STATEMENT BY THE
AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS
CONSENSUS PANEL ON CONTINUOUS GLUCOSE MONITORING

Thomas C. Blevins, MD, FACE;
Bruce W. Bode, MD, FACE;
Satish K. Garg, MD;
George Grunberger, MD, FACP, FACE;
Irl B. Hirsch, MD;
Lois Jovanovič, MD, MACE;
Elizabeth Nardacci, FNP, CDE, BC-ADM;
Eric A. Orzeck, MD, FACP, FACE;
Victor L. Roberts, MD, MBA, FACP, FACE;
William V. Tamborlane, MD;
AACE Continuous Glucose Monitoring Task Force

Address correspondence to Dr. Victor L. Roberts, Endocrine Associates of Florida, PA,
1561 West Fairbanks Ave, Ste 200, Winter Park, FL 32789-4678. E-mail: victorlrobertsmd@gmail.com.

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS CONTINUOUS GLUCOSE MONITORING TASK FORCE

Task Force Authors

Thomas C. Blevins, MD, FACE
Bruce W. Bode, MD, FACE
Satish K. Garg, MD
George Grunberger, MD, FACP, FACE
Irl B. Hirsch, MD*
Lois Jovanovič, MD, MACE
Elizabeth Nardacci, FNP, CDE, BC-ADM
Eric A. Orzeck, MD, FACP, FACE
Victor L. Roberts, MD, MBA, FACP, FACE*
William V. Tamborlane, MD

Medical Writer
Caitlin Rothermel, MA

*Cochairpersons.

Abbreviations:
AACE = American Association of Clinical Endocrinologists; **CGM** = continuous glucose monitoring; **CPT** = Current Procedural Terminology; **CSII** = continuous subcutaneous insulin infusion; **DM** = diabetes mellitus; **FDA** = US Food and Drug Administration; **GDM** = gestational diabetes mellitus; **HbA$_{1c}$** = glycated hemoglobin; **JDRF** = Juvenile Diabetes Research Foundation; **SMBG** = self-monitoring of blood glucose

Definitions:
Personal CGM = Personal CGM devices are owned by patients. With personal real-time CGM, glucose values are visible continuously; this allows for immediate therapeutic adjustments based on "real-time" glucose results.

Professional CGM = CGM equipment is owned by the health care professional, clinic, or hospital. With masked CGM, patients remain unaware of monitoring results until they are downloaded and analyzed.

EXECUTIVE SUMMARY

Professional and Personal Continuous Glucose Monitoring

Professional continuous glucose monitoring (CGM) equipment is owned by the health care professional and is typically worn by the patient for 3 to 5 days. With professional CGM, the patient remains unaware of blood glucose monitoring results until they are downloaded and analyzed by the health care professional. Personal CGM devices are owned by the patient. Glucose values are visible continuously, allowing for immediate therapeutic adjustments on the basis of "real time" glucose results.

Evidence Supporting the Use of CGM

A number of randomized, controlled clinical trials have evaluated the effects of CGM in the treatment of type 1 diabetes (DM). Summary descriptions are provided in the Executive Summary Table (see page 733).

Patient Selection Recommendations

On the basis of the available evidence, the American Association of Clinical Endocrinologists (AACE) recommends personal CGM for the following patients:

- Those with type 1 DM and the following characteristics:
  - Hypoglycemic unawareness or frequent hypoglycemia

- Hemoglobin A$_{1c}$ (HbA$_{1c}$) over target, or with excess glycemic variability (eg, hypoglycemia judged to be excessive, potentially disabling, or life-threatening)
  - Requiring HbA$_{1c}$ lowering without increased hypoglycemia
  - During preconception and pregnancy
- Children and adolescents with type 1 DM who have achieved HbA$_{1c}$ levels less than 7.0% (these patients and their families are typically highly motivated)
- Youth with type 1 DM who have HbA$_{1c}$ levels of 7.0% or higher and are able to use the device on a near-daily basis

The following patients might be good candidates for personal CGM, and a trial period of 2 to 4 weeks is recommended:

- Youth who frequently monitor their blood glucose levels
- Committed families of young children (younger than 8 years), especially if the patient is having problems with hypoglycemia

Intermittent use of professional CGM may be useful for youth with type 1 DM who are experiencing changes to their diabetes regimen or have problems with:

- Nocturnal hypoglycemia/dawn phenomenon
- Hypoglycemia unawareness
- Postprandial hyperglycemia

Conclusion and Future Research Opportunities

We recommend the following next steps for research:

- Longer-term (3- to 5-year) health outcomes studies to assess CGM durability beyond 6 to 12 months
- Health outcomes analyses to assess the cost-effectiveness of CGM in insulin-requiring DM
- Research to pinpoint which patients are the best candidates for CGM technology
- Research on the use of CGM in the hospital setting
- Assessment of the effects of preprandial glycemia and glycemic load on postprandial glycemia
- Examination of the efficacy of controlling postprandial glycemic excursions through carbohydrate counting and the use of correction dose insulin

We recommend the following next steps for CGM technology and product development:

- Improved blood glucose-reading accuracy
- Development of single-platform, intuitive software for CGM devices, glucose meters, and pumps

Executive Summary Table
Randomized Controlled Clinical Trials Evaluating the Effects of
Continuous Glucose Monitoring in the Treatment of Type 1 Diabetes Mellitus

	Trial Name	Description	Outcomes

ADULTS AND ADOLESCENTS	**STAR-1**	Primary end point: HbA_{1c} change from baseline
		
		Also evaluated hyperglycemia and/or hypoglycemia incidence
		
		Evaluated CSII patients 12 to 72 years of age
			6-Month HbA_{1c} (vs baseline HbA_{1c} 8.44%)
			  CGM + SMBG-treated patients: 7.77%
			  SMBG patients: 7.84%
			
			Patients with ≥60% sensor utilization compliance experienced significant HbA_{1c} reduction compared with less-compliant patients (*P*<.05)
			
			Severe hypoglycemia rates were higher in the CGM group[a]

	JDRF	Primary end point: HbA_{1c} change from baseline in CSII and MDI patients
		
		Also evaluated hypoglycemia incidence
		
		Evaluated patients 15 to 24 and ≥25 years of age (adult groups)
			26-Week HbA_{1c} (vs baseline):
			Age 15 to 24 years (baseline HbA_{1c} 7.9%-8.0%)
			  Mean HbA_{1c} difference of 0.08% for CGM + SMBG patients vs SMBG alone[b]
			Age ≥25 years (baseline HbA_{1c} 7.6%)
			  Mean HbA_{1c} difference of − 0.53% for CGM + SMBG patients vs SMBG alone[a]
			
			Severe hypoglycemic events were rare and occurred at the same rate for both study groups; both study groups also demonstrated similar biochemical hypoglycemia rates
			
			Patients aged ≥25 years showed increased sensor use compared with other patients
			
			Frequency of CGM monitoring was associated with significantly greater HbA_{1c} reductions in all study groups

	Key takeaway: More consistent CGM use predicts HbA_{1c} reductions		
YOUTH	**DirecNet**	Two, 13-week pilot studies (DirecNet); randomized clinical trial (JDRF CGM) Primary end point: HbA_{1c} change Safety end point: Hypoglycemia incidence	HbA_{1c} among CSII users improved from 7.1% at baseline to 6.8% at 13 weeks[a] Hypoglycemia frequency changed from 4.5% at baseline to 5.5% at 13 weeks[b]
	JDRF CGM		After 26 weeks, HbA_{1c} levels <7% in 27% of CSII users vs 12% of control group (age 8-14 years)[a] Patients who used the sensor 6 to 7 days a week were able to lower their HbA_{1c} level by a mean of 0.8% and maintain this improvement for 12 months Hypoglycemia rates did not differ between treatment groups
	Key takeaway: Youth were much less likely than adults to use CGM devices on a near-daily basis; the best HbA_{1c}-lowering results were seen in patients who used the sensor 6 to 7 days a week		
PREGNANCY	Several studies have used professional CGM to evaluate previously unknown hyperglycemia in pregnant women with type 1 diabetes mellitus; these studies identified 94 to 390 minutes/day of undetected hyperglycemia An additional study evaluated the effectiveness of professional CGM on maternal glycemic control, infant birth weight, and macrosomia risk in women with type 1 or type 2 diabetes mellitus; positive results were observed for professional CGM for all 3 outcome measures		

Abbreviations: CGM, continuous glucose monitoring; CSII continuous subcutaneous insulin infusion; DirecNet, Diabetes Research in Children Network; HbA_{1c}, hemoglobin A_{1c}; JDRF, Juvenile Diabetes Research Foundation Sensor Study; MDI, multiple daily injections; SMGB, self-monitoring of blood glucose; STAR-1, Sensor-augmented pump Therapy for A1C Reduction.
[a] Statistically significant.
[b] Not significant.

- Uniform integration of personal CGM devices with insulin pumps (eg, a single platform) and connectivity between personal CGM devices and insulin pens
- CGM algorithms that are proactive (ie, responsive to the rate of glucose change) rather than only reactive to the rise or fall of glucose values

1. BRIEF REVIEW OF CONTINUOUS GLUCOSE MONITORING TECHNOLOGY: HISTORY, CHEMISTRY, ACCURACY, LAG TIMES, INTERFERENCES

Over the past 10 years, continuous glucose monitoring (CGM) has evolved from being a research tool to a device useful in daily clinical practice. Designed to successfully improve glucose control without the addition of medication, CGM provides information about glucose concentration, direction, and rate of change over a period of several days.

The story of CGM today is reminiscent of self-monitoring of blood glucose (SMBG). About 3 decades ago, when urine glucose measurements were the standard of care for determining dosage adjustments to hypoglycemic agents (in particular, insulin), the utility of blood glucose meters was questioned, even though their overall accuracy was superior. Today, SMBG is widely used, and the utility of CGM is questioned, even though this technology also greatly increases the overall accuracy of glucose measurements.

The first attempt at continuous, remote glucose monitoring was made by Updike and Hicks in 1967 using animal models (1,2). The first CGM device made available in the United States was the GlucoWatch biographer (no longer in use), approved in 1999 by the US Food and Drug Administration (FDA) for retrospective use. Since that time, the FDA has approved 4 additional personal CGM devices (with or without concomitant insulin pump use). Personal CGM devices currently available include the Abbott Diabetes Care FreeStyle Navigator (Alameda, California, Fig. 1a), the DexCom SEVEN PLUS (San Diego, California, Fig. 1b), the Medtronic Guardian REAL-Time (Northridge, California, Fig. 1c), and the Medtronic MiniMed Paradigm REAL-Time (Northridge, California, Fig. 1d). All of these devices use hexokinase-based systems combined with mathematic algorithms and measure fluid obtained from the interstitial space to calculate blood glucose levels (Fig. 1e).

Device features of the most commonly used personal CGM sensors are provided in Table 1. Some personal CGM devices are wireless; their sensors are inserted into the subcutaneous tissue of the abdomen or upper arm.

Accuracy, Lag Times, and Interferences

All CGM devices are approved only as adjunctive devices to SMBG. This is partly because CGM accuracy
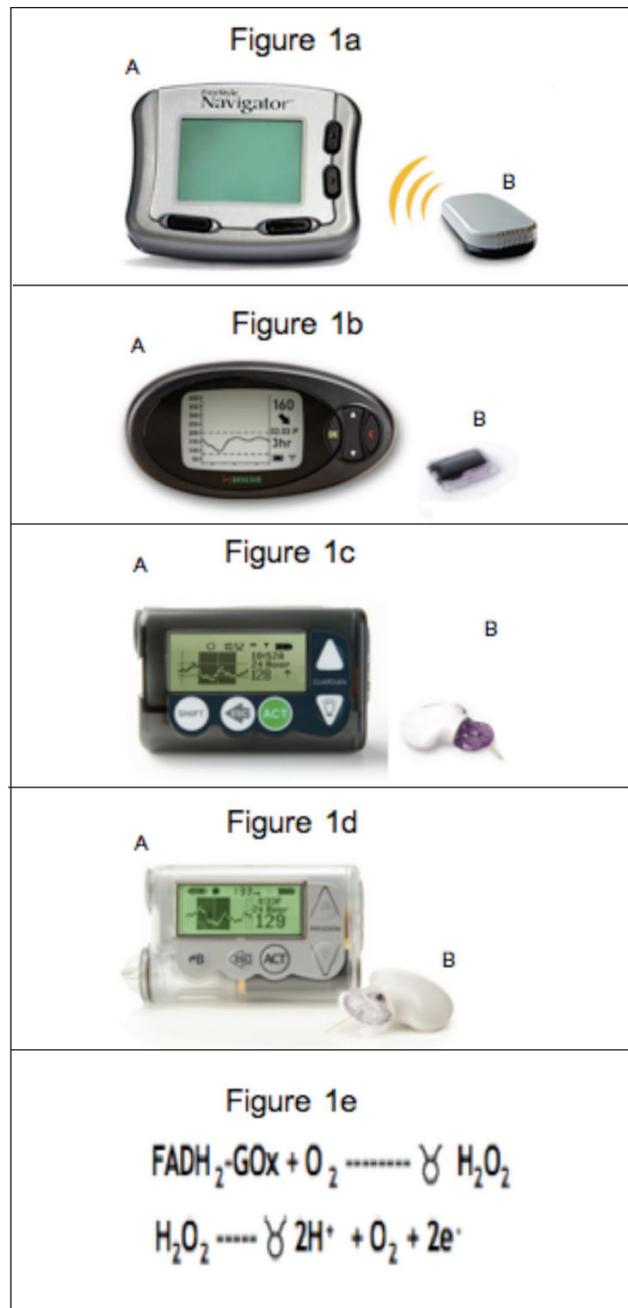
Fig. 1. US Food and Drug Administration–Approved Personal Continuous Glucose Monitoring Systems: Specifications and Algorithm. *Panel a*, FreeStyle Navigator (A, Navigator receiver unit, dimensions 6.35 × 8.1 × 2.3 cm; B, Navigator transmitter unit, dimensions 5.3 × 3.0 × 1.0 cm). *Panel b*, DexCom SEVEN PLUS (A, DexCom receiver unit, dimensions 11.4 × 5.8 × 2.2 cm; B, DexCom sensor and transmitter, dimensions 3.8 × 2.3 × 0.4 cm). *Panel c*, Medtronic Guardian REAL-Time (A, Guardian receiver unit, dimensions 5.1 × 8.1 × 2.0 cm; B, MiniLink transmitter and sensor, dimensions 3.6 × 2.8 × 0.8 cm). *Panel d*, MiniMed Paradigm REAL-Time (A, Insulin pump and Real-Time CGMS dimensions 4.8 × 7.6 × 2.0 cm; B, MiniLink transmitter and sensor, dimensions 3.6 × 2.8 × 0.8 cm). *Panel e*, Reaction of reduced GOx with oxygen followed by reaction of hydrogen peroxide on an electrode surface with most continuous glucose monitoring devices.

Table 1
Food and Drug Administration–Approved Personal Continuous Glucose Monitoring Devices
Available in the United States (3)

Features	Personal Continuous Glucose Monitoring Products			
	Abbott FreeStyle Navigator	DexCom SEVEN PLUS	Medtronic Guardian Real-Time	MiniMed Paradigm REAL-Time Revel System
FDA Approval	≥18 years of age: 5 days	≥18 years of age: 7 days	≥7 years of age: 3 days	≥7 years of age: 3 days
Integration with pump	No	No[a]	Yes	Yes
Integration with meter	Yes	No	No	Yes
Alarms/alerts				
Adjustable high/low thresholds	Yes	Yes	Yes	Yes
Predictive	Yes	No	Yes	Yes
Rate of change	Yes	Yes	Yes	Yes
Other features				
Days of wear	5	7	3	3
Needle/sensor size	21 gauge/5 mm	26 gauge/12 mm	22 gauge/12 mm	22 gauge/12 mm
Compatible software	Co-Pilot Health Management	Data Manager 3	Carelink Personal Therapy Management Carelink ProTherapy Management (office use)	Carelink Personal Therapy Management Carelink ProTherapy Management (office use)

Abbreviation: FDA, US Food and Drug Administration.
[a] Approval pending for integration with Animas Corporation and Insulet Corporation. Information current as of June 2010.

is not equivalent to that of glucose meters. Most available CGM data show a mean absolute relative difference (a standard error calculation tool used to measure the average absolute value of the relative [or percentage] difference between 2 measurements) in the range of 10% to 20% for different glucose ranges. Furthermore, only 60% to 80% of the glucose readings fall in the Clark's A zone, which is significantly lower than what can be achieved with SMBG (4-8). This may be in part due to the need to calibrate SMBG sensors in a home setting.

In addition, there is a physiologic lag between blood (SMBG) and interstitial space glucose of approximately 5 to 10 minutes; this lag is accentuated when glucose levels are undergoing rapid change (9-11). Figure 2 provides a conceptual graphic representation of this phenomenon (12). In clinical practice, this lag creates the potential for nonadherence, as patients cannot rely on the glucose values provided by the sensor and may overreact based on rises observed using SMBG readings. Therefore, this time lag can be associated with patient-driven insulin stacking or overtreatment of hypoglycemia (ie, without allowing time for insulin action or food absorption). Because of this, patients should calibrate sensors when blood glucose levels are stable.

Currently, acetaminophen and vitamin C intake may interfere with some CGM devices (13). In addition, patients must be instructed to avoid wearing a sensor when undergoing computed tomography or magnetic resonance imaging.

2. CGM DEVICE SELECTION: PROFESSIONAL AND PERSONAL OPTIONS

CGM equipment can be divided into 2 categories: professional and personal devices. Professional CGM equipment (also sometimes referred to as retrospective CGM) is owned by the health care professional, clinic, or hospital, and is generally used for masked data collection. Patients remain unaware of monitoring results until they are downloaded and analyzed by the health care professional; this allows for an unbiased assessment of patients' glucose control. Professional CGM is used in patients with type 1 diabetes mellitus (DM) or type 2 DM who are not at their hemoglobin A_{1c} (HbA_{1c}) target, who have recurrent hypoglycemia or hypoglycemia unawareness, or who are pregnant. Patients are typically asked to attend an office visit, receive instruction, wear a sensor for 3 to 5 days, keep a food and activity logbook, and then return to the
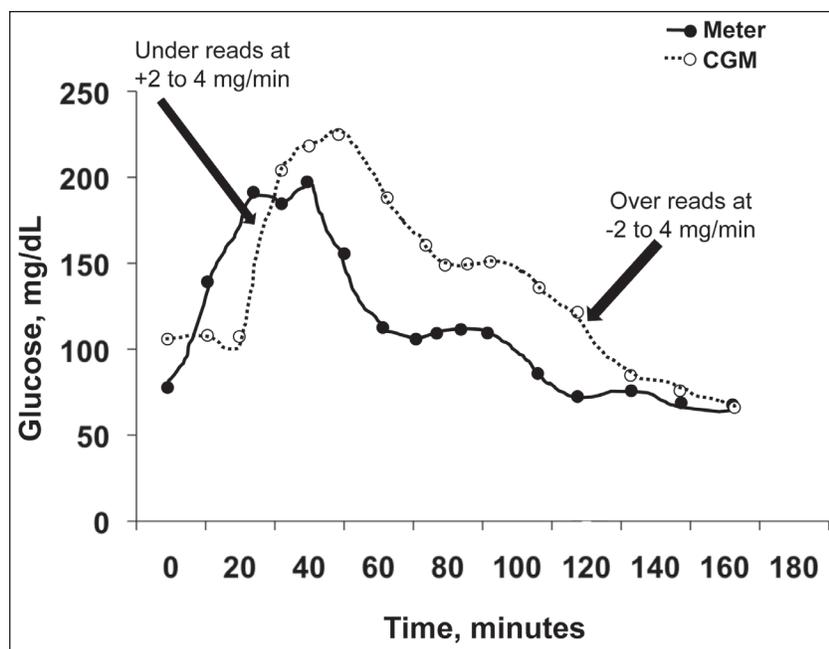
Fig. 2. Interstitial glucose sensor (continuous glucose monitoring) vs self-monitoring of blood glucose readings showing continuous glucose monitor lags when blood glucose rapidly rises or falls (12). Abbreviation: CGM, continuous glucose monitoring.

office for interpretation. Professional CGM does not have alerts to indicate hyperglycemia or hypoglycemia. Patients are recommended to use professional CGM on an episodic basis. Since professional CGM requires minimal training and setup time, it may be easier for patients to use than personal CGM. In addition, insurance reimbursement is more readily available for professional CGM than for personal CGM. Available professional CGM devices include the Medtronic iPro and the DexCom SEVEN PLUS (this device can be adapted for professional monitoring).

In contrast, a personal CGM device is owned by the patient. With personal CGM, glucose values are visible continuously; this allows for immediate therapeutic adjustments on the basis of "real-time" glucose results (personal CGM is also referred to as real-time CGM). Personal CGM is typically used by patients with type 1 DM who are not at their HbA_{1c} target level and (a) have the ability to use and understand the information supplied; (b) have hypoglycemia or hypoglycemic unawareness; and/or (c) are pregnant. In addition, any patient who could benefit from the continuous feedback of glucose readings and/or the hyperglycemia and hypoglycemia alarms in available personal CGM devices (such as patients with type 1 DM with HbA_{1c} levels less than 7.0%) are potentially good candidates for this technology. Some personal CGM devices also have alarms that indicate a rapid rate of glucose change using trend markers or arrows, and some have "predictive alarms," which calculate whether high or low glucose thresholds will be crossed, depending on rate of change and current glucose level (ie, they predict a low

or high glucose level). The setup requirements for personal CGM are more intensive than for professional CGM and include programming customized glucose targets and alarm thresholds (14). Currently, 4 FDA-approved personal CGM monitoring devices are available in the United States.

3. EVIDENCE SUPPORTING THE USE OF CGM

Over the past few years, a number of randomized controlled clinical trials have been undertaken to evaluate the impact of personal CGM devices in the treatment of type 1 DM. Several important observations have emerged. The most important is that the devices must be used on a near-daily basis to be effective in achieving and maintaining target HbA_{1c} levels.

Adults

Theoretically, by watching glucose levels rise and fall, it seems reasonable to assume that patients with type 1 DM would be able to improve their glycemic control with personal CGM, as measured by HbA_{1c} and frequency of hypoglycemia. The Sensor-Augmented Pump Therapy for HbA_{1c} Reduction (STAR-1) study was the first randomized controlled study to assess this hypothesis (15). STAR-1 enrolled 98 adults and 40 adolescents (age range, 12 to 72 years) and assigned patients to receive either continuous subcutaneous insulin infusion (CSII) with SMBG only or CSII with SMBG and personal CGM. After 6 months, HbA_{1c} levels were similarly reduced in both groups, but no

significant differences were observed between the 2 study arms. However, much was learned from this study. Patients who wore the CGM device the least often and had the highest HbA_{1c} levels experienced the least benefit. Furthermore, although not well documented, adults older than 65 years required more time for training with the CGM device and to review the downloaded data.

The largest CGM trial to date is the Juvenile Diabetes Research Foundation (JDRF) Sensor Study (7). Adults 25 years or older using personal CGM and either CSII or multiple daily insulin injections had a significant 0.53% reduction (*P*<.001) in HbA_{1c} compared with the HbA_{1c} levels of control patients who used only SMBG plus insulin. Across all age groups, severe hypoglycemia occurred in 5% to 10% of subjects, and its frequency did not differ between the 2 treatment groups. Like the STAR-1 study, more frequent personal CGM use predicted successful HbA_{1c} reductions (17). Following a 6-month extension phase, HbA_{1c} levels remained 0.4% below baseline (*P*<.001) (18). In another cohort of this study, 51 adults 25 years or older with HbA_{1c} levels less than 7% (mean HbA_{1c} 6.4%) experienced less overall hypoglycemic exposure compared with the control group, without a change in HbA_{1c} (19). In this group, HbA_{1c} levels remained stable at 6.4% for all 12 months of study follow-up (18). No data exist to suggest CSII is a better option than multiple daily injections in patients using personal CGM.

Youth

The Diabetes Research in Children Network (DirecNet) performed two 13-week, nonrandomized, pilot studies using the FreeStyle Navigator, a personal CGM system, in children and adolescents with type 1 DM. Although the observed lowering of HbA_{1c} levels was modest (0.3% to 0.6%), this research demonstrates the feasibility of these systems in youth with type 1 DM using CSII or glargine-based multiple daily injection therapy (7,16,20).

The JDRF CGM randomized clinical trials demonstrated that personal CGM could be used to assist youth with type 1 DM, 8 years or older, with HbA_{1c} levels less than 7.0% to maintain target HbA_{1c} levels while reducing exposure to hypoglycemia (19). However, the JDRF CGM trials failed to demonstrate a HbA_{1c}-lowering advantage for personal CGM vs SMBG among patients younger than 25 years with a baseline HbA_{1c} of 7.0% or higher (7). In this case, personal CGM was less successful in youth than in adults because children and adolescents with type 1 DM were much less likely to use the devices on a near-daily basis. Nonetheless, JDRF CGM trial patients between 8 and 18 years of age who used the sensor 6 to 7 days a week lowered their HbA_{1c} level by a mean of 0.8% and maintained this improvement for 12 months (21). Unfortunately, only about 22% of children and adolescents in the JDRF

Trial maintained this commitment for a full 12 months of follow-up. A similar dose-dependent effect of personal CGM use on HbA_{1c} lowering in youth has been demonstrated in the DirecNet GlucoWatch 2 Biographer [6] (22), Guard Control (6), and STAR-1 (15) studies.

In the JDRF CGM trial, the only clinical characteristic that predicted which pediatric patients would be able to successfully use personal CGM was the frequency of SMBG before study entry (17). Although CSII-treated patients outnumbered multiple daily injection users in many of the randomized pediatric clinical trials of personal CGM, patient outcomes have been similar for both methods of insulin administration (7,19,23). Randomized trials in younger age groups have been initiated, but no results have been reported. However, limited data from nonrandomized studies indicate that personal CGM devices can be used successfully in patients younger than 8 years (24).

Pediatric patients who successfully lowered their HbA_{1c} levels in the JDRF CGM trials did so without increasing their rates of severe hypoglycemia (21). In fact, the rates of severe hypoglycemic events in these randomized trials were much lower in pediatric patients in both the SMBG and personal CGM groups compared with previously reported data for intensively treated adolescents in the Diabetes Control and Complications Trial. These data indicate that insulin analogues and new and improved insulin pumps, as well as other advances, have had a positive impact on the safety of intensive insulin treatment in this population.

4. PATIENT SELECTION

Currently, not enough direct evidence is available to propose a specific algorithm to identify patients likely to experience the best outcomes with CGM. The following recommendations are based on expert opinion and are intended to provide a guide to decision making on the basis of the best available data. It is the responsibility of the individual health care professional to determine which patients will be the best candidates for this imperfect, yet powerful tool.

Ambulatory Care

Personal CGM has a widening application in DM management in the ambulatory care setting and has the potential to become the expert recommendation for select patient types. Personal CGM results in lower HbA_{1c} and lower incidence of hypoglycemia in adult patients with type 1 DM (7,25). When compared with SMBG, lower HbA_{1c} levels have been observed with the use of personal CGM in patients with baseline HbA_{1c} levels both less than 7% (19) and greater than 7% (6,15). Studies demonstrate that the more consistently personal CGM is used, the greater the benefit (7,15,25). Additionally, this benefit

can be sustained for 12 months (18). Therefore, on the basis of the available evidence, the American Association of Clinical Endocrinologists (AACE) recommends personal CGM for the following patients:

- Those with type 1 DM and the following characteristics:
  - Hypoglycemic unawareness or frequent hypoglycemia
  - HbA$_{1c}$ over target, or with excess glycemic variability (eg, hypoglycemia judged to be excessive, potentially disabling, or life-threatening)
  - Requiring HbA1c lowering without increased hypoglycemia
  - During preconception and pregnancy

Although the evidence supporting the use of personal CGM is derived from studies in patients with type 1 DM, it is reasonable to expect that similar results would be seen in patients using basal-bolus insulin regimens or CSII.

Pediatric Patients

On the basis of the evidence presented in Section 3, personal CGM is strongly recommended for children and adolescents with type 1 DM who have achieved HbA$_{1c}$ levels less than 7.0%. Personal CGM will assist these highly motivated and successful patients and families in maintaining target HbA$_{1c}$ levels and reducing hypoglycemia frequency. Personal CGM is also recommended for youth with type 1 DM who have HbA$_{1c}$ levels of 7.0% or greater and are able to use the device on a near-daily basis. Youth who monitor their blood glucose levels frequently are more likely to use personal CGM consistently, and a trial period of 2 to 4 weeks may also help to identify good candidates.

While scant data exist regarding the use of personal CGM in young children (<8 years of age), committed families of young children should also qualify for a trial period of CGM use, especially if the patient is having problems with hypoglycemia.

Last, the intermittent use of professional CGM may be useful in youth with nocturnal hypoglycemia, hypoglycemia unawareness, the dawn phenomenon, and postprandial hyperglycemia and in patients experiencing important changes in their DM regimen.

During Pregnancy

Postprandial glucose during pregnancy has been identified as the best predictor of neonatal macrosomia (26-28). Macrosomic infants are oversized, with a birth weight greater than the 90th percentile for gestational age and sex, or a birth weight greater than 2 standard deviations above the mean of a normal population of neonates (29). Macrosomia is the most common and critical neonatal complication associated with gestational diabetes mellitus (GDM). Therefore, SMBG protocols for women with GDM, type 1 DM, or type 2 DM during pregnancy stress the importance of measuring blood glucose after meals (30).

One possible reason that the frequency of macrosomia has persisted despite intensified care protocols is that physicians and patients do not know the times of the day that glucose levels are elevated. Glucose excursions can reach their maximal levels at varying times of day, based on the size and number of meals. Meal size also dictates the number of hours a patient remains in the postprandial state (31). The most rigorous SMBG protocols only require postprandial glucose measurements 3 times a day, despite the fact that many pregnant patients indulge in large between-meal snacks. As such, SMBG may miss both hyperglycemic and hypoglycemic events. By providing a complete glucose profile, CGM during pregnancy may facilitate the detection of all postprandial peaks and facilitate opportunities for intervention.

Three existing studies have used professional CGM to identify previously unknown hyperglycemia in pregnant women (32-34). These studies evaluated women with both GDM and type 1 DM. In patients using professional CGM, the total minutes per day of previously undetected hyperglycemia across 3 studies were 390, 192, and 94. One additional study evaluated the effectiveness of professional CGM on maternal glycemic control, infant birth weight, and macrosomia risk in women with type 1 DM or type 2 DM; results were positive for professional CGM for all 3 outcome measures (35,36). Summaries of these studies are provided in Table 2.

A large prospective study examining maternal and neonatal outcomes with CGM is still needed to evaluate the clinical implications of this new monitoring technique. However, the literature has shown that CGM in pregnant women with DM can reveal high postprandial blood glucose levels unrecognized by intermittent blood glucose determinations, and provides a useful educational tool to help patients improve adherence to their management regimens (32,33).

Based on the frequency of missed postprandial glucose peaks, it is recommended that all pregnant women with type 1 DM to receive CGM. The existing studies of CGM in pregnant women have used professional, or retrospective, CGM (32-34,36); however, the use of personal, or real-time, CGM may also be valuable in pregnancy because it allows immediate response to eating and glucose level patterns that can vary on a day-to-day basis (33). Women with type 2 DM or insulin-requiring GDM are typically able to maintain adequate glucose control if they are adherent to a monitoring schedule requiring 6 SMBG readings per day. For these patients, CGM may facilitate treatment adherence, but its use is not absolutely indicated.

Table 2
Studies Evaluating the Efficacy of Professional Continuous Glucose Monitoring in
Pregnant Women With Diabetes Mellitus[a] (32-36)

Study	Goal	Patients	Duration	Intervention	Outcomes
Jovanovič (2000) (32)	Evaluate professional CGM to detect previousl unknown hyperglycemia in women with GDM	10 women with GDM (no gestational data provided)	72 hours	Professional CGM	Mean total min/24 h previously undetected hyperglycemia: ~390 min
Yogev et al (2003) (33)	Comparison of daily glycemic profiles in pregnant women with type 1 DM measured by professional CGM vs intermittent glucose monitoring	34 pregnant women with type 1 DM, gestational age 16 to 32 weeks, receiving multiple insulin injections	72 hours	Professional CGM vs fingerstick glucose measurements performed 6 to 8 times a day	Average of 780 ± 54 glucose measurements recorded for CGM patients; mean total hyperglycemia in professional CGM arm (undetected by fingerstick): 192 ± 28 min/24 h; nocturnal hypoglycemic events recorded in a total of 26 patients
Chen et al (2003) (34)	Evaluate daily glucose level in pregnant women with GDM using professional CGM vs SMBG	57 women with GDM, gestational age 24 to 35 weeks; 23 treated by diet alone, 34 by diet and insulin	30 days	Professional CGM vs SMBG with fingerstick	Average of 763 ± 62 glucose measurements recorded for CGM patients; mean total hyperglycemia (undetected by fingerstick): 132 ± 31 min/24 h in insulin-treated group and 94 ± 23 min/24 h in diet-treated group; 14 patients, all insulin-treated, experienced nocturnal hypoglycemia
Murphy et al (2008) (36)	Evaluate the effectiveness of professional CGM during pregnancy on maternal glycemic control, infant birth weight, and risk of infant macrosomia in women with type 1 DM and type 2 DM	46 women with type 1 DM and 25 women with type 2 DM, gestational age 8 to 32 weeks	3 years	Antenatal care plus professional CGM (n = 38) or standard antenatal care (n = 33); professional CGM offered for ≤7 days every 4 to 6 weeks	Patients using professional CGM had lower mean hemoglobin A_{1c} levels (5.8% vs 6.4%); infants of CGM-using women had decreased median birth weight percentiles (69% vs 93%) and a reduced risk of macrosomia (odds ratio 0.36; 95% CI, 0.13-0.98; *P* = .05)

Abbreviations: CGM, continuous glucose monitoring; CI, confidence interval; DM, diabetes mellitus; GDM, gestational diabetes mellitus; SMBG, self-monitoring of blood glucose.
[a] All studies evaluated the use of professional CGM.

Hospital Setting

Professional real-time (retrospective) CGM has the potential to improve glucose control in the hospital setting while minimizing the risk of severe hypoglycemia, which has been shown to be an independent risk factor for mortality in the intensive care unit (37). Currently, none of the 4 FDA-approved personal CGM devices have been validated for accuracy or precision vs blood glucose measurements obtained in the hospital setting; thus, they are not approved for use in this environment.

Several small, single-center studies with microdialysis sensors and current CGM devices have demonstrated a reasonable correlation between abdominal interstitial fluid and arterial blood glucose measurements in critically ill patients in the intensive care unit (38,39). A recently published study compared real-time interstitial fluid CGM vs point-of-care blood glucose measurements to guide intravenous insulin infusion over 72 hours in 124 patients on mechanical ventilation. Patients receiving CGM achieved similar mean glucose control (106 ± 18 vs 111 ± 10 mg/dL in the control group, *P* = .076), but had significantly less risk of severe hypoglycemia (1.6% vs 11.5%, respectively, *P* = .031) (40).

Automated blood glucose measurement systems that reside in the peripheral vein are under development and may be more accurate than the current FDA-approved CGM systems that monitor glucose via interstitial fluid (41,42). However, more research and development must be conducted before CGM use becomes a management consideration in the hospital environment.

5.　PROPER FACILITY INFRASTRUCTURE TO HANDLE CGM LOGISTICS

By providing detailed feedback on what patients' 24-hour blood glucose profiles look like, CGM supplies clinicians and patients with key information that enables the identification of periods of suboptimal glucose control. Although personal CGM is growing in popularity, the educational investment required to successfully use this technology, combined with reimbursement challenges, have limited its use. However, professional or diagnostic CGM devices are owned by health care professionals and "borrowed" by patients to be worn for approximately 3 successive days for data collection. With professional CGM, patients are unaware of the glucose data generated. This means that minimal patient training is required, although both patient and physician benefit from the advantages of continuous data analysis (14).

When implementing professional CGM in the clinical environment, consider selecting a dedicated practice champion to manage the process and equipment. Box 1 outlines the technological requirements for conducting in-office professional CGM. Any treatment room or educational space will suffice for setting up the equipment and providing patient training. Box 2 provides a detailed summary of staff responsibilities (clinical and administrative) for scheduling, providing, and applying for reimbursement for professional CGM.

Professional CGM is not always reimbursable. However, with diligent administrative management and follow-up, it is possible to achieve good coverage for CGM. Details of medical coding requirements for CGM are covered in Section 6 of this document.

If a patient prefers to use personal CGM, the clinical practice may be asked to prepare and submit a letter of medical necessity. Patient training, however, is usually provided by the CGM device's manufacturer (either one-on-one or in a group setting). This training may take place in the health care professional's office or the patient's home. Generally, 60 to 90 minutes will be required to set up and train patients to use real-time CGM.

Patients who are most successful with personal CGM engage in regular follow-up with the health care professional. Box 3 provides details of follow-up requirements and resources available to office staff.

6.　ECONOMIC CONSIDERATIONS: REIMBURSEMENT ISSUES

Coding for CGM

Reimbursement for CGM can be a challenge. Although coverage overall is increasing at a rapid pace, different payers have different criteria, and the coding structures applied for reimbursement change frequently. Furthermore, payment amounts tend to vary by location and office site. Nonetheless, proper, precise diagnostic coding can go a long way to improving reimbursement for CGM.

To be reimbursed for professional services, physicians and other licensed professionals must use the American Medical Association's copyrighted Current Procedural Terminology (CPT) codes, which are recognized by all private and public payers. Two codes were recently revised by the CPT Panel to provide the required information to bill for CGM reimbursement: 95250 for data collection and 95251 for data interpretation. Box 4 provides a summary of these codes and their use.

Presently, US Centers for Medicare and Medicaid Services carriers only reimburse for professional, not personal, CGM (3). Other carriers, such as private insurers, have specific coding requirements that use underlying *International Classification of Diseases, Ninth Revision* diabetes codes to determine if they will cover personal CGM. Using the "bare bones" codes of 250.00 and 250.01, which signify DM (type 2 DM or type 1 DM, respectively), not stated as uncontrolled, will often lead to a denial. The *International Classification of Diseases, Ninth Revision* codes related to DM allow for the specific identification of complications if present, and can also be used to describe whether the patient's DM is uncontrolled.

CGM Coverage Policies for Select Private Health Plans

Information available from the JDRF (http://www.jdrf.org/index.cfm?page_id=111281, Table 3) indicate that the many large, private US health plans provide some coverage for personal CGM, particularly for patients with type 1 DM who are older than 25 years and/or have recurrent,

---

Box 1
Professional Continuous Glucose Monitoring: Technology Requirements

- Continuous glucose monitoring system, including the following: transmitter, receiver, sensors, software, cables and chargers for downloading, and other supported meters and cables
- Computer (to download data)
- Color printer (ideal, but not mandatory, to print data)

Box 2
Professional Continuous Glucose Monitoring: Staff Responsibilities

Before first visit
- Determine whether prior authorization is required
- Schedule patient

First visit
- Request patient sign a waiver agreeing to accept financial responsibility for equipment
- Set up CGM device
- Educate patient and reinforce instructions
  - Outline testing frequency and calibration requirements using compatible meter
  - Reinforce log-keeping (food, medication, activity)
  - Emphasize importance of return visit
- Insert device sensor and start up
- Provide patient with log to record food, medication, and activity
- Schedule return date to maximize device utility (typically 3 to 7 days, depending on device's approved duration of use)

Return visit
- Remove sensor from recorder, download data
- Set preferences for individual target values, generate report
- Interpret report and provide recommendations (this can be conducted face-to-face or remotely)
- Inform patient about the effects of food, activity, and medications on blood glucose levels
- Provide patient with copy of a report as an educational tool
- Clean and disinfect CGM equipment

Reimbursement
- Understand national and local payer policies for CGM reimbursement, and be familiar with CPT codes 95250 and 95251
- Submit claims for reimbursement, track submissions; appeal when denied

Abbreviations: CPT, Current Procedural Terminology; CGM, continuous glucose monitoring.

Box 3
Personal Continuous Glucose Monitoring: Follow-Up Requirements and Resources

- Medical office should be proactive in arranging patient follow-up for data interpretation
- Physician, nurse practitioner, or physician assistant must provide interpretation
- Interpretation can be conducted over phone, remotely via Internet report, or in face-to-face appointment
- As needed, manufacturers can typically provide information on industry certification of products, educational materials, or one-on-one guidance
- Product manufacturer Web sites typically offer additional information
  - Educational print-outs
  - Online tutorials
  - Product user guides (to supplement face-to-face training)
  - Toll-free customer service numbers

---

severe hypoglycemia. Other plans have broader inclusion criteria (ie, all patients with type 1 DM), while some plans do not have formal CGM coverage policies. The information in Table 3 is limited to plans that cover personal CGM use; other plans may cover professional CGM (ie, for ≤72 hours).

7. CONCLUSION AND FUTURE RESEARCH OPPORTUNITIES

First attempts to clinically use CGM have required a steep learning curve. Patients, health care professionals, and payers have been slow to accept that, for certain

---

Box 4
Current Procedural Terminology Codes for Continuous Glucose Monitoring

CPT code 95250 is described in the CPT manual (43) as "Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; sensor placement, hook-up, calibration of monitor, patient training, removal of sensor, and printout of recording." This code is usually used in conjunction with an evaluation and management code for the office visit. For returning patients, this code will be in the 99213 to 99215 range. A modifier, -25, must be appended to the evaluation and management code to show that this code is being billed with code 95250. This modifier indicates a significant, separately identifiable evaluation and management service provided by the same physician on the same day of the procedure or other service. Professional CGM can be billed on either the day the device is inserted and monitoring is initiated, or when the sensor is removed. Personal CGM is billed when the data are downloaded.

CPT code 95251 is described as "Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; interpretation and report." This code can be used for either professional or personal data collection and does not have to take place in the context of a face-to-face meeting. If code 95251 is billed at a time separate from another evaluation and management service such as an office visit, no modifier is needed.

Both codes have a caveat in that they cannot be billed more frequently than every 30 days.

Abbreviations: CPT, Current Procedural Terminology; CGM, continuous glucose monitoring.

---

individuals, CGM should be a cornerstone of overall DM management. That said, the technology itself is far from perfect; its accuracy and lag time errors due to interstitial fluid delays cause frustration for patients and clinicians alike. CGM devices could also be designed to be more comfortable and convenient. Added to these concerns, endocrinologists face a more fundamental issue: limited reimbursement for both the technology itself and for health care professionals' investment of time and resources. It is for these reasons that CGM use has not been as widespread as some would have predicted.

Still, we must appreciate that CGM technology is not only novel, but it can improve the lives of patients who incorporate it into a comprehensive DM management plan. While "early adopters" have clearly been in the minority, it is possible that, over time, CGM will become a key component of intensive DM management among insulin-requiring patients with DM. This is particularly the case for the treatment of type 1 DM. With this in mind, what next steps should we consider in terms of ongoing clinical research, research that guides reimbursement decisions, and potential areas for product refinement and/or new technology development?

First, to demonstrate that the benefits of personal CGM are durable beyond 6 to 12 months, longer-term (3- to 5-year) health outcomes studies like the Diabetes Control and Complications Trial or United Kingdom Prospective Diabetes Study may be needed before wider use is accepted. In the short-term, CGM devices need to have improved accuracy. This may be difficult because the capillary blood glucose devices used for calibration often

also have substantial accuracy challenges (44). Since some calibration will always be required—but "factory calibration" is not currently available—it seems that the first requirement for improved CGM accuracy is improved glucose meter accuracy. A reasonable goal for device accuracy would be a mean absolute relative difference of less than 10%. This seems feasible, as current mean absolute relative differences are not much higher (10% to 20%) (45).

Last, additional health outcomes analyses will be required to assess the cost-effectiveness of CGM in insulin-requiring DM. A literature review indicates that only 2 direct economic analyses of personal CGM have been conducted to date; neither demonstrate strong evidence for the cost-effectiveness of this technology (46,47). It is worth noting, however, that one recent analysis, conducted by the JDRF using clinical trial data from patients with type 1 DM, found that personal CGM use was associated with an increase in quality-adjusted life-years. In addition, a sensitivity analysis indicated that if patients receiving CGM were required to use only 2 SMBG test strips per day (to ensure device calibration), personal CGM would be a cost-saving technology compared with SMBG (46). It is hoped that additional analyses will provide a more detailed exploration of CGM cost-effectiveness.

Additional areas of research and analysis should include:
- Pinpointing which patients are the best candidates for CGM technology
- Research on the use of CGM in the hospital setting

Table 3
Continuous Glucose Monitoring Coverage for Select Health Care Plans[a]

Insurer	Coverage
Aetna	Patients with type 1 DM older than 25 years and those younger than 25 years with recurrent, severe hypoglycemia
BCBS MA	Patients with type 1 DM with recurrent, unexplained severe hypoglycemia or patients with type 1 DM who are pregnant
BCBS IL	Patients with type 1 DM older than 25 years
Harvard Pilgrim	Patients with type 1 DM, when determined to be medically necessary
CIGNA	Patients with type 1 DM older than 25 years and those younger than 25 years with recurrent, severe hypoglycemia
Highmark BCBS (PA)	Patients with type 1 DM with recurrent, severe hypoglycemia or hypoglycemia unawareness
Horizon BCBS (NJ)	No formal coverage
Group Health (WA)	No formal coverage
Humana	Patients with type 1 DM with recurrent, severe hypoglycemia or hypoglycemia unawareness
Kaiser Permanente (CA)	Patients with type 1 DM
Tufts (MA)	Patients with type 1 DM with hypoglycemia unawareness
United	Patients with type 1 DM who have not achieved optimum control or have experienced hypoglycemia unawareness
Wellpoint/Anthem	Patients with type 1 DM 25 years or older; coverage for other ages with recurrent, severe hypoglycemia

Abbreviation: DM, diabetes mellitus.
[a] Updated April 22, 2010.

- Assessment of the effects of preprandial glycemia and glycemic load on postprandial glycemia
- Examination of the efficacy of controlling postprandial glycemic excursions through carbohydrate counting and the use of correction dose insulin

In terms of product development, a short-term target should include more uniform integration of personal CGM devices with insulin pumps. Currently, each CGM sensor device uses a different "platform." Although there is a business reason to integrate each CGM device only with a single partner pump, a single-platform universe would be ideal for patients. With this, individuals who prefer one pump brand could pick the personal CGM system that best matches their needs.

In addition, only a few companies have successfully developed intuitive software for downloading CGM results. However, patients and endocrinologists find this helpful, if not critical. Again, from the patient and health care professional perspective, a single platform would be ideal for all CGM devices, glucose meters, and pumps. Importantly, any downloading should be simple for patients to perform at home before their clinic/office visits.

Along with these improvements in device accuracy, system integration, and software, it will be important that personal CGM is eventually approved for reimbursement as a stand-alone device (rather than only as adjunctive to SMBG). For this to happen, and for clinicians and payers to accept interstitial glucose values in place of SMBG on an ongoing basis, improvements in CGM sensitivity and specificity are critical. Last, with health care costs rising exponentially, and with cost-effectiveness considerations likely to have an ongoing role in medical decision making, CGM must become more affordable.

Over the long term, it must be appreciated that CGM in and of itself is not an end, but 1 component of a closed-loop system. The JDRF is committed to this concept through their Artificial Pancreas Project (48). Short of a true closed-loop system, other important advances would include connectivity and interactivity between CGM devices and insulin pens. The capability exists to create a "smart" insulin pen device with a memory chip, bolus calculator, and downloading capacity, but this has not been developed because of a perception of minimal market demand. However, this technology, integrated with a CGM device, would be potentially appealing, and is a potential future research opportunity. Other novel technologies, such as

near infrared ray, microdialysis, and long-term (≥1-year) implantable sensors for measuring glucose continuously, are also under development (49). Finally, in the future it will be important to create CGM algorithms that are proactive (ie, responsive to the rate of glucose change) rather than just reactive to the rise or fall of glucose values.

As CGM technology continues to mature, it will be critical that clinical endocrinologists are involved in the research and implementation of both short- and long-term advances. In that way, we will be able to help the greatest number of patients partake of this emerging technology and hopefully achieve the best care.

DISCLOSURE

Dr. Thomas C. Blevins reports being a speaker for Medtronic and DexCom and participating in clinical research studies for Abbott and Medtronic.

Dr. Bruce W. Bode reports being on the speakers' bureau, being on the medical advisory board, and consulting for Medtronic; being on the speakers' bureau for and receiving research/grant support from Lilly; receiving research/grant support from DexCom; and consulting for Abbott.

Dr. Satish K. Garg reports receiving grant support and speakers' honoraria from DexCom, Medtronic, and Abbott.

Dr. George Grunberger reports that he does not have a multiplicity of interest to disclose.

Dr. Irl B. Hirsch reports receiving research support from Novo Nordisk and Mannkind Corp and being a consultant for Roche, Johnson & Johnson, Bayer Pharmaceuticals, and Abbott.

Dr. Lois Jovanovič reports being an advisor to Medtronic, DexCom, and LifeScan and receiving research grants from these 3 companies.

Dr. Elizabeth Nardacci reports being a speaker for Eli Lilly and serving on the Medtronic Diabetes Technology Medical Advisory Board.

Dr. Eric A. Orzeck reports that he does not have a multiplicity of interest to disclose.

Dr. Victor L. Roberts reports that he does not have a multiplicity of interest to disclose.

Dr. William V. Tamborlane reports being a consultant for Medtronic.

REFERENCES

1. **Clark L**. Monitor and control of blood and tissue oxygen tensions. *Trans Am Soc Artif Intern Organs*. 1956;2:41.
2. **Updike SJ, Hicks GP**. The enzyme electrode. *Nature*. 1967;214:986-988.
3. **Harrell RM, Orzeck EA; American Association of Clinical Endocrinologists Socioeconomics and Member Advocacy Committee**. Coding guidelines for continuous glucose monitoring. *Endocr Pract*. 2010;16:151-154.
4. **Garg SK**. The future of continuous glucose monitoring. *Diabetes Technol Ther*. 2009;11(Suppl 1):S1-S3.
5. **Garg S, Zisser H, Schwartz S, et al**. Improvement in glycemic excursions with a transcutaneous, real-time continuous glucose sensor: A randomized controlled trial. *Diabetes Care*. 2006;29:44-50.
6. **Deiss D, Bolinder J, Riveline JP, et al**. Improved glycemic control in poorly controlled patients with type 1 diabetes using real-time continuous glucose monitoring. *Diabetes Care*. 2006;29:2730-2732.
7. **Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Tamborlane WV, Beck RW, et al**. Continuous glucose monitoring and intensive treatment of type 1 diabetes. *N Engl J Med*. 2008;359:1464-1476.
8. **Rodbard D, Bailey T, Jovanovič L, Zisser H, Kaplan R, Garg SK**. Improved quality of glycemic control and reduced glycemic variability with use of continuous glucose monitoring. *Diabetes Technol Ther*. 2009;11:717-723.
9. **Ellis SL, Bookout T, Garg SK, Izuora KE**. Use of continuous glucose monitoring to improve diabetes mellitus management. *Endocrinol Metab Clin North Am*. 2007;36(Suppl 2):46-68.
10. **Garg SK, Voelmle M, Gottlieb PA**. Time lag characterization of two continuous glucose monitoring systems. *Diabetes Res Clin Pract*. 2010;87:348-353.
11. **Moser EG, Crew LB, Garg SK**. Role of continuous glucose monitoring in diabetes management. *Avances en Diabetología*. 2010;26:73-78.
12. **Ellis SL, Naik RG, Gemperline K, Garg SK**. Use of continuous glucose monitoring in patients with type 1 diabetes. *Curr Diabetes Rev*. 2008;4:207-217.
13. **Kiechle FL**. The impact of continuous glucose monitoring on hospital point-of-care testing programs. *Diabetes Technol Ther*. 2001;3:647-650.
14. **Nardacci EA, Bode BW, Hirsch IB**. Individualizing care for the many: The evolving role of professional continuous glucose monitoring systems in clinical practice. *Diabetes Educ*. 2010;36(Suppl 1):4S-19S.
15. **Hirsch IB, Abelseth J, Bode BW, et al**. Sensor-augmented insulin pump therapy: Results of the first randomized treat-to-target study. *Diabetes Technol Ther*. 2008;10:377-383.
16. **Diabetes Research in Children Network (DirecNet) Study Group, Buckingham B, Beck RW, et al**. Continuous glucose monitoring in children with type 1 diabetes. *J Pediatr*. 2007;151:388-393.
17. **Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Beck RW, Buckingham B, et al**. Factors predictive of use and of benefit from continuous glucose monitoring in type 1 diabetes. *Diabetes Care*. 2009;32:1947-1953.
18. **Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Bode B, Beck RW, et al**. Sustained benefit of continuous glucose monitoring on A1C, glucose profiles, and hypoglycemia in adults with type 1 diabetes. *Diabetes Care*. 2009;32:2047-2049.
19. **Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group**. The effect of continuous glucose monitoring in well-controlled type 1 diabetes. *Diabetes Care*. 2009;32:1378-1383.
20. **Weinzimer S, Xing D, Tansey M, et al; Diabetes Research in Children Network (DirecNet) Study Group**. FreeStyle navigator continuous glucose monitoring system use in children with type 1 diabetes using glargine-based multiple daily dose regimens: Results of a pilot trial Diabetes Research in Children Network (DirecNet) Study Group. *Diabetes Care*. 2008;31:525-527.

21. **Chase HP, Beck RW, Xing D, et al**. Continuous glucose monitoring in youth with type 1 diabetes: 12-month follow-up of the Juvenile Diabetes Research Foundation continuous glucose monitoring randomized trial. *Diabetes Technol Ther*. 2010;12:507-515.

22. **Chase HP, Beck R, Tamborlane W, et al**. A randomized multicenter trial comparing the GlucoWatch Biographer with standard glucose monitoring in children with type 1 diabetes. *Diabetes Care*. 2005;28:1101-1106.

23. **Diabetes Research in Children Network Study Group, Weinzimer S, Xing D, et al**. Prolonged use of continuous glucose monitors in children with type 1 diabetes on continuous subcutaneous insulin infusion or intensive multiple-daily injection therapy. *Pediatr Diabetes*. 2009;10:91-96.

24. **Jeha GS, Karaviti LP, Anderson B, et al**. Continuous glucose monitoring and the reality of metabolic control in preschool children with type 1 diabetes. *Diabetes Care*. 2004; 27:2881-2886.

25. **Raccah D, Sulmont V, Reznik Y, et al**. Incremental value of continuous glucose monitoring when starting pump therapy in patients with poorly controlled type 1 diabetes: The RealTrend study. *Diabetes Care*. 2009;32:2245-2250.

26. **de Veciana M, Major CA, Morgan MA, et al**. Postprandial versus preprandial blood glucose monitoring in women with gestational diabetes mellitus requiring insulin therapy. *N Engl J Med*. 1995;333:1237-1241.

27. **Moses RG, Lucas EM, Knights S**. Gestational diabetes mellitus. At what time should the postprandial glucose level be monitored? *Aust N Z J Obstet Gynaecol*. 1999; 39:457-460.

28. **Jovanovič L, Ilic S, Pettitt DJ, et al**. Metabolic and immunologic effects of insulin lispro in gestational diabetes. *Diabetes Care*. 1999;22:1422-1427.

29. **Langer O, Mazze R**. The relationship between large-for-gestational-age infants and glycemic control in women with gestational diabetes. *Am J Obstet Gynecol*. 1988;159: 1478-1483.

30. **Jovanovič L**. *Medical Management of Pregnancy Complicated by Diabetes*. 4th ed. Alexandria, VA: American Diabetes Association, 2009.

31. **Polonsky KS, Given BD, Hirsch LJ, et al**. Abnormal patterns of insulin secretion in non-insulin-dependent diabetes mellitus. *N Engl J Med*. 1988;318:1231-1239.

32. **Jovanovič L**. The role of continuous glucose monitoring in gestational diabetes mellitus. *Diabetes Technol Ther*. 2000;2(Suppl 1):S67-S71.

33. **Yogev Y, Chen R, Ben-Haroush A, Phillip M, Jovanovič L, Hod M**. Continuous glucose monitoring for the evaluation of gravid women with type 1 diabetes mellitus. *Obstet Gynecol*. 2003;101:633-638.

34. **Chen R, Yogev Y, Ben-Haroush A, Jovanovič L, Hod M, Phillip M**. Continuous glucose monitoring for the evaluation and improved control of gestational diabetes mellitus. *J Matern Fetal Neonatal Med*. 2003;14:256-260.

35. **Murphy HR, Rayman G, Duffield K, et al**. Changes in the glycemic profiles of women with type 1 and type 2 diabetes during pregnancy. *Diabetes Care*. 2007;30:2785-2791.

36. **Murphy HR, Rayman G, Lewis K, et al**. Effectiveness of continuous glucose monitoring in pregnant women with diabetes: randomised clinical trial. *BMJ*. 2008;337: a1680.

37. **Van den Berghe G, Wilmer A, Hermans G, et al**. Intensive insulin therapy in the medical ICU. *N Engl J Med*. 2006;354:449-461.

38. **De Block C, Vertommen J, Manuel-y-Keenoy B, Van Gaal L**. Minimally-invasive and non-invasive continuous glucose monitoring systems: Indications, advantages, limitations and clinical aspects. *Curr Diabetes Rev*. 2008;4: 159-168.

39. **Joseph JI, Hipszer B, Mraovic B, Chervoneva I, Joseph M, Grunwald Z**. Clinical need for continuous glucose monitoring in the hospital. *J Diabetes Sci Technol*. 2009;3: 1309-1318.

40. **Holzinger U, Warszawska J, Kitzberger R, et al**. Real-time continuous glucose monitoring in critically ill patients: A prospective randomized trial. *Diabetes Care*. 2010;33:467-472.

41. **Ganesh A, Hipszer B, Loomba N, Simon B, Torjman MC, Joseph J**. Evaluation of the VIA Blood Chemistry Monitor for Glucose in Healthy and Diabetic Volunteers. *J Diabetes Sci Technol*. 2008;2:182-193.

43. **Rooyackers O, Blixt C, Mattsson P, Wernerman J**. Continuous glucose monitoring by intravenous microdialysis. *Acta Anaesthesiol Scand*. 2010;54:841-847.

44. American Medical Association. CPT Assistant: Your Practical Guide to Current Coding, 2009.

45. **Kimberly MM, Vesper HW, Caudill SP, et al**. Variability among five over-the-counter blood glucose monitors. *Clin Chem Acta*. 2006;364:292-297.

46. **Hirsch IB**. Clinical review: Realistic expectations and practical use of continuous glucose monitoring for the endocrinologist. *J Clin Endocrinol Metab*. 2009;94:2232-2238.

47. **Huang ES, O'Grady M, Basu A, et al; Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group**. The cost-effectiveness of continuous glucose monitoring in type 1 diabetes. *Diabetes Care*. 2010;33: 1269-1274.

48. **Newman SP, Cooke D, Casbard A, et al**. A randomised controlled trial to compare minimally invasive glucose monitoring devices with conventional monitoring in the management of insulin-treated diabetes mellitus (MITRE). *Health Technol Assess*. 2009;13:iii-iv, ix-xi,1-194.

49. JDRF Forms Partnership with Animas to Develop First-Generation Automated System for Managing Type 1 Diabetes 2010. Available at: http://www.jdrf.org/index.cfm?fuseaction=home.viewPage&page_id=2458B97B-1279-CFD5-A70D0580F67A16A9. Accessed March 2010.

50. **Garg SK, Schwartz S, Edelman SV**. Improved glucose excursions using an implantable real-time continuous glucose sensor in adults with type 1 diabetes. *Diabetes Care*. 2004;27:734-738.