreted as if the number of proCGM interpretation visits was the determining factor for seeing differences between groups. Alternatively, adjusting for insulin at baseline was an attempt to remove variance from insulin use and better determine factors that do have an effect. As such, the adjusted analysis suggests that pharmacist-driven proCGM implementation is more effective at improving A1c, even with the same number of encounters for CGM data interpretation.

Figure 2. Mean Number of Overall Interventions, Pharmacological Interventions, and Medication Classes Changed, Analyzed for All Patients Included in the Study for Each proCGM Interpretation Encounter (n = 315)



	RPh1	RPh2, First Encounter	RPh2, Second Encounter	MD1
All interventions (pharmacological and nonpharmacological)	2.34	2.31	1.80	1.25
Pharmacological interventions	1.33	1.63	1.34	1.17
Medication classes changed	1.26	1.57	1.29	1.02

MD1 = patients with 1 physician-driven encounter; proCGM = professional continuous glucose monitoring; RPh1/2 = patients with 1 or 2 pharmacist-driven encounters.

Although the baseline comparison of A1c reduction achieved for the RPh2 cohort was greater than RPh1, the difference between groups was statistically significant only in the sub-population of patients treated with insulin at baseline. A potential reason this difference is limited to the insulin-treated population is that the additional encounter in the RPh2 cohort allowed for more fine-tuning of insulin therapy that may not be necessary or as impactful for noninsulin treatment options. Aside from directly comparing RPh2 to RPh1, it is noted that unadjusted analyses revealed that RPh2 but not RPh1 patients had a statistically significantly greater A1c reduction compared with MD1. While these data suggest that the clinical methods used for RPh2 patients were more effective at loweringA1c than those for RPh1 for patients with insulin-dependent diabetes, a larger sample size is needed to further investigate whether a second office visit to interpret proCGM data is a cost-effective use of resources to improve diabetes outcomes. As seen in Appendix B, only 88.6% of RPh2 patients experienced any intervention at the second encounter compared with 93.1%for RPh1, 97.1% for RPh2 first encounter, and 94.1% for MD1.Still, more RPh2 patients experienced a pharmacological intervention at the second encounter compared with the number of pharmacological interventions at the first and only encounter for RPh1 patients (77.1% and 70.7%, respectively).

More clinical interventions were made through pharma-cist-driven than physician-driven proCGM implementation, though it is possible the communication method for the MD1interventions led to fewer interventions because of potential communication issues with messages being relayed via phone. Insulin was by far the most common type of medication changed, and interventions to increase medication use were more common than those to decrease medication use, which could be expected with the inclusion criteria of baseline A1cof at least 7%. Data suggest an association between increased number of pharmacological interventions and greater A1c lowering across the 3 study groups.

Only 1 published study investigating the implementation of proCGM by clinical pharmacists was found. In this pre-/post-interventional study of 29 patients by Van Dril and Schumacher (2019), pharmacist-driven proCGM did not reveal a statistically significantly lower A1c compared with baseline.13 The authors noted that while not powered to detect a statistically significant difference, the observed 0.7% reduction in A1c was a “substan-tial improvement.” A total of 54 pharmacological interventions were made across the 29 patients, averaging 1.86 interventions per patient. When compared with Van Dril and Schumacher, a greater decrease in mean A1c from baseline was observed in the current study, which did achieve statistical significance. A greater total number of pharmacological interventions was made in the RPh2 cohort (2.97 interventions for both encounters), but not for a single encounter for RPh2 or RPh1 patients. This study addresses a limitation acknowledged by Van Driland Schumacher of lack of control group by comparing to physician-driven proCGM implementation. Demographics varied between the 2 studies, with the study by Van Dril and Schumacher consisting of mostly African American patients compared with the predominantly white population of the current study. The results of the current study build upon the limited literature in this area by expanding the sample size and patient population while comparing pharmacist-driven to physician-driven implementation.

Table 3. Prevalence of Clinical Interventions Made During proCGM Interpretation Encounters (n = 315)

	RPh1 (n=58)	RPh2 at First Encounter (n=35)	RPh2 at Second Encounter (n =35)	MDI (n=222)
Medication changes, n (%)				
Biguanide	10 (17.2)	5 (14.3)	3 (8.6)	0 (0.0)
Sulfonylurea	8 (13.8)	6 (17.1)	3 (8.6)	6 (2.7)
SGLT2 inhibitor	8 (13.8)	3 (8.6)	7 (20.0)	0 (0.0)
DPP-IV inhibitor	7 (12.1)	3 (8.6)	1 (2.9)	1 (0.5)
Thiazolidinedione	1 (1.7)	3 (8.6)	0 (0.0)	0 (0.0)
GLP-1 receptor agonist	12 (20.7)	3 (8.6)	4 (11.4)	0 (0.0)
Long-acting insulin	18 (31.0)	19 (54.3)	17 (48.6)	57 (25.7)
Intermediate-acting insulin	0 (0.0)	0 (0.0)	0 (0.))	28 (12.6)
Short-acting insulin	0 (0.0)	0 (0.0)	0 (0.0)	6 (2.7)
Rapid-acting insulin	7 (12.1)	11 (31.4)	8 (22.9)	59 (26.6)
Mixed insulin	2 (3.4)	1 (2.9)	0 (0.0)	59 (26.6)
Insulin pump	0 (0.0)	1 (2.9)	2 (5.7)	11 (5.0)
Lifestyle interventions, n (%)				
Diet	26 (44.8)	15 (42.9)	9 (25.7)	16 (7.2)
Exercise	8 (13.8)	2 (5.7)	1 (2.9)	1 (0.5)
Weight loss	6 (10.3)	0 (0.0)	0 (0.0)	0 (0.0)
Patient education, n (%)				
Hypoglycemia management	11 (19.0)	5 (14.3)	4 (11.4)	1 (0.5)
Medication administration	4 (6.9)	0 (0.0)	1 (2.9)	0 (0.0)
Medication adherence	4 (6.9)	2 (5.7)	1 (2.9)	1 (0.5)

Note: Medication changes included any of the following: initiation, discontinuation, increase or decrease in dosage, change of formulation or delivery, or shift in administration time.
DPP-IV = dipeptidyl peptidase 4; GLP-1 = glucagon-like peptide-1; MD1 = patients with 1 physician-driven encounter; proCGM = professional continuous glucose monitoring; RPh1/2 = patients with 1 or 2 pharmacist-driven encounters; SGLT2 = sodium-glucose cotransporter 2.

In addition to highlighting the pharmacist's role in implementing proCGM technology, this study also adds to the literature by including patients not using insulin at baseline to manage diabetes. While some data exist exploring the use of real-time CGM in patients on noninsulin therapy, literature on proCGM and intermittently scanning CGM for patients with noninsulin-dependent diabetes is lacking.[7,16] Although only approximately one fifth of study patients were not treated with insulin therapy at baseline, this study showed benefit of proCGM use in noninsulin-dependent patients across all study groups. Furthermore, patients not treated with

insulin experienced even greater A1c lowering than those on insulin therapy at baseline. While duration of disease was not evaluated in this study, the aforementioned finding may be because of patients having early disease, less insulin resistance, and more room for clinical intervention and effect. Nonetheless, this study demonstrates that the use of proCGM technology can span the spectrum of diabetes care and that glucose data obtained from proCGM use in patients not treated with insulin may present an opportunity to guide clinical decisions regarding initiating and titrating medications and determining if and when insulin therapy should be introduced. Moreover, since Medicare requires patients to be insulin-dependent with 3 or more insulin injections per day for coverage of perCGM, proCGM allows patients who may not otherwise be eligible for this technology to benefit from the advances of CGM through professional-use devices.

Although not a focus of this article, it is important to acknowledge that the use of proCGM provides an avenue for pharmacists to bill for their services and generate revenue. The study by Van Dril and Schumacher cited above found that the mean payment was $126.87 for use of CPT code 95250 and $39.17 for 95251 (2017).[13] The reimbursement potential combined with improved clinical outcomes demonstrates the benefit of pharmacist-driven proCGM implementation in improving patient care while promoting clinical pharmacy services.

By allowing pharmacists to participate in diabetes management with the use of proCGM technology, several of the goals of managed care can be achieved. Specifically, improved clinical outcomes were observed via decreases in A1c for patients seen by pharmacists. There is the potential for cost savings for patients and the health care system overall, as these improved clinical outcomes may lead to fewer hospitalizations and emergency room visits as well as the prevention or delay of advanced diabetes-related complications. Lastly, quality and accessibility of health care are achieved because pharmacists may be more accessible to patients to have face-to-face encounters as opposed to phone interventions.

Limitations

There are several limitations present in this study. The retrospective nature makes it susceptible to inconsistencies in clinical procedures or documentation of interventions, as well as potential bias and confounding based on patient inclusion in1 study group versus another. The single-center design may limit generalizability as only a small number of practitioners were compared within 1 facility. The patient population included in this study may also affect generalizability, as patients were mostly white, whereas, the highest prevalence of diabetes is seen in the American Indian/Alaska Native, Hispanic, and non-Hispanic black populations.[17] Additionally, other variables besides the health care professional providing the service may have affected the results of this study, such as the potential for longer or more frequent encounters for cRPh patients compared with MD1 patients, including differences in the number of diabetes-related follow-up encounters after proCGM implementation. The type of encounter also has the potential to affect the results, as communicating results via phone in the MD1 group may have affected patients' understanding of their results and the perceived importance of the recommended interventions. Furthermore, there is potential bias in that more patients in the MD1 group had a documented indication for proCGM implementation of hypoglycemia or deprescribing than RPh1 or RPh2 patients.

Future Directions

Several needs still exist in the realm of CGM research. A well-designed prospective multicenter trial could improve generalizability and internal validity. A prospective study with pharmacists relaying proCGM results and interventions via phone may help answer the question of whether improved A1cas seen in this study was because of the type of practitioner or communication method. This could also be addressed by having physicians provide office visits to interpret proCGM data and make interventions. As this study did not reach statistical significance when directly comparing RPh1 to RPh2for all patients, further research should be done to determine if a 2-step pharmacist-driven proCGM implementation leads to better outcomes and additional meaningful interventions compared with a 1-step pharmacist-driven proCGM implementation. While this study uncovered interesting patterns in insulin-treated versus nontreated patients, additional studies are needed to further elucidate the role of proCGM in patients not treated with insulin. Lastly, as this study excluded patients with baseline A1c below 7%, future studies could explore the pharmacist's role in using proCGM technology to deprescribe medications and reduce hypoglycemia in patients with baseline A1c less than 7%.

Conclusions

Despite recent major advances in CGM technology, literature on the optimal implementation method of these devices is lacking. This study demonstrated that pharmacist-driven implementation of proCGM with 2 planned in-person follow-up visits was associated with greater reductions in A1c and more clinical interventions compared with physician-driven implementation with 1 follow-up encounter via phone. This study also showed that patients not treated with insulin therapy can benefit from proCGM use. As the role of the clinical pharmacist continues to expand, proCGM affords an opportunity for pharmacists to contribute to high levels of patient care while improving diabetes outcomes.

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Appendix A. Raw Number of Medication Changes by Class and Study Cohort (n=315)

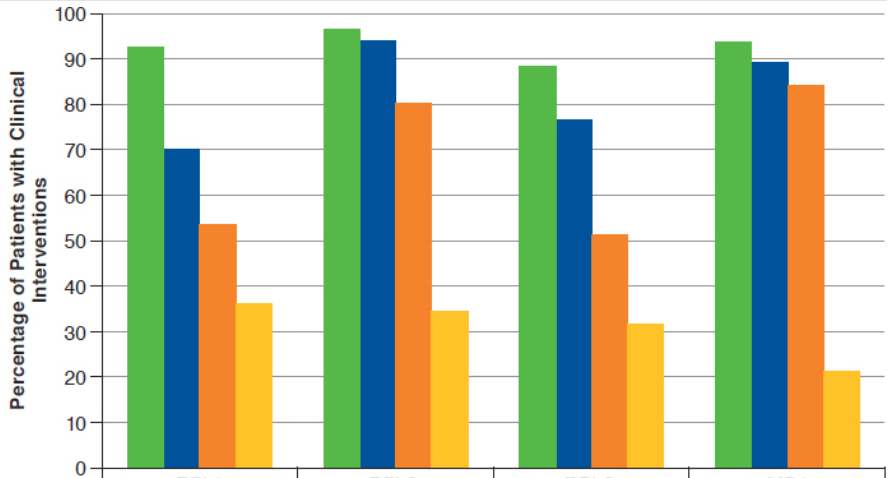
	RPh1 (n = 58)	RPh2 at First Encounter (n = 35)	RPh2 at Second Encounter (n=35)	MDI (n = 222)
Biguanide				
Initiation	3	0	0	0
Increase dosage	0	3	2	0
Discontinuation	2	0	0	0
Decrease Dosage	3	0	0	0
Sulfonylurea				
Initiation	0	3	0	1
Increase dosage	2	1	0	5
Discontinuation	4	2	0	0
Decrease dosage	1	0	2	0
SGLT2 inhibitor				
Initiation	7	2	3	0
Increase dosage	0	1	3	0
Discontinuation	1	0	0	0
Decrease dosage	0	0	0	0
DPP-IV inhibitor				
Initiation	0	0	0	1
Increase dosage	0	0	1	0
Discontinuation	0	3	0	0
Decrease dosage	0	0	0	0
Thiazolidinedione				
Initiation	0	0	0	0
Increase dosage	0	0	0	0
Discontinuation	0	3	0	

	RPh1 (n= 58)	RPh2 at First Encounter (n= 35)	Rh2 at Second Encounter (n=35)	MDI (n=222)
Long-acting insulin				
Initiation	3	3	0	0
Increase dosage	8	11	9	47
Discontinuation	0	0	1	0
Decrease dosage	5	5	6	14
Intermediate-acting insulin				
Initiation	0	0	0	0
Increase dosage	0	0	0	24
Discontinuation	0	0	0	1
Decrease dosage	0	0	0	12
Short-acting insulin				
Initiation	0	0	0	0
Increase dosage	0	0	0	5
Discontinuation	0	0	0	0
Decrease dosage	0	0	0	1
Rapid-acting insulin				
Initiation	1	2	0	1
Increase dosage	2	7	4	52
Discontinuation	1	2	0	1
Decrease dosage	0	1	5	5
Mixed insulin				
Initiation	0	0	0	2
Increase dosage	0	0	0	57
Discontinuation	2	1	0	1

Decrease dosage	1	0	0	0	Decrease dosage	0	0	0	13
GLP-1 receptor agonist					**Insulin pump**				
Initiation	12	2	3	0	Initiation	0	0	0	0
Increase dosage	0	0	0	0	Increase dosage	0	1	0	11
Discontinuation	0	0	1	0	Discontinuation	0	0	0	0
Decrease dosage	0	1	0	0	Decrease dosage	0	0	0	2

DPP-IV = dipeptidyl peptidase 4; GLP-1 = glucagon-like peptide-1; MD1 = patients with 1 physician-driven encounter; proCGM = professional continuous glucose monitoring; RPh1/2 = patients with 1 or 2 pharmacist-driven encounters; SGLT2 = sodium-glucose cotransporter 2.

Appendix B. Percentage of Patients with Any Intervention, Pharmacological Intervention, Increase in Medication Use, and Decrease in Medication Use, Analyzed for All Patients Included in the Study for Each proCGM Interpretation Encounter (n = 315)



	RPh1	RPh2, First Encounter	RPh2, Second Encounter	MD1
Any intervention	93.1	97.1	88.6	94.1
Pharmacological intervention	70.7	94.3	77.1	89.6
Increase in medication use	53.4	80.0	51.4	84.7
Decrease in medication use	36.2	34.3	31.4	21.2

MD1 = patients with 1 physician-driven encounter; proCGM = professional continuous glucose monitoring; RPh1/2 = patients with 1 or 2 pharmacist-driven encounters.