ISSN 2472-1972

A Practical Approach to Using Trend Arrows on the Dexcom G5 CGM System to Manage Children and Adolescents With Diabetes

Lori M. Laffel,[1] Grazia Aleppo,[2] Bruce A. Buckingham,[3] Gregory P. Forlenza,[4] Lisa E. Rasbach,[5] Eva Tsalikian,[6] Stuart A. Weinzimer,[7] and Dennis R. Harris[8]

[1]Pediatric, Adolescent and Young Adult Programs, Joslin Diabetes Center, Harvard Medical School, Boston, Massachusetts 02215; [2]Division of Endocrinology, Metabolism and Molecular Medicine, Feinberg School of Medicine, Northwestern University, Chicago, Illinois 60611; [3]Department of Pediatric Endocrinology, Stanford University, Stanford, California 94305; [4]Barbara Davis Center, University of Colorado Denver, Aurora, Colorado 80045; [5]Division of Pediatric Endocrinology, Johns Hopkins Children's Center, Baltimore, Maryland 21287; [6]Division of Endocrinology and Diabetes, Department of Pediatrics, University of Iowa Carver College of Medicine, Iowa City, Iowa 52242; [7]Department of Pediatrics, Yale University School of Medicine, New Haven, Connecticut 06510; and [8]Endocrine Society, Washington, District of Columbia 20036

Freeform/Key Words: continuous glucose monitoring, fine-tuning, insulin dose adjustment, insulin dosing, pediatric, type 1 diabetes

Safe and effective use of intensive insulin therapy is challenging for pediatric patients with diabetes and their caregivers [1]. Parents/caregivers must consider numerous factors such as variable dietary intake, exercise, school activities, intercurrent illnesses, and changes in metabolism with growth and puberty when selecting and adjusting insulin doses for the management of type 1 diabetes (T1D) [2–7]. Despite advanced therapeutic options for the management of T1D in childhood, the majority of youth fail to achieve glycemic targets of hemoglobin A1c values <7.5% [8]. Fear of hypoglycemia by caregivers may lead to avoidance of "lows" in exchange for higher glucose values [9–11].

Studies showed improved glycemic control without increased hypoglycemia in pediatric patients with diabetes using real-time continuous glucose monitoring (rtCGM) [12–16]; however, these benefits were observed mainly in patients who consistently used their device for 6 or more days per week [13, 14, 17]. As accuracy and ease of use of rtCGM devices has improved with newer devices, many persons with T1D and some parents/caregivers of youth with T1D increasingly rely on rtCGM data to select and adjust insulin doses [18].

In December 2016, the US Food and Drug Administration further improved usability with the approval of the Dexcom G5 Mobile CGM system (Dexcom G5, Dexcom, Inc., San Diego, CA) for nonadjunctive insulin dosing for patients aged 2 years and older. Although treatment algorithms for utilizing CGM data to establish insulin dosing parameters have been used in earlier clinical trials [19–21], recommendations for using rtCGM trend arrow data non-adjunctively in routine care are lacking.

Abbreviations: CF, correction factor; ICR, insulin-to-carbohydrate ratio; MDI, multiple daily injection; rtCGM, real-time continuous glucose monitoring; T1D, type 1 diabetes.

Received 2 October 2017
Accepted 3 November 2017
First Published Online 20 November 2017

Notably, there are four previously published methods for using trend arrow data to adjust insulin doses [21–24]. However, each method has limitations in its complexity and utility.

The purpose of this perspective is to provide safe, practical guidance for using rtCGM trend arrow data to adjust insulin doses in pediatric patients with T1D, aged 2 years and older, assuming the use of currently available rapid-acting insulin analogs. We base our approach on previous algorithms used in clinical trials [19–21], our clinical experiences as endocrinologists, and guidance from other diabetes specialists [23, 25, 26]. Notably, the Klonoff/Kerr formula was published following the development of our guidance and was therefore not used in our comparisons; however, we note the similarities to our own approach and differences in application. Specifically, we aim to address the needs of clinicians treating pediatric patients using the Dexcom G5, which is the only system currently approved for nonadjunctive use for insulin dosing in pediatric patients. It is likely that others may be approved in the near future, especially following the recent Food and Drug Administration approval of the FreeStyle Libre Flash Glucose Monitoring System for nonadjunctive use in patients ages 18 and older [27].

We recognize our own approach has certain limitations. Currently, there are no clinical trials that have used the approach we provide. We also recognize that other CGM systems, although not yet approved in the United States for nonadjunctive use in pediatric patients, are available and provide useful information based on trend arrows, and we expect that additional nonadjunctive CGM systems will become available in the near future. It is important to note that there are no standard conventions for displaying rates of change information in CGM devices and trend arrows often display rates of change differently; future standardization would be helpful.

The suggested approach is a starting point of an iterative discussion on how to best use the Dexcom G5 trend arrow data, which has held nonadjunctive insulin dosing approval since December 2016. We hope that our approach will be useful for future CGM systems considering that the transfer, display, and meaning of trend arrow data may be specific for each brand.

1. Safe and Effective rtCGM Use: Selection of Patients and Education/Training

Recognizing which patients are most likely to benefit from rtCGM and being able to provide adequate education are paramount to the success of rtCGM. Use of rtCGM is recommended for pediatric patients with T1D treated with multiple daily injections (MDIs) or insulin pump therapy, especially for youth with severe hypoglycemia, nocturnal hypoglycemia, hypoglycemia unawareness, those not meeting recommended glycemic targets, and those wanting to improve glycemic control [28–32]. Table 1 outlines patient considerations.

Education on using rtCGM is a lengthy topic on its own. However, we highlight the importance of teaching patients and parents/caregivers the fundamentals of sensor insertion, sensor lag time, calibration, and setting alerts, as well as providing patients and parents/caregivers with realistic expectations (*e.g.,* rtCGM will not eliminate the need for checking fingerstick glucose levels). Table 2 presents a suggested list of education topics [33–35]. Table 3 lists common medications containing acetaminophen, which is an important consideration when using rtCGM.

2. Data Sharing

Data sharing is an important feature of rtCGM, and the Dexcom G5 Mobile and Follow apps allow patients to share real-time data with up to five individuals. The apps require compatible smart devices for both the user and individuals monitoring remotely. Dexcom G5 Mobile only requires Bluetooth capability and can use Wi-Fi to send data, and Dexcom Follow can receive data via Wi-Fi, obviating the need for costly mobile data plans for young patients sharing as well as adult caregivers who want to "follow."

Use of data sharing varies, especially across the pediatric age span. It is the clinical opinion and experience of the authors that parents/caregivers of very young children often value

Table 1. Considerations for Recommending rtCGM

Patients Meeting One or More of the Following Criteria May Be Considered for rtCGM:
▸ Patient is 2 years of age or greater
▸ Currently treated by intensive insulin therapy
▸ Experiencing frequent hypoglycemia
▸ Hypoglycemia unawareness
▸ Excessive glucose variability
▸ Varying and/or intensive activity
▸ Desire to improve glycemic control
▸ Understands behaviors that influence glycemic control
▸ Willing and able to use rtCGM on a nearly daily basis
▸ Willing and able to learn how to use device and receive ongoing education
▸ Pregnant or wants to get pregnant[a]

The following is not an exhaustive list of considerations. It is based on prior publications by the Endocrine Society and American Association of Clinical Endocrinologists, as well as the clinical experience of the authors. A foundation criterion is that a patient/parent/guardian or caregiver must be willing and able to understand, use, and learn more about rtCGM.
Abbreviation: rtCGM, real-time continuous glucose monitor.
[a]Currently, no rtCGM system is indicated for use in pregnancy.

remote monitoring to help supervise diabetes management. For school-age patients, data sharing can link patients, parents, school staff, and/or after-school caregivers, underscoring the importance of education across caregivers. Indeed, recommendations regarding rtCGM in school settings with variable staffing require attention and guidance. Finally, in adolescent patients, rtCGM data sharing with parents requires "rules of engagement" with the intended goal of monitoring for safety rather than "policing" behavior [16].

3. How to Use Trend Arrows to Adjust Insulin Dose

At a basic level, patients requiring intensive insulin therapy rely on the current glucose value, target glucose value, food intake (if any), and insulin dosing parameters [insulin-to-carbohydrate ratio (ICR) and correction factor (CF); also known as insulin sensitivity] to calculate insulin doses when bolusing for carbohydrate intake and/or corrections. This standard glucose "point in time" monitoring is limited; the glucose value used for calculating insulin dose is an isolated, static measurement.

Trend arrows add context to this static measurement. Instead of standard "point in time" monitoring, trend arrows allow individuals to "anticipate" future glucose levels and proactively adjust the insulin dose and food intake based on the directionality of trend arrows. Upward trend arrows indicate rising glucose levels and may suggest a need for additional insulin; downward trend arrows indicate falling glucose levels and may suggest a need for less insulin, or possible carbohydrate intake. This conceptual shift from "point-in-time" monitoring to "anticipating" future glucose levels is essential to using rtCGM optimally. Figure 1 provides an example of how these trend arrows appear and the anticipated glucose change they represent in Dexcom G5 displays [*i.e.,* Dexcom Receiver and Dexcom smart device apps (Dexcom G5 Mobile and Dexcom Follow)].

Most importantly, adjusting insulin doses using trend arrows does not replace standard calculations. Adjusting, or fine tuning, the insulin dose using trend arrows is an additional step that increases or decreases the insulin dose that has been calculated using standard parameters. There are caveats—as there are with all diabetes management approaches—and the extent of insulin dose adjustment may be impacted by common factors such as meal composition, time since last meal, insulin-on-board, and exercise among other considerations. We recommend patients become as comfortable as possible with the general application of rtCGM data and learn how their body responds to various meals (quantity/composition) and physical activity before applying any approach to adjusting insulin doses using trend arrows.

Table 2. Education Checklist When Using rtCGM

The Following are Fundamental Principles and Skills That a Patient and/or Caregiver Should Learn When Using rtCGM. At the End of Training, Patients and/or Caregivers Should be Able to:
❑ Describe the difference between interstitial fluid and capillary glucose and understand the meaning of lag time.
❑ Recognize the importance of handwashing prior to fingerstick monitoring.
❑ Summarize the calibration procedure and explain when calibration is needed.[a]
❑ Summarize the limitations in rtCGM data accuracy within the first 24 hours following insertion and beyond the manufacturer's recommended wear time.[b]
❑ Demonstrate the procedures for setting alarms/alerts.[c]
❑ Explain the significance of alarms/alerts, glucose trend data, and trend arrows in making treatment decisions.[c]
❑ Explain how to use trend arrows in individualized treatment decisions.
❑ Explain the dangers associated with frequent insulin dosages following meals *(i.e.,* "stacking").
❑ Explain how to use rtCGM during sick days or illness.[d]
❑ Explain individualized monitoring and treatment strategies during exercising (*e.g.,* temporary basal rates, insulin adjustment, carbohydrate adjustment, adjusting for trend arrows).
❑ Demonstrate sensor insertion procedure and list appropriate insertion sites.[b]
❑ When share functions are available: Demonstrate the procedure for uploading the rtCGM data (*e.g.,* via Dexcom G5 Mobile app or Dexcom Clarity) and with others (*e.g.,* Dexcom Follow app or Dexcom Clarity for clinics).[e]

Abbreviations: rtCGM, real-time continuous glucose monitor.

[a]The Dexcom G5 device should be calibrated twice daily according to the manufacturer's instructions. Persons who check fingersticks frequently should be informed to not enter every fingerstick value. It is important that patients use the proper fingerstick monitoring technique (*e.g.,* thoroughly washing hands with soap and water before checking). Dexcom G5 calibration is reliant on a properly functioning and accurate blood glucose meter. Therefore, we recommend patients use blood glucose meters with proven accuracy and performance.

[b]Dexcom recommends that sensors be placed in subcutaneous tissue on the abdomen and upper buttock (including lipohypertrophic areas); however, a recent study found comparable accuracy with placement on the back of the arm [33]. Importantly, patients should be instructed not to rely solely on their rtCGM data during first 24 hours after inserting the sensor.

[c]When reviewing alarms/alerts, it is important to discuss how to deal with "alert fatigue," which may prompt patients to switch them off or underutilize their rtCGM system.

[d]rtCGM can be used during periods of illness but will require additional confirmatory fingerstick checks. Importantly, patients should be cautioned about use of medications that contain acetaminophen, which can cause the rtCGM system to display false high readings for up to and beyond 6 hours following ingestion [34, 35].

[e]If the patient chooses to use data sharing, it is important that caregivers receive training in rtCGM use, specifically, use of trend arrows, interpretation, and appropriate response.

4. Previous Methods to Adjust Insulin Dose Using Trend Arrows

To date, there are four previously published methods to adjust insulin doses using trend arrows: DirecNet Applied Treatment Algorithm [21], Scheiner method [22], Pettus/Edelman method [23], and Klonoff/Kerr formula [24]. Notably, the DirecNet, Scheiner, and Klonoff/Kerr methods include CGM systems other than Dexcom in their approach.

In brief, the DirecNet method determines insulin dose adjustment by calculating percent increase/decrease based on trend arrow directionality. Notably, the net increase/decrease will vary depending on food intake because the DirecNet method considers total insulin dose—*e.g.*, meal and correction dose as appropriate—when determining percent insulin adjustment. The Scheiner and Pettus/Edelman methods use a different approach. Both use anticipated glucose values to recommend an adjustment in insulin dose. The patient can then use predetermined CF and the recommended corrective parameter to add or subtract insulin based on insulin sensitivity. Although the two methods have a similar approach, the Scheiner method has more conservative recommendations for correction parameters to use in insulin adjustment. The recently published Klonoff/Kerr formula offers a simplified approach by using rate of change midpoints for each trend arrow scenario and extrapolating anticipated glucose in the next 45 minutes [24]. Simplified insulin dose adjustments are provided as insulin units, which is similar to our approach. To assess potential safety, the authors consider the impact of insulin dose adjustments using minimum total daily insulin doses and

Table 3. Commonly Used Over-the-Counter and Prescription Medications Containing Acetaminophen

Common Over-the-Counter Medicines Containing Acetaminophen[a]			
▸ Actifed®	▸ Dayquil®	▸ Midol®	▸ Sudafed®
▸ Alka-Seltzer Plus LiquidGels®	▸ Dimetapp®	▸ Nyquil®	▸ Theraflu®
▸ Anacin®	▸ Dristan®	▸ Panadol®	▸ Triaminic®
▸ Benadryl®	▸ Excedrin®	▸ Robitussin®	▸ TYLENOL® Brand Products
▸ Cepacol®	▸ Feverall®	▸ Saint Joseph®	▸ Vanquish®
▸ Contac®	▸ Equation 44®	▸ Aspirin-Free Singlet®	▸ Vicks®
▸ Coricidin®	▸ Goody's® Powders	▸ Sinutab®	▸ Zicam®
	▸ Liquiprin		

Common Prescription Medicines Containing Acetaminophen[a]		
▸ Endocet®	▸ Lortab®	▸ Tylenol® with Codeine
▸ Fioricet®	▸ Percocet®	▸ Tylox®
▸ Hycotab	▸ Phenaphen®	▸ Ultracet®
▸ Hydrocet®	▸ Sedapap®	▸ Vicodin®
▸ Hydrocodone Bitartrate	▸ Tapanol®	▸ Zydone®

Acetaminophen is known to interfere with certain rtCGM sensors causing falsely high glucose readings. Patients using rtCGM are cautioned to check with the manufacturer's information and review labels of over-the-counter medicines for acetaminophen and to ask their provider and/or pharmacist whether their prescribed medication(s) contain acetaminophen.
[a]Includes store and other generic brands.

the 1500 and 1960 rules to infer correction doses [36]. In the Klonoff/Kerr calculations, the proposed doses reflect a limited range of CF values and/or total daily insulin doses, which restricts more insulin-sensitive individuals from applying adjustments. It is the clinical experience and opinion of the authors that the Klonoff/Kerr formula, presumably most applicable for adults, may not apply as readily to the pediatric population given the wide range of insulin sensitivities seen in pediatric patients. Due to the limited application across a broad range of insulin sensitivities and the fact that we did not consider their formula in the development of our approach, we have not included the Klonoff/Kerr formula in our illustrated comparisons. Figure 2 provides a comparison of the DirecNet, Scheiner, and Pettus/Edelman methods; the Klonoff/Kerr formula is described above.

Despite some differences, insulin adjustments for prandial and correction insulin doses are relatively similar and appear to be safe among the described approaches. Each method appears to offer a safe and effective approach to adjusting insulin doses using trend arrows. However, these approaches are limited by their complexity and need for numeracy skills. Additionally, the Scheiner and Pettus/Edelman methods indirectly ask individuals to enter information that is different from actual measurement into their records and do not take into consideration the limitation of MDI users with minimum insulin dose increments/decrements of 1.0 or 0.5 U as well as the need for rounding insulin doses. For the Scheiner and Pettus/Edelman methods, we recognize that bolus calculators, either as an integrated tool in an insulin pump or as a standalone app, can be used to overcome the challenge of requiring additional calculations. However, these methods may be overly reliant on use of bolus calculators, and as a related concern, clinicians should be aware of the apps their patients use to calculate insulin doses. It is the clinical opinion of the authors that many bolus calculator apps have not been rigorously evaluated for accuracy and performance [37]. The Klonoff/Kerr formula takes a similar approach to our method by providing adjustments in insulin units; however, the formula has limitations in the pediatric population where there is a broad range of insulin sensitivities.

5. New Approach to "Adjusting for the Arrows" in Pediatric Patients

We preferred the Scheiner and Pettus/Edelman methods because they rely on insulin sensitivity and recognize the CF as most important when adjusting insulin dose using trend

Dexcom G5 Trend Arrows			Change in Glucose
Receiver	App	Glucose Direction	
⬆⬆		Increasing	**Glucose is rapidly rising** Increasing >3 mg/dL/min or >90 mg/dL in 30 minutes
⬆		Increasing	**Glucose is rising** Increasing 2–3 mg/dL/min or 60–90 mg/dL in 30 minutes
⬈		Increasing	**Glucose is slowly rising** Increasing 1–2 mg/dL/min or 30–60 mg/dL in 30 minutes
➡		Increasing or Decreasing	**Glucose is steady** Not increasing/decreasing >1 mg/dL/min
⬊		Decreasing	**Glucose is slowly falling** Decreasing 1–2 mg/dL/min or 30–60 mg/dL in 30 minutes
⬇		Decreasing	**Glucose is falling** Decreasing 2–3 mg/dL/min or 60–90 mg/dL in 30 minutes
⬇⬇		Decreasing	**Glucose is rapidly falling** Decreasing >3 mg/dL/min or >90 mg/dL in 30 minutes
No Arrow	N/A	System cannot calculate the velocity and direction of the glucose change	

Figure 1. Dexcom G5 trend arrows. Dexcom G5 presents trend arrow data as icons on the Dexcom G5 Receiver and on the Dexcom G5 Mobile and Follow mobile apps (App) on compatible smart devices. According to the manufacturer, trend arrows indicate rates of glucose change (mg/dL per minute) and can be described as the anticipated glucose change in 30 minutes. Notably, the FLAT arrow (➡) indicates steady but does not indicate zero change. Note that trend arrows are determined by recent rtCGM measurements (generally the most recent 10 minutes of glucose values). In general, anticipated glucose may be less accurate when trying to predict changes over extended periods of time (e.g., beyond 20 to 30 minutes) due to the many factors that may influence glucose levels. Conversion: mg/dL × 0.0555 = mmol/L.

arrows. Therefore, in pediatric patients, we sought a simplified approach that addresses the limitations described above while accounting for the wide range of insulin sensitivities observed in the pediatric population. Figure 3 outlines our approach, which is based on typical insulin sensitivity ranges for pediatric patients. For each insulin sensitivity range, we suggest an insulin dose adjustment in insulin units rather than as corrective values. In this manner, insulin adjustments can be more simply added or subtracted to standard calculations and can be used with MDI or insulin pump therapy. The adjustments also take into consideration the limitations of 0.5-U increment/decrement minimums for MDI-treated individuals. Figure 4 is a visual comparison of insulin dose adjustments according to previous methods based on anticipated glucose (Scheiner and Pettus/Edelman) and our suggested approach based on insulin sensitivity ranges (Endocrine Society approach). The illustration shows that our approach aligns well with existing methods that indirectly use insulin sensitivity to adjust insulin doses while overcoming some of the limitations (*e.g.,* a need for additional calculations and the minimum increments/decrements possible for MDI-treated patients).

Our approach divides insulin dose adjustments into five insulin sensitivity ranges that relate to pediatric developmental stages: ≥125 (highly sensitive, often used in toddlers/preschoolers), 75 to <125 (sensitive, often used in young school-age children), 50 to <75 (fairly sensitive, generally used in older school age children), 25 to <50 (less sensitive, often used in young, early pubertal teens), and <25 (least sensitive; generally used in pubertal teens). Patients or parents/caregivers calculate the insulin dose using standard information (*i.e.,* current glucose value, ICR, and CF) and can then add or subtract insulin based on trend arrow information and the patient's insulin sensitivity (*e.g.,* CF) using these suggestions as a starting point. In the event of adjusting insulin dose for downward arrows results in a negative insulin dose, the individual or parent/caregiver should consider if fast-acting carbohydrate is warranted based on the current sensor glucose, taking into account previous exercise and/or anticipated exercise. We provide several

Other Methods to Adjust Insulin Dose Using Trend Arrows				
Trend Arrows	**Insulin Adjustment**	**DirecNet**	**Scheiner**	**Pettus/Edelman**
⇈	**Increase**	20% increase of total dose	Increase to cover current sensor glucose plus 60 mg/dL	Increase to cover current sensor glucose plus 100 mg/dL
↑	**Increase**	20% increase of total dose	Increase to cover current sensor glucose plus 30 mg/dL	Increase to cover current sensor glucose plus 75 mg/dL
↗	**Increase**	10% increase of total dose	Cover current sensor glucose	Increase to cover current sensor glucose plus 50 mg/dL
→	**No adjustment**	0% increase	Cover current sensor glucose	Cover current sensor glucose
↘	**Decrease***	10% decrease of total dose	Cover current sensor glucose	Decrease to cover current sensor glucose minus 50 mg/dL
↓	**Decrease***	20% decrease of total dose	Decrease to cover current sensor glucose minus 30 mg/dL	Decrease to cover current sensor glucose minus 75 mg/dL
⇊	**Decrease***	20% decrease of total dose	Decrease to cover current sensor glucose minus 60 mg/dL	Decrease to cover current sensor glucose minus 100 mg/dL
*May require suspension or delay of insulin administration and/or remedial action (e.g., carbohydrate intake), depending on current sensor glucose value and potential risk for hypoglycemia.				

Figure 2. Other methods to adjust insulin doses using trend arrows. Three published methods for adjusting insulin dose using rtCGM trend arrow data are compared [DirecNet (Abbott system) [21], Scheiner (Medtronic and Dexcom systems) [22], and Pettus/Edelman (Dexcom system)] [23]. The DirecNet method takes total insulin dosage, including carbohydrate consumption (if any) into consideration. Scheiner and Pettus/Edelman methods are based on anticipated change in blood glucose with the Scheiner method being more conservative in insulin adjustment. Notably, the author of the Scheiner method has presented slightly modified values in recent presentations (personal communication) relative to past publication [22]. We use the more recently presented values in this comparison. All three require calculations beyond managing the correction and carbohydrate consumption. All three assume the patient has insulin requiring diabetes and is using rapid-acting insulin for meals and correction doses. Note that the recently published Klonoff/Kerr formula recommends adjusting insulin doses by 1, 1.5, or 2 U supplements/decrements for rates of change of 1 to 2, 2 to 3, and >3 mg/dL/min, respectively [24]. Conversion: mg/dL × 0.0555 = mmol/L.

additional case examples to illustrate how our approach may be used in real-life scenarios in Table 4.

Patients and parents/caregivers should individualize adjustments based on the suggestions, according to the patient's CF, and subsequent observation of responses to dose adjustments. For missed boluses and miscalculations, patients and parents/caregivers should not use the suggested approach to adjust for trend arrows. Instead, they should take the insulin dose calculated from the glucose value at the time of the food consumption and use their ICR, preferably within 2 hours of the missed dose. Adjusting insulin doses using trend arrows should also be avoided in cases of underestimating carbohydrate intake (*i.e.,* miscalculations) and overcorrecting for hypoglycemia with fast-acting carbohydrate. At these times, the trend arrows can serve an important role as reminders to patients/families of a missed dose or a miscalculation.

6. Safety

Insulin stacking (*i.e.,* repeated injection of bolus insulin correction doses at close intervals when glucose-lowering of initial insulin bolus dose is ongoing) can lead to hypoglycemia; thus, it is important to avoid additional insulin bolus dosing when patients/parents/caregivers

Suggested Approach to Adjusting Insulin Dose Using Trend Arrows in Pediatric Patients: Pre-meal and ≥3 Hours Post-meal

Trend Arrows		Correction Factor* (CF)	Insulin Dose Adjustment (U)
Receiver	App		
⬆⬆		<25	+4.0
		25–<50	+3.0
		50–<75	+2.0
		75–<125	+1.0
		≥125	+0.5
⬆		<25	+3.0
		25–<50	+2.0
		50–<75	+1.0
		75–<125	+0.5
		≥125	No adjustment
➚		<25	+2.0
		25–<50	+1.0
		50–<75	+0.5
		75–<125	No adjustment
		≥125	No adjustment
➡		<25	No adjustment
		25–<50	No adjustment
		50–<75	No adjustment
		75–<125	No adjustment
		≥125	No adjustment
➘		<25	-2.0
		25–<50	-1.0
		50–<75	-0.5
		75–<125	No adjustment
		≥125	No adjustment
⬇		<25	-3.0
		25–<50	-2.0
		50–<75	-1.0
		75–<125	-0.5
		≥125	No adjustment
⬇⬇		<25	-4.0
		25–<50	-3.0
		50–<75	-2.0
		75–<125	-1.0
		≥125	-0.5

Insulin adjustments using trend arrows do not replace standard calculations using ICR and CF. Adjustments are increases or decreases of rapid-acting insulin in addition to calculations using ICR and CF. Adjustments using trend arrows are an additional step to standard care.

Note on insulin sensitivity with developmental stages in pediatric patients: We provide five insulin sensitivity ranges. Notably, younger patients tend to be more insulin sensitive (higher CF) and older patients tend to be less insulin sensitive (lower CF). Typical decrease in insulin sensitivity is an important consideration in long-term care. Outliers may exist in any group.

Pre-School-Age/Toddlerhood (ages 2–6): often use CF ≥125
School Age/Middle-Childhood (ages 7–12): greatest variability
Adolescence/Young Adulthood (ages 13–22): often use CF 25–50 or <25

Considerations when adjusting for trend arrows:
If sensor glucose is rapidly rising (2 UP arrows; ⬆⬆) at pre-meal, consider administering insulin 15–30 minutes before eating.

If sensor glucose is rapidly falling (2 DOWN arrows; ⬇⬇) at pre-meal, consider administering insulin closer to the meal.

At bedtime, adjustments may be considered; however, use caution when adding insulin at that time. Suggest a bedtime target of 130 mg/dL with FLAT (➡) or ANGLE UP (➚) arrow.

Approach does not require insulin on board to be set to 3 hours.

*Correction factor (CF) is in mg/dL and indicates glucose lowering per unit of rapid-acting insulin.

Figure 3. New approach to adjust insulin doses using trend arrows in pediatric patients with diabetes. This figure outlines our approach to adjusting insulin doses using trend arrow data from the Dexcom G5 system in pediatric patients with diabetes receiving rapid acting insulin analogs. The approach is based on anticipated glucose change and typical insulin sensitivity ranges in pediatric patients that correspond to developmental stages. It should be noted that insulin sensitivity is generally greater in younger, prepubertal patients and

decreases over time as youth age with decreasing insulin sensitivity associated with pubertal growth and development. The approach to adjusting insulin doses using trend arrows is suggested for premeal boluses and for corrections 3 or more hours following a meal. In general, the authors recommend avoiding adjustments using trend arrows immediately following meals due to the variability that ingested carbohydrates can have on trend arrows. Generally, one should begin with conservative adjustments to understand how the dose changes impact the individual. It is essential to understand that adjusting insulin doses using trend arrows does not replace but adds to standard calculations using ICR and CF. The approach assumes the patient has insulin requiring diabetes, is using rapid-acting insulin for meals and correction, and is using ICR and CF factors that have been accurately determined by the patient's health care team (*e.g.,* determining CF using the 1500 to 1800 rule) [36]. Conversion: mg/dL × 0.0555 = mmol/L. CF, correction factor in mg/dL, indicates glucose lowering per unit of rapid-acting insulin; U, units of rapid-acting insulin.

see rapid rises in postprandial glucose values using rtCGM, especially if there is substantial insulin on board. Rapid increases in glucose levels can be especially problematic if insulin is given postprandially, as may be the case in very young children [38]. In general, we suggest pediatric patients using rapid-acting insulin analogs wait at least 3 hours after the prandial bolus before giving a subsequent correction dose. For individuals using an insulin pump, this assumes active insulin duration of at least 3 hours. For pediatric patients, especially younger patients, who tend to "graze" throughout the day, dose adjustments using trend arrows can potentially lead to undue insulin stacking with risk of hypoglycemia and should be avoided. Importantly, our approach is designed for premeals and 3 or more hours postprandially.

7. Important Considerations When "Adjusting for the Arrows"

We recognize insulin dosing decisions at bedtime, with exercise, and during sick day management are complex and multifactorial. During these special circumstances, food intake, physical activity, and stressors among other factors impact insulin dosing decisions. We reiterate that our suggestions are not comprehensive in these special circumstances and should serve as a starting point for future discussion. We recognize these areas are of great concern and further consideration on how our suggested approach may apply under these circumstances needs to be addressed in the near future.

A. Bedtime

Nocturnal hypoglycemia is common and potentially dangerous, particularly when patients engage in intensive physical activity during the day. Children also tend to be deeper sleepers, engage in sporadic unpredictable exercise, experience changing metabolism, and may have blunted overnight counter-regulatory hormone responses, which puts them at increased risk for nocturnal hypoglycemia compared with adults [39]. We recommend a bedtime glucose target of ~130 mg/dL with a FLAT or ANGLE UP trend arrow [21]. Other trend arrows may provide guidance in determining a bedtime snack or correction bolus. For example, if bedtime glucose levels are near target and are accompanied by downward trending arrows, an extra snack may be needed. Conversely, a modest correction might be given if glucose levels are over target and accompanied by upward arrows. Although our approach to adjustments may be considered at bedtime, patients and parents/caregivers should use caution when adding insulin at that time, with follow-up assessment of glucose levels overnight as indicated. Patients or parents/caregivers should also consider altering the CGM alerts for trend arrows and/or the high/low threshold alert levels following a day of atypical physical activity or illness to reduce glucose levels out of range.

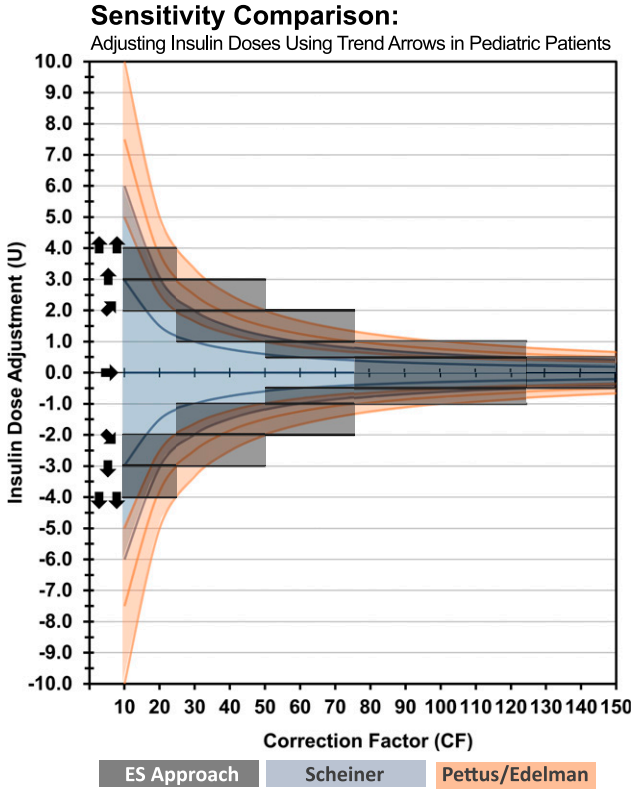

Figure 4. Sensitivity comparison of CF based methods to adjust insulin doses using trend arrows in pediatric patients. The figure is a visual comparison of insulin dose adjustments according to previous methods based on anticipated glucose (Scheiner and Pettus/Edelman) and our suggested approach based on insulin sensitivity ranges (Endocrine Society approach). The illustration shows that our approach aligns well with existing methods that indirectly use insulin sensitivity to adjust insulin doses while overcoming some of the limitations (*e.g.,* a need for additional calculations and minimum increments possible for MDI-treated patients). Notably, our suggestion is relatively more conservative when applied to insulin-resistant individuals using lower CF ranges (*e.g.,* <30) and more aggressive in the midrange (*e.g.,* 40 to 75). However, one must consider that the calculations used in our approach are based on anticipated glucose at 30 minutes. When considering the anticipated glucose at 1 hour, the suggested insulin dose adjustments become more conservative. For example, a single UP trend arrow indicates that glucose is rising 2 to 3 mg/dL/min. At 30 minutes, the anticipated glucose would be 60 to 90 mg/dL higher. However, the anticipated glucose could be as much as 120 to 180 mg/dL at 60 minutes if unexposed to other perturbations. If a child's CF was 60, our approach suggests adding 1 U of rapid-acting insulin to the premeal bolus. The additional 1 U of insulin would be expected to provide additional glucose lowering of 60 mg/dL over the 60 minutes. Given that the 60-minute anticipated glucose could potentially be much higher at 1 hour, our suggestion could be considered conservative. The expected glucose would be closer to target, postprandially, without overcorrecting and without increasing risk for hypoglycemia. As noted, these recommendations are starting points and should be readjusted as experience increases and responsiveness is observed and understood. Conversion: mg/dL × 0.0555 = mmol/L. CF, correction factor in mg/dL indicates glucose lowering per unit of rapid-acting insulin; U, units of rapid-acting insulin.

B. Exercise/Physical Activity

Exercise is a fundamental component of diabetes management and paramount to children's well-being. rtCGM trend arrows and alerts/alarms are particularly beneficial before, during, and after exercise/physical activity. These features alert patients and parents/caregivers to rapid changes and onset of hypoglycemia, which are less noticeable during exertion. The alerts and alarms also provide overnight safety following a day of intense exercise/physical activity by detecting nocturnal hypoglycemia.

Table 4. Case Examples to Put Our Approach Into Practice for Children and Adolescents

The Case Examples are Applicable to Both MDI and Insulin Pump Treated Individuals. Examples Assume ICR and CF Values Have Been Accurately Determined by the Patient's Health Care Team and That the Patient is Administering Rapid-Acting Insulin for Bolus Doses for Carbohydrate Coverage and Corrections. Examples Assume the Patients Have Insulin-Requiring Diabetes and Are Using Dexcom G5 rtCGM.

A A 9-year-old school-age child is about to eat dinner. The CGM indicates that the glucose is above target with a SINGLE UP arrow. A calculated insulin dose is determined using predetermined parameters. Due to the SINGLE UP arrow and no recent or planned exercise, an adjustment of +0.5 U is suggested. This increases the total insulin dose to 3.0 U.

Sensor Glucose	Trend Arrow	Target Glucose	Carb	Parameters	Calculated Insulin Dose	Trend Arrow Adjustment	Total Insulin Dose
160 mg/dL	↑	120 mg/dL	50 g	CF–80 ICR–1:25	0.5 U + 2.0 U = 2.5 U	+0.5 U	3.0 U

B A 16-year-old teen is going to eat breakfast with DOUBLE UP arrows present. Her glucose is below target, and she uses reverse corrections. An insulin dose is determined using ICR and CF values. Due to DOUBLE UP arrows, an adjustment of +3.0 U is suggested to account for the rising glucose. This increases the total insulin dose to 12.0 U.

Sensor Glucose	Trend Arrow	Target Glucose	Carb	Parameters	Calculated Insulin Dose	Trend Arrow Adjustment	Total Insulin Dose
75 mg/dL	↑↑	100 mg/dL	70 g	CF–25 ICR–1:7	−1.0 U + 10.0 U = 9.0 U	+3.0 U	12.0 U

C A 3-year-old toddler is about to eat lunch. The child tends to be a good eater. The parent sees an elevated glucose with DOUBLE DOWN trend arrows on the CGM display. An insulin dose is calculated based on correction and carbohydrate intake. Due to the DOUBLE DOWN arrows, a negative adjustment of −0.5 U is suggested to account for the falling glucose. This decreases the total insulin dose to 2.5 U.

Sensor Glucose	Trend Arrow	Target Glucose	Carb	Parameters	Calculated Insulin Dose	Trend Arrow Adjustment	Total Insulin Dose
275 mg/dL	↓↓	150 mg/dL	40 g	CF–125 ICR–1:20	1.0 U + 2.0 U = 3.0 U	−0.5 U	2.5 U

D A 7-year-old boy is having lunch at school. His CGM display shows a sensor glucose of 300 mg/dL with SINGLE UP arrow. The caregiver notes that recess is planned to take place after lunch. An insulin dose is determined that includes the correction dose and carbohydrate intake. However, due to the planned exercise, using the adjustment table may not be recommended. This conservative approach is suggested because there is typically less monitoring oversight during school hours. (Note: An adjustment may be considered with a parent's more watchful monitoring or when exercise is not a factor with a suggested adjustment of +0.5 U, which increases the total insulin dose to 5.5 U. In general, use trend adjustments conservatively in special situations such as exercise.)

Sensor Glucose	Trend Arrow	Target Glucose	Carb	Parameters	Calculated Insulin Dose	Trend Arrow Adjustment	Total Insulin Dose
300 mg/dL	↑	100 mg/dL	60 g	CF–100 ICR–1:20	2.0 + 3.0 = 5.0 U	NA (or +0.5 U if with parents)	5.0 U (or 5.5 U if with parents)

E A 12-year-old girl just completed afternoon soccer practice. Two hours later, she is preparing for supper, which is usually a large meal after practice. Her sensor glucose is in range; however, DOUBLE DOWN arrows are also present. With her parents, she calculates her insulin dose for the planned carbohydrate intake; no correction is needed. To prevent later hypoglycemia, a negative adjustment of −2.0 U is suggested. This decreases the total insulin dose to 3.0 U.

Sensor Glucose	Trend Arrow	Target Glucose	Carb	Parameters	Calculated Insulin Dose	Trend Arrow Adjustment	Total Insulin Dose
105 mg/dL	↓↓	100 mg/dL	75 g	CF–60 ICR–1:15	5.0 U	−2.0 U	3.0 U

Table 4. Continued

The Case Examples are Applicable to Both MDI and Insulin Pump Treated Individuals. Examples Assume ICR and CF Values Have Been Accurately Determined by the Patient's Health Care Team and That the Patient is Administering Rapid-Acting Insulin for Bolus Doses for Carbohydrate Coverage and Corrections. Examples Assume the Patients Have Insulin-Requiring Diabetes and Are Using Dexcom G5 rtCGM.

F A 5-year-old is preparing for bedtime. His CGM glucose is near his bedtime target of 130 mg/dL and his CGM shows a SINGLE DOWN arrow. The parents calculate the insulin dose for the bedtime snack and decide no correction dose is needed with the glucose of 150 mg/dL. They then consider the suggested negative adjustment of −0.5 U. In this case, the parents decide to decrease the total insulin dose to reduce the risk of nocturnal hypoglycemia, which brings the net dose to 0.0 U.

Sensor Glucose	Trend Arrow	Target Glucose	Carb	Parameters	Calculated Insulin Dose	Trend Arrow Adjustment	Total Insulin Dose
150 mg/dL	↓	130 mg/dL	15 g	CF–120 ICR–1:30	0.5 U	−0.5 U	0.0 U

G It is bedtime for a 17-year-old male. Today, he participated in a rigorous hockey tournament. Before going to bed, he plans to eat a large snack because he is very hungry. His sensor glucose is 210 mg/dL with an ANGLE UP arrow present. He calculates the insulin dose for the correction and planned carbohydrate intake. He then considers if he should use the adjustment table following his rigorous exercise that afternoon. He chooses to act conservatively and not adjust the insulin dose because he is going to bed following an unusually active day. This decision should reduce his risk of nocturnal hypoglycemia. (Note: An adjustment of 2.0 U might be added in the absence of rigorous exercise)

Sensor Glucose	Trend Arrow	Target Glucose	Carb	Parameters	Calculated Insulin Dose	Trend Arrow Adjustment	Total Insulin Dose
210 mg/dL	↗	130 mg/dL	40 g	CF–20 ICR–1:8	4.0 + 5.0 = 9.0 U	NA (or +2.0 U if no exercise)	9.0 U (or 11.0 U if no exercise)

Calculated Insulin Dose includes insulin needed to cover carbohydrate intake and correction to reach target glucose. The calculations use the predetermined ICR and CF values and assume these values have been accurately determined by the patient's health care team and that the patient is using rapid-acting insulin for carbohydrate intake and correction.

Abbreviations: CF, correction factor in mg/dL indicates glucose lowering per unit of rapid-acting insulin; U, units of rapid-acting insulin. Conversion: mg/dL × 0.0555 = mmol/L.

Glycemic response to exercise/physical activity can be influenced by the glucose concentrations prior to exercise, amount of active insulin during and after exercise, insulin infusion/injection site, composition of previous meal, as well as intensity, duration, and type of exercise [aerobic (*e.g.,* running, swimming, biking) or anaerobic (*e.g.,* resistance training)] [40]. Pediatric patients of all ages may engage in unplanned activities. Notably, most young pediatric patients engage in aerobic exercise.

Very young patients do not prepare for exercise; they play at any time. School-age/adolescent patients are more likely to be involved in organized sports, generally in the afternoon after school. Nocturnal hypoglycemia is particularly common after afternoon exercise [41, 42].

Due to the complexities associated with exercise, we generally suggest refraining from using our suggested approach during and after exercise. However, trend arrows can be helpful indicators during exercise to determine when extra carbohydrates are required and can be used to prevent impending hypoglycemia [43]. A simple approach before and during exercise when glucose level is ≤125 mg/dL and downward arrow are present may be to ingest between 8 and 30 g of fast-acting carbohydrate and monitor trends carefully. The amount of carbohydrate should be based on several factors including the child's age, anticipated response to exercise, and directionality of downward trend arrows (*e.g.,* single downward arrow requires less carbohydrate than two downward arrows). This should be followed by reassessment of glucose levels and trend arrows as the exercise continues. The use of trend arrows with

exercise needs to be individualized to the person and sport and modified according to prior experience.

C. Sick Day Management

When ill, there is increased risk of hyperglycemia, diabetic ketoacidosis, and acetaminophen ingestion (intentional or inadvertent). An important concern with rtCGM is falsely elevated glucose readings due to acetaminophen interference; trend arrows are most impacted during the onset and tailing off of acetaminophen use [34, 35]. rtCGM users should be aware of each manufacturer's recommendations regarding acetaminophen interference. A recent study reported significant differences between rtCGM and fingerstick glucose readings for up to 6 hours after acetaminophen ingestion [35]. Notably, acetaminophen interference will likely be eliminated in future CGM models [44].

On sick days, it is advisable to check glucose by confirmatory fingerstick every 2 to 4 hours and consider insulin correction doses every 2 to 3 hours (with appropriate ketone testing). Additionally, patients and parents/caregivers should consider using fingerstick monitoring for treatment decisions when glucose is >250 mg/dL and ketones (blood or urine) are present and when glucose is <70 mg/dL or symptoms of hypoglycemia are present.

Patients and parents/caregivers should be counseled to carefully read labels of medications to avoid acetaminophen-containing formulations, and if they choose a medication that contains acetaminophen, they should base **all treatment decisions** on fingerstick glucose values for up to 6 hours following ingestion. A list of common medications that contain acetaminophen is included in Table 3.

D. Environmental Factors

There are no indications that environmental factors, such as temperature, altitude, or humidity impact rtCGM accuracy, but they do affect fingerstick blood glucose monitoring results [45]. Because accurate calibration is essential to rtCGM accuracy, patients and parents/caregivers should be advised to perform calibration prior to exposure to these environmental conditions.

8. Summary

Our goal was to provide a safe, practical approach to using Dexcom G5 trend arrow data. The approach we present here is based on review of previously published and presented methods. Instead of percentage or corrective values, our approach focuses on typical insulin sensitivity ranges and provides a range of adjustments in terms of insulin units that corresponds to pediatric developmental stages. We believe our simplified approach minimizes the complexity and number of additional steps, and that it will help patients/parents/caregivers improve glucose control, increase time in range without hypoglycemia, and promote clinical discussion.

A major difference of pediatric care from adult care is the gradual shift of responsibility from caregiver to patient. Young children with insulin requiring diabetes rely on parents/caregivers; whereas older children, adolescents, and young adults must gradually assume increasing amounts of responsibility for self-care [46]. Transitioning adolescent patients from pediatric to adult care is often a challenge. Ensuring continuity of care and supporting patients during transition can involve multiple care teams and changes in therapy or therapeutic goals in addition to life challenges. As a starting point, we offer the complementary approach to adjusting insulin doses using trend arrows in adult patients, which is included in this issue.

In summary, rtCGM can be a valuable tool for predictive fine-tuning of insulin dosing when "adjusting for the arrows" and for overall diabetes care. With this as a starting point, we hope

to see more empirically based information and similar guidance developed for other currently available and emerging glucose monitoring devices.

Acknowledgments

The authors thank the Endocrine Society for convening and facilitating the writing group and Christopher G. Parkin, MS, for editorial support in developing this manuscript.

Financial Support: This publication was supported by an unrestricted educational grant to the Endocrine Society from Dexcom, Inc., San Diego, California.

Author Contributions: L.M.L. led the writing group as chair and facilitated development and group consensus of the methods proposed. All authors contributed equally in manuscript review, discussion of the results and implications, and commented on the manuscript at all stages.

Correspondence: Lori M. Laffel, MD, MPH, Chief, Pediatric, Adolescent, and Young Adult Section, Senior Investigator, Co-Head, Section on Clinical, Behavioral and Outcomes Research, Joslin Diabetes Center, Professor of Pediatrics, Harvard Medical School, One Joslin Place, Boston, Massachusetts 02215. E-mail lori.laffel@joslin.harvard.edu.

Disclosure Summary: L.M.L. has served as a consultant to AstraZeneca, Boehringer Ingelheim Pharmaceuticals, Dexcom, Eli Lilly and Company, Insulet, Johnson & Johnson, MannKind Corporation, Menarini Diagnostics, Novo Nordisk, Roche Diabetes Care, and Sanofi U.S. G.A. has served as an advisor board member for Novo Nordisk, has served as a consultant to Boehringer Ingelheim and Dexcom, and her institution has received research support from AstraZeneca. B.A.B. receives research funding from Bigfoot Biomedical, Dexcom, Insulet Corp., Medtronic, Tandem, and Type Zero, and is an advisory board member for Convatec, Novo Nordisk, and Sanofi. G.P.F. receives research funding from Animas, Bigfoot Biomedical, Dexcom, Insulet Corp., Medtronic, Novo Nordisk, Tandem, and Type Zero, and is a speaker and advisory board member for Dexcom. S.A.W. serves as a consultant and speaker for Medtronic and Insulet. E.T., L.E.R., and D.R.H. have no disclosures to report.

References and Notes

1. Danne T, Bangstad HJ, Deeb L, Jarosz-Chobot P, Mungaie L, Saboo B, Urakami T, Battelino T, Hanas R; International Society for Pediatric and Adolescent Diabetes. ISPAD Clinical Practice Consensus Guidelines 2014. Insulin treatment in children and adolescents with diabetes. *Pediatr Diabetes*. 2014; **15**(Suppl 20):115–134.
2. Weinzimer SA, Tamborlane VW. Diabetes mellitus in children and adolescents. In: Fonseca V, ed. *Clinical Diabetes*. Philadelphia, PA: Saunders Elsevier; 2006:505.
3. Streisand R, Mackey ER, Elliot BM, Mednick L, Slaughter IM, Turek J, Austin A. Parental anxiety and depression associated with caring for a child newly diagnosed with type 1 diabetes: opportunities for education and counseling. *Patient Educ Couns*. 2008;**73**(2):333–338.
4. Whittemore R, Jaser S, Chao A, Jang M, Grey M. Psychological experience of parents of children with type 1 diabetes: a systematic mixed-studies review. *Diabetes Educ*. 2012;**38**(4):562–579.
5. Grey M. Coping and psychosocial adjustment in mothers of young children with type 1 diabetes. *Child Health Care*. 2009;**38**(2):91–106.
6. Mitchell SJ, Hilliard ME, Mednick L, Henderson C, Cogen FR, Streisand R. Stress among fathers of young children with type 1 diabetes. *Fam Syst Health*. 2009;**27**(4):314–324.
7. Streisand R, Swift E, Wickmark T, Chen R, Holmes CS. Pediatric parenting stress among parents of children with type 1 diabetes: the role of self-efficacy, responsibility, and fear. *J Pediatr Psychol*. 2005; **30**(6):513–521.
8. Miller KM, Foster NC, Beck RW, Bergenstal RM, DuBose SN, DiMeglio LA, Maahs DM, Tamborlane WV; T1D Exchange Clinic Network. Current state of type 1 diabetes treatment in the U.S.: updated data from the T1D Exchange clinic registry. *Diabetes Care*. 2015;**38**(6):971–978.
9. Lowes L, Lyne P, Gregory JW. Childhood diabetes: parents' experience of home management and the first year following diagnosis. *Diabet Med*. 2004;**21**(6):531–538.
10. Barnard K, Thomas S, Royle P, Noyes K, Waugh N. Fear of hypoglycaemia in parents of young children with type 1 diabetes: a systematic review. *BMC Pediatr*. 2010;**10**(1):50.
11. Haugstvedt A, Wentzel-Larsen T, Graue M, Søvik O, Rokne B. Fear of hypoglycaemia in mothers and fathers of children with Type 1 diabetes is associated with poor glycaemic control and parental emotional distress: a population-based study. *Diabet Med*. 2010;**27**(1):72–78.

12. Beck RW, Hirsch IB, Laffel L, Tamborlane WV, Bode BW, Buckingham B, Chase P, Clemons R, Fiallo-Scharer R, Fox LA, Gilliam LK, Huang ES, Kollman C, Kowalski AJ, Lawrence JM, Lee J, Mauras N, O'Grady M, Ruedy KJ, Tansey M, Tsalikian E, Weinzimer SA, Wilson DM, Wolpert H, Wysocki T, Xing D; Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group. The effect of continuous glucose monitoring in well-controlled type 1 diabetes [published correction appears in *Diabetes Care*. 2009;32(10):1944]. *Diabetes Care*. 2009;**32**(8):1378–1383.
13. Battelino T, Phillip M, Bratina N, Nimri R, Oskarsson P, Bolinder J. Effect of continuous glucose monitoring on hypoglycemia in type 1 diabetes. *Diabetes Care*. 2011;**34**(4):795–800.
14. Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group. Effectiveness of continuous glucose monitoring in a clinical care environment: evidence from the Juvenile Diabetes Research Foundation continuous glucose monitoring (JDRF-CGM) trial. *Diabetes Care*. 2010;**33**(1):17–22.
15. Battelino T, Conget I, Olsen B, Schütz-Fuhrmann I, Hommel E, Hoogma R, Schierloh U, Sulli N, Bolinder J; SWITCH Study Group. The use and efficacy of continuous glucose monitoring in type 1 diabetes treated with insulin pump therapy: a randomised controlled trial. *Diabetologia*. 2012;**55**(12):3155–3162.
16. Cemeroglu AP, Stone R, Kleis L, Racine MS, Postellon DC, Wood MA. Use of a real-time continuous glucose monitoring system in children and young adults on insulin pump therapy: patients' and caregivers' perception of benefit. *Pediatr Diabetes*. 2010;**11**(3):182–187.
17. Bergenstal RM, Tamborlane WV, Ahmann A, Buse JB, Dailey G, Davis SN, Joyce C, Perkins BA, Welsh JB, Willi SM, Wood MA; STAR 3 Study Group. Sensor-augmented pump therapy for A1C reduction (STAR 3) study: results from the 6-month continuation phase. *Diabetes Care*. 2011;**34**(11):2403–2405.
18. Pettus J, Price DA, Edelman SV. How patients with type 1 diabetes translate continuous glucose monitoring data into diabetes management decisions. *Endocr Pract*. 2015;**21**(6):613–620.
19. Hirsch IB, Abelseth J, Bode BW, Fischer JS, Kaufman FR, Mastrototaro J, Parkin CG, Wolpert HA, Buckingham BA. Sensor-augmented insulin pump therapy: results of the first randomized treat-to-target study. *Diabetes Technol Ther*. 2008;**10**(5):377–383.
20. JDRF CGM Study Group. JDRF randomized clinical trial to assess the efficacy of real-time continuous glucose monitoring in the management of type 1 diabetes: research design and methods. *Diabetes Technol Ther*. 2008;**10**(4):310–321.
21. Buckingham B, Xing D, Weinzimer S, Fiallo-Scharer R, Kollman C, Mauras N, Tsalikian E, Tamborlane W, Wysocki T, Ruedy K, Beck R; Diabetes Research In Children Network (DirecNet) Study Group. Use of the DirecNet Applied Treatment Algorithm (DATA) for diabetes management with a real-time continuous glucose monitor (the FreeStyle Navigator). *Pediatr Diabetes*. 2008;**9**(2):142–147.
22. Scheiner G. *Practical CGM: Improving Patient Outcomes Through Continuous Glucose Monitoring*. 4th ed. Alexandria, VA: American Diabetes Association; 2015.
23. Pettus J, Edelman SV. Recommendations for using real-time continuous glucose monitoring (rtCGM) data for insulin adjustments in type 1 diabetes. *J Diabetes Sci Technol*. 2017;**11**(1):138–147.
24. Klonoff DC, Kerr D. A simplified approach using rate of change arrows to adjust insulin with real-time continuous glucose monitoring. *J Diabetes Sci Technol*. 2017;**11**(6):1063–1069.
25. Forlenza GP, Argento NB, Laffel LM. Practical considerations on the use of continuous glucose monitoring in pediatrics and older adults and nonadjunctive use. *Diabetes Technol Ther*. 2017;**19**(S3): S13–S20.
26. Scheiner G. Continuous glucose monitoring. Making sense of your numbers. *Diabetes Self Manag*. 2008; **25**(3):42, 44, 48–50.
27. U.S. Food and Drug Administration. Press Announcements - FDA approves first continuous glucose monitoring system for adults not requiring blood sample calibration. In: Health and Human Services, ed. Office of the Commissioner; 2017.
28. Bailey TS, Grunberger G, Bode BW, Handelsman Y, Hirsch IB, Jovanovič L, Roberts VL, Rodbard D, Tamborlane WV, Walsh J; American Association of Clinical Endocrinologists (AACE)American College of Endocrinology (ACE). American Association of Clinical Endocrinologists and American College of Endocrinology 2016 Outpatient Glucose Monitoring Consensus Statement. *Endocr Pract*. 2016;**22**(2): 231–261.
29. Phillip M, Danne T, Shalitin S, Buckingham B, Laffel L, Tamborlane W, Battelino T; Consensus Forum Participants. Use of continuous glucose monitoring in children and adolescents (*). *Pediatr Diabetes*. 2012;**13**(3):215–228.
30. Rewers MJ, Pillay K, de Beaufort C, Craig ME, Hanas R, Acerini CL, Maahs DM; International Society for Pediatric and Adolescent Diabetes. ISPAD Clinical Practice Consensus Guidelines 2014. Assessment and monitoring of glycemic control in children and adolescents with diabetes. *Pediatr Diabetes*. 2014;**15**(Suppl 20):102–114.

31. Buckingham B, Beck RW, Tamborlane WV, Xing D, Kollman C, Fiallo-Scharer R, Mauras N, Ruedy KJ, Tansey M, Weinzimer SA, Wysocki T. Continuous glucose monitoring in children with type 1 diabetes. *J Pediatr*. 2007;**151**:388–393.
32. Weinzimer S, Xing D, Tansey M, Fiallo-Scharer R, Mauras N, Wysocki T, Beck R, Tamborlane W, Ruedy K; Diabetes Research in Children Network (DirecNet) Study Group. FreeStyle navigator continuous glucose monitoring system use in children with type 1 diabetes using glargine-based multiple daily dose regimens: results of a pilot trial Diabetes Research in Children Network (DirecNet) Study Group. *Diabetes Care*. 2008;**31**(3):525–527.
33. Faccioli S, Del Favero S, Visentin R, Bonfanti R, Iafusco D, Rabbone I, Marigliano M, Schiaffini R, Bruttomesso D, Cobelli C; PedArPan Study Group. Accuracy of a CGM sensor in pediatric subjects with type 1 diabetes. comparison of three insertion sites: arm, abdomen, and gluteus. *J Diabetes Sci Technol*. 2017;**11**(6):1147–1154.
34. Basu A, Veettil S, Dyer R, Peyser T, Basu R. Direct evidence of acetaminophen interference with subcutaneous glucose sensing in humans: a pilot study. *Diabetes Technol Ther*. 2016;**18**(Suppl 2): S243–S247.
35. Maahs DM, DeSalvo D, Pyle L, Ly T, Messer L, Clinton P, Westfall E, Wadwa RP, Buckingham B. Effect of acetaminophen on CGM glucose in an outpatient setting. *Diabetes Care*. 2015;**38**(10):e158–e159.
36. Walsh J, Roberts R, Bailey T. Guidelines for insulin dosing in continuous subcutaneous insulin infusion using new formulas from a retrospective study of individuals with optimal glucose levels. *J Diabetes Sci Technol*. 2010;**4**(5):1174–1181.
37. Schmidt S, Nørgaard K. Bolus calculators. *J Diabetes Sci Technol*. 2014;**8**(5):1035–1041.
38. Hirsch IB. Insulin analogues. *N Engl J Med*. 2005;**352**(2):174–183.
39. Diabetes Research in Children Network (DirecNet) Study Group. Impaired overnight counter-regulatory hormone responses to spontaneous hypoglycemia in children with type 1 diabetes. *Pediatr Diabetes*. 2007;**8**(4):199–205.
40. Bally L, Laimer M, Stettler C. Exercise-associated glucose metabolism in individuals with type 1 diabetes mellitus. *Curr Opin Clin Nutr Metab Care*. 2015;**18**(4):428–433.
41. Davey RJ, Howe W, Paramalingam N, Ferreira LD, Davis EA, Fournier PA, Jones TW. The effect of midday moderate-intensity exercise on postexercise hypoglycemia risk in individuals with type 1 diabetes. *J Clin Endocrinol Metab*. 2013;**98**(7):2908–2914.
42. Riddell MC, Gallen IW, Smart CE, Taplin CE, Adolfsson P, Lumb AN, Kowalski A, Rabasa-Lhoret R, McCrimmon RJ, Hume C, Annan F, Fournier PA, Graham C, Bode B, Galassetti P, Jones TW, Millán IS, Heise T, Peters AL, Petz A, Laffel LM. Exercise management in type 1 diabetes: a consensus statement. *Lancet Diabetes Endocrinol*. 2017;**5**(5):377–390.
43. Riddell MC, Milliken J. Preventing exercise-induced hypoglycemia in type 1 diabetes using real-time continuous glucose monitoring and a new carbohydrate intake algorithm: an observational field study. *Diabetes Technol Ther*. 2011;**13**(8):819–825.
44. Lynn Kennedy AB. Dexcom's G6 Sensor Shines in Early Accuracy Study. 2016; Dexcom CEO interview. Available at: https://diatribe.org/dexcom-g6-sensor-shines-early-accuracy-study. Accessed 18 October 2017.
45. Erbach M, Freckmann G, Hinzmann R, Kulzer B, Ziegler R, Heinemann L, Schnell O. Interferences and limitations in blood glucose self-testing: an overview of the current knowledge. *J Diabetes Sci Technol*. 2016;**10**(5):1161–1168.
46. Cameron F. Teenagers with diabetes–management challenges. *Aust Fam Physician*. 2006;**35**(6): 386–390.