



# PUSHING THE LIMITS of WHAT SENSING CAN DO for Type 1 and Type 2 DIABETES

Focus on Pivotal Advantages in **Dual Monitoring—Glucose and Ketones**—for Improving Glycemic Metrics and Reducing the Risk of DKA



Leveraging Dual Analyte Sensing to **Optimize Therapeutic Interventions in Diabetes**

## Fernando Gómez-Peralta, MD, PhD

Coordinator of the SCLEDyN Diabetes Group  
and Diabetes Area of the Spanish Society of  
Endocrinology and Nutrition (SEEN)  
Endocrinology and Nutrition Unit  
General Hospital of Segovia (Spain)



# Disclosures

F. Gomez-Peralta has taken part in advisory panels for Insulcloud S.L., Abbott Diabetes, Dexcom, Novartis, Astra Zeneca, Sanofi and Novo Nordisk; has participated as principal investigator in Clinical Trials funded by Sanofi, Novo Nordisk, Boehringer Ingelheim Pharmaceuticals, and Lilly; and has acted as a speaker for Abbott Diabetes, Novartis, Sanofi, Novo Nordisk, Boehringer Ingelheim Pharmaceuticals, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Co., and Lilly.

- ▶ I may present recommendations regarding the use of drugs or devices from companies with which I have a financial relationship.
- ▶ Additionally, my presentation will adhere to the following criteria:
  - My recommendations will be based on data and findings from peer-reviewed sources OR in the absence of adequate peer-reviewed material, my recommendations will rely on the best available evidence-based medicine.
  - Content will be fair and balanced, and if any product, specific drugs, or devices are discussed, alternate drugs or devices will also be discussed when appropriate.

This **CME-certified simulcast symposium** is jointly provided by the UMASS Chan Medical School and CMEducation Resources.

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# My Task Today: Introducing...

- ▶ Introducing the **agenda and speakers**
- ▶ Introducing the **main protagonists: THE KETONES!**
- ▶ Introducing **DKA**
- ▶ Introducing **KB and T2D...**

# Program Agenda

**14:40 – 15:10**

## **Ketones, What They Are and What They Can Tell Us About Preventing DKA**

**Dr Fernando Gomez-Peralta, MD, PhD - Program Chair**

Coordinator Diabetes Area, Spanish Endocrinology and Nutrition Society  
Head of Endocrinology and Nutrition Unit  
Segovia General Hospital  
Segovia, Spain

**15:10 – 15:35**

## **Beyond CGM: Dual Sensing Technology as a Cornerstone of DKA Prevention**

**Professor Ketan Dhatariya, MBBS, MSc, MD, MS, FRCP, PhD**

Consultant Diabetes & Endocrinology / Honorary Professor, Endocrinology & Diabetes  
Norwich, Norfolk UK  
Norwich Medical School, University of East Anglia  
Elsie Bertam Diabetes Centre  
Chair, Association of British Clinical Diabetologists

**15:35 – 16:00**

## **CGM for Transforming Clinical Outcomes in Non-Intensive T2D Therapy**

**Dr Emma Wilmot MB ChB BSc (hons) PhD FRCP**

Associate Professor, University of Nottingham  
Honorary Consultant Diabetologist, University Hospitals of Derby and Burton NHS FT  
Founder, Diabetes Technology Network UK

## **Interactive Question and Answer Session**



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Focus on Pivotal Advantages in **Dual Monitoring—Glucose and Ketones**—for Improving Glycemic Metrics and Reducing the Risk of DKA



*Leveraging Dual Analyte Sensing to Optimize Therapeutic Interventions in Diabetes*

# Ketones: What They Are and What They Can Tell Us About Preventing DKA

**Fernando Gómez-Peralta, MD, PhD**

Coordinator of the SCLEDyN Diabetes Group and Diabetes Area of the Spanish Society of Endocrinology and Nutrition (SEEN)  
Endocrinology and Nutrition Unit  
General Hospital of Segovia (Spain)



# Relationship of Blood Acetoacetate and 3-Hydroxybutyrate in Diabetes

Jennifer M. Stephens, B.Sc., M. J. Sulway, M.R.A.C.P.,  
and P. J. Watkins, M.D., M.R.C.P., Birmingham, England

## SUMMARY

The ratio of blood ketone bodies 3-hydroxybutyrate to acetoacetate, once thought to be fairly constant, has been shown to vary from 0.6:1 to 4.8:1. In untreated, ketoacidotic patients, it is directly related to the plasma free fatty acid level. Administration of insulin lowers the ratio because the fall of blood 3-hydroxybutyrate occurs earlier and more rapidly than that of acetoacetate. During the treatment of ketoacidosis there is usually an initial increase of the acetoacetate which may persist at a high level for several hours despite improvement in the 3-hydroxybutyrate.

July, 1971

**DIABETES** 20:485-89,  
July, 1971.

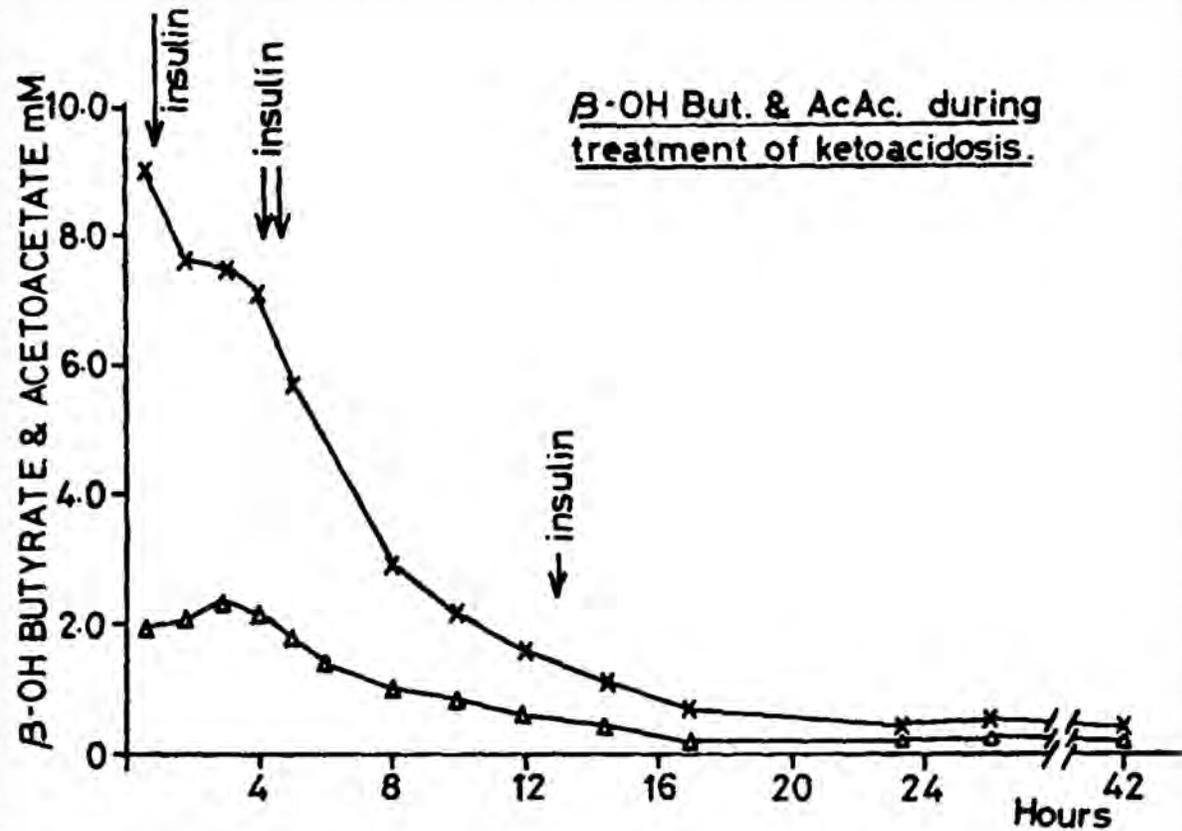
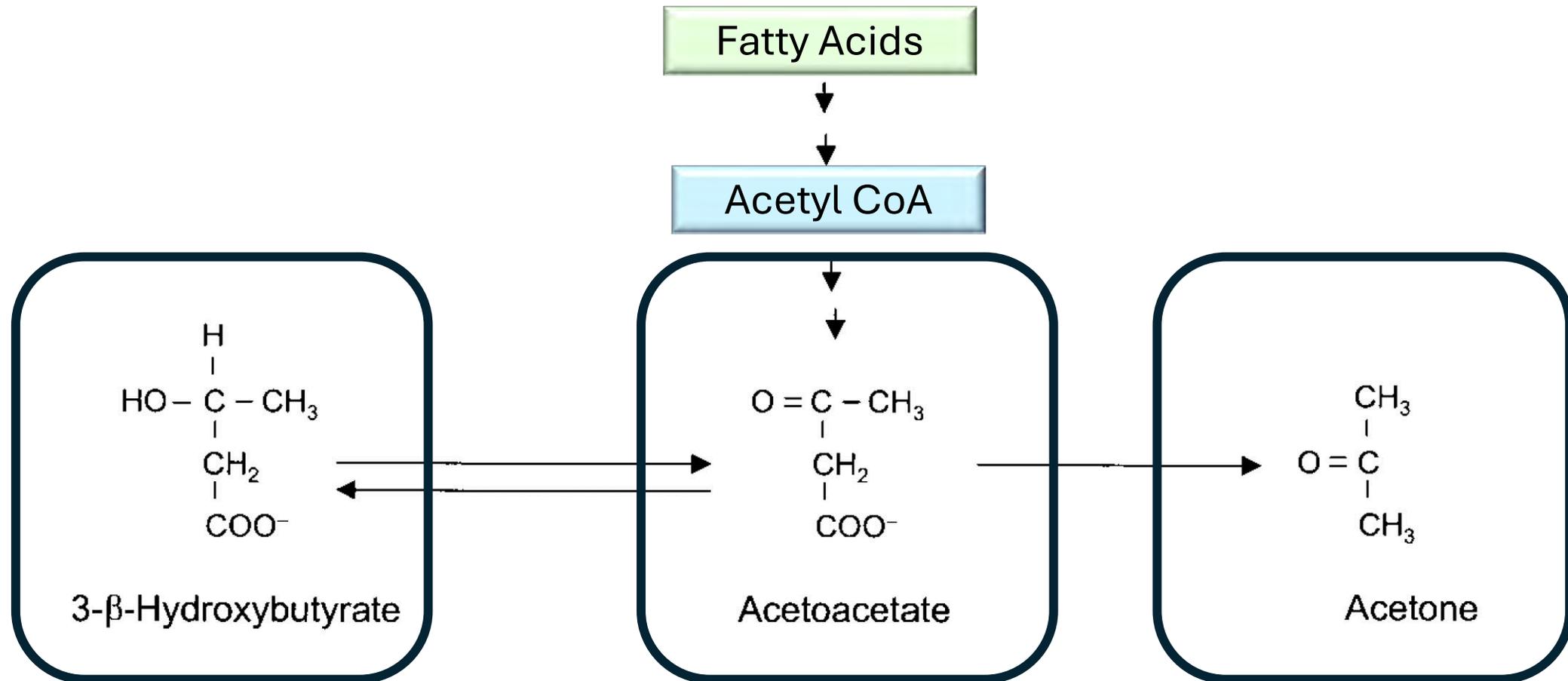


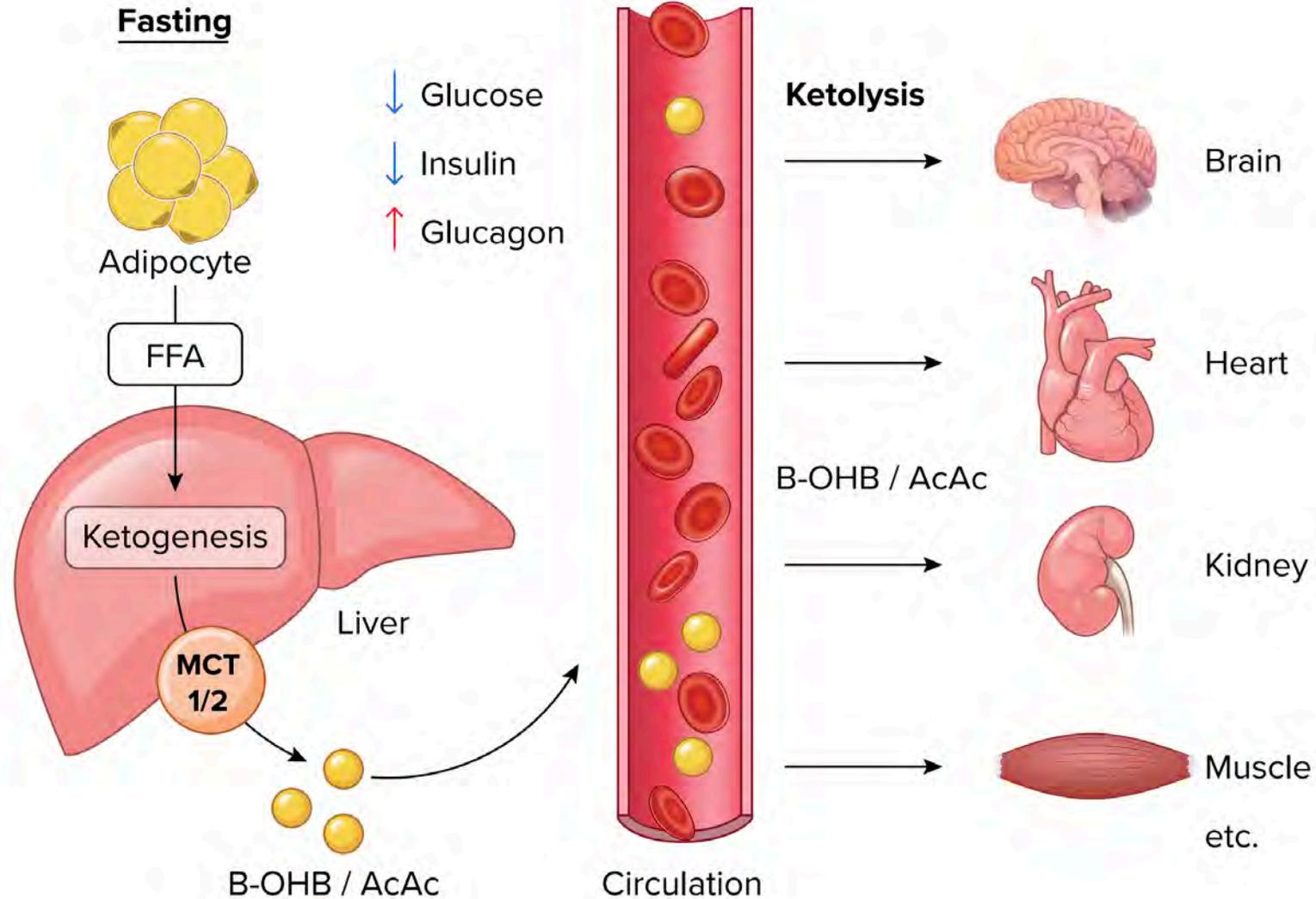
FIG. 4. Blood 3-hydroxybutyrate and acetoacetate changes in a woman of fifty-three years admitted in severe diabetic ketoacidosis precipitated by a respiratory infection. The initial blood glucose was 635 mg. per 100 ml. and the blood pH 7.02.

# Introducing the Main Protagonists

## Structures of Major Ketone Bodies



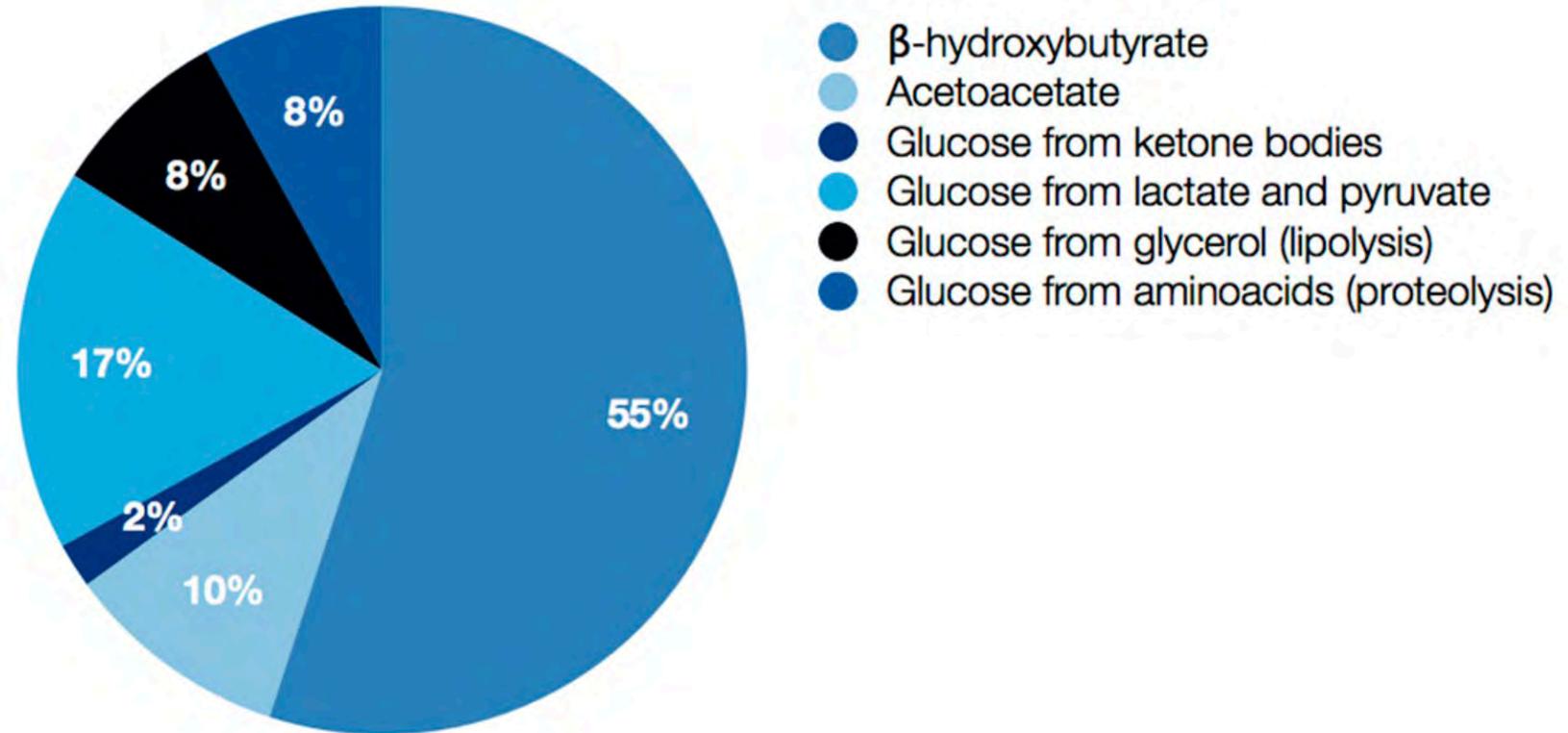
# Ketone Body Production and Utilization During Fasting



# Introducing the Main Protagonists

Ketone bodies provide nearly 2/3 of the brain's energy needs during periods of prolonged fasting and starvation.

Energy substrates for neurons during fasting



# Relationship of Blood Acetoacetate and 3-hydroxybutyrate in Diabetes

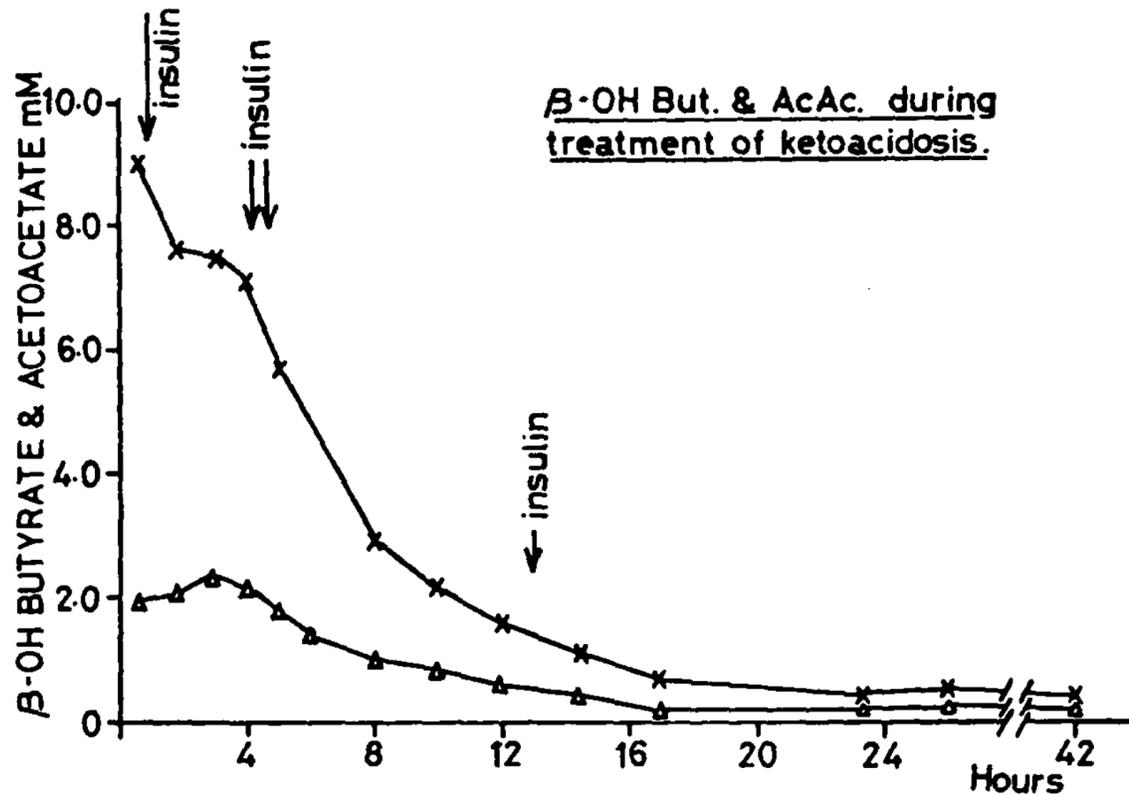


FIG. 4. Blood 3-hydroxybutyrate and acetoacetate changes in a woman of fifty-three years admitted in severe diabetic ketoacidosis precipitated by a respiratory infection. The initial blood glucose was 635 mg. per 100 ml. and the blood pH 7.02.

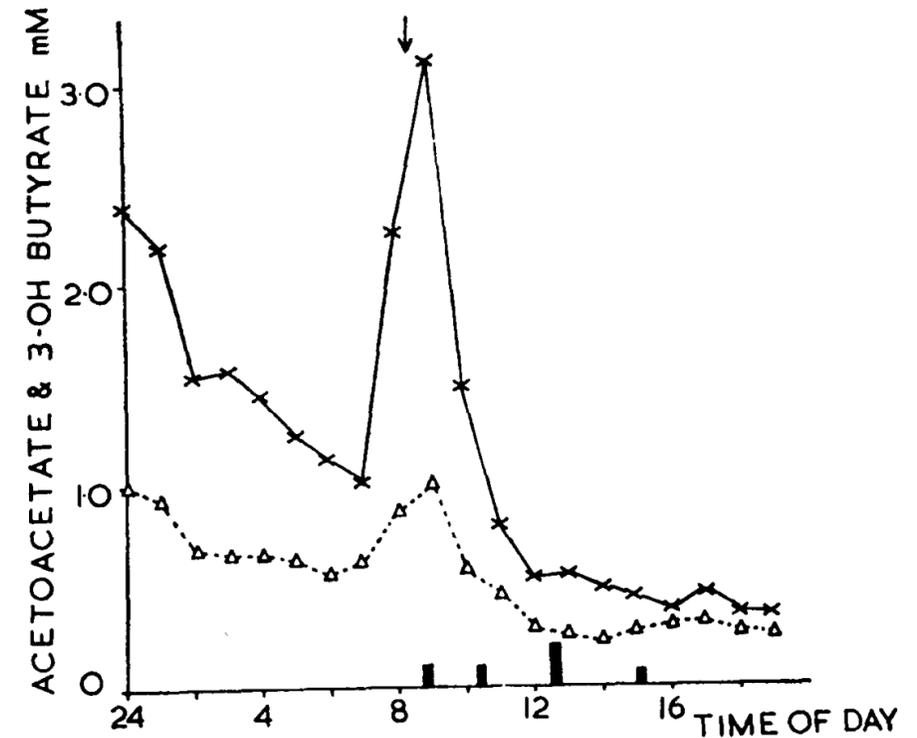
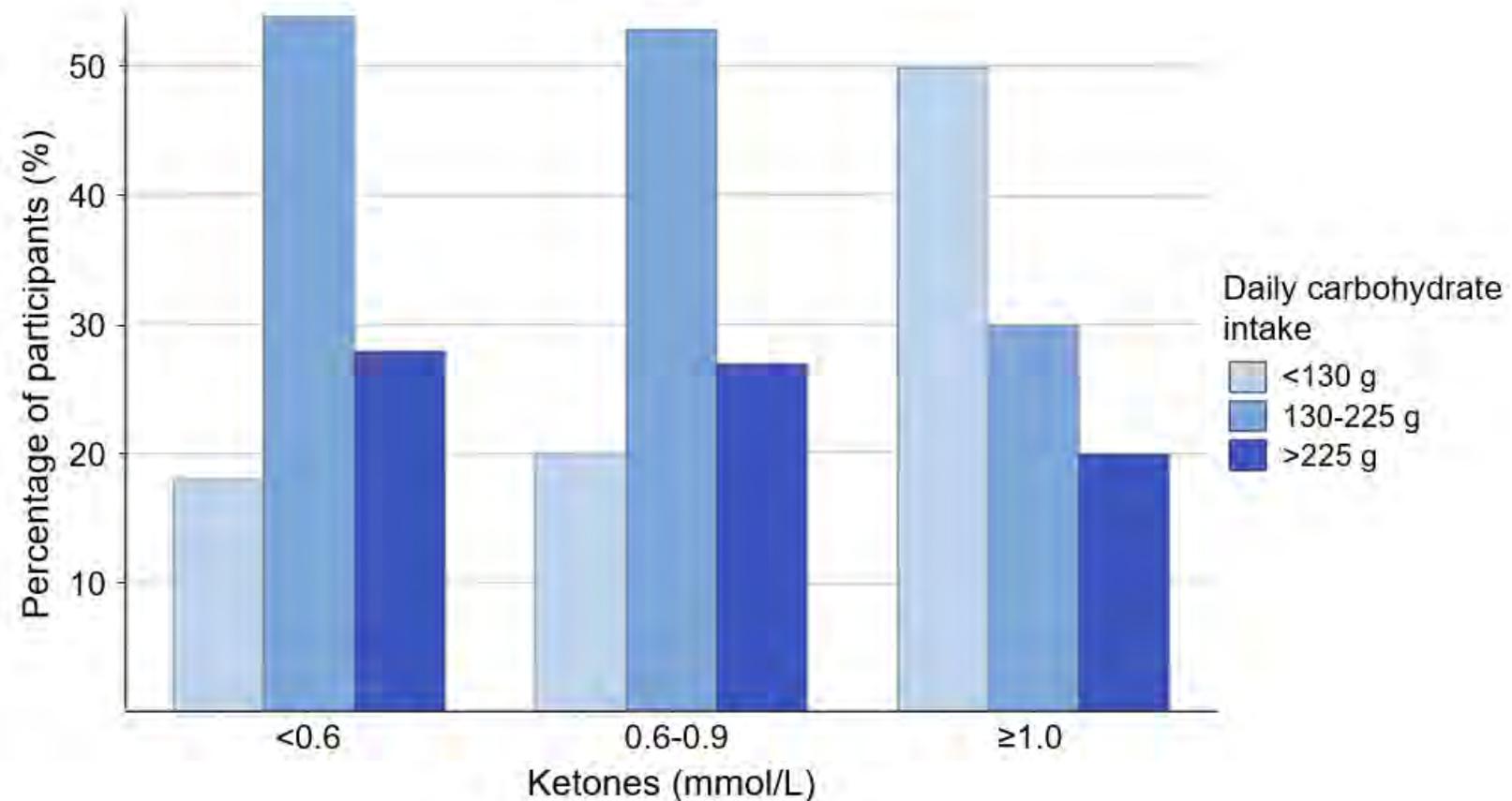


FIG. 5. Blood 3-hydroxybutyrate and acetoacetate changes in an ambulant patient of twenty years, admitted for stabilization of diabetes. The vertical arrow indicates administration of 80 units of soluble insulin subcutaneously and the black bars show mealtimes and their relative carbohydrate content. The blood glucose at 8 a.m. was 320 mg. per 100 ml.

X ——— X 3-hydroxybutyrate  
 Δ ——— Δ acetoacetate

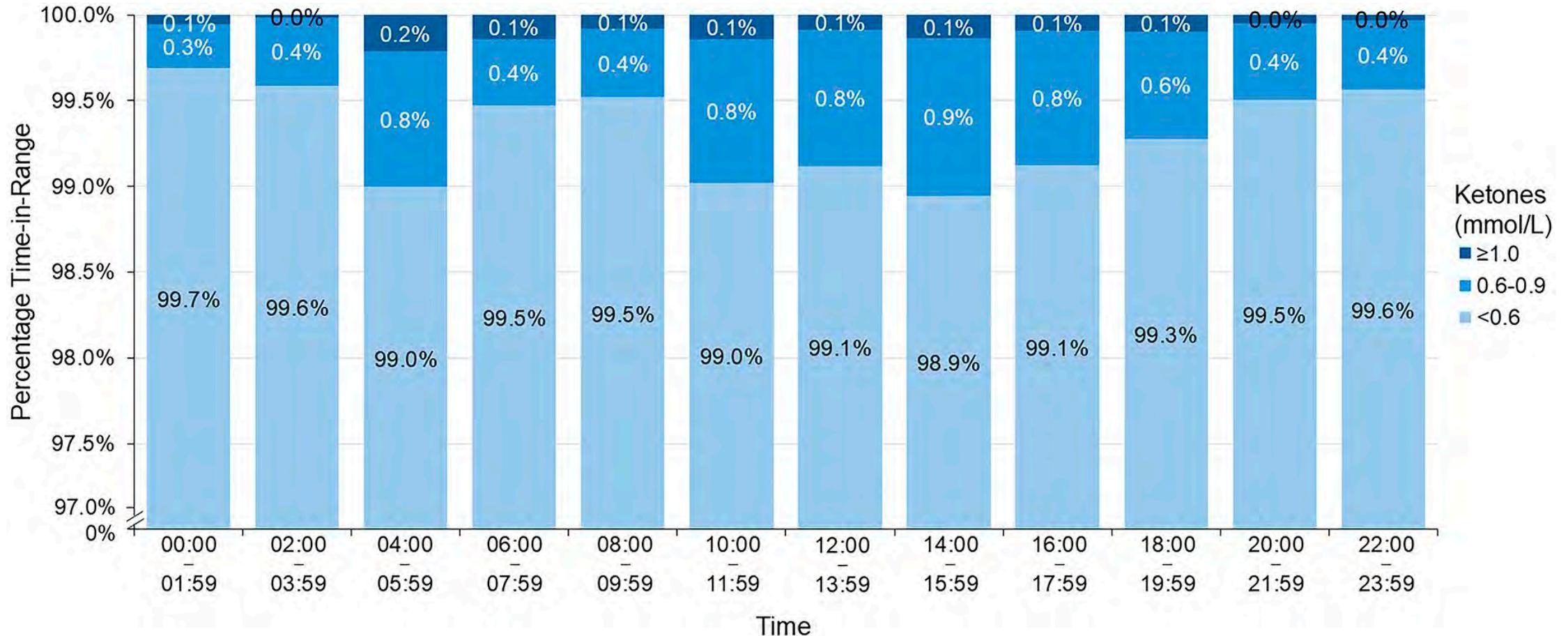
# Ketone Profiles in Community-Dwelling Adults with T1D Using Continuous Ketone Monitoring

Distribution of average daily carbohydrate intake by maximum CKM ketone level measured



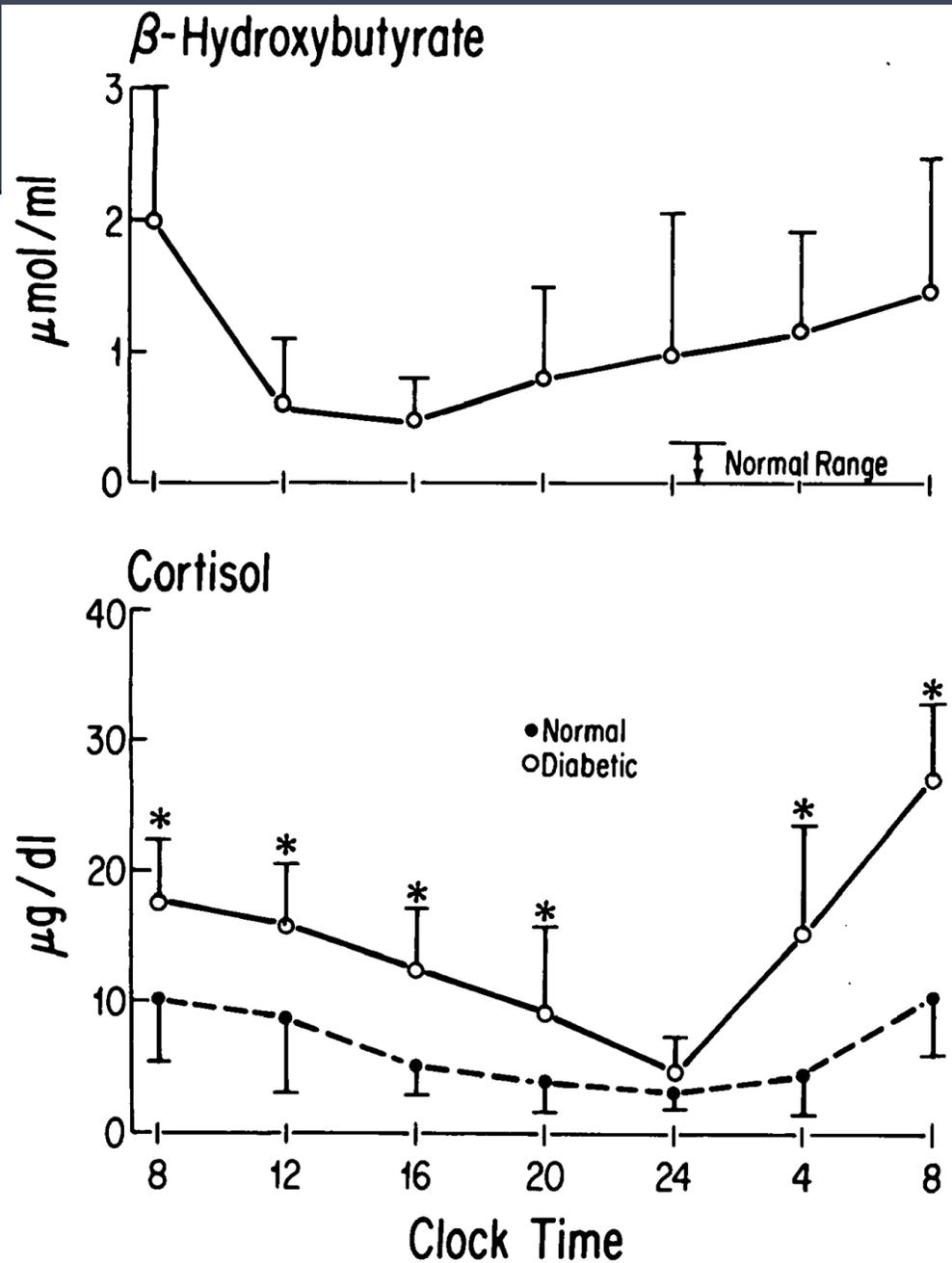
# Ketone Profiles in Community-Dwelling Adults with T1D Using Continuous Ketone Monitoring

**CKM ketone percentage time-in-range over the 24 h period**

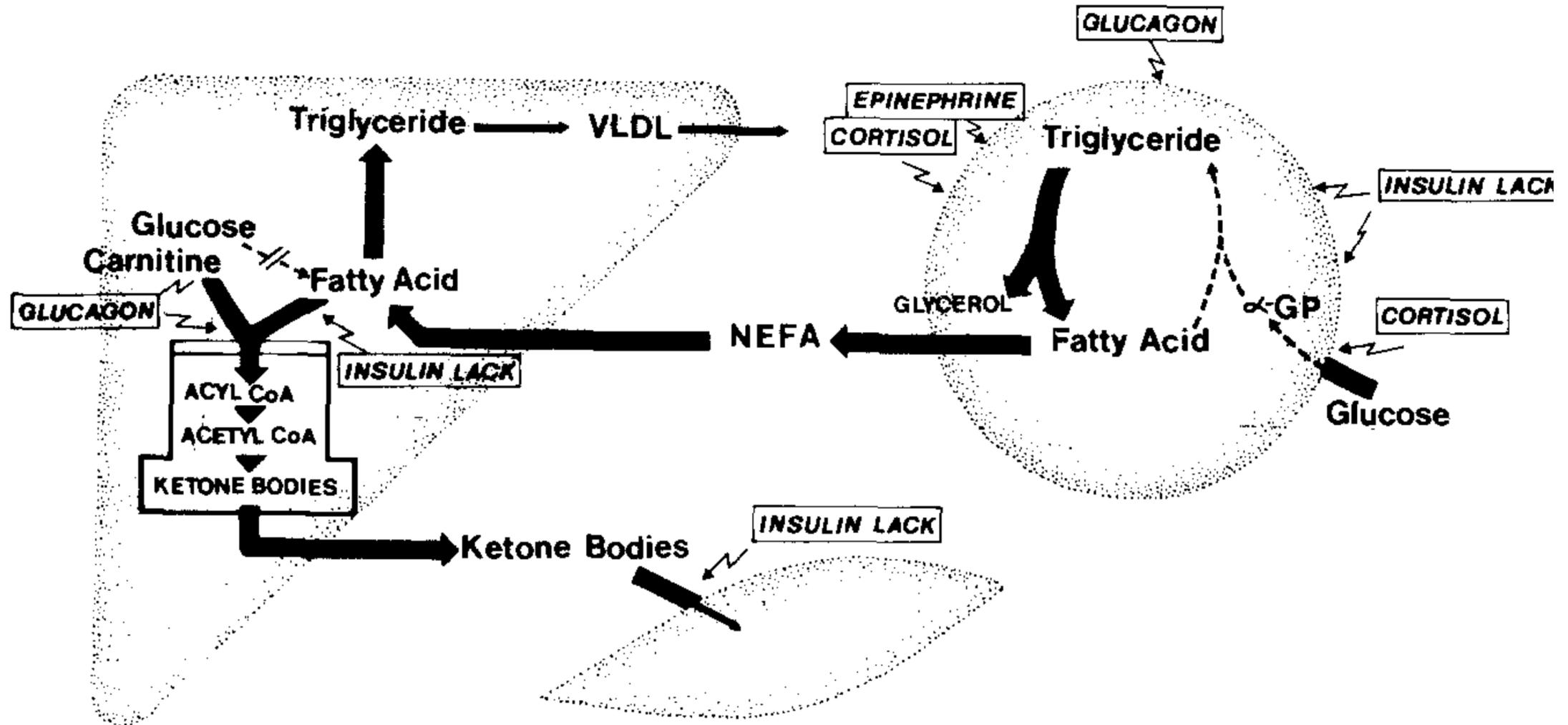


Percentage time-in-range in 64 participants over a 2-week period (median CKM wear duration was 13.4 [IQR: 13.1–13.5] days). CKM, continuous ketone monitor.

**“The association of elevated plasma BHB levels and hypercortisolemia in our diabetic patients suggests that KB kinetics may be influenced by abnormalities in glucocorticoid production as well as insulin availability.”**



# Effects of Major Catabolic Hormones on Ketone Body Metabolism in Insulin Deficiency



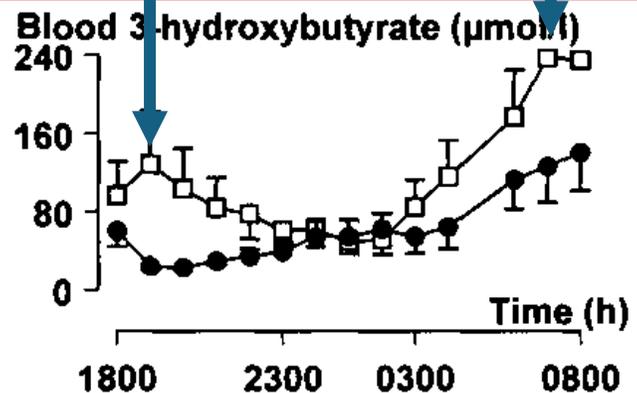
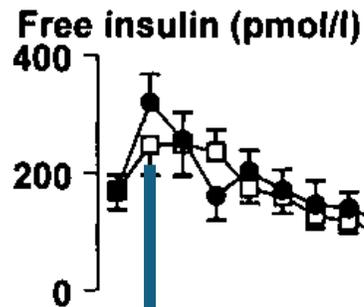
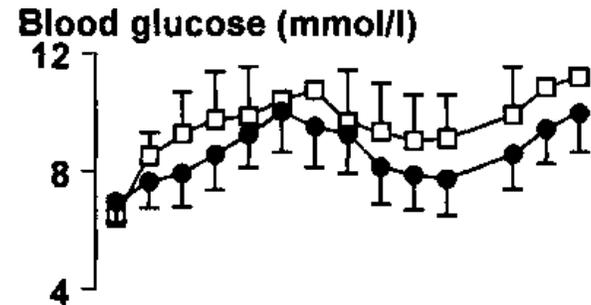
# Quantification of BHB Levels in Type 1 Diabetes

## Can quantification of BHB levels in Type 1 diabetes be used to help monitor diabetes control and guide insulin therapy?

Evening and nighttime (6:00 P.M. to 8:00 A.M.):

- ✓ blood glucose
- ✓ plasma free insulin
- ✓ blood 3-hydroxybutyrate

□ human insulin  
■ lispro



# Ketosis

## Physiological (in response to fasting)

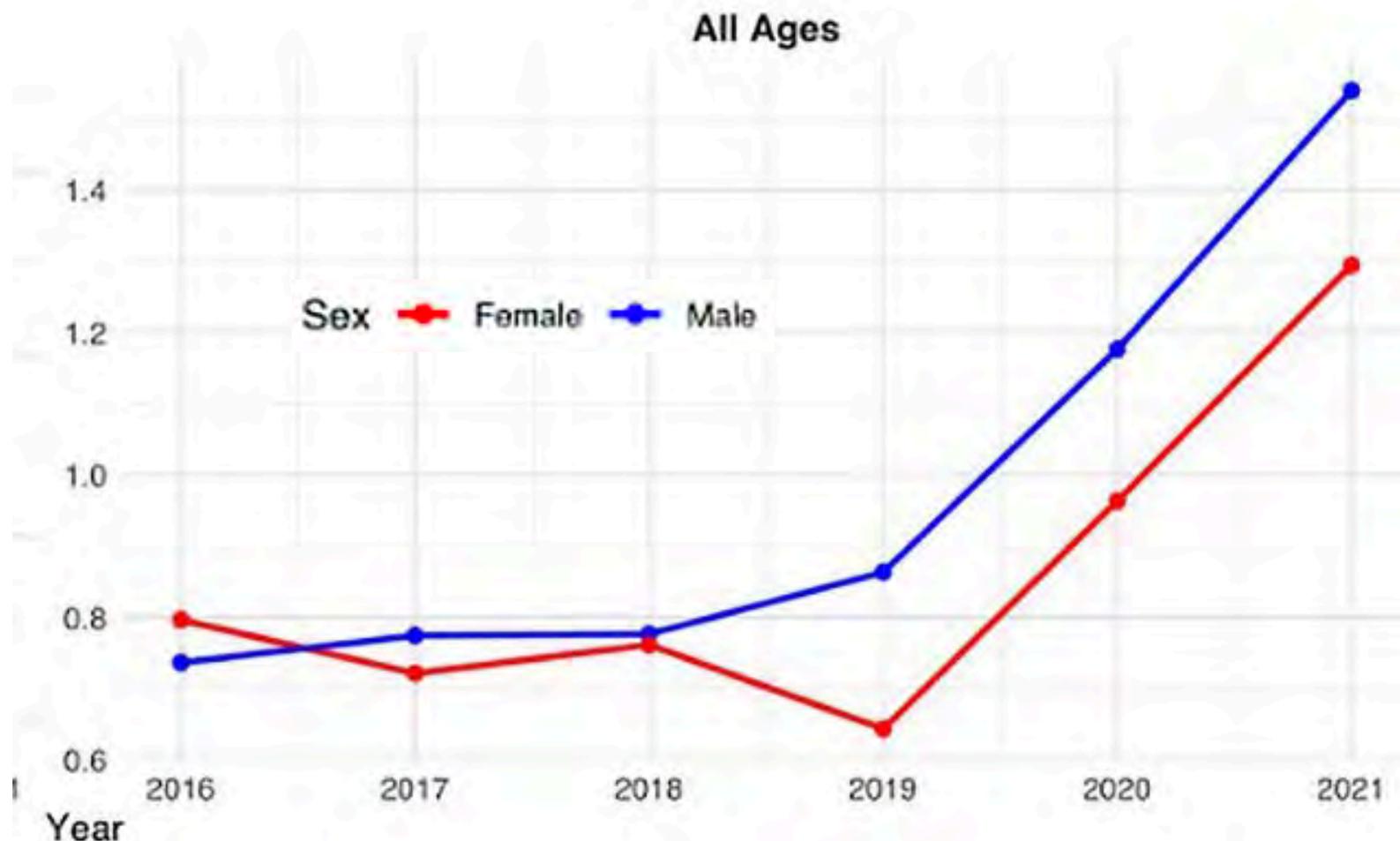
- ▶ Starvation
- ▶ Infancy or pregnancy
- ▶ Prolonged exercise
- ▶ Ketogenic (high-fat) diet

## Pathological Processes

- ▶ Obesity
- ▶ ***Diabetes mellitus***
  - ***Diabetic ketoacidosis (DKA)***
  - ***SGLT2 use: “Euglycemic DKA”***
- ▶ Cortisol / growth hormone deficiency
- ▶ Hyperthyroidism
- ▶ Toxic ingestions of ethanol or salicylates
- ▶ Certain rare inborn errors of metabolism

# Trend of In-Hospital Mortality Among Hospitalizations with DKA 2016-2021

“Global reports clearly show an **increase in the number of DKA admissions** during the past decade, with a 55% increase in the rate of DKA hospitalizations”



Umpierrez GE et al. *Diabetes Care* 2024;47:1257–1275

USA n=594 230

Chia JE, et al. *BMJ Open Diab Res Care* 2026;14:e005817

# ATTD 2026 Late-Breaking Abstracts

**ATTD**

*Advanced Technologies  
& Treatments for Diabetes*

**11-14 MARCH 2026  
BARCELONA & ONLINE**

# Rising Burden of Diabetic Ketoacidosis in the UK

## 21-Year Trends, Recurrence, and Predictors from Linked Primary–Secondary Care Data

- Long-term real-world data on diabetic ketoacidosis (DKA) in UK adults remain limited.
- Adults  $\geq 18$  years with diabetes and  $\geq 1$  glucose-lowering prescription (thus excluding most newly diagnosed individuals) for at least a year.
- Recurrent DKA was defined as  $\geq 2$  episodes during follow-up.
- **Results: Recent DKA was the strongest predictor of recurrence** (IRR 11.4 and 109 in T1DM and T2DM). Other predictors of DKA included female sex, younger age, socioeconomic deprivation and multimorbidity.

### **Conclusion**

**DKA rates have increased steadily in both diabetes types**, with evidence of health inequalities and unmet clinical need, clustering in younger, socioeconomically deprived, and medically complex adults.

Given the strong association of recent DKA with future events, proactive strategies – such as **personalised education and access to real-time ketone monitoring** – are warranted.

# Rising Burden of Diabetic Ketoacidosis in the UK

21-Year Trends, Recurrence, and Predictors from Linked Primary–Secondary Care Data

## Adjusted predictors of first DKA

Predictor	T1DM IRR (95 % CI)	T2DM IRR (95 % CI)
Female vs male	1.42 (1.34–1.50)	1.27 (1.19–1.35)
Age 40–64 y vs 18–39 y	0.47 (0.43–0.50)	0.40 (0.35–0.45)
Age ≥ 75 y vs 18–39 y	0.48 (0.36–0.62)	0.41 (0.30–0.55)
IMD quintile 5 vs 1	2.66 (2.42–2.93)	1.47 (1.33–1.63)
CCI ≥ 3 vs 0	2.25 (1.99–2.53)	1.46 (1.33–1.61)
Recent DKA ≤ 28 d	11.4 (10.1–12.8)	108.7 (88.5–133.5)

# FreeStyle Libre Use: Decrease in Hospitalizations for DKA

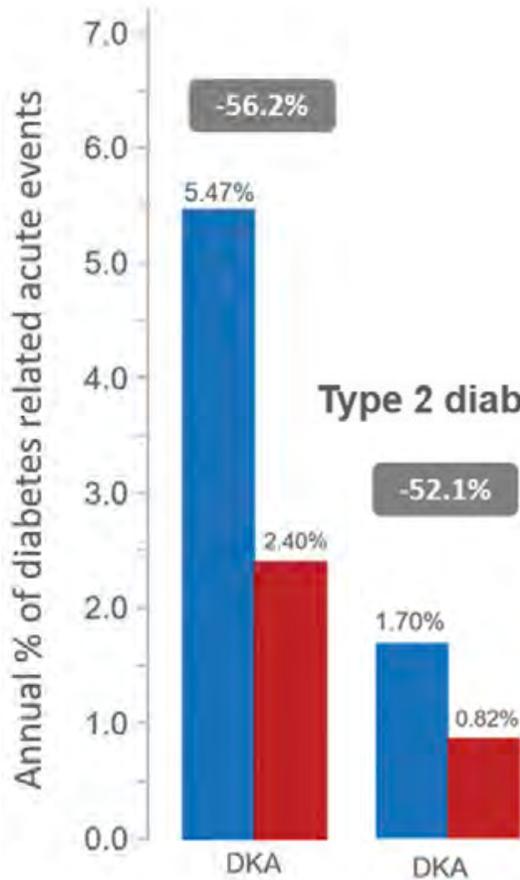
## RELIEF study (France)



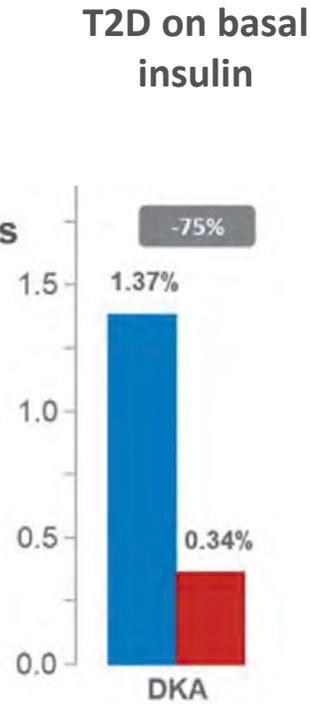
## Eeg-Olofsson study (Sweden)



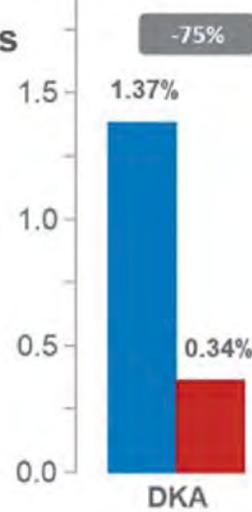
### Type 1 diabetes



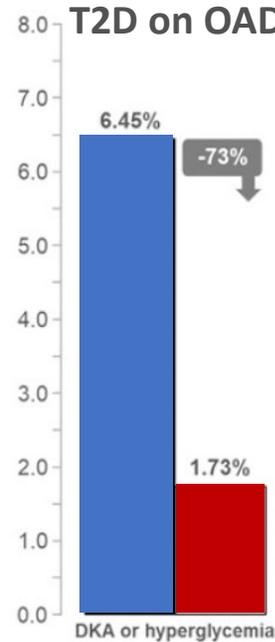
### Type 2 diabetes



### T2D on basal insulin

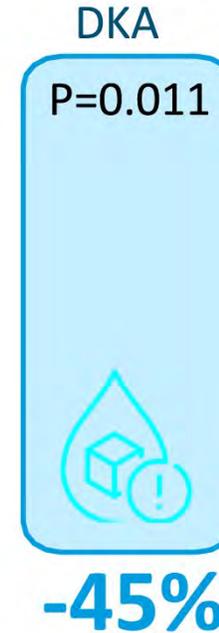


### T2D on OADs



■ 12 months prior to FreeStyle Libre ■ 12 months following FreeStyle Libre

### T1DM vs BGM

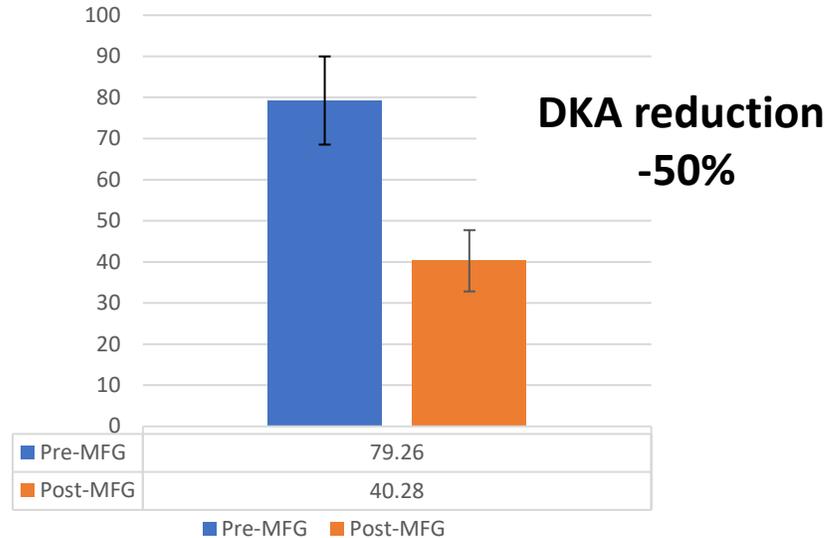


# FreeStyle Libre Use: Decrease in Hospitalizations for DKA



## Andalucia Study (Spain)

### T1D



DKA Events/10,000 person- years

n = 13,616

## T2D on MDI

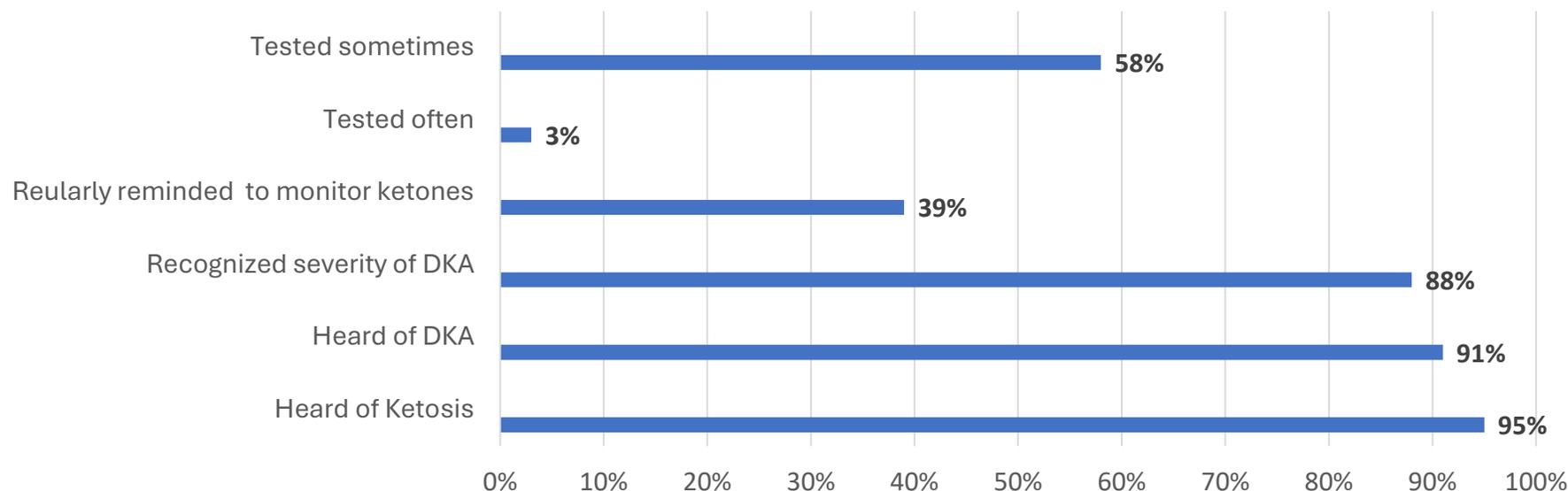
**DKA  
reduction  
-27,6%**

# Patients' Knowledge and Barriers to Ketone Self-Monitoring

## Results From a Prospective Survey of T1DM Patients From the French SFDT1 Cohort

- ▶ International guidelines recommend ketone monitoring in specific situations. This study assessed patients' awareness of ketosis and DKA, and identified barriers to self-monitoring.
- ▶ A total of 553 adults surveyed. 62% reported prior DKA.

### Awareness



**Interest in a dual glucose-ketone sensor was high (82%)**

### Conclusion

Despite strong awareness, challenges remain around symptom recognition, equipment, and time.

Leading barriers were: poor symptom recognition (56%); lack of equipment (52%), and time constraints (52%), particularly among CSII/AID users or those with TIR<70%.

**High interest in dual glucose-ketone sensors highlights limitations of current methods and the need for accessible, patient-centric solutions to support DKA prevention.**

# Provider Perspectives on Hyperketonemia, Diabetic Ketoacidosis Healthcare Burden and Ketone Monitoring in T1D and T2D

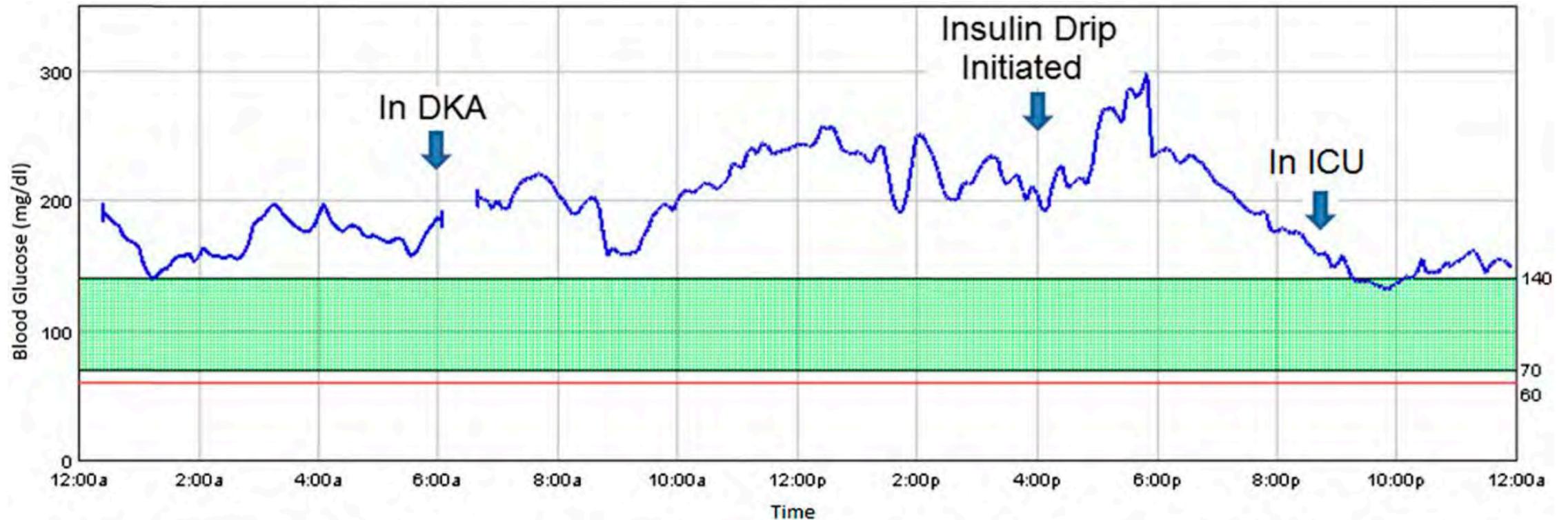
- ▶ Ketone monitoring is an essential step in early detection of hyperketonemia and prevention of DKA, but previous research has revealed barriers amongst PWD; clinical perspectives on ketone management and monitoring require further investigation.
- ▶ **Results:** Qualitative findings will highlight providers' clinical perspectives and knowledge gaps regarding ketone monitoring and management.
- ▶ Additional findings will highlight current approaches to preventing and managing ketosis, hyperketonemia, and diabetic ketoacidosis, as well as their implications for clinical practice.

## Conclusion

This qualitative study will capture the perspectives, beliefs, and values that influence provider behaviors around ketone management. **These insights will highlight needs around ketone management, which could include increased awareness and access to ketone monitoring tools to help fill the current gaps in ketone management for PWD.**

# Euglycemic Diabetic Ketoacidosis (euDKA)

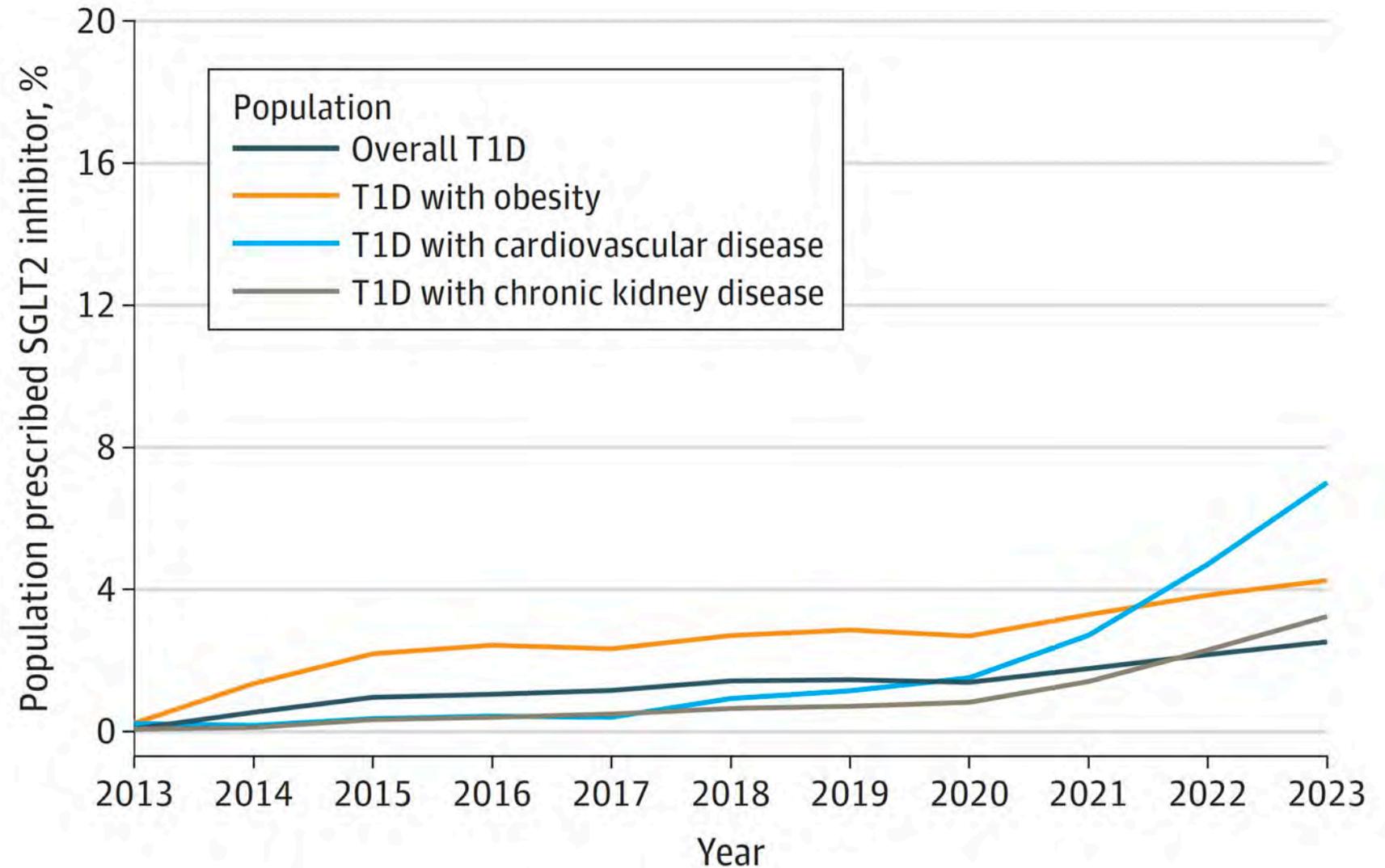
A Potential Complication of Treatment With SGLT2i



*One-day CGM reading of a case patient in the day of admission to the ICU in euDKA.*

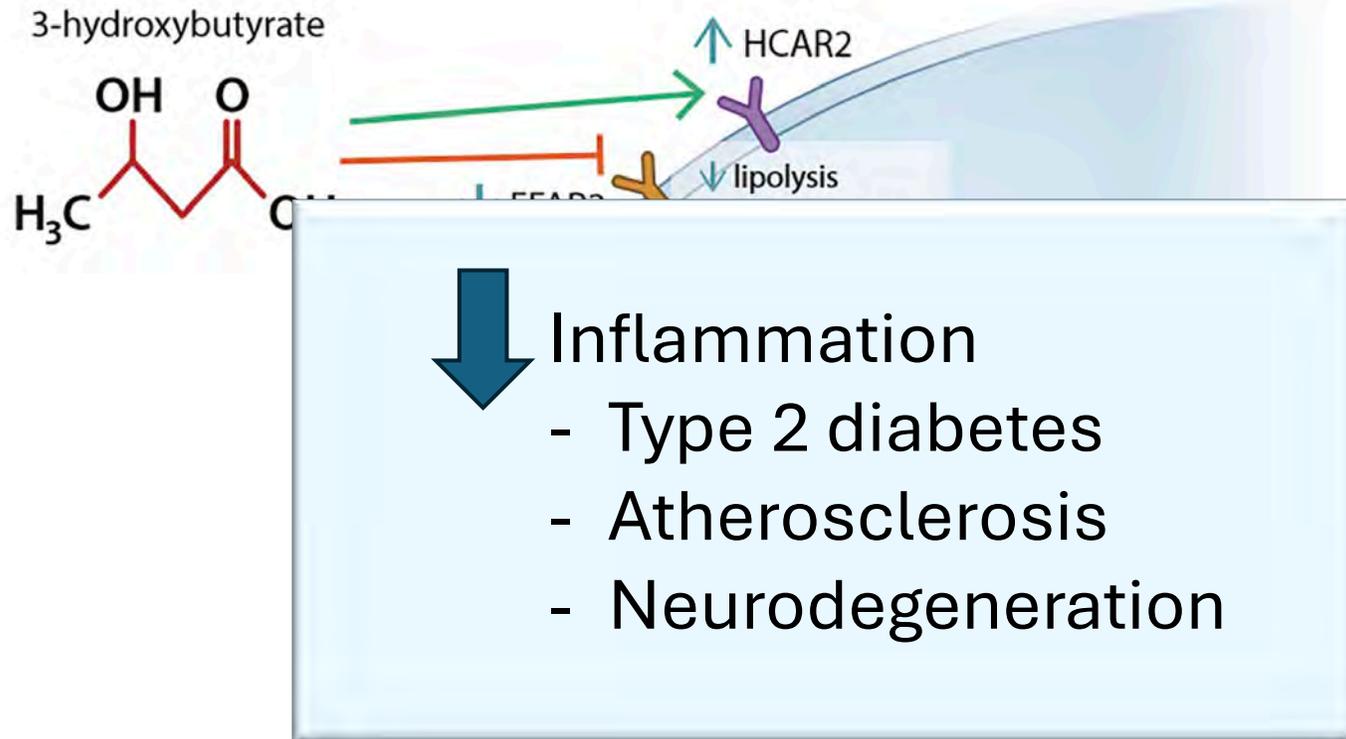
# T1D Population Prescribed SGLT2i

Pooled cross-sectional analysis of EHRs from an integrated database including **257 million across 50 USA states**

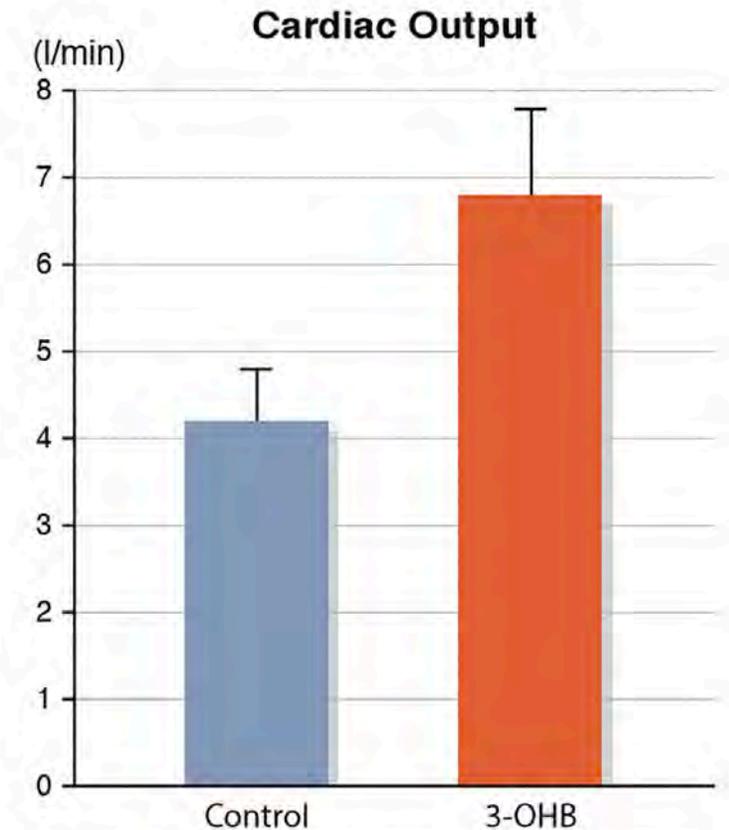


# Ketones Role in T2D, Long-Term Complications, Heart Failure,...

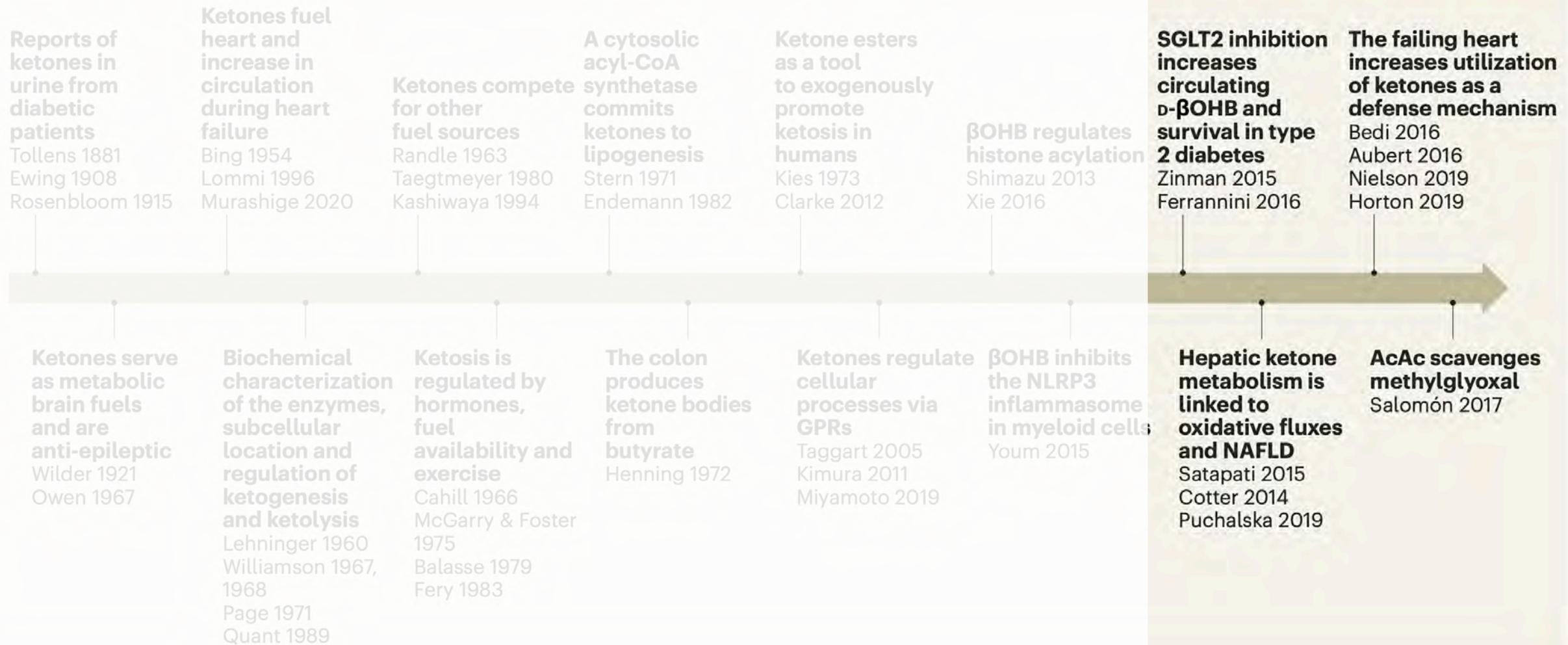
Intracellular signaling mediated by 3-hydroxybutyrate (3-OHB).



Cardiovascular effects of treatment with the ketone body 3-hydroxybutyrate in chronic heart failure patients.



# Timeline of Major Discoveries Related to Ketone Bodies



GPR, G-protein-coupled receptor; NAFLD, nonalcoholic fatty liver disease; SGLT, sodium glucose cotransporter.



**Thank you very much for your  
attention! ¡Muchas gracias!**

[fgomezp@saludcastillayleon.es](mailto:fgomezp@saludcastillayleon.es)

# Beyond CGM: Dual Sensing Technology as a Cornerstone of DKA Prevention

**Prof Ketan Dhatariya MBBS MSc MD MS FRCP PhD**

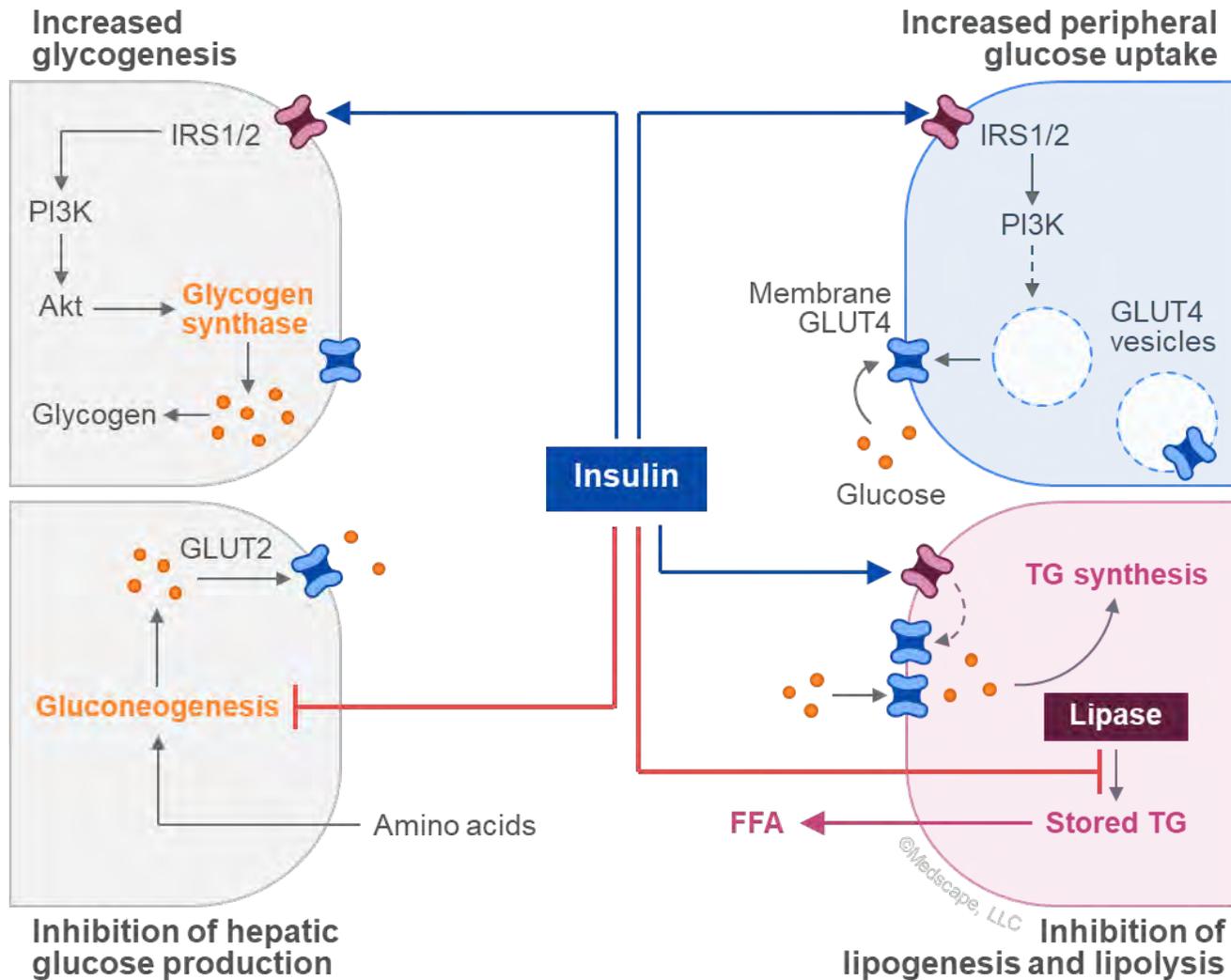
Consultant in Diabetes and Endocrinology  
Norfolk and Norwich University Hospitals



# Disclosures

- ▶ In the last 12 months I have received honoraria, travel, fees for speaking or advisory boards from
  - Abbott Diabetes
  - AstraZeneca
  - Boehringer-Ingelheim
  - Eli Lilly
  - Menarini
  - Novo Nordisk
  - Roche
  - Sanofi Diabetes

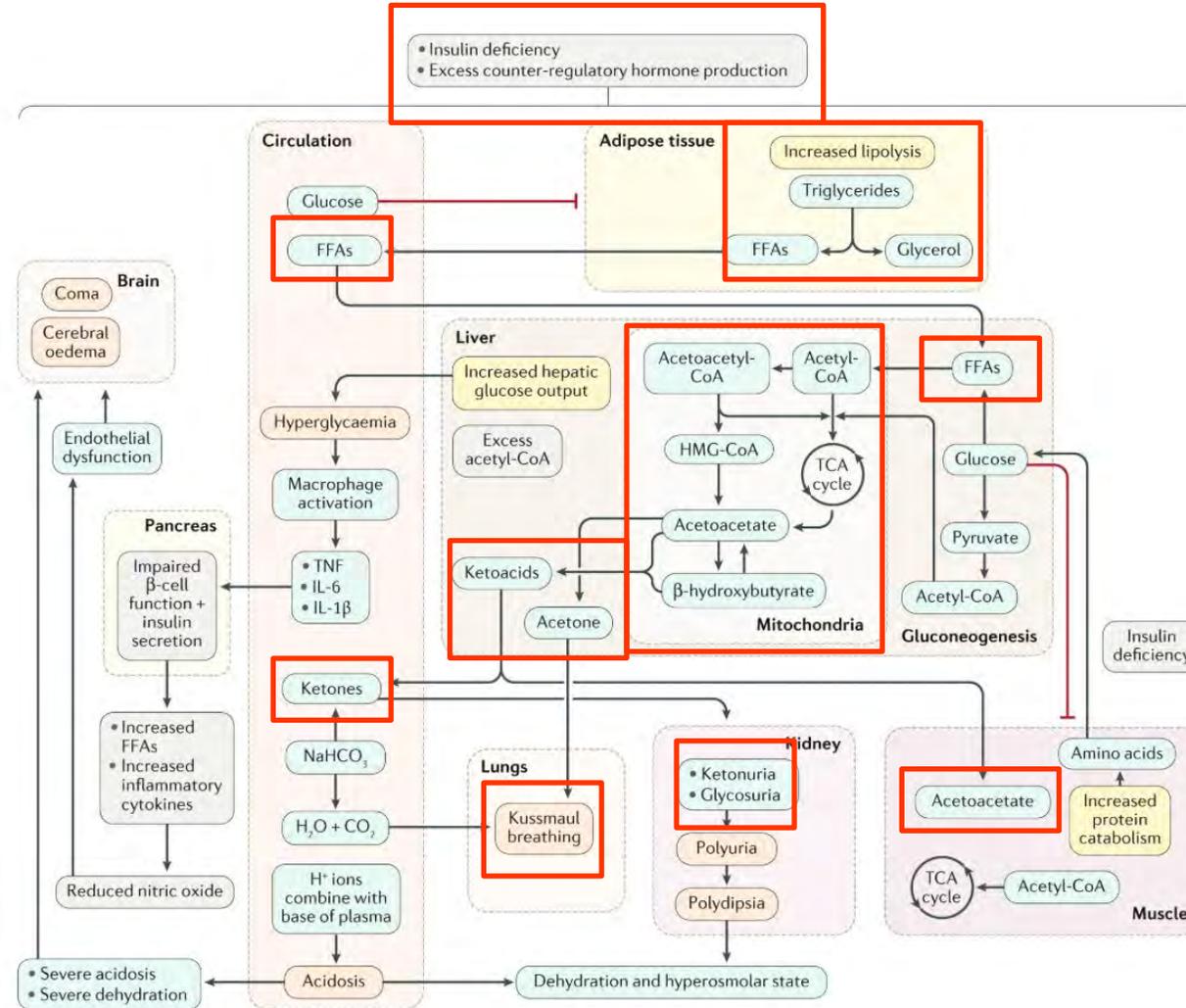
# Back to Basics



At different plasma concentrations, insulin has different effects

- ▶ At the very lowest concentrations, it suppresses ketogenesis
- ▶ Then it stops gluconeogenesis and skeletal muscle catabolism
- ▶ Then it causes glucose uptake and glycogen synthesis
- ▶ Finally, it is an anabolic hormone

# Physiology

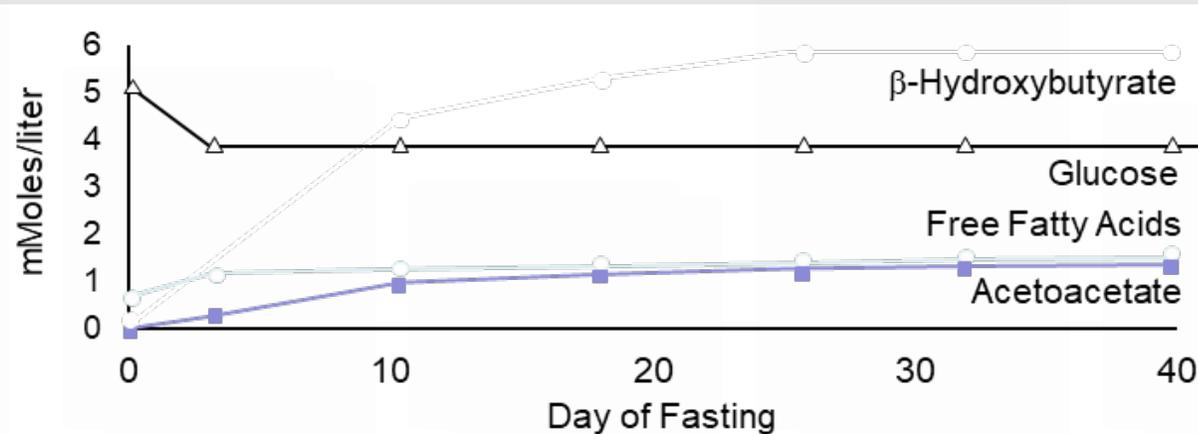


# Ketones – Why Are They Important?

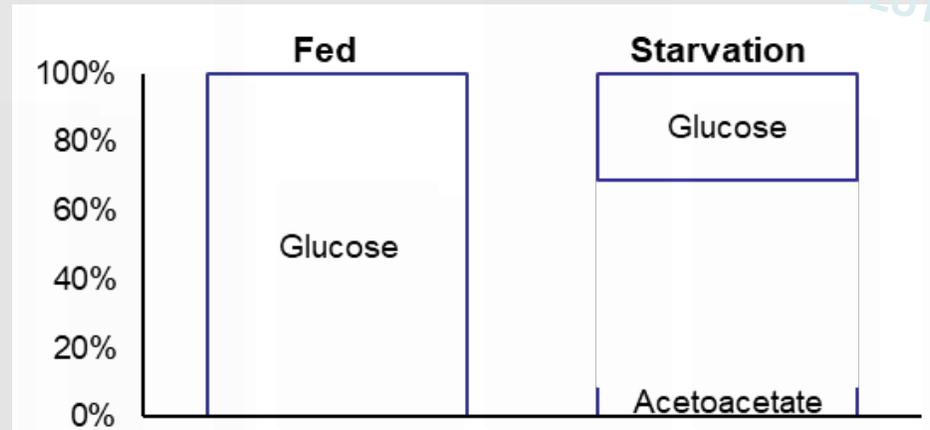
Levels of Circulating Substrates

Period of observation	Glucose mg/100 ml	Free fatty acids	Acetoacetate	$\beta$ -Hydroxybutyrate mM	Glycerol	Amino acids	Lactate	Pyruvate
Post-absorptive	80	0.5	0.01	0.01	0.06	4.5	0.6	0.1
After 1 wk fast	65	1.5	1.0	4.0	0.1	4.5	0.6	0.1
After 4–5 wks fast	65	1.5	1.5	6.0	0.1	3.5	0.6	0.1

Blood Glucose, Free Fatty Acids and Ketone Body Levels During Fast



Brain Fuel



EVOLUTION!

# Living Longer on Starvation Diets

## Dietary deprivation extends lifespan in *Caenorhabditis elegans*

Garrick D. Lee,<sup>1</sup> Mark A. Wilson,<sup>2</sup> Min Zhu,<sup>1</sup> Catherine A. Wolkow,<sup>2</sup> Rafael de Cabo,<sup>1</sup> Donald K. Ingram<sup>1,3</sup> and Sigge Zou<sup>1</sup>

dietary restriction (DR) (Masoro, 2005). DR has been shown to extend lifespan in many species, ranging from invertebrates to mammals. In addition, DR enhances resistance to a variety of



## A Ketogenic Diet Extends Longevity and Healthspan in Adult Mice

Megan N. Roberts,<sup>1</sup> Marita A. Wallace,<sup>2</sup> Alexey A. Tomilov,<sup>1</sup> Zeyu Zhou,<sup>1</sup> George R. Marcotte,<sup>2</sup> Dianna Tran,<sup>1</sup> Gabriella Perez,<sup>1</sup> Elena Gutierrez-Casado,<sup>7</sup> Shinichiro Koike,<sup>3</sup> Trina A. Knotts,<sup>1</sup> Denise M. Imai,<sup>4</sup> Stephen M. Griffey,<sup>1</sup> Kyoungmi Kim,<sup>5</sup> Kevork Hagopian,<sup>1</sup> Marissa Z. McMackin,<sup>1</sup> Fawaz G. Haj,<sup>9</sup> Keith Baar,<sup>2,6</sup> Gino A. Cortopassi,<sup>1</sup> Jon J. Ramsey,<sup>1,9,\*</sup> and Jose Alberto Lopez-Dominguez<sup>1,8,\*</sup>

<sup>1</sup>Department of Molecular Biosciences, School of Veterinary Medicine



## LETTER

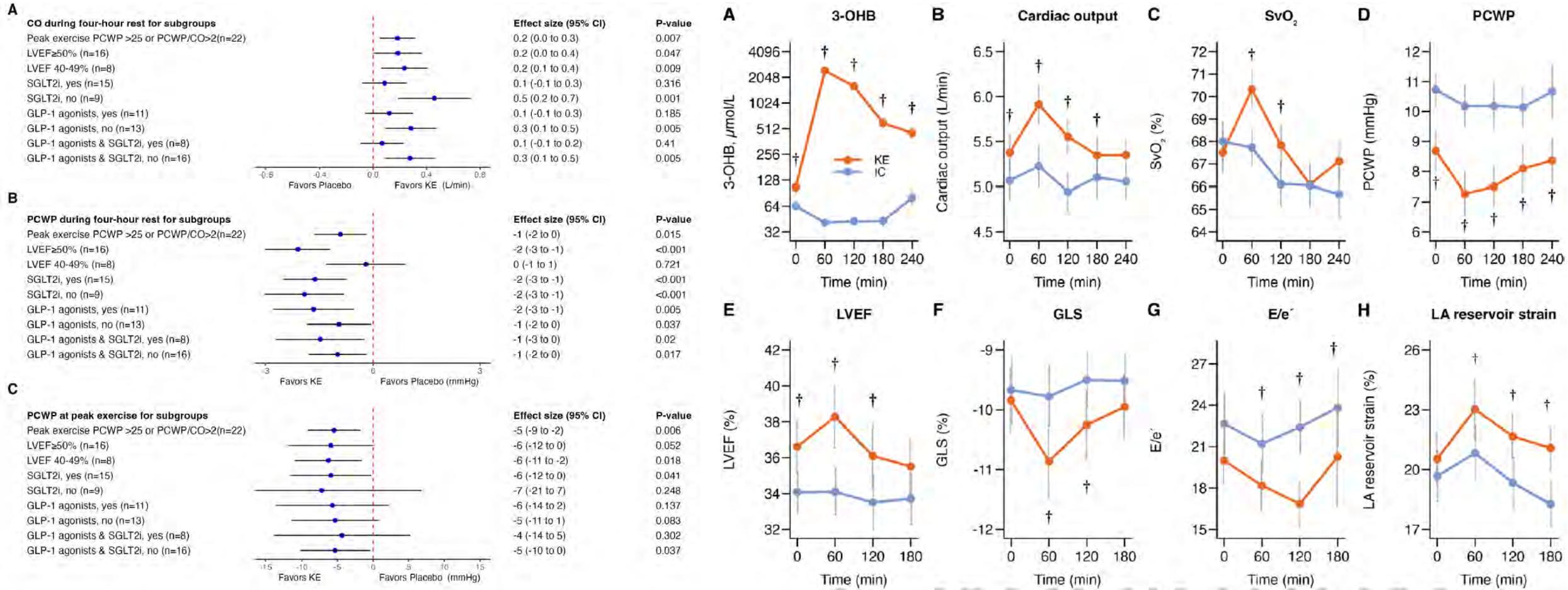
doi:10.1038/nature11432

## Impact of caloric restriction on health and survival in rhesus monkeys from the NIA study

Julie A. Mattison<sup>1</sup>, George S. Roth<sup>2</sup>, T. Mark Beasley<sup>3</sup>, Edward M. Tilmont<sup>1</sup>, April M. Handy<sup>1,4</sup>, Richard L. Herbert<sup>5</sup>, Dan L. Longo<sup>6</sup>, David B. Allison<sup>7</sup>, Jennifer E. Young<sup>1</sup>, Mark Bryant<sup>8</sup>, Dennis Barnard<sup>9</sup>, Walter F. Ward<sup>10</sup>, Wenbo Qi<sup>11</sup>, Donald K. Ingram<sup>12</sup> & Rafael de Cabo<sup>13</sup>

Lee GD et al Ageing Cell 2006;5(6):515-524  
Roberts MN et al Cell Metabol 2017;26(3):P539-546.E5  
Mattison JA et al Nature 2012;489(7415):318-321

# Failing Hearts Prefer Ketones



# Published in August 2024

Diabetologia (2024) 67:1455–1479

<https://doi.org/10.1007/s00125-024-06183-8>

CONSENSUS REPORT



## Hyperglycaemic crises in adults with diabetes: a consensus report

Guillermo E. Umpierrez<sup>1</sup> · Georgia M. Davis<sup>1</sup> · Nuha A. ElSayed<sup>2,3</sup> · Gian Paolo Fadini<sup>4,5</sup> ·  
Rodolfo J. Galindo<sup>6</sup> · Irl B. Hirsch<sup>7</sup> · David C. Klonoff<sup>8</sup> · Rozalina G. McCoy<sup>9,10</sup> · Shivani Misra<sup>11,12</sup> ·  
Robert A. Gabbay<sup>2,3</sup> · Raveendhara R. Bannuru<sup>2</sup> · Ketan K. Dhatariya<sup>13,14</sup>

Diabetes Care Volume 47, August 2024

1257



### Hyperglycemic Crises in Adults With Diabetes: A Consensus Report

Diabetes Care 2024;47:1257–1275 | <https://doi.org/10.2337/dci24-0032>



Guillermo E. Umpierrez,<sup>1</sup>  
Georgia M. Davis,<sup>1</sup> Nuha A. ElSayed,<sup>2,3</sup>  
Gian Paolo Fadini,<sup>4,5</sup> Rodolfo J. Galindo,<sup>6</sup>  
Irl B. Hirsch,<sup>7</sup> David C. Klonoff,<sup>8</sup>  
Rozalina G. McCoy,<sup>9,10</sup> Shivani Misra,<sup>11,12</sup>  
Robert A. Gabbay,<sup>2,3</sup>  
Raveendhara R. Bannuru,<sup>2</sup> and  
Ketan K. Dhatariya<sup>13,14</sup>

CONSENSUS REPORT

Umpierrez GE et al Diabetes Care 2024;47(8):1257-1275

Umpierrez GE et al Diabetologia 2024;67(8):1455-1479

# New DKA Diagnostic Criteria

DKA	<b>Diabetes/hyperglycaemia</b>	Glucose $\geq 200$ mg/dl (11.1 mmol/l) or prior history of diabetes
	<b>Ketosis</b>	$\beta$ -hydroxybutyrate $\geq 3.0$ mmol/l or urine ketone strip 2+ or greater
	<b>Metabolic Acidosis</b>	pH $< 7.3$ and/or bicarbonate concentration $< 18$ mmol/l

# Why 3.0mmol/l?

## IDM

### The hospital and home use of a 30-second hand-held blood ketone meter: guidelines for clinical practice

T. M. Wallace, N. M. Meston\*, S. G. Gardnert and D. R. Matthews

**Conclusion** Near patient blood ketone testing is a useful adjunct to blood glucose monitoring in distinguishing between ketosis and simple hyperglycaemia. The data suggest that  $\beta$ -OHB levels  $\geq 1$  mmol/l require further action and levels  $> 3$  mmol/l necessitate medical review. In addition, the rate of fall of  $\beta$ -OHB in DKA can be used as an indicator of the adequacy of treatment.

# Physiological vs Pathological

- ▶ It's the rate of appearance and the ability for renal and respiratory compensation for the drop in pH
- ▶ A rise of  $\beta$  hydroxybutyrate of  $\geq 0.2$  mmol/l/hr might be considered 'pathological'
- ▶ But there are currently no technologies available to allow prediction or prevention other than glucose meters that say 'Hi' and 'Check ketones' or point of care capillary ketone meters

# Any Age and Any Kind of Diabetes



Most common **hyperglycemic emergency** in persons living with diabetes



DKA is a **leading cause of death** among children and adults (< 58) with diabetes



**1%–13% annual prevalence** of DKA in adults with T1D across countries

## DKA and T2D



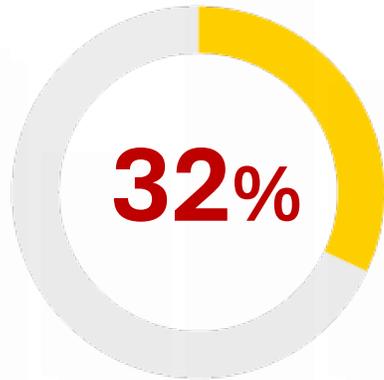
**Hospitalization for DKA:** 1 in 5 cases attributed to T2D



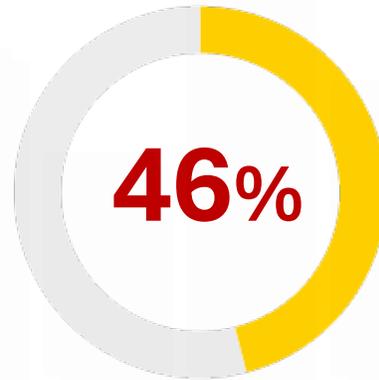
**Higher mortality** for T2D (0.85%) with DKA than T1D (0.2%)

# DKA Unawareness

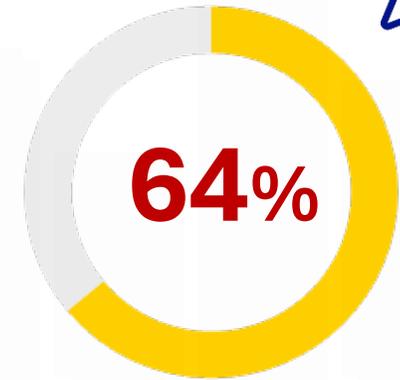
MULTINATIONAL, MULTICENTER SURVEY OF ENDOCRINE OUTPATIENT CLINIC PATIENTS WITH AVERAGE DURATION OF T1D OF 22 YEARS (N=333)



Were not familiar with the term DKA



Were unable to name a single symptom of DKA



Did not test for ketones at all



# No Self-Monitoring

A green circle containing the text "< 20%".

< 20%

---

Test ketone levels, even when glucose is > 16.7 mmol/L for 1 hour or more

A dark blue circle containing the text "38%".

38%

---

Never test ketones when nauseated and/or vomiting

A yellow circle containing the text "45%".

45%

---

Never test ketone levels when they detect a fever

# Barriers to DKA Prevention

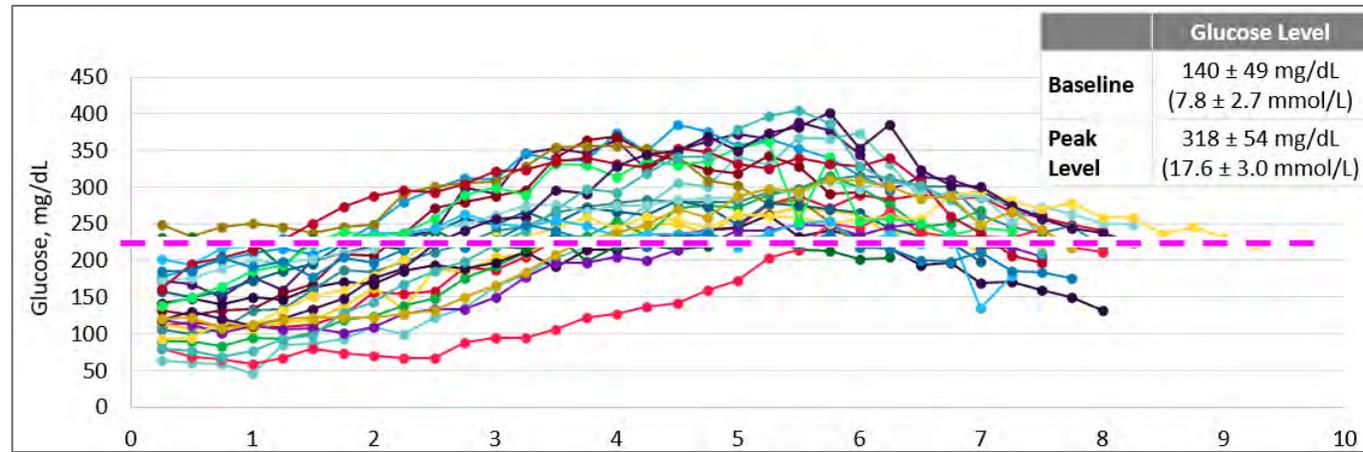
- ▶ Lack of knowledge of what ketones are, what DKA is, when to check ketone levels, how to interpret ketone level results, and when to seek emergency medical care
- ▶ Some individuals with T1D experience feelings of responsibility for their disease and its management and are consequently less likely to seek help from healthcare providers
- ▶ Individuals with T1D do not expect that they could get DKA and that it could be life-threatening, or that it truly would require emergency medical care

# Barriers to DKA Prevention

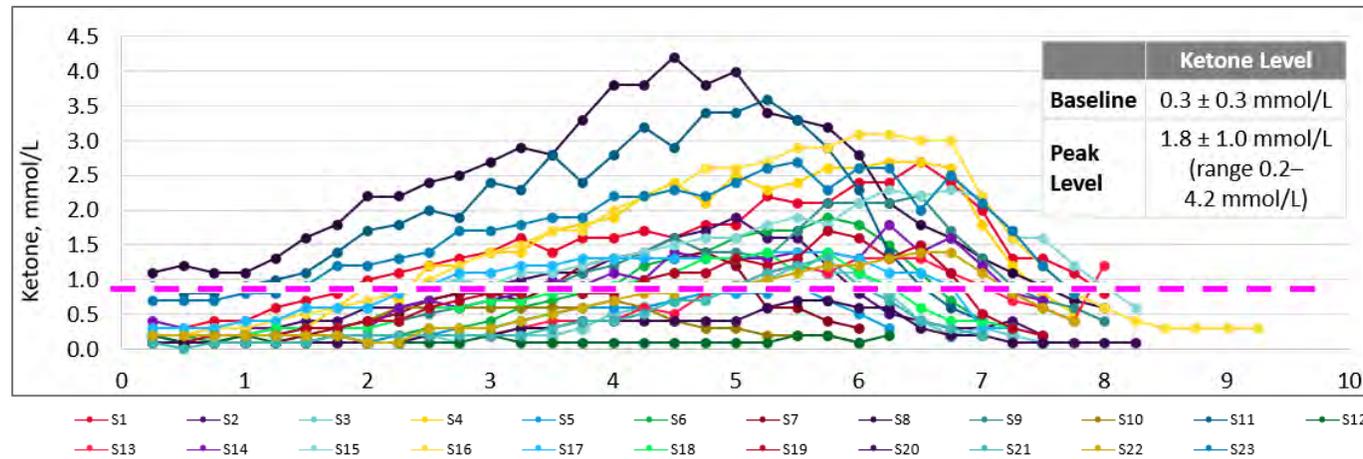
- ▶ Individuals with T1D could benefit from frequent reinforcement regarding preparing for sick days and healthcare providers could benefit from frequent reinforcement to counsel on DKA
- ▶ It is difficult for individuals with T1D to remember information that will help them recognize and prevent DKA given all the other self-management burdens
- ▶ Support from loved ones and others with T1D improves ability to engage in DKA prevention
- ▶ There is financial inaccessibility to resources and outdated existing DKA preventative guidelines

# Glucose and Ketone Variability

Glucose Profiles  
During Pump  
Suspension

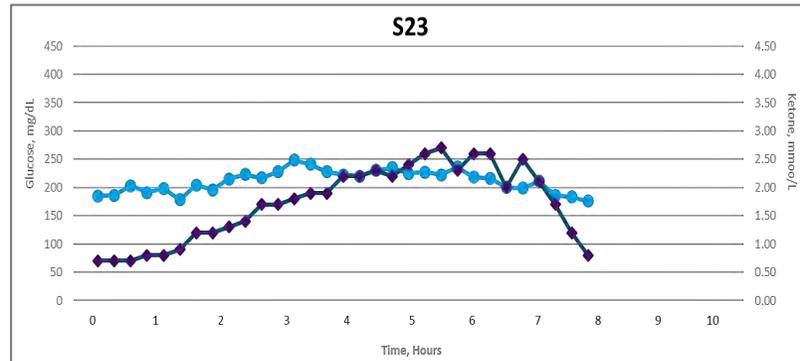
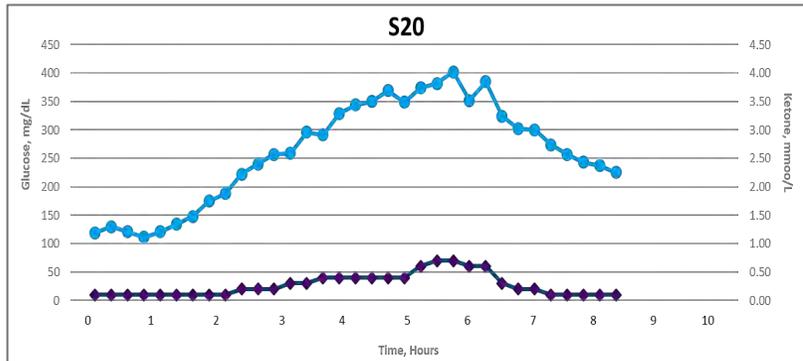
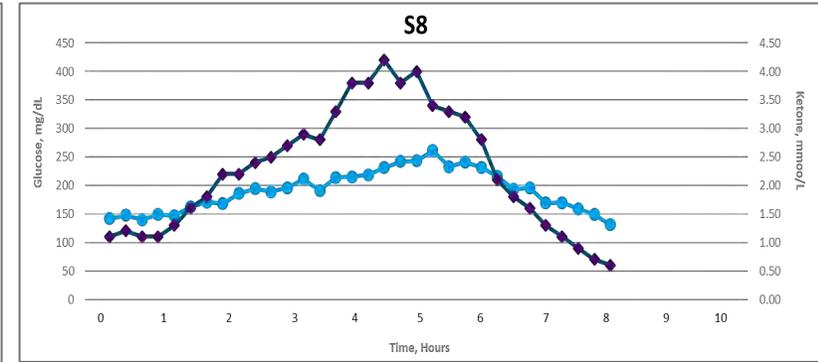
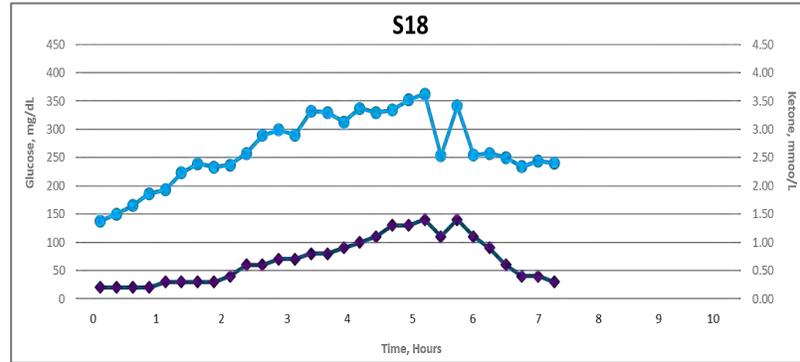
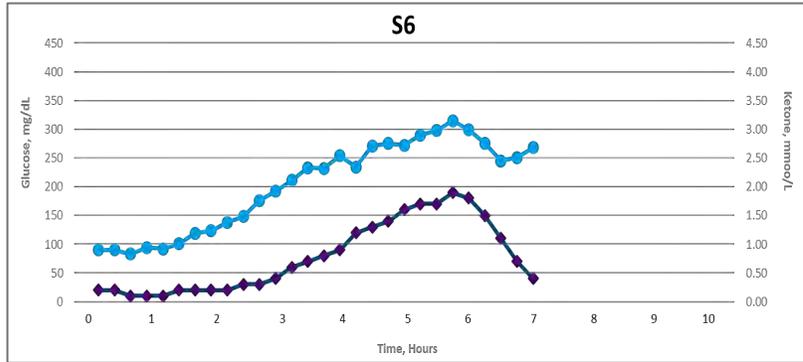


Ketone Profiles  
During Pump  
Suspension



● S1    ● S2    ● S3    ● S4    ● S5    ● S6    ● S7    ● S8    ● S9    ● S10    ● S11    ● S12  
● S13    ● S14    ● S15    ● S16    ● S17    ● S18    ● S19    ● S20    ● S21    ● S22    ● S23

# Glucose and Ketone Variability

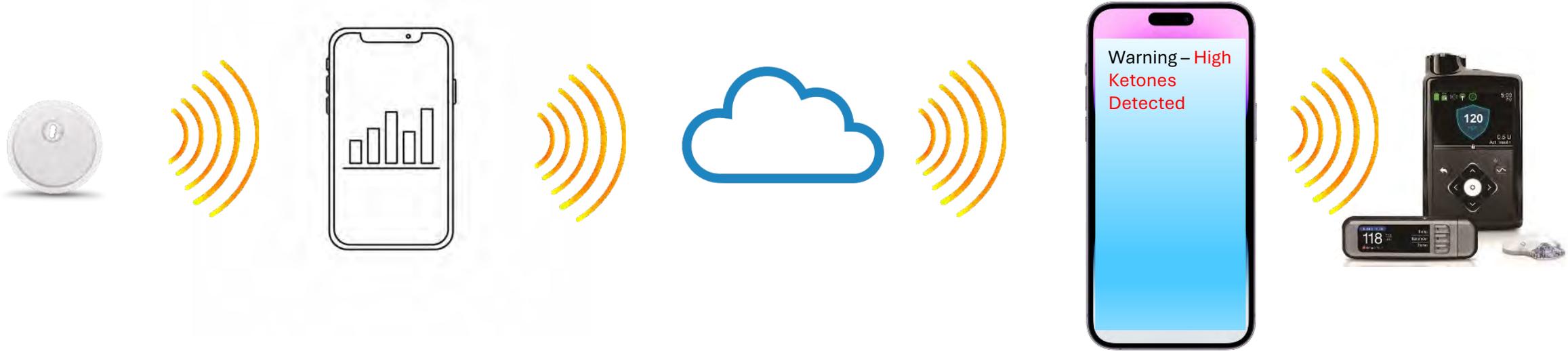


● Glucose    ◆ Ketone

**Notes:**

- (S6) G and K rise together at about same rate
- (S18) G rises faster than K
- (S8) K rises faster than G
- (S20) G rises, K stays flat
- (S23) G stays flat, K rises

# On the Horizon – CKM and AID



## SENSOR

- Continuously monitors glucose and ketone levels every minute without user calibration
- 10-14 days of data storage

## MOBILE APP

- Automatically displays glucose result (value, trend arrow and graph)
- Optional, customizable glucose and ketone alarms

## CLOUD SOFTWARE

- Cloud-based software
- Glucose and ketone reports

## MOBILE DEVICE APP

- Shared glucose and ketone alarms

## AID SYSTEM

# Suggested Use

## ■ Personal View

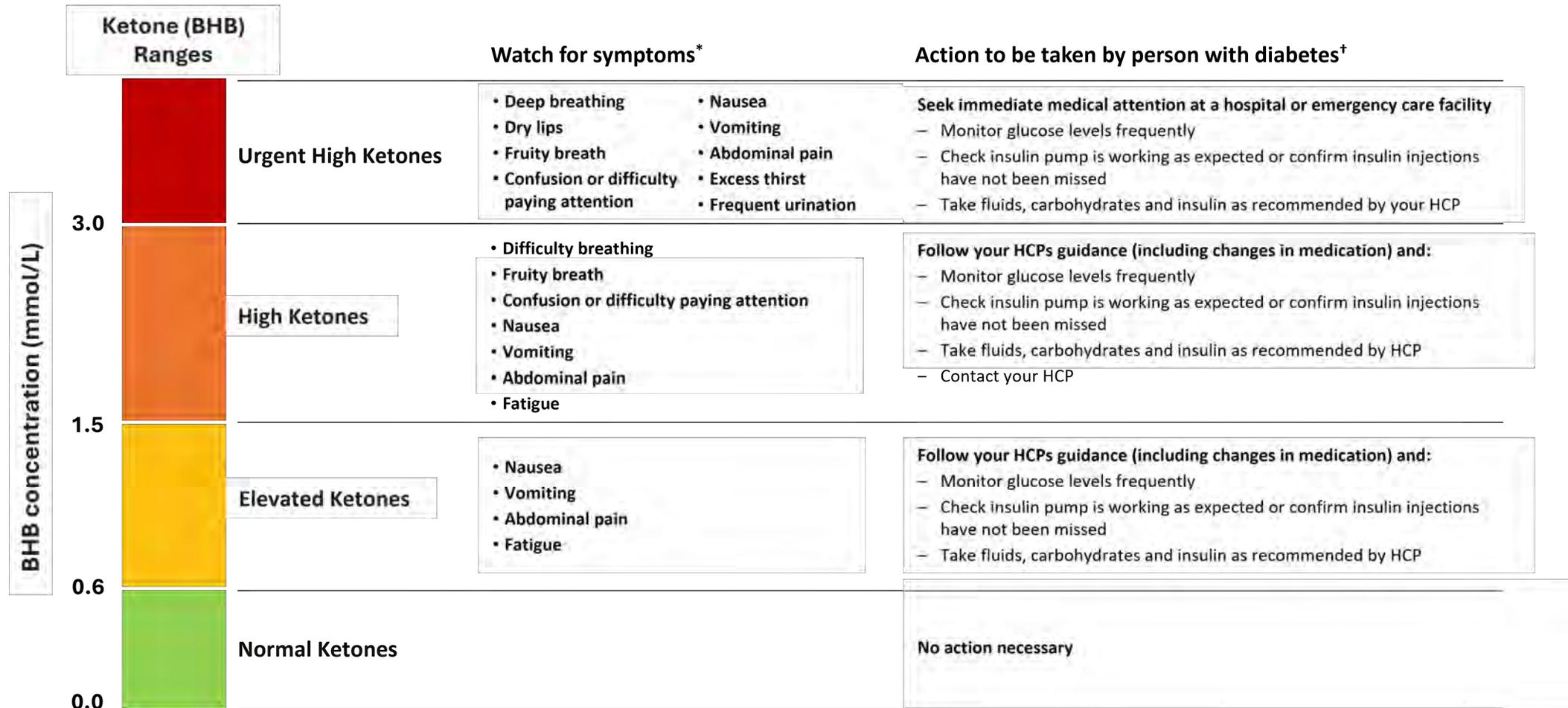
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### Continuous ketone monitoring for people with diabetes: international expert recommendations on the application of a new technology

*Ketan Dhatariya\*, Richard M Bergenstal\*, Mohammed Al-Sofiani, Anastasia Albanese-O'Neill, Tadej Battelino, Kelly Close, Christophe De Block, Sanjoy Dutta, Rodolfo J Galindo, Amin GhavamiNejad, Ahmad Haidar, Julie Heverly, Davida Kruger, Lori M Laffel, Julianne Lally, David M Maahs, Claudio Maffei, Chantal Mathieu, Eden Miller, Medha Munshi, Rimei Nishimura, Kirsten Nørgaard, Tal Oron, David N O'Neal, Monica Oxenreiter, Bruce A Perkins, Moshe Phillip, Eric Renard, Jonathan Rosen, Mauro Scharf, Jennifer Sherr, Carol Wysham, Thomas Danne*

# Suggested Thresholds



# Suggested Graphics

Orientation	Interpretation
	Ketones are <b>rising faster</b> than <b>0.4 mmol/L/h</b>
	Ketones are <b>changing slowly</b> , less than or equal to <b>0.4 mmol/L/h</b>
	Ketones are <b>falling faster</b> than <b>0.4 mmol/L/h</b>

# Suggested Actions

<b>STOP DKA considerations for bolus insulin and CHO</b>			
Continuous ketone concentration (mmol/L)	Blood glucose meter / CGM value (check every hour)*		
	4.0-8.0 mmol/L (70-150 mg/dL)	8.1-14.0 mmol/L (151-250 mg/dL)	>14 mmol/L (>250 mg/dL)
<b>&lt;0.6</b> <b>Normal</b>	<ul style="list-style-type: none"> <li>No extra insulin</li> <li>Usual bolus to cover CHO + usual correction</li> </ul>		<ul style="list-style-type: none"> <li>5-10% TDD supplemental insulin or usual correction bolus</li> <li>Usual bolus to cover CHO</li> </ul>
<b>0.6–1.5</b> <b>Elevated Ketonemia</b> <i>Consider rate of change arrow</i>	<ul style="list-style-type: none"> <li>5% TDD supplemental insulin + usual bolus to cover CHO</li> <li>30 - 45 g CHO every 2-4 hours</li> </ul>	<ul style="list-style-type: none"> <li>10% TDD supplemental insulin or 1.5x correction bolus</li> <li>Usual bolus to cover CHO</li> <li>30 g CHO every 2-4 hours</li> </ul>	<ul style="list-style-type: none"> <li>10% TDD supplemental insulin or 1.5x correction bolus</li> <li>Usual bolus to cover CHO every 2-4 hours</li> </ul>
<b>1.6–2.9</b> <b>High Impending DKA</b> <i>Consider rate of change arrow</i>	<ul style="list-style-type: none"> <li>10% TDD supplemental insulin + usual bolus to cover CHO</li> <li>30 - 45 g CHO every 2-4 hours</li> </ul>	<ul style="list-style-type: none"> <li>20% TDD supplemental insulin or 2x correction bolus</li> <li>Usual bolus to cover CHO</li> <li>30 - 45 g CHO every 2-4 hours</li> </ul>	<ul style="list-style-type: none"> <li>20% TDD supplemental insulin or 2x correction bolus</li> <li>Usual bolus to cover CHO every 2-4 hours</li> </ul>
<b>≥3.0</b> <b>Urgent High Probable DKA</b>	<ul style="list-style-type: none"> <li>10% TDD supplemental insulin + usual bolus to cover CHO</li> <li>30 - 45 g CHO every 2-4 hours</li> </ul>	<ul style="list-style-type: none"> <li>20% TDD supplemental insulin or 2x correction bolus</li> <li>Usual bolus to cover CHO</li> <li>30 - 45 g CHO every 2-4 hours</li> </ul>	<ul style="list-style-type: none"> <li>20% TDD supplemental insulin or 2x correction bolus</li> <li>Usual bolus to cover CHO every 2-4 hours</li> </ul>

DKA is likely if ketones remain  $\geq 3$  mmol/L (**Continuous Ketone System Alarm**) despite supplemental insulin

# Potentials

## **There are several!**

- ▶ Helping to identify a rise in ketones allowing the implementation of 'Sick Day Rules'
- ▶ Early warning of pump / infusion set failure
- ▶ Preventing acute illness / hospital admission
- ▶ Fewer pieces of 'kit' to carry about
- ▶ Developing an AID algorithm that incorporates ketones / sick day rules



### Adolescents and young adults

- Potential causes may include hormonal changes in puberty, transition from pediatric to adult care
- Psychosocial aspects can increase risks for DKA, e.g., eating disorders



### Pregnancy

- Most common with pregestational T1D
- Associated with significant adverse fetal outcomes
- Risks for DKA heightened by 'morning sickness' in 2<sup>nd</sup> and 3<sup>rd</sup> trimester
- Pregnancy-specific symptoms include vaginal bleeding, uterine contractions
- Higher rates of euglycemic DKA



### Older and frail individuals

- Symptoms may differ, with higher rates of respiratory distress, cognitive impairment, fever
- Recurrent DKA more common
- Greater risk of in-hospital mortality
- Care-home staff require education

## The 'At Risk' Population



### SGLT2 inhibitors

- Used for glucose-lowering and cardiorenal protection
- DKA risk doubled in T1D compared to other glucose-lowering agents
- Higher rates of euglycemic DKA
- Associated with delayed DKA diagnosis



### Insulin pump users

- Associated with catheter occlusion and other infusion-site issues
- Risks for DKA increased compared to daily insulin injection regimens
- DKA due to infusion-site failure is a real-world clinical management concern



### Chronic kidney disease (CKD)

- Chronic metabolic acidosis in CKD can mask symptoms of DKA
- Euglycemic DKA more common with CKD than without, especially ESRD
- Treatment of DKA in CKD requires specific fluid and electrolyte management



### Mental health & psychiatric disorders

- Three-fold increased risk of DKA compared to individuals without mental or psychiatric illness
- Comorbid psychiatric illness can impact insulin adherence, increasing DKA risk
- Atypical antipsychotic drugs associated with DKA



### Rural populations

- Up to 68% additional risks for DKA compared to urban locations
- Association between DKA risk and indices of socio-economic deprivation



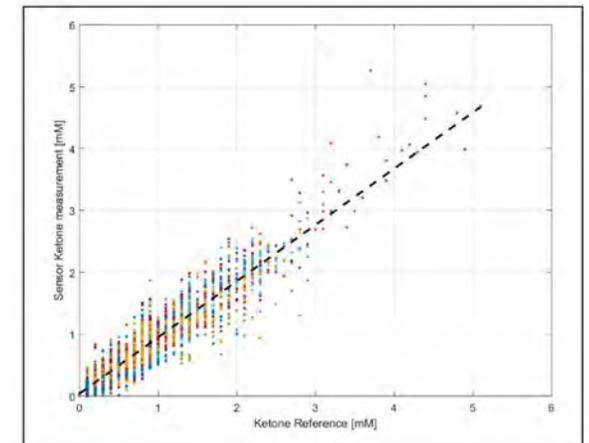
### Low carbohydrate & ketogenic diets

- Increased risk for DKA in T2D during weight-loss therapies
- Exacerbated with SGLT2 inhibitors
- Guidelines discourage low carbohydrate/ ketogenic dieting in T1D or in T2D using SGLT2 inhibitors

# Challenges & Unknowns

## There are several!

- ▶ Education of people with diabetes – what do the numbers mean?
- ▶ Education of health care professionals – what do the numbers mean?
- ▶ When does physiological become pathological?
- ▶ Are there significant differences between blood / capillary and interstitial fluid?
- ▶ T1DM vs T2DM
- ▶ How to manage euglycaemic ketonaemia/DKA
- ▶ Reimbursement?



# Preventing Diabetic Ketoacidosis with Continuous Ketone Monitoring: **Insights from a Clinical Case**



**Peter is a 55 year old man**

## Medical history

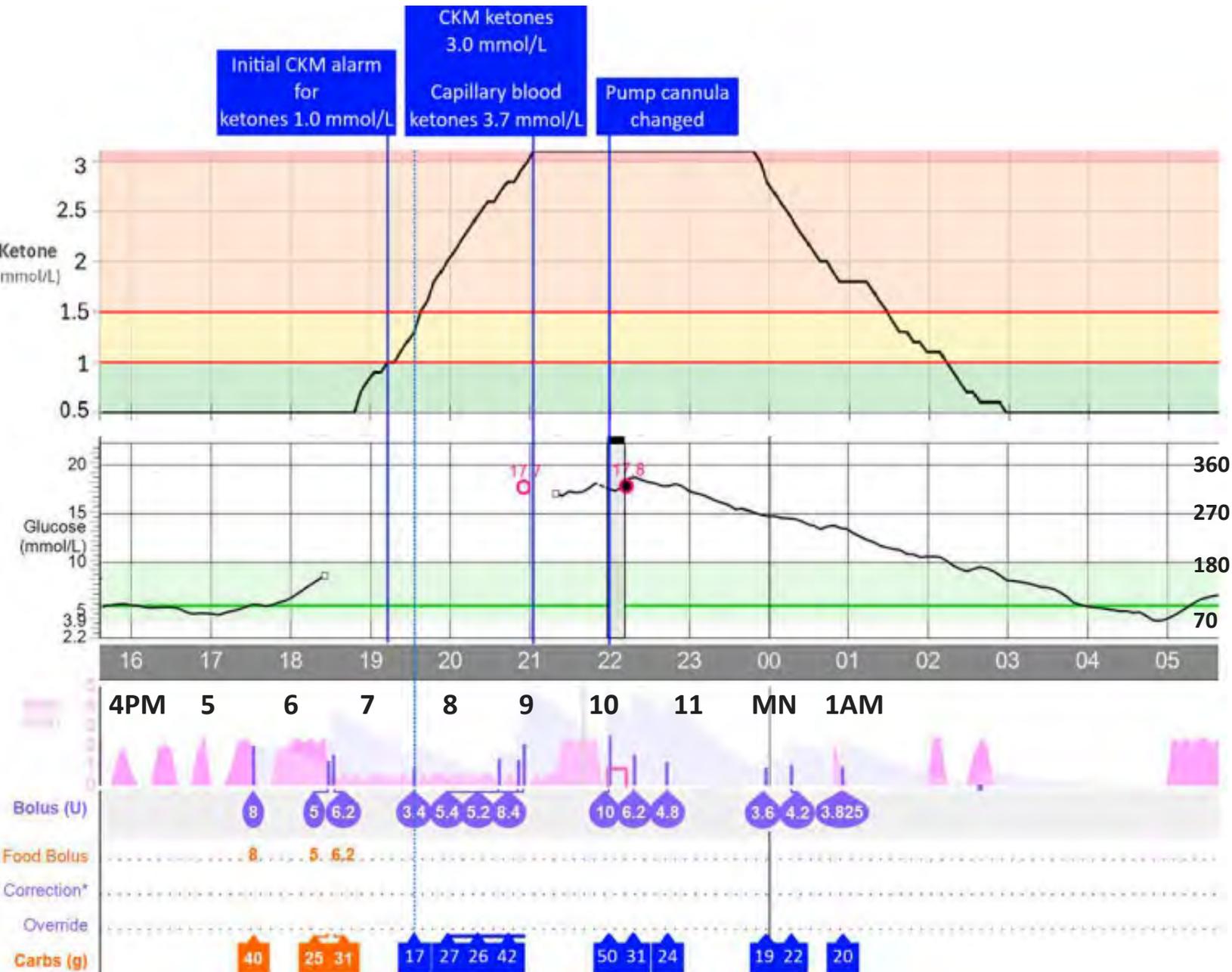
Type 1 diabetes for 53 years

## Profile

- Undetectable C-peptide
- **AID system** with a tubed insulin pump
- Total daily insulin dose was 0.5 units/kg/day
- CGM TIR 83%, TAR 14%, HbA1c was 6.9% (51.9 mmol/mol)
- Last episode of DKA was during childhood

## Management

- In clinical trial on **Dapagliflozin** 10 mg/d or Placebo
- **Using CKM system in development** - alarms at 1.0
  - ✓ BHB 0.6 -1.0 – review data q2-4 hr
  - ✓ 1.0-1.5 – suggest change pump sites, hydrate, insulin pen/pump pen/pump
  - ✓ Over 1.5 – mandate site change and insulin via pen



- Worked in the garden in the afternoon
  - Premeal pump boluses 5:30 and 6:30 PM ---- glucose started up post-meal
- 6:30 PM** CGM expired and was changed and 2hr warm up and one more hr charge transmitter (3hr no sensor)
- 7:15 PM** CKM 1.0 ketone alarm
- 7:30 PM** Alarm still >1 approaching 1.5 – gave insulin bolus via pump
- 8:00 PM** Ketones 2.0
- 9:00 PM** >3.1 CKM **alarm** (capillary glucose 319 mg/dL (17.7 mmol/L))
- CGM started to work**
- 9:30 PM** Noted pump cannula site noted to be dislodged
- By 10PM** Replaced cannula and gave insulin via pump
- By MN – Ketones falling. Glucose and ketones normalized over 4-5 hrs.**

# In Summary

- ▶ Ketones are an evolutionary adaptation to prolonged starvation
- ▶ Their presence can be beneficial or harmful – depending on the rate of appearance in the circulation
- ▶ Continuous ketone measurement seems to be the next logical step in the management of type 1 diabetes, and incorporation into an AID system seems likely
- ▶ Challenges remain but the potential for benefit is huge

# Beyond CGM: Dual Sensing Technology as a Cornerstone of DKA Prevention

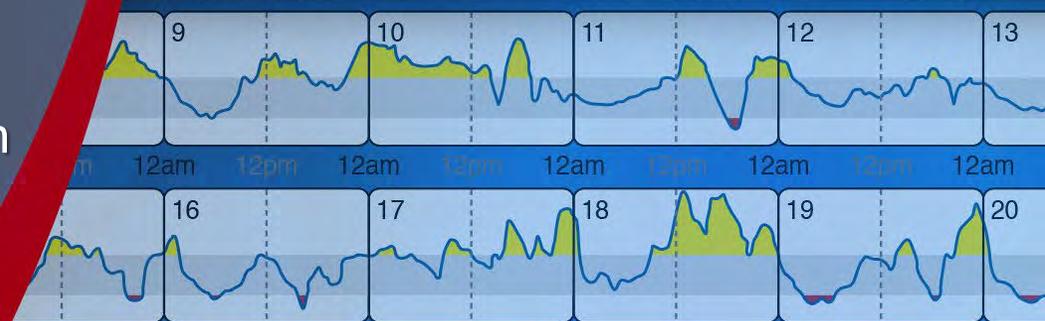
- [www.norfolkdiabetes.com](http://www.norfolkdiabetes.com)
- [ketan.dhatariya@nnuh.nhs.uk](mailto:ketan.dhatariya@nnuh.nhs.uk)
- @ketandhatariya
- @ketandhatariya.bsky.social
- @JBDSIP
- @ABCDiab



# CGM for Transforming Clinical Outcomes in Non-Intensive T2D Therapy

**Dr Emma Wilmot**

Associate Professor University of Nottingham  
Honorary Consultant, University Hospitals of Derby & Burton  
NHS FT  
Founder, ABCD Diabetes Technology Network UK



# Disclosures

- ▶ **Emma Wilmot** has received personal fees from Abbott, AstraZeneca, Dexcom, Eli Lilly, Embecta, Insulet, Medtronic, Novo Nordisk, Roche, Sanofi, Sinocare, Ypsomed and research support from Abbott, Embecta, Insulet, Novo Nordisk, Sanofi.

# Overview

## Evidence base for continuous glucose monitoring

- ▶ Insulin treated
- ▶ Non insulin treated

## Interactive case study

### What next?

- ▶ Consider emerging research



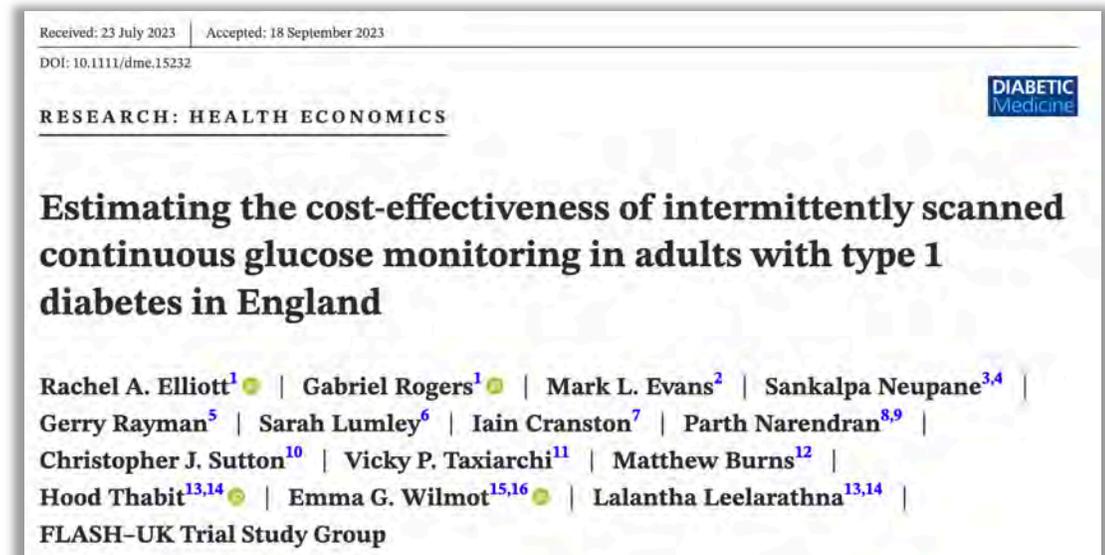
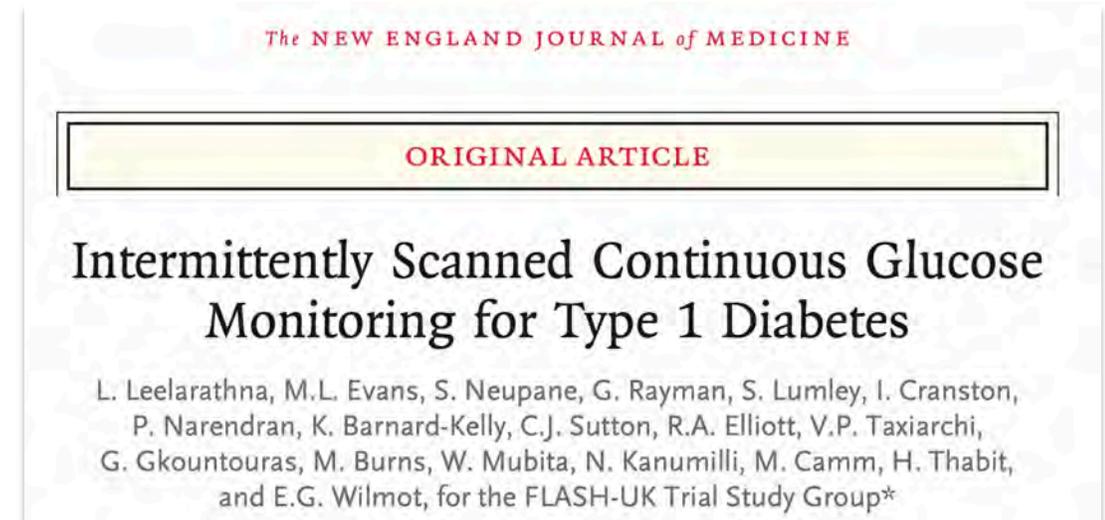
# Flash UK Summary

## isCGM in T1 diabetes

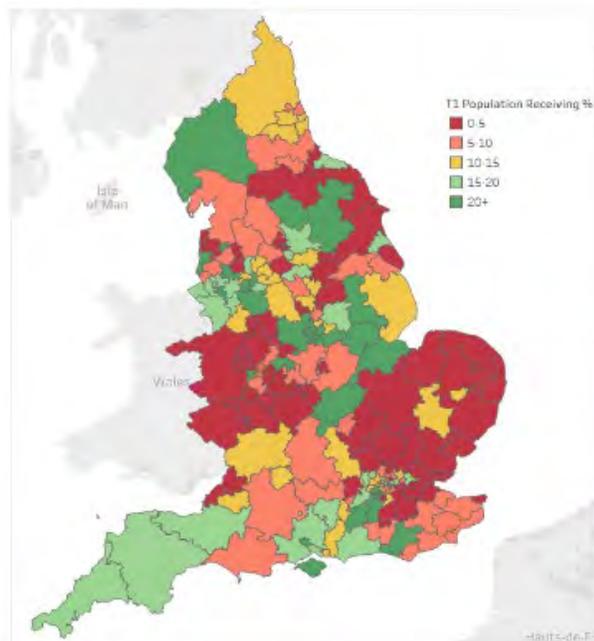
- ▶ Significant improvement in HbA1c
- ▶ Less hypoglycaemia
- ▶ Improved treatment satisfaction

## Cost Effectiveness

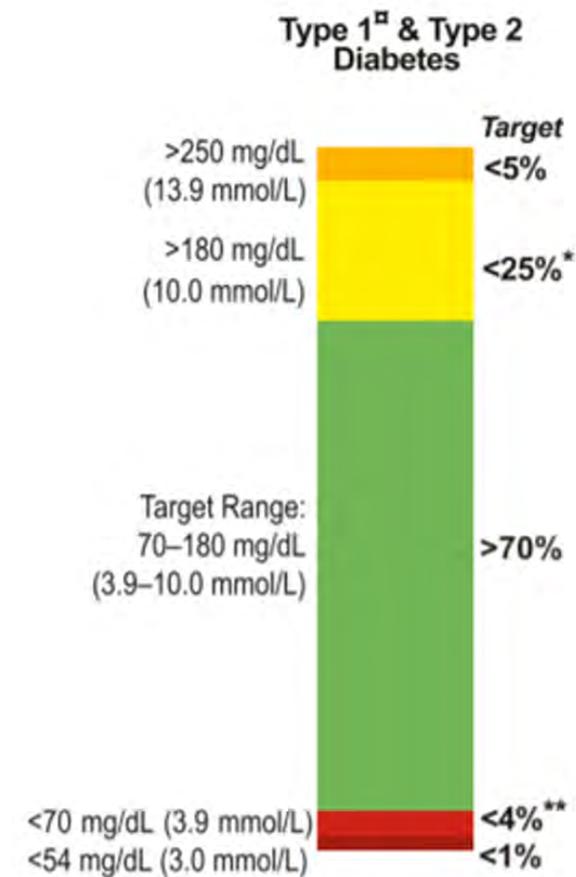
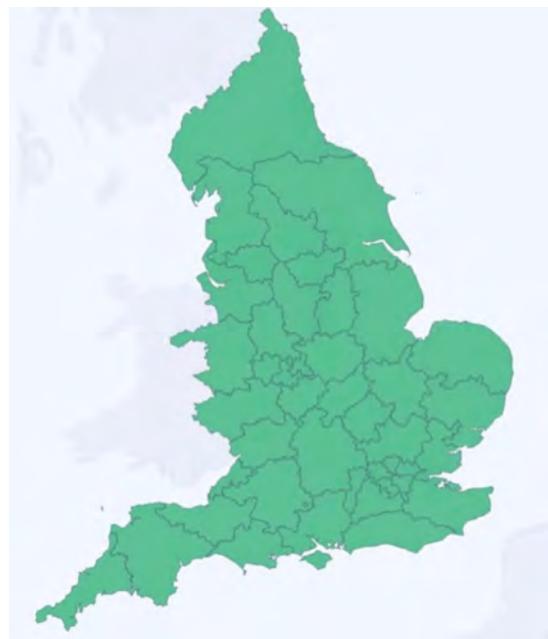
- ▶ Incremental cost-per-QALY of £4477
- ▶ For people with HbA1c >75 mmol/mol (9.0%), cost-saving



# Impact of CGM in T1DM in England



*>95% of people living with T1DM in the UK now have access to NHS funded CGM*



# UK NICE Recommendations (2022)

## Continuous glucose monitoring

1.6.17 Offer intermittently scanned [continuous glucose monitoring](#) (isCGM, commonly referred to as 'flash') to adults with type 2 diabetes on [multiple daily insulin injections](#) if any of the following apply:

- they have [recurrent hypoglycaemia](#) or [severe hypoglycaemia](#)
- they have impaired hypoglycaemia awareness
- they have a condition or disability (including a learning disability or cognitive impairment) that means they cannot self-monitor their blood glucose by capillary blood glucose monitoring but could use an isCGM device (or have it scanned for them)
- they would otherwise be advised to self-measure at least 8 times a day.

For guidance on [continuous glucose monitoring](#) (CGM) for pregnant women, see the [NICE guideline on diabetes in pregnancy](#). [2022]

1.6.18 Offer isCGM to adults with insulin-treated type 2 diabetes who would otherwise need help from a care worker or healthcare professional to monitor their blood glucose. [2022]

NICE define MDI as two or more daily insulin injections

## Type 2 diabetes in adults: management

# RCTs of CGM

Received: 18 October 2022 | Revised: 7 December 2022 | Accepted: 16 December 2022  
DOI: 10.1111/dom.14949

ORIGINAL ARTICLE

WILEY

## Impact of flash glucose Monitoring in pEople with type 2 Diabetes Inadequately controlled with non-insulin Antihyperglycaemic ThERapy (IMMEDIATE): A randomized controlled trial

Ronnie Aronson MD | Ruth E. Brown PhD | Lisa Chu PhD | Harpreet S. Bajaj MD | Hasnain Khandwala MD | Alexander Abitbol MDCM | Nadia Malakieh MD | Ronald Goldenberg MD

Research

JAMA | Original Investigation

## Effect of Continuous Glucose Monitoring on Glycemic Control in Patients With Type 2 Diabetes Treated With Basal Insulin A Randomized Clinical Trial

Thomas Martens, MD; Roy W. Beck, MD, PhD; Ryan Bailey, MS; Katrina J. Ruedy, MSPH; Peter Calhoun, PhD; Anne L. Peters, MD; Rodica Pop-Burusa, MD, PhD; Athena Philis-Tsimikas, MD; Shichun Bao, MD, PhD; Guillermo Umpierrez, MD; Georgia Pop-Burusa, MD, PhD; Davida Kruger, MSN, APN-BC; Anuj Bhargava, MD; Laura Young, MD, PhD; Janet B. McGill, MD; Grazia Aleppo, MD; Quang T. Nguyen, DO; Ian Orozco, MD; William Biggs, MD; K. Jean Lucas, MD; William H. Polonsky, PhD; John B. Buse, MD, PhD; David Price, MD; Richard M. Bergenstal, MD, for the MOBILE Study Group

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Intermittently Scanned Continuous Glucose Monitoring for Type 1 Diabetes

L. Leelarathna, M.L. Evans, S. Neupane, G. Rayman, S. Lumley, I. Cranston, P. Narendran, K. Barnard-Kelly, C.J. Sutton, R.A. Elliott, V.P. Taxiarchi, G. Gkountouras, M. Burns, W. Mubita, N. Kanumilli, M. Camm, H. Thabit, and E.G. Wilmot, for the FLASH-UK Trial Study Group\*

Research

JAMA | Original Investigation

## Effect of Continuous Glucose Monitoring on Glycemic Control in Adults With Type 1 Diabetes Using Insulin Injections The DIAMOND Randomized Clinical Trial

Roy W. Beck, MD, PhD; Tonya Riddlesworth, PhD; Katrina Ruedy, MSPH; Andrew Ahmann, MD; Stacie Haller, RD, LD, CDE; Richard Bergenstal, MD; Stacie Haller, RD, LD, CDE; Craig Kollman, PhD; Davida Kruger, MSN, APN-BC; Janet B. McGill, MD; William Polonsky, PhD; Elena Toschi, MD; Howard Wolpert, MD; David Price, MD; for the DIAMOND Study Group

Multicenter Randomized Trial of Intermittently Scanned Continuous Glucose Monitoring Versus Self-Monitoring of Blood Glucose in Individuals With Type 2 Diabetes and Recent-Onset Acute Myocardial Infarction: Results of the LIBERATES Trial

Ramzi A. Ajan,<sup>1</sup> Simon R. Heller,<sup>2</sup> Colin C. Everett,<sup>3</sup> Armando Vargas-Palacios,<sup>4</sup> Ruchi Higham,<sup>2</sup> Linda Sharples,<sup>5</sup> Diana A. Gorog,<sup>6,7</sup> Alice Rogers,<sup>8</sup> Catherine Reynolds,<sup>1</sup> Catherine Fernandez,<sup>2</sup> Pedro Rodrigues,<sup>4</sup> Thozhukat Sathyapalan,<sup>9</sup> Robert F. Storey,<sup>10</sup> and Deborah D. Stocken<sup>3</sup>

Diabetes Care 2023;46:441-449 | <https://doi.org/10.2337/dc22-1219>

Research

JAMA | Original Investigation

## Continuous Glucose Monitoring vs Conventional Therapy for Glycemic Control in Adults With Type 1 Diabetes Treated With Multiple Daily Insulin Injections The GOLD Randomized Clinical Trial

Marcus Lind, MD, PhD; William Polonsky, PhD; Iril B. Hirsch, MD; Tim Heise, MD; Jan Bolinder, MD, PhD; Sofia Dahlqvist; Erik Schwarz, MD, PhD; Arndt Finna Olafsdottir, RN; Anders Frid, MD, PhD; Hans Wedel, PhD; Eba Ahlén, MD; Thomas Nyström, MD, PhD; Jari Hellman, MD

Annals of Internal Medicine

ORIGINAL RESEARCH

## Continuous Glucose Monitoring Versus Usual Care in Patients With Type 2 Diabetes Receiving Multiple Daily Insulin Injections A Randomized Trial

Roy W. Beck, MD, PhD; Tonya D. Riddlesworth, PhD; Katrina Ruedy, MSPH; Andrew Ahmann, MD; Stacie Haller, RD, LD, CDE; Davida Kruger, MSN, APN-BC; Janet B. McGill, MD; William Polonsky, PhD; David Price, MD; Stephen Aronoff, MD; Ronnie Aronson, MD; Elena Toschi, MD; Craig Kollman, PhD; and Richard Bergenstal, MD; for the DIAMOND Study Group\*

## Effect of Flash Glucose Monitoring Technology on Glycemic Control and Treatment Satisfaction in Patients With Type 2 Diabetes

Marianna Yaron,<sup>1,2</sup> Eytan Roitman,<sup>1</sup> Genya Aharon-Hananel,<sup>1</sup> Zohar Landau,<sup>1,2,3</sup> Tali Ganz,<sup>3</sup> Ilan Yanuv,<sup>4</sup> Aliza Rozenberg,<sup>4</sup> Moshe Karp,<sup>1</sup> Maya Ish-Shalom,<sup>1,2</sup> Joelle Singer,<sup>1,2</sup> Julio Wainstein,<sup>1,2,3</sup> and Itamar Raz<sup>1,4</sup>

<https://doi.org/10.2337/dc18-0166>

# CGM in Type 2 Diabetes

## Randomised Controlled Trials: Intensive Insulin Tx



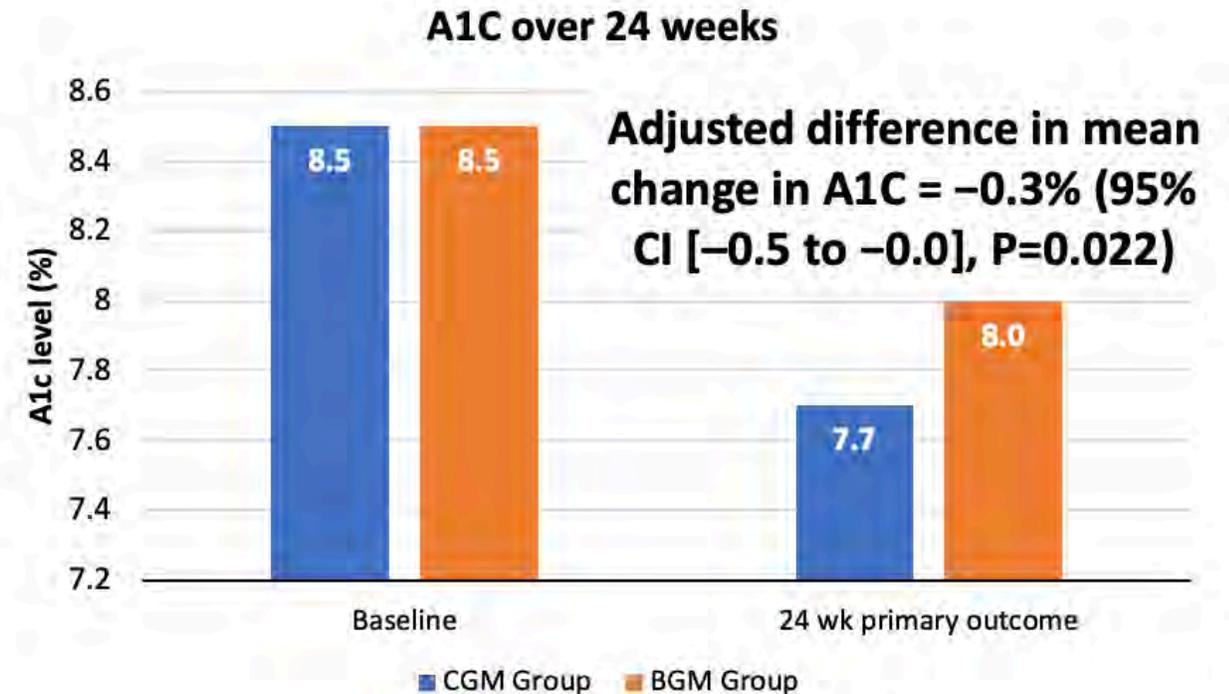
## Continuous Glucose Monitoring Versus Usual Care in Patients With Type 2 Diabetes Receiving Multiple Daily Insulin Injections

### A Randomized Trial

Roy W. Beck, MD, PhD; Tonya D. Riddlesworth, PhD; Katrina Ruedy, MSPH; Andrew Ahmann, MD; Stacie Haller, RD, LD, CDE; Davida Kruger, MSN, APN-BC; Janet B. McGill, MD; William Polonsky, PhD; David Price, MD; Stephen Aronoff, MD; Ronnie Aronson, MD; Elena Toschi, MD; Craig Kollman, PhD; and Richard Bergenstal, MD; for the DIAMOND Study Group\*

- ▶ To determine the effectiveness of rtCGM in adults with **T2DM on MDI**
- ▶ Age >25 years old attending endocrinology practices in N. America
- ▶ HbA1c 7.5 %-10.0 %
- ▶ Mean SMBG frequency  $\geq$  2/day

# DIAMOND T2 Study



# Flash Glucose-Sensing Technology as a Replacement for Blood Glucose Monitoring for the Management of Insulin-Treated Type 2 Diabetes: a Multicenter, Open-Label Randomized Controlled Trial

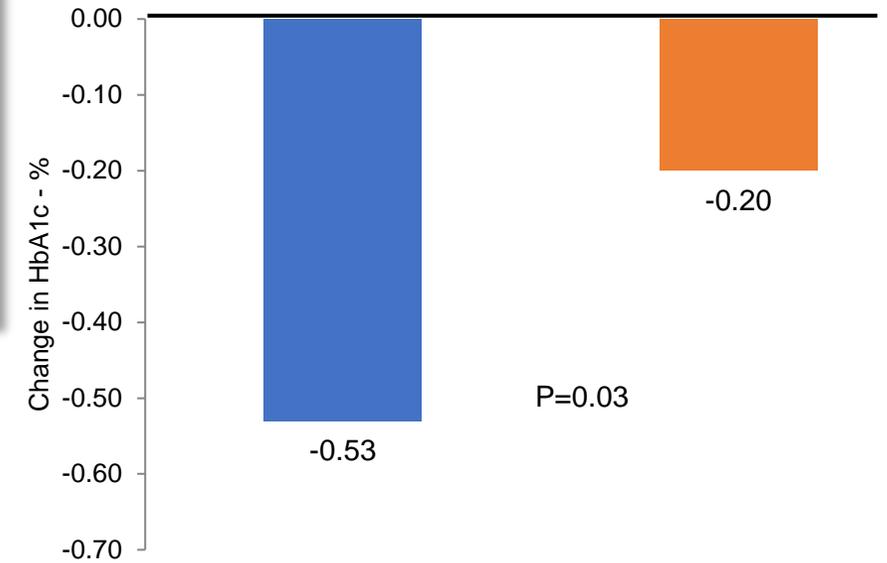
Thomas Haak · H el ene Hanaire · Ramzi Ajjan · Norbert Hermanns ·

Jean-Pierre Riveline · Gerry Rayman

- RCT with T2DM adults on **intensive insulin therapy**, 26 European diabetes centers
- Randomised to isCGM or SMBG
- Primary outcome: difference in HbA1c at 6 months

## Results:

- No difference in HbA1c overall
- <65 years subgroup mean change HbA1c - 0.33%, p = 0.03 favouring isCGM (blue intervention, orange control)



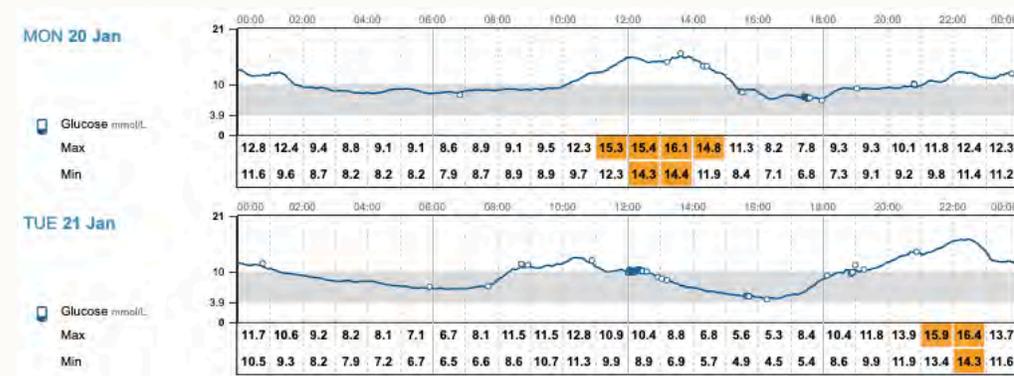
Glucose Level	Difference (vs control)	P value	Reduction vs control
<3.9mmol/l	-0.47h (-28 min)	P<0.001	<b>43%</b>
<3.1 mmol/l	-0.22h (-13 min)	P=0.0014	<b>53%</b>
<2.5mmol/l	-0.14h (-8 min)	P=0.0013	<b>64%</b>



# Continuous glucose monitoring with structured education in adults with type 2 diabetes managed by multiple daily insulin injections: a multicentre randomised controlled trial

Article | Published: 19 April 2024

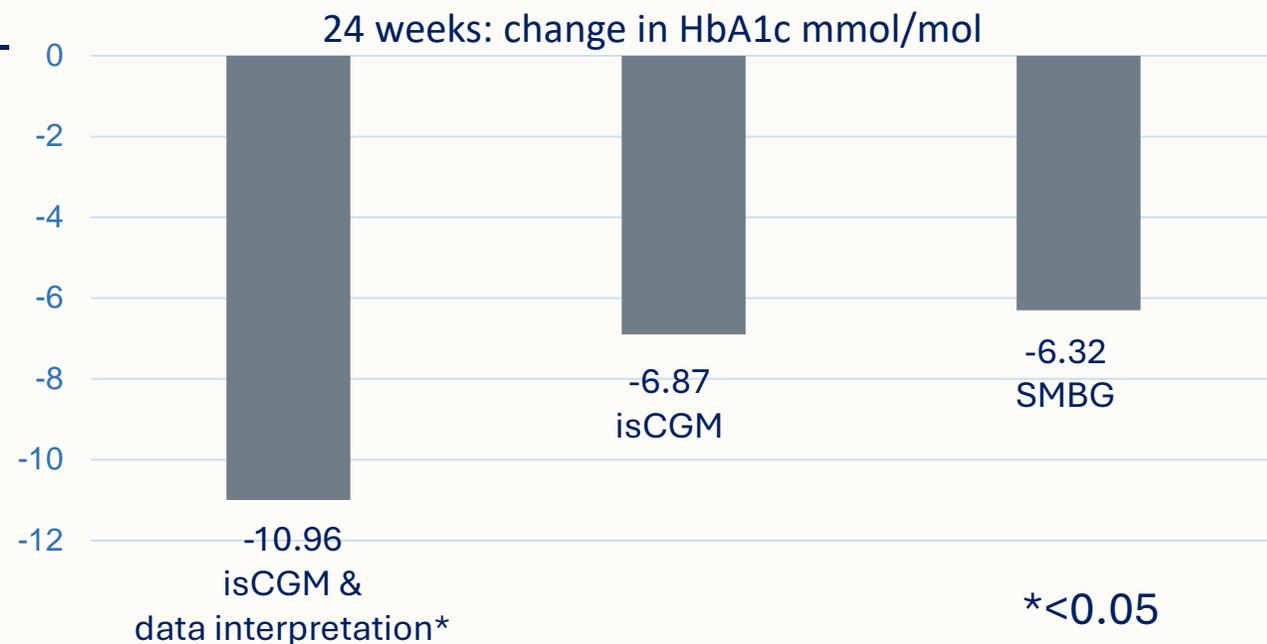
Volume 67, pages 1223–1234, (2024) [Cite this article](#)



Aimed to compare the effectiveness of isCGM +/- structured education programme vs. SMBG in adults T2DM MDI.

24 week RCT, randomly assigned:

- **isCGM with a structured education on adjusting insulin dose/timing according to CGM patterns**
- isCGM with education
- SMBG with education



**Take home: Education on CGM data matters!**

Kim JY, Diabetologia 2024

# CGM in Type 2 Diabetes

## Basal Insulin



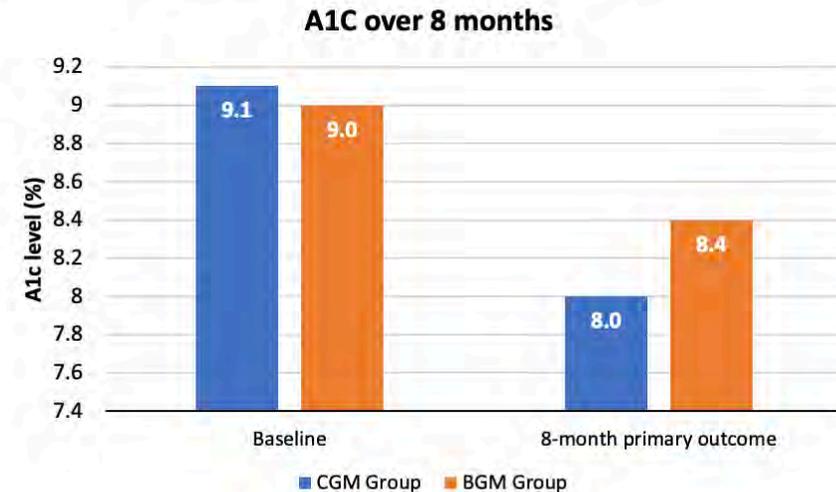
JAMA | Original Investigation

## Effect of Continuous Glucose Monitoring on Glycemic Control in Patients With Type 2 Diabetes Treated With Basal Insulin A Randomized Clinical Trial

Thomas Martens, MD; Roy W. Beck, MD, PhD; Ryan Bailey, MS; Katrina J. Ruedy, MSPH; Peter Calhoun, PhD; Anne L. Peters, MD; Rodica Pop-Busui, MD, PhD; Athena Philis-Tsimikas, MD; Shichun Bao, MD, PhD; Guillermo Umpierrez, MD; Georgia Davis, MD; Davida Kruger, MSN, APN-BC; Anuj Bhargava, MD; Laura Young, MD, PhD; Janet B. McGill, MD; Grazia Aleppo, MD; Quang T. Nguyen, DO; Ian Orozco, MD; William Biggs, MD; K. Jean Lucas, MD; William H. Polonsky, PhD; John B. Buse, MD, PhD; David Price, MD; Richard M. Bergenstal, MD; for the MOBILE Study Group

- ▶ To determine the effectiveness of Dexcom G6 CGM in adults with T2DM treated with **basal insulin (no prandial)**
- ▶ HbA1c 7.8 % to 11.5% (62 to 102 mmol/mol)
- ▶ 22 Endocrinology practices in USA, participant under primary care physician for diabetes care

**Adjusted difference in mean change in HbA1C -0.4%**  
(95% CI [-0.8% to -0.1%], P=0.02)



No difference of basal / total daily insulin between groups

**% TIR 3.9 to 10 mmol/L**

- **59% CGM vs. 43% BGM** (adjusted difference, 15%, P<0.001)

**% TBR <3.9 mmol/L**

- **0.2% CGM vs. 0.5% BGM** (adjusted difference, -0.24%, P=0.02)

*Martens et. al. JAMA. 2021;325 (22): 2262-2272*

# MOBILE Study

Open access

Original research

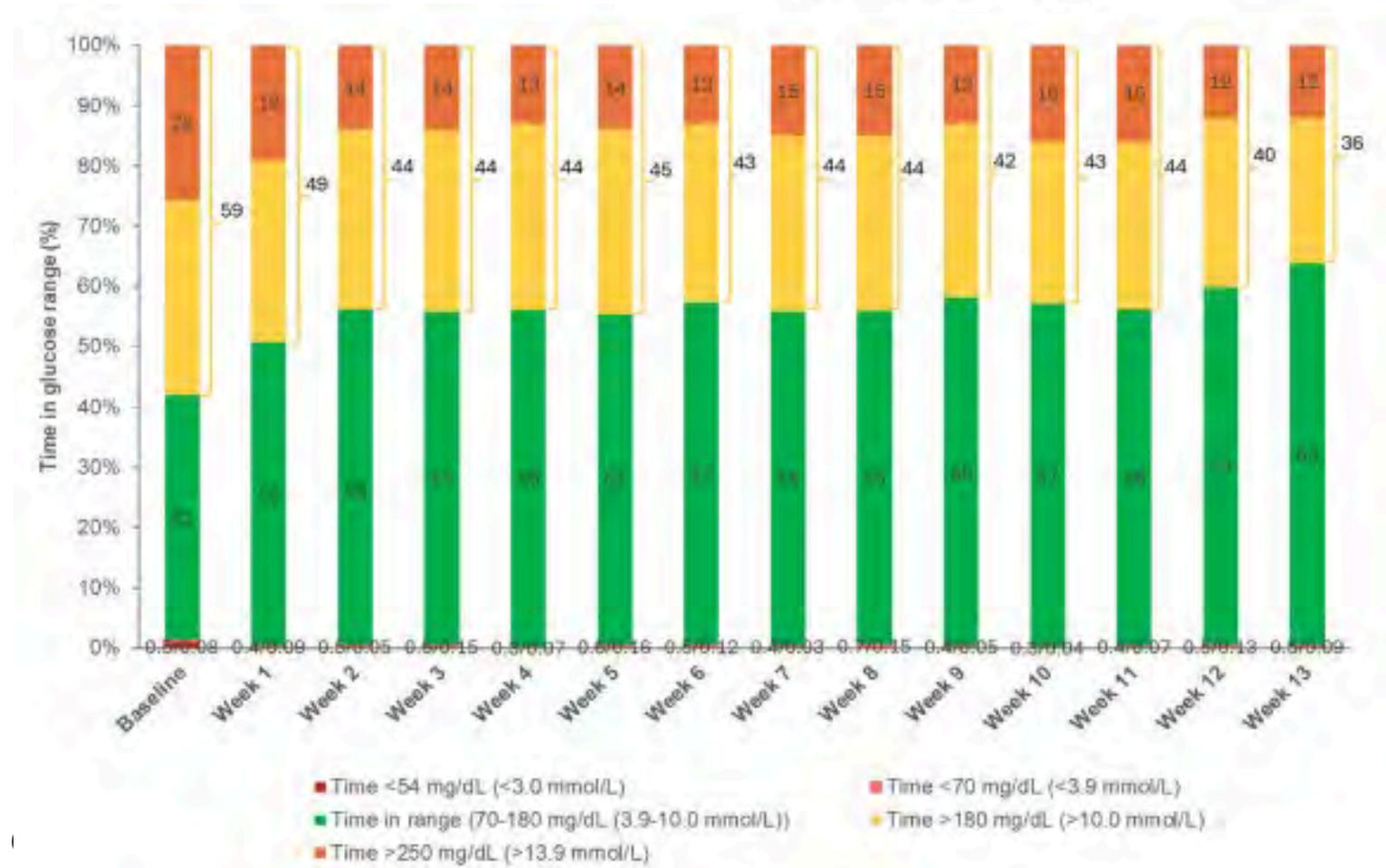
BMJ Open  
Diabetes  
Research  
& Care

Rapid improvements in glycemic management with use of continuous glucose monitoring in adults with type 2 diabetes treated with basal insulin: 3-month analysis of the MOBILE study

Thomas W Martens,<sup>1,2</sup> Roy W Beck,<sup>3</sup> Corbin Griffen,<sup>4</sup> Junrui Di,<sup>4</sup> Karen Elkind-Hirsch,<sup>4</sup> Matthew L Johnson,<sup>4</sup> Jessica R Castle,<sup>4</sup> Stayce E Beck,<sup>4</sup> Richard M Bergenstal<sup>1</sup>

At 3 months:

- ▶ 9.1±1.0% to 8.0±1.2% CGM group
- ▶ 9.0±0.9% to 8.5±1.5% BGM group
- ▶ Adjusted difference, **-0.6%** (95% CI -0.9% to -0.3%); p<0.001)





Effects of Patient-Driven Lifestyle Modification Using Intermittently Scanned Continuous Glucose Monitoring in Patients With Type 2 Diabetes: Results From the Randomized Open-label PDF Study

Hun Jee Choe,<sup>1,2</sup> Eun-Jung Rhee,<sup>3</sup>  
Jong Chul Won,<sup>4</sup> Kyong Soo Park,<sup>1,2</sup>  
Won-Young Lee,<sup>3</sup> and Young Min Cho<sup>1,2</sup>

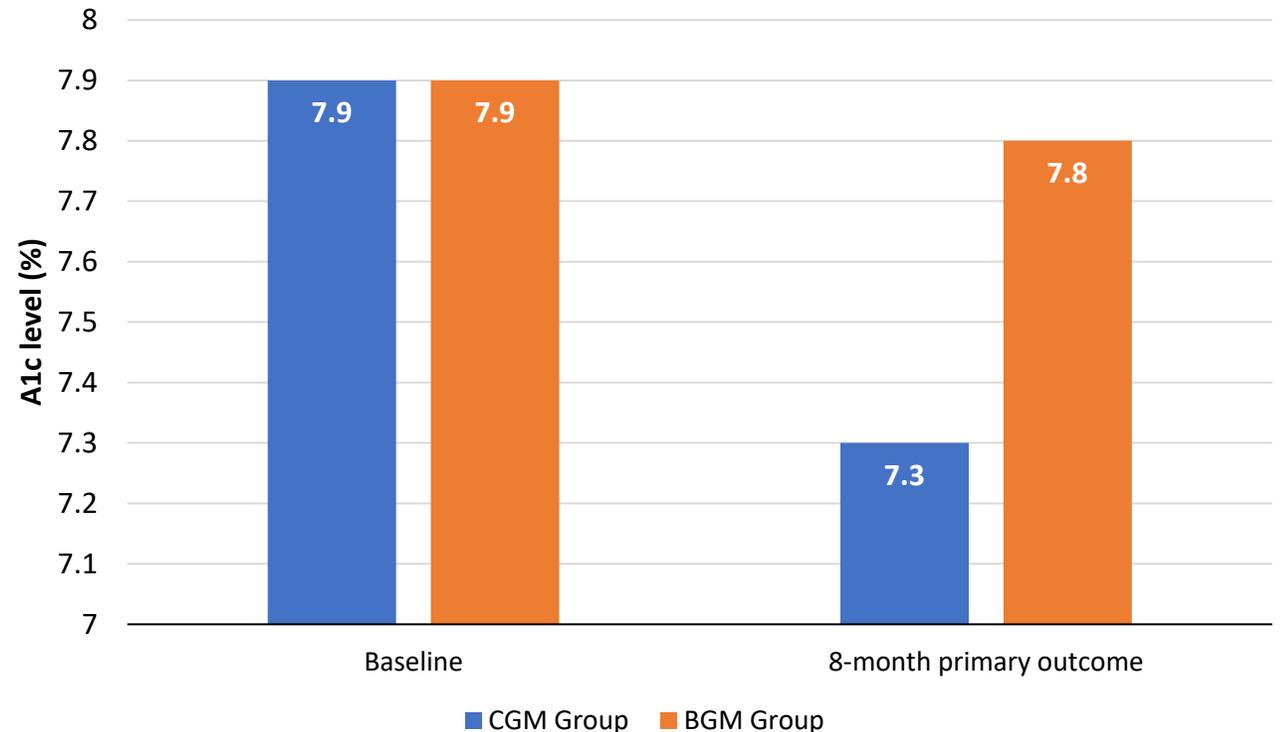
Diabetes Care 2022;45:2224–2230 | <https://doi.org/10.2337/dc22-0764>

- ▶ 12 week RCT (n=126)
- ▶ HbA1c >7% on oral and/or basal insulin therapy
- ▶ Primary end point HbA1c
- ▶ isCGM + diabetes education vs SMBG

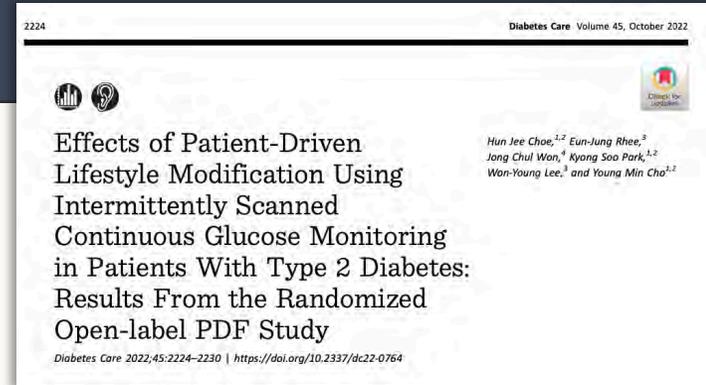
# PDF Study

**Risk-adjusted difference  
-0.50% (0.74 to 0.26) <0.001**

A1C over 3 months



# Keep It Simple



## Healthy food?

Post meal  
high glucose?

	Yes	No
No	Stay on current eating pattern	Cut down the amount
Yes	Cut down the amount	Stay away

# Clinical Case Discussion

## Basal Insulin-Treated Type 2 Diabetes



# Clinical Case Discussion



**52-year-old female**

## Medical history

Type 2 diabetes, smoker

## Profile

- ▶ BMI 29kg/m<sup>2</sup>
- ▶ HbA1c 9.6% (chronically elevated)
- ▶ Only checks blood glucose for a few days before diabetes

## Management

- ▶ Diabetes tx
  - Humulin i 19u BD
  - Empagliflozin 25mg OD
- ▶ Declined statin, intolerant metformin and GLP-1

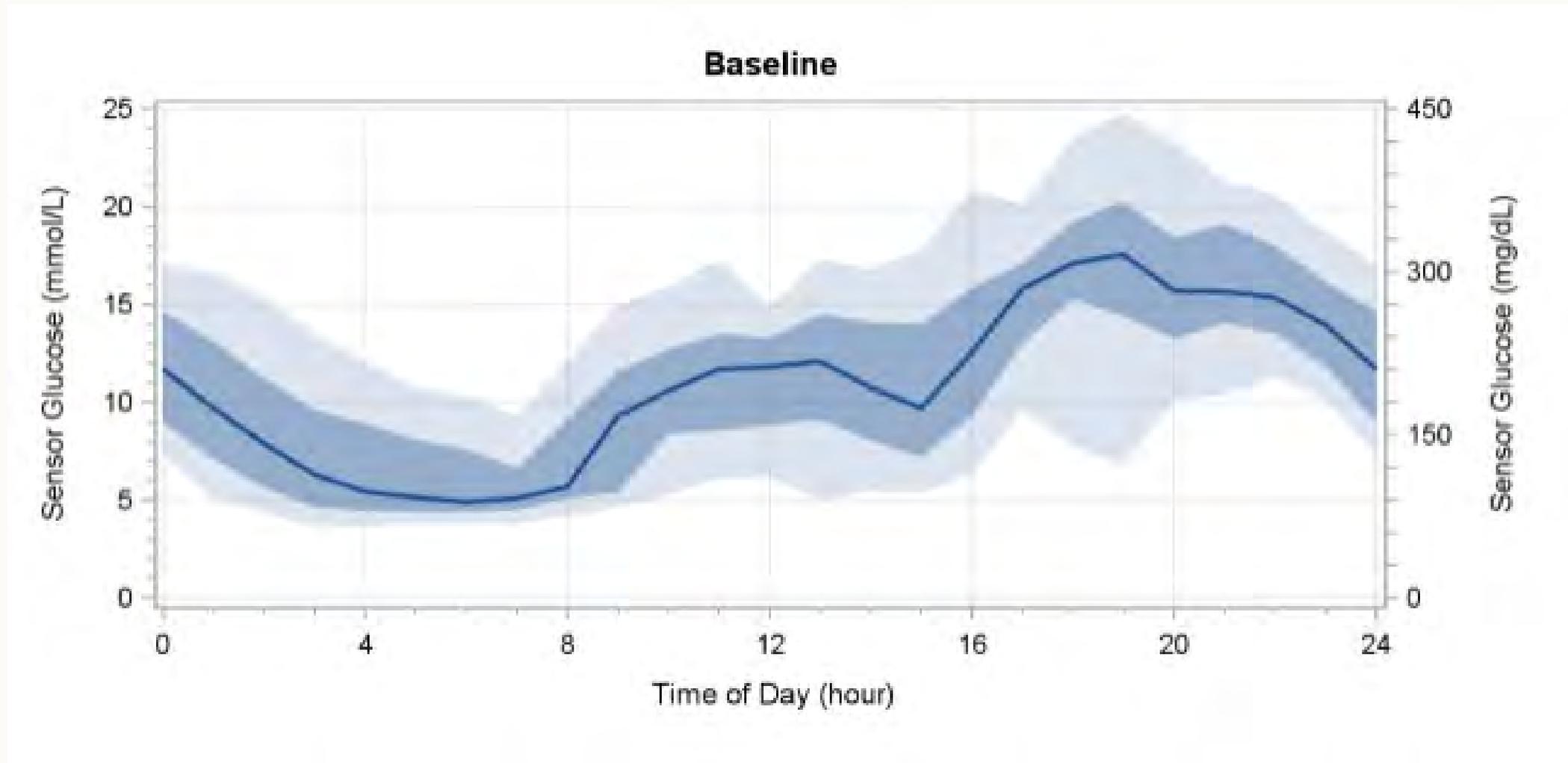
# Glucose Data

	Pre-breakfast	Pre-lunch	Pre-dinner	Pre-bed
Sunday	4.9 mmol/L			
Monday	5.2 mmol/L			
Tuesday				
Wednesday	6.3 mmol/L			
Thursday	5.1 mmol/L			

**Question: How will you alter the insulin dosing (Humulin i 19 units BD)?**

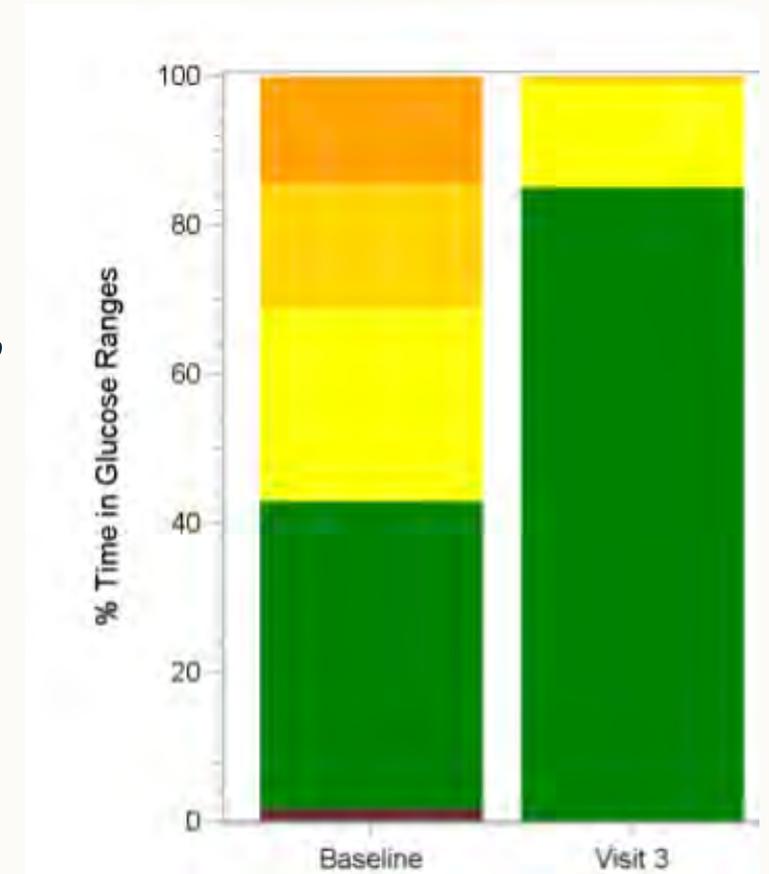
- 1) Increase the morning dose
- 2) Increase the evening dose
- 3) Add in prandial insulin
- 4) Wait for more blood glucose data first
- 5) Wait and give a trial of rtCGM first

# Blind CGM Data

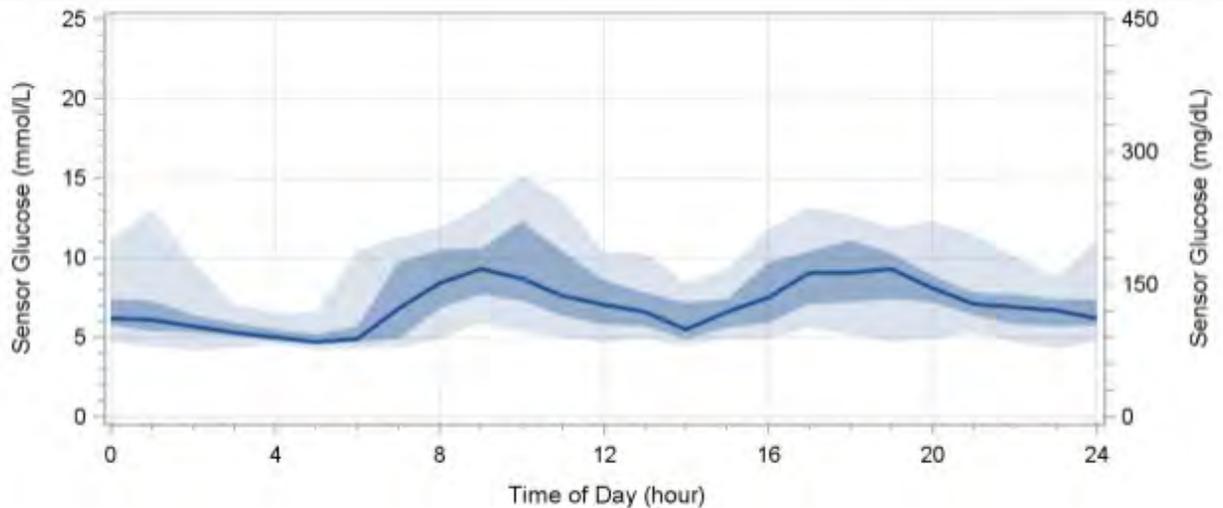
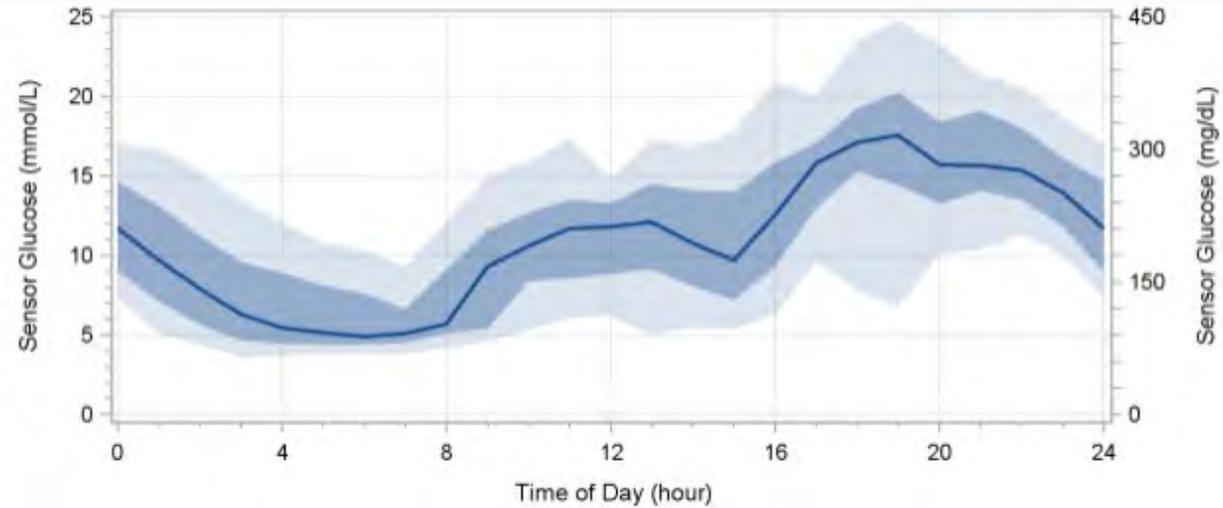


# By Four Months

- ▶ Patient used rtCGM for four months
- ▶ Gained insight into the impact of foods on her glucose levels
- ▶ Made changes to her diet: avoiding chocolates, sweets and eating less bread
- ▶ By 4 months she had reduced her insulin dose from 19u BD to 14u BD
- ▶ Time in Range improved from **41 to 85%**
- ▶ HbA1c improved from **9.6% to 6.9%**



# Before and Four Months Later

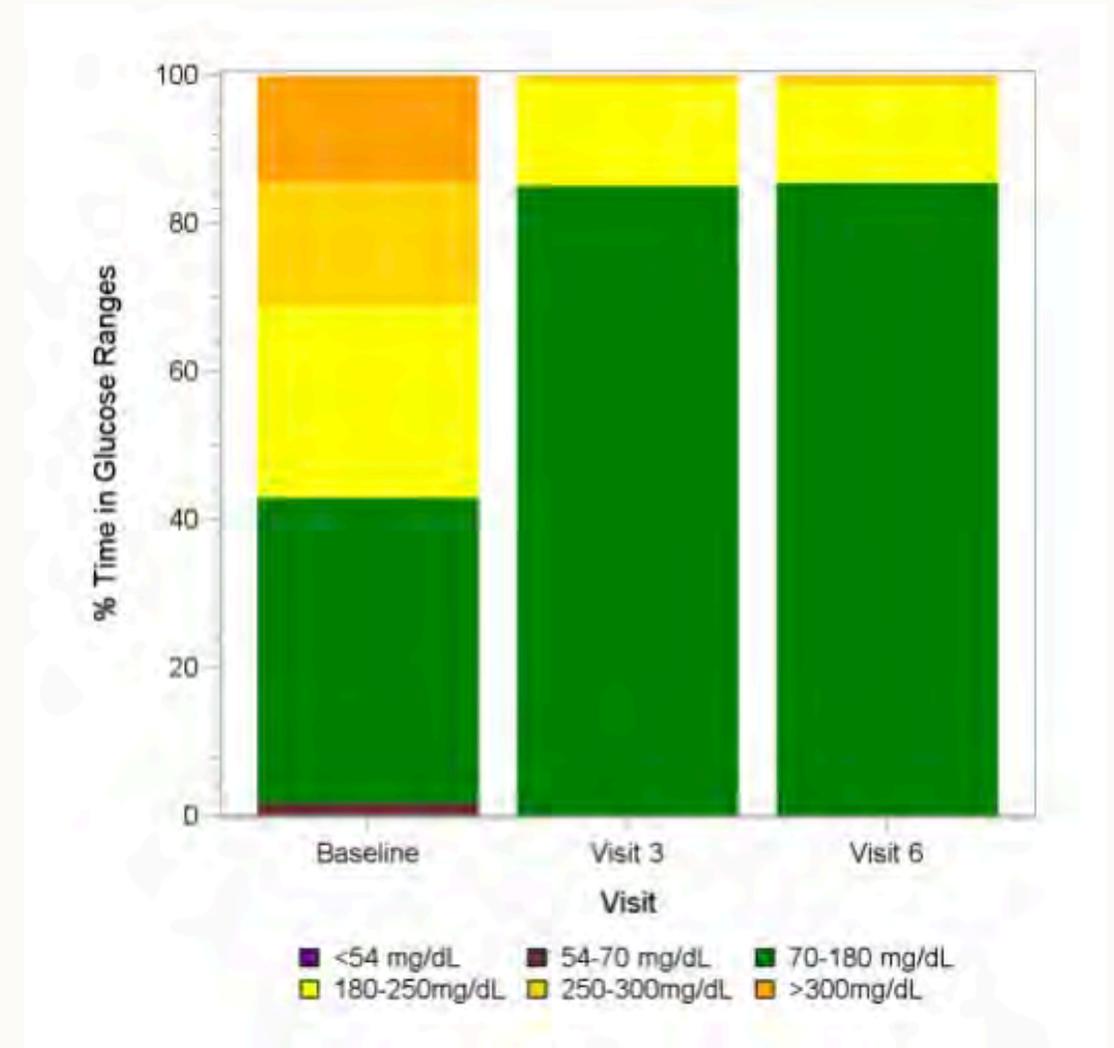


**HbA1c 9.6%**  
**TIR 41%**

**HbA1c 6.9%**  
**TIR 85%**

# After Eight Months of rtCGM

- ▶ By eight months she had further reduced her insulin dose to 10 units morning, 12 units at night
- ▶ Sustained improvements in dietary intake
- ▶ Time in Range 85%
- ▶ HbA1c improved
  - 9.6% at start
  - 6.9% at 4 months
  - 6.5% at 8 months
  - 6.6% at 12 months
- ▶ Weight reduced 96 to 87kg



# Access to Technology

## Non-Intensive Insulin Therapy



# Access to Technology

Can you currently access funding for rtCGM for all your patients with T2DM who are on non intensive insulin therapy (basal only)?

- 1) Yes
- 2) Yes, but only if they have insurance
- 3) No

# CGM in Type 2 Diabetes

## Non-Insulin Therapy

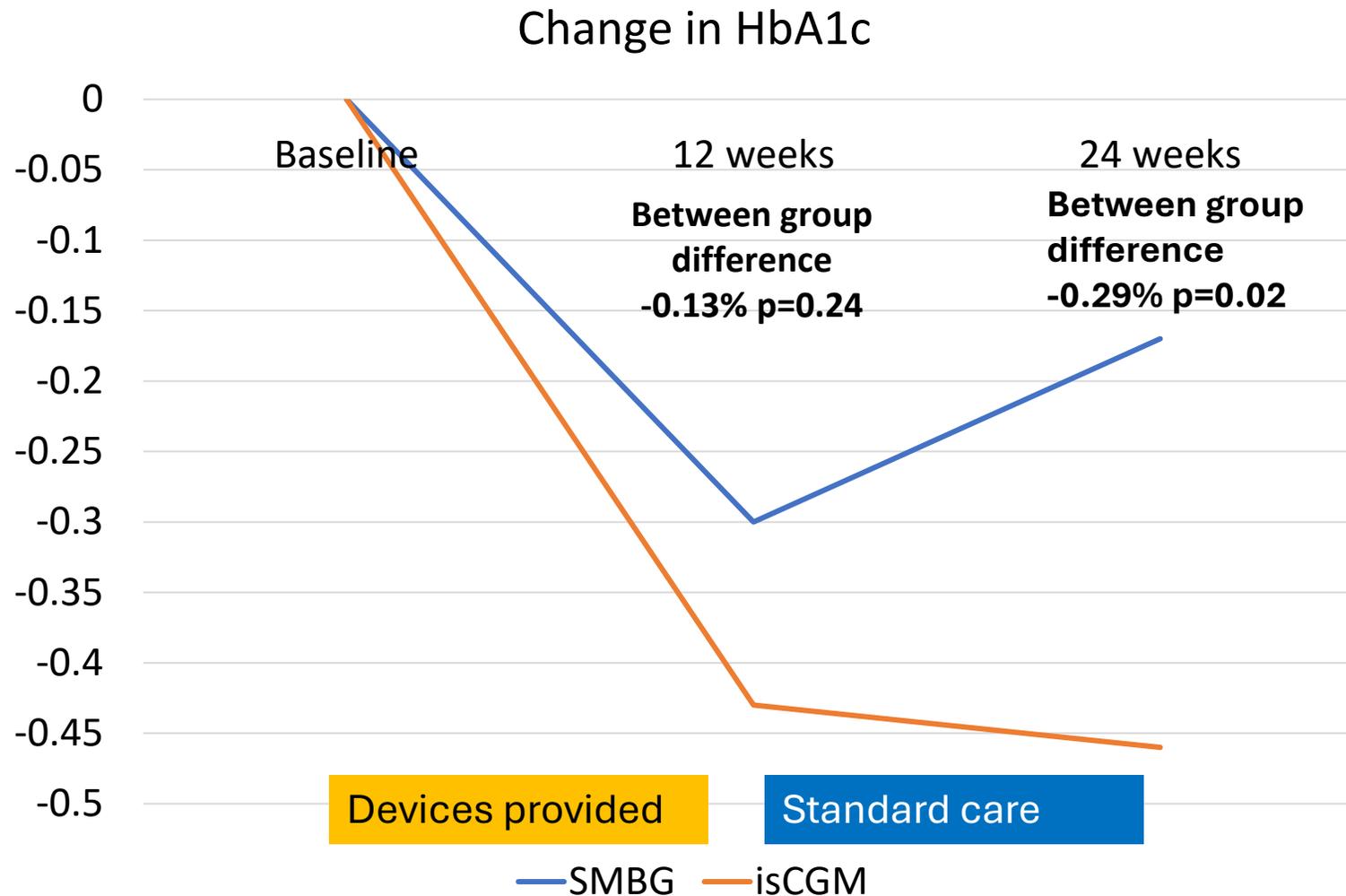


# Wada et al

Open access Original research

**BMJ Open Diabetes Research & Care** Flash glucose monitoring helps achieve better glycemic control than conventional self-monitoring of blood glucose in non-insulin-treated type 2 diabetes: a randomized controlled trial

Eri Wada,<sup>1</sup> Takeshi Onoue,<sup>1</sup> Tomoko Kobayashi,<sup>1</sup> Tomoko Handa,<sup>1</sup> Ayaka Hayase,<sup>1</sup> Masaaki Ito,<sup>1</sup> Mariko Furukawa,<sup>1</sup> Takayuki Okuji,<sup>1</sup> Norio Okada,<sup>1</sup> Shintaro Iwama,<sup>1</sup> Mariko Sugiyama,<sup>1</sup> Taku Tsunekawa,<sup>1</sup> Hiroshi Takagi,<sup>1</sup> Daisuke Hagiwara,<sup>1</sup> Yoshihiro Ito,<sup>1,2</sup> Hidetaka Suga,<sup>1</sup> Ryoichi Banno,<sup>1,3</sup> Yachiyo Kuwatsuka,<sup>4</sup> Masahiko Ando,<sup>4</sup> Motomitsu Goto,<sup>1</sup> Hiroshi Arima<sup>1</sup>



- ▶ RCT **non-insulin- treated** T2DM
- ▶ HbA1c 7.5-8.5% in Japan
- ▶ Randomised to isCGM or SMBG for 12 weeks
- ▶ Primary outcome HbA1c
- ▶ Significant improvements with isCGM:
  - ↑ Diabetes Treatment Satisfaction
  - ↓ Mean glucose
- ▶ No difference in hypoglycaemia

# IMMEDIATE Study

- ▶ Multi-site RCT (n=116)
- ▶ HbA1c of >7.5% on **non-insulin therapy**
- ▶ Follow-up 16 weeks, 1:1 Randomisation
- ▶ isCGM (Libre) + diabetes education vs diabetes education alone
- ▶ Primary outcome: Time in range



# IMMEDIATE: Key Outcomes

**TABLE 2** CGM metrics between the isCGM + DSME and the DSME arms at follow-up

	isCGM + DSME	DSME	Adjusted mean difference (95% CI)	Adjusted P value
n	51	48		
% TIR (3.9-10.0 mmol/L)	76.3 ± 17.4	65.6 ± 22.6	-9.9 (-17.3 to -2.5)	.009
% time in the tight glycaemic range (3.9-7.8 mmol/L)	50.3 ± 21.9	40.4 ± 23.1	-8.5 (-16.6 to -0.3)	.042
% TAR (> 10.0 mmol/L)	21.2 ± 18.1	30.7 ± 24.5	8.1 (0.5 to 15.7)	.037
% TBR (< 3.9 mmol/L)	1.9 ± 3.5	3.0 ± 6.5	1.3 (-0.8 to 3.3)	.218
% TBR level 2 (< 3.0 mmol/L)	0.6 ± 2.3	0.9 ± 3.1	0.3 (-0.8 to 1.4)	.553

- ▶ Adjusted mean difference for follow-up HbA1c -0.3% lower (P = 0.048) in isCGM
- ▶ Glucose monitoring satisfaction survey higher (P<0.01)
- ▶ Non-insulin antihyperglycaemic therapies were added among less than 10% of participants in each arm over the trial follow-up period
  - Improvement in glycaemia more to do with life-style change?



# CGM with Remote Support

Can CGM with **remote telemonitoring-enabled virtual diabetes educator** visits improve glycaemic management in adults with T2DM, not on insulin?

- ▶ 6-week RCT of CGM with telemonitoring vs. usual care
- ▶ Both groups received educator support
- ▶ **CGM 0.65 % greater HbA1c reduction at 12 weeks p = 0.008**
- ▶ CGM participants
  - Lost more weight (difference in weight reduction 2.17 kg p = 0.029)
  - More satisfied with their treatment

***Take home: CGM with remote support is superior***

Lau et al. DRCP 2024

# Access to Technology

## Non-Insulin Therapy



# Access to Technology

Can you currently access funding for rtCGM for all your patients with T2DM who are on non-insulin therapy?

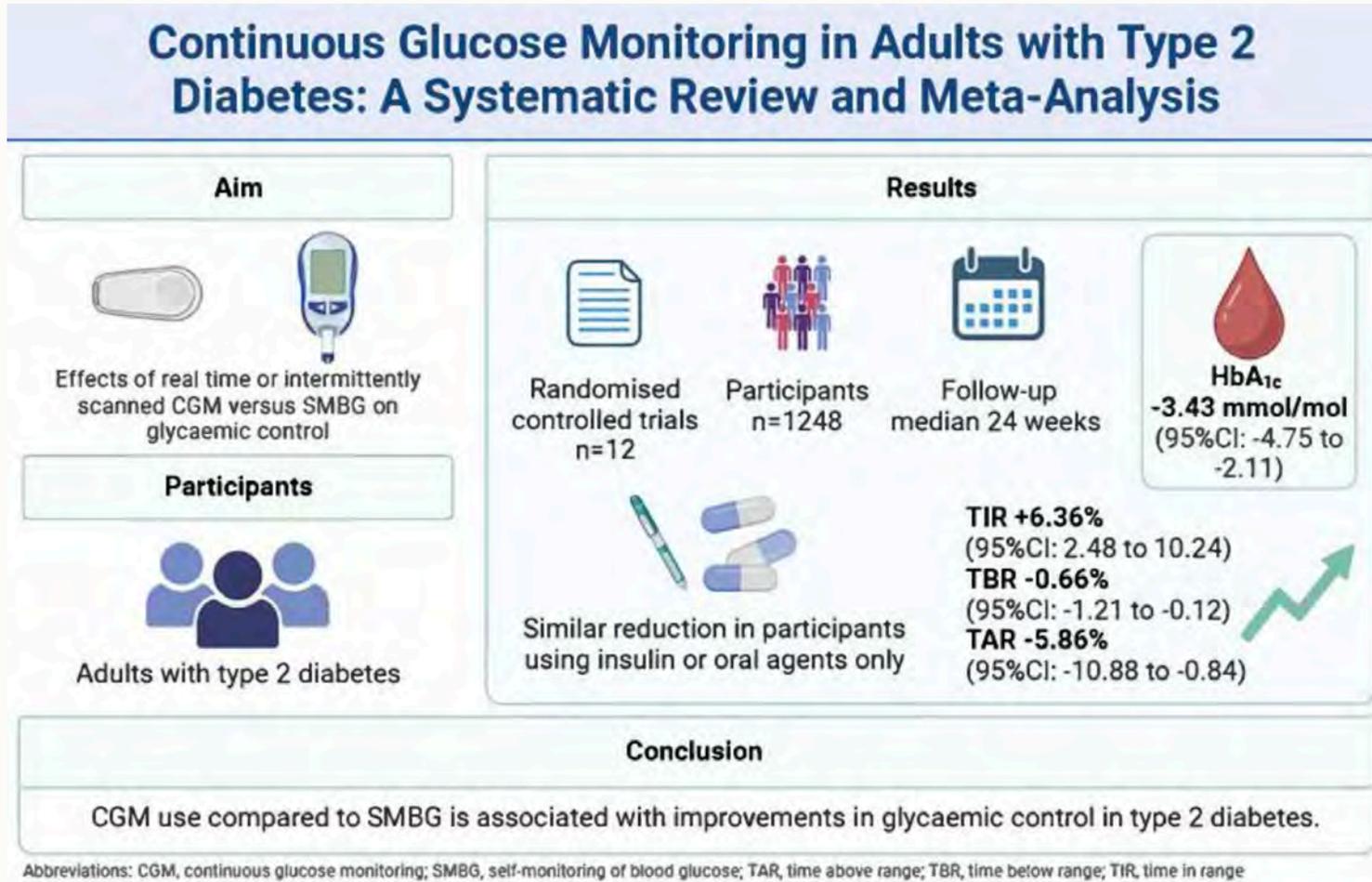
- 1) Yes
- 2) Yes, but only if they have insurance
- 3) No

# CGM in Type 2 Diabetes

## In Summary

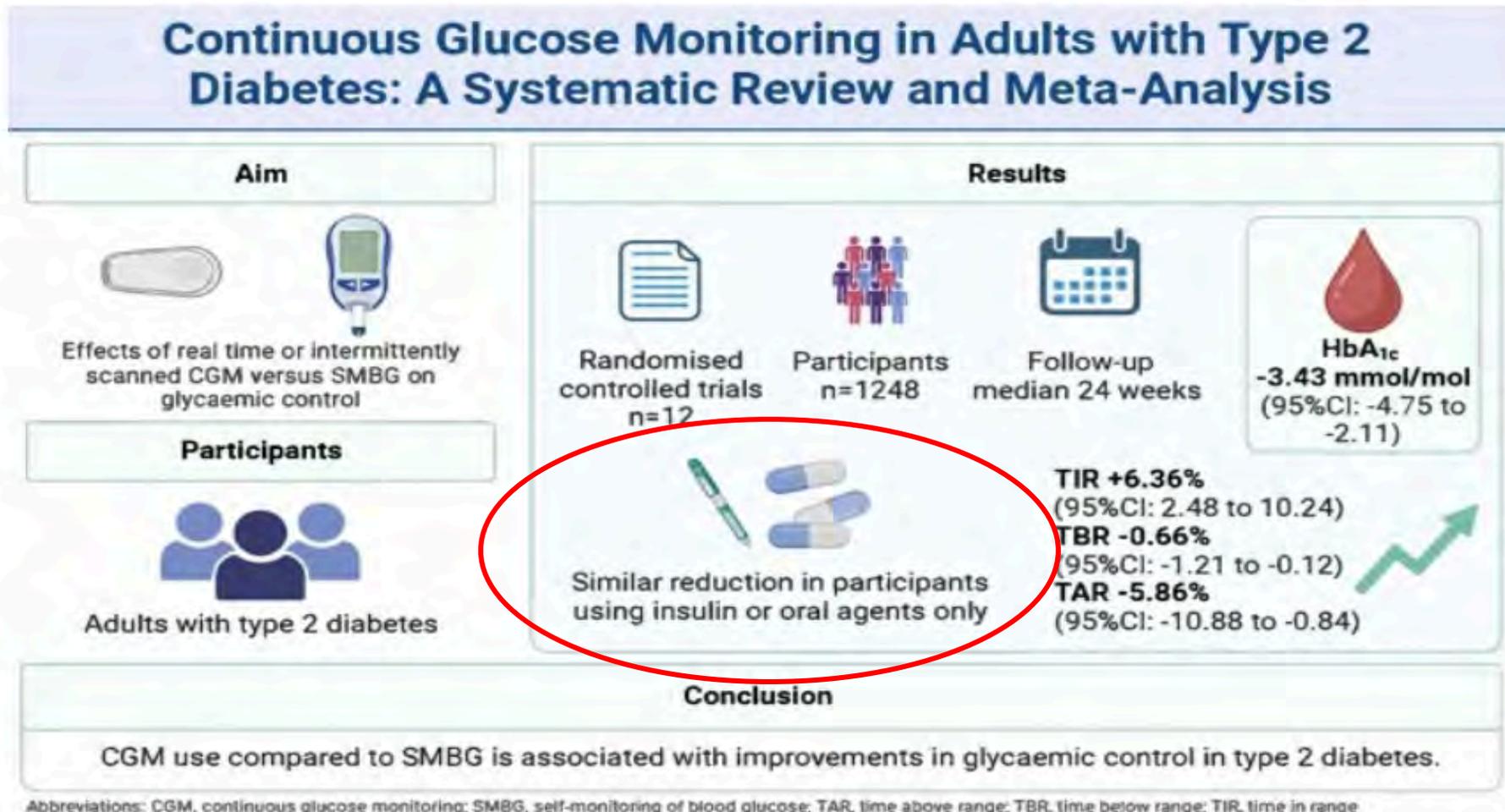


# CGM Systematic Review



Excluded studies with pregnant women or individuals with type 1 diabetes, studies that investigated GlucoWatch or a professional CGM device or an intervention that consisted of CGM combined with an additional glucose-lowering treatment strategy

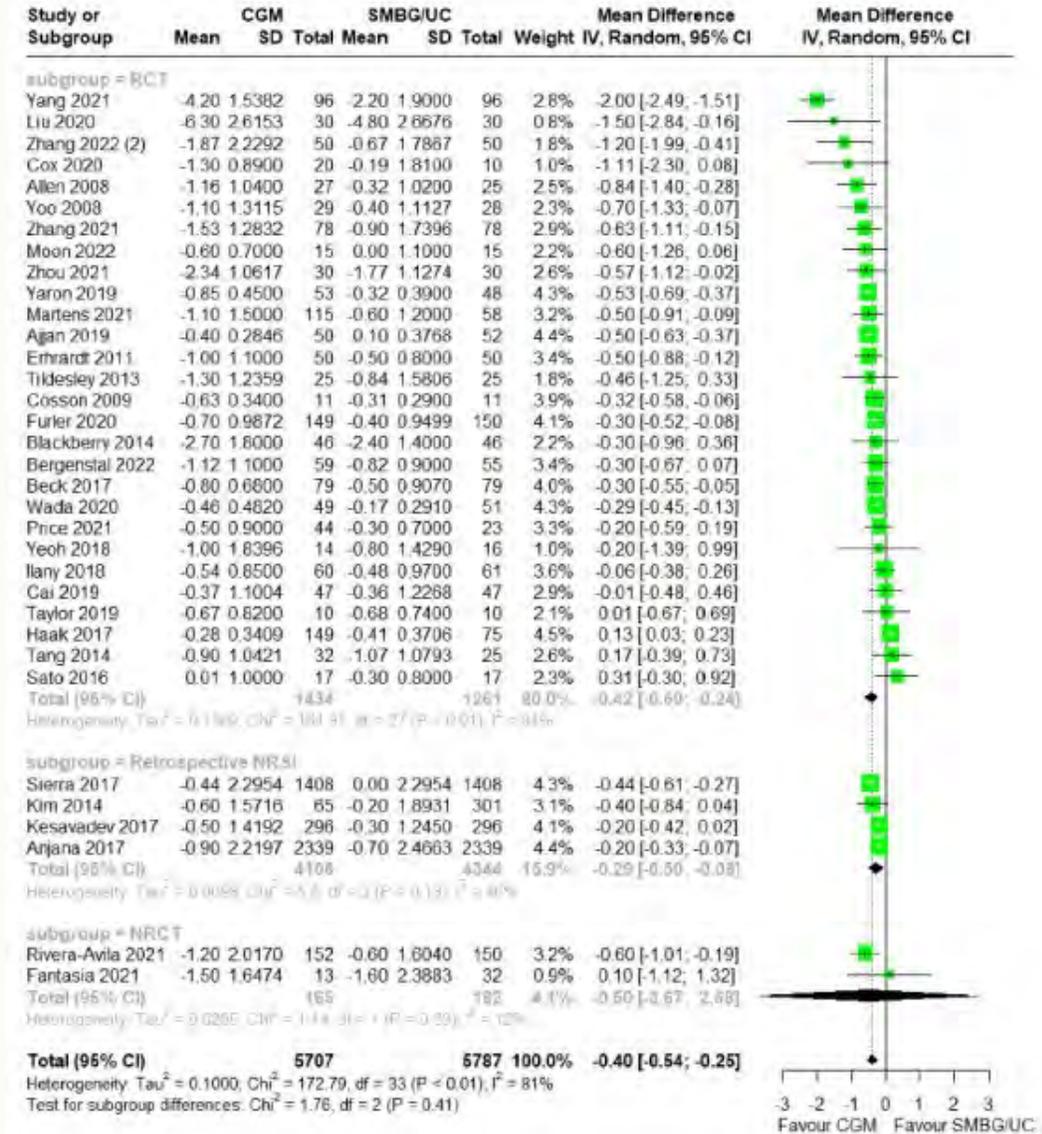
# CGM Systematic Review



Excluded studies with pregnant women or individuals with type 1 diabetes, studies that investigated GlucoWatch or a professional CGM device or an intervention that consisted of CGM combined with an additional glucose-lowering treatment strategy

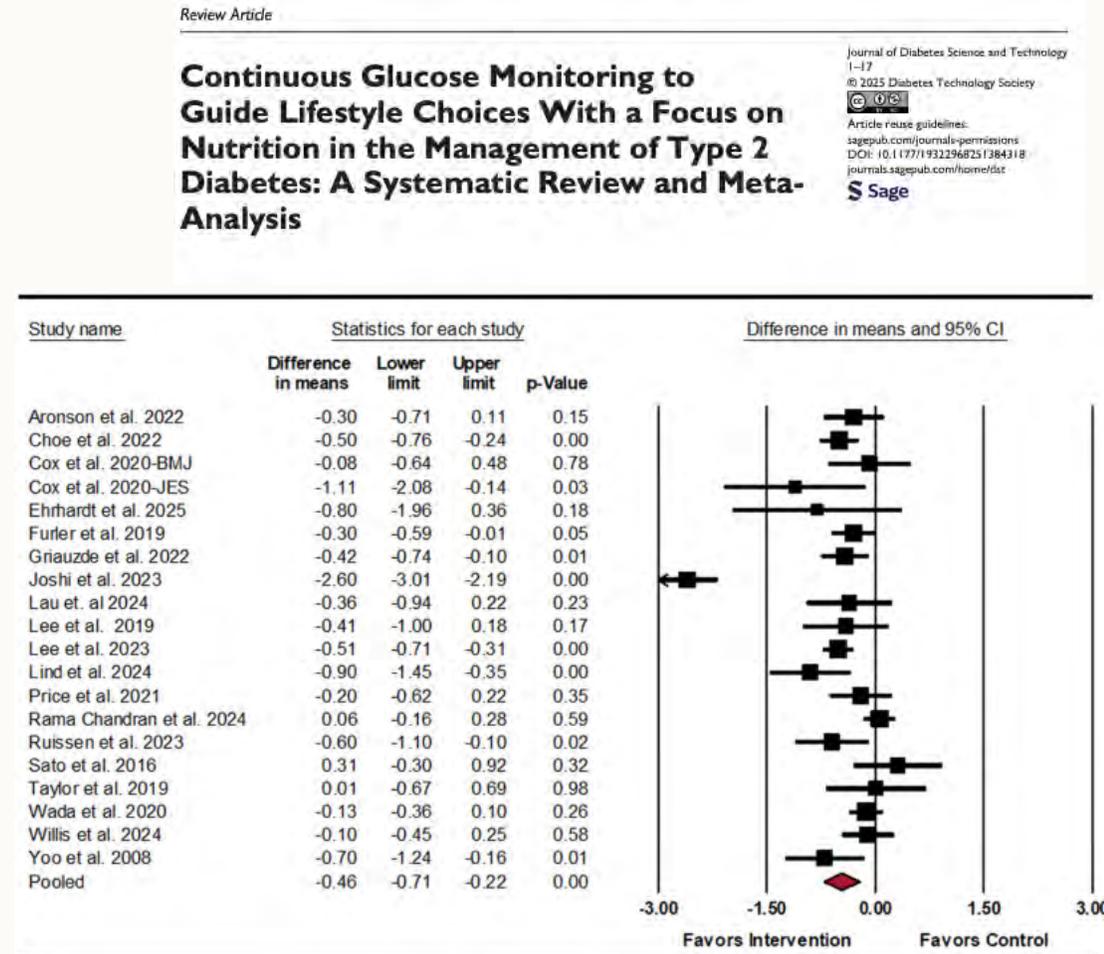
# Umbrella Review

- ▶ CGM was associated with
  - **HbA1c decrease** (MD = -0.40% [95% CI: -0.54 to -0.25]),
  - **TIR increase** (MD = 6.00% [95%CI: 3.13 to 8.88])
  - **TAR decrease** (MD = -4.33% [95%CI: -8.37 to -0.28])
- ▶ Findings invariant with CGM modality, study funding, **pre-existing insulin treatment**, risk-of-bias.
- ▶ Conclusion: CGM could lead to better clinical outcomes than SMBG/UC and was of moderate evidence certainty (GRADE)
- ▶ “We recommend the introduction of CGM into standard care alongside SMBG for T2DM”



# Focus on Nutrition

- ▶ Systematic review and meta-analysis examined the role of CGM in guiding lifestyle choices with a focus on nutrition in the management of T2D
- ▶ CGM intervention vs control:
  - 0.46% (95% CI: -0.71, -0.22) greater reduction in HbA1c
  - 2.06 kg (95% CI: -3.74, -0.38) greater reduction in body weight (or approximately 2.5% reduction)



# CGM in Type 2 Diabetes

## What's Next?

BMJ Open

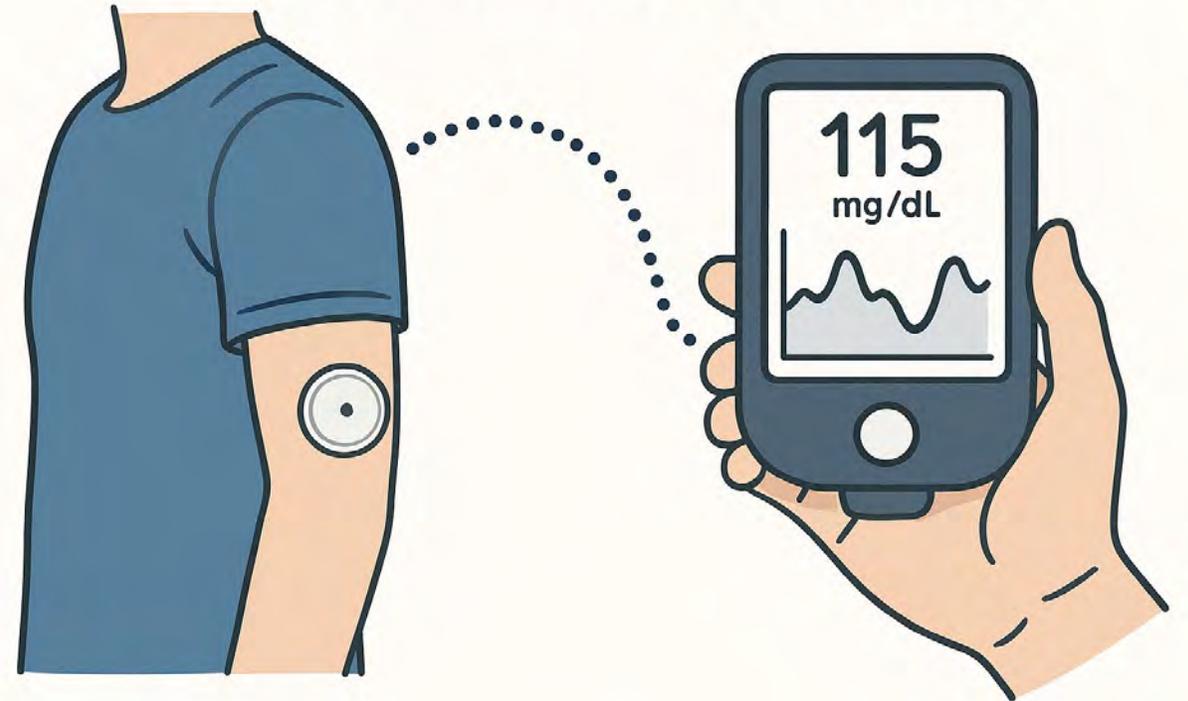
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Journal **BMJ**

BMJ Open. 2025 Apr 15;15(4):e090154. doi: [10.1136/bmjopen-2024-090154](https://doi.org/10.1136/bmjopen-2024-090154)

### Impact of real-time glucose monitoring using FreeStyle Libre 3 on glycaemia in type 2 diabetes managed with basal insulin plus SGLT2 inhibitor and/or GLP-1 agonist: the FreeDM2 randomised controlled trial protocol

[Emma G Wilmot](#)<sup>1,2</sup>, [Ramzi A Ajjan](#)<sup>3,4</sup>, [Yee S Cheah](#)<sup>5</sup>, [Pratik Choudhary](#)<sup>6</sup>, [Iain Cranston](#)<sup>7</sup>, [Rachel Ann Elliott](#)<sup>8</sup>, [Mark Evans](#)<sup>9,10</sup>, [Ahmed Iqbal](#)<sup>11,12</sup>, [Shafie Kamaruddin](#)<sup>13</sup>, [Katharine Barnard-Kelly](#)<sup>14</sup>, [Alistair Lumb](#)<sup>15,16</sup>, [Thinzar Min](#)<sup>17</sup>, [Patrick Moore](#)<sup>18</sup>, [Parth Narendran](#)<sup>19</sup>, [Sankalpa Neupane](#)<sup>20,21</sup>, [Gerry Rayman](#)<sup>22</sup>, [Thozhukat Sathyapalan](#)<sup>23,24</sup>, [Hood Thabit](#)<sup>25,26</sup>, [Thomas Yates](#)<sup>27,28</sup>, [Lalantha Leelarathna](#)<sup>26,29,∞</sup>

## Continuous Glucose Monitoring



# FreeDM2 Study Aims

- ▶ Individuals treated with basal insulin, SGLT2i and GIP/GLP-1 therapy represent an **increasingly significant proportion** of those living with **T2DM**.
- ▶ Despite combination therapy, many **do not** achieve **glycaemic targets**.
- ▶ There is a **lack** of high quality RCT evidence supporting the use of **CGM** in people with T2DM treated with the combination of **basal insulin** with **GIP/GLP-1** or **SGLT2i** therapy.
- ▶ Our **understanding** of **behavioral changes** associated with CGM use are limited

## Aim:

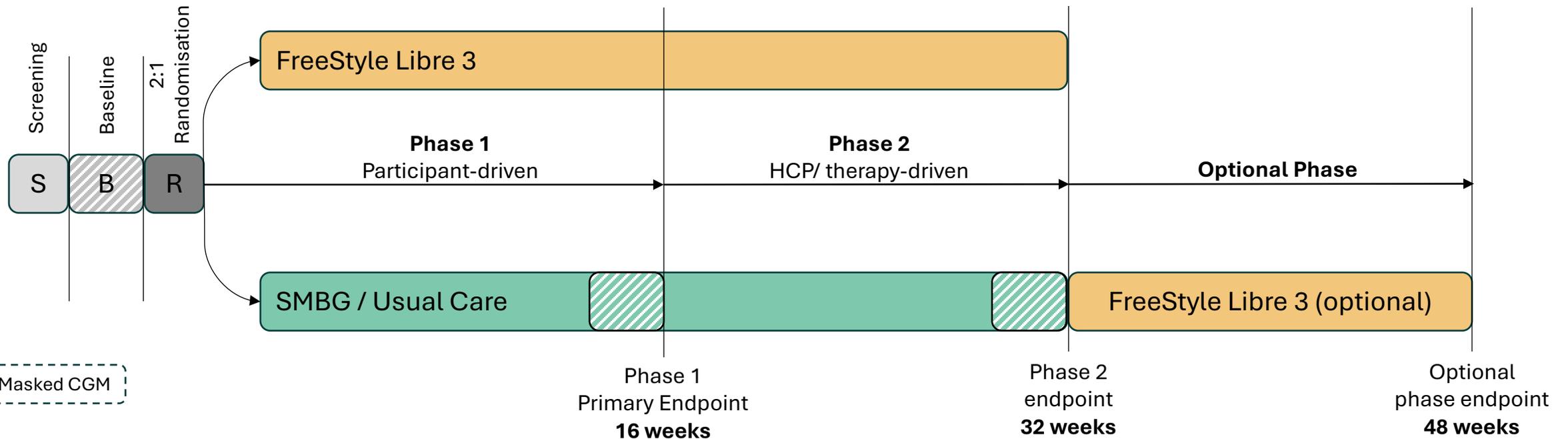
To determine whether the FreeStyle Libre 3 CGM system improves HbA1c over 16-weeks compared to SMBG in adults with suboptimal glycaemia

# Study Design

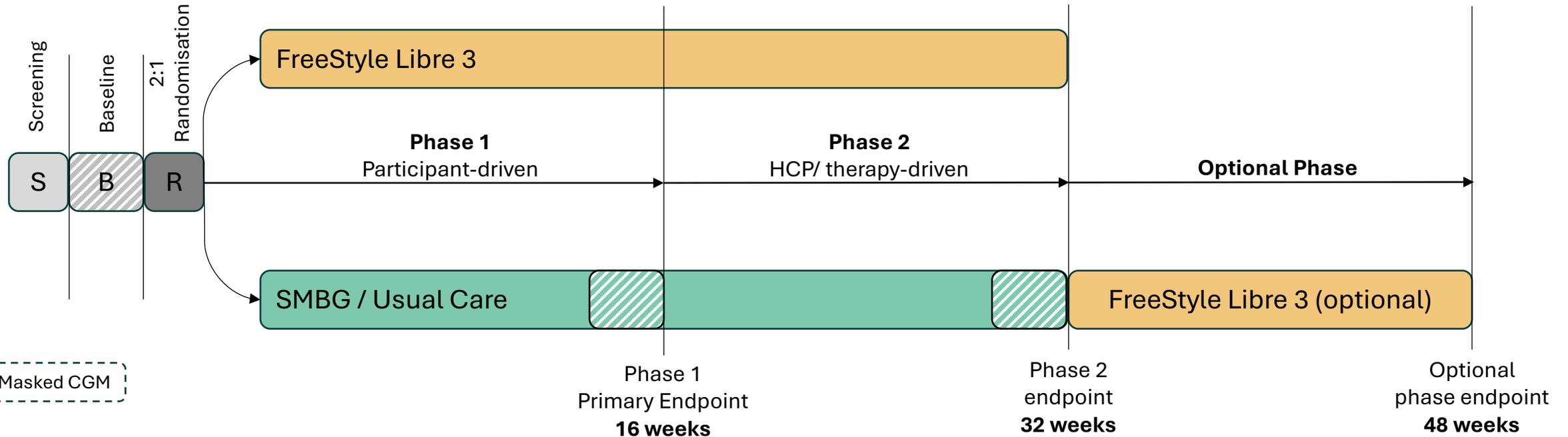
UK study: recruitment from 24 secondary & primary care centres & nationally via self-referral.

## Key inclusion criteria

- Adults with T2DM
- Basal-only insulin plus SGLT2i and/or GLP-1 dual GIP/GLP-1-RA
- HbA1c  $\geq 59$  and  $\leq 97$  mmol/mol ( $\geq 7.5$  and  $\leq 11.0\%$ )



# Analysis Endpoints



## Primary endpoint

 Between group difference in HbA1c change at 16 weeks

## Secondary endpoints

 Between group difference in HbA1c change at 32 weeks

 Weight and blood pressure

 Accelerometer data

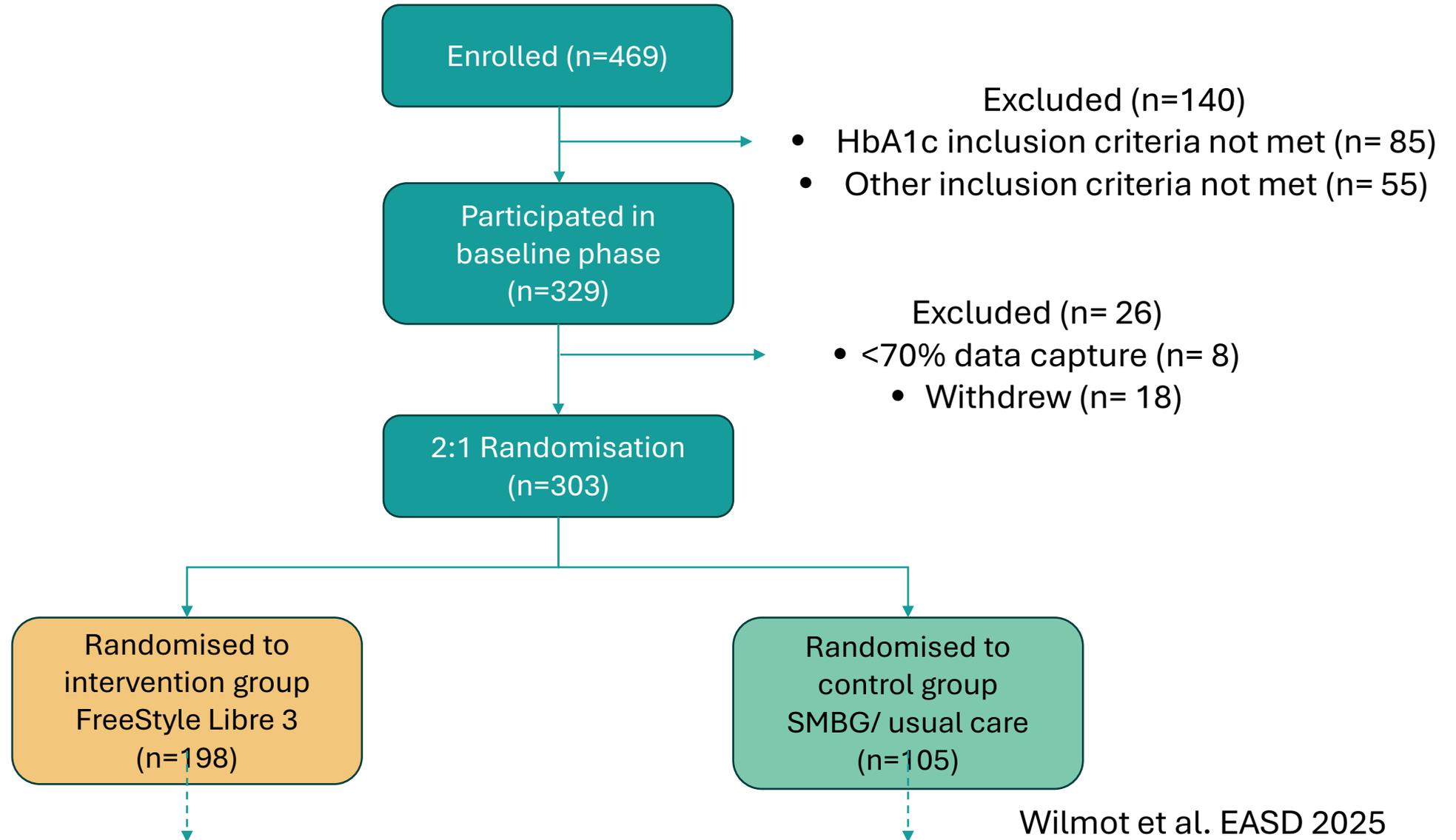
 PROMs (including EQ-5D-5L, GMSS, UKDDQ, HCS, HFS-II) and qualitative interviews.

 CGM metrics

 Changes to insulin doses and non-insulin medications

 Safety

# Participant Flow Diagram



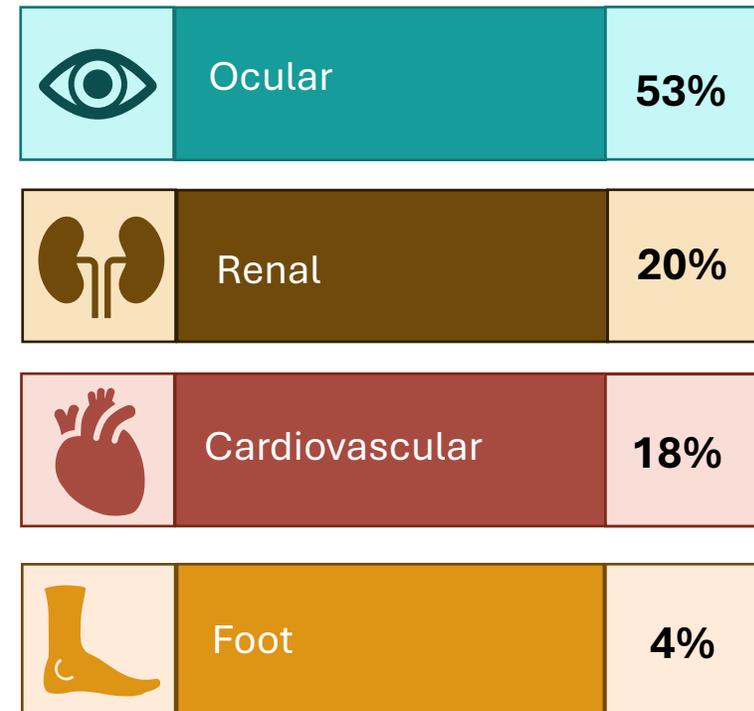
# Baseline Data

## Demographics and Medical History

Demographic	All (n=303)	FSL3 Intervention (n=198)	SMBG/ Usual Care (n=105)
Age, years	60.7 ± 9.8	61.2 ± 10.2	59.8 ± 9.1
Male sex, %	67.3	66.7	68.6
BMI, kg/m <sup>2</sup>	31.2 ± 5.6	31.1 ± 5.6	31.3 ± 5.7
Diabetes duration, years	16.7 ± 6.9	17.1 ± 6.6	15.9 ± 7.4

mean± SD unless stated otherwise

### Diabetes related complications at baseline



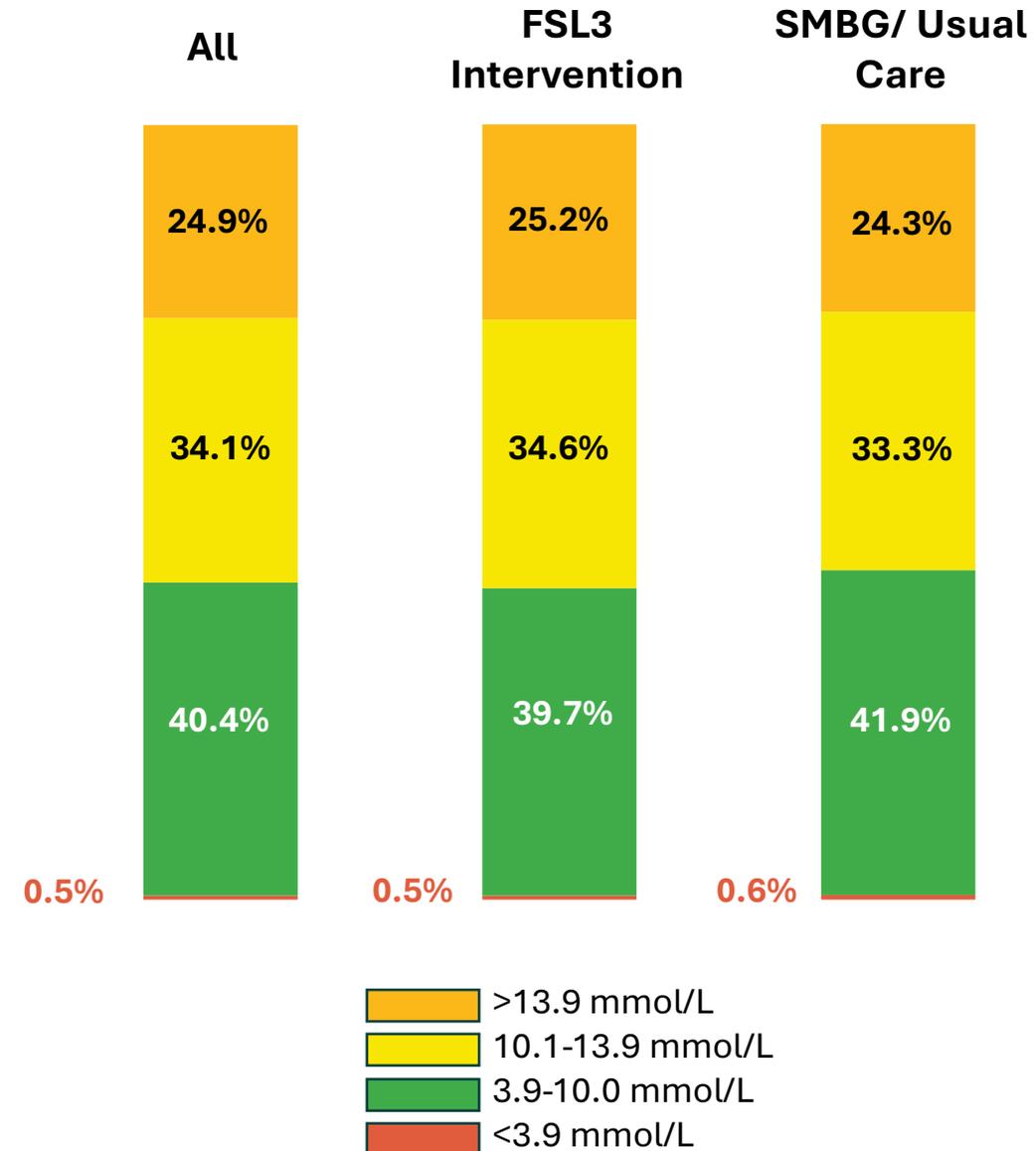
# Baseline Data

## Glycaemia

Mean % time in glucose ranges at baseline

Parameter	All (n=303)	FSL3 Intervention (n=198)	SMBG/ Usual Care (n=105)
HbA1c, mmol/mol	73 ± 11	73 ± 11	73 ± 11
HbA1c, %	8.8 ± 1.0	8.8 ± 1.0	8.8 ± 1.1
Mean daily fingerstick frequency	2.0 ± 1.9	1.9 ± 1.8	2.1 ± 2.0

mean ± SD unless stated otherwise



# FreeDM2 RCT

- ▶ FreeDM2 will provide information on the **efficacy** of the FreeStyle Libre 3 system on glycaemic outcomes in adults with T2DM with suboptimal HbA1c levels despite basal insulin plus SGLT2i and/or incretin therapy.
- ▶ The **two-phase design** will provide insight into the impact of
  - **Patient-driven insulin titration**
  - **Therapy escalation**

**Presentation of  
combined 4- and  
8-month data**

**ATTB**  
Advanced Technologies  
& Treatments for Diabetes

**11-14 MARCH 2026  
BARCELONA, SPAIN**

Hot From The Oven Session, Thursday 8am

# ATTD 2026 Late-Breaking Abstracts

**ATTD**

*Advanced Technologies  
& Treatments for Diabetes*

**11-14 MARCH 2026  
BARCELONA & ONLINE**

# Screening for and Prevention of Type 2 Diabetes

## CURRENT GMI CAN OVER DIAGNOSE PREDIABETES WITH UPDATED GMI AND TITR MITIGATING THIS RISK

Session Name 0740 - ORAL PRESENTATIONS 04: SCREENING, PREVENTION AND CURE OF DIABETES (ID 37)

Session Type ORAL PRESENTATIONS SESSION

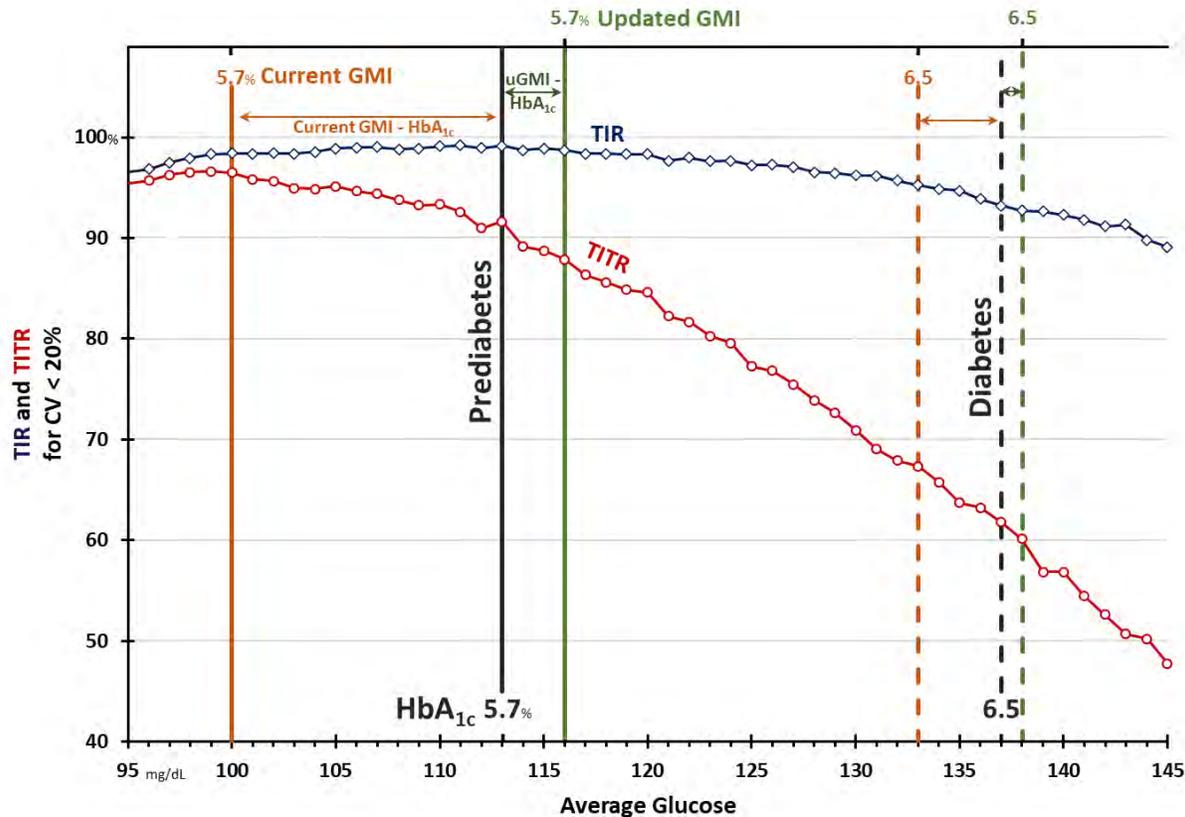
Date Fri, 13.03.2026

Session Time 09:30 - 10:30

Room Hall 212

Presenter Ramzi Ajjan (United Kingdom)

Lecture Time 10:00 - 10:10

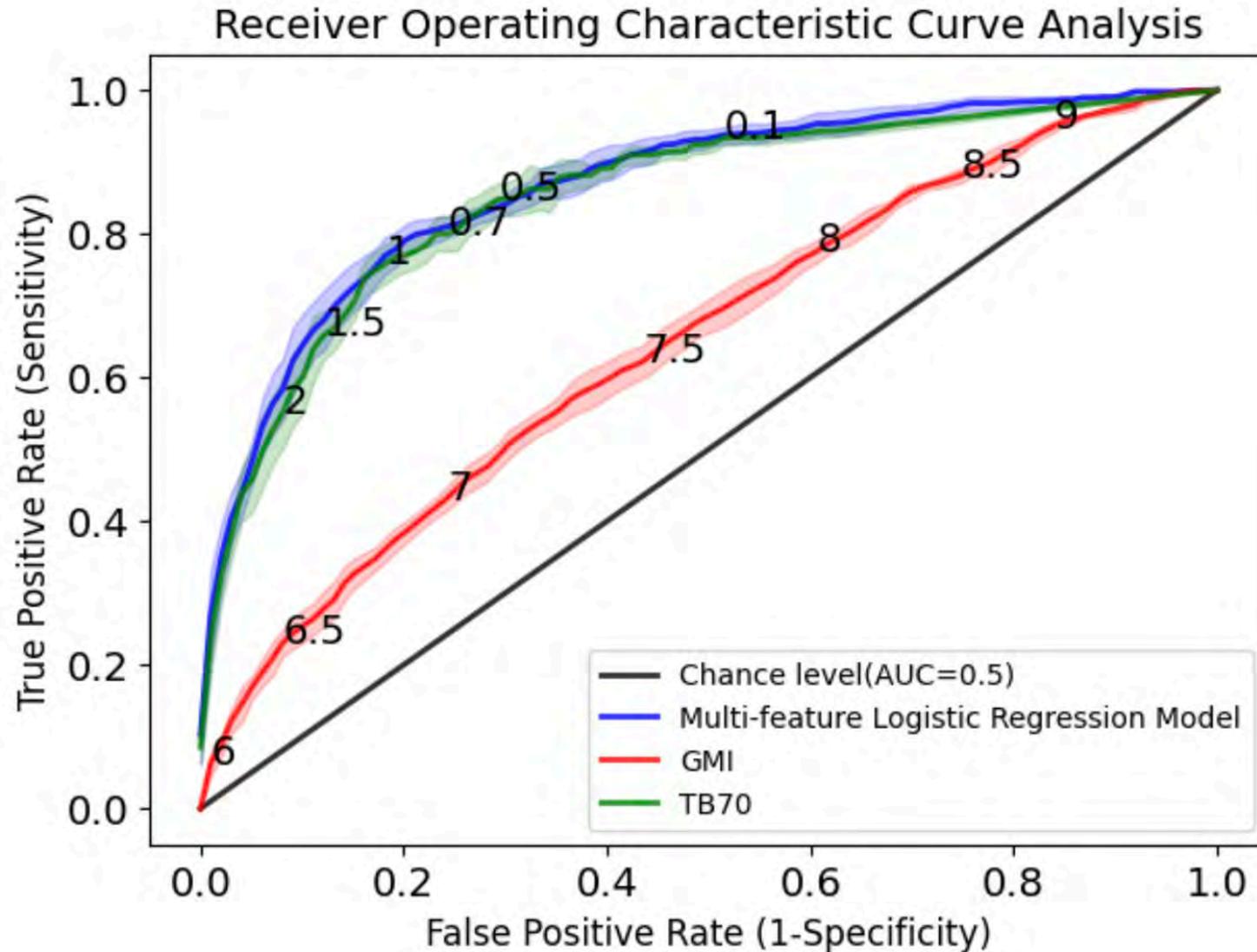


Updated GMI (uGMI) and time in tight range (TITR) are more sensitive to HbA1c cut off values for the diagnosis of prediabetes.

Current GMI can over diagnose prediabetes and should be replaced with **updated GMI, which aligns more closely with HbA1c.**

Similarly, TITR should replace TIR as a measure of normoglycaemia and prediabetes.

# Data-Driven Identification of Patients Requiring Insulin Reduction Using Continuous Glucose Monitoring Prior to GLP-1 RA Initiation



**CGM data before GLP-RA initiation helps identify patients likely to experience hypoglycemia post-initiation, enabling preemptive insulin reduction.**

# Budget Impact Analysis of Freestyle Libre Systems for People with T2D on Basal Insulin

- ▶ Reimbursement of FSL in most European countries remains restricted to people T1D and T2D on intensively managed insulin regimens.
- ▶ This study estimated the budget impact of expanding FSL access to people with T2D on basal insulin only (T2B) from a European payer perspective.
- ▶ **Results:** Expanding reimbursement of FSL to the T2B population resulted in a **net cost savings of €444** per patient per year.
- ▶ At a cohort level, this translated to a **net annual cost savings of €443,803** for the payer. OWSA identified the baseline rate of hospitalization and cost of all-cause healthcare resource utilization as key model drivers.

## Conclusion

This budget impact analysis showed **the acquisition cost of FSL is offset by HCRU reduction in the T2B population.**

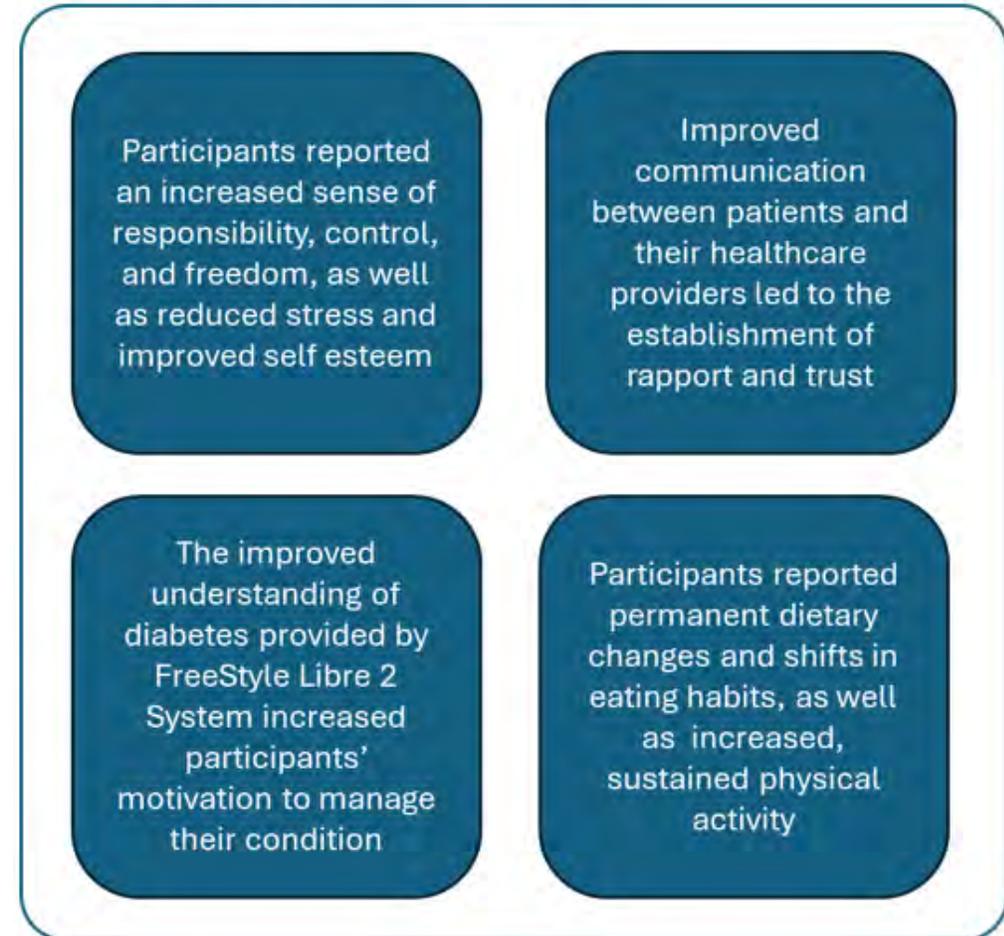
As such, reimbursement expansion of FSL in this population can result in significant net cost savings to European health systems.

# Experiences of Diabetes Management With Freestyle Libre 2

## A Focus Group Study Among People Living With Type 2 Diabetes In Quebec

- ▶ A focus group of 16 adults with T2DM living in Quebec and using FSL2
- ▶ Focus group participants found that **FSL2 improved their diabetes self-management, communication with healthcare providers, stress levels, and facilitated short- and long-term lifestyle changes.**

Figure 2. Key insights



# Conclusion

- ▶ Undisputed benefits of CGM in people with T1DM
- ▶ Evidence so far suggest CGM is beneficial in Type 2 diabetes
- ▶ Benefits in some groups may be more to do with lifestyle modification?
- ▶ FreeDM2 RCT results will be presented on Thursday

**Presentation of  
combined 4- and  
8-month data**

**ATTD**  
Advanced Technologies  
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**11-14 MARCH 2026  
BARCELONA, SPAIN**

Hot From The Oven Session, Thursday 8am

# CGM for Transforming Clinical Outcomes in Non-Intensive T2D Therapy

Thank You

