

CONVEGNO SID AMD UMBRIA

Nel Cuore del Diabete: cardio-diabetologia, approccio integrato, multidisciplinarietà, nuove tecnologie, engagement del paziente/operatore

Perugia, 28 OTTOBRE 2017

I sistemi di monitoraggio: dalla glicemia capillare ai sensori

Paola Lucidi

Dipartimento di Medicina Interna,
Sezione di Medicina Interna, Endocrinologia e Metabolismo,
Università degli Studi di Perugia.

AMD ASSOCIAZIONE MEDICI DIABETOLOGI 1974 ANNO DI FONDAZIONE

SID Società Italiana di Diabetologia fondata nel 1964

Ai sensi dell'art. 3.3 sul conflitto di interessi, pag 17 del Regolamento Applicativo Stato-Regioni del 5/11/2009, dichiaro che negli ultimi 2 anni ho avuto rapporti diretti di finanziamento (travel grants for national and international meetings) con i seguenti soggetti portatori di interessi commerciali in campo sanitario:

- Menarini
- Sanofi
- Theras
- Abbot

In fede, Paola Lucidi

Autocontrollo glicemico

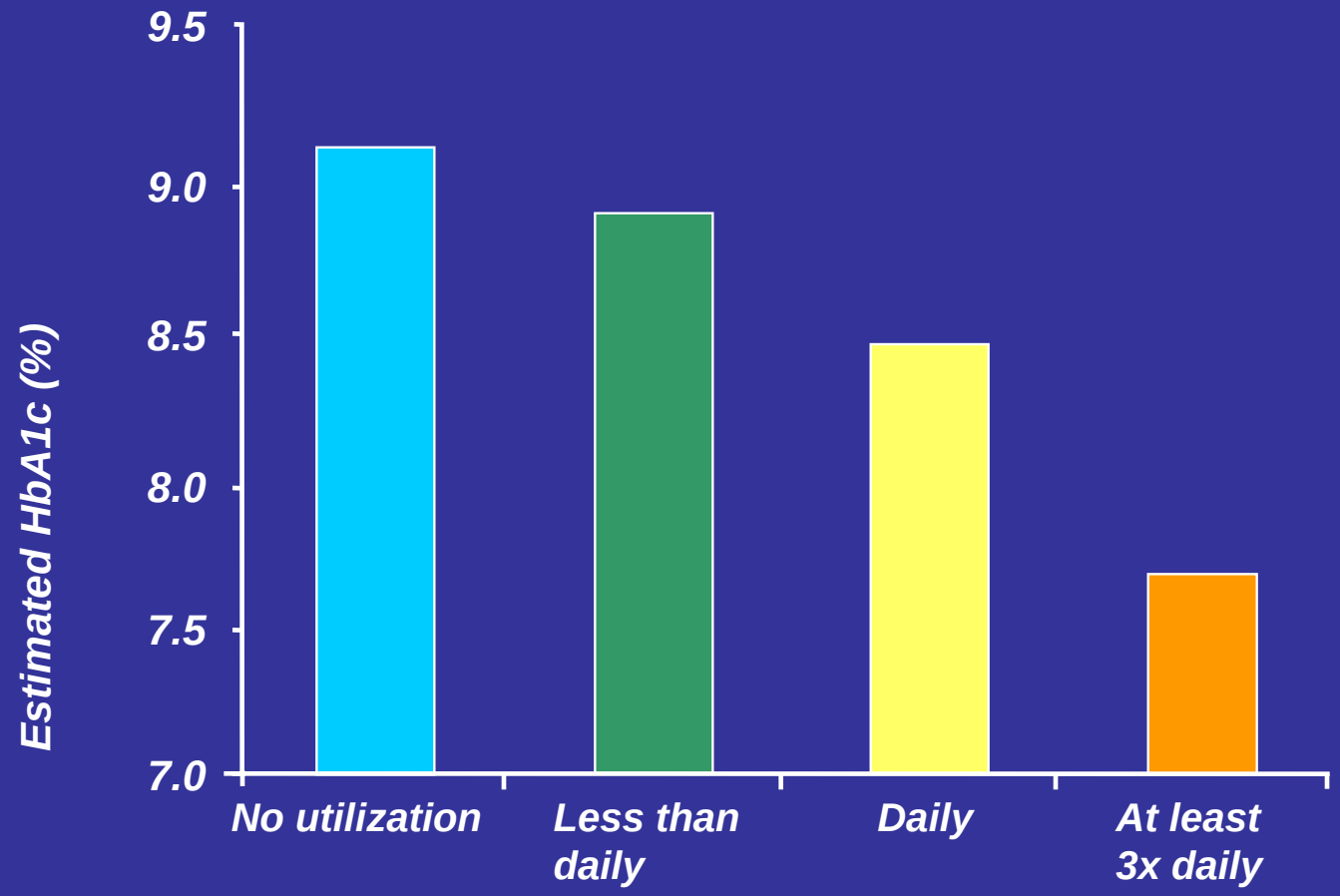
L’automonitoraggio è parte integrante del percorso di educazione terapeutica strutturata che comprende:

- Misurazione della glicemia
- Interpretazione dei risultati e gli interventi terapeutici coerenti finalizzati al miglioramento del controllo glicemico, alla prevenzione delle ipoglicemie e delle complicanze .

Automonitoraggio
Terapia insulinica intensiva

- Frequenza e periodicità
- Scelta dello strumento (Glucometro, calcolatore di bolo, CGM)
- Ottimizzazione terapia insulinica (conta CHO)
- Prevenzione e trattamento ipoglicemie

SMBG ≥ 3-times per day associated with better glycemic control in T1DM



Adjusted HbA1c by strip use (average strips per day)

Reproduced from Karter AJ, et al. Am J Med 2001; 111:1–9.

Copyright 2001 with permission from Elsevier.

Evidence of a Strong Association Between Frequency of Self-Monitoring of Blood Glucose and Hemoglobin A_{1c} Levels in T1D Exchange Clinic Registry Participants

KELLEE M. MILLER, MPH[1]
ROY W. BECK, MD, PHD[1]
RICHARD M. BERGENSTAL, MD[2]
ROBIN S. GOLAND, MD[3]
MICHAEL J. HALLER, MD[4]
JANET B. MCGILL, MD[5]
HENRY RODRIGUEZ, MD[6]
JILL H. SIMMONS, MD[7]
IRL B. HIRSCH, MD[8]
FOR THE T1D EXCHANGE CLINIC NETWORK

20555 T1DM

CONCLUSIONS—There is a strong association between higher SMBG frequency and lower HbA_{1c} levels. It is important for insurers to consider that reducing restrictions on the number of test strips provided per month may lead to improved glycemic control for some patients with type 1 diabetes.

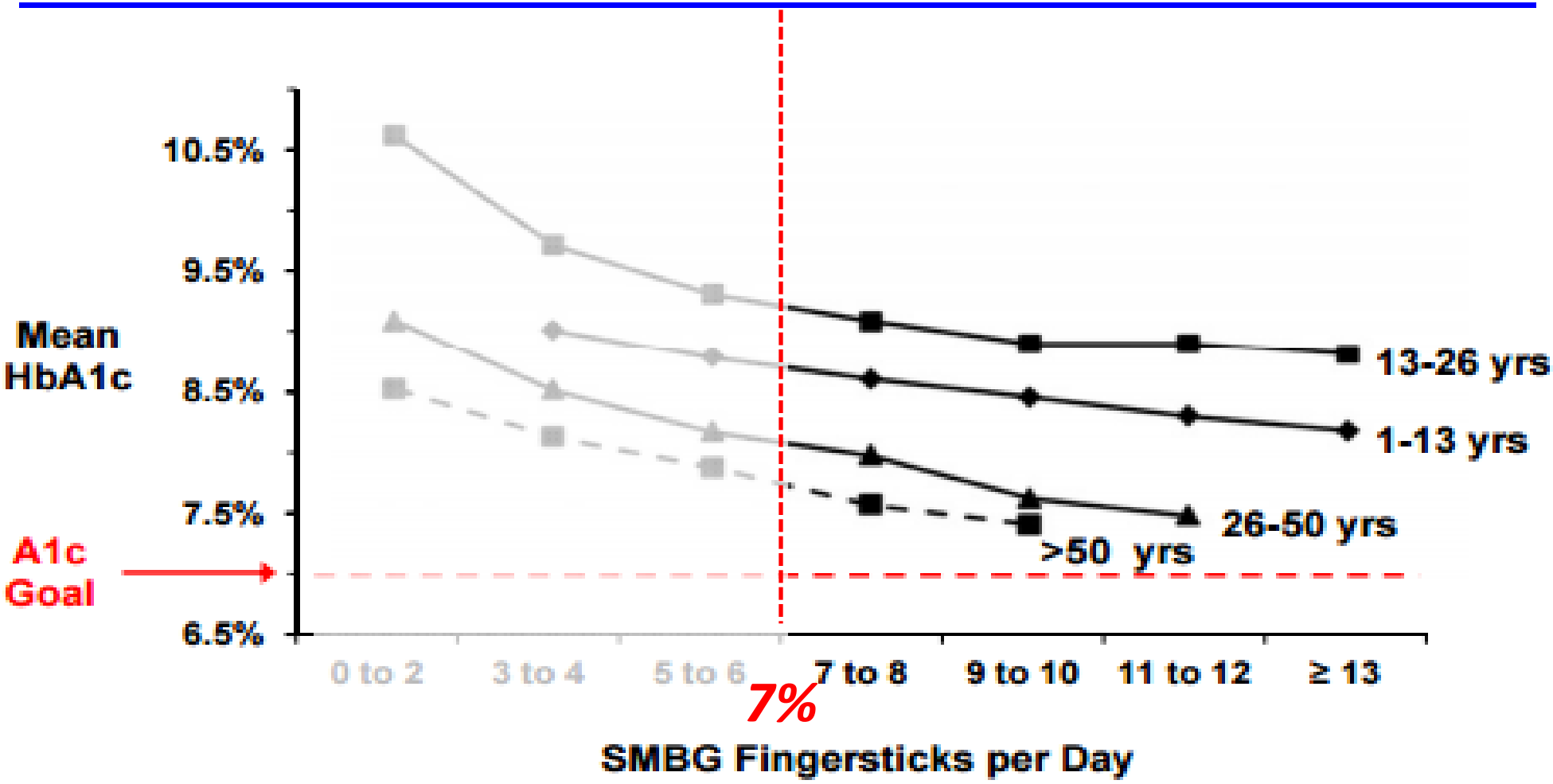
Diabetes Care 36:2009–2014, 2013

***CONCLUSIONS** There is a strong association between higher SMBG frequency and lower HbA_{1c} levels. It is important for insurers to consider that reducing restrictions on the number of test strips provided per month may lead to improved glycemic control for some patients with type 1 diabetes.*

	SMBG 0-2 times per day		SMBG 3-4 times per day		SMBG 5-6 times per day		SMBG 7-9 times per day		SMBG >10 times per day		P
Mean HbA_{1c}*	*n*	HbA_{1c} Mean, %	*n*	HbA_{1c} Mean, %	*n*	HbA_{1c} Mean, %	*n*	HbA_{1c} Mean, %	*n*	HbA_{1c} Mean, %	*P*
Age 1 to <6 years	3	–	124	8.5	281	8.4	260	8.1	151	7.8	0.002
Age 6 to <13 years	22	–	840	8.7	2,172	8.4	1,725	8.1	686	7.8	<0.001
Age 13 to <18 years	302	10.3	2,056	9.0	1,929	8.5	820	8.2	270	8.0	<0.001
Age 18 to <26 years	564	9.6	1,489	8.6	795	8.0	320	7.7	139	7.5	<0.001
Age 26 to <50 years	393	8.6	1,190	8.0	965	7.6	551	7.4	252	7.1	<0.001
Age 50 to <65 years	112	8.4	553	8.0	526	7.7	331	7.3	124	7.2	<0.001
Age ≥65 years	21	–	201	7.6	219	7.5	135	7.2	34	6.9	<0.001
HbA_{1c} < 7.0%†	*n*	% with HbA_{1c} <7.0%	*n*	% with HbA_{1c} <7.0%	*n*	% with HbA_{1c} <7.0%	*n*	% with HbA_{1c} <7.0%	*n*	% with HbA_{1c} <7.0%	
Age 1 to <6 years	3	–	124	6	281	6	260	11	151	17	0.06
Age 6 to <13 years	22	–	840	9	2,172	8	1,725	11	686	17	<0.001
Age 13 to <18 years	302	4	2,056	9	1,929	11	820	14	270	18	<0.001
Age 18 to <26 years	564	8	1,489	13	795	21	320	26	139	35	<0.001
Age 26 to < 50 years	393	13	1,190	21	965	30	551	39	252	50	<0.001
Age 50 to <65 years	112	15	553	17	526	25	331	34	124	44	<0.001
Age ≥65 years	21	–	201	31	219	27	135	46	34	53	0.01

*Means are unadjusted. *P* values are from general linear regression models adjusted for insulin delivery method, sex, race/ethnicity, insurance status, and household income (treated as ordinal variables with a missing indicator). †Percentages are unadjusted. *P* values are from logistic regression models adjusted for insulin delivery method, sex, race-ethnicity, insurance status, and household income (treated as ordinal variables with a missing indicator). ‡The median HbA_{1c} for the 127 participants who reported 0 SMBG checks per day was 9.6

Even High Frequency Fingerstick Testing Does Not Lead to Sufficient HbA1c Control



Miller et al., (2013)

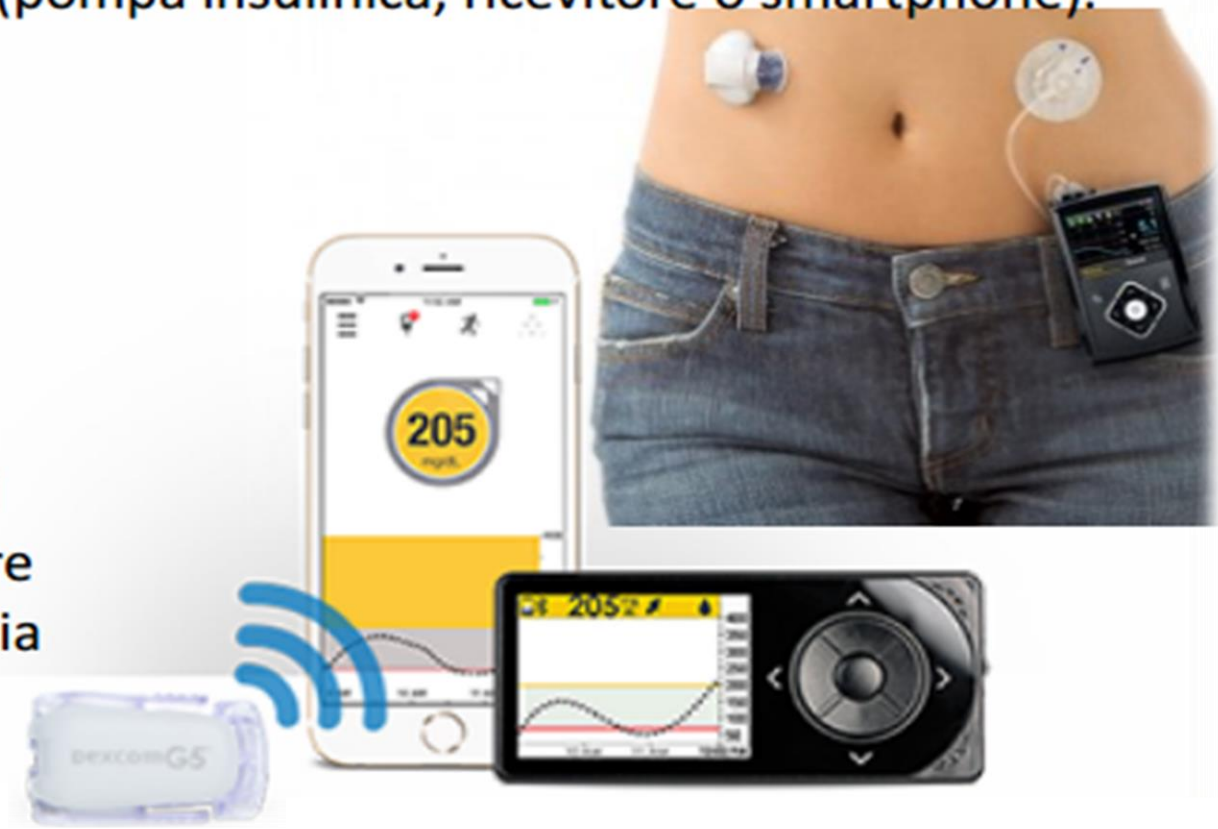
Monitoraggio Glicemico Continuo (CGM)

CGM è un sistema per la rilevazione dei livelli di glucosio nel fluido interstiziale.
Esso consiste di 3 componenti:

- Sensore sottocutaneo;
- Unità elettronica per la trasmissione del segnale;
- ricevitore/unità di archiviazione (pompa insulinica, ricevitore o smartphone).

<u>Retrospettivo "holter-like"</u>: i dati vengono visualizzati dopo che il paziente ha utilizzato il sensore.

<u>Real-time</u> : il paziente può leggere i dati rilevati dal sensore sul ricevitore o sulla pompa e modificare la terapia



Indicazioni CGM Retrospettivo

Utilizzo diagnostico puro:

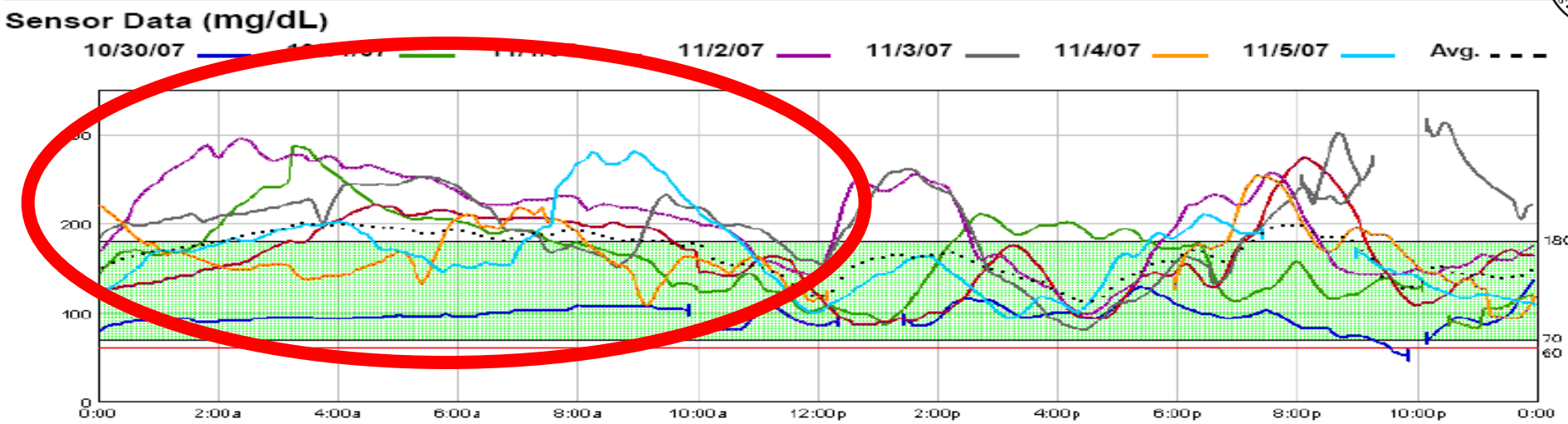
- In sospette alterazioni glucidiche non diabetiche (S. ipoglicemiche, Glicogenosi, Fibrosi cistica)
- In sospetta gastroparesi diabetica

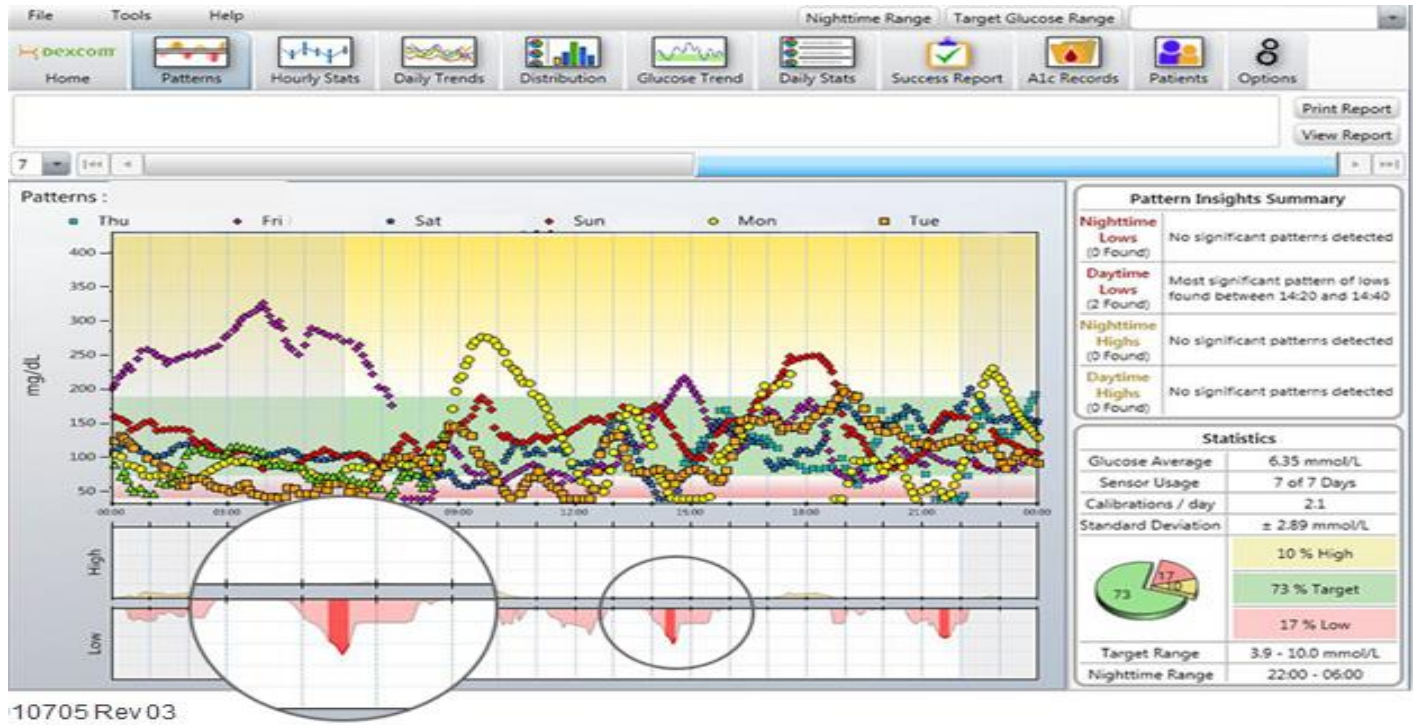
Utilizzo diagnostico-terapeutico:

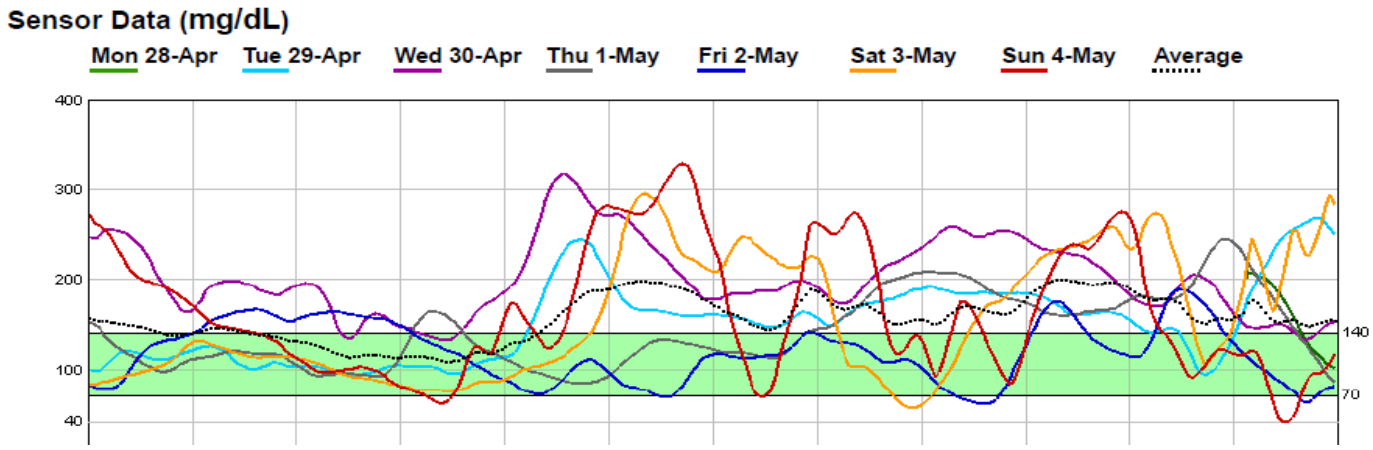
Valutazione profilo glicemico, e conseguente adeguamento degli schemi terapeutici

- Nei pazienti diabetici di tipo 1 in compenso non ottimale, sia in età pediatrica, sia adulti
- In presenza di ricorrente iperglicemia al risveglio
- Nel sospetto di "Hypoglycemia Unawareness"
- In gravidanza
- Nei pazienti di tipo 2 fragili/instabili (es. anziani con ipoglicemie non evidenti al SMBG)

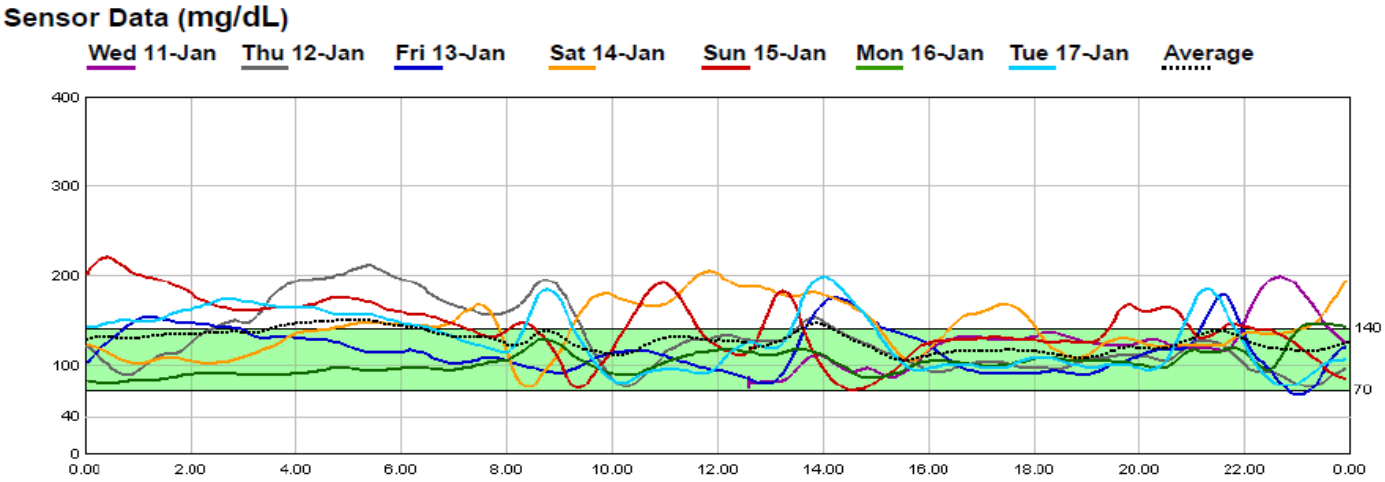
Retrospective data



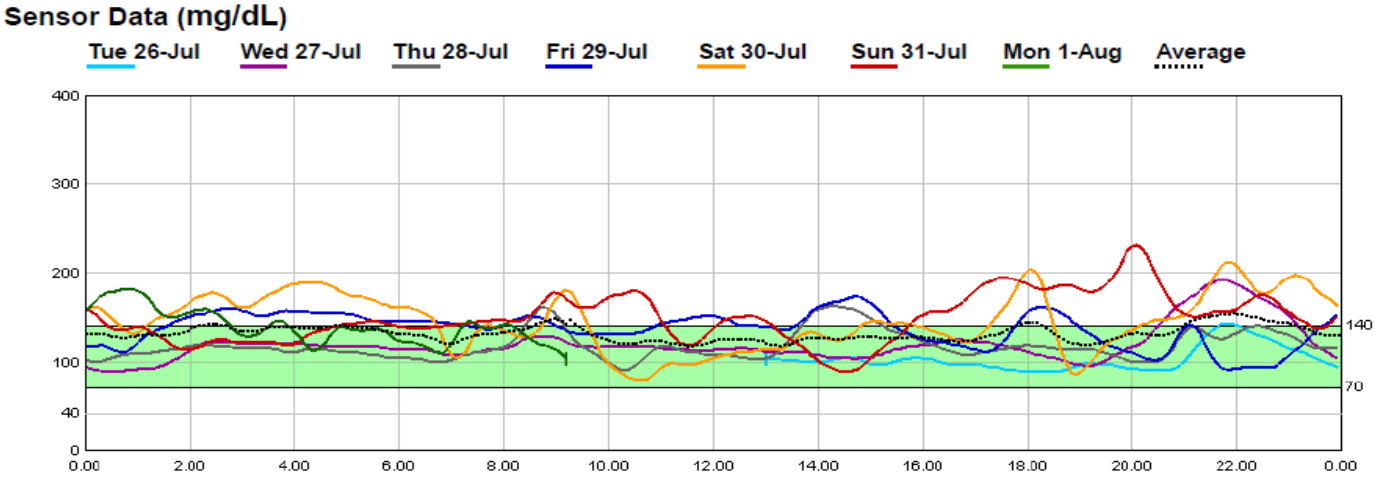




A1c: 8.4%



A1c: 7.4%



A1c: 6,3

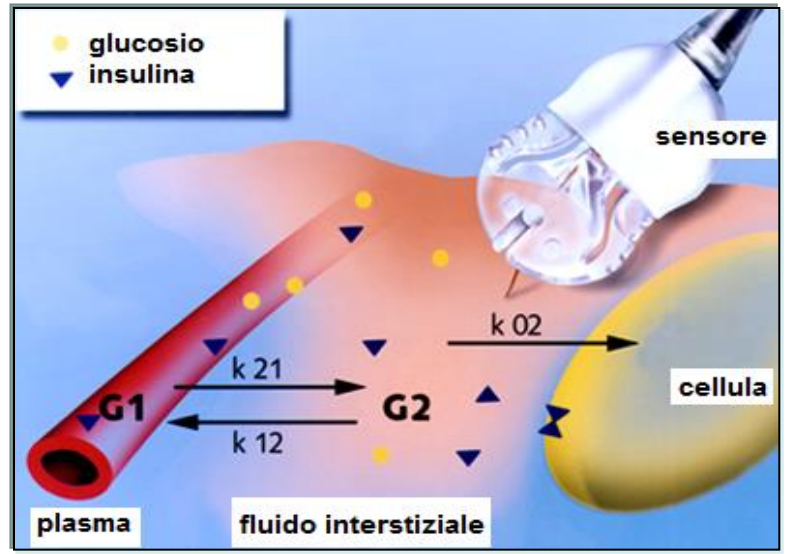
CGM e liquido interstiziale

Le concentrazioni di glucosio interstiziale dipendono da:

- ***livello di glicemia plasmatico***
- ***velocità di perfusione dal sangue allo spazio interstiziale***
- ***velocità di utilizzo del glucosio da parte del tessuto***

ritardo nelle letture =Lag Time

(7-20 min)



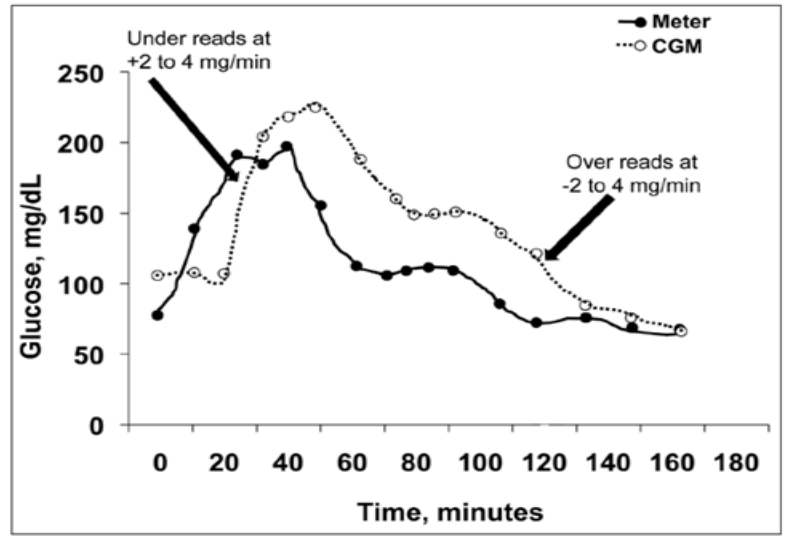


Grafico tratto da Consensus ADA/AACE. Endocr Pract 2010;16(5): 731

Accuratezza del CGM/FGM

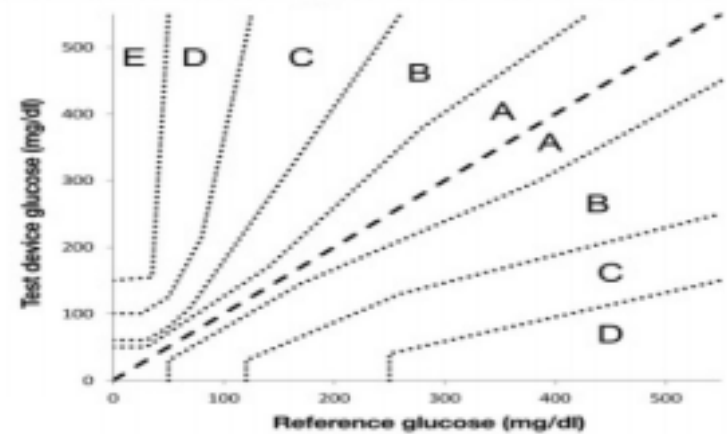
Per l'utilizzo cui è destinato, l'accuratezza e la precisione del CGM sono delle caratteristiche di fondamentale importanza.

Nel corso degli anni sono stati sviluppati diversi indici per valutare l'accuratezza del CGM:

- MARD – Differenza media assoluta relativa

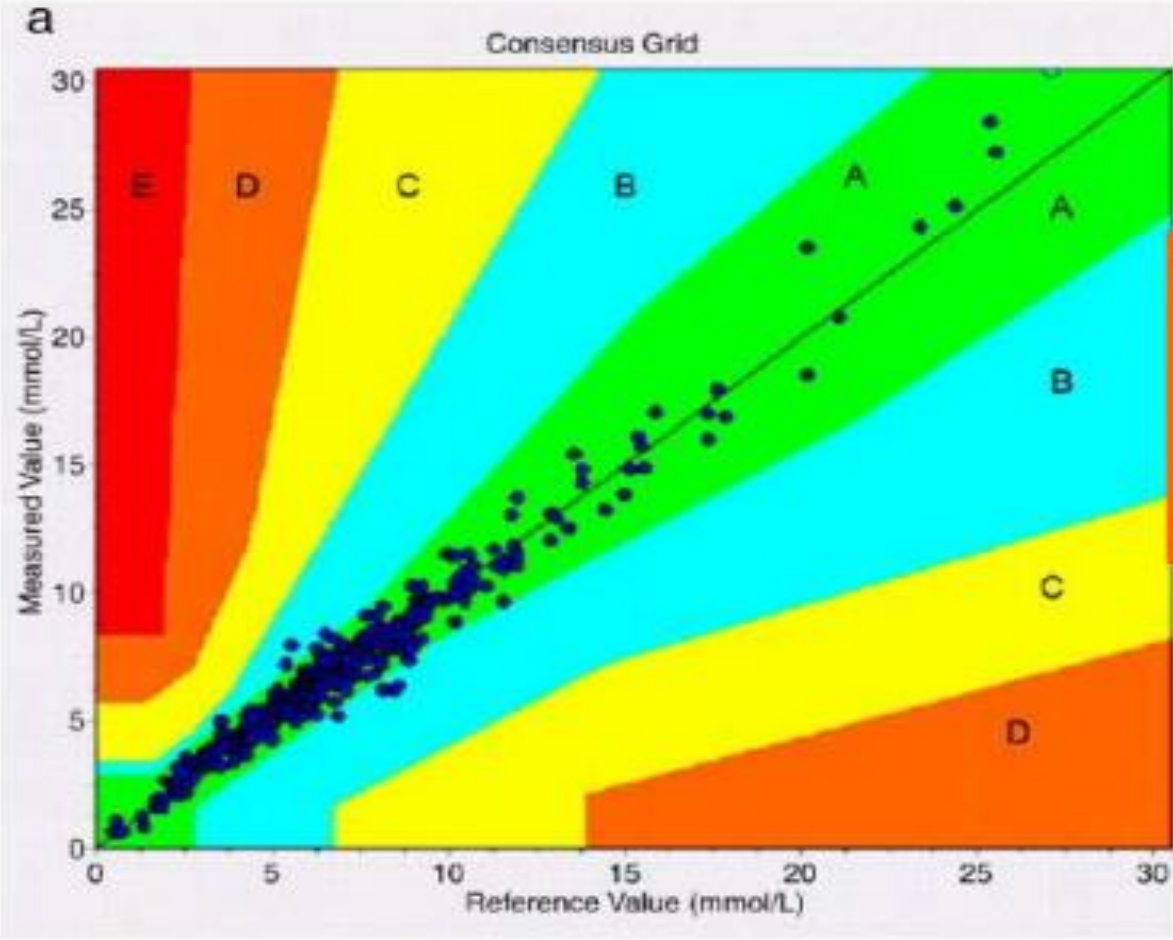
  MARD può essere diversa nei diversi contesti iperglicemico, euglicemico ed ipoglicemico, quindi deve essere valutata in ciascuna delle situazioni.

- Parkes/Consensus Error Grid



Quanto è importante l'accuratezza?

la capacità di uno strumento di misura di dare un risultato quanto più vicino a quello reale



Zone	Description	Meaning
A	Clinically accurate, would lead to correct treatment decisions	Clinically acceptable
B	Would lead to benign decisions or no treatment	
C	Would lead to overcorrection of normal glucose levels	Clinically significant errors
D	Would lead to failure to detect and treat high or low glucose levels	
E	Would lead to erroneous treatment decisions	

Maggiore è il numero di valori presenti nelle zone A e B, più sono CLINICAMENTE ACCURATI i dispositivi in termini di accuratezza

ACCURATEZZA CGM 2013

		Navigator (Abbot)	Guardian (Medtronic)	Seven Plus (Dexcom)	G4 (Dexcom)
Giorni da 1 a 7	**MARD (%)**	**12,6 ± 12**	**16,7 ± 19,3**	**16,7 ± 17,1**	**11 ± 10**
	PARD (%)	10,1 ± 8,5	18,1 ± 18,5	15,3 ± 15,7	7,3 ± 8,1
< 70 mg/dL	**MARD (%)**	**23,3 ± 21,3**	**34,3 ± 41**	**31,7 ± 31,6**	**13,7 ± 10,4**
	PARD (%)	13,6 ± 11,4	28,2 ± 23,7	21,8 ± 18,3	14,2 ± 12,2
70-180 mg/dL	**MARD (%)**	**11,6 ± 10,7**	**14,9 ± 15,3**	**16 ± 16**	**7,3 ± 7,8**
	PARD (%)	9,6 ± 8,4	17,8 ± 18,3	15,8 ± 16,1	7,3 ± 1,7
> 180 mg/dL	**MARD (%)**	**10,9 ± 8,8**	**16,6 ± 15**	**13,5 ± 12,5**	**8,5 ± 7,2**
	PARD (%)	8,9 ± 6,6	17,3 ± 15,4	17,8 ± 17	5 ± 5,4

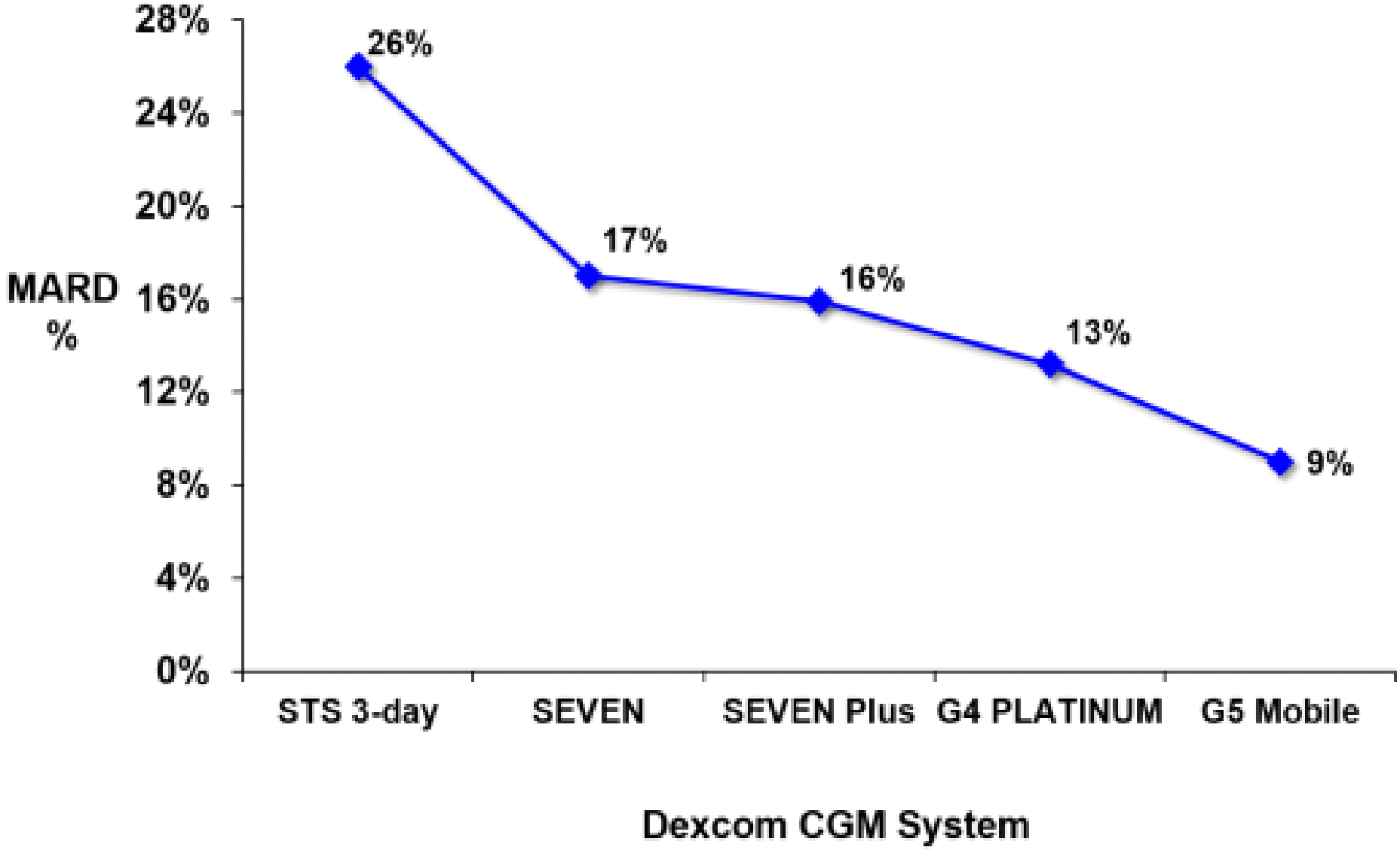
Pleius S et al. J Diab Sci Technol 2013; 7(4): 833-41

Freckmann G et al. J Diab Sci Technol 2013; 7(4): 842-53

ACCURATEZZA sistemi CGM più recenti

	LIBRE (Bailey TS et al. Diab Technol Ther 2015)	DEXCOM 5 (Bailey TS et al. J Diabetes Sci Technol 2015)	ENLITE (Minimed 640G) (Cohen O et al, Abs n° 0317, ATTD 2016)
Performance parameters	CGM vs YSI	CGM vs YSI	CGM vs YSI
MARD (%)	12	9	9.1±8.29
MAD hypoglycemia	13.4 mg/dl (< 100 mg/dl)	6.4mg/dl (≤70 mg/dl)	10.6±8.5 (≤75 mg/dl)
MARD at euglycaemia	11.4 (>100 mg/dl)	9.7 (70-180mg/dl)	10.3±7.5 (75-180 mg/dl)
MARD >180 mg/dl	-	8	6.3±4.8
Overall CEG A+B (%)	99.7	99.5	98.6%

Figure 2: Evolution of Dexcom CGM Accuracy



Indicazioni CGM Real-time

Adulti DMT1

- Ipoglicemia

  asintomatica, ricorrente, severa ≥2/anno (intervento di una terza persona)

- Insoddisfacente controllo metabolico

  HbA1c stabilmente superiore al target desiderabile per lo specifico paziente [>8% (MDI); >7,5% (CSII); >7% (prima e durante gravidanza)]

- Condizioni lavorative o stili di vita in cui un controllo molto frequente è consigliabile ma non praticabile (ad es. autisti, personale sanitario, sportivi)

Bambini DMT1

Ipoglicemia

asintomatica, ricorrente, severa ≥2/anno

Insoddisfacente controllo metabolico

rt Continuous Glucose Monitoring Systems





Medtronic Enlite

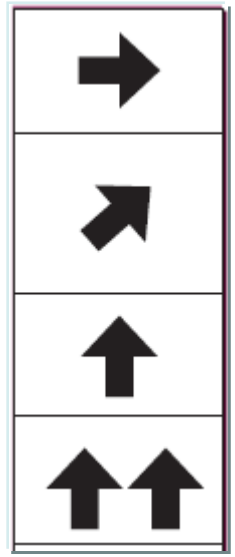


Dexcom G5



REAL-TIME CGM: OPPORTUNITA'

- Allarmi per ipo- e iperglicemia
- Evidenziazione
- del "trend"



Costante: la glicemia è stabile (non aumenta/diminuisce di oltre 1 mg/dL al minuto)

In lento aumento: la glicemia aumenta di 1-2 mg/dL al minuto

In aumento: la glicemia aumenta di 2-3 mg/dL al minuto

In rapido aumento: la glicemia aumenta di oltre 3 mg/dL al minuto

- Possibili correzioni immediate
- Approccio terapeutico aggressivo in sicurezza
- Migliore qualità di vita (minore paura dell'ipoglicemia)
- Possibili target glicemici più fisiologici

CGM in T1DM on MDI: The DIAMOND Study

Effect of Continuous Glucose Monitoring on Glycemic Control in Adults With Type 1 Diabetes Using Insulin Injections

The DIAMOND Randomized Clinical Trial

158 soggetti con Diabete Mellito Tipo 1, in terapia con MDI.

- Età ≥25 anni
- HbA1c 7.5-10.0%
- Non utilizzo di CGM per 2 mesi prima dell'arruolamento.

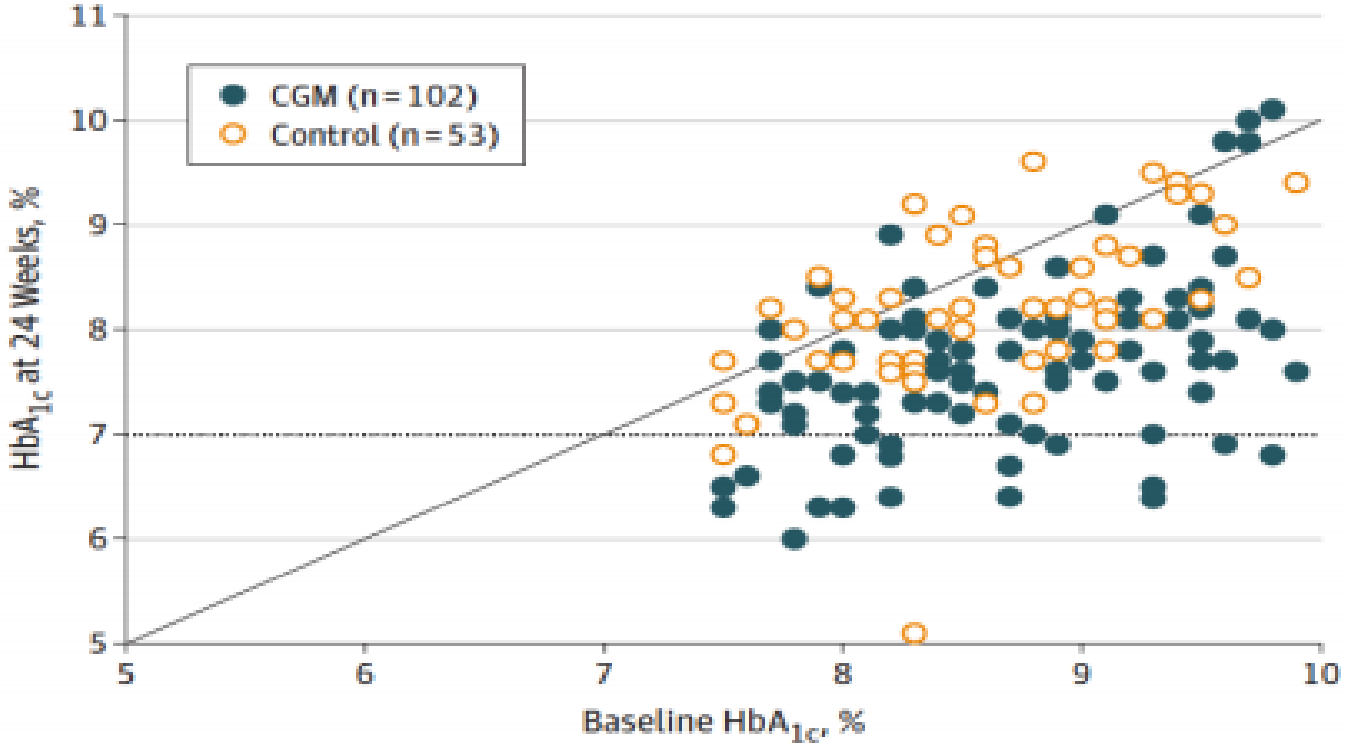
Randomizzazione a CGM:SMBG=2:1.

105 soggetti randomizzati a CGM (Dexcom G4) e 53 soggetti randomizzati a SMBG.

Beck et al. JAMA, 2017

Maggiore riduzione dei livelli di HbA1c nel gruppo CGM

	12 Weeks		24 Weeks			
	CGM Group (n = 103)	Control Group (n = 52)	CGM Group (n = 105)[b]	Control Group (n = 53)	Between-Group Difference[c,d]	*P* Value[c,d]
Primary outcome, mean (SD), %					Mean adjusted difference, % (95% CI)	
HbA_{1c}	7.6 (0.7)	8.1 (0.7)	7.7 (0.8)	8.2 (0.8)	**-0.6%**	
Change in HbA_{1c} from baseline	−1.1 (0.7)	−0.5 (0.7)	−1.0 (0.8)	−0.4 (0.7)	−0.6 (−0.8 to −0.3)	<.001



Beck et al. JAMA, 2017

Riduzione della variabilità glicemica nel gruppo CGM: minor tempo in ipo- ed iperglicemia.

	Baseline		12 and 24 Weeks Pooled[a]			
	CGM Group (n = 105)	Control Group (n = 53)	CGM Group (n = 103)	Control Group (n = 53)	Mean Adjusted Difference (99% CI)[b]	*P* Value[b]
Hours of data, mean (SD)	322 (50)	325 (51)	301 (41)	301 (54)		
Prespecified secondary outcomes						
Glucose variability: coefficient of variation, mean (SD), %	42 (7)	42 (7)	38 (6)	42 (7)	−4 (−6 to −2)	<.001
Minutes per day in range 70-180 mg/dL, mean (SD)	660 (179)	650 (170)	736 (206)	650 (194)	77 (6 to 147)	.005
Hypoglycemia, median (IQR)						
Minutes per day <70 mg/dL	65 (33 to 103)	72 (35 to 136)	43 (27 to 69)	80 (36 to 111)		.002
Minutes per day <60 mg/dL	32 (15 to 61)	39 (15 to 78)	20 (9 to 30)	40 (16 to 68)		.002
Minutes per day <50 mg/dL	13 (5 to 29)	18 (4 to 39)	6 (2 to 12)	20 (4 to 42)		.001
Hyperglycemia, median (IQR)						
Minutes per day >180 mg/dL	687 (554 to 810)	725 (537 to 798)	638 (503 to 807)	740 (625 to 854)		.03
Minutes per day >250 mg/dL	301 (190 to 401)	269 (184 to 383)	223 (128 to 351)	347 (241 to 429)		<.001
Minutes per day >300 mg/dL	129 (66 to 201)	109 (71 to 204)	78 (36 to 142)	167 (89 to 226)		<.001

Riduzione del numero di rilevazioni capillari/die a 24 settimane: 3.1/die per CGM vs 4.1/die per SMBG (p<0.001)

Beck et al. JAMA, 2017

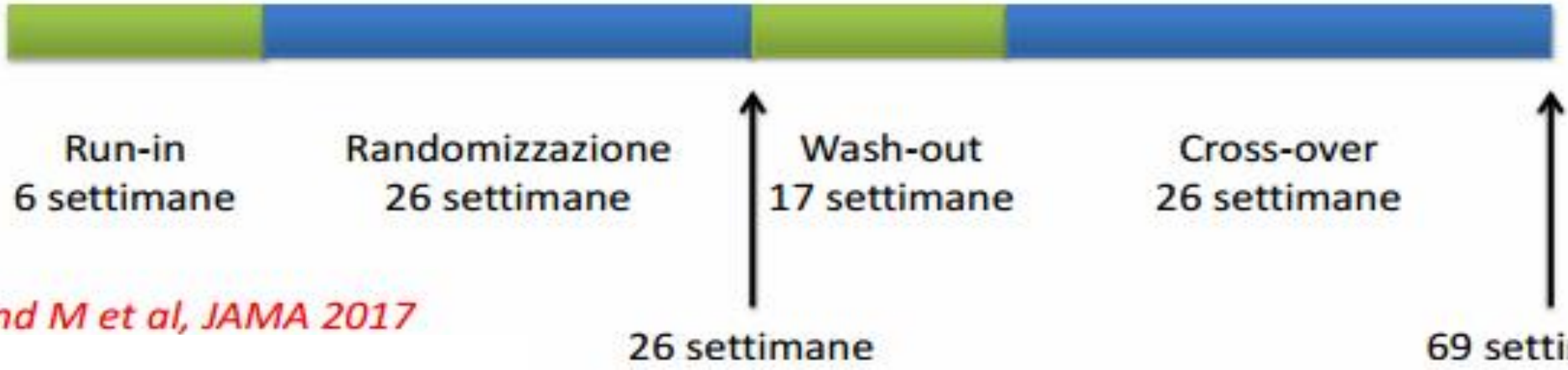
CGM in T1DM on MDI: The GOLD Cross-over Study

Continuous Glucose Monitoring vs Conventional Therapy for Glycemic Control in Adults With Type 1 Diabetes Treated With Multiple Daily Insulin Injections

The GOLD Randomized Clinical Trial

RCT cross-over open-label della durata di 69 settimane, che ha coinvolto 161 soggetti con DMT1 in terapia MDI con livelli di HbA1c ≥7.5%

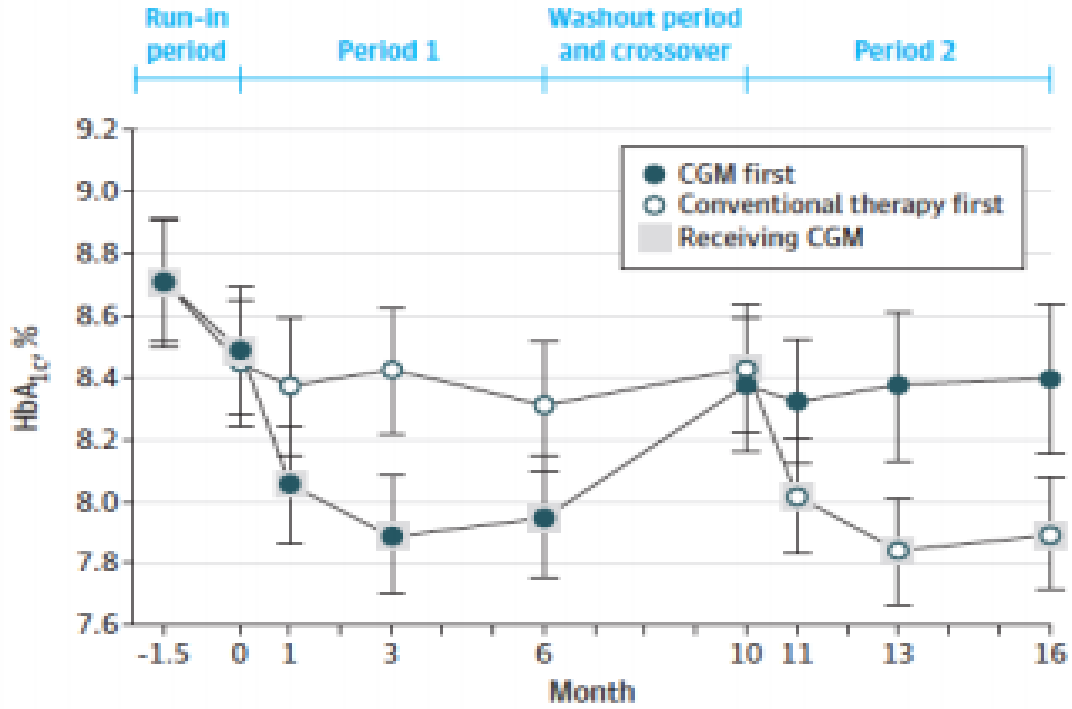
Outcome primario: variazione dei livelli di HbA1c a 26 e 69 settimane



Lind M et al, JAMA 2017

Maggiore riduzione dei livelli di HbA1c nel gruppo CGM

	CGM, Mean (95% CI)	Conventional Therapy, Mean (95% CI)	Least Square Means or Mean for Difference: CGM−Conventional Treatment (95% CI)[a]	*P* Value
Primary end point				
HbA_{1c}, %[b]	7.92 (7.79 to 8.05)	8.35 (8.19 to 8.51)	−0.43 (−0.57 to −0.29)	<.001
HbA_{1c}, mmol/mol	63 (61.6 to 64.5)	68 (66.0 to 69.4)	−4.7 (−6.27 to −3.13)	
No. of patients	142	142		



No. of patients									
CGM first	69	69	69	69	69	66	67	68	69
Conventional therapy first	73	72	71	73	73	73	70	73	73

Lind M et al, JAMA 2017

Miglioramento degli outcomes secondari nel gruppo CGM

	CGM, Mean (95% CI)	Conventional Therapy, Mean (95% CI)	Least Square Means or Mean for Difference: CGM–Conventional Treatment (95% CI)[a]	*P* Value
Secondary end points (sequential testing performed)[c]				
Mean glucose level, mg/dL[d]	186.93 (181.66 to 192.20)	193.68 (188.31 to 199.04)	−6.61 (−12.01 to −1.20)	.02
No. of patients	133	133		
Mean amplitude glycemic excursions, mg/dL[d]	161.93 (156.94 to 166.91)	180.96 (175.72 to 186.20)	−19.36 (−24.26 to −14.46)	<.001
No. of patients	123	127		
SD of glucose levels, mg/dL[d]	68.49 (66.36 to 70.63)	77.23 (74.96 to 79.50)	−8.69 (−10.76 to −6.61)	<.001
No. of patients	133	133		
DTSQ status version, scale total	30.21 (29.47 to 30.96)	26.62 (25.61 to 27.64)	3.43 (2.31 to 4.54)	<.001
No. of patients	136	137	131	
DTSQ change version, scale total[e]	13.20 (12.13 to 14.28)	5.97 (3.64 to 8.30)	3.76 (1.70 to 5.82)	<.001
No. of patients	69	67	136	

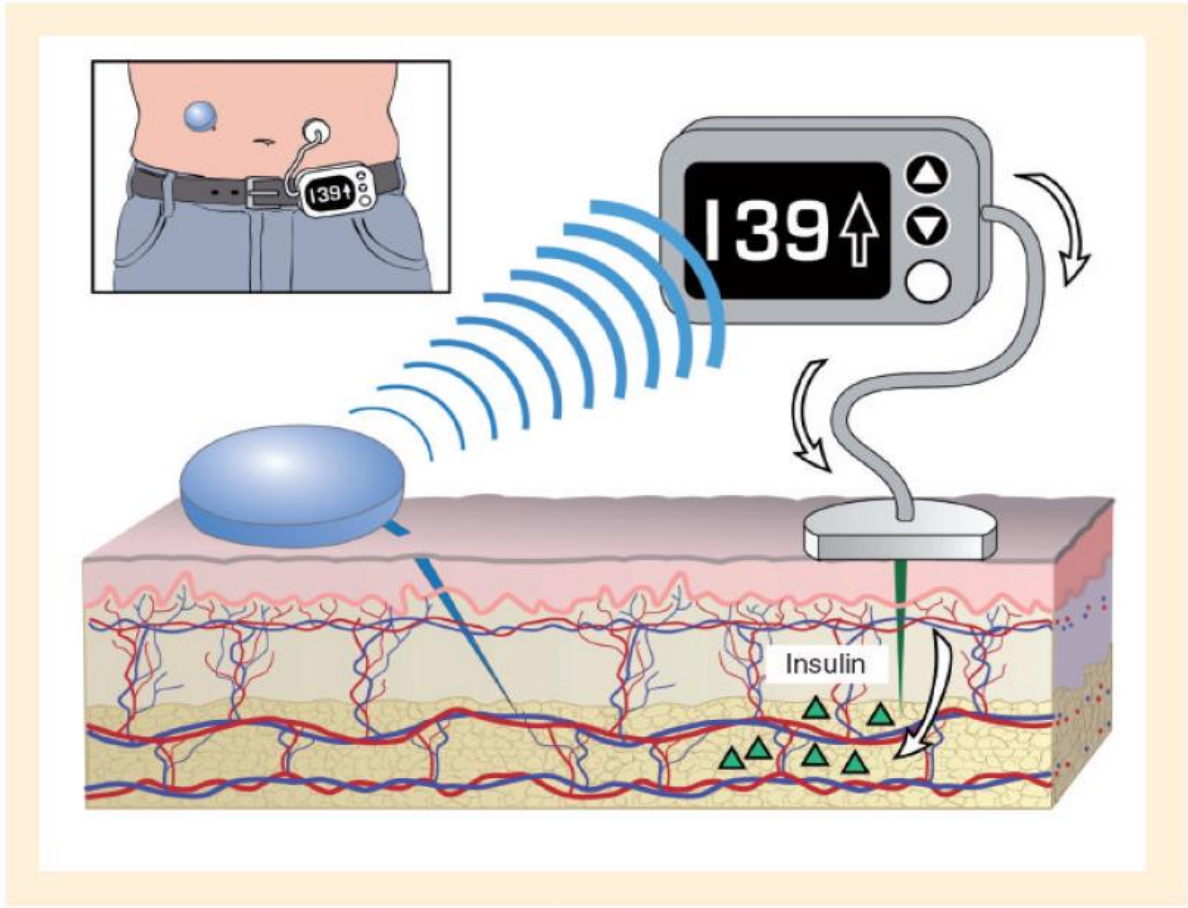
Lind M et al, JAMA 2017

CGM vs SMBG: Meta-analysis of Randomized Controlled Trials

- CGM associated with significant reduction in A1C, with greatest reductions in patients
  - With highest A1C at baseline
  - Who most frequently used sensors >80%
- CGM reduced hypoglycemia

"The most cost effective or appropriate use of continuous glucose monitoring is likely to be when targeted at people with T1DM who have continued poor control during intensified insulin therapy and who frequently use continuous glucose monitoring."

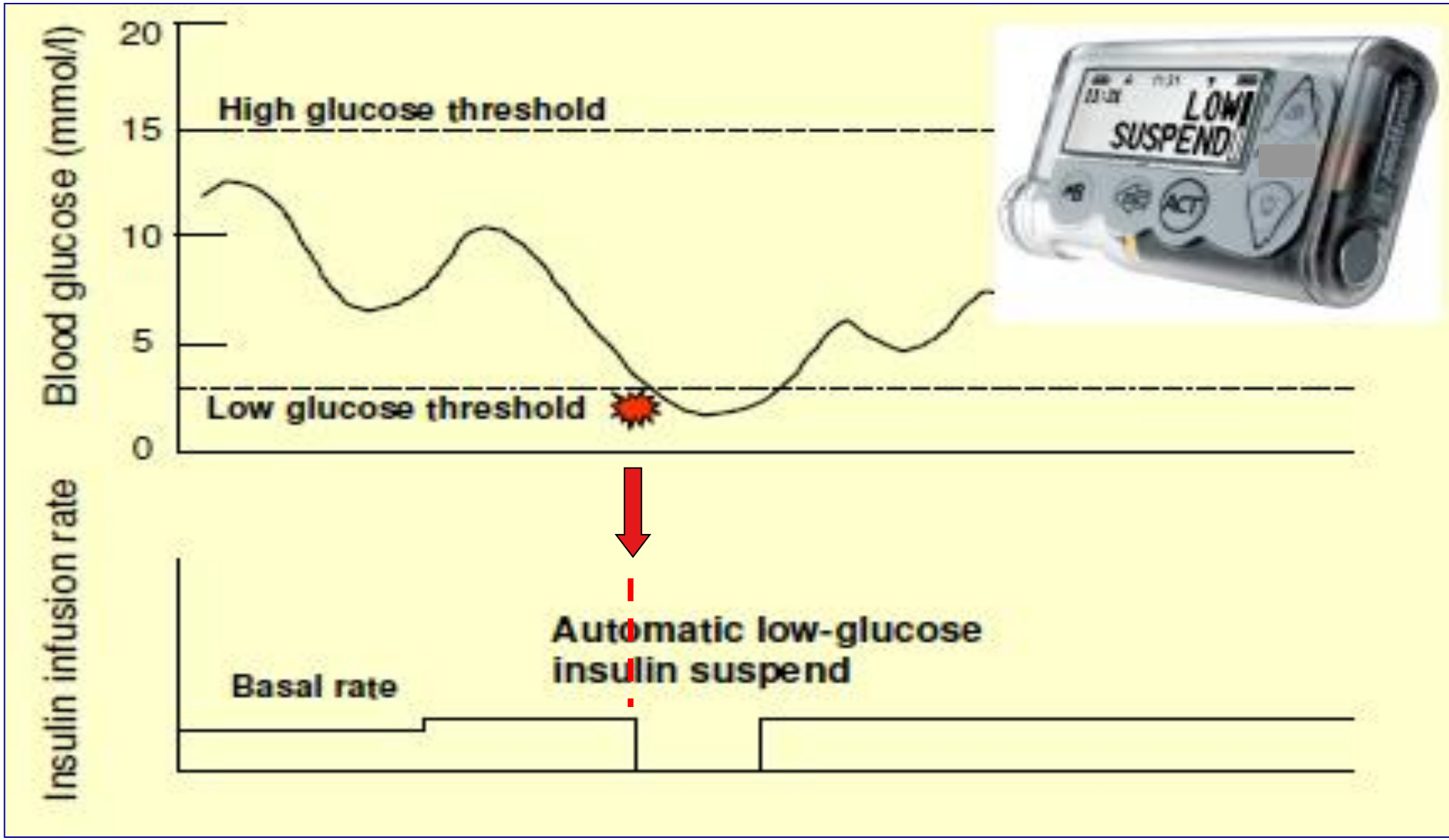
Sensor Augmented Pumps (SAPs)



Real-time glucose sensor (in blue), sitting on the skin surface with its tip inserted in the tissue interstitial fluid, measures glucose levels. The glucose value is transmitted to the insulin pump by radiofrequency, and sensor glucose values, graphs and trend arrows are displayed on its screen. An appropriate insulin dose is calculated based on the glucose value by insulin pump software and can be administered, if approved by the user, through the pump infusion set (in gray) with its catheter in the subcutaneous tissue delivering insulin.

Cengiz et al, Expert Rev Med Devices. 2011 July ; 8(4): 449

SAP and hypoglycemia: the "Low Glucose Suspend" Feature



Sensor-Augmented Insulin-Pump Therapy in Type 1 Diabetes

NICE National Institute for Health and Care Excellence

Integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (the MiniMed Paradigm Veo system and the Vibe and G4 PLATINUM CGM system)

NICE guidance

Published: 12 February 2016
nice.org.uk/guidance/dg21

Al momento non esistono linee-guida internazionali che identifichino la popolazione da trattare con SAP piuttosto che con CSII tradizionale. L'unica indicazione deriva da una recente valutazione del NICE, pubblicata nel febbraio 2016, che ha analizzato le evidenze relative esclusivamente ai sistemi MiniMed Paradigm Veo e Vibe con sensore G4 Platinum e che suggerisce l'uso del sistema Paradigm VEO nei pazienti tipo 1 con ipoglicemia invalidante nonostante la terapia con CSII. Le indicazioni del NICE sottolineano come l'impiego del sistema SAP richieda la capacità del paziente a comprendere e usare il sistema, la disponibilità all'uso continuativo del sensore (almeno il 70% del tempo) e l'adesione a un programma strutturato di educazione terapeutica.

Standard Italiani per la cura del Diabete Mellito 2016

Effect of Sensor-Augmented Insulin Pump Therapy and Au Th A

Trang
Adam
Timot

Severe hypoglycemia[a]		
Baseline		
Rate per 100 patient-months (95% CI)	2.1 (0.8 to 4.6)	1.8 (0.6 to 4.3)
No. of events (total No. of patients)	6 (49)	5 (46)
End point		
6-Month rate per 100 patient-months (95% CI)	2.2 (0.5 to 6.5)	0 (0 to 2.4)
No. of events (total No. of patients)	6 (45)	0 (41)
Incidence rate difference from baseline to end point (95% CI)		1.5 (0.3 to 2.7)
P value		.02

JAMA. 2013;310(12):1240-1247. doi:10.1001/jama.2013.277818

Original Investigation

Effect of Sensor-Augmented Insulin Pump Therapy and Automated Insulin Suspension vs Standard Insulin Pump Therapy on Hypoglycemia in Patients With Type 1 Diabetes A Ra

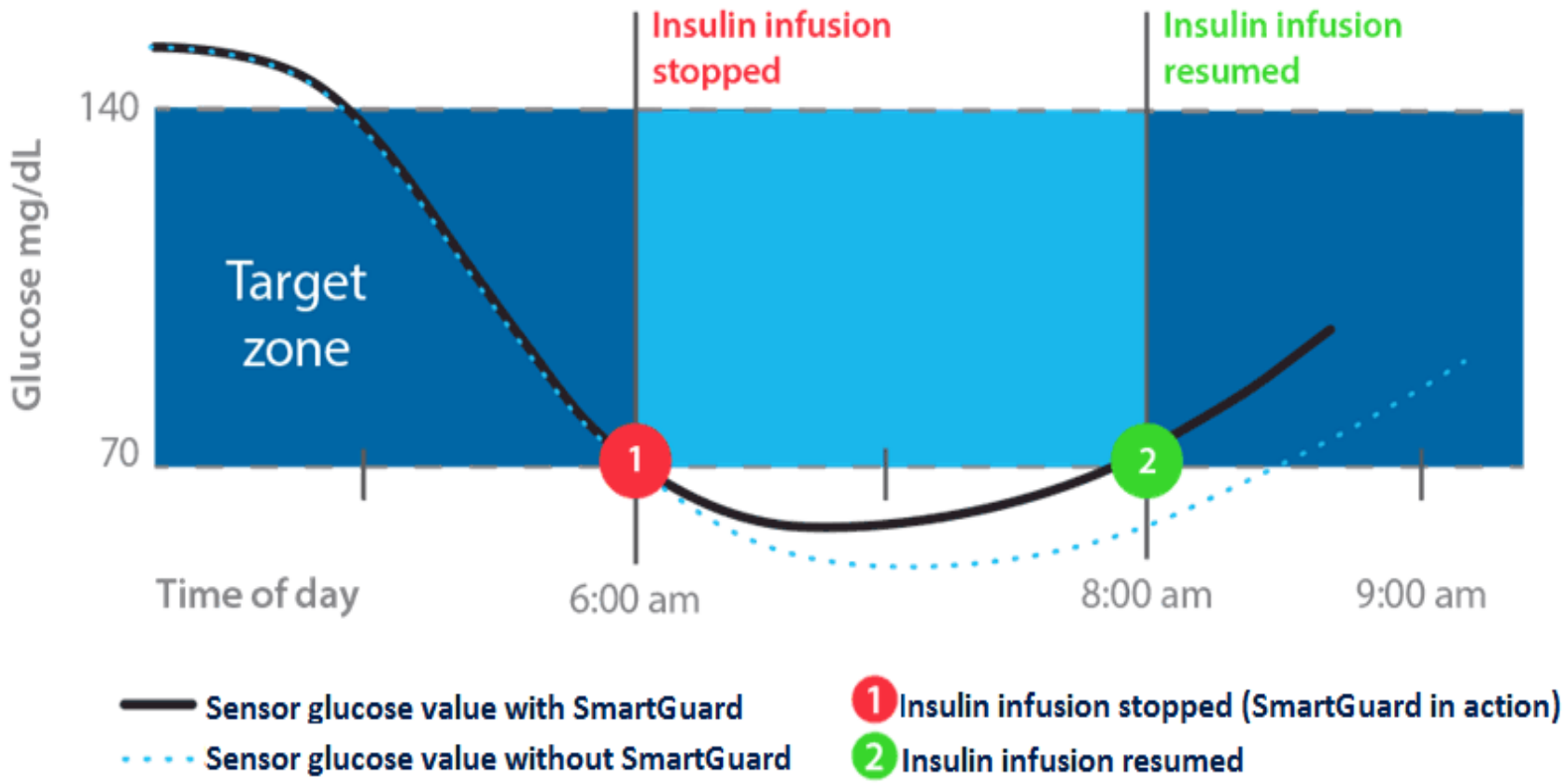
Trang T. Ly
Adam Rett
Timothy W

Table 2. Clinical Outcomes

	Insulin Pump (n = 49)	Sensor-Augmented Pump With Low-Glucose Suspension (n = 46)
Sum of Severe and Moderate Hypoglycemia		
Baseline		
Rate per 100 patient-months (95% CI)[a]	20.7 (13.8 to 30)	129.6 (111.1 to 150.3)
No. of events (total No. of patients)	28 (45)	175 (45)
End point		
6-Month rate per 100 patient-months (95% CI)[a]	11.9 (6.8 to 19.3)	28.4 (19.8 to 39.6)
No. of events (total No. of patients)	13 (45)	35 (41)
Incidence rate per 100 patient-months (95% CI)[b]	34.2 (22.0 to 53.3)	9.5 (5.2 to 17.4)
Patients modeled	45	41
Incidence rate ratio per 100 patient-months (95% CI)[b]		3.6 (1.7 to 7.5)
P value		<.001

JAMA. 2013;310(12):1240-1247. doi:10.1001/jama.2013.277818

Predictive Low Glucose Suspend (PLGS)

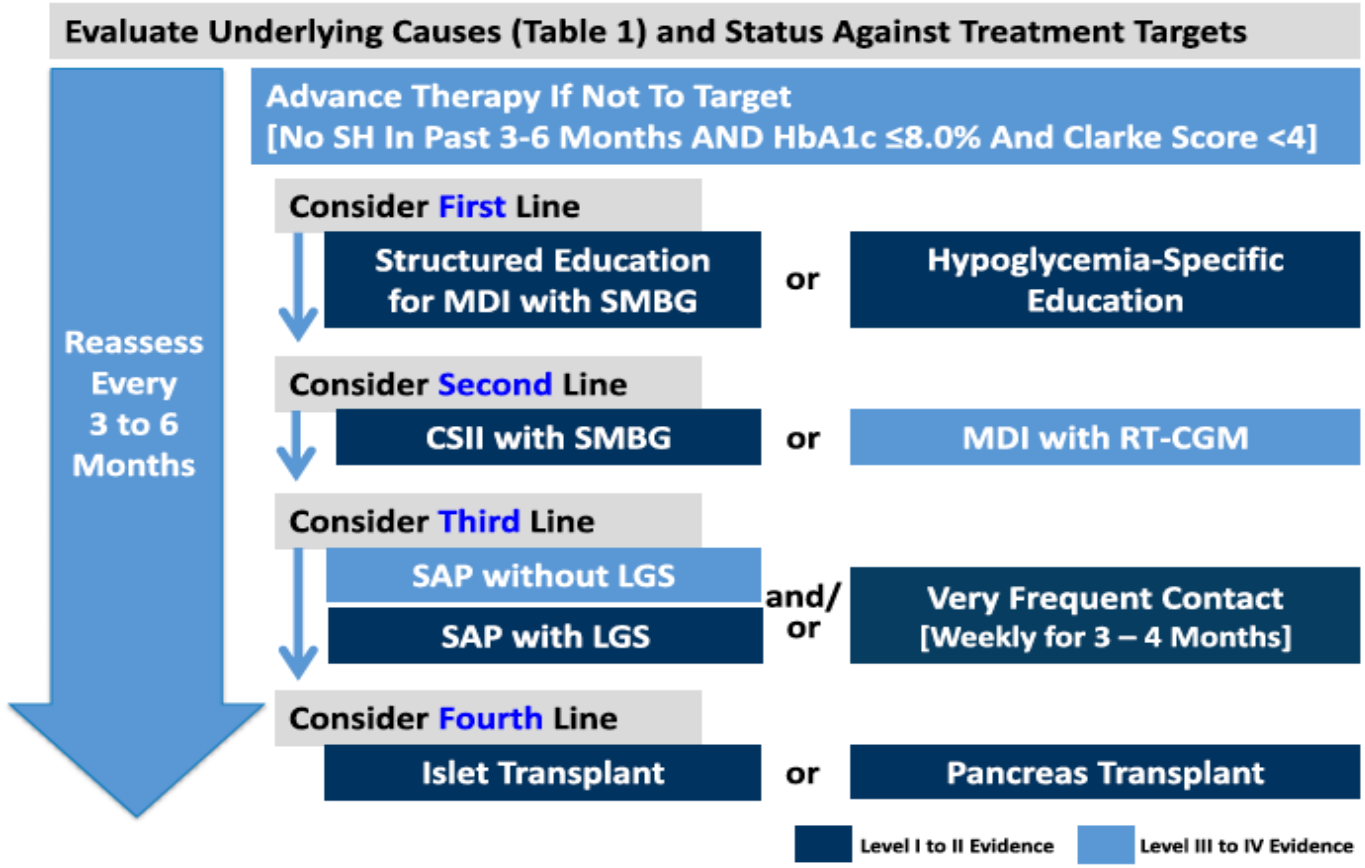


Date submitted 11 December 2014; date of first decision 5 February 2015; date of final acceptance 10 July 2015

Evidence-Informed Clinical Practice Recommendations for Treatment of Type 1 Diabetes Complicated by Problematic Hypoglycemia

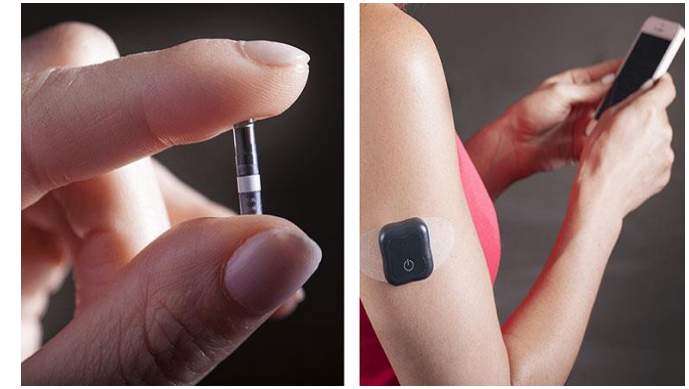
Pratik Choudhary,[1] Michael R. Rickels,[2] Peter A. Senior,[3] Marie-Christine Vantyghem,[4] Paola Maffi,[5] Thomas W. Kay,[6] Bart Keymeulen,[7] Nobuya Inagaki,[8] Frantisek Saudek,[9] Roger Lehmann,[10] and Bernhard J. Hering[11]

Diabetes Care 2015;38:1016–1029 | DOI: 10.2337/dc15-0090



CGM Versus FGM; or, Continuous Glucose Monitoring Is Not Flash Glucose Monitoring

Lutz Heinemann, PhD[1], and Guido Freckmann, MD[2]



Senseonics EverSense





Medtronic Enlite



Dexcom G5

FreeStyle Libre Abbott



Journal of Diabetes Science and Technology
2015, Vol. 9(5) 947–950

Il sistema di monitoraggio flash del glucosio FreeStyle Libre: una nuova categoria di dispositivi



Il lettore
FreeStyle Libre



Il sensore
FreeStyle Libre

14 gg
No calibration
No alarms



Il software
FreeStyle Libre

The Performance and Usability of a Factory-Calibrated Flash Glucose Monitoring System

Timothy Bailey, MD, FACE, FACP,[1] Bruce W. Bode, MD, FACE,[2]
Mark P. Ch

TABLE 2. DIFFERENCE ANALYSIS COMPARED WITH CAPILLARY AND VENOUS REFERENCE UNDER VARIOUS CONDITIONS

Reference, glucose range, parameter	*Days 1–14*			*Days 2–14*			*Day (7 a.m.–11 p.m.)*	*Night (11 p.m.–7 a.m.)*	*Without hypoglycemia/rapid change[a]*	
	All	*Home*	*Clinic*	*All*	*Home*	*Clinic*			*All*	*Clinic*
Capillary, BG										
< 100 mg/dL										
MAD (mg/dL)	11.3	11.3	11.8	11.0	11.0	10.6	11.5	10.4	10.3	8.4
n	2,153	1,946	207	1,985	1,813	172	1,787	366	905	97
≥ 100 mg/dL										
MARD (%)	10.7	10.5	11.8	10.2	10.2	10.4	10.8	9.9	10.2	11.1
n	11,042	9,642	1,400	9,987	8,878	1,109	9,717	1,325	9,341	1,236
All										
%	11.4	11.3	12.1	11.0	11.0	10.7	11.5	10.8	10.4	11.0
n	13,195	11,588	1,607	11,972	1,0691	1,281	11,504	1,691	10,246	1,333
Venous, YSI										
< 100 mg/dL										
MAD (mg/dL)	—	—	13.4	—	—	12.6	—	—	—	10.2
n	—	—	1,475	—	—	1,327	—	—	—	620
≥ 100 mg/dL										
MARD (%)	—	—	11.4	—	—	10.3	—	—	—	10.9
n	—	—	10,697	—	—	8,789	—	—	—	9,722
All										
%	—	—	12.0	—	—	11.0	—	—	—	11.0
n	—	—	12,172	—	—	10,116	—	—	—	1,0342

[a]Excluding rapidly changing/hypoglycemia (80 mg/dL) and impending hypoglycemia.
BG, blood glucose; MAD, mean absolute difference, MARD, mean absolute relative difference.

using the FreeStyle Precision meter built into the Reader.

DIABETES TECHNOLOGY & THERAPEUTICS
Volume 17, Number 11, 2015
DOI: 10.1089/dia.2014.0378

Novel glucos
type 1 diabet
controlled tr

Jan Bolinder, Ramiro Antuna, I

Background Tight control o
complications; however, gl
whether a factory-calibrate
testing reduced exposure t

Method In this multicentr
well controlled type 1 diabe
participants wearing the bl
(1:1) to flash sensor-based
capillary strips (control gr
dependent on study centre
masked to group allocation
between baseline and 6 m
positive pregnancy test dur

	Intervention (n=119)	Control (n=120)
Men	77 (65%)*	59 (49%)*
Women	42 (35%)	61 (51%)
Race		
White	119 (100%)	119 (99%)
Black	0	1 (1%)
Age (years)	42 (33-51)	45 (33-57)
BMI (kg/m²)	25·2 (3·6)	24·8 (3·5)
Duration of diabetes (years)	20 (13-27)	20 (12-32)
Screening HbA_{1c} (%; mmol/mol)	6·7 (0·5); 50·1 (5·7)	6·7(0·6); 50·2 (6·5)
Self-reported blood glucose frequency per day	5·4 (2·0)	5·6 (2·3)
Insulin administration method		
Multiple daily injections	81 (68%)	80 (67%)
Continuous subcutaneous insulin infusion	38 (32%)	40 (33%)
Insulin, total daily dose		
Basal (units)	25·7 (13·9)	20·9 (10·0)
Bolus (units)	24·2 (13·5)	22·2 (13·4)
Continuous subcutaneous insulin infusion (units)	41·4 (17·1)	35·9 (15·6)

Data are n (%), median (IQR), or mean (SD). *p=0·0153.

Table 1: **Baseline characteristics**

	Baseline		Study end		Difference in adjusted means in intervention vs control	Difference in intervention vs control (%)	p value
	Intervention (n=119)	Control (n=119)	Intervention (n=119)	Control (n=119)			
HbA_{1c} (mmol/mol)	50·7 (5·7)	50·6 (7·0)	52·4 (7·2)	52·4 (7·2)	0·0 (0·65)	NA	0·9543
HbA_{1c} (%)	6·79 (0·52)	6·78 (0·64)	6·94 (0·65)	6·95 (0·66)	0·00 (0·059)	NA	0·9556
Time with glucose 3·9–10·0 mmol/L (70–180 mg/dL) in h	15·0 (2·5)	14·8 (2·8)	15·8 (2·9)	14·6 (2·9)	1·0 (0·30)	NA	0·0006
Glucose <3·9 mmol/L (70 mg/dL) within 24 h							
Events	1·81 (0·90)	1·67 (0·80)	1·32 (0·81)	1·69 (0·83)	−0·45 (0·089)	−25·8%	<0·0001
Time in h	3·38 (2·31)	3·44 (2·62)	2·03 (1·93)	3·27 (2·58)	−1·24 (0·239)	−38·0%	<0·0001
AUC (hxmg/dL)	53·42 (43·46)	58·34 (57·22)	28·58 (31·15)	54·67 (60·08)	−25·14 (5·32)	−46·7	<0·0001
Glucose <3·9 mmol/L (70 mg/dL) at night (2300–0600 h) within 7 h							
Events	0·47 (0·32)	0·46 (0·29)	0·27 (0·23)	0·40 (0·29)	−0·14 (0·029)	−33·2%	<0·0001
Time in h	1·32 (1·07)	1·48 (1·29)	0·68 (0·97)	1·23 (1·10)	−0·47 (0·118)	−39·8%	<0·0001
Glucose <3·1 mmol/L (55 mg/dL) within 24 h							
Events	0·96 (0·65)	0·92 (0·73)	0·56 (0·55)	0·92 (0·74)	−0·38 (0·074)	−41·3%	<0·0001
Time in h	1·59 (1·42)	1·77 (1·86)	0·80 (0·96)	1·65 (1·97)	−0·82 (0·175)	−50·3%	<0·0001
AUC (hxmg/dL)	16·04 (17·46)	18·94 (23·22)	7·59 (10·25)	17·69 (26·34)	−9·67 (2·29)	−56·1%	<0·0001
Glucose <3·1 mmol/L (55 mg/dL) at night (2300–0600 h) within 7 h							
Events	0·34 (0·27)	0·36 (0·34)	0·19 (0·24)	0·30 (0·28)	−0·11 (0·03)	−34·9%	0·0005
Time in h	0·62 (0·60)	0·75 (0·83)	0·31 (0·43)	0·66 (0·080)	−0·32 (0·07)	−48·9%	<0·0001

Il sistema CGM Eversense®



Sensore

Smart Transmitter

Mobile App

90 giorni di uso continuativo

Allarmi tramite vibrazione sul corpo

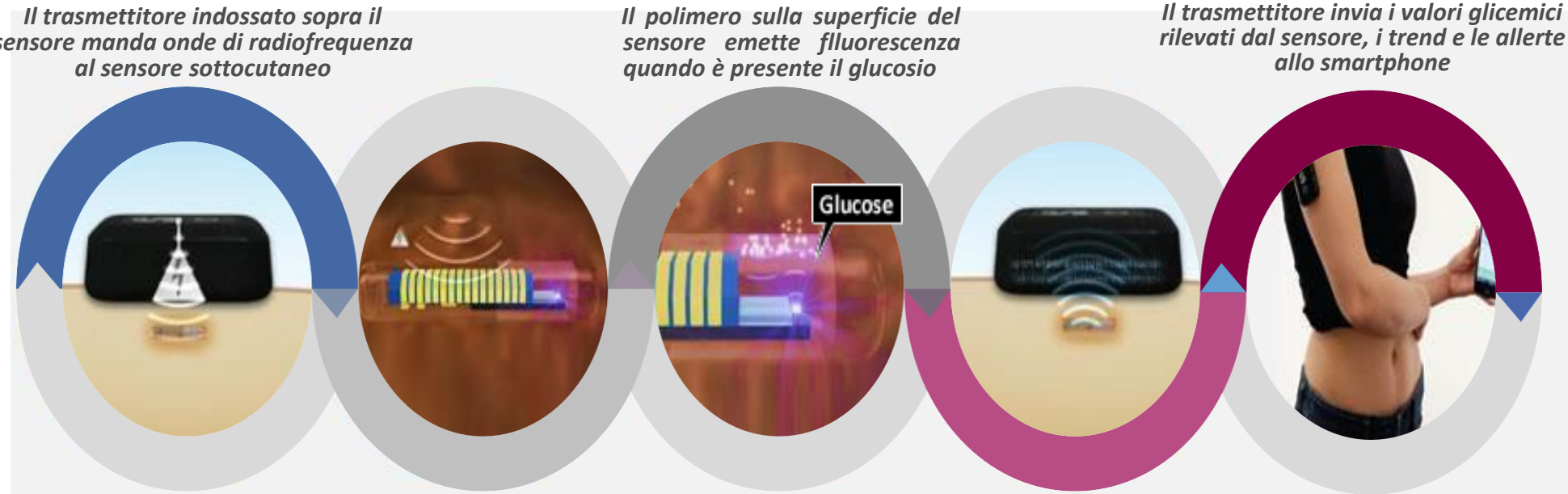
Nessun ricevitore aggiuntivo

Come funziona Eversense

Il trasmettitore indossato sopra il sensore manda onde di radiofrequenza al sensore sottocutaneo

Il polimero sulla superficie del sensore emette flluorescenza quando è presente il glucosio

Il trasmettitore invia i valori glicemici rilevati dal sensore, i trend e le allerte allo smartphone



L'antenna del sensore riceve le onde di radiofrequenza dal trasmettitore per alimentare il device

Il sensore invia i dati al trasmettitore, che calcola i valori glicemici

L'idrogel co-polimerizzato con un indicatore fluorescente è responsabile della creazione del segnale direttamente proporzionale alla quantità di glucosio interstiziale rilevato

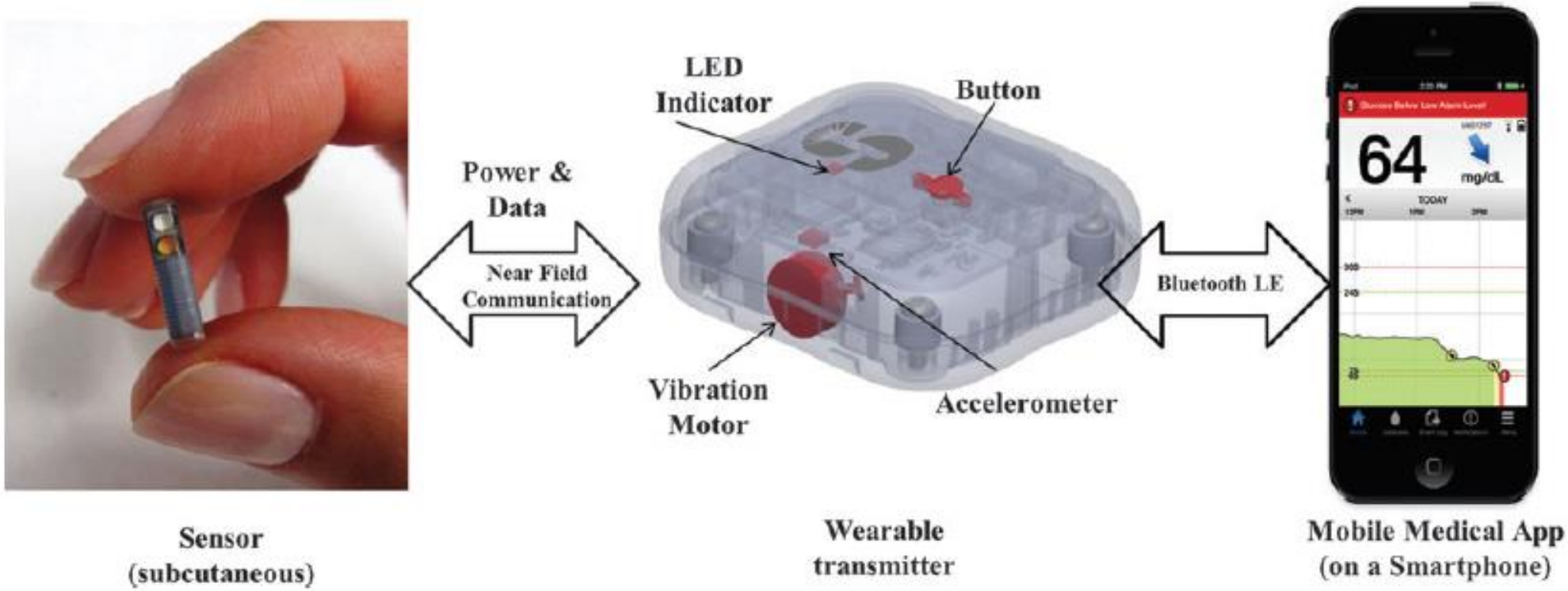
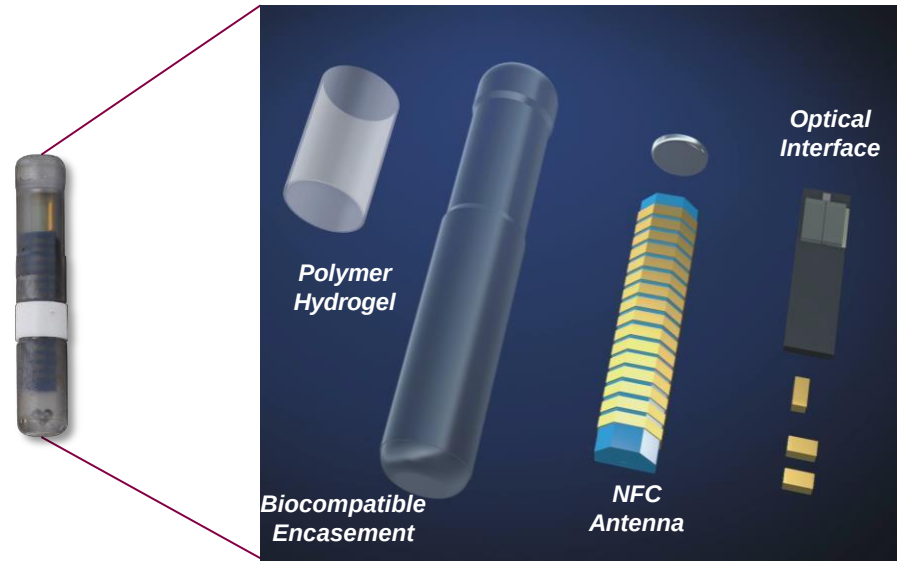


FIG. 1. Components of the continuous glucose monitoring system. App, application; LE, low energy; LED, light-emitting diode. (Color graphics available at www.liebertonline.com/dia)

Sensore

- ***Microfluorometro***
- ***Tecnologia non enzimatica con trasduttore a fluorescenza***



ESTERNAMENTE:

•Il **desametasone acetato** contenuto nelle microsfere eluisce in modo controllato per tutta la durata del tempo dell'impianto con tasso di eluizione a regime di 1,8 ug al giorno.

•Questo significa che nei 90 giorni di impianto il dosaggio complessivo ammonta a 0,162 mg, molto al di sotto di qualsiasi dosaggio terapeutico della molecola







	Eversense	Dexcom G4/G5	Medtronic	Libre
Sensor Life	90 days	7 days	6 days	14 days
Sensors / insertions per year	4 per year	52 per year	60 per year	26 per year

grazie alla stabilità del sensore non enzimatico che dura 90 giorni si verifica una riduzione del numero di «cambi» (4 anno)

Predittività







	Eversense	Dexcom G4/G5	Medtronic	Libre
Predictive Low/High Alerts	Yes	No; coming soon	Yes	No

Eversense ha avvisi predittivi in grado di dare un avvertimento in «previsione» 10, 20 o 30 minuti prima.

su tre livelli glicemici e sulle impostazioni basso o alto, è in grado di prevedere se la glicemia supererà i limiti impostati nei 10, 20 o 30 minuti successivi.







	Eversense	Dexcom G4/G5	Medtronic	Libre
Sensor Technology	Non-enzymatic	Enzyme based	Enzyme based	Enzyme based

L'idrogel co-polimerizzato con un indicatore fluorescente crea un segnale
direttamente proporzionale alla quantità di glucosio interstiziale rilevato
= reazione è stabile
= non dipende dalle caratteristiche di instabilità tipiche degli enzimi
= nessun prodotto chimico

1_Colvin AE, Jiang H. 2013. J Biomed Mater Res Part A 2013:101A:1274–1282.

2_Tankiewicz S, Schaefer J, DeHennis, NJ: IEEE, 2013:523–526.

3_ Wang X, Mdingi, C, DeHennis A, et al.:. Conf Proc IEEE Eng Med Biol Soc 2012;2012:3492–3495

4_Mortellaro_performance characterization of an abiotic and fluorescent-based CGM_Biosensor and Bioelectronics 2014.

Studio PRECISE

A Prospective, Multicenter Evaluation of the Accuracy of a Novel Continuous Implanted Glucose Sensor

Diabetes Care Volume 40, January 2017 63

Accuracy and Longevity of an Implantable Continuous Glucose Sensor in the PRECISE Study: A 180-Day, Prospective, Multicenter, Pivotal Trial

Jort Kropff,[1] Pratik Choudhary,[2] Sankalpa Neupane,[3] Katharine Barnard,[4] Steve C. Bain,[5] Christoph Kapitza,[6] Thomas Forst,[7] Manuela Link,[8] Andrew Dehennis,[9] and J. Hans DeVries[1]

Diabetes Care 2017;40:63–68 | DOI: 10.2337/dc16-1525

pubblicato su Diabetes Care (gennaio 2017)

eversense® Continuous Glucose Monitoring System

ACCU-CHEK®

Caratteristiche della popolazione in studio

Table 1—Baseline patient characteristics

Variable	Intent-to-treat population (n = 71)
Age (years)	41.7 [12.6]
Sex	
Male	42 (59.2)
Female	29 (40.8)
Type 1 diabetes	66 (93.0)
Type 2 diabetes	5 (7.0)
Diabetes duration (years)	22.2 [12.5]
Insulin delivery mode, CSII	42 (59.2)
BMI (kg/m^2)	27.0 [4.2]
HbA_{1c} (%)	7.6 [1.1]
HbA_{1c} (mmol/mol)	60 [12]
Any history of	
Ketoacidosis	15 (21.1)
Severe hypoglycemia	17 (23.9)
Long-term diabetes complications	
Retinopathy	16 (22.5)
Nephropathy	0 (0)
Neuropathy	7 (9.9)
Cardiovascular disease	21 (29.6)
Foot problems	4 (5.6)

For categorical variables, n (%) is presented. For continuous variables, mean [SD] is presented.
CSII, continuous subcutaneous insulin infusion.

età media 40 anni

93% con DM1

Durata malattia da >20 anni CSII 60% HbA1c 7,6%

Obiettivo primario: MARD

Table 2—Accuracy of the CGM system versus YSI over time

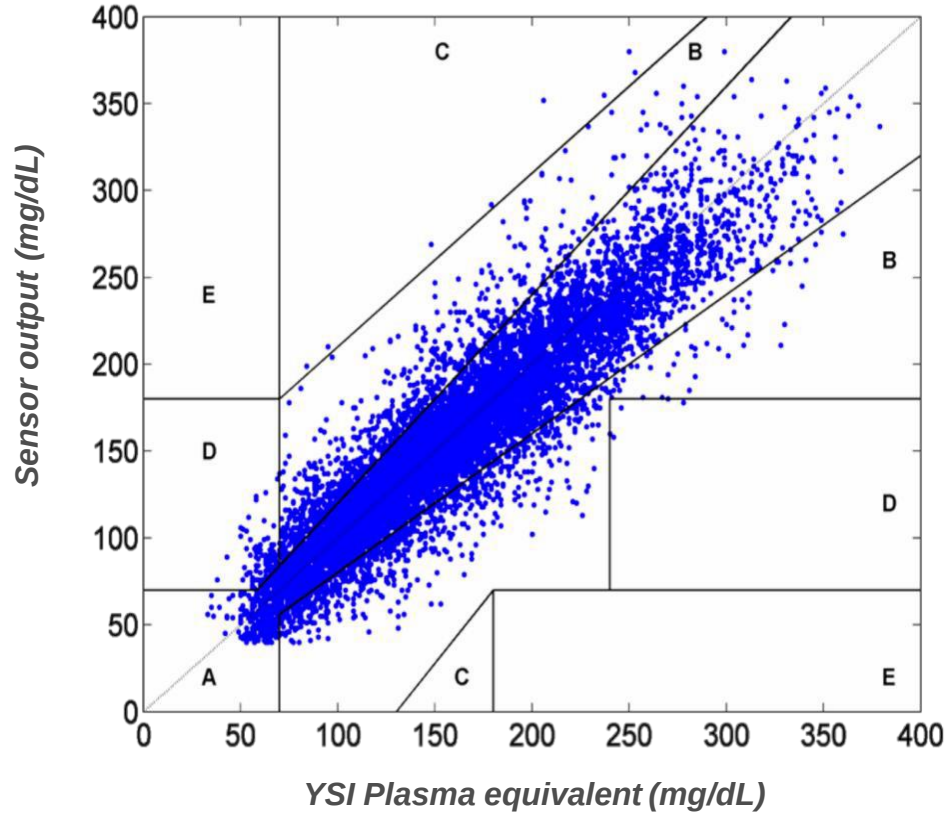
	Sensor accuracy, MARD (%), over the range of 2.2–22 mmol/L or 40–400 mg/dL			
Day	MARD, % (*n*)	SD	95% CI	15 mg/dL or 20%,* transitioning at 75 mg/dL
0–180	11.6 (21,527)	11.2	11.5, 11.8	84.0%
1–30	11.6 (10,761)	11.4	11.4, 11.8	83.9%
31–60	11.2 (4,382)	9.8	10.9, 11.5	85.5%
61–90	11.4 (1,429)	10.5	10.9, 11.9	84.3%
91–120	11.9 (2,672)	11.6	11.5, 12.3	82.6%
121–150	12.0 (975)	12.6	11.2, 12.8	84.3%
151–180	12.9 (1,308)	12.6	12.2, 13.6	81.9%

In-clinic accuracy is assessed per venous YSI reference measurement. *Performance of the sensor stability was assessed by calculating the percentage of system readings within 15 mg/dL (for YSI ≤4.2 mmol/L or 75 mg/dL) or 20% (for YSI >4.2 mmol/L or 75 mg/dL) of the paired YSI values.

La MARD del sensore nel range 40-400 mg/dL è pari a 11,6% .

Negli ultimi 30 giorni è stata rilevato un peggioramento dei parametri di accuratezza (MARD da 11,6% a 12,9%)

Obiettivo secondario: Clarke Error Grid



A: 84%

B: 15%

C: 0%

D: 1%

E: 0%

Il 99,2% dei valori rilevati dal sensore rientrano nelle sezioni A e B della griglia di Clarke (sezioni di scostamento clinicamente accettabile rispetto ai valori di riferimento)

Uso clinico del CGM

- Migliora il controllo glicemico
- Riduce il numero di eventi ipoglicemici
- Riduce la variabilità glicemica
- Educa il paziente alla gestione del diabete

Floyd B. et al., J Diabetes Sci Technol 6: 1094-1102, 2012; Poolsup N.et al., Diabetology & Metabolic Syndrome 5: 39-52, 2013; Pickup J C et al. BMJ 2011;343:bmj.d3805; Vigersky RA et al., Diabetes Care 35: 32-38, 2012.

Il successo del RT-CGM è basato su:

- Selezione, educazione e formazione del paziente
- Capacità del paziente di trasferire i dati del CGM nelle decisioni riguardanti la gestione del diabete
- Follow-up e rivalutazioni periodiche
- Eucazione e formazione del team diabetologico

Improving the Clinical Value and Utility of CGM Systems: Issues and Recommendations

A Joint Statement of the European Association for the Study of Diabetes and the American Diabetes Association Diabetes Technology Working Group

John R. Petrie,[1] Anne L. Peters,[2] Richard M. Bergenstal,[3] Reinhard W. Holl,[4] G. Alexander Fleming,[5] and Lutz Heinemann[6]

https://doi.org/10.2337/dci17-0043

1. ***More systematic and structured premarketing evaluation of the performance of CGM systems.***
2. ***Greater investment in trials to provide evidence of GCM value and reliability for all patient groups***
3. ***Standardization of CGM.measured glucose data reporting from clinical trials.***
4. ***Improved consistency and accessibility of safety reports to regulatory authorities after market approval***
1. ***Increased communication and cooperation across stakeholder groups***

- GRAZIE PER L’ ATTENZIONE