Using Flash/CGM in people with type 2 diabetes

Ramzi Ajjan
Professor of Metabolic Medicine
University of Leeds and Leeds Teaching Hospitals Trust
Leeds, United Kingdom

UNIVERSITY OF LEEDS

The Leeds Teaching Hospitals NHS
NHS Trust

Our main glycaemic measure in T2D remains HbA1c

Why?

- Predicts complications
- Easy to understand/explain (familiarity)
- Clear cut targets (most of the time!)

Used for

- Glycaemic management
- Diagnosis of diabetes

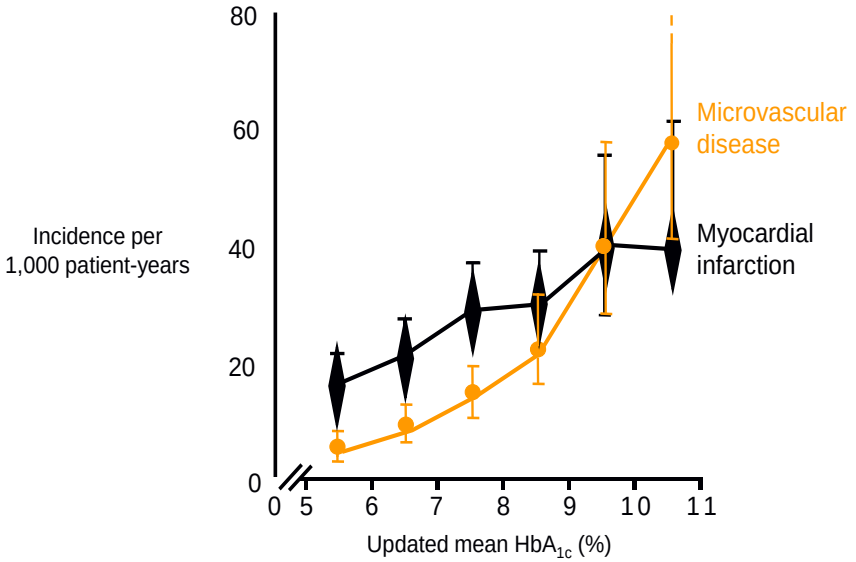
Our main glycaemic measure in T2D remains HbA1c

Why?

- Predicts complications
- Easy to understand/explain (familiarity)
- Clear cut targets (most of the time!)

Used for

- Glycaemic management
- Diagnosis of diabetes



Adapted from Stratton IM, et al. BMJ 2000; 321:405-12
ADA, Diabetes Care 2021; 44:S15–S33

HbA1c: an old friend of the diabetologist but…

HbA1c has a number of weaknesses

- Several factors affect accuracy
- Slow at assessing effectiveness of new therapies/management strategies
- Unable to provide data on the role of daily life activities on glucose control

HbA1c does not measure

- Hypoglycaemia
- Glycaemic variability (GV)

HbA1c: an old friend of the diabetologist but…

HbA1c has a number of weaknesses

- **Several factors affect accuracy**
- Slow at assessing effectiveness of new therapies/management strategies
- Unable to provide data on the role of daily life activities on glucose control

HbA1c does not measure

- Hypoglycaemia
- Glycaemic variability (GV)

HbA1c and RBC Lifespan

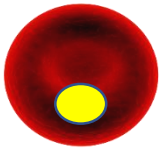
Xu et al, Elife 2021, 10:e69456

HbA1c and RBC Lifespan

Similar Average Blood Glucose

HbA1c

Average RBC lifespan



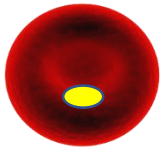
Xu et al, Elife 2021, 10:e69456

HbA1c and RBC Lifespan

Similar Average Blood Glucose

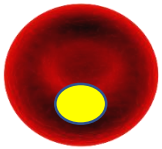
HbA1c

Short RBC lifespan



Undertreatment
(risk of complications)

Average RBC lifespan



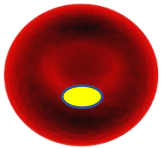
Xu et al, Elife 2021, 10:e69456

HbA1c and RBC Lifespan

Similar Average Blood Glucose

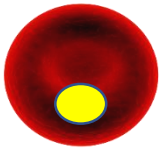
HbA1c

Short RBC lifespan

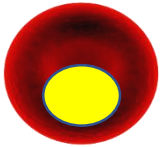


Undertreatment
(risk of complications)

Average RBC lifespan



Long RBC lifespan



Overtreatment
(risk if hypoglycaemia)

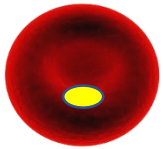
Xu et al, Elife 2021, 10:e69456

HbA1c and RBC Lifespan

Similar Average Blood Glucose

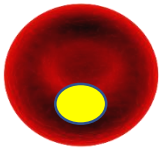
HbA1c

Short RBC lifespan

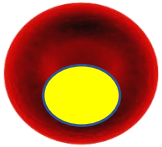


Undertreatment
(risk of complications)

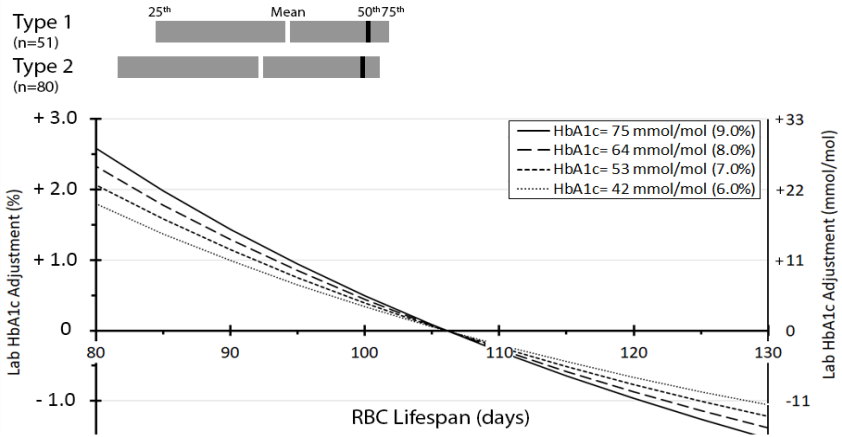
Average RBC lifespan



Long RBC lifespan



Overtreatment
(risk if hypoglycaemia)



Xu et al, Elife 2021, 10:e69456

Some of the Factors Modulating Accuracy of HbA_{1c}

	Erythropoiesis	Hemolysis (erythrocytes lifespan)	Altered hemoglobin
↓ **Falsely low HbA_{1c}**	**Increased erythropoiesis** • Hemorrhage • Administration of erythropoietin • Pregnancy • High altitude	**Decreased erythrocytes lifespan** • Chronic liver / kidney disease • Hemolytic anemia • Hemoglobinopathies • Antiretroviral treatment	• Hemoglobinopathies • Methemoglobin
↑ **Falsely high HbA_{1c}**	**Decreased erythropoiesis** • Different anaemia (iron deficiency, infections, tumor)	**Increased erythrocytes lifespan** • Splenectomy • Different anaemia • Hemoglobinopathies	• Hemoglobinopathies

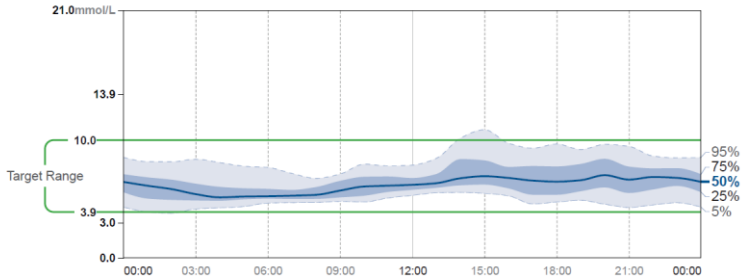
Gallagher et al., J Diabetes. 2009;1(1):9-17
https://www.consultant360.com/articles/when-a1c-unreliable
Campbell L. et al., J Clin Pathol. 2019;72:12-19

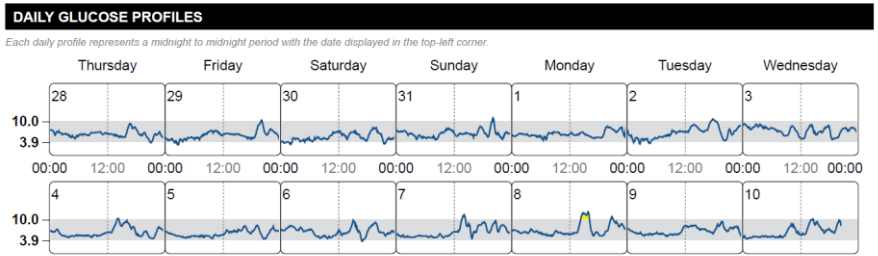
Clinical Case 1

- **41 year old lady found to have :**

HbA1c 49 mmol/mol (6.6%)

Fasting glucose of 5.4 mmol/l (97 mg/dl)



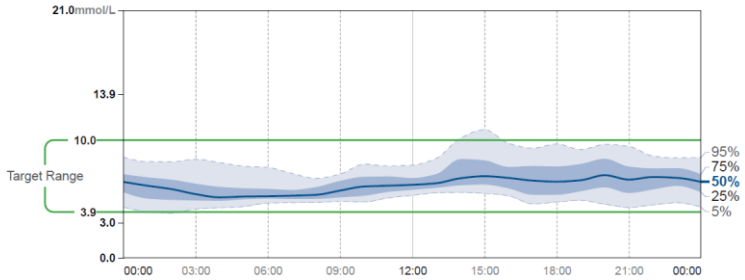


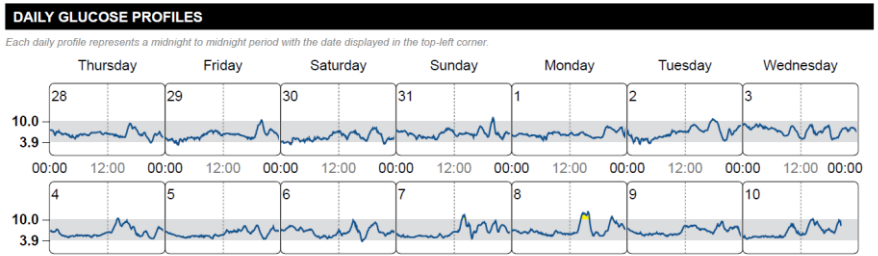
Clinical Case 1

- **41 year old lady found to have :**

HbA1c 49 mmol/mol (6.6%)

Fasting glucose of 5.4 mmol/l (97 mg/dl)





- **OGTT**

0 min: 5.2 mmol/l (94 mg/dl)

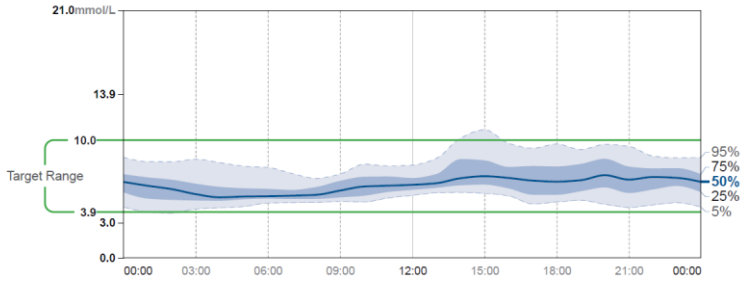
120 min: 7.1 mmol/l (128 mg/dl)

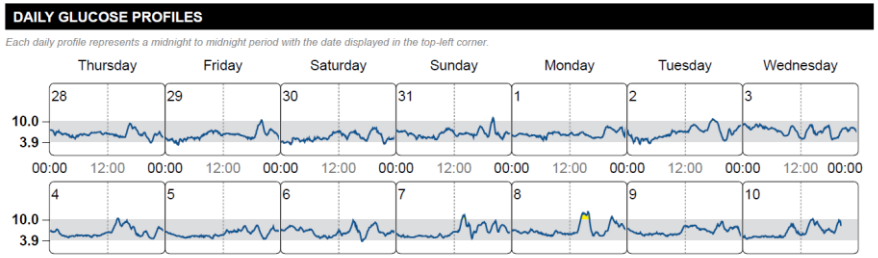
Clinical Case 1

- **41 year old lady found to have :**

HbA1c 49 mmol/mol (6.6%)

Fasting glucose of 5.4 mmol/l (97 mg/dl)





- **OGTT**

0 min: 5.2 mmol/l (94 mg/dl)

120 min: 7.1 mmol/l (128 mg/dl)

- **Further investigations:**

Hb 106 g/L (115-165)

MCV 70 fL (80-100)

Ferritin 4 ng/mL (10-300)

- **Treated with ferrous sulphate**

Repeat HbA1c 39 mmol/mol (5.7%)

HbA1c: an old friend of the diabetologist but…

HbA1c has a number of weaknesses

- Several factors affect accuracy
- **Slow at assessing effectiveness of new therapies/management strategies**
- Unable to provide data on the role of daily life activities on glucose control

HbA1c does not measure

- Hypoglycaemia
- Glycaemic variability (GV)

Case 2

Case 2

67 year gentleman with T2D for 11 years and recent myocardial infarction (second in 5 years).

- Glycaemic treatment prior to MI
  - Metformin 1 g bd
  - Glimepiride 2 mg od

Case 2

67 year gentleman with T2D for 11 years and recent myocardial infarction (second in 5 years).

- Glycaemic treatment prior to MI
  - Metformin 1 g bd
  - Glimepiride 2 mg od

Results

- HbA_{1c} 100 mmol/mol (11.3%)

Case 2

67 year gentleman with T2D for 11 years and recent myocardial infarction (second in 5 years).

- Glycaemic treatment prior to MI
  - Metformin 1 g bd
  - Glimepiride 2 mg od

Results

- HbA_{1c} 100 mmol/mol (11.3%)

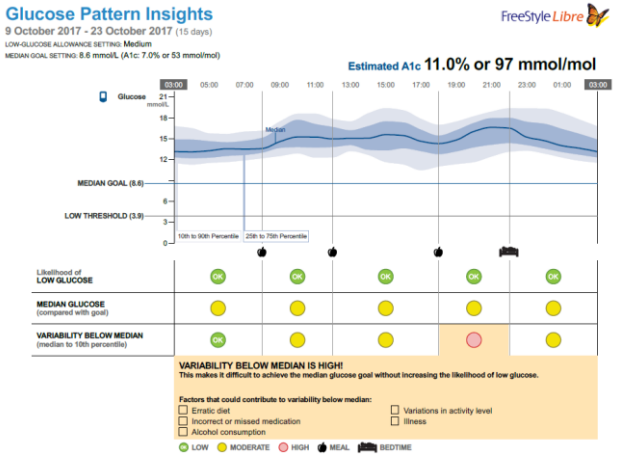
Monitoring response to any new treatment using HbA1c is problematic

Case 2

67 year gentleman with T2D for 11 years and recent myocardial infarction (second in 5 years).

- Glycaemic treatment prior to MI
  - Metformin 1 g bd
  - Glimepiride 2 mg od

TIR=21%



Results

- HbA_{1c} 100 mmol/mol (11.3%)

Monitoring response to any new treatment using HbA1c is problematic

Case 2

67 year gentleman with T2D for 11 years and recent myocardial infarction (second in 5 years).

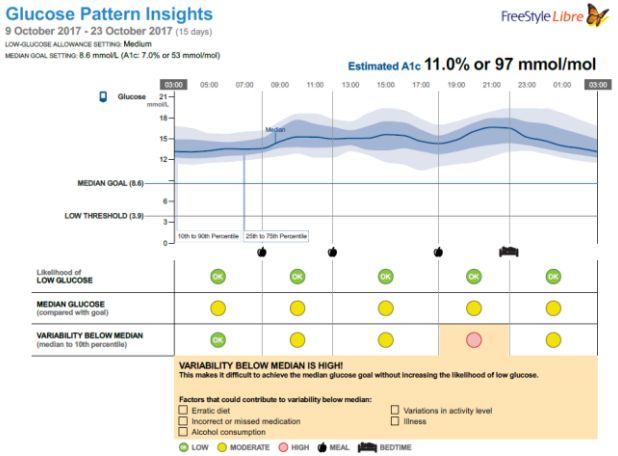
- Glycaemic treatment prior to MI
  - Metformin 1 g bd
  - Glimepiride 2 mg od

Results

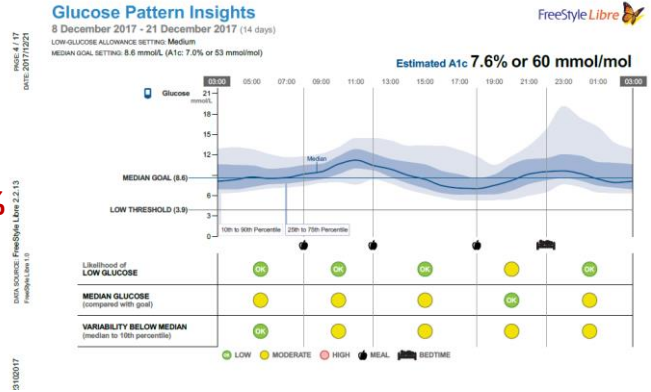
- HbA_{1c} 100 mmol/mol (11.3%)

Monitoring response to any new treatment using HbA1c is problematic

TIR=21%



TIR=62%



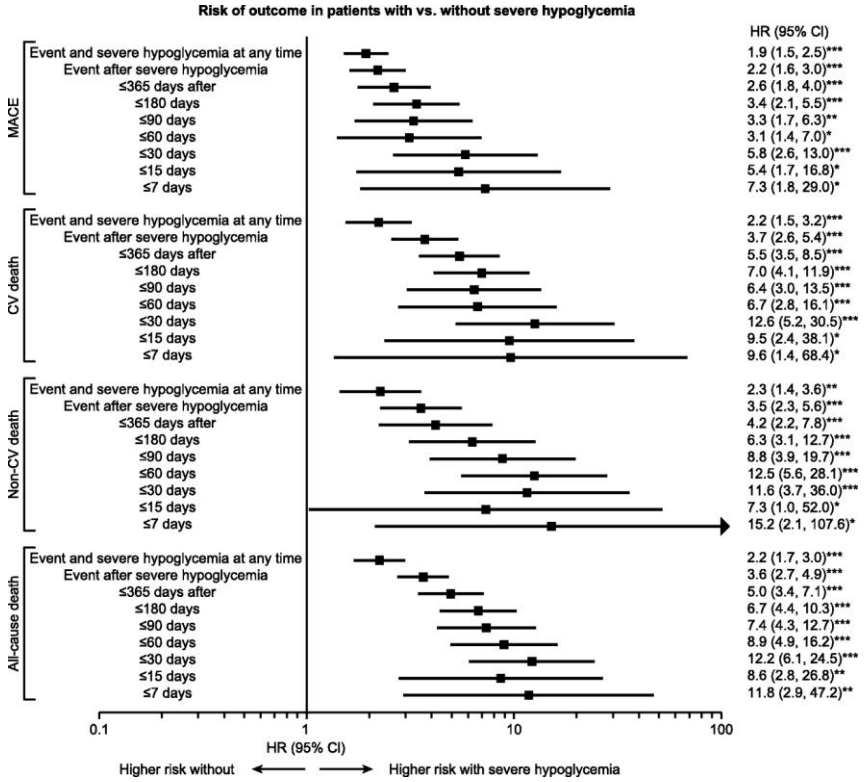
What about hypoglycaemia?

HbA1c Does Not Address Hypoglycaemia

Zinman et al, Diabetes Care 2018; 41(8):1783

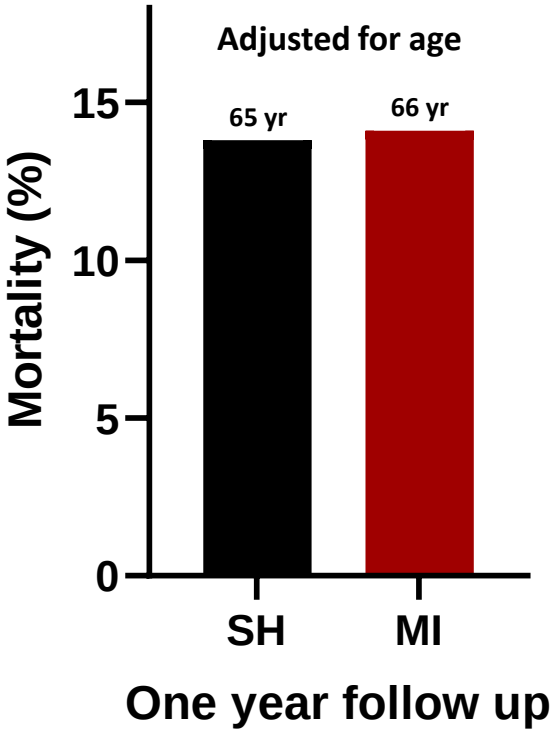
HbA1c Does Not Address Hypoglycaemia

Severe hypoglycaemia and CV events/death
LEADER trial; n=9,304



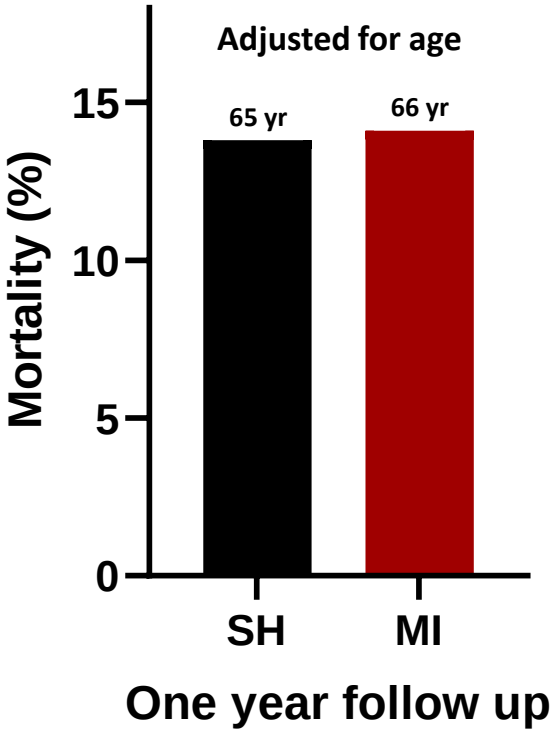
Zinman et al, Diabetes Care 2018; 41(8):1783

Mortality Following Severe Hypoglycaemia (SH) or Myocardial Infarction (MI) in Individuals with Type 2 Diabetes

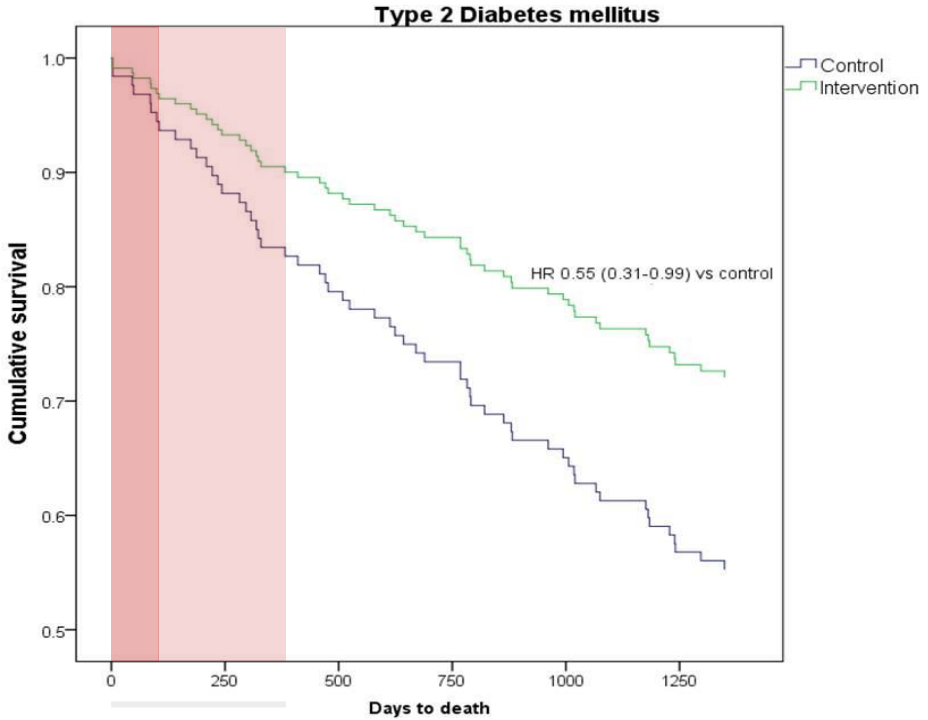


Adapted from:
Kahn et al, Diab Vasc Dis Res 2012, 9:3
Elwen et al, BMJ Diabetes 2015; 3:e94
Pearson et al, Cardiovasc Diabetol 2021; 20:18

Mortality Following Severe Hypoglycaemia (SH) or Myocardial Infarction (MI) in Individuals with Type 2 Diabetes



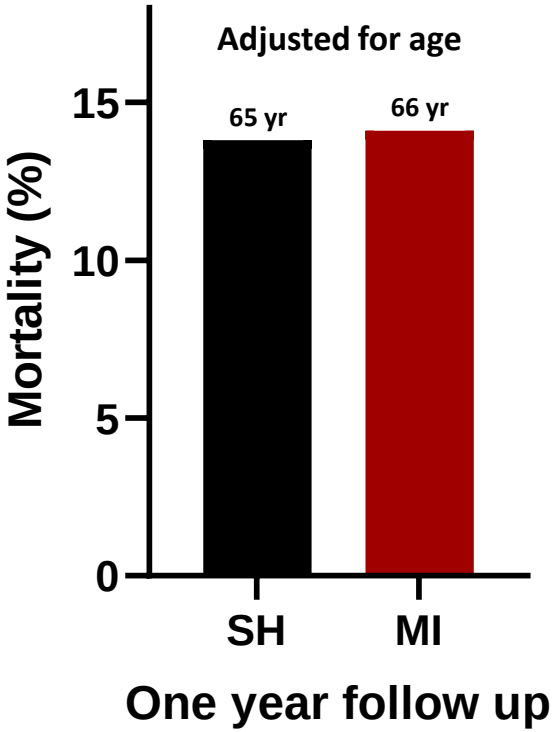
One year follow up

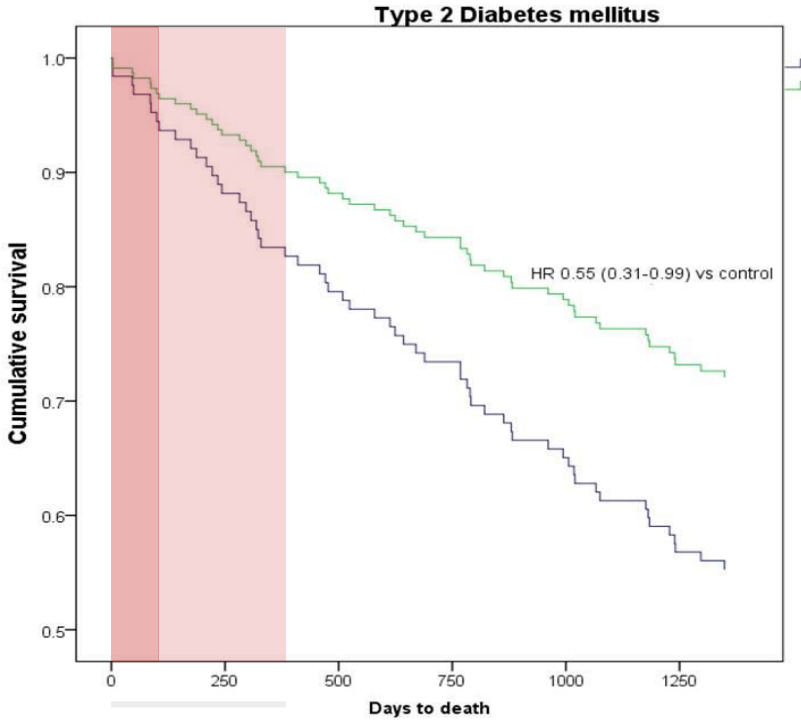


Nurse-led intervention

Adapted from:
Kahn et al, Diab Vasc Dis Res 2012, 9:3
Elwen et al, BMJ Diabetes 2015; 3:e94
Pearson et al, Cardiovasc Diabetol 2021; 20:18

Mortality Following Severe Hypoglycaemia (SH) or Myocardial Infarction (MI) in Individuals with Type 2 Diabetes





CV mortality: 2%

Adjusted for age

CV mortality: 18%

Nurse-led intervention

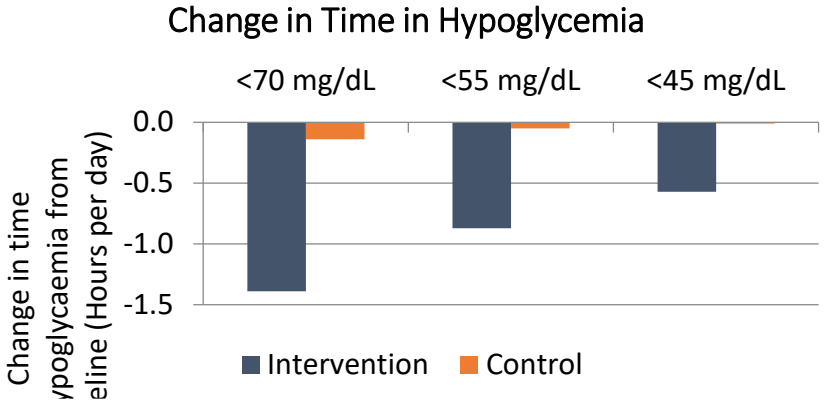
Adapted from:
Kahn et al, Diab Vasc Dis Res 2012, 9:3
Elwen et al, BMJ Diabetes 2015; 3:e94
Pearson et al, Cardiovasc Diabetol 2021; 20:18

Time in Hypoglycaemia

Bolinder et al, Lancet. 2016 Nov 5;388(10057):2254
Haak et al, Diabetes Ther. 2017 Feb;8(1):55

Time in Hypoglycaemia

IMPACT

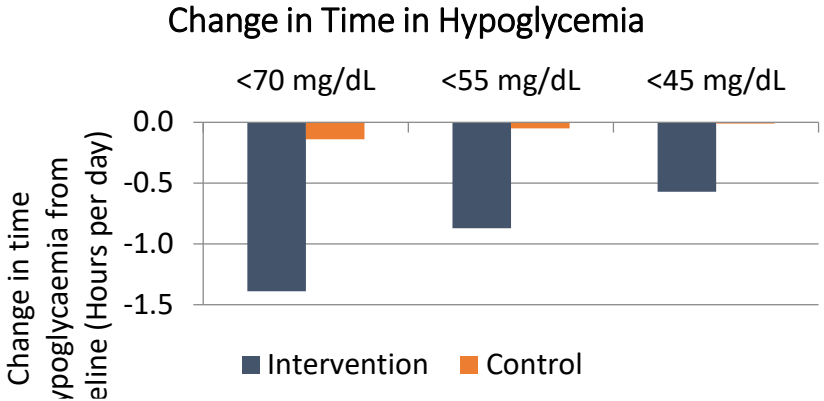


Glucose Level	Difference (vs control) in change from baseline per day	Significance (vs control)	Reduction vs control
<70 mg/dL	-1.24h (-74 min)	P<0.0001	38%
<55 mg/dL	-0.82h (-49 min)	P<0.0001	50%
<45 mg/dL	-0.55h (-33 min)	P<0.0001	60%

Bolinder et al, Lancet. 2016 Nov 5;388(10057):2254
Haak et al, Diabetes Ther. 2017 Feb;8(1):55

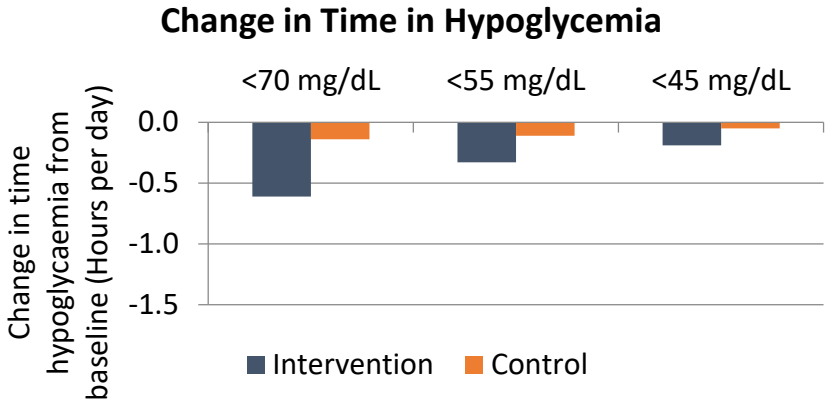
Time in Hypoglycaemia

IMPACT



Glucose Level	Difference (vs control) in change from baseline per day	Significance (vs control)	Reduction vs control
<70 mg/dL	-1.24h (-74 min)	P<0.0001	38%
<55 mg/dL	-0.82h (-49 min)	P<0.0001	50%
<45 mg/dL	-0.55h (-33 min)	P<0.0001	60%

REPLACE



Glucose Level	Difference (vs control) in change from baseline per day	Significance (vs control)	Reduction vs control
<70 mg/dL	-0.47h (-28 min)	P<0.001	43%
<55 mg/dL	-0.22h (-13 min)	P=0.0014	53%
<45 mg/dL	-0.14h (-8 min)	P=0.0013	64%

Bolinder et al, Lancet. 2016 Nov 5;388(10057):2254
Haak et al, Diabetes Ther. 2017 Feb;8(1):55

Clinical Case 3

Yasmin is a 69 year old lady T2D for 19 years and has been on insulin for 6 years.

Treatment:

- Insulin glargine 60 units/day
- Insulin aspart 24–34 units with meals
- Metformin 1 gram twice daily (intolerant to GLP1-RA and SGLT2i)
- Ramipril, amlodipine, aspirin, atorvastatin, ibuprofen, paracetamol

Feels great and the only complaint in morning headaches on/off, which she feels is stress-related

Results:

- HbA_{1c} 48 mmol/mol (6.5%)

Clinical Case 3

Yasmin is a 69 year old lady T2D for 19 years, on insulin for 6 years
HbA1c 48 mmol/mol (6.5%)

SMBG: mg/dL (mmol/L)

D	0-6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
M			128 (7.1)				146 (8.1)									160 (8.9)	
T			112 (6.2)					130 (7.2)								97 (5.4)	
W			103 (5.7)					149 (8.3)									114 (6.3)
T							103 (5.7)									175 (9.7)	
F				137 (7.6)				124 (6.9)								88 (4.9)	
S			106 (5.9)					164 (9.1)								122 (6.8)	

Clinical Case 3

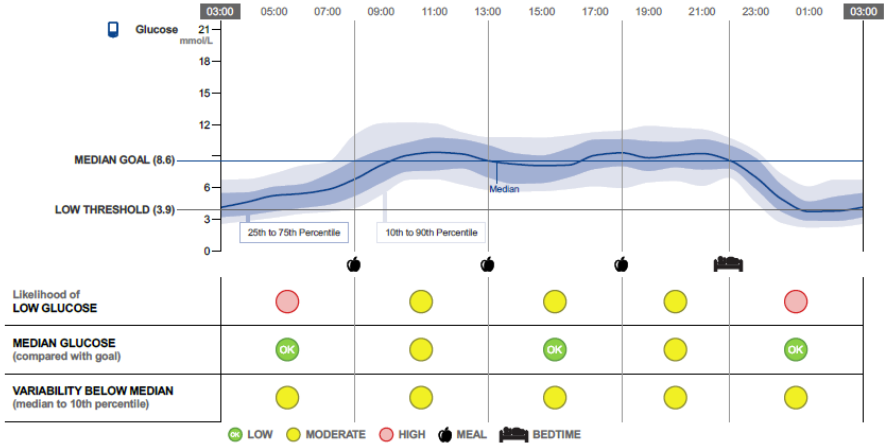
Clinical Case 3

Glucose Pattern Insights

27 June 2018 – 10 July 2018 (14 days)

LOW-GLUCOSE ALLOWANCE SETTING: **Medium**

MEDIAN GOAL SETTING: **8.6 mmol/L (A1c: 7.0% or 53 mmol/mol)**



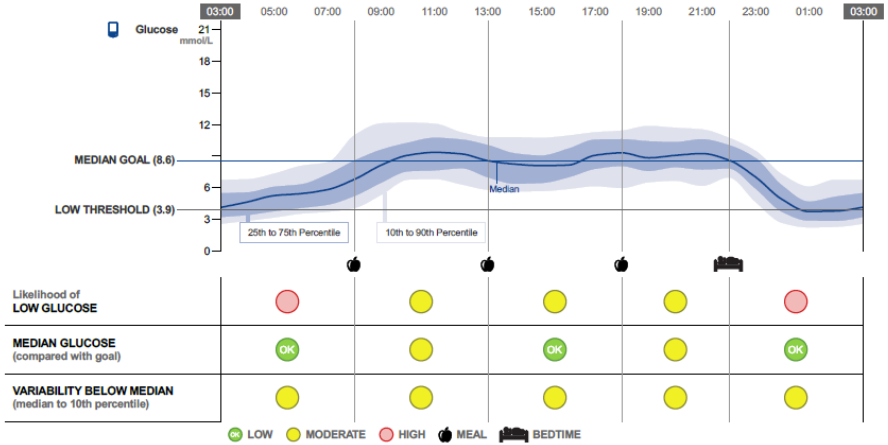
Clinical Case 3

Glucose Pattern Insights

27 June 2018 – 10 July 2018 (14 days)

LOW-GLUCOSE ALLOWANCE SETTING: **Medium**

MEDIAN GOAL SETTING: **8.6 mmol/L (A1c: 7.0% or 53 mmol/mol)**

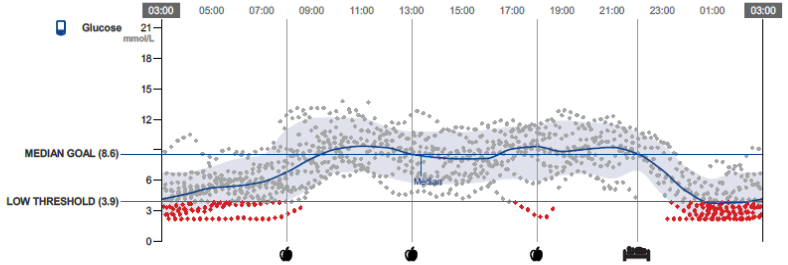


Glucose Pattern Insights (with glucose readings)

27 June 2018 – 10 July 2018 (14 days)

LOW-GLUCOSE ALLOWANCE SETTING: **Medium**

MEDIAN GOAL SETTING: **8.6 mmol/L (A1c: 7.0% or 53 mmol/mol)**



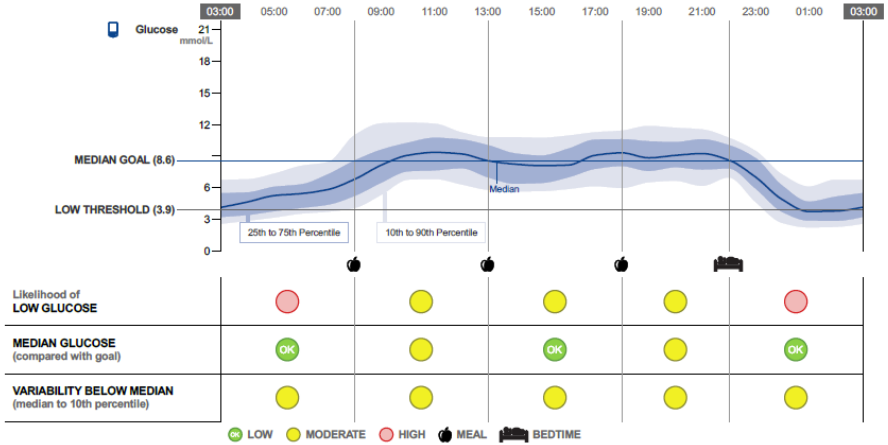
Clinical Case 3

Glucose Pattern Insights

27 June 2018 – 10 July 2018 (14 days)

LOW-GLUCOSE ALLOWANCE SETTING: **Medium**

MEDIAN GOAL SETTING: **8.6 mmol/L (A1c: 7.0% or 53 mmol/mol)**

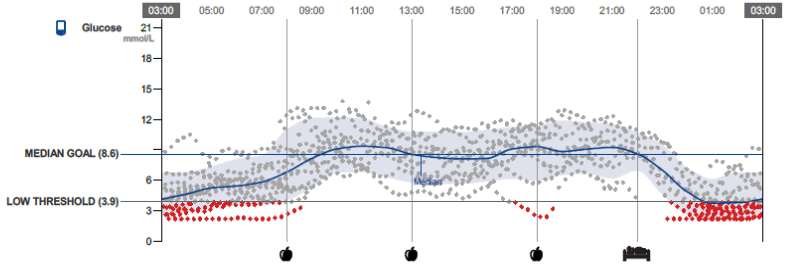


Glucose Pattern Insights (with glucose readings)

27 June 2018 – 10 July 2018 (14 days)

LOW-GLUCOSE ALLOWANCE SETTING: **Medium**

MEDIAN GOAL SETTING: **8.6 mmol/L (A1c: 7.0% or 53 mmol/mol)**



Reason for morning headaches is becoming more obvious

Is it time to say goodbye to our old friend?

No (or at least not yet!)

- ►HbA1c still has a role for many years to come

However, HbA1c is getting old and needs help from CGM-generated glycaemic markers, including:

- ►Ambulatory glucose profile (AGP): identification of glycaemic patterns
- ►Time below range (TBR): avoidance of hypoglycaemia is important
- ►Glycaemic variability (GV): there is a reason why people without diabetes keep glucose levels in a tight range

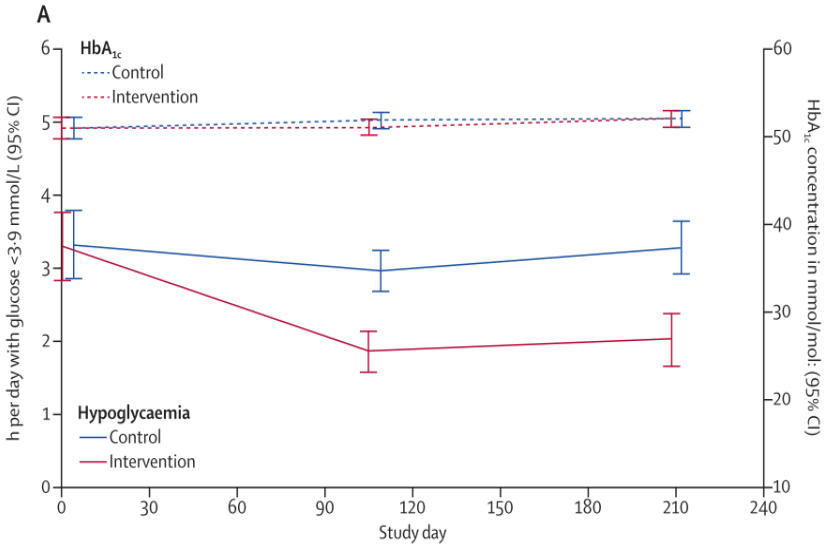
CGM for T1D

Libre use in T1D

Bolinder J et al. Lancet. 2016; 388(10057): 2254-2263
Leelarathna et al, N Engl J Med 2022; 387:1477-1487

Libre use in T1D

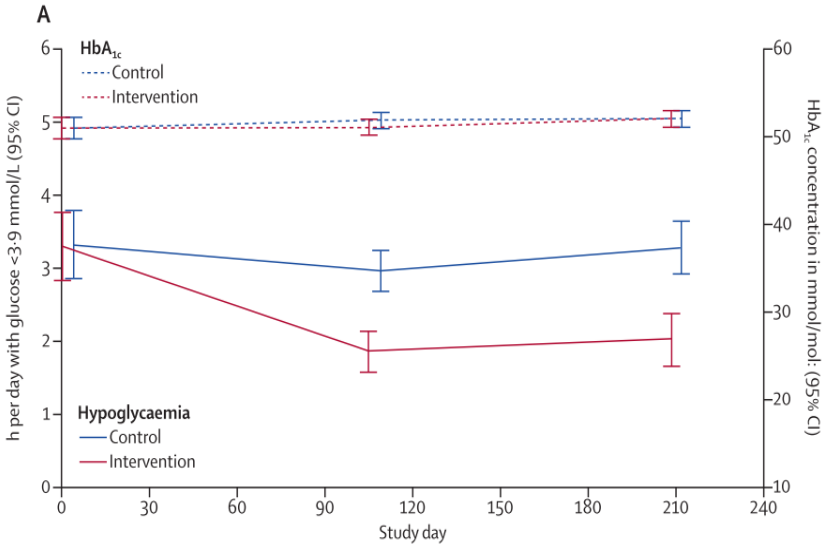
Reduction of hypoglycaemia in those with good HbA1c



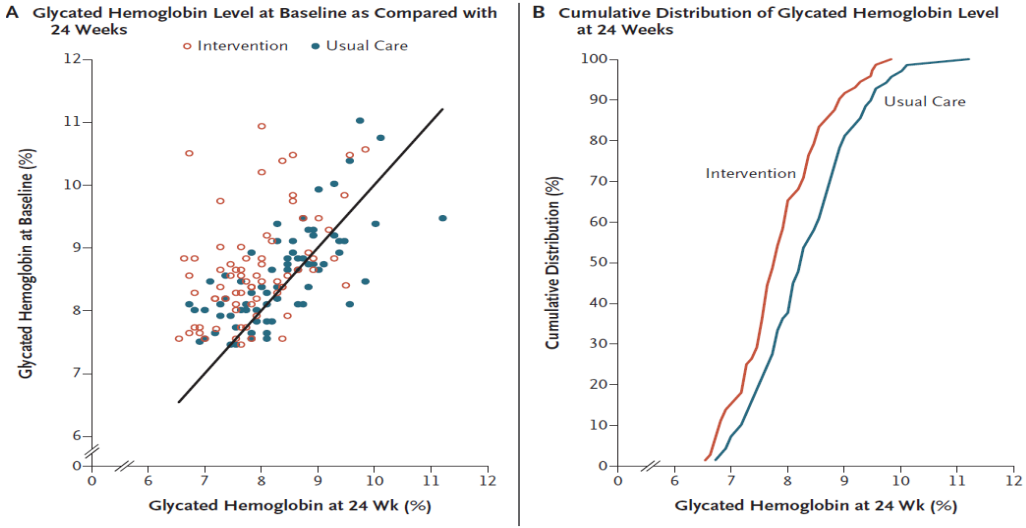
Bolinder J et al. Lancet. 2016; 388(10057): 2254-2263
Leelarathna et al, N Engl J Med 2022; 387:1477-1487

Libre use in T1D

Reduction of hypoglycaemia
in those with good HbA1c



Reduction of HbA1c
in those with poor glycaemic control



Bolinder J et al. Lancet. 2016; 388(10057): 2254-2263
Leelarathna et al, N Engl J Med 2022; 387:1477-1487

CGM for T2D

(do we have any studies in T2D)?

CGM in T2D MDI - DIAMOND

- USA, n=158(MDI)
- Age 60 yrs, A1c 8.5%
- Primary outcome: A1c

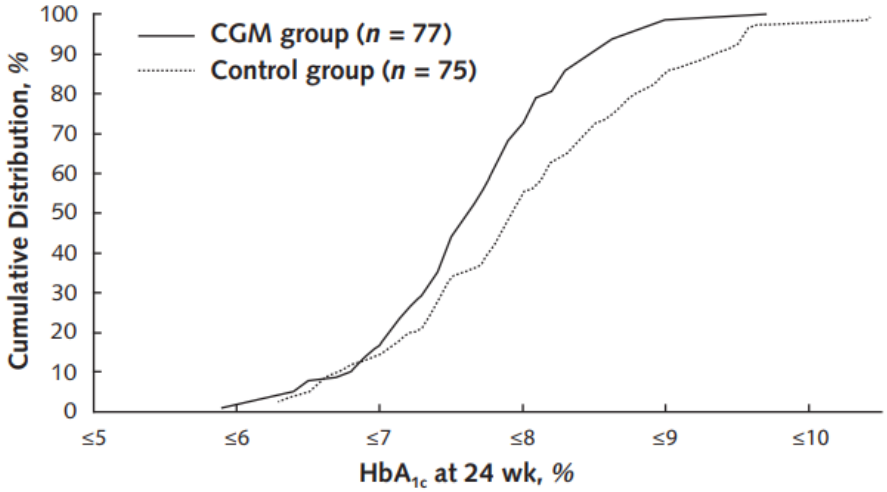


Table 2. Comparison of HbA_{1c} Outcomes at 12 and 24 Weeks in the CGM and Usual Care Groups*

Outcome	12 wk			24 wk		
	CGM Group (*n* = 77)	Control Group (*n* = 75)	Adjusted Difference (95% CI); *P* Value†	CGM Group (*n* = 79)	Control Group (*n* = 79)	Adjusted Difference (95% CI); *P* Value†
Primary outcome						
Mean HbA_{1c} level (95% CI), %	7.5 (7.4 to 7.7)	7.9 (7.7 to 8.1)	–	7.7 (7.5 to 7.8)	8.0 (7.8 to 8.2)	
Mean change in HbA_{1c} level from baseline (95% CI), %	−1.0 (−1.2 to −0.8)	−0.6 (−0.8 to −0.4)	−0.3 (−0.6 to −0.1); 0.005	−0.8 (−1.0 to −0.7)	−0.5 (−0.7 to −0.3)	−0.3 (−0.5 to 0.0); 0.022

Beck et al., Ann Intern Med. 2017; 167(6):365-374

CGM in T2D with MDI or CSII – REPLACE

- **Europe, n=224 (Insulin treated)**
- **Age 59 yrs, A1c 8.7%**
- **Primary outcome: A1c**

Haak T et al., Diabetes Ther. 2017; 8(1): 55–73

CGM in T2D with MDI or CSII – REPLACE

- **Europe, n=224 (Insulin treated)**
- **Age 59 yrs, A1c 8.7%**
- **Primary outcome: A1c**

Table 2 Glycemic and glucose variability measures

Glycemic measure	Baseline mean (SD)		Study end mean (SD)		Difference in adjusted means in intervention vs control (SE)	Difference in intervention vs control (%)	*p* value
	Intervention ($n = 149$)	Control ($n = 75$)	Intervention ($n = 149$)	Control ($n = 75$)			
HbA1c (mmol/mol)	71.0 (11.1)	72.1 (10.7)	68.0 (9.0)	67.7 (12.4)	0.3 (1.25)	N/A	0.8259
HbA1c (%)	8.65 (1.01)	8.75 (0.98)	8.37 (0.83)	8.34 (1.14)	0.03 (0.114)	N/A	0.8222
Time with glucose 3.9–10.0 mmol/L (70–180 mg/dL) (h)	13.9 (4.5)	13.5 (5.2)	13.6 (4.6)	13.2 (4.9)	0.2 (0.58)	1.1	0.7925
Glucose <3.9 mmol/L (70 mg/dL) within 24 h							
Events	0.64 (0.63)	0.63 (0.66)	0.38 (0.45)	0.53 (0.59)	−0.16 (0.065)	−27.7	0.0164
Time (h)	1.30 (1.78)	1.08 (1.58)	0.59 (0.82)	0.99 (1.29)	−0.47 (0.134)	−43.1	0.0006
AUC (h × mg/dL)	20.15 (35.21)	14.05 (26.35)	7.23 (12.35)	13.59 (22.31)	−7.80 (2.20)	−51.1	0.0005

Haak T et al., Diabetes Ther. 2017; 8(1): 55–73

CGM in T2D with MDI or CSII – REPLACE

- **Europe, n=224 (Insulin treated)**
- **Age 59 yrs, A1c 8.7%**
- **Primary outcome: A1c**

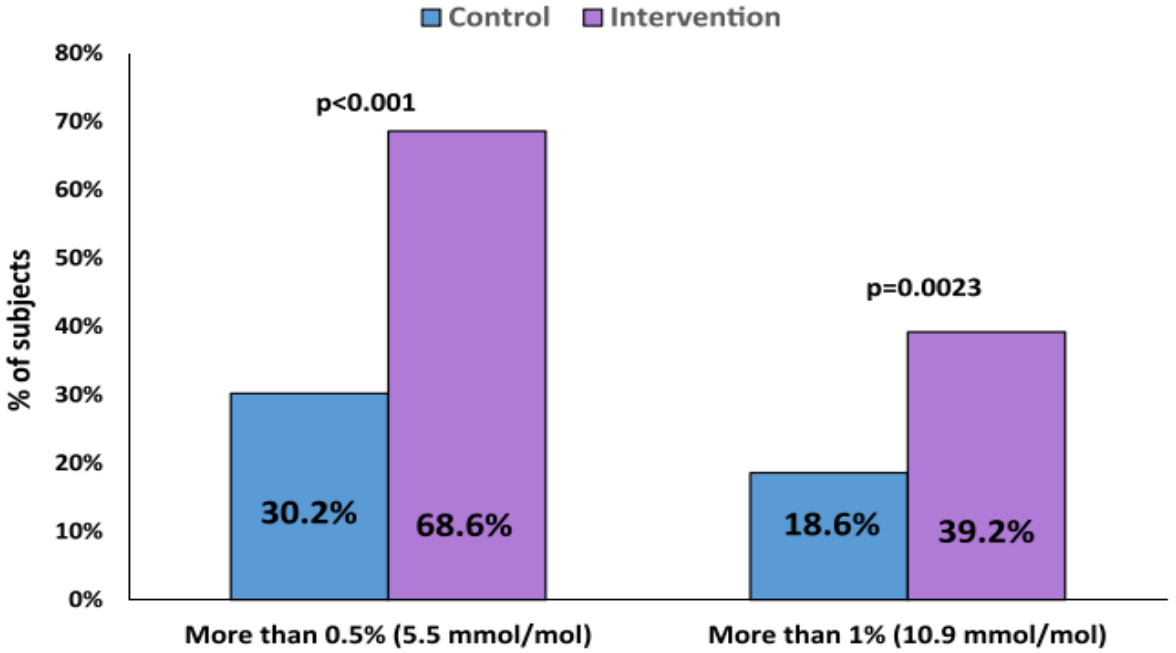
Table 2 Glycemic and glucose variability measures

Glycemic measure	Baseline mean (SD)		Study end mean (SD)		Difference in adjusted means in intervention vs control (SE)	Difference in intervention vs control (%)	*p* value
	Intervention ($n = 149$)	Control ($n = 75$)	Intervention ($n = 149$)	Control ($n = 75$)			
HbA1c (mmol/mol)	71.0 (11.1)	72.1 (10.7)	68.0 (9.0)	67.7 (12.4)	0.3 (1.25)	N/A	0.8259
HbA1c (%)	8.65 (1.01)	8.75 (0.98)	8.37 (0.83)	8.34 (1.14)	0.03 (0.114)	N/A	0.8222
Time with glucose 3.9–10.0 mmol/L (70–180 mg/dL) (h)	13.9 (4.5)	13.5 (5.2)	13.6 (4.6)	13.2 (4.9)	0.2 (0.58)	1.1	0.7925
Glucose <3.9 mmol/L (70 mg/dL) within 24 h							
Events	0.64 (0.63)	0.63 (0.66)	0.38 (0.45)	0.53 (0.59)	−0.16 (0.065)	−27.7	0.0164
Time (h)	1.30 (1.78)	1.08 (1.58)	0.59 (0.82)	0.99 (1.29)	−0.47 (0.134)	−43.1	0.0006
AUC (h × mg/dL)	20.15 (35.21)	14.05 (26.35)	7.23 (12.35)	13.59 (22.31)	−7.80 (2.20)	−51.1	0.0005

Haak T et al., Diabetes Ther. 2017; 8(1): 55–73

CGM in T2D MDI with education – Yaron et al.

- Israel, n=101 (Insulin treated)
- Primary outcome: Satisfaction (DTSQ)

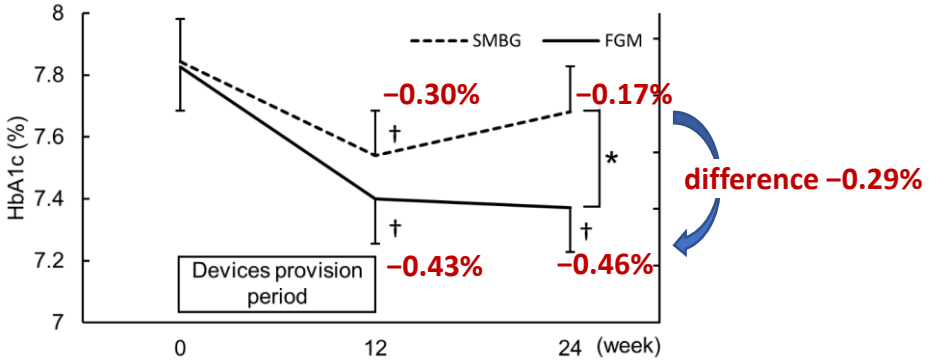


Reduction of A1c by more than 0.5% A1C and by more than 1.0% A1c.

Yaron M et al. Diabetes Care. 2019; 42(7): 1178

CGM in T2D without Insulin – Wada et al.

- Japan, n=100
- Freestyle Libre
- Age 58 yrs, A1c 7.8%

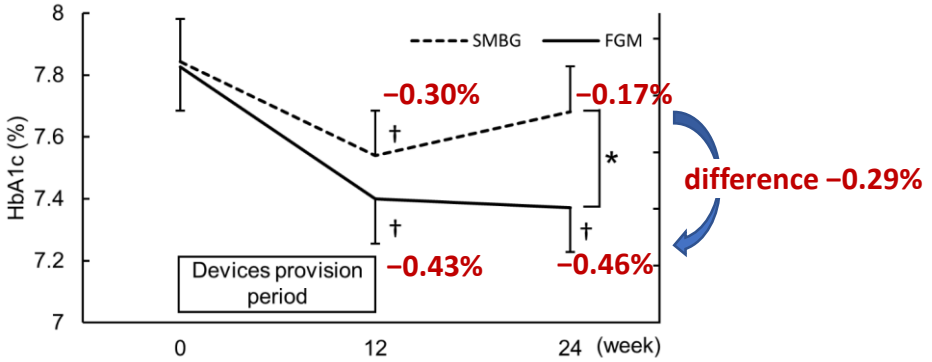


Glycemic outcomes	Baseline mean (SD) FGM (n=41)	Baseline mean (SD) SMBG (n=35)	Intervention end mean (SD) FGM (n=41)	Intervention end mean (SD) SMBG (n=35)	Difference in adjusted means in FGM vs SMBG (95% CI)	P value
Mean glucose (mg/dL)	170 (29)	158 (32)	146 (19)	156 (31)	−15 (−22 to −8)	**<0.001**
SD of glucose (mg/dL)	46 (11)	44 (11)	38 (9)	43 (13)	−5 (−8 to −2)	**<0.001**
Glucose CV (%)	26.9 (5.0)	28.4 (5.9)	26.6 (6.8)	27.4 (5.1)	0.2 (−1.2 to 1.7)	0.762
MAGE (mg/dL)	110 (27)	111 (30)	91 (22)	108 (33)	−17 (−24 to −9)	**<0.001**
BGRI	9.8 (3.8)	9.1 (4.2)	6.9 (3.4)	8.4 (4.1)	−1.7 (−2.8 to −0.5)	**0.005**
CONGA 2 hour (mg/dL)	136 (25)	125 (27)	117 (18)	124 (26)	−12 (−18 to −6)	**<0.001**
MODD (mg/dL)	41 (14)	38 (10)	33 (11)	37 (12)	−5 (−8 to −1)	**0.006**
Glucose 70–180 mg/dL (3.9–10.0 mmol/L) within 24 hours period						
Duration (hours)	14.36 (4.79)	15.62 (4.27)	18.71 (3.15)	16.65 (4.35)	2.36 (1.21 to 3.51)	**<0.001**
Glucose <70 mg/dL (3.9 mmol/L) within 24 hours period						
Duration (hours)	0.10 (0.42)	0.78 (3.11)	0.38 (1.10)	0.41 (1.12)	0.13 (−0.19 to 0.45)	0.423

Wada E. et al., BMJ Open Diabetes Res Care. 2020; 8:e001115

CGM in T2D without Insulin – Wada et al.

- Japan, n=100
- Freestyle Libre
- Age 58 yrs, A1c 7.8%

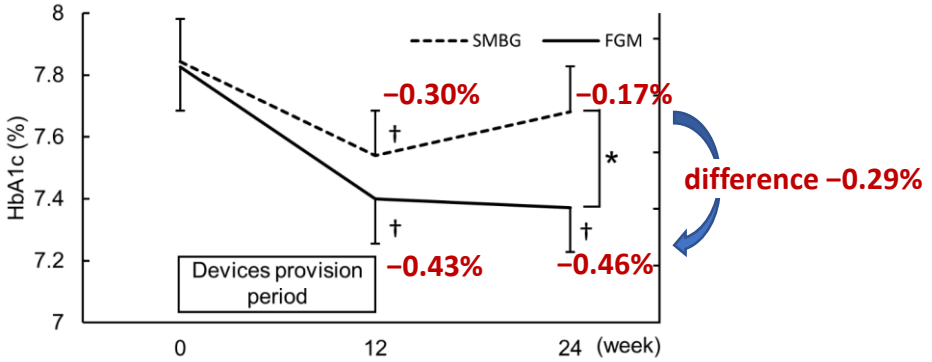


Glycemic outcomes	Baseline mean (SD) FGM (n=41)	Baseline mean (SD) SMBG (n=35)	Intervention end mean (SD) FGM (n=41)	Intervention end mean (SD) SMBG (n=35)	Difference in adjusted means in FGM vs SMBG (95% CI)	P value
Mean glucose (mg/dL)	170 (29)	158 (32)	146 (19)	156 (31)	−15 (−22 to −8)	**<0.001**
SD of glucose (mg/dL)	46 (11)	44 (11)	38 (9)	43 (13)	−5 (−8 to −2)	**<0.001**
Glucose CV (%)	26.9 (5.0)	28.4 (5.9)	26.6 (6.8)	27.4 (5.1)	0.2 (−1.2 to 1.7)	0.762
MAGE (mg/dL)	110 (27)	111 (30)	91 (22)	108 (33)	−17 (−24 to −9)	**<0.001**
BGRI	9.8 (3.8)	9.1 (4.2)	6.9 (3.4)	8.4 (4.1)	−1.7 (−2.8 to −0.5)	**0.005**
CONGA 2 hour (mg/dL)	136 (25)	125 (27)	117 (18)	124 (26)	−12 (−18 to −6)	**<0.001**
MODD (mg/dL)	41 (14)	38 (10)	33 (11)	37 (12)	−5 (−8 to −1)	**0.006**
Glucose 70–180 mg/dL (3.9–10.0 mmol/L) within 24 hours period						
Duration (hours)	14.36 (4.79)	15.62 (4.27)	18.71 (3.15)	16.65 (4.35)	2.36 (1.21 to 3.51)	**<0.001**
Glucose <70 mg/dL (3.9 mmol/L) within 24 hours period						
Duration (hours)	0.10 (0.42)	0.78 (3.11)	0.38 (1.10)	0.41 (1.12)	0.13 (−0.19 to 0.45)	0.423

Wada E. et al., BMJ Open Diabetes Res Care. 2020; 8:e001115

CGM in T2D without Insulin – Wada et al.

- Japan, n=100
- Freestyle Libre
- Age 58 yrs, A1c 7.8%

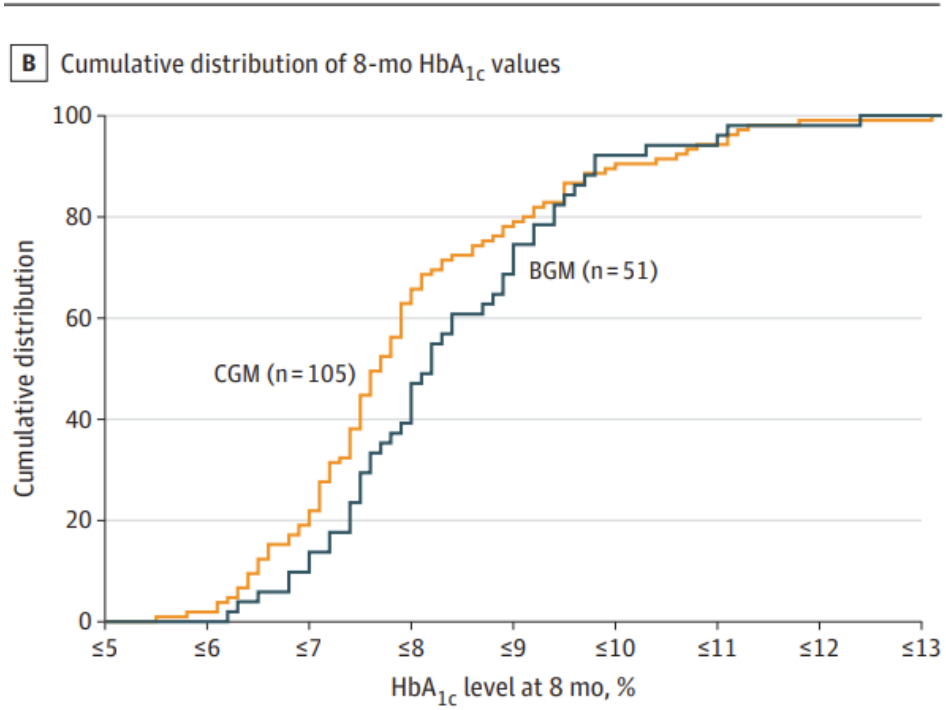


Glycemic outcomes	Baseline mean (SD) FGM (n=41)	Baseline mean (SD) SMBG (n=35)	Intervention end mean (SD) FGM (n=41)	Intervention end mean (SD) SMBG (n=35)	Difference in adjusted means in FGM vs SMBG (95% CI)	P value
Mean glucose (mg/dL)	170 (29)	158 (32)	146 (19)	156 (31)	−15 (−22 to −8)	**<0.001**
SD of glucose (mg/dL)	46 (11)	44 (11)	38 (9)	43 (13)	−5 (−8 to −2)	**<0.001**
Glucose CV (%)	26.9 (5.0)	28.4 (5.9)	26.6 (6.8)	27.4 (5.1)	0.2 (−1.2 to 1.7)	0.762
MAGE (mg/dL)	110 (27)	111 (30)	91 (22)	108 (33)	−17 (−24 to −9)	**<0.001**
BGRI	9.8 (3.8)	9.1 (4.2)	6.9 (3.4)	8.4 (4.1)	−1.7 (−2.8 to −0.5)	**0.005**
CONGA 2 hour (mg/dL)	136 (25)	125 (27)	117 (18)	124 (26)	−12 (−18 to −6)	**<0.001**
MODD (mg/dL)	41 (14)	38 (10)	33 (11)	37 (12)	−5 (−8 to −1)	**0.006**
Glucose 70–180 mg/dL (3.9–10.0 mmol/L) within 24 hours period						
Duration (hours)	14.36 (4.79)	15.62 (4.27)	18.71 (3.15)	16.65 (4.35)	2.36 (1.21 to 3.51)	**<0.001**
Glucose <70 mg/dL (3.9 mmol/L) within 24 hours period						
Duration (hours)	0.10 (0.42)	0.78 (3.11)	0.38 (1.10)	0.41 (1.12)	0.13 (−0.19 to 0.45)	0.423

Wada E. et al., BMJ Open Diabetes Res Care. 2020; 8:e001115

CGM in T2D with Basal Insulin - MOBILE

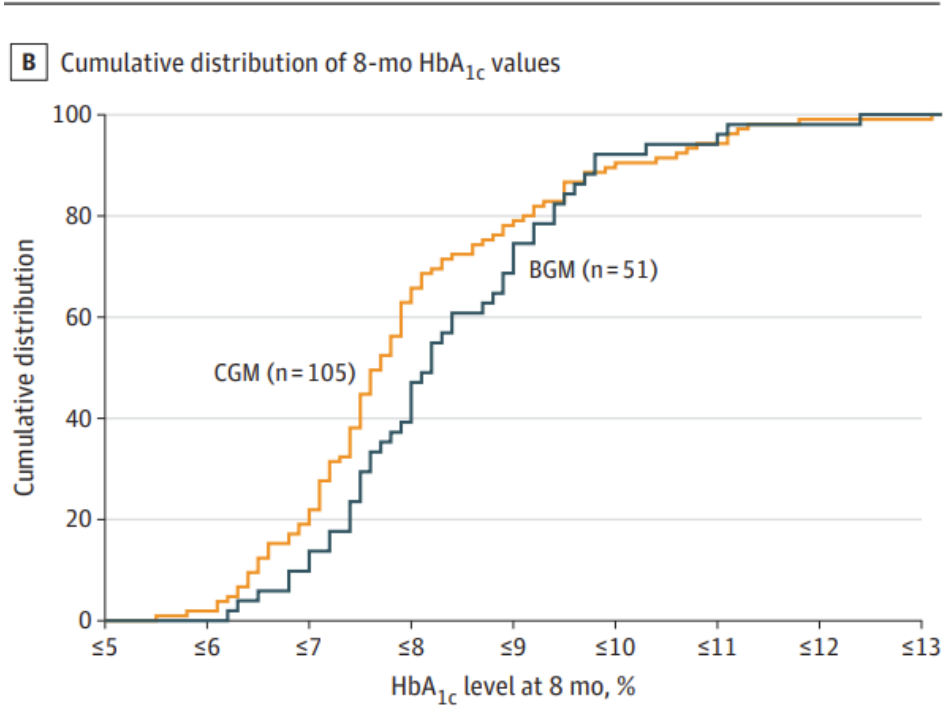
USA, n=116
Basal insulin, SMBG ≥3 times/weeks
Age 57 yrs, A1c 9.1%, 8 months
Primary outcome: A1c
(G6 CGM)



Martens T et al., JAMA. 2021; 8;325(22):2262-2272
G Aleppo et al., Diabetes Care. 2021; 44(12):2729-2737

CGM in T2D with Basal Insulin - MOBILE

USA, n=116
Basal insulin, SMBG ≥3 times/weeks
Age 57 yrs, A1c 9.1%, 8 months
Primary outcome: A1c
(G6 CGM)

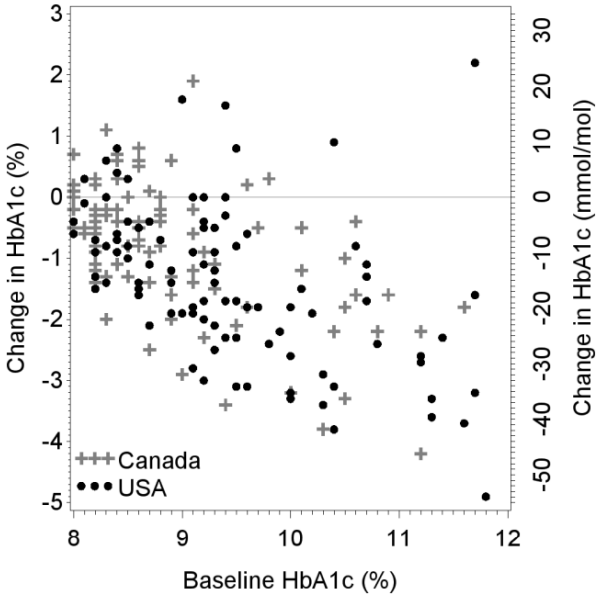


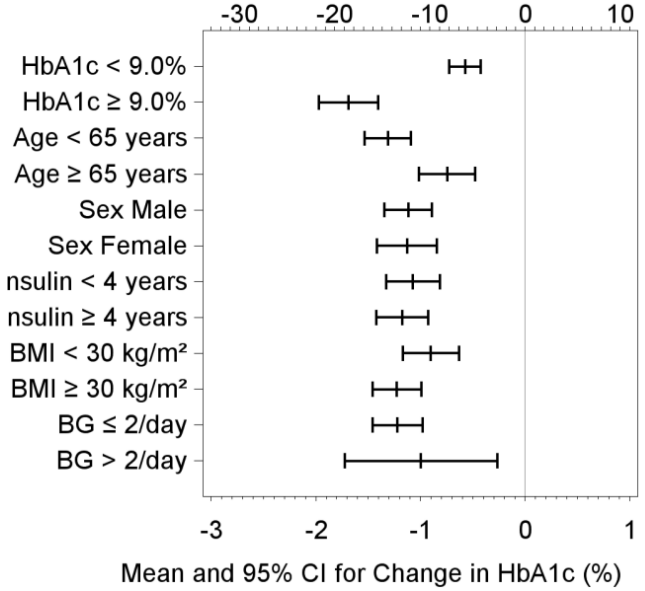
% Time in range of 70-180 mg/dL	40 (26)	40 (25)	59 (25)	43 (26)	15 (8 to 23)	<.001
% Time <70 mg/dL[e]	0.3 (0.5)	0.3 (0.6)	0.2 (0.4)	0.5 (0.8)	−0.24 (−0.42 to −0.05)	.02

Martens T et al., JAMA. 2021; 8;325(22):2262-2272
G Aleppo et al., Diabetes Care. 2021; 44(12):2729-2737

FSL in T2D with Basal Insulin (Retrospective Study)

- USA and Canada, n=191 (Basal insulin),
- Single Arm, Retrospective study
- Age 60 yrs, A1c 9.2%, 6m

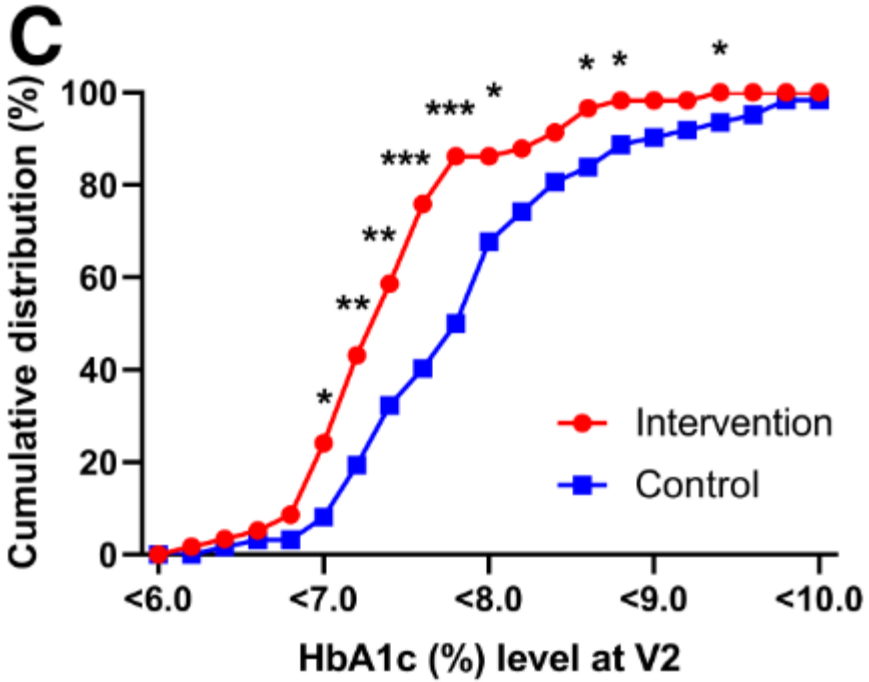




Carlson AL et al., BMJ Open Diabetes Res Care. 2022; 10(1):e002590.

CGM in T2D with OAD or basal insulin – PDF Trial

- Korea, n=126, 3m
- OAD and/or basal insulin (27.5%)
- Structured education + isCGM vs Standard care with BGM
- Mean Age 58, A1c 7.9%



Cheo HJ. et al., Diabetes Care. 2022; 45(10):2224-2230

CGM in T2D with ACS (SU or Insulin) – LIBERATES

- **UK, Multicentre, n=141, 3m**
- **Need to be on SU and/or insulin (with or without any other hypoglycaemic therapies**

[9%]

[8.4%]

[8.8%]

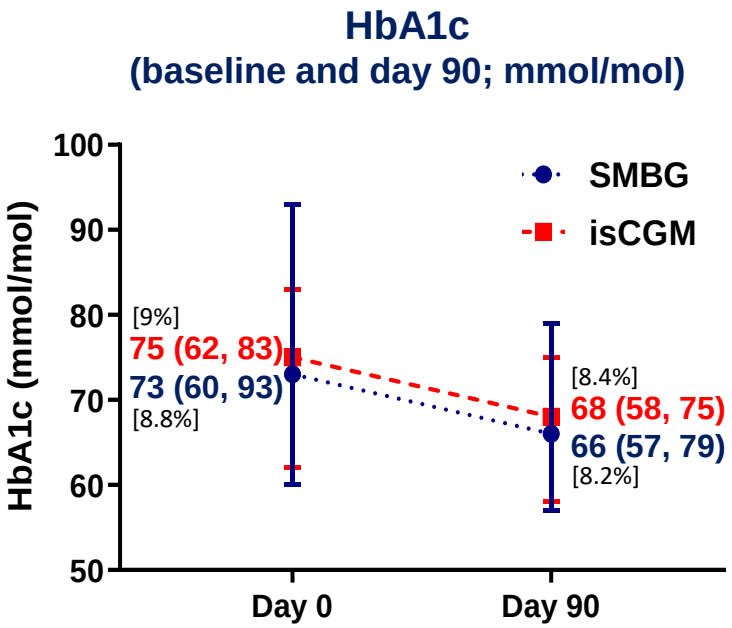
[8.2%]

SMBG: self-monitoring of blood glucose
isCGM: intermittently-scanned continuous glucose monitoring
SU: sulphonylurea

Ajjan et al, Diabetes Care, 2023; 46(2):441–449

CGM in T2D with ACS (SU or Insulin) – LIBERATES

- UK, Multicentre, n=141, 3m
- Need to be on SU and/or insulin (with or without any other hypoglycaemic therapies



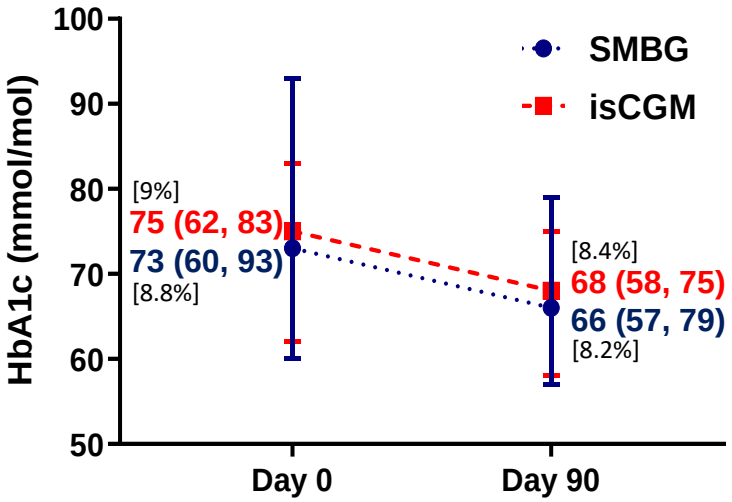
SMBG: self-monitoring of blood glucose
isCGM: intermittently-scanned continuous glucose monitoring
SU: sulphonylurea

Ajjan et al, Diabetes Care, 2023; 46(2):441–449

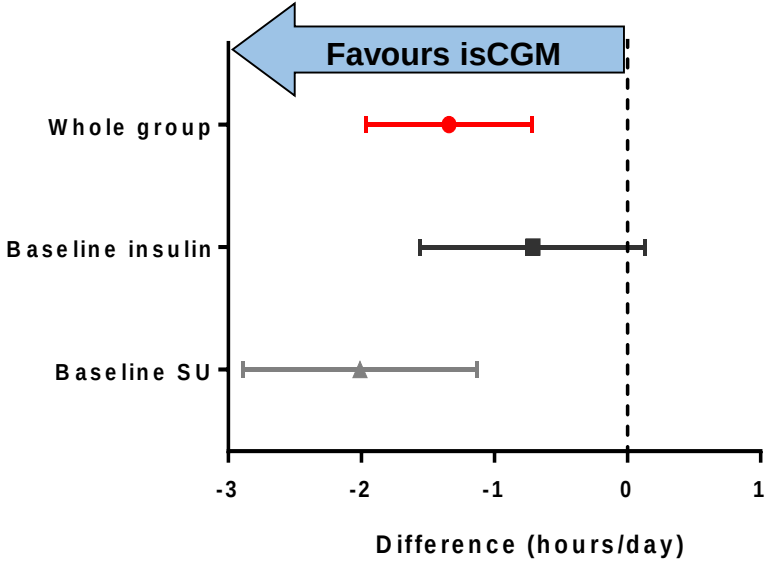
CGM in T2D with ACS (SU or Insulin) – LIBERATES

- UK, Multicentre, n=141, 3m
- Need to be on SU and/or insulin (with or without any other hypoglycaemic therapies

HbA1c
(baseline and day 90; mmol/mol)



Hypoglycaemia
(days 76-90; <3.9 mmol/l, <70 mg/dl)

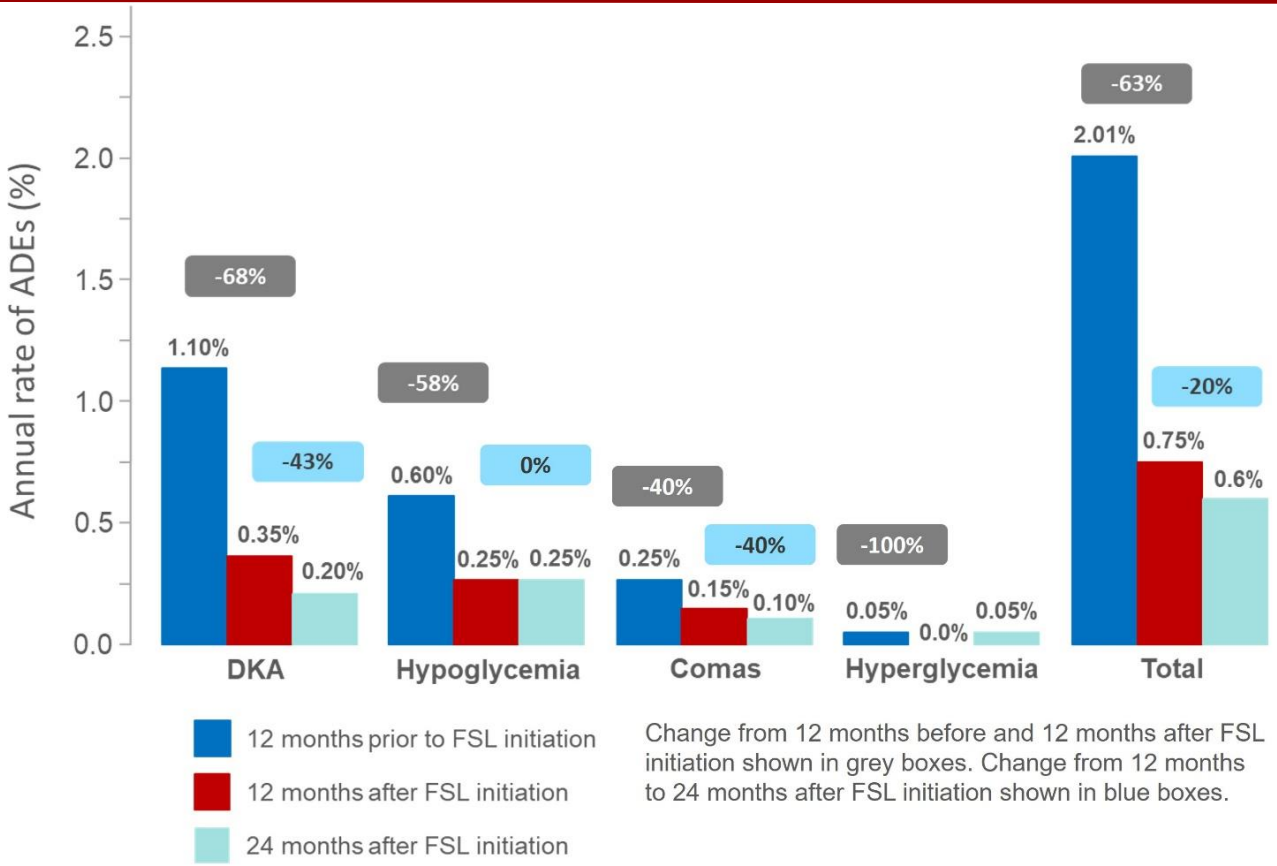


SMBG: self-monitoring of blood glucose
isCGM: intermittently-scanned continuous glucose monitoring
SU: sulphonylurea

Ajjan et al, Diabetes Care, 2023; 46(2):441–449

What about the real world and hard clinical outcomes?

Riveline study: Hospital admissions for people with T2D on Basal Insulin Therapy before and after initiation of flash CGM (isCGM)



Riveline JP, et al. EASD 2022

Summary of Flash CGM RCTs

Bolinder et al, Lancet. 2016; 388(10057):2254
Leelarathna et al, NEJM 2022; EPub
Haak et al, Diabetes Ther. 2017 Feb;8(1):55
Yaron et al, Diabetes Care. 2019; 42(7): 1178
Cheo HJ. et al., Diabetes Care. 2022; 45(10):2224-2230
Wada et al, BMJ Diab Res Care 2020; 8:e001115
Ajjan et al, LIBERATES trial, Diabetes Care, 2023; 46:441-48

Summary of Flash CGM RCTs

- **In T1D**
  - Significant reduction in hypoglycaemia in well controlled T1D individuals
  - Significant reduction in HbA1c in poorly controlled T1D individuals (FSL2)

Bolinder et al, Lancet. 2016; 388(10057):2254
Leelarathna et al, NEJM 2022; EPub
Haak et al, Diabetes Ther. 2017 Feb;8(1):55
Yaron et al, Diabetes Care. 2019; 42(7): 1178
Cheo HJ. et al., Diabetes Care. 2022; 45(10):2224-2230
Wada et al, BMJ Diab Res Care 2020; 8:e001115
Ajjan et al, LIBERATES trial, Diabetes Care, 2023; 46:441-48

Summary of Flash CGM RCTs

- **In T1D**
  - Significant reduction in hypoglycaemia in well controlled T1D individuals
  - Significant reduction in HbA1c in poorly controlled T1D individuals (FSL2)

- **In T2D**
  - Reduction in HbA1c or reduction in hypoglycaemia in MDI-treated patients
  - Reduction in HbA1c in T2D on basal insulin or on oral therapy
  - T2D patients with MI (SU- and insulin-treated): similar reduction in HbA1c to controls (7 mmol/mol at 3 months) but with a much lower hypoglycaemic exposure (-1.3 hour/day)

- **In T1D and T2D**
  - Improved quality of life measures

Bolinder et al, Lancet. 2016; 388(10057):2254
Leelarathna et al, NEJM 2022; EPub
Haak et al, Diabetes Ther. 2017 Feb;8(1):55
Yaron et al, Diabetes Care. 2019; 42(7): 1178
Cheo HJ. et al., Diabetes Care. 2022; 45(10):2224-2230
Wada et al, BMJ Diab Res Care 2020; 8:e001115
Ajjan et al, LIBERATES trial, Diabetes Care, 2023; 46:441-48

CGM - NICE

https://www.nice.org.uk/guidance/ng28/chapter/Recommendations#blood-glucose-management

CGM - NICE

Offer intermittently scanned continuous glucose monitoring (isCGM, commonly referred to as 'flash') to adults with T2D on MDI (two or more injections of insulin) if:

- recurrent hypoglycaemia, severe hypoglycaemia or impaired awareness
- condition or disability (learning disability/cognitive impairment) preventing SMBG
- advised to self-measure at least 8 times a day

https://www.nice.org.uk/guidance/ng28/chapter/Recommendations#blood-glucose-management

CGM - NICE

Offer intermittently scanned continuous glucose monitoring (isCGM, commonly referred to as 'flash') to adults with T2D on MDI (two or more injections of insulin) if:

- recurrent hypoglycaemia, severe hypoglycaemia or impaired awareness
- condition or disability (learning disability/cognitive impairment) preventing SMBG
- advised to self-measure at least 8 times a day

Offer isCGM to adults with insulin-treated type 2 diabetes who would otherwise need help from a care worker or HCP to monitor glucose

https://www.nice.org.uk/guidance/ng28/chapter/Recommendations#blood-glucose-management

CGM - NICE

Offer intermittently scanned continuous glucose monitoring (isCGM, commonly referred to as 'flash') to adults with T2D on MDI (two or more injections of insulin) if:

- recurrent hypoglycaemia, severe hypoglycaemia or impaired awareness
- condition or disability (learning disability/cognitive impairment) preventing SMBG
- advised to self-measure at least 8 times a day

Offer isCGM to adults with insulin-treated type 2 diabetes who would otherwise need help from a care worker or HCP to monitor glucose

- Consider real-time continuous glucose monitoring (rtCGM) as an alternative to isCGM for adults with insulin-treated T2D type 2 diabetes available for same or lower cost

https://www.nice.org.uk/guidance/ng28/chapter/Recommendations#blood-glucose-management

CGM - NICE

Offer intermittently scanned continuous glucose monitoring (isCGM, commonly referred to as 'flash') to adults with T2D on MDI (two or more injections of insulin) if:

- recurrent hypoglycaemia, severe hypoglycaemia or impaired awareness
- condition or disability (learning disability/cognitive impairment) preventing SMBG
- advised to self-measure at least 8 times a day

Offer isCGM to adults with insulin-treated type 2 diabetes who would otherwise need help from a care worker or HCP to monitor glucose

- Consider real-time continuous glucose monitoring (rtCGM) as an alternative to isCGM for adults with insulin-treated T2D type 2 diabetes available for same or lower cost
- CGM should be provided by a team with expertise in its use

https://www.nice.org.uk/guidance/ng28/chapter/Recommendations#blood-glucose-management

Should all T2D diabetes patients be eligible for CGM?

There are cost implications and therefore we need to be pragmatic. T2D individuals who can be considered for CGM include:

Should all T2D diabetes patients be eligible for CGM?

There are cost implications and therefore we need to be pragmatic. T2D individuals who can be considered for CGM include:

1. MDI-treated patients T2D: no brainer.

Should all T2D diabetes patients be eligible for CGM?

There are cost implications and therefore we need to be pragmatic. T2D individuals who can be considered for CGM include:

1. MDI-treated patients T2D: no brainer.

2. Basal insulin, fixed insulin doses and sulphonylurea use: intermittently, particularly in older people.

Should all T2D diabetes patients be eligible for CGM?

There are cost implications and therefore we need to be pragmatic. T2D individuals who can be considered for CGM include:

1. MDI-treated patients T2D: no brainer.

2. Basal insulin, fixed insulin doses and sulphonylurea use: intermittently, particularly in older people.

3. History of severe hypoglycaemia (particularly if repeated).

Should all T2D diabetes patients be eligible for CGM?

There are cost implications and therefore we need to be pragmatic. T2D individuals who can be considered for CGM include:

1. MDI-treated patients T2D: no brainer.

2. Basal insulin, fixed insulin doses and sulphonylurea use: intermittently, particularly in older people.

3. History of severe hypoglycaemia (particularly if repeated).

4. When rapid “optimisation” in glucose is needed (such as myocardial infarction, foot infection, pre-surgery and others).

Should all T2D diabetes patients be eligible for CGM?

There are cost implications and therefore we need to be pragmatic. T2D individuals who can be considered for CGM include:

1. MDI-treated patients T2D: no brainer.

2. Basal insulin, fixed insulin doses and sulphonylurea use: intermittently, particularly in older people.

3. History of severe hypoglycaemia (particularly if repeated).

4. When rapid “optimisation” in glucose is needed (such as myocardial infarction, foot infection, pre-surgery and others).

5. Oral therapies (other than SU) and injectable GLP-1RA: during therapy escalations.

Should all T2D diabetes patients be eligible for CGM?

There are cost implications and therefore we need to be pragmatic. T2D individuals who can be considered for CGM include:

1. MDI-treated patients T2D: no brainer.

2. Basal insulin, fixed insulin doses and sulphonylurea use: intermittently, particularly in older people.

3. History of severe hypoglycaemia (particularly if repeated).

4. When rapid “optimisation” in glucose is needed (such as myocardial infarction, foot infection, pre-surgery and others).

5. Oral therapies (other than SU) and injectable GLP-1RA: during therapy escalations.

6. Inability to perform/interpret SMBG and at risk of hypoglycaemia (rheumatoid, Parkinson’s, learning difficulties...etc…).

Should all T2D diabetes patients be eligible for CGM?

There are cost implications and therefore we need to be pragmatic. T2D individuals who can be considered for CGM include:

1. MDI-treated patients T2D: no brainer.

2. Basal insulin, fixed insulin doses and sulphonylurea use: intermittently, particularly in older people.

3. History of severe hypoglycaemia (particularly if repeated).

4. When rapid “optimisation” in glucose is needed (such as myocardial infarction, foot infection, pre-surgery and others).

5. Oral therapies (other than SU) and injectable GLP-1RA: during therapy escalations.

6. Inability to perform/interpret SMBG and at risk of hypoglycaemia (rheumatoid, Parkinson’s, learning difficulties...etc…).

7. When HbA1c is unreliable (dialysis, Hb variant…etc…)

General conclusions

General conclusions

- While HbA1c served us well, we should use additional glycaemic markers (**CGM-derived metrics**) to optimise management in some T2D patients

Ajjan, EASD 2014

General conclusions

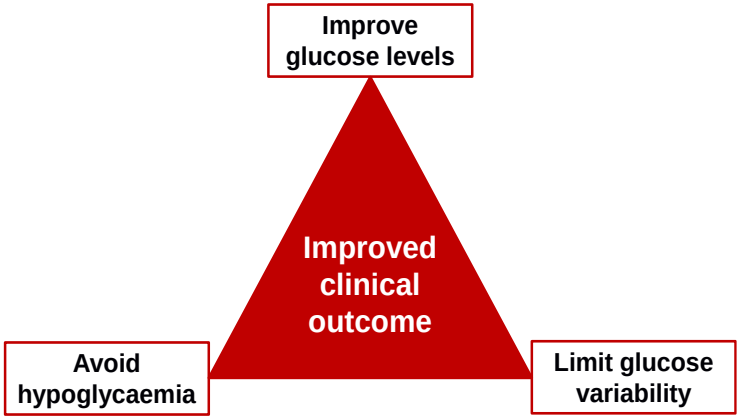
- While HbA1c served us well, we should use additional glycaemic markers (**CGM-derived metrics**) to optimise management in some T2D patients
- We need to have practical guidance for the use of CGM in non-T1D taking into account resources and financial burden

General conclusions

- While HbA1c served us well, we should use additional glycaemic markers (**CGM-derived metrics**) to optimise management in some T2D patients
- We need to have practical guidance for the use of CGM in non-T1D taking into account resources and financial burden
- Technology on its own is not enough – this should be accompanied by the right expertise (education and sharing experiences)

General conclusions

- While HbA1c served us well, we should use additional glycaemic markers (**CGM-derived metrics**) to optimise management in some T2D patients
- We need to have practical guidance for the use of CGM in non-T1D taking into account resources and financial burden
- Technology on its own is not enough – this should be accompanied by the right expertise (education and sharing experiences)



Ajjan, EASD 2014

Thank you for your kind attention