

**CONTINUOUS GLUCOSE MONITORING:
A CONSENSUS CONFERENCE OF THE
AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS
AND AMERICAN COLLEGE OF ENDOCRINOLOGY**

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This document represents the position of the American Association of Clinical Endocrinologists and the American College of Endocrinology Consensus Conference Writing Committee. Where there were no randomized controlled trials or specific U.S. FDA labeling for issues in clinical practice, the participating clinical experts utilized their judgment and experience. Every effort was made to achieve consensus among the committee members. Position and consensus statements are meant to provide guidance, but they are not to be considered prescriptive for any individual patient and cannot replace the judgment of a clinician.

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ABSTRACT

Objective/Methods: Barriers to continuous glucose monitoring (CGM) use continue to hamper adoption of this valuable technology for the management of diabetes. The American Association of Clinical Endocrinologists and the American College of Endocrinology convened a public consensus conference February 20, 2016, to review available CGM data and propose strategies for expanding CGM access.

Results: Conference participants agreed that evidence supports the benefits of CGM in type 1 diabetes and that these benefits are likely to apply whenever intensive insulin therapy is used, regardless of diabetes type. CGM is likely to reduce healthcare resource utilization for acute and chronic complications, although real-world analyses are needed to confirm potential cost savings and quality of life improvements. Ongoing technological advances have improved CGM accuracy and usability, but more innovations in human factors, data delivery, reporting, and interpretation are needed to foster expanded use. The development of a standardized data report using similar metrics across all devices would facilitate clinician and patient understanding and utilization of CGM. Expanded CGM coverage by government and private payers is an urgent need.

Conclusion: CGM improves glycemic control, reduces hypoglycemia, and may reduce overall costs of diabetes management. Expanding CGM coverage and utilization is likely to improve the health outcomes of people with diabetes. (*Endocr Pract.* 2016;22:1008-1021)

Abbreviations:

A1C = glycated hemoglobin; **AACE** = American Association of Clinical Endocrinologists; **ACE** = American College of Endocrinology; **ASPIRE** = Automation to Simulate Pancreatic Insulin Response; **CGM** = continuous glucose monitoring; **HRQOL** = health-related quality of life; **ICER** = incremental cost-effectiveness ratio; **JDRF** = Juvenile Diabetes Research Foundation; **MARD** = mean absolute relative difference; **MDI** = multiple daily injections; **QALY** = quality-adjusted life years; **RCT** = randomized, controlled trial; **SAP** = sensor-augmented pump; **SMBG** = self-monitoring of blood glucose; **STAR** = Sensor-Augmented Pump Therapy for A1C Reduction; **T1D** = type 1 diabetes; **T2D** = type 2 diabetes

EXECUTIVE SUMMARY

Continuous glucose monitoring (CGM) has been commercially available since the early 2000s but has not been widely adopted in the management of diabetes. In light of advances in CGM technology and a growing

body of evidence supporting CGM benefits, the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) convened a public consensus conference February 20, 2016, to review available CGM data and develop strategies for overcoming barriers to CGM use and access (see Appendix for agenda and participants). Representatives from medical and scientific societies, patient advocacy organizations, government, health insurance providers, and device and pharmaceutical manufacturers met to discuss 4 key questions related to CGM use (Table 1). A detailed report on the scientific evidence supporting the consensus conference's conclusions follows this summary.

Question 1. How would patients, clinicians, and payers benefit from expanded use of personal and professional CGM?

- Extensive data from randomized controlled and other trials support the use of CGM in children and adults with type 1 diabetes (T1D). CGM may have similar benefits in insulin-using patients with type 2 diabetes (T2D) and pregnant women with diabetes.
- Advances in CGM technology have improved the accuracy and reliability of these devices.
- CGM is likely to reduce costs associated with hypoglycemia and severe hyperglycemia by alerting patients to impending or actual low or high glucose values and thereby facilitating prompt action and prevention of hospitalizations. CGM use may also reduce healthcare costs due to chronic diabetes complications, although more studies of the economic impact of CGM are needed.

Question 2. What CGM data are relevant and how should they be reported?

- The primary display of all CGM devices should highlight actionable data, such as:
 - Current glucose level
 - Glucose trend arrows
 - Graphs showing glucose trends over past day
- The default trigger for hypoglycemia alerts should be <70 mg/dL, which matches the generally agreed upon threshold for hypoglycemia and also allows for a window of safety to compensate for potential disparities between the CGM measurement of interstitial glucose and blood glucose values. Additional alerts at other modifiable trigger values may be useful.
- The downloadable report of all CGM devices should include a standardized report that includes such metrics as time in range, glycemic variability, patterns of hypoglycemia and hyperglycemia, and other customizable parameters deemed essential by the clinician and patient.

- CGM data should be evaluated in context with other variables such as meals, treatments, exercise, illness, insulin boluses, and automated insulin delivery activity.
- Standardized metrics and reporting among available CGM devices would facilitate understanding by patients and clinicians and promote wider adoption of CGM technology.
- Automated, rapid access to CGM data is essential for utilization by clinicians and useful for patients.
 - Patients older than 65 years with comorbidities and/or at risk for severe hypoglycemia
 - Women with diabetes who are or are planning to become pregnant as well as women with gestational diabetes
 - Patients with kidney disease
 - Patients with diagnosed hypoglycemia unawareness
- Cost-effectiveness studies are needed to further document healthcare cost reductions associated with CGM.

Question 3. How should the data and reporting be interpreted?

- Whether CGM is used intermittently or continuously, patients should generally be able to see and react to glucose data. However, CGM without data display (i.e., masked CGM) may be beneficial when used intermittently with advice and supervision from clinicians. Masked CGM can also serve as an important outcome measure for clinical trials in diabetes.
- CGM reports should be interpreted by trained clinicians but should include summary reports designed to be understood by patients.
- CGM training for clinicians should be made widely available to all involved in diabetes management and should encompass the use and interpretation of CGM data as well as the delivery of CGM patient education. CGM certification should not be required, as this would add another barrier and hinder wider adoption of CGM technology.

Question 4.1. What clinical data are currently available to support expanded CGM coverage by payers as pertains to questions 1 and 3?

- Data consistently support CGM-associated improvements in glycated hemoglobin (A1C) and reduced risk of hypoglycemia in patients using intensive insulin therapy for T1D.

Question 4.2. What additional data are needed?

- CGM is likely to provide significant benefits to the following patient populations, although additional studies are needed:

Call for Action

- Reimbursement should be expanded to cover clinician time spent reviewing and interpreting CGM data and advising patients outside of as well as during patient visits.
- Advancements in data delivery and interpretation through cloud-connected devices, electronic medical records, standardized reports, and other improvements are needed to increase clinician efficiency in reviewing and interpreting CGM data, facilitating better patient care and outcomes.

INTRODUCTION

CGM consists of a subcutaneously inserted sensor that measures interstitial glucose and delivers glucose values to a recording device. Most devices have a real-time display and other features that permit patients to respond to changing glucose values, and all can generate reports for later analysis. CGM use facilitates modest improvements in glucose control as measured by A1C without increasing, and sometimes reducing, the risk of hypoglycemia, thus facilitating safer intensification of glucose control. Technological advancements have also improved the accuracy and wearability (comfort, size, data display, fit, etc.) of these devices. However, CGM has been used on a regular basis by only a small minority of patients with diabetes: about 15% of T1D patients and even fewer with T2D (1). In February 2016, the AACE and ACE convened a public consensus conference to examine the evidence supporting CGM and the barriers to its adoption. Representatives from medical and scientific societies, patient advocacy organiza-

Table 1
Pillar Questions

1. How would patients, clinicians, and payers benefit from expanded use of personal and professional CGM?
2. What CGM data are relevant and how should they be reported?
3. How should the data and reporting be interpreted?
4. What clinical data are currently available to support expanded CGM coverage by payers as pertains to questions 1 and 3? What additional data are needed?

Abbreviation: CGM = continuous glucose monitoring.

tions, government, health insurance providers, and device and pharmaceutical manufacturers met to discuss 4 key questions related to CGM use. Each question was divided into 4 to 5 subquestions, as detailed below.

In this document, *professional use* refers to CGM devices owned by the clinician's office and used intermittently to assess glycemic patterns for therapeutic decision-making, whereas *personal use* refers to CGM devices owned by patients who use it for making real-time and retrospective adjustments to diabetes management. *Masked CGM* refers to professional devices without a data display, which may be used intermittently in conjunction with advice from clinicians or in clinical trials to clarify the action and evaluate the efficacy and safety of investigational medications. The CGM Consensus Conference Writing Committee acknowledges the limitations of CGM, including variable accuracy in the first hours of sensor use, the lead-lag phenomenon that occurs with rapid glucose changes and that contributes to differences between CGM readings and self-monitoring of blood glucose (SMBG) results, and larger mean absolute relative differences (MARDs; a measure of the average disparity between the CGM measurement and a reference blood glucose measurement) occurring in the hypoglycemic range. These concerns have been described in detail elsewhere (2-4).

Question 1. How would patients, clinicians, and payers benefit from expanded use of personal and professional CGM?

Question 1.1. What data support the use of CGM for either personal or professional use?

Personal use of real-time CGM on a frequent basis in children and adults with T1D is strongly supported by evidence from randomized, controlled trials (RCTs; e.g., Juvenile Diabetes Research Foundation [JDRF] CGM Study, the Sensor-Augmented Pump Therapy for A1C Reduction [STAR] 3 study, and the Automation to Simulate Pancreatic Insulin Response [ASPIRE] study), as well as observational data from the Type 1 Diabetes Exchange (T1D Exchange) clinic registry.

Conducted in 2007, the JDRF CGM trial included 322 adults and children with T1D and was designed to compare use of a CGM device (DexCom Seven™ [DexCom, San Diego, CA], the MiniMed Paradigm Real-Time Insulin Pump and Continuous Glucose Monitoring System [Medtronic, Minneapolis, MN], or the FreeStyle Navigator™ [Abbott Diabetes Care, Alameda, CA], chosen according to investigator/patient preference) with traditional SMBG using meters and test strips (5). Study results demonstrated that using CGM >6 times per week reduced mean hemoglobin A1C by 0.5 to 0.8% across all age groups from a mean baseline A1C of 7.6 to 8.0% without an increased incidence of severe hypoglycemia (5-9). CGM users with baseline A1C levels <7.0% maintained

A1C values between 6.4 and 6.5% and also experienced a 33 to 50% reduction in sensor values <70 mg/dL compared to patients in the control group. In the low baseline A1C cohort, the control group experienced significantly increased A1C levels (9,10).

In the STAR3 Study (conducted in 2007-2008), T1D patients were randomly assigned to therapy with a sensor-augmented pump (SAP) device that integrated an insulin pump with CGM (MiniMed Paradigm REAL-Time System™ [Medtronic]) or multiple daily injections (MDI) of insulin plus SMBG. A1C in children and adults using the SAP device decreased by 0.8%, with a net difference of 0.6% relative to the MDI+SMBG control group. Hypoglycemia rates were similar in the 2 groups (11). Similar results were seen across age groups, and the benefits increased with increasing frequency of CGM use (11-13). An observational study using data from the Medtronic CareLink database showed that patients who used CGM with an insulin pump ≥75% of the time over a 6-month period experienced significantly greater A1C reductions and up to 50% decreased incidence of hypoglycemia compared to patients who used their CGM devices <25% of the time (14).

Most studies of stand-alone CGM (i.e., CGM not integrated with an insulin pump) have shown A1C reductions without increased risk of hypoglycemia, but they have not shown *decreases* in hypoglycemia. Hypoglycemia reductions were demonstrated in the ASPIRE study, which compared a SAP device with a more advanced threshold suspend system (Paradigm Veo™ [Medtronic]) that stops insulin delivery when glucose readings fall below a given threshold (usually 70 mg/dL). Threshold suspend significantly reduced the frequency of nocturnal hypoglycemia by 32% ($P<.001$). Moreover, no severe hypoglycemic events occurred in the threshold suspend group compared with 4 events in the control group (15). Similar results were seen in patients with low baseline A1C and in those whose A1C decreased during the study period (15,16).

A 2012 meta-analysis that included 10 trials comparing real-time CGM to SMBG and 4 studies comparing SAP with MDI+SMBG supported the superiority of CGM over SMBG and SAP devices over MDI+SMBG in terms A1C reduction without increased risk of hypoglycemia (17).

Most RCTs were conducted prior to 2010 and demonstrated benefits despite relatively primitive CGM technology, which contributed to low adherence and high discontinuation rates. Problems with wearability and accuracy have hampered adoption of CGM. Only 6% of the initial enrollment population of the T1D Exchange clinic registry, which began in September 2010, used CGM, and in a 2014 report, 41% of CGM users (9% of T1D Exchange participants at the time of the survey) stopped using their device within a year because of difficulty wearing the device, technical problems, or concerns about data accuracy. The majority of these patients were using older devices (18).

Even with older technology, however, patients are more likely to use CGM more frequently and consistently when they see improvements in glucose trend data, out-of-range glucose levels, and detection of hypoglycemia. Changes that reduce or improve problems with insertion pain, bothersome system alerts, body-fit issues, and other barriers will also improve adherence (19,20). In the DirectNet study (conducted in 2009-2010), children 4 to 10 years of age and their caregivers reported high satisfaction with their devices despite no improvement in A1C or hypoglycemia rates. The DirectNet study also demonstrated the feasibility of CGM for children <4 years of age (21-23).

Technological progress has addressed barriers to CGM, including accuracy, which for many devices now approaches <10% of MARDs, which is considered safe for insulin dosing (4,24). Meanwhile, although CGM usage remains low, it is growing. The number of users in the T1D Exchange clinic registry has more than doubled to 15% in 2016 (1,25,26), and observational data collected in 2014-2015 from the T1D Exchange clinic registry support the benefits of newer devices. In the latest analysis, A1C levels were significantly lower in patients using CGM than those not using CGM, regardless of whether patients administered insulin via a pump (A1C 7.7% versus 8.2%; $P<.001$) or MDI (7.8% versus 8.6%; $P<.001$) (1). No RCTs with newer devices have yet been published, but several are underway.

Professional CGM consists of a real-time or masked (i.e., no data display) CGM that is owned by the clinician and worn by patients for short periods (typically 3 to 5 days; also known as intermittent CGM). The clinician uses the data to provide patient education and/or make changes to treatment regimens to achieve better glycemic control. Several small-scale studies have shown that professional CGM can lead to reductions in A1C, weight loss, and/or reductions in incidence of hypoglycemia in patients with T2D when the clinician uses the data to guide therapeutic changes (27-32). Notably, intermittent real-time CGM use in T2D patients for 12 weeks significantly reduced A1C compared with SMBG, and the difference in A1C was sustained over a 40-week follow-up period. Only about half of the 100 study participants used insulin to control hyperglycemia in this study (32). When used as an educational tool for pregnant women with T1D or T2D, intermittent masked CGM was associated with improved glycemic control in the third trimester, lower birth weight, and a 74% lower risk of macrosomia (33). Masked CGM has also provided valuable insight into the effects of medications in clinical trials and has helped establish normative values for glycemia (34-37).

CGM can be used to identify hypoglycemia in elderly patients and those with hypoglycemia unawareness (30,38,39). Recent studies have pointed to improvements in health-related quality of life (HRQOL), including reduced fear of hypoglycemia (40) and fewer missed school days (41).

Question 1.2. Which patient populations are best served by this technology based on the research?

Consensus conference participants unanimously agreed that real-time CGM should be available to all insulin-using patients regardless of diabetes type, although this conclusion is based entirely on studies conducted in T1D (1,7,9,11,15). Few studies have been conducted in patients with hypoglycemia unawareness due to challenges recruiting a suitable patient population, but it is likely that this population would also benefit from CGM (39). Other patients at risk from hypoglycemia, including the elderly, patients with renal impairment, and athletes should receive next priority (30,38,42). T2D patients who use antihyperglycemic agents other than insulin might also benefit from CGM (32), but the evidence base is inadequate to make a strong recommendation.

Question 1.3. What are the implications for the healthcare system of not addressing glycemic variability that results in short-term acute hypoglycemic episodes/hospitalizations and long-term complications/hyperglycemia?

The most recent estimate of direct medical expenditures for diabetes in the U.S. is \$218 billion per year (43); hospitalizations for hypoglycemic and hyperglycemic crises may account for up to \$5 billion, based on an estimated cost of approximately \$17,500 per hospitalization (44-47). Real-time CGM has the potential to substantially reduce these costs by helping patients prevent hypoglycemia and diabetic ketoacidosis. In the Diabetes Control and Complications Trial, severe hypoglycemia rose exponentially with decreasing A1C (48), whereas no increased or a reduced risk of hypoglycemia occurred with the A1C reductions observed in the JDRF-CGM, STAR3, and ASPIRE studies (5,11,15). A recent modeling study estimated that real-time CGM could reduce annual hospitalizations for hypoglycemia by 32%, which would reduce associated costs by \$54 million in a hypothetical population of 46,500 T1D patients (49). Another study conducted in Australia demonstrated an incremental cost-effectiveness ratio (ICER) of \$18,257 (AUS dollars) per severe hypoglycemic event avoided (50).

Few studies assessing the cost-effectiveness of CGM have been completed. In a modeling study based on data from the JDRF-CGM, the ICER was \$98,679 per quality-adjusted life year (QALY) gained, which is below a recently updated ICER threshold of \$109,000/QALY (values below this threshold indicate the therapy is cost-effective) (51,52). In sensitivity analyses, the authors determined that if only 2 glucose monitoring test strips were used per day for device calibration and CGM data were used for insulin dosing, long-term CGM use would produce cost savings compared with standard SMBG (51). Other modeling studies have estimated ICERs ranging from \$45,033 to \$229,675 (49). Cost-effectiveness studies based on quality of life analyses may not reflect real-world experience,

however, because HRQOL surveys are often insensitive to the effects of CGM. As a result, ICERs may be inflated.

Question 1.4. Is it necessary to review data in different groups to determine the impact on improved control of diabetes, not necessarily only a lower A1C, but a better quality of life?

Although studies conducted to date consistently show the benefits of CGM, additional studies in other populations are needed to substantiate the benefits in those groups (e.g., those with hypoglycemia unawareness). In addition to A1C, studies should assess glycemic variability. HRQOL surveys sensitive to the effects of CGM should be developed and, along with a measure of fear of hypoglycemia, should also be used as endpoints in future studies.

Research Gaps

Prospective RCTs evaluating personal CGM devices in insulin-using patients with T2D are needed to confirm that benefits seen in T1D also apply to this population. Prospective clinical trials are also needed to support CGM benefits as well as determine the suitability of personal versus professional CGM in at-risk groups such as the elderly, pregnant women, patients with kidney disease, patients with hypoglycemia unawareness or otherwise at risk from hypoglycemia, and athletes.

Although modeling studies have highlighted the potential for CGM to reduce healthcare costs, to date, real-world analyses have not demonstrated actual cost reductions by comparing healthcare costs among CGM users versus nonusers. In addition, there is a need for CGM-specific, validated HRQOL surveys, as currently available surveys are insensitive to the effects of CGM.

Question 2. What CGM data are relevant and how should they be reported?

Question 2.1. What information from CGM technology is critical for patients and clinicians to manage diabetes and improve outcomes?

The primary purpose of CGM is to identify glucose patterns, hypoglycemia, and hyperglycemia. Patients using personal CGM should use real-time data to prevent and/or treat hypoglycemia and hyperglycemic excursions, as well as retrospectively to adjust their treatment regimens. On the other hand, clinicians primarily use reports downloaded from personal or professional CGM to make retrospective treatment adjustments. In both cases, the goal is to maximize time in the desired glucose range.

Both patients and clinicians should recognize that blood glucose fluctuations are a dynamic process characterized by the current blood glucose value and the rate and direction of change. Modal day graphs that superimpose multiple days on the same plot are useful for highlighting time of day patterns as well as hypoglycemic and hypergly-

cemic periods and trends. Meal-related glucose excursions and nighttime glucose patterns should also be assessed. Sensor accuracy is vital and has significantly improved in the past decade. Now most CGM devices have MARD values close to 10% when compared with SMBG or Yellow Springs Instrument glucose values (4,24). No CGM devices are currently approved in the U.S. for insulin dosing or taking action to correct a hypoglycemia event without first confirming the glucose with SMBG. However, most patients use their CGM glucose values for the desired action (insulin dosing or food intake for hypoglycemia) in lieu of SMBG confirmation. Insulin dosing using data from a currently available CGM device is being evaluated (53).

Question 2.2. What key metrics should be considered?

Individual metrics have been discussed in detail elsewhere, including the 2016 AACE/ACE Consensus Statement on Glucose Monitoring (3,54,55). Table 2 summarizes some key metrics discussed by the CGM consensus group, along with their advantages, limitations, and supporting evidence (3,54-62).

Consensus conference participants generally agreed that personal CGM displays should include the following:

- Current glucose value
- Trend arrows showing direction of glucose changes (increases or decreases) and the rate of change for the past few hours
- Glucose values for the past 3, 5, or 7 days at the current time (i.e., modal day)
- Factory-programmed (nonmodifiable) trigger for a hypoglycemic alert set to <70 mg/dL, with optional/programmable alerts at lower values (e.g., <55 mg/dL and <45 mg/dL)
- Factory-programmed (nonmodifiable) hyperglycemic trigger set to >300 mg/dL, with customizable alerts at other hyperglycemic values set by patient and clinician
- Insulin pump data (as applicable), which should be downloadable on the same platform to review insulin dose and glucose excursions simultaneously, such that necessary action can be recommended or taken

Predictive alerts signal CGM users of impending high and low glucose values, whereas rate of change alerts signal when glucose rises or falls at a specified rate. These features may be useful, although the alerts and display information should be clearly distinguishable from the trigger alerts. Users should be able to customize alerts to be discreet (e.g., vibratory or flashing) or audible, but they should be escalating (e.g., with increasing volume or intensity if the user does not respond).

Reports downloaded from personal or professional CGM vary widely in how data are organized and shown (54), and no consensus has yet been reached on optimal

Table 2
Advantages and Limitations of Metrics Recommended for Inclusion in Standardized CGM Reports

Metric	Advantages	Limitations	Supporting evidence and/or detailed discussion
Glucose control measures			
Percent time in glucose range of 70-180 mg/dL ^a	Widely accepted "safe" range of glycemic exposure	May not be appropriate for all patients	Garg and Jovanovic 2006 (56) Bailey et al 2007 (57) Rodbard 2009 (54) Bergenstal et al 2013 (55)
Percent time with glucose >180 mg/dL, >250 mg/dL, >300 mg/dL ^a	Values align with generally accepted levels of extreme hyperglycemia and DKA thresholds	May not be appropriate for all patients	Garg and Jovanovic 2006 (56) Bailey et al 2007 (57) Rodbard 2009 (54) Bergenstal et al 2013 (55)
Percent time with glucose <70 mg/dL, <55 mg/dL, and <45 mg/dL ^a	Values align with generally accepted levels of hypoglycemia and severe hypoglycemia	May not be appropriate for all patients Thresholds at <70, <60, and <50 mg/dL preferred by many clinicians and organizations	Garg and Jovanovic 2006 (56) Bailey et al 2007 (57) Rodbard 2009 (54) Bergenstal et al 2013 (55)
Glycemic variability, reported as SD or %CV	Classic statistical methods generally understood by clinicians; SD of glucose correlates with mean glucose; %CV usually varies systematically depending on glucose level	Reducing glycemic variability not yet proven to independently affect diabetes outcomes in ambulatory patients Values not widely understood by patients SD tends to be higher in patients with higher mean glucose values	Kohnert et al 2009 (58) Rodbard 2009 (54) Bergenstal et al 2013 (55) Bailey et al 2016 (3)
Graphic presentation of glucose values over 1-5 days, including mean at specific times, SD, 95% CI, and mean daily glucose over time, with ability to stratify by weekday, weekend, and day of week	Facilitates detection of consistent patterns in glucose excursions	Graphs may be difficult to interpret due to wide variation in glucose data obtained over several days No agreement among clinicians and industry on optimal modal day presentations	Bailey et al 2016 (3)
Statistics over 7, 15, and 30 days, including mean glucose in the morning, noon, and night; mean daily glucose; percentage of time in range (70-180 mg/dL ^a); number of hypoglycemic episodes; percentage of time in hypoglycemia (<70 mg/dL ^a)	Provides information on glycemic trends over time	Potentially difficult and/or time-consuming to report and interpret	Bailey et al 2016 (3)
Calculated (estimated) A1C	Reflects mean glucose and is readily understood by patients and clinicians	Does not reflect hypoglycemic or hyperglycemic values	Rodbard 2009 (54) Bergenstal et al 2013 (55) Bailey et al 2016 (3)
Risk assessment			
LBGI	Weights risk according to more severe hypoglycemic levels	Mathematical formula may need further validation Concept needs to be shown to relate to diabetes outcomes in clinical trials	Kovatchev et al 1998 (59) Rodbard 2009 (54) Fabris et al 2015 (60)
HBGI	Weights risk according to more severe hyperglycemic levels	Mathematical formula may need further validation Concept needs to be shown to relate to diabetes outcomes in clinical trials	Kovatchev et al 1997 (61) Rodbard 2009 (54) Fabris et al 2015 (60)
ADRR (optional)	Combines HBGI and LBGI in one measure	Mathematical formula may need further validation Concept needs to be shown to relate to diabetes outcomes in clinical trials May be more useful/appropriate for SMBG than CGM	Kovatchev et al 2006 (62) Rodbard 2009 (54)

Abbreviations: A1C = glycated hemoglobin; ADRR = average daily risk range; CGM = continuous glucose monitoring; CI = confidence interval; CV = coefficient of variance; DKA = diabetic ketoacidosis; HBGI = high blood glucose index; LBGI = low blood glucose index; SMBG = self-monitoring of blood glucose.

^aShould include option to customize parameter for individual patients.

graphic displays. The ambulatory glucose profile (AGP), first introduced in 1987 (63) and adapted more recently for CGM (55), or a 24-hour tracing with superimposed insulin, meals, and other markers (64) are useful graphics. A limitation of the AGP and all other modal presentations is that patients do not always keep consistent schedules for meals, snacks, exercise, work, and sleep.

Consensus conference participants agreed that a standardized, “default” report downloadable from all CGM devices should include the parameters described in Table 2 as well as device-related data such as frequency of calibration, frequency of sensor interactions, and point accuracy. Reports should also show the CGM data in context with other variables such as meals, treatments, exercise, illness, insulin boluses, and automated insulin delivery activity. Moreover, systems should permit integration with commonly used step counters, heart rate monitors, and mobile device apps that track meals, exercise, etc., to minimize or avoid manual entry by patients. Innovations such as Bluetooth insulin pens would facilitate passive accumulation of essential insulin dosing data.

Question 2.3. Would standardized reporting support patient management, clinician utilization, and training of clinicians and patients?

Standardized metrics and reporting among available CGM devices would facilitate understanding by patients and clinicians and promote wider adoption of CGM technology. The goal of standardization should be to make CGM reports as universally understandable by clinicians as an electrocardiogram, and reports should also include summary pages geared for patients.

An urgent need is for improved ease of accessing CGM data in terms of both simplicity and speed. Future systems could include automatic uploads to secured data clouds to facilitate remote access by clinicians and caregivers.

Question 2.4. What data are necessary and how should they be standardized?

The default reports from all CGM devices, whether personal or professional (with either masked or real-time displays), should include the metrics listed in Table 2. Manufacturers may differentiate their products by customizing features and data analyses beyond the basic metrics.

Question 2.5. Can unnecessary data distract from key findings? If so, should a series of algorithms be developed to assist with a focused and meaningful analysis and interpretation?

Metrics not listed in Table 2 should be displayed on subsequent pages of CGM reports so they are available to clinicians but do not interfere with review and interpretation of hypoglycemic and hyperglycemic patterns. Pattern-recognition software that identifies high-risk patterns could facilitate interpretation and utilization by clinicians.

Research Gaps

Recommendations for the metrics listed in Table 2 are based primarily on expert opinion of consensus conference participants and others (3,54,55). For example, no clinical studies have examined whether CGM hypoglycemia alerts set at <55 and <45 mg/dL versus <60 and <50 mg/dL would have different effects on patient safety. The risk indices are generally believed to be useful and were shown to predict outcomes in patients with T2D (65), but the impact of changes in the low blood glucose index (LBGI), high blood glucose index (HBGI), and average daily risk range (ADRR) has not been assessed in CGM users.

Question 3. How should the data and reporting be interpreted?

Question 3.1. Are there standard metrics that should inform therapy adjustment?

As discussed under Question 2, a standardized basic report downloadable from all devices would facilitate data interpretation by clinicians and patients. Therapy adjustments should be made on the basis of percent of time within the optimal range (70 to 180 mg/dL for most patients), percent of time above and below this range, and indices of hypoglycemic risk (e.g., LBGI) and glycemic variability (e.g., HBGI and ADRR).

Question 3.2. Should additional patient descriptors based on standardized CGM reporting be included, such as “hypo-unaware,” “hyper-unaware,” and “high variability”? What are the most important factors clinicians need to focus on when interpreting CGM data?

For patients and clinicians, the identification of nocturnal hypoglycemia, hypoglycemia unawareness, and other hypoglycemia events are of paramount importance in diabetes management, followed by detection of high glycemic variability and hyperglycemia unawareness. CGM reports should not include qualitative descriptors or labels, because these assessments should be left to the clinician as part of the diagnostic process. However, a diagnosis of hypoglycemia unawareness, frequent nocturnal hypoglycemia, or extreme glycemic excursions could be used to justify reimbursement for CGM.

Question 3.3. Who should interpret data to utilize it in an effective way? Who should be authorized to interpret a standardized CGM report that will allow it to be part of permanent medical records and billable service? Is special training or certification necessary? Should the provider interpretation of data be standardized as well?

Patients manage their own diabetes on a day-to-day basis, and their health and safety would benefit from access to CGM data; therefore, whether CGM is used continuously or intermittently, patients should generally be able to see and respond to glucose data and should receive education and

support from their clinicians to ensure acute problems are appropriately addressed. Manufacturers of CGM devices and software are encouraged to provide more patient training courses and materials, especially with online resources.

As described in Question 1.1, CGM without data display (i.e., masked CGM) has demonstrated benefit in T2D when used intermittently in conjunction with advice from clinicians, although more trials of masked CGM with modern devices are needed. In T1D, only near-daily use of personal CGM has been shown to be of benefit (5-9,14,66). Masked CGM is of great value in clinical trials to clarify the action of investigational medications, and CGM results may be used as endpoints in the evaluation of medication efficacy and safety.

Although CGM interpretation has recently become a standard component of endocrinology fellowship training (a practice fully endorsed by AACE/ACE), a large number of clinicians who manage diabetes have not received adequate training in the use and interpretation of CGM, including many practicing endocrinologists, primary care physicians, nurse practitioners, physician assistants, nurses, and certified diabetes educators. CGM training—including the science behind CGM, CGM accuracy, utilization of CGM in clinical practice, interpretation of CGM data, and the delivery of patient education on CGM—should be made widely available to all clinicians involved in diabetes management through relevant medical and diabetes education associations, CGM manufacturers, and continuing medical education providers. Ideally, educational programs and materials would be available through live education as well as print and online materials. However, formal certification in CGM should not be required, as this would result in more barriers and hinder wider adoption of this valuable technology.

AACE/ACE strongly recommends that downloading and interpretation of glucose monitoring data (both SMBG and CGM) should be considered a diabetes management standard of care. As discussed under Question 2, a 1- to 2-page standardized report would facilitate this care process. These reports should be interpreted by trained clinicians but should include summary pages designed to be understood by patients.

Question 3.4. What would be the impact of CGM on patients' frequency of SMBG?

SMBG is currently required for daily calibration of all CGM devices available in the U.S., as well as for insulin dosing, but patient-related errors in SMBG are common (67). CGM innovations have the potential to reduce or eliminate the need for SMBG. A <10% MARD has been suggested as the threshold for CGM accuracy that would permit safe dosing of insulin with CGM, so long as the sensor relays reliable data without signal interruption or loss of sensitivity throughout its lifetime (4). Currently, no CGM devices consistently meet this requirement, and

none are yet approved in the U.S. for use in insulin dosing. However, as CGM technology has continued to improve, MARDs have begun to approach the 10% threshold (24), and a factory-calibrated device currently marketed in Europe was shown to have comparable accuracy to SMBG (68). In practice, many patients already use their CGM data without confirmatory SMBG values for insulin dosing. This approach is being assessed in an ongoing trial with a current CGM device (53).

Question 3.5. What outcome measures (behavioral, clinical, laboratory, etc.) can be used by providers and payers to assess the benefits of CGM in their patients and justify decisions on continued need and coverage?

CGM users who lacked full reimbursement were 50% more likely to discontinue CGM in a study involving >10,000 CareLink participants (14), highlighting the need for more studies demonstrating a positive impact on both direct and indirect healthcare spending. Clinical assessments relevant to the benefits of CGM include improvements in glycemic control measures (calculated A1C and glycemic variability metrics) and reductions in the frequency of hypoglycemia, severe hypoglycemia, and number of emergency room visits. Behavioral measurements include changes in the number of days the CGM device was used, frequency of CGM downloads, and frequency of SMBG. In addition, CGM studies could examine endpoints such as improved sleep quality for patients and caregivers; positive changes in absenteeism, workplace disruptions, and work/school performance (e.g., so-called presenteeism, in which individuals' functioning is impaired by diabetes-related events such as hypo- or hyperglycemia); and reduced burden on school resources.

Research and Practice Gaps

Nearly all proposals herein regarding data interpretation are based on expert consensus from the conference rather than clinical studies or other forms of evidence. Research is needed to confirm that CGM devices can be safely used for insulin dosing and to demonstrate the effectiveness and safety of factory-calibrated devices relative to traditional patient-calibrated CGM. Whether approval for insulin dosing and factory calibration would reduce healthcare costs related to SMBG also needs to be studied.

There is a need for pattern recognition software to identify the highest risk patterns, which would facilitate interpretation and utilization of data by clinicians. There was broad consensus at the conference that clinician training programs should be expanded to all healthcare professionals involved in diabetes management. As described in Question 3.5, the impact of CGM on various HRQOL endpoints should be examined to help justify CGM reimbursement.

Question 4. What clinical data are currently available to support expanded CGM coverage by payers as pertains to questions 1 and 3? What additional data are needed?

As described in the preceding sections, a wealth of evidence supports CGM-associated improvements in A1C and reduced risk of hypoglycemia in individuals with T1D, and these benefits are likely for patients with other forms of diabetes using intensive insulin therapy. Furthermore, CGM is likely to provide significant benefits to patients with hypoglycemia unawareness; patients older than 65 years, particularly those at risk from hypoglycemia; women with diabetes who are or are planning to become pregnant and those with gestational diabetes; and patients with kidney disease. Nevertheless, CGM provides benefits only if worn as prescribed and if the data are accessed and used appropriately. Not all patients and/or their caregivers will be willing and able to use the technology, although acceptance and adherence should increase as technological innovations improve wearability, reliability, and accuracy and as economic factors drive down device cost. Additional cost-effectiveness studies are needed to document these changes.

Question 4.1. In view of recent scientific evidence and progress in CGM technology, what are the current gaps in CGM reimbursements and in what priority should reimbursement gaps be addressed?

Two main gaps in reimbursement are the lack of reimbursement for Medicare patients >65 years (pending legislation addresses this gap) and inadequate reimbursement for the time required for clinicians to access and interpret CGM data, as well as provide advice outside of patient visits. In addition, future Current Procedural Technology codes should include personal as well as professional use of CGM to better reflect current practice.

With most currently available CGM technology, data downloads and report printing are time-consuming activities that drain office resources. However, despite the frequency of CGM data downloads being a commonly used and well-accepted quality of care measure, these activities are not currently reimbursed, nor is the time clinicians spend outside of office visits reviewing and analyzing CGM data. All CGM data should be accessible from the electronic medical records, which would improve care and help justify reimbursement.

Question 4.2. What future clinical or technological needs should be addressed to improve outcomes related to CGM?

CGM is a strong research tool, and CGM data should be recognized by governing bodies as a valuable and meaningful endpoint to be used in clinical trials of new drugs and devices for diabetes treatment. The identifica-

tion of hypoglycemia is as important as the measurement of glycemic reductions in clinical trials.

Efficiency-related improvements would facilitate better patient care as well as reduce care costs. These include advancements in data delivery through cloud-connected or other wireless devices (e.g., Bluetooth) and standardized reports as discussed in prior sections.

CALL FOR ACTION

Patients, clinicians, legislators, patient advocates, insurance companies, regulators, and other interested parties should work together to overcome current barriers to CGM adoption, including those related to reimbursement, patient and clinician training, and ease of use and interpretation. CGM improves glycemic control, reduces hypoglycemia, and may reduce overall costs of diabetes management. Therefore, expanding CGM coverage and use would improve the health of the diabetes population.

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Dr. Henry Anhalt has served as independent director for Tandem Diabetes Care and consultant and/advisor for Abbott Diabetes Care and Eli Lilly.

Dr. Timothy S. Bailey has served as a consultant and/or speaker for Novo Nordisk, Bayer, BD, Medtronic, and Sanofi. He has received research support from Abbott, ACON, Alere, Animas, Bayer, BD, Bristol Myers Squibb, Cebix, Dexcom, GlaxoSmithKline, Halozyme, Insulet, Lifescan, Lilly, Mannkind, Medtronic, Merck, Novo Nordisk, Orexigen, Sanofi, and Tandem.

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APPENDIX 1

The Consensus Conference report was based on a 2-day international experts workshop: AACE/ACE Consensus Conference on Continuous Glucose Monitoring

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The writing committee, AACE, and ACE are grateful to participants for their contribution to the consensus.

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General Session	
Agenda, February 20, 2016	
8:00 AM – 8:10 AM	Welcome & Introductions Dr. George Grunberger, AACE President
8:10 AM – 8:20 AM	AACE Perspective Dr. Vivian Fonseca, Chair, Consensus Conference on Continuous Glucose Monitoring
8:20 AM – 9:05 AM	State-of-the-Art of Glucose Monitoring Technology Dr. Bruce Buckingham
9:05 AM – 9:15 AM	Pillar Breakout Instructions Dr. Vivian Fonseca
9:15 AM – 9:30 AM	Break
Pillar Breakout Sessions	
9:30 AM – 12:00 PM	Medical/Scientific, Professional & Educational Societies <i>Co-Moderators: Dr. Victor Roberts & Dr. William Tamborlane</i>
	Patient/Lay Organizations <i>Co-Moderators: Dr. Irl Hirsch, Dr. Henry Anhalt & Dr. Thomas Blevins</i>
	Government/Regulatory, Payers & Employers <i>Co-Moderators: Dr. Eric Orzeck & Dr. Satish Garg</i>
	Industry Organizations <i>Co-Moderators: Dr. Timothy Bailey & Dr. Yehuda Handelsman</i>
12:00 PM – 1:30 PM	Lunch
Pillar Forum	
1:30 PM – 2:15 PM	Question 1: How would patients, clinicians and payers benefit from expanded use of personal and professional CGM?
2:15 PM – 3:00 PM	Question 2: What CGM data are relevant and how should they be reported?
3:00 PM – 3:15 PM	Break
3:15 PM – 4:00 PM	Question 3: How should the data and reporting be interpreted?
4:00 PM – 4:45 PM	Question 4: What clinical data are currently available to support expanded CGM coverage by payers as it pertains to Questions 1 and 3? What additional data are needed?
4:45 PM – 5:00 PM	Conclusion

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