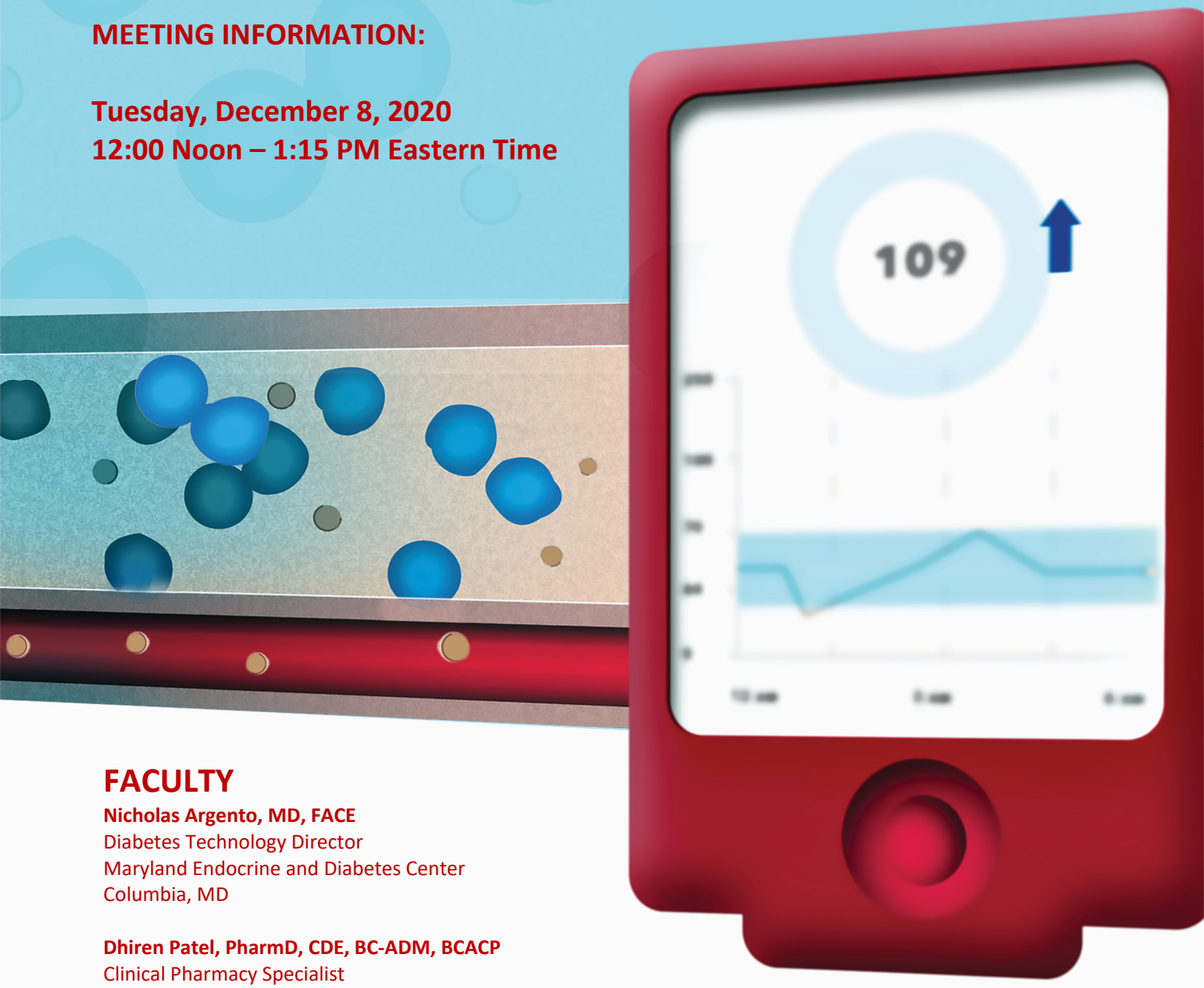
Harnessing Technology to Improve
Glycemic Control:
THE ROLE OF CONTINUOUS GLUCOSE MONITORING

MEETING INFORMATION:

Tuesday, December 8, 2020
12:00 Noon – 1:15 PM Eastern Time



FACULTY

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This activity is provided by Med Learning Group.
This activity is co-provided by Ultimate Medical Academy/Complete Conference Management (CCM).
This activity is supported by an independent educational grant from DEXCOM, INC.

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The Role of Continuous Glucose Monitoring

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LEARNING OBJECTIVES

- Analyze clinical trial data that provide the rationale for CGM
- Compare the benefits and limitations of self-monitoring blood glucose vs. continuous CGM
- Select between real-time CGM and intermittently scanned CGM based on product features and patient characteristics
- Determine optimal approaches to the interpretation and clinical use of CGM data

TARGET AUDIENCE

This educational activity is intended for endocrinologists, primary care physicians, hospitalists, physician assistants, nurse practitioners, pharmacists, certified diabetes educators, managed care healthcare providers, and other healthcare providers who care for patients with diabetes.

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Credits: 1.25 ANCC Contact Hour(s)

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Dr. Patel discloses that he has received consulting fees from Amarin, Astra Zeneca, Bayer, Boehringer Ingelheim, Dexcom, Eli Lilly, Insulet, Merck, Novo Nordisk, and Sanofi. Dr. Patel is on the speakers' bureaus for Amarin, Astra Zeneca, Boehringer Ingelheim, Dexcom, Eli Lilly, Merck, Novo Nordisk, Valeritas, Xeris and Zealand.

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CNE Content Review

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1. Read the CME/CNE information and faculty disclosures.
2. Participate in the virtual- live activity.
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This activity is supported by an educational grant from DEXCOM, INC

AGENDA

I. Diabetes overview

II. Assessment of glycemic control

   a. Whiteboard animation #1: CGM Devices

III. Interpreting CGM data
   a. Whiteboard animation #2: CGM Metrics

IV. Conclusion

V. Questions and answers

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1

Dr. Argento Disclosures

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Learning Objectives

- Analyze clinical trial data that provide the rationale for continuous glucose monitoring (CGM)
- Compare the benefits and limitations of self-monitoring blood glucose vs. CGM
- Select between real-time CGM and intermittently-scanned CGM based on product features and patient characteristics
- Determine optimal approaches to the interpretation and clinical use of CGM data

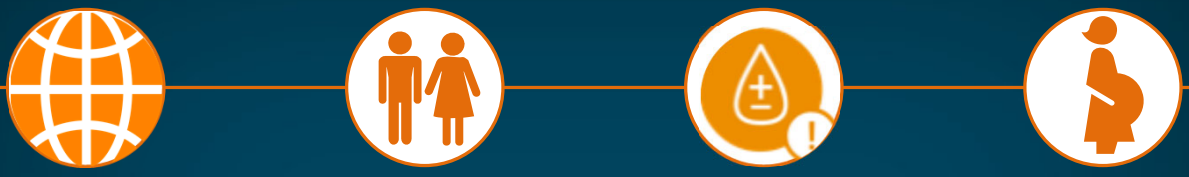
3

Diabetes Overview

Prevalence, Cost, Goals, and Progression

4

Diabetes in US and Among US Veterans



10.5%

of the US population has diabetes at a cost of $327 billion (2017); 72% was for direct medical costs (e.g. hospitalization, medications to treat complications)[1]

25%

of veterans have diabetes, and **diabetes is leading cause of blindness, ESRD, and amputations in veterans**[2]

7.5%

of veterans had documented hypoglycemia in past 2 years[3]

↑ HR 1.4

Posttraumatic stress disorder in pregnant female veterans is associated with increased likelihood of gestational diabetes[2]

ESRD = end-stage renal disease; HR = hazard ratio.

1. American Diabetes Association (ADA). Diabetes statistics (www.diabetes.org/resources/statistics/statistics-about-diabetes).
2. VA diabetes fact sheet. (www.research.va.gov/pubs/docs/va_factsheets/ diabetes.pdf). 3. VA Choosing Wisely Health Hypoglycemia Safety Initiative (www.qualityandsafety.va.gov/choosingwiselyhealthsafetyinitiative/hypoglycemiasite/for_clinicians.asp). Assessed 11/8/20.

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ADA Recommended HbA1c Goals

- An HbA1C goal for many nonpregnant adults of <7% is appropriate
- On the basis of provider judgment and patient preference, achievement of lower HbA1C levels (such as <6.5%) may be acceptable **if this can be achieved safely without significant hypoglycemia** or other adverse effect of treatment
- Less stringent HbA1C goals (such as <8%) may be appropriate for patients **with a history of severe hypoglycemia**, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, or long-standing diabetes

HbA1c = glycosylated hemoglobin.

ADA. *Diabetes Care.* 2020;43(suppl 1):S66-S76.

6

Hypoglycemia in Veterans: Learnings from Veterans Affairs Diabetes Trial and Other Trials

Intensive insulin treatment is associated with a **5-fold** higher risk of hypoglycemia and a **~3-fold** higher risk of severe hypoglycemia[1, 2]

Hypoglycemia or non-severe hypoglycemia[3]
<70 mg/dL;
45% nocturnal

Severe hypoglycemia[3] (requiring assistance)
<55 mg/dL; **55% nocturnal**
Seizure, coma, and death

Hypoglycemia unawareness[4]
63% in T1DM
49–64% in T2DM

Fear of hypoglycemia[5]
may impair ability to get glucose to goal

Severe hypoglycemia in past 3 months associated with increased mortality[6]
CV events, and CV mortality.

T2DM = type 2 diabetes mellitus; T1DM = type 1 diabetes mellitus; CV = cardiovascular.

1. Duckworth W, et al. *N Engl J Med* 2009; 360:129-139. 2. Diabetes Control and Complications (DCCT) research group. Trial. *Diabetes*. 1997;46:271-286. 3. DCCT research group. *Am J Med*. 1991;90:450-459. 4. Ostenson CG, et al. *Diabetes Med*. 2014;31:92-101. 5. Brod M, et al. *Qual Life Res*. 2009; 18; 23-32. 6. Davis SN, et al. *Diabetes Care*. 2019;42:157-163.

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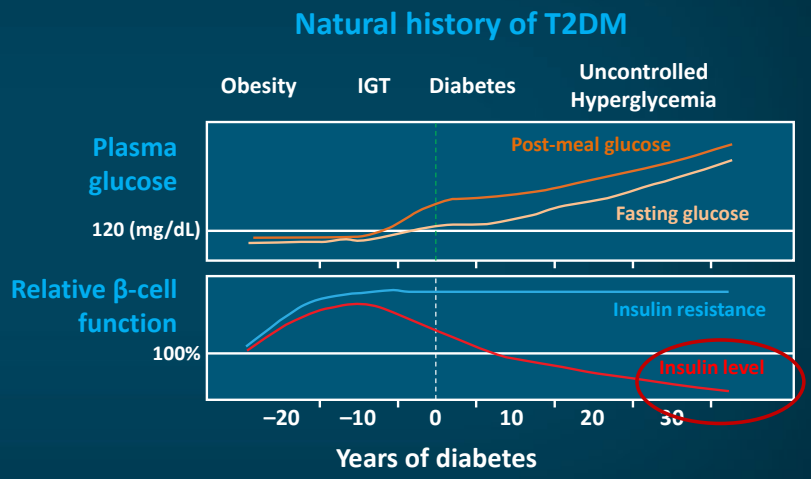
For Many, Insulin Is Inevitable

Progressive Loss of Beta Cells in T2DM and Late Onset of T1DM

- T1DM is not a kid's disease; more than 30% of patients with T1DM present after age 30
- Many type 2 patients eventually require basal + meal insulin due to loss of beta-cell capacity over time



IGT = impaired glucose tolerance.
Adapted from Simonson G, et al. *Diabetes Manage*. 2011;1:175-189.

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Assessing Glycemia in Diabetes: HbA1c

9

Glycemic Control Cannot Be Assessed and Challenges Addressed by HbA1c Used in Isolation

HbA1C, %	mg/dL	95% CI
5	97	(76–120)
6	126	(100–152)
7	154	(123–185)
8	183	(147–217)
9	212	(170–249)
10	240	(193–282)
11	269	(217–314)
12	298	(240–347)

1. May underestimate or overestimate an individual's average glucose ***(example: HbA1C of 7% could represent a range between 123–185 mg/dL)***
2. Does not indicate extent or timing of either hypoglycemia or hyperglycemia
3. Does not reveal glycemic variability
4. Limited utility for insulin-dosing decisions
5. Unreliable in patients with hemolytic anemia, some hemoglobinopathies, or iron deficiency
6. Underestimates glycemia in patients with ESKD or during pregnancy
7. Correlation with mean glucose can vary among races

ESKD = end-stage kidney disease.

Nathan DM, et al. *Diabetes Care*. 2008;31:1473-1478.

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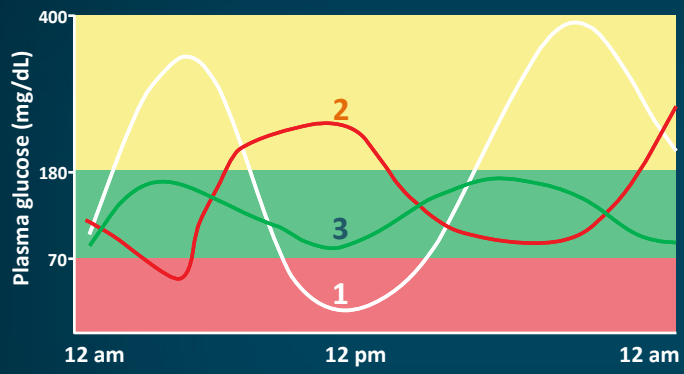
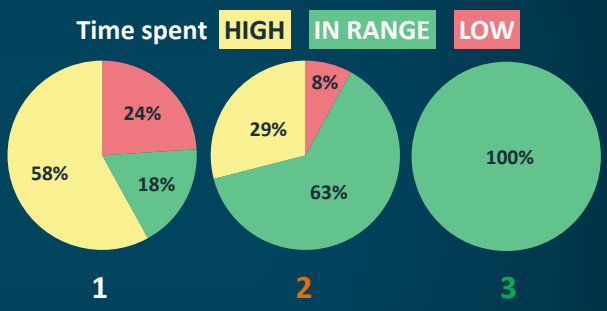
Same HbA1C, but CGM Reveals Vastly Different Glycemic Patterns



The many faces of a 7% HbA1c



Using HbA1c alone as a measure of diabetes outcomes, current regulatory standards would treat therapies the same if they resulted in the different profiles above, even though each pattern has a far different benefit-risk profile.

CGM = continuous glucose monitoring.

Brown A, et al. *diaTribe*. 2016 (https://diatribe.org/BeyondA1c). Accessed 11/8/2020.

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Assessing Glycemia in Diabetes: Blood Glucose Monitoring (BGM)

12

Accuracy Requirements per FDA for New Home Blood Glucose Meters

- 95% of BGM BG values must be within 15% of the reference value
  - 99% of BGM BG values must be within 20% of the reference value
- **Note: meters previously approved are not required to, and most do not, meet these standards…**

FDA = US Food and Drug Administration; BG = blood glucose.

Klonoff DC, et al. *Diabetes Care.* 2018;41:1681-1688.

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Assessing Glycemia in Diabetes Continuous Glucose Monitoring (CGM)

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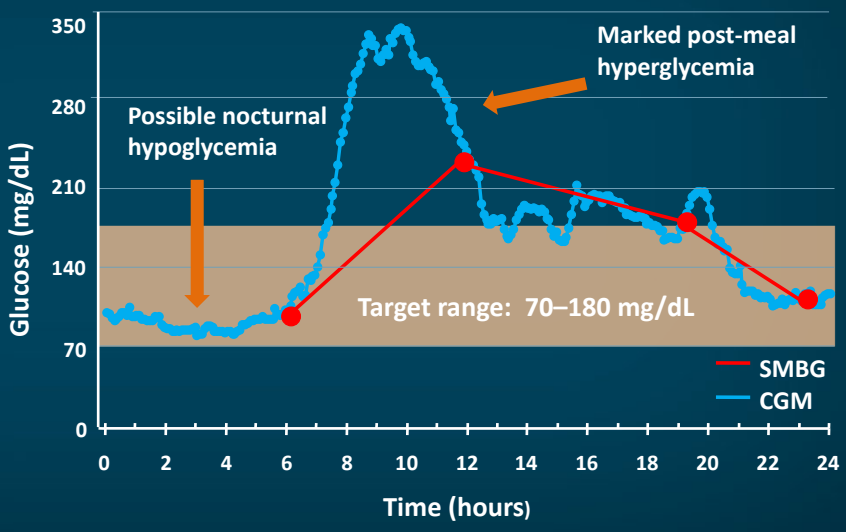
BGM Tells You Where You Are Now While CGM Tells You Where You Have Been, Where You Are, and Where You Are Going Now…



SMBG = self-monitoring of blood glucose.

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CGM Arrows, Alerts, and Alarms Support Self-Management of Glucose Levels to Improve Time in Range

Rate-of-change arrows show where glucose levels are headed, so action can be taken

- Glucose levels are steady. No action needed.
- Glucose levels are increasing. Add more insulin.
- Glucose levels are decreasing. Add less insulin. Eat carbs.

Double arrows indicate more rapid change and more urgent need for action.

Immediate sound or vibrate alerts indicate glucose levels that are above or below target ranges

Target ranges are customizable.

Alerts that are set are always functioning, night and day.

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Whiteboard #1

Distinctions Between CGM Systems

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Personal Use CGM Systems in US

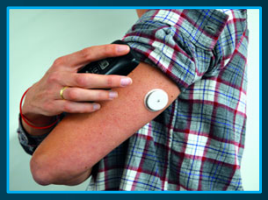
Real Time CGM: provides **continuous and automatic** readout updated every 5 min to receiver-phone-pump, with customized alerts and alarms

Intermittently scanned CGM: requires scanning for current and last 8 hours of readings, with optional high and low alerts in Libre 2

Dexcom G6
10 day
No calibration needed
CMS coverage

Medtronic Guardian
7 day
Calibration needed
No CMS coverage

Eversense Implanted CGM
(every 3 mo, 6 mo pending)
Calibration needed
CMS coverage



Freestyle Libre 14 day and Libre 2
14 day
No calibration possible
CMS coverage

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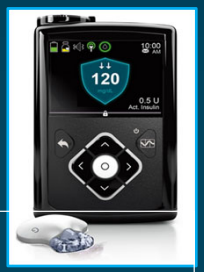
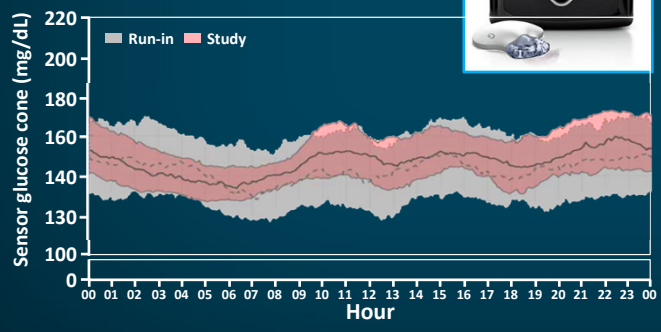
Hybrid Closed Loop—Using CGM to Guide an Insulin Pump

Lower HbA1c, More Time in Range, Less Hypoglycemia, Less Variability

Medtronic 670 G[1]

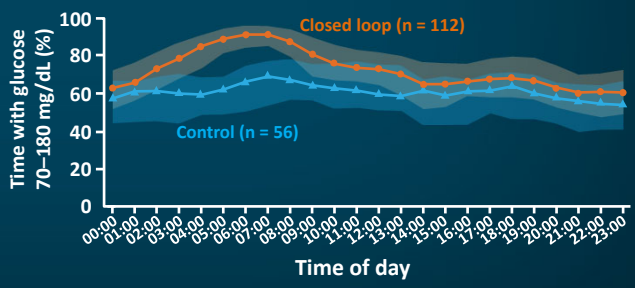
- Uses Medtronic CGMS to adjust basal insulin to goal of 120 mg/dL
- Patient still needs to bolus for meals and calibrate 3–4 times/day





T-Slim X2 with Control IQ[2]

- Uses Dexcom G6 CGM to guide T-Slim X2 pump
- Patient still needs to bolus for meals but not calibrate



1. Garg SK, et al. *Diabetes Technol Ther.* 2017;19:155-163. 2. Brown SA, et al. *N Engl J Mrd.* 2019;381:1707-1717.

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ADA 2020 Standards of Care

Recommendations for Continuous Glucose Monitoring in Adults

American Diabetes Association®

RT-CGM should be used **continuously** for maximal benefit.

IS-CGM should be scanned frequently throughout the day (minimum of once every 8 hours)

CGM and T1DM

- Real-time CGM (rtCGM) and intermittently scanned CGM (isCGM) are useful to lower HbA1C and/or reduce hypoglycemia in adults who are not meeting glycemic targets, have hypoglycemia episodes, and/or unawareness
- rtCGM may be used to improve HbA1C levels, time-in-range and neonatal outcomes in pregnant women

CGM and T2DM

- Useful tool, when used in conjunction with insulin therapy, to lower HbA1C and/or reduce hypoglycemia in adults with T2DM who are not meeting glycemic targets

ADA. *Diabetes Care*. 2020;43(suppl 1):S77-S88.

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Diabetes: Considerations in Senior Population

- >25% of people aged >65 years have diabetes.
- Diabetes management requires regular assessment of medical, mental, functional, and social domains.
- Older adults with diabetes have higher rates of premature death, functional disability, and coexisting chronic health conditions.
- Diabetes in elderly is associated with higher incidences of dementia.
  - Hypoglycemia can contribute to cognitive decline and can cause major adverse outcomes.
- Cognitive dysfunction makes self-care tasks more challenging to perform, such as glucose monitoring and complex insulin regimens.
- Possible Benefits of CGM for Elderly
  - Do not have to “remember” to check BG if real time CGM
  - May avoid or t least reduce need for fingersticks if calibration not needed
  - Modern systems simple to use
  - Ability to share data with caregivers/loved ones with some systems- May help maintain independence
  - Data can be shared with provider clinic for remote uploads

Beck RW, et al. *JAMA*. 2017;317:371-378. Beck RW, et al. *Ann Intern Med*. 2017;167:365-374. ADA. *Diabetes Care*. 2020;43(suppl 1):S77-S88. ADA. *Diabetes Care*. 2020;43(suppl 1):S152-S162.

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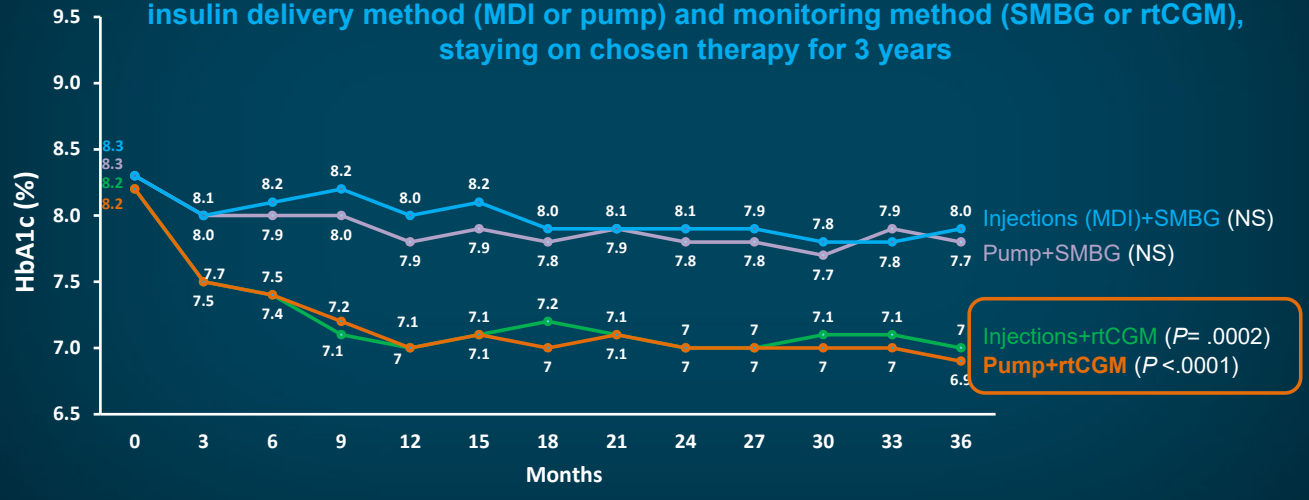
CGM Clinical Trial Evidence

23

COMISAIR Study: HbA1C Decreases With rtCGM Regardless of Insulin Delivery Method in T1DM

Observational prospective COMISAIR study in patients with T1DM who chose insulin delivery method (MDI or pump) and monitoring method (SMBG or rtCGM), staying on chosen therapy for 3 years



MDI = multiple daily injections; NS = not significant.

Šoupal J, et al. *Diabetes Care*. 2020;43:37-43.

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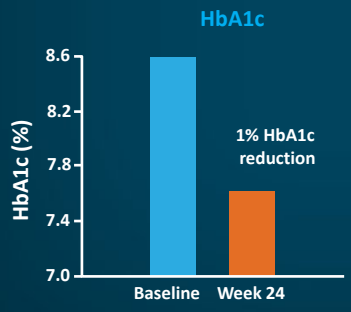
The DIAMOND Study in T1DM

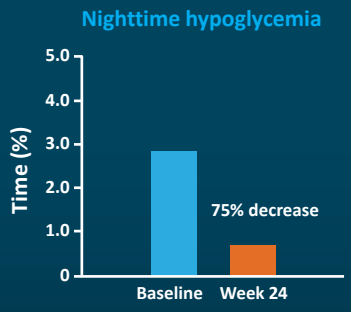
rtCGM vs BGM in Patients with T1DM on Multiple Daily Injections

Randomized, controlled 24-week trial in 158 adults (aged >25 years) with T1DM (mean baseline HbA1C = 8.6%)

HbA1c reduction
CGM users had a mean 1.0% HbA1C reduction from baseline (0.6% lower than SMBG; *P* <.001); **52% of CGM users had ≥1% HbA1C reduction.**

Reduced time in nighttime hypoglycemia (<60 mg/dL)
CGM group had 75% reduction in the median time spent in hypoglycemia at night. CGM users spent significantly less time in hypoglycemia vs BGM users (0.6% vs 2.4%; *P* <.005).





OTHER RESULTS

SIGNIFICANT HbA1c REDUCTIONS
regardless of patients' education level, math ability, and age

HIGH RATE OF ADHERENCE
at week 24, 93% of patients were still using the CGM system ≥6 days/week

Beck RW, et al. *JAMA*. 2017;317:371-378.

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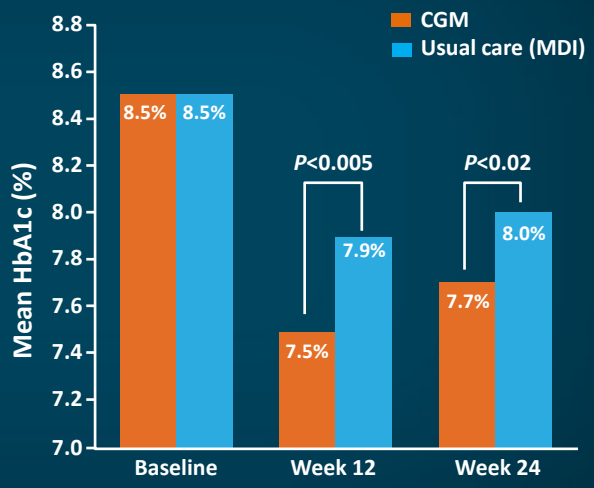
The DIAMOND Study in T2DM

rtCGM vs BGM in 158 Patients with T2DM on Multiple Daily Injections

Significant improvement across key measures at 24 weeks:

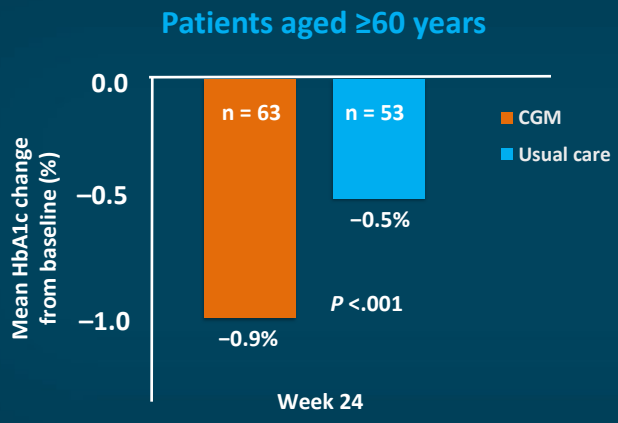
- CGM group: average 0.8% HbA1C reduction compared with baseline of 8.5%
- Avg 1.4% HbA1C reduction for HbA1Cs ≥9.0% compared with baseline
- HbA1c reductions occurred with minimal changes in insulin and no additions of non-insulin diabetes meds
- Significant HbA1C reductions regardless of education, math ability, and age
- High adherence: 93% of subjects using rtCGM ≥6 days/ week at end of study



Beck RW, et al. *Ann Intern Med*. 2017;167:365-374.

26

DIAMOND Outcomes Demonstrated Similar HbA1C Reduction in T1DM and T2DM Seniors on MDI Using CGM vs BGM



High Adherence: 97% used CGM>6 days/week in month 6

Reudy KJ, et al. *J Diabetes Sci Technol.* 2017;11:1138-1146.

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WISDM: Wireless Innovation for Seniors With Diabetes Mellitus

- 6 mo RCT of rtCGM vs BGM in patients >60 y/o with T1DM
  - 203 participants (assigned 1:1), half on pumps, mean HbA1c = 7.5%
  - Compared
    - Full time personal rtCGM with 2 calibrations per day
    - BGM with blinded CGM at weeks 8, 16, 26
- **Primary objective was to determine if use of rtCGM can reduce hypoglycemia**

VS

BGM represents no intervention/usual care control group.

RCT = randomized controlled trial; rtCGM = real-time CGM; y/o = years old.

Pratley RE, et al. *JAMA*. 2020;3232397-2406.

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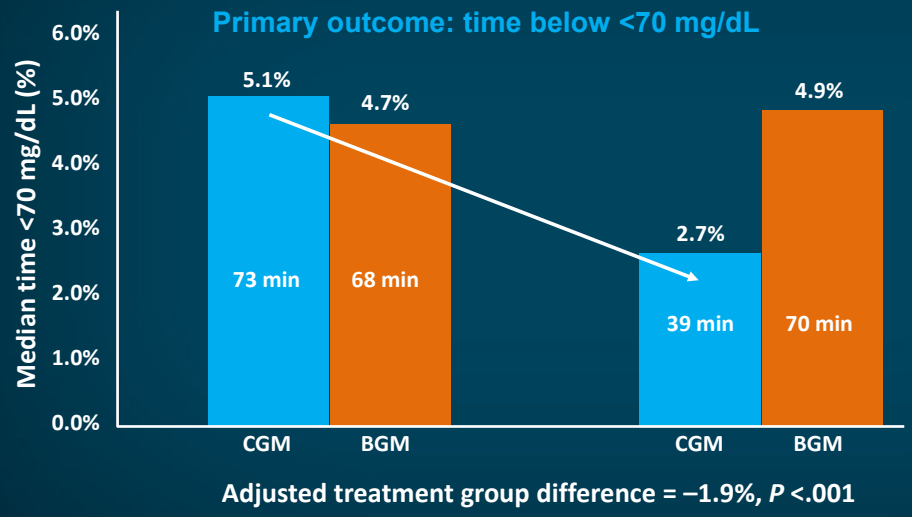
WISDM: Seniors With T1DM Using RT-CGM Spent Less Time in Hypoglycemia (<70 mg/dL) Compared With BGM



Number with a severe hypoglycemic event:
CGM = 1 vs BGM = 10
(5 with LOC or seizure)
P= .02

Mean reduction in HbA1C of 0.4%
Increased TIR by 8.8%
(*P* <.001)

Similar reduction in HbA1C for MDI and CSII

LOC = loss of consciousness; CSII = continuous subcutaneous insulin injection; TIR = time in range.

Pratley RE, et al. *JAMA*. 2020;3232397-2406.

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CONCEPTT STUDY

rtCGM vs BGM in T1DM Pregnancies with MDI or Open-Loop Pump

- Compared BGM + CGM with BGM alone during pregnancy, n = 325[1]
- **Benefit for mothers with CGM**[1]
  - **Small but significant difference in maternal HbA1c** (mean difference −0.19%; *P*= .0207)
  - **Almost 2 hours more time in pregnancy target range** of 63–140 mg/dL (68% *vs* 61%; *P*= .0034)
  - **Less time hyperglycemic** >140 (27% *vs* 32%; *P*= .0279)
  - **Comparable time in hypoglycemia** and severe hypoglycemia episodes
- **Fetal health outcomes significantly improved with CGM**[1]
  - Lower incidence of large for gestational age (odds ratio [OR] = 0.51, *P*= .0210)
  - Fewer neonatal intensive-care admissions lasting more than 24 hours (OR = 0.48, *P*= .0157)
  - Fewer incidences of neonatal hypoglycemia (OR = 0.45; *P*= .0250)
  - 1-day shorter length of hospital stay (*P*= .0091)
- Highly cost effective, using UK data[2]

1. Feig DS, et al. *Lancet.* 2017;390:2347-2359. 2. Murphy HR, et al. *Diabetes.* 2019;68(suppl 1): abstract 351-OR.

30

CGM: Reports from Real World Experience

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rtCGM Real-World Experience

Reduction in Diabetes Hospitalizations and Work Absenteeism

	Before CGM Reimbursement (n = 496)	12 Months of CGM Reimbursement (n = 379)	*P* Value
Patients, n (%)			
Hospitalizations due to hypoglycemia and/or ketoacidosis	77 (16%)	14 (4%)	<.0005
Hospitalizations due to hypoglycemia	59 (11%)	12 (3%)	<.0005
Hospitalizations due to ketoacidosis	23 (5%)	4 (1%)	.092
Work absenteeism*	123 (25%)	36 (9%)	<.0005
Days, n/per 100 patient years			
Hospitalizations due to hypoglycemia and/or ketoacidosis	53.5	17.8	<.0005
Hospitalizations due to hypoglycemia	38.5	12.5	.001
Hospitalizations due to ketoacidosis	14.9	5.3	.220
Work absenteeism	494.5	233.8	.001

*Work absenteeism of at least half a day

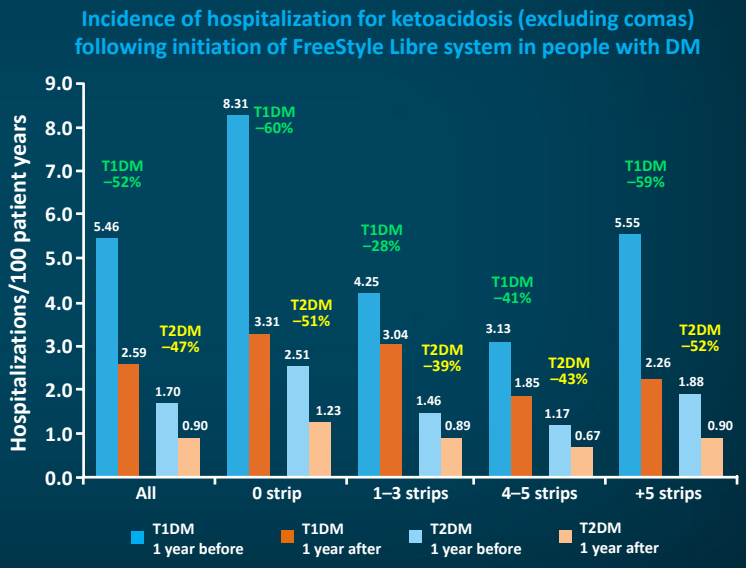
Charleer S, et al. *J Clin Endocrinol Metab*. 2018;103:1224-1232.

32

Reduced DKA Rates Per Claims Data With isCGM in France

Year Before and Year After First Use

- 33,203 with T1DM and 40,955 with T2DM initiated intermittently scanned CGM system during study period
- DKA rates reduced by 52% in T1DM and 47% in T2DM patients
- Benefit seen regardless of baseline strip use, with those T1DM patients using no strips at baseline showing highest reduction (60%)



DKA = diabetic ketoacidosis; isCGM = intermittently scanned CGM; DM = diabetes mellitus.

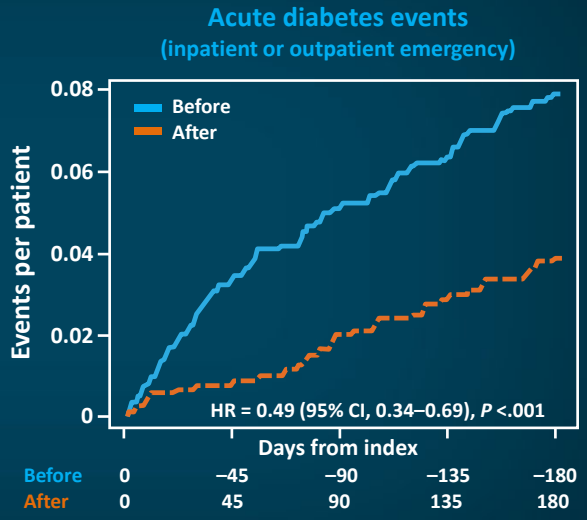
Roussel R, et al. *Diabetes.* 2020;69(suppl 1): abstract 68-OR.

33

Real-World Data From Patients With T2DM Using isCGM

ADA—June 2020

- 1244 patients with T2DM on insulin new to using isCGM showed 51% reduction in acute diabetes events requiring ED visit or hospital stay and 28% reduction in all hospitalizations[1]
- 1183 patients with T2DM not on bolus insulin and with HbA1c above 8% baseline new to isCGM were able to reduce HbA1c from 10.16% to 8.78% at 6 months (P <.001)[2]
- 774 patients with T2DM on basal insulin or non-insulin were able to reduce HbA1c from 8.5% to 7.7% at 6 months (P <.0001)[3]



HR = hazard ratio; CI = confidence interval.

ED = emergency department

1. Bergenstal RM, et al. *Diabetes.* 2020;69(suppl 1): abstract 69-OR. 2. Wright E Jr, et al. *Diabetes.* 2020;69(suppl 1): abstract 78-LB. 3. Miller E, et al. *Diabetes.* 2020;69(suppl 1): abstract 84-LB.

34

Real-World Data: Implanted CGM

- Registry data from 945 patients with T1DM and T2DM having at least 4 sensor placements (90 or 180 day)[1]
- High utilization by patients, who had data 84% of time possible[1]
- Blood glucose data: no change over cycles seen[1]
  - Good accuracy compared with BGM (MARD ~11.5%)
  - Mean BG ~157 mg/dL (calculated HbA1c or GMI 7.06%)
- Time in ranges, compared with recommended targets[2]:
  - Hyperglycemia >180 mg/dL: 32% (<25%)
  - TIR (70–180): 64% (>70%)
  - Hypoglycemia <70: 4.8% (<4%)
  - Serious or level 2 hypoglycemia <54 mg/dL: 1.2% (<1%)
- Few adverse events- all <1% of subjects: site infection, inability to remove prior sensor on first try, and adhesive irritation

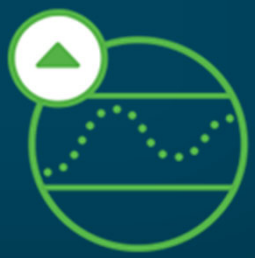
MARD = mean absolute relative difference.

1. Tweden KS, et al. *Diabetes Technol Ther.* 2020;22:422-427. 2. Battelino T, et al. *Diabetes Care*. 2019;42:1593-1603. 3. Deiss D, et al. *Diabetes Technol Ther.* 2020;22:48-52.

35

Summary: Proven Clinical Benefits of CGM

- Reduction in HbA1c and improved time in target range in diverse populations[1–5]
- Reduction in time spent in hypoglycemia[1,4,5] and reduced severe hypoglycemic events[6]
- Improved overall quality of life and well-being[7–9] with reduced ER visits and admissions for acute diabetes complications and reduced absenteeism[10]



1. Beck RW, et al. *JAMA*. 2017;317:371-378. 2. Beck RW, et al. *Ann Intern Med*. 2017;167:365-374. 3. Lind M, et al. *JAMA*. 2017;317:379-387. 4. Šoupal J, et al. *Diabetes Care*. 2020;43:37-43. 5. Reddy M, et al. *Diabet Med*. 2018;35:483-490. 6. Heinemann L, et al. *Lancet*. 2018;391:1367-1377. 7. Polonsky WH, et al. *Diabetes Care*. 2017;40:736-741. 8. Ólafsdóttir AF, et al. *Diabetes Technol Ther*. 2018;20:274-284. 9. Ehrmann D, et al. *Diabetes Technol Ther*. 2019;21:86-93. 10 . Charleer S, et al. *Clin Endocrinol Metab*. 2018;103:1224-1232.

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Overcoming Barriers to Use of CGM

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National CGM Policy for Veterans Affairs[1]

- Patient must have type1, type 2 or other unspecified diabetes and meet all the following criteria:

✓ Requires an intensive insulin regimen (e.g. ≥3 injections a day, or insulin pump) to achieve desired glycemic control (target range) based upon shared-decision making)
✓ Requires frequent blood glucose monitoring (≥4 or more times a day)
✓ Has the knowledge and skill set necessary to successfully utilize CGM
✓ Agrees to ongoing medical appointments with multidisciplinary team at least every six months to assess the adherence and benefit derived from CGM

- **And meets at least one of the following criteria:**

✓ At risk for hypoglycemia
✓ Unable to meet glycemic control despite adherence to the treatment regimen
✓ Performing job-related activities where a hypoglycemic event could put them at risk of harm
✓ Unable to perform self-monitoring of blood glucose due to disability or disease

1. Use of Continuous Glucose Monitoring Systems (CGMS). January 31, 2019 – Department of Veteran Affairs, Prosthetics & Sensory Aid Services.

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Overcoming Patient Obstacles to CGM

- **Help them see the value…**
  - Replaces fingersticks
  - Warnings about and therefore protection from hypoglycemia
  - Empowers patients to take control of their diabetes by seeing connections between actions and their BG response
- **Training on CGM**
  - Many younger patients can learn from online videos
  - Older patients may benefit from hands-on training
  - Consider group training sessions

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Fitting CGM into Clinic Workflow

- CGM workflow for clinic:
  - Set up Clarity or other CGM clinic account
- Minimal staff training needed but best to have a primary person or champion
  - know how to download to clinic account and to set up Clarity or another CGM system on the patient's phone and link to clinic account right in the office
  - Access data via the CGM system and decide on preferred reports
- CGM workflow for patient
  - 2-week follow-up after initial start to review download, identify needs, make adjustments
  - Encourage use of CGM system weekly summaries or daily TIR notifications if using a smart phone and linking for automatic data download or weekly download and review with other systems
  - Encourage receiver download before coming to the visit, if possible

Clarity = diabetes management application.

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Interpreting CGM Data

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Continuous Glucose Monitoring Definitions

Standardized CGM Metrics for Clinical Care
Number of days CGM is worn 14 days is recommended
Percentage of time CGM is active 70% of data from 14 days is recommended
Glucose Measures:
Glucose management indicator (GMI) Formula to convert CGM-derived mean glucose to an estimate of current HbA1C level
Coefficient of variation (CoV) Measure of glycemic variability: CoV of ≤36% is considered acceptable; >36% is considered unstable and intervention is needed
Very high time above range (TAR) % of readings and time >250 mg/dL; target is <5% of the day
High time above range (TAR) % of readings and time 181–250 mg/dL, target is <25% of the day
Time In range (TIR) % of readings and time 70–180 mg/dL, target is >70% per day
Low time below range (TBR) % of readings and time 54–69 mg/dL, target is <4% per day
Very low time below range (TBR) % of readings and time <54 mg/dL, target is <1% per day

CoV = coefficient of variation; GMI = glucose management indicator; TAR = time above range; TBR = time below range.

Battelino T, et al. *Diabetes Care*. 2019;42:1593-1603.

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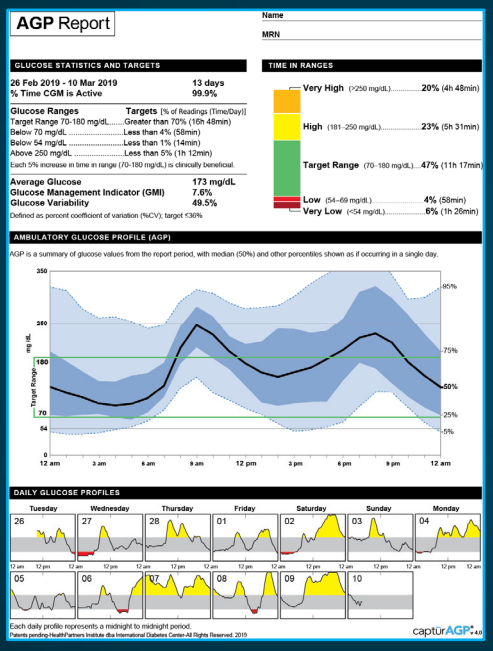
Standardized Report Content



- **The Ambulatory Glucose Profile (AGP) is a standardized report for retrospective CGM interpretation created by International Diabetes Center (IDC) and recommended by American Association of Clinical Endocrinologists (AACE).**
- This report has three distinct sections that:
  - **Summarize glucose values to help assess the overall quality of glucose control**
  - **Show variability around the median glucose and patterned areas of highs and lows**
  - **Show single-day glucose values to help identify patterns and progress**

Johnson et al. Diabetes Technology & Therapeutics. 2019;21(S2):S217-S225

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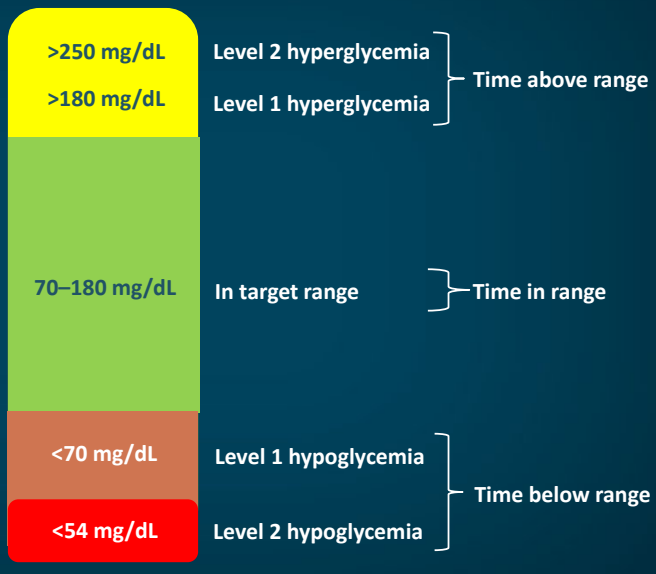
CGM Metrics

1. Number of days CGM worn (14 days)
2. Percentage of time CGM is active (70% of data captured from 14 days)
3. Mean glucose
4. Glucose management indicator (GMI)
5. Glycemic variability (%CoV) target ≤36% (some studies suggest <33%)



Battelino T, et al. *Diabetes Care*. 2019;42:1593-1603.

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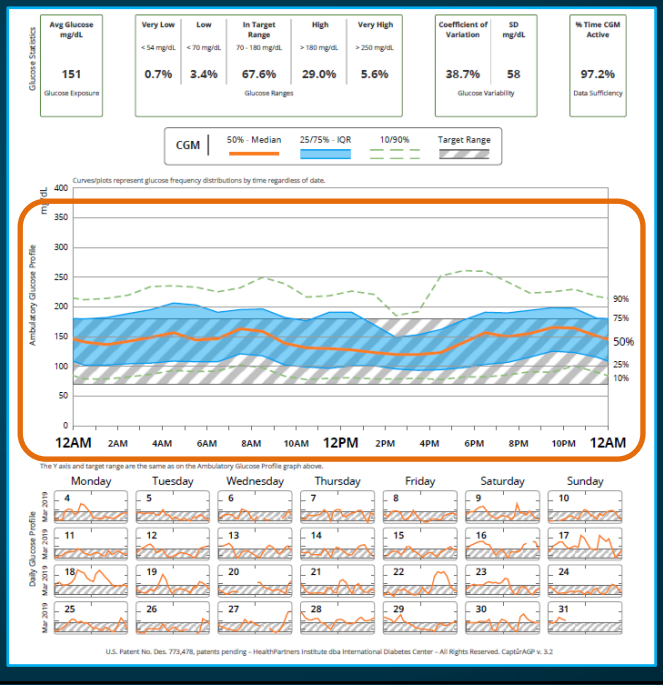
Ambulatory Glucose Profile

AGP: define the time period

- Minimum time thought sufficient to generate MBG and other measures is 14 days
- 30 days only slightly better

Graphic Display of median glucose and variability – points out when problems are occurring



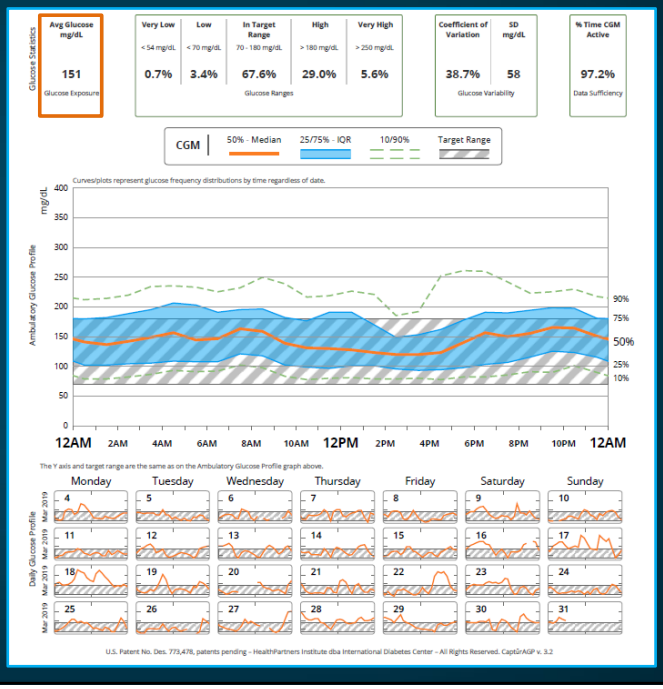
MBG = mean blood glucose.

Riddlesworth TD, et al. *Diabetes Technol* Ther. 2018;20:314-316.

45

Mean Blood Glucose

- CGM is direct measure of MBG
- Population average for an HbA1c of **7.0% ~155 mg/dL**
  - **6.5% ~135 mg/dL**
- Each 1% change = 41 mg/dL
- MBG used to generate the **glucose management indicator (GMI)**
- Calculator available at **www.jaeb.org/gmi/**



HbA1c = glycosylated hemoglobin.

Beck RW, et al. *Diabetes Care.* 2017;40:994-999.
Bergenstal RM, et al. *Diabetes Care* 2018;41:2275-2280.

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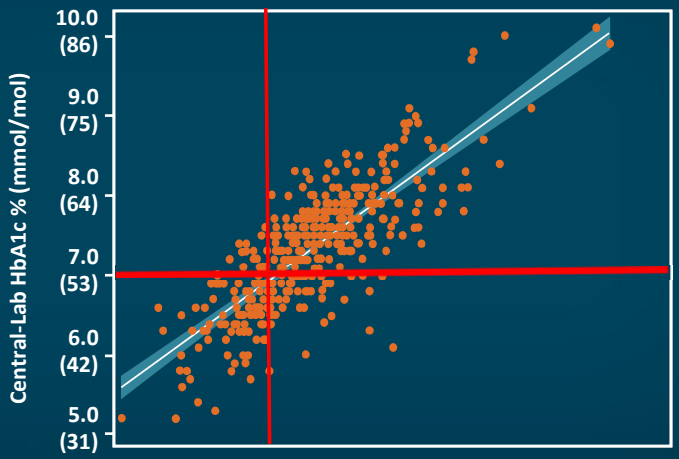
Glucose Management Indicator (GMI)

HbA1c as dependent variable (GMI)

Each change in HbA1c point ~41 mg/dL



CGM-Measured Mean Glucose (mg/dL)	100	125	150	175	200	225	250	275	300
eHbA1c % (mmol/mol)	5.7 (39)	6.3 (46)	6.9 (52)	7.5 (58)	8.1 (65)	8.7 (71)	9.2 (78)	9.8 (84)	10.4 (90)

Beck RW, et al. *Diabetes Care.* 2017;40:994-999.

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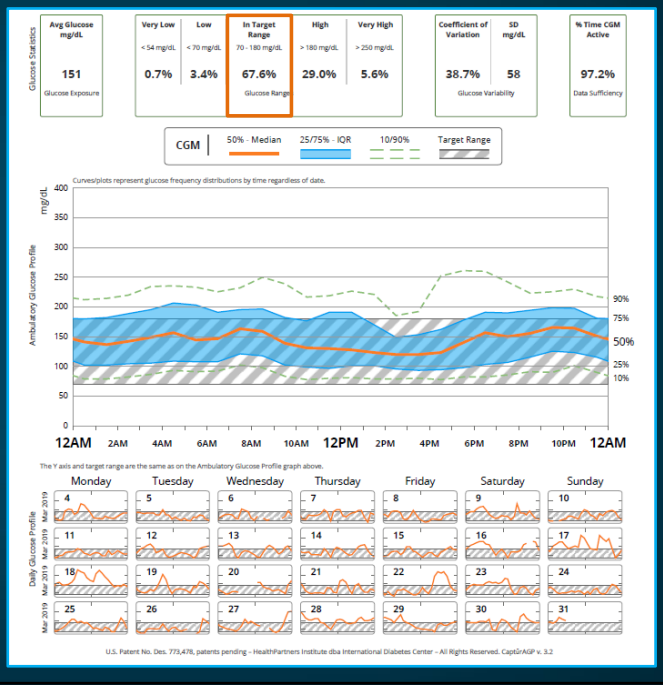
Time in Range (TIR)

- **70–180 mg/dL** accepted as target outside of pregnancy
- Pregnancy target 63-140
- TIR targets based on Vigersky and McMahon analyses of multiple CGM data sets:
  - >65% for HbA1c of 7.0%
  - >70% for HbA1c of 6.5%



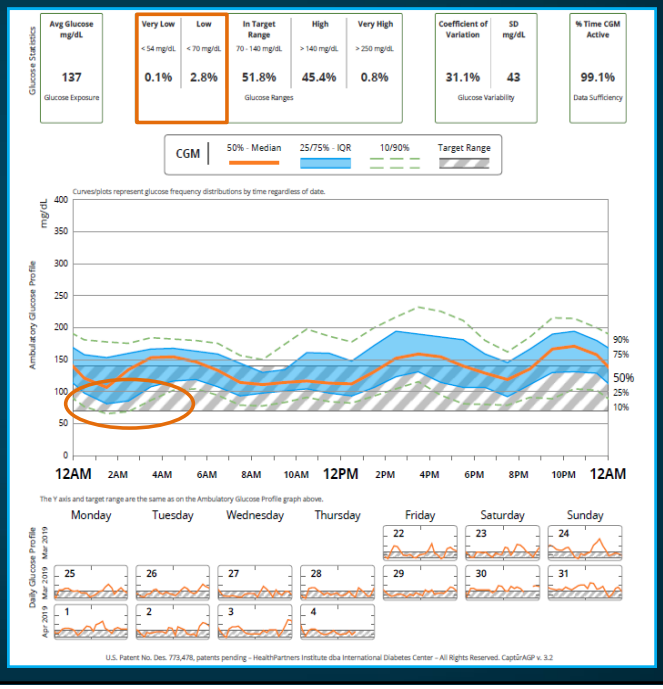
ADA = American Diabetes Association; FBG = fasting blood glucose; PPG = postprandial glucose.

ADA. Standards of Medical Care in Diabetes. *Diabetes Care.* 2020;43(suppl 1):S66-S76. ADA. *Diabetes Care.* 2020;43(suppl 1):S183-S192. Vigersky RA, McMahon C. *Diabetes Technol Ther.* 2019;21: 81-85.

48

Time Below Range: Hypoglycemia

- **1% = 15 minutes a day**
- Low <70 mg/dL—target <4%
- Very low <54 mg/dL (3 mmol) <1%
  - Critical safety indicator
  - Correlates with severe events
  - Associated with worsening of hypoglycemia unawareness
  - **Goal—minimize time in this range**
- Look for frequency, timing, persistence, rebounding



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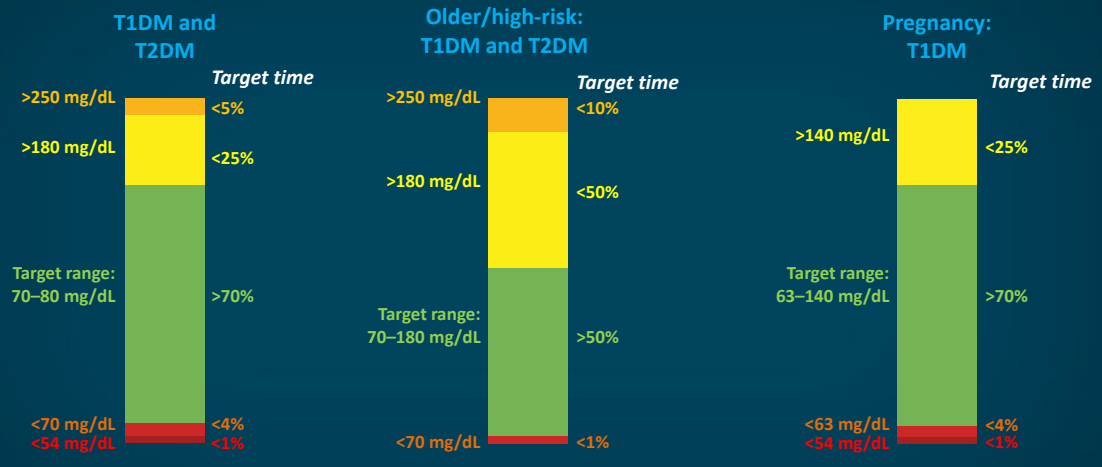
CGM-Based Targets for Different Populations



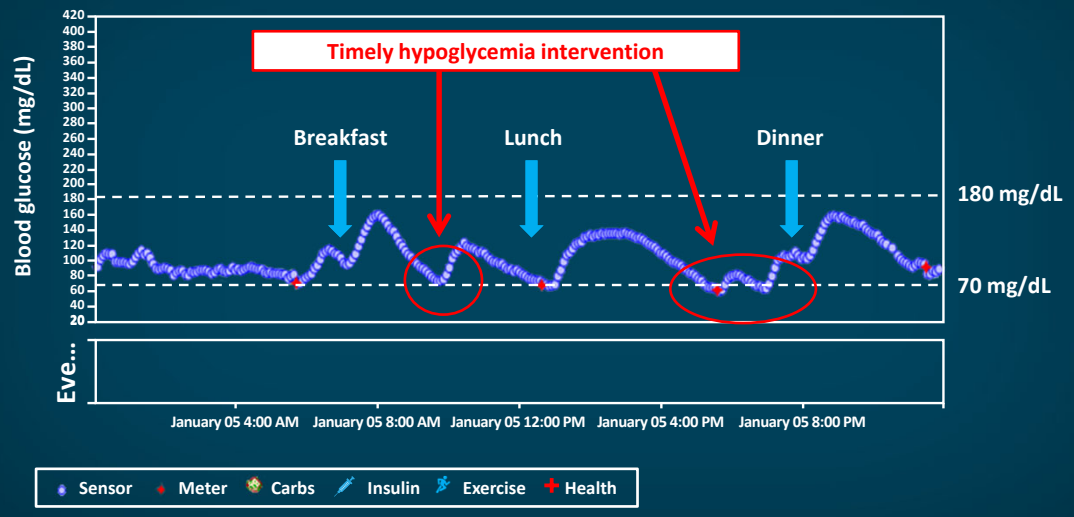
1% of the day is ~15 minutes

Battelino T et al. *Diabetes Care*. 2019;42:1593-1603.

50

Reducing Hypoglycemia with rtCGM

Acting on Trends and Alarms



rtCGM = real-time CGM.

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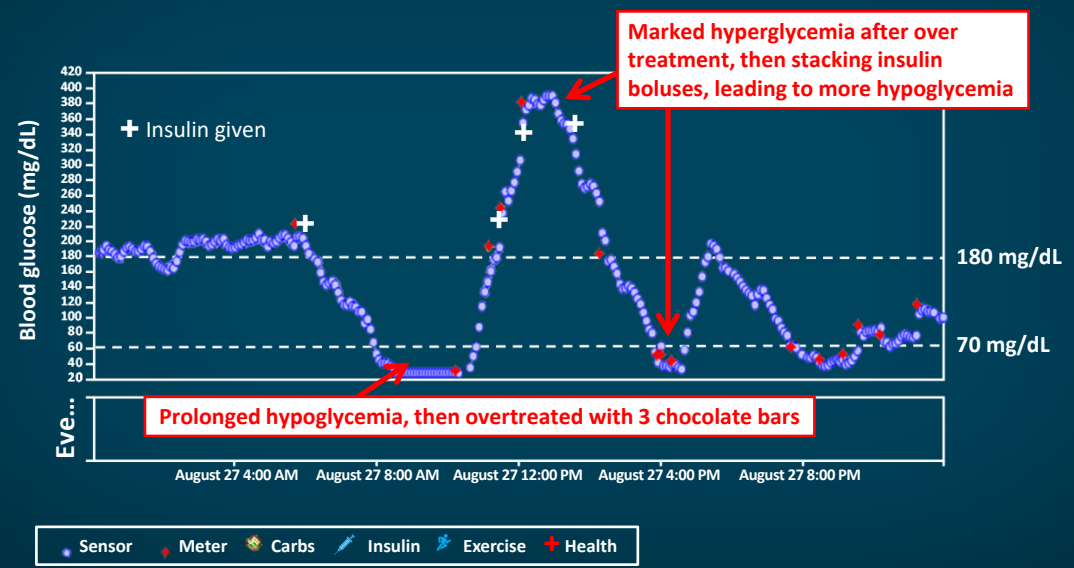
Prolonged Hypoglycemia, Over-Treatment of Hypoglycemia, Followed by Stacking Insulin



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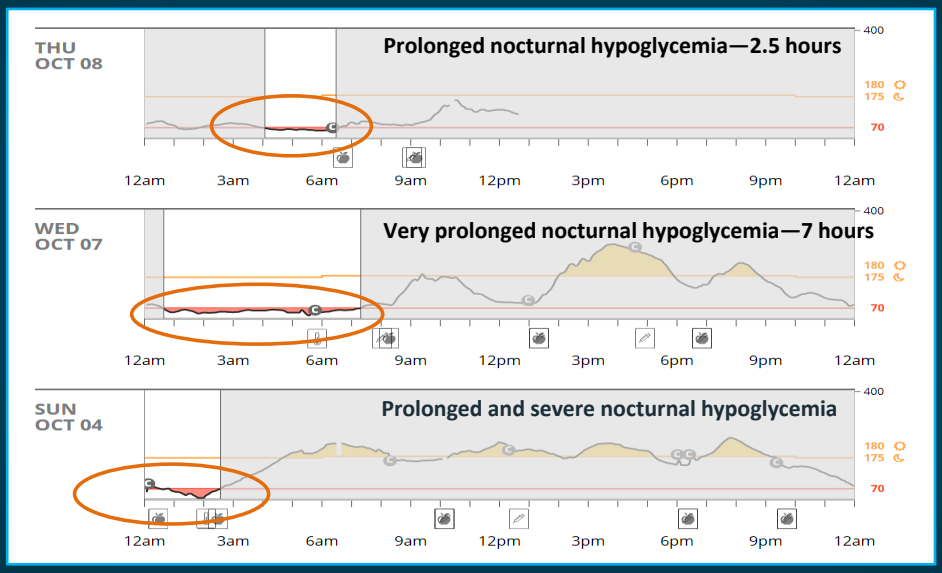
Individual Daily Tracings: Alarming Lack of Response to Alarms!



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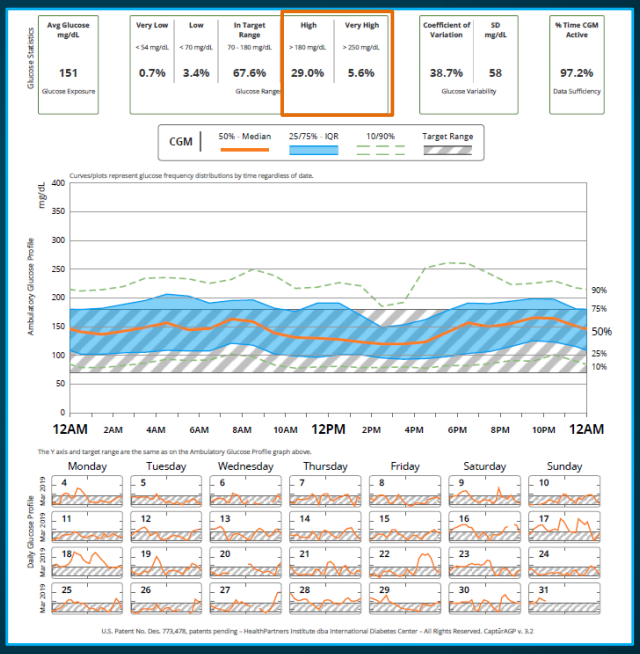
Time Above Range: Hyperglycemia

- High = >180 mg/dL
  - Very high = >250 mg/dL
- Pre-meal and fasting levels mostly reflect basal
  - Unless persistent post-meal hyperglycemia
- Daytime hyperglycemia—think **eating-related behaviors**
- Also common—over-treatment of hypoglycemia



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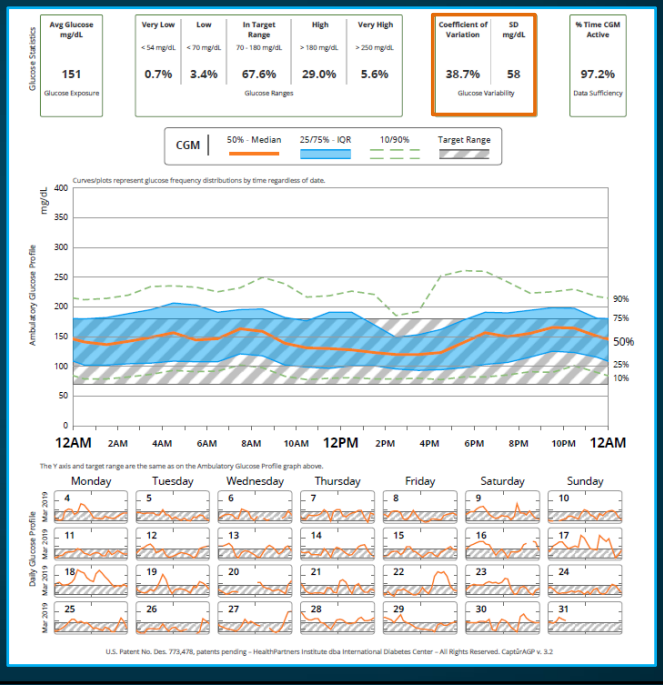
Variability

- SD or coefficient of variation (SD/MBG) [1]
- Target: <36% CV[1] or <33%
  - ~3-fold higher rate of BG <56 mg/dL with a CV of 36% or higher
- Main drivers: post-meal hyperglycemia, frequency of and reactions to hypoglycemia or exercise



1. Monnier L, et al, *Diabetes Care*. 2017;40:832-838.

55

Using Trends: Based on Previous 15–20 Minutes

Project in which arrow predicts where it will be in 30 minutes for a correction if using a bolus calculator or correction factor

Medtronic	30-minute change	Libre	30-minute change	Eversense	30-minute change	Dexcom	30-minute change
						↑↑	90+ rise
↑↑	60+ rise	↑	60+ rise	↑	60+ rise	↑	60–90 rise
↑	30–60 rise	↗	30–60 rise	↗	30–60 rise	↗	30–60 rise
——	<30	——	<30	→	<30	→	<30
↓	30–60 fall	↘	30–60 fall	↘	30–60 fall	↘	30–60 fall
↓↓	60+ fall	↓	60+ fall	↓	60–90 fall	↓	60–90 fall
						↓↓	90+ fall

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Keys To Setting Alarms That Make Sense

- Individualize
  - Always set low alarms—safety first!
  - Consider not setting high alarms at first in those patients with high HbA1c levels
- Emphasize to patients that they are never to ignore low alarms
- Alarms don't help if they are turned off or are silent at night!
- Repeat times are extremely helpful, if available
  - 30 minutes on lows
  - Never less than 2 hours on highs

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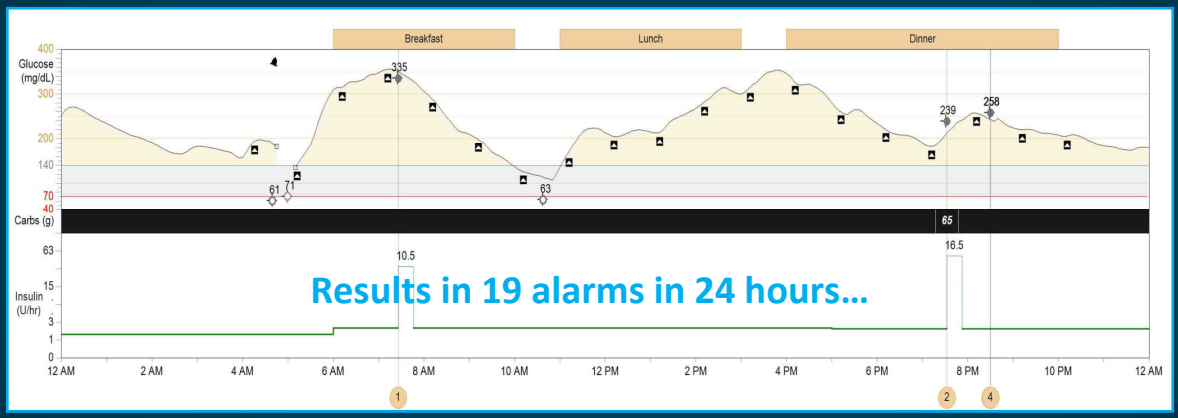
Example of Alarms in Case of Patient With HbA1c of 9.4%...

High alarm setting: >140 mg/dL, with repeat time every 60 minutes…



Results in 19 alarms in 24 hours…

Patient response to so many alarms was to turn off alarms at night and ignore them during the day…

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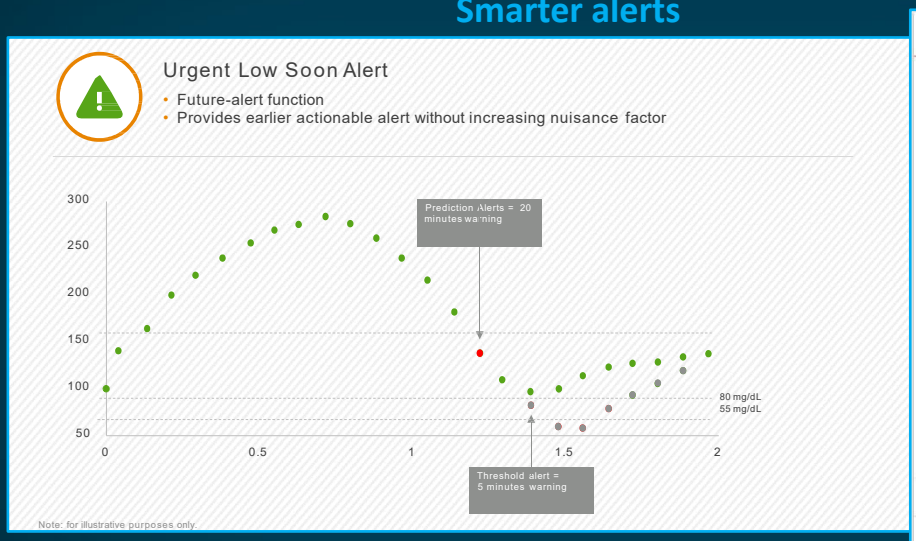
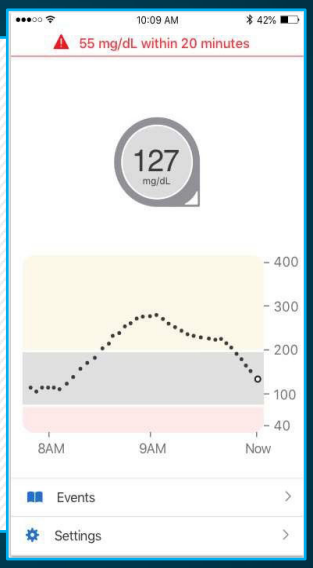
Urgent Low-Soon Alert

Smarter alerts





Dexcom CGM: Integrating data science and clinical application to support patient glycemic management. ATTD (Advanced Technologies and Treatments in Diabetes) 2020. 2/19–22/2020. Madrid Spain. Dexcom G6 CGM user guide (https://s3-us-west-2.amazonaws.com/dexcompdf/G6-CGM-Users-Guide.pdf). Accessed 11/10/2020.

59

Clinical Significance

- Regular CGM use increases glucose awareness, helping to optimize diabetes management.[1] It has been shown to deliver the following benefits:
  - Reduces both HbA1C and time spent in hypoglycemia (low glucose)[1,2]
  - Decreases time in hyperglycemia (high glucose)[1,2]
  - Increases time in range[1]
  - Improves overall quality of life[2]
- Provides a holistic view of your patients' diabetes management by highlighting glucose patterns, trends, and statistics
- Can help guide your conversations with patients and align on diabetes management plans for both in-office and telemedicine visits

1. Beck RW et al. *JAMA*. 2017;317:371-378. 2. Lind M, et al. *JAMA*. 2017;317:379-387.

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Whiteboard #1

CGM Metrics

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Standardized Report Interpretation Summary

Step 1 Data interpretation should be based on adequate amount of data; 14 days is recommended with 70% of the data captured. 3 fewer days are needed when professional CGM systems are used.

Step 2 Review AGP with patient. Garner insight as to daily habits (for example, food eaten, exercise, when a bolus is taken, if they count carbs, etc.)

Step 3 Discuss AGP with patients and assess their understanding of diabetes regimen. This interactive discussion allows them to better understand how insulin, food, and other factors affect their glucose levels and also helps clinicians identify knowledge deficits or behaviors that may not support glycemic goals.

Step 4 Look for glycemic patterns in following order of priority: hypoglycemia, hyperglycemia, and wide glycemic variability. Review overall glucose profile (initial view) to determine time of day when patterns are occurring, then review daily graphs to double-check patterns to see if they are clustered on certain days.

Step 5 This is a good opportunity to have patients reflect on what they think may be causing problems with their glucose levels and discuss potential solutions.

Step 6 Collaboratively develop an action plan with the individual patient.

Step 7 Save reports and enter them into EMR.

EMR = electronic medical record.

Adapted from Kruger DF, et al. *Diabetes Educ*. 2019;45(1 suppl):3S-20S.

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Summary

- The AGP is the key to setting the agenda for the visit
  - Mean blood glucose <155 mg/dL
  - Fix hypoglycemia, and emphasize avoiding prolonged or severe lows, ie, <55 mg/dL
  - TIR >70%—look at eating behaviors
  - high CV or SD usually means problems with eating behaviors or hypoglycemia overreaction
- Pre-meal bolus, lower carbs, and new agents to lower post-meal BG
- Extra insulin is necessary for high-fat foods
- Empower patients to act on trends with dosing
- Alarms are critically important to reduce hypoglycemia in those patients at risk

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Patient Case Studies

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Case 1—T1DM: Presentation

- Joe is 38 y/o male with T1DM; on multiple daily injections
- **Current meds**
  - Insulin degludec 24 units
  - Insulin aspart 1:15 g with correction 1:40
- **Recommendations for LR**
  - Increase insulin degludec by ~ 10% to 26 units
  - Dose insulin aspart with bedtime snack

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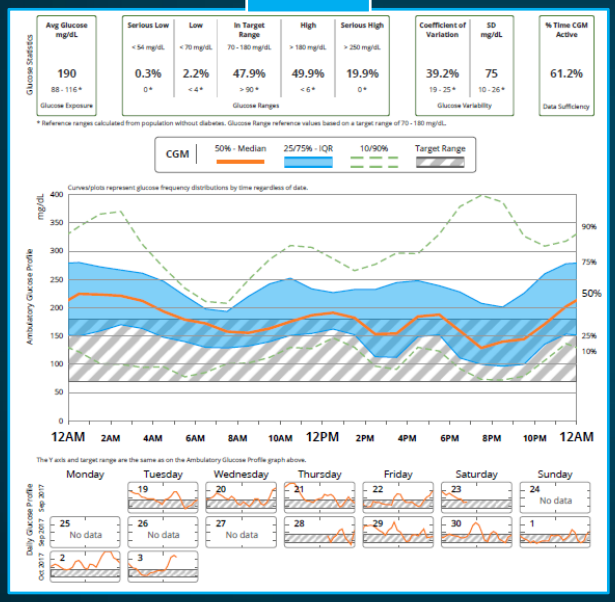
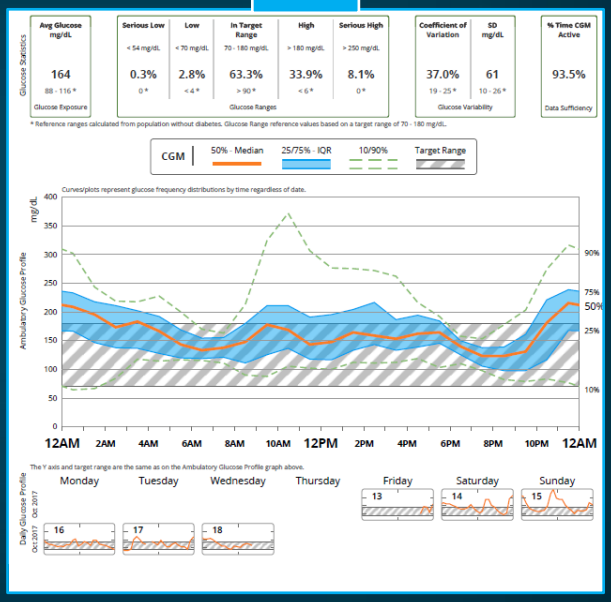
Case 1—T1DM: Before and After…

Before



After



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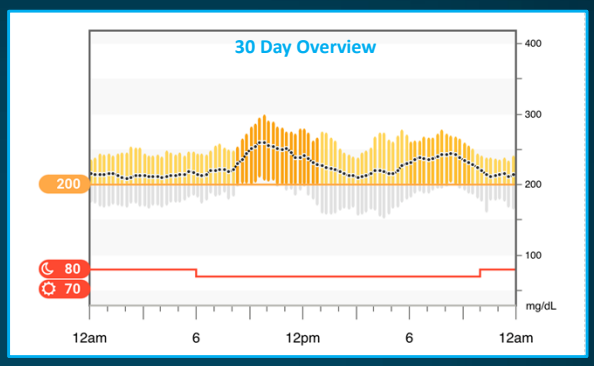
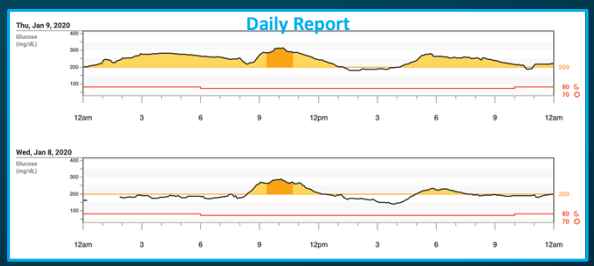
Case 2—T2DM: Presentation

- Mark is 68 y/o male with T2DM
- **Current meds**
  - Metformin 2000 mg/day
  - Insulin glargine 60 units/day
  - Insulin aspart 10 units bid with breakfast and supper
- **Recommendations for MJ**
  - Add long-acting GLP-1RA to lower fasting and post-prandial readings
  - Start dulaglutide 0.75mg weekly
  - Reduce aspart to 5 units at breakfast and supper





GLP-1RA = glucagon-like pepoide-1 receptor agonist.

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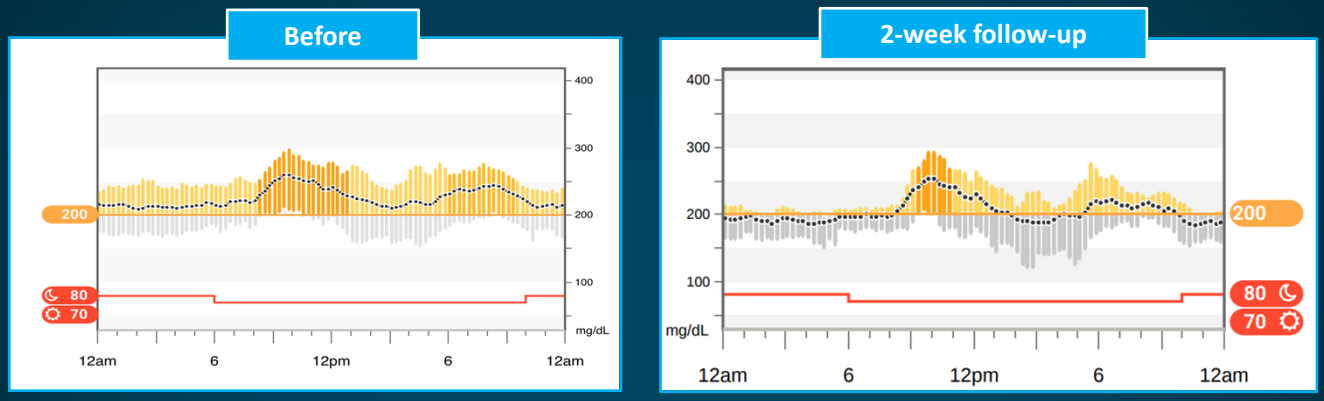
Case 2—T2DM: Before and at 2 Weeks



Recommendations for Mark

- Increase dulaglutide
- Stop supper insulin
- Reduce insulin glargine by 5 units per day if BG drops <90
- Return to clinic in 2 weeks

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Case 2—T2DM: Before and at 30-Day Follow-Up

- **Medications at follow-up**
  - Insulin glargine—55 units
  - Insulin aspart—5 units with breakfast
  - Dulaglutide—1.5 mg weekly
- **Recommendations for Mark**
  - Continue dietary counseling—consider lower carb breakfast. Reduce insulin doses as able with more time on therapy

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Questions?

Thank you!

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