International Consensus on Use of Continuous Glucose Monitoring

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Measurement of glycated hemoglobin (HbA$_{1c}$) has been the traditional method for assessing glycemic control. However, it does not reflect intra- and interday glycemic excursions that may lead to acute events (such as hypoglycemia) or postprandial hyperglycemia, which have been linked to both microvascular and macrovascular complications. Continuous glucose monitoring (CGM), either from real-time use (rtCGM) or intermittently viewed (iCGM), addresses many of the limitations inherent in HbA$_{1c}$ testing and self-monitoring of blood glucose. Although both provide the means to move beyond the HbA$_{1c}$ measurement as the sole marker of glycemic control, standardized metrics for analyzing CGM data are lacking. Moreover, clear criteria for matching people with diabetes to the most appropriate glucose monitoring methodologies, as well as standardized advice about how best to use the new information they provide, have yet to be established. In February 2017, the Advanced Technologies & Treatments for Diabetes (ATTD) Congress convened an international panel of physicians, researchers, and individuals with diabetes who are expert in CGM technologies to address these issues. This article summarizes the ATTD consensus recommendations and represents the current understanding of how CGM results can affect outcomes.

Glucose measurements are critical to effective diabetes management. Although measurement of glycated hemoglobin (HbA$_{1c}$) has been the traditional method for assessing glycemic control, it does not reflect intra- and interday glycemic excursions that may lead to acute events (such as hypoglycemia) or postprandial hyperglycemia, which have been linked to both microvascular and macrovascular complications. Moreover, although self-monitoring of blood glucose (SMBG) has been shown to improve glycemic control and quality of life in both insulin-treated and noninsulin-treated diabetes when used within a structured testing regimen (1–4) [C,C,C,C], it cannot predict impending hypoglycemia or alert for hypoglycemia (5,6) [C,C] (7).

Real-time continuous glucose monitoring (rtCGM) and intermittently viewed CGM (iCGM) address many of the limitations inherent in HbA$_{1c}$ testing and SMBG. rtCGM uniformly tracks the glucose concentrations in the body's interstitial fluid, providing near real-time glucose data; iCGM uses similar methodology to show continuous glucose measurements retrospectively at the time of checking. Both rtCGM and iCGM facilitate monitoring of time spent in the target glucose range ("time in range"). However, only rtCGM can warn users if glucose is trending toward hypoglycemia or hyperglycemia. With iCGM, these trends can only be viewed after physically scanning the sensor. It is often difficult to distinguish between technologies regarding issues such as calibrations, alarms/alerts, human factors of applying and wearing sensors, and the cost, which are device specific. As these technological details are subject to constant change, the term CGM is used for all issues related to the device class unless indicated otherwise.

In February 2017, the Advanced Technologies & Treatments for Diabetes (ATTD) Congress convened an international panel of physicians, researchers, and individuals

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with diabetes who are expert in CGM to address these issues. The purpose of the conference was to provide guidance for clinicians, patients, and researchers in utilizing, interpreting, and reporting CGM data in clinical care and research. The panel was divided into subgroups to review the literature and provide evidence-based recommendations for relevant aspects of CGM utilization and reporting. Primary citations were identified for each topic, assigned a level of evidence (7) (indicated next to the corresponding citation in the text), and verified by the expert panel.

This article summarizes the ATTD consensus recommendations and represents the current state of knowledge on CGM results affecting outcomes. The content represents the consensus of the panel members' comprehensive evaluation of the issues. Supporting evidence is included in the online Supplementary Data identified at the end of each section.

1. LIMITATIONS OF HbA_{1c}

Key Findings

- The Diabetes Control and Complications Trial (DCCT), followed by the Epidemiology of Diabetes Interventions and Complications (EDIC), demonstrated how elevated HbA$_{1c}$ contributes to complications in type 1 diabetes. The UK Prospective Diabetes Study (UKPDS) confirmed the importance of glycemic control as well as other components of metabolic control, namely blood pressure, on health outcomes in individuals with type 2 diabetes (8,9) [**A,A**].
- Most global organizations recommend target HbA$_{1c}$ levels of <7.0% (53 mmol/mol) for adults and <7.5% (58 mmol/mol) for children, although several organizations suggest an HbA$_{1c}$

target of ≤6.5% for adults (10) [**E**] and children (11) [**E**]. However, all organizations agree that HbA$_{1c}$ targets should be individualized to each patient.
- Although HbA$_{1c}$ remains the reference marker for assessing glycemic control and predicting the risk of development of long-term complications, it has several limitations: HbA$_{1c}$ *1)* provides only an average of glucose levels over the previous past 2–3 months; *2)* does not detect hypoglycemia or hyperglycemia on a daily basis; *3)* is an unreliable measure in patients with anemia (12) [**B**], hemoglobinopathies (13) [**B**], or iron deficiency (14) [**B**] and during pregnancy (15) [**B**]; *4)* does not reflect rapid changes in daily glucose control; and *5)* does not provide data as to how to adjust the treatment regimen when HbA$_{1c}$ levels are elevated. In summary, although HbA$_{1c}$ has proved extremely valuable in patient management, is a valuable measure of population health, and remains a validated indicator of glycation as a risk factor for complications, it is not as helpful for personalized diabetes management.
- The literature suggests that ethnic and racial differences exist in glycation rates (16–18) [**B,C,C**], which affects the accuracy of HbA$_{1c}$ measurements; however, a racial difference was not found in the relationship between mean glucose and fructosamine or glycated albumin levels. This suggests that the racial discordance in glycation rates is specific to red blood cells. The effects of ethnic differences on average HbA$_{1c}$ cannot be entirely explained by measured differences in glycemia, differences in sociodemographic or clinical

factors, or differences in access to care or quality of care (19) [**E**].
- An estimated HbA$_{1c}$ (eA1C) can be calculated if adequate rtCGM/iCGM data (70% or 10 days of the 14 days of CGM data) are available. The eA1C and laboratory-measured HbA$_{1c}$ may differ to some degree for a given individual because there are many factors that affect an HbA$_{1c}$ reading and tables that convert HbA$_{1c}$ to a mean glucose and vice versa are based on mean values for a population. Knowing how an individual's CGM-derived eA1C compares to their laboratory-measured HbA$_{1c}$ may be helpful for safe and effective clinical management (20) [**E**].

Recommendations

- HbA$_{1c}$ should be measured with a device that is certified by the NGSP (National Glycohemoglobin Standardization Program, www.ngsp.org) or the IFCC (International Federation of Clinical Chemistry and Laboratory Medicine, www.ifcchba1c.net).
- Clinicians and patients should target an HbA$_{1c}$ as close to normal as possible without severe hypoglycemia or a significant amount of nonsevere hypoglycemia while at the same time individualizing glycemic targets according to patient age, duration of diabetes, comorbidities, and expected life expectancy, with "less-strict" HbA$_{1c}$ targets for those more frail (21) [**A**].
- When there is a discrepancy between actual HbA$_{1c}$ and the eA1C based on mean glucose, other glucose measurement methods such as fructosamine, glycated albumin, SMBG, and in particular CGM should be used in conjunction with HbA$_{1c}$ measurements

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when assessing glycemic control and adjusting therapy.

- CGM data should be used to assess hypoglycemia and glucose variability.

Additional discussion of these recommendations and supporting evidence is presented in Appendix 1 of the Supplementary Data.

2. USE OF GLUCOSE MONITORING METHODOLOGIES (SMBG AND CGM) TO GUIDE MANAGEMENT AND ASSESS OUTCOMES IN DIFFERENT PATIENT POPULATIONS

Key Findings

- SMBG has been shown to be helpful or to correlate with effective management in insulin-treated and noninsulin-treated diabetes (1–4,22,23) [**C,C,C,C,A,C**]; however, SMBG has notable limitations. First, it requires a fingerstick to obtain a blood sample. Moreover, it only provides a single "point-in-time" measurement, which provides no indication of the direction or rate of change of glucose levels. Thus, using SMBG data alone may result in inappropriate therapy decisions (such as administering correction insulin when blood glucose levels are falling). Second, obtaining glucose data via SMBG is dependent upon the patient's decision to self-monitor. Accordingly, SMBG often fails to detect nocturnal and asymptomatic hypoglycemia (5,6) [**C,C**].
- iCGM provides the current glucose value plus retrospective glucose data for a specified time period upon "scanning." At the time of this writing, only one iCGM system, also known as "flash" monitoring, was available. This system utilizes two components: a glucose sensor, which is inserted the user's upper arm, and a separate touch screen reader device. When the reader device is swiped close to the sensor, the sensor transmits both an instantaneous glucose level and an 8-h trend graph to the reader. The only currently available iCGM device is factory calibrated, lasts up to 14 days, and does not need to be calibrated by the user. However, iCGM lacks alarms for low and high glucose values, and, as with SMBG, measurements are only visualized when the user of the device chooses to make a measurement. Two studies using iCGM have demonstrated significant improvements in hypoglycemia, time

in range, glycemic variability, and user satisfaction (24,25) [**B,B**]. The flash device is also available without the need for scanning in a blinded mode for clinical research or retrospective glucose pattern evaluation.

- rtCGM in unblinded mode provides real-time numerical and graphical information about the current glucose level, glucose trends, and the direction/rate of change of glucose. Devices with programmable alerts/alarms that warn users of current and/or impending high or low glucose offer additional safety advantages. In Europe, a new type of implantable rtCGM system is available as an alternative for transcutaneous CGM (26) [**C**].
- Numerous studies have shown that use of rtCGM improves glycemic control and quality of life in both children and adults with type 1 diabetes treated with either continuous subcutaneous insulin infusion or multiple daily insulin injection therapy, improving HbA$_{1c}$, shortening the time spent in hypoglycemia and hyperglycemia, and reducing moderate-to-severe hypoglycemia (27–38) [**C,C,B,B,C,C,A,C,B,C,B**]. The benefit of rtCGM was seen primarily in those patients who regularly used their devices (27,29,36) [**C,B,B**]. In a lifetime analysis, rtCGM reduced overall diabetes-related complications (39) [**B**]. Similar results of the cost-effectiveness of rtCGM versus SMBG were reported using a larger, population-based model (40).
- Using data collected from a meta-analysis of patient-level data (36) [**B**], sensor-augmented pump therapy was determined to be cost-effective for the treatment of type 1 diabetes in the Swedish health care system (41) [**C**]. Sensitivity analyses indicated further cost-effectiveness benefit of increasing the amount of rtCGM use from 5 to 7 days a week, and decreasing the use of SMBG was incrementally cost-effective at every level.
- Subsequent studies have determined that sensor-augmented pump systems with a low-glucose suspend feature are also cost-effective relative to insulin pump therapy alone, in the Australian (42) [**C**], U.K. (43) [**C**], and French (44) [**C**] health care systems, due to improved glycemic control and reduction in hypoglycemia.
- Benefits of rtCGM use have also been reported in individuals with type 2

diabetes who are managed with or without intensive insulin treatment (45–47) [**B,C,C**]. There are limited data regarding the benefit of rtCGM as an outcome measure for individuals with gestational diabetes mellitus and type 2 diabetes, especially for those who do not use insulin (48) [**C**].

- The benefit of rtCGM is directly correlated to persistence and frequency of use. A meta-analysis by Pickup et al. (36) [**B**] found that every 1-day increase of sensor usage per week increased the effect of CGM; the effect on HbA$_{1c}$ is more pronounced the higher the initial HbA$_{1c}$.

Recommendations

- CGM should be considered in conjunction with HbA$_{1c}$ for glycemic status assessment and therapy adjustment in all patients with type 1 diabetes and patients with type 2 diabetes treated with intensive insulin therapy who are not achieving glucose targets, especially if the patient is experiencing problematic hypoglycemia.
- Structured testing regimens should be defined for patients when SMBG is prescribed.
- All patients should receive training in how to interpret and respond to their glucose data regardless of the monitoring method used. Patient education and training for CGM should utilize standardized programs with follow-up to improve adherence and facilitate appropriate use of data and diabetes therapies.

Additional discussion of these recommendations and supporting evidence is presented in Appendix 2 of the Supplementary Data.

3. MINIMUM REQUIREMENTS FOR CGM PERFORMANCE

Key Findings

- No internationally accepted standard exists for CGM system performance comparable with the International Organization for Standardization (ISO) 15197 standard for SMBG, which specifies design verification procedures and the validation of performance by the intended users. However, ISO/IEEE FDIS 11073-10425 provides a normative definition of the communication between CGM devices and managers (such as cell phones, personal computers,

personal health appliances, and set-top boxes) in a manner that enables plug-and-play interoperability.

- In contrast to iCGM, the accuracy of current rtCGM systems is dependent on SMBG testing for calibration. Therefore, it is important to have an accurate glucose meter. Successful calibration also requires several conditions; for example, it is best performed when glucose is not changing rapidly. Importantly, users must be educated in the appropriate techniques.
- The mean absolute relative difference (MARD) is currently the most common metric used to assess the performance of CGM systems. MARD is the average of the absolute error between all CGM values and matched reference values. A small percentage indicates that the CGM readings are close to the reference glucose value, whereas a larger MARD percentage indicates greater discrepancies between the CGM and reference glucose values.
- Comparing MARD values from different clinical studies has several limitations, and thus head-to-head studies should be performed. Additional metrics, such as precision absolute relative difference, can be used as well to obtain an additional evaluation of the CGM performance (49) [**C**].
- Although controversy exists regarding the exact cut point for accuracy, in silico testing has shown that a further lowering of MARD ≤10% from reference values has little additional benefit for insulin dosing (50) [**C**].

Recommendation

- Only CGM systems that provide an acceptable level of sensor accuracy should be used.

Additional discussion of this recommendation and supporting evidence is presented is presented in Appendix 3 of the Supplementary Data.

4. DEFINITION AND ASSESSMENT OF HYPOGLYCEMIA IN CLINICAL STUDIES

Key Findings

- Hypoglycemia remains a major barrier for glycemic control and a common complication of diabetes treatment, especially in type 1 diabetes (51) [**E**].
- In adults with type 1 diabetes, severe hypoglycemia is more related to duration of diabetes and socioeconomic status than HbA$_{1c}$ (35) [**C**]. Similarly, in children aged 6–17 years old with type 1 diabetes (52) [**C**] or adults with type 2 diabetes (mostly receiving insulin or sulfonylureas [53] [**B**]), severe hypoglycemia was most common among those with the lowest and highest HbA$_{1c}$ levels.
- Needing assistance is the usual concise definition for severe hypoglycemia. Most children require assistance with all hypoglycemia, not just severe hypoglycemia (54) [**C**]. Therefore, severe hypoglycemia in children is often defined as an event associated with a seizure or loss of consciousness or requiring emergency medical personnel, a visit to the emergency department, or a hospital admission. In adults, the definition of severe hypoglycemia often includes episodes associated with coma or seizure, for which the patient, perhaps being on their own, recovered spontaneously.
- The degree of hypoglycemia that causes clinical symptoms and counter-regulatory response is specific to the individual and depends on the personal level of glycemic control (54) [**C**].
- Studies indicate that hypoglycemia for two or more hours impairs hormonal responses (55,56) [**C,B**].
- Gradation of hypoglycemic events may be valuable: specifically, that of a prolonged hypoglycemic event, in which the CGM levels indicate glucose levels <54 mg/dL (3.0 mmol/L) for ≥120 min. While this metric is somewhat arbitrary, a study by Öz et al. (57) [**B**] found that the glycogen signal decreases with a rate of ~10% per hour in the human brain at blood glucose levels of <54 mg/dL (3.0 mmol/L), indicating a mobilization rate commensurate with the severity of hypoglycemia.
- The low blood glucose index (LBGI) is a metric specifically designed to calculate the risk for hypoglycemia as reflected by SMBG data (58) [**B**]. However, LBGI calculations based on CGM data tend to slightly underestimate risk, particularly in the low-risk range (59) [**C**].

Recommendations

- The definition of hypoglycemia should take into consideration several parameters: the compartment of measurement (arterial, venous, and capillary blood or interstitial), the nadir level of blood glucose measured, and the duration of the event and related symptoms.
- When assessing hypoglycemia using CGM, the accuracy of the data in the lower glycemic range should be considered.
- The following classifications of hypoglycemia, based on clinical evaluation, should be used in categorizing levels of hypoglycemia.
  - Level 1: a hypoglycemia alert glucose value of <70–54 mg/dL (3.9–3.0 mmol/L) with or without symptoms. This should be considered an alert that the individual may be at risk for developing hypoglycemia and should work to minimize the time spent in this range to reduce the risk of developing more clinically significant hypoglycemia. This need not be reported routinely in clinical studies, although that would depend on the purpose of the study. Nevertheless, most clinicians want to know how often patients are <70–54 mg/dL (3.9–3.0 mmol/L) and would act to reduce the time spent in this range to minimize the risk of more clinically significant hypoglycemia occurring.
  - Level 2: a glucose level of <54 mg/dL (3.0 mmol/L) with our without symptoms. This should be considered clinically significant hypoglycemia requiring immediate attention.
  - Level 3: severe hypoglycemia. This denotes cognitive impairment requiring external assistance for recovery (7) [**E**] but is not defined by a specific glucose value.
- For clinical study CGM outcomes reports, hypoglycemia values <54 mg/dL (3.0 mmol/L) should be given more weight or importance than those <70–54 mg/dL (3.9–3.0 mmol/L).
- When assessing hypoglycemia in clinical care, other important consequences or adverse patient-reported outcomes should be considered.
  - Reduced awareness of subsequent hypoglycemia.
  - Associated cardiac arrhythmia, confusion, or abnormal or combative behavior.
  - Weight gain.
  - Fear of hypoglycemia.
- Hypoglycemia should be quantified in the following ways.
  - As the percentage of CGM values that are below a given threshold (<70 mg/dL [3.9 mmol/L] or <54 mg/dL

[3.0 mmol/L]) or the number of minutes or hours below these thresholds.
  ○ As the number of hypoglycemic events that occur over the given CGM reporting period.
- A hypoglycemic event should be defined as follows.
  ○ Beginning of a CGM event: readings below the threshold for at least 15 min is considered an event. For example, at least 15 min <54 mg/dL (3.0 mmol/L) to define a clinically significant (level 2) hypoglycemic event.
  ○ End of a CGM event: readings for 15 min at ≥70 mg/dL (3.9 mmol/L).
  ○ A second hypoglycemic event outcome of prolonged hypoglycemia is considered when CGM levels are <54 mg/dL (3.0 mmol/L) for consecutive 120 min or more.
- LBGI should be reviewed when assessing hypoglycemia risk.

Additional discussion of these recommendations and supporting evidence is presented in Appendix 4 of the Supplementary Data.

5. ASSESSMENT OF GLYCEMIC VARIABILITY

Key Findings

- Numerous studies have focused on glycemic variability as an independent risk factor for diabetes complications, particularly cardiovascular disease (60–63) [C,E,C,C], and on the effects of glycemic variability on cognitive function and quality of life (64) [C].
- Acceptance of glycemic variability as a clinically valuable marker of glycemic control has greatly expanded the understanding of glycemic control beyond HbA$_{1c}$ alone (65–68) [E,E,E,E].
- The interpretation of average blood glucose is relatively straightforward, providing a direct relationship to HbA$_{1c}$. However, because glycemic variability is a reflection of a dynamic process, understanding and measuring it is more complex (69,70) [E,C]. Beyond the setting of laboratory experiments, the data sources available for routine estimation of glycemic variability include episodic SMBG records and CGM traces (71) [B]. The density of the available data determines what properties of glycemic variability can be investigated.

- Glycemic variability is a process characterized by the amplitude, frequency, and duration of the fluctuation.
- Both the amplitude and the timing of blood glucose fluctuations contribute to the risks for hypoglycemia and hyperglycemia associated with diabetes (72) [C]. Increased glucose variability is consistently associated with mortality in the intensive care unit (73,74) [C,B] and is a consistent predictor of hypoglycemia, both in prospective studies and within the setting of randomized clinical trials (64,75) [C,B].
- When quantifying glucose variability from CGM data, the following physiological and statistical factors should be considered.
  ○ In healthy individuals, the metabolic system has a physiological equilibrium range (e.g., fasting blood glucose) to which it returns if left undisturbed; with the progression of diabetes, this equilibrium range moves up.
  ○ This physiological equilibrium range is relatively universal (hence the diagnostic criteria for prediabetes and diabetes). Therefore, the objective of diabetes control is to keep blood glucose levels in the vicinity of a commonly accepted range (not the mean for a person, which is individual).
  ○ Deviations from the range in both directions carry risks. These risks increase with the amplitude of the deviations, nonlinearly and asymmetrically, into the hypoglycemic and hyperglycemic ranges.
  ○ The timing of the deviations is of essence as it reflects system (person) dynamics and system stability. However, most of the traditional glycemic variability metrics ignore the time axis of CGM data.
  ○ Mathematical methods (e.g., risk analysis, time series) are well developed and can be adapted to diabetes, keeping in mind the objectives of diabetes control.
- CGM data reflect the dynamics of glucose fluctuations by including all of these dimensions. A recent analysis of CGM data in comparison with blood glucose data obtained in a large study with patients with type 1 diabetes showed how glycemic variability indices are related and demonstrated the impact of CGM use on glycemic variability (76) [C].

- SD, coefficient of variation (CV), and mean amplitude of glucose excursions are widely used to quantify glycemic variability. The CV (which is the SD divided by the mean) has the advantage of being a metric relative to the mean, which makes it more descriptive of hypoglycemic excursions than the SD alone. For example, a population with a mean glucose of 150 mg/dL and an SD of 60 would have a CV of 40%.
- Stable glucose levels are defined as a CV <36%, and unstable glucose levels are defined as CV ≥36% (77) [E].

Recommendations

- Glycemic variability evaluated from CGM data should be considered among other factors of the overall clinical representation of glycemic control.
- CV should be considered the primary measure of variability; however, many clinicians may want to see SD reported as a key secondary glycemic variability measure since it is a metric with which they are familiar.
- The recommended metrics for glycemic variability should be included in summary statistics for data downloaded from CGM devices into reports.

Additional discussion of these recommendations and supporting evidence is presented in Appendix 5 of the Supplementary Data.

6. TIME IN "RANGES"

- Time in range (TIR) generally refers to the time spent in an individual's target glucose range (usually 70–180 mg/dL [3.9–10 mmol/L] but occasionally 70–140 mg/dL [3.9–7.8 mmol/L]). TIR measurements add valuable information to assess the level of current glycemic control in addition to what is known from the HbA$_{1c}$. However, clinicians, researchers, and regulators now know that time in target range alone is not an adequate description of overall glycemic control. It is also necessary to quantitate the times below and above target range, using a few severity thresholds for each level (78) [E]. Thus, time in "ranges" (TIRs) provides a more illustrative metric for clinical and research purposes.
- TIRs are useful for a research comparison of interventions and can help patients understand whether the amount

of clinically significant hypoglycemia or hyperglycemia they are experiencing is improving over time. Breaking out the time in hypoglycemia and hyperglycemia into level 1 (monitor and take action if needed) and level 2 (immediate action required due to the more potentially clinically significant nature of the glucose levels) can guide the urgency and degree of clinical response.

Composite Measures

- Because the function of CGM use is to monitor glucose levels with the ultimate goal of improving glycemic control, it makes clinical sense to combine TIRs data with other measures.
  - HbA$_{1c}$ level and time in level 2 (clinically significant/immediate action required) hypoglycemia is one such combined measure.
  - Time in target range combined with time in level 2 hypoglycemia is

another such combined measure. This combined set of measures could be set up as a coprimary outcome for a clinical trial asking whether one therapy is more effective than another in achieving an increased time in target range (70–180 mg/dL) while also being noninferior for the level 2 hypoglycemia achieved. One then needs to further define the parameters of judging noninferior status. These examples make clinical sense, since one wants to improve glucose control (HbA$_{1c}$ or TIR) while also reducing or at least not increasing hypoglycemia.

  - Even broader combined measures of diabetes management such as targets for desired diabetes management are being explored (e.g., HbA$_{1c}$ + hypoglycemia + weight

gain or HbA$_{1c}$ + blood pressure + LDL or HbA$_{1c}$ + blood pressure + LDL + aspirin use if high-risk cardiovascular disease + no tobacco use). These composites emphasize the importance of taking a multifactorial approach to reducing diabetes complications, particularly cardiovascular disease.

Recommendations

- Percentages of time in ranges (target, hypoglycemia, and hyperglycemia) should be assessed and reported.
- Different TIRs in conjunction with a measure of glycemic variability should be reported as key diabetes control metrics in clinical studies.

Additional discussion of these recommendations and supporting evidence is presented in Appendix 6 of the Supplementary Data.

Table 1—Key metrics for CGM data analysis and reporting

CGM metric	Measures	ATTD consensus
1	Mean glucose	$\sqrt{}$ (calculated)
	Severe hypoglycemia*	Clinical diagnosis: event requiring assistance (level 3)
	Percentage of time in hypoglycemic ranges, mg/dL (mmol/L)	
2	Clinically significant/very low/immediate action required	<54 (<3.0) (level 2)
3	Alert/low/monitor	<70–54 (<3.9–3.0) (level 1)
	Percentage of time in target range, mg/dL (mmol/L)	
4	Default	70–180 (3.9–10.0)
	Secondary	70–140 (3.9–7.8)
	Percentage of time in hyperglycemic ranges, mg/dL (mmol/L)	
5	Alert/elevated/monitor	>180 (>10) (level 1)
6	Clinically significant/very elevated/immediate action required	>250 (>13.9) (level 2)
	Diabetic ketoacidosis*	Clinical diagnosis: ketones, acidosis, and usually hyperglycemia (level 3)
	Glycemic variability	
7	Primary glycemic variability	CV
	Stable	CV <36%,
	Unstable	CV ≥36%
	Secondary glycemic variability	SD
8	eA1C	$\sqrt{}$ (calculated)
9	Three time blocks: sleep, wake, 24 h	12:00 A.M.–6:00 A.M., 6:00 A.M.–12:00 A.M., 12 A.M.–12:00 A.M.
	Recommended data sufficiency	
10	Collection period (minimum no. of weeks)	2
11	Percentage of expected CGM readings (minimum percentage)	70–80 (10 of 14 days)
12	Episodes of hypoglycemia/hyperglycemia (minimum no. of minutes) (with beginning and end of episode defined)	15 min
13	Area under the curve	$\sqrt{}$ (calculated)
14	Risk of hypoglycemia and hyperglycemia	LBGI/HBGI recommended
15	Standardized CGM visualization of data	AGP recommended

*Severe hypoglycemia (level 3) and diabetic ketoacidosis (level 3) are not key CGM metrics per se. However, these conditions are included in the table because they are important clinical categories that must be assessed and documented.

7. VISUALIZATION, ANALYSIS, AND DOCUMENTATION OF KEY CGM METRICS

Key Findings

- Standardizing glucose reporting and analysis similar to electrocardiogram output is vital to optimizing clinical decision-making in diabetes. Further optimizing of such tools and expanding them into shared decision-making guides is needed.

- Reporting CGM data in a standardized way, in conjunction with an HbA$_{1c}$ value and other clinical conditions (e.g., severe hypoglycemia, diabetic ketoacidosis) would foster a precise definition of this composite goal. Using a standardized composite goal, the medical community could establish with more confidence whether a particular insulin formulation, new technology for insulin delivery, or an innovative patient-centered approach to care was an important factor in helping individuals with diabetes reach optimal glycemic control.

- Standardized tools such as the Ambulatory Glucose Profile (AGP [79]), Pattern Snapshot (Medtronic) (80), Clarity (Dexcom) (81), and others from various device makers and data management companies are now available. Use of the AGP approach was previously endorsed by an expert panel of clinicians in a consensus conference held in 2012 (82) [E] and is recommended by this consensus group as a standard for visualization of CGM data.

- Integration of standardized metrics into electronic health records is important to maximize the clinical workflow and facilitate remote communications with patients.

- Patient responses to the current glucose level, trend arrows indicating rate of change of glucose, and qualitative analysis of a graphical display of glucose versus time do not require stability of patterns. However, retrospective analysis of CGM is dependent on stability of patterns from day to day (83) [B].

- A minimum of 14 consecutive days of data with approximately 70% of possible CGM readings over those 14 days appears to generate a report that enables optimal analysis and decision-making; standard reporting and visualization of CGM data are important.

Recommendations

- Fourteen key metrics should be utilized to assess glycemic control and documented.

1. Mean glucose.
2. Percentage of time in level 2 hypoglycemic range (<54 mg/dL [3.0 mmol/L]). Urgency for action: clinically significant/very low/immediate action required.
3. Percentage of time in level 1 hypoglycemic range (<70–54 mg/dL [3.9–3.0 mmol/L]). Urgency for action: alert/low/monitor.
4. Percentage of time in target range: 70–180 mg/dL (3.9–10.0 mmol/L) (default); 70–140 mg/dL (3.9–7.8 mmol/L) (secondary); individual targets closer to the physiological range can be defined, depending on age, comorbidities, and/or patient adherence.
5. Percentage of time in level 1 hyperglycemic range (>180 mg/dL [10.0 mmol/L]). Urgency for action: alert/elevated/monitor.
6. Percentage of time in level 2 hyperglycemic range (>250 mg/dL [13.9 mmol/L]). Urgency for action: clinically significant/very elevated/immediate action.
7. Glycemic variability, reported as CV (primary) and SD (secondary).
8. eA1C.
9. Data for glucose metrics (1–6,8) [C,C,C, C,C,C,A] reported in three time blocks (sleep, wake, 24 h) with the default times for the sleep (12:00 A.M.–6:00 A.M.) and wake (6:00 A.M.–12:00 A.M.) often written as midnight to 6:00 A.M. and 6:00 A.M. to midnight, respectively.
10. Data sufficiency: minimum 2 weeks of data.
11. Data sufficiency: 70–80% of possible CGM readings over a 2-week period.
12. Episodes of hypoglycemia and hyperglycemia, using a standard definition of episodes.
13. Area under the curve (recommended for research purposes). This can be calculated from CGM analysis software and is recommended for research purposes, as it is a measure that integrates to some extent the severity of a high or low glucose along with the duration of the abnormality.
14. Risk of hypoglycemia and hyperglycemia (LBGI and high blood glucose index [HBGI] recommended).
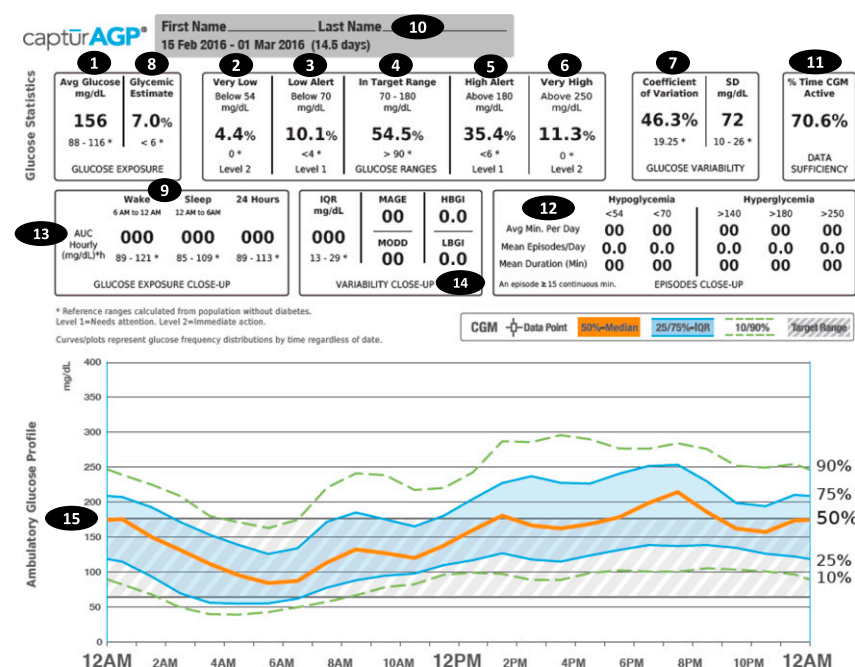
Figure 1—The electronic AGP report visualizes the key CGM metrics: 1) mean glucose, 2) hypoglycemia: clinically significant/very low/immediate action required, 3) hypoglycemia: alert/low/monitor, 4) target range, 5) hyperglycemia: alert/elevated/monitor, 6) hyperglycemia: clinically significant/very elevated/immediate action required, 7) glycemic variability, 8) eA1C, 9) time blocks, 10) collection period, 11) percentage of expected readings, 12) hypoglycemia/hyperglycemia episodes, 13) area under the curve, 14) hypoglycemia/hyperglycemia risk, and 15) standardized rtCGM/iCGM visualization. AUC, area under the curve; Avg; average; IQR, interquartile range; MAGE, mean amplitude of glucose excursions; MODD, mean of daily differences.

- Standardized software for visualization and reporting of the 14 key CGM metrics should be considered an additional component (no. 15) of analysis and documentation (use of the AGP is recommended).
- Although severe hypoglycemia (level 3 hypoglycemia) and diabetic ketoacidosis (level 3 hyperglycemia) are not CGM data–based determinations, they should be reported and documented.
- For research purposes, median and interquartile range should be presented for all measurements.
- Conduct further studies in a variety of patient groups (including the pediatric population, pregnant individuals, those with renal insufficiency, and the elderly) to determine acceptable and achievable time in range and the accompanying acceptable rates of hypoglycemia.

The key metrics for CGM analysis and reporting are presented in Table 1. Figure 1 illustrates how these metrics are presented in the AGP.

CONCLUSIONS

CGM is a robust research tool, and continuous glucose data should be recognized by governing bodies as a valuable and meaningful end point to be used in clinical trials of new drugs and devices for diabetes treatment. The identification of hypoglycemia is as important as the measurement of time in range in clinical trials. Quantifying the duration and magnitude of glycemic excursions provides another means of assessing glucose control. The unifying theme of trials investigating the usefulness of CGM technologies is that the device must be worn on a near-daily basis to optimize its benefits.

The expert panel concludes that, in clinical practice, the advanced metrics of assessing continuous glucose data presented here are appropriate as outcome parameters that complement HbA_{1c} for a wide range of patients with diabetes and should be considered for use to help them improve glycemic control provided that appropriate educational and technical support is available.

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