Interprofessional Continuous Glucose Monitoring for Underserved Adults with Type 2 Diabetes on Insulin or Secretagogues

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Abstract
***Background**: Literature describing continuous glucose monitoring for underserved patients, including those with type 2 diabetes or at risk for hypoglycemia, is lacking. **Methods**: An interprofessional internal medicine residency team implemented a blinded CGM service for underserved adults with type 2 diabetes with at-goal glycated hemoglobin (A1C) taking insulin or secretagogues. **Results**: The 2-week blinded CGM service (N=44) significantly reduced time in hypoglycemia (<70 mg/dL) by 4.1% (P=0.0038). Time-in-target-range increased significantly (4.31%, P=0.025). Body weight, number of medications, and daily insulin dose decreased significantly. Overall, A1C remained stable, indicating no worsening of diabetes control associated with the service. **Conclusions**: The interprofessional blinded CGM service influenced improved glycemic control in this vulnerable population.*

Keywords: continuous glucose monitoring, healthcare disparities, hypoglycemia risk, interprofessional patient care, type 2 diabetes, underserved patients

Introduction

Glycated hemoglobin (A1C) is essential for evaluating glycemic control and has a strong predictive value for diabetes complications.[1] In some cases, incorporating other glycemic measurement tools may be necessary due to A1C limitations. Since A1C conveys average blood glucose over 3 months, glycemic variability, intra- or inter-day glucose variations, and the confounding impact of some conditions (e.g. anemia, pregnancy) may lead to discrepancies between A1C and true mean glycemia.[1,2]

Continuous glucose monitoring (CGM) uses interstitial levels to promote diabetes monitoring and management precision, facilitating timely and patient-centered therapy decisions.[1] The American Diabetes Association (ADA) Standards of Medical Care provide recommendations supporting use of CGM. Since CGM may not be necessary, appropriate, or accessible for all patients, more research is needed to determine which populations may benefit the most. Overall, more studies have focused on type 1 than type 2 diabetes. Studies primarily involved real-time or intermittently-scanned CGM which provide immediate results to the patient, with fewer studies involving professional CGM which provide retrospective results. Research in patients with hyperglycemia has demonstrated improved A1C, while, in some studies, reducing risk of hypoglycemia. For patients with hypoglycemia, mores studies focused on type 1 than type 2 diabetes, and CGM contributed to less time spent in hypoglycemia, with improved or unaffected A1C.[3] Recent meta-analyses of patients with type 2 diabetes showed A1C improvements in most studies; however, no significant impact on hypoglycemic events was identified.[4,5]

Hypoglycemia is responsible for 1 in 4 adverse drug event-related emergency hospitalizations.[6] Severe hypoglycemia increases risk of falls, accidents, cardiovascular disease, dementia, and death. The risk of hypoglycemia is better-understood in type 1 than type 2 diabetes. Hypoglycemia is one of the most frequent adverse events among patients with type 2 diabetes. However, the risk varies widely and there is no validated method for predicting hypoglycemia risk in type 2 diabetes. Insulin and secretagogues (sulfonylureas or meglitinides) are known to increase the risk of hypoglycemia.[1] Notably, low-income status is an important hypoglycemia risk factor, possibly due to lack of access to resources for safe diabetes management.[7] Low income poses a hypoglycemia risk similar to insulin use and almost double that of high-income patients. This study aims to describe an interprofessional blinded CGM service for underserved adults with type 2 diabetes with at-goal A1C who are taking insulin or secretagogues.

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Methods

Clinical Process

The CGM service was implemented in an interprofessional internal medicine residency primary care clinic serving adult patients regardless of financial or insurance status. Of approximately 2,000 patients, 45% have Medicare, 17% have Medicaid, 19% have commercial insurance, and 20% are uninsured. Approximately 70% of patients are black or African American, 25% are white or Caucasian, 60% are female, and

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40% are male. Income information is only collected for patients without insurance or reporting financial challenges, but it is estimated that more than half of the population has a household income at or below the Federal Poverty Level.

In July 2019, the CGM process (appointments, follow up plans, billing) was developed and implemented by a physician leader, pharmacist, and dietician. The clinic director funded and managed CGM supply inventory. The dietician facilitated initial access to CGM supplies, implemented software, and provided staff education. The pharmacist identified patients meeting study criteria and provided 1-hour staff education on ADA guideline-based medication therapy using a live lecture format. The pharmacist with pharmacy students, or the dietician with dietician students, contacted patients by phone, provided education about the initiative, and offered the CGM service.

All patients were contacted within 1 month. For patients who consented to the CGM service, 3 appointments were scheduled, each visit was spaced one week apart due to the 14-day CGM systems available to the clinic. The first appointment involved CGM placement and education (billing codes: CPT 99211-5 in addition to G95250 for CGM placement); second and third appointments involved data download and therapy changes with education (billing codes: CPT 99211-5 in addition to G95251 for CGM analysis, interpretation, and report).[8] At the third visit, the CGM sensor was removed and patients were offered prescriptions for personal CGM if interested, accessible, and deemed appropriate or necessary by the provider.

At each of the three visits, the dietician, pharmacist, or clinic phlebotomists downloaded CGM data and shared with the physician seeing the patient that day. Patients were asked to bring their home glucose monitor to each visit to compare against CGM data and help correlate findings of hypoglycemia via CGM as well as to encourage adherence with and understanding of SMBG. The dietician or pharmacist implemented therapy changes in collaboration with, or provided recommendations to, attending or resident physicians. The pharmacist managed inventory for diabetes sample medications and assisted with overcoming medication access barriers to support real-time guideline-based[1] therapy changes and allow for evaluation of response to therapy and titration.

Study Design

The research was a single-center, retrospective quasi-experimental study conducted 3 months after implementation of the CGM service. The study was approved by the institutional review board. Inclusion criteria was age 18 years or older, type 2 diabetes, treatment with insulin, secretagogues, or both, A1C < 7% if younger than 65 years, and A1C < 8.5 if 65 years and older. The pharmacist created an electronic medical record report to identify patients using the inclusion criteria. Patients were excluded if they refused or could not be reached by phone, had a home CGM, completed a blinded CGM in the past year indicating no hypoglycemia, or did not complete at least 10 days of CGM to allow enough time to implement and monitor the impact of therapy changes.

The primary outcome is the percentage of time experiencing hypoglycemia (glucose < 70 mg/dL). Secondary outcomes include other CGM data [percentage of time with glucose < 54 mg/dL, percentage of time in target range (70-180 mg/dL),[2] percentage of time > 180 mg/dL, and average glucose]; A1C and body weight prior to and at least 3 months after CGM; CGM-associated medication interventions; number of diabetes medications and total daily insulin units before and at the end of CGM; and adverse effects after CGM associated medication changes. Data was collected using double chart review (one investigator checked the chart review data collected by another investigator for data accuracy). Continuous data was analyzed with paired t-tests using JMP®, Version 15.1.0 (SAS Institute Inc., Cary, NC, 1989-2019).[9] Patient characteristics, hypoglycemia subgroups, interventions, and adverse effects were evaluated using descriptive statistics.

Results

Of 134 patients who were offered the service, 44 completed at least 10 days of CGM (Figure 1), with a mean age of 67.7 years (Table 1). Thirty-one (70.5%) were female; 34 (77.3%) were black or African American; 31 (70.5%) had ≥ 3 hypoglycemia risk factors[1] (Table 2); and 22 (50%) had at least 1 condition influencing lower A1C than expected (e.g. anemia).[2] Prior to CGM, 35 patients (79.5%) were on insulin therapy (22 on basal-only regimens, 12 on basal-bolus, and 1 on bolus-only). Twelve patients (27.3%) were on a secretagogue, three of whom were concomitantly on insulin; 9 of the 12 were on glipizide, 2 were on glimepiride, and 1 was on repaglinide.

The average time in hypoglycemia was significantly reduced from the first week to the second week of CGM [11.1% vs 7.0%, respectively, 95% confidence interval (CI) -6.80 to -1.40, P=0.0038] (Table 3). Twenty-three patients (52.3%) had hypoglycemia > 5% of the time during the first week, compared to 17 (38.6%) during the second week; for hypoglycemia > 10% of the time, there were 21 patients (47.7%) the first week compared to 8 (18.2%) the second week; and patients with hypoglycemia > 25% of the time decreased from 4 (9.1%) the first week to 1 (2.3%) the second week. The average percent of time within target range increased from 72.5% to 76.8% (95% CI 0.58 to 8.03, P=0.025). The A1C did not change significantly (Table 3), but weight decreased by 1.7 kg (P=0.0008).

Out of 86 CGM-related guideline-based[1] medication interventions (Figure 2), 58 interventions occurred during the first week and 28 the second week; 34% involved dose reduction, 26% discontinuation, 19% switching agents, and 21% intensification (12% increased doses, 9% add-on therapy). The average number of diabetes medications per patient decreased from 2.4 to 2.0 (95% CI 0.12 to 0.51, P=0.0019), and average total daily insulin dose decreased from 30 units to 18.3 units

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(95% CI 6.76 to 16.56, P<0.001). Therapy changes were associated with hypoglycemia in 3 patients and acute kidney injury in 1 patient undergoing simultaneous titration of furosemide; all patients recovered without clinical sequelae. No significant time out of target range or CGM-related severe adverse events occurred.

Discussion

Overall, our study adds to the body of literature in some areas where CGM research is lacking as previously described (type 2 diabetes and hypoglycemia risk, underserved patients, professional CGM). Clinically, the CGM service helped to identify a population with hypoglycemia risk who may not have otherwise been identified due to the lack of a standardized evidence-based method to identify patients with type 2 diabetes at risk for hypoglycemic events.[6] In addition to generally serving a population with socioeconomic challenges, we included medications (insulin and secretagogues) and narrowed A1C in our criteria. We also found that most patients were older adults, and older age is known to be a hypoglycemia risk factor. Our CGM service revealed that almost half of patients were experiencing hypoglycemia > 10% of the time.

Although our clinic does not collect income information for all patients, it is estimated that a large proportion of our patients are indigent even though many are insured. Low-income insured patients may go unrecognized as impoverished unless they report financial hardships. Underserved patients have a higher risk of diabetes and related complications including hypoglycemia.[7,10,11] Improving access to services such as CGM can help to minimize disparities for this population and improve outcomes.[12,13] To date, only 1 published CGM study in a low-income population was identified.[14] Adults with type 1 diabetes were included with over 80% reporting that CGM helped to prevent hypoglycemia and improve hypoglycemia management. There was no significant A1C change, which is consistent with ours and previous studies. In our study, CGM revealed a 61.8% relative reduction in the percent of patients experiencing hypoglycemia > 10% of the time, with a 6% relative increase in time within target range.

Professional CGM can be used to identify and address blood glucose patterns or when CGM access is challenging for the patient, but there is a dearth of research exploring its utility.[1] In our experience, professional CGM facilitated safe transition to newer guideline-based treatments which confer cardiovascular, renal, and weight benefits,[1] including glucagon-like peptide 1 agonists and sodium-glucose cotransporter-2 inhibitors, given that insulin and sulfonylureas are the most common therapies added to metformin for type 2 diabetes.[15] Abrupt discontinuation of insulin or secretagogues without monitoring could inadvertently result in hyperglycemia.[16,17] We also felt professional CGM was beneficial for individualizing monitoring plans. Instead of depending on subjective feedback, clinical results were used to guide recommendations for long-term CGM use. Almost half of patients experienced hypoglycemia < 5% of the time and therefore may potentially proceed with SMBG and/or A1C.

Limitations of our study include a small sample size and quasi-experimental, retrospective design, and short timeframe. The study was conducted in a clinic setting and some patients did not wear the CGM for the entire 14 days. This may lead to an underestimate of the full impact. We did not collect SMBG data due to lack of a streamlined standardized process for all health professionals involved. We also did not collect data specific to intra- or inter-day glucose or other variations. Some patients did present with nocturnal hypoglycemia but were unaware. We did not provide free CGM access after the initiative due to lack of funding, but we facilitated access when feasible (e.g. covered by patient's insurance, affordable via cash pay) for patients who were interested or whose provider recommended continuing CGM. We did notify patients they can repeat the professional CGM process again in the future if clinically beneficial. Since the time of this study, the process was implemented to identify patients every 3-6 months. Team members are also free to refer patients based on clinical judgement, and patients can request the service if concerns arise (e.g. symptoms, fluctuating SMBG results).

We also did not track revenue or cost avoidance. In addition to clinic appointment or telehealth billing, it is possible to generate benefits for the health system, as well as the patient, associated with clinical improvements. Examples include reduced emergency department visits and hospitalizations for hypoglycemia, fewer diabetes-related complications, decreased prescription costs due to de-prescribing, increased productivity, quality of life, and satisfaction. From a community pharmacy perspective, CGM can help to identify medication adherence needs and can be incorporated into medication therapy management services to support diabetes management.

In our setting, multidisciplinary collaboration and administrative support enabled successful implementation of this initiative. Patient education provided by a variety of team members may have helped to engage and empower patients. Additionally, the use of CGM provides patients with feedback about their behaviors, indicating the CGM can promote accountability and patient motivation.

Conclusions

The interprofessional blinded CGM service influenced improved glycemic control for underserved adults with type 2 diabetes and at-goal A1Cs who were taking insulin or secretagogues.

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Approved by Institutional Review Board (expedited review)

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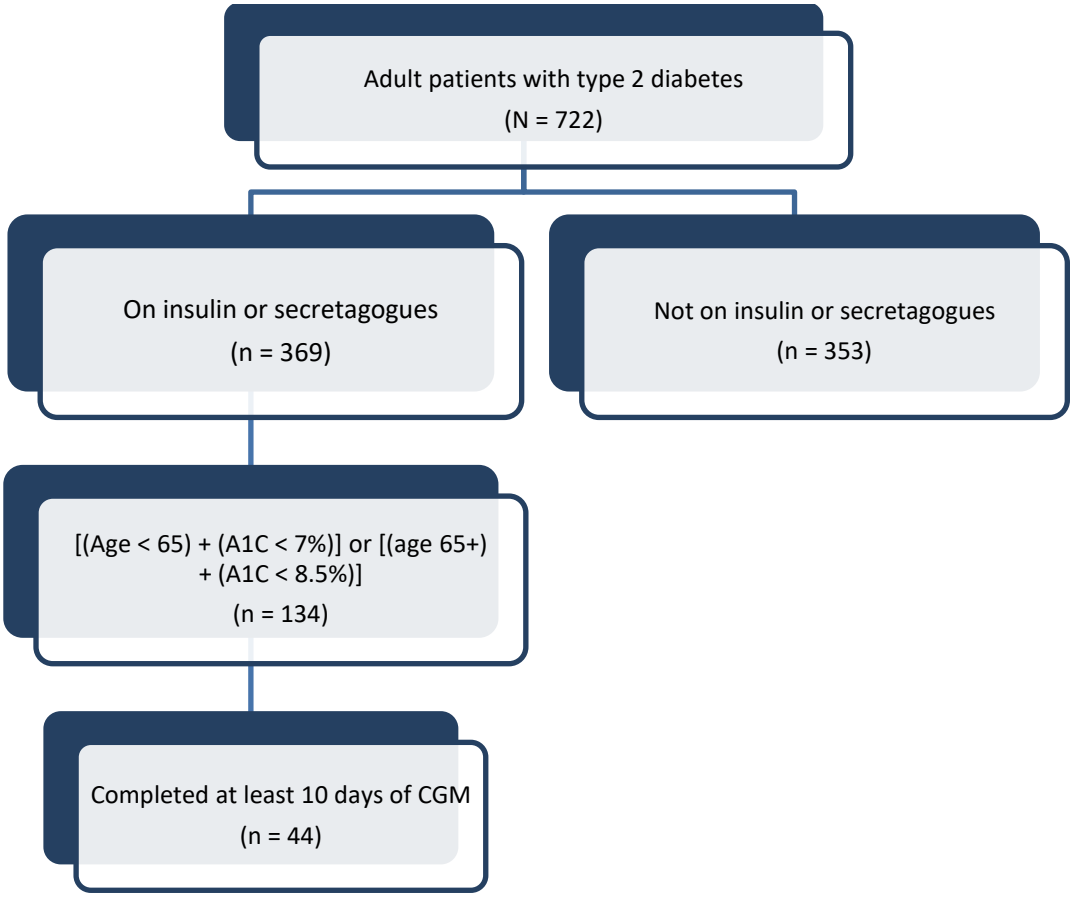
Figure 1. Patient selection for continuous glucose monitoring (CGM) initiative



A1C, glycated hemoglobin

Table 1. Participant characteristics

Characteristic	Quantity
Mean age, years (SD)	67.7 (7.47)
Male, n (%)	13 (29.5)
Female, n (%)	31 (70.5)
Black or African American, n (%)	34 (77.3)
White or Caucasian, n (%)	10 (22.7)
Insulin without secretagogue, n (%)	32 (72.7)
Sulfonylurea without insulin, n (%)	9 (20.5)
Insulin plus sulfonylurea, n (%)	2 (4.5)
Insulin plus meglitinide, n (%)	1 (2.3)
Conditions influencing lower A1C than expected,[2] n (%)	22 (50.0)
Chronic kidney disease (CKD), n (%)	20 (45.5)
Anemia, n (%)	12 (27.3)
CKD plus anemia, n (%)	10 (22.7)
Medicare, n (%)	35 (79.5)
None, n (%)	6 (13.6)
Medicaid, n (%)	2 (4.5)
Commercial, n (%)	1 (2.3)

A1C, glycated hemoglobin

Table 2. Hypoglycemia risk factors[1]

Characteristic	Quantity
Polypharmacy, n (%)	40 (90.9)
Longer duration of diabetes, n (%)	37 (84.1)
Older age, n (%)	33 (75.0)
Chronic kidney disease, n (%)	20 (45.5)
Hypoglycemia unawareness, n (%)	6 (13.6)
Cognitive dysfunction, n (%)	2 (4.5)
Alcohol use, n (%)	2 (4.5)
≥ 3 hypoglycemia risk factors, n (%)	31 (70.5)

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Table 3. Continuous glucose monitoring outcomes (N = 44)

Endpoints	CGM week #1	CGM week #2	P value	Difference, 95% CI
Time with glucose < 70 mg/dL, mean % (SD)	11.1 (12.5)	7.0 (12.9)	0.0038	-4.10, -6.80 to -1.40
Time with glucose < 54 mg/dL, mean % (SD)	4.2 (7.9)	2.9 (10.2)	0.1618	-1.29, -3.13 to 0.54
Time with glucose 70-180 mg/dL, mean % (SD)	72.5 (16.2)	76.8 (18.4)	0.0247	4.31, 0.58 to 8.03
Time with glucose > 180 mg/dL, mean % (SD)	16.3 (17.3)	16.3 (16.8)	0.9808	0.05, -4.30 to 4.41
Overall glucose, mean mg/dL (SD)	125.2 (34.9)	131.0 (28.9)	0.2938	5.83, -5.24 to 16.90
Number of DM medications, mean n (SD)	2.4 (1.0)	2.0 (0.9)	0.0019	-0.32, -0.51 to -0.12
Insulin total daily dose, mean units (SD)	30.0 (28.9)	18.3 (26.5)	<0.001	-11.66, -16.56 to -6.76
	3 months before CGM	**3 months after CGM**		
A1C, mean % (SD)	7.0 (0.8)	7.1 (1.5)	0.5631	0.16, -0.40 to 0.73
Weight, mean kg (SD)	90.4 (21.9)	88.7 (21.5)	0.0008	-1.69, -2.64 to -0.75

CGM, continuous glucose monitoring; CI, confidence interval; DM, diabetes mellitus; A1C, glycated hemoglobin

Figure 2. Description of medication interventions performed during continuous glucose monitoring