Conflitto di Interessi

Il Dr. Domenico Greco
dichiara di NON aver ricevuto negli ultimi due anni finanziamenti da Aziende Farmaceutiche e/o Diagnostiche

Le nuove tecnologie nella gestione dell'ipoglicemia: quale sensore e quale microinfusore e per quale paziente?

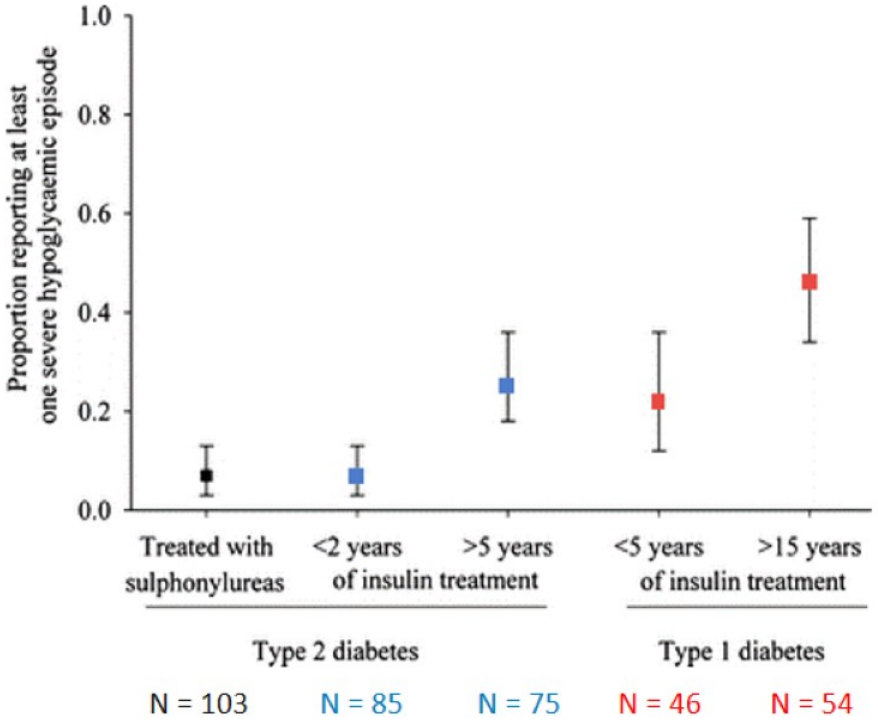
Dr. Domenico Greco

UOC "Malattie Endocrine, del Ricambio e della Nutrizione"

P.O. "Paolo Borsellino" - Marsala

ASP TRAPANI

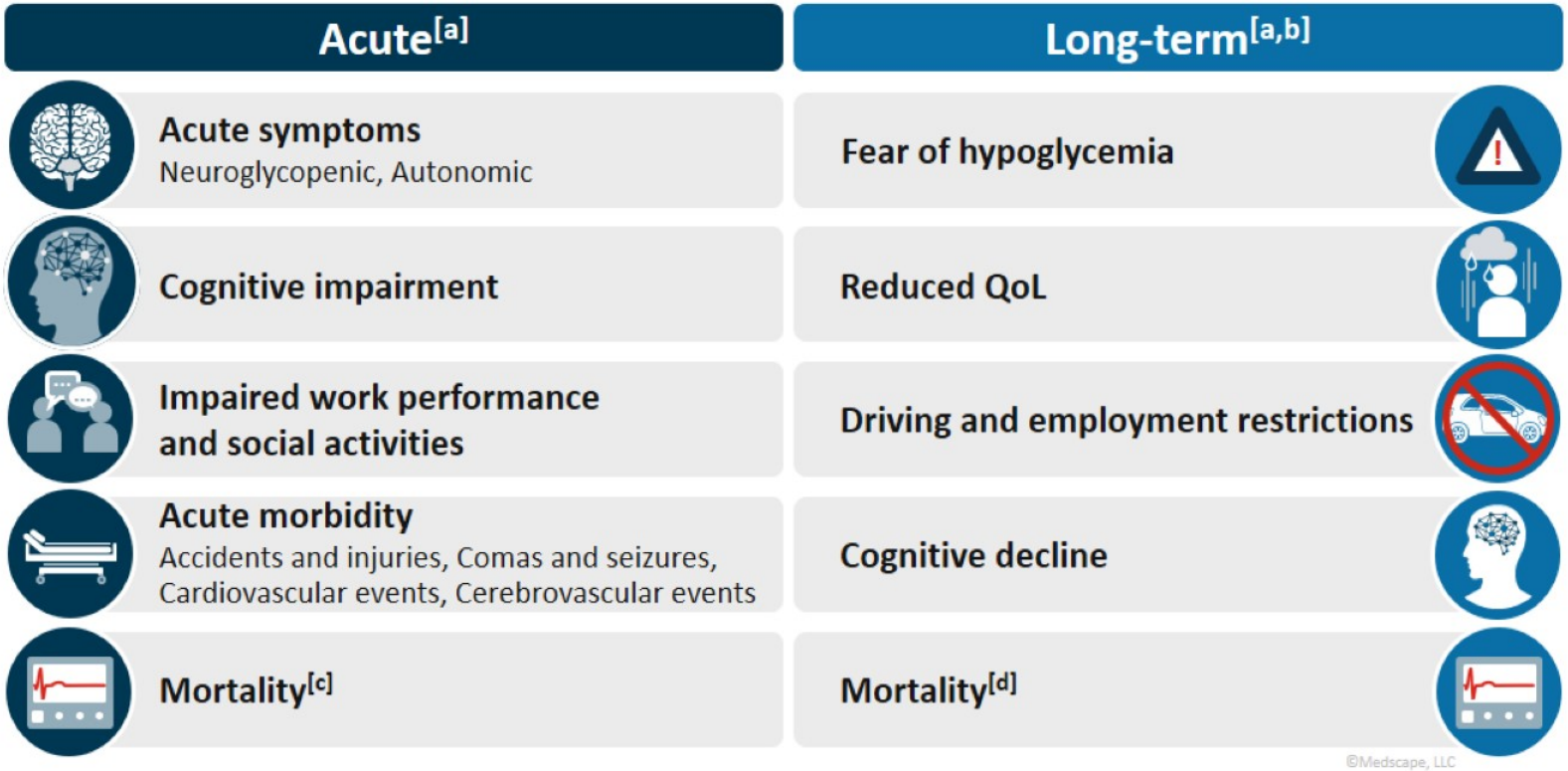
Risk of Hypoglycemia in T1DM and T2DM



Severe hypoglycemia was defined as any episode requiring third-party assistance
Error bars = 95% confidence intervals.
UK Hypoglycaemia Study Group. *Diabetologia.* 2007;50:1140-1147.

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

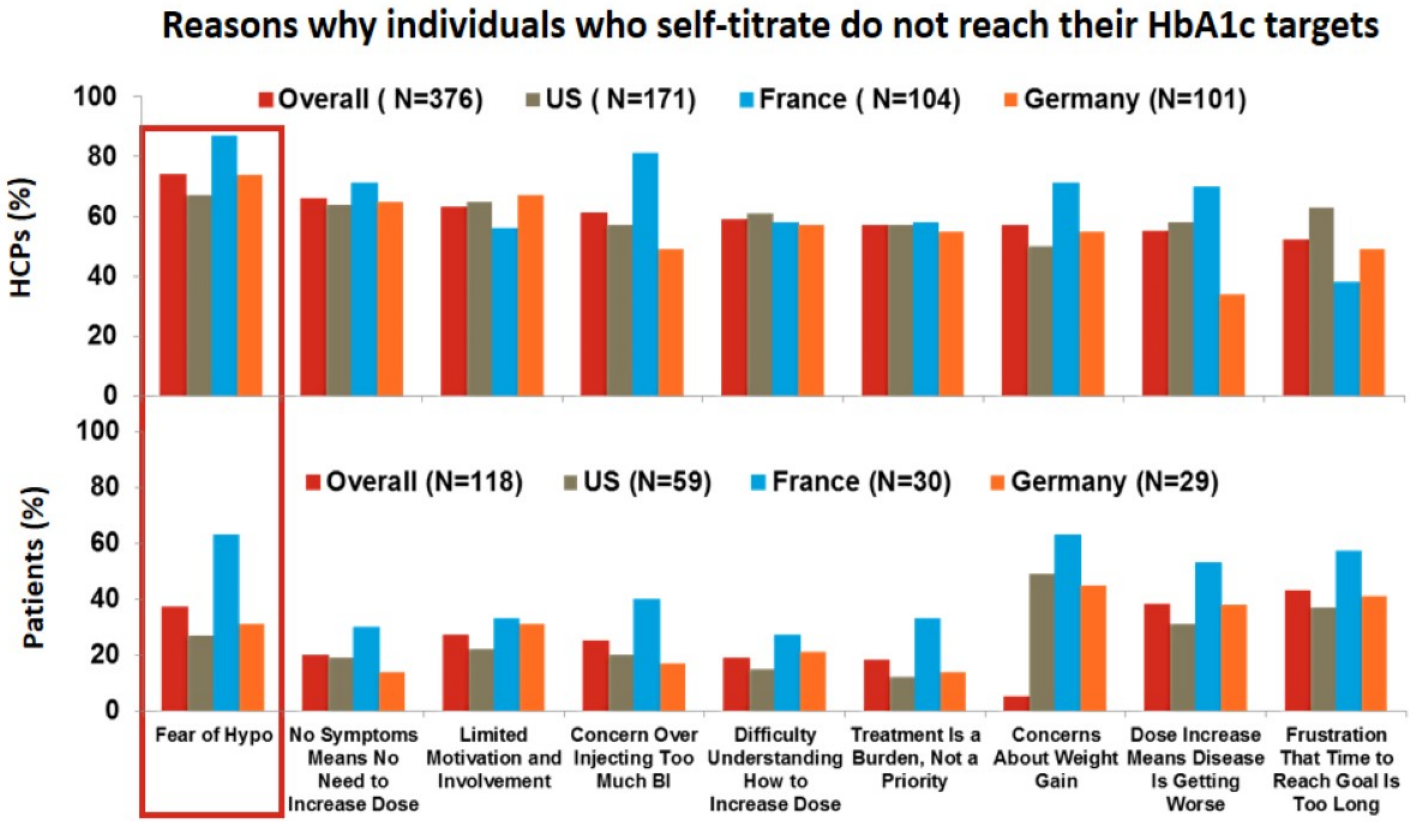
Severe Hypoglycemia Is Life Threatening and Has Negative Acute and Long-Term Consequences



a. Frier BM. *Nat Rev Endocrinol.* 2014;10:711-722; b. Seaquist ER, et al. *Diabetes Care.* 2013;36:1384-1395; c. Bonds DE, et al. *BMJ.* 2010;340:b4909; d. Cryer PE. *Diabetes Care.* 2012;35:1814-1816.

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

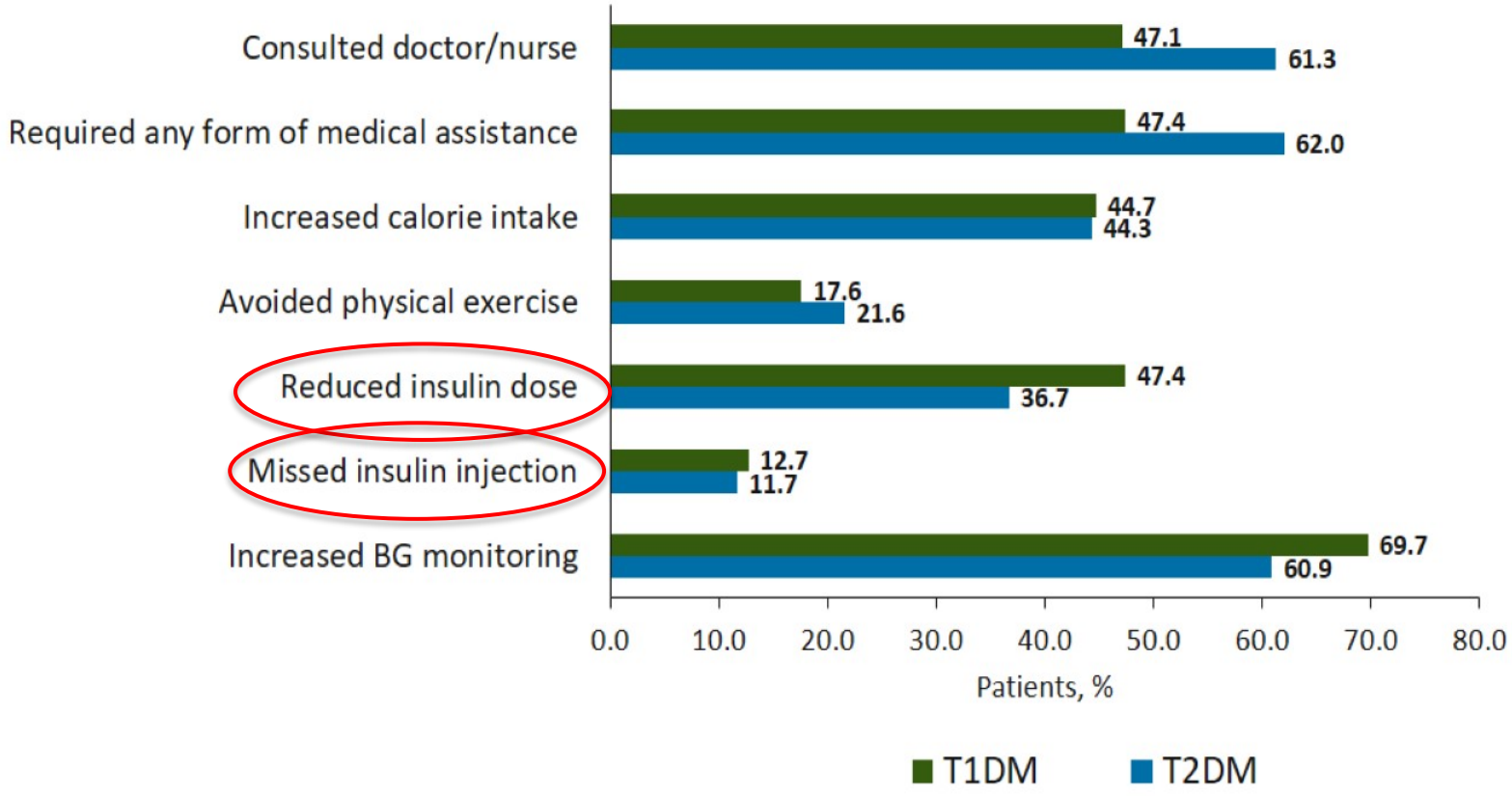
Fear of Hypoglycemia Is a Barrier to Optimal Insulin Titration



Berard LD, et al. ATTD 2017.

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Actions After Experiencing Hypoglycemia



Khunti K, et al. *Diab Res Clin Pract.* 2017;130:121-129.

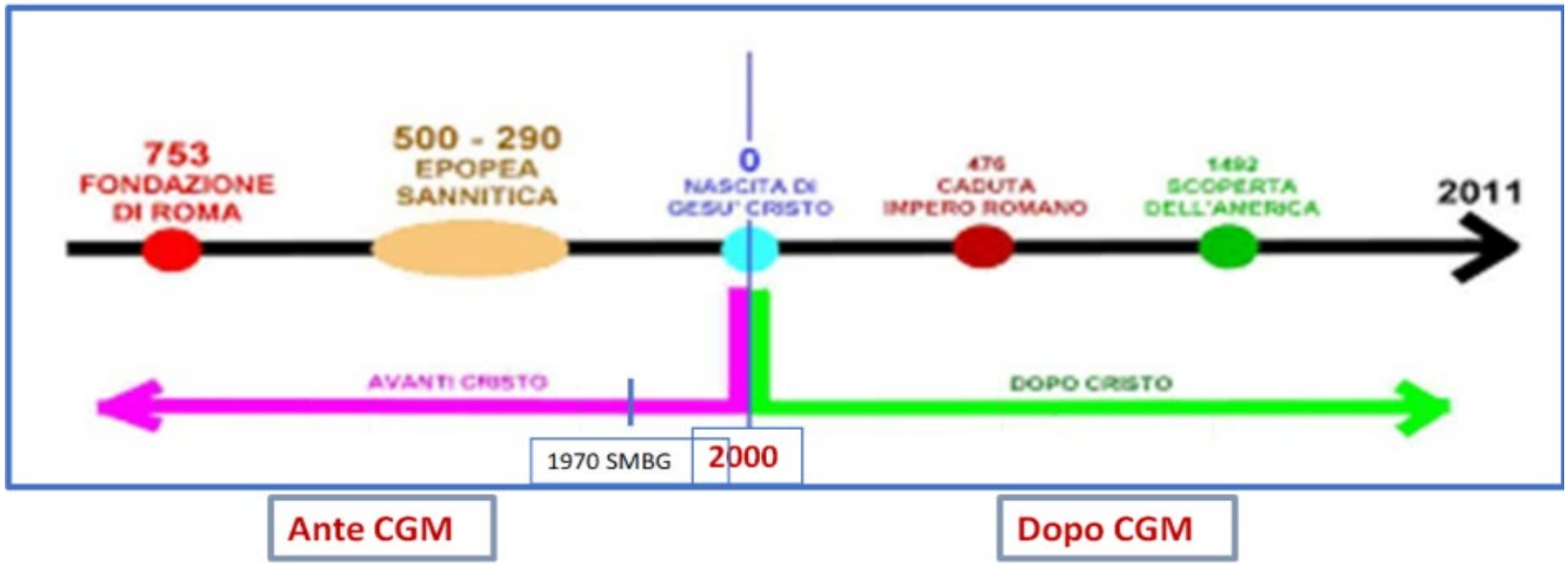
Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Nuove Tecnologie:

un contributo fondamentale nella conoscenza, nella prevenzione e nella gestione dell'ipoglicemia

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Il monitoraggio in continuo della glicemia è il vero spartiacque della *"linea del tempo diabetologica"*

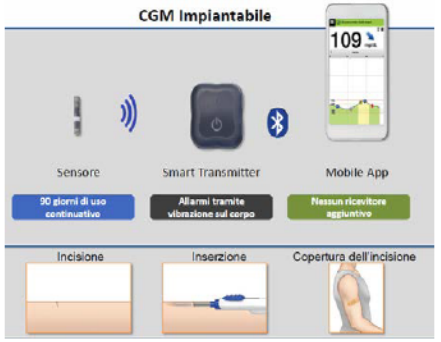


Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Monitoraggio Glicemico Continuo (CGM)

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

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

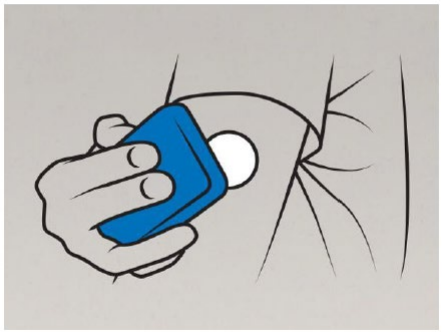


<u>Retrospettivo "holter-like"</u>
i dati vengono visualizzati dopo che il paziente ha utilizzato il sensore

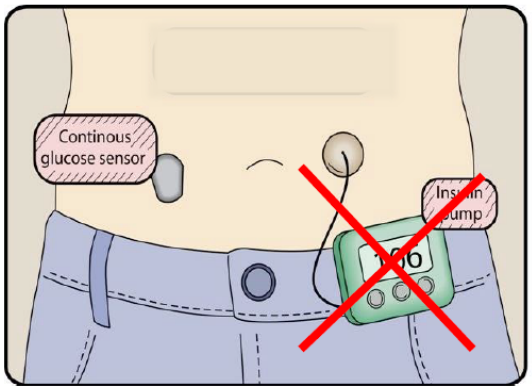
<u>Real-time</u>
il paziente può leggere i dati rilevati dal sensore sul ricevitore o sulla pompa e modificare la terapia

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

FGM

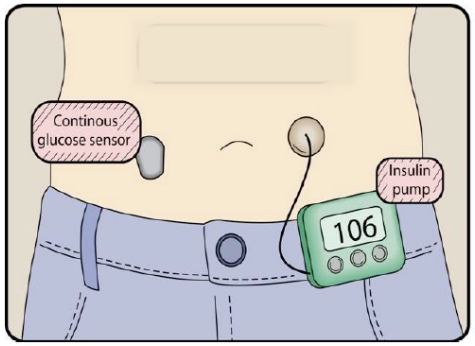


rtCGM



Stand-alone

rtCGM



Impiantabile

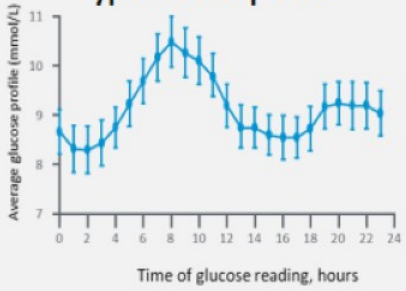
Hybrid Closed-Loop System

Sensor-augmented pump (SAP) therapy

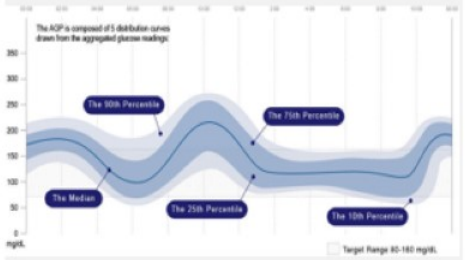
Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

From 7-Point SMBG to Ambulatory Glucose Profile

Distinguishes between **fasting**, **preprandial**, and **postprandial glucose excursions**, but only provides a snapshot[a]



Provides information on **direction**, **magnitude**, and **frequency of fluctuations** in blood glucose over 24 hours[b]



Average of CGM profiles to generate a **modal day** single curve, which can help in **identifying trends**[c] and visually represent **glycemic patterns**[d]

a. Parkin CG, et al. *J Diabetes Sci Technol.* 2009;3:500-508; b. De Block C, et al. *J Diabetes Sci Technol.* 2008;2:718-727; c. Hammond P. *Br J Diabetes.* 2016;16:S10-S15; d. Bergenstal RM, et al. *J Diabetes Sci Technol.* 2013;7:562-578.

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

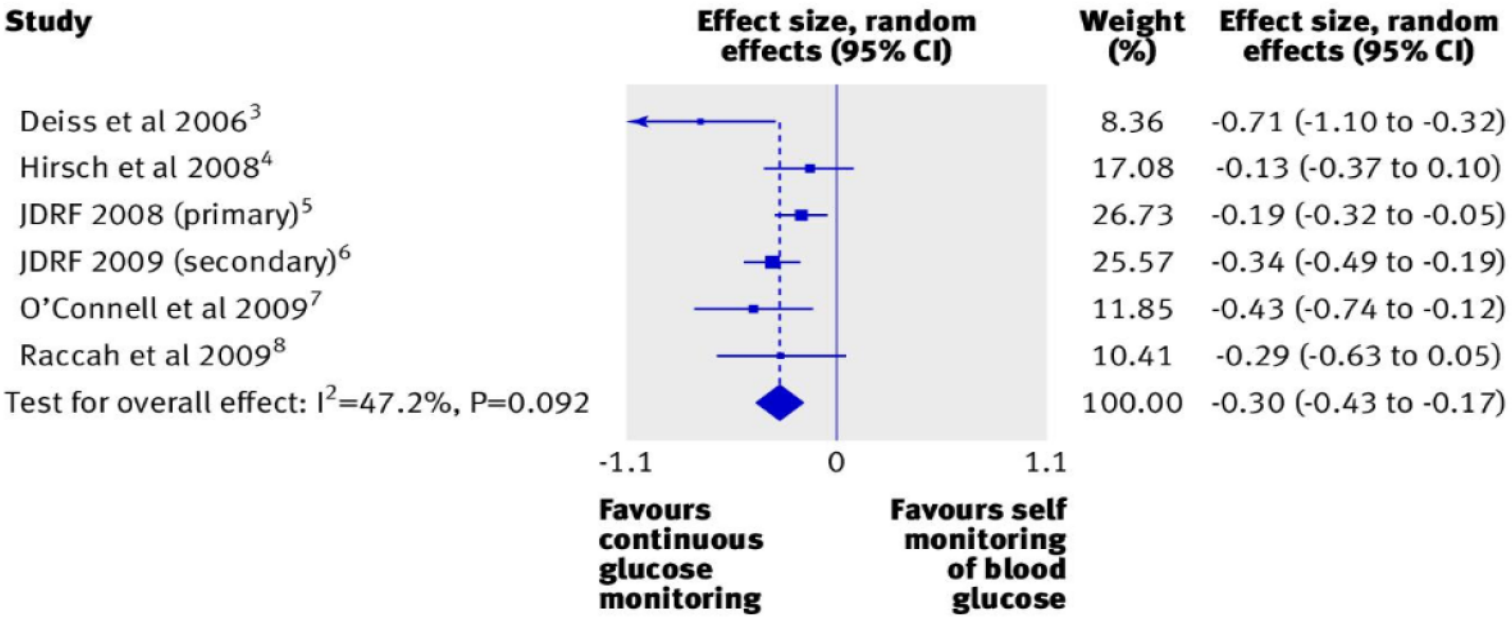
*In tutti gli studi, il vantaggio derivato dall'uso del CGM correla con il grado di aderenza all'uso **continuativo**.*

rtCGM vs. SMBG

BMJ

Glycaemic control in type 1 diabetes during real time continuous glucose monitoring compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data

John C Pickup *professor of diabetes and metabolism*[1], Suzanne C Freeman *medical statistics student*[2 3], Alex J Sutton *professor of medical statistics*[2]



Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Diabetes Care 1

Glycemic Outcomes in Adults With T1D Are Impacted More by Continuous Glucose Monitoring Than by Insulin Delivery Method: 3 Years of Follow-Up From the COMISAIR Study

Jan Šoupal,[1] Lenka Petruželková,[2] George Grunberger,[3,4,5] Aneta Hásková,[1] Milan Flekač,[1] Martin Matoulek,[1] Ondřej Mikeš,[1] Tomáš Pelcl,[1] Jan Škrha Jr.,[1] Eva Horová,[1] Jan Škrha,[1] Christopher G. Parkin,[6] Štěpán Svačina,[1] and Martin Prázný[1]

https://doi.org/10.2337/dc19-0888

94 soggetti adulti con DM1 in terapia con:
- microinfusore con rt-CGM
- microinfusore senza rt-CGM
- MDI con rt-CGM
- MDI senza rt-CGM

Durata osservazione: 3 anni

Risultati:
- i due gruppi con rt-CGM avevano una glicata significativamente inferiore;
- i due gruppi con rt-CGM avevano la maggiore percentuale di HbA1c < 7%;
- i due gruppi con rt-CGM avevano il maggiore aumento del "time in range"

"Real World Study"

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Diabetes Care 1

Glycemic Outcomes in Adults With T1D Are Impacted More by Continuous Glucose Monitoring Than by Insulin Delivery Method: 3 Years of Follow-Up From the COMISAIR Study

Jan Šoupal,[1] Lenka Petruželková,[2] George Grunberger,[3,4,5] Aneta Hásková,[1] Milan Flekač,[1] Martin Matoulek,[1] Ondřej Mikeš,[1] Tomáš Pelcl,[1] Jan Škrha Jr.,[1] Eva Horová,[1] Jan Škrha,[1] Christopher G. Parkin,[6] Štěpán Svačina,[1] and Martin Prázný[1]

https://doi.org/10.2337/dc19-0888

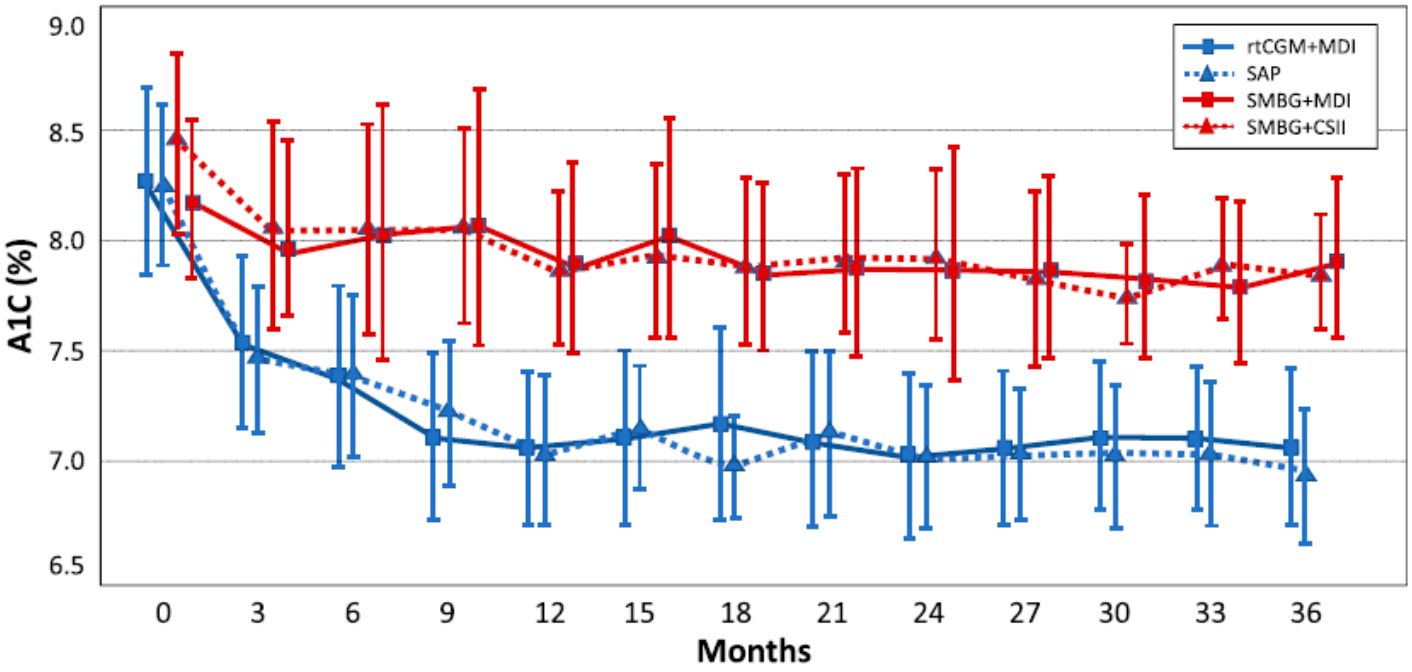


Figure 1—Change in A1C from baseline by study group. SAP, sensor-augmented pump.

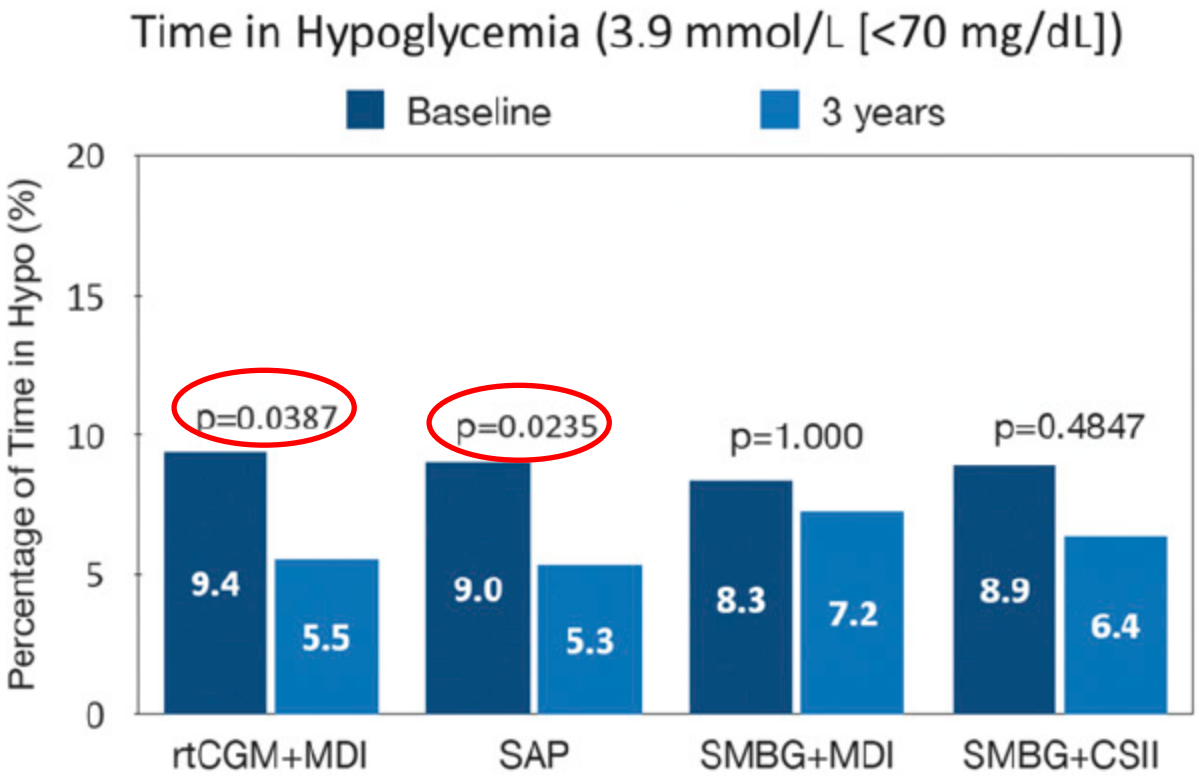
Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Diabetes Care 1

Glycemic Outcomes in Adults With T1D Are Impacted More by Continuous Glucose Monitoring Than by Insulin Delivery Method: 3 Years of Follow-Up From the COMISAIR Study

Jan Šoupal,[1] Lenka Petruželková,[2] George Grunberger,[3,4,5] Aneta Hásková,[1] Milan Flekač,[1] Martin Matoulek,[1] Ondřej Mikeš,[1] Tomáš Pelcl,[1] Jan Škrha Jr.,[1] Eva Horová,[1] Jan Škrha,[1] Christopher G. Parkin,[6] Štěpán Svačina,[1] and Martin Prázný[1]

https://doi.org/10.2337/dc19-0888



Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Diabetes Technology & Therapeutics, VOL. 21, NO. 1 | Original Articles

Glycemic Outcomes with Early Initiation of Continuous Glucose Monitoring System in Recently Diagnosed Patients with Type 1 Diabetes

Giacomo Mulinacci, G. Todd Alonso, Janet K. Snell-Bergeon, and Viral N. Shah

Published Online: 8 Jan 2019 | https://doi.org/10.1089/dia.2018.0257

Abstract

Background: We investigated the efficacy and safety of continuous glucose monitoring (CGM) initiation within 1 year of type 1 diabetes (T1D) diagnosis among children, adolescents, and adults.

Methods: Differences in mean A1c (primary outcome) and diabetes-related emergency visits (secondary outcome) for 2.5 years between early CGM users and non-CGM users were studied among 396 newly diagnosed patients with T1D (94% children [age <18 years], 5% adults, 46% females) between January 2013 and December 2015 at Barbara Davis Center for Diabetes. The primary outcome was adjusted by age at diagnosis and gender. $P < 0.05$ was considered significant.

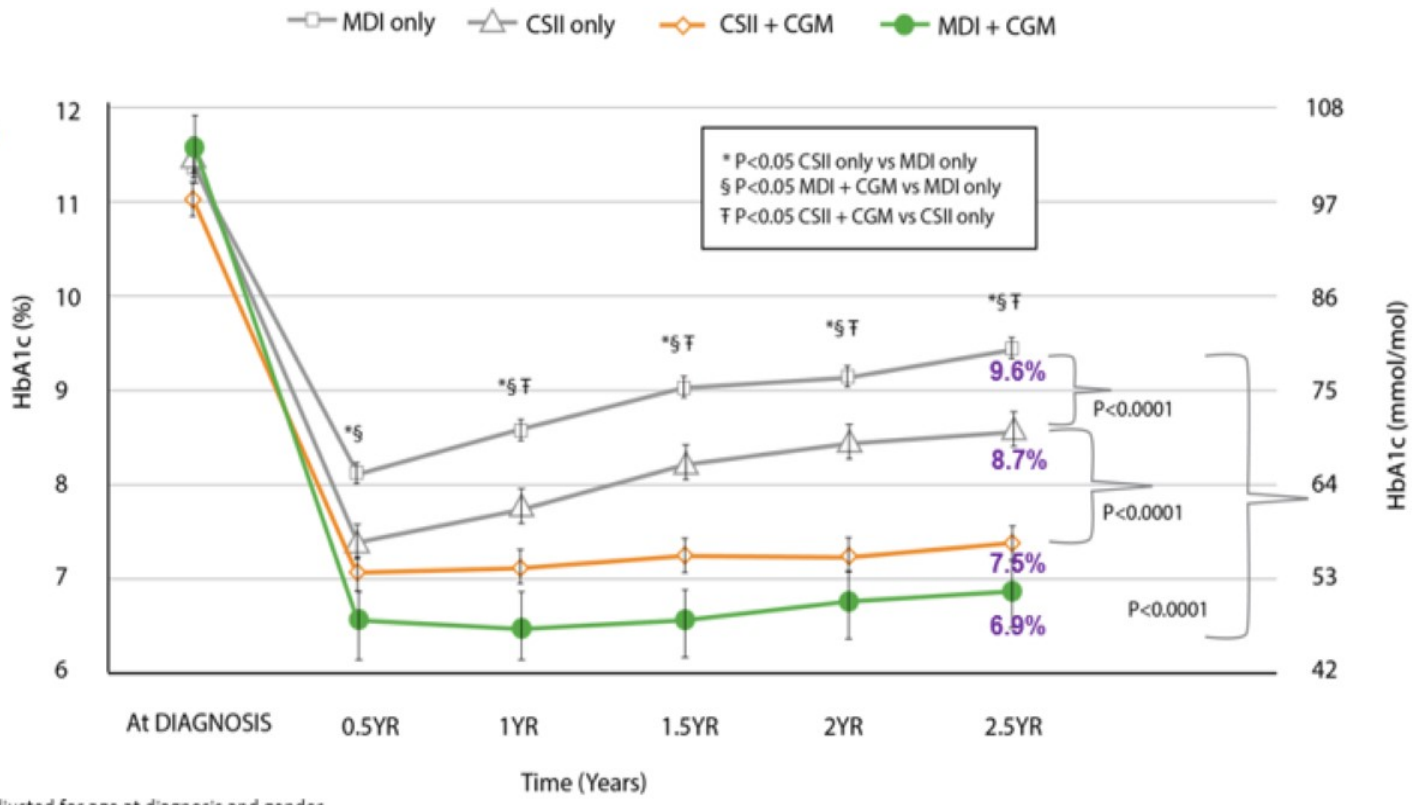
Results: Gender, ethnicity, body mass index, and A1c at diagnosis were similar between the groups. Irrespective of insulin delivery methods, CGM users had a significantly greater improvement in glycemic control than non-CGM users at 1, 1.5, 2, and 2.5 years. For 2.5 years of follow-up, the multiple daily injection (MDI)+CGM group ($n = 19$) had 1.5% ± 0.2% lower A1c than the MDI only group ($n = 225$) (7.7% ± 0.2% vs. 9.2% ± 0.04%, $P < 0.0001$), and the insulin pump (continuous subcutaneous insulin infusion [CSII])+CGM group ($n = 62$) had 0.7% ± 0.1% lower A1c than the CSII only group ($n = 90$) (8.0% ± 0.08% vs. 8.7% ± 0.07%, $P < 0.0001$). The MDI+CGM group had significantly lower A1c than the CSII only group (7.7% ± 0.2% vs. 8.7% ± 0.07%, $P < 0.0001$). The number of diabetes-related (severe hypoglycemia or hyperglycemia) emergency department visits was significantly lower among early CGM users compared with non-CGM users ($P = 0.003$).

Conclusion: Irrespective of insulin delivery system, early initiation of CGM within 1 year from T1D diagnosis was associated with better glucose control and fewer diabetes-related emergency visits.

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Irrespective of Insulin Delivery, HbA_{1c} Reductions Greater With CGM

N = 396
94% (n=372) <18y/o
6% (n=24) ≥18y/o



Linear mixed model adjusted for age at diagnosis and gender

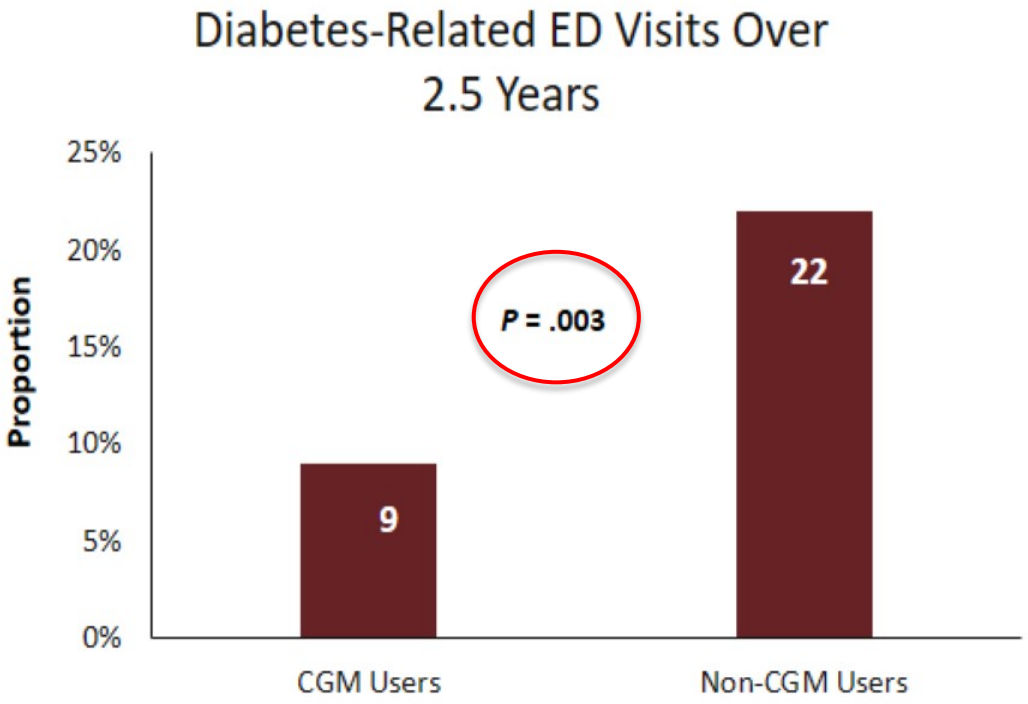
Mullinacci G, et al. *Diabetes Technol Ther.* 2019;21:6-10.

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Early Initiation of CGM Improves HbA_{1c} and Decreases ED Visits

Outcomes adjusted for a higher rate of private insurance among the CGM group. Results at 2.5 years demonstrated:

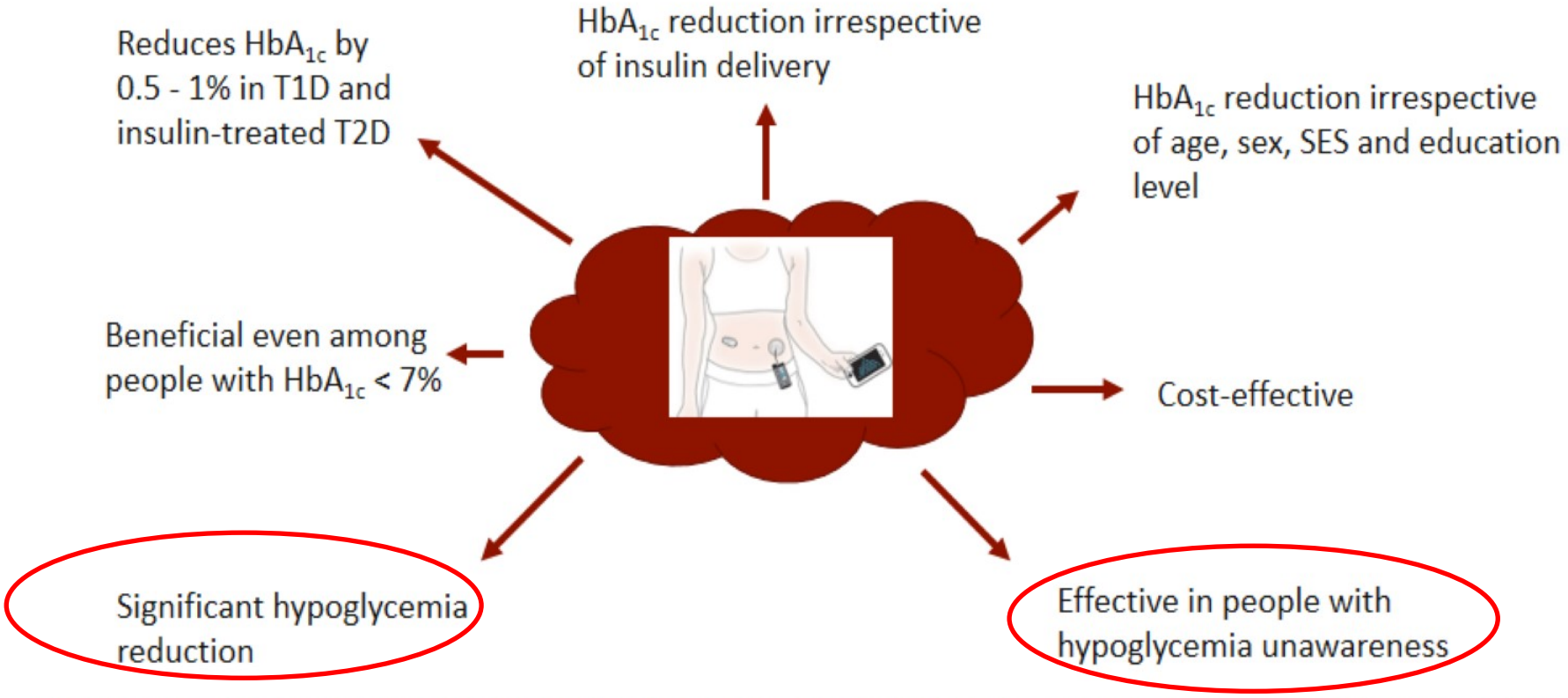
No statistically significant difference between MDI + CGM vs CSII + CGM



Mulinacci G, et al. *Diabetes Technol Ther*. 2019;21:6-10.

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Evidence With rtCGM



JDRF-CGM, Guard Control, SWITCH, DIAMOND T1D, DIAMOND T2D, GOLD, STAR-3, HypoCompass, HypoDE, InControl, CITY, SENCE, WISDM

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

141 soggetti DM1
con precedenti IPO severe
e/o "Hypo Unawareness"

RT-CGM vs autocontrollo
tradizionale x 6 mesi

Real-time continuous glucose monitoring in adults with type 1 diabetes and impaired hypoglycaemia awareness or severe hypoglycaemia treated with multiple daily insulin injections (HypoDE): a multicentre, randomised controlled trial

Lutz Heinemann, Guido Freckmann, Dominic Ehrmann, Gabriele Faber-Heinemann, Stefania Guerra, Delia Waldenmaier, Norbert Hermanns

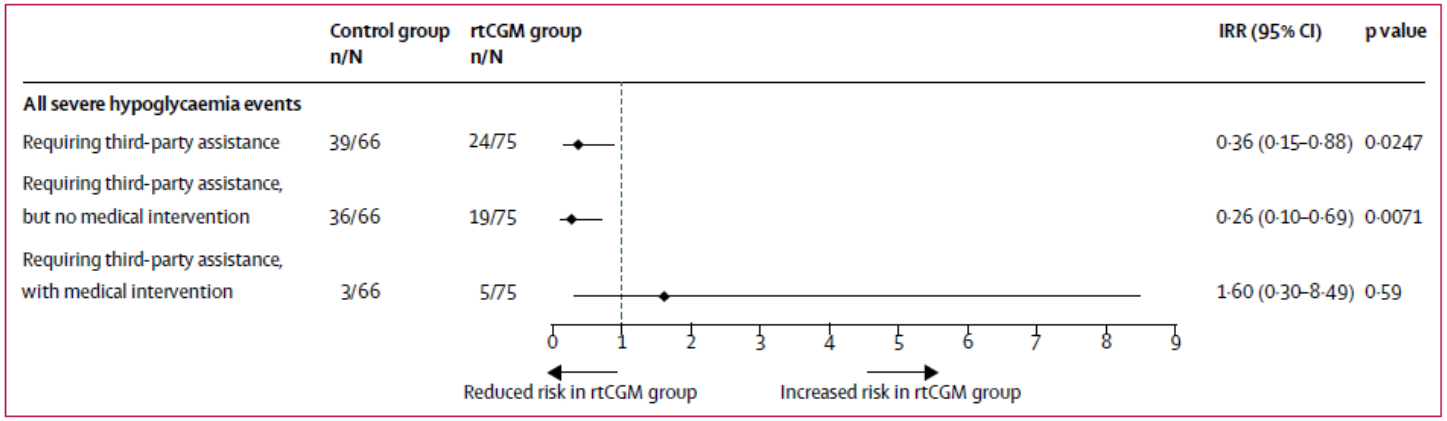


Figure 4: **Severe hypoglycaemia events in the rtCGM group and the control group**
rtCGM=real-time continuous glucose monitoring. IRR=incidence rate ratio.

Interpretation Usage of rtCGM reduced the number of hypoglycaemic events in individuals with type 1 diabetes treated by MDI and with impaired hypoglycaemia awareness or severe hypoglycaemia.

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

DIABETICMedicine

DOI: 10.1111/dme.14362

Research: Complications

People with type 1 diabetes and impaired awareness of hypoglycaemia have a delayed reaction to performing a glucose scan during hypoglycaemia: a prospective observational study

O. Moser[1], H. Ziko[1], H. Elsayed[1], D. A. Hochfellner[1], T. Pöttler[1], A. Mueller[1,2], M. L. Eckstein[1], H. Sourij[1,3] and J. K. Mader[1] on behalf of the Hypo-RESOLVE Consortium

[1]Division of Endocrinology and Diabetology, Department of Internal Medicine, Medical University of Graz, [2]Exercise Physiology, Training & Training Therapy Research Group, Institute of Sports Science, University of Graz, Graz, Austria and [3]Zayed Center for Health Sciences (ZCHS), United Arab Emirates University, Al Ain, United Arab Emirates

What's new?

- Assessment of impaired awareness of hypoglycaemia (IAH) is based mainly on scoring systems such as the Gold score, Clarke score and Pedersen-Bjergaard score.
- Our data revealed that time until scan after reaching hypoglycaemia while using a flash glucose monitoring system (flash GM) is delayed significantly in people with type 1 diabetes and IAH compared with those with type 1 diabetes without IAH, when IAH was assessed by Gold score and Pedersen-Bjergaard score.

DIABETICMedicine
DOI: 10.1111/dme.13561

Research: Treatment

A randomized controlled pilot study of continuous glucose monitoring and flash glucose monitoring in people with Type 1 diabetes and impaired awareness of hypoglycaemia

M. Reddy, N. Jugnee, A. El Laboudi, E. Spanudakis, S. Anantharaja and N. Oliver

Division of Diabetes, Endocrinology and Metabolism, Faculty of Medicine, Imperial College, London, UK

Abstract

Aim Hypoglycaemia in Type 1 diabetes is associated with mortality and morbidity, especially where awareness of hypoglycaemia is impaired. Clinical pathways for access to continuous glucose monitoring (CGM) and flash glucose monitoring technologies are unclear. We assessed the impact of CGM and flash glucose monitoring in a high-risk group of people with Type 1 diabetes.

Methods A randomized, non-masked parallel group study was undertaken. Adults with Type 1 diabetes using a multiple-dose insulin-injection regimen with a Gold score of ≥ 4 or recent severe hypoglycaemia were recruited. Following 2 weeks of blinded CGM, they were randomly assigned to CGM (Dexcom G5) or flash glucose monitoring (Abbott Freestyle Libre) for 8 weeks. The primary outcome was the difference in time spent in hypoglycaemia (below 3.3 mmol/l) from baseline to endpoint with CGM versus flash glucose monitoring.

Results Some 40 participants were randomized to CGM ($n = 20$) or flash glucose monitoring ($n = 20$). The participants (24 men, 16 women) had a median (IQR) age of 49.6 (37.5–63.5) years, duration of diabetes of 30.0 (21.0–36.5) years and HbA_{1c} of 56 (48–63) mmol/mol [7.3 (6.5–7.8)%]. The baseline median percentage time < 3.3 mmol/l was 4.5% in the CGM group and 6.7% in the flash glucose monitoring. At the end-point the percentage time < 3.3 mmol/l was 2.4%, and 6.8% respectively (median between group difference –4.3%, $P = 0.006$). Time spent in hypoglycaemia at all thresholds, and hypoglycaemia fear, were different between groups, favouring CGM.

Conclusion CGM more effectively reduces time spent in hypoglycaemia in people with Type 1 diabetes and impaired awareness of hypoglycaemia compared with flash glucose monitoring. (Clinical Trial Registry No: NCT03028220)

Diabet. Med. 35, 483–490 (2018)

OBJECTIVE

Use of real-time continuous glucose monitoring (RT-CGM) systems in the inpatient setting is considered investigational. The objective of this study was to evaluate whether RT-CGM, using the glucose telemetry system (GTS), can prevent hypoglycemia in the general wards.

RESEARCH DESIGN AND METHODS

In a randomized clinical trial, insulin-treated patients with type 2 diabetes at high risk for hypoglycemia were recruited. Participants were randomized to RT-CGM/GTS or point-of-care (POC) blood glucose testing. The primary outcome was difference in inpatient hypoglycemia.

Reducing Inpatient Hypoglycemia in the General Wards Using Real-time Continuous Glucose Monitoring: The Glucose Telemetry System, a Randomized Clinical Trial

Lakshmi G. Singh,[1] Medha Satyarengga,[2] Isabel Marcano,[3] William H. Scott,[1] Lillian F. Pinault,[1] Zhaoyong Feng,[4] John D. Sorkin,[5] Guillermo E. Umpierrez,[6] and Elias K. Spanakis[1,3]

Diabetes Care 2020;43:2736–2743 | https://doi.org/10.2337/dc20-0840

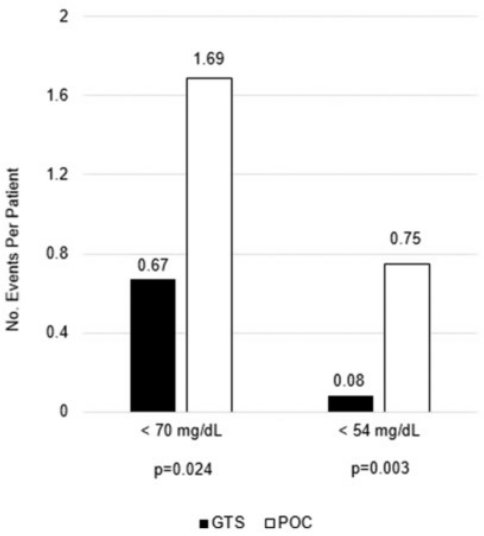


Figure 1—Hypoglycemic events per patient.

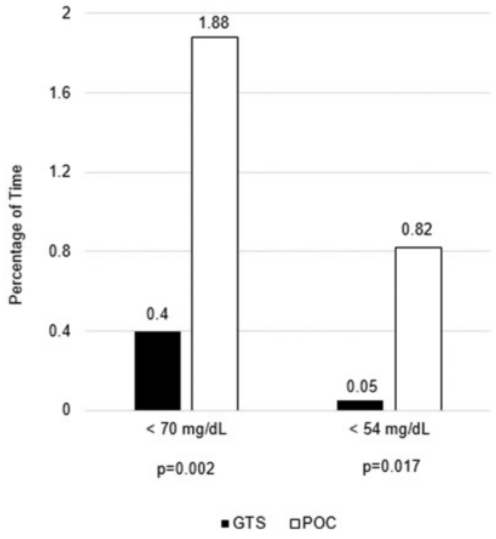


Figure 2—Percentage of TBR.

CONCLUSIONS

RT-CGM/GTS can decrease hypoglycemia among hospitalized high-risk insulin-treated patients with type 2 diabetes.

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Diabetologia (2020) 63:2501–2520
https://doi.org/10.1007/s00125-020-05263-9

POSITION STATEMENT

Check for updates

Glucose management for exercise using continuous glucose monitoring (CGM) and intermittently scanned CGM (isCGM) systems in type 1 diabetes: position statement of the European Association for the Study of Diabetes (EASD) and of the International Society for Pediatric and Adolescent Diabetes (ISPAD) endorsed by JDRF and supported by the American Diabetes Association (ADA)

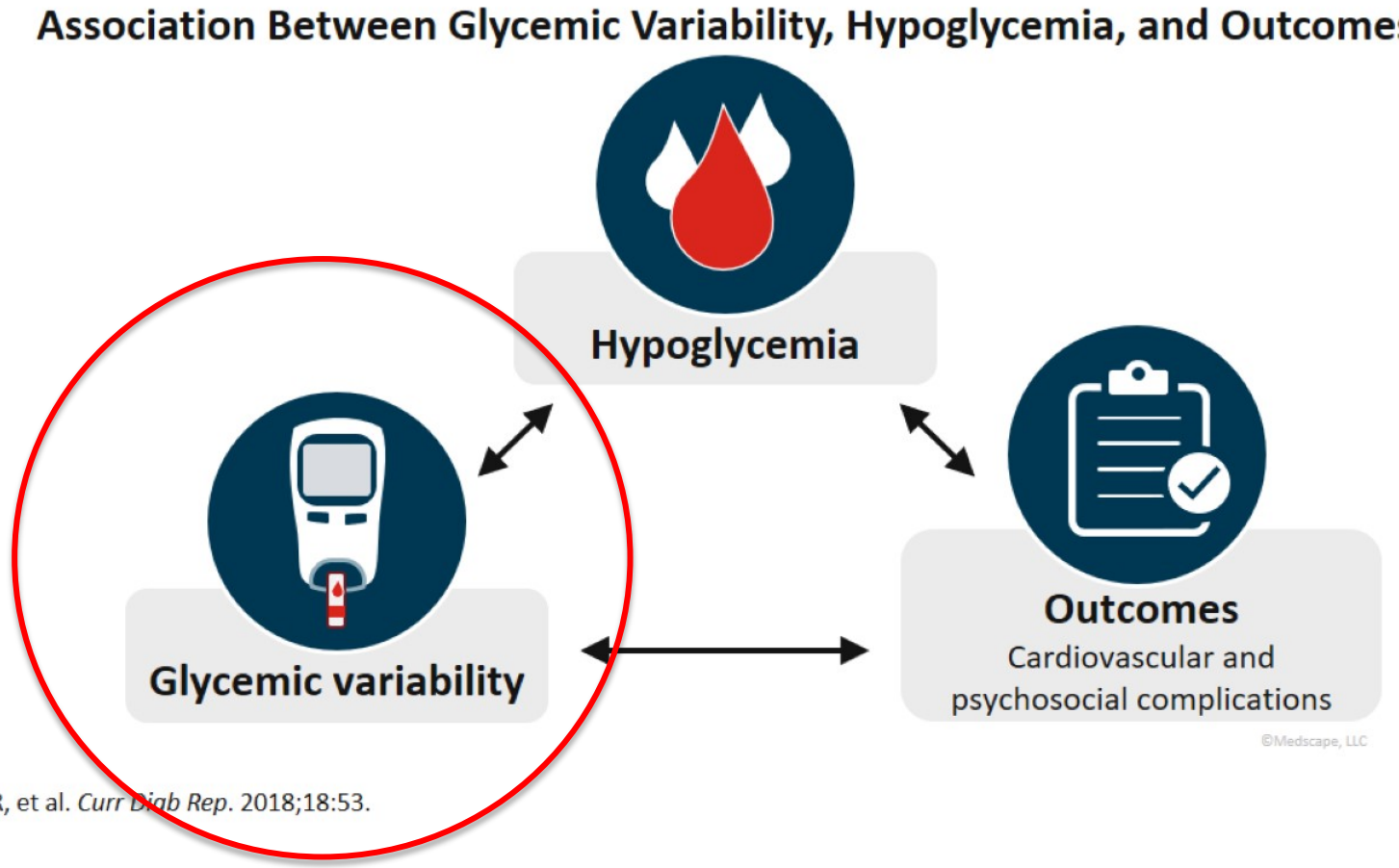
Othmar Moser[1,2] · Michael C. Riddell[3] · Max L. Eckstein[1] · Peter Adolfsson[4,5] · Rémi Rabasa-Lhoret[6,7,8,9] · Louisa van den Boom[10] · Pieter Gillard[11] · Kirsten Nørgaard[12] · Nick S. Oliver[13] · Dessi P. Zaharieva[14] · Tadej Battelino[15,16] · Carine de Beaufort[17,18] · Richard M. Bergenstal[19] · Bruce Buckingham[14] · Eda Cengiz[20,21] · Asma Deeb[22] · Tim Heise[23] · Simon Heller[24,25] · Aaron J. Kowalski[26] · Lalantha Leelarathna[27,28] · Chantal Mathieu[11] · Christoph Stettler[29] · Martin Tauschmann[30] · Hood Thabit[27] · Emma G. Wilmot[31,32] · Harald Sourij[1] · Carmel E. Smart[33,34] · Peter G. Jacobs[35] · Richard M. Bracken[36] · Julia K. Mader[1]

Abstract

Physical exercise is an important component in the management of type 1 diabetes across the lifespan. Yet, acute exercise increases the risk of dysglycaemia, and the direction of glycaemic excursions depends, to some extent, on the intensity and duration of the type of exercise. Understandably, fear of hypoglycaemia is one of the strongest barriers to incorporating exercise into daily life. Risk of hypoglycaemia during and after exercise can be lowered when insulin-dose adjustments are made and/or additional carbohydrates are consumed. Glycaemic management during exercise has been made easier with continuous glucose monitoring (CGM)

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

The Hypo Triad



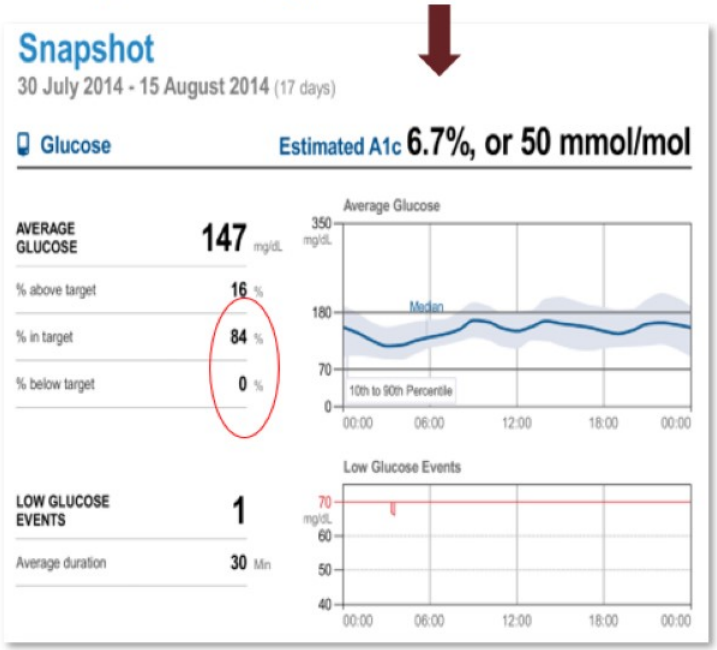
Silbert R, et al. *Curr Diab Rep*. 2018;18:53.

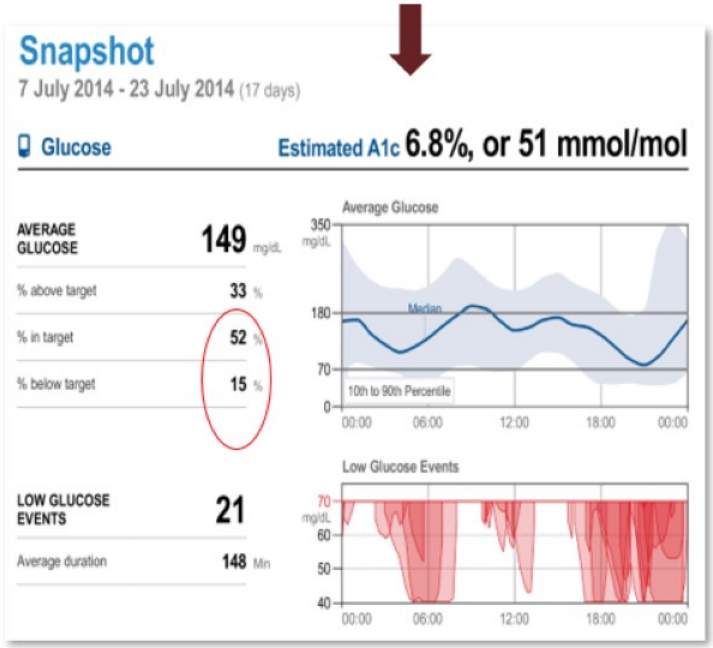
Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Why TIR Is Important

Clinical Examples With Same HbA1c

TiR 70-180/< 70 mg/dL





84 / 0 %

52 / 15 %

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Scopo: fornire una guida ai medici, ricercatori e persone con diabete, per l'uso, l'interpretazione e la comunicazione dei dati CGM nella pratica quotidiana e nella ricerca.

Diabetes Care 1

Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range

Tadej Battelino,[1] Thomas Danne,[2] Richard M. Bergenstal,[3] Stephanie A. Amiel,[4] Roy Beck,[5] Torben Biester,[2] Emanuele Bosi,[6] Bruce A. Buckingham,[7] William T. Cefalu,[8] Kelly L. Close,[9] Claudio Cobelli,[10] Eyal Dassau,[11] J. Hans DeVries,[12,13] Kim C. Donaghue,[14] Klemen Dovc,[1] Francis J. Doyle III,[11] Satish Garg,[15] George Grunberger,[16] Simon Heller,[17]

Table 2—Standardized CGM metrics for clinical care: 2019

1. Number of days CGM worn (recommend 14 days) (42,43)	
2. Percentage of time CGM is active (recommend 70% of data from 14 days) (41,42)	
3. Mean glucose	
4. Glucose management indicator (GMI) (75)	
5. Glycemic variability (%CV) target ≤36% (90)*	
6. Time above range (TAR): % of readings and time >250 mg/dL (>13.9 mmol/L)	Level 2
7. Time above range (TAR): % of readings and time 181–250 mg/dL (10.1–13.9 mmol/L)	Level 1
8. Time in range (TIR): % of readings and time 70–180 mg/dL (3.9–10.0 mmol/L)	In range
9. Time below range (TBR): % of readings and time 54–69 mg/dL (3.0–3.8 mmol/L)	Level 1
10. Time below range (TBR): % of readings and time <54 mg/dL (<3.0 mmol/L)	Level 2
Use of Ambulatory Glucose Profile (AGP) for CGM report	

CV, coefficient of variation. *Some studies suggest that lower %CV targets (<33%) provide additional protection against hypoglycemia for those receiving insulin or sulfonylureas (45,90,91).

Sono stati selezionati i 10 parametri più utili nella pratica clinica

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Profilo Glicemico Ambulatoriale (AGP).

AGP Report

Name

MRN

GLUCOSE STATISTICS AND TARGETS

26 Feb 2019–10 Mar 2019 **13 days**
% Time CGM is Active **99.9%**

Glucose Ranges	**Targets** [% of Readings (Time/Day)]
Target Range 70–180 mg/dL	Greater than 70% (16h 48min)
Below 70 mg/dL	Less than 4% (58min)
Below 54 mg/dL	Less than 1% (14min)
Above 180 mg/dL	Less than 25% (6h)
Above 250 mg/dL	Less than 5% (1h 12min)

Each 5% increase in time in range (70–180 mg/dL) is clinically beneficial.

Average Glucose	**173 mg/dL**
Glucose Management Indicator (GMI)	**7.6%**
Glucose Variability	**49.5%**

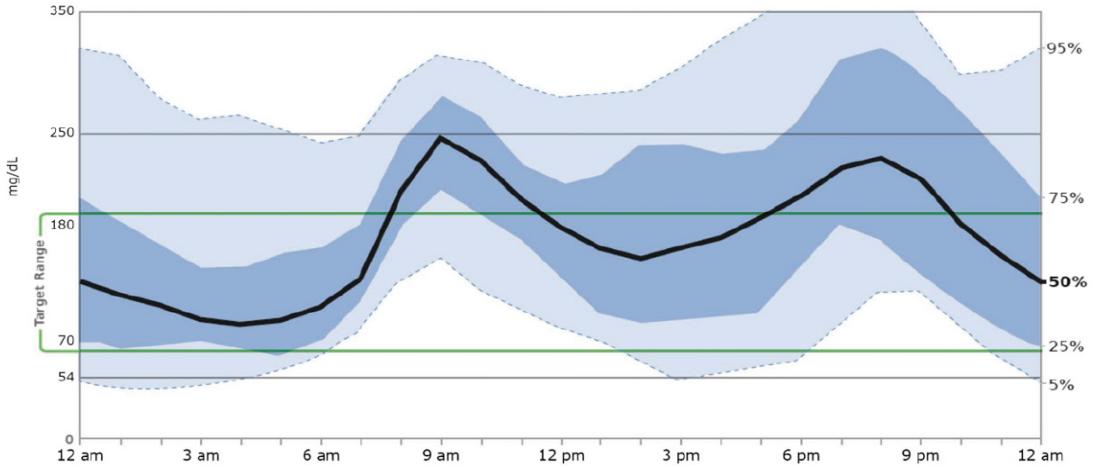
Defined as percent coefficient of variation (%CV); target ≤36%

TIME IN RANGES

Very High (>250 mg/dL) **20%** (4h 48min)
High (181–250 mg/dL) **23%** (5h 31min)
Target Range (70–180 mg/dL) **47%** (11h 17min)
Low (54–69 mg/dL) **4%** (58min)
Very Low (<54 mg/dL) **6%** (1h 26min)

AMBULATORY GLUCOSE PROFILE (AGP)

AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if occurring in a single day.



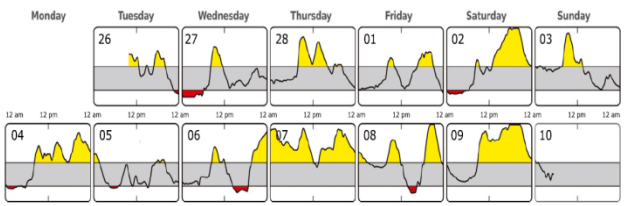
Diabetes Care 1

Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range

Tadej Battelino,[1] Thomas Danne,[2] Richard M. Bergenstal,[3] Stephanie A. Amiel,[4] Roy Beck,[5] Torben Biester,[2] Emanuele Bosi,[6] Bruce A. Buckingham,[7] William T. Cefalu,[8] Kelly L. Close,[9] Claudio Cobelli,[10] Eyal Dassau,[11] J. Hans DeVries,[12,13] Kim C. Donaghue,[14] Klemen Dovc,[1] Francis J. Doyle III,[15] Satish Garg,[16] George Grunberger,[16] Simon Heller,[17]

·Ambulatory Glucose Profile.

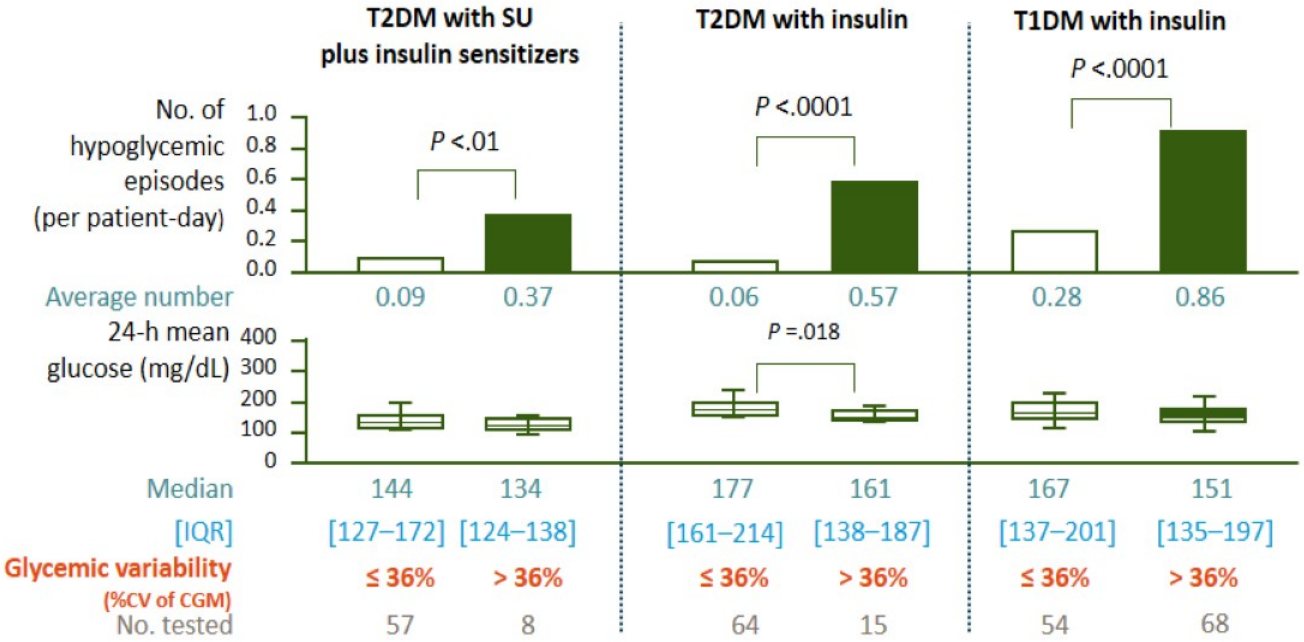
DAILY GLUCOSE PROFILES



Each daily profile represents a midnight-to-midnight period.

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Coefficient of Variation: Glucose Variability Assessed by CGM And Hypoglycemia



Glycemic variability based on %CV of glucose at 36%

- Could be used as a threshold to discern between stable and unstable glucose homeostasis
- Increased frequency of hypoglycemia observed in patients with T1DM and T2DM on insulin therapy when threshold is transgressed

Monnier L, et al. *Diabetes Care*. 2017;40:832-838.

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

JAMD THE JOURNAL OF AMD

JAMD 2020 | VOL. 23 | N° 1

RESEARCH ARTICLE

Real Time Continous Glucose Monitoring, Flash Glucose Monitoring e sensori glicemici impiantabili: caratteristiche e peculiarità

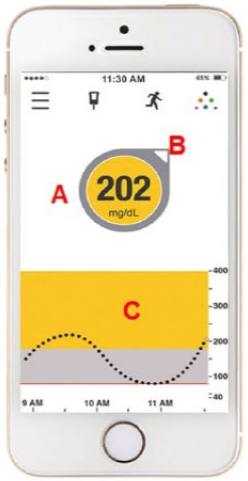
Real Time Continous Glucose Monitoring, Flash Glucose Monitorin and implantable glycemic sensors: features and peculiarities

G. Papa[1], M.P. Iurato[1], C. Licciardello[1], D. Moretti[1], C. Toscano[2], C. Finocchiaro[1]
[1]Centro Catanese di Medicina e Chirurgia, Unità Funzionale di Malattie Endocrine e Dismetaboliche, Catania. [2]S.C. Diabetologia Territoriale Sud, A.S.L. Città di Torino, Torino.

I sistemi CGM <u>non sono tutti uguali</u> e per una corretta gestione delle risorse la scelta del CGM/FGM dovrebbe essere quanto più possibile "*sartoriale*".

Frecce di "Tendenza" o di "Variazione"

Reference Guide for Integrating Continuous Glucose Monitoring Into Clinical Practice



Kruger et al

The Diabetes EDUCATOR

Volume 45, Supplement 1, February 2019

Arrow	Meaning	Arrow	Meaning	Arrow	Meaning	Arrow	Meaning
↑↑	**Glucose rapidly rising** >3 mg/dL/min >0.2 mmol/L/min	↑↑↑	**Glucose rapidly rising** >3 mg/dL/min >0.2 mmol/L/min	—	—	—	—
↑	**Glucose rising** 2–3 mg/dL/min 0.1-0.2 mmol/L/min	↑↑	**Glucose is rising** 2–3 mg/dL/min 0.1-0.2 mmol/L/min	↑	**Glucose rapidly rising** >2 mg/dL/min >0.1 mmol/L/min	↑	**Glucose rapidly rising** >2 mg/dL/min >0.1 mmol/L/min
↗	**Glucose slowly rising** 1–2 mg/dL/min 0.06-0.1 mmol/L/min	↑	**Glucose slowly rising** 1–2 mg/dL/min 0.06-0.1 mmol/L/min	↗	**Glucose rising** 1–2 mg/dL/min 0.06-0.1 mmol/L/min	↗	**Glucose slowly rising** 1–2 mg/dL/min 0.06-0.1 mmol/L/min
→	**Glucose steady** *Increasing/decreasing* <1 mg/dL/min <0.06 mmol/L/min	—	**Glucose steady** Increasing/decreasing <1 mg/dL/min <0.06 mmol/L/min	→	**Glucose steady** *Increasing/decreasing* <1 mg/dL/min <0.06 mmol/L/min	→	**Glucose steady** *Increasing/decreasing* <1 mg/dL/min <0.06 mmol/L/min
↘	**Glucose slowly falling** 1–2 mg/dL/min 0.06-0.1 mmol/L/min	↓	**Glucose slowly falling** 1–2 mg/dL/min 0.06-0.1 mmol/L/min	↘	**Glucose slowly falling** 1–2 mg/dL/min 0.06-0.1 mmol/L/min	↘	**Glucose slowly falling** 1–2 mg/dL/min 0.06-0.1 mmol/L/min
↓	**Glucose falling** 2–3 mg/dL/min 0.1-0.2 mmol/L/min	↓↓	**Glucose is falling** 2–3 mg/dL/min 0.1-0.2 mmol/L/min	↓	**Glucose rapidly falling** >2 mg/dL/min >0.1 mmol/L/min	↓	**Glucose rapidly falling** >2 mg/dL/min >0.1 mmol/L/min
↓↓	**Glucose rapidly falling** >3 mg/dL/min >0.2 mmol/L/min	↓↓↓	**Glucose rapidly falling** >3 mg/dL/min >0.2 mmol/L/min	—	—	—	—

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Table 1: Currently available Continuous Glucose Monitors (CGM)[15]

CGM	Receiver	Size and weight	Warm-up/ calibration	Dosing decisions	Duration	Alerts	Share feature	Age	MARD	Software
	Reader; Sensor stores 8 hours of data if not read	1.38 in. diameter x 0.2 in; 0.18 oz.	1-hour warm up; no calibration required.	Yes	14 days	No	No	≥18 years and older	10%	
	Receiver or app	1.5 x 0.9 x 0.5 in; 0.4 oz. with sensor	2-hour warm up; calibration required every 12 hours.	Yes	7 days	Yes	Yes	≥2 years and older	9%	
	Receiver or app (Apple and Android devices) or integrated with pump	4.02 x 2.44 x 0.46 in; 3.3 oz.	2-hour warm up; no calibration required.	Yes	10 days	Yes	Yes	≥2 years and older	9%	
	Integrated with insulin pumps	1.4 x 1.12 x 0.37 in; 0.19 oz. without sensor	2-hour warm up; calibration required every 12 hours.	No	7 days	Yes	No	≥7 years and older	9.1% (8.7% with 3-4 calibrations a day	
	phone app (Apple devices only)	1.41 x 1.13 x 0.38 in; 0.04 oz.	2-hour warm up; calibration required every 12 hours.	No	7 days	Yes	Yes	≥14 years and older	9.1% (8.7% with 3-4 calibrations a day	
	Smart phone app (Apple and Android devices)	1.48 x 1.89 x 0.35 in; 0.39 oz.	24-hour warm up; calibration required every 12 hours.	No	90 days in US; 180 days in Europe	Yes and transmitter vibrates alerts when away from phone	Yes	≥18 years and older	8.8%	

CGM = continuous glucose monitor; MARD = Mean absolute relative difference.

Reference Guide for Integrating Continuous Glucose Monitoring Into Clinical Practice

rtCGM:

- **Allarmi raggiungimento soglie IPO**
- **Avvisi predittivi per soglie IPO**

Kruger et al

The Diabetes EDUCATOR

Volume 45, Supplement 1, February 2019

Active alarms/alerts

The availability of active alarms/alerts that automatically warn users of current or impending adverse glycemic events is an important feature of rtCGM devices. This feature is extremely important for patients with frequent severe hypoglycemia, nocturnal hypoglycemia, impaired hypoglycemia awareness, fear of hypoglycemia, and extreme hyperglycemia as well. The downside of active alarms/alerts is the potential for "alarm fatigue," defined as situations in which patients (and families) are repeatedly disturbed by both false and frequent alarms.[20]

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

FGM "2": Allarmi

Allarme Glucosio Basso
Può essere impostato tra 60-100 mg/dl

Allarme Glucosio Alto
Può essere impostato tra 120-400 mg/dl

Allarme Perdita Segnale
Succede quando il sensore perde il segnale con reader o smartphone

FGM "3": new

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

DOCUMENTO DEL GRUPPO DI STUDIO INTERSOCIETARIO AMD - SID - SIEDP "TECNOLOGIA E DIABETE"

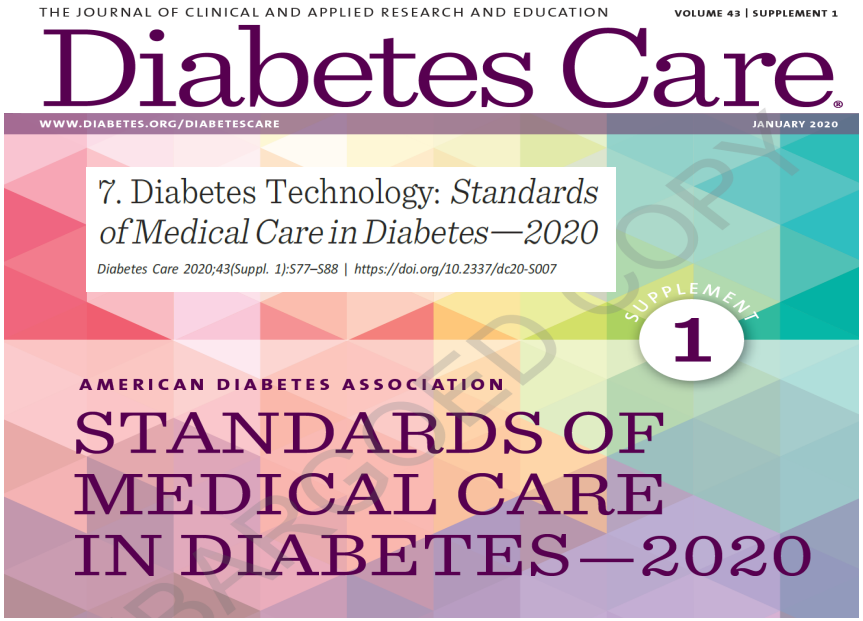
Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

CONTINUOUS GLUCOSE MONITORING DEVICES

7.9 When used properly, real-time continuous glucose monitors in conjunction with insulin therapy are a useful tool to lower A1C levels and/or reduce hypoglycemia in adults with type 1 diabetes who are not meeting glycemic targets, have hypoglycemia unawareness, and/or have episodes of hypoglycemia. **A**

7.10 When used properly, intermittently scanned continuous glucose monitors in conjunction with insulin therapy are useful tools to lower A1C levels and/or reduce hypoglycemia in adults with type 1 diabetes who are not meeting glycemic targets, have hypoglycemia unawareness, and/or have episodes of hypoglycemia. **C**

7.11 When used properly, real-time and intermittently scanned continuous glucose monitors in conjunction with insulin therapy are useful tools to lower A1C and/or reduce hypoglycemia in adults with type 2 diabetes who are not meeting glycemic targets. **B**



Primary Outcome: Hypoglycemia

In studies in adults where reduction in episodes of hypoglycemia was the primary end point, significant reductions were seen in individuals with type 1 diabetes on MDI or CSII

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Monitoraggio della glicemia interstiziale (CGM e FGM)

Nei pazienti con diabete di tipo 1 con insufficiente controllo glicemico persistente nel tempo e/o con ipoglicemie gravi o inavvertite nonostante l'ottimizzazione della terapia insulinica è raccomandato il monitoraggio in continuo del glucosio (RT-CGM). *I A*

L'uso di RT-CGM è consigliato durante la gravidanza nelle donne con diabete di tipo 1. *IIA*

L'impiego di RT-CGM può essere utile in pazienti in cui, per condizioni lavorative o stili di vita in cui un controllo molto frequente è consigliabile ma non praticabile (ad es., minatori, subacquei, lavoratori dell'edilizia, ecc.) *VI B*

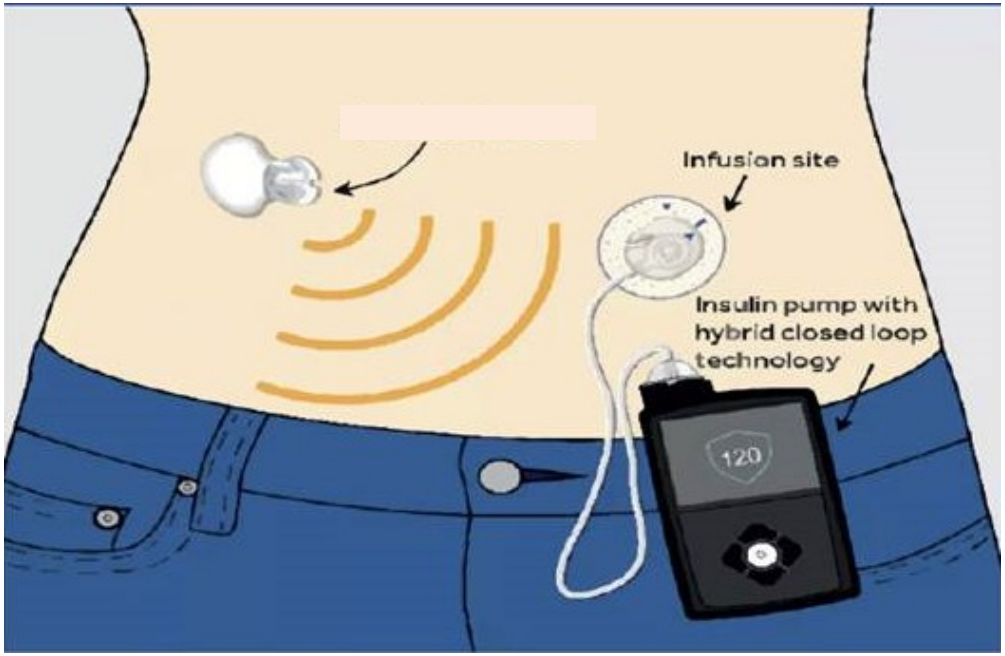
L'uso di RT-CGM intermittente o continuativo può essere utile in persone con diabete tipo 2 in compenso non ottimale come strumento di ottimizzazione della gestione *II B*

L'uso retrospettivo o diagnostico del CGM può essere utile nei pazienti con sospette alterazioni glucidiche non diabetiche (sindromi ipoglicemiche, glicogenosi, fibrosi cistica) o sospetta gastroparesi diabetica. Può essere utilizzato anche in pazienti con diabete tipo 1, per valutare l'andamento del profilo glicemico e adattare opportunamente la terapia insulinica, o in pazienti con diabete tipo 2 fragili e/o instabili. *III A*

Nei pazienti con diabete di tipo 1 in buon controllo glicemico senza ipoglicemie inavvertite è raccomandato l'uso di FGM. *II B*

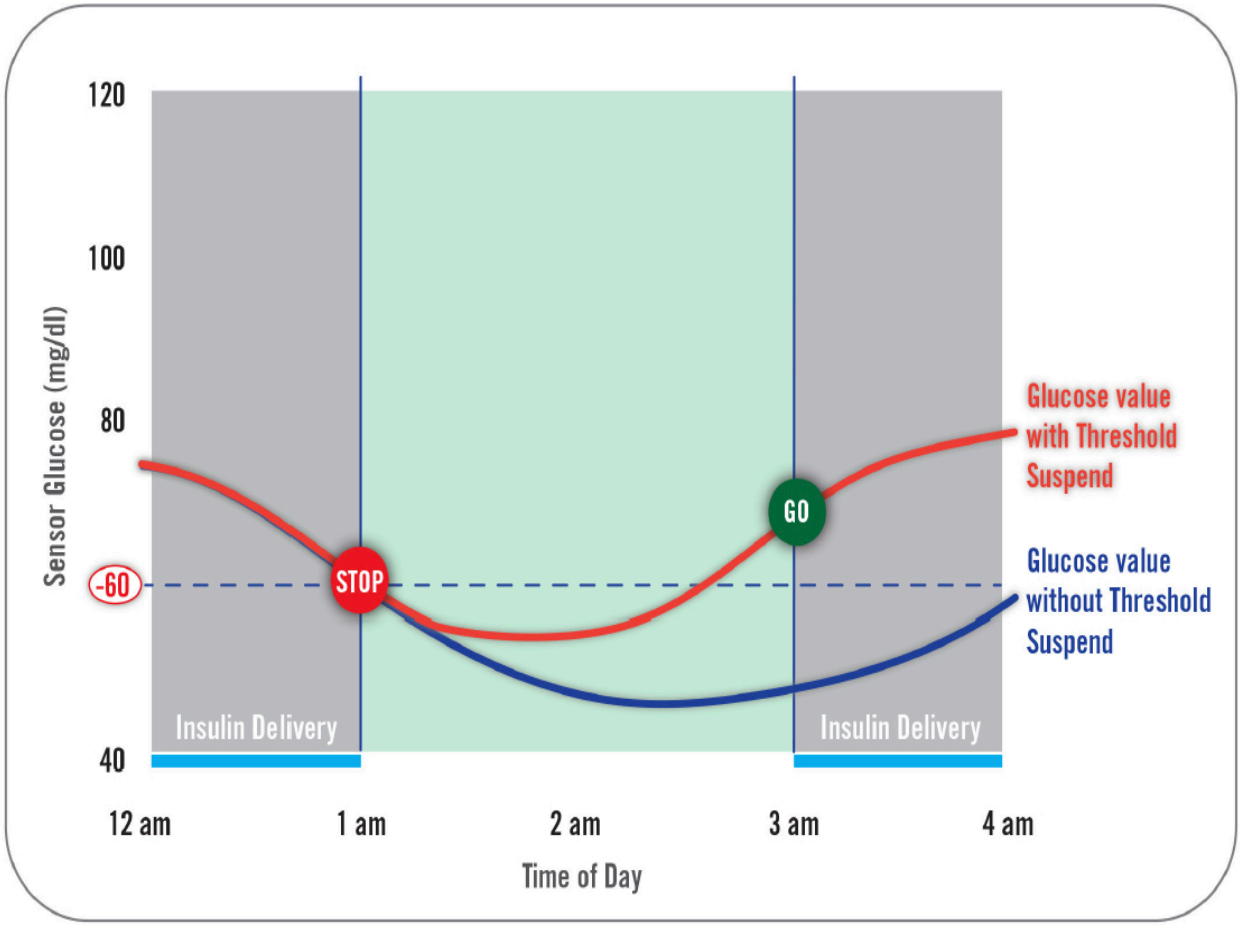
Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

…… e se al CGM associamo il microinfusore….
….. e se li mettiamo in comunicazione tra loro….



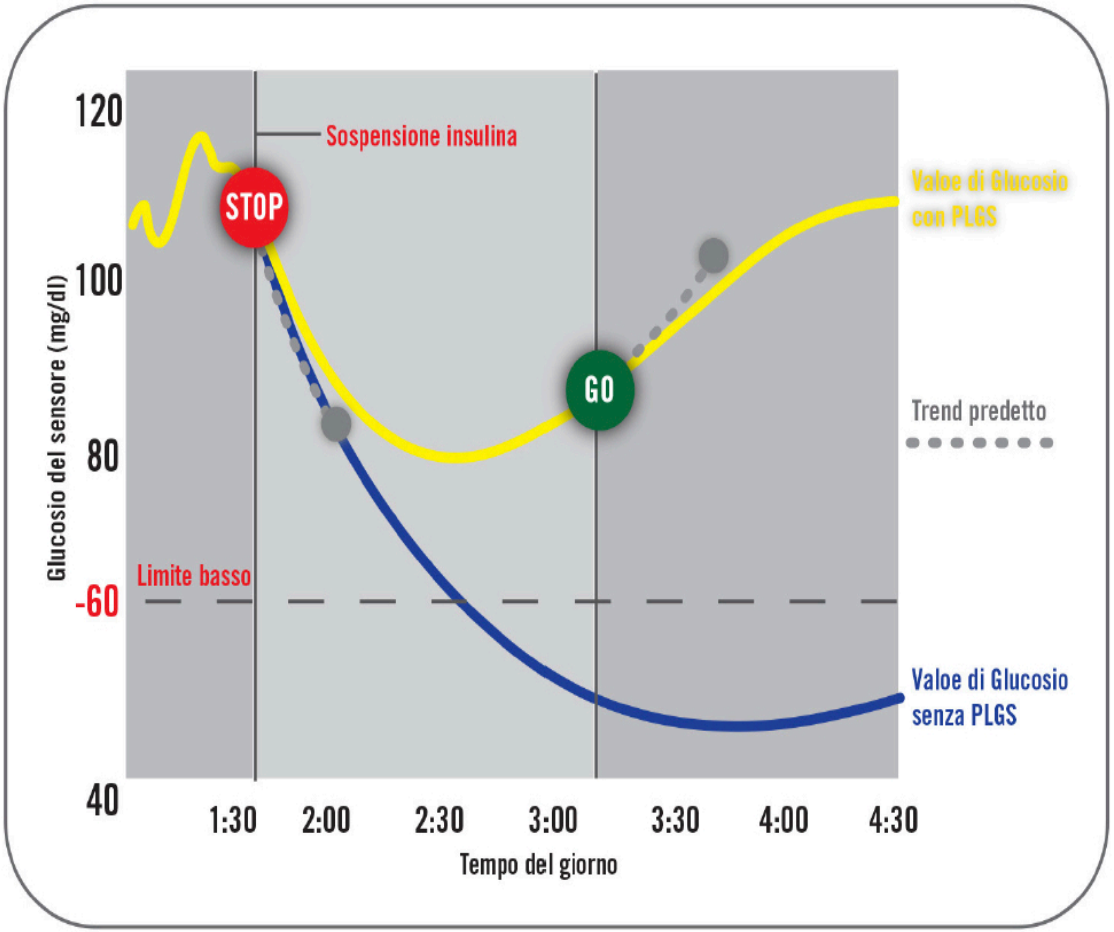
Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Funzione *Low Glucose Suspends* (LGS): la pompa sospende l'infusione per circa 2 ore se la glicemia (CGM) scende sotto la soglia stabilita per quel paziente



Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Funzione *Predictive Low Glucose Suspends* (PLGS): la pompa sospende l'infusione in caso di previsione di ipoglicemia e riprende quando il rischio di ipoglicemia è superato



Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Componenti principali di un pancreas artificiale

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Sistema di pancreas artificiale ibrido

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Tecnologia "Control – IQ"

Cos'è la tecnologia Control-IQ?

- Control-IQ è un ***Advanced Hybrid Closed Loop*** system (AHCL)
- E' progettato per aiutare i pazienti ad aumentare il loro Time In Range (70-180 mg), come da rilevazione da CGM
- Regola la somministrazione di insulina in base ai valori CGM previsti a 30 minuti, inclusa la somministrazione di boli di correzione automatica (fino a uno all'ora) secondo necessità

Componenti:

- Pompa per insulina
- Algoritmo Control-IQ incorporato

Le impostazioni della pompa sono le «fondamenta»

L'algoritmo utilizza i profili personali come input per il calcolo delle regolazioni

Quando Control-IQ technology è ON

- Il Target BG è impostato automaticamente a 110 mg/dL per tutti i boli di correzione e non può essere modificato
- La durata dell'insulina è impostata a 5 ore e non può essere modificata

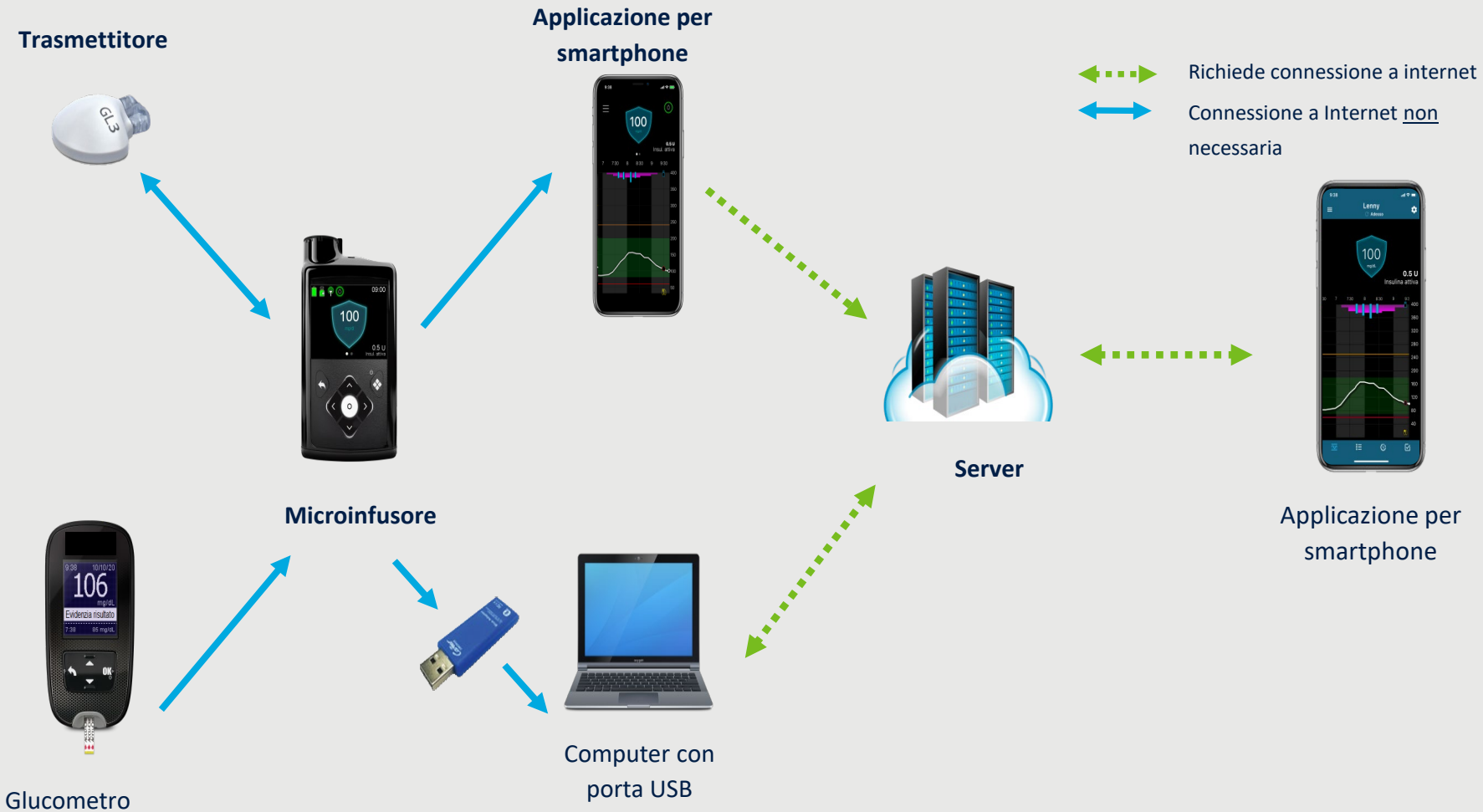
Quando Control-IQ technology è OFF:

- Tutte le impostazioni ritornano alle impostazione originali del Profilo Personale

Note: *Recommend review patients' profiles at every visit.*

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

TECNOLOGIA "SMART GUARD"



Le frecce indicano la direzione primaria del flusso di dati.

*È necessario utilizzare l'**adattatore Bluetooth USB** se non è possibile effettuare il trasferimento automatico dei dati via app*

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

REGOLA E CORREGGE I LIVELLI DI GLUCOSIO OGNI 5 MINUTI, IN BASE ALLA NECESSITÀ

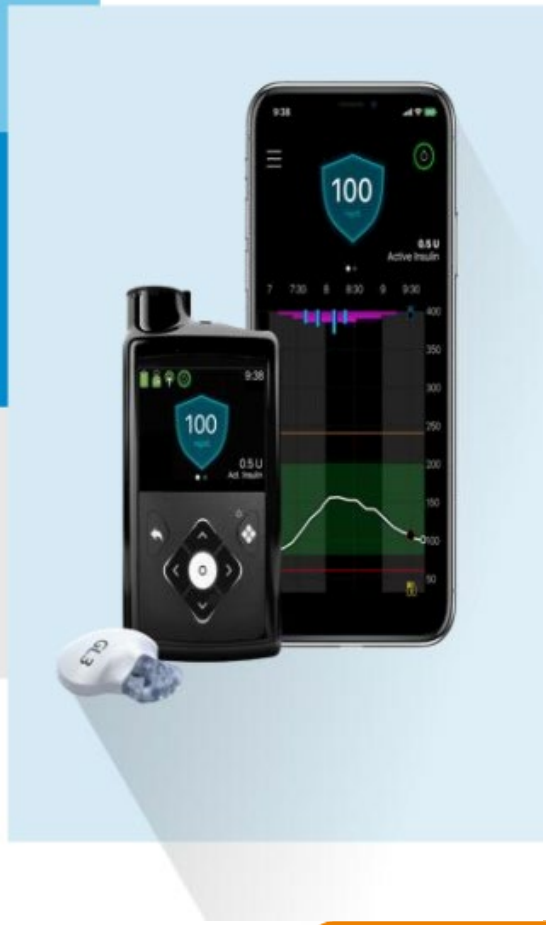
Aiuta a prevenire iperglicemie e ipoglicemie con minore fatica[1,2]

TARGET BASALE PREDEFINITO RIDOTTO A 100 mg/dl

con la possibilità di personalizzare il target selezionando anche livelli più elevati a 110 mg/dl o 120 mg/dl.*

CONNETTIVITÀ E AGGIORNAMENTI**

L'utilizzatore può verificare l'andamento del proprio glucosio, ricevere avvisi direttamente su smartphone, condividere i dati con le proprie persone di supporto e avere accesso a futuri aggiornamenti e versioni del software del sistema.

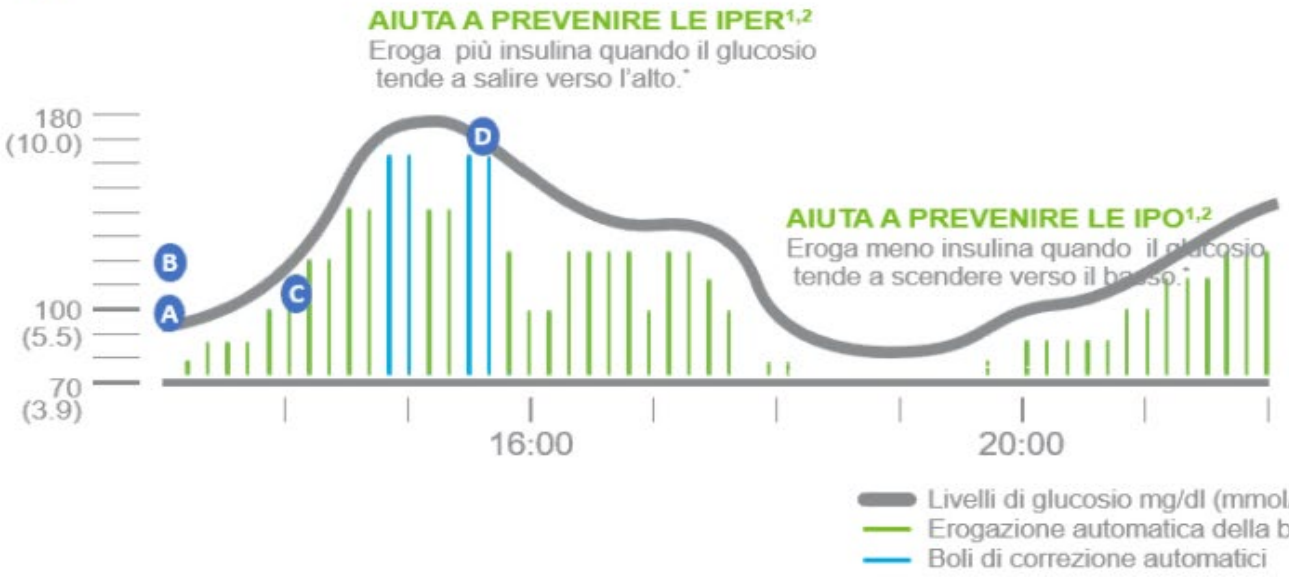


Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

CORREGGE

AUTOMATICAMENTE I LIVELLI DI GLUCOSIO, 24 ORE SU 24, 7 GIORNI SU 7*

LA TECNOLOGIA SMARTGUARD™ AIUTA A PREVENIRE IPERGLICEMIE E IPOGLICEMIE[1,2]



A **Il target dell'erogazione basale è configurabile** tra 100 mg/dl (impostazione predefinita), 110 mg/dl o 120 mg/dl

B Il **target delle correzioni automatiche** è fissato a 120 mg/dl.

C **L'erogazione dell'insulina basale** viene adattata ogni 5 minuti sulla base dei valori di glucosio sensore

D

Le correzioni automatiche vengono erogate solo quando l'algoritmo ne determina la necessità, con una frequenza massima di 5 minuti e solo quando:

- si raggiunge l'**erogazione basale massima**
- E il glucosio sensore è > **120mg/dl**
- E **non** è attivo il **Target temporaneo**

CORREGGE LE IPERGLICEMIE AUTOMATICAMENTE E IN MANIERA PREVENTIVA, PRIMA CHE SI VERIFICHINO[1,2]

Adatta ed eroga automaticamente piccole correzioni, al massimo ogni 5 minuti.*

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

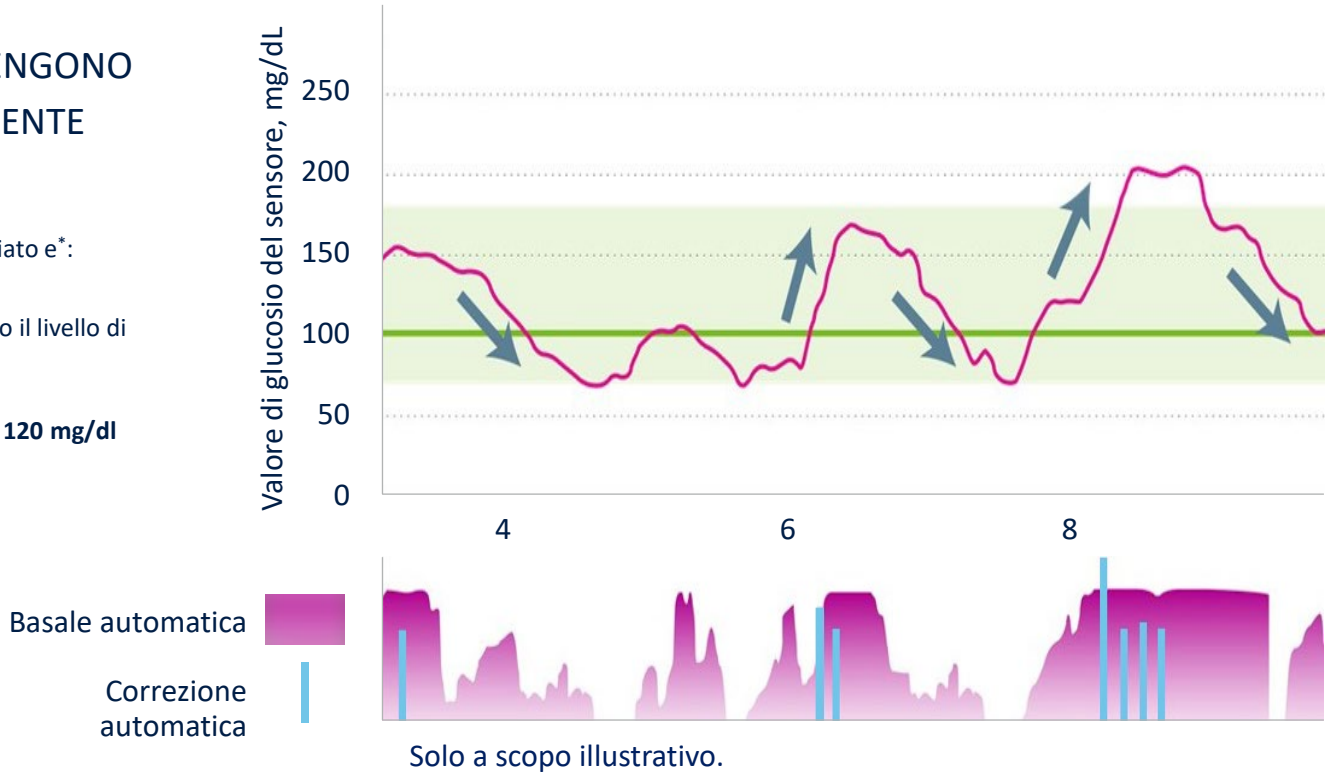
CORREZIONI AUTOMATICHE DELLA FUNZIONE SMARTGUARD™

ANTICIPA, ADATTA E CORREGGE[2]

I BOLI DI CORREZIONE VENGONO EROGATI AUTOMATICAMENTE FINO A 1 **OGNI 5 MINUTI**

quando l'algoritmo lo ritiene appropriato e*:

- la **basale automatica** ha raggiunto il livello di **erogazione massima**
- **e** il valore di glucosio sensore è **> 120 mg/dl**



Solo a scopo illustrativo.

L'algoritmo verificherà sempre che sia sicuro erogare il bolo di correzione in considerazione del valore di glucosio del sensore, del tasso di variazione e della stima del livello di insulina totale in azione nel corpo

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

STUDIO PILOTA SU AHCL EFFETTUATO IN AMERICA* (CARLSON, ET. AL. ADA 2020)

DISEGNO DELLO STUDIO[1]

DISEGNO DELLO STUDIO

A braccio singolo

n=157 adulti e adolescenti con T1D

Progettato per comprovare la sicurezza dell'algoritmo AHCL

PERIODO DI RIFERIMENTO

2 settimane (67% di pazienti in SAP; 33% in HCL)

FOLLOW-UP

90 giorni in AHCL

IMPOSTAZIONI

Target della basale automatica a 100 mg/dL e 120 mg/dL (6 settimane ciascuno); Impostazione del tempo di insulina attiva secondo valutazione dei ricercatori.

Età	+ 14 anni
Media	39 anni
14-21 anni	39 pazienti
Più di 21 anni	118 pazienti
Time in range di partenza	69%
HbA1c di partenza	7,5% ±0.8

STUDIO PILOTA SU AHCL EFFETTUATO IN AMERICA

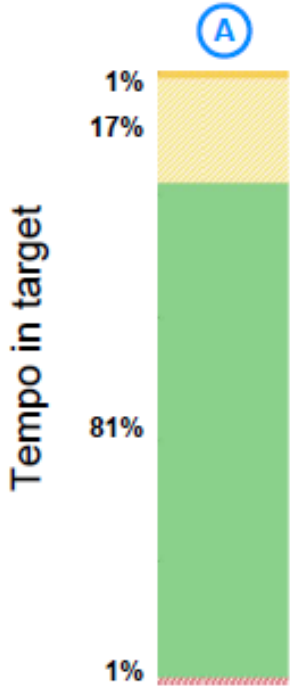
RISULTATI DELLO STUDIO (N=157 PAZIENTI)[1]

ENDPOINT DI SICUREZZA	ENDPOINT DI EFFICACIA				
Obiettivo: nessun evento avverso severo	HbA1c	Time in range	Tempo > 180 mg/dL	Tempo < 70 mg/dL	Valore medio di glucosio del sensore (mg/dl)
Nessun caso di ipoglicemia severa	7,0%	74,5%	23,1%	2,3%	148
	p<0,001	p<0,001	p<0,001	p<0,001	p<0,001
Nessun caso di DKA	↓ 0,5% dal riferimento iniziale	↑ 6% dal riferimento iniziale	↓ 5% dal riferimento iniziale	↓ 1% dal riferimento iniziale	↓ 5 mg/dL dal riferimento iniziale

Il Pancreas Artificiale: aspettative del paziente e ruolo del medico

- fornisce una gran quant… e molte calibrazioni e misurazioni della glicemia… il paziente abbia delle aspettative corrette altrim… con spreco di tempo e risorse economiche;
- il paziente deve in parti… e i sistemi ibridi non sono completamente autonom… matica di basale non rimpiazza l'insulina neces…
- è necessario un training … opriato dello strumento.

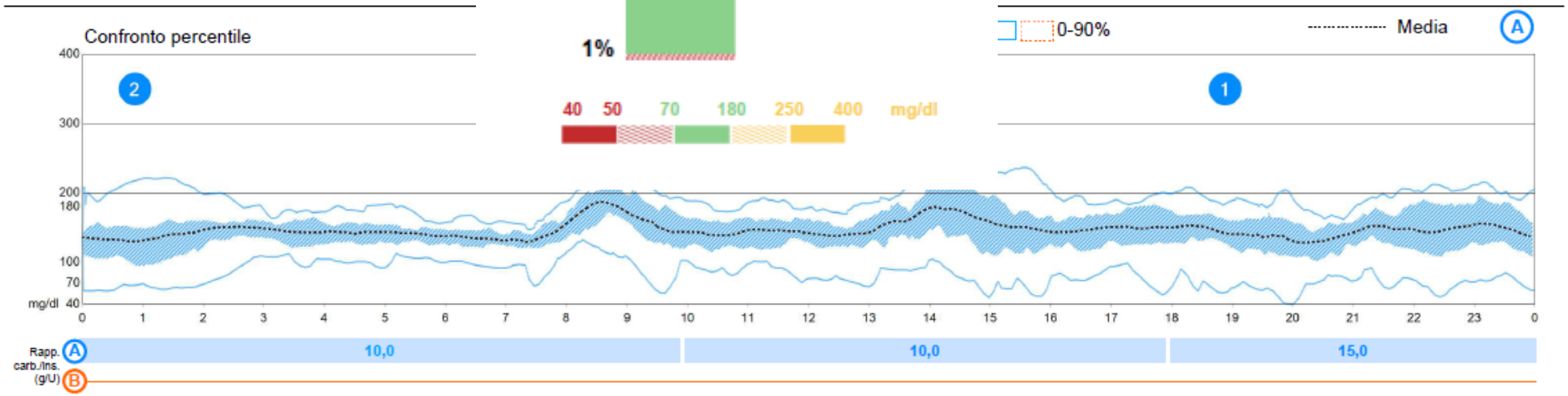
Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala



Donna, 40 anni
15 anni di durata di DM1

3 ricorsi al 118 negli ultimi 6 mesi per "ipo" inavvertite

Sistema ibrido: … dopo 6 mesi



A	Andamenti ipoglicemici (2)	Andamenti iperglicemici (1)
	1 17:36- 20:11 (4 volte) 2 23:46- 1:58 (3 volte)	3 8:25- 8:55

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

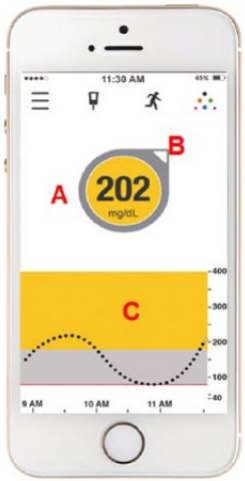
Therapeutic Advances in Endocrinology and Metabolism Systematic Review

The road from intermittently scanned continuous glucose monitoring to hybrid closed-loop systems.

Ther Adv Endocrinol Metab
2019, Vol. 10: 1–17
DOI: 10.1177/2042018819871903

Francesca De Ridder, Marieke den Brinker and Christophe De Block

Conclusions: Recent technologies have dramatically changed the course of T1DM. They are proving useful in controlling glycaemia in patients with T1DM, without increasing the treatment burden.



Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Conclusioni

Le strategie tecnologiche per prevenire e meglio gestire le ipoglicemie sono ormai diventate numerose e sempre più accurate e diffuse:

- ***la terapia con CSII rispetto a MDI è già un mezzo efficace ai fini della riduzione degli eventi ipoglicemici moderati/severi;***
- ***un mezzo ancora più efficace appare tuttavia essere il monitoraggio glicemico continuo in "real time", sia esso utilizzato in "stand alone" nella terapia MDI che in associazione alla terapia CSII;***
- ***i sistemi integrati microinfusore + sensore glicemico e i più recenti sistemi "ibridi" hanno dimostrato di poter offrire un ulteriore salto di qualità;***
- ***tuttavia, l'uso di qualsiasi mezzo tecnologico risulta efficace, solo se preceduto da una accurata selezione del paziente e accompagnato da una adeguata motivazione ed educazione terapeutica dello stesso da parte di un team multidisciplinare dedicato ed esperto.***

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala

Grazie per l'attenzione

P.O. "Paolo Borsellino"
Marsala (TP)

Dr. Domenico Greco
UOC Malattie Endocrine
P.O. "P. Borsellino" - Marsala