Stepping Forward With Real-Time Continuous Glucose Monitoring in the Primary Care Practice

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CONTINUING MEDICAL EDUCATION

CME INFORMATION

CME / CE
Release Dates: 9/15/2022
Expiration Date: 9/15/2023

GOAL STATEMENT

The goal of this activity is that learners will be better able to use real-time CGM (rtCGM) in appropriate patients with type 2 diabetes.

LEARNING OBJECTIVES

Upon completion of this activity, participants will:

Have increased knowledge regarding the
- Data supporting use of rtCGM in practice

Have greater competence related to
- Implementing practical strategies for using rtCGM in practice

TARGET AUDIENCE

This activity is intended for primary care physicians and internal medicine physicians.

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- Research funding from: Dexcom; Merck; Novo Nordisk

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INTRODUCTION

Whose responsibility is it to bring new diabetes technologies and standards of care to patients' attention? From new insulin pumps to continuous glucose monitoring (CGM) devices, a revolution in diabetes technology is happening. In 2022, the American Diabetes Association (ADA) expanded its guideline recommendation on CGM for diabetes management by adults on multiple daily doses of insulin to include adults on once-daily or long-acting insulin.[1] In this interview, Dr. Nicole Ehrhardt, assistant professor of medicine and adult endocrinologist from the University of Washington Diabetes Institute in Seattle, Washington, explores the impact of CGM technology in primary care practices.

Can you briefly describe CGM?

Nicole M. Ehrhardt, MD: CGM involves a small device with a sensor that sits under the skin and, depending on the device, measures interstitial glucose every 1 to 5 minutes. The measurements are sent wirelessly to a smartphone/smart device or a receiver/reader and the patient can view their glucose measurements, the real-time change in glucose, and trends over time. CGM is considered either professional, meaning that the clinic owns the device, or personal, meaning that the patient owns the device.

CGM technology has 2 distinct types: real-time CGM (rtCGM), which continuously captures glucose levels, and intermittently scanned CGM (or flash technology), which captures glucose levels when

a receiver is placed near the sensor. With intermittent CGM technology, glucose data is backfilled as long as the patient scans the sensor every 8 hours. Currently available rtCGM systems include Eversense (implantable CGM), G6, and Guardian Connect. Most recently, Libre 3, which sends glucose readings to a smartphone every 1 minute, was cleared by the FDA. Intermittently scanned CGM systems include FreeStyle Libre 14-day and Libre 2.

How does CGM differ from glycated hemoglobin (HbA1c) and fingerstick glucose measurements?

Dr. Ehrhardt: HbA1c is the 3-month average of a patient's overall glucose. An HbA1c of 7% or lower is the goal for most patients.[2] However, a patient with blood glucose levels of 300 mg/dL during the day and 50 mg/dL overnight could still have an HbA1c of 7% (**FIGURE 1**). Their average blood glucose level would be 150 mg/dL, and their HbA1c

FIGURE 1. Blood Glucose Readings and HbA1c
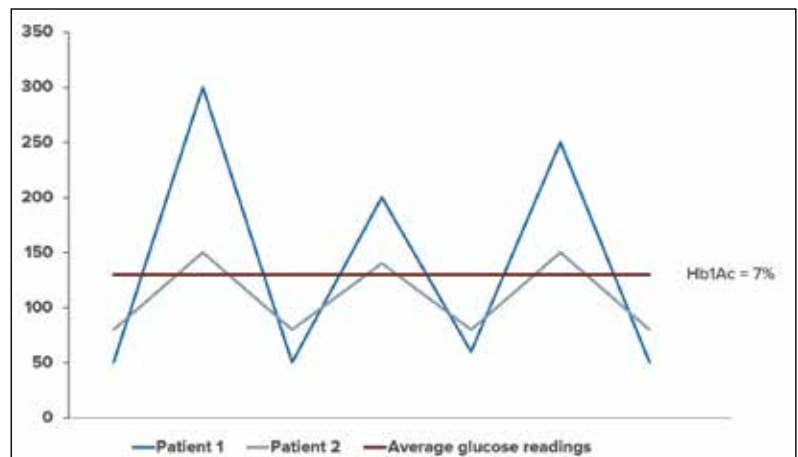
FIGURE 2. Blood Glucose Monitoring and Continuous Glucose Monitoring

● Fingerstick Tests ••••• CGM Readings
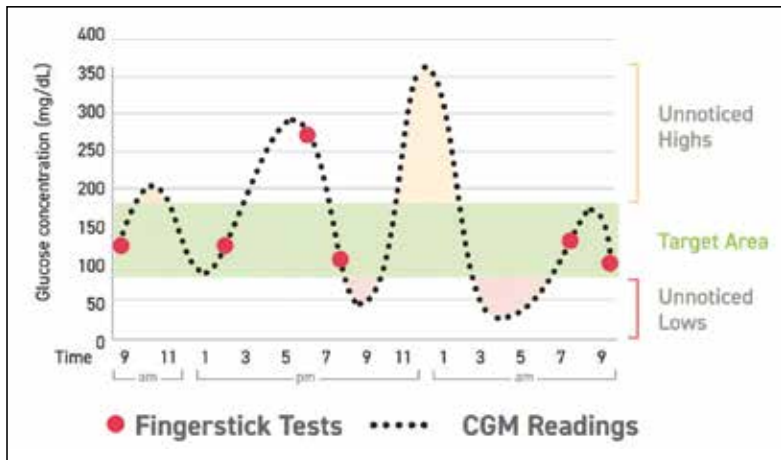
would be at goal, but the patient is spending most of their time either hyperglycemic or hypoglycemic.

Blood glucose monitoring (BGM), using fingersticks, tells the patient their blood glucose level at that exact moment (**FIGURE 2**). While helpful, HbA1c and BGM are snapshots in time, and overall they both lack information about glycemic excursions and glucose variations. CGM provides a more complete picture, showing current directions, predictive directions, and glucose trends over time. Patients can see the impact of food choices, physical activity, and medications on their glucose levels in real-time or after scanning.

In which patients do the guidelines recommend CGM technology as being most useful for managing diabetes?

Dr. Ehrhardt: Previously, the ADA recommended CGM only for patients on intensive insulin therapy, which is 3 or more insulin injections a day. This guidance typically applied to patients with type 1 diabetes (T1D). However, a smaller proportion of patients with type 2 diabetes (T2D) are also treated with multiple daily injection insulin. The DIAMOND T2D study evaluated CGM for diabetes man-

agement in adult patients who had poorly controlled T2D for a median of 17 years and were treated with intensive insulin therapy.[3] Patients were randomly assigned to CGM (n = 79) or usual care (n = 79). The primary outcome was HbA1c reduction at 24 weeks. Mean HbA1c levels decreased to 7.7% in the CGM group vs 8.0% in the control group at 24 weeks; the difference between groups was significant (P = .022). The groups did not differ significantly in CGM-measured hypoglycemia or quality of life outcomes.[3]

This year, the ADA expanded its recommendation on CGM to include patients on less intensive insulin, that is, basal insulin. What does this mean for patients with T2D?

Dr. Ehrhardt: Approximately 30% of patients with T2D in the United States are treated with insulin, with about two-thirds using basal insulin without prandial insulin.[4] Ultimately, with the guideline expansion,[1] more patients with T2D on insulin are recommended to use CGM to help manage their diabetes. But, notably, the American Association of Clinical Endocrinology (AACE) and the Endocrine Society have included patients with T2D who are treated with basal insulin in their recommendations since 2021 and 2018, respectively (**TABLE 1**). Medicare also eliminated the 4-time daily fingerstick requirement to qualify for coverage of a CGM in 2021, making this technology increasingly accessible for patients with diabetes over age 65.

Up until recently, data evaluating the use of CGM in patients with T2D treated with only basal insulin was scarce. What does the evidence say now?

Dr. Ehrhardt: The evidence on CGM use in patients with T2D indicates that the devices can help those on less intensive insulin improve their day-to-day glucose management. In 2012, the first randomized controlled

TABLE 1. CGM Recommendations in Patients With Type 2 Diabetes on Basal Insulin[1,4,5]

ADA 2022	*"Real-time continuous glucose monitoring or intermittently scanned continuous glucose monitoring can be used for diabetes management in adults with diabetes on basal insulin who are capable of using devices safely."*
AACE 2021	*"CGM may be recommended for individuals with T2D who are treated with less intensive insulin therapy."*
Endocrine Society 2018	*"We suggest short-term, intermittent rtCGM use in adult patients with T2DM (not on prandial insulin) who have HbA1c levels >7% and are willing and able to use the device."*

TABLE 2. Mean HbA1c Change From Baseline

Week	SMBG, HbA1c %	Real-time CGM, HbA1c %
12	-0.5	-1.0
24	-0.5	-1.2
38	-0.5	-0.8
52	-0.2	-0.8

trial conducted in this population included 100 patients treated with oral medications, basal insulin, and/or diet and exercise.[6] Fifty patients were randomly assigned to intermittent real-time CGM and 50 patients to self-monitored blood glucose (SMBG) for 12 weeks. All patients were then followed until week 52. For patients with T2D using real-time CGM, HbA1c levels were significantly improved at week 12 and there was sustained improvement, a "legacy" effect without further CGM use for 40 weeks, compared with patients who only used SMBG (P = .04).[6] (**TABLE 2**).

If patients wore the CGM for more than 48 days, they tended to have more initial and persistent HbA1c lowering, hinting that CGM may require time for patients to acclimate to the technology. As the number of diabetes medications or doses of insulin did not increase in the CGM group compared with the SMBG group, it was hypothesized that the improvement was secondary to lifestyle modifications. However, in my opinion, a limitation of the study was that it did not evaluate behavioral and nutritional changes.

But, nearly a decade later, the MOBILE trial—conducted at 15 primary care clinics and in an ethnically diverse population—helped spur the 2022 ADA Standards of Care update.[1,7] The randomized clinical trial, which included 175 patients with T2D on basal insulin without prandial insulin, showed that using real-time CGM significantly reduced HbA1c compared with SMBG over a period of 8 months (-1.1% vs -0.6%, respectively.)[7] The risk-adjusted difference was significant (-0.4%; 95% CI: -0.8%, -0.1%; P = .02). In the Diabetes Control and Complications Trial, this same level of HbA1c improvement was shown to be associated with a more than 40% risk reduction in the progression of retinopathy.[8]

Do you think the MOBILE trial results are generalizable to most primary care practices?
Dr. Ehrhardt: Yes. Patients participating in the study represent the patients living with diabetes that we take care of every day in primary care clinics across the United States. The study included 15 primary care clinics, and approximately half of the study's participants were of a racial or ethnic minority.[7] Now, study participants did have greater contact with clinic staff than they might have typically had as part of usual care. And still, after 8 months HbA1c remained above 8% for one-third of the patients in the real-time CGM group, suggesting that more aggressive approaches to pharmacologic management may have been beneficial.[7]

Results were also published from MOBILE's 6-month extension study. What were the findings?
Dr. Ehrhardt: Compared to the SMBG group, participants in the real-time CGM group spent 3.6 more hours per day in the target glucose range of 70 mg/dL to 180 mg/dL.[9] However, when real-time CGM was discontinued after 8 months of use, approximately 50% of the benefit of real-time CGM on time in range (TIR) was erased. Data were not available to evaluate how quickly the benefit of real-time CGM was lost when the technology was discontinued.[9]

The larger randomized controlled trials investigating real-time CGM have focused on HbA1c and hypoglycemia as endpoints; none have evaluated behavior modification. The MOBILE extension study was underpowered for treatment group comparisons but begot the question of whether long-term continuation of real-time CGM is necessary to sustain the glycemic benefit provided to patients.[9] Or could a greater focus on education coupled with real-time CGM help patients change their behaviors to sustain glycemic improvement after using this technology for a finite time?

In other words, can CGM be used as a behavior modification tool?
Dr. Ehrhardt: Yes. Real-time CGM gives the patient immediate feedback on their food and activity choices, both cornerstones of glycemic management. It does not always mean that patients will choose well, but it does empower them to take an active role in their glycemic control. By coupling education with real-time CGM to support skill development, patients may modify their behavior, for example, by limiting or excluding food choices that cause high blood sugar and increasing their physical activity

in response to rising glucose levels. In the MOBILE trial, patients with a baseline HbA1c of ≥ 10% had a reduction of 2 percentage points in HbA1c with CGM vs a 0.4% decrease with SMBG, despite little change in insulin dose or medication class.[10] This finding suggests behavior modification may have contributed to the reduction in HbA1c in the real-time CGM group.[10] The potential of real-time CGM as a behavior modification tool is worth further investigation in large randomized trials.

Data from CGM devices are compiled into an Ambulatory Glucose Profile (AGP) report. How do these data help support self-management?

Dr. Ehrhardt: The AGP, created by the International Diabetes Center, is an ADA- and AACE-recommended standardized report for retrospective CGM interpretation.[2,4,11,12] The AGP report has 3 distinct sections:
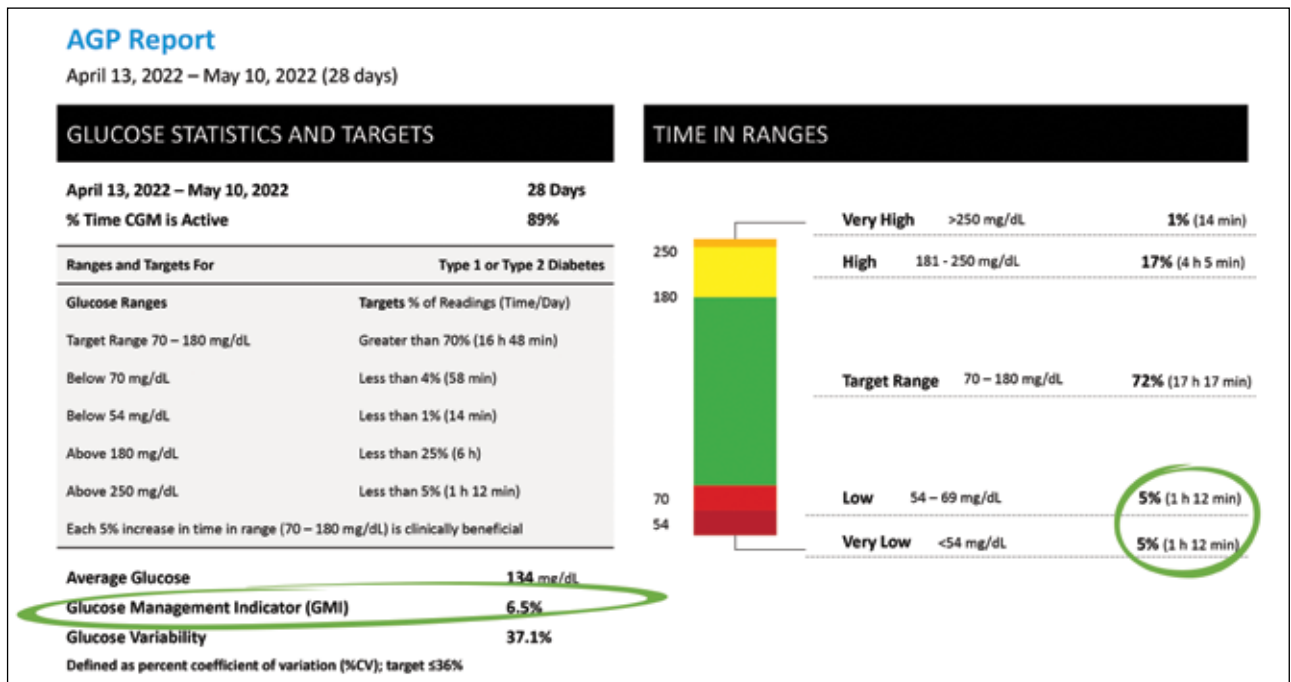
1. Glucose statistics and targets: summarizes glucose values to help assess the overall quality of glucose control.
2. Ambulatory glucose profile: shows variability in the mean glucose and patterned areas of highs and lows.
3. Daily glucose profiles: shows single-day glucose values to help identify patterns and progress.

The first section of an AGP report presents CGM statistics and time above, below, and within the target glucose range (**FIGURE 3**). The glucose measurement indicator (GMI) approximates HbA1c based on the average glucose level from 14 or more days of CGM readings. The goal for most patients with diabetes is to have their glucose levels stay within the target range of 70 to 180 mg/dL for at least 70% of the day, spending less than 5% of their time in hypoglycemia (< 70 mg/dL) and less than 5% of their time with glucose levels greater than 250 mg/dL.[12] Every 10% increase in time in range (TIR) approximates a 0.6% to 0.8% change in HbA1c.[13,14]

When reviewing a patient's AGP report, address their time below range or hypoglycemia first, and then address TIR and hyperglycemia. **FIGURE 3** shows the AGP report of a patient who has a glucose average of 134 mg/dL and GMI of 6.5% but spends 10% of the day in hypoglycemia. This patient would benefit from a care plan different than someone with a glucose average of 134 mg/dL and GMI of 6.5% who spends 1% of the day in hypoglycemia.

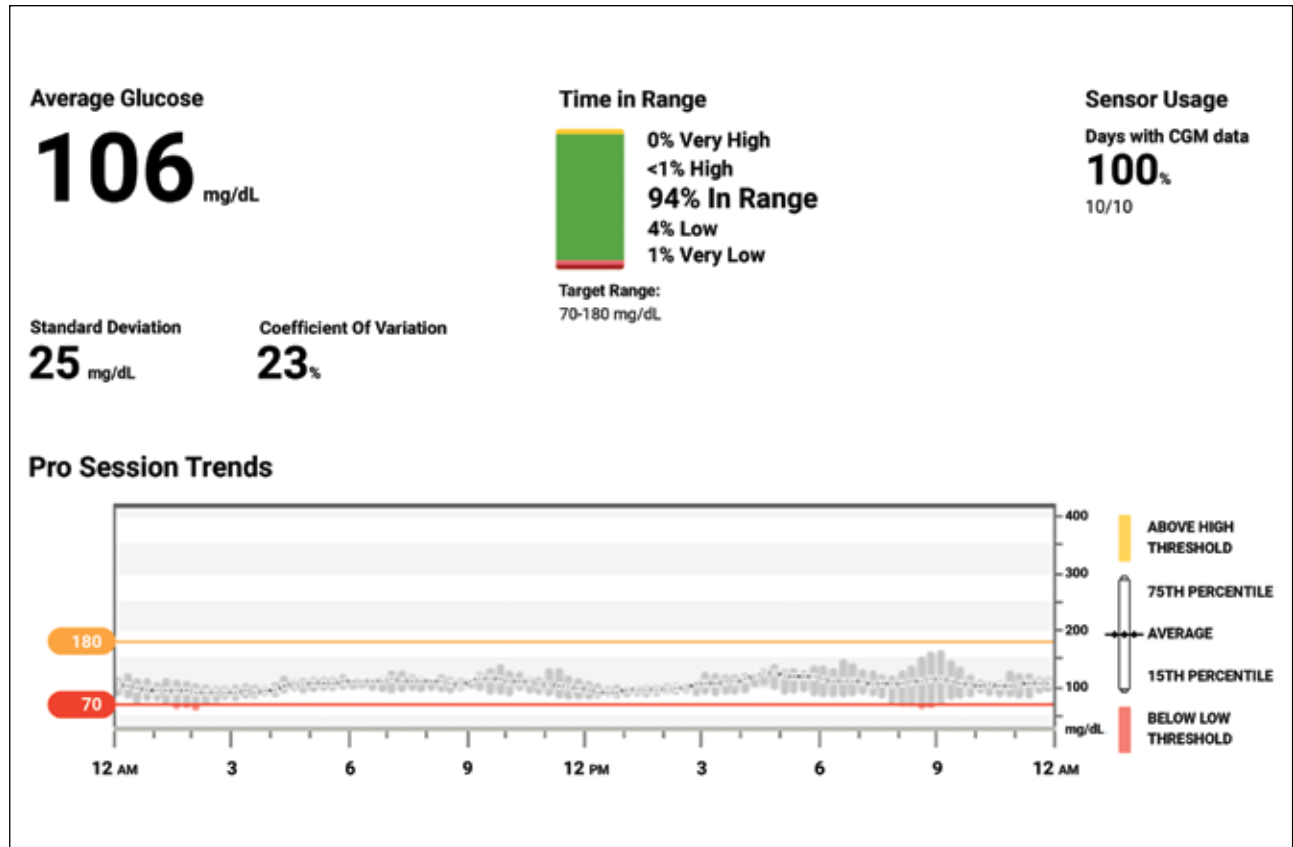There will be clinical scenarios when HbA1c is considerably higher than expected from a patient's average glucose (ie, hemoglobinopathies and hemolytic anemia). In **FIGURE 4**, this particular patient's HbA1c was 8.1% with fasting fingersticks measuring 70 mg/dL to 200

FIGURE 3. Example of a Patient's AGP Report: Glucose Statistics and Targets and Time in Ranges

Source: Image courtesy of Nicole M. Ehrhardt, MD.

FIGURE 4. AGP Report: Ambulatory Glucose Profile

Average Glucose
106 mg/dL

Standard Deviation
25 mg/dL

Coefficient Of Variation
23%

Time in Range
0% Very High
<1% High
94% In Range
4% Low
1% Very Low
Target Range:
70-180 mg/dL

Sensor Usage
Days with CGM data
100%
10/10

Pro Session Trends

ABOVE HIGH THRESHOLD
75TH PERCENTILE
AVERAGE
15TH PERCENTILE
BELOW LOW THRESHOLD

180
70

400 300 200 100 mg/dL

12 AM   3   6   9   12 PM   3   6   9   12 AM

Source: Image courtesy of Nicole M. Ehrhardt, MD.

mg/dL and bedtime glucose measuring 140 mg/dL to 150 mg/dL. Professional CGM was performed and showed a glucose average of 106 mg/dL with 5% of the day spent hypoglycemic. This illumination from CGM helped confirm that this patient's HbA1c was falsely elevated due to iron deficiency.

Collaborative review of glucose statistics, targets, and TIRs help patients determine whether they need to take action to improve glycemic management. A review of the AGP and associated daily views also helps patients determine what actions they need to take.

Would you like to provide any closing comments for your colleagues?

Dr. Ehrhardt: The good thing about technology is every year it gets better and hopefully more cost-effective. More patients can manage their diabetes if they have access to CGM as a resource between clinic visits and if their primary care physicians are adept at helping them to use it. Each CGM manufacturer provides patients with educa-

tion resources through their website, in addition to providing downloadable resources for clinicians to share with patients. ●

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