

Continuous Glucose Monitoring: A Review of Available Systems

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INTRODUCTION

More than 9% of the U.S. population—30.3 million people—currently have diabetes, according to the 2017 National Diabetes Statistics Report by the Centers for Disease Control and Prevention (CDC).¹ More than seven million of those individuals are unaware of their condition and are undiagnosed. Diabetes is generally described as a silent, chronic, and progressive disease, marked by abnormally elevated levels of serum glucose. Type-1 diabetes (T1D) is typically diagnosed and most commonly seen in children and adolescents. It is caused by the immune-mediated destruction of beta cells in the pancreas, which inhibits insulin production. Patients diagnosed with T1D, who account for approximately 5% of people diagnosed with diabetes, typically present with excessive urination, thirst, hunger, weight loss, vision changes, and fatigue. Medical treatment involves the use of the blood-glucose regulating hormone, insulin, and there are no preventive measures.^{1,2}

Type-2 diabetes (T2D) arises from the body's inability to sufficiently respond to and properly utilize insulin, otherwise known as insulin resistance. Risk factors include the following: ≥ 45 years of age, an increased body mass index, poor nutrition, smoking, a history of gestational diabetes, a family history of diabetes, and physical inactivity. Symptoms mirror that of T1D, but are gradual, less severe, and not always present, which makes the condition difficult to diagnose promptly. Patients with T2D can be properly managed through lifestyle interventions (e.g., diet and exercise), pharmacologic interventions (non-insulin and/or insulin medications), and glucose monitoring.^{1,2}

GLUCOSE MONITORING

Diabetes can lead to life-threatening consequences if it is not managed appropriately. Over time, it can cause various macrovascular and microvascular complications (e.g., cardiovascular disease, renal disease, retinopathy, and/or neuropathy), resulting in an overall reduction in blood flow. People with diabetes are twice as likely to develop heart disease or to experience a stroke, and the condition is also the leading cause of renal failure, limb amputations, and adult blindness (retinopathy). In addition, there is a 30–40% increase in prevalence in diabetics who smoke, leading to an even greater risk of heart- and kidney-disease complications. These complications affect patients' overall health and quality of life and increase the risk of mortality by 50%.^{1,2}

To help minimize the progression of diabetes and the potential complications, strict glucose control and monitoring is

recommended for patients. Glucose monitoring can aid in: (1) the proper management of symptoms; (2) evaluating responses to therapy; (3) achieving established glycemic targets; and (4) preventing or delaying the progression of complications in both T1D and T2D. It is recommended that all patients who have diabetes, especially those on around-the-clock insulin regimens, frequently self-monitor their blood glucose at home throughout the day. Self-monitoring of blood glucose (SMBG) is also recommended in certain circumstances postprandially, prior to exercising, when experiencing symptoms of hypoglycemia (and until euglycemia is achieved), and before performing tasks such as driving or operating heavy machinery. By doing so, patients can see a reduction in baseline hemoglobin A_{1c} (HbA_{1c}) and experience fewer disease complications.³ However, SMBG only provides a snapshot of current glucose levels at a specific point in time. Long-term trends in glucose fluctuations as a result of diet, medication therapy, and lifestyle choices are not accurately reflected.

Until recently, most patients with diabetes performed SMBG using a glucose meter, which required intermittent capillary-blood sampling and having various supplies (e.g., test strips, control solutions, and alcohol swabs) to hand. This process can be uncomfortable and burdensome for patients and can lead to nonadherence, thus limiting the potential benefits of SMBG. Continuous glucose monitoring (CGM) is a newer method for assessing glucose levels, with an important role in assessing treatment efficacy and safety in patients with T1D and potentially in selected patients with T2D (e.g., patients on intensive insulin regimens).³

Continuous Glucose Monitoring

Continuous glucose monitoring measures glucose levels in the interstitial fluid as a way to optimize glucose control by keeping levels in their target range for a longer period of time, thereby improving HbA_{1c}. There are various monitors available, and they are the focus of this article. Generally, the monitor itself consists of a sensor that is worn on the body and automatically obtains frequent glucose readings. The data are either manually scanned or wirelessly transmitted to a nearby receiver to display the readings. Patients and their physicians are able to assess patterns in glucose fluctuations, which helps them to make informed decisions about nutrition, physical activity, and medication. However, because of the monitor's cost and uncertainty about how to use and interpret the data, only a small percentage of patients utilize these devices.⁴⁻⁵

If we compare the benefits of continuous glucose monitoring to those of SMBG, the former has the unique ability to automatically measure blood glucose as often as every five

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minutes, which is equivalent to approximately 288 readings daily. Real-time glucose trends are observed, and alerts can be transmitted to patients during times of rising or falling glucose levels, enabling them to make immediate changes to their medication and/or lifestyle habits. It can also give patients a glimpse into what happens when they are sleeping or pre-occupied with other daily activities. There is no more pain from finger-sticks or any need for supplies apart from the sensors. Certain continuous glucose monitors (CGMs) can also be integrated with an insulin pump, which allows the monitor to automatically adjust or pause insulin delivery in response to any significant changes in glucose. The sensors have been known to fail on occasion, however, which is one disadvantage in choosing this type of technology. By contrast, SMBG produces approximately four to seven measurements daily and requires a large commitment from patients to carry out the measurements themselves. Besides often being painful, the procedure is also costly; needles, testing strips, and control solutions must be purchased monthly, in addition to the cost of the monitor itself.⁵

FreeStyle Libre System

Abbott's FreeStyle Libre System is a stand-alone CGM. The system consists of a reader and a sensor kit, which is sold separately. The reader comes fully charged with a USB cable and power adapter, and the sensor kit comes with a sensor applicator and sensor pack, and includes an alcohol wipe and product insert.⁶ The sensor is small—about the size of two quarters together—and is placed on the back of the upper arm. The sensor must then be activated by the reader, which scans it from a distance of one and a half inches. Once activated, it takes 12 hours for the sensor to adjust to the patient's body and produce accurate readings.⁷ Although this is a long period of time before activation, the sensor is then effective for up to 10 days, and no daily calibration is required during that time.⁷ In the warm-up period, patients can use the built-in test-strip port, which utilizes FreeStyle Precision Neo Test Strips to measure glucose levels.⁶

The FreeStyle Libre is approved for use in adults aged 18 years and older. It is one of two CGMs available whose reading remains accurate even with acetaminophen use.⁷ The reader contains visuals, including a trend arrow showing the patient's glucose measures, a trend graph depicting the last eight hours of glucose history, and visual alerts if the glucose reading is rapidly changing. However, unlike the Dexcom monitors, for example, there is no alarm that sounds when glucose levels are too high or too low. Also, the glucose reading is not continuous, like other CGMs; instead, the reader has to scan the sensor in a quick second for an accurate and current glucose reading.

The FreeStyle Libre reader and sensor are currently available with valid prescriptions in the United States, and covered by Medicare for patients who meet certain requirements. The system is available at major retail pharmacies, and the FreeStyle website has a tool for locating the nearest participating pharmacy to a patient's zip code. Without insurance, the out-of-pocket price for the reader (a one-time purchase) ranges from \$84 to \$100, and a one-month supply for a pack of three sensors ranges from \$129 to \$153, depending on the retail pharmacy and its location. A number of insurers cover

FreeStyle Libre monitors and many patients are expected to pay no more than \$75 for one month's supply of the sensors and no more than a one-time cost of \$65 for the reader.⁸ In October 2018, Abbott released a FreeStyle Libre 14-day system that takes only one hour to warm up and a sensor that lasts for up to 14 days. Currently, Abbott is encouraging patients to switch from the 10-day system to the 14-day system, and certain patients are eligible for the new system at no cost.^{7,10}

Dexcom G4 Platinum with Share

Dexcom has released three CGMs, all of which take two hours for the readings to be adjusted and accurate after the sensor has been inserted.⁹ The CGMs are approved for adults and for children from the age of 2 years, which is an advantage over the FreeStyle Libre. Unlike the FreeStyle Libre, Dexcom sensors only last seven days, necessitating the use of an extra sensor or two every month. Dexcom monitors also must be calibrated every 12 hours in the case of mandatory blood glucose levels that are between 40 and 400 mg/dL.⁹ In addition, the Dexcom monitors' range is a lot wider, with an unobstructed 20 feet between the sensor and transmitter.⁹

The first Dexcom monitor to be released was the G4 Platinum with Share. This system consists of a sensor that is placed just underneath the skin, a transmitter fastened on top of the sensor that sends data to the receiver, and a receiver that displays glucose levels.⁹ The receiver contains built-in Bluetooth wireless communication and has a screen that shows glucose trends in color, with various alarms for high or low glucose readings.⁹ The main marketing feature of the G4 Platinum is that glucose data can be shared with family members via the iOS app, something the FreeStyle Libre lacks as its data can only be shared via the Cloud, with LibreView, and not on an app.⁶

Dexcom G5 Mobile

Dexcom's second monitor is also their most popular, the G5 Mobile. It sends glucose data wirelessly to a smartphone compatible with the Dexcom G5 app or to the receiver via Bluetooth.¹⁰ The smartphone app, which is available on iOS and Android, allows data to be shared with up to five followers. The app also has audio alerts for glucose levels that are too high or too low.¹⁰ The G5 Mobile system consists of a sensor and applicator, a transmitter, and a display device. The sensor lasts for seven days and the transmitter three months, at which time they both need to be replaced. One box comes with two transmitters, so it lasts for a six-month period. The transmitters also come with a limited three-month warranty effective from the first day of use. The display device is not essential for viewing glucose data as it can be viewed on the app, but patients can choose to use both the display device and the app.

Dexcom G6

Dexcom's most recent monitor is the Dexcom G6. Like the G5, it is compatible with the app, or patients can choose to use the display device to monitor their glucose levels. The system contains a one-touch applicator that inserts a small sensor just underneath the skin, a sensor and transmitter, and a display device. The Dexcom G6 is the only CGM on the market, aside from the FreeStyle Libre, that can obtain accurate readings even when the patient is taking acetaminophen.¹¹ Further, the G6

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Table 1 Special Features of CGM-Only Products

	No daily calibration needed	Accurate readings even with acetaminophen	Sound alarms for low/high glucose levels	Automatic glucose-data sharing	iOS app available	Predictive software (Sugar IQ)
FreeStyle Libre	✓	✓			✓	
Dexcom G4			✓	✓	✓	
Dexcom G5			✓	✓	✓	
Dexcom G6		✓	✓	✓	✓	
Medtronic Guardian Connect				✓	✓	✓

is unique because it is FDA-permitted to make diabetes treatment decisions without the use of confirmatory finger-sticks or calibration; however, if the glucose alerts and readings do not match the patient's symptoms, a blood glucose meter is required to make treatment decisions.¹⁵ Dexcom G6 has been proven to help patients in lowering their HbA_{1c} and in reducing hypoglycemic incidents.¹¹

Regarding cost, Dexcom monitors are more expensive than the FreeStyle Libre monitor; the three parts to the Dexcom monitors—the receiver, sensors, and transmitter—all have separate costs. For the Dexcom G4 and G5, a one-year supply of the receiver costs \$599 plus shipping and taxes, a four-week supply of the sensors costs \$349 plus tax, and a six-month supply of the transmitter costs \$599 plus shipping and taxes. The Dexcom G6 is slightly less expensive, at \$355 plus shipping and taxes for a one-year supply of the receiver, \$349 plus tax for a one-month supply of the sensors, and \$475 plus tax for a six-month supply of the transmitter.¹¹ Eligible Medicare patients are qualified to obtain reimbursements from Dexcom, and select insurance companies also provide coverage, as indicated on the Insurance Reimbursement Grid chart on Dexcom's website.¹²

Medtronic Guardian Connect

The newest monitor on the market is Medtronic's Guardian Connect, approved for use in patients aged 14 to 75 years old.¹³ Like the Dexcom monitors, it requires calibrating every 12 hours.¹⁴ Unlike the other monitors, the Guardian Connect only contains a sensor and a transmitter, with no reader device. Glucose-level readings are viewed on the Guardian Connect app, which is currently available on iOS only. The app makes it convenient to share glucose readings and alerts with family and friends, and up to five people can be signed up to receive text messages for low-glucose alerts.¹⁵ There is also a website called CareLink, which enables patients to send glucose data to care partners. Like the Dexcom monitors, the Guardian Connect transmitter sends glucose readings to the app every five minutes via Bluetooth. The system is also waterproof up to 2.4 meters (7.8 feet) for 10-minute periods.¹³

One feature that distinguishes the Guardian Connect from the other CGMs is the Sugar IQ. Sugar IQ analyzes glucose, insulin, food, and other data to provide patients with tips and insights for a better understanding of their daily glucose patterns and the factors affecting them.¹⁴ Guardian Connect is thus the only CGM on the market that provides patients with the

information behind the highs and lows of their blood-glucose levels. It is also the only monitor that issues predictive alerts of impending highs or lows 10 to 60 minutes beforehand.¹⁵ Such unique features come at a cost, however, making Guardian Connect the priciest among the CGMs. The out-of-pocket price of a 5-pack one-month supply of the sensor is \$553 and the transmitter costs \$775, with a one-year warranty. The transmitter is a one-time purchase, but annual replacement is recommended when the warranty has expired.

Combination CGM-Insulin Pumps

Aside from stand-alone CGMs, there are also combination CGM-insulin pumps. This type of device automatically adjusts insulin delivery based on a patient's glucose levels. Medtronic has a few combination systems on the market, including the MiniMed 630G system, the 670G system, and the Paradigm Revel. Medtronic combination systems consist of the transmitter, sensor, and insulin pump. The MiniMed 630G and 670G systems offer SmartGuard technology, with an auto mode and suspend-before-low mode. Auto-mode automatically adjusts the patient's basal insulin every five minutes based on CGM readings and helps keep sugar levels within the patient's target range, avoiding lows and rebound highs.¹⁶ Suspend-before-low mode stops insulin delivery up to 30 minutes before reaching preset low limits, then automatically restarts insulin when levels recover without alerts.¹⁶ The MiniMed 630G system and Paradigm Revel are both approved for use by adults and children from the age of 16 years, and the MiniMed 670G system is approved for use by adults and children aged 14 years and older with T1D.¹⁶

Another type of combination CGM-insulin pump is the Tandem t:slim X2. This pump can be integrated with the Dexcom G6 system and contains Basal IQ technology that enables it to look ahead 30 minutes and suspend insulin to help reduce the time and frequency of low glucose events.¹⁷ Without those two components activated, the t:slim X2 is used as a regular insulin pump. The pump is waterproof up to three feet for 30 minutes and contains a rechargeable battery.¹⁷ Unlike the other combination CGM pumps, the t:slim X2 is an insulin pump only; the Dexcom G6 would also have to be purchased in order for t:slim X2 to work as a combination pump.

ROLE OF THE PHARMACIST

Pharmacists are uniquely equipped with the knowledge, skills, and opportunities to educate patients on diabetes and

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managing the condition appropriately. In addition to being able to provide information on the disease state, lifestyle modifications, and pharmacologic therapies, pharmacists are in a position to counsel patients on the importance of monitoring their glucose levels in many practice settings. Self-monitoring blood glucose, using one of the numerous glucometers available, has been the most common way for patients to monitor their levels on a daily basis. However, the CGM systems that are now available offer a more appealing and convenient method for the regular monitoring of glucose levels. The cost could prove to be a barrier for some patients, but as many insurance companies are realizing the potential impact of such technology on disease management and the prevention of related complications, they are beginning to add these systems to their formularies.

CONCLUSION

Glucose monitoring is key for the proper management of diabetes—and CGM offers patients with diabetes a new option for monitoring their glucose levels on a regular basis, without any need for the perpetual finger-sticks and myriad supplies. The features and capabilities of the CGM systems also give patients the ability to chart their glucose levels, share the results, and/or receive alerts at times of low or high glucose levels. Pharmacists should be aware of this technology and familiarize themselves with the various features of each system, which will enable them to instruct patients on their use and minimize the progression or complications of diabetes.

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