This article combines research findings and clinical experience that are unique to the use of continuous glucose monitoring in children and adolescents. It stresses the importance of realistic expectations, describes considerations related to wearability, and reviews the potential benefit of glucose alarm features for pediatric patients.

Use of Real-Time Continuous Glucose Monitoring Technology in Children and Adolescents

Jen M. Block, RN, CDE, and Bruce Buckingham, MD

The management of diabetes in children and adolescents is a delicate balancing act. It is best achieved with consideration of developmental stages, lifestyle, and psychological burden. Age-specific glucose targets reflect the importance of balancing the risk for complications with the risk for hypoglycemia in children. Although not specific to children, the fear of hypoglycemia can be a major obstacle to achieving glycemic control. The fear of hypoglycemia at night causes many parents to wake up several times each night to test their child’s glucose. A 3-year study of 657 children with type 1 diabetes found that 8.5% of participants had a seizure, 27% of participants required assistance to treat a low, and 75% of all seizures occurred at night. The risk for low blood glucose at night increases with physical activity the preceding afternoon, a common time for exercise in both children and adolescents. A Diabetes Research in Children Network (DirecNet) study in children found nocturnal hypoglycemia (≤60 mg/dl) occurred 42% of nights after 75 minutes of aerobic exercise in the afternoon, compared to 16% overnight after a sedentary afternoon.

Real-time continuous glucose monitoring (CGM) technology offers alarms for low and high glucose, information about the rate and direction of glucose change, and retrospective data about glucose control. CGM offers many benefits to children and their families, but the decision to use the technology requires careful consideration. Although we have clinical experience using all of the available CGM systems in our pediatric population, this is still a relatively new field. There are limited research data on the use of CGM systems in this age-group, and we look forward to data from the large-scale randomized clinical trial in both adults and children funded by the Juvenile Diabetes Research Foundation (JDRF) to provide more data on the use of all CGM systems in children and adolescents. A recent poll of 528 respondents on the Children With Diabetes website reported that two in five people were willing to pay for a CGM system out of pocket, and only 4% said they did not need a CGM system.

The additional glucose data provided by CGM systems offer many advantages, and in several studies in children, sensor use has resulted in improved glucose control. In a randomized clinical trial conducted in both children and adults with type 1 diabetes, use of the Medtronic Guardian CGM system resulted in a ≥1% hemoglobin A1c (A1C) reduction in half of the subjects and a ≥2% reduction in one-fourth of subjects. In the DirecNet pilot trial of children using the FreeStyle Navigator CGM system, the mean A1C improved from 7.1% at baseline to 6.8% at 13 weeks (P < 0.02), and the percentage of glucose values between 71 and 180 mg/dl increased from 52 to 60% (P < 0.01). In a 1-month pilot study of the MiniMed 722 CGM system,
10 children showed a reduction in the percentage of time spent < 70 mg/dl and > 180 mg/dl, as well as a slight, statistically insignificant reduction in their A1C levels in 1 month of CGM use. A randomized, multi-center, treat-to-target study of adolescents and adults with type 1 diabetes using the Medtronic MiniMed 722 CGM system followed 40 adolescents with a mean age of 14.2 ± 1.7 years. In this subgroup, subjects who had at least 5 days a week of CGM use were 3.3 times more likely to show a 0.5% decrease in their A1C. The statistically significant reduction in A1C occurred without an increase in hypoglycemia. Pediatric studies using the DexCom system have not been published at the time of this review.

**CGM Technology**

CGM systems measure glucose in the interstitial fluid, not blood glucose, providing interstitial glucose readings every 1–5 minutes. Rapid blood glucose changes may result in a 6- to 18-minute delay in interstitial glucose readings. Approximately 6–8 minutes of the delay is the result of a physiological lag, and up to 12 minutes of delay may result from filters on the glucose sensor.

CGM systems are currently approved for adjunctive use and should be used in addition to blood glucose testing. Blood glucose testing is used to calibrate CGM systems and should be the basis for treatment decisions, such as insulin dose adjustments and determinations of ability to drive. Blood glucose tests should also be performed to verify CGM data and alarms, as well as anytime there are symptoms of a low or high glucose level.

If an errant blood glucose test result is entered as a calibration, or if calibration is performed when the glucose level is changing rapidly, the accuracy of the CGM readings may be impaired. Calibration should be done when the glucose is not changing rapidly. Finding a good time to calibrate may be more challenging in children, whose eating and activity patterns are inconsistent and varied.

CGM systems are composed of several components. Disposable sensors are inserted in the subcutaneous tissue using an insertion device. The sensors generate a current that correlates with the level of glucose in the interstitial fluid. The transmitter then relays the information to the receiver, where it is displayed. Several CGM systems are presented in Table 1, some of which are approved for use in children.

**Special Considerations in Children and Adolescents**

**Unrealistic expectations**

The hope for a cure is a dream shared by many people with diabetes, especially children and their families. This strong desire is a positive force that provides hope and encourages research, but it can also contribute to high expectations for any novel drug or device. User expectations for CGM are no different, and having realistic expectations for the technology is an important first step in adapting its use. CGM systems are not a cure, and they are not an artificial pancreas.

These systems provide more and different data about glucose control than were previously available, but it is information that patients and their families need to be ready and willing to use. Although this technology has many advantages, it may not be suitable for all families and children with diabetes. The increased data may be overwhelming for some people, and the ability to interpret and respond to the data appropriately is an important consideration in patient selection. CGM is a behavior modification tool. Having real-time data will not prevent all hypo- or hyperglycemia, but the glucose alarms and the direction- and rate-of-change information may help prompt preemptive intervention. Children and their families should appreciate that CGM is not perfect, but the increased data can be an effective and powerful tool in diabetes management.

**Issues of wearable**

CGM technology is only effective when it is used. CGM use in children and adolescents provides unique challenges. In young children, especially those using insulin pump therapy, the addition of a transmitter may take up valuable body real estate. The smaller the child, the bigger the challenge. Transmitter size and the location of sensor insertion are important considerations in children. For children who are active or frequently perspire, the adhesion of the sensors and transmitters can be problematic and may require experimentation with various adhesives and skin preparations. Finding creative approaches to keeping receivers from getting lost, dropped, or damaged can be challenging.

It is important to consider the possibility that the desire to use CGM may lie with the parents and not the children. It is the children ultimately who will be wearing the system, and their opinion is key in the decision to use the technology. It is often beneficial to provide a trial period of sensor wear, and ideally a trial of inserting different sensors and using different CGM systems, especially if the child does not want to use the system because of anxiety about inserting or wearing the device. In older children, concerns about the violation of privacy should be addressed because this may create more conflict and result in decreased use and benefit from the technology. In this case, it may be worthwhile to work out an agreement between parents and children about how and when data will be reviewed. It is also possible that children may be willing to use the device intermittently.

Surveys of children with type 1 diabetes and their parents who were enrolled in a pilot trial using the FreeStyle Navigator system revealed a high level of satisfaction. More than 70% of both parents and children reported the use of CGM made adjusting insulin easier, made them more confident in their management decisions, and helped detect glucose patterns they were not previously aware of. Of particular interest in this small pilot trial was the finding that using CGM did not increase family conflict, and device use remained fairly constant throughout the study. During the pilot trial, which lasted 13 weeks, the CGM device was used 80% of the time in the first 4 weeks and 70% of the time in weeks 9–13.

**Glucose alarms**

All of the current CGM systems have threshold alarms for low and high glucose. For children and their families, this feature is one of the major draws of the technology. These alarms are used in addition to traditional methods of detecting hypo- and hyperglycemia. CGM systems are not, however, an infallible method of detecting low or high glucose and should not be depended on as the
<table>
<thead>
<tr>
<th>Device</th>
<th>Low/ High Alarms</th>
<th>Trend Arrows/ Trend Graphs</th>
<th>Sensor Life</th>
<th>Sensor</th>
<th>Initialization/ Warm-Up Time (hours)</th>
<th>Calibration Schedule</th>
<th>CGM Data Frequency</th>
<th>Approved for Pediatric Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>DexCom STS 7 Day</td>
<td>Yes</td>
<td>No/Yes</td>
<td>7 days</td>
<td>Angled insertion 12 mm</td>
<td>2</td>
<td>After initial two calibrations, at least one every 12 hours</td>
<td>Updated every 5 minutes</td>
<td>Approved for adults/Not approved for children</td>
</tr>
<tr>
<td>DexCom STS Investigational Short Sensor</td>
<td>Yes*</td>
<td>No*/Yes*</td>
<td>7 days*</td>
<td>Angled insertion short sensor* N/A</td>
<td>2*</td>
<td>After initial two calibrations, at least one every 12 hours*</td>
<td>Updated every 5 minutes*</td>
<td>Not yet approved for any age*</td>
</tr>
<tr>
<td>FreeStyle Navigator</td>
<td>Yes</td>
<td>Yes/Yes</td>
<td>5 days</td>
<td>Straight insertion 5 mm</td>
<td>10</td>
<td>Fixed schedule at 10, 12, 24, and 72 hours after insertion</td>
<td>Updated every 1 minute</td>
<td>Approved for adults/Not approved for children</td>
</tr>
<tr>
<td>Medtronic MiniMed 522/722 522K/722K</td>
<td>Yes</td>
<td>Low alert on 522K/722K cannot be set &lt; 90 mg/dl.</td>
<td>3 days</td>
<td>Angled insertion 16 mm</td>
<td>2</td>
<td>After initial calibration, at least one every 12 hours</td>
<td>Updated every 5 minutes</td>
<td>Yes, 522K/722K is approved for ages 7–17 years</td>
</tr>
<tr>
<td>Medtronic MiniMed Guardian Real-Time</td>
<td>Yes</td>
<td>Yes/Yes</td>
<td>3 days</td>
<td>Angled insertion 16 mm</td>
<td>2</td>
<td>After initial calibration, at least one every 12 hours</td>
<td>Updated every 5 minutes</td>
<td>Yes, pediatric model is approved for ages 7–17 years</td>
</tr>
</tbody>
</table>

*This investigational device has not yet received FDA approval. Specifications may change.
From Research to Practice / Diabetes Technology Update

only means of detecting these events. Lag time and errors in calibration, among other things, may prevent the system from alaraming. In some cases, the system may alarm but the user may not respond.

In a study of responses to alarms generated by the GlucoWatch G2 Biographer, children and their parents were videotaped overnight using an infrared camera. Children awoke to 29% of alarms. The alarm response rate increased with age: 4- to 6-year-olds responded to 17% of alarms, 7- to 11-year-olds responded to 20% of alarms, and there was a 53% response rate in adolescents. Parents who were asleep in the same room responded to 37% of alarms. It has been our experience that many patients and families do not hear the audible or feel the vibratory alarms overnight, and many feel they would benefit from louder alarms or alarms that were able to remotely alert others or turn on lights.

Children and adolescents in particular are at risk for missing meal boluses. This is especially true when they are at school. In a study of 48 children between 7 and 20 years of age (mean age of 15.3 ± 3.0 years) using insulin pump therapy but not meeting their glycemic goals, there was a correlation between the frequency of missed meal boluses and the elevation in A1C levels. This study found a 0.5% increase in A1C when two meal boluses per week were missed and an increase of 1% if four meal boluses per week were missed.

Real-time alarms for actual or projected high glucose can help alert children and adolescents to missed meal boluses and facilitate correction actions earlier than conventional blood glucose testing alone. Although preventing a missed bolus is the ideal scenario, responding rapidly to the postprandial hyperglycemia after a missed meal bolus is a step in the right direction.

Setting glucose alarms

Low and high glucose alarms and projected low and high alarms, can be a valuable adjunct to symptoms and blood glucose meter data in detecting hypo- and hyperglycemia. Alarm settings should balance sensitivity and specificity to maximize event detection and minimize nuisance alarms. Setting the low alarm at 80 mg/dl may improve the sensitivity, but if the patient and family are constantly warned of lows when the blood glucose is in the 100-mg/dl range, they may tire quickly, especially when the alarms are occurring overnight.

A study of the FreeStyle Navigator system found when the low threshold is < 70 mg/dl, the alarm sensitivity is 79.8% (defined as a glucose < 70 mg/dl within ± 30 minutes of the threshold or projected alarm). The rate of false-positive alarms (defined as a glucose > 85 mg/dl) was 7.2%. When the low alarm was raised to 80 mg/dl, the detection rate for blood glucose < 70 mg/dl increased to 92.5%, but the false alarm rate increased to 27.8%.

The glucose tattle

CGM leaves little to the imagination. The continuous stream of data identifies glycemic excursions that were previously undetected, even with frequent blood glucose testing. Given the limitations of our current therapies and the numerous variables that affect glucose control, perfect glucose control is not a realistic goal for most patients. Never before have
patients and families been so aware of the successes and missteps in care.

It is important to look at the data objectively, to identify patterns, and to work to make changes. As children gain independence with their diabetes in the age of CGM, it will be increasingly important to view the data objectively, focusing on the positives and working as a team to make changes. Children and adolescents need to understand that no one is perfect; we all make mistakes. Transitioning care from parents to children or adolescents can be very challenging, and focusing on what is working and providing positive feedback is as important as identifying areas for improvement. In fact, CGM may empower children and adolescents with the support of parents to take a more active role in their diabetes management.

The example in Figure 1 shows the improvement in glucose control for a 15-year-old between when his mother managed his diabetes and 13 weeks later, when he had gained independence in his care. For some patients, the desire to maintain autonomy and to demonstrate their diabetes management abilities may lead them to be overly aggressive with their insulin doses in response to glucose trends and alarms. In Figure 2, a 13-year-old who had received education on the dangers of over-correcting before starting CGM was alerted to a high glucose his first night of sensor use. He admitted that the high glucose was frustrating, and his instinct was to get it down as fast as possible without regard to insulin on board and without use of the bolus calculator. The figure shows that the patient gave two boluses close together, raised his basal rate, and used a square wave in attempts to achieve lower glucose values. As a result, his blood glucose dropped quickly, and he was woken again by alarms for a low glucose that needed treatment. This example highlights the need to address expectations and teaching the onset, peak, and duration of insulin to prevent over-correction.

Responding to data with DATA
When using CGM, patients and parents need to make decisions about how they will respond to the glucose readings on many levels. Data provided from CGM, including the rate and direction of glucose change and short- and long-term retrospective trend data, in combination with blood glucose tests, can guide therapy decisions. This more complete picture of glucose control warrants a comprehensive plan to maximize the use of all the data.

In the DirecNet pilot trial, subjects with a mean age of 11.2 ± 4.1 years of age using CGM tested algorithms designed to provide guidelines for the use of both real-time and retrospective data. The DirecNet Applied Treatment Algorithm (DATA) was written and tested using the FreeStyle Navigator in patients insulin pump therapy. A condensed version of the algorithms that has been modified for use in a variety of systems appears in Table 2. A complete copy of the algorithms used in the study is available in the appendix of the original article. The algorithms provided guidance for patients on how to respond to glucose alarms, adjust insulin doses, and take into account the glucose trend, as well as how to review and respond to retrospective trends. These algorithms were used as part of a research study, and it is worth emphasizing that all treatment decisions should be confirmed with a blood glucose meter test.

The use of the DATA algorithms increased subjects’ autonomy. This is evidenced by the frequency of therapy adjustments made by patients and their families. After 1 week of CGM use, 10% of subjects reported making changes to insulin-to-carbohydrate ratios, and 20% made changes in basal rates. By the end of the study, this increased to 25% reporting making a change in insulin-to-carbohydrate ratios and 32% adjusting basal rates. After only 3 weeks of use, 82% of subjects and 96% of parents felt DATA was helpful in guiding insulin management decisions. The use of algorithms decreased over time to 59% of subjects and 73% of parents by 13 weeks. This reduction may reflect increased confidence in making their own decisions and a better understanding of their individual needs as a result of CGM use.

The success of the DATA algorithms warrants further study and consideration when teaching patients how to respond to CGM data. Central to these algorithms is a thorough understanding of insulin action profiles. Teaching the onset, peak, and duration of all types of insulin patients are using is crucial. For patients using smart insulin pumps with bolus calculators, it is important to review their insulin-on-board settings and encourage the use of this feature to prevent insulin “stacking.”
Table 2. Suggestions for Using Real-Time Data

<table>
<thead>
<tr>
<th>Glucose Rate of Change</th>
<th>Receiver Trend Display</th>
<th>Expected Glucose Change Over 30 Minutes</th>
<th>Suggested Insulin Dose Adjustment*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rising at &gt; 2 mg/dl per minute</td>
<td>DexCom: see below Medtronic: ↑↑ Navigator: ↑</td>
<td>Increase of &gt; 60 mg/dl in 30 minutes</td>
<td>Increase dose by 20%</td>
</tr>
<tr>
<td>Rising at 1–2 mg/dl per minute</td>
<td>DexCom: see below Medtronic: ↑ Navigator: ↑</td>
<td>Increase of 30–60 mg/dl in 30 minutes</td>
<td>Increase dose by 10%</td>
</tr>
<tr>
<td>Changing &lt; 1 mg/dl per minute</td>
<td>DexCom: see below Medtronic: No change in display Navigator: →</td>
<td>Change of &lt; 30 mg/dl in 30 minutes</td>
<td>No change</td>
</tr>
<tr>
<td>Falling 1–2 mg/dl per minute</td>
<td>DexCom: see below Medtronic: ↓ Navigator:♭</td>
<td>Decrease of 30–60 mg/dl in 30 minutes</td>
<td>Decrease dose by 10%</td>
</tr>
<tr>
<td>Falling &gt; 2 mg/dl per minute</td>
<td>DexCom: see below Medtronic: ↓↓ Navigator: ↓</td>
<td>Decrease of &gt; 60 mg/dl in 30 minutes</td>
<td>Decrease dose by 20%</td>
</tr>
</tbody>
</table>

Note: These are general suggestions. Patients should consult with their physician before making changes to their diabetes management regimen.

* Insulin dose decisions should be confirmed with a blood glucose meter test.

Calculating Rate of Change with DexCom:
1. View the most recent 1-hour trend graph. Divide the screen in half and focus on the glucose trend during the past 30 minutes.
2. Using the change in glucose during the past 30 minutes, calculate an estimate of the rate of change. Glucose 30 minutes ago – current glucose
   • Example: 150 (CGM value from 30 minutes ago) − 110 (current CGM value) = 40 mg/dl
3. Because the glucose has fallen ~40 mg/dl in the past 30 minutes, you would follow the algorithm for a decrease of 30–60 mg/dl, which would suggest a 10% reduction in insulin dose.

Special thanks to The Jaeb Center for Health Research and The JDRF RT-CGM RCT Study Group for the use of this image.

For patients not using smart pumps, discuss how to calculate insulin on board.

Prospective versus retrospective
The ability to use direction- and rate-of-change data to prevent glucose from rising above or dropping below the threshold is an advantage not previously afforded with traditional blood glucose meters. The use of real-time data is exciting and empowering, but it is not the only benefit of CGM use. Retrospective glucose trends should be used to make medication or lifestyle modifications. When reviewing these trends, it is important to consider recurrent patterns of real-time proactive measures that were taken, so that changes can be made to basal rates, insulin sensitivity calculations, and insulin-to-carbohydrate ratios to decrease the need for recurring corrective measures.

Conclusion
A fear of hypoglycemia that keeps many parents from sleeping through the night, hormonal changes with puberty, varied activity and meal schedules, and the gradual transition of care from parents to children are all unique challenges in children and adolescents with diabetes. They are also common reasons that parents and children cite for using CGM. The additional data afforded by CGM use, especially data on overnight and postmeal glucose trends, can help increase confidence in therapy modifications. Although there are many reasons to use CGM, it is important to recognize that not everyone may be ready or willing to use the technology. For children and families who chose to add CGM to their diabetes regimen, having reasonable expectations for the therapy is important. It is also vital to have a thorough understanding of the onset, peak, and duration of all medications that affect glucose control. Education should include information about the technology itself and about how to safely use both the real-time data and the glucose trend and retrospective information.

References
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Notes of disclosure: Ms. Block has served as a consultant to and is a former employer of and stock shareholder in Abbott Diabetes Care. She is also a stock shareholder in C8 Medisensors. These companies manufacture or are developing glucose monitoring devices. Dr. Buckingham serves on a medical advisory board and a speaker’s bureau for and has received research support from Medtronic MiniMed. He is also on medical advisory boards for Lifescan, Glysen, and Arkal Medical and has received research support from Abbott Diabetes Care. All of these companies either manufacture or are developing glucose monitoring devices or products that employ glucose sensing technology.