Technology Update 2016

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Pump update

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	Omnipod patch pump	Animas Vibe*	Medtronic 640G*	Roche Insight	CellNovo patch pump
Pump features					
Weight	25 g	105 g	96 g	122 g	30 g
Basal increment	0.05 U (0.05-30)	0.025 U (0.025-25)	0.025 U (0.025-35)	0.01 U (0.02-25)	0.05 U (0.05-30)
Basal rate/d	24 @ 30 min	12	48	24	24
Basal profiles	7	4	8	5	20
Basal deliver	0.05 u pulse	3 min	10m (0.2-60)	3 min	?0.05u pulse
Extended bolus	30 min steps up to 8 h	30 min steps up to 12 h	30 min steps up to 8 h	15 min steps up to 24 h	30 min steps up to 8 h
Bolus increments	0.05 U (max 30)	0.05 U (max 35)	0.1 U (max 75)	0.05 U (max 25)	0.05 U (max 30)
Occlusion alarm	?	1.5-3h	2-3.8h	< 2h	Max 16h
Insulin vol	200 u	200 u	300 u	160 u	170 u

*Sensor augmentation option

Patch pumps?

Cellnovo, a game changer in insulin delivery

Intuitive operation, wireless Internet connectivity and real-time tracking = all industry firsts

Disposables

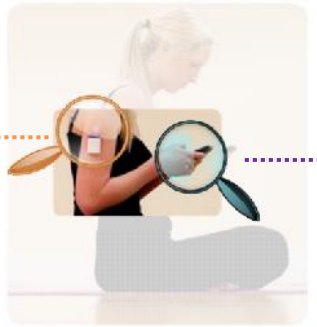
Insulin Cartridge

- The insulin reservoir
- Pumping mechanism
- Occlusion sensor

Durables

Wireless

- Pump microprocessors and memory
- Rechargeable battery
- Accelerometer
- Precision reservoir sensor



Mobile Handset

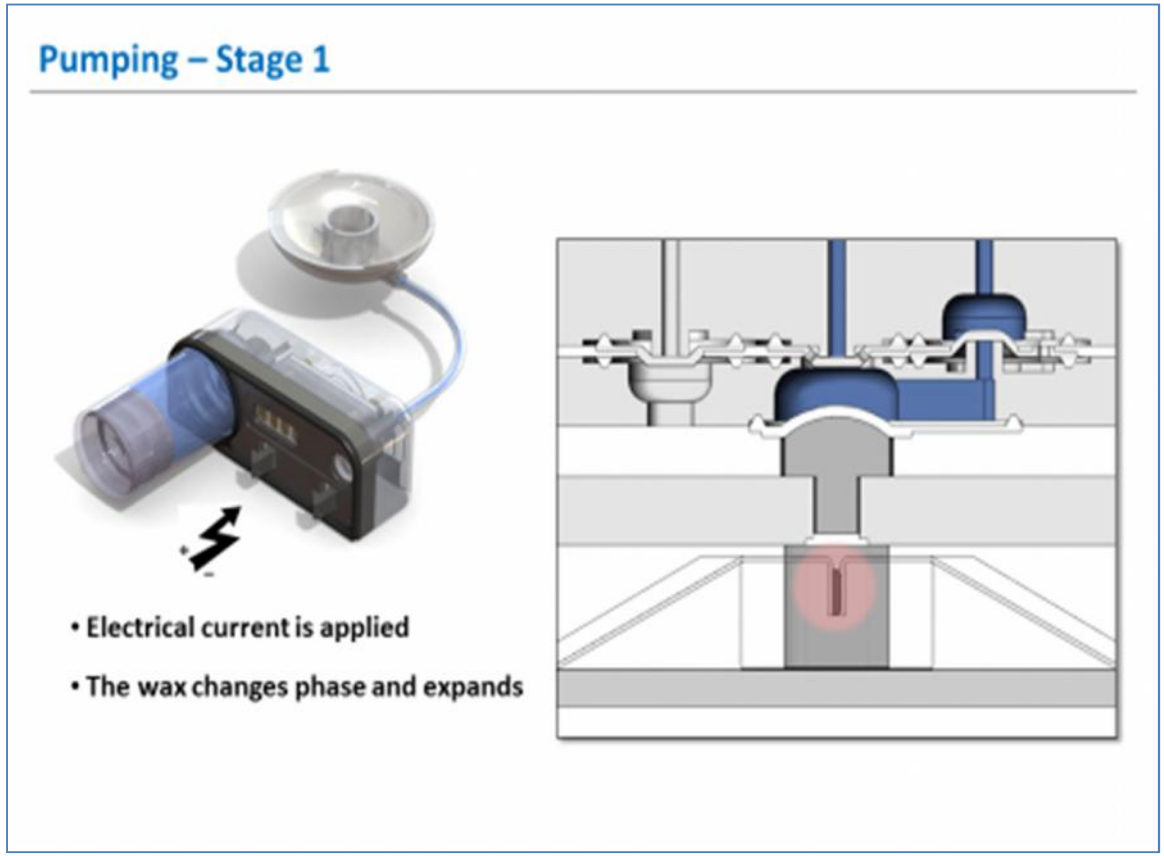
- High resolution, full colour touch screen
- GSM Modem
- Micro SD port
- Apps friendly
- BG Meter integrated, manual insertion of strips
- Insulin bolus suggestion via calculator

On-line

- Real-time data
- Automated capture of data and transmission
- Analytics and trends
- Stakeholders access

The perfect combination between a new generation of patch pump and a mobile handset to allow the best accuracy and a 24/7 health remote monitoring

How the cartridge works



Cellnovo Micro-actuator – this device is based on **heating and melting of wax**

Expansion of wax is very consistent and forces the actuation of a piston

Accuracy per pulse is very consistent, thereby ensuring accurate delivery of insulin.

Kaleido

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Bolus Patch

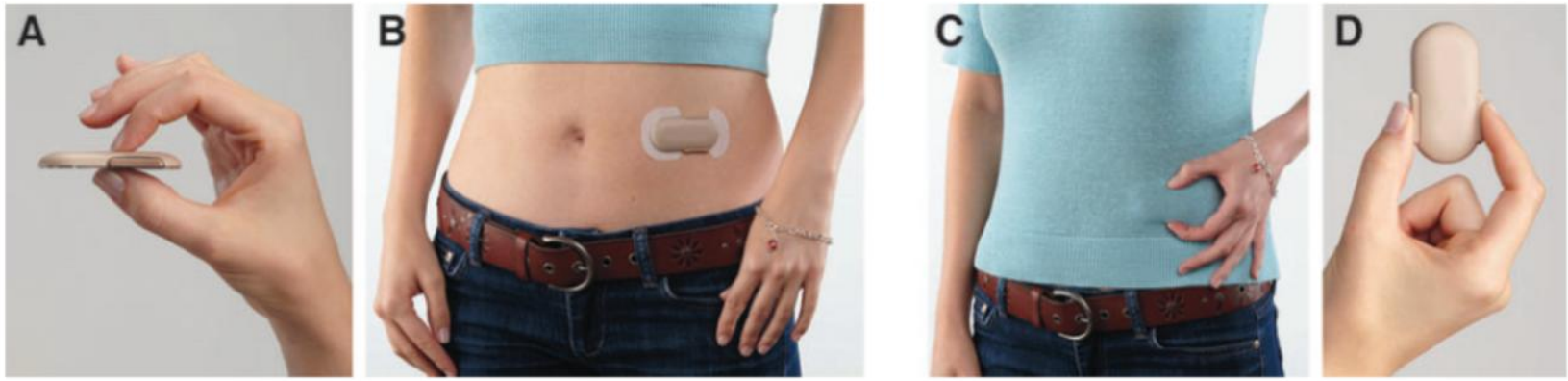

FIG. 1. Insulin bolus-patch (Finesse, Calibra Medical Inc.). (**A**) Bolus-patch size is 6×3×8 mm. (**B**) Bolus-patch is wearable for up to 3 days. (**C**) Mealtime insulin can be dosed through clothing. (**D**) Mealtime insulin is administered by actuating the buttons on both sides of the bolus-patch.

Bohannon N et al. *Diab Ther Tech* 2011;13:1031-7

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Bolus patch vs pen

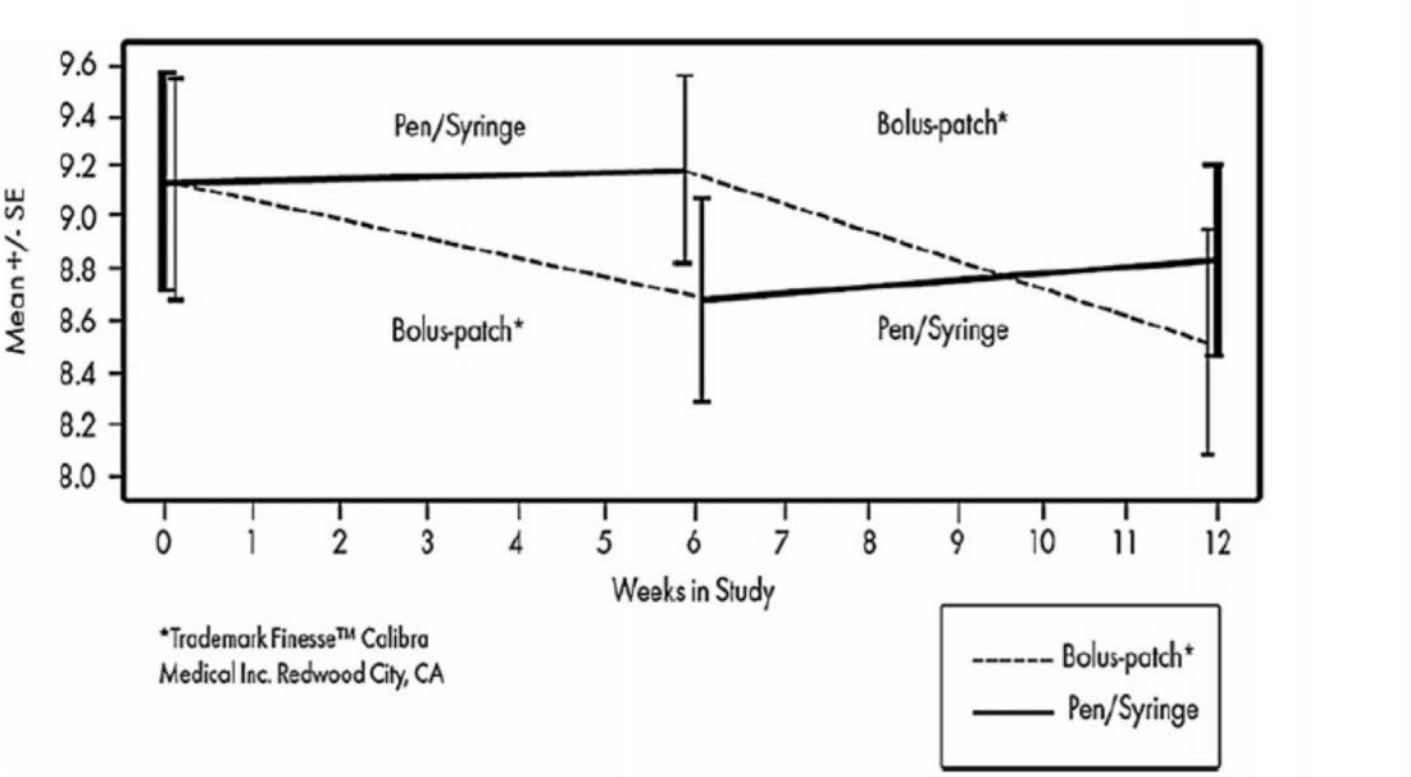

FIG. 2. Mean daily blood glucose (in mmol/L) in 38 subjects (intent-to-treat population) by treatment sequence at baseline, the 6-week crossover (end of Phase 1), and the 12-week completion (end of Phase 2). Data are mean ± SE values. The mean daily blood glucose was lower by −0.42 mmol/L using bolus-patch versus pen/syringe ($P = 0.098$). *Bolus-patch is Finesse from Calibra Medical Inc.

Bohannon N et al. *Diab Ther Tech* 2011;13:1031-7

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Adverse effects (1)

TABLE 1. CLINICAL FEATURES, TECHNOLOGY, AND INSULINS USED BY SUBJECTS COMPLETING THE SURVEY OF COMPLICATIONS OF CONTINUOUS SUBCUTANEOUS INSULIN INFUSION

Parameter	*Value*
Number of subjects	92
Age (years)	45.3 ± 12.8
Mean (range) diabetes duration (years)	28.8 ± 12.8 (2.0–67.0)
Median (range) duration of CSII (years)	3.3 (0.5–32.0)
Mean (range) duration of infusion set use (days)	3.2 ± 0.7 (2.0–6)
Pump manufacturer (% of subjects)	
Medtronic	84.8
Roche	9.8
Animas	5.4
Pump insulin (% of subjects)	
Aspart	55.8
Lispro	40.7
Glulisine	3.5
Infusion set (% of subjects)	
Medtronic Quick-Set[a]	72.0
Medtronic Mio[a]	6.5
Animas Inset[b]	5.4
ACCU-CHEK FlexLink[b]	4.3
Medtronic Silhouette[a]	4.3
Medtronic Sure-T[b]	3.2
ACCU-CHEK Tender[a]	3.2
ACCU-CHEK Rapid-D[b]	1.1

[a]Teflon.
[b]Metal.
CSII, continuous subcutaneous insulin infusion.

TABLE 2. INFUSION SET AND INFUSION SITE PROBLEMS

Problem	*%*
Infusion set	
Kinking	64.1
Frequent kinking	12
Blockage	54.3
Frequent blockage	9.8
Leakage	16.3
Infusion site	
Lipohypertrophy	26.1
Site infection	17.4
Bleeding or bruising	14.1
Pain or soreness	9.8
Adhesion problems	5.4
Irritation or itchiness	5.4

Data are percentages of all subjects reporting problem at some time during pump treatment.

Pickup JC et al. *Diab Tech Ther* 2014;16:145-149

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Adverse effects (2)

TABLE 3. RELATIVE RISK FOR INFUSION SET BLOCKAGE ASSOCIATED WITH VARIOUS FACTORS

Risk factor	*RR*	*P value*
>3 days set use with lispro	1.71 (1.03–2.85)	0.07
Insulin analog use, any duration		
Lispro	1.39 (0.95–2.10)	0.12
Aspart	0.76 (0.51–1.13)	0.27
Glulisine	0.62 (0.12–3.12)	0.60
Kinking	1.36 (0.89–2.10)	0.17
Teflon cannula use	0.76 (0.51–1.12)	0.28

RR, relative risk.

TABLE 4. PUMP PROBLEMS

Malfunction	*%*
Any pump malfunction (% of patients)	48
Types (% of all malfunctions)	
Pump stop/no delivery	26
Keypad/button problem	12
Rewind malfunction	12
Battery compartment problem	11
Belt clip broken	6
Accidental damage by user	6
Display problem	5
Software problem	5
Other (e.g., no cartridge detected, continuous alarm, O-ring leak, unknown)	17

Data are percentages of subjects reporting.

Pickup JC et al. *Diab Tech Ther* 2014;16:145-149

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Pump dosing accuracy

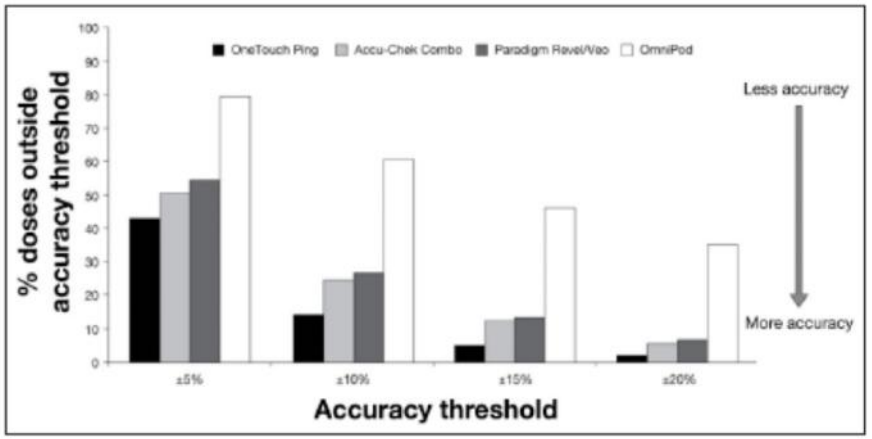

Figure 3. Single-dose accuracy. The percentage of measured deliveries (n = 12,000 for OneTouch Ping, n = 11,947 for Accu-Chek Combo, n = 11,987 for Paradigm Revel/Veo, and n = 5977 for OmniPod) that were outside the accuracy threshold of ±5%, ±10%, ±15%, and ±20% with fixed basal rate delivery. Accuracy increases with lower percentage outside threshold.

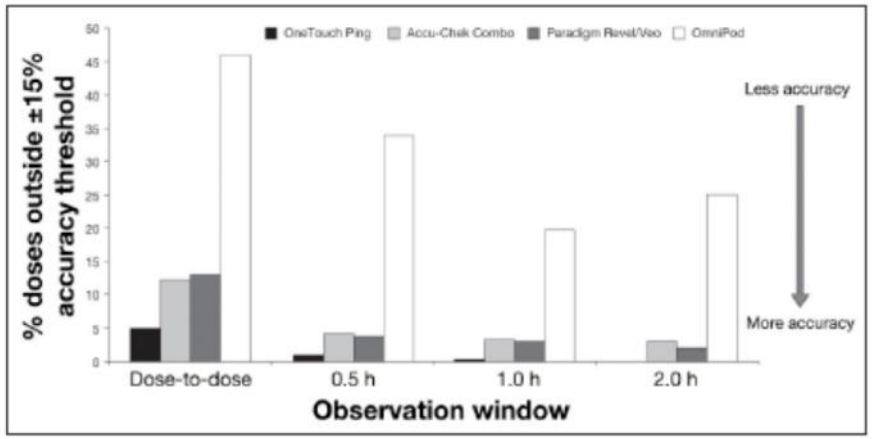

Figure 4. Averaged-dose accuracy. The graph shows the percentage of measured deliveries (n = 12,000 for OneTouch Ping, n = 11,947 for Accu-Chek Combo, n = 11,987 for Paradigm Revel/Veo, and n = 5977 for OmniPod) that were outside the accuracy threshold of ±15% averaged over the specified time interval. Accuracy increases with lower percentage outside threshold.

Jahn LG et al. *J Diab Sci Tech* 2013;7:1011-20

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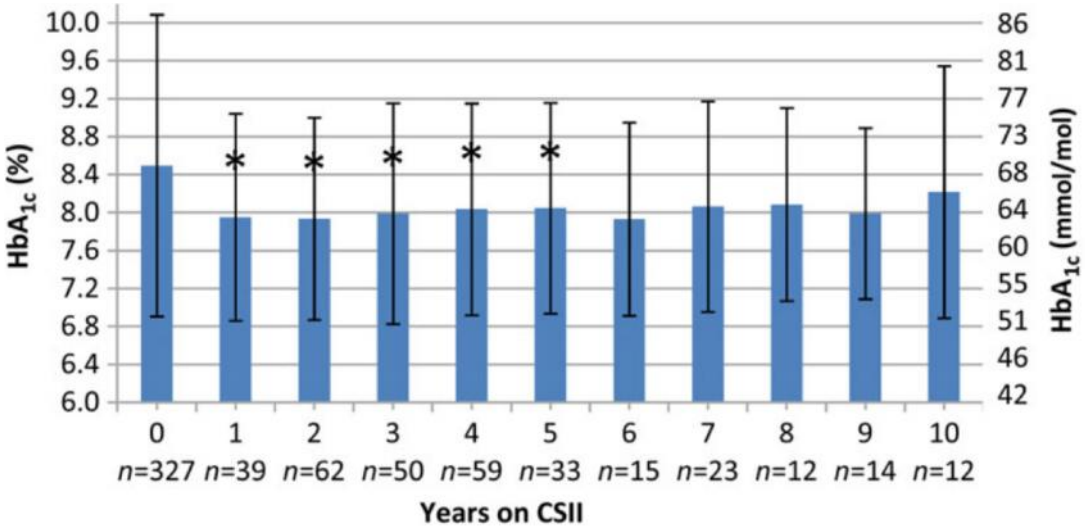
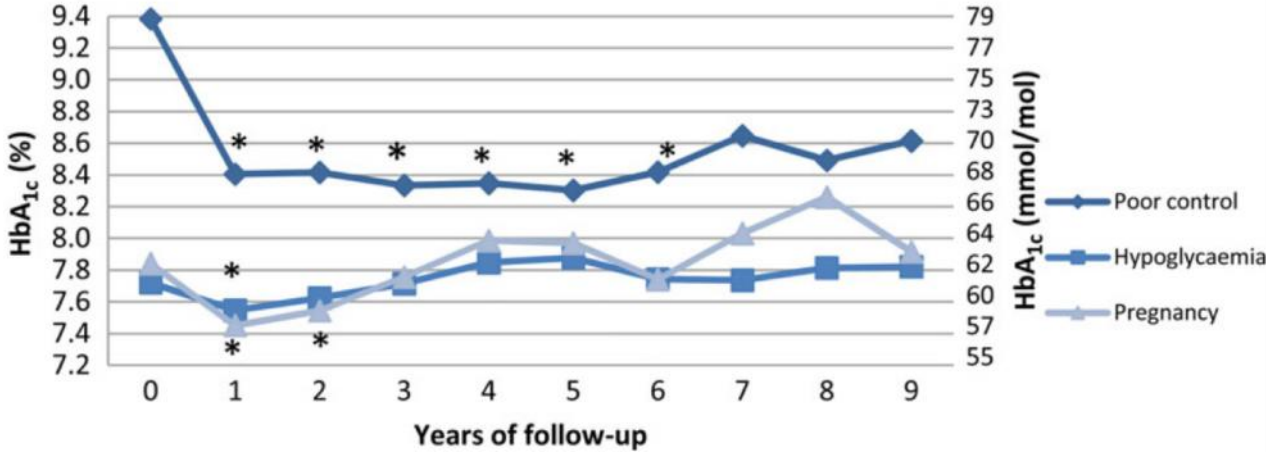
CSII: sustained improvement





Beato-Vibora P et al. *Diabet Med.* 2015;Online first

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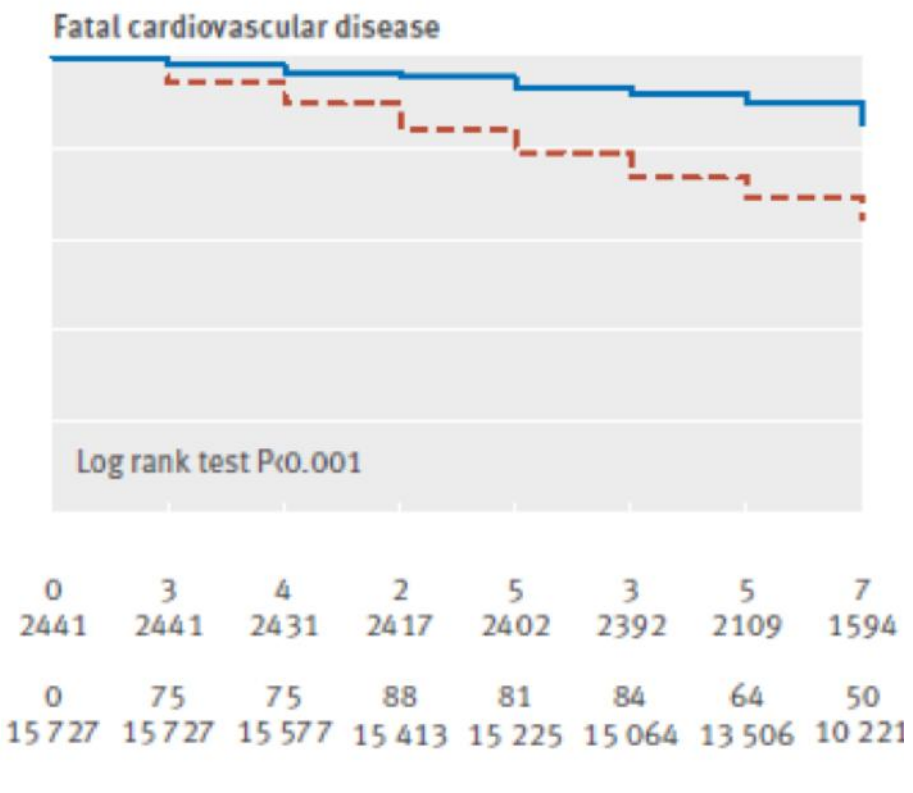
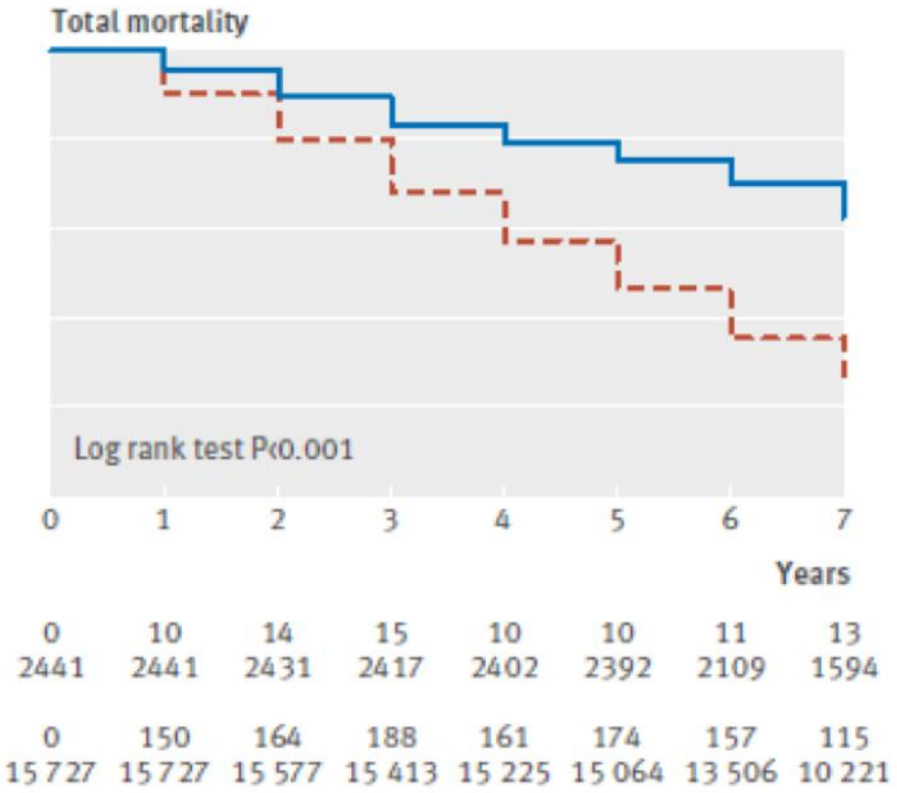
CSII and mortality





Steineck I et al. *BMJ* 2015;350:h3234

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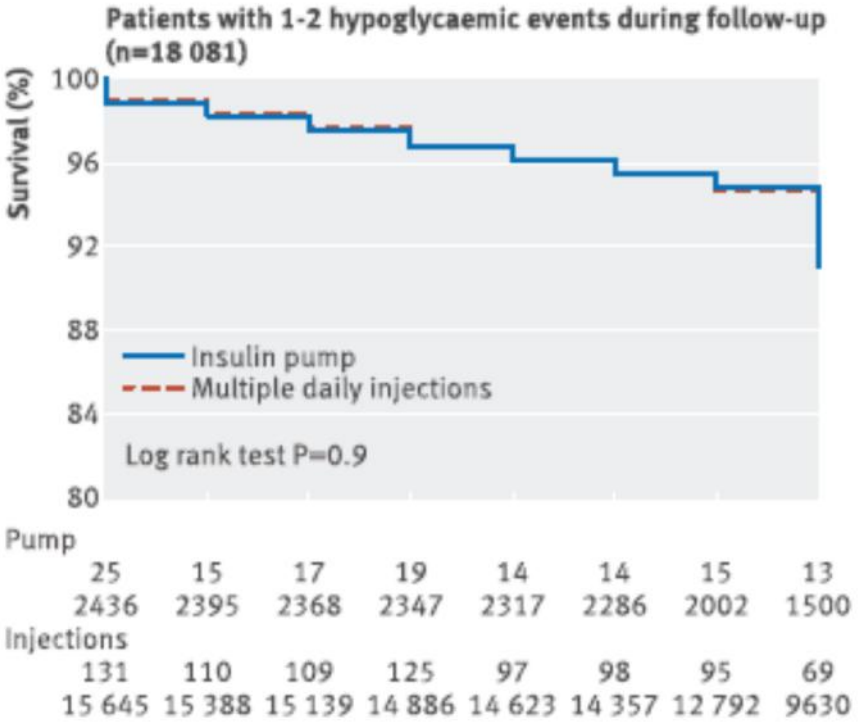
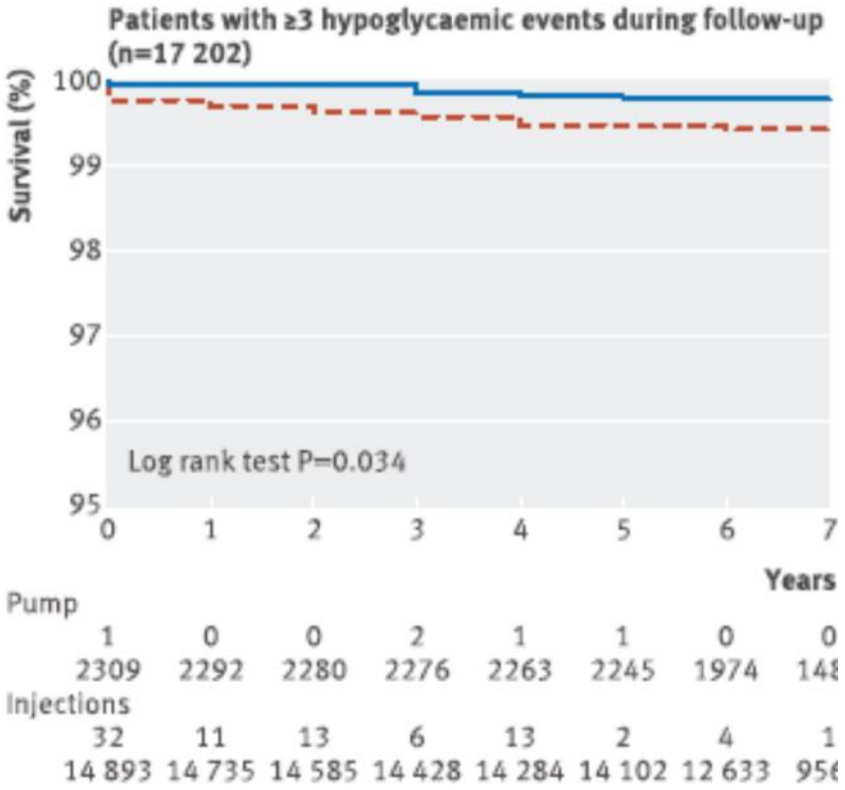
CSII and mortality

	No with events (%)	Events/1000 person years	Hazard ratio* (95% CI)	P value
Major endpoints				
Fatal/non-fatal coronary heart disease:				
MDIs	15 727/1058 (6.7)	10.7	1.0	0.05
Pump	2441/97 (4.0)	6.2	0.81 (0.66 to1.01)	
Fatal/non-fatal cardiovascular disease:				
MDIs	15 727/1294 (8.2)	13.1	1.0	0.2
Pump	2441/129 (5.3)	8.3	0.88 (0.73 to1.06)	
Fatal cardiovascular disease:				
MDIs	15 727/517 (3.3)	5.1	1.0	0.005
Pump	2441/29 (1.2)	1.8	0.58 (0.40 to 0.85)	
Total mortality:				
MDIs	15 727/1109 (7.1)	11.0	1.0	0.007
Pump	2441/83 (3.4)	5.3	0.73 (0.58 to 0.92)	
Secondary endpoints				
Fatal coronary heart disease:				
MDIs	15 727/453 (2.9)	4.5	1.0	0.004
Pump	2441/24 (1.0)	1.5	0.55 (0.36 to 0.83)	
Fatal stroke:				
MDIs	15 727/79 (0.5)	0.8	1.0	0.4
Pump	2441/5 (0.2)	0.3	0.67 (0.27 to 1.67)	
Non-cardiovascular disease mortality:				
MDIs	15 722/592 (3.8)	5.9	1.0	0.3
Pump	2441/54 (2.2)	3.4	0.86 (0.64 to 1.13)	

Steineck I et al. *BMJ* 2015;350:h3234

CSII and hypos





Steineck I et al. *BMJ* 2015;350:h3234

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OpT2mise

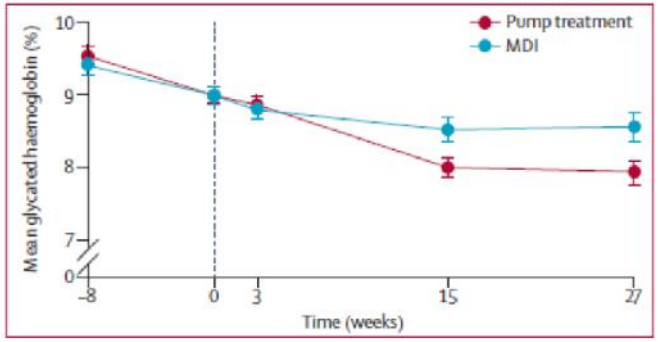


Figure 2: **Changes in glycated haemoglobin**
Error bars are 95% CIs. MDI=multiple daily injection.

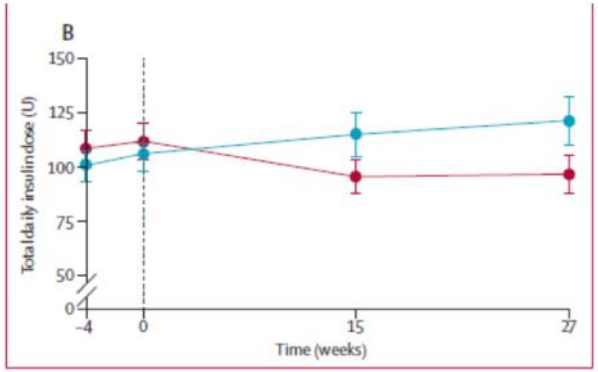
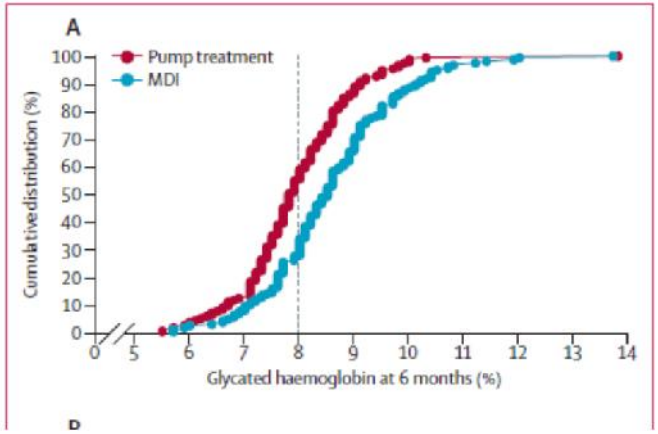


Figure 3: **Cumulative distribution of glycated haemoglobin at 6 months (A) and total daily insulin dose (B)**
Error bars are 95% CIs. MDI=multiple daily injection.



	Pump treatment	Multiple daily injection	Difference	p value
Change in 24 h mean glucose concentration (mmol/L)	−1·3 (2·4)	−0·3 (1·7)	−1·0	0·0062
AUC change >10 mmol/L (mmol/L × min)	−0·6 (1·4)	−0·1 (0·9)	−0·5	0·0047
Reduction of time spent >10 mmol/L (min)	225·6 (355·9)	56·8 (256·3)	168·7	0·0007
AUC change <3·9 mmol/L (mmol/L × min)	0·0 (0·0)	0·0 (0·1)	0·0	0·4540
Time spent <3·9 mmol/L (min)	8·8 (49·6)	5·1 (71·0)	3·7	0·7669

Data in parentheses are SD. Includes patients with at least 48 h of continuous measurement. AUC=area under the curve.

Table 2: **Glycaemic control in each treatment group**

Reznik Y et al, *Lancet* 2014;published online July 3rd

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CGM update

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NG17: CGM

- Do not offer real-time continuous glucose monitoring routinely to adults with type 1 diabetes.

- Consider real-time continuous glucose monitoring for adults with type 1 diabetes who are willing to commit to using it at least 70% of the time and to calibrate it as needed, and who have any of the following despite optimised use of insulin therapy and conventional blood glucose monitoring:
  - More than 1 episode a year of severe hypoglycaemia with no obviously preventable precipitating cause.
  - Complete loss of awareness of hypoglycaemia.
  - Frequent (more than 2 episodes a week) asymptomatic hypoglycaemia that is causing problems with daily activities.
  - Extreme fear of hypoglycaemia.
  - Hyperglycaemia (HbA1c level of 75 mmol/mol [9%] or higher) that persists despite testing at least 10 times a day (see recommendations 1.6.11 and 1.6.12). Continue real-time continuous glucose monitoring only if HbA1c can be sustained at or below 53 mmol/mol (7%) and/or there has been a fall in HbA1c of 27 mmol/mol (2.5%) or more

	Guardian RT	640G Smart guard	DexCom G4 Platinum	Freestyle Navigator II
				
Sensor life	6 days		7 days	5 days
Alarms	Multiple		1 high, low and trend	High, low and projected
Predictive	Yes		No	Yes
Trends	Yes		Yes	Yes
Rate change	Yes		No	Yes
Calibration	12 hrly		2h, then 12 hrly	1, 2, 10, 24, 72 h
MARD	13%		12.6%	11.8%

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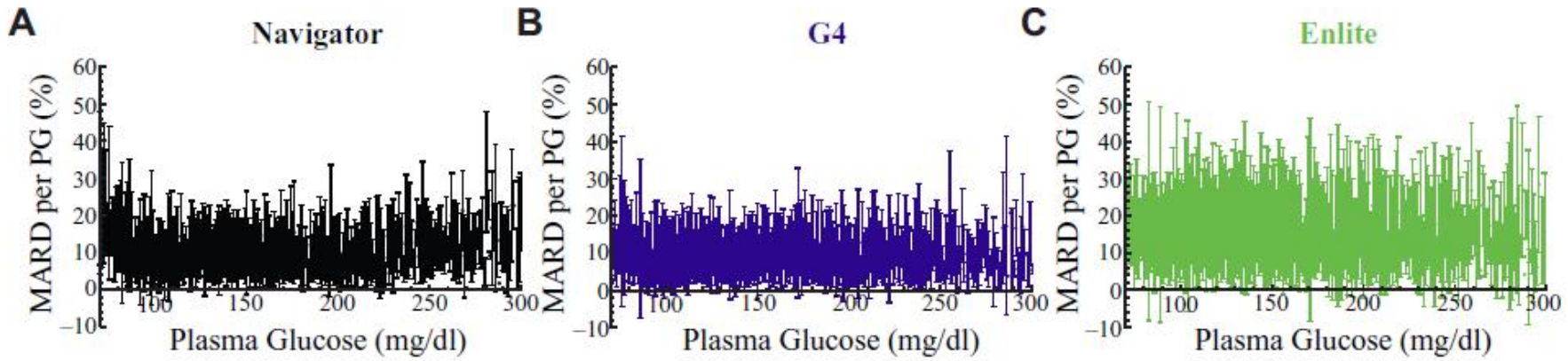
MARD

Mean Absolute Relative Difference

- Measured as the difference between sensor and reference blood glucose values taken at the same time, expressed as a percentage.
- The lower the MARD, the more accurate a sensor glucose value is considered.
- It is an average of all the readings
- It is the industry standard for CGM accuracy

MARD Ranges



Page 704.

Journal of Diabetes Science and Technology 8.4 (2014): 699-708.

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G4 vs Enlite (1)

- Over 6 days Dexcom did not display data over six days for 13 minutes, Enlite for 98.2 minutes.
- Dexcom had “greater accuracy in the hypoglycemic and euglycemic ranges.”

*Matuleviciene et al "Diabe Tech Ther.2014;16:*Web.

G4 vs Enlite (2)

1) Patients preferred G4 in their daily lives. (79.1 vs. 42.1 Enlite).

2) Patients prefer G4 Platinum over Enlite in 12 out of 13 categories,so tend to wear it more and get better results.

3) Greater accuracy in the hypoglycemic and euglycemic range for more optimal insulin dosing; more false alarms with Enlite.

*Matuleviciene et al "Diabe Tech Ther.2014;16:*Web.

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Trend accuracy

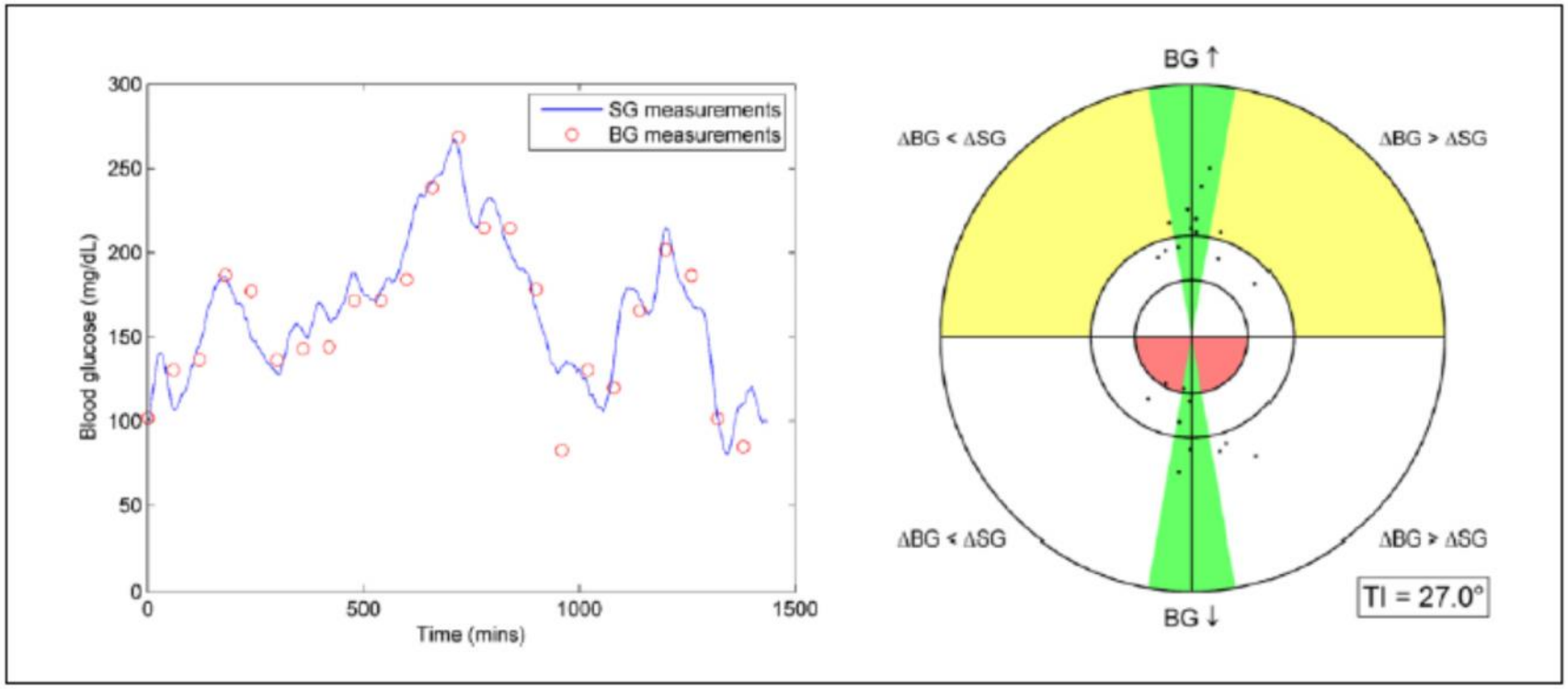

Figure 6. (left) BG and SG measurements for a variable patient with high sensor error. (right) Trend Compass plot for this data set with TI metric.

Signal M et al. *J Diab Sci Tech.* 2014;8:986-997

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CBG meter accuracy

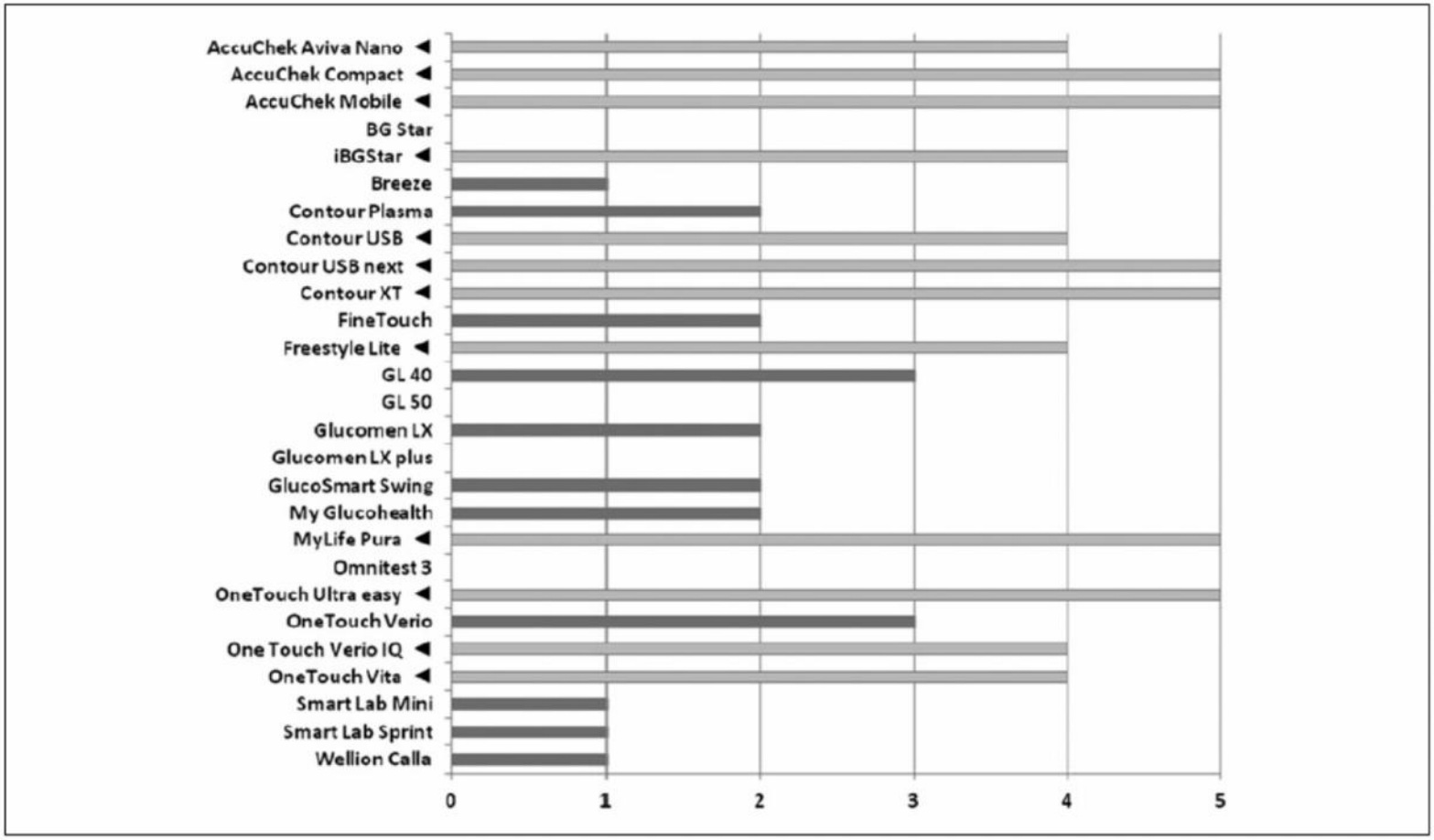

Figure 2. Number of BG ranges in which the new accuracy limits were met. Triangles mark GMS that fulfilled overall accuracy requirements shown in Table I.

Hasslacher C et al. *J Diab Sci Tech.* 2014;8:466-72

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CBG meter MARD

TABLE 1. MEAN ABSOLUTE DIFFERENCE AND MEAN ABSOLUTE RELATIVE DIFFERENCE BETWEEN MEASUREMENTS WITH THE DIFFERENT BLOOD GLUCOSE METERS AND THE YSI 2300

	Mean bias		*MARD*				
Blood glucose meter	*mg/dL*	*%*	*%*	*95% CI*	*SD (%)*	*Subjects* (n)	*Measurements* (n)
FreeStyle Lite FreeStyle	0.8	1.0	4.9	4.1 to 5.7	7.5	240	480
Freedom Lite	0.3	1.0	5.5	4.8 to 6.3	8.5	244	488
Accu-Chek Aviva	7.2	5.3	6.8	6.1 to 7.6	7.5	252	504
Contour	−1.2	−0.2	9.0	8.3 to 9.8	12.0	255	510
OneTouch UltraEasy	6.3	4.6	9.7	8.9 to 10.4	12.1	246	492

CI, confidence interval; MARD, mean absolute relative difference; *n*, number.

Tack C et al. *Diab Ther Tech* 2012;14:330-7

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Flash glucose sensing: Freestyle Libre

The FreeStyle Libre reader

The FreeStyle Libre sensor

The FreeStyle Libre software

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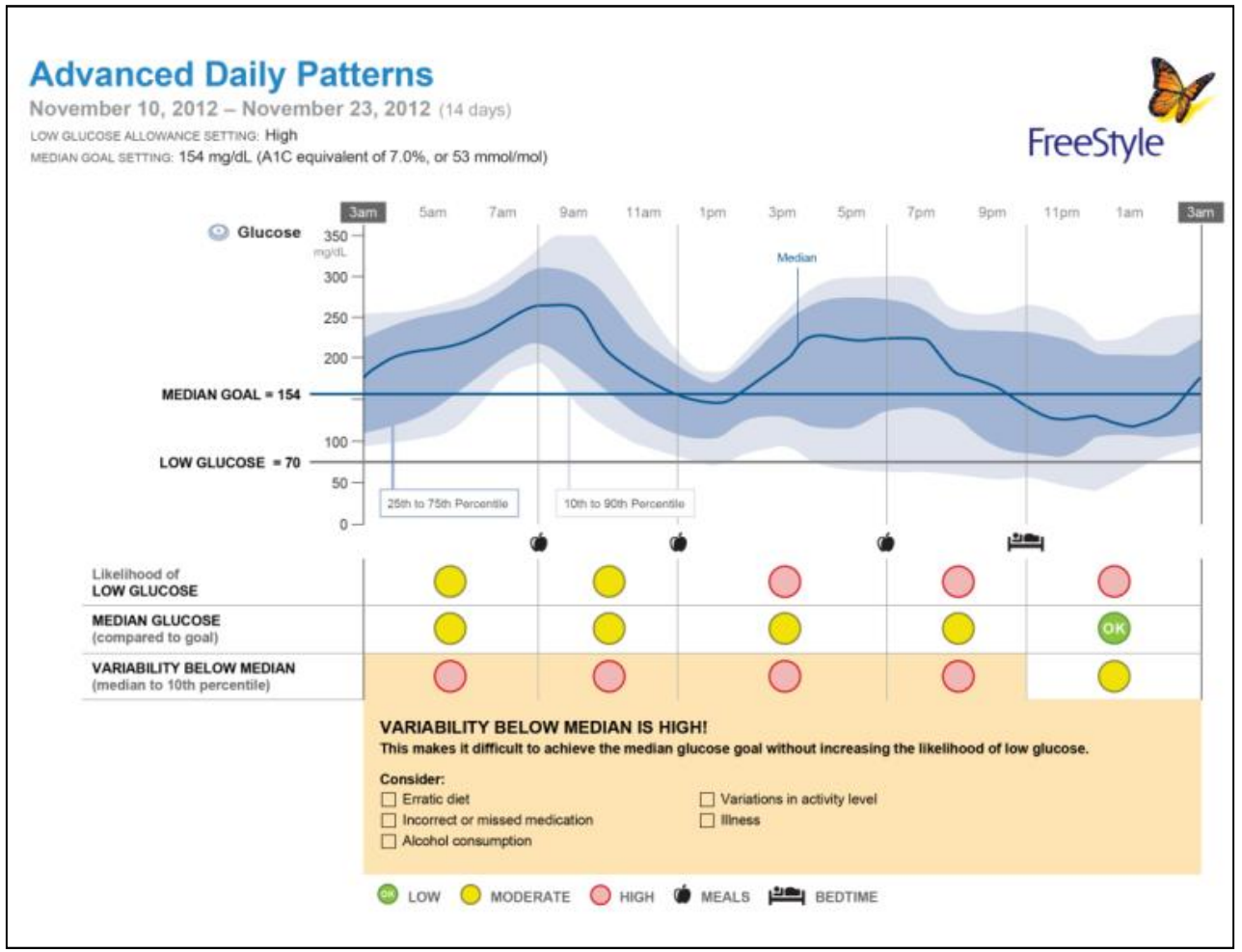
Advanced Daily Patterns



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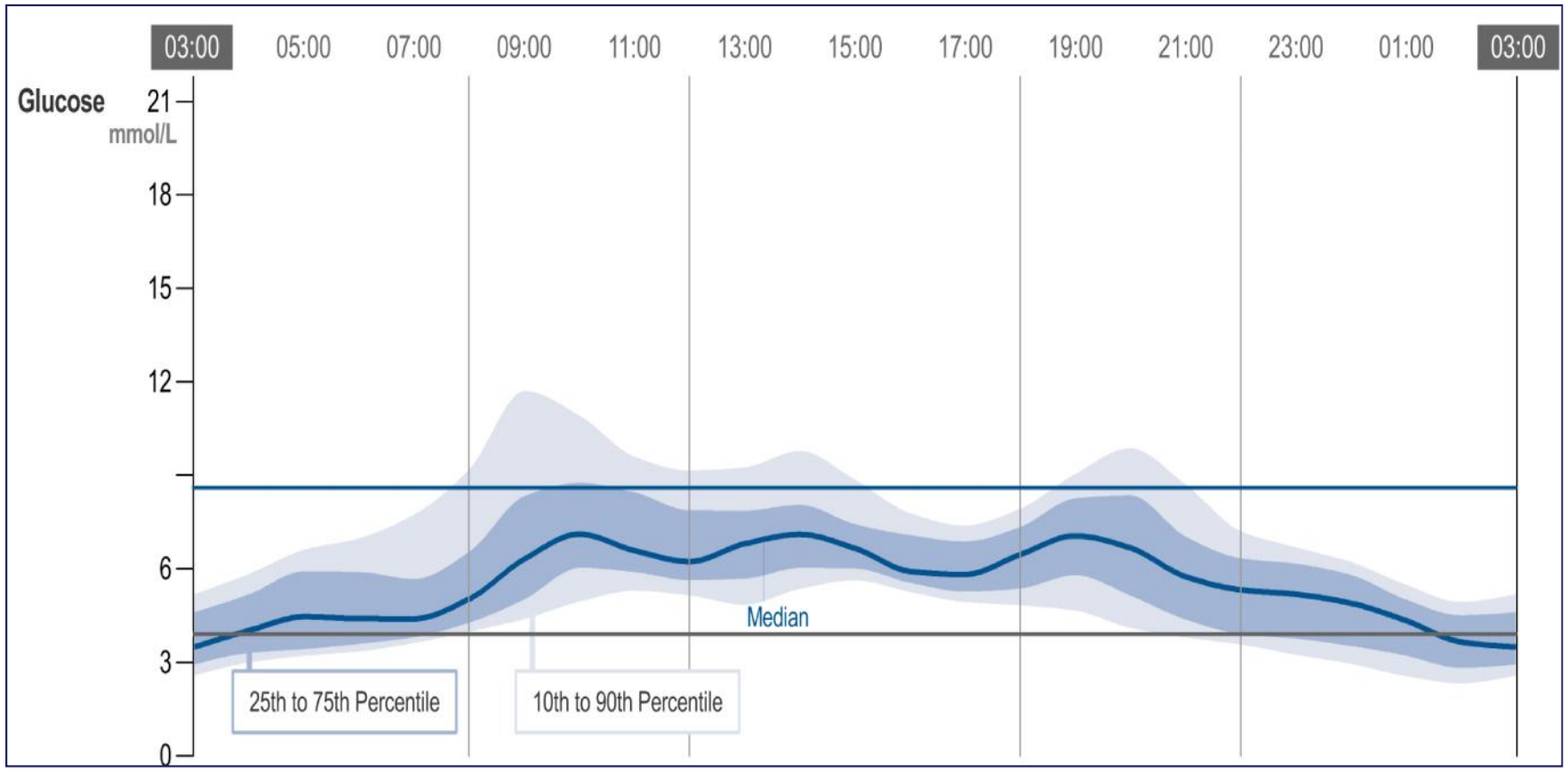
Ambulatory glucose profile (AGP)



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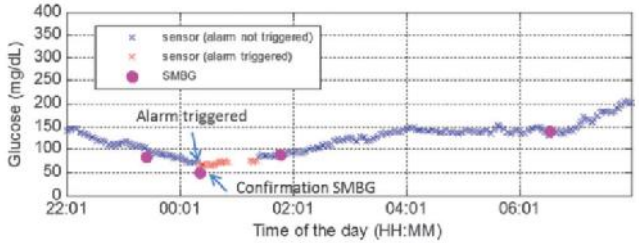
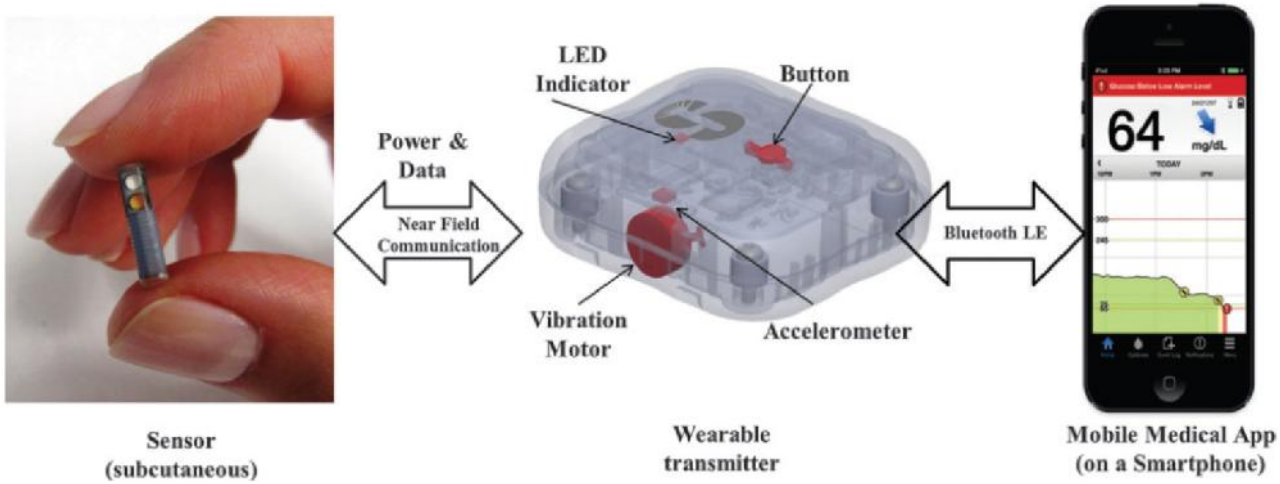
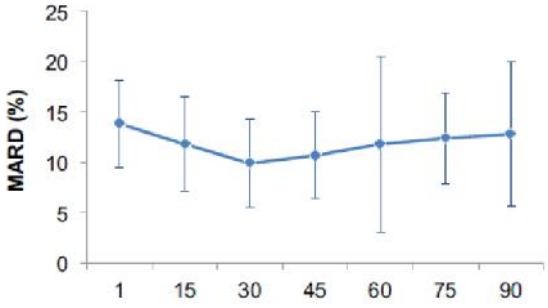
Implantable sensor



Reference glucose range (mg/dl)	Number of paired system-reference readings	MARD[a]/MAD[b]
≤70	116	9.6 mg/dl
71-180	2101	11.4%
>180	1369	11.0%





DeHennis A et al. *J Diab Sci Tech* 2015;9:951-6; Want et al. *Diabet Ther Tech 2015;17(10):1-7*

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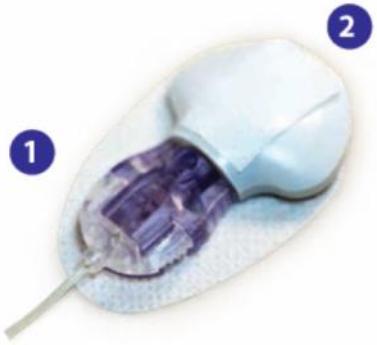
Medtronic DUO



The transmitter must be within 6 feet (183 centimeters) of the insulin pump in order to communicate sensor readings.

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Predictive low glucose suspend

Medtronic 640G Smart Guard

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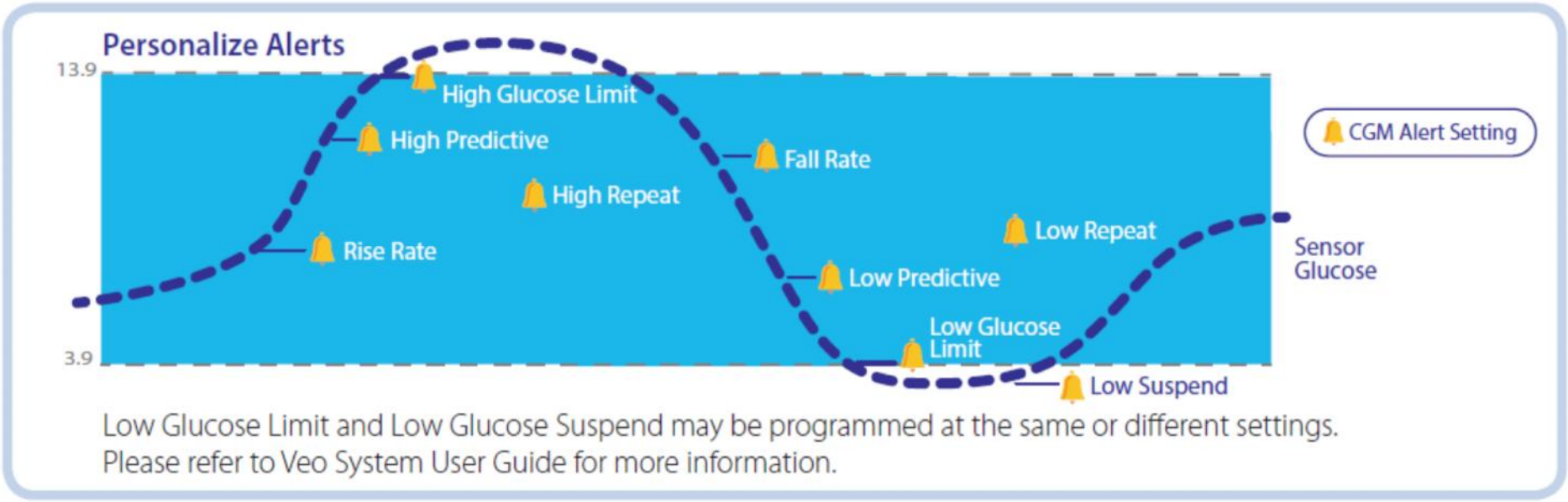


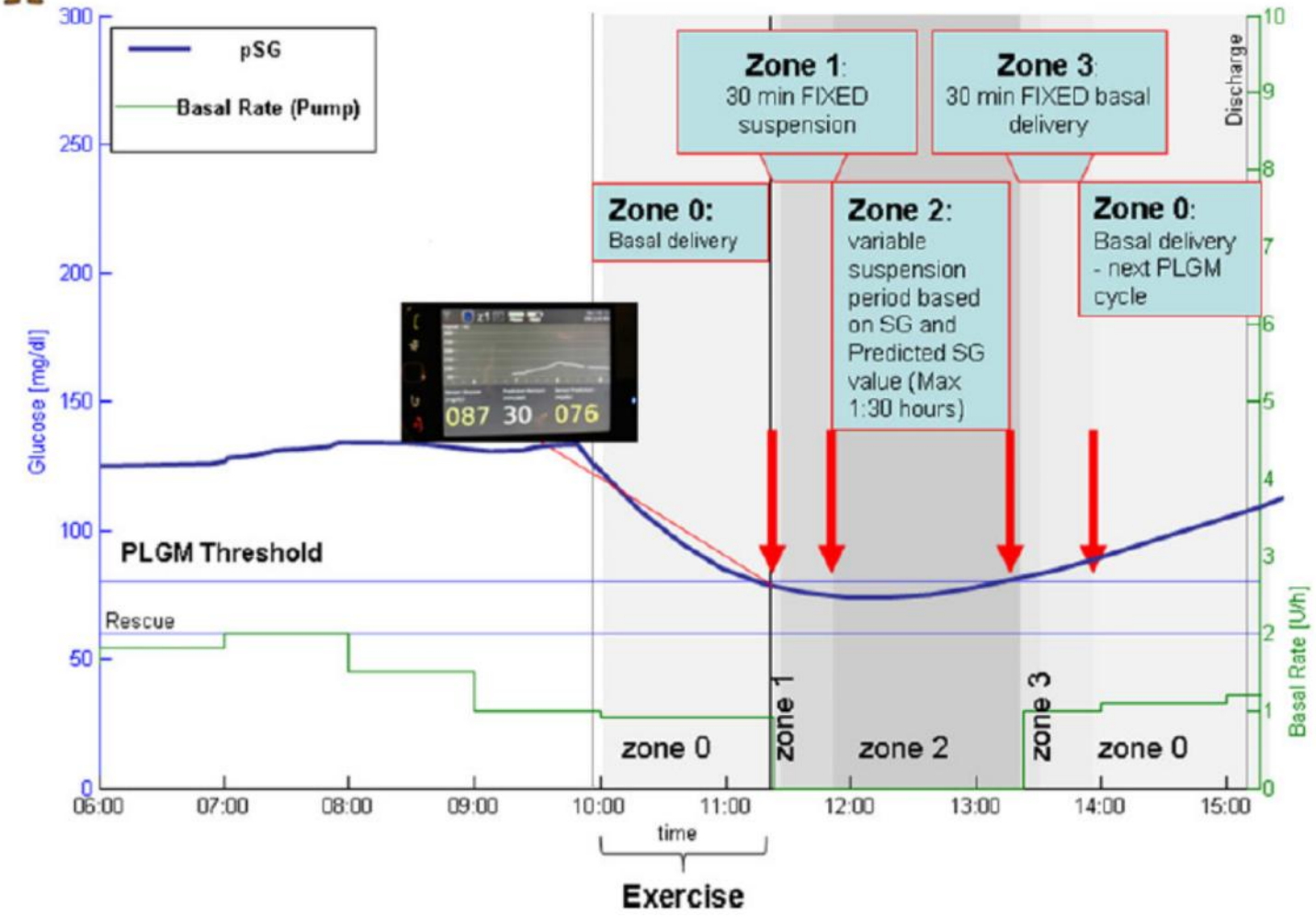
Low Glucose Limit and Low Glucose Suspend may be programmed at the same or different settings.
Please refer to Veo System User Guide for more information.

Predictive low glucose suspend

- Insulin infusion suspended when BG falling and anticipated to be 0.5 mmol/l above hypoglycaemia threshold within 30 minutes
- Insulin infusion suspended for up to 120 minutes but restarts automatically when BG rises 0.5 mmol/l above hypoglycaemia threshold

PILGRIM

PredIctive Low Glucose Management in Realtime Sensing Insulin PuMp Therapy



Danne T *et al* *Diab Tech Ther* 2014;16:6 (online)

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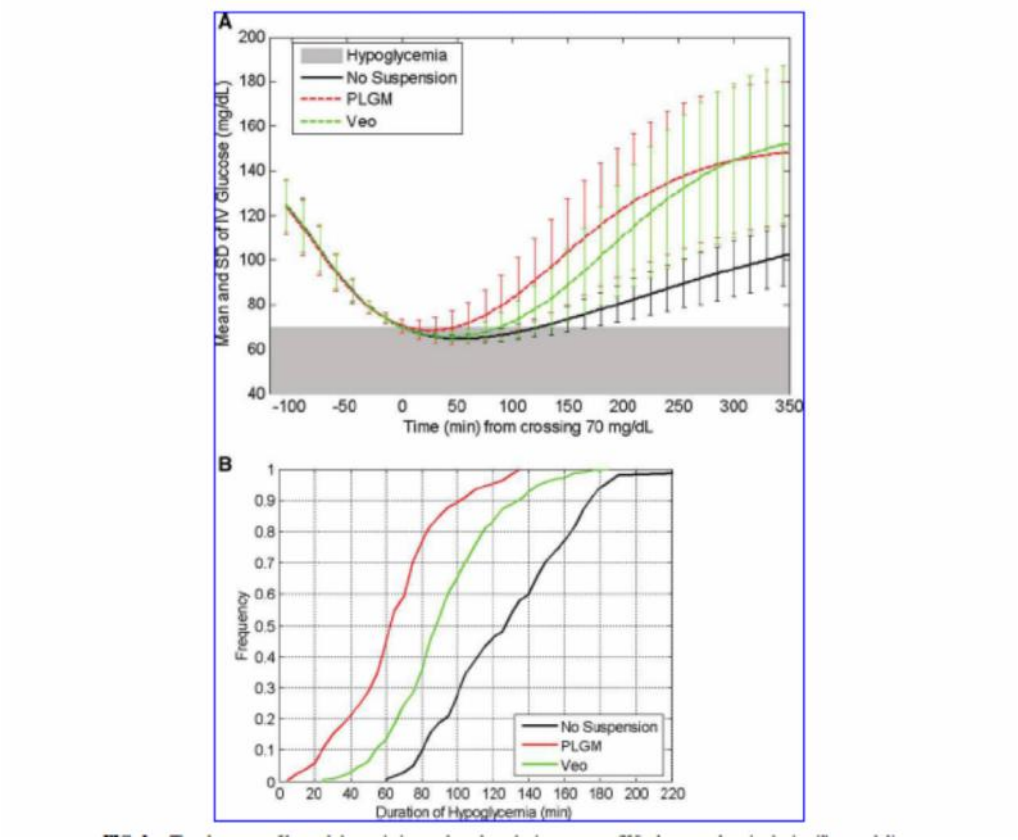
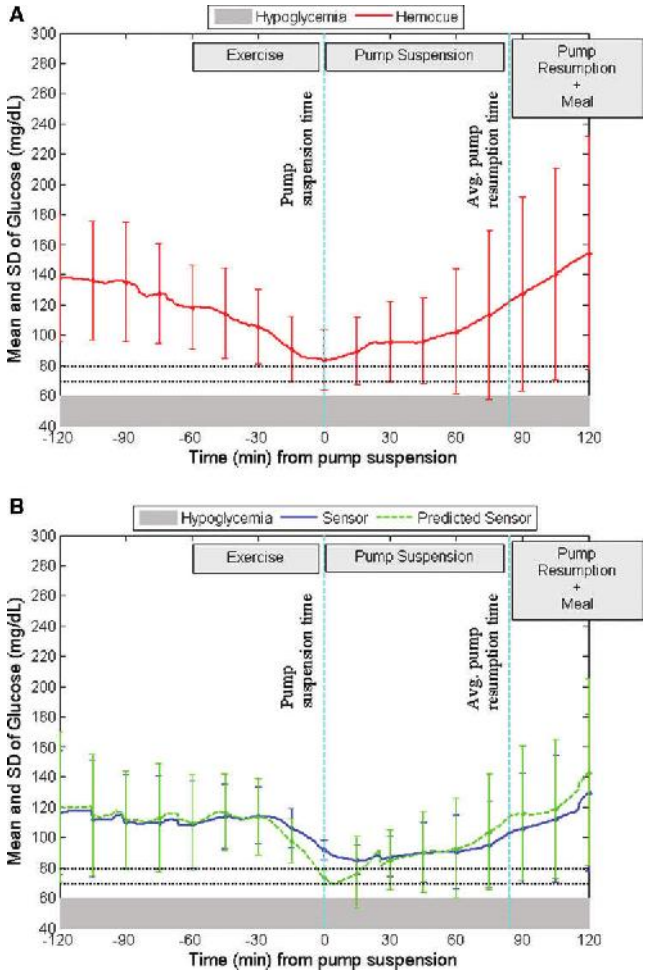
PILGRIM





80% hypoglycaemia prevention with exercise

Danne T *et al Diab Tech Ther* 2014;16:6 (online)

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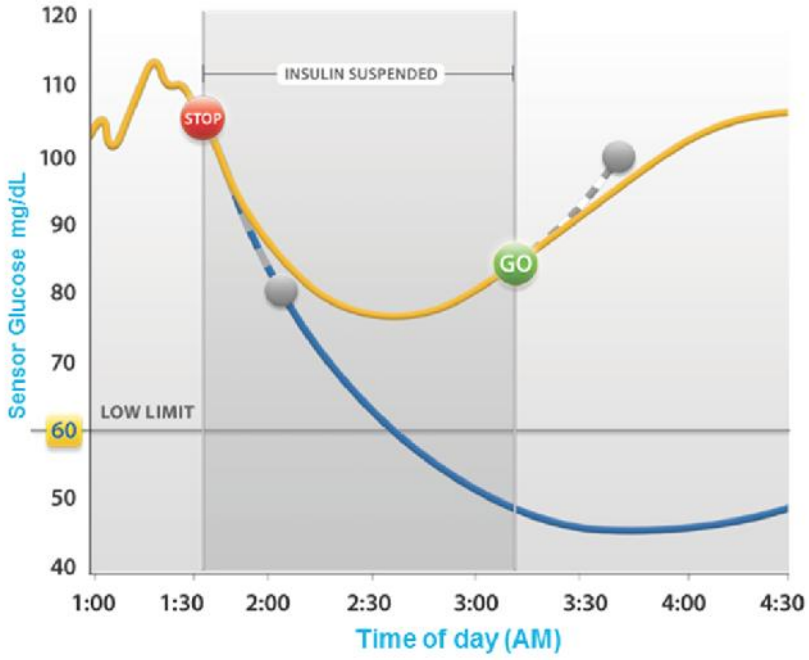
SmartGuard
Concept

The SmartGuard technology has been designed to help protect from hypoglycaemia and avoid the hyperglycemic rebound.

How SmartGuard™ Works



Once resumed manually or based on sensor glucose, basal insulin delivery will not be resuspended for a minimum of 30 minutes.

STOP **SmartGuard™ suspends** basal delivery to reduce hypoglycaemia if sensor glucose is:

- Less than 70 mg/dL above the low limit AND
- Predicted to approach the low limit within 30 minutes

GO Suspended basal insulin delivery can **resume** if:

- Your patient manually resumes OR
- Sensor glucose is above the low limit and trending upward and insulin delivery has been suspended for a minimum of 30 minutes OR
- Insulin delivery has been suspended for 2 hours

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SmartGuard in Action: Managing Hypoglycemia

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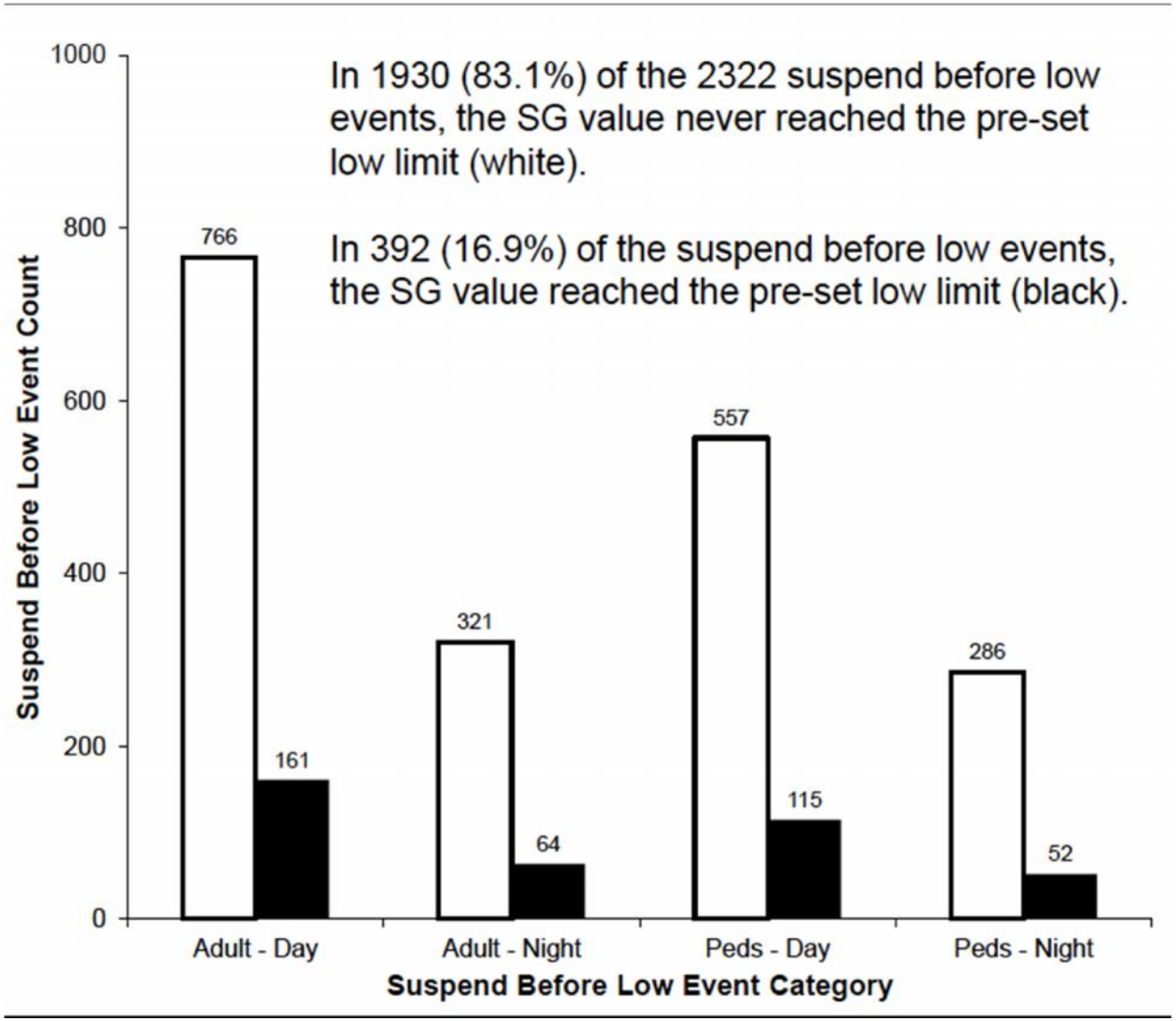
Predictive suspend events



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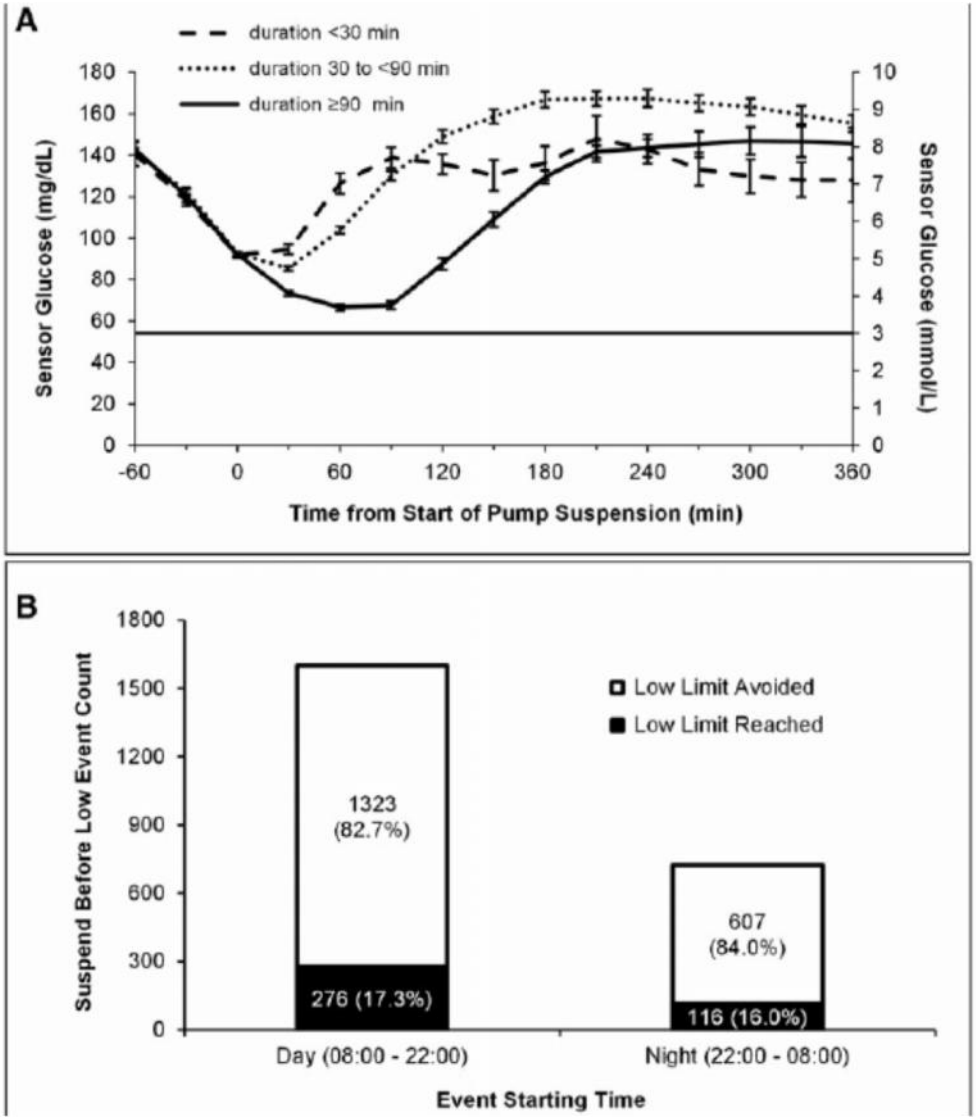
640G – hypo avoidance



Choudhary P et al. *Diab Ther Tech* 2016;e pub ahead of print

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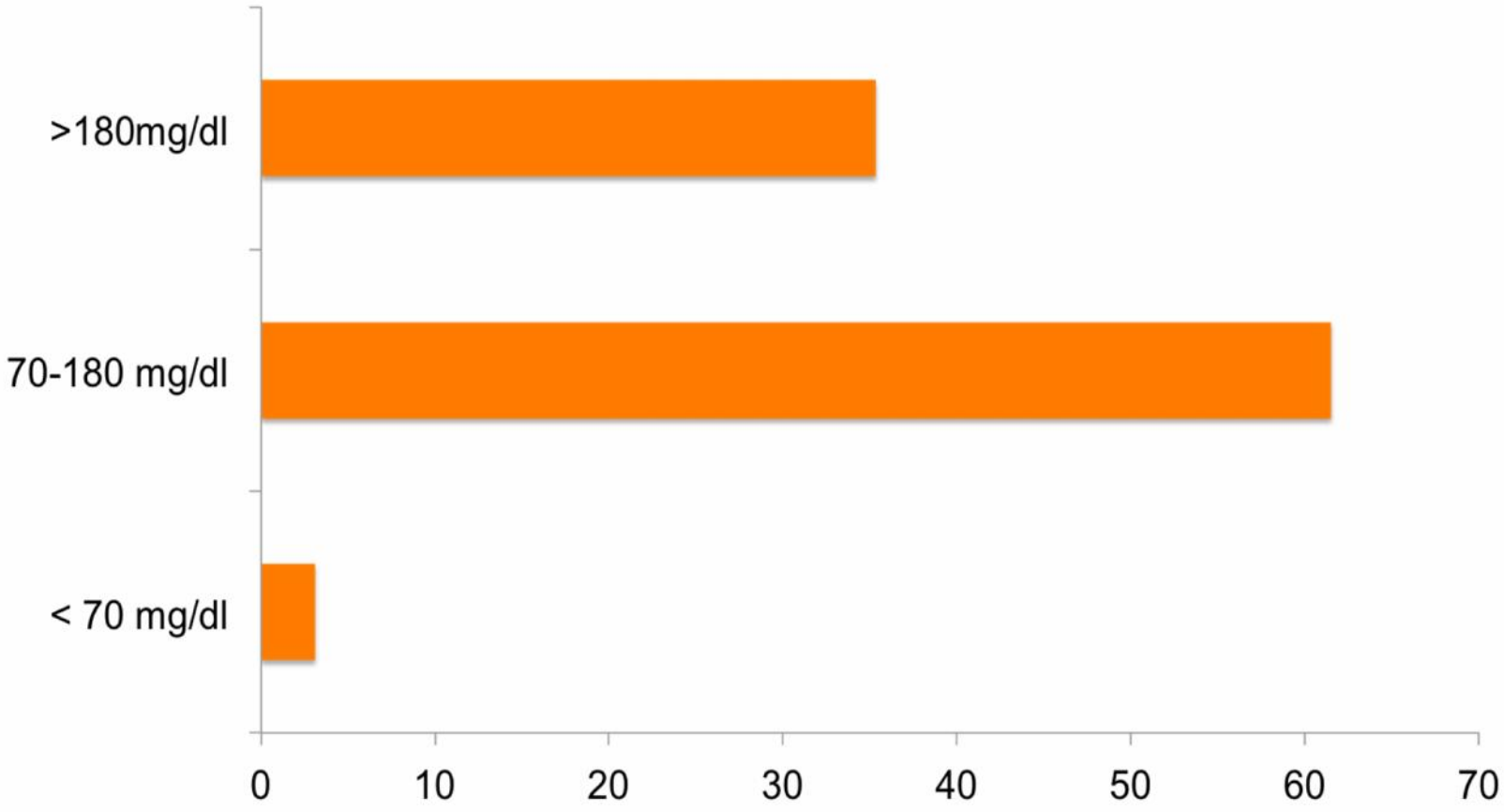
Prevention of hypoglycemia



% time in various targets

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MiniMed 640G on Social Media – What the world is saying….

Note: 4.8 mmol/L is equivalent to 86.4 mg/dL

Note: 11.6 mmol/L is equivalent to 208.8 mg/dL

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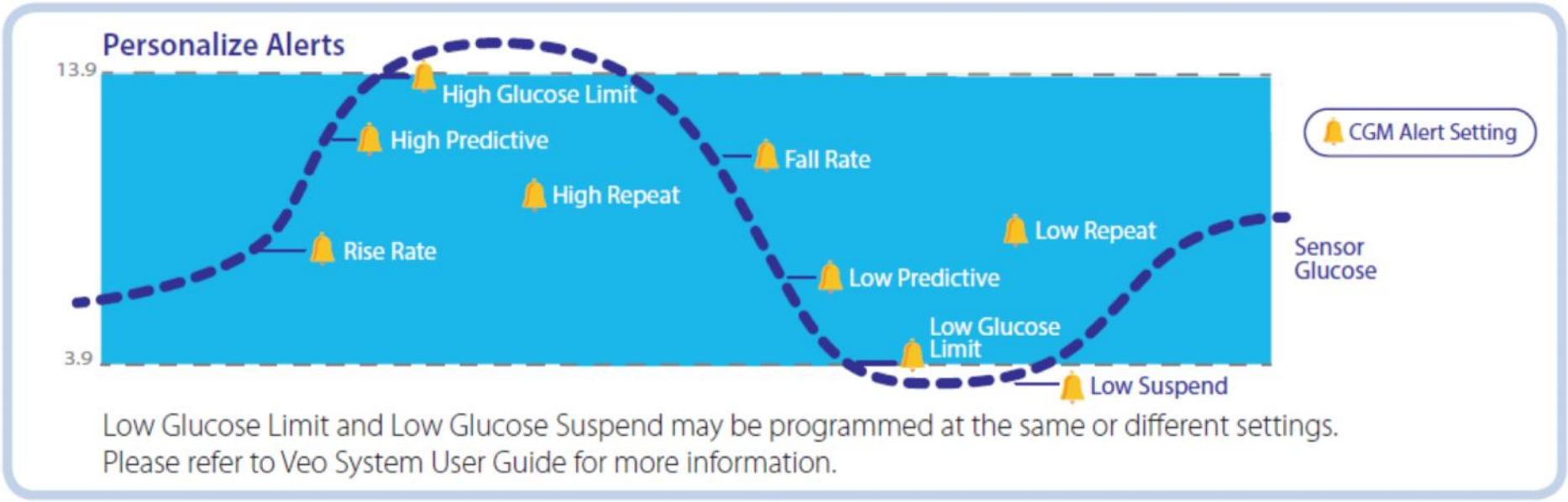

Low Glucose Limit and Low Glucose Suspend may be programmed at the same or different settings.
Please refer to Veo System User Guide for more information.

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Hypo-Hyper Minimiser

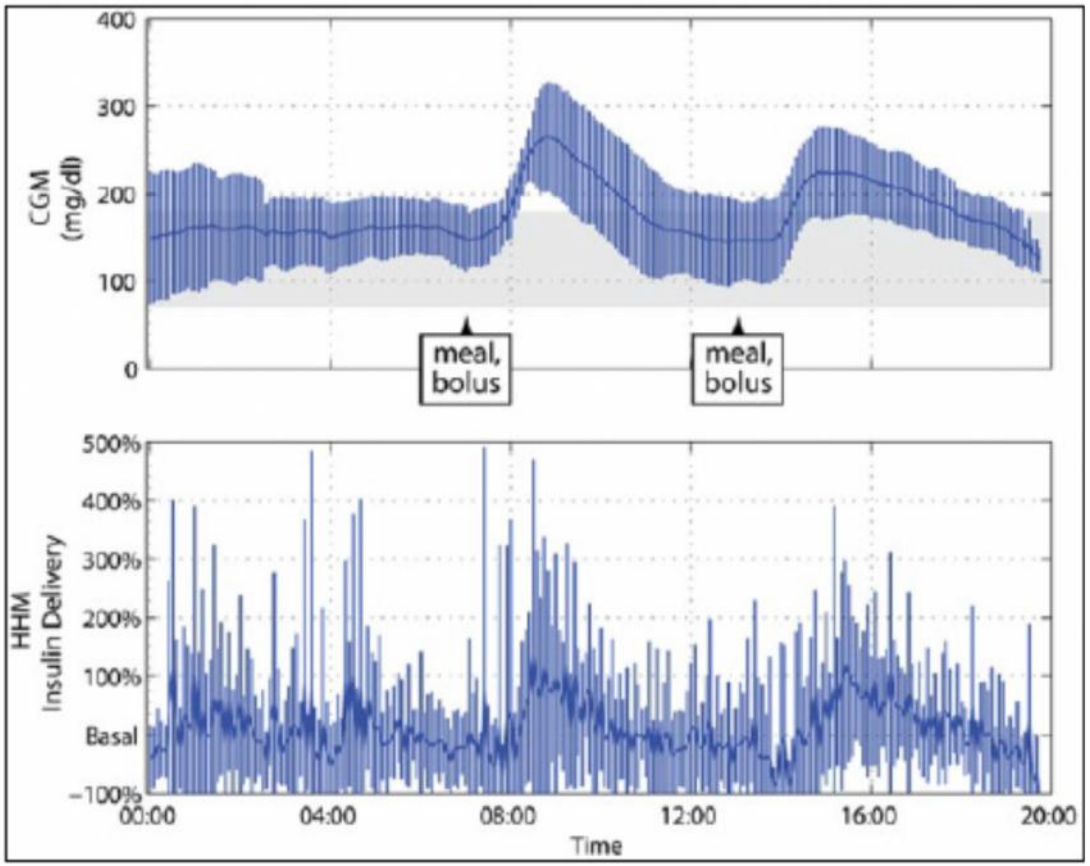

Figure 2. Average Hypoglycemia-Hyperglycemia Minimizer (HHM) System results for all participants (n = 13). Upper plot: Glucose levels (mean ± standard deviation) based on continuous glucose monitoring (CGM). Also shown are the nominal meal times. The shaded area is the approximately normoglycemic range (70-180 mg/dl). Lower plot: HHM System–determined insulin delivered during closed-loop control, as a percentage difference from the participants' respective basal rates (mean ± standard deviation).

Finan DA et al. *J Diab Sci Tech* 2014;8:35-42

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Connectivity

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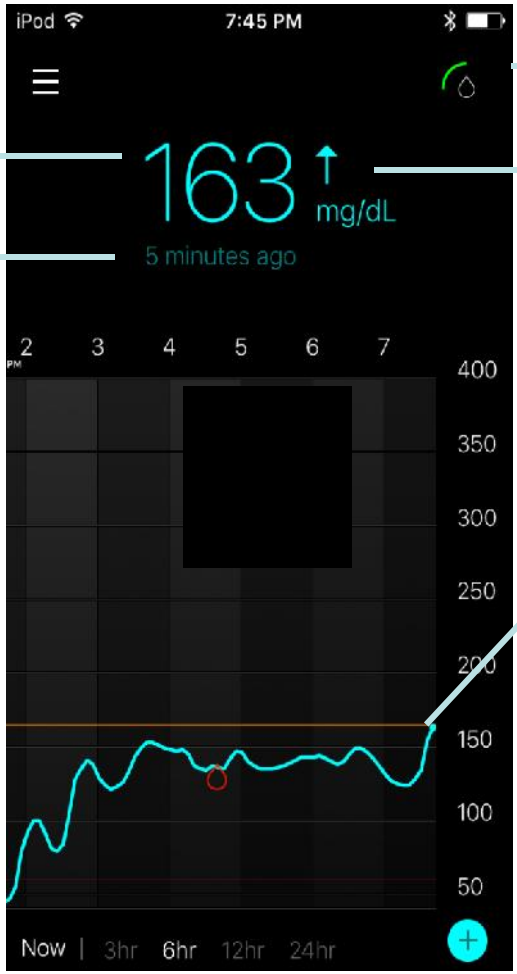
Guardian Connect

Sensor Glucose value
(will be updated every 5 minutes)

Time Since Last Sensor Glucose Reading



Time until Next Calibration

Rate of Change Arrow
(showing you medium, fast or very fast changes in your SG)

Sensor Glucose Trend Line

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