SISTEMI INTEGRATI

Andrea Laurenzi

Il Dr. Andrea Laurenzi dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

Abbott, Eli Lilly, Medtronic, Menarini, Novo Nordisk, Roche, Sanofi, Ypsomed

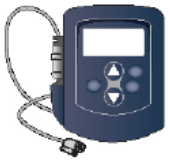
Dichiara altresì il proprio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc.).

Storia della CSII

1920s
Insulin discovered

1980s
1st commercialized SubQ insulin pump

1999
1st CGM



2006
Sensor augmented pump (SAP)

2013 / 2015
LGS / PLGS SAP

2019
Commercialized HCL (Control IQ)

2020
Commercialized HCL (CamAPS FX)

2016
Commercialized HCL (Minimed 670G)

2020
Commercialized AHCL (Minimed 780G)

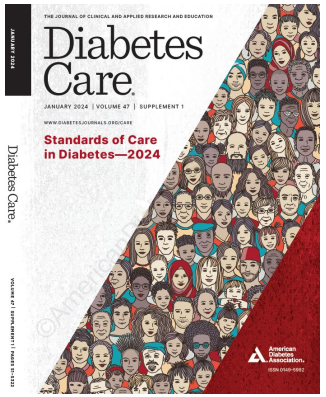
Modificato da *Diabetes Metab J* 2021;45:813-839

I target glicemici in gravidanza

gli obiettivi PRE-concepimento

- Nella fase precedente il concepimento deve essere ricercata l'ottimizzazione del controllo glicemico. L'obiettivo terapeutico è definito da **valori di HbA1c** normali o il più possibile vicini alla norma (≤48 mmol/mol, ≤6,5%), in assenza o limitando al massimo le ipoglicemie ***(III B)***

- Preconception counseling should address the importance of glycemic management as close to normal as is safely possible, ideally **A1C 6.5%** (48 mmol/mol), to reduce the risk of congenital anomalies, preeclampsia, macrosomia, and other complications ***(B)***

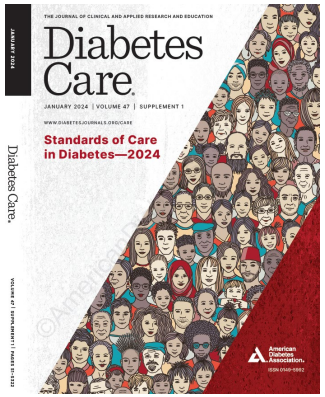


I target glicemici in gravidanza

Diabetes in pregnancy: management from preconception to the postnatal period

NICE guideline [NG3] Published: 25 February 2015 Last updated: 16 December 2020

- **a digiuno: 5.3 mmol/litre (95 mg/dl) e**
- 1 ora dopo i pasti: 7.8 mmol/litre (140 mg/dl) o
- 2 ore dopo i pasti: 6.4 mmol/litre (115 mg/dl)



- **a digiuno ≤95 mg/dL (5.3 mmol/L) e**
- un' ora post prandiale ≤140 mg/dL (7.8 mmol/L) o
- due ore post prandiale ≤120 mg/dL (6.7 mmol/L).

- **a digiuno ≤90 mg/dL**
- un' ora post prandiale <130 mg/dL
- due ore post prandiale <120 mg/dL.

I target glicemici in gravidanza

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

Diabetes Care 2019;42:1593–1603 | https://doi.org/10.2337/dci19-0028

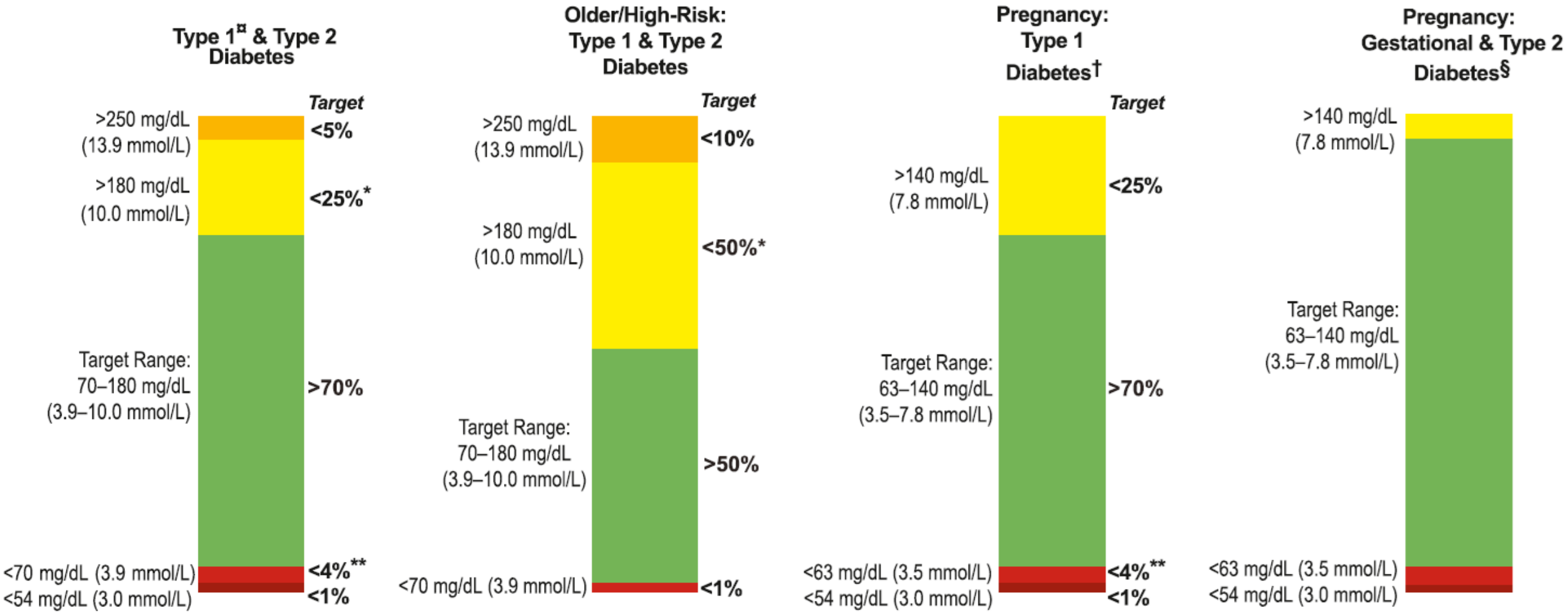
Tadej Battelino,[1] Thomas Danne,[2] Richard M. Bergenstal,[3] Stephanie A. Amiel,[4] Roy Beck,[5] Torben Biester,[2] Emanuele Bosi,[6] Bruce A. Buckingham,[7] William T. Cefalu,[8] Kelly L. Close,[9] Claudio Cobelli,[10] Eyal Dassau,[11] J. Hans DeVries,[12,13] Kim C. Donaghue,[14] Klemen Dovc,[1] Francis J. Doyle III,[11] Satish Garg,[15] George Grunberger,[16] Simon Heller,[17] Lutz Heinemann,[18] Irl B. Hirsch,[19] Roman Hovorka,[20] Weiping Jia,[21] Olga Kordonouri,[2] Boris Kovatchev,[22] Aaron Kowalski,[23] Lori Laffel,[24] Brian Levine,[9] Alexander Mayorov,[25] Chantal Mathieu,[26] Helen R. Murphy,[27] Revital Nimri,[28] Kirsten Nørgaard,[29] Christopher G. Parkin,[30] Eric Renard,[31] David Rodbard,[32] Banshi Saboo,[33] Desmond Schatz,[34] Keaton Stoner,[35] Tatsuiko Urakami,[36] Stuart A. Weinzimer,[37] and Moshe Phillip[28,38]

Improvements in sensor accuracy, greater convenience and ease of use, and expanding reimbursement have led to growing adoption of continuous glucose monitoring (CGM). However, successful utilization of CGM technology in routine clinical practice remains relatively low. This may be due in part to the lack of clear and agreed-upon glycemic targets that both diabetes teams and people with diabetes can work toward. Although unified recommendations for use of key CGM metrics have been established in three separate peer-reviewed articles, formal adoption by diabetes professional organizations and guidance in the practical application of these metrics in clinical practice have been lacking. In February 2019, the Advanced Technologies & Treatments for Diabetes (ATTD) Congress convened an international panel of physicians, researchers, and individuals with diabetes who are expert in CGM technologies to address this issue. This article summarizes the ATTD consensus recommendations for relevant aspects of CGM data utilization and reporting among the various diabetes populations.

This international consensus report has been endorsed by the American Diabetes Association, American Association of Clinical Endocrinologists, American Association of Diabetes Educators, European Association for the Study of Diabetes, Foundation of European Nurses in Diabetes, International Society for Pediatric and Adolescent Diabetes, JDRF, and Pediatric Endocrine Society.

I target glicemici in gravidanza

times in range



Battelino T et Al Diabetes Care Volume 42, August 2019

CSII+CGM: potenziali benefici

- miglior controllo dei livelli glicemici (come riflesso dal valore di emoglobina glicata, HbA1c)[3]
- riduzione della variabilità glicemica [1]
- minor frequenza di ipoglicemie severe con CSII [3,4]
- Riduzione di tutte le ipoglicemia (solo con algoritmi)
- riduzione del fabbisogno insulinico giornaliero [1]
- miglioramento della qualità della vita[2]
- maggiore flessibilità nello stile di vita [1]

[1]Cummins E et Al. *Health Technol Assess* 2010
[2]Nicolucci A at Al. *Diabet Med* 2008
[3]Misso ML et al. *Cochrane Database Syst Rev.* 2010
[4]Pickup JC, Phil D *N Engl J Med* 2012

Indicazioni a CSII, SAP

Continuous Subcutaneous Insulin Infusion (CSII)

- Emoglobina glicata persistentemente superiore al target desiderabile per il paziente, nonostante MDI intensiva e ottimizzata
- Elevato rischio di ipoglicemia, ipoglicemia grave
- Programmazione di gravidanza

Sensor Augmented Pump (SAP)

- Ipoglicemia problematica e ricorrente
- Ipoglicemia severa nonostante MDI ottimizzata
- Ipoglicemia unawareness

quale sistema scegliere?

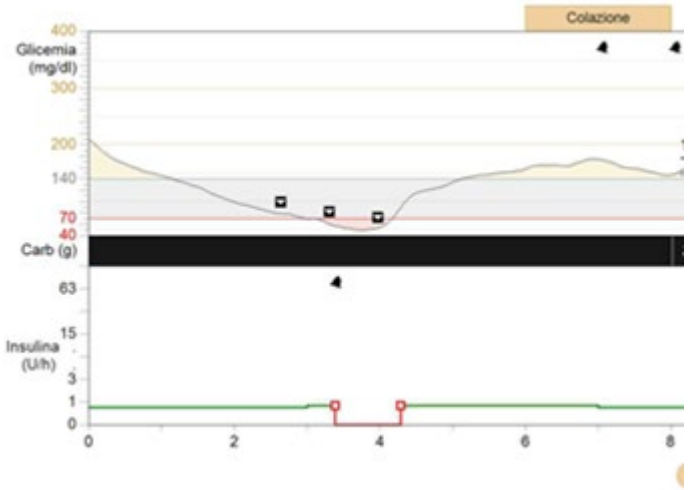
tubeless vs "tradizionale"

quale sistema scegliere?

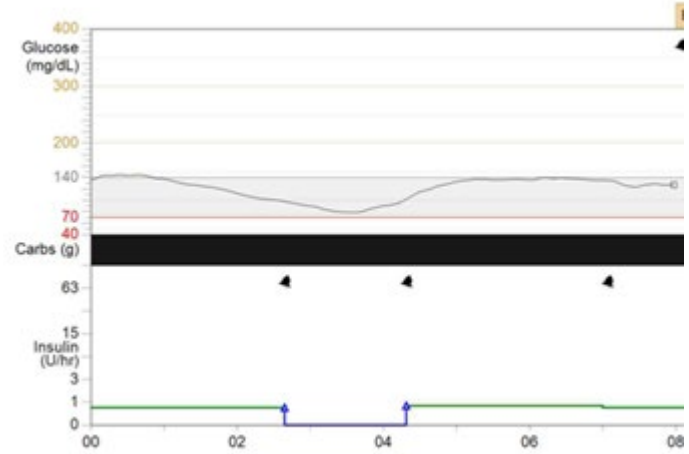
associazione con CGM e algoritmo

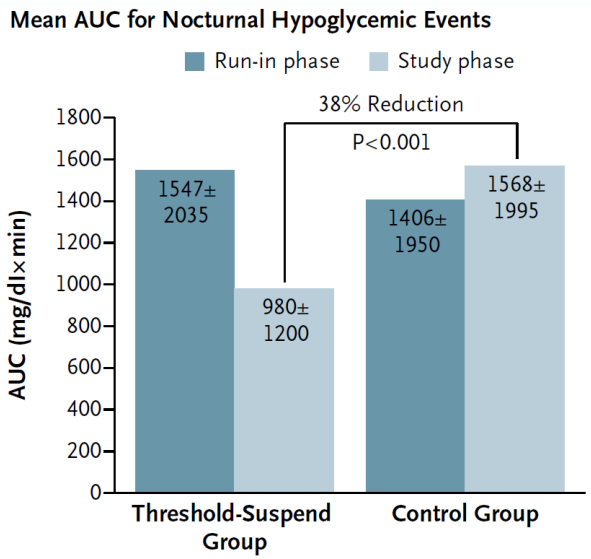
SAP con algoritmi attivi per l'ipoglicemia

Sospensione IN ipoglicemia (LGS)

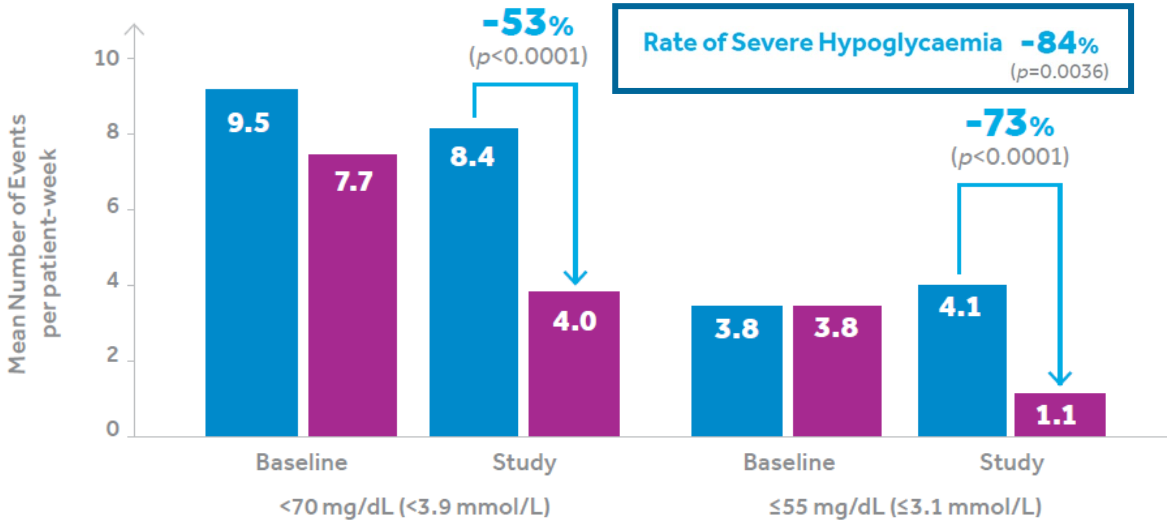


Sospensione PREDITTIVA (PLGS)



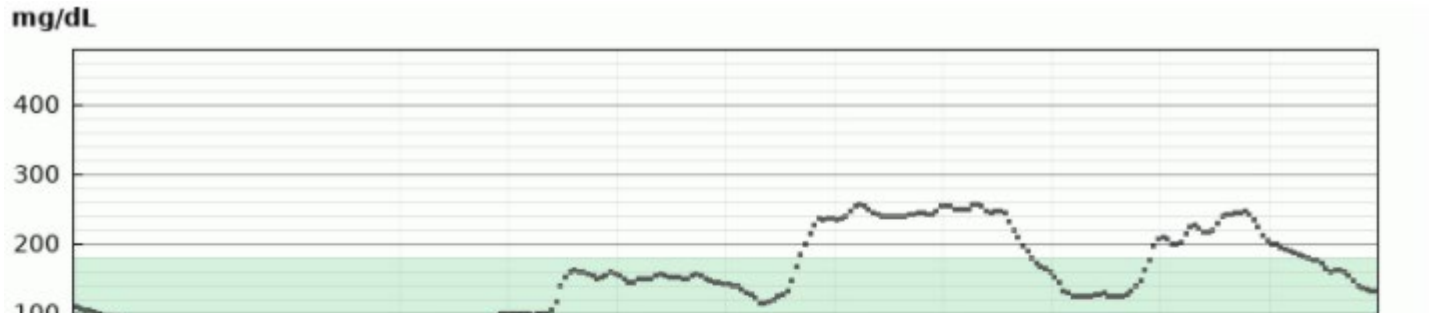


Bergenstal RM et al. *NEJM* 2013



Bosi E et al. *Lancet Endocr Metab* 2019

SAP con algoritmi attivi per l'ipoglicemia

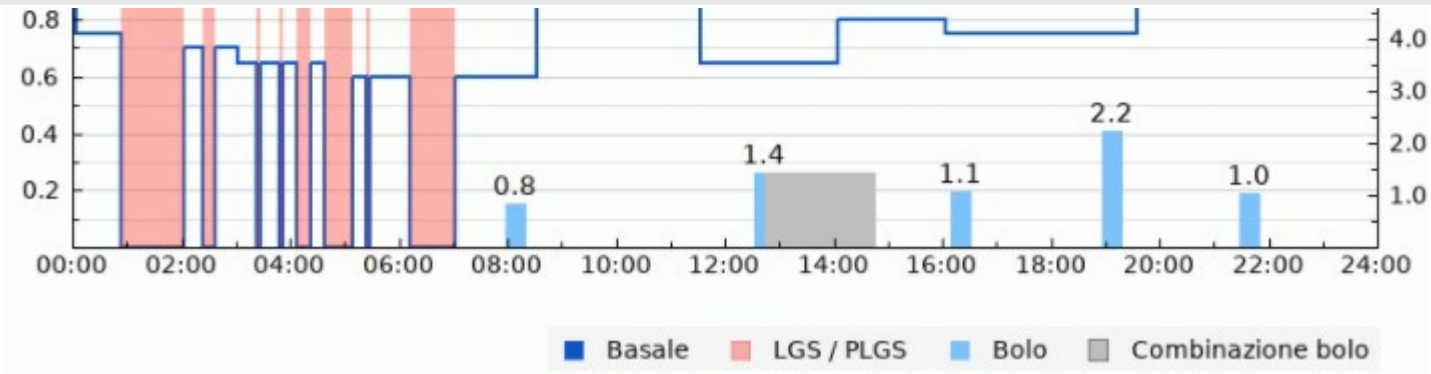


Hypoglycemia					
%Glucose <60 mg/dL	1.2 (0.6, 2.1)	0.9 (0.4, 1.6)	1.2 (0.6, 2.7)	−0.3 (−0.5, −0.2)	<0.001
%Glucose <54 mg/dL§	0.6 (0.2, 1.0)	0.4 (0.1, 0.8)	0.5 (0.2, 1.4)	−0.1 (−0.2, −0.1)	<0.001
%Glucose <50 mg/dL	0.3 (0.1, 0.6)	0.2 (0.1, 0.5)	0.3 (0.1, 0.7)	0.0 (−0.1, 0.0)‖	0.002
Area over curve <70 mg/dL	0.31 (0.19, 0.55)	0.25 (0.11, 0.40)	0.30 (0.17, 0.65)	−0.07 (−0.11, −0.05)	<0.001
Low blood glucose index	0.9 (0.6, 1.3)	0.8 (0.5, 1.1)	0.9 (0.6, 1.5)	−0.1 (−0.2, −0.1)	<0.001
Hypoglycemic events per week¶	1.1 (0.5, 2.4)	0.8 (0.3, 1.9)	1.1 (0.4, 3.0)	−0.3 (−0.4, 0.0)‖	<0.001

glucose 30 minutes ahead

insulin to help avoid the low

insulin once glucose rises



Forlenza GP et al. *Diabetes Care* 2018;41:2155–2161

PLGS in gravidanza

- A retrospective comparison between:
  - ✓ 19 women on SAP therapy plus PLGS
  - ✓ 13 on MDI plus rtCGM

Table 2 CGM metrics in the two groups divided by trimester

	I trimester($n=28$)		II trimester($n=33$)		III trimester($n=34$)	
	MDI + rtCGM($n=10$)	SAP + pLGS($n=18$)	MDI + rtCGM($n=13$)	SAP + pLGS($n=20$)	MDI + rtCGM($n=13$)	SAP + pLGS($n=21$)
Mean blood glucose	121.8 ± 42.9	139.4 ± 51.6	119.5 ± 43	133.7 ± 50.7	119.5 ± 39	141.7 ± 49.1
TAR (%) > 140 mg/dl	27.2 ± 19	42.7 ± 9.4 §	25.2 ± 13.9	39.0 ± 9.3°	23.8 ± 13	46.3 ± 10.8 *
TIR (%) 63–140 mg/dl	64 ± 15.3	53.8 ± 9.8 §	66.7 ± 12	56.9 ± 9.2 §	70.1 ± 11.7	51.3 ± 10.4 *
TBR (%) < 63 mg/dl	8.81 ± 7.81	3.53 ± 2.27 §	8.08 ± 6.65	4.08 ± 2.38 §	6.14 ± 3.70	2.42 ± 1.62 *
TBR (%) < 54 mg/dl	4.51 ± 3.72	1.60 ± 1.32°	4.09 ± 4.01	1.79 ± 1.27 §	2.77 ± 1.93	0.94 ± 0.85 *
pLGS activations/day (number)	–	3.3 ± 0.9	–	3.0 ± 1.3	–	1.9 ± 1.1 #
pLGS duration/day (min)	–	73.2 ± 24.4	–	68.7 ± 14.0	–	65.7 ± 14.0

Dodesini AR et al. *Acta Diabetologica* (2023) 60:1283–1285

CSII in gravidanza

- Medical records of 646 pregnancies in 478 women with T1D (2004-2017)
  - Pump vs. MDI use
  - CGM use vs. non-use
  - pregnancy-related outcomes using mixed effect models.

Conclusions:

- association between insulin pump use, CGM use, and better glycemic control during pregnancy among women with type 1 diabetes
- pump use was associated with increased birth weight measures
- lower HbA1c values associated with CGM use; these associations persisted even after adjustment for pump use in the sensitivity analysis, suggesting the potential beneficial effect of CGM use on glycemic control independent of pump use. These results are consistent with the findings from the CONCEPTT trial

Wang Z et al *Diabetes Research and Clinical Practice 187 (2022)*

CSII in gravidanza

	2010-2013	2016-2018
Completed questionnaire, *n*	5236	2818
Pregnant, *n* (%)	208 (4.0)	47 (1.7)
	Cohort 1 *N* = 208	Cohort 2 *N* = 47
Age (years), M ± SD	29 ± 6	30 ± 6
Diabetes duration (years), median (IQR)	15 (9, 22)	17 (13, 23)
Race/ethnicity, *n* (%)		
White non-Hispanic	178 (86)	40 (85)
Black non-Hispanic	7 (3)	3 (6)
Hispanic or Latino	19 (9)	3 (6)
Other race/ethnicity	4 (2)	1 (2)
Insurance status, *n* (%)		
Private	152 (76)	37 (80)
Other insurance	45 (23)	9 (20)
No insurance	2 (1)	0
Body mass index (kg/m^2), median (IQR)	27.6 (24.2, 31.2)	27.0 (24.1, 31.2)
Self-monitoring of blood glucose (non-CGM users; clinic-reported), *n* (%)	131 (63)	28 (59)
M ± SD	7.2 ± 3.1	5.5 ± 2.3
Self-monitoring of blood glucose (CGM users; clinic-reported), *n* (%)	74 (36)	18 (38)
M ± SD	8.3 ± 4.0	5.5 ± 2.7
CSII use (clinic-reported), *n* (%)	155 (75)	32 (70)

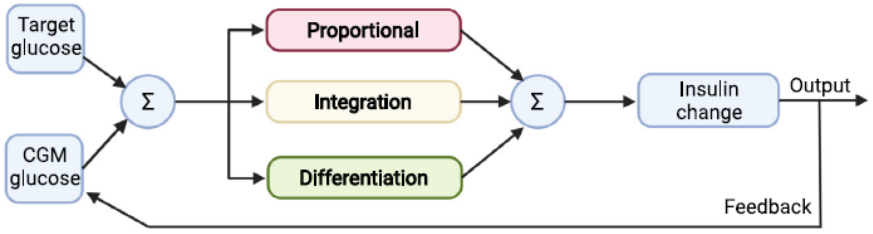
- Despites substantial improvement in glycemic outcomes, rates of macrosomia were higher in the infants of the women on CSII
- Much of the literature regarding the benefits of CSII therapy compared with MDI therapy in a pregnancy has been largely reliant on retrospective observational case series with baseline differences between CSII and MDI users

Levy CJ et al. *Journal of Diabetes Science and Technology* 15(6), 2021

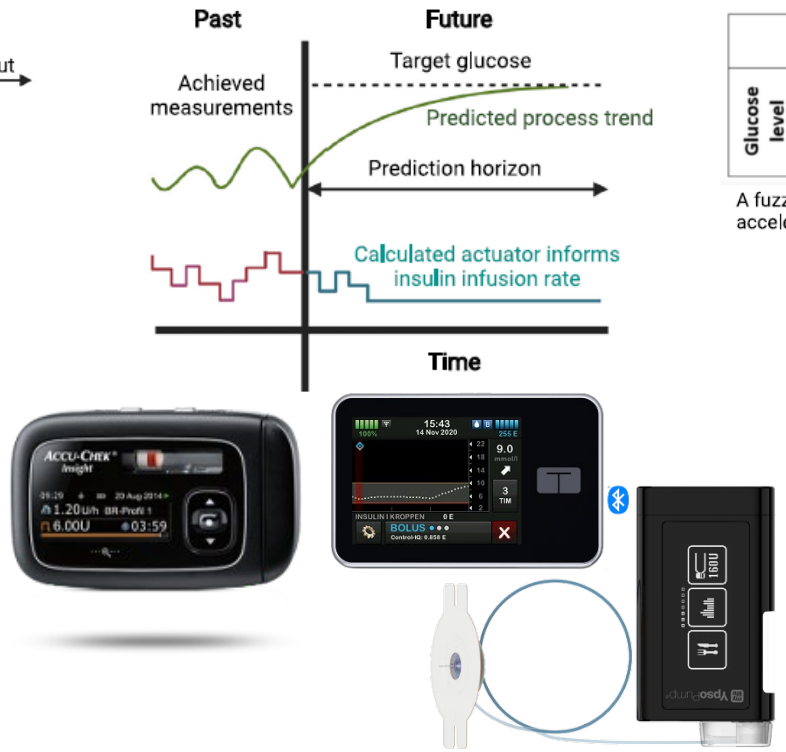
Sistemi AID

Current AID systems utilize sophisticated controller algorithms that continuously adjusts insulin delivery in response to real-time sensor glucose levels, residual insulin action and other inputs, such as meal intake and exercise announcement. The goal is to bring the predicted glucose levels into the target range.

A Proportional integral derivative (PID) controller



B Model predictive controller (MPC)



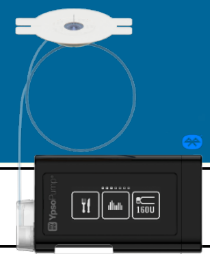
C Fuzzy logic controller

	Glucose rate	N			Z			P		
	Glucose acceleration	N	Z	P	N	Z	P	N	Z	P
Glucose level	Very high	0.05	0.10	0.20	0.10	0.20	0.30	0.10	0.20	0.50
	High	0.00	0.05	0.10	0.05	0.10	0.20	0.10	0.15	0.30
	Normal	0.00	0.00	0.05	0.00	0.05	0.10	0.05	0.10	0.20
	Low	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.05

A fuzzy logic controller using current sensor glucose level, rate of glucose change and acceleration to calculate insulin dosage. N, negative (for rate and acceleration); Z, zero; P, positive.

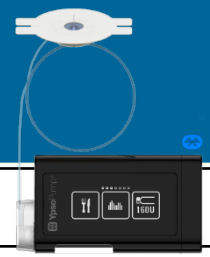
Ware J, Hovorka R *Metabolism Clinical and Experimental* 127, 2022

Sistemi AID



	Sxxxxxxxxd	Cxxxxxx-xQ	Dxxx1	CxxxxS
Età minima	7 anni	6 anni	18 anni	2 anni (con G6) o 4 anni (con FGM3)
Uso in gravidanza	NO	NO	NO	SI
Sensore	Guardian 4	Dexcom G6 o G7	Dexcom G6	Dexcom G6 o Libre 3
Tipo di Algoritmo	PID con feedback ed elementi di adattamento predittivo	Predittivo (MPC?)	MPC	MPC
Sede dell'algoritmo	Microinfusore	Microinfusore	Device in aggiunta	App per smartphone
Tipo di erogazione automatica	Basale e boli di correzione	Basale e boli di correzione	Basale e boli di correzione	Basale
Target	Un singolo valore: 100, 110 o 120 mg/dl	Un intervallo: 112.5–160 mg/dl	Un singolo valore: personalizzabile fra 100 e 130 mg/dl	Un singolo valore: personalizzabile fra 80 e 200 mg/dl
Fasce orarie del target	Unico nelle 24 ore	Unico nelle 24 ore	Unico nelle 24 ore	48 possibili nelle 24 ore (regolabile ogni 30 min)

Sistemi AID



	Sxxxxxxxxd	Cxxxxxx-xQ	Dxxx1	CxxxxS
Attività fisica	Target temporaneo a 150 mg/dL (disattivazione dei boli automatici)	Intervallo target 140–160 mg/dl	aumenta soglie e target di 70 mg/dl per la durata programmata	“Ease off”: somministrazione meno aggressiva di insulina
Altre modalità possibili	-	Modalità sonno: intervallo target 112,5–120 mg/dl (disattivazione dei boli automatici)	Modalità ZEN (aumenta il target di 10–40 mg/dl per 1–8 ore)	“Boost”: somministrazione più aggressiva di insulina
Parametri da inserire per il bolo	Grammi di CHO	Grammi di CHO o unità di insulina	Grammi di CHO o specifica del pasto	Grammi di CHO o unità di insulina
Paramenti modificabili per regolare il funzionamento automatico	Target glicemico I/CHO Tempo di insulina attiva	Infusione basale I/CHO FSI Peso corporeo Total Daily Dose	Target glicemico Aggressività Peso corporeo Total Daily Dose	Target glicemico I/CHO

AID in gravidanza

15. Management of Diabetes in Pregnancy: *Standards of Care in Diabetes—2024*

Diabetes Care 2024;47(Suppl. 1):S282–S294 | https://doi.org/10.2337/dc24-S015

- While many health care professionals prefer insulin pumps in pregnancy, it is not clear that they are superior to multiple daily injections
- None of the current automated insulin delivery (AID) systems approved by the U.S. Food and Drug Administration (FDA) have algorithms set to achieve pregnancy goals. It may be appropriate to continue or initiate AID therapy in carefully selected pregnant individuals with type 1 diabetes in the setting of using assistive techniques with expert guidance
- In addition, individuals who use AID systems that do not have pregnancy specific glucose targets often benefit from assistive techniques for pump management as determined by expert guidance from an experienced interprofessional team

AID in gravidanza

TABLE 3. APPROACH TO ASSISTED HYBRID CLOSED-LOOP THERAPY DURING PREGNANCY

Principle	*Possible adaptations to assist HCL therapy in pregnancy*
Assess/re-assess AID use throughout pregnancy	• Examine glucose control at each pregnancy visit • Examine psychosocial burdens at each pregnancy visit • Consider continuing current therapy or changing to alternate therapy at each visit (e.g., AID → SAPT, SAPT → AID)

Assist commercial AID system for use in pregnancy	• Use lowest glucose level/range for AID system
	• Correct for hyperglycemia often
	  • Use bolus calculator, when possible
	  • Provide pregnant women with glucose threshold above which corrections should be initiated
	• Enter manual boluses or "fake carbs" when required (when using the bolus calculator will not allow a bolus)
	  • Consider marking "fake carbs" with an event marker label (e.g., "other")
	  • Provide a range for manual bolus or "fake carb" input (start conservatively, watch for treatment effect, adjust as needed)
	  • Avoid stacking insulin by limiting frequency of these boluses to once every 2 h
	• Avoid overcorrection for hypoglycemia
	  • Consume fewer carbohydrates for corrections
	  • Check capillary glucose (not sensor glucose) before treatment and re-treatment
	• Adjust pump settings to avoid prolonged basal insulin suspensions and thereby reduce rebound hyperglycemia
	• Advise proper nutrition and bolusing techniques
	  • Adhere to recommended carbohydrate consumption levels for pregnancy
	  • Alter premeal bolus time with stage of pregnancy
	  • Split boluses for high-fat/high-carbohydrate meals
	• Alter pump settings around meal times
	  • Adjust carbohydrate-to-insulin ratios frequently
	  • "Steal" from basal 2–3 h after meal times
	• Consider exiting automated mode overnight and re-initiating each morning
	  • SAPT overnight and AID during the day
	  • Partial closed loop overnight and AID during the day

Szmuilowicz ED et al *Diabetes Technology & Therapeutics* Volume 25, Number 5, 2023

Primo sistema AID

Martedì 29/09

Dose tot giorn. 59,4U | Tot basale 36% | 21,3U | Tot bolo 64% | 38,1U

Tempo in target

9%

91%

Glucosio (mg/dl)

400
300
180
100
70
40

169 131 203 98 163

00 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 00

Basale (U/h)

Bolo (U) 0,6 6 13,8 17,7

Bolo prand.

Correttivo*

Differenza

Carb (g) 12 54 69

*Con considerazione dell'insulina attiva

Glicemia
Calibrazione
Basale Auto
Sosp. glucosio basso
Basale
Sosp. Pre glucosio basso
Basale temp
Avvisi
Bolo + Insulina attiva
Iniezione
Target + target temp
Attiv. fisica
Fuori grafico
Modifica ora
Altro
Modalità Manuale
Sosp. manuale
Tempo in target (mg/dl)
40 54 70 180 250 400

Primo sistema AID in gravidanza

TABLE 2. GLYCEMIC OUTCOMES BY RANDOMIZATION GROUP, ADJUSTED FOR CLINIC

	SAPT (n=12)	*HCL* (n=12)[ab]	p-*value*
Average HbA1c (%)			
First trimester	6.7 (0.2)	6.7 (0.2)	0.8811
Second trimester	6.1 (0.2)[c]	6.2 (0.2)[c]	0.6936
Third trimester	6.1 (0.2)[c]	6.7 (0.2)[d]	**0.0406**
Post-partum	6.2 (0.2)[c]	6.7 (0.2)[d]	0.0659
CGM measures in the run-in phase			
Average sensor glucose (mg/dL)	117 (4)	123 (4)	0.3765
Glucose management index (%)	6.1 (0.1)	6.3 (0.1)	0.3770
Time spent <54 mg/dL	4.2 (0.7)	4.0 (0.8)	0.8820
Time spent <63 mg/dL	8.5 (1.3)	7.9 (1.3)	0.7425
Time spent 63-140 mg/dL	64.3 (3.1)	62.3 (3.2)	0.6515
Time spent >140 mg/dL	28.4 (3.4)	30.9 (3.5)	0.6109
Time spent >180 mg/dL	10.4 (2.3)	13.8 (2.4)	0.3134
CGM measures in the first trimester			
Average sensor glucose (mg/dL)	123 (4)	126 (4)	0.6270
Glucose management index (%)	6.3 (0.1)	6.3 (0.1)	0.7249
Time spent <54 mg/dL	4.0 (0.7)	4.1 (0.8)	0.8563
Time spent <63 mg/dL	8.0 (1.3)	7.5 (1.3)	0.7674
Time spent 63–140 mg/dL	61.7 (3.1)	61.2 (3.2)	0.9037
Time spent >140 mg/dL	31.4 (3.4)	32.5 (3.5)	0.8222
Time spent >180 mg/dL	13.2 (2.3)	15.3 (2.4)	0.5370
CGM measures in the second trimester			
Average sensor glucose (mg/dL)	126 (4)	137 (4)[c]	0.0674
Glucose management index (%)	6.3 (0.1)	6.6 (0.1)[c]	0.0543
Time spent <54 mg/dL	2.8 (0.7)	1.7 (0.8)[c]	0.2880
Time spent <63 mg/dL	6.2 (1.3)	3.5 (1.3)[c]	0.1471
Time spent 63–140 mg/dL	60.5 (3.1)	57.2 (3.2)	0.4697
Time spent >140 mg/dL	34.5 (3.4)	40.3 (3.5)	0.2410
Time spent >180 mg/dL	13.1 (2.3)	17.8 (2.4)	0.1650
CGM measures in the third trimester			
Average sensor glucose (mg/dL)	119 (4)	132 (4)	**0.0475**
Glucose management index (%)	6.2 (0.1)	6.5 (0.1)	0.0515
Time spent <54 mg/dL	2.0 (0.7)[c]	1.3 (0.8)[c]	0.4747
Time spent <63 mg/dL	5.1 (1.3)	2.8 (1.3)[c]	0.2237
Time spent 63–140 mg/dL	68.2 (3.1)[d]	61.9 (3.2)	0.1667
Time spent >140 mg/dL	27.9 (3.4)	36.3 (3.5)	0.0987
Time spent >180 mg/dL	8.5 (2.3)	13.7 (2.4)	0.1346

The HCL group had total insulin from fake Carbohydrates:

- 5.73% of in the second trimester
- 5.13% in the third trimester
- 4.41 % in postpartum.

Time in auto mode (HCL) was:

- 68.6% in the
- second trimester
- 77.3% in the third trimester
- 61.4% postpartum

	High use of HCL (n=5)	*Low use of HCL* (n=6)
CGM measures in the run-in phase		
Average sensor glucose (mg/dL)	117.4±19.4	126.1±20.5
Glucose management index (%)	6.1±0.5	6.3±0.5
Time spent <54 mg/dL	3.8±2.8	4.3±3.9
Time spent <63 mg/dL	7.4±4.0	8.6±5.8
Time spent 63–140 mg/dL	66.7±17.6	59.4±15.6
Time spent >140 mg/dL	27.0±18.4	33.2±16.8
Time spent >180 mg/dL	10.8±9.6	15.9±12.3
CGM measures in the first trimester		
Average sensor glucose (mg/dL)	124.3±13.6	126.1±11.4
Glucose management index (%)	6.3±0.3	6.3±0.3
Time spent <54 mg/dL	3.4±2.5	4.8±3.4
Time spent <63 mg/dL	6.6±3.8	8.4±4.1
Time spent 63–140 mg/dL	63.4±8.2	60.1±11.6
Time spent >140 mg/dL	31.2±11.1	32.6±9.3
Time spent >180 mg/dL	13.5±7.0	16.3±8.8
CGM measures in the second trimester		
Average sensor glucose (mg/dL)	133.9±14.4	139.3±15.8
Glucose management index (%)	6.5±0.3	6.7±0.4
Time spent <54 mg/dL	1.7±1.4	1.8±0.9
Time spent <63 mg/dL	3.6±2.5	3.7±1.5
Time spent 63–140 mg/dL	60.5±10.6	55.3±12.1
Time spent >140 mg/dL	37.0±12.3	42.1±12.4
Time spent >180 mg/dL	15.1±8.3	19.6±9.9
CGM measures in the third trimester		
Average sensor glucose (mg/dL)	130.1±11.5	132.4±12.0
Glucose management index (%)	6.4±0.3	6.5±0.3
Time spent <54 mg/dL	1.2±1.1	1.4±0.9
Time spent <63 mg/dL	2.7±2.2	3.2±1.1
Time spent 63–140 mg/dL	65.0±8.2	60.2±11.0
Time spent >140 mg/dL	33.4±9.7	37.7±10.7
Time spent >180 mg/dL	12.0±6.5	14.5±7.7

Grosman B et al. *Journal of Diabetes Science and Technology* 2016, Vol. 10(3) 708–713

AID in gravidanza

$$CB_{init} = (SG-120)/ISF-IOB$$

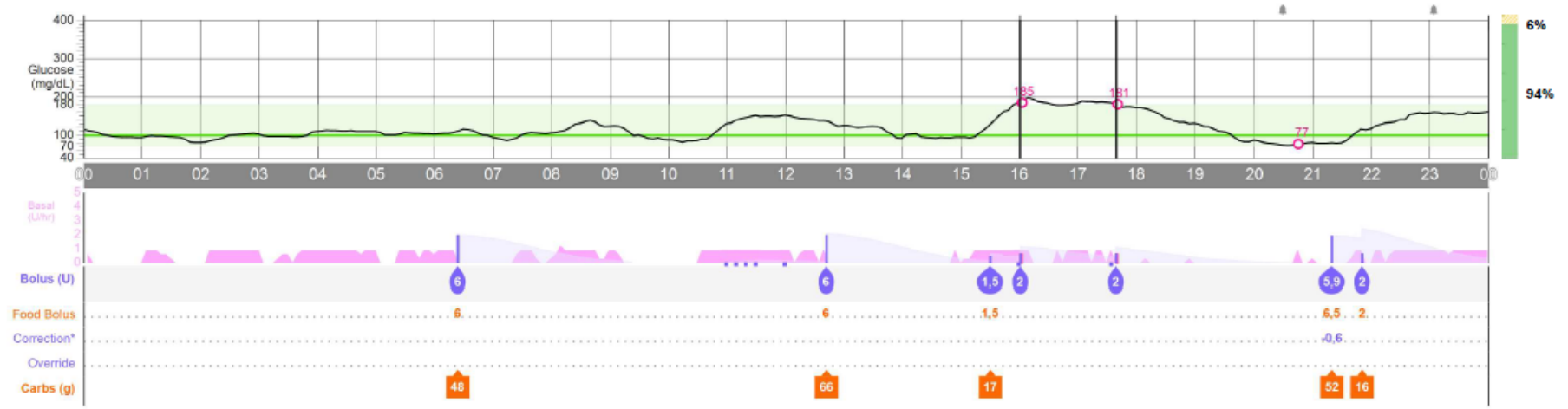
AID in gravidanza

Daily Review (3 of 7)
08/04/2024, 09/04/2024

Generated: 07/06/2024, 15:17 Page 19 of 23

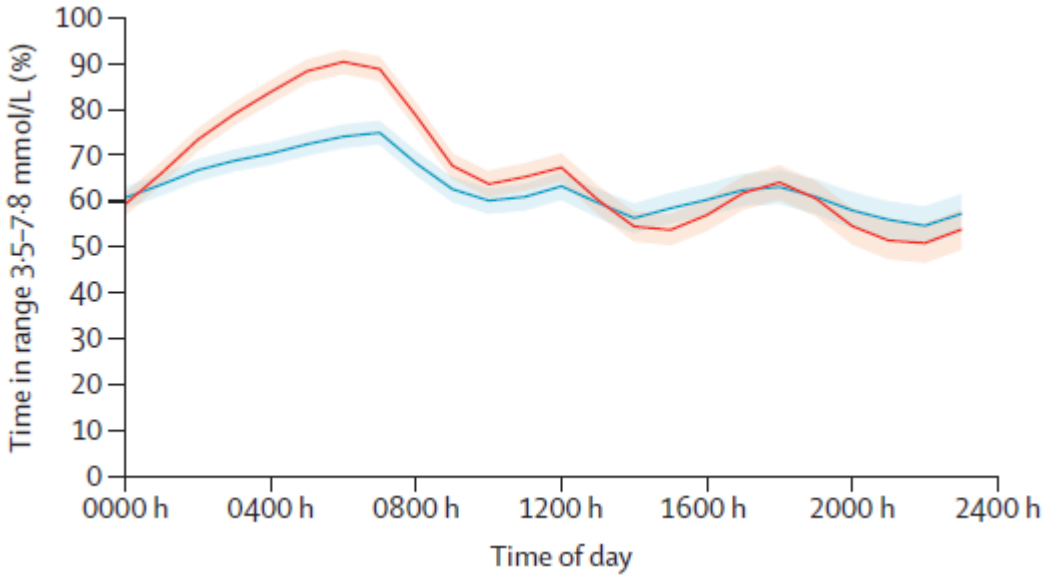
Monday 08/04 TDD 38,7U | Total Basal 29% | 11,4U | Total Bolus 71% | 27,3U { Bolus 95% | 26,0U + Auto Correction 5% | 1,3U }

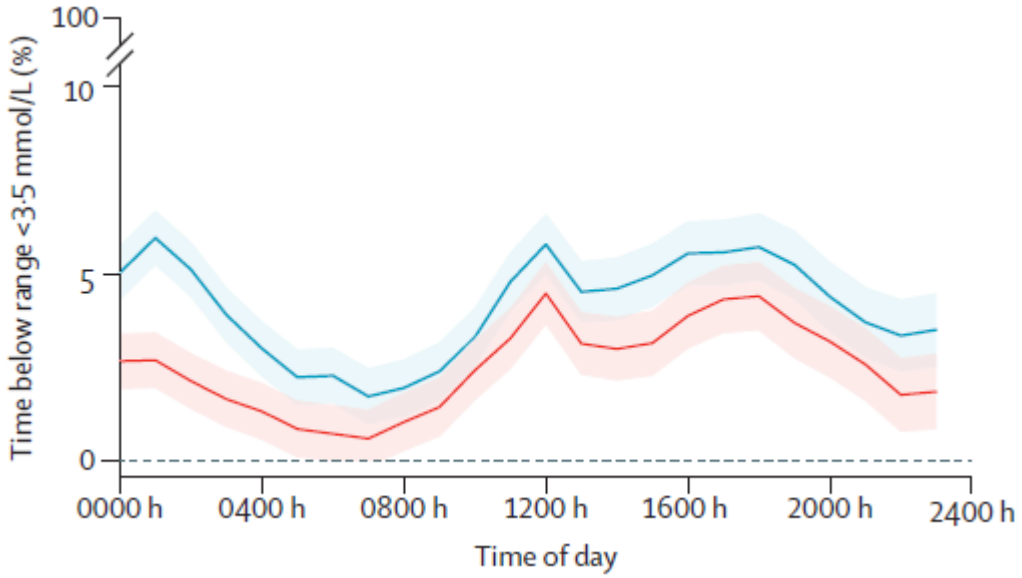
Tuesday 09/04 TDD 36,6U | Total Basal 28% | 10,2U | Total Bolus 72% | 26,4U { Bolus 97% | 25,5U + Auto Correction 3% | 0,9U }



AID in gravidanza

- CRISTAL Study: double-arm, parallel-group, open-label, randomised controlled trial
- 101 participants were screened, and 95 were randomly assigned to AID therapy (n=46) or standard insulin therapy (n=49)





AHCL therapy did not improve overall time in target range, improved overnight time in target range, reduced overall time below range, and improved treatment satisfaction

Benhalima K et al. *Lancet Diabetes Endocrinology* Vol 12 June 2024

AID in gravidanza

- CRISTAL Study: double-arm, parallel-group, open-label, randomised controlled trial
- 101 participants were screened, and 95 were randomly assigned to AID therapy (n=46) or standard insulin therapy (n=49)

	Advanced hybrid closed loop therapy (n=43)	Standard insulin therapy (n=46)
Obstetric and maternal outcomes		
Gestational hypertension	4/43 (9·3%)	6/46 (13·0%)
Pre-eclampsia	4/42 (9·5%)	2/46 (4·3%)
HELLP syndrome	1/42 (2·4%)	0/46 (0·0%)
Mode of delivery		
Vaginal	16/43 (37·2%)	14/45 (31·1%)
Vacuum pump (instrumental)	6/43 (13·9%)	2/45 (4·4%)
Caesarean section (total)	21/43 (48·8%)	29/45 (64·4%)
Planned or elective caesarean section	14/21 (66·7%)	19/29 (65·5%)
Unplanned or emergency caesarean section	7/21 (33·3%)	10/29 (34·5%)
Repeat caesarean section	10/21 (47·6%)	9/29 (31·0%)
Total gestational weight gain (kg)*	11·8 (4·2)	13·9 (5·7)
Excessive gestational weight gain†	14/43 (32·6%)	26/46 (56·5%)
Median duration of postpartum hospital stay (days)	4·0 (3·0–5·0)	4·0 (3·0–4·0)
Breastfeeding‡	33/41 (80·5%)	37/45 (82·2%)
Fetal and neonatal outcomes		
Miscarriage (<20 weeks)§	2/45 (4·4%)	1/47 (2·1%)
Death in utero or stillbirth (≥20 weeks)¶	1/45 (2·2%)	0/47 (0·0%)
Neonatal death	0/42 (0·0%)	0/46 (0·0%)
Gestational age at delivery (weeks and days)	37 weeks and 2 days (1 week and 1 day)	37 weeks and 5 days (1 week and 1 day)
Preterm birth (<37 weeks)‖	12/43 (27·9%)	9/46 (19·6%)
Birthweight outcomes**		
Birthweight (kg)	3·6 (0·6)	3·7 (0·5)
Small for gestational age	0/43 (0·0%)	0/46 (0·0%)
Large for gestational age	24/43 (55·8%)	31/46 (67·4%)
Extremely large for gestational age (>P97)	16/43 (37·2%)	20/46 (43·5%)
Macrosomia (>4 kg)	13/43 (30·2%)	15/46 (32·6%)
Birthweight >4·5 kg	2/43 (4·7%)	4/46 (8·7%)
Median sum of skinfolds (mm)	18·8 (15·1–19·8)	18·4 (15·8–21·8)
Median neonatal body fat mass (g)	1514·4 (1381·7–1619·6)	1436·4 (1262·5–577·0)
Median neonatal body fat mass (%)	39·0 (39·0–39·0)	39·0 (39·0–39·0)

(Table 4 continues on next page)

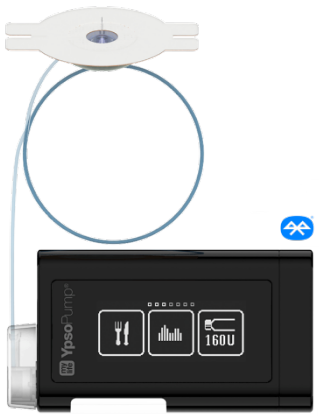
	Advanced hybrid closed loop therapy (n=43)	Standard insulin therapy (n=46)
(Continued from previous page)		
Neonatal complications		
Congenital malformation††	2/41 (4·9%)	4/46 (8·7%)
Birth trauma‡‡	1/41 (2·4%)	0/45 (0·0%)
Shoulder dystocia	3/40 (7·5%)	3/44 (6·8%)
Respiratory distress§§	6/41 (14·6%)	5/46 (10·9%)
Hypoglycaemia (<40 mg/dL)	12/38 (31·6%)	19/42 (45·2%)
Hypoglycaemia treated with intravenous glucose	2/11 (18·2%)	5/18 (27·8%)
Hyperbilirubinaemia with need for phototherapy	9/34 (26·5%)	5/39 (12·8%)
Neonatal (intensive) care hospital admission (≥1 day)¶¶	14/42 (33·3%)	11/45 (24·4%)
Neonatal (intensive) care hospital admission for neonatal hypoglycaemia‖‖	2/14 (14·3%)	7/11 (63·6%)
Median duration of hospital stay (days)	4·0 (3·0–5·0)	4·0 (3·0–4·0)
Median duration of neonatal (intensive) care hospital admission (days)	4·5 (2·0–11·0)	6·5 (3·0–9·0)

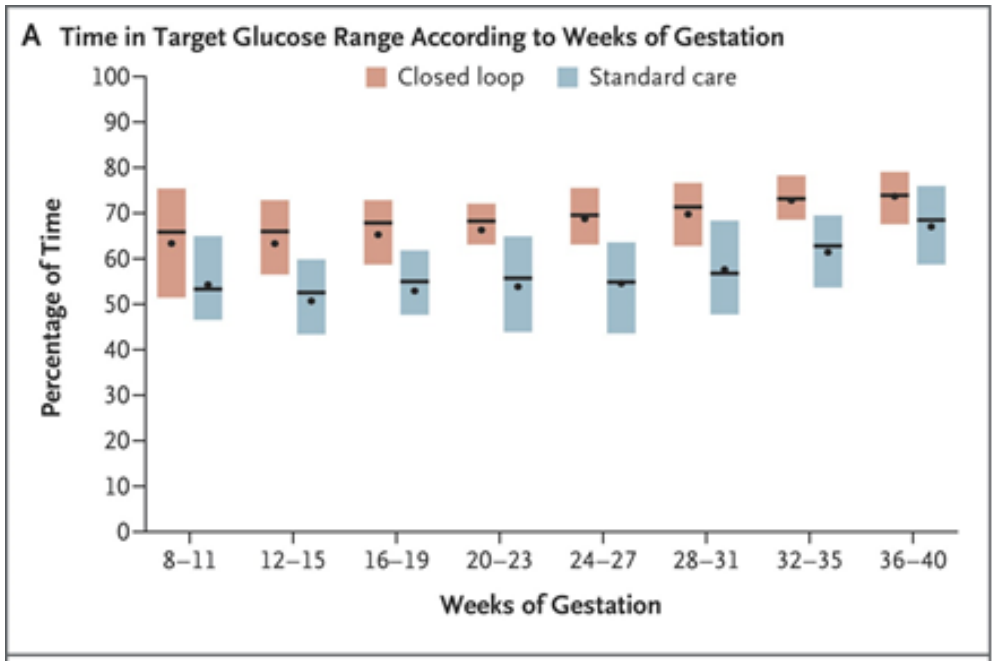
Excessive gestational weight gain was lower in women using AHCL therapy, NICU admissions due to neonatal hypoglycaemia occurred less frequently in the AHCL therapy group

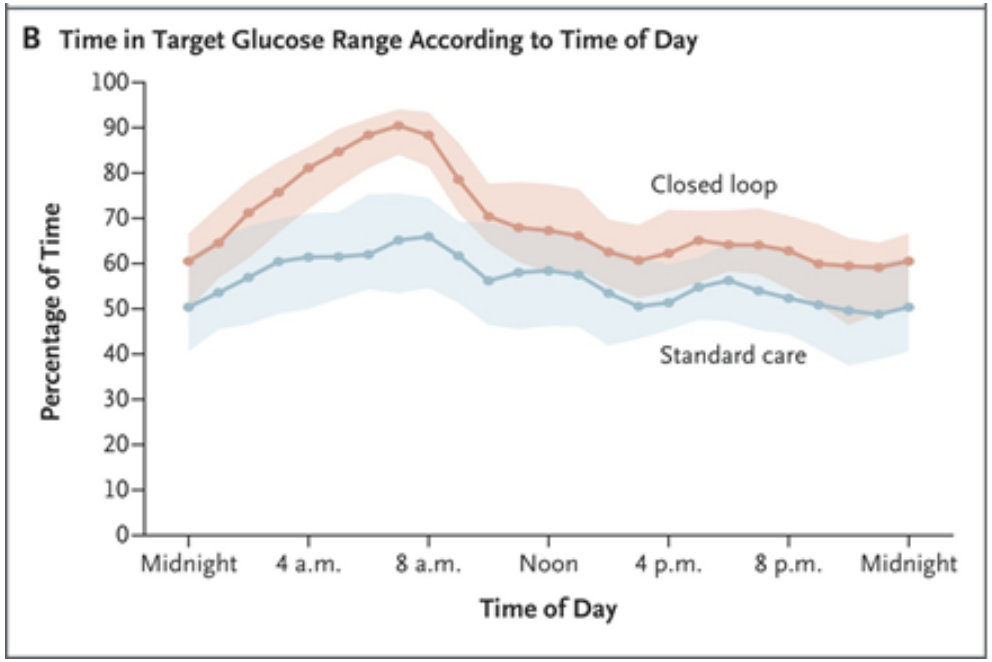
Benhalima K et al. *Lancet Diabetes Endocrinology* Vol 12 June 2024

AID in gravidanza

- AiDAPT Study: double-arm, parallel-group, open-label, randomised controlled trial
- 124 participants were randomly assigned to HCL or standard insulin therapy plus rtCGM







HCL therapy improved TIR in during all pregnancy and in overall daily times, in particular in night-time

Lee TTM et al. *N Engl J Med* Vol.389(17):1566-1578 October 26, 2023

AID in gravidanza

- AiDAPT Study: double-arm, parallel-group, open-label, randomised controlled trial
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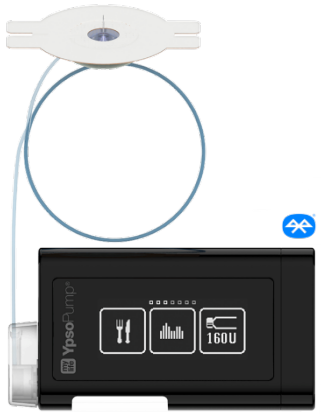


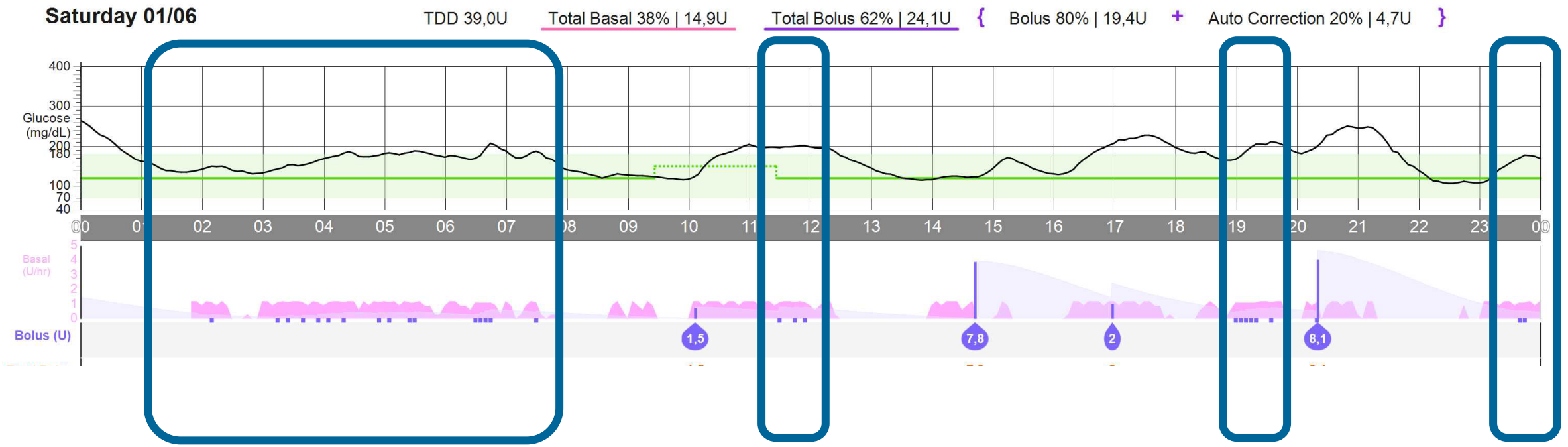
Table 3. Maternal and Neonatal Outcomes.*

Outcome	Closed Loop (N=59)	Standard Care (N=60)
Maternal outcomes		
Any hypertensive disorder — no. (%)	12 (20)	25 (42)
Worsening of existing hypertension	4 (7)	2 (3)
New onset hypertension	6 (10)	19 (32)
Preeclampsia	4 (7)	12 (20)
Mode of delivery — no. (%)†		
Vaginal	10 (17)	15 (25)
Primary cesarean section	24 (41)	34 (57)
Repeat cesarean section	25 (42)	11 (18)
Cesarean type — no./total no. (%)		
Planned or elective	27/49 (55)	22/45 (49)
Unplanned or emergency	22/49 (45)	23/45 (51)
Maternal weight gain — kg	11.1±6.1	14.1±6.1
Median length of hospital stay (IQR) — days	6 (4–9)	6 (4–8)
Fetal and neonatal outcomes		
Pregnancy loss at <20 wk — no.‡	1	3
Neonatal death — no.§	0	1
Baby alive at discharge — no./total no. (%)¶	59/60 (98)	59/63 (94)
Gestational age at delivery	36 wk 3 days (±2 wk)	37 wk 1 day (±1 wk)
Preterm birth, at <37 wk — no./total no. (%)‖	27/60 (45)	14/63 (22)
Birth weight**		
Mean — kg	3.3±0.6	3.5±0.5
Median customized percentile (IQR)	80.7 (53–97)	90.1 (71–99)
Small for gestational age — no. (%)	3 (5)	1 (2)
Large for gestational age — no. (%)	23 (39)	30 (50)
Extremely large for gestational age — no. (%)	13 (22)	19 (32)
Macrosomia >4.0 kg — no. (%)	4 (7)	9 (15)
Neonatal complications		
Serious birth injury — no. (%)††	1 (2)	4 (7)
Respiratory distress — no. (%)	5 (8)	8 (13)
Hypoglycemia treated with intravenous or oral glucose — no. (%)	26 (44)	25 (42)
Hyperbilirubinemia — no. (%)	40 (68)	37 (62)
Readmission within 7 days — no. (%)	8 (14)	3 (5)
Neonatal intensive care unit stay ≥1 day — no. (%)	13 (22)	15 (25)
Median length of hospital stay (IQR) — days	6 (3–10)	5 (3–7)

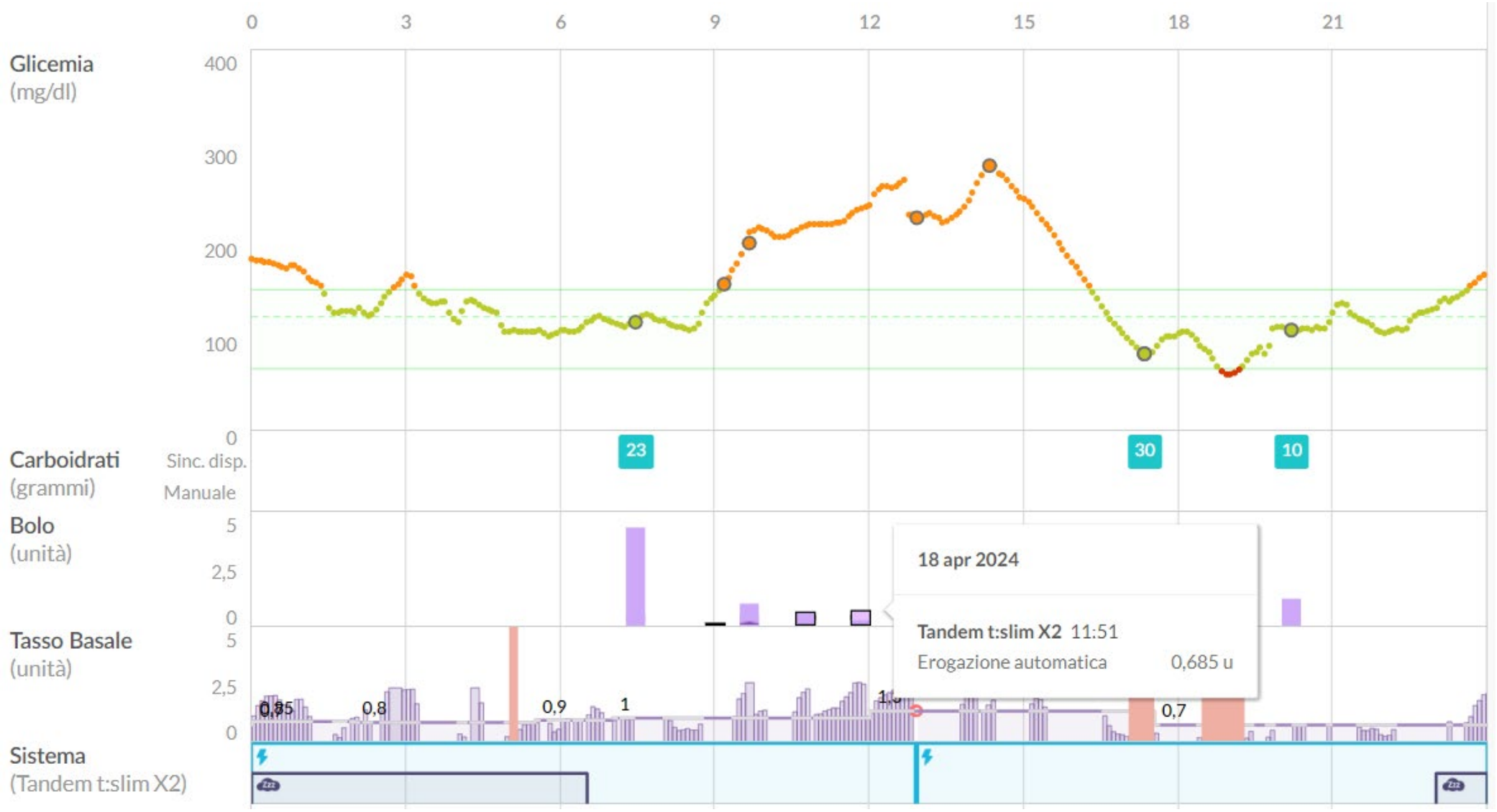
Lee TTM et al. *N Engl J Med* Vol.389(17):1566-1578 October 26, 2023

AID: definizioni

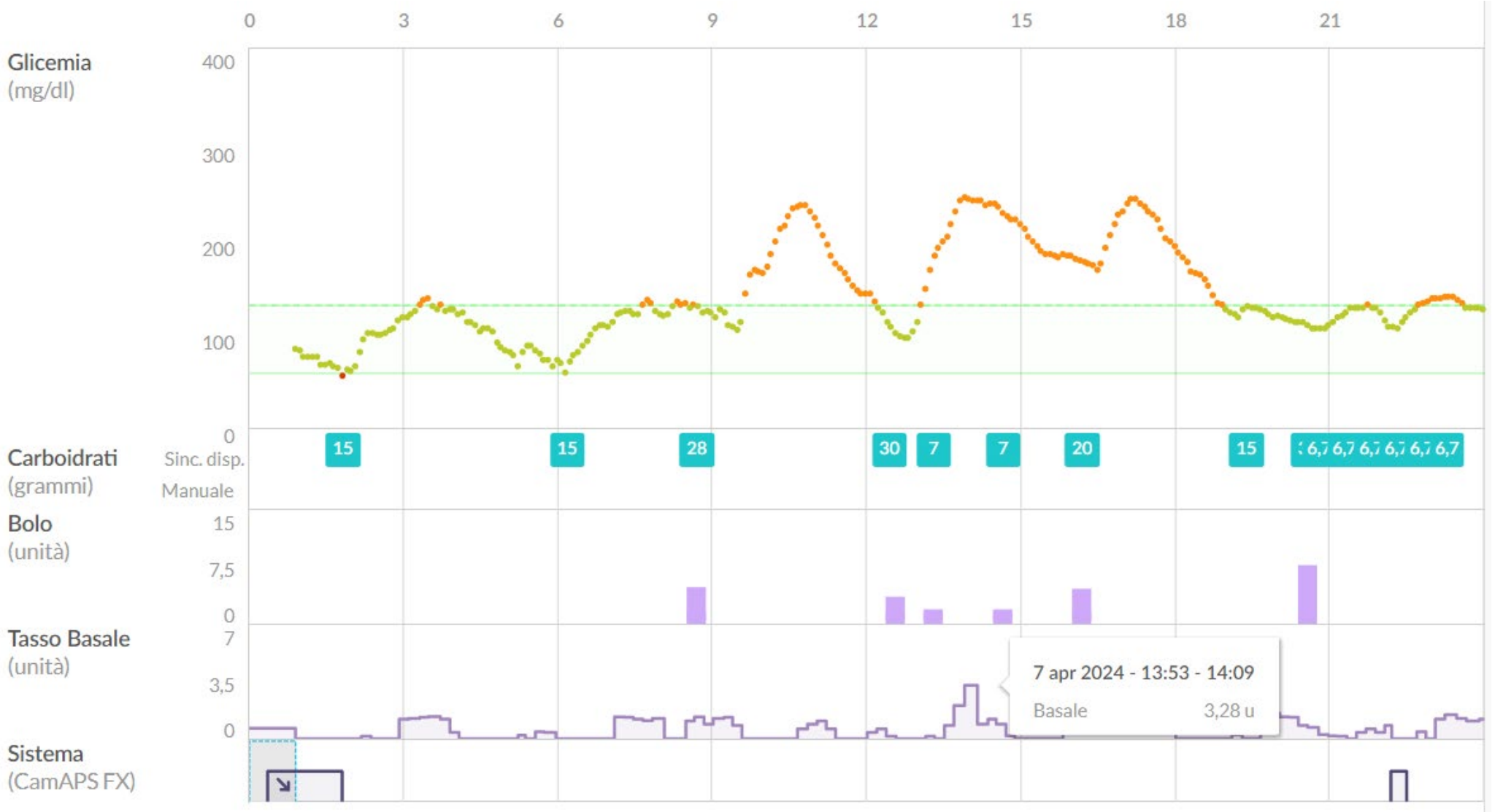
- Semi-Automated (or Hybrid)
  - Hybrid Close Loop
  - Avanced-Hybrid Close Loop
- Fully-Automated Closed Loop



AID: definizioni



AID: definizioni



AID: real world data

Study	Technology (* = isCGM)	# of participants	Ped / Adult	Final TIR (%) 70-180 mg/dL	Final TBR (%) < 70 mg/dL
Battelino T, DC 2011	MDI, CSII (65%)	120	Ped 27%, Adult	63	3.8
Battelino T, Diabetologia 2012	CSII	147	Ped 45%, Adult	54	1.3
Bergenstal RM, NEJM 2013	LGS	247	Adult	Not reported	5.3
Bolinder J, Lancet 2016	* MDI	238	Adult	65.8	8.4
Beck RW, JAMA 2017	MDI	102	Adult	50	3.7
Lind M, JAMA 2017	MDI	142	Adult	42.3	2.8
Allepo G, DC 2017	MDI	149	Adult	65	3.7
Battelino T, DC 2017	PLGS	97	Ped	56.3	2.6
Piona C, PedDiab 2018	* CSII	45	Ped	50	3.2

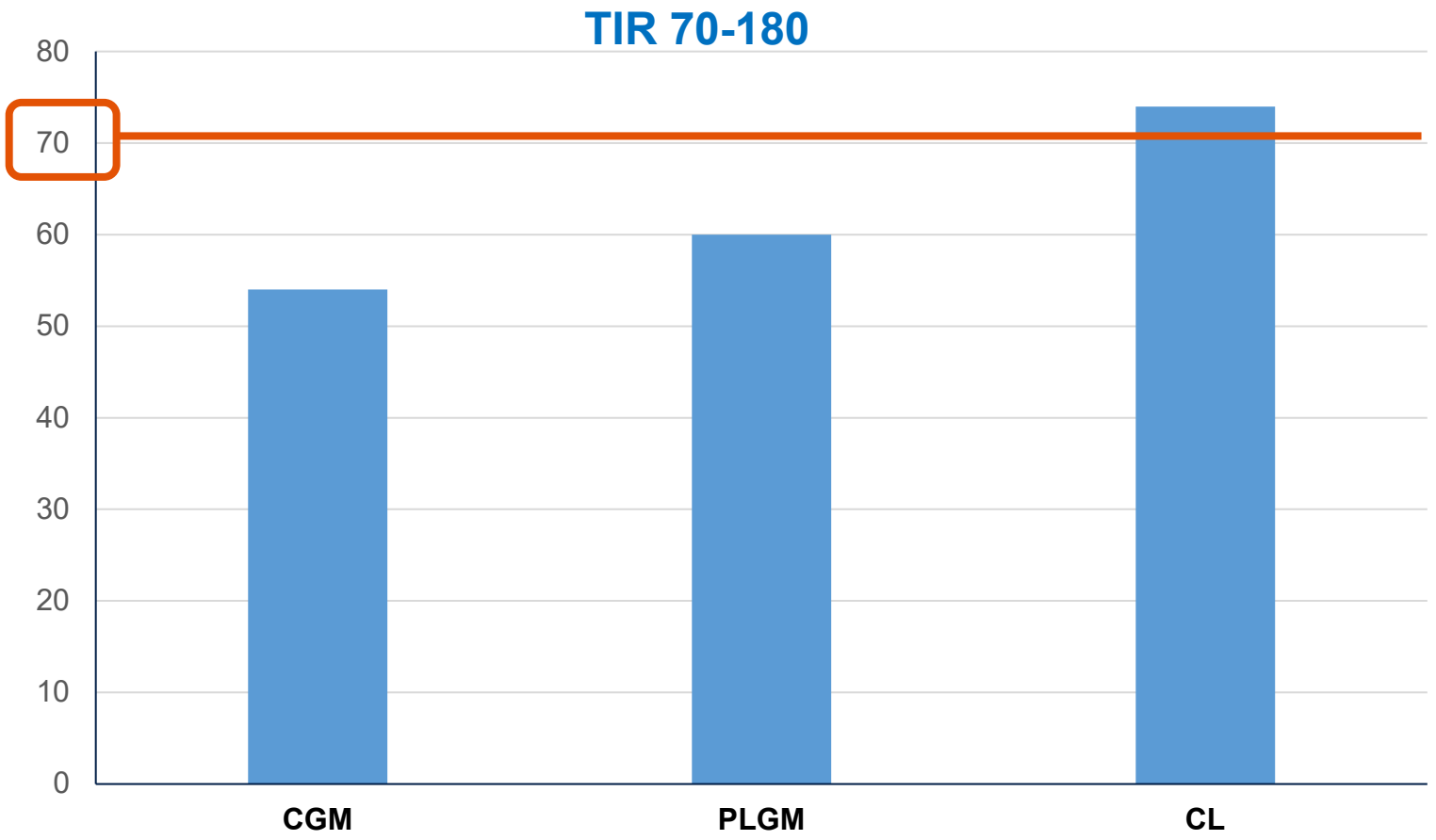
AID: real world data

Study	Technology (* = isCGM)	# of participants	Ped / Adult	Final TIR (%) 70-180 mg/dL	Final TBR (%) < 70 mg/dL
Heinemann L, Lancet DE 2018	MDI	141	Adult	58.5	1.6
Forlenza GP, DC 2018	PLGS	102	Ped	65	2.6
Bosi E, Lancet DE 2019	PLGS	153	Adult	59.9	2.8
Thabit H, NEJM, 2015	CL	33	Adult	67.7	2.9
		25	Ped	61.2	3.1
Russell SJ, NEJM, 2015	CL (bihorm)	20	Adult	79.5	4.1
		32	Ped	75.9	3.1
Russell SJ, Lancet DE, 2016	CL (bihorm)	19	Ped	80.6	2.9
Tauschmann M, DC 2016	CL	12	Ped	72	2.9

AID: real world data

Study	Technology (* = isCGM)	# of participants	Ped / Adult	Final TIR (%) 70-180 mg/dL	Final TBR (%) < 70 mg/dL
Bergenstal RM, JAMA 2016[#]	CL	124	Ped +Adult	72.2	3.3
Anderson SM, DC, 2016	CL	30	Adult	73	1.7
Haidar A, JCEM, 2016	CL	28	Ped +Adult	76	5
	CL (bihorm)	28	Ped +Adult	81	1
El-Khatib FH, Lancet 2017	CL (bihorm)	39	Adult	78.4	1.8
Bally L, Lancet DE, 2017	CL	29	Adult	76.2	2.9
Tauschmann M, Lancet 2018	CL	86 (subopt.)	Ped +Adult	65	2.6
Tauschmann M, DC 2019	CL	24	Ped (5 y)	72	4.5
Brown SA, NEJM, 2019	CL	168	Ped (27%) + A	71	1.6
Haidar A, DC 2020	CL + pramlint	27	Adult	84	0.1

AID: real world data



More technology is associated with higher TIR

AID: indications

Endocrine Reviews, 2023, **44**, 254–280
https://doi.org/10.1210/endrev/bnac022
Advance access publication 6 September 2022
Review

Consensus Recommendations for the Use of Automated Insulin Delivery Technologies in Clinical Practice

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Table 6. Summary of recommendations: target populations

- Strongly consider recommending AID systems to all people with T1D to improve glycemic control
  - School-aged children (7–14 years) (2, 3, 5, 20, 46, 63–67) **A**
  - Adolescents/Adults (3, 6, 68) **A**
- Consider recommending to:
  - Older adults (above 65 years) (2, 29, 68, 69) **B**
  - Preschool children (<7 years) (31, 32, 56, 57, 70–73) **B**
  - People with moderate/severe hypoglycemia and hypoglycemia unawareness (74–77) **C**
  - Pregnancy complicated with T1D (58, 60, 78–81) **C**
  - People with comorbidities: chronic renal failure and gastroparesis (82–84) **C**
- Consider recommending appropriate AID systems to people with other types of diabetes treated with intensive insulin therapy (multiple daily injections or pump therapy):
  - People with type 2 diabetes (60, 61) **C**
  - People after pancreatectomy **E**
  - People with cystic fibrosis–related diabetes (85, 86) **C**
- Use of AID under supervision should be allowed in hospital settings if not contraindicated by clinical status or treatment needs **E**

Take home messages

- La CSII rappresenta una valida opzione per il trattamento del diabete pregestazionale
- Ma è l'associazione con il sensore che rende la CSII efficace in termini di outcomes glicemici e materno-fetali
- Gli algoritmi per la gestione della ipoglicemia (LGS e PLGS) sono stati il primo passo per ottimizzare il controllo glicemico in gravidanza
- I sistemi AID, in particolare se con il target glicemico adeguato alla gravidanza, sono già il presente del trattamento del diabete pregestazionale
- È importante conoscere bene l'algoritmo che si propone alla paziente, per farlo rendere al meglio e ottenere il miglioramento degli outcomes glicemici e, di conseguenza, materno-fetali