# Approaches for Successful Outcomes with Continuous Glucose Monitoring

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Successful management of diabetes requires regular monitoring of glucose levels for all patients (1), with greater frequency recommended for those with type 1 or insulin-treated type 2 diabetes (2). However, daily self-monitoring of blood glucose (SMBG) may be painful, inconvenient, costly, and difficult to maintain. In 2017, a study using Cloud-based analysis software revealed that rates of glucose monitoring in Europe and North America ranged between 2.7 and 4.4 times/day in people with any type of diabetes (3). Individuals who perform SMBG typically focus on pre-meal or bedtime glucose levels, obtaining only a static snapshot of points in time. In the past two decades, continuous glucose monitoring (CGM), using subcutaneous sensors to measure interstitial glucose levels, has emerged to provide a better understanding of glucose trends and patterns.

Real-time CGM devices, alone or integrated into insulin pump systems, display data continuously and provide alerts and alarms for current and impending hypoglycemia and hyperglycemia (4,5). In 2017, a novel factory-calibrated, sensor-based system for daily use by people with diabetes, the FreeStyle Libre (Abbott, Alameda, CA), became available in the United States (6). The Libre's technology has been alternately referred to as flash CGM (FCGM) and intermittently scanned CGM because continuous data are viewable to the user only when a dedicated reader is scanned (or "flashed") over the sensor (7). The FreeStyle Libre has no alarms, but a distinct audible tone is provided when alerts to perform fingerstick testing are displayed. This may occur during scanning when glucose is <70 or >240 mg/dL, projected to be <70 or >240 mg/dL, "hi" or "lo," projected to be "hi" or "lo," or when glucose is rapidly changing or no trend arrow displays. A built-in glucose meter and individually foil-packed glucose strips facilitate measurement of glucose levels in these situations (8). The FreeStyle Libre does not require fingerstick testing for calibration.

The accuracy of CGM systems has improved over time, and presently, several available systems are approved as tools for making treatment decisions. All have similar accuracy at glucose levels >80–200 mg/dL. However, in the hypoglycemic range, the FreeStyle Libre system is not as accurate as in the euglycemic range (9), and sensor readings should be confirmed with blood glucose measurements. All personal CGM systems provide current glucose trend arrows. Because the meaning of the arrows is system-specific (see the article on p. 8 of this compendium), health care providers must learn the differences among the devices and guide patients based on each one's ecosystem for therapy adjustment. In the United States, the Dexcom G5 Mobile and FreeStyle Libre systems are approved by Medicare for beneficiaries with diabetes who use intensive insulin therapy (three or more injections per day), perform fingerstick glucose testing four times per day, and require frequent adjustment in therapy (10–13).

Outcomes of CGM in people with type 1 and insulin-treated type 2 diabetes are reviewed in the article on p. 3 of this compendium (14–18). Results in more heterogeneous groups with type 2 diabetes show variable effectiveness and acceptability (19). With high adherence to CGM, increased physical activity, reduced calorie intake, and decreased body weight were observed. This is consistent with findings that increased frequency of SMBG and CGM correlate with positive outcomes in type 1 diabetes (14–18,20). Benefits of FCGM have also been demonstrated in the IMPACT and REPLACE studies for type 1 and type 2 diabetes, respectively, with overall time spent in hypoglycemia reduced by 38% (type 1 diabetes) and 43% (type 2 diabetes) (21,22). Previously, improved glycemic control for up to 1 year was observed in patients not on prandial insulin using intermittent real-time CGM (23).

For some people, fatigue from alerts and alarms may thwart improved glucose outcomes with real-time CGM (24,25). FCGM, which has no alarms and sounds a distinct audible tone during scanning when alerts to perform fingerstick testing are displayed, offers a viable alternative; in studies of FCGM to date, patient satisfaction and adherence have been high (21,22).

### Frequency of Looking at Receiver/Reader Data

It is difficult to quantify how often users check real-time CGM data during the day and night, either actively before insulin dosing or passively when alerted to hypoglycemia or hyperglycemia; however, a reasonable estimate is at least 4–12 times/day, including before meals, at bedtime, for physical activity, and in response to alerts and alarms. Quantification of FCGM is easier, as the number of scans per day is provided on the reader and available when uploading data to the LibreView software. In two recent studies using FCGM, the average number of scans per day was reported to be 15 for type 1 diabetes and 8 for type 2 diabetes patients (21,22). A recent analysis of FCGM in >50,000 users worldwide provided additional insight into real-world experience. In this report, the number of scans per day positively correlated with glycemic outcomes, with less time spent in hypoglycemia and hyperglycemia and more time spent in range with increasing number of scans per day. The number of scans per day ranged from 4.4 (every 5.4 hours) to 48 (every 30 minutes) (26). Health care

providers should address the ideal frequency of scanning on an individual basis and modify recommendations based on each patient's treatment regimen and needs.

## Patient Selection

Careful patient selection is important when recommending CGM therapy. The article on p. 11 of this compendium provides more details about appropriate candidates. Successful outcomes will depend in large part on a person's trust in the system, willingness to calibrate the system per product specifications, the number of times the person scans or looks at the system, and the type of intervention plan set up with the health care provider. Guidelines for CGM patient selection have been developed by professional societies and other expert forums (27–29).

Regardless of baseline A1C or the degree of glucose variability at CGM initiation, users should be willing to check or scan their device on a near-daily basis to realize the greatest benefit (14–18,21,22). Users should also understand the concept of interstitial fluid versus capillary blood glucose measurements and calibration procedures for systems that require calibration. Of note, for real-time CGM systems, setting alerts and alarms with realistic expectations is essential to avoid alarm fatigue (24). Establishing a plan for sick-day or illness management with CGM is greatly encouraged. Dexcom CGM users should also consider taking advantage of the Share feature, which allows a "follower" (person chosen by the user, such as a parent, family member, or friend) to receive CGM information on a smartphone. Such data, including alerts and alarms, would allow the recipient to potentially assist the user if necessary, such as in the event of hypoglycemia. Educating family members or other caretakers about the CGM system and, for older adults, ensuring that they can see or hear the alerts and alarms, are also fundamental to successful outcomes.

## Patient and Provider Education

The importance of patient and provider education cannot be overemphasized. People with diabetes should receive training on the meaning of the messages displayed on their system reader. Additionally, setting procedures for alerts and alarms, individualizing trend arrow-based treatment decisions, and reinforcing the dangers of insulin stacking (administering insulin while the previous dose is still active) are crucial to promoting adherence to CGM and improving glycemic outcomes. Although training videos are provided by manufacturers, they should not be seen as a substitute for in-depth patient education, especially when initiating CGM. Without appropriate training, CGM users may not be able to take full advantage of the information provided. Additionally, because most health care providers lack training in the interpretation of CGM data, including retrospective analysis during office visits, the availability of educational resources for health care providers is essential to achieving positive outcomes.

## Hypoglycemia

Hypoglycemia is a serious concern for people with diabetes and the major limiting factor in achieving glycemic targets with intensive management. Hypoglycemia risks and frequency are well established in people with type 1 diabetes (30,31), and even self-reported severe hypoglycemia is associated with a 3.4-fold increased risk of death (32). However, hypoglycemia frequency may be underestimated in people with type 2 diabetes; whether on insulin or other antihyperglycemic regimens, these individuals can also have hypoglycemia unawareness (33). CGM technology has been demonstrated to reduce hypoglycemia frequency and hypoglycemia unawareness in people with diabetes (14–18,21,22,34–37).

When recommending CGM to patients, the presence of hypoglycemia unawareness should be evaluated and discussed to aid in selecting the most appropriate system.

## Interpretation of Data

Interpretation of data for users and providers still lacks a cohesive approach. When reviewing data, time spent in the various ranges (<54, <70, 70–180, >180, and >250 mg/dL) as well as coefficient of variation should be addressed. This can be accomplished with Ambulatory Glucose Profile reports available in various software platforms (Dexcom Clarity, Glooko-Diasend, Tidepool, Medtronic CareLink, and LibreView) (38–42). Nocturnal hypoglycemia should be addressed first, with intervention to reduce its severity and frequency. Subsequently, fasting glucose levels should be evaluated, and modifications to basal insulin doses or insulin-pump basal rate settings should be implemented. CGM systems offer great advantage in identifying prandial glycemic excursions; in such cases, mealtime insulin doses and the timing of the boluses should be addressed by instructing patients to monitor glucose before and 2–4 hours after meals to better understand glucose fluctuations and make appropriate regimen adjustments. Recently, use of FCGM was associated with a significant increase in delivering bolus insulin 15–20 minutes in advance of meals (compared to immediately before or after meals) (36). People using insulin should be cautioned against making frequent dose changes in response to above-target post-meal CGM readings on their display tools because insulin stacking is a well-known and avoidable cause of hypoglycemia.

## Trend Arrows

As mentioned previously, CGM systems feature trend arrows that provide information on the predicted change of glucose levels over a specific time period. It is important to be aware that the arrows correspond to different rates of glucose change depending on the brand of CGM system. Training users on the meaning of arrows displayed on their particular device will ensure that they take appropriate actions guided by the specific system they use. (See the table on p. 9 of this compendium for details about each available system.) Although approaches to adjusting insulin

doses on the basis of trend arrows are frequently discussed and constitute an important aspect of therapeutic CGM, proposed methods have yet to be validated in randomized controlled trials (43–47). The most recently published method is specific to the Dexcom G5 Mobile (47). With this in mind, it is imperative that health care providers take an individualized approach when applying trend arrows to treatment decisions (Table 1).

In view of the aforementioned caveats, the published recommendations made with respect to the Dexcom G5 arrows cannot be extrapolated to the FreeStyle Libre system. However, using a correction factor for trend arrow–guided insulin dose adjustments in combination with mealtime dose calculations based on an insulin-to-carbohydrate ratio offers an advantage over other published methods in that it allows for personalized dose calculations based on insulin sensitivity. A proposed working algorithm for the FreeStyle Libre incorporating this concept is shown in Table 2, and sample dose adjustments are provided in Box 1. The rationale for this non-validated method is to be more aggressive when the reader displays one up-trending arrow because the predicted glucose change over time with the FreeStyle Libre in reality could be much higher than 2 mg/dL per minute. Moreover, readings in the hypoglycemic range must be confirmed with fingerstick glucose testing because of potential sensor inaccuracy; when glucose is rapidly falling and sensor glucose levels are <100 mg/dL, additional rapid-acting carbohydrate intake (15–30 g) should be considered in the pre-meal period. In the postprandial period, insulin dosing based on trend arrows should be calculated 4 hours after an insulin dose, although this recommendation may change with the recent introduction of insulin analogs with a faster onset of action (48).

Before using trend arrows for insulin dose adjustments, patients should first become familiar with their CGM systems. Because users will work within their own CGM ecosystem, education should be targeted toward patients' specific device. Although there are no head-to-head trials, all available CGM systems have decreased accuracy in the hypoglycemic range (9,49,50), but in the United States, only the FreeStyle Libre label requires confirmation with fingerstick testing in this range. Thus, individualized guidance may be needed on using trend arrows for insulin dose adjustments when glucose levels are <70 mg/dL. This is especially true in older adults with diabetes, who are at highest risk for severe hypoglycemia and hypoglycemia unawareness (51). For certain high-risk geriatric patients, use of trend arrows for insulin dose changes with the FreeStyle Libre should be assessed on a case-by-case basis, and it may be prudent to confirm glucose levels via fingerstick glucose testing when adjusting insulin per instructions from the reader display; in the setting of rapid glucose changes toward hypoglycemia, fingerstick glucose checks should be strongly recommended for safety, especially when the "check blood glucose" symbol appears on the reader display. Of note, in a small cohort of nursing home residents with type 2 diabetes, FCGM overestimated hypoglycemia, with 51.4% of the interstitial glucose readings <70 mg/dL being falsely low compared to capillary blood glucose levels (52). More studies of FCGM in geriatric populations are needed.

### Non-Insulin-Using Patients

Formal studies of CGM in non-insulin-using patients on antihyperglycemic regimens are scant. For such people, the main goal of CGM should be to achieve target fasting glucose levels and decrease postprandial glycemic excursions with appropriate regimen adjustments, meal quality modifications, and lifestyle interventions (2,53). For people with type 2 diabetes, especially those on sodium–glucose cotransporter 2 inhibitors or glucagon-like peptide 1 receptor agonists, CGM therapy could have significant

**TABLE 1** Published Trend Arrow Methods for Insulin Dose Adjustment

| Trend Arrow | DirecNet (43) | Scheiner (44) | Pettus and Edelman (45) | Klonoff and Kerr (46) | Endocrine Society (Dexcom G5 only) (47) |
|---|---|---|---|---|---|
| ⇈ | 20% increase | +60 mg/dL | +100 mg/dL | +2 units | +1.5–4.5 based on correction factor |
| ↑ | 20% increase | +30 mg/dL | +75 mg/dL | +1.5 units | +1–3.5 based on correction factor |
| ↗ | 10% increase | 0 | +50 mg/dL | +1 units | +0.5–2.5 based on correction factor |
| → | No changes | No changes | No changes | No changes | No changes |
| ↘ | 10% decrease | 0 | −50 mg/dL | −1 units | −0.5–2.5 based on correction factor |
| ↓ | 20% decrease | −30 mg/dL | −75 mg/dL | −1.5 units | −1–3.5 based on correction factor |
| ⇊ | 20% decrease | −60 mg/dL | −100 mg/dL | −2 units | −1.5–4.5 based on correction factor |

**TABLE 2** Suggested Insulin Dose-Adjustment Algorithm for FreeStyle Libre Trend Arrows

| Trend Arrow | FreeStyle Libre Trend Definition | Correction Factor (mg/dL)* | Insulin Dose Adjustment (Units)† |
|---|---|---|---|
| ↑ | Glucose is rising quickly (>2 mg/dL per minute) | <25<br>25–50<br>50–75<br>>75 | +4<br>+3<br>+2<br>+1 |
| ↗ | Glucose is rising (1–2 mg/dL per minute) | <25<br>25–50<br>50–75<br>>75 | +3<br>+2<br>+1<br>No changes |
| → | Glucose is changing slowly (<1 mg/dL per minute) | <25<br>25–50<br>50–75<br>>75 | No changes<br>No changes<br>No changes<br>No changes |
| ↘ | Glucose is falling (1–2 mg/dL per minute) | <25<br>25–50<br>50–75<br>>75 | −3<br>−2<br>−1<br>No changes |
| ↓ | Glucose is falling quickly (>2 mg/dL per minute) | <25<br>25–50<br>50–75<br>>75 | −4‡<br>−3‡<br>−1‡§<br>No changes‡§ |

*Amount of blood glucose-lowering expected from 1 unit of rapid-acting insulin.

†For pre-meal sensor glucose levels <100 or >300 mg/dL, individualized plans with the health care provider are strongly recommended. Target glucose levels should be established with the health care team. For falling glucose trends or when FCGM glucose levels are approaching 70 mg/dL, users should measure glucose levels if prompted by the reader to confirm the presence of hypoglycemia in pre-meal situations; doing so will help prevent unnecessary reduction of pre-meal insulin doses if the glucose value measured by fingerstick testing is not in the hypoglycemic range. Older adults with a history of hypoglycemia unawareness or severe hypoglycemia episodes should be counseled on a case-by-case basis.

‡Consider fingerstick glucose testing if instructed by the reader.

§Consider additional rapid-acting carbohydrate intake (15–30 g).

educational and therapeutic benefits, with the additional advantage of obtaining data relatively painlessly. Developing a plan to review CGM trends in the postprandial period, whether by setting up alerts or by instructing users to scan their FCGM at specific times after meals, can convey the dynamics of post-meal glucose fluctuations to patients and guide providers in personalizing diabetes regimen adjustments based on data accumulated between visits. More studies are needed to address the potential value of FCGM in this clinical setting.

Ideally, all systems should display glucose data on a mobile app so that users do not have to carry multiple tools; this strategy would potentially contribute to acceptance and increase uptake of CGM use in non-insulin-using people with diabetes.

## Best Practice for Exercise

Standards of care recommend that most adults with type 1 or type 2 diabetes engage in daily physical activity, allowing no more than two consecutive days without activity (2,53).

**BOX 1** Examples of Trend Arrow–Guided Insulin Dose Adjustments with FreeStyle Libre

**PATIENT 1** is a 35-year-old man with type 1 diabetes who is planning to eat 50 g of carbohydrate. His insulin-to-carbohydrate ratio is 1:10, his correction factor is 30, and his glucose target is 120 mg/dL. His pre-meal FCGM glucose level is 180 mg/dL with one up-trending arrow. His dose will be adjusted by adding 3 units to his calculated insulin dose.

*Calculation:* (meal) 5 units + (correction) 2 units = 7 units. Insulin dose adjustment for trend arrow: +3 units. Total dose: 7 + 3 = 10 units

**PATIENT 2** is a 60-year-old woman with type 2 diabetes who is planning to eat 50 g of carbohydrate. Her insulin-to-carbohydrate ratio is 1:5, her correction factor is 20, and her glucose target is 100 mg/dL. Her pre-meal FCGM glucose level is 280 mg/dL with one down-trending arrow. Her dose will be adjusted by subtracting 4 units from her calculated insulin dose.

*Calculation:* (meal) 10 units + (correction) 9 units = 19 units. Insulin dose adjustment for trend arrow: −4 units. Total dose: 19 − 4 = 15 units

**PATIENT 3** is a 73-year-old man with type 2 diabetes complicated by renal insufficiency and a creatinine of 2.1 mg/dL. At 11:30 a.m., his FCGM glucose reads 65 mg/dL. He follows the FCGM reader prompt to "check blood glucose." His blood glucose level is 63 mg/dL. He ingests 15 g of rapid-acting carbohydrate in the form of apple juice. Thirty minutes later, he is ready to eat a lunch, which will include 45 g of carbohydrate. He notices an FCGM glucose level of 105 mg/dL with one up-trending arrow. Per the algorithm, he should increase his dose of insulin by 3 units. His insulin-to-carbohydrate ratio is 1:15, his correction factor is 50, and his glucose target 120 mg/dL.

*Calculation:* (meal) 3 units + (correction) 0 units = 3 units. Total dose should be 6 units (3 units for the meal + 3 units for algorithm). However, he feels uncomfortable with this dose and decides to take only 1 additional unit of insulin to compensate for the rapidly increasing glucose level. When he scans the FCGM reader 2.5 hours after lunch, he notices an FCGM glucose level of 155 mg/dL, which is acceptable to him. The patient discusses this episode with his health care provider, and together, they modify the algorithm to better suit the specific needs of this geriatric patient with increased risk for hypoglycemia due to decreased renal function.

However, blood glucose responses to physical activity, especially in individuals with type 1 diabetes, can be highly variable depending on many factors, including the type and timing of activity, previous food ingestion, and level of insulin on board. Adjustments in medication doses and carbohydrate intake are often required to maintain adequate glucose levels during and after physical activity (54,55).

CGM can be of benefit by providing users with glucose-trend data at any time, thereby decreasing fear of exercise-induced hypoglycemia. This is especially relevant when sensor glucose levels are trending toward hypoglycemia. However, very few studies have addressed this issue, and the accuracy of CGM has not been fully validated with different types of exercise. For example, intermittent high-intensity interval exercise is associated with metabolic changes (e.g., changes in pH, microcirculation, and oxygen tension) that may potentially interfere with CGM accuracy. In a small study using the Dexcom G4 Platinum system, the accuracy was comparable during continuous moderate and intermittent high-intensity exercise during a cycling session (56). Similarly, the accuracy of real-time CGM (Medtronic Guardian REAL-Time) measured at various prescribed workloads was acceptable for all types of exercises with the exception of continuous high-intensity exercise, where lower accuracy was detected (57). A recent survey of 502 adults from the T1D Exchange's online patient community, 276 of whom were using CGM either alone or in combination with CSII, showed that, although most respondents adjusted carbohydrate intake and insulin doses around exercise, the majority still reported experiencing hypoglycemia after exercise and having significant difficulties with blood glucose control around exercise (58).

Using CGM trend arrows adds another level of complexity. Although trend arrows are helpful in determining the direction of glucose during exercise and guiding users in the consumption of additional carbohydrate to prevent or reduce hypoglycemia, using them to adjust insulin doses during and after exercise is more challenging. As previously suggested (47), users should be conservative when adjusting their insulin doses before exercise and should refrain from increasing their insulin dose in the presence of up-trending arrows during the active period. In the post-exercise period, as previously recommended by Riddell et al. (55), close glucose monitoring is essential. In particular, attention should be paid to the direction of trend arrows in the immediate or even late-post-exercise period to correct impending hypoglycemia with rapid-acting carbohydrate intake, if indicated. Trend arrows may also signal the need for additional carbohydrate or an insulin dose reduction at bedtime to avoid nocturnal hypoglycemia, especially when exercise takes place in the late afternoon or evening (55). It is hoped that additional studies of newer CGM systems and their accuracy in response to various exercise protocols will better define best practice for the use of CGM trend arrows during physical activity.

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