TITLE:

Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations from the International Consensus on Time-in-Range

RUNNING TITLE:

CGM Time-In-Range Consensus

AUTHORS:

Tadej Battelino, Department of Pediatric Endocrinology, Diabetes and Metabolism, University Medical Centre-University Children's Hospital, and Faculty of Medicine, University of Ljubljana, Slovenia

Thomas Danne, Diabetes Centre for Children and Adolescents, AUF DER BULT, Kinder- und Jugendkrankenhaus, Hannover, Germany

Stephanie A. Amiel, Diabetes Research Group, King's College London, London, United Kingdom

Roy Beck, Jaeb Center for Health Research, Tampa, Florida, USA

Richard M. Bergenstal, International Diabetes Center at Park Nicollet, Minneapolis, MN, USA

Torben Biester, Diabetes Centre for Children and Adolescents, AUF DER BULT, Kinder- und Jugendkrankenhaus, Hannover, Germany

Emanuele Bosi, Diabetes Research Institute, IRCCS San Raffaele Hospital, Vita-Salute San Raffaele University, Milan, Italy.

Bruce Buckingham, Stanford Medical Center, Department of Pediatrics, Division of Endocrinology and Diabetes, Stanford, CA, U.S.A

William Cefalu, American Diabetes Association, Alexandria, VA, USA

Kelly L. Close, Close Concerns and diaTribe, San Francisco, California, USA

Claudio Cobelli, Department of Information Engineering, University of Padova, Padova, Italy.

Eyal Dassau, Harvard John A. Paulson School of Engineering and Applied Sciences, Harvard University, Cambridge, Massachusetts, USA

J. Hans DeVries, Profil, Neuss, Germany and Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

Kim Donaghue, The Children's Hospital at Westmead, University of Sydney, Australia,

Klemen Dovc, Department of Pediatric Endocrinology, Diabetes and Metabolism, University Medical Centre-University Children's Hospital, Ljubljana, Slovenia

Francis J. Doyle III, Harvard John A. Paulson School of Engineering and Applied Sciences, Harvard University, Cambridge, Massachusetts, USA

Satish Garg, University of Colorado Denver and Barbara Davis Center for Diabetes, Aurora, Colorado USA

George Grunberger, Grunberger Diabetes Institute, Bloomfield Hills, Michigan, USA

Simon Heller, Academic Unit of Diabetes, Endocrinology and Metabolism, University of Sheffield, Sheffield, United Kingdom

Lutz Heinemann, Science Consulting in Diabetes, Neuss, Germany

Irl B. Hirsch, Department of Medicine, Division of Metabolism, Endocrinology, & Nutrition, University of Washington School of Medicine, Seattle, Washington, USA

Roman Hovorka, Wellcome Trust-MRC Institute of Metabolic Science, and Department of Paediatrics, University of Cambridge, Cambridge, United Kingdom

Weiping Jia, Department of Endocrinology & Metabolism, Shanghai Clinical Center of Diabetes, Shanghai Diabetes Institute, Shanghai Key Laboratory of Diabetes Mellitus, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China

Olga Kordonouri, Diabetes Centre for Children and Adolescents, AUF DER BULT, Kinder- und Jugendkrankenhaus, Hannover, Germany

Boris Kovatchev, Center for Diabetes Technology, University of Virginia, Charlottesville, VA, U.S.A

Aaron Kowalski, Juvenile Diabetes Research Foundation, New York, New York, USA

Lori Laffel, Pediatric, Adolescent and Young Adult Section and Section on Clinical, Behavioral and Outcomes Research, Joslin Diabetes Center, Harvard Medical School, Boston, MA, U.S.A

Brian Levine, Close Concerns and diaTribe, San Francisco, California, USA

Aleksander Mayorov, I.M. Sechenov First Moscow State Medical University, Moscow, Russia

Chantal Mathieu, MD, Clinical and Experimental Endocrinology, KU Leuven, Leuven, Belgium

Helen R. Murphy, Norwich Medical School, University of East Anglia, Norwich, United Kingdom

Revital Nimri, The Jesse Z and Sara Lea Shafer Institute for Endocrinology and Diabetes, National Center for Childhood Diabetes, Schneider Children's Medical Center of Israel, Petah Tikva, and Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel

Kirsten Nørgaard, Steno Diabetes Center Copenhagen, Gentofte, Denmark

Christopher G. Parkin, CGParkin Communications, Inc., Boulder City, NV, USA

Eric Renard, Montpellier University Hospital, Department of Endocrinology, Diabetes, Nutrition, Montpellier, and Institute of Functional Genomics, University of Montpellier, Montpellier, and INSERM Clinical Investigation Centre, Montpellier, France.

David Rodbard, Biomedical Informatics Consultants LLC, Potomac, Maryland, USA

Banshi Saboo, DiaCare, Ahmedabad, Gujarat, India

Desmond Schatz, University of Florida, Pediatric Endocrinology, Gainesville, FL, USA

Keaton Stoner, dQ&A Market Research, Inc., San Francisco, California, USA

Tatsuiko Urakami, Department of Pediatrics, Nihon University School of Medicine, Tokyo, Japan

Stuart A. Weinzimer, Department of Pediatrics, Yale School of Medicine, New Haven, Connecticut, USA

Moshe Phillip, The Jesse Z and Sara Lea Shafer Institute for Endocrinology and Diabetes, National Center for Childhood Diabetes, Schneider Children's Medical Center of Israel, Petah Tikva, and Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel

CORRESPONDING AUTHOR

Tadej Battelino, Department of Pediatric Endocrinology, Diabetes and Metabolism, University Medical Centre-University Children's Hospital, and Faculty of Medicine, University of Ljubljana, Slovenia, (+386 1 522 9235), tadej.battelino@mf.uni-lj.si

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ABBREVIATIONS

A1C=glycated hemoglobin; AGP=ambulatory glucose profile; ATTD=Advanced Technologies & Treatments for Diabetes; AUC= area under the curve; CGM=continuous glucose monitoring; CI=confidence interval; DR=diabetic retinopathy; GMI=glucose management indicator; GV=glycemic variability; HBGI-high blood glucose index; HCL=hybrid closed-loop; iCGM= intermittently-scanned continuous glucose monitoring; MDI=multiple daily injections; NPDR=mild nonproliferative diabetic retinopathy; rtCGM=real-time continuous glucose monitoring; LBGI-low blood glucose index; SD=standard deviation; SGLT-2=sodium glucose cotransporter-2; TAR=time above range; TBR=time below range; TIR=time in range; VTDR=vision-threatening diabetic retinopathy

(ABSTRACT)

Improvements in sensor accuracy, greater convenience and ease of use and expanding reimbursement have led to growing adoption of continuous glucose monitoring (CGM). However, successful utilization of CGM technology in routine clinical practice remains relatively low. This may be due in part to the lack of clear and agreed upon glycemic targets that both diabetes teams and people with diabetes can work towards. Although unified recommendations for use of key CGM metrics have been established in three separate peer reviewed articles, formal adoption by diabetes professional organizations, and guidance in the practical application of these metrics in clinical practice has been lacking. In February 2019, 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 this issue. This article summarizes the ATTD consensus recommendations for relevant aspects of CGM data utilization and reporting among the various diabetes populations.

Adoption of continuous glucose monitoring (CGM), which includes both real-time CGM (rtCGM) and intermittently-scanned CGM (isCGM), has grown rapidly over the past few years due to improvements in sensor accuracy, greater convenience and ease of use and expanding reimbursement. Numerous studies have demonstrated significant clinical benefits of CGM use in people with diabetes regardless of insulin delivery method (1-15). In many countries, the benefits and utility of CGM are now recognized by national and international medical organizations for individuals with insulin-requiring diabetes and/or those at risk for hypoglycemia (16-21). However, despite increased CGM adoption (22; 23), successful utilization of CGM data in routine clinical practice remains relatively low. This may be due in part to the lack of clear and agreed upon glycemic targets toward which both diabetes teams and people with diabetes can work.

In 2012 the Helmsley Charitable Trust sponsored the first expert panel to recommend the standardization of CGM metrics and CGM report visualization (24). This was followed by a series of CGM consensus statements refining the core CGM metrics but the conclusions were never in alignment. In 2017, several articles supported use of systematic approaches to CGM data evaluation (18-20). To date, the key CGM metrics remain as unified recommendations in three separate peer reviewed articles, yet formal adoption by diabetes professional organizations and guidance in the practical application of these metrics in clinical practice has been lacking (19).

In February 2019, the Advanced Technologies and Treatments for Diabetes (ATTD) Congress convened an international panel of individuals with diabetes and clinicians and researchers expert in CGM. Our objective was to develop evidence-based, clinical CGM targets to supplement the currently agreed-upon metrics for CGM derived times in glucose ranges (within target range, below target range, above target range) in order to provide guidance for clinicians, researchers, and individuals with diabetes in utilizing, interpreting and reporting CGM data in routine clinical care and research. Importantly, in order to make the recommendations generalizable and comprehensive, the consensus panel included individuals living with diabetes and had international representation from physicians and researchers from all geographic regions.

The panel was divided into subgroups to review literature and provide evidence-based recommendations for relevant aspects of CGM data utilization and reporting among the various diabetes populations. Because long-term trials demonstrating how CGM metrics relate to and/or predict clinical outcomes have not been conducted, there is suggestive evidence from a number of recent studies, one a cross-sectional study correlating current retrospective 3-day TIR with varying degrees of diabetes retinopathy (25) and an analysis of the 7-point SMBG data from the DCCT (26) have shown correlations of time in target range (70-180 mg/dL [3.9-10.0 mmol/L]) with diabetes complication. Relationships between time in target range and A1C (25; 26) and number of severe and non-severe hypoglycemic events (27-31) have also been observed. Recommendations from each subgroup were then presented to the full panel and voted upon. This article summarizes the consensus recommendations and represents the panel members' evaluation of the issues.

Need for Metrics Beyond A1C

A1C is currently recognized as the key surrogate marker for the development of long-term diabetes complications in people with type 1 and type 2 diabetes and has been used the primary endpoint for many CGM studies (1; 3; 4; 6; 32; 33). While A1C reflects the average glucose over the last 2-3 months, its limitation is the lack of information about acute glycemic excursions and the acute complications of hypo- and hyperglycemia. A1C also fails to identify the magnitude and frequency of intra- and inter-day glucose variation (34; 35). Moreover, certain conditions such as anemia (36), hemoglobinopathies (37), iron deficiency (38), and pregnancy (39) can confound A1C measurements. Importantly, as reported by Beck and colleagues, the A1C test can at times fail to accurately reflect mean glucose even when none of these conditions are present (40). Despite these limitations, A1C is the only prospectively evaluated tool for assessing the risk for diabetes complications and its importance in clinical decision-making should not be undervalued. Rather, the utility of A1C is further enhanced when used in combination with CGM data.

Unlike A1C measurement, use of CGM allows for the direct observation of glycemic excursions and daily profiles, which can inform on immediate therapy decisions and/or lifestyle modifications. CGM also provides the ability to assess glucose variability (GV) and identify patterns of hypo- and hyperglycemia.

Effective use of CGM data to optimize clinical outcomes requires the user to interpret the collected data and act upon them appropriately. This requires: 1) common metrics for assessment of CGM glycemic status; 2) graphical visualization of the glucose data and CGM daily profile; and 3) clear evidence-based clinical targets.

Standardization of CGM Metrics

In February 2017, the Advanced Technologies and Treatments for Diabetes (ATTD) Congress convened an international panel of expert clinicians and researchers to define core metrics for assessing CGM data (18). (**Table 1**)

Table 1. Standardized CGM Metrics

2017 International Consensus on CGM Metrics (18)
1. Number of Days CGM Worn
2. Percentage of time CGM is active
3. Mean Glucose
4. Estimated A1c (eA1C)
5. Glycemic Variability (%CV or SD)
6. Time >250 mg/dL (>13.9 mmol/L)
7. Time >180 mg/dL (>10.0 mmol/L)
8. Time 70-180 mg/dL (3.9-10.0 mmol/L)
9. Time <70 mg/dL (<3.9 mmol/L)
10. Time <54 mg/dL (<3.0 mmol/L)
11. LBGI & HBGI (risk indices)
12. Episodes (hypoglycemia and hyperglycemia) 15 min
13. Area under the curve (AUC)
14. Time Blocks (24-h, day, night)
Use of Ambulatory Glucose Profile (AGP) for CGM report

CV=Coefficient of variation; SD=standard deviation; LBGI=low blood glucose index; HBGI=high blood glucose index.

The list of core CGM metrics has now been streamlined for use in clinical practice based on the expert opinion of this International Consensus Group (18). Of the 14 core metrics, the panel selected that 10 metrics that may be most useful in clinical practice (**Table 2**).

Table 2. Standardized CGM Metrics for Clinical Care

2019 Core CGM Metrics for Clinical Care (18)	
1. Number of Days CGM Worn (recommend 14 days) (41; 42)	
2. Percentage of time CGM is active (recommend 70% of data from 14 days) (41; 42).	
3. Mean Glucose	
4. Glucose Management Indicator (GMI) (43)	
5. Glycemic Variability (%CV) Target ≤36% (44)*	
6. Time Above Range (TAR) - % of readings and time >250 mg/dL (>13.9 mmol/L)	Level 2
7. Time Above Range (TAR) - % of readings and time 181-250 mg/dL (10.1-13.9 mmol/L)	Level 1
8. Time In Range (TIR) - % of readings and time 70-180 mg/dL (3.9-10.0 mmol/L)	In Range
9. Time Below Range (TBR) - % of readings and time 54-69 mg/dL (3.0-3.8 mmol/L)	Level 1
10. Time Below Range (TBR) - % of readings and time <54 mg/dL (<3.0 mmol/L)	Level 2
Use of Ambulatory Glucose Profile (AGP) for CGM report	

CV=Coefficient of variation; SD=standard deviation; LBGI=low blood glucose index; HBGI=high blood glucose index.
* Some studies suggest that lower %CV targets (<33%) provide additional protection against hypoglycemia for those receiving insulin or sulfonylureas: <33% (44-46)

Fundamental to accurate and meaningful interpretation of CGM is ensuring that adequate glucose data are available for evaluation. As shown in studies, >70% use of CGM over the recent 14 days correlates strongly with 3 months of mean glucose, time in ranges, and hyperglycemia metrics (41; 42). In individuals with type 1 diabetes, correlations are weaker for hypoglycemia and glycemic variability; however, these correlations have not been shown to increase with longer sampling periods (42). Longer CGM data collection periods may be required for individuals with more variable glycemic control (e.g., 4 weeks of data to investigate hypoglycemia exposure).

Time in Ranges

The development of blood glucose testing in 1965 provided individuals with diabetes the ability to obtain immediate information about their current glucose levels and adjust their therapy accordingly. Over the past decades, national and international medical organization have been successful in developing, harmonizing, and disseminating standardized glycemic targets based on risk for acute and chronic complications. CGM technology greatly expands the ability to assess glycemic control throughout the day, presenting critical data to inform daily treatment decisions and quantifying time below, within, and above the established glycemic targets.

Although each of the core metrics established in the 2017 ATTD consensus conference (18) provides important information about various aspects of glycemic status, it is often impractical to assess and fully utilize many of these metrics in real-world clinical practices. To streamline data interpretation, the consensus panel identified "time in ranges" as a composite metric of glycemic control that provides more actionable information than A1C alone. The panel agreed that establishing target percentages of time in the various glycemic ranges with the ability to adjust the percentage cutpoints to address the specific needs of special diabetes populations (e.g., pregnancy, high-risk) would facilitate safe and effective therapeutic decision-making within the parameters of the established glycemic goals.

The composite metric includes three key CGM measurements: percentage of reading and time per day within target glucose range (TIR), time below target glucose range (TBR), and time above target glucose range (TAR) (**Table 3**). The primary goal for effective and safe glucose control is to increase the TIR while reducing the TBR. The consensus group agreed that expressing time in the various ranges can be done as the percentage (%) of CGM, average hours and minutes spent in each range or both, depending on the circumstances.

It was agreed that CGM based glycemic targets must be personalized to meet the needs of each individual with diabetes. In addition, the group reached consensus on glycemic cutpoints (a target range of 70-180 mg/dL [3.9-10.0 mmol/L] for individuals with type 1 diabetes and type 2 diabetes and 63-140 mg/dL [3.5-7.8 mmol/L] during pregnancy, along with a set of targets for the time per day [% of CGM readings or minutes/hrs]) individuals with type 1 diabetes and type 2 diabetes (**Table 3)** and women during pregnancy (**Table 4**) should strive to achieve. It should be noted that premeal and postprandial targets remain for diabetes in pregnancy (ADA Standards

of medical care-2019. Diabetes Care 2019: 42 (Suppl 1)) in addition to the new TIR targets for overall glycemia.

Table 3. Recommended cutpoints for assessment of glycemic control: Type 1 / Type 2 and Older / High-Risk Individuals

Diabetes Group	Time in Range (TIR)		Time Below Range (TBR)		Time Above Range (TAR)	
	% of readings time/day	Target Range	% of readings time /day	Below Target Level	% of readings time/ day	Above Target Level
Type 1* / Type 2	**>70%** **>16hr, 48 min**	70-180 mg/dL 3.9 -10.0 mmol/L	**<4%** **<1 hr**	<70 mg/dL <3.9 mmol/L	**<25%** **<6 hr**	>180 mg/dL >10.0 mmol/L
			<1% **<15 min**	<54 mg/dL <3.0 mmol/L	**<5%** **<1 hr, 12 min**	>250 mg/dL >13.9 mmol/L
Older/High-Risk Type 1 / Type 2	**>50%** **>12 hr**	70-180 mg/dL 3.9-10 mmol/L	**<1%** **<15 min**	<70 mg/dL <3.9 mmol/L	**<10%** **<2 hr, 24 min**	>250 mg/dL >13.9 mmol/L
Each incremental 5% increase in TIR is associated with clinically significant benefits for Type 1 / Type 2 (25; 26)						

* For age <25 yr., if the A1C goal is 7.5% then set TIR target to approximately 60%. (See "Clinical Applications of Times in Range" in the text for additional information regarding target goal setting in pediatric management)

Table 4. Consensus guidance on cutpoints for assessment of glycemic control: Pregnancy

Diabetes Group	Time in Range (TIR)		Time Below Range (TBR)		Time Above Range (TAR)	
	% of readings time/day	Target Range	% of readings time /day	Below Target Level	% of readings time/ day	Above Target Level
Pregnancy Type 1 §	**>70%** **>16 hr, 48 min**	63-140 mg/dL† 3.5-7.8 mmol/L†	**<4%** **<1 hr**	<63 mg/dL† <3.5 mmol/L†	**<25%** **<6 hr**	>140 mg/dL >7.8 mmol/L
			<1% **<15 min**	<54 mg/dL <3.0 mmol/L		
Pregnancy § Type 2 / GDM	see *Pregnancy* section	63-140 mg/dL† 3.5-7.8 mmol/L†	see *Pregnancy* section	<63 mg/dL† <3.5 mmol/L†	see *Pregnancy* section	>140 mg/dL >7.8 mmol/L
				<54 mg/dL <3.0 mmol/L		
Each incremental 5% increase in TIR is associated with clinically significant benefits for Pregnancy Type 1 (47; 48)						

† Glucose levels are physiologically lower during pregnancy

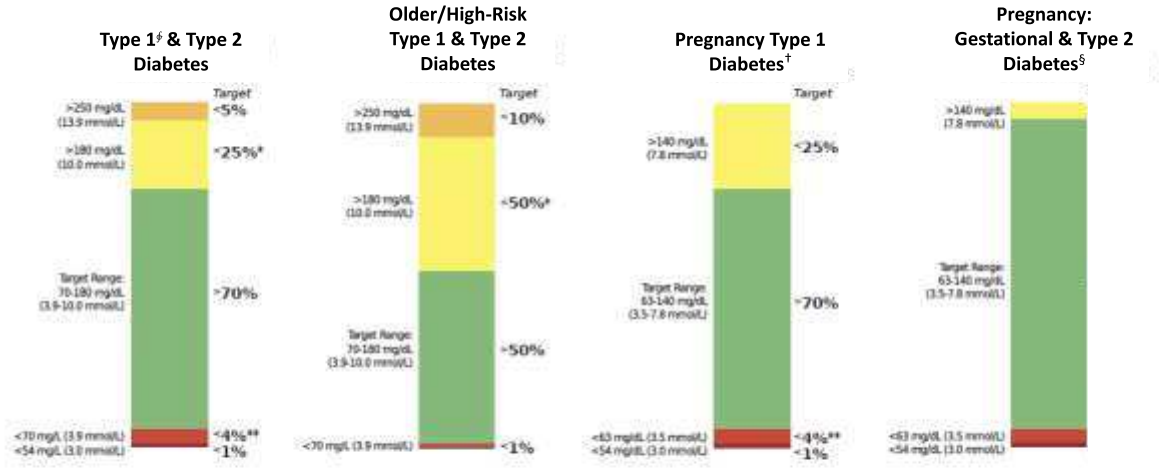
§ Percentages of time in range are based on limited evidence. More research is needed.

Although the composite metric includes TIR, TBR and TAR, achieving the TBR and TIR goals would result in reduced time spent above range and thereby improve glycemic control. However, some clinicians may choose to target the reduction of the high glucose values and minimize hypoglycemia, thereby arriving at more time in the target range. In both approaches, the first priority is to reduce TBR to target levels and then address TIR or TAR targets.

Note that for people with type 1 diabetes, the targets are informed by the ability to reach the targets with hybrid closed-loop therapy (11), the first example of which is now commercially available, with several more systems in final stages of testing. Importantly, recent studies have shown the potential of reaching these targets with CGM in individuals using multiple daily injections (MDI) (6). In type 2 diabetes, there is generally less glycemic variability and hypoglycemia than in type 1 diabetes (46). Thus, people with type 2 diabetes can often achieve more time in target range while minimizing hypoglycemia (4). As demonstrated by Beck et al., individuals with type 2 diabetes increased their TIR by 10.3% (from 55.6% to 61.3%) after 24 weeks of CGM use with slight reductions in TBR (4). Most recently, the beneficial effects of new medications, such as sodium glucose cotransporter-2 (SGLT-2) agents have helped individuals with type 1 diabetes increase TIR (49-51). Targets for type 1 diabetes and type 2 diabetes were close enough to combine them into one set of targets, outside of pregnancy.

Another way to visualize the CGM-derived targets for the four categories of diabetes is shown in **Figure 1** which displays and compares the targets for time in range (TIR - green), time below range (TBR - 2 categories in light and dark red) and time above range (TAR -2 categories in yellow and orange). It becomes clear at a glance that there are different expectations for the various time in ranges relating to safety concerns and efficacy based on currently available therapies and medical practice.

Figure 1. International consensus on time in range: CGM-based targets for different types of diabetes



ϕ For age <25 yr., if the A1C goal is 7.5% then set TIR target to approximately 60%. (See *Clinical Applications of Time in Ranges* section in the text for additional information regarding target goal setting in pediatric management).
† Percentages of time in ranges are based on limited evidence. More research is needed.
§ Percentages of time in range have not been included because there is very limited evidence in this area. More research is needed. Please see *Pregnancy* section in text for more considerations on targets for these groups.
* Includes percentage of values >250 mg/dL (>13.9 mmol/L).
** Includes percentage of values <54 mg/dL (<3.0 mmol/L).

Clinical Validity of Measures

To fundamentally change clinical care with use of the new metrics, it would be important to demonstrate that the metrics relate to and predict clinical outcomes. In this regard, longer-term studies relating to time spent within specific CGM glycemic ranges, diabetes complications, and other outcomes are required. However, there is evidence from a number of recent studies that have shown correlations of TIR (70-180 mg/dL [3.9-10.0 mmol/L]) with diabetes complications (52; 53) as well as a relationship between TIR and A1C (25; 26). Although there is no evidence regarding time in range for older and/or high-risk individuals, numerous studies have shown the elevated risk for hypoglycemia in these populations (54-59). We have lowered the TIR target from >70% to >50% and reduced TBR to <1/% at <70 mg/dL (<3.9 mmol/L) to place greater emphasis on reducing hypoglycemia with less emphasis on maintaining target glucose levels (**Table 3**).

Type 1 Diabetes and Type 2 Diabetes

Association with Complications

Associations between TIR and progression of both diabetic retinopathy (DR) and development of microalbuminuria were reported by Beck and colleagues, using the Diabetes Control and Complications Trial (DCCT) data set (7-point blood glucose profiles) to validate the use of TIR as an outcome measure for clinical trials (53). Their analysis showed that the hazard rate for retinopathy progression increased by 64% for each 10% reduction in TIR. The hazard rate for microalbuminuria development increased by 40% for 10% reduction in TIR. A post-hoc analysis of the same DCCT data set showed a link between glucose of <70 mg/dL (<3.9 mmol/L) and <54 mg/dL (<3.0 mmol/L) and an increased risk for severe hypoglycemia (60).

Similar associations between DR and TIR were reported in a recent study by Lu and colleague in which 3,262 individuals with type 2 diabetes were evaluated for DR, which was graded as: non-DR; mild nonproliferative DR (NPDR); moderate NPDR; or vision-threatening DR (VTDR) (52). Results showed that individuals with more advanced DR spent significantly less time within target (70-180 mg/dL [3.9-10.0 mmol/L) and that prevalence of DR decreased with increasing TIR.

Relationship Between TIR and A1C

Analyses were conducted utilizing datasets from four randomized trials encompassing 545 adults with type 1 diabetes who had central-laboratory measurements of A1C (25). TIR (70-180 mg/dL [3.9-10.0 mmol/L]) of 70% and 50% strongly corresponded with an A1C of approximately 7% (53 mmol/mol) and 8% (64 mmol/mol), respectively. An increase in TIR of 10% (2.4 hours per day) corresponded to a decrease in A1C of approximately 0.5% (5.0 mmol/mol); similar associations were seen in an analysis of 18 RCTs by Vigersky et al. that included over 2,500 individuals with type 1 diabetes and type 2 diabetes over a wide range of ages and A1C levels (26). (**Table 4**)

Table 4. Estimate of A1C for a given TIR level based on type 1 diabetes and type 2 diabetes studies

Beck et al. (n=545 type 1 diabetes participants) (25)			**Vigersky et al.** (n=1,137 type 1/type 2 participants) (26)	
TIR 70-180 mg/dL (3.9-10.0 mmol/L)	**A1C % (mmol/mol)**	**95% CI for predicted values**	**TIR 70-180 mg/dL (3.9-10.0 mmol/L)**	**A1C % (mmol/mol)**
20%	9.4 (79)	(8.0, 10.7)	20%	10.6 (92)
30%	8.9 (74)	(7.6, 10.2)	30%	9.8 (84)
40%	8.4 (68)	(7.1, 9.7)	40%	9.0 (75)
50%	7.9 (63)	(6.6, 9.2)	50%	8.3 (67)
60%	7.4 (57)	(6.1, 8.8)	60%	7.5 (59)
70%	7.0 (53)	(5.6, 8.3)	70%	6.7 (50)
80%	6.5 (48)	(5.2, 7.8)	80%	5.9 (42)
90%	6.0 (42)	(4.7, 7.3)	90%	5.1 (32)
Every 10% increase in TIR = ~0.5% (5.5 mmol/mol) A1C reduction			***Every 10% increase in TIR = ~0.8% (8.7 mmol/mol) A1C reduction***	

*The difference between findings from the two studies likely stems from differences in number of studies analyzed and subjects included (RCTs with type 1 vs. RCTs with type 1/type 2 with CGM and SMBG).

Pregnancy

During pregnancy, the ambition is to safely increase TIR as quickly as possible, while reducing TAR and glycemic variability. The first longitudinal CGM data demonstrated a 13-percentage point increase in TIR (43% to 56% TIR 70-140 mg/dL [3.9-7.8 mmol/L]) (61). The TBR < 50 mg/dL reduced from 6% to 4%, although the higher TBR <70 mg/dL was high (13-15%) using older generation sensors. With improved sensor accuracy, recent type 1 diabetes pregnancy studies report a lower threshold of <63 mg/dL (<3.5 mmol/L) for TBR and ≥63 mg/dL (≥3.5 mmol/L) for TIR (47; 48). Data from Sweden, and the CONCEPTT control group, report 50% TIR in the first trimester, improving to 60% TIR in the third trimester, reflecting contemporary antenatal care. Of note, these data confirm that the TBR <63 mg/dL (<3.5 mmol/L) recommendation of <4% is safely achievable, especially after the first trimester. Furthermore, 33% of women achieved the recommendation of 70% TIR 63-140 mg/dL (3.5-7.8 mmol/L) in the final (>34) weeks of pregnancy. Preliminary data suggest that closed-loop may allow pregnant women to safely achieve 70% TIR, at an earlier (>24 weeks) gestation (62; 63).

Law et al analyzed data from two early CGM trials (64; 65) describing the associations between CGM measures and risk of large for gestational age (LGA) infants. Taken together, the Swedish and CONCEPTT data confirm that a 5-7% higher TIR during the second and third trimesters is associated with decreased risk of LGA and neonatal outcomes, including macrosomia, shoulder dystocia, neonatal hypoglycemia and NICU admissions. More data are needed to define the clinical CGM targets for pregnant women with type 2 diabetes, who spend one third less time hyperglycemic than women with type 1 diabetes, and achieve TIR of 90% (61). Because of the lack of evidence on CGM targets for women with GDM or type 2 diabetes in pregnancy, percentages of time spent in range, below range, and above range have not been included in this report. Recent data suggest that even more stringent targets (66) and greater attention to overnight glucose profiles may be required to normalize outcomes in pregnant women with gestational diabetes (67).

Older and/or High-Risk Individuals with Diabetes

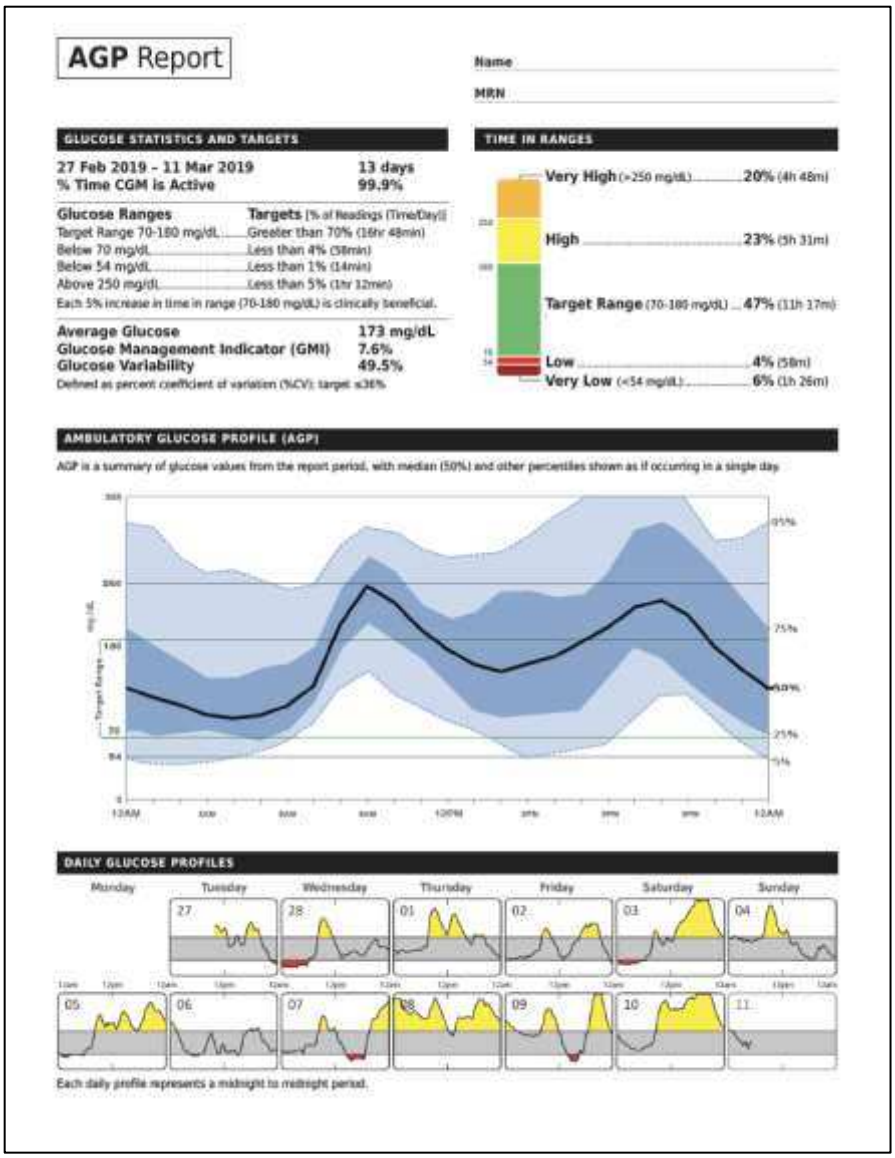
Older and/or high-risk individuals with diabetes are at notably higher risk for severe hypoglycemia due to age, duration of diabetes, duration of insulin therapy, and greater prevalence of hypoglycemia unawareness (54-58). The increased risk of severe hypoglycemia is compounded by cognitive and physical impairments and other co-morbidities (56; 59). High-risk individuals include those with a higher risk of complications, comorbid conditions (e.g., cognitive deficits, renal disease, joint disease, osteoporosis, fracture, and/or cardiovascular disease), and often require assisted care, which can complicate treatment regimens (59). Therefore, when setting glycemic for high-risk and/or elderly people, it is important to individualize and be conservative, with a strong focus on reducing the percentage of time spent <70 mg/dL (<3.9 mmol/L) and preventing excessive hyperglycemia.

Standardization of CGM Data Presentation

As noted above, in 2013, a panel of clinicians with expertise in CGM published recommendations for use of the Ambulatory Glucose Profile (AGP) as a template for data presentation and visualization. Originally created by Mazze et. al. (68), the standardized AGP report was further developed by the International Diabetes Center and now incorporates all the core CGM metrics and targets along with a 14-day composite glucose profile as an integral

component of clinical decision making (24). This recommendation was later endorsed at the aforementioned international consensus conference on CGM metrics (18) and is referenced as an example in the American Diabetes Association (ADA) 2019 Standards of Care (16) and in an update to the American Association of Clinical Endocrinologists (AACE) consensus on use of CGM (69). The AGP report, in slightly modified formats, has been adopted by most of the CGM device manufacturers in their download software. An example of the AGP report, updated to incorporate targets, is presented in **Figure 2**. In the AGP report, glucose ranges are defined as "Very High" (Level 2), "High" (Level 1), "Low" (Level 1) and "Very Low" (Level 2). A "mmol/L" version is provided in **Supplemental Figure 1**.

Figure 2. Ambulatory Glucose Profile



There is a general consensus that a useful CGM report is one that can be understood by clinician and people with diabetes. While there may be some terms (e.g., glucose variability) that are less familiar for many people with diabetes to understand, the value of a single-page report that the medical team can review and file in the electronic medical record and can be used as a shared decision-making tool with people with diabetes was considered to be of value (70-73). More detailed reports (e.g., adjustable data ranges, detailed daily reports) should remain available for individualized review by or with people with diabetes.

Clinical Application of Time in Ranges

Despite its demonstrated value, clinical utilization of CGM data has remained suboptimal. Although time constraints and reimbursement issues are clearly obstacles, clinician inexperience in data interpretation and lack of standardization software for visualization of CGM data have also played a role (74). The proposed standardized report enables clinicians to readily identify important metrics such as the percentage of time spent within, below and above each individual's target range, allowing for greater personalization of therapy through shared decision making.

Using the standardized report the clinician can also address glucose variability (e.g., %CV metric) (75) or use glucose management indicator (GMI) metric (43) to discuss the possible discrepancies noted in glucose exposure derived from CGM data versus the individual's laboratory-measured A1C (40; 76). With appropriate educational materials, time and experience, clinicians will develop a systematic approach to CGM data analysis and the most effective ways to discuss the data with patients in person or remotely.

Goal Setting

Numerous studies have demonstrated the clinical benefits of early achievement of near-normal glycemic control in individuals with type 1 diabetes and type 2 diabetes (77-83). However, when advising people with diabetes, goal-setting must be collaborative and take into account the individual needs/capabilities of each patient and start with the goals that are most achievable. An early study by DeWalt and colleagues found that setting small, achievable goals not only enhances people's ability to cope with their diabetes, but that people with diabetes who set and achieved their goals often initiated additional behavioral changes on their own (84). One approach to consider is the S.M.A.R.T. Goal (Specific, Measurable, Achievable, Relevant, Time bound) intervention, which is directly applicable to setting targets for times in ranges. First described by Lawlor and Hornyak in 2012 (85), this approach incorporates four key components of behavioral change relevant to goal setting: 1) the goal is specific and defines exactly what is to be achieved; 2) the goal is measurable and there is tangible evidence when it has been achieved; 3) the goal is achievable but stretches the patient slightly so that he/she feels challenged; and 4) the goal should be attainable over a short period of time.

Effective goals should utilize CGM data to identify specific instances for the patient to take measurable action to prevent hypoglycemia. Although analysis of the AGP reports provides

an opportunity for meaningful discussion, individuals should be counseled to look at patterns throughout the day to see when low glucose events are occurring and make adjustments in their therapy to reduce these events.

When applying the CGM metrics in clinical practice, it may be more meaningful and motivating to communicate to people with diabetes the importance of working to reduce the time spent <70 mg/dL (<3.9 mmol/L) to less than one hour per day and less than 15 minutes per day <54 mg/dL (<3.0 mmol/L) rather than using <4% and <1% respectively, as the goal. However, as discussed earlier, targets must be personalized to meet the needs and capabilities of each person, focusing on small steps and small successes. Individuals with diabetes should work with their physician and/or educator to develop a SMART goal to reduce time below range.

Individualized goals are particularly important for pediatric and young adult populations. The International Society for Pediatric Diabetes (ISPAD) recommends that targets for individuals ≤25 years aim for the lowest achievable A1C without undue exposure to severe hypoglycemia balances with quality of life and burden of care (86). An A1C target of 7.0% (53 mmol/mol) can be used in children, adolescents and adults ≤25 years who have access to comprehensive care (86). However, a higher A1C goal (e.g., <7.5% [<58 mmol/mol] may be more appropriate in the following situations: inability to articulate hypoglycemia symptoms; hypoglycemia; hypoglycemia unawareness; history of severe hypoglycemia, lack of access to analog insulins and/or advanced insulin delivery technology, inability to regularly check glucose (86). This would equate to a TIR target of ~60% (**Table 4**).

The consensus group recognized that achieving the targets for the various time in ranges is aspirational in some situations and many individuals will require ongoing support, both educational and technological, from their healthcare team. Importantly, as demonstrated by Beck et al. (25), Vigersky et al. (26) and Feig et al. (47), even small, incremental improvements yield significant glycemic benefits. Therefore, when advising individuals with diabetes (particularly children, adolescents, high-risk) about their glycemic goals, it important to take a step-wise approach, emphasizing that what may appear to be small, incremental successes (e.g. 5% increase in TIR) are, in fact, clinically significant in improving their glycemic control (25; 26; 47). However, when counseling women planning pregnancy and pregnant women, greater emphasis should be placed on getting to goal as soon as possible (47; 48).

Conclusions

Use of CGM continues to expand in clinical practice. As a component of diabetes self-management, daily use of CGM provides the ability to obtain immediate feedback on current glucose levels, direction and rate of change in glucose levels. This information allows people with diabetes to optimize dietary intake and exercise, make informed therapy decisions regarding meal-time and correction of insulin dosing and, importantly, react immediately and appropriately to mitigate or prevent acute glycemic events (87-89). Retrospective analysis of CGM data, utilizing standardized data management tools such as the AGP, enables clinicians and people with diabetes to work collaboratively in identifying problem areas and then set achievable goals (71-73). We conclude that, in clinical practice, time in ranges (within target range, below range, above range) are both appropriate and useful as clinical targets and outcome measurements that complement A1C for a wide range of people with diabetes, and that the target values specified in this paper should be considered an integral component of CGM data analysis and day-to-day treatment decision making.

Author Contributions

T.B., R.M.B., W.C., T.D., S.G., L.H. I.M..B., C.M., H.M., S.A., R.N., K.D., C.G.P. and M.P. wrote and revised the initial manuscript drafts. All authors reviewed, provided input, and approved the final manuscript. T.B. is the guarantor of this work and takes full responsibility for the integrity of the information included in the report.

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Stephanie A. Amiel - S.A.A. declared no conflicts of interest.

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Bruce Buckingham - B.B. declared no conflicts of interest.

William Cefalu - W.C. declared no conflicts of interest.

Kelly L. Close - K.L.C. is an employee of Close Concerns and diaTribe, which receive funding CGM manufacturers, including Medtronic, Dexcom and Abbott Diabetes Care.

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Brian Levine - B.L. is an employee of Close Concerns and diaTribe, which receive funding CGM manufacturers, including Medtronic, Dexcom and Abbott Diabetes Care.

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