



Trends-in-Medicine

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Quick Pulse

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Trends-in-Medicine

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CONTINUOUS GLUCOSE MONITORING SYSTEMS (CGMS)

As a preview to the American Diabetes Association meeting in Atlanta June 9-15, 2006, endocrinologists and one RN were interviewed to determine how Continuous Glucose Monitoring Systems in general – and DexCom's DexCom STS in particular – are being accepted by doctors and patients. The systems use glucose sensors implanted under the skin of the abdomen to provide a continuous reading. The sensor is about the size of an AA battery, and it transmits radio signals to a pager-sized receiver. Glucose levels are measured about every 30 seconds, and data are transmitted to the receiver every few minutes. Vibrations and auditory alarms go off when glucose levels are too high or too low.

Medtronic's Guardian was approved by the FDA in August 2005, and it is being rolled out in a controlled release in the U.S. The DexCom STS was approved by the FDA in March 2006. The Abbott Navigator is awaiting FDA approval.

Few patients are asking for CGMS, doctors said, explaining that this is due to a lack of education, marketing, and availability. However, they predicted that, as patients learn about the devices, they will start asking more questions.

- *Dr. Fernando Ovalle of the University of Alabama at Birmingham:* "Patients aren't asking about it. There hasn't been a lot of press on this locally yet. Endocrinologists are aware of it, but internists and primary care doctors aren't. A few patients ask about it, usually those who are really into their diabetes and who look at the web. Maybe 2% specifically ask about continuous glucose monitoring systems in general, but not products by name."
- *Dr. Samuel Andrews of the Ochsner Medical Center in New Orleans LA:* "A few are asking, not many. I think a lot of pump patients want to get the new MiniMed (Medtronic) pump, and I'm trying to switch them over."
- *Dr. Robert Vigersky, Director of the Diabetes Institute of the Walter Reed Health Care System in Washington DC:* "I think patients will love these devices, and a few are asking about them, but they are still not on the radar screen yet for most patients...The Diabetes Technology Society puts on a clinical program once a year...At the last program there was a panel of six users of these devices who told the audience what their impressions were...It was really powerful to hear what a leap in their ability to manage their diabetes these (devices) provided for them. I think five of the six were on an insulin pump, and for each, going on the pump was a major leap, and basically this was an equivalent leap."

Doctors predicted that CGMS will be used mostly by Type 1 diabetics, although some doctors said they could be helpful for Type 2 patients on insulin.

- *Dr. Andrews:* "The devices will be mostly for Type 1 diabetics on an insulin pump or on four or more injections a day."

Comparison of Continuous Glucose Monitoring Systems

Issue	Abbott Freestyle Navigator	Medtronic Guardian RT	DexCom STS
Availability	Pending FDA approval	Available to adults and children who are willing to travel to get a prescription in any of the 7 locations: Austin, Boston, Chicago, Houston, Minneapolis/St. Paul, San Antonio, Tampa	Across the U.S. Still recruiting sales reps
FDA approval	Pending	Approved in August 2005 for adults age 18 and older	Approved in March 2006 for adults age 18 and older
Price	Not set yet	\$1,995 + \$395 docking station + \$35-\$40 per sensor	\$500 for receiver, transmitter, and 2 sensors, with reduced pricing until the end of 2006. Then, \$800 for the unit and \$175 for 5 sensors.
Reimbursement	---	Some plans are currently covering	Not yet
Sensor life	Seeking approval for 5 days	Shuts off at 72 hours (FDA stipulation) but has gone longer in trials	72 hours
Size of sensor cannula	6 mm	14 mm	6 mm
Angle of sensor insertion	90 degrees	45 degrees	45 degrees
Insertion device available	Each sensor has a disposable inserter	Sens-serter, manual insertion also possible	DexCom STS applicator
Monitor size	3" x 2.5"	3.5" x 2.5"	3" x 2.5"
Start-up initialization time	10 hours	2 hours 20 minutes	2 hours
Calibration	Calibrate at 10, 12, 24, and 72 hours with no further calibration for final 2 days of 5-day wear	First calibration is 2 hours after insertion, then 6 hours afterwards. Then every 12 hours. Will alarm if calibration value not entered	Every 12 hours. With One Touch Ultra, cannot be entered manually.
Transmitter/sensor body surface size	2"x1" (both combined)	Sensor the size of a nickel. Transmitter is 2"x1.5" with a cable that connects the two.	2.5" (both combined)
Alarms on user-set low and high thresholds	Yes	Yes – different sounds for different alarms, different volumes. Loud backup alarm if no response to the first alarm.	Yes
Displays glucose numbers	Every minute	Every 5 minutes	Every 5 minutes
Displays directional trends	Yes. Always has directional and rate of change arrow. Can view 2-, 4-, 6-, 12-, and 24-hour graph. Can go back 28 days.	No. Must manually scroll backward and wait to upload data to software to make graphs.	Yes. Can display a 1-, 3-, or 9-hour glucose graph.
Displays rate of change	Yes. Sideways arrow means dropping at <1 mg/dL/minute. Up or down arrow means raising/dropping at more than 2 mg/dL/minute. 45 degree arrow means dropping/raising between 1 and 2 mg/dL/minute.	No	No
Alarms on vector technology	Yes. Will alarm on 10, 20, or 30 minutes before it thinks that you will hit that number based on the current trend. It estimates a future number by using algorithms and vector technology.	No	No
Alarms, vibrate, or both	Alarm or vibrate	Vibrate, escalating alarm, or both	Alarm or vibrate – low first vibrate, then alarm
Transmitter waterproof	Yes	Yes	No. Can shower with shower patch but shouldn't swim.
Transmitter batteries	Watch battery should be replaced monthly	Non-replaceable. Transmitter life is about 1 year (will usually be covered by insurance). Additional transmitter \$500.	Non-replaceable. Transmitter life unknown. Additional transmitter is \$250.
Monitor batteries	2 AAA batteries that need to be replaced every 3 months.	2 AAA batteries. Monitor alerts when change is needed.	Must recharge the battery every 5 days. Charge time is 3 hours.
Range of monitor to transmitter (factory stated)	10 ft	6 ft	5 ft
Sensor storage	Room temperature, 4 month life	Refrigerated	Room temperature, 4 month life
Snooze alarm feature	Yes, 1 hour silence	Yes, only for high alarm, 1-12 hours	N/A
BG monitor	Built-in Freestyle Flash Monitor	No	Must calibrate with One Touch Ultra
Computer software	Freestyle CoPilot	Guardian Solutions	None yet
Warranty	N/A	1 year	6 month warranty for receiver and transmitter
Upgrade program	N/A	Medtronic Pathway Program	N/A
Money-back guarantee	N/A	N/A	90-day money back guarantee if not happy.
Developing technology	Open loop system with new Abbott Pump-Aviator	Pump/CGMS monitor combination has been submitted to the FDA for approval and is already available in Canada.	Long-term (about 1 year/outpatient procedure) implantable sensor.

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- *Dr. Vigersky*: “The devices certainly have utility in Type 1 diabetes, and Type 2 diabetics certainly would benefit. Whether there is any utility in Type 2 diabetes patients who are not on insulin remains to be seen – maybe and maybe not – but I wouldn’t rule it out. But the primary target is Type 1 diabetics because they have the most erratic blood sugars and are usually much more difficult to control.”
- *Dr. Howard Wolpert, Director of the Insulin Pump Program at Joslin Diabetes Center in Boston MA*: “For us it’s primarily Type 1. It can be valuable in Type 2, but mainly in Type 1.”
- *Doris Roberts RN of Kaiser Permanente in Bellflower CA*: “We use (CGMS) mostly for the pregnant and pediatric populations. We have used the sensors on some pediatric patients to evaluate 24-hour control, but not often.”
- *Dr. Ovalle*: “Type 1 diabetics who really care about their disease – which is about half of them – will mostly use this type of device. I don’t know about Type 2 diabetics. I think the cost may be a little too much for them. For the most part you really don’t need it in most Type 2s; most times they are well-controlled and won’t do anything with the extra information. It would just be a burden and hassle for them. The market will be mostly Type 1 or some very insulin-sensitive Type 2s (maybe 5%-10% of Type 2s).”

Doctors said they are not yet recommending CGMS to patients, in part because of:

1. Availability. A doctor commented said, “I tell patients they can go to Tampa (to get a Medtronic Guardian) but they would have to pay for it out-of-pocket...I had a lawyer recently who I told about it (the Guardian), and he said he would pay for it, but that is a rare situation.”

2. Insurance coverage. One doctor said, “People are asking for the DexCom STS, certainly, but the challenging issue is that it’s not covered by insurance.” Another said, “The Medtronic device isn’t available here yet. I heard from a patient who got a Medtronic pump in Minnesota (where Blue Cross Blue Shield covers it) that there isn’t much difference in price (from DexCom). Medtronic is sold only in seven test markets around the country. I heard that Medtronic wants to gain insight into the insurance market and negotiate deals before they hit tougher markets.” A third doctor said, “With reimbursement, all my Type 1 patients will be on it as well as my insulin-dependent Type 2 diabetics.”

Most physicians said their patients would not pay for the devices out-of-pocket. One doctor said, “Those who can, will pay for it, but I think it will be pretty pricey, and probably 25% of interested patients could afford it.” Another commented, “Some patients will pay out-of-pocket, but I don’t think continuous glucose monitoring will take off even after

insurance has (approved it). I’ve been in meetings with managed care to see about their interest in covering sensors, and I think in the next 18-24 months, there will be data that will help in terms of overcoming that hurdle.”

Once reimbursement is available for the devices, doctors estimated that an average of 51% of their Type 1 patients (which is about 10% of all diabetics) and 5% of their Type 2 patients will use a CGMS within 6-12 months, though there were wide ranges in these estimates.

- “Half of my Type 1 patients and 5%-10% of my Type 2 patients might be on a CGMS.”
- “In a year, perhaps 1%-2% of Type 1 insulin pump or multi-injection patients would be on it. First, you have to have a very, very motivated patient, and then that patient has to be willing to spend the money. It won’t, suddenly, in one year, see that much use.”
- “In a year, I’ll be recommending it for all my Type 1 patients.”
- “There will be prospects for ultimately getting insurance using it even as an adjunctive device if trials can show that the sensor, used adjunctively, can optimize hypoglycemia. The insurers will be hard-pressed to deny coverage for both sensors and the finger sticks...Once (the reimbursement problem) is overcome, there will be a huge explosion in sensor use.”

3. Waiting for newer products. A doctor said, “(I’m not recommending DexCom) because I’m waiting for the Medtronic pump. The DexCom sales rep was in my office this week. We will start using it, but I like the Medtronic device...The Medtronic will be used more than the DexCom.” Another doctor said, “We have 20 patients in the Medtronic trial, and 10 patients are using DexCom, so that’s not many.”

More doctors were familiar with all of the devices, but they generally knew more about the Medtronic device than the other CGMS. One doctor said, “I’ve seen the DexCom, and I’ve used the Medtronic.” Another said, “We’ve seen presentations on it (the DexCom STS), and the literature looks good. We use the MiniMed (Medtronic’s System Gold, a physician system) for retrospective analyses of patient blood sugar over 72-hour periods, not for real-time monitoring yet.” A third commented, “We aren’t using the DexCom in our clinic. We’re planning to implement a program to initiate Medtronic’s Paradigm device. We didn’t use the (Medtronic) Guardian because we were waiting for the next generation device, and we hope to start using it soon.”

Doctors familiar with both Medtronic and DexCom systems seemed to prefer the Medtronic devices. One doctor said, “I like the Medtronic (Guardian) best. It has a little more technology behind it. It’s more user friendly and more adaptable to the pumps that are out there, and the Medtronic pump is the most commonly used pump.” A New England

doctor said he has patients on both the Medtronic and DexCom devices, “The (Medtronic) 722 is linked to a pump, and the DexCom is standalone. The DexCom center is smaller and easier to insert, but there is no software available yet for downloading and reviewing data, whereas Medtronic has good software. Both are first generation technology, and we are going to see more product refinement. There are other devices coming out. There will be a lot of improvements on the horizon in both devices, in use and in accuracy. At this stage, the technology needs a lot of guidance for people. A big challenge in the long-term will be in training patients...So I think the challenge is going to be beyond the refinement of the technique.” A third doctor declared, “I like the Medtronic pump better.”

There were a few doctors who critiqued the DexCom STS. One pointed out that it has a display, but he said the device lacks the ability to download information, explaining, “You can’t download the data to review the tracings, so it’s not as if patients can go into their doctor’s office with copies of their tracings to get guidance. It’s difficult to write down – it’s not a number – it’s a continuous tracing, so that is challenging... People can use it at home, but the problem is...that they don’t have the data to review with clinicians.” He cited another problem with the DexCom device: “They don’t have approval for the DexCom device to be used in kids. That’s one patient population where there is a lot of demand and interest (in CGMS).”

Most sources have not yet been detailed on the DexCom STS, but those who have or who know their DexCom sales rep said sales and service are good. It does not appear that Abbott and Medtronic are doing any really negative counter marketing to the DexCom STS. A source said, “Medtronic’s sales reps don’t say anything bad about STS, but they point out that it won’t communicate with their pump, and their device will. That is the advantage to the Guardian, they emphasize. They don’t talk about cost, but I heard the DexCom is cheaper. I know other companies are working on continuous glucose monitoring systems. Roche said it has one coming out, but I didn’t hear any specifics.” Another doctor speculated that Johnson & Johnson and Roche both make pumps, but they reportedly need a sensor and are potential buyers of DexCom, “Having pumps as Medtronic does, they both realize they’re going to have to move into that space.”

Other comments included:

- “I haven’t seen a DexCom sales rep. The Medtronic reps come in but only unofficially. Medtronic sales and support is good, a little above average, but not great. They had problems when they first bought MiniMed, and then they solved that problem and now offer mostly good service.”
- “(DexCom reps) are good. They are willing to come and help us with patient education, and our sales rep is bright and enthusiastic.”

- “DexCom is quite open in acknowledging that they want to sell out, but at this point there’s not much focus on clinical use; they tend to minimize or underplay what the clinical needs are going to be...So its focus is short-term only; they just want to sell the company. Once one of the other bigger players comes into the field, they’ll understand that they have to develop clinical support in order to get more widespread use of the technology.”

Two physicians said they think the Abbott Navigator looks promising. A doctor who has used all three devices said, “The data for the Abbott actually looks better than either Medtronic or DexCom.” Another doctor said, “When the Abbott and Medtronic devices are (both) available, I’ll compare them individually, but from the data I’ve seen, the Abbott Navigator looks like it might perform better than the other two because it lasts longer – five days instead of three. But the disadvantage to the Abbott device is that there is a warm-up period of 12 to 14 hours; it has to be equilibrated before you can use the readings, so you have to have overlapping sensors and do sticks for a day. Whether this is a problem, I don’t know. At least from what I’ve seen, in terms of the performance characteristics, the Abbott device looked to have the best data in terms of accuracy. We all recognize that these devices don’t need to be as accurate as a finger stick because the feature of knowing the direction is so powerful that it trumps any inaccuracies. If you know your blood sugar is 80 and falling fast, you will stop what you are doing and eat something, and vice versa. That functionality is so powerful that the degree of accuracy doesn’t actually have to be as good as finger sticks. But the FDA has required manufacturers to say in the package insert that before patients take any action – change insulin – they should confirm the reading with a finger stick. But even with that, this trumps finger sticks. Instead of accuracy in the range of 3%-5% for finger sticks, you are talking about a range of 10%-15% with continuous glucose monitoring systems.”

Finger sticks won’t go away

Continuous glucose monitoring systems are unlikely to completely replace finger sticks to draw blood for a glucose meter, doctors agreed. One said, “There is a limitation on what information this gives you. It doesn’t take the place of sticks. It is not as accurate as finger sticks or as rapid, so if the patient is having a rapid change in blood sugar, there is a lag before it is picked up, but they do have alarms that alert you to rapid changes either up or down.” Another said, “At the moment they’re all adjunctive...and all need finger sticks.”

Patients are expected to eventually stop using finger sticks to calibrate their devices as they get more comfortable with the devices and trust the readings. One doctor said, “They will calibrate sometimes, but they will start to trust the readings, and I think they are accurate enough.” Another recommended, “It might be something they use periodically, but I’m not sure patients need to use it 24 hours all the time...Patients only have to do two sticks a day...People who don’t have an

interest in finger sticks won't be interested because they don't follow their blood sugar that closely." A third said, "Probably patients won't calibrate as much as they are supposed to (i.e., four times a day). I think most people will do it twice a day. I wore one (CGMS) myself, and I tried to fool the thing, but I couldn't leave the (device) behind no matter what I did – even if I didn't calibrate, or if I ate something high in sugar. No matter what I did, it stayed right next to the test strip, so I'm very impressed by the technology."

Replacement sensors

The cost of replacement sensors is considered a problem by some but not all doctors. Asked about the reasonableness of a \$35 cost for a replacement sensor, doctors said:

- "That is a reasonable price because if you use test strips at 70 to 80 cents each and use six a day, that is \$5 a day, or \$15 for three days, so you have already offset \$15 of the \$35, so for an extra \$20 you can have additional sensing."
- "It is quite expensive and lasts only two to four days."
- "Strips (for finger sticks) are about 70 cents each, and if a patient is doing four of those a day, that's \$2 to \$3 a day or about \$20 a week, so the sensors are adding a lot of money."
- "None of these are replacement sensors. All of them are adjunctive (to finger sticks) at the moment."
- "Thirty-five dollars seems a little steep, especially if it's out-of-pocket."

Thus, most doctors said they expect patients will use the DexCom STS for longer than the three days for which it is intended. They explained that the devices probably can be stretched an extra day or two – and one doctor claimed that the devices get more accurate over time.

- "These devices are supposed to be for three days, but if you just unhook it, and then re-hook it up again, the device will be recognized as new and will keep working for another three days, so you can extend it for another three days. If you do that, then it becomes the same cost as the test strip. That isn't to say you shouldn't do test strips, but if you do fewer strips, maybe two a day at first, and more on the last three of the six days, then overall, probably the cost is close to coming out even. The extra expense is very small for the added advantage. At that price, it is reasonable."
- "Some patients stretch it up to five days...The sensor is supposed to last three days, but it lasts longer. After a while it will stop transmitting, and you have to replace it. I think it's okay to use it as long as it is transmitting data. Some will abuse the device and take too much insulin. They'll see their sugar climbing, take insulin, and get hypoglycemic. We use continuous glucose monitoring systems mainly to look at trends, to see if there are trends toward hypoglycemic reactions at night when a patient is

sleeping. The devices have a memory, about 30 days, and you can upload the data into our computer in the office."

- "They have to subterfuge the system...but there are data coming out that shows accuracy actually improves when one keeps them in for longer, and certainly the companies are applying for longer term use. It's opposite than with pump infusion."

