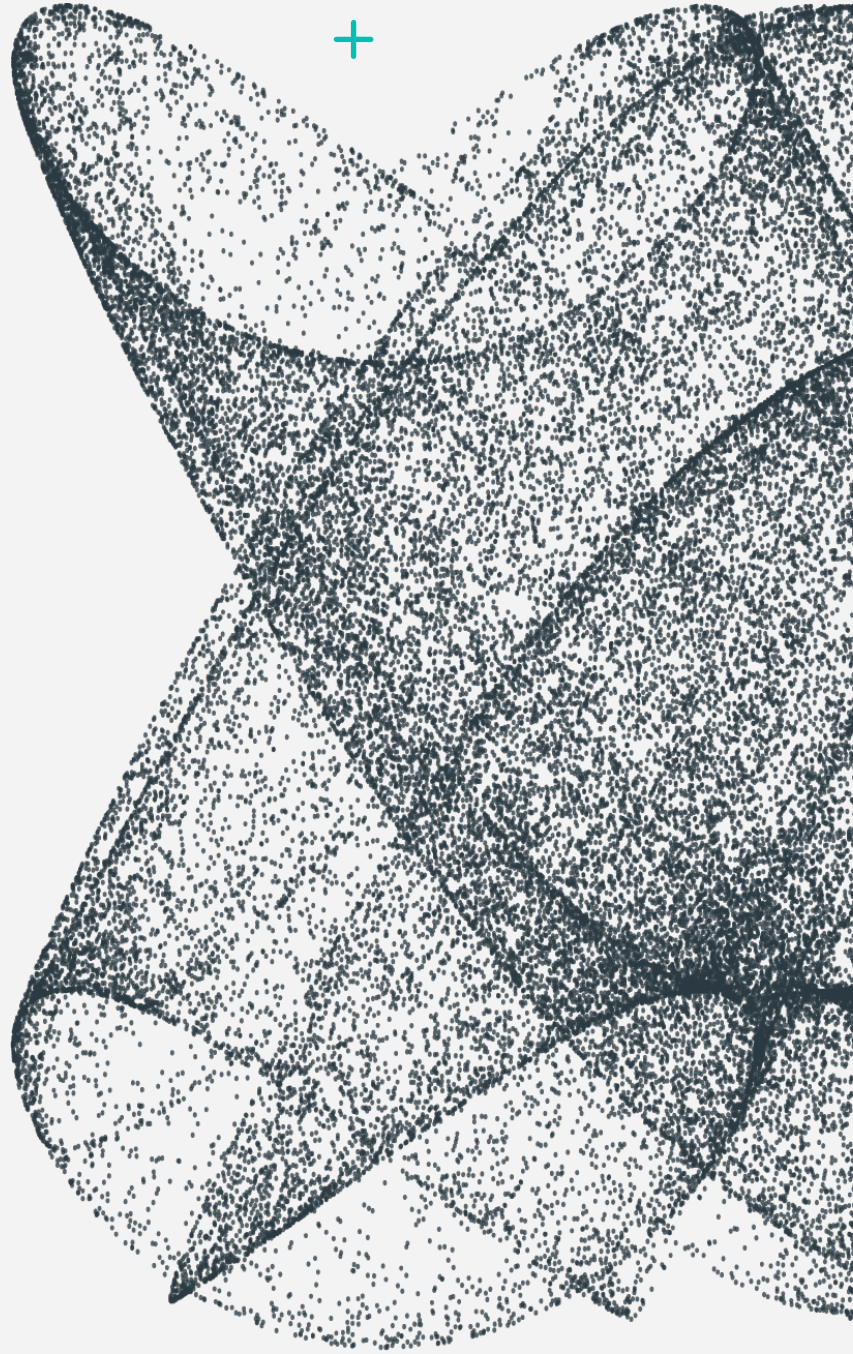
IQVIA INSTITUTE FOR HUMAN DATA SCIENCE

A Movement in Diabetes: Using Time-in-Range

Webinar

November 12, 2019



Speakers

Executive Director, IQVIA Institute

Senior Vice President, IQVIA

Founder and Chair of the Board, The diaTribe Foundation

President, Close Concerns

Vice President, Head, CV, Metabolism, Renal, and Reproductive Health Centers of Excellence, IQVIA

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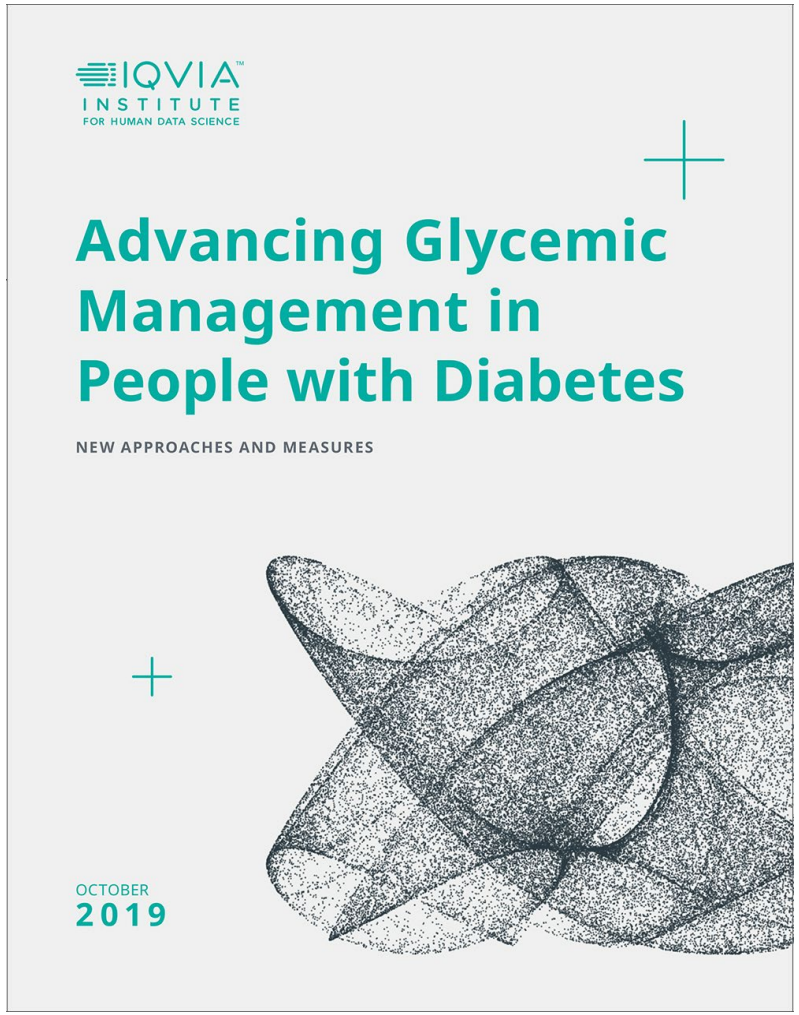
Advancing Glycemic Management in People with Diabetes

A look at the components of the IQVIA Institute report



Type 1 and Type 2 Diabetes in the United States

Evolution of blood glucose management in Diabetes

Reduction in complications and costs by improving TIR

Approaches to further use of TIR in the U.S. PwD population

This study is based on research and analysis undertaken by IQVIA Real World & Analytics Solutions with support and funding from Eli Lilly and Company

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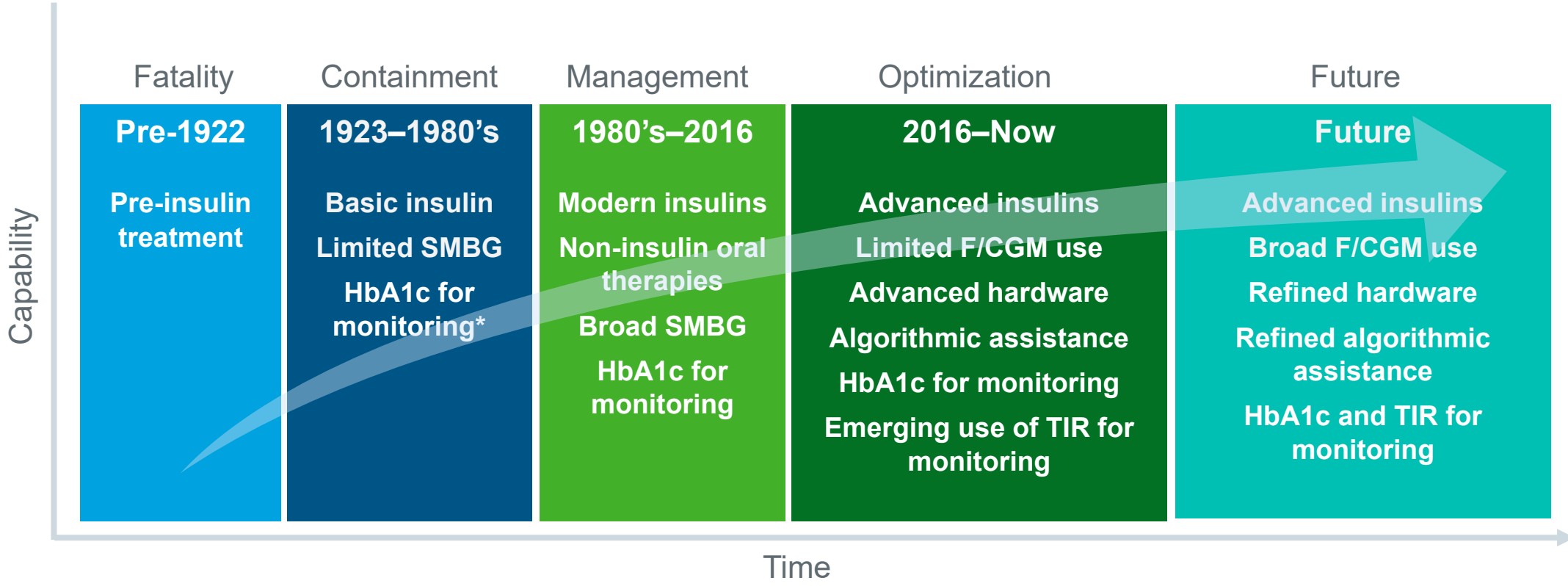
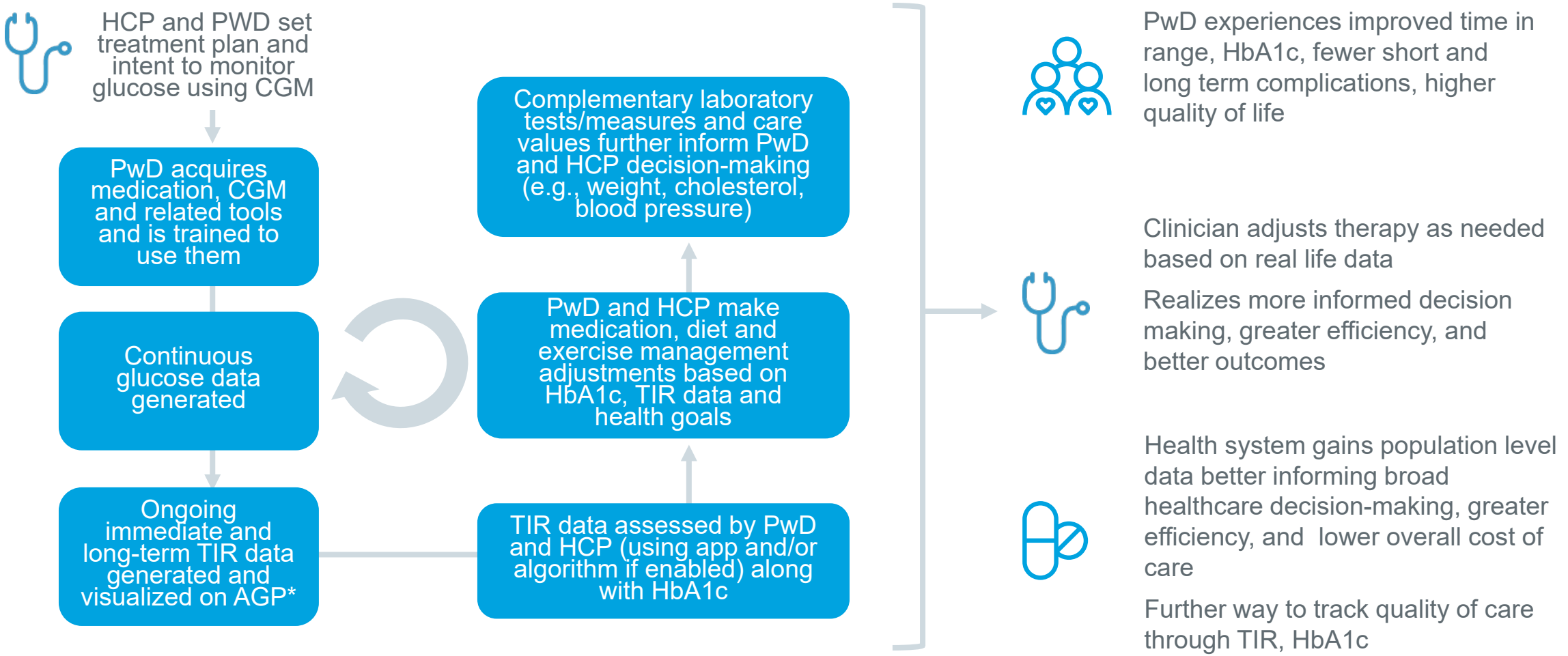
Eras of Diabetes control



Source: IQVIA, Aug 2019

Notes: SMBG = self-monitoring of blood glucose. F/CGM = flash/continuous glucose monitoring. *HbA1c measurements were available for monitoring in the latter part of this era. Fatality refers primarily to people with Type 1 Diabetes. Advanced hardware includes various technologies such as smart insulin pens and hybrid closed loop pumps, which are an automatic insulin delivery system that regulates basal insulin levels and typically integrate a CGM data sensor, transmitter and insulin delivery system.

The ecosystem of blood glucose management incorporating continuous glucose monitoring



Source: IQVIA, Aug 2019

Notes: The ecosystem of CGM and digital health apps for tracking TIR. *AGP or ambulatory glucose profile is a standardized, single page glucose report, developed by RS Mazze, D Lucido, O Langer, K Hartmann, D Robard and further developed by International Diabetes Center.25 It is recommended by an ATTD consensus group as standard for visualization of CGM data (Petrie et al., 2017). In patients with T1DM, RT-CGM use is associated with lower health care costs, fewer hospital admissions, and better glycemic management (Gill et al., 2018). Use of RT-CGM in T1DM patients is associated decrease in HbA1c level and health care system utilization compared with traditional SMBG (Parkin et al., 2017). CGM measurements are taken from interstitial fluid and not directly from blood.

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Methodology for assessing reduction in complications and associated costs achieved by improving TIR

1

- A relationship between HbA1c and TIR was needed as there is limited longitudinal TIR-claim data available and not yet a validated model using TIR as a primary input
- Two peer-reviewed articles indicating a mathematical relationship between TIR percentage achievement and HbA1c were identified
  - $HbA1c = 9.65 - 0.041 \times TIR^{70\text{-}180}$ *
  - $HbA1c = 12.31 - 0.08 \times TIR^{70\text{-}180}$ **

2

- Based on selected peer-reviewed articles, a conservative average current TIR of 58% was used for the analysis*^^
- 70% TIR was used as the minimum consensus target based on the ATTD working group consensus paper***
- Additionally, 80% was used as a target for the analysis which has recently been demonstrated by advanced insulin pump-CGM-treatment algorithm combination****

3

- The HbA1c values associated with TIR of 58%, 70% and 80% were calculated using the peer-reviewed articles
- These were used as input for the IQVIA Core Diabetes Model, a validated, peer-reviewed model, which simulates clinical outcomes and costs for individuals with either Type 1 or Type 2 Diabetes^ (For more details see Appendix and: https://www.core-Diabetes.com/)
- Associated complications and costs were estimated by the model

Source: IQVIA, Aug 2019; *Beck et al., 2019; **Vigersky et al., 2019, ***Battelino T, Danne T, Bergenstal RM et al., 2019; ****Lewis DM, Swain RS and Donner TW, 2018; ^See endnotes 42,43.
^^The current average is based on clinical trials. The average TIR for the overall US population may be lower.
Notes: Currently available risk equations do not include TIR as a variable but have HbA1c. As HbA1c is a core input of the model, TIR values are required to be converted into HbA1c prior to being modelled, per Beck et al., 2019 and Vigersky and McMahon, 2019.The model then takes HbA1c, in addition to other surrogate inputs such as blood pressure, weight and lipids, and generates long-term endpoints including life expectancy, incidence of macro/micro-vascular events and costs. Slope equations used to convert TIR into HbA1c were developed predominantly based on Type 1 Diabetes datasets per Beck et al., 2019, with a small Type 2 Diabetes population derived from Vigersky and McMahon, 2019.
Advancing Glyemic Control in Diabetes - New Approaches and Measures ~ Report by the IQVIA Institute for Human Data Science

The current and proposed alternate state of treatment for People with Diabetes

CURRENT STATE

Key Statistics

Age	41 years	TIR[70-180 23,24]	58%^
Indication	Type 1	TAR[>180 23,24]	37%
Duration of Diabetes	20 years	TBR[<70 23,24]	5%
HbA1c[23,24]	7.3-7.5%	No. of hypoglycemic[29] events/week	4.1

Current Management

- **Treatment:** Multiple daily injections of insulin
- **Blood Glucose Measurement:** SMBG using fingerstick and HbA1c; No CGM use

Key Complication Risks*

10-year cumulative incidence of developing complications

Myocardial infarction	3.29	Severe vision loss	9.12
End-state renal disease	3.85	Amputation	3.96

Psychosocial Profile

Anxiety related to blood glucose levels and fear of hypoglycemia

ALTERNATE STATE

Key Statistics

Age	41 years	TIR[70-180]	>70%
Indication	Type 1	TAR[>180]	<25%
Duration of Diabetes	20 years	TBR[<70]	<4%
HbA1c	6.5-7.0%	No. of hypoglycemic events/week	1.1

Current Management

- **Treatment:** Insulin pump delivery system of next-generation insulins*

Blood Glucose Measurement: CGM-TIR. Ambulatory Glucose Profile** and HbA1c

Key Complication Risks

10-year cumulative incidence of developing complications

Myocardial infarction	2.65-2.97	Severe vision loss	7.99-8.44
End-state renal disease	3.79-3.81	Amputation	3.73-3.82

Psychosocial Profile

Increased confidence in overall glucose management

Source: Beck et al., 2019; Vigersky and McMahon, 2019; Bosi et al., 2019; Battelino et al., 2019; + Estimated by IQVIA Core Diabetes Model, v9.0 2019
Notes: ^ Current average TIR is based on clinical trials, the TIR in the US population may be lower. PwD vignette illustrating the current and proposed alternate state for PwD. * Insulin pump systems may not be needed for all PwDs. ** AGP; ambulatory glucose profile is a standardized, single page glucose report, developed by RS Mazze, D Lucido, O Langer, K Hartmann, D Robard and further developed by International Diabetes Center.25 This visual is produced automatically by CGM-supporting software and provides the individual with a summarized profile of their glucose metrics over a set period of time, including TIR, TAR and TBR. The average TIR, TAR, TBR is based on Beck et al., 2019 where a masked baseline CGM was used to collect the baseline data, this data represents the best estimate of PwD currently not on CGMs. SMBG = self-monitoring of blood glucose. Hypo events refer to both severe and non-severe hypoglycemic events.

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10-year incidence of developing Diabetes-related complications after improving TIR in PwD with Type 1 and Type 2 Diabetes

TYPE 1 Diabetes

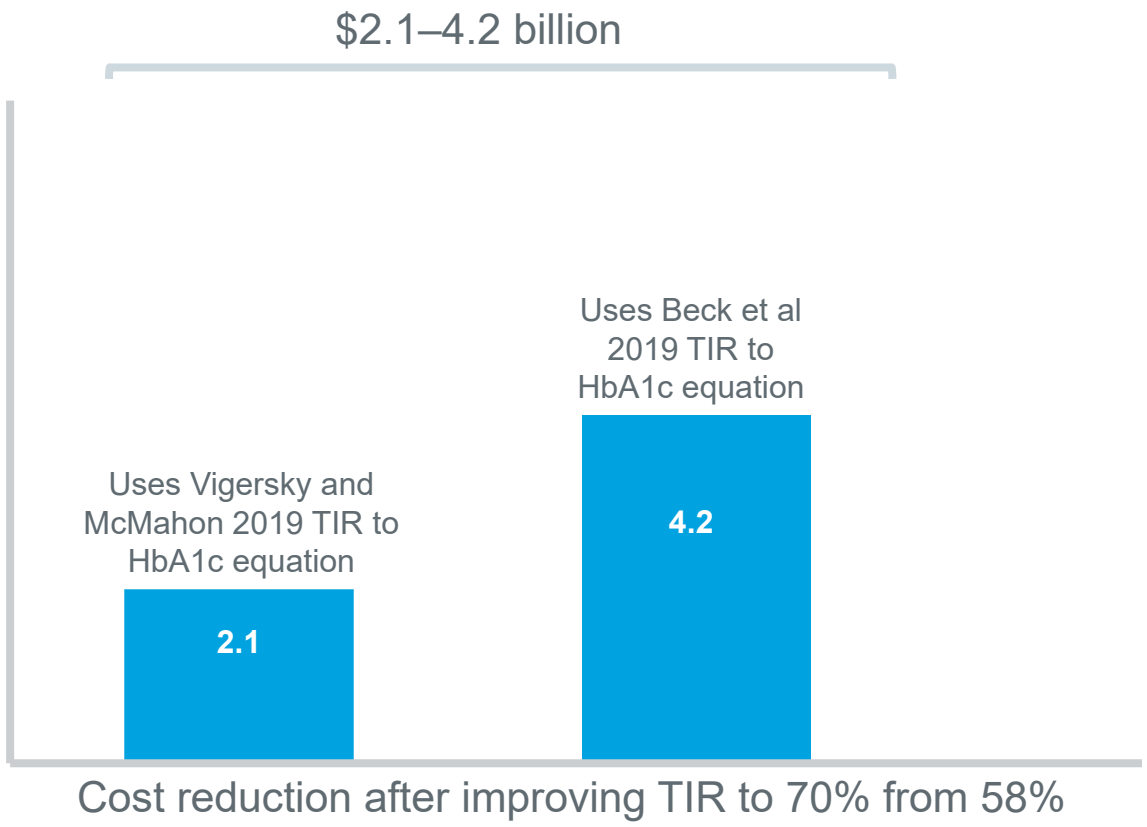
COMPLICATION	58% TIR	70% TIR	80% TIR
Myocardial infarction	3.29	2.65 – 2.97	2.25 – 2.70
End-stage renal disease	3.85	3.79 – 3.81	3.72 – 3.73
Severe vision loss	9.12	7.99 – 8.44	7.55 – 8.00
Amputation	3.96	3.73 – 3.82	3.57 – 3.73

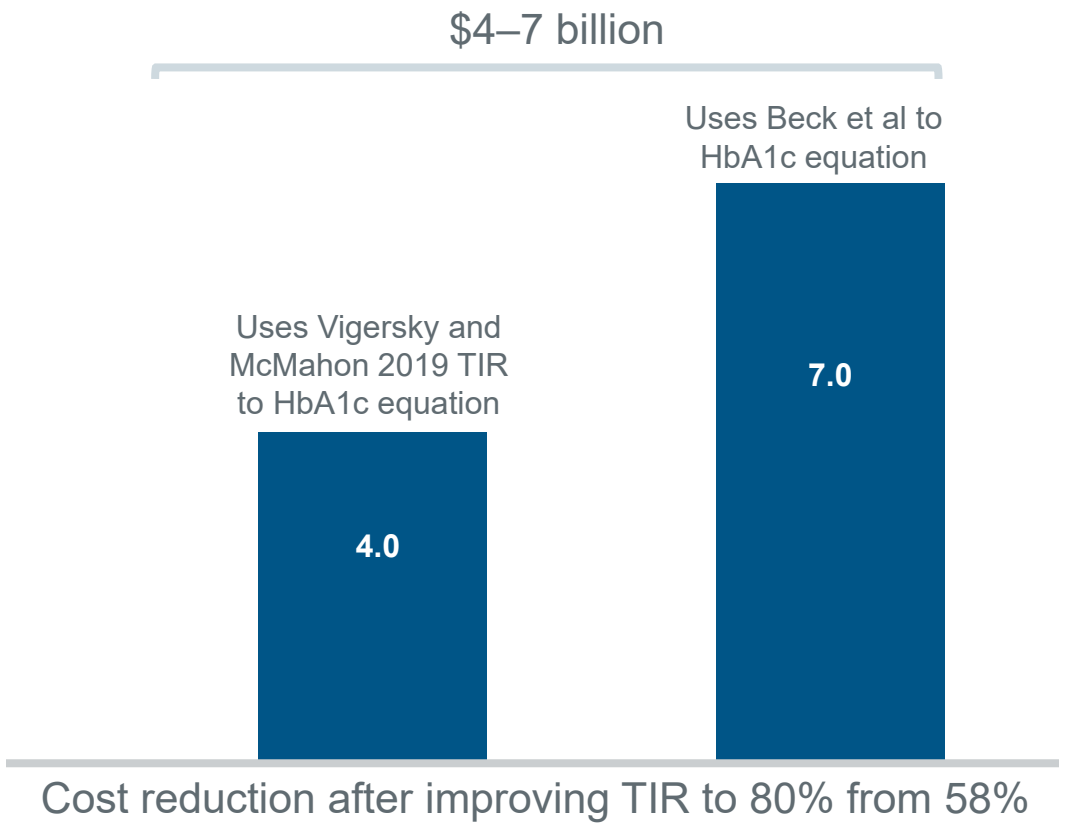
TYPE 2 Diabetes

COMPLICATION	58% TIR	70% TIR	80% TIR
Myocardial infarction	12.76	11.99 – 12.39	11.37 – 11.97
End-stage renal disease	2.84	1.94 – 2.34	1.42 – 1.98
Severe vision loss	5.18	4.78 – 4.98	4.56 – 4.83
Amputation	1.00	0.97	0.95-0.96

Source: IQVIA Core Diabetes Model, 2019
Notes: The IQVIA Core Diabetes Model was used to calculate the cumulative incidence of developing major Diabetes-related complications over a 10-year time horizon in people with Type 1 and Type 2 Diabetes. Currently available risk equations do not include TIR as a variable but have HbA1c. As HbA1c is a core input of the model, TIR values are required to be converted into HbA1c prior to being modelled, per Beck et al., 2019 and Vigersky and McMahon, 2019. 10-year cumulative incidence refers to the percentage of patients having a complication over a ten-year period.

10-year cost reduction by improving TIR in people with Type 1 and Type 2 Diabetes to 70% and 80%, US$Bn

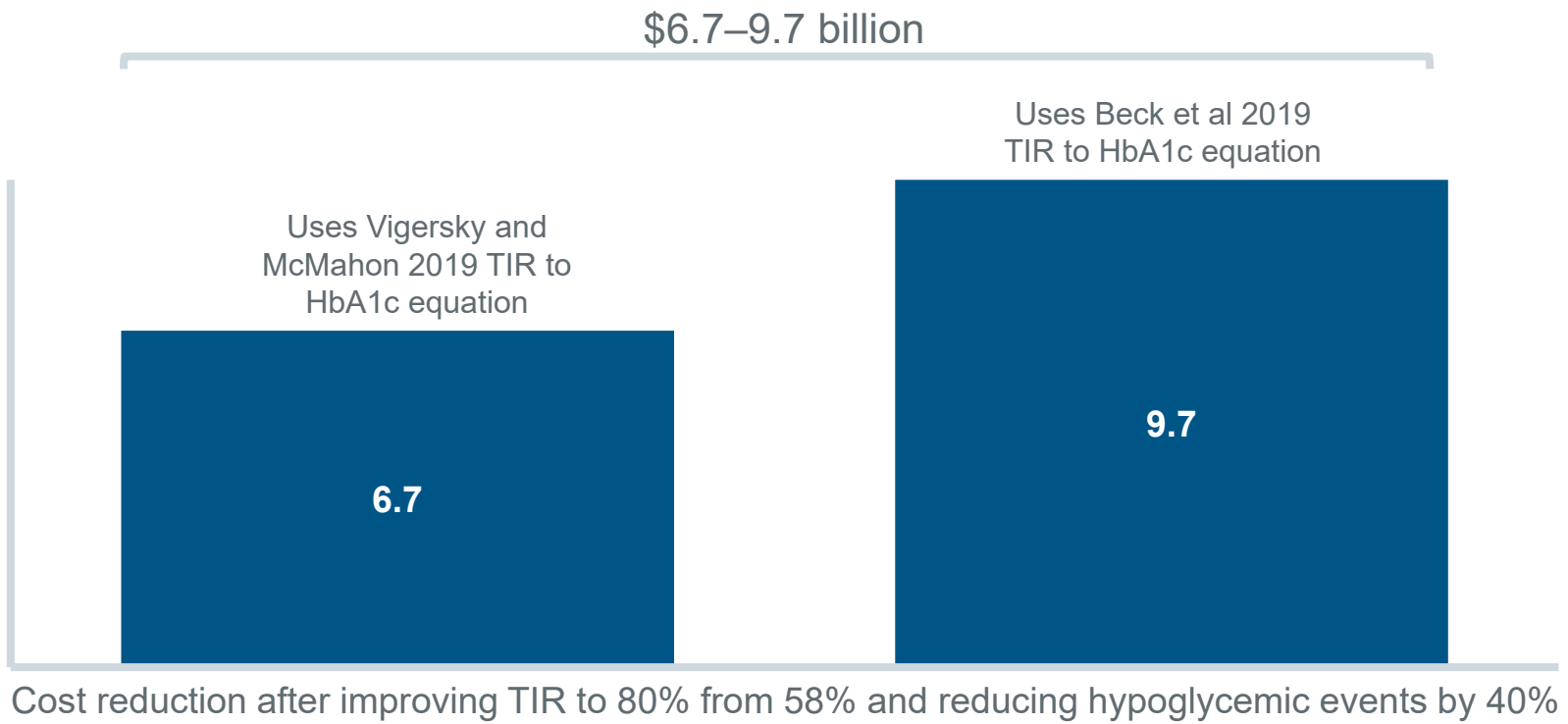




Source: IQVIA Core Diabetes Model, 2019

Notes: Shown is a summary of the 10-year cost ($Bn) reduction after improving TIR from the current average of 58% to 80% in people with Type 1 and Type 2 Diabetes. Currently available risk equations do not include TIR as a variable but have HbA1c. As HbA1c is a core input of the model, TIR values are required to be converted into HbA1c prior to being modelled, per Beck et al., 2019 and Vigersky and McMahon, 2019. Outputs from the model are provided on a per PwD basis, and therefore required multiplying by the total number of U.S. insulin-dependent people with Type 1 and Type 2 Diabetes to generate the figures shown. Population sizes used to make these calculations were 1.25Mn for Type 1 Diabetes (per the ADA), and 5.86Mn for Type 2 Diabetes (per the CDC National Diabetes Statistics Report, 2017). The total complication costs at different TIR values are as follows: At 58% = $207.4Bn; at 70% = $203.1-205.3Bn; at 80%= $200.4-203.4Bn.

Summary of 10-year cost reduction after improving TIR to 80% and reducing the rate of hypoglycemic events, US$Bn



Source: IQVIA Core Diabetes Model, 2019

Notes: Shown is a summary of the 10-year cost ($Bn) reduction after improving TIR from the current average of 58% to 80% in people with Type 1 and Type 2 Diabetes, as well as the costs reduced after reducing hypoglycemic event rate by 40% in people with Type 1 Diabetes. Currently available risk equations do not include TIR as a variable but have HbA1c. As HbA1c is a core input of the model, TIR values are required to be converted into HbA1c prior to being modelled, per Beck et al., 2019 and Vigersky and McMahon, 2019. The range of values shown are driven by the differences in equations linking HbA1c and TIR in Beck et al., 2019 and Vigersky and McMahon, 2019. Outputs from the model are provided on a per PwD basis, and therefore required multiplying by the total number of U.S. insulin-dependent people with Type 1 and Type 2 Diabetes to generate the figures shown. Population sizes used to make these calculations were 1.25Mn for Type 1 Diabetes (per the ADA), and 5.86Mn for Type 2 Diabetes (per the CDC National Diabetes Statistics Report, 2017). The total complication costs at different TIR values were as follows: At 58% = $207.4Bn, At 80% = $200.4-203.4Bn, and with reduction in Hypoglycemic events = $197.7-200.6Bn.

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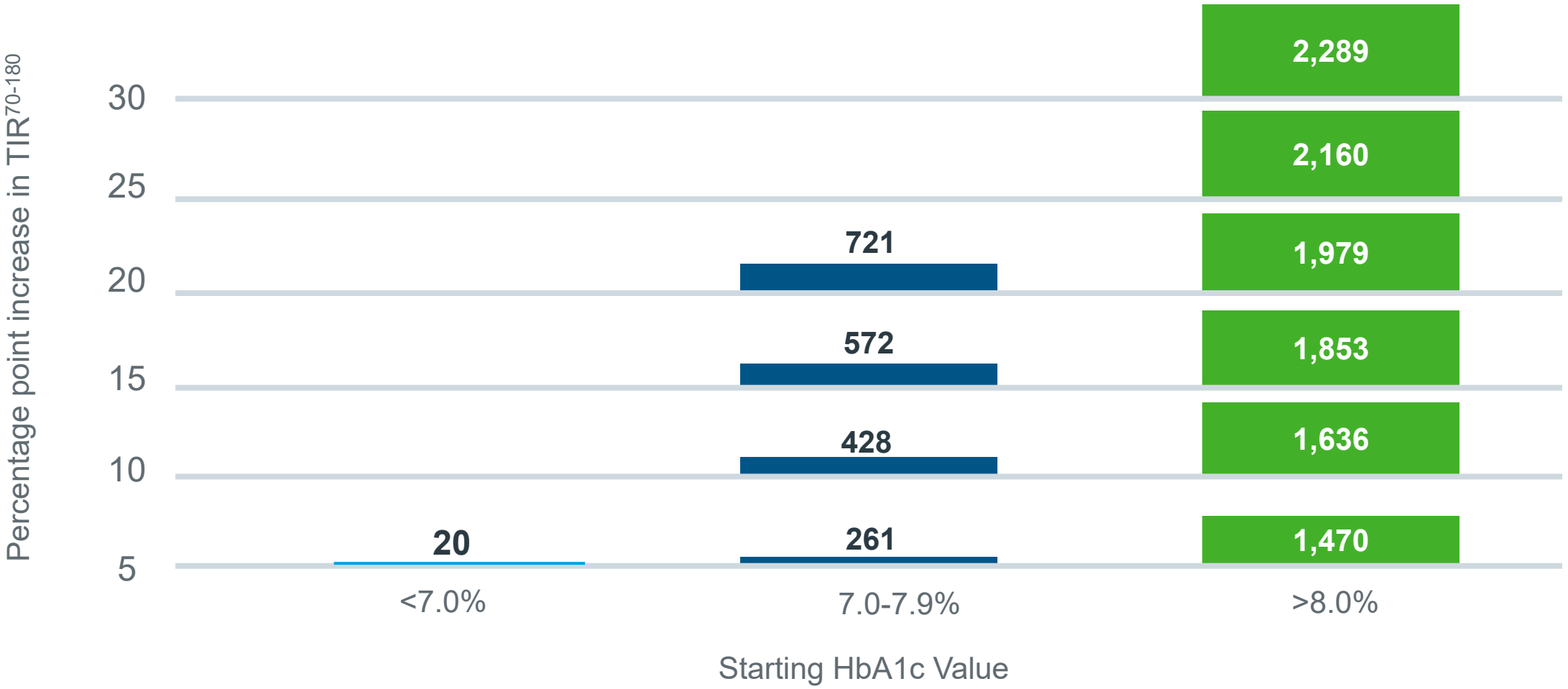
10-year per person cost reduction associated with incrementally improving TIR in Type 1 Diabetes, US$



Source: IQVIA Core Diabetes Model, 2019
Notes: The IQVIA Core Diabetes Model was used to determine the per person 10-year reduction in costs ($) associated with incrementally improving TIR at different starting HbA1c levels in people with Type 1 diabetes. Currently available risk equations do not include TIR as a variable but have HbA1c. As HbA1c is a core input of the model, TIR values are required to be converted into HbA1c prior to being modelled, per Beck et al., 2019 and Vigersky and McMahon, 2019.

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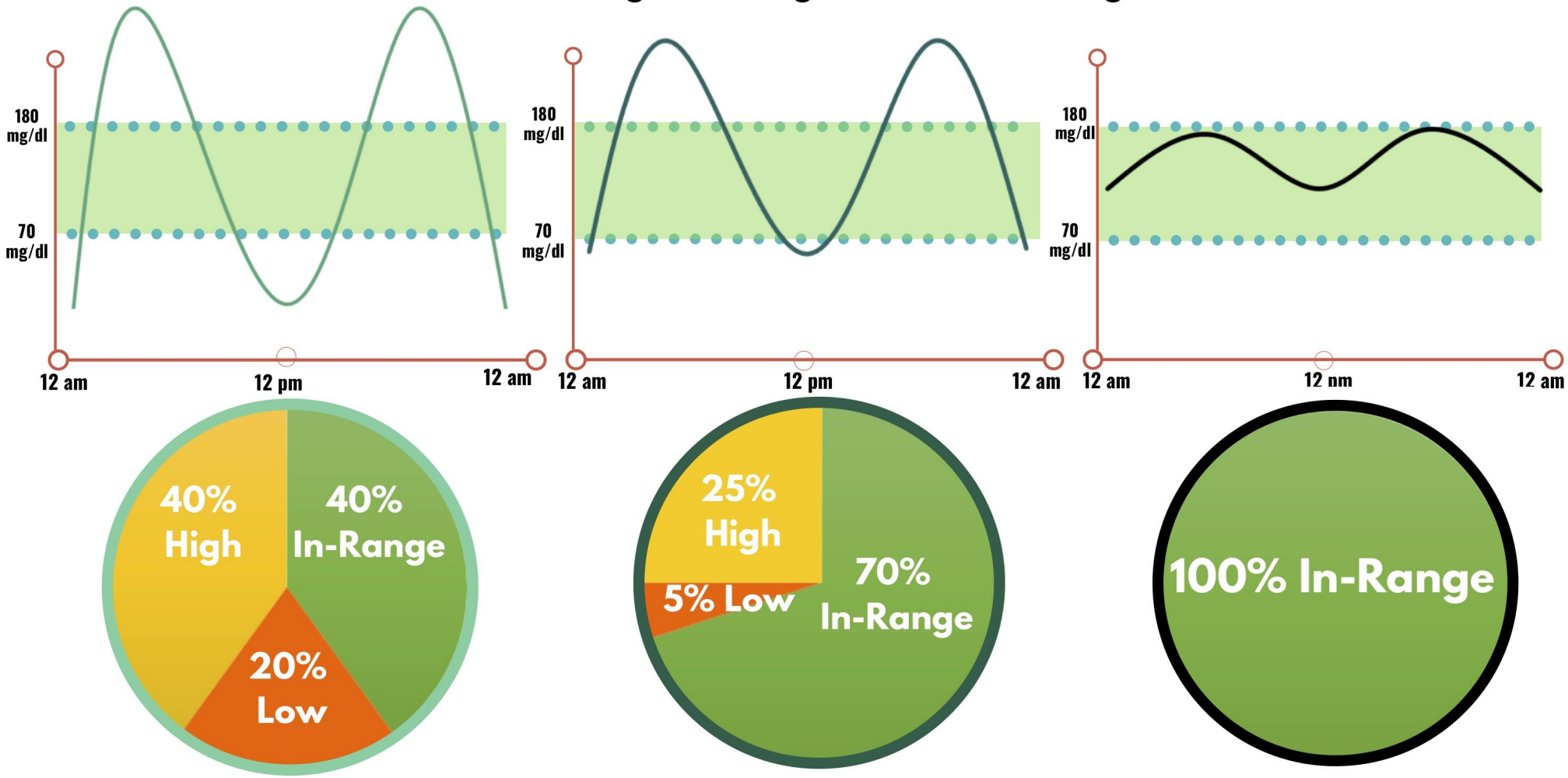
Why People with Diabetes Love Time-in-Range

THE MANY FACES OF A 7% A1C

(and an average blood glucose of 154 mg/dl)



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One-click access to my CGM patterns = Gamechanger!

7 days Oct 23, 2019 - Oct 29, 2019

Time in Range

29% High
65% In Range
4% Low
2% Urgent Low

Glucose Management Indicator (GMI)

Not enough data available

Average Glucose (CGM)

148 mg/dL

Patterns

Nighttime Highs

Best Day

Sunday, October 27

7 days Oct 5, 2019 - Oct 11, 2019

Time in Range

6% High
86% In Range
6% Low
2% Urgent Low

Glucose Management Indicator (GMI)

Not enough data available

Average Glucose (CGM)

117 mg/dL

Patterns

No patterns detected

Best Day

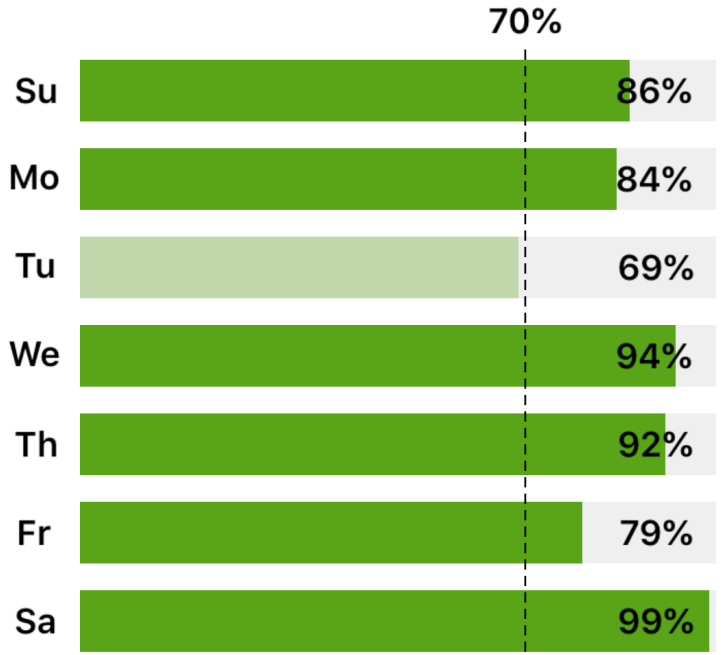
Wednesday, October 9

7 Days

You reached your Goal: Time in Range 6 out of 7 days.

Edit Goal

Oct 6, 2019 - Oct 12, 2019



Data: Kelly Close, Dexcom CLARITY app

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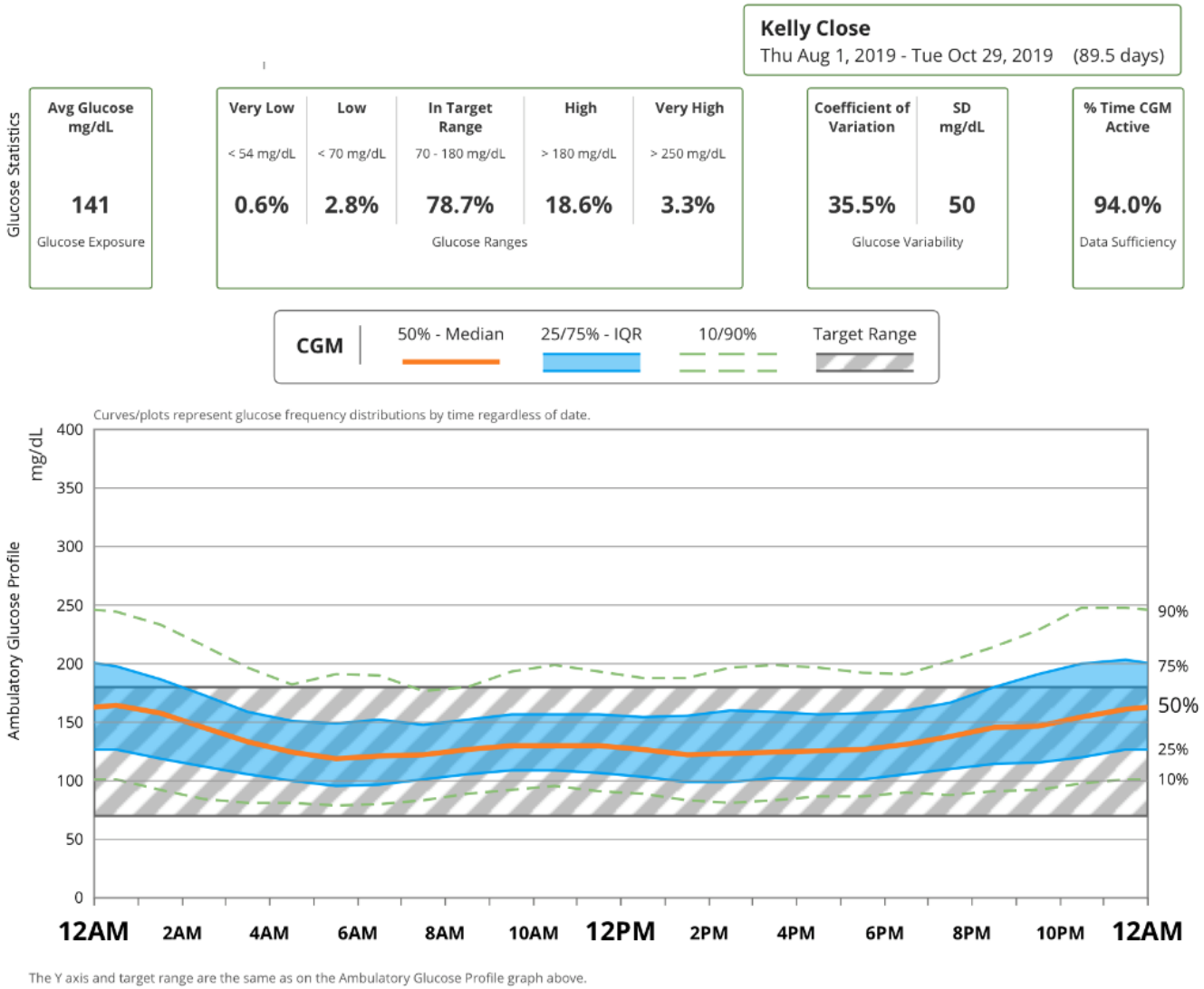
Ambulatory Glucose Profile (AGP) shows my 90-day blood glucose trends



Data Source: Kelly Close, Dexcom CLARITY app

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Automated weekly emails and notifications: frictionless data insights

Weekly Summary

Sun Sep 29, 2019 - Sat Oct 5, 2019

Time in Range

81%

-2%
Decrease since last week

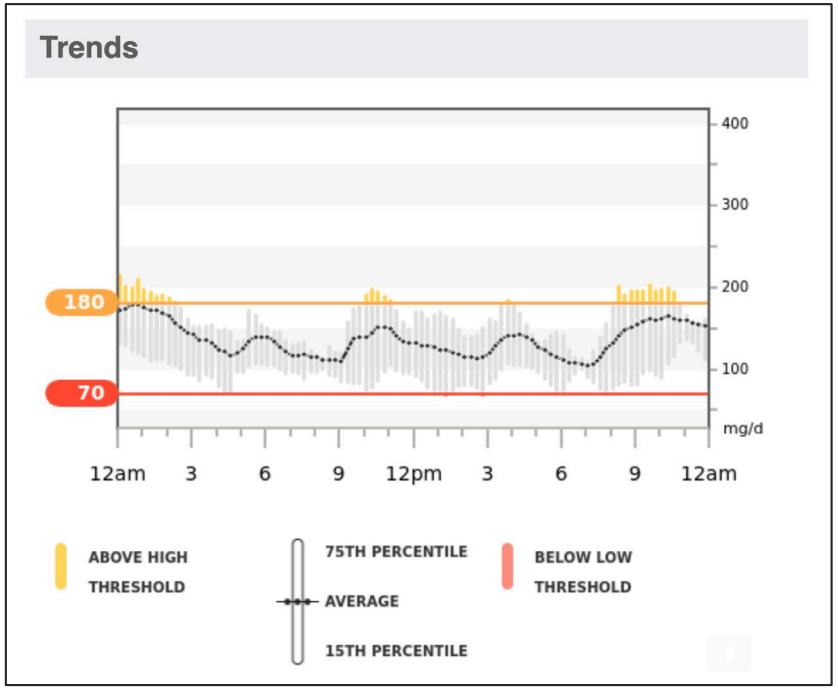
136 mg/dL
Average glucose

44 mg/dL
Standard deviation

Target Range Settings:
Daytime (6:00 AM – 10:00 PM): 70 – 180 mg/dL
Nighttime (10:00 PM – 6:00 AM): 70 – 180 mg/dL

dQ&A (2019):
78% of Dexcom users currently use the CLARITY app

dQ&A (2018):
57% of Dexcom G5 and t:slim X2 users use the CLARITY app



Data Source: Kelly Close, Dexcom CLARITY app

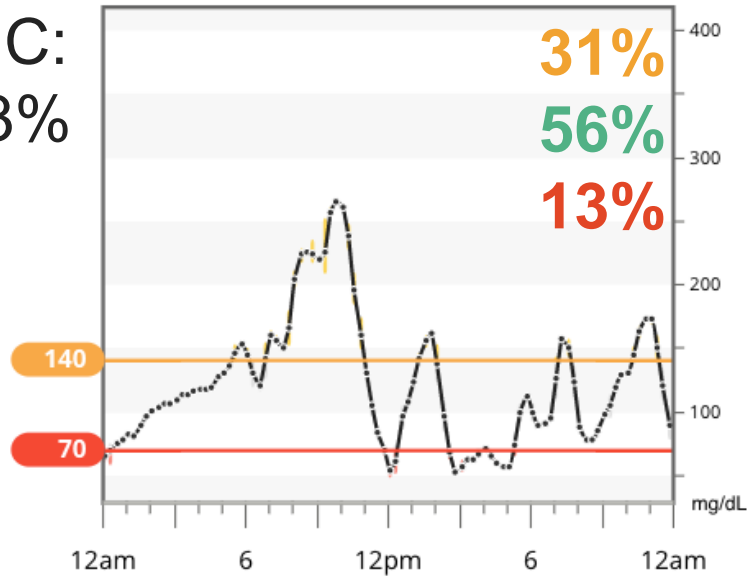
Questions we wonder about quarterly A1Cs:

- What times of day are in-range BGs, highs, and lows occurring? Why?
- Should medication dose be adjusted? Timing?
- What's going on with food, sleep, exercise, stress, decisions? What is working? What is not working?
- I just made a change – but did it make a difference?
- What is my quality of life and level of Diabetes burden?
- What experiments should I try going forward?

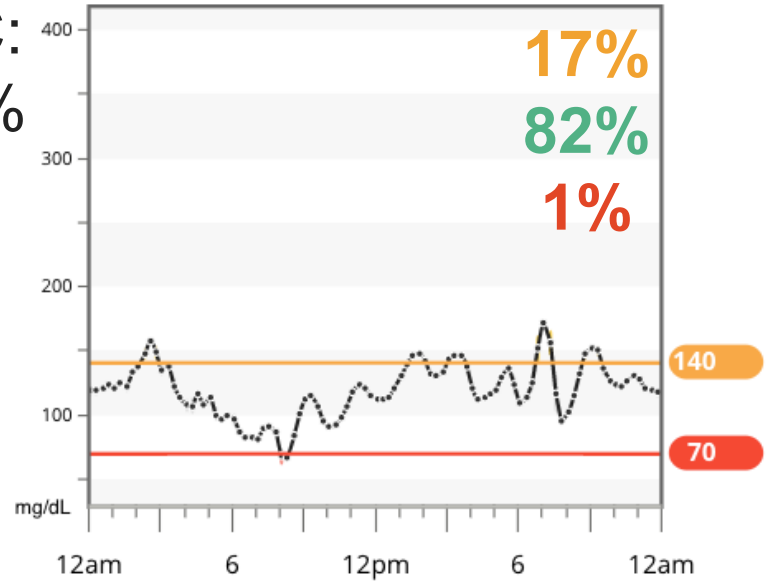
A1C Does Not Give Enough Data to Answer These Q's!

TIR can help to contextualize A1C

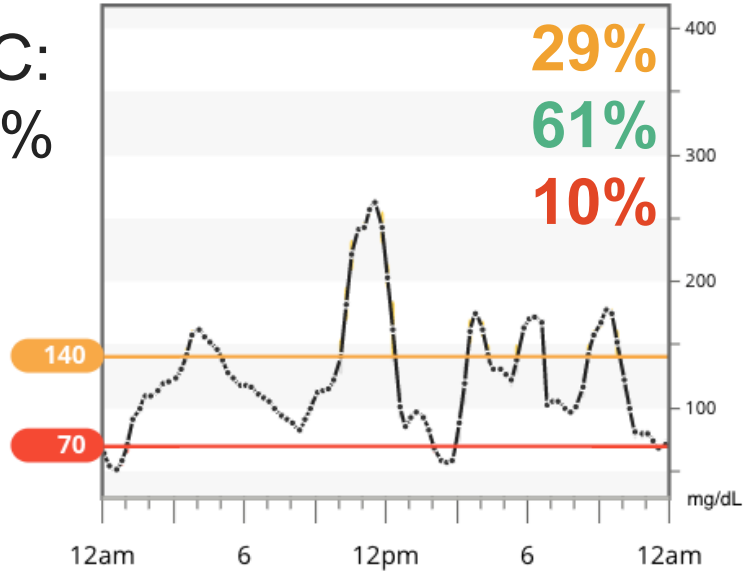
A1C: 6.3%



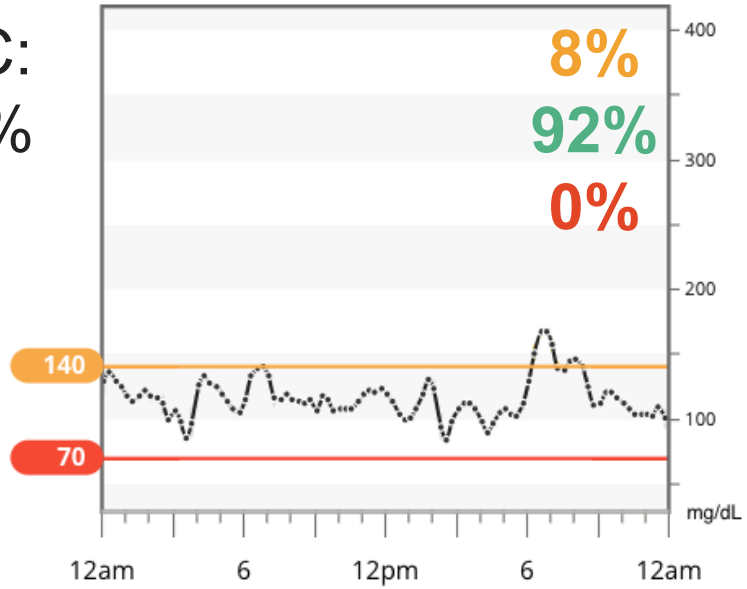
A1C: 6.2%



A1C: 6.3%



A1C: 6.1%



Source: Adam Brown

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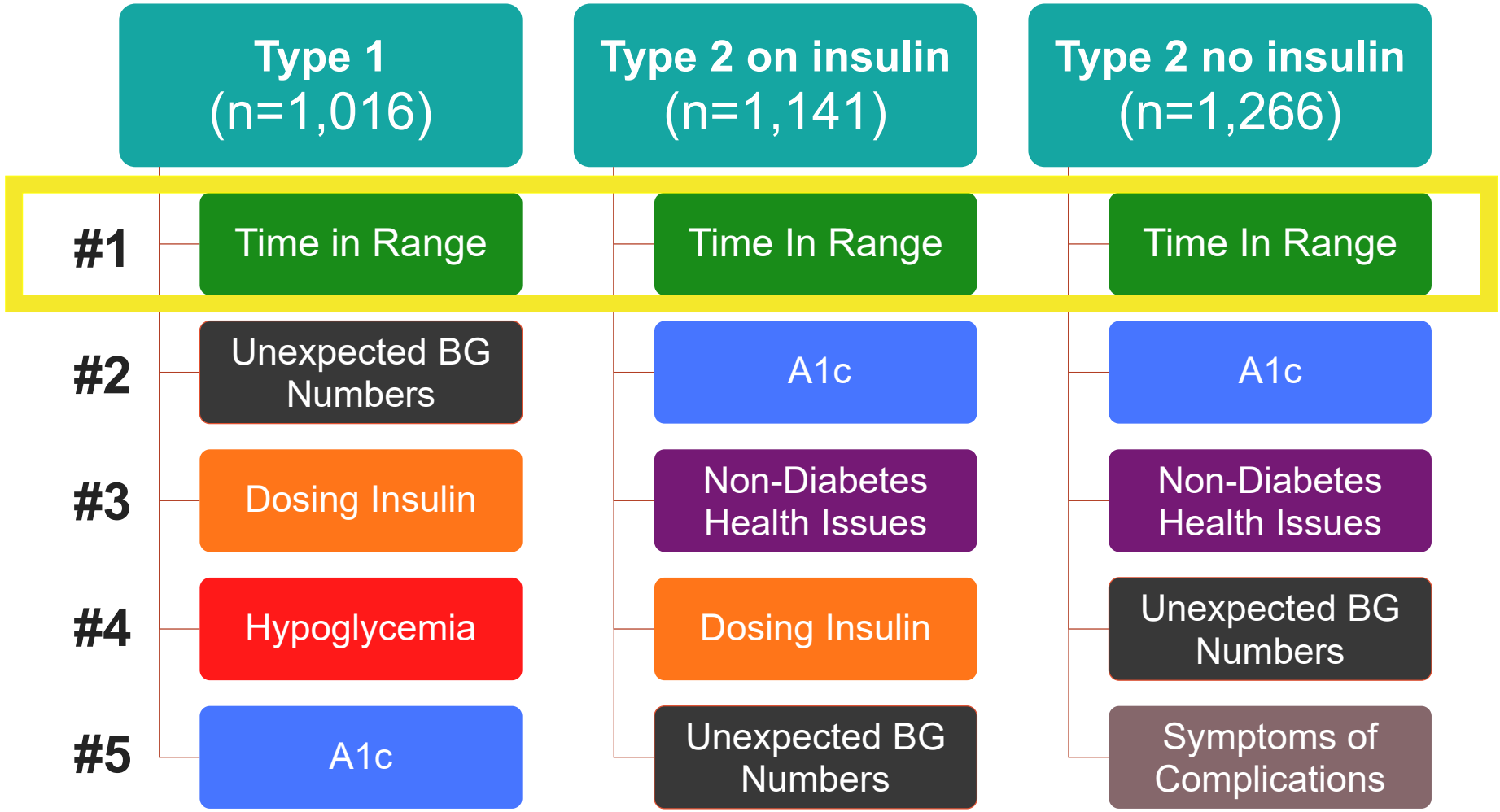
Time-in-Range has “A Big Impact” on daily life



Gopisetty et al., “How Does Diabetes Affect Daily Life? A Beyond-A1C Perspective on Unmet Needs” *Clinical Diabetes* 2018

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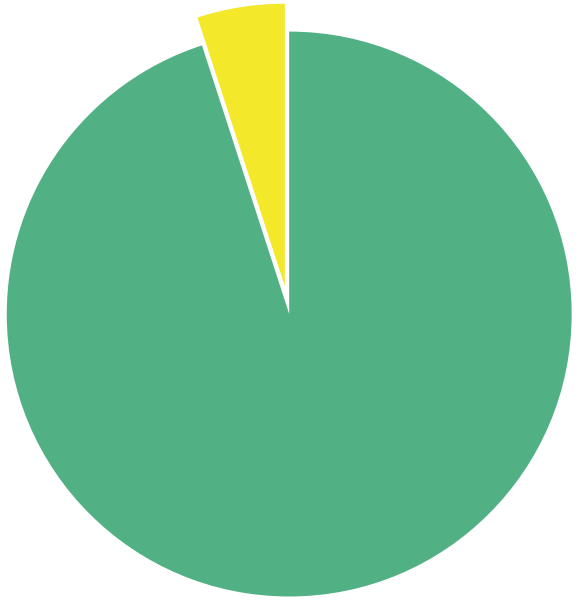
+5% TIR = +1 hour per day



+8% TIR per day = 1 extra month *per year* in-range

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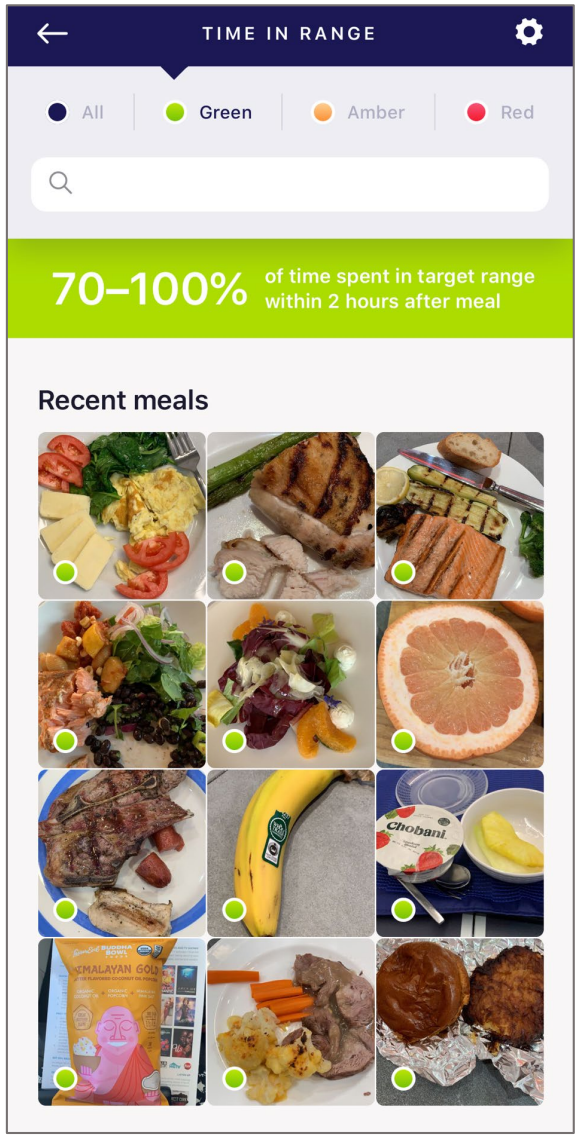
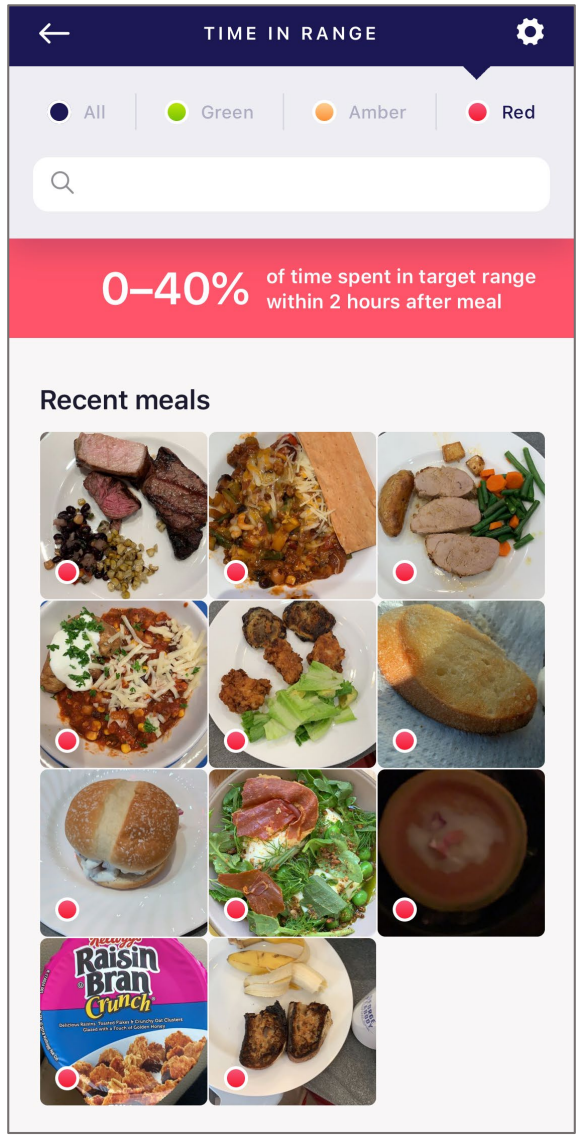
People with Diabetes can *use* TIR:

What happens when I eat different foods?

Photos + CGM = Magic!





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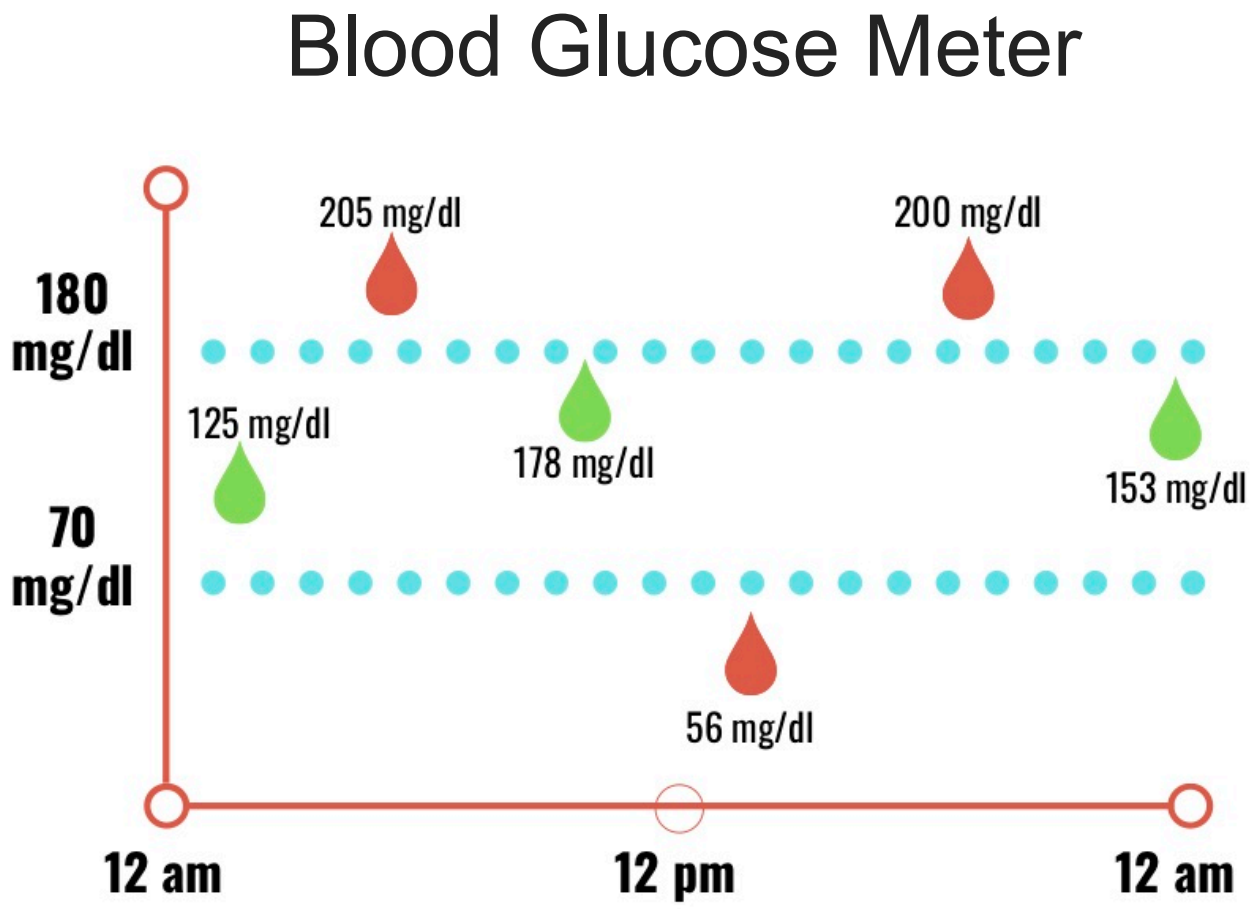
TIR exists whether or not it's being measured with CGM using professional CGMs



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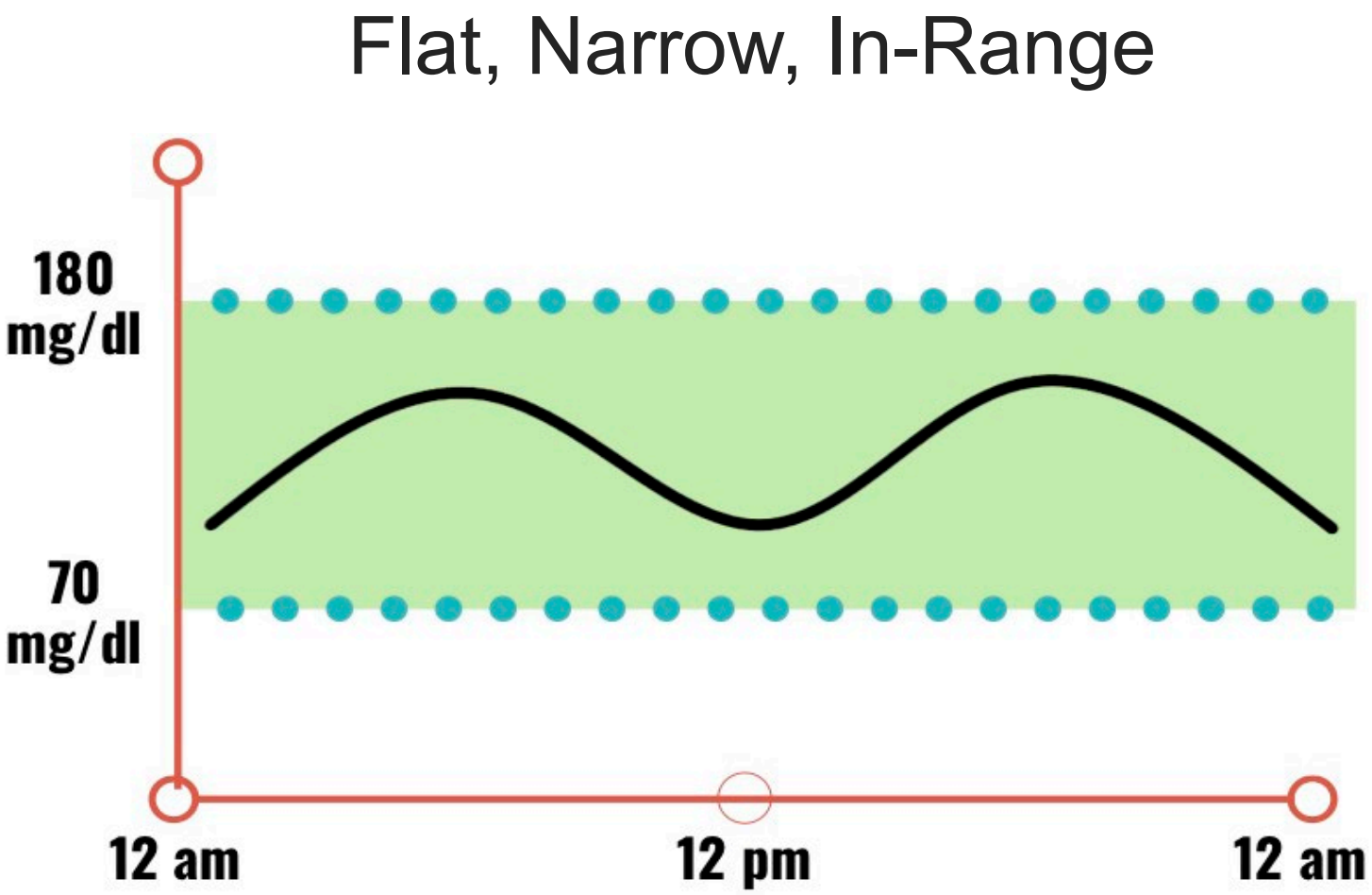
Diabetes is not destiny: striving for FNIR!



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What can we learn from ~500,000 CGM users?

N=470,643 readers	**Median CGM User 10 Scans/Day**	**Lowest-Scan Users 4 Scans/Day**	**Highest-Scan Users 40 Scans/Day**
Estimated A1c	7.5%	8.2%	6.7%
Time-in-Range (70-180 mg/dl)	56% 13.5 hours/day	48% 11.7 hours/day	70% 16.9 hours/day
Time ≤54 mg/dl	2% 34 minutes/day	2% 34 minutes/day	1.6% 24 minutes/day
Time >240	17% 4 hours/day	25% 6 hours/day	9% 2.2 hours/day

Source: Abbott Freestyle Libre RWD, Abbott Poster, ATTD 2019

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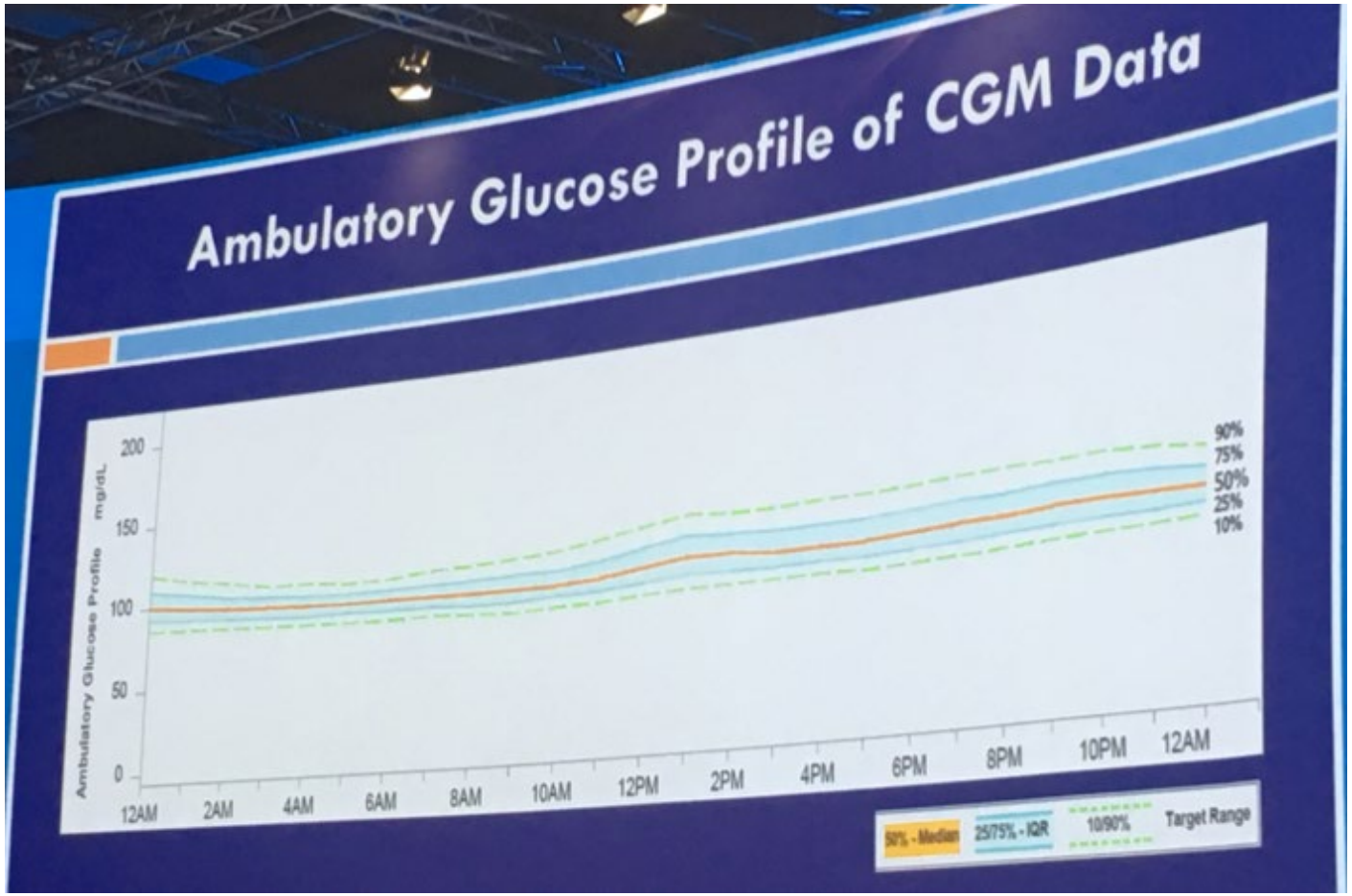
Normoglycemia—the goal.



10 days blinded CGM (n=153 without Diabetes)

T1D Exchange®

Mean glucose:
99 mg/dl

Time 70–140 mg/dl:
97%

Coefficient of Variation:
17%

Beck, EASD 2019

diaTribe®

CITY study. 6 months of RT-CGM in Type 1s Ages 14-25

Mean A1c

8.9% 8.5%

Mean Time-in-Range

37% 43%

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Mean Time >180 mg/dl

58% 54%

Mean Time>300 mg/dl

18% 14%

Mean Coefficient of Variation (CV)

42% 39%

Laffel, ADA 2019

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WISDM study. 6 months of RT-CGM in Type 1s Ages 60+

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JDRF IMPROVING LIVES. CURING TYPE 1 DIABETES.

Mean A1c

7.6% 7.2%

Mean Time-in Range

56% 63%

Mean Time >180 mg/dl

37% 34%

Mean Time <70 mg/dl

5% 3%

Mean Coefficient of Variation (CV)

41% 37%

Carlson, ENDO 2019

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“It’s not just giving CGM to those with A1cs
of 7.2% and getting them down to 6.9%.
We won’t see a flattening of the curve
if we only do that…***We need to be more equitable, regardless of A1c, ability to pay, race, or ethnicity***. It’ll take more work
on our part but we’ve got to make it happen
if we’re going to flatten that curve.”

— Dr. Rich Bergenstal, ATTD 2019

Progress! ADA posters show promise of CGM in:

Youth with Type 2 Diabetes (973-P; LaRoche et al.)

Newly Diagnosed Type 1s (1358-P; Prahalad et al.)

Primary Care (1280-P; Martens et al.)

Emerging standard of care includes TIR, based on CGM developments

J Diabetes Sci Technol. 2019 Jul;13(4):614-626. doi: 10.1177/1932296818822496. Epub 2019 Jan 13.

The Relationships Between Time in Range, Hyperglycemia Metrics, and HbA1c.

Beck RW[1], Bergenstal RM[2], Cheng P[1], Kollman C[1], Carlson AL[2], Johnson ML[2], Rodbard D[3].

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1 1 Jaeb Center for Health Research, Tampa, FL, USA.
2 2 International Diabetes Center, Park Nicollet and HealthPartners, St. Louis Park, MN, USA.
3 3 Biomedical Informatics Consultants, LLC, Potomac, MD, USA.

Diabetes Care. 2019 Mar;42(3):400-405. doi: 10.2337/dc18-1444. Epub 2018 Oct 23.

Validation of Time in Range as an Outcome Measure for Diabetes Clinical Trials.

Beck RW[1], Bergenstal RM[2], Riddlesworth TD[3], Kollman C[3], Li Z[3], Brown AS[4], Close KL[5].

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1 Jaeb Center for Health Research, Tampa, FL rbeck@jaeb.org.
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Learn more at diaTribe.org/time-in-range

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Benefits of Time in Range: New Study Shows Cost Savings

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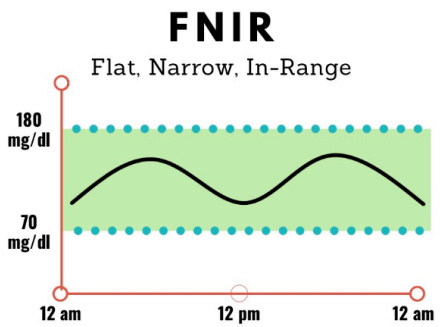
By Eliza Skoler and Albert Cai

A new paper suggests that as people with diabetes increase their time in range, healthcare costs decrease



IQVIA, a healthcare consulting firm, published a 22-page paper describing the limitations of A1C and the potential financial benefits of improving time in range, the time a person spends with blood glucose levels between 70-180 mg/dl. The paper was sponsored by Lilly

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Time-in-Range: What's an Achievable Goal with Diabetes?

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By Adam Brown

My approach to time-in-range goals, five key tips to spend more time-in-range each day, and what's still to come from experts…

Q: "What do you think is an attainable percent time in range? My son's doctor is happy about his A1c around 7.1%, and I think that can lead to being complacent or thinking he is good enough. What is a good goal for percent time in range on a daily basis?" – Madeline G.

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CGM and Time-in-Range: What Do Diabetes Experts Think About Goals?

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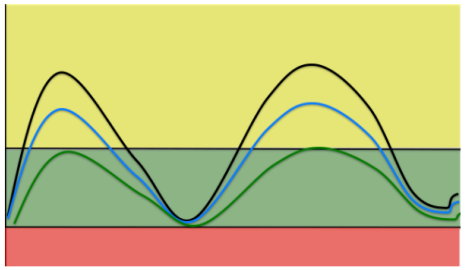
By Kelly Close and Adam Brown



We interviewed 15 experts about time-in-range goals for those wearing CGM. Here's what they said…

It's been a big year in continuous glucose monitoring (CGM)! Talking with Dr. Roy Beck over the weekend, he in fact said, "If I had to pick one thing that is most important for diabetes management among faster insulins, using a pump, and using CGM, it would be CGM."

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Time-in-Range Tips: Expert-Defined Goals, Plus Insights from Almost 500,000 FreeStyle Libre Users

5/1/19 - NEW NOW NEXT

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By Emma Ryan

The latest updates on time-in-range goals for people with all types of diabetes, and insights linking FreeStyle Libre scanning frequency to outcomes

Time-in-range goes beyond A1C describe the amount of time spent "in range" (70-180 mg/dl) and at high and low blood

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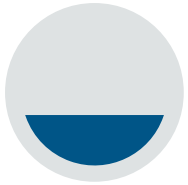
Time-in-Range: Thoughts from an Endocrinologist

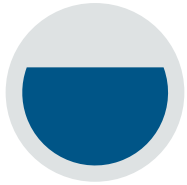
Three pillars to manage dysglycemia

The whole is greater than the sum of its parts



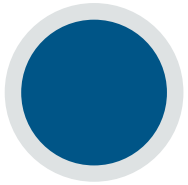
Chronic Hyperglycemia

DCCT (T1D) and UKPDS (T2D) have clearly demonstrated a link between A1c and development of Diabetes related complications



Hypoglycemia

The limiting factor in treating People with Diabetes



Glycemic Variability

Emerging glycemic target

TIR and GV are mathematically and conceptually linked, they are not interchangeable

Glycemic Variability

Measurements of fluctuations of glucose over an interval of time

	Computation	Interpretation	Advantages and limitations
SD of mean glucose concentration	From the mean SD (variance)	Short-term within-day glucose variability	Traditional measure of dispersion for large quantities of data such as those recorded with CGM systems and directly calculated by devices
CV for glucose	Calculated as %: (SD ÷ mean glucose) x 100	Short-term within-day glucose variability in diabetes	Adjusted on the mean glucose concentration and easily calculated from SD and mean
MAGE	Mean differences from peaks to nadirs	Short-term within-day glucose variability	Major glucose fluctuations; not directly reported by CGM devices but is simple to calculate
MODD	24 h mean absolute differences between two values measured at the same timepoint	Short-term between-day glucose variability	Not directly reported by CGM devices; requires additional computation, but is easy to interpret
CONGA	Integrates the duration and degree of glucose excursions	Short-term within-day temporal glucose variability	Complex calculation
ADRR	Sum of the daily peak risks for hypoglycaemia and hyperglycaemia	Composite of short-term within-day and between-day temporal glucose variability	Complex calculation
LBGI and HBGI	Preceded by a log transformation to render symmetrical the skewed distribution of glucose values	Risk indices for predicting hypoglycaemia (LBGI) or hyperglycaemia (HGBI)	Complex calculation; more oriented towards capturing the risk for severe hypoglycaemia and hyperglycaemia than assessing glycaemic variability
MAG	Incremental or decremental changes in glucose	Short-term within-day temporal variability	Fairly complex calculation
IQR of AGP	Distribution of glucose data at a given timepoint calculated from non-parametric statistics	Reflects the presence or absence of day-to-day synchrony in glucose patterns at a given time	Measure of dispersion for small amount of data such as those recorded at a given timepoint over several days (directly reported by the Abbott FreeStyle Libre)
Visit-to-visit changes	Measures of variability (SD, CV) of HbA_{1c}, FPG, etc between sequential visits	Long-term variability in glucose homoeostasis	Measures that are very heterogeneous in design

CGM=continuous glucose monitoring. CV=coefficient of variation. MAGE=mean amplitude of glycaemic excursions. MODD=mean of daily differences. CONGA=continuous overlapping net glycaemic action. ADRR=average daily risk range. LBGI=low blood glucose index. HBGI=high blood glucose index. MAG=mean absolute glucose variation. AGP=averaged glycaemic profile over several consecutive days (14 days with the Abbott FreeStyle Libre). FPG=fasting plasma glucose.

Short-term GV: within-day and between day

Long-term GV: based on serial determinations over a longer period of time, usually involving HbA1c

There is no consensus on how short-term or longer-term GV should be measured and the appropriate metrics for characterizing it clinically

Antonio Ceriello, Louis Monnier, David Owens www.thelancet.com/Diabetes-endocrinology Vol 7 March 2019

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Glycemic Variability* *TIR and GV are mathematically and conceptually linked, they are not interchangeable*

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Antonio Ceriello, Louis Monnier, David Owens www.thelancet.com/diabetes-endocrinology Vol 7 March 2019

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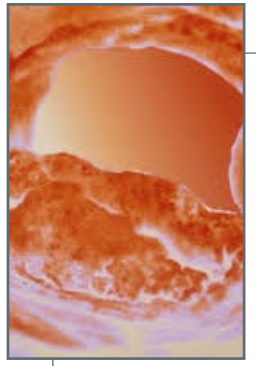
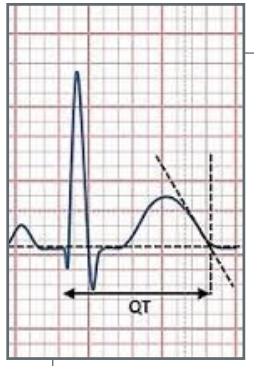
GV and CV clinical outcomes

Before 2015: Several studies had shown a positive association between GV and macro (and micro)vascular complications

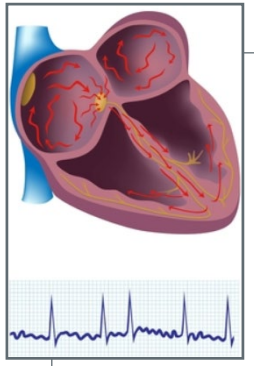
Since 2015: Studies have supported this is an independent risk factor for total mortality and CV death in both T1 and T2



Adversely affect plaque stability in both T1D and T2D



Extends cQT interval duration and dispersion



Increased risk of A Fib and HF

Gohbara M, Hibi K, Mitsuhashi T, et al. Glycemic variability on continuous glucose monitoring system correlates with non-culprit vessel coronary plaque vulnerability in patients with first-episode acute coronary syndrome—Optical Coherence Tomography Study. Circ J 2016; 80: 202–10.
Gu J, Fan YQ, Zhang JF, Wang CQ. Association of hemoglobin A1c variability and the incidence of heart failure with preserved ejection fraction in patients with type 2 Diabetes mellitus and arterial hypertension. Hellenic J Cardiol 2017; published online Aug 15. DOI:10.1016/j.hjc.2017.08.001.
Sertbas Y, Ozdemir A, Sertbas M, Dayan A, Sancak S, Uyan C. The effect of glucose variability on QTc duration and dispersion in patients with type 2 Diabetes mellitus. Pak J Med Sci 2017; 33: 22–26.

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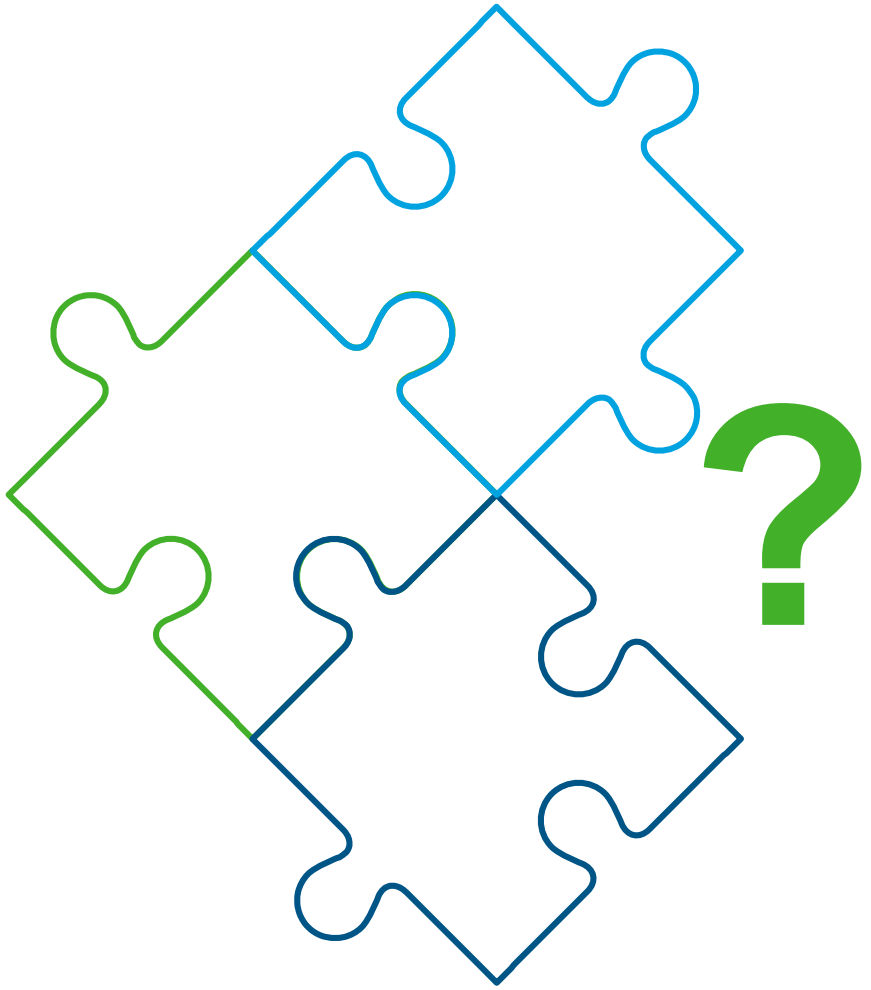
Diabetic Kidney Disease

Diabetes is the leading cause of CKD in the world

- The most important RF for developing DKD is hyperglycemic burden (hyperglycemic exposure over time)
  - The structural abnormalities seen in DKD are unique to Diabetes and develop only in the context of elevated glucose levels
  - Not everyone with poor glycemic control develop renal disease
  - Those with intensive control can develop DKD
- Are we missing a something…such as the limitations of A1c…GV?



Diabetic Kidney Disease

GV and DKD

T2D

A1c variability was found to associate with worsening albuminuria in cohort of individuals with T2D.

HbA1c variability in type 2 diabetes is associated with the occurrence of new-onset albuminuria within three years, possibly improving 3-year prediction of new-onset albuminuria.

T1D

The longitudinal Finnish Diabetic nephropathy study of individuals with T1D, long-term **A1c variability** predicted the development and progression of renal disease.

DCCT post-hoc analysis showed an association between **A1c variability** and the microvascular complications of diabetes.

There is limited to no data on the impact of day-to-day glycemic variability on DKD in T1D or T2D.

Evidence exists that **hypo ➡ hyper** leads to worsening endothelial function and increasing oxidative stress and inflammation in in patients with T1D and non-diabetic, but not **hypo ➡ normal.**

Diabetes Res Clin Pract. 2017 Jun;128:32-39. doi: 10.1016/j.diabres.2017.02.007. Epub 2017 Feb 14.
Diabetes 2009 Nov; 58(11): 2649-2655.

ATTD Consensus Statement Values for TIR

Advanced Technologies & Treatments for Diabetes (ATTD)

Table 3—Guidance on targets for assessment of glycemic control for adults with type 1 or type 2 diabetes and older/high-risk individuals

	TIR		TBR		TAR	
Diabetes group	% of readings; time per day	Target range	% of readings; time per day	Below target level	% of readings; time per day	Above target level
Type 1*/type 2	>70%; >16 h, 48 min	70–180 mg/dL (3.9–10.0 mmol/L)	<4%; <1 h <1%; <15 min	<70 mg/dL (<3.9 mmol/L) <54 mg/dL (<3.0 mmol/L)	<25%; <6 h <5%; <1 h, 12 min	>180 mg/dL (>10.0 mmol/L) >250 mg/dL (>13.9 mmol/L)
Older/high-risk# type 1/type 2	>50%; >12 h	70–180 mg/dL (3.9–10 mmol/L)	<1%; <15 min	<70 mg/dL (<3.9 mmol/L)	<10%; <2 h, 24 min	>250 mg/dL (>13.9 mmol/L)

Each incremental 5% increase in TIR is associated with clinically significant benefits for individuals with type 1 or type 2 diabetes (26,27). *For age <25 years, if the A1C goal is 7.5%, set TIR target to approximately 60%. See the section CLINICAL APPLICATION OF TIME IN RANGES for additional information regarding target goal setting in pediatric management. #See the section OLDER AND/OR HIGH-RISK INDIVIDUALS WITH DIABETES for additional information regarding target goal setting.

This international consensus report has been endorsed by the American Diabetes Association, American Association of Clinical Endocrinologists, American Association of Diabetes Educators, European Association for the Study of Diabetes, Foundation of European Nurses in Diabetes, International Society for Pediatric and Adolescent Diabetes, JDRF, and Pediatric Endocrine Society

Diabetes Care 2019 Aug; 42(8): 1593-1603.

Approaches to Further the Use of Time-in-Range Across Three Stages of Maturity

ESTABLISH

Objective:
Establish importance of TIR for blood glucose management across key stakeholders

- Finalize consensus and overall understanding of the benefits of TIR targets
- Raise awareness and educate key stakeholders on the drivers of optimal TIR (including diet), importance of this metric in management of blood glucose and the subsequent economic, psychosocial, societal and health benefits

ADVANCE

Objective:
Advance importance of TIR and promote ease of use of technologies to enable use of TIR

- Elevate importance and relevance of TIR
- Engage key stakeholders and demonstrate the value of TIR to increase regular use of these measures and associated technologies across stakeholders
- Develop and implement approaches to overcome access and affordability issues related to digital health solutions in Diabetes

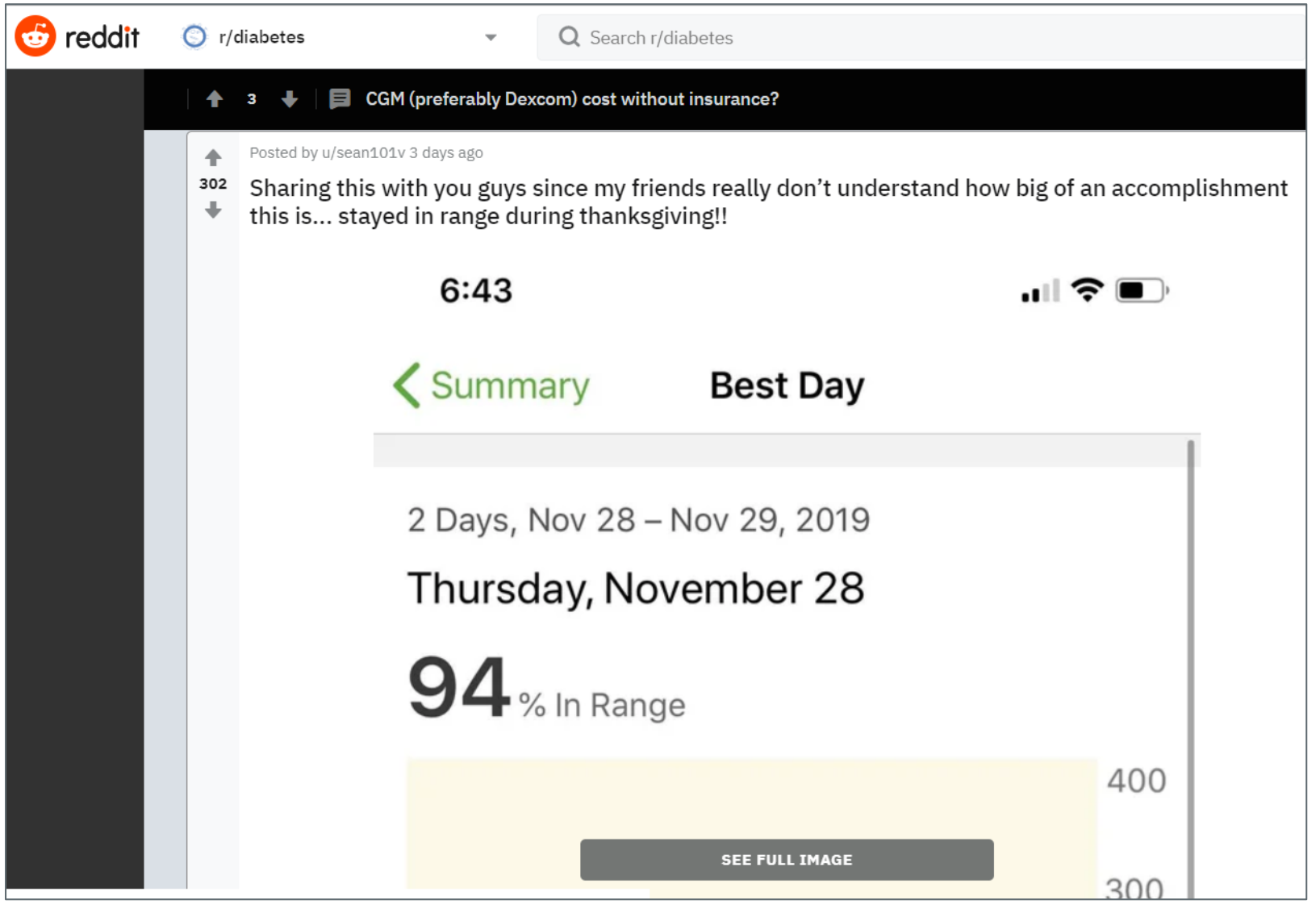
PERPETUATE

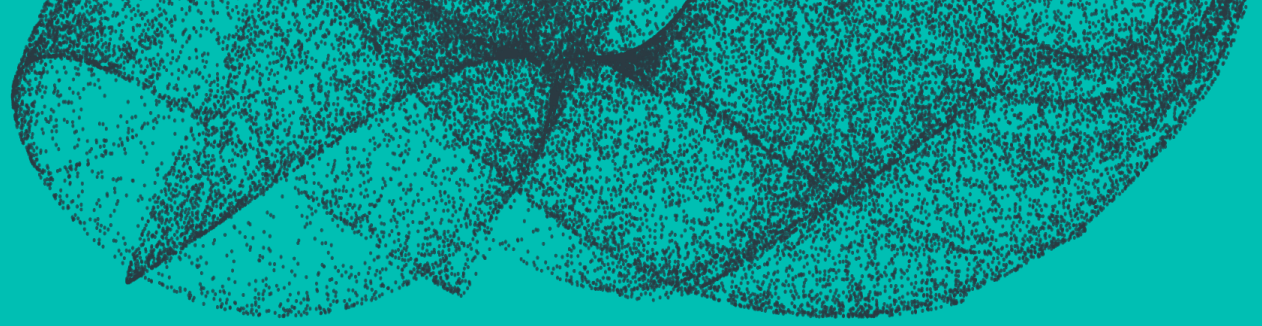
Objective:
Perpetuate the use of TIR to sustain blood glucose management across all PwD populations

- Ensure that adopted TIR targets are met regularly by PwD
- Continue HCP and PwD education about the health benefits of improving TIR using FGM/CGM
- Collaborate with payers, regulators and industry to broaden technology access to new PwD populations
- Develop case management programs to improve PwD adherence
- Enhance HCP ability to use/interpret data from digital technologies

Source: IQVIA, Aug 2019
Notes: Potential approaches to furthering the use of TIR as a Diabetes management tool. FGM/CGM = Flash Glucose Monitoring/Continuous Glucose Monitoring.
Advancing Glyemic Control in Diabetes - New Apporaches and Measures ~ Report by the IQVIA Institute for Human Data Science

Mission (can be) Accomplished!





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