Continuous Glucose Monitoring:
The Next Big Thing in Diabetes Self-Management?

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Not All Innovations are Good Ideas!

Hydroelectric Power:
The Home Edition

# Yeah, but we got it done under budget!

The Glycemic Control Era in Diabetes

- **HbA1c** for accurately estimating glycemic average over time
  - Limitations
    - Does not reflect glycemic lability
    - Does not identify hypoglycemia

- **Capillary blood glucose** (fingerstick) monitoring for
  - Daily trends and variation
  - Urgent detection of hypoglycemia
  - Decision-making at point of care

The Double Edge of Glycemic Control

HbA$_1$c vs. Incident Retinopathy
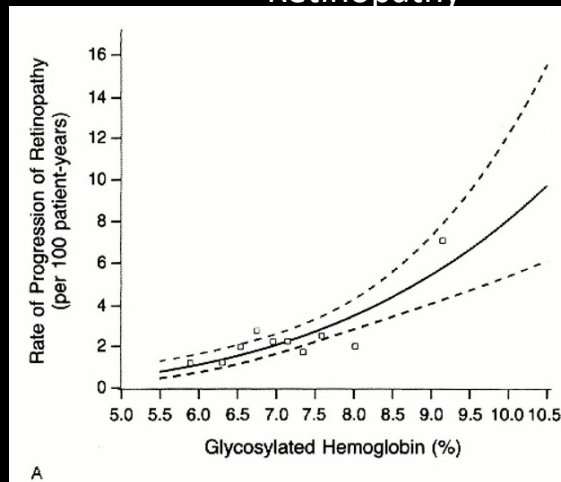
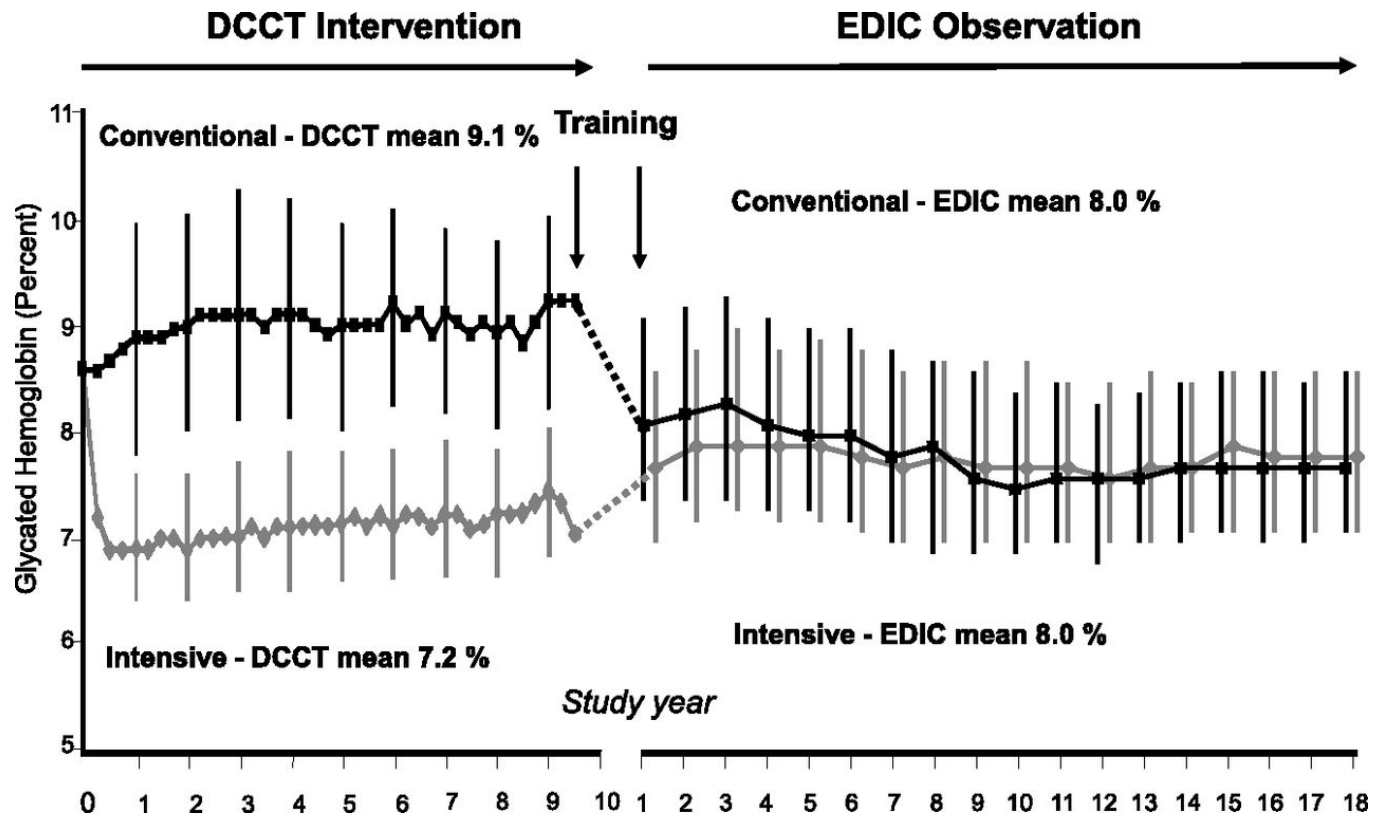HbA$_1$c vs. Incident Hypoglycemia
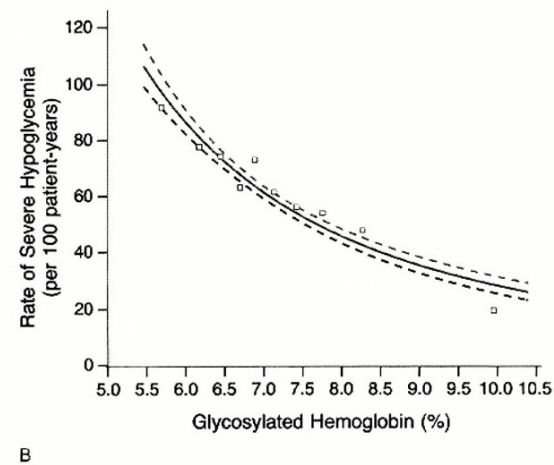
The Diabetes Control and Complications Trial Research Group. N Engl J Med 1993;329:977-986

HbA1c Over Time in DCCT/EDIC:

## What's "Average" Control?

Ideal Glycemic Measurement Day-to-day

- Accurate

- Comfortable

- Timely
  - Identify actionable trends
  - Provide data in real-time

- Convenient

- Merge blood glucose monitoring with other ADL's (work/home/recreation)

1950's-1970's: European Vacation
Urine Dipstick Testing for Glucose

1980's: Color-Matching Blood Glucose Testing

1st film-based colourimetric test-strip
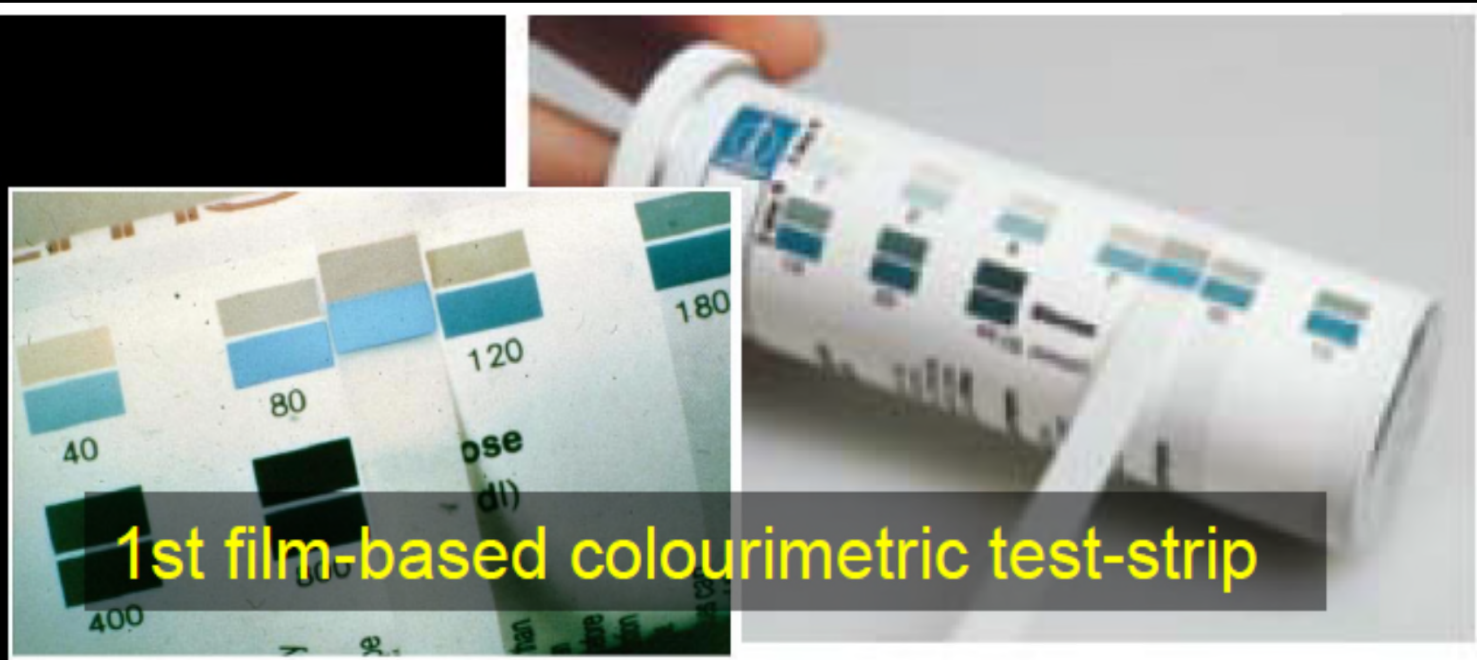
1990's: Rise of the Machines
(Digital Display Blood Glucose Meters)

2000's: Fast and Furious

2010-Present: The Clone Wars

Traditional Blood Glucose Self-Monitoring

Candidates for CGM

Qualifying Criteria (for insurance coverage)

- Using insulin (MDI or pump)

- Performing SMBG at least 4 times daily
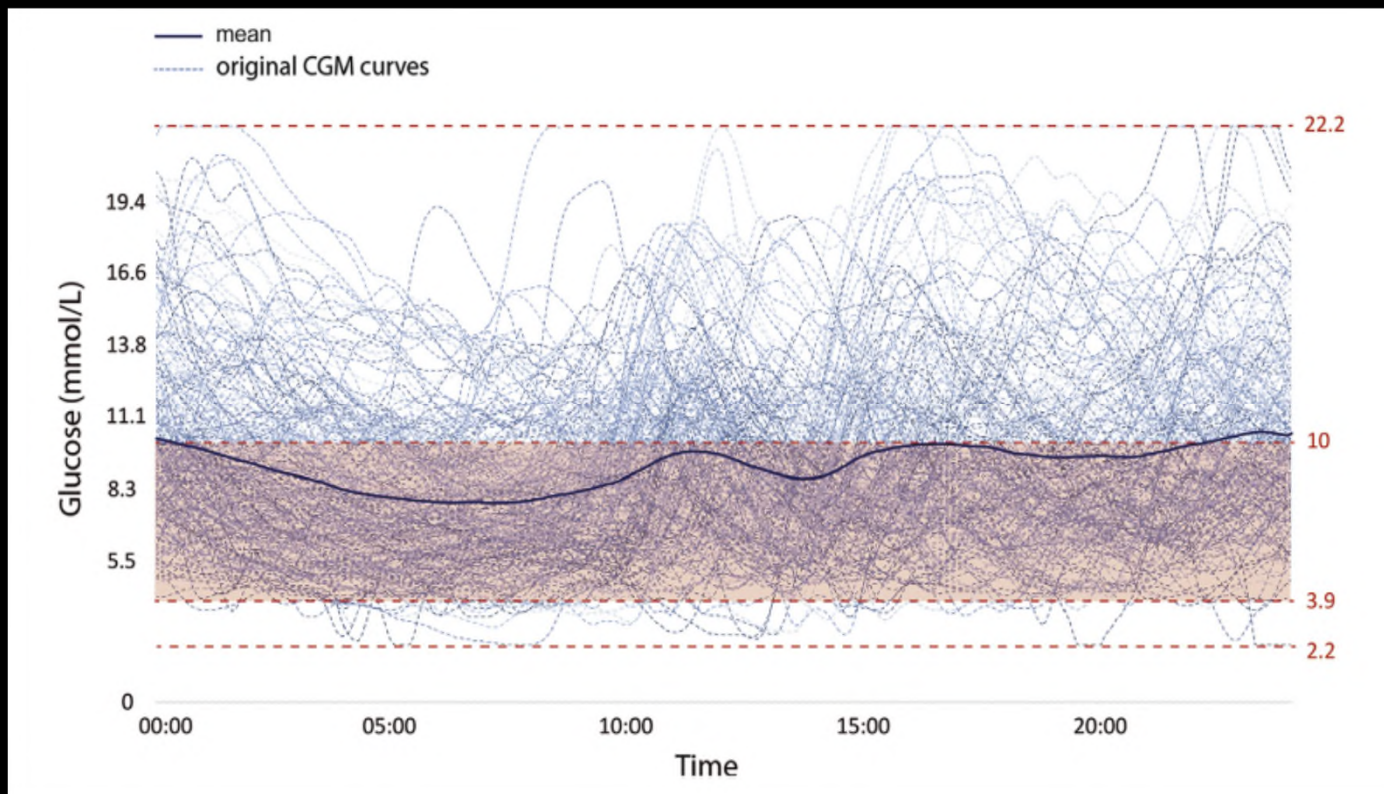
Major Indications

- Patients who are *motivated* to use one!

- Hx of hypoglycemia unawareness

- Hx of extreme glycemic lability

- Very active or highly variable daily routines

Basic Types of CGM Devices

- Continuous
  - Dexcom G4/G5/G6
  - Medtronic
- Flash
  - Freestyle Libre
  - Eversense

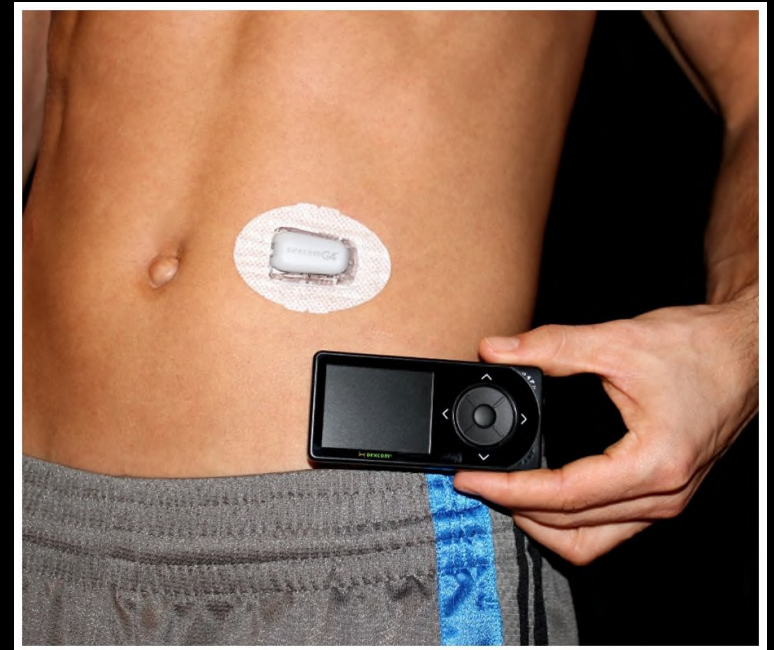# CGM Tracings from a Clinical Trial
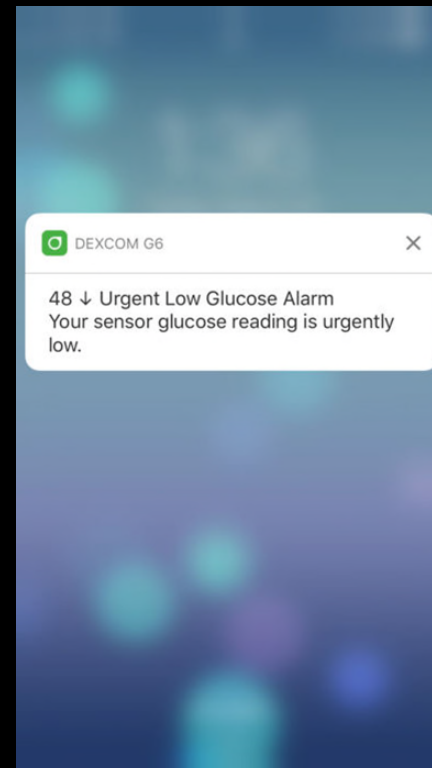## Pazos-Couselo M. *Can J Diabetes* 2015; 39:428-433

Anatomy of a CGM Sensor

Dexcom Transmitter & Receiver Options

Cell Phone App for Dexcom

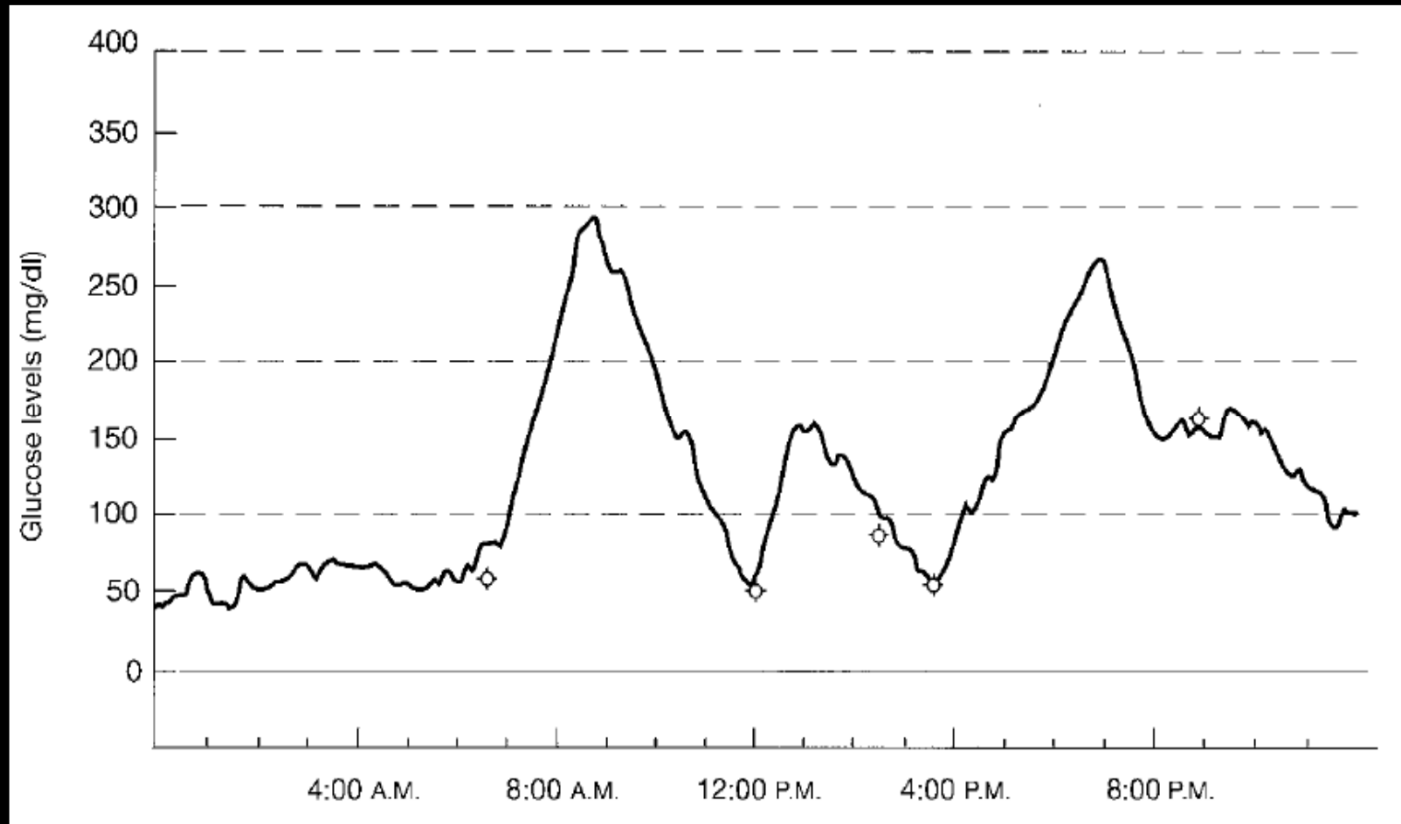**Freestyle Libre CGM System**

Eversense Implantable CGM System

Introducing the Eversense
Continuous Glucose Monitoring System

109 mg/dL

90-Day Implantable
Sensor

Removable / rechargeable
Smart Transmitter

Clear, concise
Mobile App

How Accurate are CGM Devices?
Aberer F et al. Diabetes Obes Metab 2017; 19:1051-1055

	Abbott	Dexcom	Medtronic
MARD ± s.d., %			
Overall	13.2 ± 10.9	16.8 ± 12.3	21.4 ± 17.6
	(n = 462)	(n = 540)	(n = 502)
Exercise	8.7 ± 5.9	15.7 ± 14.6	19.4 ± 13.5
	(n = 13)	(n = 24)	(n = 22)
Hypoglycaemia	14.6 ± 10.2	23.8 ± 15.7	26.9 ± 20.0
	(n = 81)	(n = 88)	(n = 87)
Euglycaemia	13.7 ± 11.5	16.3 ± 11.6	21.0 ± 15.3
	(n = 301)	(n = 362)	(n = 334)
Hyperglycaemia	10.1 ± 7.9	11.6 ± 7.2	17.1 ± 21.9
	(n = 80)	(n = 90)	(n = 81)
ΔGlucose (maximum; minimum), mmol/L			
Exercise	1.7 (1.0; 4.5)	1.5 (1.3; 4.5)	1.9 (0.4; 4.3)
Breakfast	3.6 (3.4; 6.5)	3.6 (2.5; 6.7)	3.4 (2.4; 6.4)
Lunch	4.3 (2.6; 5.9)	4.8 (3.6; 7.3)	3.9 (2.3; 6.8)
Dinner	0.4 (0.3; 0.4)	1.3 (0.2; 3.3)	1.8 (0.2; 2.7)

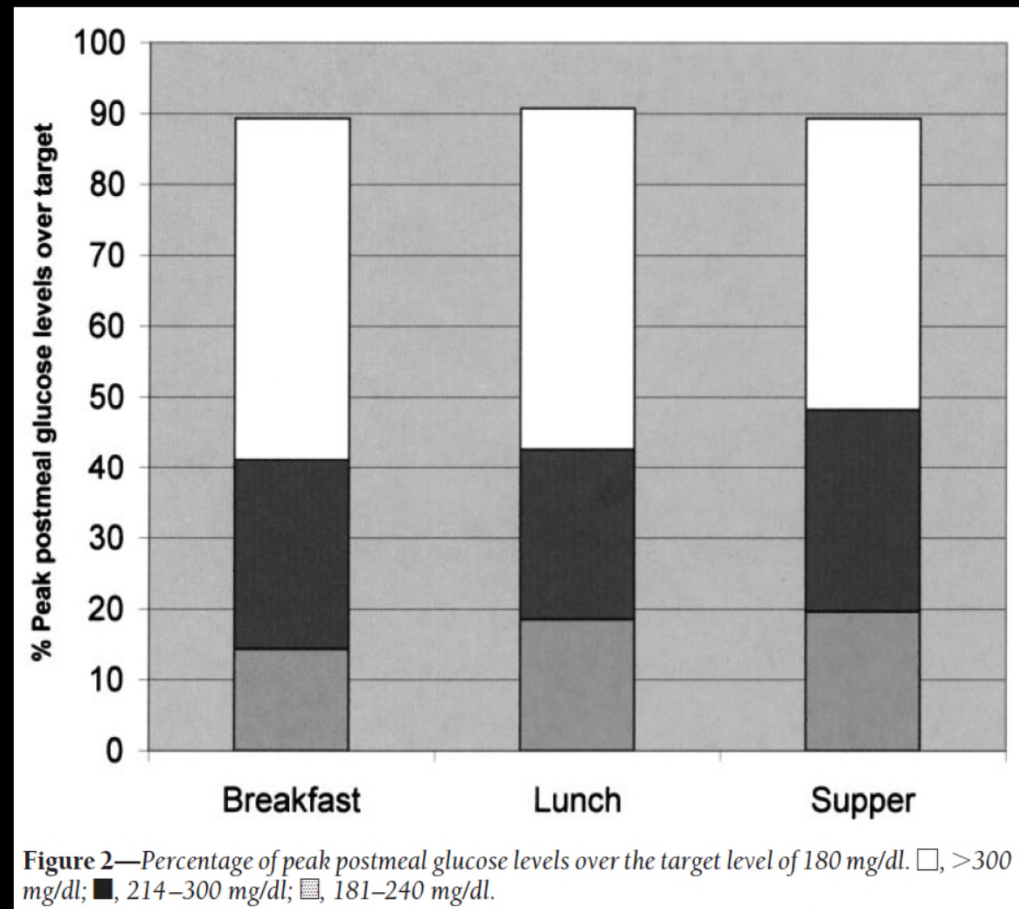# New Concepts in Glycemic Control Introduced by CGM

- Time in Range
- % Hypoglycemic
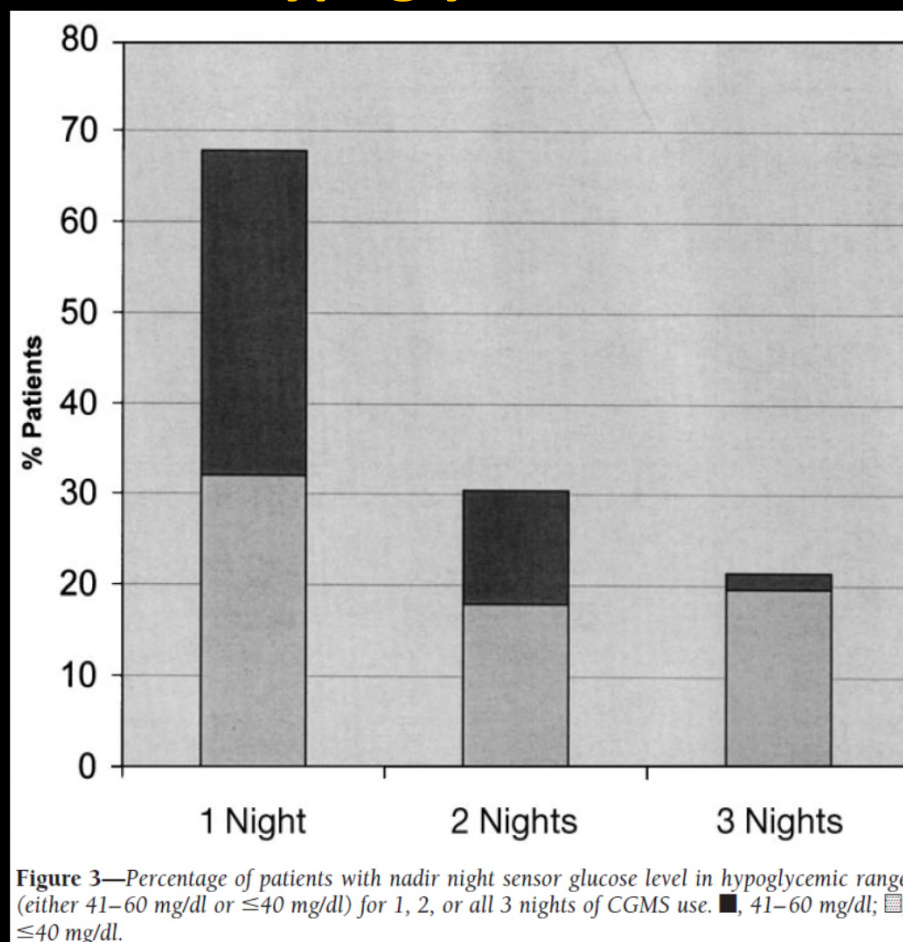- % Hyperglycemic

What Do We Learn From CGM's?

Boland E et al. *Diabetes Care* 24: 1858-1862; 2001

Excessive Postprandial Hyperglycemia is Common

Figure 2—Percentage of peak postmeal glucose levels over the target level of 180 mg/dl. □, >300 mg/dl; ■, 214–300 mg/dl; ▨, 181–240 mg/dl.

Boland E et al. *Diabetes Care* 24: 1858-1862; 2001

Nocturnal Hypoglycemia is Common

Figure 3—Percentage of patients with nadir night sensor glucose level in hypoglycemic range (either 41–60 mg/dl or ≤40 mg/dl) for 1, 2, or all 3 nights of CGMS use. ■, 41–60 mg/dl; ▨, ≤40 mg/dl.

Boland E et al. *Diabetes Care* 24: 1858-1862; 2001

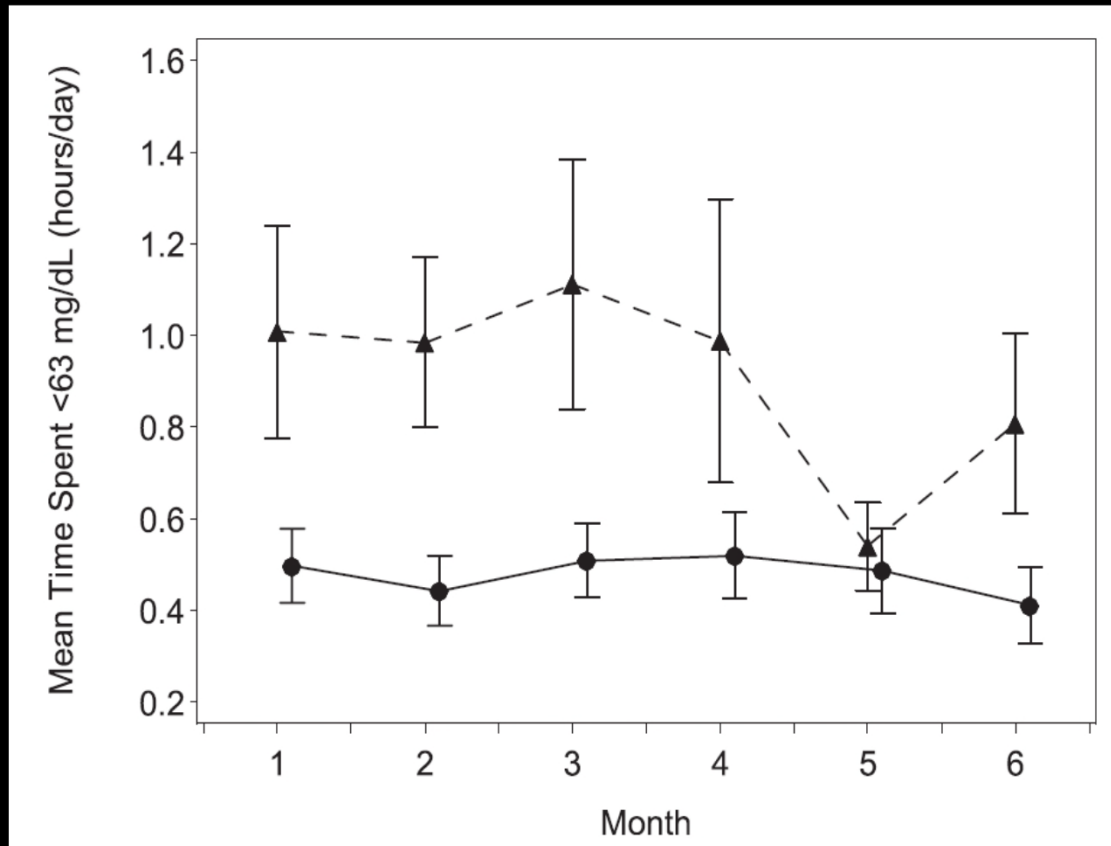# Self-Reported vs. CGM-detected Hypoglycemia in 4-T Trial (UK; Insulin + Orals)
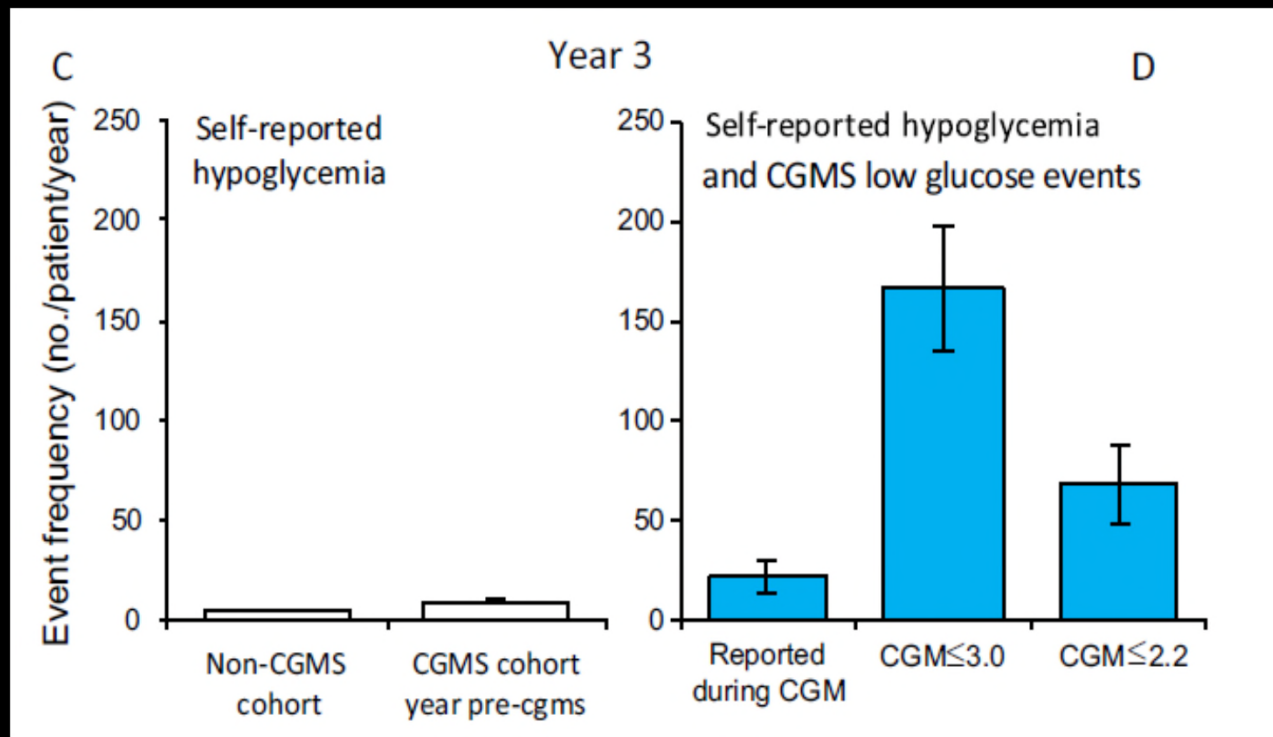
Levy JC et al. *Diab Research Clin Pract* 2017; 131: 161-168.

CGM vs SMBG: Effect on Hypoglycemia in T1DM

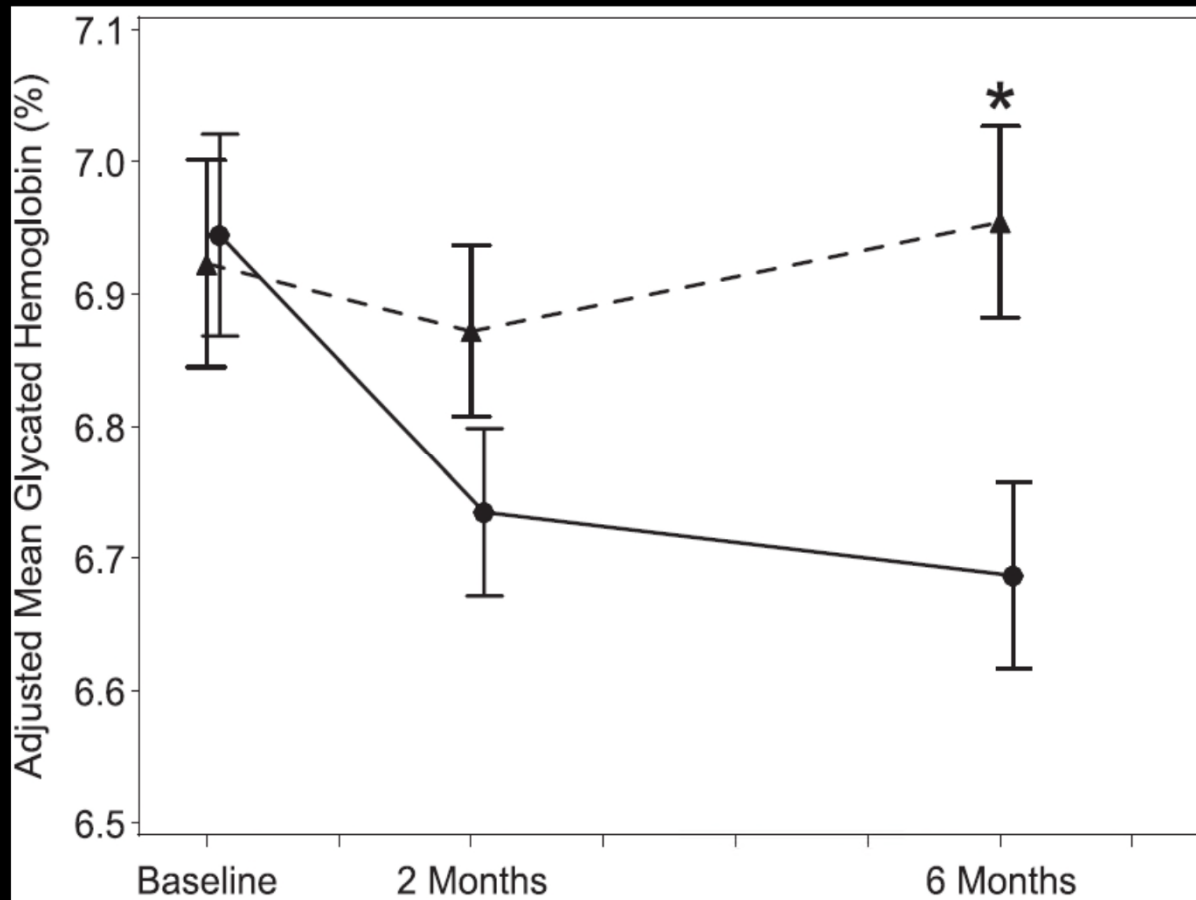|	CGM (n=62)	Control (n=58)
Age	25.7 ± 14.1	26.0 ± 14.6
% Male	58	67
BMI (Kg/m^2)	22.4 ± 3.8	22.0 ± 3.8
HbA1c(%)	6.9 ± 0.6	6.9 ± 0.7
SMBG tests per day	5.3 ± 2.2	5.1 ± 2.5

Battelino T et al. *Diabetes Care* 34:795-800; 2011

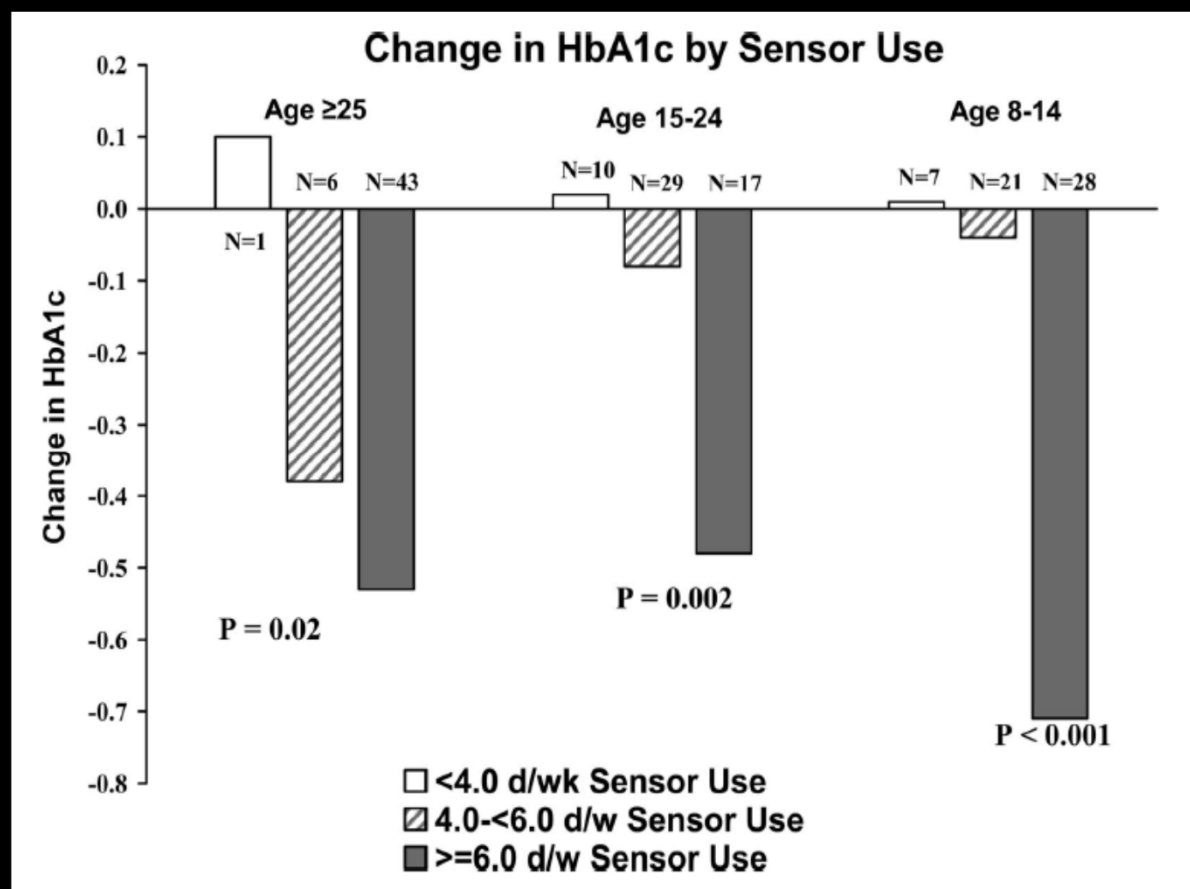# Time in Hypoglycemia Range: FSG vs. CGM

Battelino T et al. *Diabetes Care* 34:795-800; 2011

HbA1c at 6 months: FSG vs. CGM

Battelino T et al.   *Diabetes Care* 34:795-800; 2011

Change in HbA1c vs. Frequency of CGM Use

GOLD Study: Impact of CGM on HbA1c in T1DM on MDI Crossover Design (Sweden)

- N = 161
- Mean age 44 years
- 55% male
- Mean Duration T1DM = 22 years
- Baseline HbA1c = 8.7%

GOLD Study: Adult Patients with T1DM, on MDI Regimens Effect of CGM (Crossover Design)
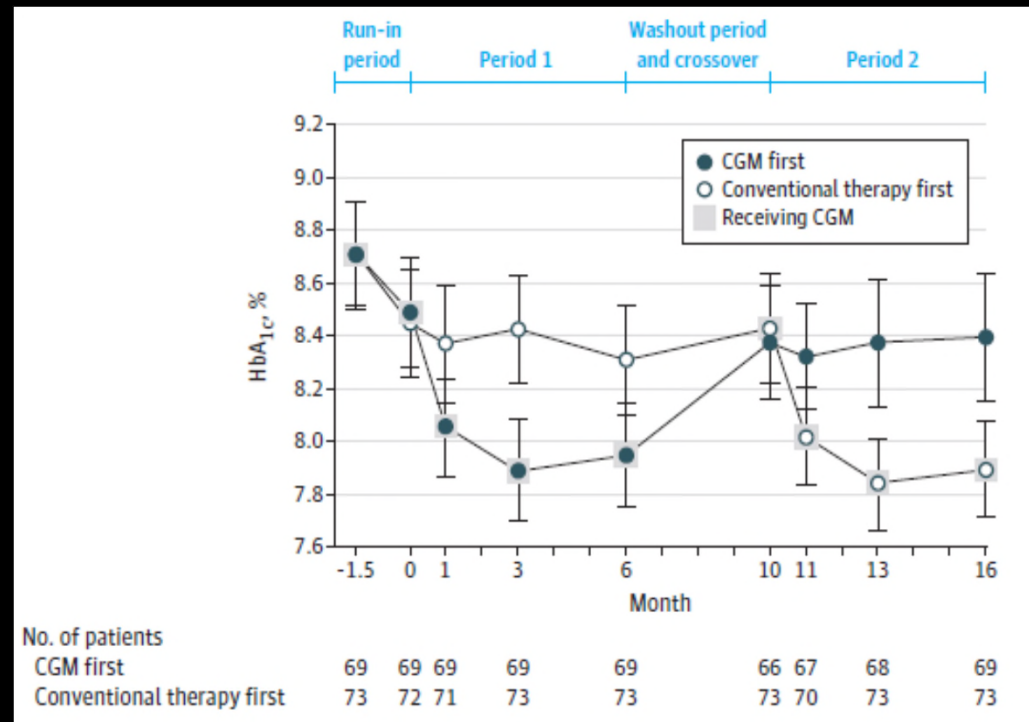
GOLD Study Group.   *JAMA* 317: 379-387; 2017

CGM vs. FSG in Intensive Insulin Rx for T1DM (Age ≥ 25 only)

	CGM (n = 52)	FSG [Control] (n = 46)
Age (years)	41.2 ± 11.2	44.6 ± 12.3
% Female	60%	57%
Duration of T1DM (years)	23.6 ± 10.6	21.8 ± 10.4
HbA1c (%)	7.6 ± 0.5	7.6 ± 0.5
Insulin pump	83%	85%
# of FSG tests per day	6.5 ± 2.3	6.6 ± 2.2

JDRF Study Group. *NEJM* 2008; 359: 1464-1476.

Additive Effect of CGM to Intensive Rx T1DM: JDRF Study
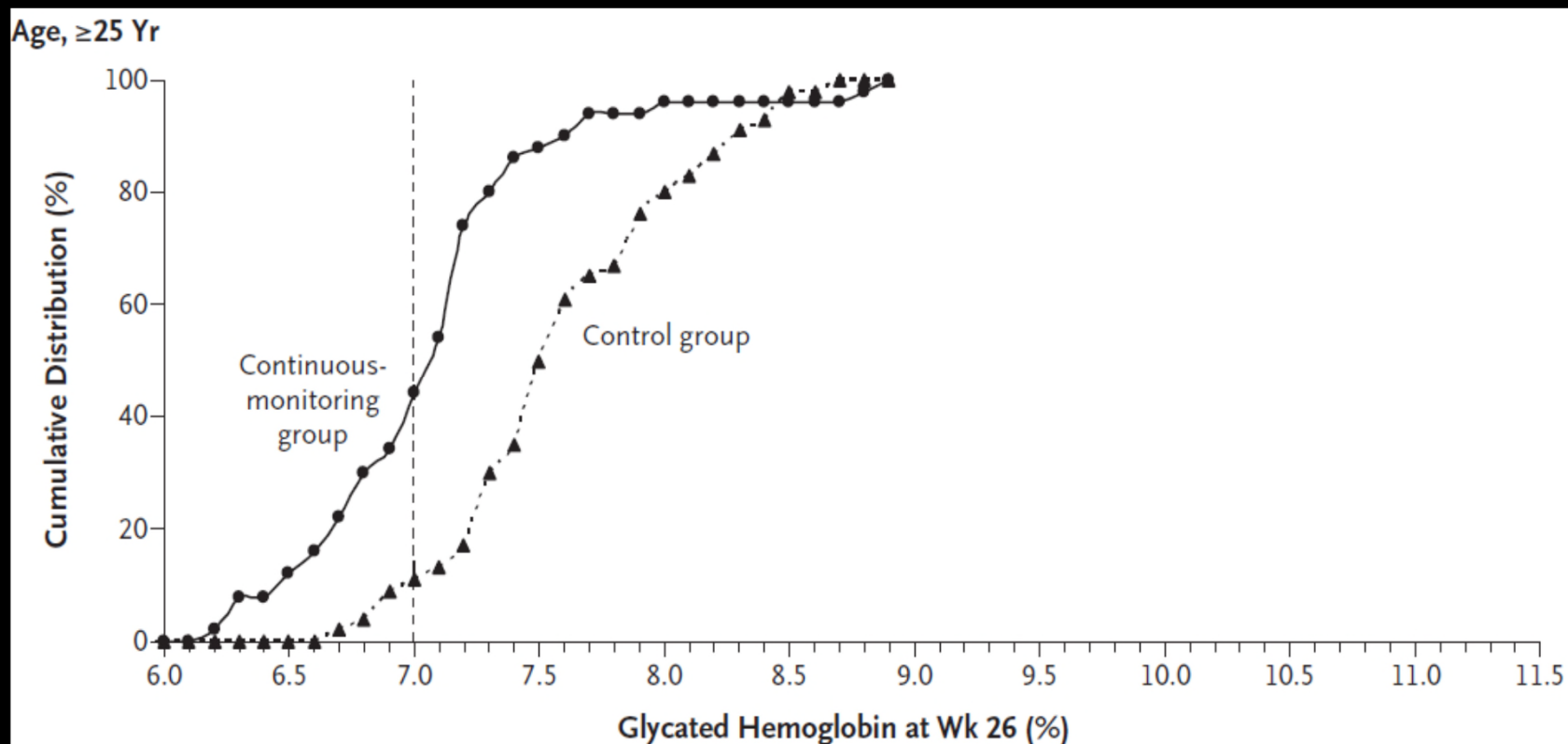
JDRF Study Group. *NEJM* 2008; 359: 1464-1476.

Adult Patients with T1DM, on MDI Regimens: Effect of CGM
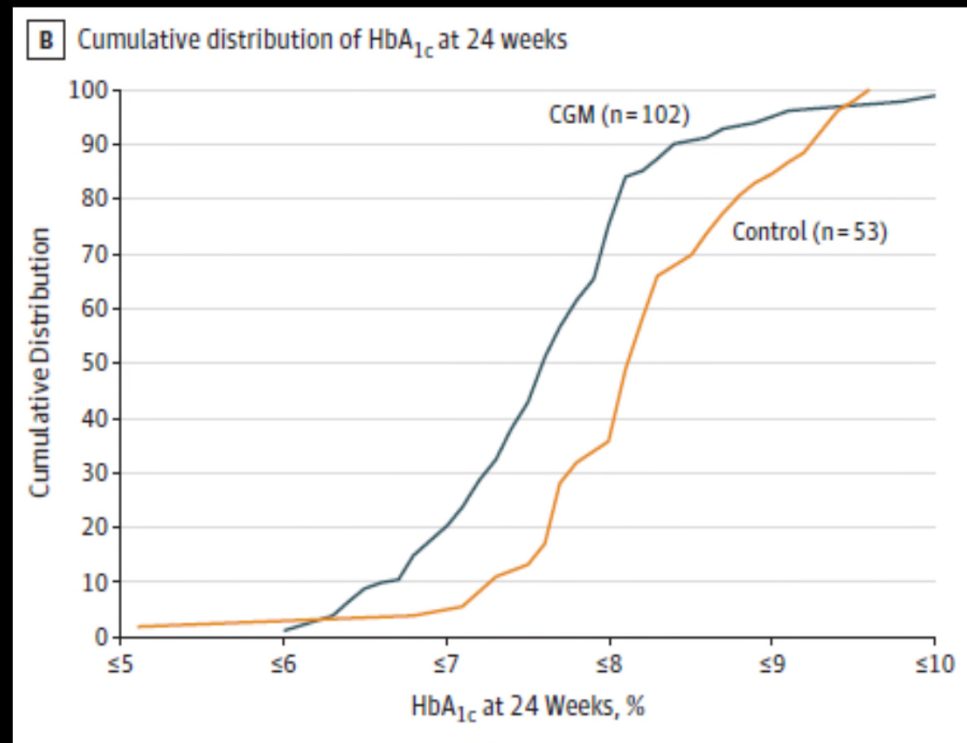
DIAMOND Study Group.   *JAMA* 317: 371-378; 2017

Patient Snapshot #1: 39 y/o man, T1DM x 10 years, on MDI

Hemoglobin A1c

Dexcom

Generalized Normal High

Generalized Normal Low

Patient Snapshot #2:   41 y/o man with T1DM x 26 years; on MDI
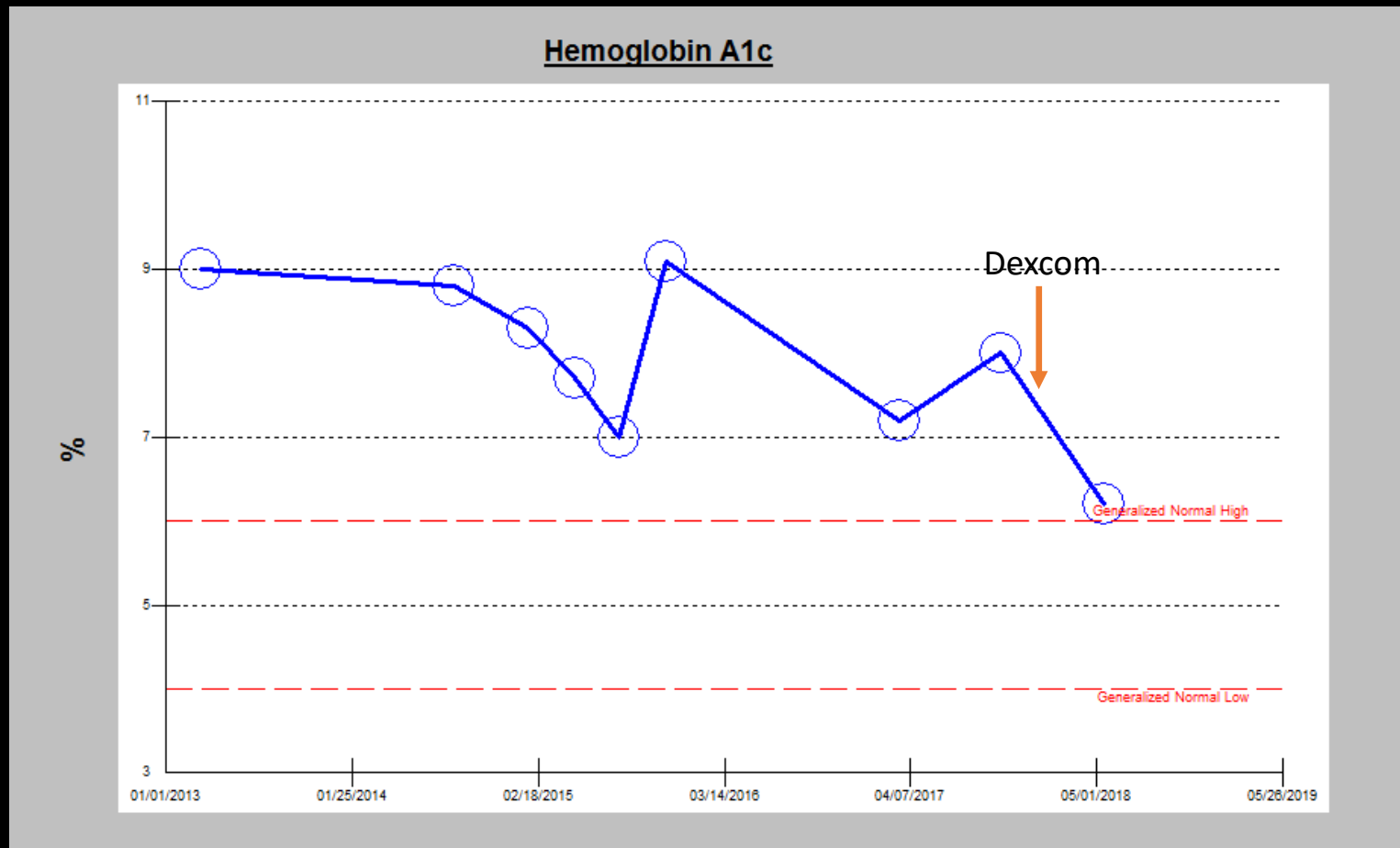
DIAMOND Study: CGM in T2DM on MDI Insulin Regimens Subject Characteristics
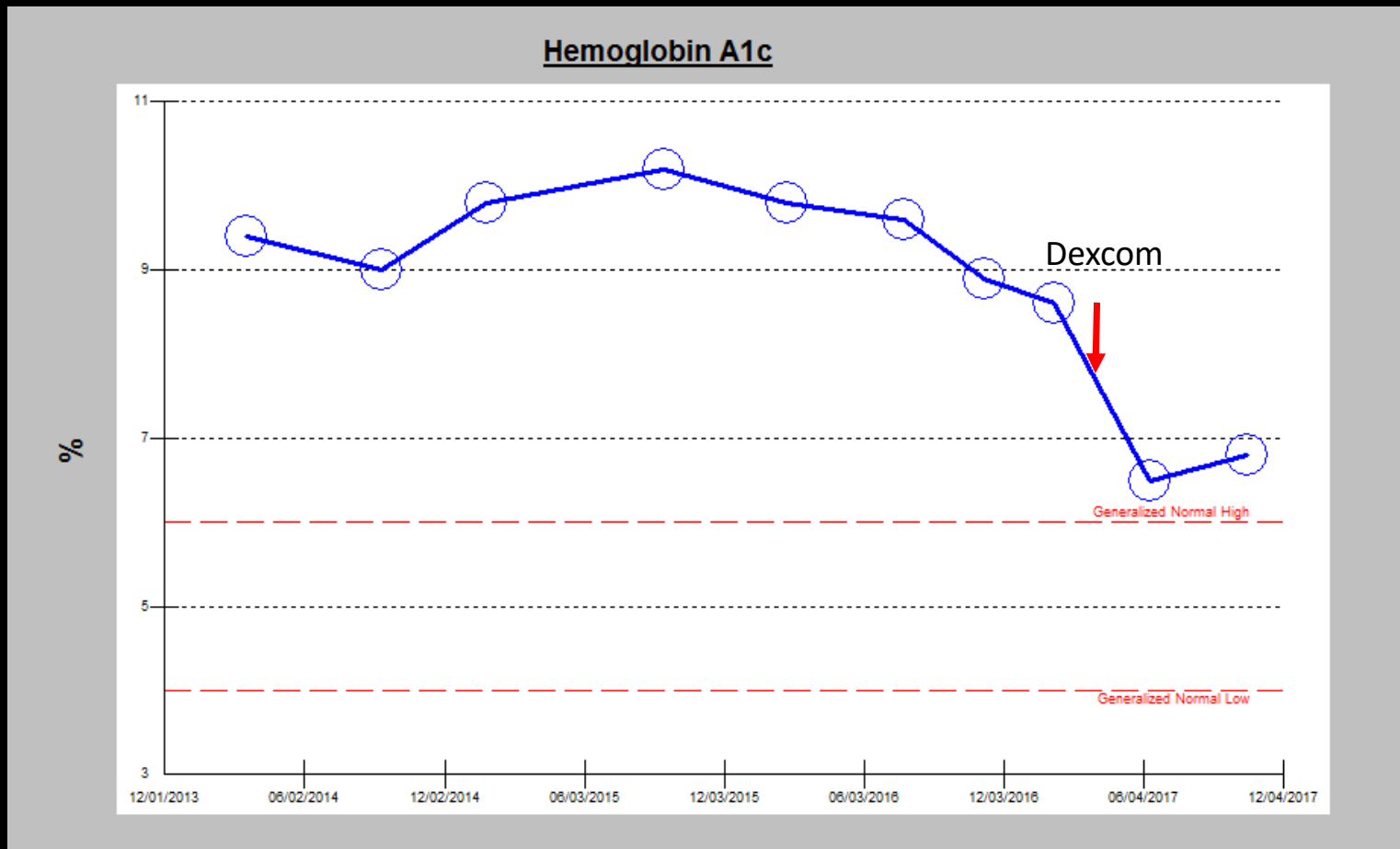
	CGM (n=79)	Control (n=79)
HbA1c	8.5%	8.5%
Age (years)	60 ± 11	60 ± 9
BMI (kg/m^2)	35 ± 8	37 ± 7
Non-insulin Rx	71%	66%
Reduced hypoglycemic awareness	32%	22%

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

Impact of CGM in T2DM with MDI Regimens: DIAMOND Study

@ 24 Weeks	CGM Group	SMBG Group	P value
HbA1c	7.7%	8.0%	0.02
Mean blood glucose	171 mg/dl	171 mg/dl	N.S.
Time in Range (70-180 mg/dl)	882 min/24 hrs	836 min/24 hrs	<0.001
Time < 70 mg/dl	4 min/24 hrs	12 min/24 hrs	<0.001

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

CGM vs. SMBG (Fingerstick) Testing: T1DM (children)
Poolsup N. Diabetol Metab Syndr 2013;5: 39-53.

Figure 8 Mean difference (95% confidence interval) in HbA1c for CGM versus SMBG according to quality of included studies in T1DM pediatrics.
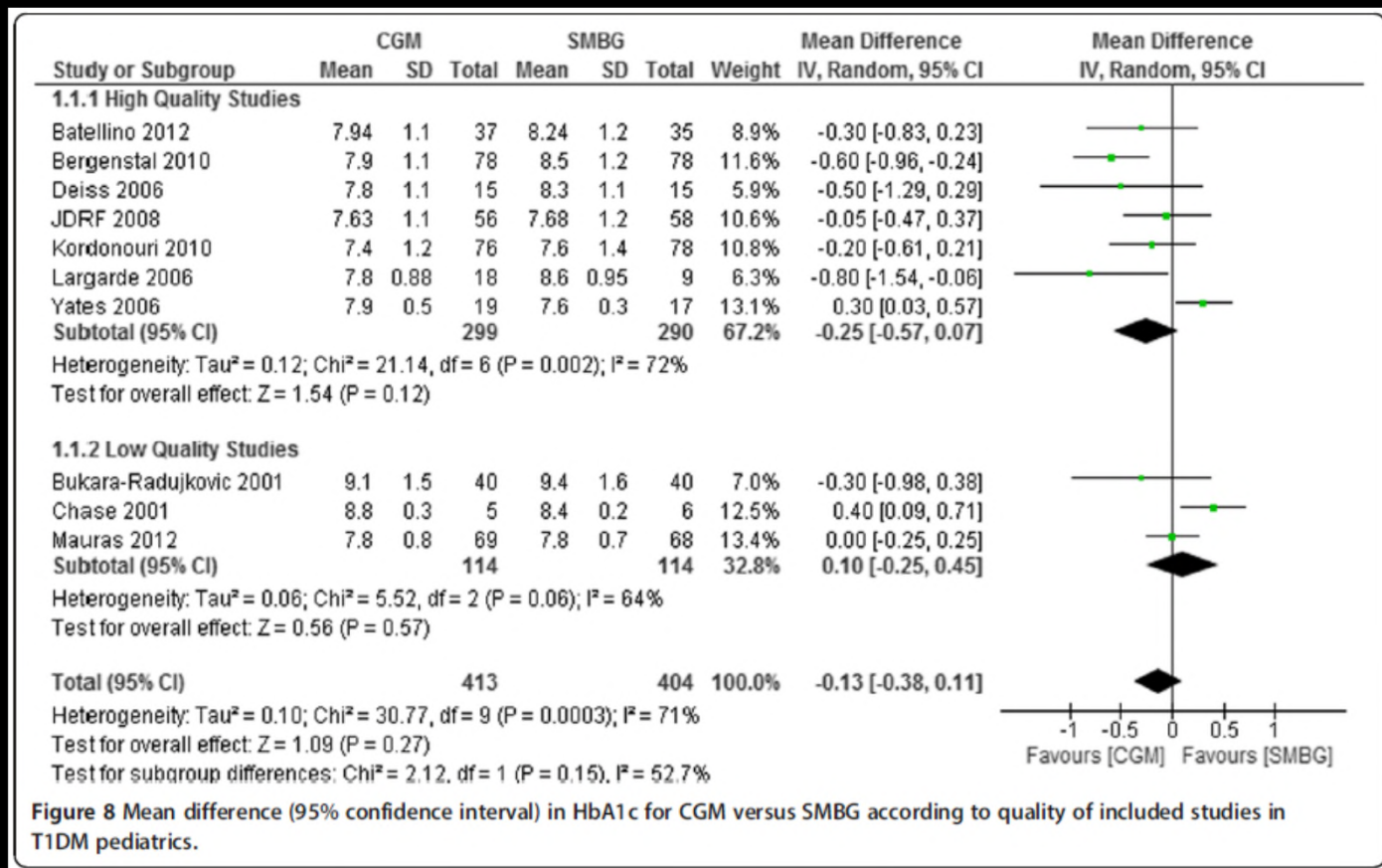
CGM vs. SMBG (Fingerstick) Testing: T2DM (adults)
## Poolsup N. Diabetol Metab Syndr 2013;5: 39-53.
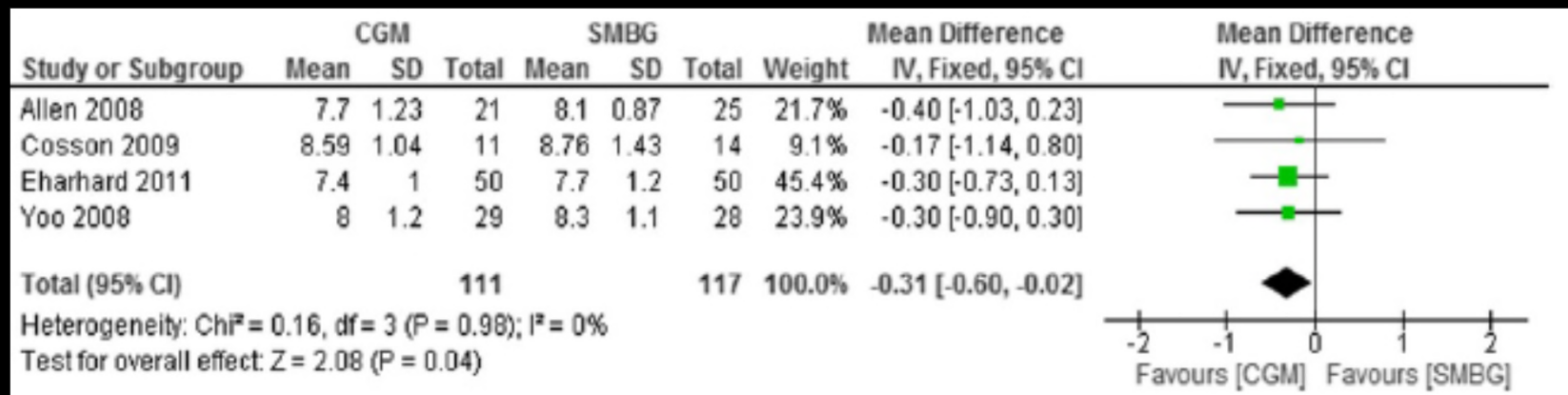
Impact of CGM on Hospitalizations & Missed Work in Insulin Pump-Treated T1DM: Belgian Study

	Before Reimbursement (n = 496)	12 Months of Reimbursement (n = 379)	P Value
Patients with			
Hospitalizations due to hypoglycemia and/or ketoacidosis	77 (16%)	14 (4%)	<0.0005
Hospitalizations due to hypoglycemia	59 (11%)	12 (3%)	<0.0005
Hospitalizations due to ketoacidosis	23 (5%)	4 (1%)	0.092
Work absenteeism[a]	123 (25%)	36 (9%)	<0.0005
Days (per 100 patient years) of			
Hospitalizations due to hypoglycemia and/or ketoacidosis	53.5	17.8	<0.0005
Hospitalizations due to hypoglycemia	38.5	12.5	0.001
Hospitalizations due to ketoacidosis	14.9	5.3	0.220
Work absenteeism	494.5	233.8	0.001

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

Impact of CGM on Hospital and ED Admissions and Cost
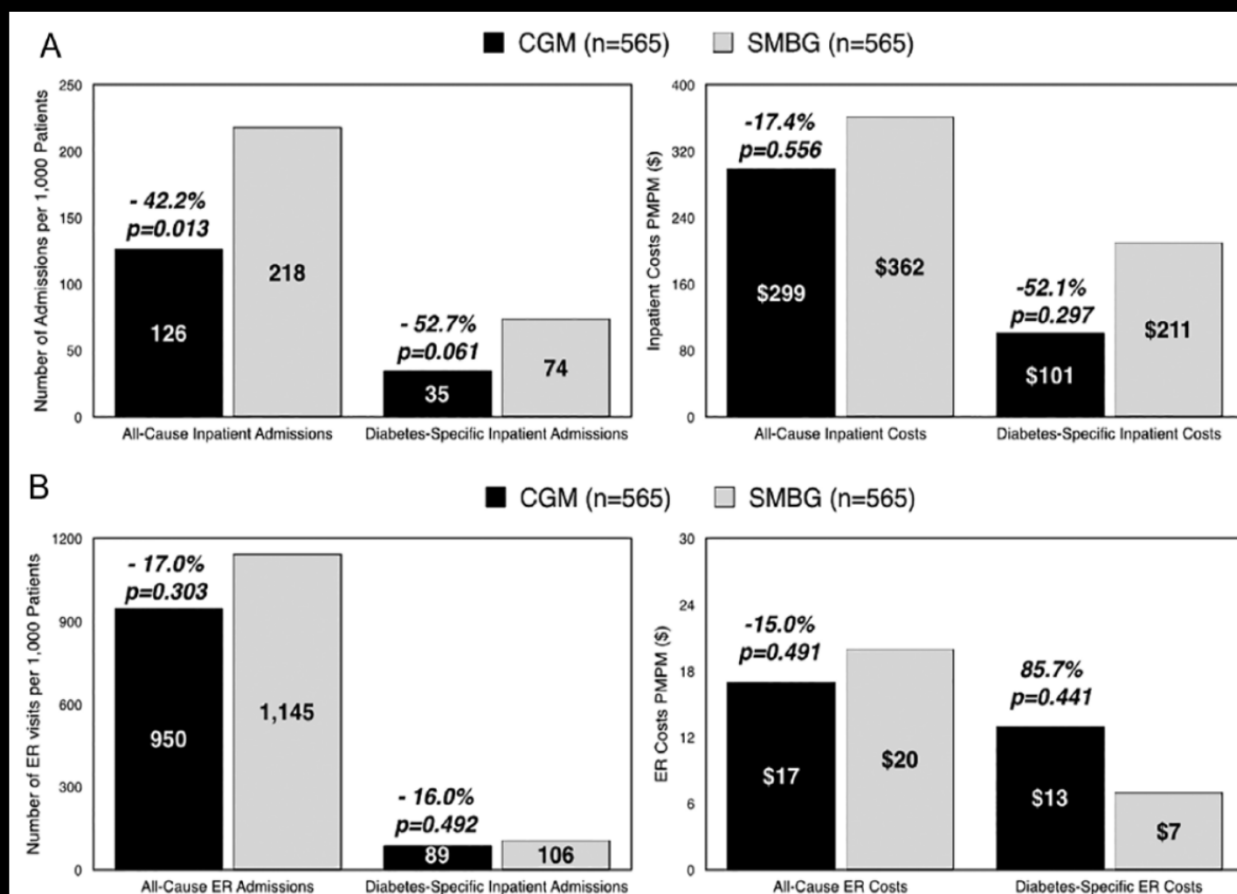
Parkin CG. *J Diabetes Sci Technol* 2017; 11: 522-528.

CGM in Hospital Inpatients

Bally L et al. Closed-Loop Insulin Delivery for glycemic control
in non-critical care. *NEJM*; June 25 2018 on-line

Subject Characteristics:
Closed Loop Insulin Pump vs. MDI w/CGM in T2DM

**Table 1. Characteristics of the Patients at Baseline.***

Characteristic	Closed-Loop Group (N=70)	Control Group (N=66)
Male sex — no. (%)	50 (71)	43 (65)
Age — yr	67.7±10.1	67.1±13.0
Body-mass index†	32.7±8.2	32.3±8.1
Glycated hemoglobin		
Percentage	8.1±1.9	8.0±1.9
Mean value — mmol/mol	65±21	64±21
Duration of diabetes — yr	17.1±11.2	15.5±11.2
Duration of insulin therapy — yr	10.0±9.1	8.0±9.1
Total daily insulin dose — U	64.2±59.4	50.6±38.9

Set-Up for Closed Loop Insulin Pump with CGM
(Inpatient Study)

Figure S1. Automated fully closed-loop insulin delivery prototype (FlorenceD2W-T2) used in the study (photo obtained with consent).

Closed Loop Insulin vs. MDI Insulin in T2DM Inpatients
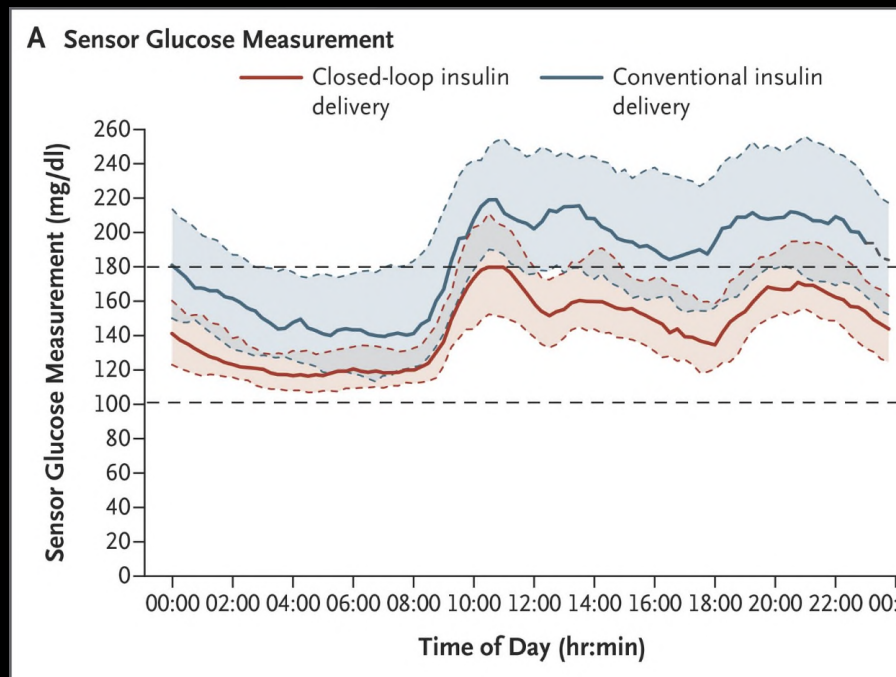
Outcomes: Closed Loop Insulin Pump vs. MDI with CGM in T2DM Inpatients

	Closed-Loop	MDI	P value
Nocturnal BG avg.	129 ± 24	160 ± 49	<0.001
% Time in Range (100-180 mg/dl)	74 ± 19	54 ± 25	<0.001
Daytime BG avg.	165 ± 36	204 ± 46	<0.001
% Time in Range (100-180 mg/dl)	62 ± 19	35 ± 19	<0.001
% Hypoglycemia (< 60 mg/dl)	0	0	N.S.
Mean Daily Insulin Dose	44	40	N.S.

Predicting the Future
of Continuous Glucose Monitoring

Predicting the Future
of Continuous Glucose Monitoring

- Contact lens
- Salivary sampling
- 365-day implantable sensor
- Glucose-sensing tattoo

Conclusions

- At present time, CGM can be recommended for most patients with either T1DM or T2DM who
  - Use MDI or CSII (insulin pump)
  - Perform at least 4 SMBG tests per day
  - Are motivated and willing to wear the device 24/7
- Accuracy of monitoring can largely obviate SMBG fingersticks
- Payers are gradually taking the hint
  (getting MediCare/CMS on board was huge!)
- Can expect this technology to improve rapidly,
  possibly becoming non-invasive in next iterations

Well-Koalafied for Success with Diabetes!