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A new glucose monitoring option

These new devices allow patients to measure glucose continuously, via a tiny sensor in the skin. Here's how they work, and which patients may benefit from using them.

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PRACTICE RECOMMENDATIONS

› *Practitioners and patients can use continuous glucose monitoring (CGM) data to modify medications and institute lifestyle alterations.* (A)

› *CGM systems must be calibrated with conventional blood glucose monitors to ensure accuracy.* (A)

› *CGM systems can set off an alarm to alert patients to glucose thresholds above and below established norms.* (A)

Strength of recommendation (SOR)

(A) Good-quality patient-oriented evidence

(B) Inconsistent or limited-quality patient-oriented evidence

(C) Consensus, usual practice, opinion, disease-oriented evidence, case series

We all know that the key to optimal diabetes management is tight glucose control, which can be achieved with multiple daily fingersticks, good record keeping of the results, and appropriate modification of the medication regimen, diet, and exercise schedule.

But patients find the routine burdensome, and many skip fingersticks or abandon the process entirely. And even those who follow the program faithfully may find that it fails to protect them from unpleasant and potentially dangerous episodes of hyper- and hypoglycemia.

The newer technology of continuous glucose monitoring systems (CGMS) offers the promise of overcoming these limitations. But how do these new systems work and what does the evidence tell us about their potential benefits and remaining uncertainties? Read on.

The old way: Take a snapshot

The variables that affect blood glucose levels—meals and snacks, exercise or the lack of it, dosages and timing of medication, and stress, among others—keep changing throughout the day and night. The impact of these variables cannot be adequately captured in snapshot blood glucose levels taken at isolated moments in the patient's day. Achieving glycemic control with blood glucose monitors can be difficult for some patients, especially since the data generated are dependent on the patient's willingness and ability to self-monitor his or her glucose levels.

The new way: Monitor continuously

CGMS measure the amount of glucose in the interstitial fluid—not in the blood. These measurements are taken every 5 minutes or so, depending on the system. Each system consists of a sensor, transmitter, and receiver. The sensor is a fine wire—about the diameter of 2 human hairs—that sticks into the skin of the abdomen or upper arm and is kept in place by an adhesive pad. The transmitter fits on the sensor pad and sends information to the receiver via radio waves. Sensors are

Continuous glucose monitoring systems measure the amount of glucose in the interstitial fluid every 5 minutes, throughout the day and night.

disposable; they last for 3 to 5 days and then must be replaced. The system is wireless, so your patient isn't tethered to the equipment.

Calibration with a glucose meter is still necessary. To be sure that interstitial glucose measurements reflect actual blood glucose levels, currently available systems require daily calibration with conventional blood glucose monitors. Patients will still have to do fingersticks, but far less frequently. The FDA has approved CGMS for use only in conjunction with conventional glucose testing. Traditional glucose self-monitoring may also be necessary when CGM results do not correspond to symptoms patients are experiencing.

Receiver displays data, can set off an alarm. Glucose measurements from the CGMS are displayed and stored in the receiver, and the data can be downloaded to a computer using the manufacturer's data software. Continuous readings over a 24-hour period for up to 7 days allow the user to detect variation and identify trends. High and low glucose value thresholds can be customized for the individual patient and fed into the system. When these thresholds are exceeded, an alarm will sound. The receiver displays directional arrows showing the rate of change in glucose levels, allowing the patient to predict—and possibly prevent—hypoglycemic episodes.

Impact of events can be noted. The systems also allow for input of additional information about events that may affect blood glucose levels, such as medication, exercise, and food intake. Patients can use information about how these events affect their glucose levels to adjust the prandial or basal insulin dose, modify the insulin correction algorithm, or adjust their diet. Patients can bring computer-generated charts and graphs to office visits as a basis for joint decision-making about their care. Short-term, periodic use of a CGMS in patients with type 2 diabetes may identify times when patients need more frequent self-testing or guide further therapy selection.

These systems are available now

The systems available in the United States include:

- the iPro Continuous Glucose Monitor, Guardian Real-Time System, and MiniMed Paradigm Real-Time System—all from Medtronic, Inc.
- the SEVEN PLUS, from DexCom
- the FreeStyle Navigator, from Abbott.[1-3]

The SEVEN PLUS and the FreeStyle Navigator are FDA approved for adults only. Pediatric versions of Medtronic's MiniMed Paradigm and Guardian systems are approved for use in patients ages 7 to 17. All these systems require a prescription. For detailed comparisons of the features of these systems, see the **TABLE**.

Patients with severe diabetes benefit most

Patients with type 1 diabetes who use an insulin pump or are being switched from multiple injections to pumps, and patients who have problems with hypoglycemia are good candidates for CGMS. The latter group includes those who are not aware of their hypoglycemic state, those who have nighttime hypoglycemia, and those who experience severe episodes of hypoglycemia. The category also includes patients who keep their blood glucose levels higher than appropriate goals would indicate, because of their fear of hypoglycemia.

An additional group of patients who might benefit, although they do not fit currently approved indications for these devices, are pregnant women who should maintain tight glucose control. Other patients who might find CGMS useful are those with glycemic variability or those who have not achieved their A1C goal and want to be proactive.

Your letter of medical necessity can qualify patients like these for Medicare or private insurance reimbursement for the CGMS and for ongoing sensor supplies. You may also choose to purchase a system yourself for patients to use, and bill the patient's insurance company for the service.

Accuracy continues to be a concern

Currently available systems are more accurate than the first generation of these devices. When glucose is rapidly changing, users need to be aware that there may be a time lag before the interstitial glucose reaches the same level as the blood glucose. So, while medication changes can be made based on CGMS, values should be confirmed with a fingerstick.

JOIN THE DISCUSSION

Do you use continuous glucose monitoring with your patients, and what has your experience been?

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SEVEN and Navigator are comparable

A number of studies have confirmed the accuracy of CGMS.[4-7] A study by Garg and colleagues compared the accuracy of the DexCom SEVEN and the FreeStyle Navigator.[6] Fourteen patients wore sensors from both systems for 3 consecutive, 5-day periods. Laboratory reference measurements of venous blood glucose were taken every 15 minutes through an 8-hour period on days 5, 10, and 15 in clinic using the YSI STAT Plus Glucose Analyzer. Sensors were replaced at the end of the clinic day on days 5 and 10, and the sensors were removed at the end of day 15. The mean absolute relative difference for CGM compared with laboratory glucose measures was 16.8% for the SEVEN and 16.1% for the Navigator (P=.38), an insignificant difference between the 2 systems.

The 2 systems were also compared using continuous glucose error grid analysis, which evaluates how accurately CGM data lead to an appropriate clinical response by the patient. The error grid is divided into 5 zones and superimposed on the correlation plot. Plots in Zone A are a perfect fit and plots in Zone B are "benign error" that does not result in an inaccurate clinical response. The percentage of data points in Zones A or B was 94.8% for the SEVEN and 93.2% for the Navigator. The SEVEN provided better agreement with laboratory glucose measures for the range 40 to 80 mg/dL (P<.001).

Guardian evaluation has similar results

A similar study done by Medtronic in 2004 evaluated the Guardian RT, an earlier version of the Guardian, in 16 patients.[7] Values from the Guardian RT were compared with reference YSI STAT Plus glucose analyzer glucose values taken every 30 minutes in clinic. The mean absolute percent difference was 19.7%±18.4%. Of the 3941 total paired glucose measurements, 96% fell in the clinically acceptable error grid Zones A or B. For low glucose values between 40 and 80 mg/dL, 76.1% of readings fell in Zones A or B; for high values, over 240 mg/dL, 86.8% of readings fell in Zones A or B. Accuracy in the hypoglycemic ranges declined as the time increased from insertion of the sensor.

Safety risks are few, minor

Insertion of the sensor can pose minor safety risks, including infection, inflammation, and

TABLE

Continuous glucose monitoring systems: The options

	SEVEN PLUS	FreeStyle Navigator	Guardian Real-Time System	MiniMed Paradigm Real-Time System	iPro Continuous Glucose Monitor*
Manufacturer	DexCom	Abbott	Medtronic, Inc.	Medtronic, Inc.	Medtronic, Inc.
URL	www.dexcom.com	www.freestyle navigator.com	www.minimed.com	www.minimed.com	www.minimed.com
Price	$799 for system; $399 for 4 sensors; $79 for software	$1250 for system; $450 for 6 sensors	$1350 for system, including 4 sensors; $350 for 10 sensors	$999, plus cost of insulin pump; $35 per sensor	$1090 for start-up; $350 for 10 sensors
Receiver range	5 feet	10 feet	6 feet	6 feet	
Sensor life	Up to 7 days	Up to 5 days	Up to 3 days	Up to 3 days	Up to 3 days
Calibration	2 hours after insertion, then every 12 hours	At least 4 times over a 5-day period at 10, 12, 24, and 72 hours after insertion	2 hours after insertion, again within 6 hours, then every 12 hours	2 hours after insertion, then within next 6 hours, then every 12 hours	
User-set alarm for highs/lows	Yes, plus factory alarm at 55 mg/dL that can't be disabled	Yes	Yes	Yes	
Glucose reading display frequency	Every 5 minutes	Once every minute	Measures every minute, displays an average of every 5 minutes	Measures every minute, displays an average of every 5 minutes	
Displays directional trends	Yes	Yes	Yes	Yes	

Sources: Diabetes Network. Diabetes technology. Available at: www.diabetesnet.com/diabetes_technology/continuous_monitoring.php. Accessed January 6, 2010.
DexCom. Available at: www.dexcom.com. Accessed January 6, 2010.
FreeStyle Navigator. Available at: www.freestylenavigator.com. Accessed January 6, 2010.
Medtronic. Available at: www.minimed.com. Accessed January 6, 2010.
Conversations with Robert Sala, sales representative, DexCom, on May 1 and May 8, 2009.
*iPro consists of sensor and transmitter only; no receiver. Sensor is inserted by provider; data are uploaded in provider's office to help guide therapeutic decision-making.

bleeding. Adverse events reported in 1 study consisted mainly of mild sensor site reactions such as blisters, bullae, edema, and erythema, none of which required treatment.[6] The CGMS must be removed prior to magnetic imaging studies and the devices are not approved for use on airplanes. When the FreeStyle Navigator sensor is removed, a portion of the membrane polymer is left in the skin. The company reports no health effects in clinical studies, aside from sensor site reactions mentioned above, but long-term effects of sensor membrane fragments remaining in the skin are unknown.[8]

CGMS have the potential to reduce diabetic complications

Glycemic fluctuations that occur throughout the day may be an independent risk factor in the development of diabetic complications.[9-11]

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Continuous monitoring that can detect such fluctuations could, potentially, reduce complications, but further studies are needed to determine whether CGMS users actually experience fewer complications. Several studies have shown a relationship between postprandial glucose fluctuations and macrovascular disease.[12-14] An analysis of data from the Diabetes Control and Complications Trial (DCCT) showed that A1C, mean blood glucose, and glycemic variability were independent risk factors for severe hypoglycemia.[15] Reducing glycemic fluctuations may, therefore, reduce the risk of severe hypoglycemia.

CGMS data can change behavior, reduce hypoglycemia. The data a CGMS generates could be used to adjust medications or diet on the basis of real-time glucose levels, identify glucose trends, and aid in pattern management by providing retrospective, nearly continuous glucose values. One study evaluated the benefit of using a CGM in 90 type 1 and type 2 patients receiving insulin.[4] All patients wore the monitor at home and at work during daily activities. Patients were randomized to a control group that was blinded to their glucose data and an experimental group that saw the display readings, could review trends, and received alerts and alarms from the system.

The results showed that the group that saw the display spent 21% less time in a hypoglycemic state and 26% more time in the target glycemic range than the control group. Nocturnal hypoglycemia was also significantly reduced in the group that had access to the display. These improvements were seen even though no prescribed plan to adjust therapy on the basis of glucose readings was in place, and must therefore have been the result of diet or insulin changes patients made on their own initiative in response to their CGM readings. Thus, in this study, providing more frequent glucose readings to patients improved safety of insulin and glycemic control.

Studies have also been done comparing the efficacy of CGM and traditional monitoring systems on hemoglobin A1C.[16] These studies revealed a trend toward lower A1C with the use of CGMS, but the results were not statistically significant (0.22%; 95% confidence interval, -0.439% to 0.004%; *P*=.055).

Crossing the barriers to adoption

Before CGMS can become widespread in the primary care setting, barriers to their adoption must be addressed. Some clinicians continue to be dubious about the accuracy of the readings because CGMS measure interstitial glucose levels, rather than blood glucose. As we have seen, studies have been published that indicate a high level of accuracy for CGM readings, but more research needs to be done.

In the real world of the caregiver's office, physicians and patients will have much to learn before CGMS come into widespread acceptance. Patients and providers both need to learn to use the new equipment and how to apply the data it provides. Physicians and patients will need to take account of the time lag before a CGMS reading catches up with a standard reading, and check with a standard blood glucose meter before making medication adjustments. Patients will need to understand the time to onset and peak of their insulins so that they can make appropriate adjustments.

Providers will have to find ways to incorporate the technology into their already busy clinical practice. Integrating CGMS data into electronic medical records or downloading data before scheduled office visits may streamline the process.

So where does this leave you, the busy family physician?

CGMS can provide useful information to select patients, making it possible for them to alter their diet and lifestyle choices and make better insulin treatment decisions. Although CGMS may not be able to eliminate the need for traditional self-monitoring of blood glucose entirely, using the 2 methods together does offer additional advantages. These new devices may help prevent hypo- and hyperglycemic episodes, improve patients' quality of life, and potentially reduce the likelihood that complications will develop. Long-term studies will be necessary to confirm these potential benefits. JFP

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Glycemic fluctuations may be an independent risk factor in the development of diabetic complications.

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