

Real-Time Continuous Glucose Monitoring Clinical Implementation Aspects

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High lights

- History of glucose monitoring
- SMBG and various glucometers
- Barriers of SMBG
- CGM
- Availability of Various CGMS
- Pediatric patient selections
- Advantages of rtCGM
- Disadvantages
- Comparisons between various types
- AGP (ambulatory glucose profile)
- Summery

Glucose Monitoring : History

From appearance, color, sediment and often taste



Clinitest was introduced by Ames in 1945, and utilised a copper reagent tablet that contained all the reagents required for a urine glucose test.



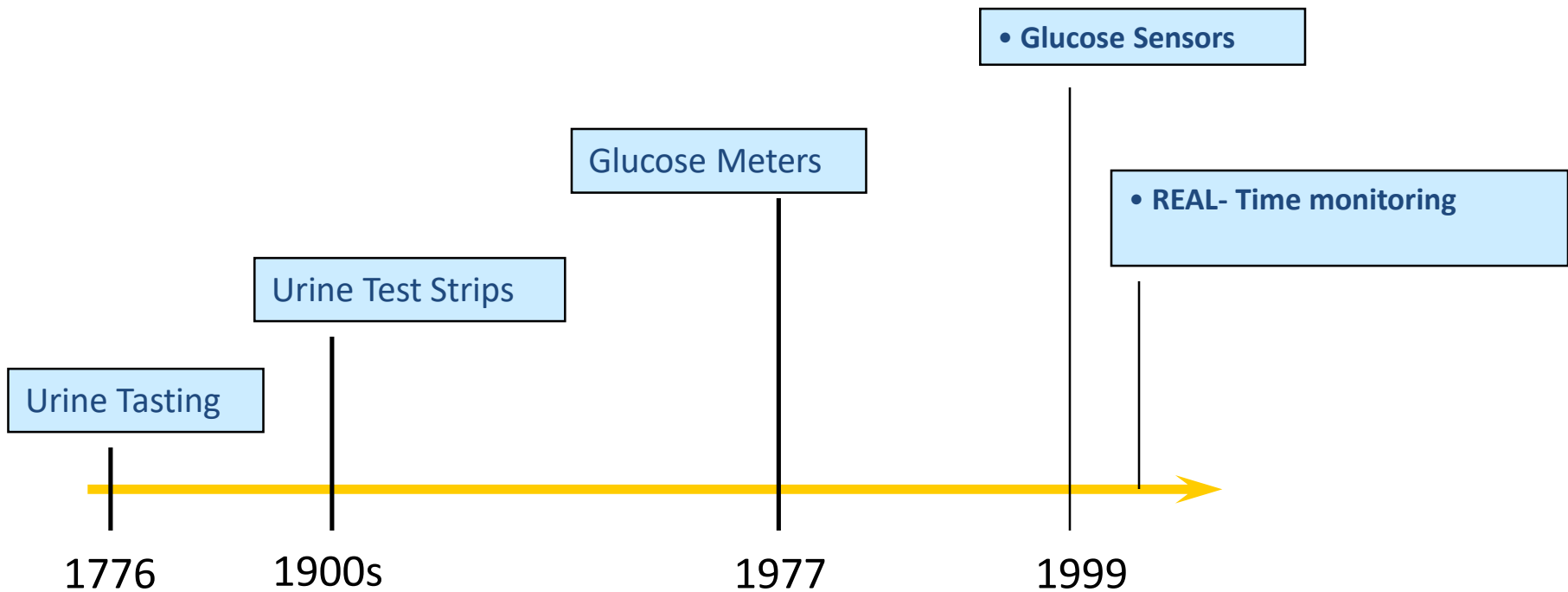
In 1954 Glucotest/Testape roll



1960's the "dipstix"



Evolution of Diabetes Technology



First Glucose Meter: 1977



Current various glucometers



SMBG supplies

Carrying case



Lancing device



Lancet



Control solution



Test strip



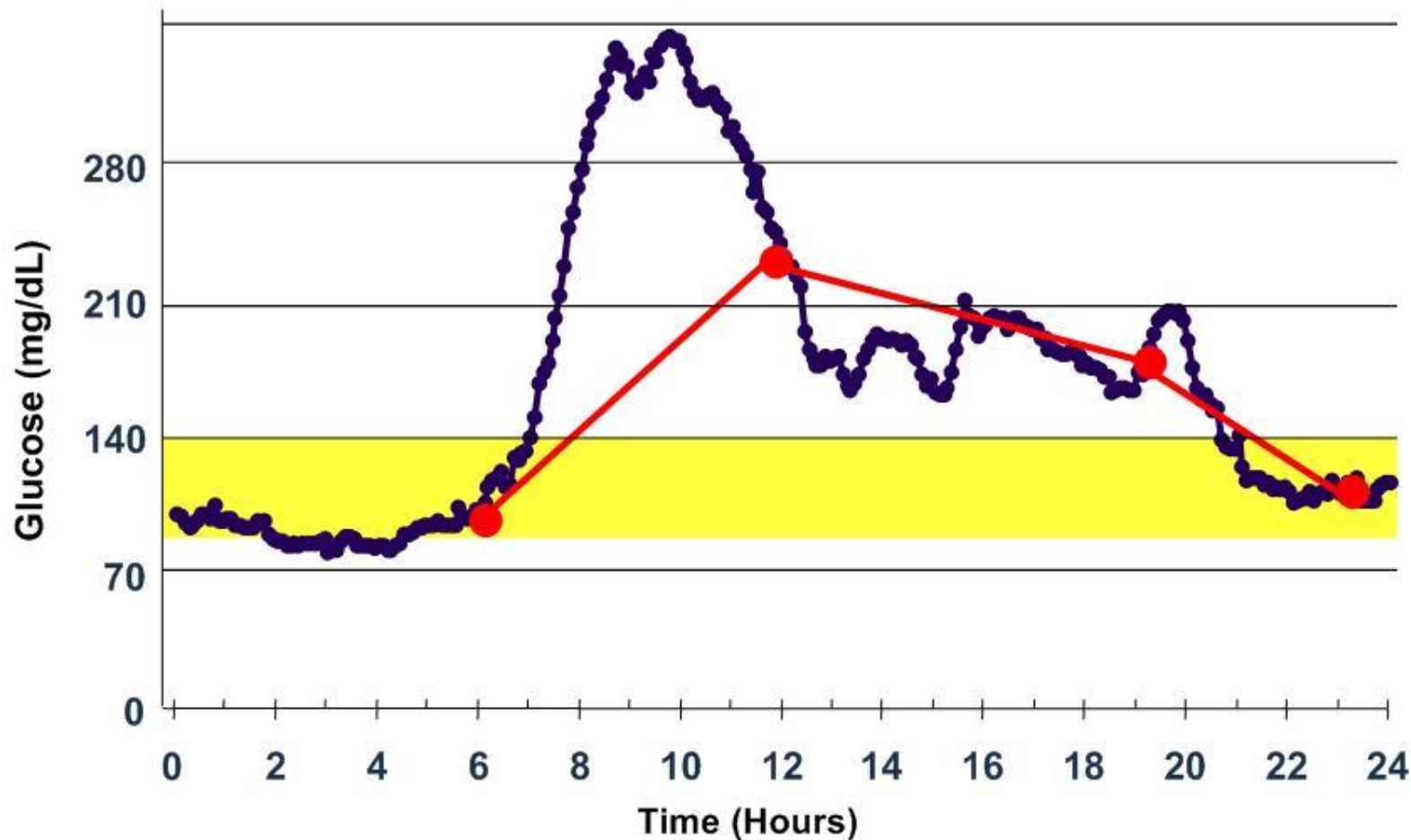
Self-test logbook



Meter



SMBG Does Not Give Patients the Whole Picture



Based on simulated data.

SMBG: A “Snapshot”

- + No information on
 - What glucose levels have been/will be
 - Direction or rate of change of glucose
- + Today, many patients do not achieve glycemic targets despite focused efforts¹



**Where Is
the Ball
Going?**



**Without Additional
Trend Information,
Patients Are Prone
to Increased
Glucose Excursions
and Increased
Hypoglycemia.**





**Continuous
Glucose
Monitoring:
Part of the
Solution**



**Help take the
blindfold off!**

CGM Provides Real-Time Information, Feedback, Warnings, Alerts

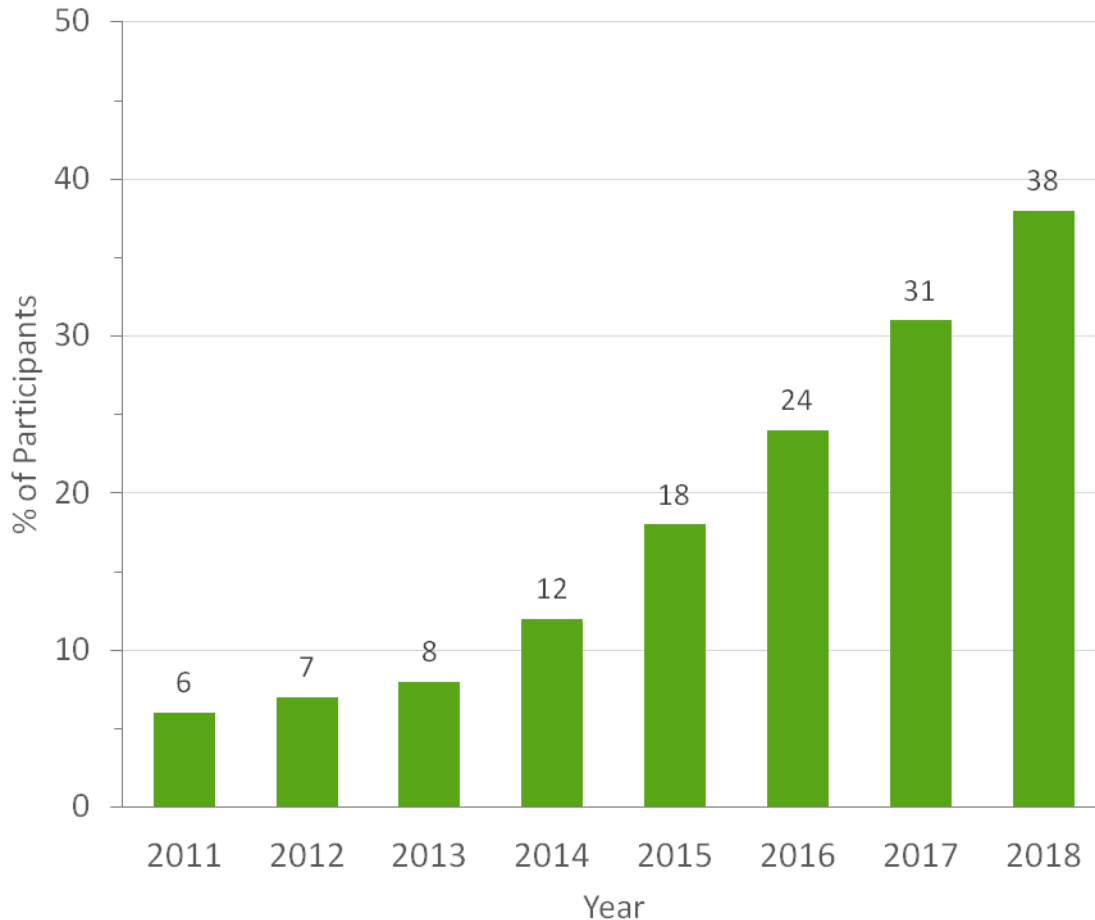
- + Both SMBG and CGM report estimates of glucose levels at a point in time
- + CGM represents a significant advance because it monitors blood glucose levels every 1 to 5 minutes and therefore also provides¹:
 - Real time information about current glucose levels, glucose direction, trends, rate of change
 - Feedback regarding effectiveness of interventions
 - Warnings when glucose levels become too high, too low or are outside of the glucose target range
 - Alerts to help preemptively avoid hypo- and hyperglycemia

1. Burge MR, et al. *Diabetes Spectrum*. 2008;21(2):112-119.

CGM Provides More Information than SMBG

- Up to 288 readings per day
- No pain
- Accurate, stable and consistent
- Glucose trends/arrow systems
- Alerts and alarms with low and high
- Remote monitoring
- AGP-based reports to visualize comprehensive glucose data

CGM use over time



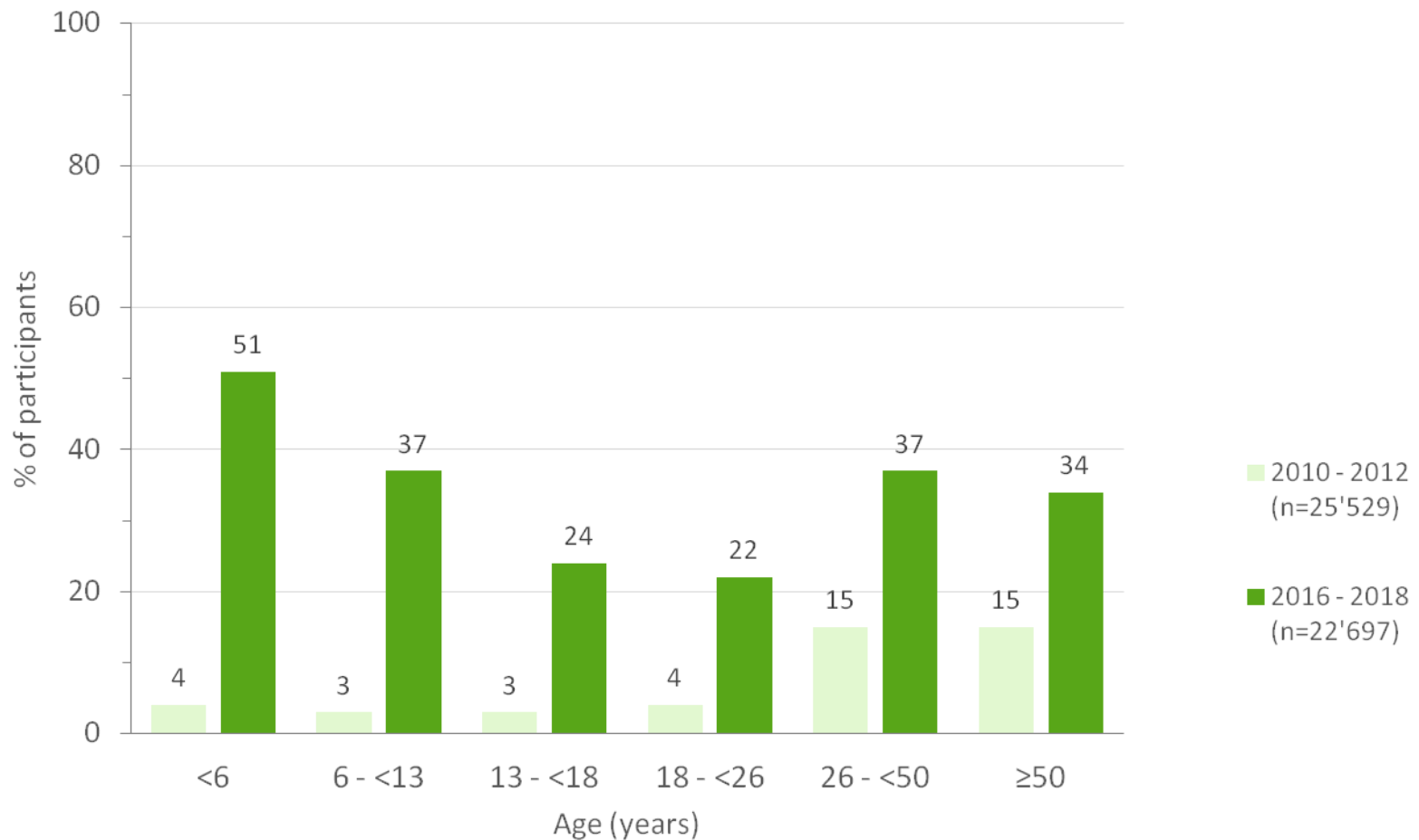
Data from 81 U.S.-based pediatric and adult endocrinology practices*.

Between 2016 and 2018 data from 22'697 individuals with T1D were collected and analysed, between 2010 and 2012 data from 25'529 participants.

77% of the 2016-2018 cohort were using a Dexcom CGM system.

*Foster N. C. et al. "State of Type 1 Diabetes Management and Outcomes from the T1D Exchange in 2016–2018". DTT (2019), Vol. 21 (2), 66-72

2010-2012 versus 2016-2018 by age groups*



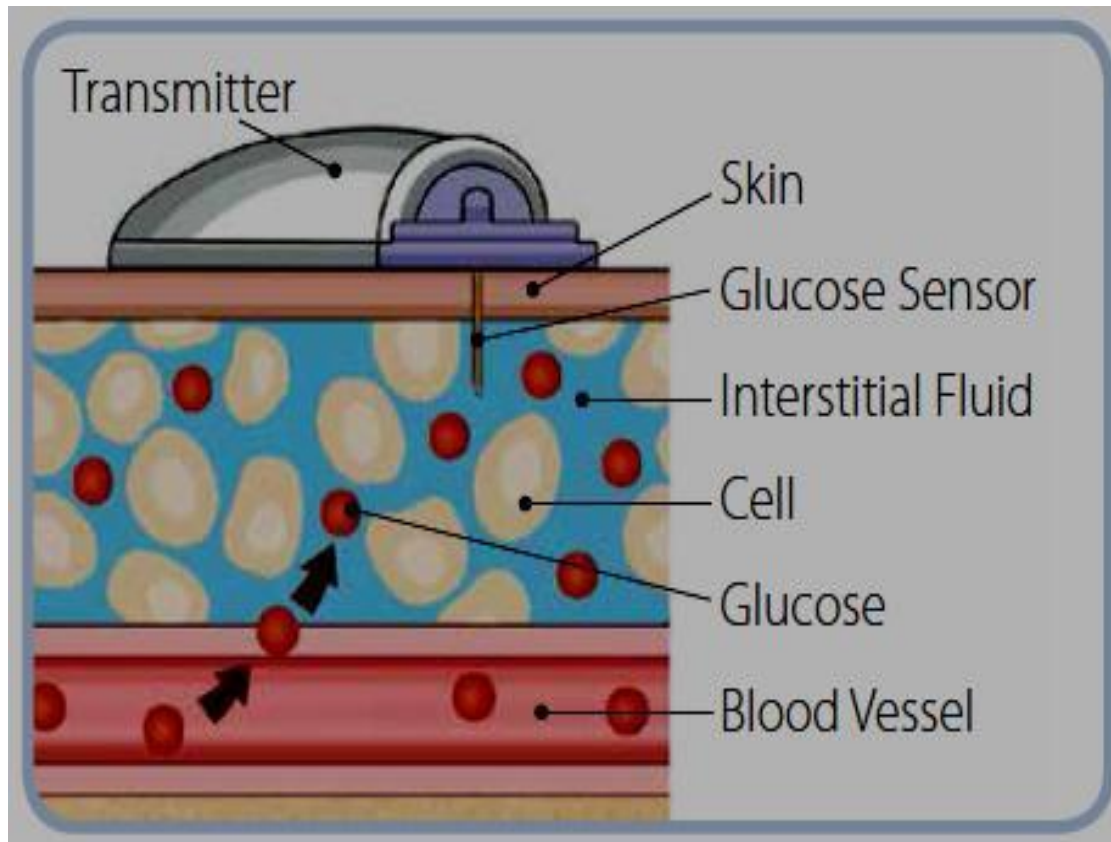
*Foster N. C. et al. "State of Type 1 Diabetes Management and Outcomes from the T1D Exchange in 2016–2018". DTT (2019), Vol. 21 (2), 66-72
7 March 2019

Availability of various CGMS



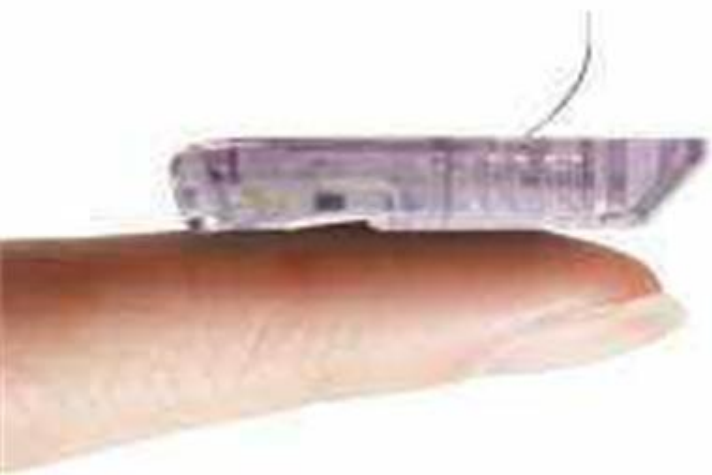
The Dexcom G4 PLATINUM System with Share and the Dexcom Share2 and Follow apps are available in the US only

- CGM Measures Interstitial Glucose related to capillary glucose
- CGM values usually lag behind blood glucose.
- There is a physiologic delay associated with the transfer of glucose from the blood to the interstitial compartments .



Continuous Glucose Monitoring Provides Full Dimensions of the Trend

- + **Sensor** inserted under the skin measures fluid in between tissues (interstitial fluid space, or ISF)
- + In the presence of glucose, a current is generated
- + Sensor is attached to a **transmitter**



Transmitter Sends Sensor Signal to a CGM Receiver



Dexcom G5 CGM System

- Stand alone CGM system
- Display devices = Receiver and/or Android or iOS smart devices
- Calibration once every 12 hours
- Confirmatory finger sticks when:
 - Symptoms do not match
 - No CGM number and arrow
 - Taking acetaminophen
- Remote monitoring
- Real-time data available to 5 users on their iPhone, iPad or iPod touch
- 7 day wear
- Approved for 2 years and older

Dexcom G6 system

- No calibration needed
- 10 - Day session duration
- Cannot restart sensor session
- Acetaminophen blocking intended for use for ages 2 and Older
- Applicator: Less Painful, Simple, Push Button Sensor Applicator Tiny Insertion Needle (26G)
- Transmitter: 30% Thinner
- Direct Transmission of CGM data to receiver & mobile device
- Receiver: Touch screen

Guardian Connect (Stand-alone CGM system) Medtronic

- No receiver; display device is iOS phone
- Predictive Alert Schedules
- 10-60 minute prediction of hypo-/ hyperglycemia based on threshold settings
- Calibration at least once every 12 hours (4x/day recommended)
- 7 day sensor use
- Acetaminophen sensitive
- Approved for 18 and older

Freestyle Libre Pro

- Flash glucose monitoring
- No calibration
- Reasonable price in comparison to other sensors
- 14 days of data



Pediatric Patients With T1DM

- Challenges of glycemic control in pediatric patients:
 - Changing insulin requirements
 - Unpredictable food intake and physical activity
 - Concerns about hypoglycemic risk
 - Close monitoring needed to recognize when the patient outgrows their insulin dose(s)¹

CGM should be considered for regular daily use in pediatric patients with T1DM who perform frequent blood glucose testing and have:²

- Severe hypoglycemic episodes
- Hypoglycemic unawareness (especially in young children)
- Nocturnal hypoglycemia
- Wide glucose excursions, regardless of A1C
- Suboptimal glycemic control, with A1C exceeding target range
- A1C levels <7%, to maintain target glycemic control while limiting hypoglycemia risk

T1DM = type 1 diabetes mellitus; A1C = glycated hemoglobin; CGM = continuous glucose monitoring.

1. Nidel S. *J Health Services Research Policy*. 2013; 2. Phillip M. *Pediatr Diabetes*. 2012;13(3):215-228.

Patient selection - 2019 ADA Standards of Care*

- rtCGM should be considered in children and adolescents with type 1 diabetes, whether using MDI or insulin pumps, as an additional tool to help improve glucose control and reduce the risk of hypoglycemia
- When used properly, rtCGM in conjunction with intensive insulin regimens is a useful tool to lower A1C in patients with type 1 diabetes who are not meeting glycemic targets
- rtCGM may be a useful tool in those with hypoglycemia unawareness and/or frequent hypoglycemic episodes
- rtCGM may be used effectively to improve A1C levels and neonatal outcomes in pregnant women with type 1 diabetes
- (flash) or isCGM use may be considered as a substitute for self-monitoring of blood glucose in children with diabetes requiring frequent glucose testing

SMBG



- **Measurement has to be carried out by patient**
- Detection of hypoglycemia only by chance
- No alarms/warnings
- Therapy management by patient (dose adjustments, correction boluses, etc.)

FGM



- **Reduces need for SMBG**
- Displays glucose trend (retrospectively)
- **Requires direct patient action (scanning)**
- No alarms / heads-up in critical metabolic situations:
 - Limited therapy support and limited prevention of hypos (compared to RT-CGM)
 - No automatic surveillance during night

rtCGM



- Direct access to glucose values (w/o patient action)
- **Alarm system: Automatic information about critical metabolic situations, also during night time**
- Prevention of hypos requires patient action following alarms

- **Option to avoid hypoglycemia automatically**
- No immediate patient reaction required, but possible

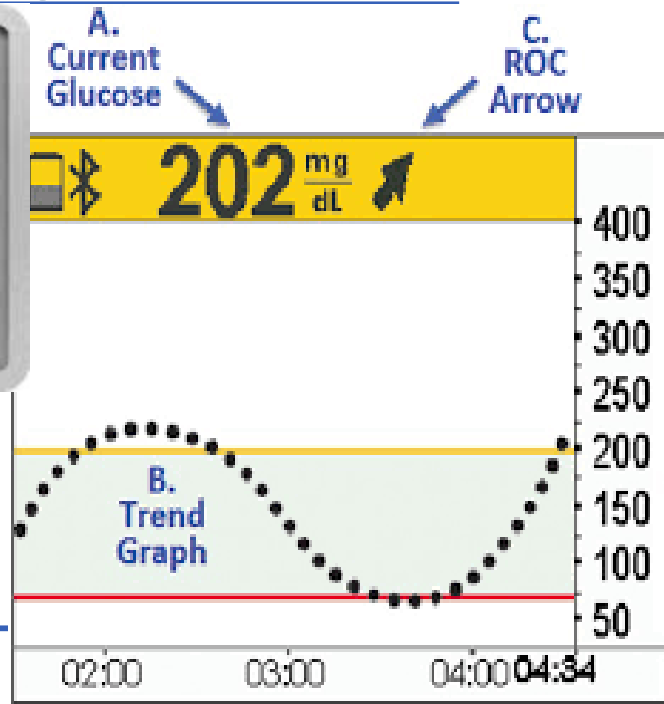
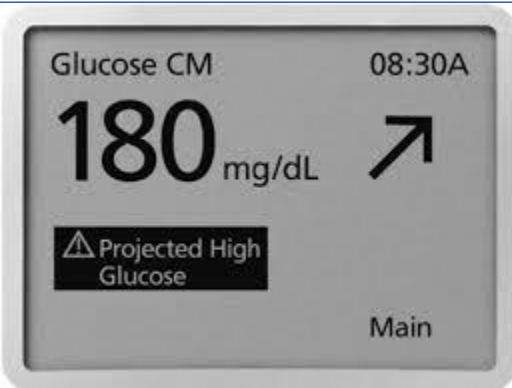
Feature	rtCGM					
	FreeStyle Libre	Dexcom G6	Dexcom G5 *	Guardian 3	Enlite	Eversense
Minimum age for use, years	≥18 (U.S.) ≥4 (ex-U.S.)	≥ 2	≥2	≥7	≥16	≥18
Indicated for use in pregnancy	No (U.S.) Yes (ex-U.S.)	No	No	No	No	No
Sensor wear time, days	10 (U.S.) ^f 14 (ex-U.S.)	10	7	7	6	≤90 (U.S.) ≤180 (ex-U.S.)
Calibration with SMBG is required	No	No	2xday	2x/day	2x/day	2x/day
Allows optional calibration	No	Yes	Yes	Yes	Yes	Yes
Warm-up period, h	12 (U.S.) ^f 1 (ex-U.S.)	2	2	2	2	24 (only upon insertion of sensor)
Insulin dosing approved without confirmatory fingerstick testing	Yes	Yes	Yes	No	No	No

Feature	FreeStyle Libre	rtCGM				
		Dexcom G6	Dexcom G5 *	Guardian 3	Enlite	Eversense
Provides trend arrows	Yes	Yes	Yes	Yes	Yes	Yes
Provides active alarms/alerts for current and impending hyperglycemia and hypoglycemia	No	Yes	Yes	Yes	Yes	Yes
Real-time remote monitoring (data sharing)	No	Yes	Yes	No	Yes	Yes
Connects with insulin pump	No	Yes	Yes	Yes	Yes	No
Interoperability with other devices	No	Yes	Yes	No	Yes	Yes
Accuracy: overall MARD, %†	9.7	9.0	9.0‡	10.6‡	16.1‡	8.8‡

Rend Arrows

Rate of Change Arrows

Gives the up-to-the-minute glucose value and a rate of change arrow



Glucose rising quickly
>2 (mg/dL)/min



Glucose going up
1 to 2 (mg/dL)/min



Fairly stable glucose
-1 to 1 (mg/dL)/min



Glucose going down
-1 to -2 (mg/dL)/min



Glucose falling quickly
>-2 (mg/dL)/min

What does “Calibration” mean?

- Calibration is a process that gives a fingerstick BG value to the CGM system so the values will align with each other
- Number of Calibrations vary by device
- Best times to calibrate are when the BG values are stable: before meals and before bed
- Do not calibrate when arrows are present

Ambulatory Glucose Profile (AGP)

- AGP is constructed from a modal day plot, which collapses glucose data over several days or weeks. The data are plotted according to time as if they occurred over 24 hours.
- AGP is a visual snapshot of a patient's typical day, revealing patterns of:
 - Hypoglycemia
 - Hyperglycemia
 - Glycemic Variability

Snapshot

18 March 2014 - 31 March 2014 (14 days)

Glucose

Estimated A1c **8.2% or 66 mmol/mol**

Logged Carbs

DAILY CARBS **221** grams/day

Logged Insulin

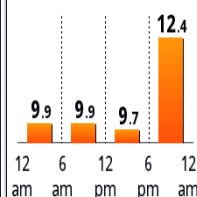
Rapid-Acting Insulin **8.8** units/day

Long-Acting Insulin **7.4** units/day

TOTAL DAILY INSULIN **16.2** units/day

Average Glucose

Average: **10.4** mmol/L



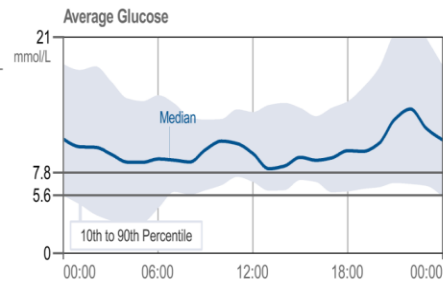
PAC: 1/7/23
DATE: 2014/04/23

AVERAGE GLUCOSE **10.4** mmol/L

% above target **73 %**

% in target **17 %**

% below target **10 %**



Time In Target

Above **73%**

In Target **17%**

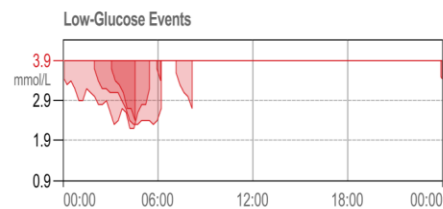
Below **10%**

Target Range
5.6-7.8 mmol/L

1827 For R&D Use Only

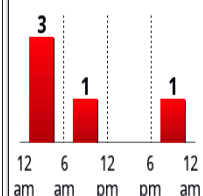
LOW-GLUCOSE EVENTS **5**

Average duration **177** Min



Low-Glucose Events

Total Events: **5**

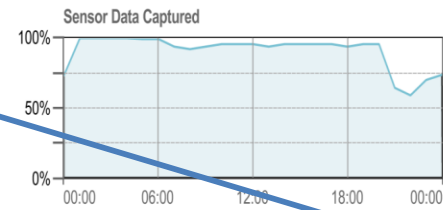


Last 14 Days

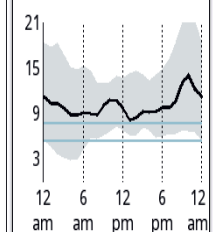
Sensor Usage

SENSOR DATA CAPTURED **92 %**

Daily scans **14**



Daily Patterns (mmol/L)



Last 14 Days

Sensor Usage

Scans Per Day **14**

Sensor data captured **92%**

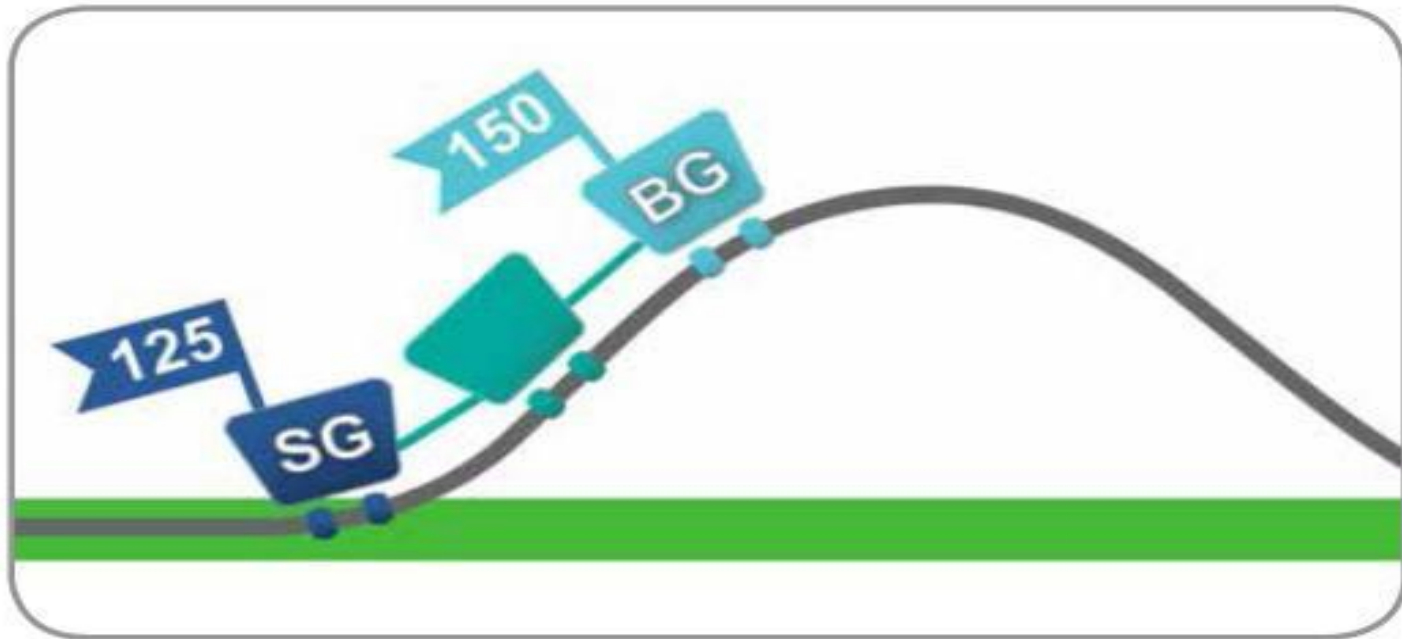
Last 14 Days

Comments

DCR1009_RAR ID#:

Limitations of CGMS

- During rapid states of change, SG and BG may differ more than 20%
- The CGM needs calibrations a minimum of twice a day (once every 12 hours)



Sensor Glucose (SG) vs. Blood Glucose(BG)

Limitations of CGMS

- Interference with glucose readings by sensor can occur with certain substances

 - i.e. glutathione, ascorbic acid, uric acid, salicylates

- Lag-time for up to 15 minutes when glucose changes rapidly

- **MARD = mean average reading deviations**

 - Overall percentage of error –near 15%

 - Guardian REAL-Time –12%
 - DexCom - 9 %
 - Navigator 12-14%



Lessons Learned From CGM Clinical Trials

- + It is difficult to achieve glycemic goals with fingersticks alone
- + Use of CGM substantially improves glycemic control without increasing hypoglycemia
- + Fear of hypoglycemia and lack of understanding about glycemic excursions keep patients from adjusting insulin dose appropriately in many instances
 - CGM helps reduce A1c without increasing hypoglycemia
- + Consistency of use on a daily basis is the most important factor for success with CGM
- + Patients with both high and low A1c values obtain clinical benefit from use of CGM

Summery

- SMBG is done sporadically and has limited patient acceptance
- rtCGM has a high level of acceptance and enables actions on predicted glucose levels in a much safer way
- To make the right treatment decisions a high level of accuracy has to be guaranteed (especially in the low glucose range)
- Only rtCGM has the potential for treatment automatisation regarding glucose homeostasis leading to semi-“closed loop”

Questions & Answers

