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*International Diabetes Center*

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# **The Role of CGM in the Wide & Narrow Spectrum of Diabetes**

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Minneapolis, MN

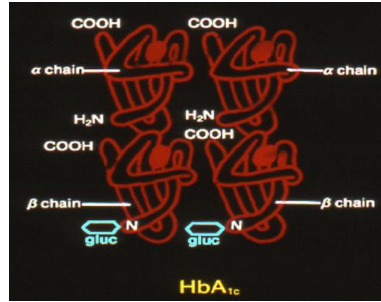
# Disclosures: Richard M. Bergenstal, MD

## I have no personal financial disclosures

- My employer, the non-profit HealthPartners Institute, contracts for my services, and I receive no personal income from the following activities:
  - I have participated in clinical research, been a member of a scientific advisory board, and served as a consultant for:
    - Abbott Diabetes Care, Ascensia, CeQur, Dexcom, Eli Lilly, Hygieia, Insulet, Johnson & Johnson, Medtronic, Novo Nordisk, Onduo, Roche, Sanofi, united Healthcare AND Zealand
  - My institution receives NIH/NIDDK funding: T1D (DCCT/EDIC) & T2D (GRADE) and Technology (SBIR with Hygieia) and automated insulin delivery systems (FLAIR)

40-50 yr.

## Hemoglobin A1c



40-50 yr.

## Fingerstick Glucose Testing



Day/Night	BREAKFAST			LUNCH			DINNER			BEDTIME	
	BG	Med	BG	BG	Med	BG	BG	Med	BG	Med	
1/24	79									272	
1/25	148										
1/26	165										
1/27	195										
1/28	197										
1/29	153										
1/30	181										
1/31	189										
2/1	210										
2/2	173										

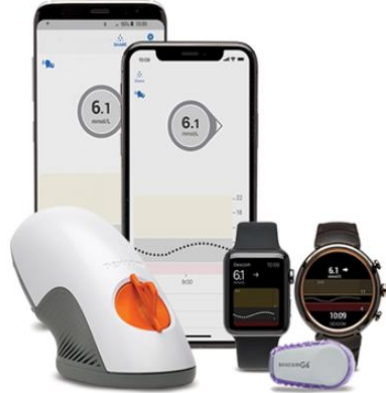
15-20 yr.

## Continuous Glucose Monitoring (CGM)

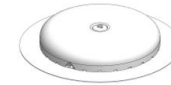


# CGM Devices/Systems

**Dexcom G6  
and G6 Pro**



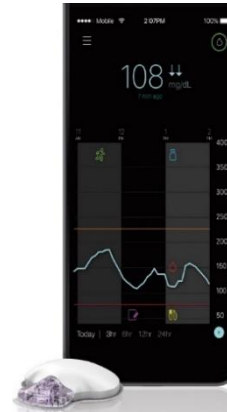
**Abbott FreeStyle  
Libre, Libre 2  
and Libre Pro**



**Eversense  
CGM (90 day)  
(Eversense E3-  
180 day system  
FDA approved)**

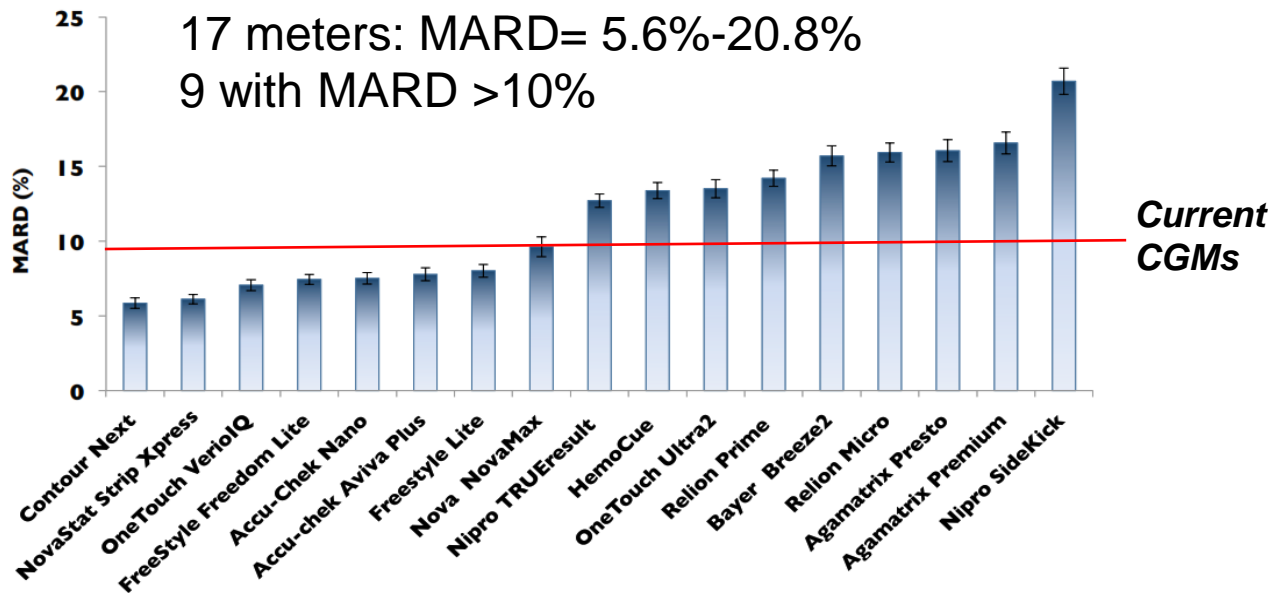


**Medtronic Guardian  
Sensor 3/ Guardian  
Connect CGM  
(iPro2)**



# Is CGM accurate enough?

## Is SMBG much more accurate than CGM?



March 27, 2018  
(iCGM)

FDA authorizes first fully interoperable CGM system

*Current  
CGMs*

THE LANCET

# Continuous glucose monitoring: transforming diabetes management step by step

*Richard M Bergenstal*

International Diabetes Center at Park Nicollet



## Wide and Narrow Impact on Diabetes Management



Published online February 16, 2018

# Triple Aim to Improve Healthcare Value (outcomes/cost)



## Healthcare *triple aim*<sup>1</sup>

Patient experience

Improved quality

Value

Reduced cost

## Diabetes *triple aim*

Reduce the Burden<sup>2</sup>

Improve Quality  
A1C+ TIR & TBR  
CVD & CKD  
Weight loss?

Value

Reduce therapeutic inertia

## CGM *triple aim*

CGM/TIR  
Clinical Trial  
& Regulatory  
Measures<sup>4</sup>

CGM/TIR  
Digital  
Quality  
Measures<sup>3</sup>

Value

CGM/TIR Guided  
Clinical Care  
Strategies



<sup>1</sup>Berwick D et al.  
*Health Affairs* 2008

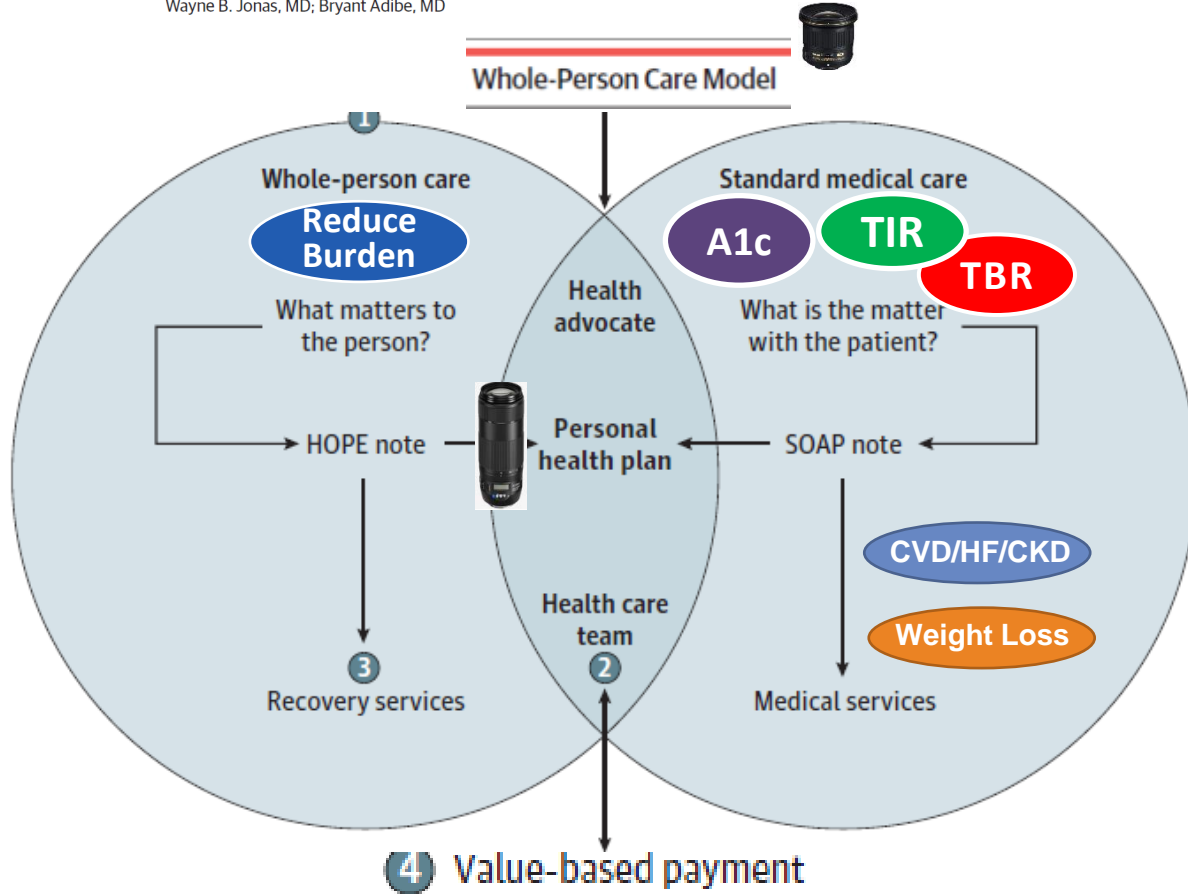
<sup>2</sup> Reduce diabetes distress  
Patient feels listened to

<sup>3</sup> TIR/TBR; GMI; Diabetes distress  
<sup>4</sup> CGM data in drug package insert

Viewpoint

## An Integrated Framework for Achieving National Health Goals

Wayne B. Jonas, MD; Bryant Adibe, MD





# DCCT (1983-1993): Relationship of HbA1c to Risk of Microvascular Complications

The New England  
Journal of Medicine

©Copyright, 1993, by the Massachusetts Medical Society

Volume 329 SEPTEMBER 30, 1993 Number 14

## THE EFFECT OF INTENSIVE TREATMENT OF DIABETES ON THE DEVELOPMENT AND PROGRESSION OF LONG-TERM COMPLICATIONS IN INSULIN-DEPENDENT DIABETES MELLITUS

THE DIABETES CONTROL AND COMPLICATIONS TRIAL RESEARCH GROUP\*

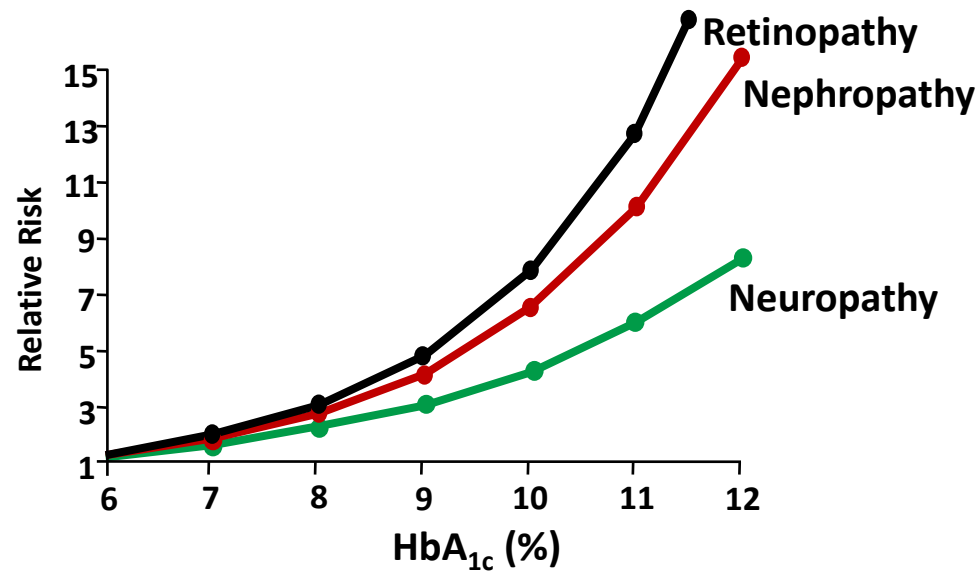
**Abstract Background.** Long-term microvascular and neurologic complications cause major morbidity and mortality in patients with insulin-dependent diabetes mellitus (IDDM). We examined whether intensive treatment with the goal of maintaining blood glucose concentrations close to the normal range could decrease the frequency and severity of these complications.

**Methods.** A total of 1441 patients with IDDM — 726 with no retinopathy at base line (the primary-prevention cohort) and 715 with mild retinopathy (the secondary-intervention cohort) were randomly assigned to intensive therapy administered either with an external insulin pump or by three or more daily insulin injections and guided by frequent blood glucose monitoring or to conventional therapy with one or two daily insulin injections. The patients were followed for a mean of 6.5 years, and the appearance and progression of retinopathy and other complications were assessed regularly.

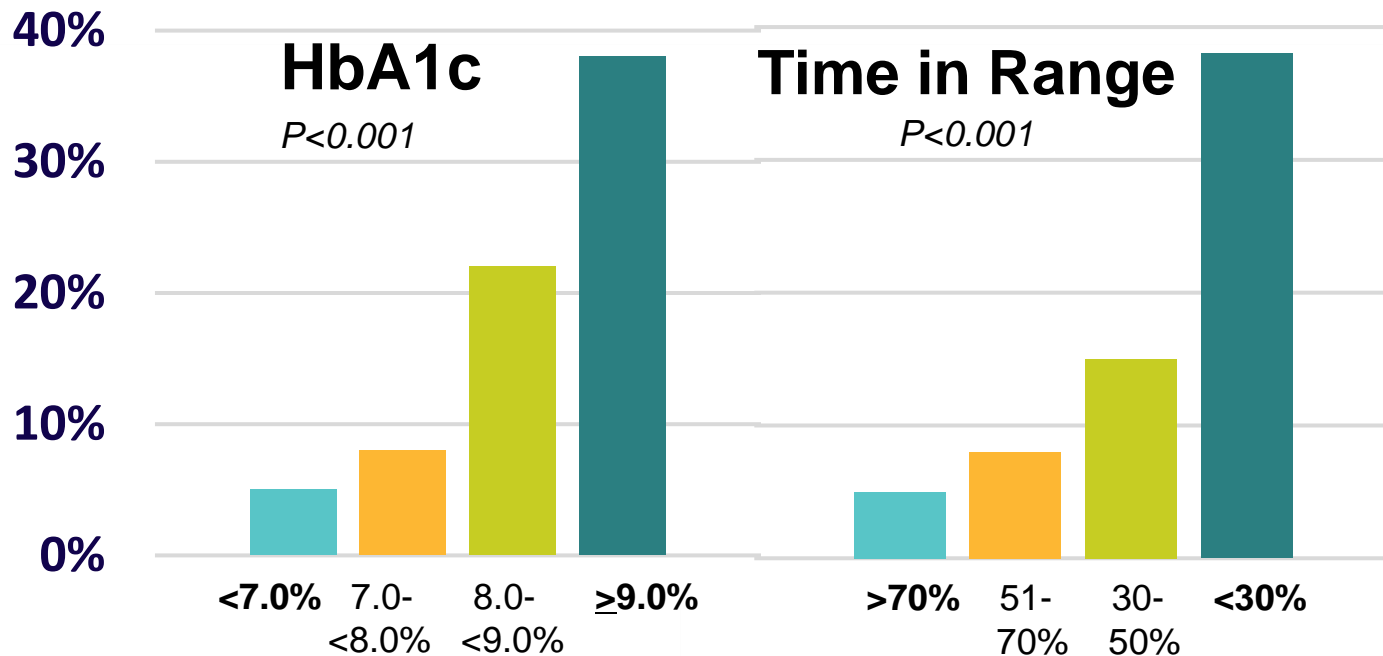
**Results.** In the primary-prevention cohort, intensive therapy reduced the adjusted mean risk for the development of retinopathy by 76 percent (95 percent confidence

interval, 62 to 85 percent), as compared with conventional therapy. In the secondary-intervention cohort, intensive therapy slowed the progression of retinopathy by 54 percent (95 percent confidence interval, 39 to 66 percent) and reduced the development of proliferative or severe nonproliferative retinopathy by 47 percent (95 percent confidence interval, 14 to 67 percent). In the two cohorts combined, intensive therapy reduced the occurrence of microalbuminuria (urinary albumin excretion of  $\geq 40$  mg per 24 hours) by 39 percent (95 percent confidence interval, 21 to 52 percent), that of albuminuria (urinary albumin excretion of  $\geq 300$  mg per 24 hours) by 54 percent (95 percent confidence interval, 19 to 74 percent), and that of clinical neuropathy by 60 percent (95 percent confidence interval, 38 to 74 percent). The chief adverse event associated with intensive therapy was an increase in severe hypoglycemia.

**Conclusions.** Intensive therapy effectively delays the onset and slows the progression of diabetic retinopathy, nephropathy, and neuropathy in patients with IDDM. (N Engl J Med 1993;329:977-86.)

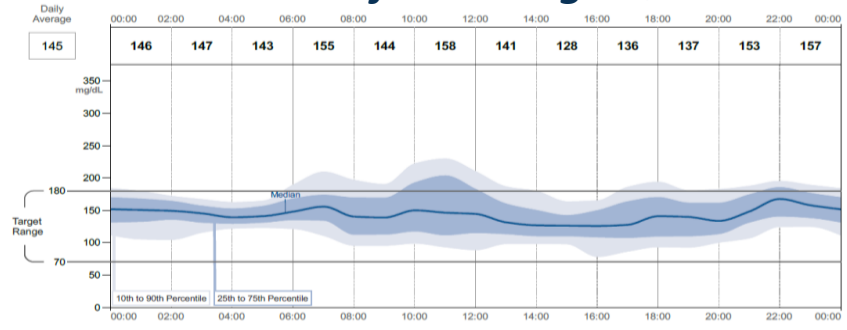


# Retinopathy Progression According to HbA1c and Time in Range

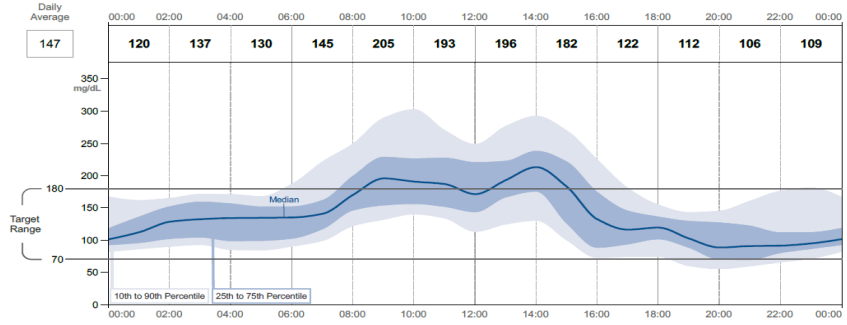


Retinopathy progression rate increased by:  
32% for each 0.5% higher HbA1c and for 6.2 percentage points lower TIR

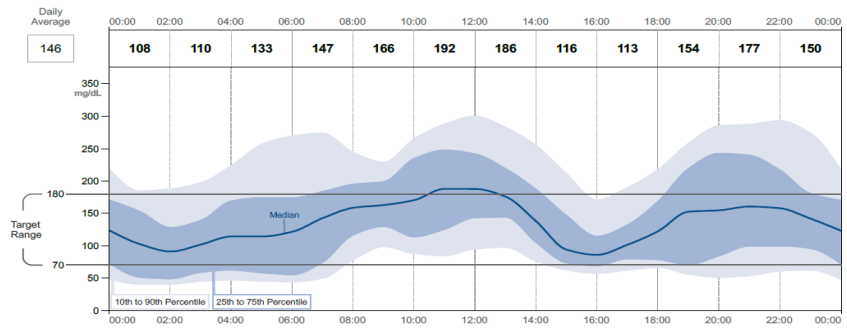
# A1C or CGM for Management?



A1C (%)	% Time Hypo (< 70 mg/dL)	% Time TIR (70-180 mg/dL)
6.7%	1%	83%



6.7%	6%	69%
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6.7%	9%	51%
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CV= coefficient of variation



Wide Angle

# CGM FIRST – for ALL PwT1D

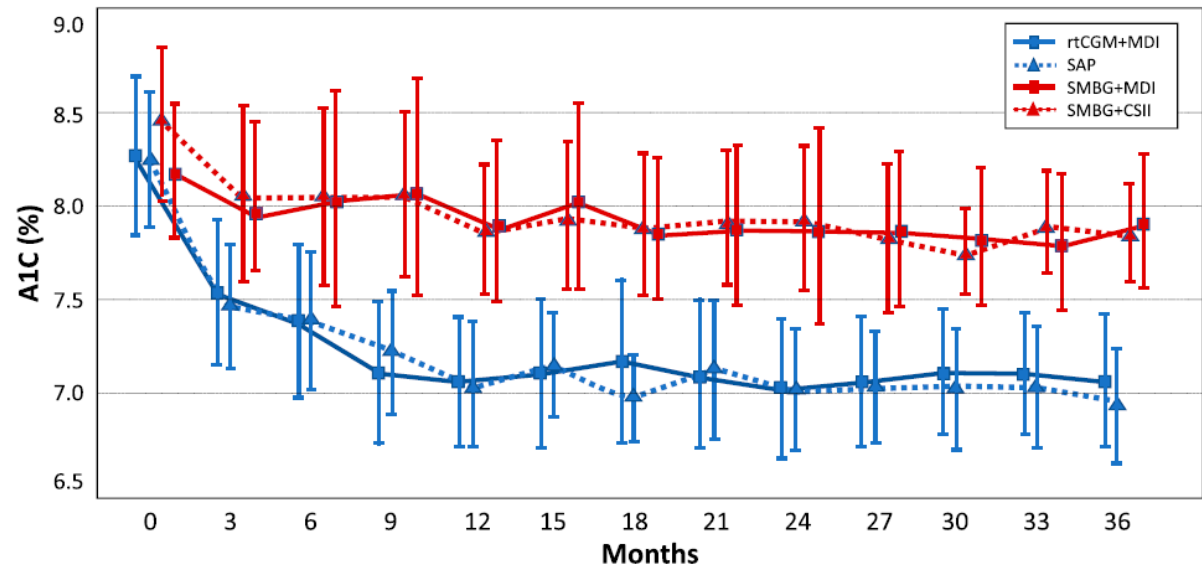
COMISAIR<sup>1</sup>

**3 year follow up** of 94 adults with **Type 1 diabetes** 4 treatment groups:

1. Real time CGM\* + MDI<sup>†</sup>
2. SAP<sup>~</sup> (CGM + pump)
3. SMBG<sup>‡</sup> + MDI
4. SMBG + pump

- Only **CGM groups** had significant improvements in **TIR** and **significant reductions in TBR**
- A1C was lower in the rtCGM groups than SMBG groups

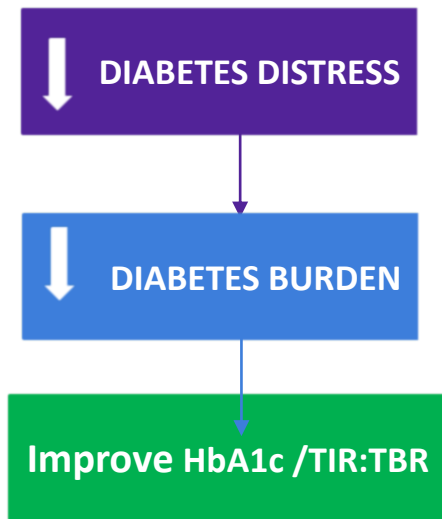
\* Real time continuous glucose monitoring <sup>†</sup>Multiple dose injections <sup>~</sup>Sensor augmented pump <sup>‡</sup>Self monitoring blood glucose



Note: 3 year non-randomized prospective real world clinical trial.

<sup>1</sup>Soupal J et al. Diabetes Care. 2020;43(1):37-43.

# Minimizing diabetes distress: a key strategy to reduce the burden of diabetes



Nagel KE et al. *Diabetes distress and glycaemic control in young adults with type 1 diabetes: Associations by use of insulin pumps and continuous glucose monitors.* *Diabet Med* 2021;38:e14660.

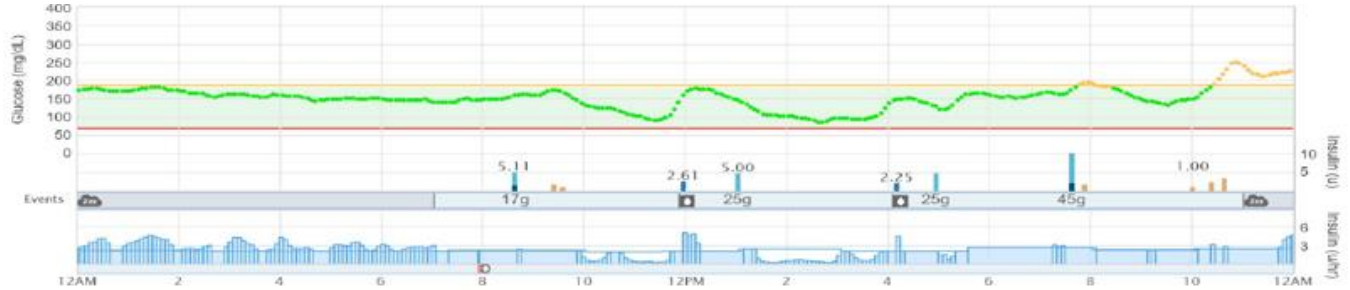
## Automated Insulin Delivery

Computerized control of insulin delivery based on data from a continuous glucose sensor

Continuous  
Glucose  
Monitor

Algorithm

Insulin  
Pump



**Insulin increased** to  
reduce hyperglycemia

**Insulin reduced** to  
avoid hypoglycemia

MINIMED® 670G / 770G



MiniMed® 670G

MiniMed® 770G

MINIMED® 780G\*



\*AVAILABLE OUTSIDE US, NOT FDA APPROVED.

t:SLIM X2 WITH CONTROL-IQ



OMNIPOD 5\*



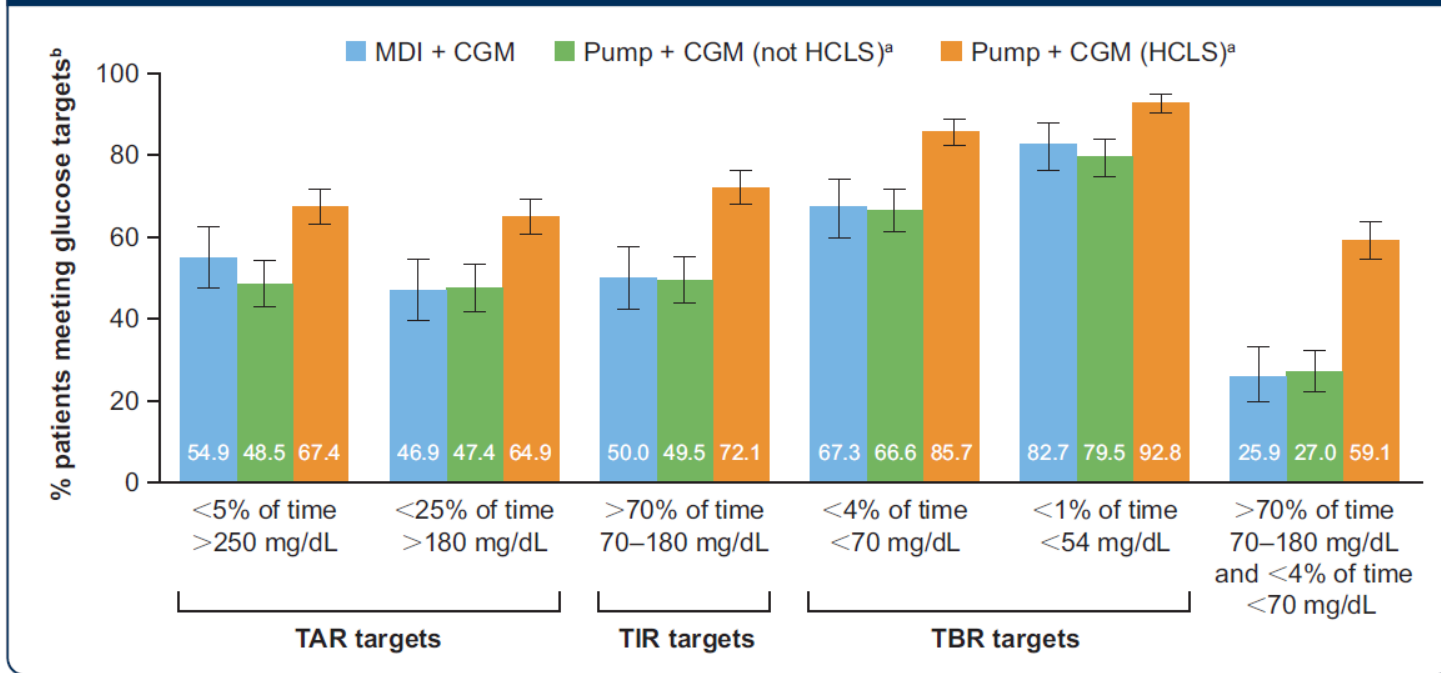
\* FDA APPROVED DOWN TO AGE 6, DETAILS SUBJECT TO CHANGE WHEN DEVICE BECOMES AVAILABLE.

iLet dual hormone



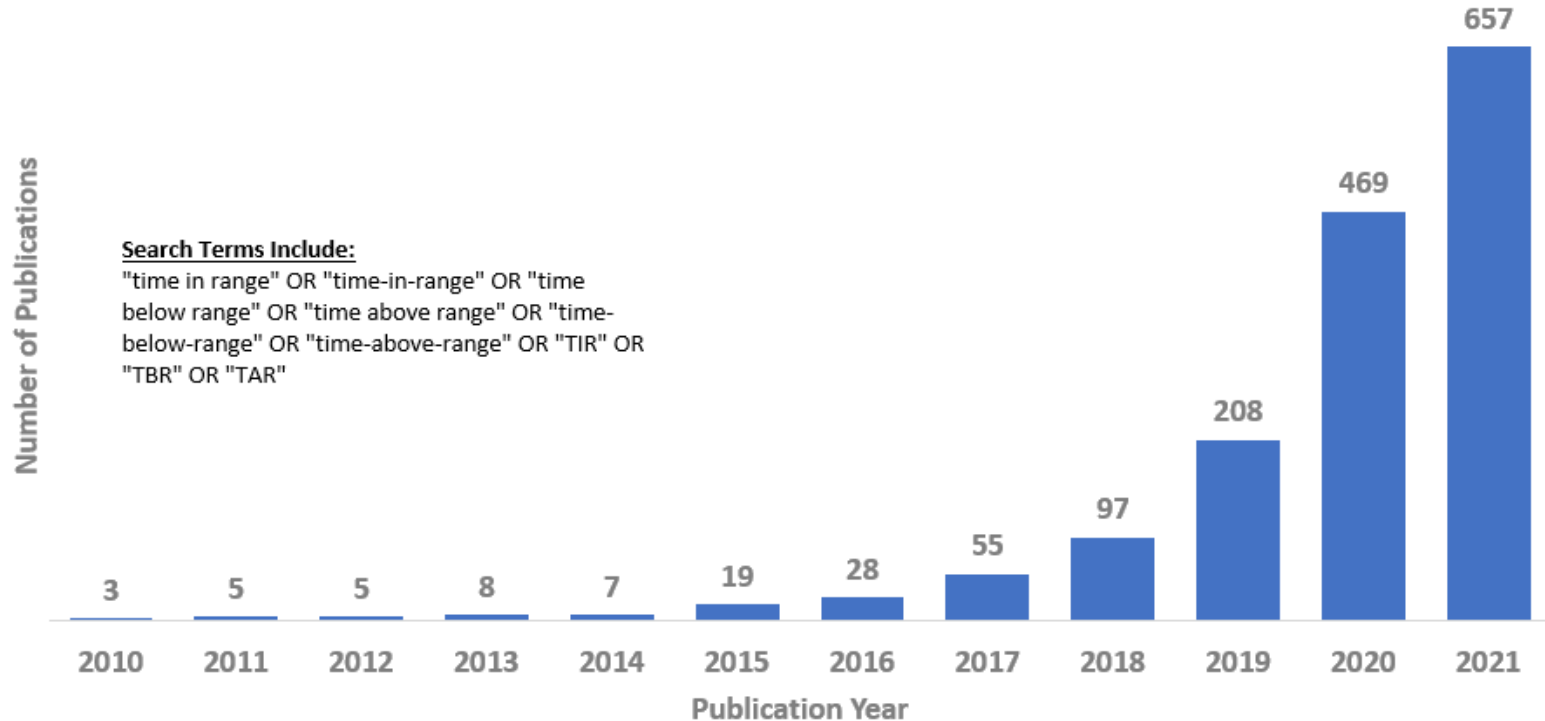
# T1D Exchange participants (N=926) on various approaches to insulin delivery willing to share their CGM data

**Figure 6. Proportion of Patients Meeting Various Glucose Targets**



# Time In Range as a Clinical Outcome: Results of a Longitudinal Analysis of the Literature and Clinical Trials

**Figure 1: Number of Publications Reporting Time-in-Range as a Clinical Outcome**

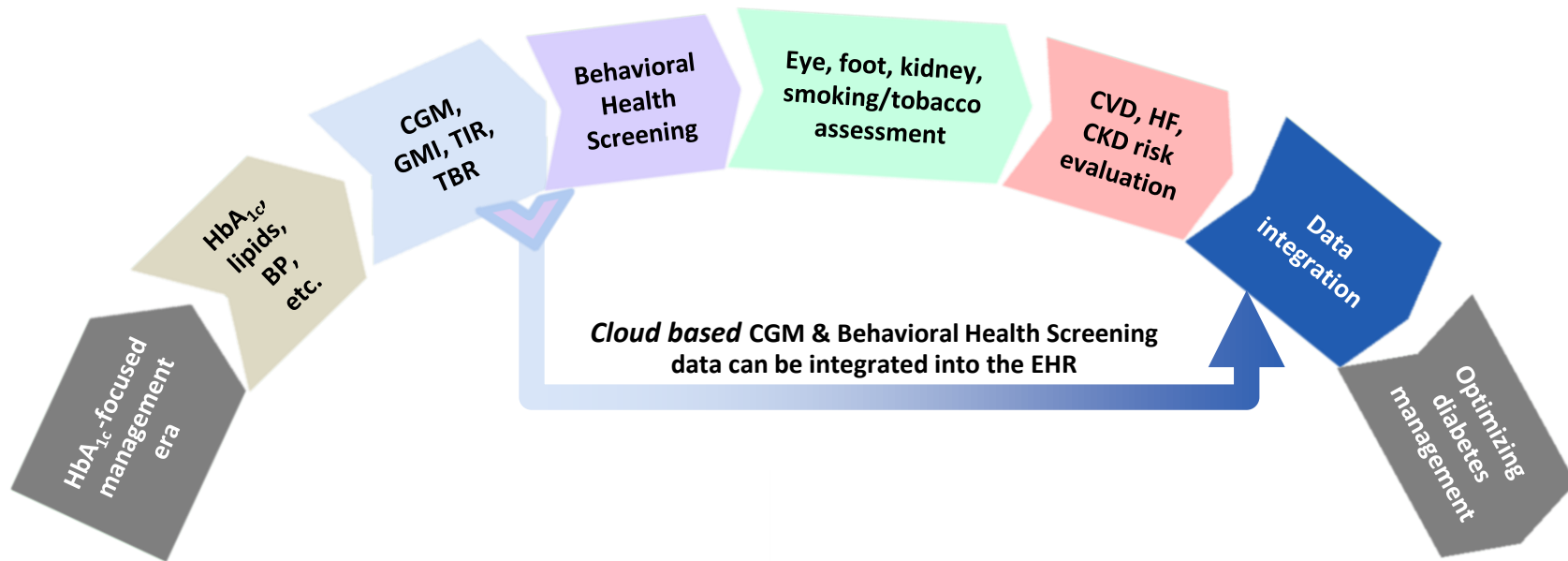




# Rethinking diabetes care in the digital age



## Building a Bridge Toward Optimal Diabetes Management



Modified from R Bergenstal presentation at NCQA Digital Quality Summit July, 2021

Rethinking Diabetes Care In The Digital Age. Findings from the 2021 Digital Quality Summit.

Available at: <https://www.ncqa.org/wp-content/uploads/2022/02/NCQA-DQS-WhitepaperRethinkDiabetes.pdf> Accessed 9 March 2022

BP, blood pressure; CVD, cardiovascular disease; CKD, chronic kidney disease; GMI, glucose management indication (formerly estimated HbA<sub>1c</sub>); HF, heart failure; TIR, Time in range (70–180mg/dL); TBR, Time below range (<70 mg/dL)



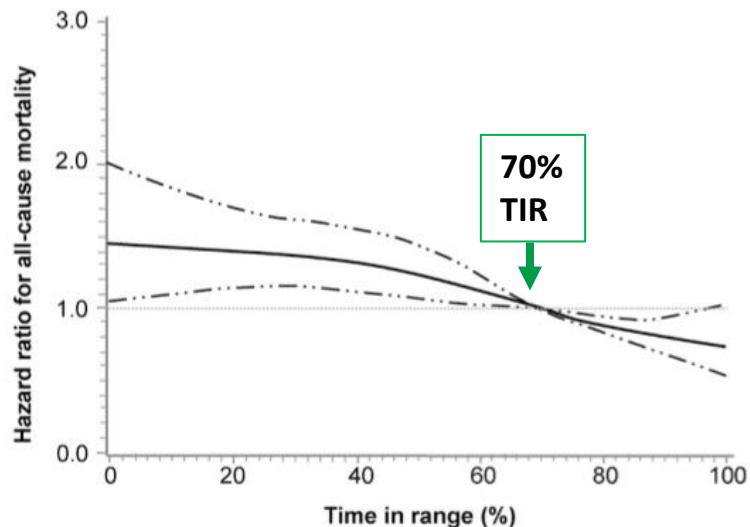
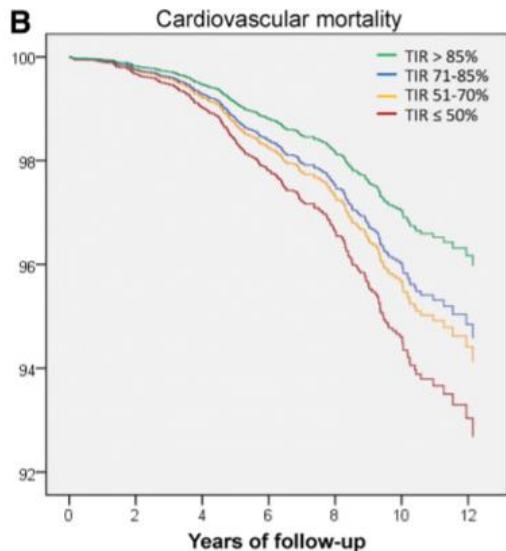
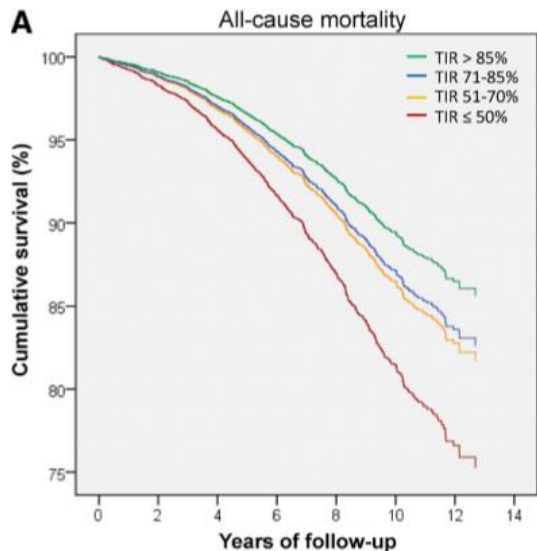
**Park Nicollet**  
International Diabetes Center

# Time in Range in Relation to All-Cause and Cardiovascular Mortality in Patients With Type 2 Diabetes: A Prospective Cohort Study

**Diabetes Care 2021 Feb; 44(2): 549-555**

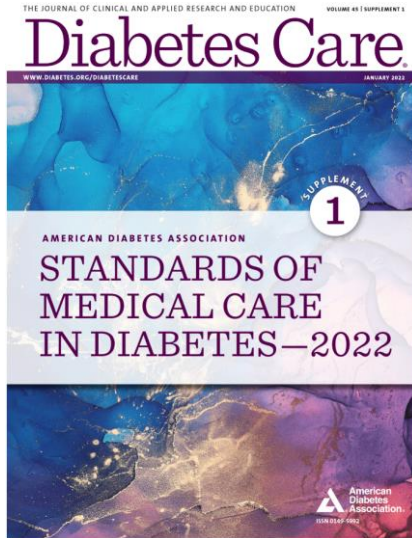
Jingyi Lu,<sup>1</sup> Chunfang Wang,<sup>2</sup> Yun Shen,<sup>1</sup> Lei Chen,<sup>2</sup> Lei Zhang,<sup>1</sup> Jinghao Cai,<sup>1</sup> Wei Lu,<sup>1</sup> Wei Zhu,<sup>1</sup> Gang Hu,<sup>3</sup> Tian Xia,<sup>2</sup> and Jian Zhou<sup>1</sup>

- 6,225 T2D – CGM (72 hrs)
- Followed 10 years (2005-2015)
- Association baseline TIR & Mortality
  - All cause & CV mortality

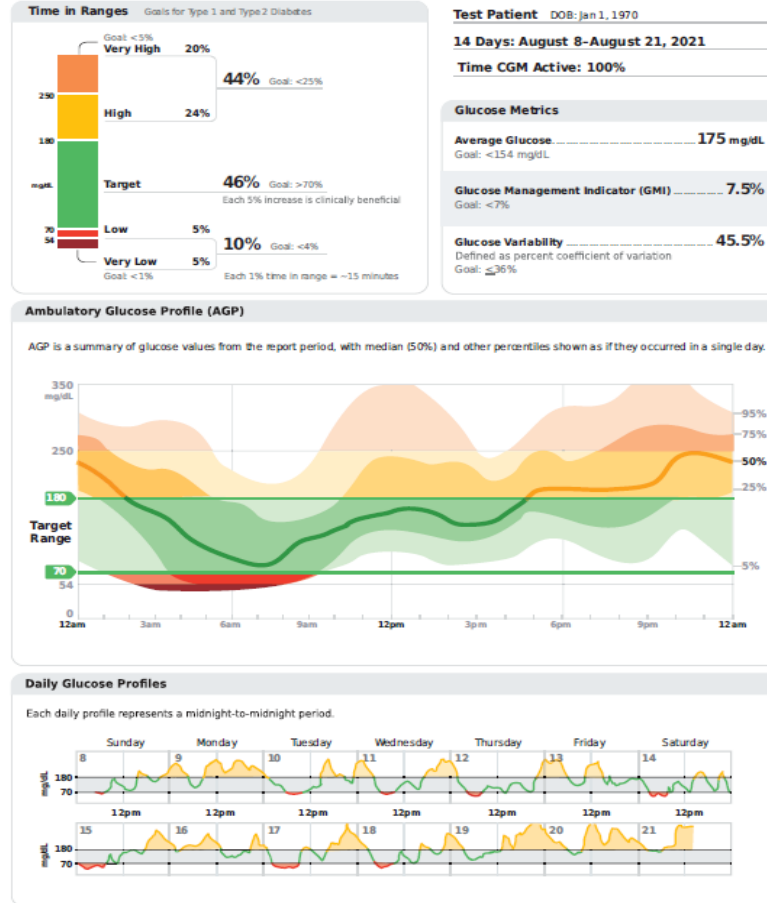


**Figure 1**—Multivariate-adjusted cumulative survival curves of all-cause (A) and cardiovascular (B) mortality by different levels of TIR. Adjusted for age, sex, BMI, diabetes duration, systolic blood pressure, triglyceride, HDL cholesterol, LDL cholesterol, smoking status, history of cancer and CVDs, and using antihypertensive drugs, aspirin, and statins.

# AGP Report Recommended



## AGP Report: Continuous Glucose Monitoring



Glycemic Targets: |

Figure 6.1—Key points included in standard ambulatory glucose profile (AGP) report. Reprinted from Holt et al. (33).

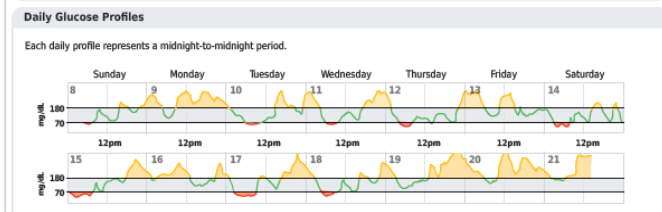
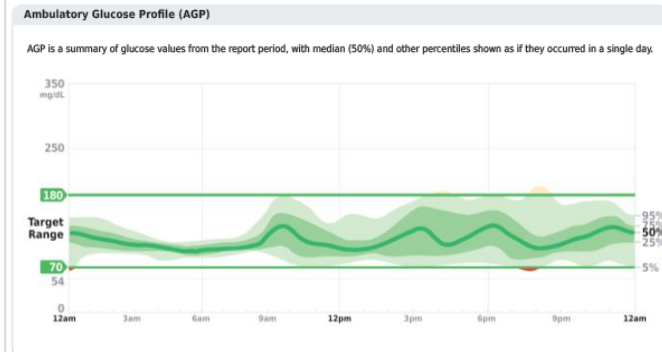
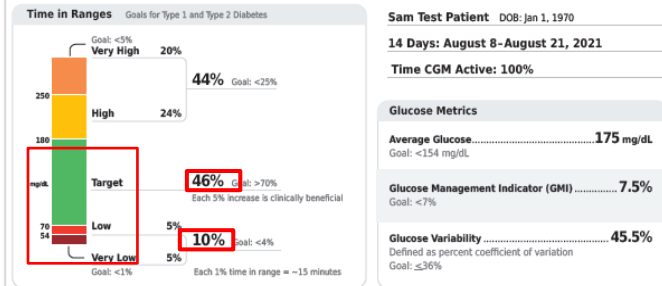
*Standards of Medical Care in Diabetes - 2022. Diabetes Care 2022;45(Suppl. 1)*

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ational Diabetes Center

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# CGM Clinician Guided Management

## AGP Report: Continuous Glucose Monitoring



1. Is there a glucose control problem?

More Green, Less Red

2. Where is the problem?

FNIR

Flat Narrow In Range

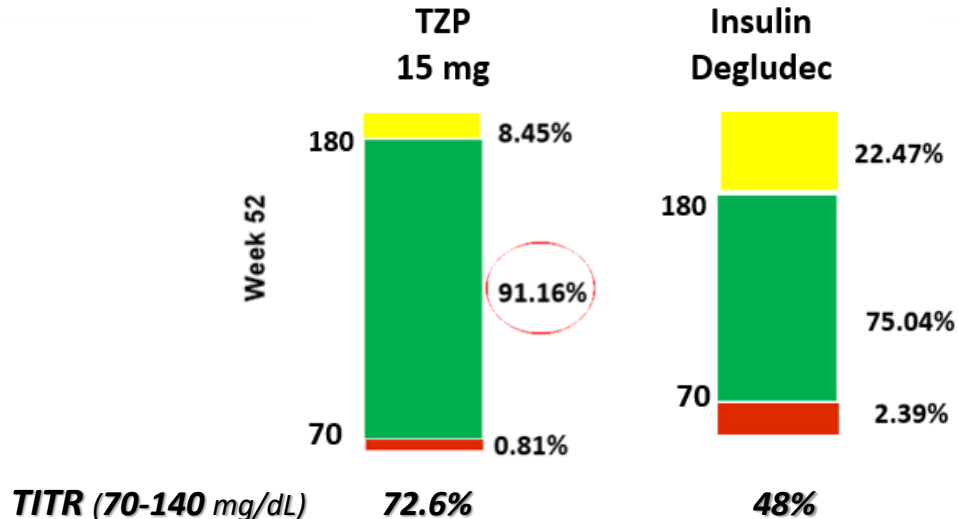
3. Continue to titrate on a timely basis

Titrate, Titrate, Titrate



# SURPASS-3: *Tirzepatide* vs insulin degludec

## SURPASS-3 CGM substudy: TIR at 52 weeks



Do we need to add ***Time in Tight Range (TITR) 70-140 mg/dL***  
to the current ***Time in Range (TIR) 70-180 mg/dL***

# Glucose-lowering medication in type 2 diabetes: ADA Standards of Care in Diabetes - 2021

**FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle (including weight management and physical activity)**

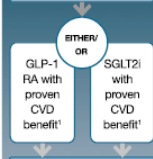
**INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD, OR HF<sup>1</sup>**



**CONSIDER INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE\***

**+ASCVD/Indicators of High Risk**

- Established ASCVD
- Indicators of high ASCVD risk (age  $\geq 55$  years with coronary, carotid, or lower-extremity artery stenosis  $>50\%$ , or LVH)



**If A1C above target**

If further intensification is required or patient is unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV benefit and/or safety:

- For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit and vice versa<sup>2</sup>
- TZD<sup>3</sup>
- DPP-4i if not on GLP-1 RA
- Basal insulin<sup>4</sup>
- SU<sup>4</sup>

**+HF**

Particularly HF<sup>1</sup>EF (LVEF  $<45\%$ )

**SGLT2i with proven benefit in this population<sup>5,6,7</sup>**

**+CKD**

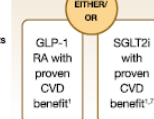
DKD and Albuminuria<sup>8</sup>

**PREFERABLY** SGLT2i with primary evidence of reducing CKD progression

**OR** SGLT2i with evidence of reducing CKD progression in CVOTs<sup>9,10</sup>

**OR** GLP-1 RA with proven CVD benefit<sup>1</sup> if SGLT2i not tolerated or contraindicated

**For patients with TZD and CKD<sup>11</sup> (e.g., eGFR  $<60$  mL/min/1.73 m<sup>2</sup>) and thus at increased risk of cardiovascular events**



**NO**

**IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW**

**COMPPELLING NEED TO MINIMIZE HYPOGLYCEMIA**

DPP-4i    GLP-1 RA    SGLT2i    TZD

**If A1C above target**    **If A1C above target**    **If A1C above target**    **If A1C above target**

SGLT2i    SGLT2i    GLP-1 RA    SGLT2i

**OR**    **OR**    **OR**    **OR**

TZD    TZD    DPP-4i    DPP-4i

**OR**    **OR**    **OR**    **OR**

GLP-1 RA    SGLT2i    GLP-1 RA

**OR**    **OR**    **OR**

TZD    TZD    TZD

**If A1C above target**

Continue with addition of other agents as outlined above

**If A1C above target**

**If A1C above target**

Consider the addition of SU<sup>4</sup> OR basal insulin:

- Choose later generation SU with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia<sup>2</sup>

**COMPPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS**

GLP-1 RA with good efficacy for weight loss<sup>12</sup>    **OR**    SGLT2i

**If A1C above target**

**If A1C above target**

SGLT2i

**If A1C above target**

GLP-1 RA with good efficacy for weight loss<sup>12</sup>

**If A1C above target**

If quadruple therapy required, or SGLT2i and/or GLP-1 RA not tolerated or contraindicated, use regimen with lowest risk of weight gain

**PREFERABLY**

DPP-4i (if not on GLP-1 RA) based on weight neutrality

**If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:**

- SU<sup>4</sup> • TZD<sup>3</sup> • Basal insulin

**COST IS A MAJOR ISSUE<sup>11,12</sup>**

SU<sup>4</sup>    TZD<sup>3</sup>

**If A1C above target**

TZD<sup>3</sup>    SU<sup>4</sup>

**If A1C above target**

**Insulin therapy** basal insulin with lowest acquisition cost

**OR**

Consider other therapies based on cost

- Proven CVD benefit means it has label indication of reducing CVD events
- Low dose may be better tolerated though less well studied for CVD effects
- Degludec or U-100 glargine have demonstrated CVD safety
- Choose later generation SU to lower risk of hypoglycemia; glibenclamide has shown similar CV safety to DPP-4i
- Be aware that SGLT2i labeling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use
- Empagliflozin, canagliflozin, and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin and dapagliflozin have primary renal outcome data. Dapagliflozin and empagliflozin have primary heart failure outcome data.

- Proven benefit means it has label indication of reducing heart failure in this population
- Refer to Section 11: Microvascular Complications and Foot Care
- Degludec / glargine U-300 < glargine U-100 / detemir < NPH insulin
- Semaaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
- If no specific comorbidities (e.g., no established CVD, low risk of hypoglycemia, and lower priority to avoid weight gain or no weight-related comorbidities)
- Consider country- and region-specific cost of drugs. In some countries TZDs are relatively more expensive and DPP-4i are relatively cheaper.

<sup>†</sup> Acted on whenever these become new clinical considerations regardless of background glucose-lowering medications.  
<sup>\*</sup> Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.

**2021**  
**Non-Glycemic (CVD/HF/CKD) & Glycemic**

**2022**  
**Non-Glycemic (CVD/HF/CKD) & Glycemic & Weight Loss**

**More:**

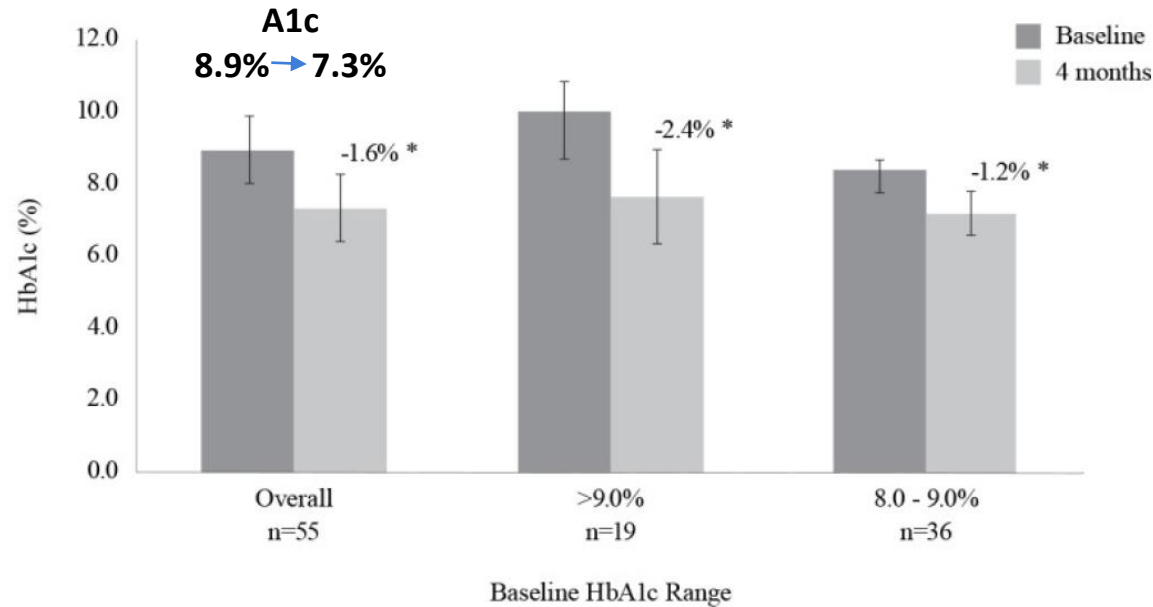
- GLP-1 RA<sup>+</sup>, SGLT2i

***Role of CGM guided management?***

Figure 9.1—: 2021 ADA Professional Practice Committee (PPC) adaptation of Davies et al. and Buse et al.

# Does remote monitoring of digital CGM data improve outcomes?

## Patients with T2D followed in a CGM-based virtual diabetes clinic (Onduo)

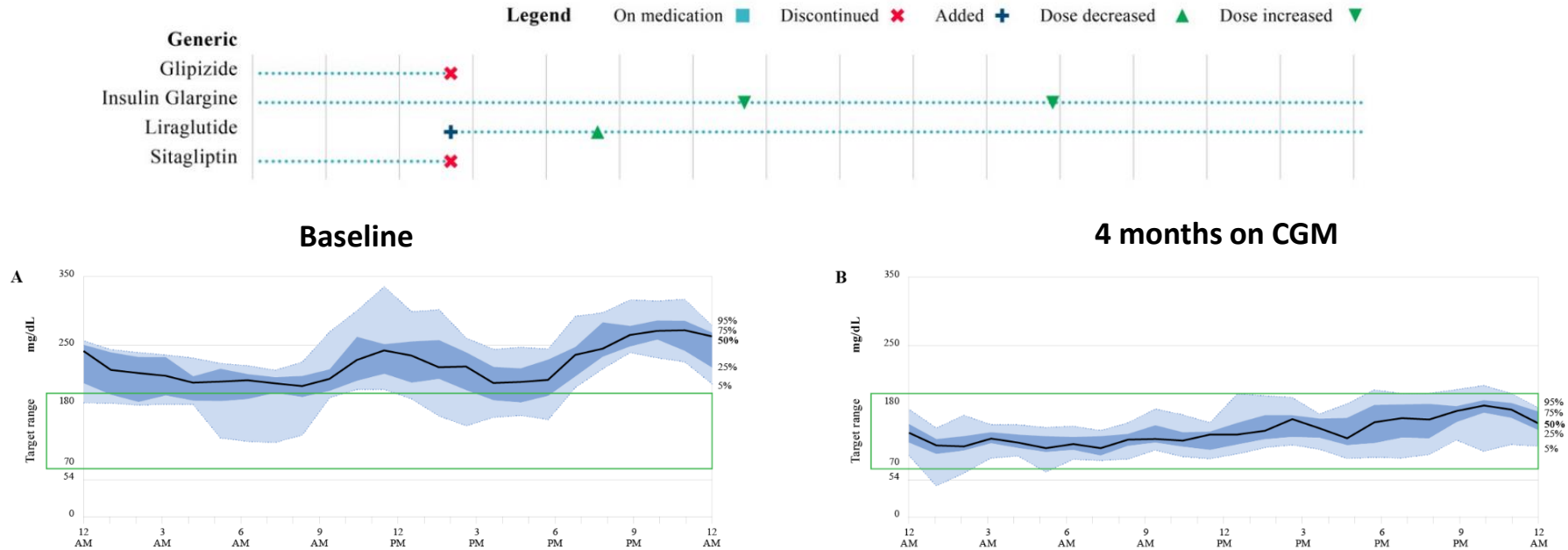


CGM, continuous glucose monitoring; SD, standard deviation

Majithia AR et al. *J Med Internet Res* 2020;22:e21778. doi: 12.2196/21778

# Does remote monitoring of digital CGM data improve outcomes?

## Timely access to guideline-based diabetes medications and technologies



CGM, continuous glucose monitoring  
Majithia AR et al. *JMIR Form Res* 2022 doi: 10.2196/31629 [Epub ahead of print]



# The EKG Informing the Future of CGM

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Eric J. Topol, MD, Scripps Research Translational Institute

*The Lancet* Vol 397: February 27, 2021

## Digital medicine

### What's lurking in your electrocardiogram?

For decades one of my favourite tasks in medicine has been reading 12-lead electrocardiograms (ECGs). I've always thought the wealth of information provided was impressive—

**Discussed that papers that showed how ECG could tell you**

- Gender
- Anemia
- CV outcome prediction

# ***AGP – EKG of glucose management***

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## Digital medicine

What's lurking in your ***continuous glucose monitor?*** \*

***For a decade one of my favorite tasks in medicine has been looking for patterns in the CGM/AGP report. I think CGM/AGP will transform diabetes management-***

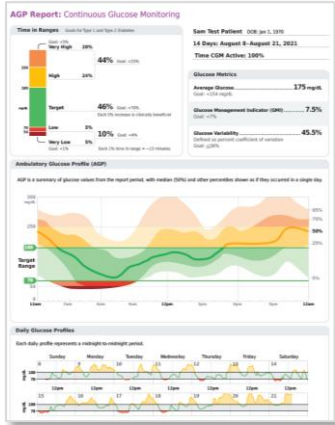
**\* CGM has been used to show:**

**Different people have very different glycemic responses to the same foods**

Hall H, et. al. Glucotypes reveal new patterns of glucose dysregulation. *PLoS Biol.* 2018;16(7):e2005143

Berry SE et al. Human postprandial responses to food and potential for precision nutrition. *Nat Med.* 2020 Jun;26(6):964-973.

# In Summary: *CGM using AGP* and taking a wide and narrow perspective is achieving both the *CGM & Diabetes Triple Aim*



## CGM triple aim

CGM/TIR  
Clinical Trial  
& Regulatory  
Measures

CGM/TIR  
Digital  
Quality  
Measures

CGM/TIR Guided  
Clinical Care Strategies

Value

## Diabetes triple aim

Reduce  
the  
Burden

Improve Quality  
A1C + TIR & TBR  
CVD & CKD

Reduce  
therapeutic inertia

Value



**Wide  
&  
Narrow**

**Thank you!**