IN DOCTRINA ET IN USU

Praticamente ... diabetologia

TORINO 01.06.24

HOMO EST QUOD EST

Nutrire il futuro: strategie di prevenzione e cura

POLLENZO 23.11.24

PRIMA SESSIONE | **“Il mestiere di vivere” C. Pavese**

Fully Closed Loop: a che punto siamo?

Silvana Bertaina

Vivere con il diabete tipo1

42 Factors *that affect* Blood Glucose

FOOD
- 1 Carbohydrate quantity
- 2 Carbohydrate type
- 3 Fat
- 4 Protein
- 5 Caffeine
- 6 Alcohol
- 7 Meal timing
- 8 Dehydration
- ? 9 Personal microbiome

MEDICATION
- 10 Medication dose
- 11 Medication timing
- 12 Medication interactions
- 13 Steroid administration
- 14 Niacin (Vitamin B3)

ACTIVITY
- 15 Light exercise
- 16 High-intensity & moderate exercise
- 17 Level of fitness/training
- 18 Time of day
- 19 Food and insulin timing

BIOLOGICAL
- 20 Too little sleep
- 21 Stress and illness
- 22 Recent hypoglycemia
- 23 During-sleep blood sugars
- 24 Dawn phenomenon
- 25 Infusion set issues
- 26 Scar tissue / lipodystrophy
- 27 Intramuscular insulin delivery
- 28 Allergies
- 29 A higher BG level (glucotoxicity)
- 30 Periods (menstruation)
- 31 Puberty
- 32 Celiac disease
- 33 Smoking

ENVIRONMENTAL
- 34 Expired insulin
- 35 Inaccurate BG reading
- 36 Outside temperature
- 37 Sunburn
- ? 38 Altitude

BEHAVIOR & DECISIONS
- 39 More frequent BG checks
- 40 Default options and choices
- 41 Decision-making biases
- 42 Family and social pressures

diaTribe

Di quante cose mi devo occupare?
Il tempo per me?
Il tempo per vivere la mia vita?

“Lavorare stanca ” C.Pavese

the **remaining life expectancy** of a 10-year-old child diagnosed with type 1 diabetes in 2021 ranged from a mean of **13 years in low-income** countries to **65 years in high-income** countries

International Diabetes Federation Diabetes Atlas Type 1 Diabetes in Adults Special Interest Group. Global incidence, prevalence, and mortality of type 1 diabetes in 2021 with projection to 2040: a modelling study. Lancet Diabetes Endocrinol 2022

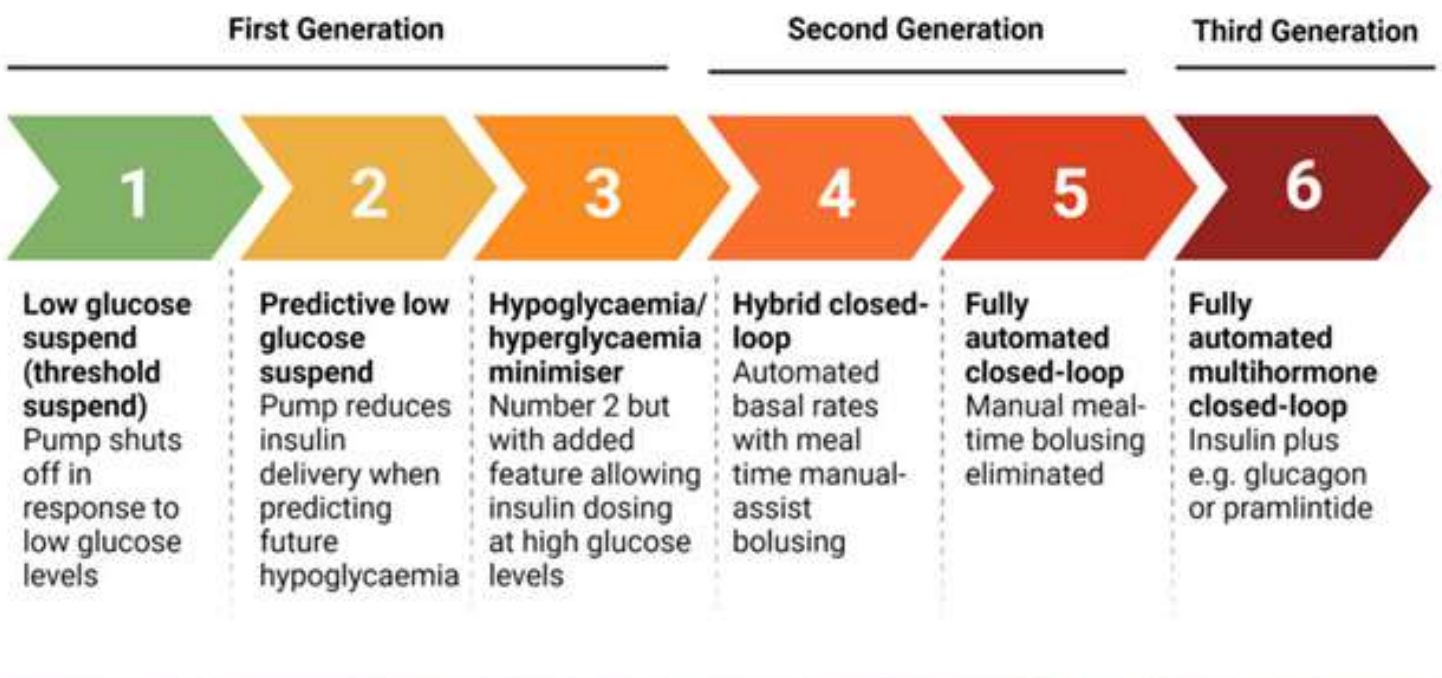


Figure 3
The six developmental stages of artificial pancreas device systems as originally described by JDRF (https://www.jdrf.org/blog/2011/02/09/artificial-pancreas-and-fda-the-latest/). (Created with BioRender.com).

JDRF/NIDDK ArtificialPancreas Project Consortium

DIABETES TECHNOLOGY & THERAPEUTICS
Volume 23, Number 7, 2021
Mary Ann Liebert, Inc.
DOI: 10.1089/dia.2020.0618

DTT

ORIGINAL ARTICLE

The SWEET Project 10-Year Benchmarking in 19 Countries Worldwide Is Associated with Improved HbA1c and Increased Use of Diabetes Technology in Youth with Type 1 Diabetes

CGM

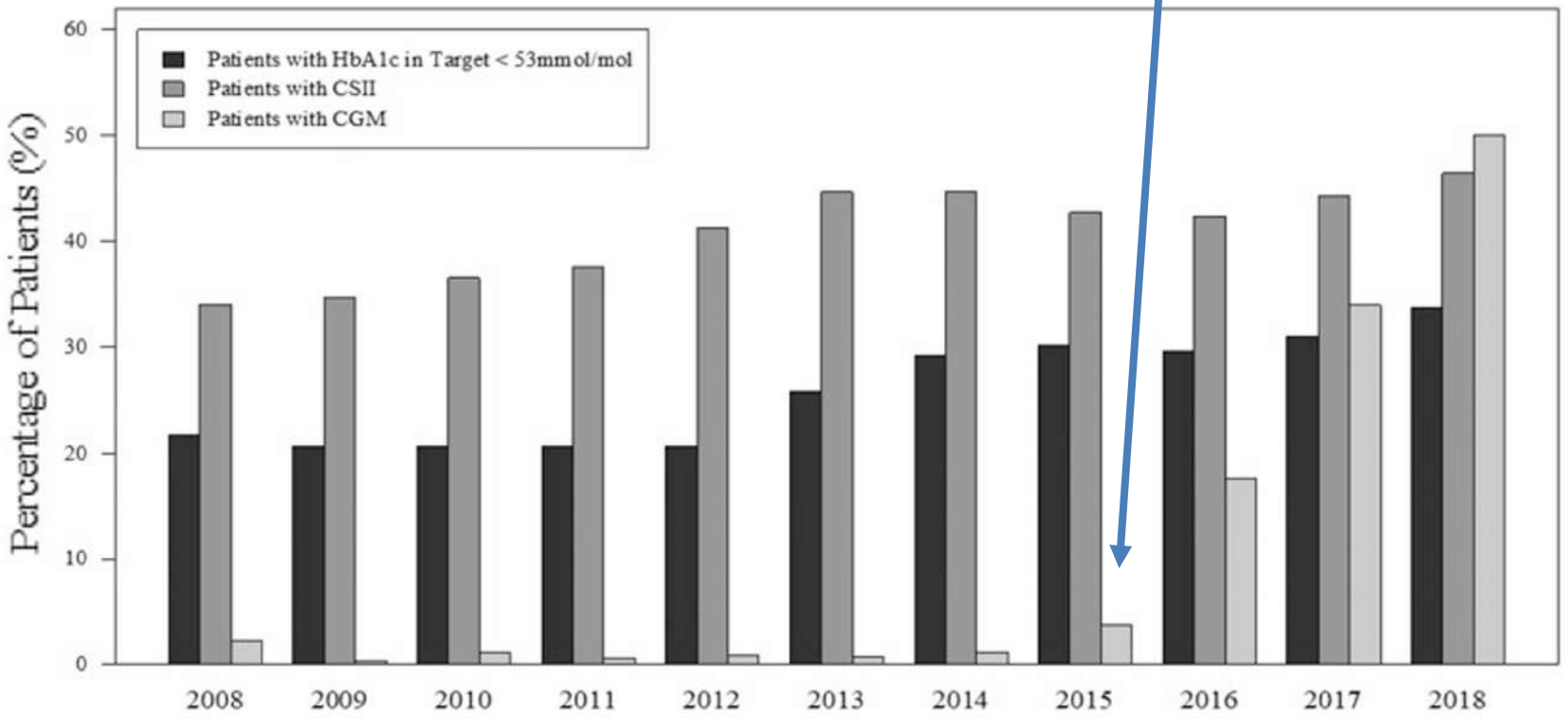


FIG. 4. Temporal patterns of CSII and CGM use in centers and HbA1c. HbA1c data of the entire cohort were aggregated for each year of treatment from 2008 to 2018. CGM, continuous glucose monitoring.

Studi real world hanno confermato pivotal studi

Table 5. Key real-world studies

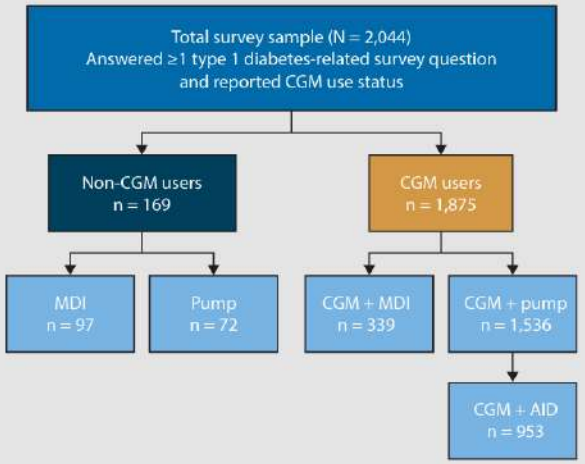
Closed-loop system (author & publication year)	Study design (type, duration, comparison group)	Study population (number of participants & age, mean baseline HbA1c)	Number of participants by age category	Glycemic outcomes (start to end of study)					
				ΔMean sensor glucose	ΔTIR 70–180 mg/dL	ΔTBR < 70 mg/dL	ΔTBR < 54 mg/dL	ΔTAR > 250 mg/dL	ΔHbA1c
670G Stone MP et al, 2018 (37)	3-mo retrospective, CareLink system data comparing baseline	N = 3141, >7 yo, T1D, no baseline HbA1c	N = 2066, 22–60 yo N = 649, ≥ 60 yo	−7 mg/dL −6 mg/dL	+8% +6%	−0.7% −0.4%	−0.1%	−2.7%	
			N = 105, 7–13 yo N = 244, 14–21 yo	−17 mg/dL −10 mg/dL	+11% +8%	+0.5% −0.3%			
670G Akturk et al, 2019 (38)	6-mo retrospective single-center study comparing study period with baseline SAP use	N = 127, 21–68 yo, T1D, baseline mean HbA1c: 7.6%		−12 mg/dL	+11%	−1%	−0.2%	−0.5%	−0.4%
780G Da Silva et al, 2022 (40)	2-mo retrospective, CareLink system data comparing study period with baseline	N = 812, T1D, baseline mean estimated HbA1c: 7.2%	No data	−15.7 mg/dL	+12%	−0.3%	−0.1%	−4.2%	−0.4%
Control-IQ Breton & Kovatchev 2021 (35)	12-mo retrospective, real-world observational study, comparing study period with baseline (PLGS)**	N = 9010, 6–91 yo, T1D or T2D, baseline mean estimated HbA1c: 7.3% (N = 7813 T1D)	N = 5616, 19–63 yo N = 1773, >63 yo	−13 mg/dL −12 mg/dL	+10% +9%	−0.8% 0%	+0.1% 0%	−3% −2%	−0.3% GMI for all group
			N = 716, 6–13 yo N = 905, 14–18 yo	−15.5 mg/dL −13 mg/dL	+12% +12%	+0.1% +0.1%	+0.1% +0.1%	−5% −6%	
Control-IQ Messer et al, 2021 (41)	6-mo prospective, real-world single-center comparing study period with baseline	N = 191, children and adolescents with T1D, baseline mean HbA1c: 7.6%		−12.5 mg/dL	+9.4%	−0.4%	0%	−4.3%	−0.3% GMI
Loop Open Source Lum et al, 2021 (27)	6-mo prospective, real-world observational study comparison of study period with baseline**	N = 558, 1–71 yo, T1D, baseline mean HbA1c: 6.8%		−10 mg/dL	+7%	−0.2%	−0.05%	−2%	−0.3%

**Time in range change from baseline estimated from median.
Abbreviations: GMI, glucose management index; HbA1c, glycated hemoglobin; mo, month; yo, years old.

Endocrine Reviews, 202

A retrospective, observational study using an online survey to describe glycemic metrics, severe hypoglycemic events, and impaired awareness of hypoglycemia in individuals with type 1 diabetes

Survey participants



Participants were aged 18 years and older from the T1D Exchange Registry/ online community

Participant demographics

Mean (SD) age	43.0 (15.6) years
72.1% Female	95.4% White
Mean (SD) BMI	27.7 (6.2) kg/m²
Mean (SD) daily insulin dose	49.7 (33.1) units
Mean (SD) overall HbA_{1c}	6.9% (1.1%)
Mean (SD) duration since diagnosis	26.3 (15.3) years

Key results

Only **57.7%** of all respondents reported **achieving target HbA_{1c} <7%**

~20% of all respondents reported having **≥1 SHEs in past 12 months** including CGM users (16.6% of AID users, 19% of pump users, and 23% of MDI users)

12% of respondents had **≥2 SHEs** in previous 12 months

Approximately one-third of all respondents **reported IAH in past 12 months**, regardless of CGM or AID usage

AID, automated insulin delivery; BMI, body mass index; CGM, continuous glucose monitoring; HbA_{1c}, hemoglobin A1c; IAH, impaired awareness of hypoglycemia; MDI, multiple daily injections; SHE, severe hypoglycemic event

Conclusion: Despite use of currently available advanced diabetes technologies, a high proportion of people with type 1 diabetes do not achieve glycemic targets and continue to experience SHEs and IAH, suggesting an ongoing need for improved treatment strategies

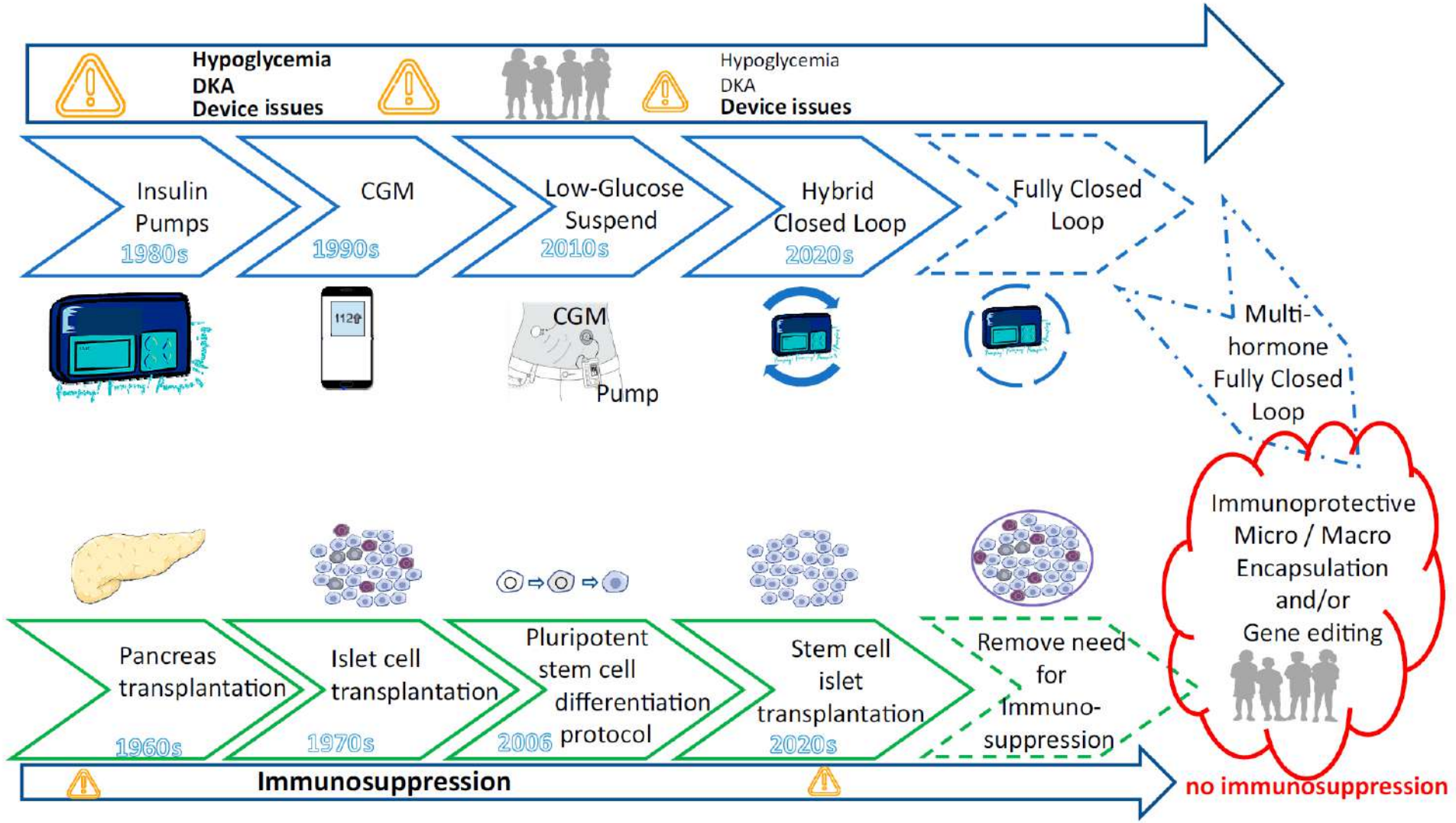
16% AID users

Diabetes Care 2024

Il nostro fine

non la nostra fine

è l'insulino indipendenza



Diabetes Care Volume 47, June 2024

” Poesie del disamore ” e altre poesie disperse C.Pavese

- **Accurato conteggio carboidrati**
- **Bolo manuale prima del pasto**

Prima che il gallo canti

- **Meal announcements (simplified)**

-iLet Bionic Pancreas (Beta Bionics)

Meals : usual,more,less

(**OK FDA 6.2023**)

-MiniMED 780 system RCT

(scelta tra 3 quantità di CHO)

- **Bihormonal fully closed-loop systems**

-Inreda (Olanda) EU 2020 ma non in commercio

Insulina e glucagone (2 pompe)

-iLet

Insulina e dasiglucagon (analogo sintetico)

-Insulina + pramlintide

- **Fully closed loop com ultrafast insulina**

Bihormonal fully closed-loop system for the treatment of type 1 diabetes: a real-world multicentre, prospective, single-arm trial in the Netherlands

A C van Bon*, H Blauw*, T J P Jansen, G D Laverman, T Urgert, J Geessink-Mennink, A H Mulder, M Out, R Groote Veldman, A J Onvlee, B J J W Schouwenberg, M A R Vermeulen, M J M Diekman, M N Gerding, J P H van Wijk, M Klaassen, M Witkop, J H DeVries

Lancet Digit Health 2024; 6: e272–80

Inreda AP

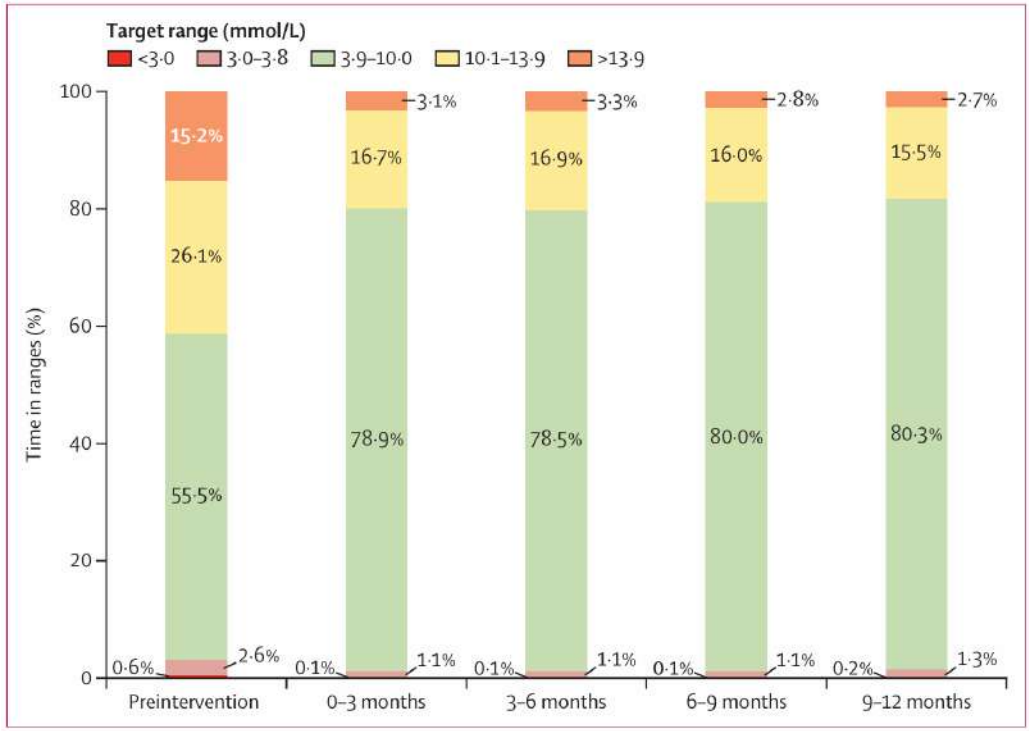


Figure 3: Proportion of time spent in the different glycaemic ranges preintervention and during fully closed-loop treatment

Interpretation: Real-world data obtained in this trial demonstrate that use of the bihormonal FCL system was associated with good glycaemic control in patients who completed 1 year of treatment, and could help relieve these individuals with type 1 diabetes from making treatment decisions and the burden of carbohydrate counting.

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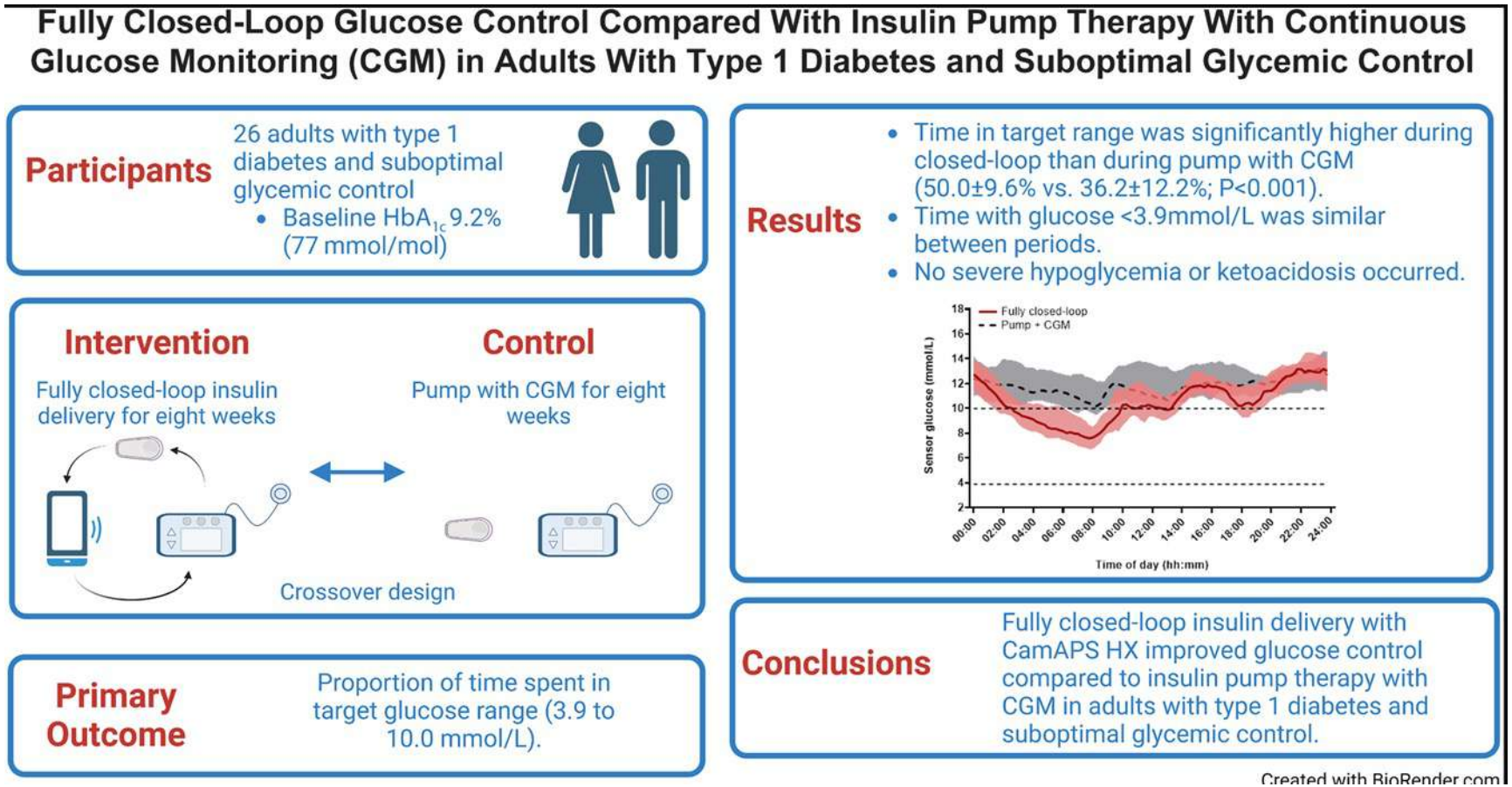
POLLENZO 23.11.24

Randomized Controlled Trial > Diabetes Care. 2023 Nov 1;46(11):1916-1922.
doi: 10.2337/dc23-0728.

Fully Closed-Loop Glucose Control Compared With Insulin Pump Therapy With Continuous Glucose Monitoring in Adults With Type 1 Diabetes and Suboptimal Glycemic Control: A Single-Center, Randomized, Crossover Study

Charlotte K Boughton [1,2], Sara Hartnell [2], Rama Lakshman [1], Munachiso Nwokolo [1], Malgorzata E Wilinska [1], Julia Ware [1,3], Janet M Allen [1], Mark L Evans [1,2], Roman Hovorka [1]



ultrarapid insulin lispro

A fully artificial pancreas versus a hybrid artificial pancreas for type 1 diabetes: a single-centre, open-label, randomised controlled, crossover, non-inferiority trial

Michael A Tsoukas*, Dorsa Majdpour*, Jean-François Yale, Anas El Fathi, Natasha Garfield, Joanna Rutkowski, Jennifer Rene, Laurent Legault, Ahmad Haidar

***Lancet Digit Health* 2021**

In conclusion, we have performed the first randomised trial to assess the efficacy of a Fiasp-plus-pramlintide fully closed-loop system without full carbohydrate counting. **Non-inferiority of the fully closed-loop system compared with the Fiasp-alone hybrid closed-loop system was not shown**. We observed **transient hyperglyceamia in the first 2 h after meals with the fully closed-loop system**

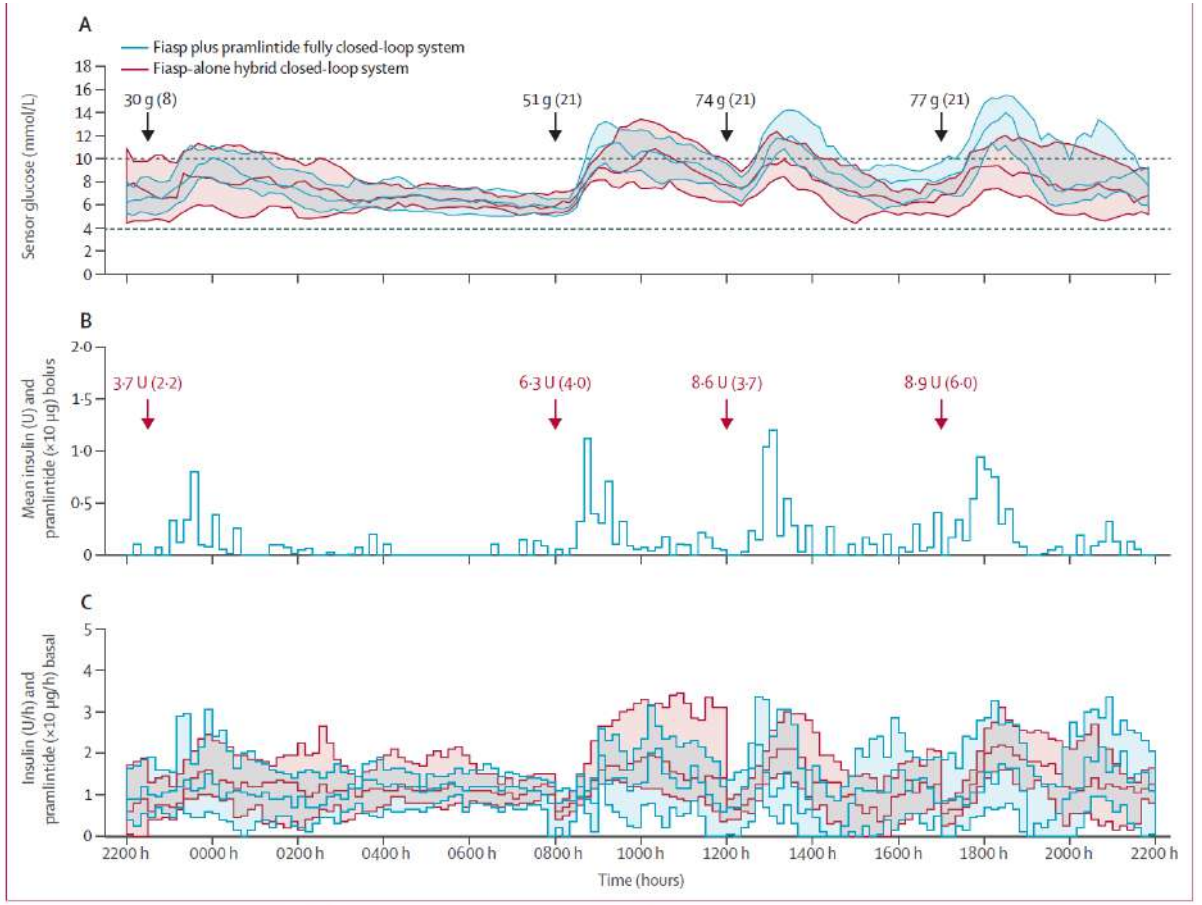


Figure 2: **Glucose levels and bolus and basal delivery with the Fiasp-alone hybrid closed-loop system and Fiasp plus pramlintide fully closed-loop system (n=24)**
(A) Median (IQR) glucose values of the fully closed-loop (blue) and hybrid closed-loop (red) interventions. The arrows indicate the time of delivery and average carbohydrate content of each meal. (B) Blue line represents mean insulin and co-delivered pramlintide boluses (1U insulin:10 µg pramlintide) during the fully closed-loop intervention. The red arrows indicate mean (SD) insulin boluses during the hybrid closed-loop intervention. (C) Median (IQR) insulin basal delivery for the fully closed-loop (blue) and hybrid closed-loop (red) during the interventions.The shaded areas indicate the IQR. Fiasp=faster-acting insulin aspart.

AID con terapie aggiuntive

- SGLT2i
- GLP1AR

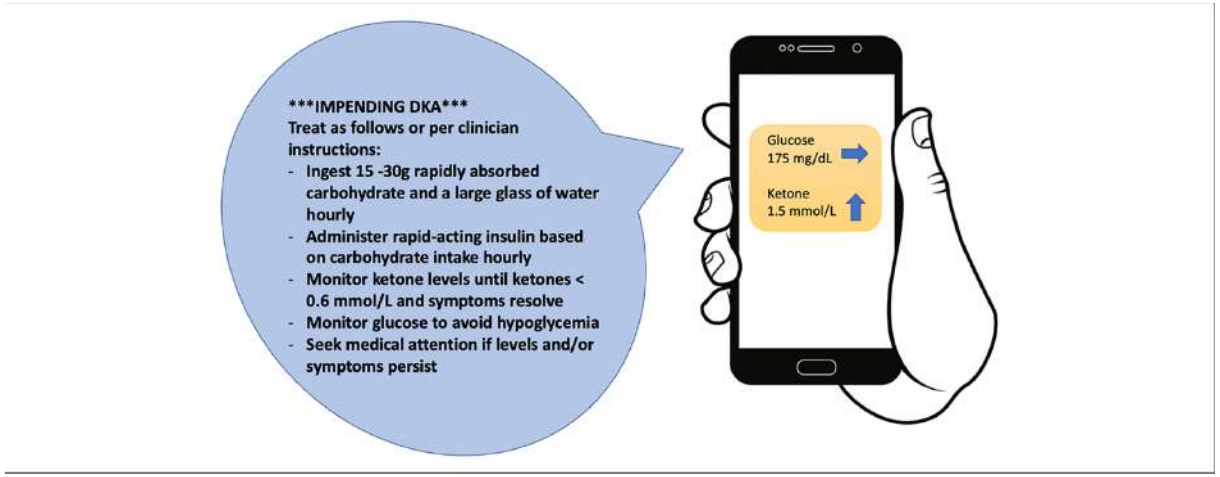


Figure 5. An example of an alert based on continuous ketone monitor data with behavioral suggestions to prevent ketoacidosis. Figure courtesy of Kristin Castorino. Abbreviation: DKA, diabetic ketoacidosis.

CKMs are under development.

CKMs could measure interstitial beta hydroxybutyrate using a similar electrochemical technology and form factor as existing glucose monitoring devices.

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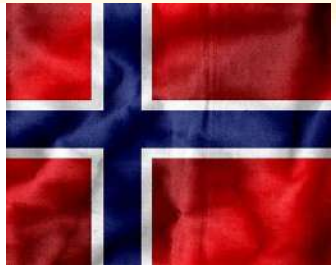
Journal of Endocrinological Investigation (2024) 47:513–521
https://doi.org/10.1007/s40618-023-02193-2

REVIEW

The artificial pancreas: two alternative approaches to achieve a fully closed-loop system with optimal glucose control

M. K. Åm[1] · I. A. Teigen[1,2] · M. Riaz[1,4] · A. L. Fougner[3] · S. C. Christiansen[1,4] · S. M. Carlsen[1,4]



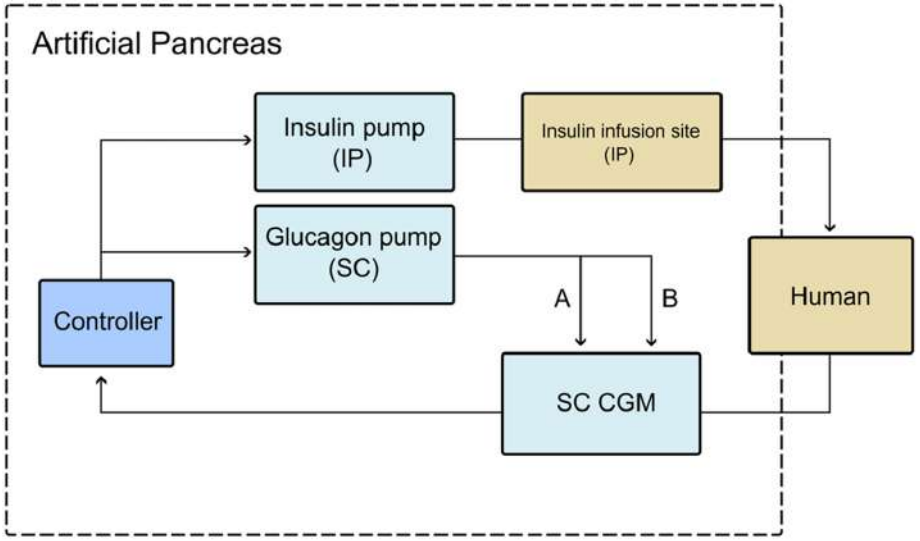
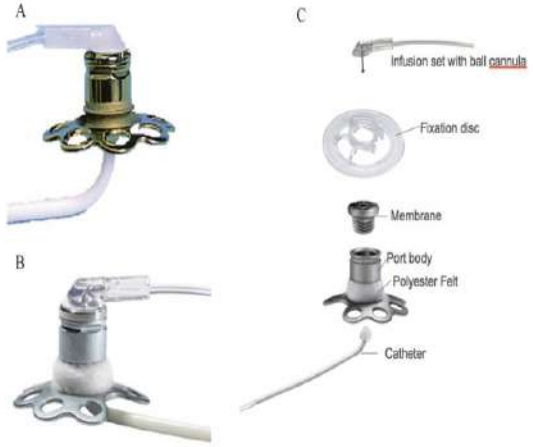


Fig. 1 Illustration of an intraperitoneal (IP) artificial pancreas with possible use of glucagon to achieve a fully closed-loop system; **A** glucagon is used to prevent or treat hypoglycemia, **B** glucagon micro-boluses are used to enhance continuous glucose monitoring (CGM) performance by increasing local SC blood flow. If glucagon is not used to enhance CGM performance, it will be delivered at another SC site than CGM



Accu-Chek DiaPort system

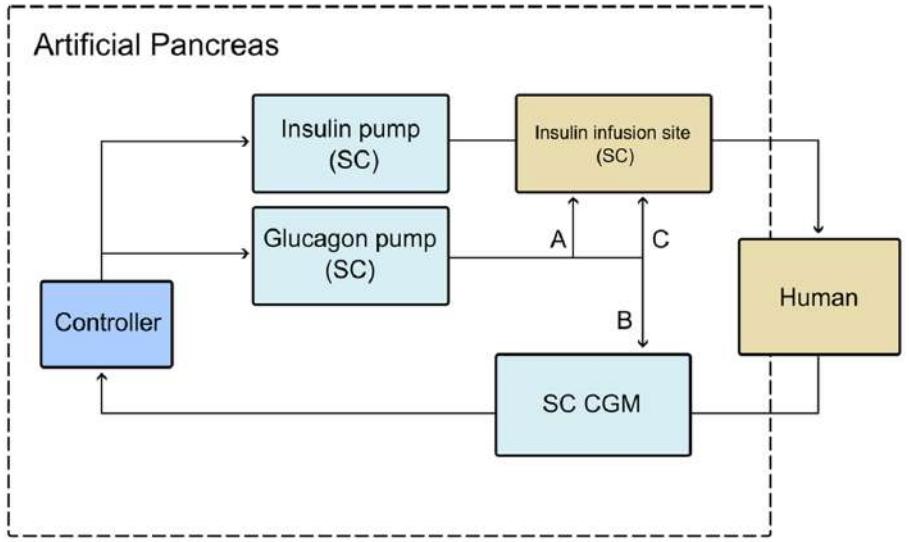


Fig. 2 Illustration of a subcutaneous (SC) artificial pancreas with possible uses of glucagon to achieve a fully closed-loop system; **A** glucagon is used to prevent or treat hypoglycemia, **B** glucagon micro-boluses are used to enhance continuous glucose monitoring (CGM) performance by increasing local SC blood flow, **C** glucagon micro-boluses are used to accelerate absorption of insulin by increasing local SC blood flow

1° giugno.

Perché la gente prende delle pose, e fa il *dandy*, o lo scettico, o lo stoico, o il *sans-souci*, ecc.? Perché sente che c'è una superiorità nell'affrontare la vita secondo una forza, una disciplina che ci si dà se non altro ai pensieri.

È infatti questo il segreto della felicità: assumere un atteggiamento, uno stile, uno stampo in cui devono cadere e modellarsi tutte le nostre impressioni ed espressioni.

Ogni vita vissuta secondo uno stampo coerente e comprensivo e vitale, è classica.

Cesare Pavese
Il mestiere di vivere

Vi auguro una

(La) Bella estate C.Pavese