



INNOVAZIONE TECNOLOGICA
E SOSTENIBILITÀ NELLA GESTIONE
DEL DIABETE MELLITO

Penne Intelligenti

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Il Dottor Boscari Federico dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

- Relazioni a congresso

- Novo Nordisk
- Sanofi Aventis
- Movì

- Advisory Board

- Tandem
- Roche
- Glooko
- Sanofi Aventis

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.).

Ancora Penne??

Insulin Pumps and Automated Insulin Delivery Systems

Recommendations

7.26 AID systems should be the preferred insulin delivery method to improve glycemic outcomes and reduce hypoglycemia and disparities in youth and adults with type 1 diabetes **A** and other types of insulin-deficient diabetes **E** who are capable of using the device (either by themselves or with a caregiver). Choice of an AID system should be made based on the individual's circumstances, preferences, and needs. **A**

7.27 Insulin pump therapy, preferably with CGM, should be offered for diabetes management to youth and adults on MDI with type 2 diabetes who can use the device safely (either by themselves or with a caregiver). The choice of device should be made based on the individual's circumstances, preferences, and needs. **A**

1.6 In soggetti con diabete mellito di tipo 1 è preferibile l'utilizzo di sistemi ad ansa chiusa costituiti da microinfusore e sensore con automatismo oppure sistemi senza automatismo?

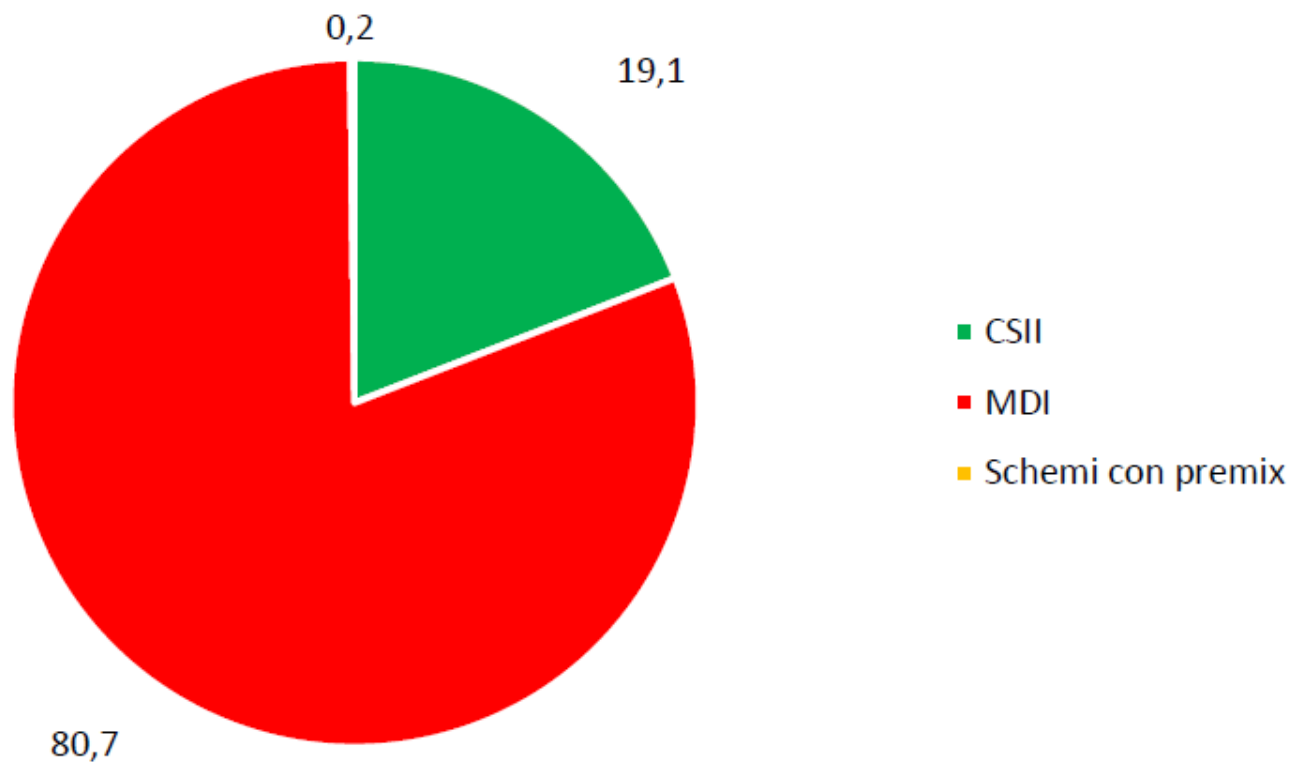
In soggetti con diabete mellito di tipo 1 si raccomanda l'utilizzo di sistemi ad ansa chiusa costituiti da microinfusore e sensore con automatismo rispetto all'uso di sistemi senza automatismo.

Raccomandazione forte a favore dell'intervento

Qualità delle prove: alta.

Ancora penne...nel DM1

Distribuzione dei pazienti per schema di trattamento insulinico (%)



Ancora penne...

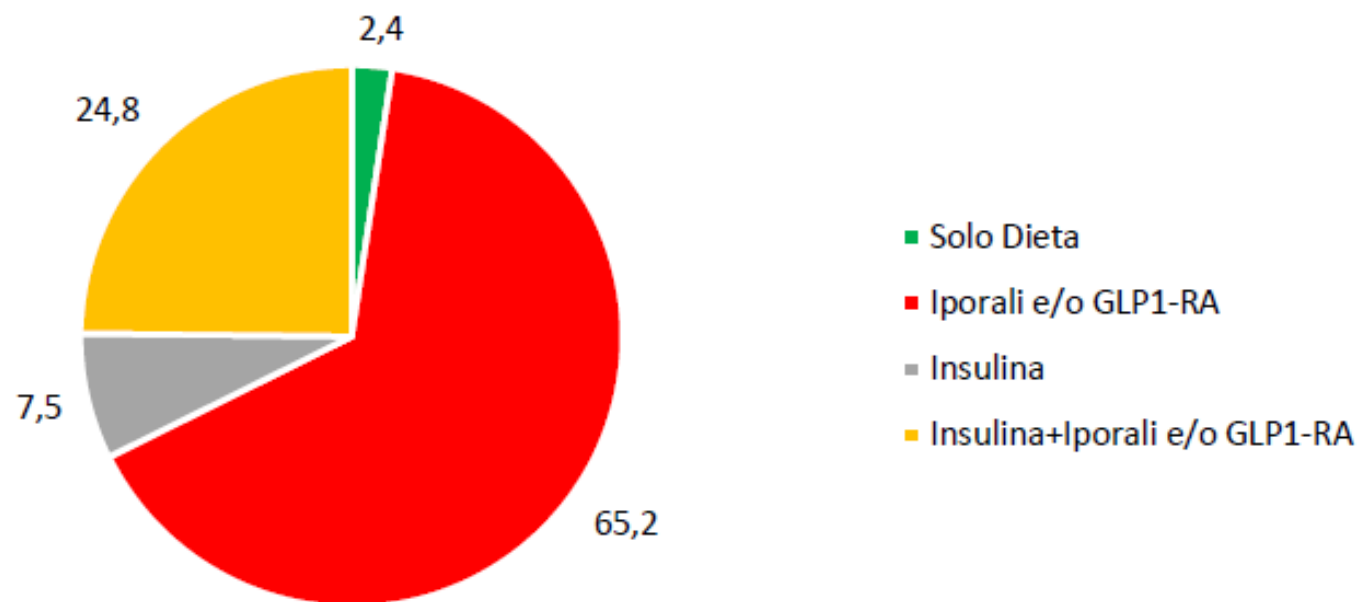
Indicatori di intensità/appropriatezza terapeutica	Annali 2023 Italia	Annali 2023 Veneto
Terapia insulinica		
Insulina basal-bolus	79,6	89,8
CSII	19,8	9,9
Pre-mix	0,6	0,2

**ANNALI REGIONALI
DIABETE TIPO 1
E DIABETE TIPO 2**



Ancora penne...nel DM2

Distribuzione dei pazienti per intensità di trattamento anti-iperglicemizzante (%)



Ancora penne...

- Sostenibilità economica???
- Difficoltà organizzative??
- Mancata accettazione?

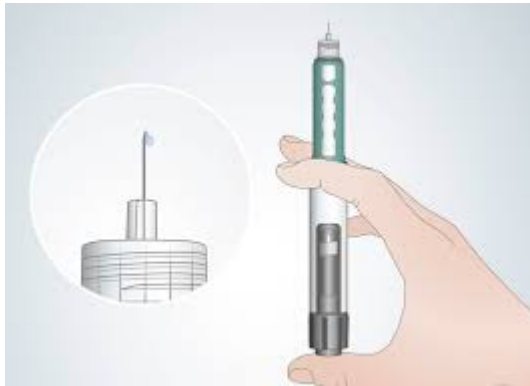
15.20 I sistemi automatizzati per l'infusione di insulina: una tecnologia per tutti:

NO: *Sergio Di Molfetta*

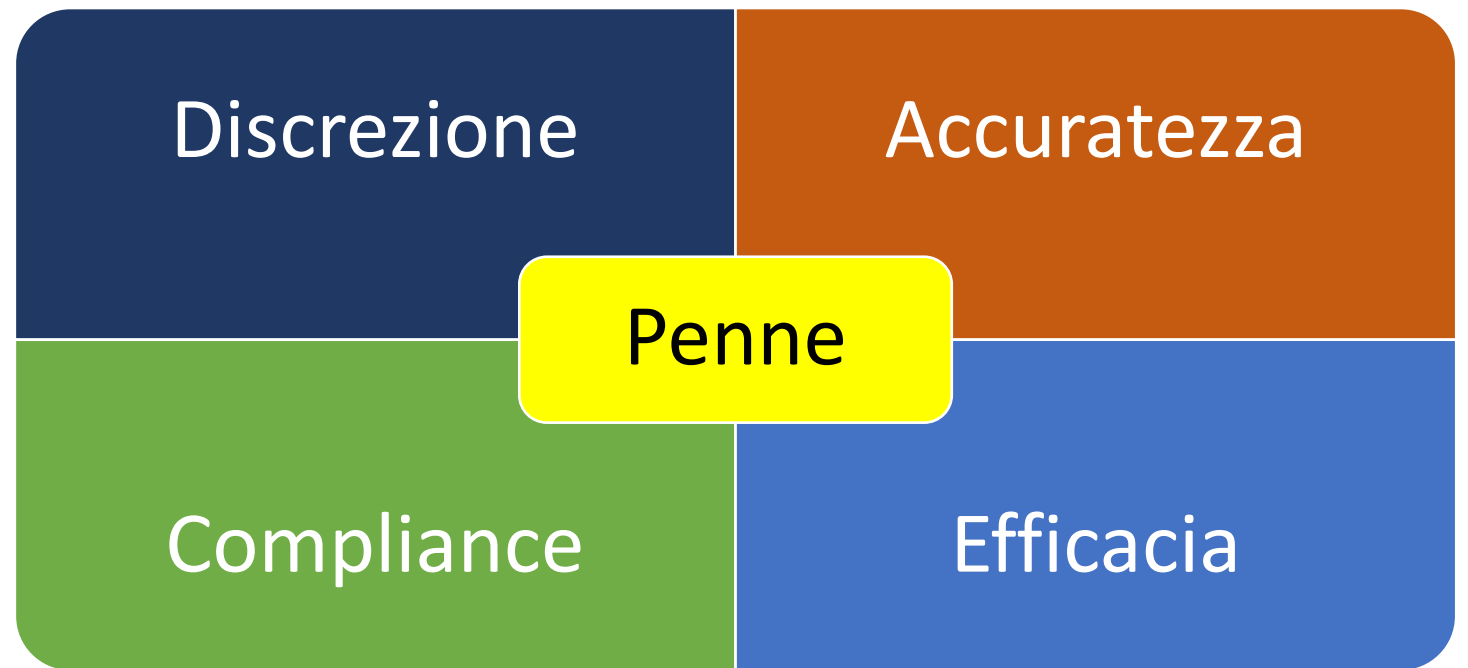
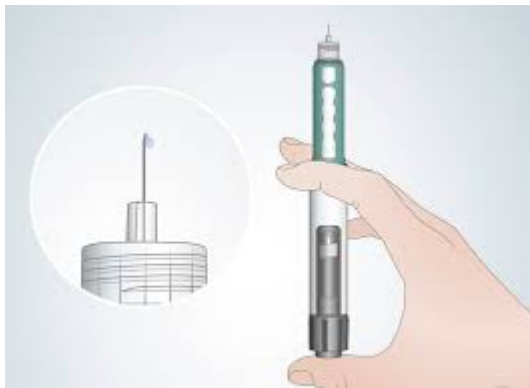
Somministrazione di insulina



Somministrazione di insulina



Penne di insulina



Efficacia delle penne

Table 3 Adherence and persistence measures

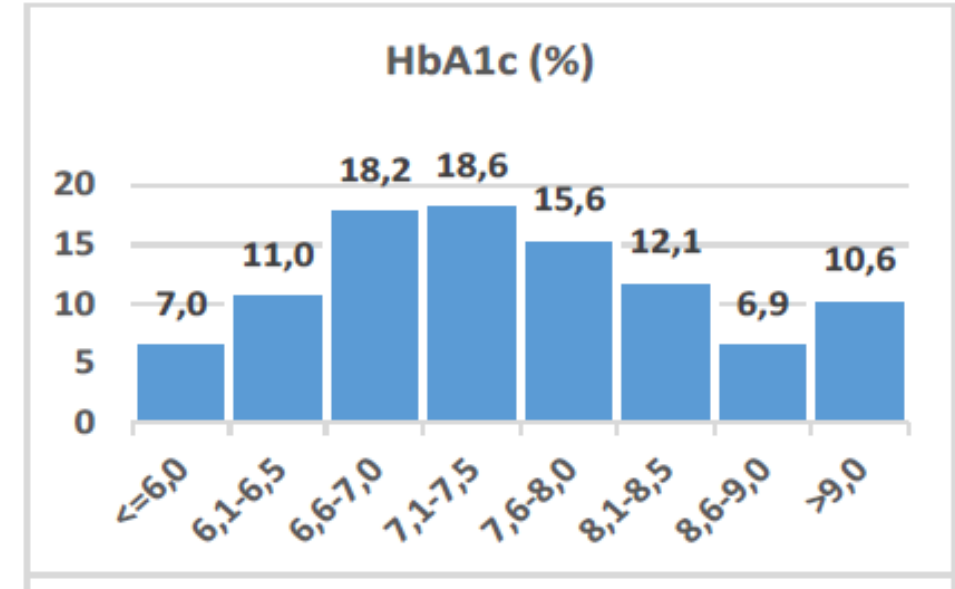
Measure	Pen cohort	Vial cohort	<i>P</i> value
Number of prescription claims prior to discontinuation, mean (SD)	2.93 (2.9)	2.13 (2.5)	<0.0001
Adherence			
Mean adherence (MPR)	0.75 (± 0.3)	0.57 (± 0.3)	<0.0001
Mean adherence (PDC)			
Unadjusted mean (95% CI)	0.71 (0.70, 0.73)	0.53 (0.52, 0.55)	<0.0001
Adjusted mean (95% CI)	0.67 (0.61, 0.72)	0.50 (0.45, 0.56)	<0.0001
Proportion adherent (MPR $\geq 80\%$), <i>n</i> (%)	1123 (57.9)	436 (35.4)	<0.0001
Proportion adherent (PDC $\geq 80\%$), <i>n</i> (%)	959 (49.4)	366 (29.7)	<0.0001
Adjusted odds of adherence (PDC $\geq 80\%$) (95% CI)	2.19 (1.86, 2.59)	Reference	<0.0001
Persistence			
Unadjusted mean persistence, days (SD)	181.0 (128.1)	93.7 (89.8)	<0.0001
Adjusted hazard ratio (95% CI)	0.415 (0.381, 0.452)	Reference	<0.0001
Mean basal insulin fills prior to discontinuation	2.93	2.13	<0.0001

All reported demographic and clinical characteristics were included in the adjusted models

CI confidence interval, *MPR* medication possession ratio, *PDC* proportion of days covered, *SD* standard deviation

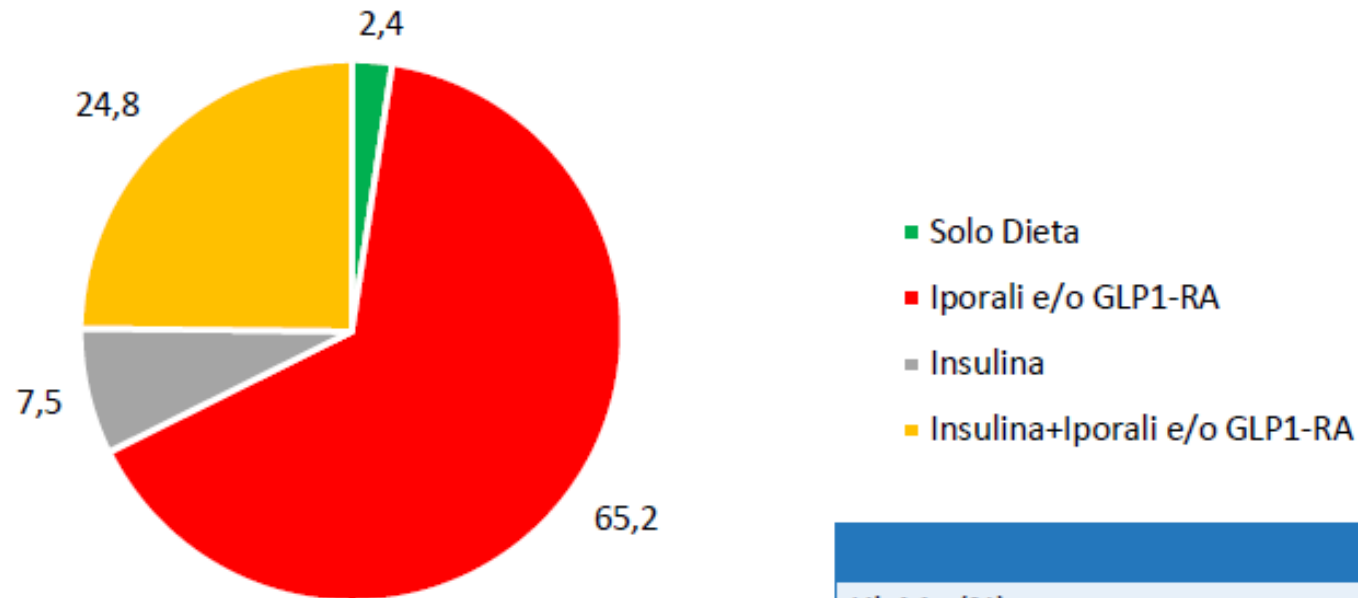
DM1 & MDI

	Media e deviazione standard
HbA1c (%)	7,6±1,3
HbA1c (%) per gruppo di trattamento:	
Microinfusore	7,1±1,0
Basal-bolus	7,7±1,3
Schemi con insulina premiscelata	7,4±1,1
Insulina + altri anti-iperglicemizzanti	7,8±1,2



DM2 & Insulina

Distribuzione dei pazienti per intensità di trattamento anti-iperglicemizzante (%)



Media e deviazione standard	
HbA1c (%)	7,1±1,2
HbA1c (%) per gruppo di trattamento:	
Solo dieta	6,2±0,6
Iporali / GLP1-RA	6,8±0,9
Insulina + Iporali / GLP1-RA	7,8±1,4
Solo insulina	7,7±1,6

Barriere all'ottimizzazione terapia insulinica

- Omissione boli

Omissione boli & Controllo glicemico

Parameter	Overall (n = 64)			T1D (n = 38)		
	Masked CGM	Unmasked CGM	P	Masked CGM	Unmasked CGM	P
MBD per day	0.74 ± 0.4	0.62 ± 0.3	0.008	0.70 ± 0.4	0.64 ± 0.3	0.237
MBD per month	22.1 ± 11.3	18.6 ± 9.3	0.008	20.9 ± 11.0	19.11 ± 9.3	0.237
Correlations			—			—
MBD/day with TIR	−0.241 (0.055)	−0.188 (0.138)	—	−0.387 (0.016)	−0.144 (0.389)	—
MBD/day with TAR	0.229 (0.069)	0.150 (0.238)	—	0.392 (0.015)	0.103 (0.539)	—
MBD/day with TBR	−0.030 (0.811)	0.127 (0.317)	—	−0.188 (0.259)	0.070 (0.674)	—
MBD/day with HbA1c	0.297 (0.017)	0.175 (0.166)	—	0.317 (0.053)	0.122 (0.467)	—

Edwards S, He X, Wang W, Poon JL, Meadows E, Price D, Johnson J, Wolpert H, Polonsky W. Use of Connected Pen as a Diagnostic Tool to Evaluate Missed Bolus Dosing Behavior in People with Type 1 and Type 2 Diabetes. *Diabetes Technol Ther*. 2022 Jan;24(1):61-66. doi: 10.1089/dia.2021.0239. Epub 2021 Nov 1. PMID: 34524010; PMCID: PMC8783630.

	Excellent HbA _{1c} <6.5% (n = 627) ^a	Fair/poor HbA _{1c} ≥8.5% (n = 1,267) ^a	P value
Number of boluses on a typical day			0.006
≤2	50 (9)	111 (10)	
3–4	316 (54)	725 (63)	
≥5	217 (37)	308 (27)	
Bolus given for daytime snacks			0.0003*
Never/ rarely	165 (29)	415 (35)	
Sometimes/most of the time	287 (51)	619 (52)	
Always	108 (19)	148 (13)	
Timing of mealtime insulin bolus			<0.0001
Not given regularly	10 (2)	68 (6)	
Before meal	420 (69)	648 (54)	
During or after meal	87 (14)	328 (27)	
Depends on glucose level prior to meal	89 (15)	167 (14)	
Insulin:carbohydrate ratio used to determine amount of insulin bolus			<0.0001
No/do not know	130 (23)	310 (28)	
Yes, all three meals the same	285 (51)	621 (56)	
Yes, three meals not all the same	141 (25)	176 (16)	
Frequency of missing insulin dose			<0.0001*
Never	426 (70)	390 (32)	
<1 time/week	141 (23)	274 (23)	
1–2 times/week	31 (5)	286 (24)	
≥3 times/week	7 (1)	261 (22)	

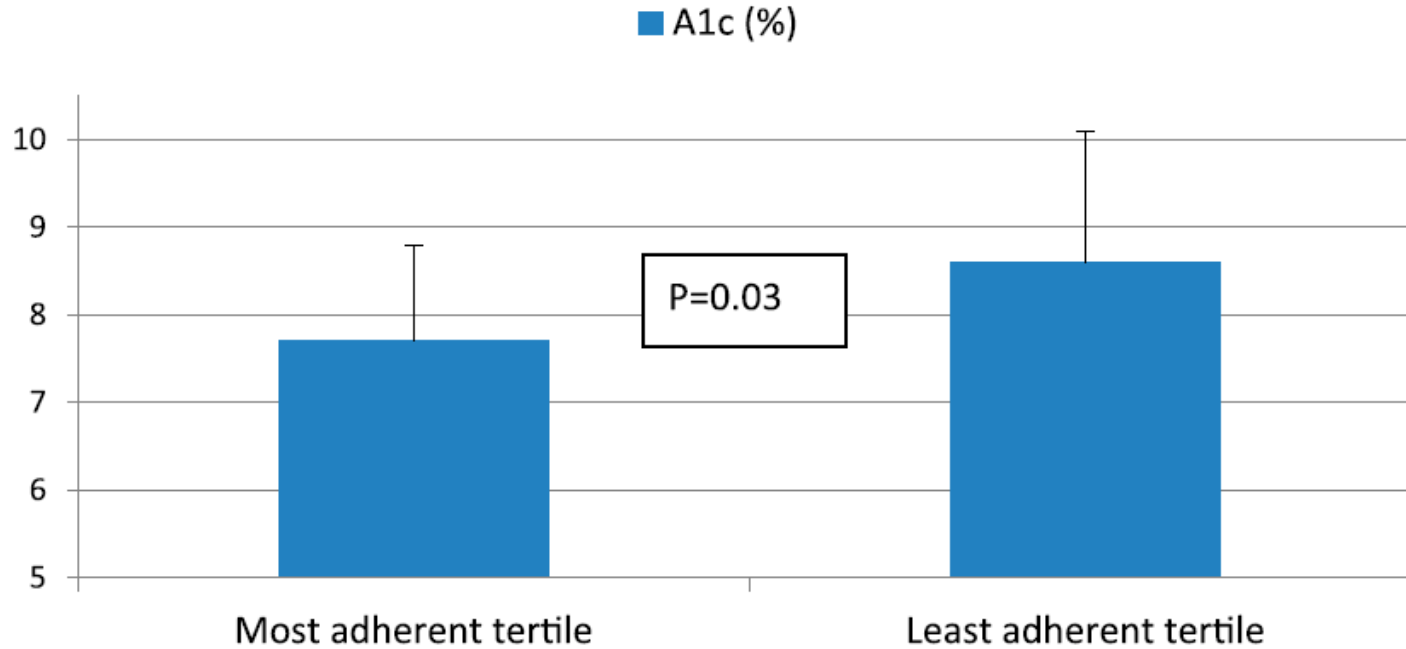
Simmons JH, Chen V, Miller KM, McGill JB, Bergenstal RM, Goland RS, Harlan DM, Largay JF, Massaro EM, Beck RW; T1D Exchange Clinic Network. Differences in the management of type 1 diabetes among adults under excellent control compared with those under poor control in the T1D Exchange Clinic Registry. *Diabetes Care*. 2013 Nov;36(11):3573-7. doi: 10.2337/dc12-2643. Epub 2013 Sep 11. PMID: 24026543; PMCID: PMC3816911.

Barriere all'ottimizzazione terapia insulinica

- Omissione boli
- Errori boli

Errori Boli & Controllo glicemico

Glycemic Control by Tertile of Adherence



Mancanza aderenza

- 24% boli

- 36% basale

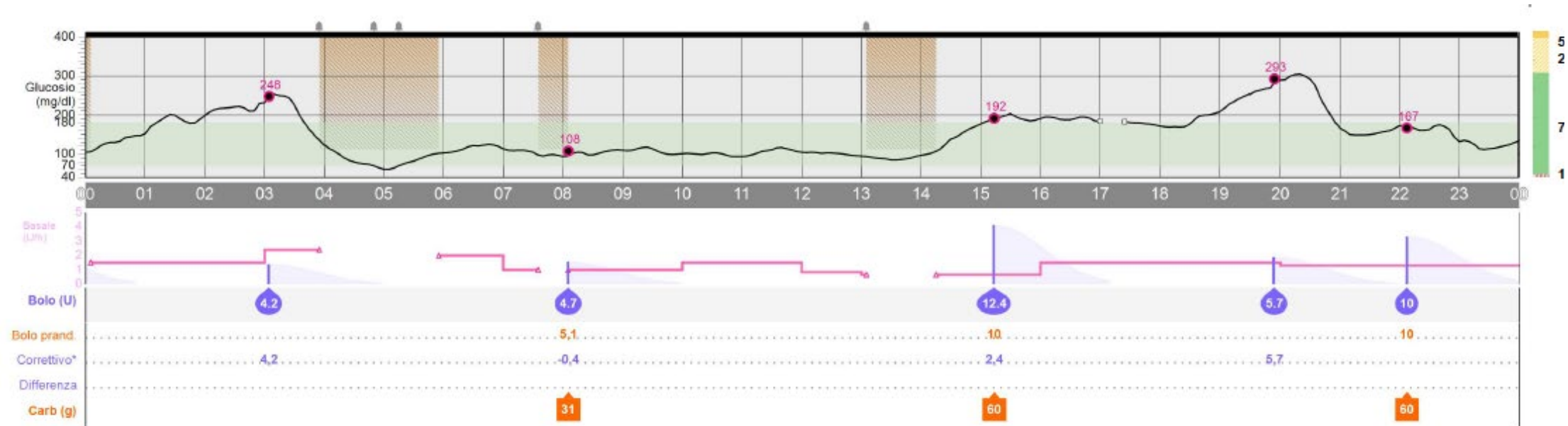
Munshi MN, Slyne C, Greenberg JM, Greaves T, Lee A, Carl S, Atakov-Castillo A, Toschi E. Nonadherence to Insulin Therapy Detected by Bluetooth-Enabled Pen Cap Is Associated With Poor Glycemic Control. *Diabetes Care*. 2019 Jun;42(6):1129-1131. doi: 10.2337/dc18-1631. Epub 2019 Mar 12. PMID: 30862650.

Figure 1—Glycemic control by tertiles of adherence.

Barriere all'ottimizzazione terapia insulinica

- Omissione boli
- Errori boli
- Mancanza dati

Microinfusore...

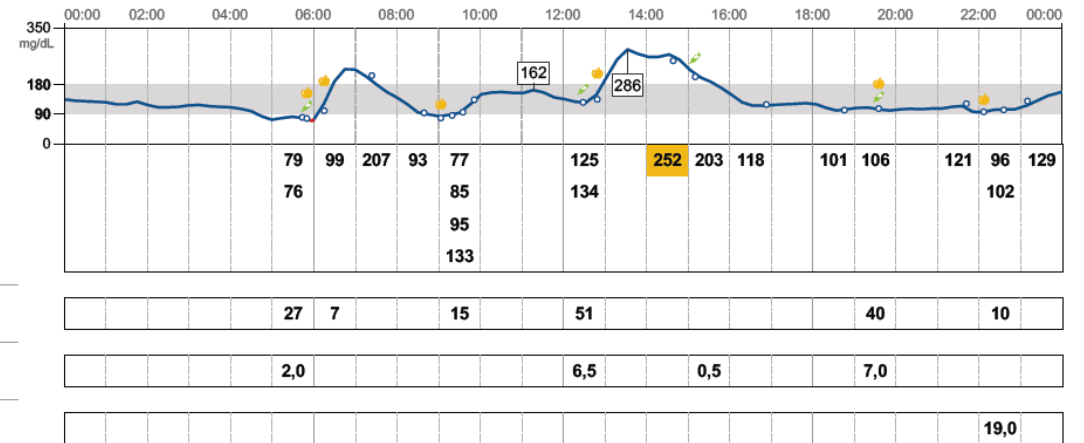


... vs Multiniettiva

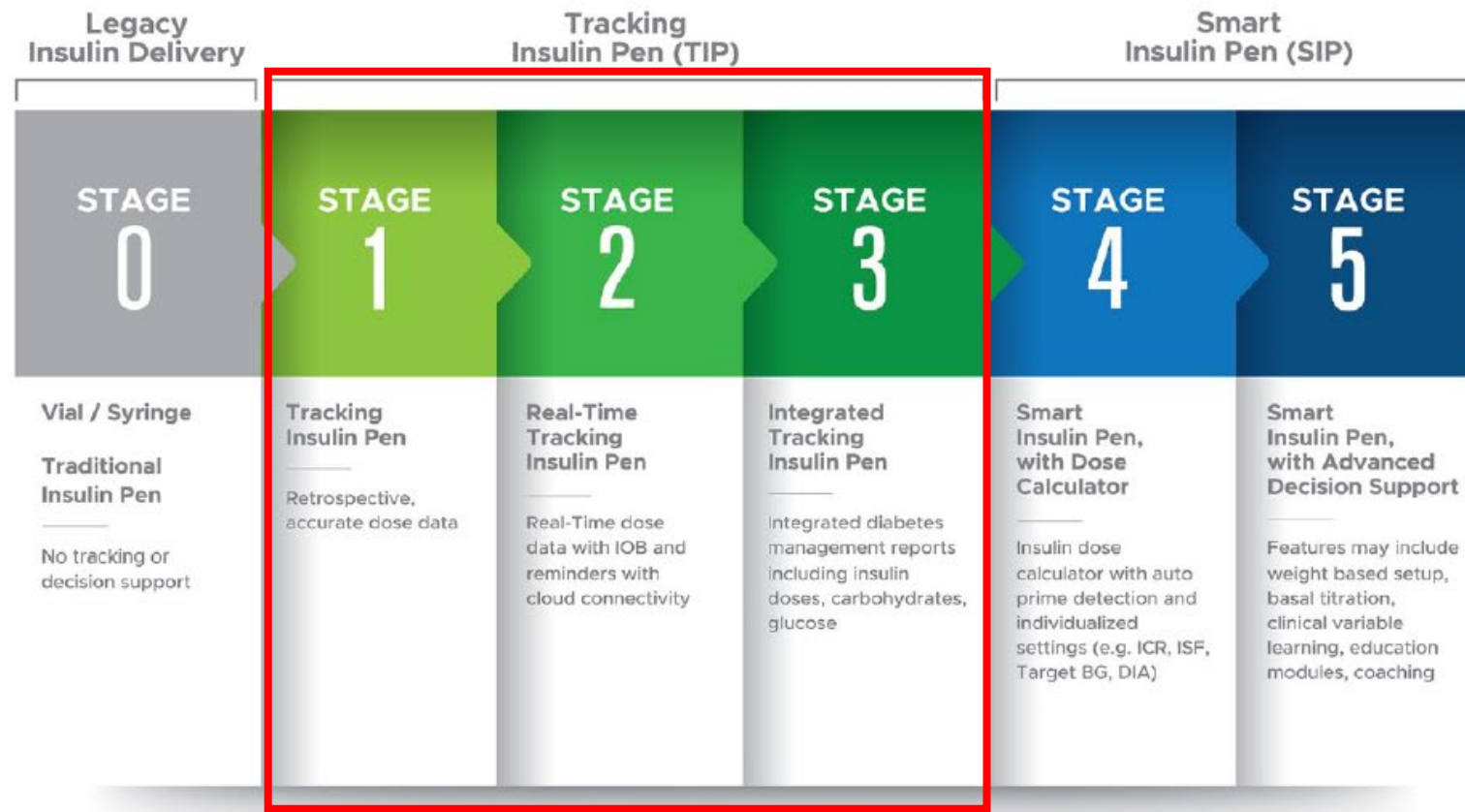
 Glucosio
mg/dL

 **Insulina ad azione rapida**
unità

 **Insulina ad azione lenta**
unità



Device per somministrazione insulina



Dose remind

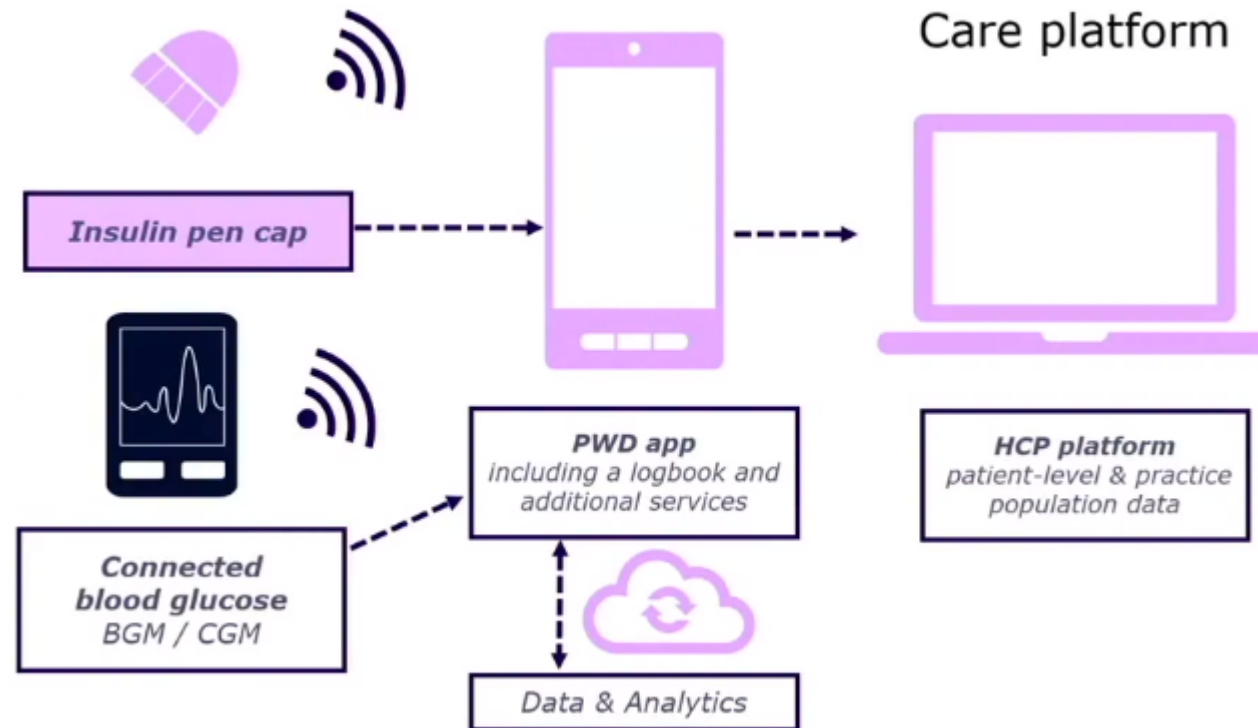
- Registrazione dose e tempo da ultima somministrazione



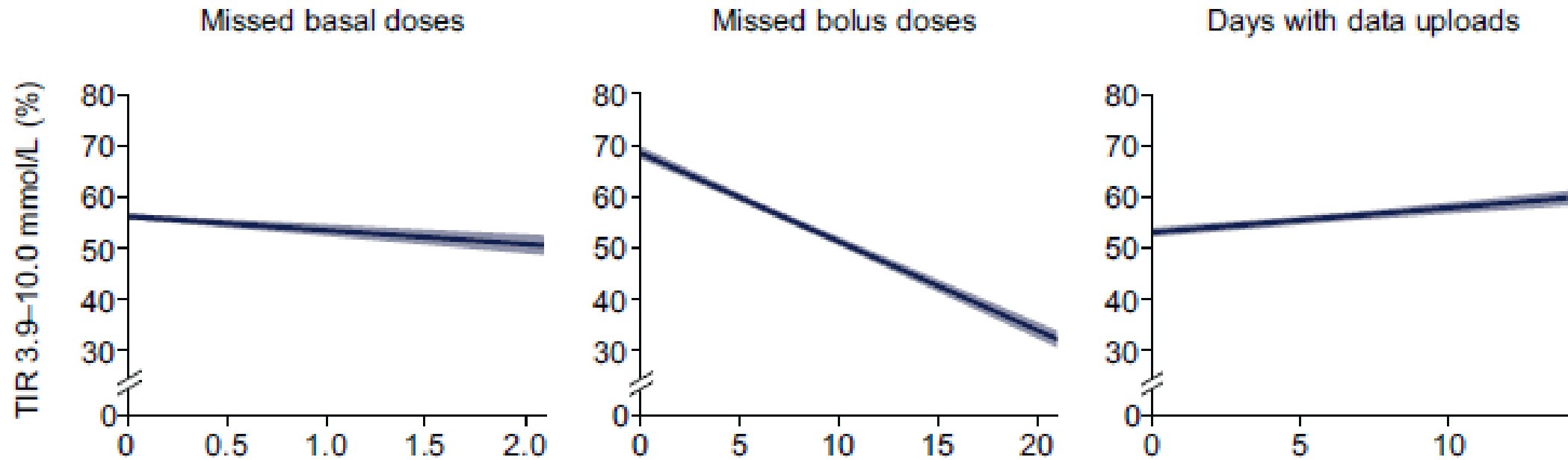
Penne connesse

- Penne in grado di raccogliere dati relativi a dosaggi insulinici
- Comunicazione dato all'app e condivisione del dato
- Possibile integrazione con dato glicemico
- Possibile creazione di diario

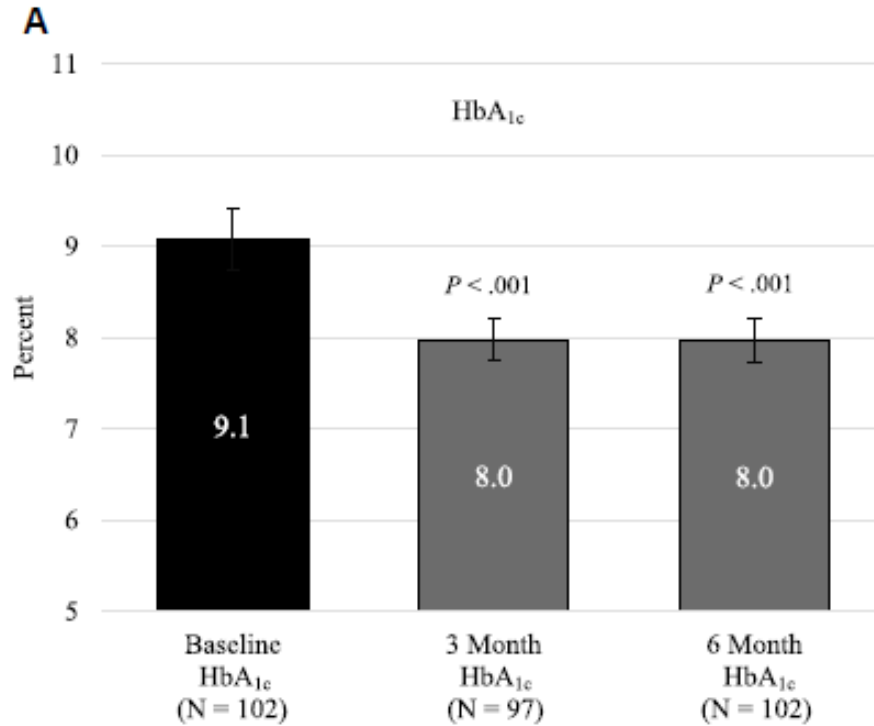
Insulin pen cap



Efficacia

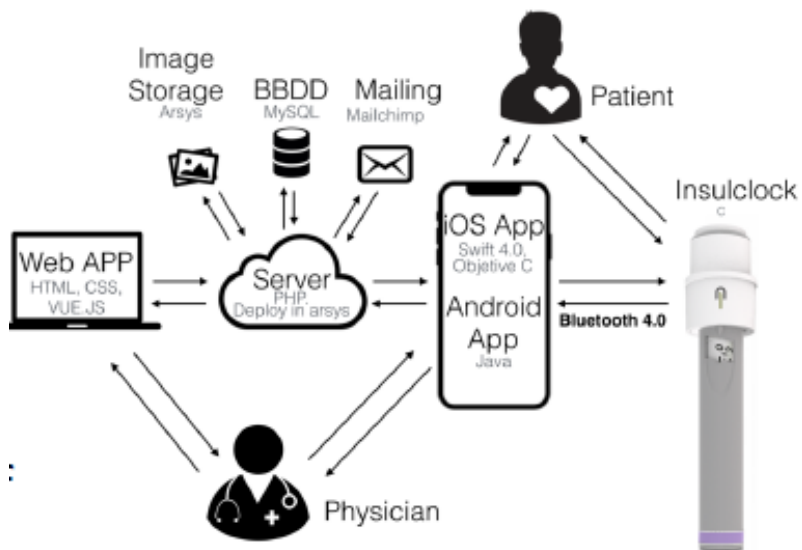


DM2



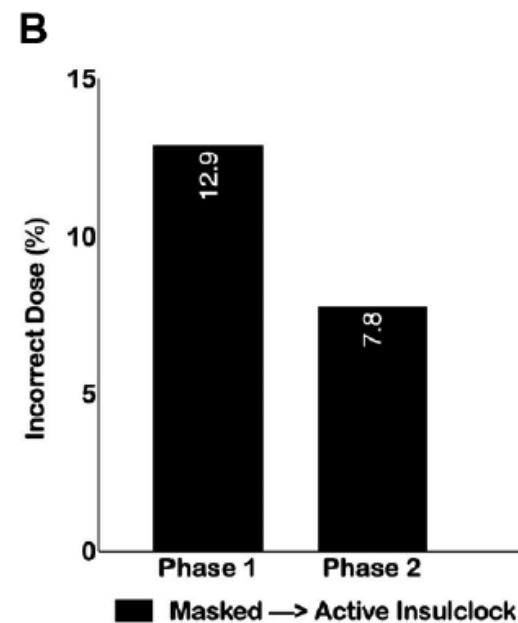
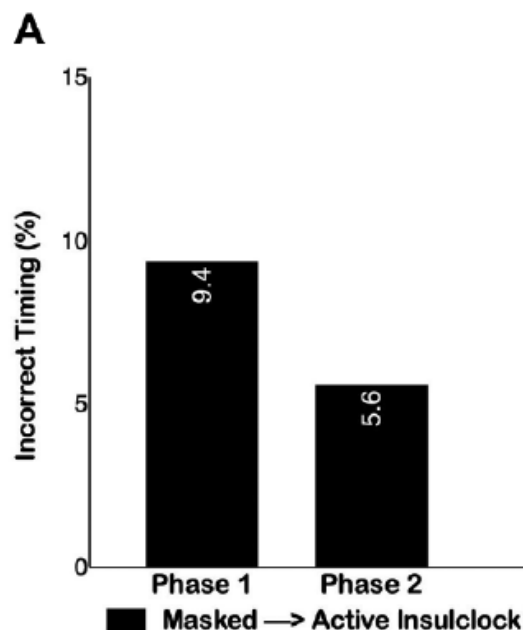
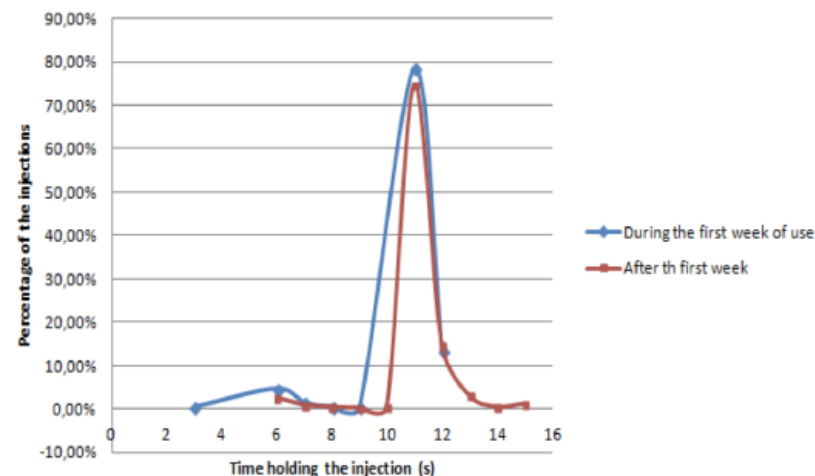
Parameter	Baseline	3 Month	3 month change from baseline (95% CI) [<i>P</i> value]	6 Month	6 month change from baseline (95% CI) [<i>P</i> value]
Diabetes Distress Scale (DDS)	N = 91	N = 94	N = 99	N = 95	N = 99
Total	2.4 ± 0.9	1.6 ± 0.6	−0.7 (−0.9, −0.5) [<i><.001</i>]	1.7 ± 0.6	−0.7 (−0.9, −0.5) [<i><.001</i>]
Powerlessness	2.9 ± 1.3	2.0 ± 1.0	−0.9 (−1.1, −0.6) [<i><.001</i>]	2.0 ± 0.9	−0.9 (−1.1, −0.6) [<i><.001</i>]
Management Distress	3.0 ± 1.2	1.7 ± 0.8	−1.3 (−1.5, −1.0) [<i><.001</i>]	1.7 ± 0.8	−1.3 (−1.5, −1.0) [<i><.001</i>]
Hypoglycemia Distress	2.2 ± 1.3	1.6 ± 0.8	−0.6 (−0.8, −0.3) [<i><.001</i>]	1.7 ± 0.9	−0.5 (−0.8, −0.3) [<i><.001</i>]
Negative Social Perceptions	1.6 ± 0.9	1.4 ± 0.7	−0.2 (−0.4, 0.0) [.02]	1.4 ± 0.7	−0.2 (−0.4, −0.1) [0.01]
Eating Distress	3.0 ± 1.2	2.0 ± 1.0	−1.0 (−1.2, −0.8) [<i><.001</i>]	2.0 ± 1.0	−1.0 (−1.2, −0.7) [<i><.001</i>]
Physician Distress	1.8 ± 1.2	1.2 ± 0.5	−0.6 (−0.8, −0.4) [<i><.001</i>]	1.3 ± 0.7	−0.5 (−0.8, −0.3) [<i><.001</i>]
Friend/Family Distress	1.9 ± 1.2	1.4 ± 0.7	−0.4 (−0.7, −0.2) [<i><.001</i>]	1.6 ± 0.8	−0.3 (−0.6, −0.1) [.003]
Hypoglycemia Confidence Scale (HCS)	N = 91	N = 94	N = 99	N = 95	N = 99
Total	2.8 ± 0.7	3.2 ± 0.6	0.4 (0.2, 0.5) [<i><.001</i>]	3.1 ± 0.7	0.4 (0.2, 0.5) [<i><.001</i>]
System Usability Scale (SUS)	—	N = 93	—	N = 95	—
Total	—	78.1 ± 18.5	—	80.7 ± 17.3	—

Data reflect mean ± SD; change from baseline reflect mean (95% CI). The median timing of baseline questionnaire completion was 6 days prior to System start. *P* values were estimated using a longitudinal linear model and have been adjusted for multiplicity using the two-step adaptive Benjamini-Hochberg procedure.



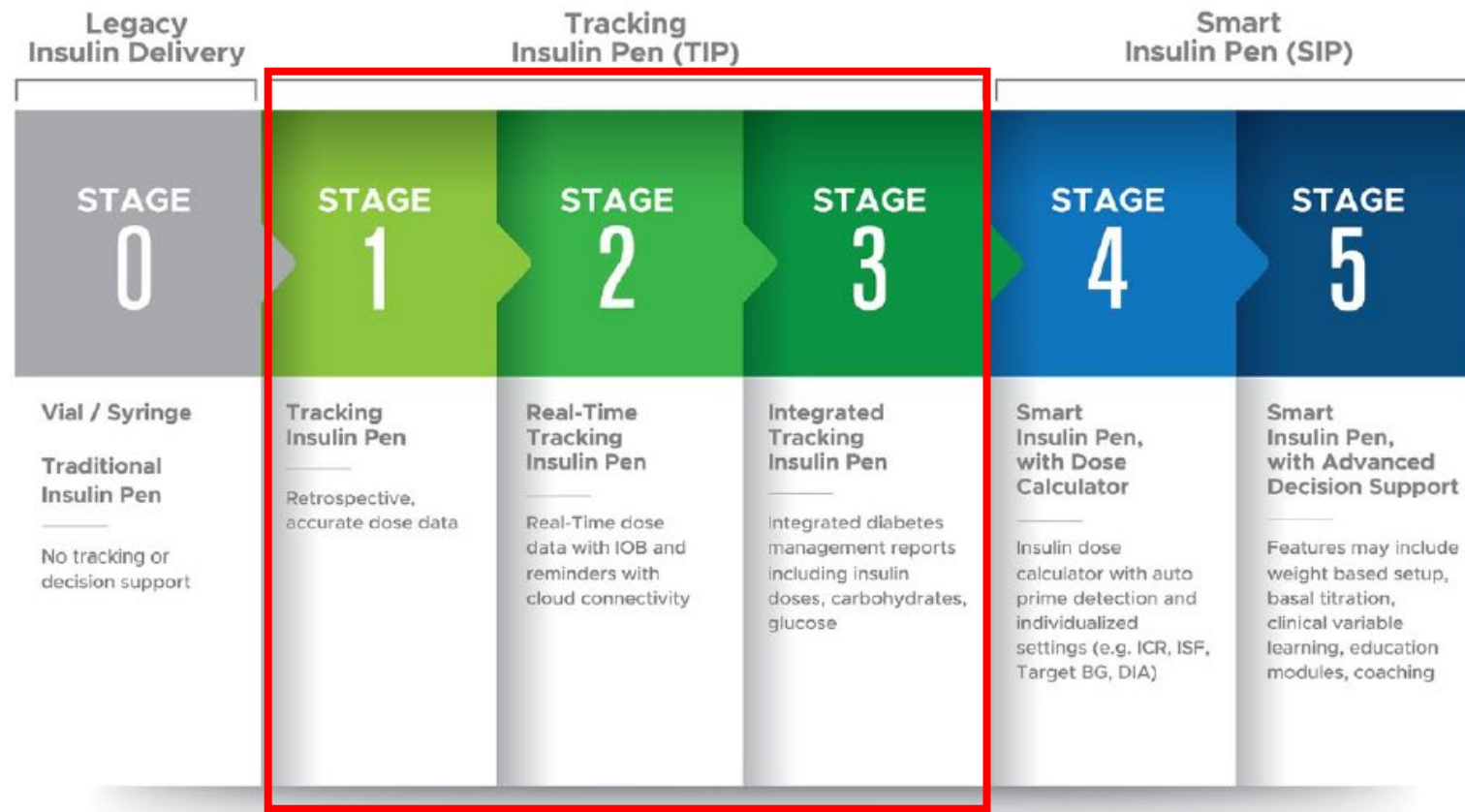
Gomez-Peralta F, Abreu C, Gomez-Rodriguez S, Ruiz L. Insulclock: A Novel Insulin Delivery Optimization and Tracking System. *Diabetes Technol Ther.* 2019 Apr;21(4):209-214. doi: 10.1089/dia.2018.0361. Epub 2019 Mar 21. PMID: 30896261.

Figure 1. Duration of the injection before and after setting the *Insulclock*[®] alarm.

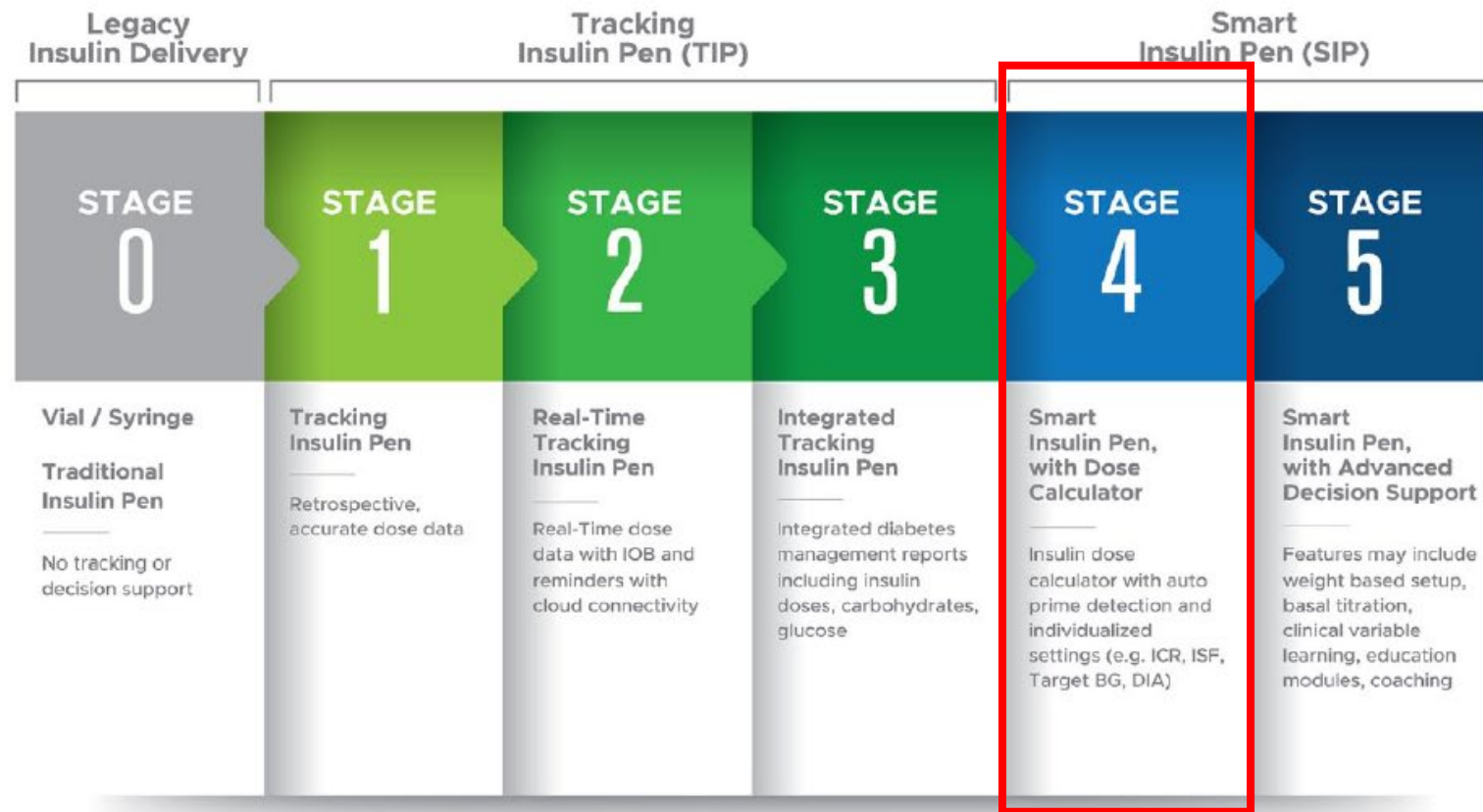


Galindo RJ, Ramos C, Cardona S, Vellanki P, Davis GM, Oladejo O, Albury B, Dhruv N, Peng L, Umpierrez GE. Efficacy of a Smart Insulin Pen Cap for the Management of Patients with Uncontrolled Type 2 Diabetes: A Randomized Cross-Over Trial. *J Diabetes Sci Technol.* 2021 Jul 22:19322968211033837. doi: 10.1177/19322968211033837. Epub ahead of print. PMID: 34293955.

Device per somministrazione insulina



Device per somministrazione insulina



Smart Pen Ideale

Box 1. Characteristics of an Ideal Smart Multiple Daily Injection (Smart MDI) System.

Glucose sensor: A Smart MDI system includes a sensor to monitor interstitial glucose levels (CGM) and provides real-time data to inform dynamic adjustments in insulin dosage.

Connected insulin injection device: A Smart MDI system includes a smart/connected insulin pen, cap, or attachment that records and transmits data on insulin administration and storage.

Connectivity: A Smart MDI system connects the sensor and insulin pen to a companion app and data platform to enable seamless communication between the system, patient, caregivers, and HCPs.

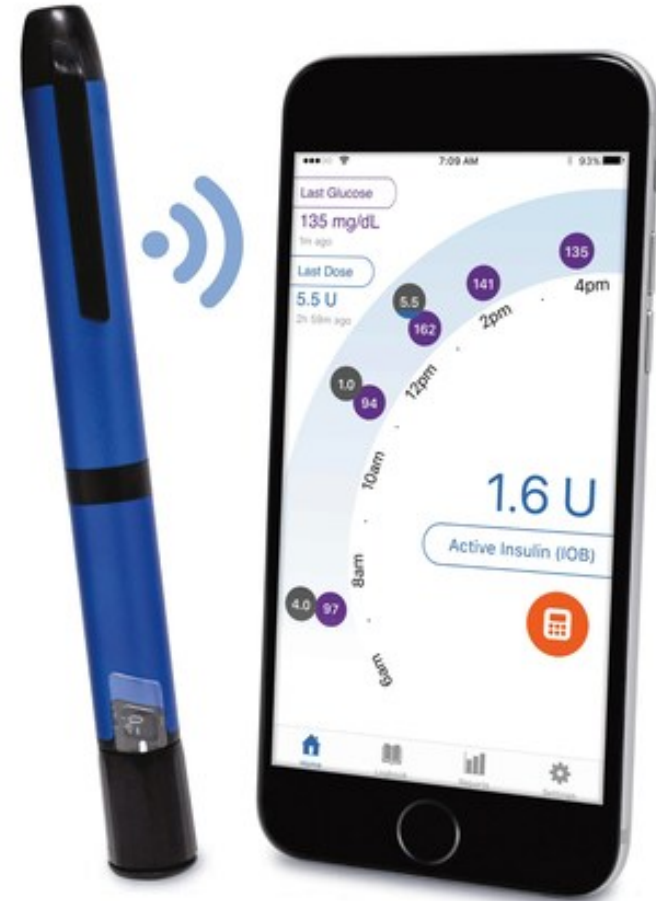
Data analysis: AI algorithms analyze the sensor data in the context of current glucose levels, the expected carbohydrate intake, insulin dose history, insulin sensitivity, and provide personalized insulin dosage suggestions and dose adjustments in real-time in response to preset parameters. People with diabetes and HCPs customize settings to match individual preferences and treatment plans, setting glucose target ranges and insulin delivery times, and adapt the settings in response to changing situations, such as acute illness.

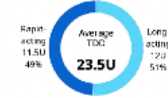
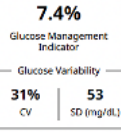
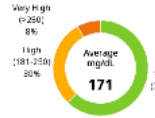
System interfaces:

- **People with diabetes** receive a graphic representation of glycemic parameters over time, reminders for insulin doses, alerts for abnormal glucose levels, and suggestions for lifestyle modifications.
 - **HCPs** have remote access to patient data through cloud-based platforms to monitor insulin usage, adherence, and overall diabetes management.
 - **Optional components.** In addition to CGM, a Smart MDI system could interface with wearable devices such as activity trackers, smart watches, and other health monitoring devices to provide useful data on activity levels and sleep patterns.
-

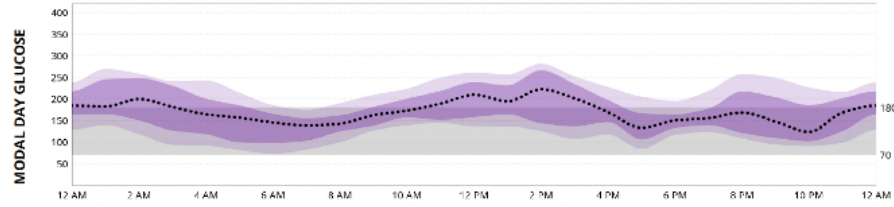
Smart Insulin Pen

- Registro boli somministrati
- Integrazione con CGM
- Calcolatore di bolo
- Allarmi dimenticanza bolo
- Suggerimenti correzione





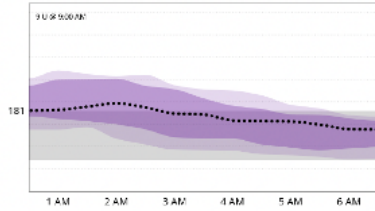
3.3 Avg. Rapid-acting Doses Per Day



Target BG	127	127	127	127	127	mg/dL
ICR	8	7	7	8	8	g/U
ISF	60	60	60	60	60	mg/dLU

Max Dose: 9 U Duration of Insulin Action: 4h

LONG ACTING ASSESSMENT

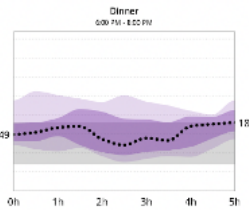
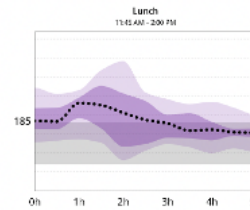
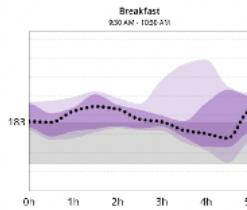


Days Included in Assessment	13 of last 14 days
Average Daily Dose Taken	12 U
# Days with Glucose < 70 mg/dL	1 ▼
Median Bedtime to Fasting (Change)	181 to 138 (-43 mg/dL) ▼

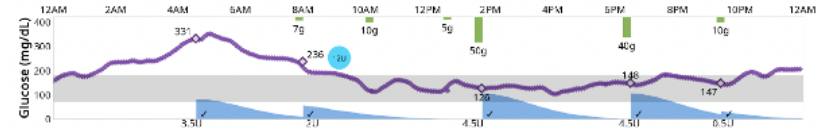
Note: Days with overnight boluses are excluded

- ▲ Rising fasting glucose of 30 mg/dL or more may indicate long-acting dose should be increased.
- ▼ Falling fasting glucose of 30 mg/dL or more or days with glucose < 70 mg/dL may indicate long-acting dose should be decreased.

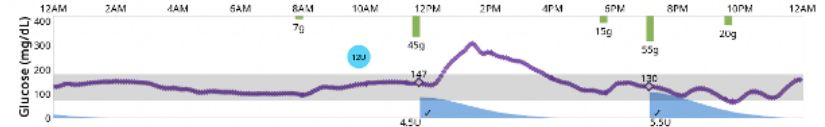
MEAL ASSESSMENT


Tuesday
April 18, 2023

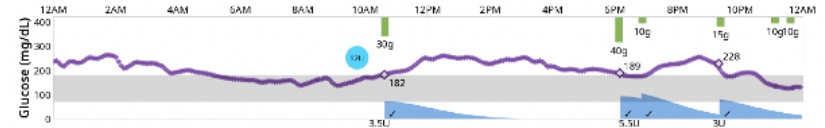
Notes:


Monday
April 17, 2023

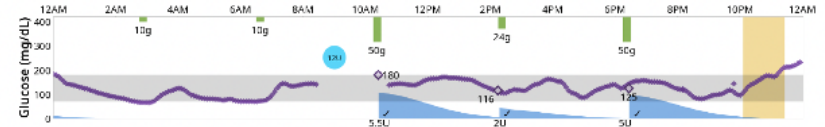
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Sunday
April 16, 2023

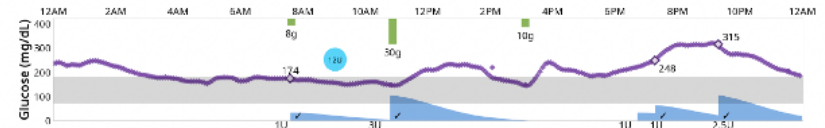
Notes:


Saturday
April 15, 2023

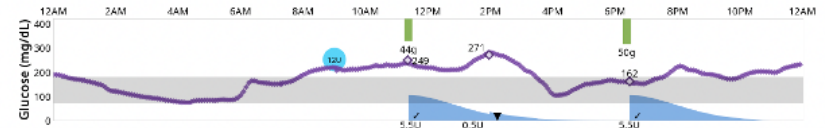
Notes:


Friday
April 14, 2023

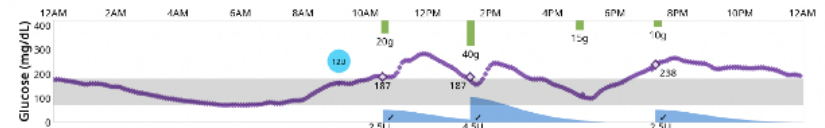
Notes:

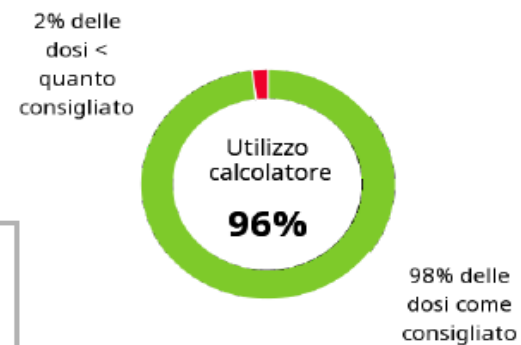
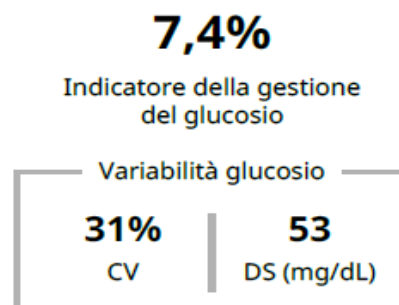
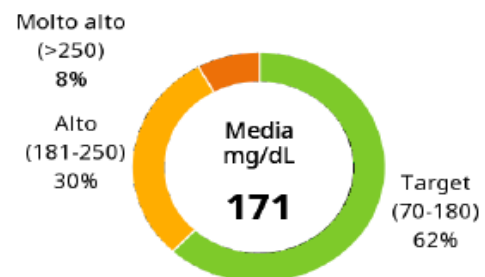

Thursday
April 13, 2023

Notes:


Wednesday
April 12, 2023

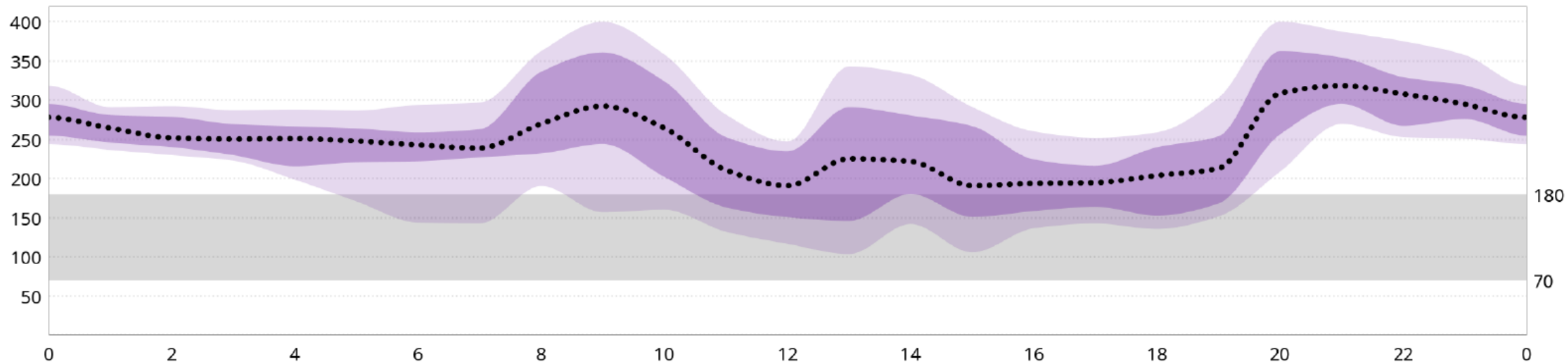
Notes:


Legend:
◆ glucose value ◇ glucose in calculation ■ bolus/dose ■ active insulin ▲ calculation override ✓ dose as advised (M-DOSE) ● long acting dose ■ mixed dose



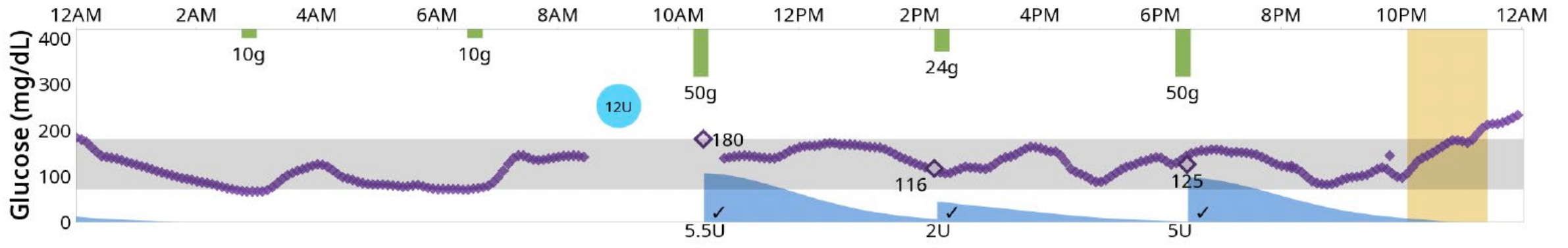
Media numero dosi analogo rapido giornaliera: 3,3

DISTRIB. GIORNALIERA GLUCOSIO

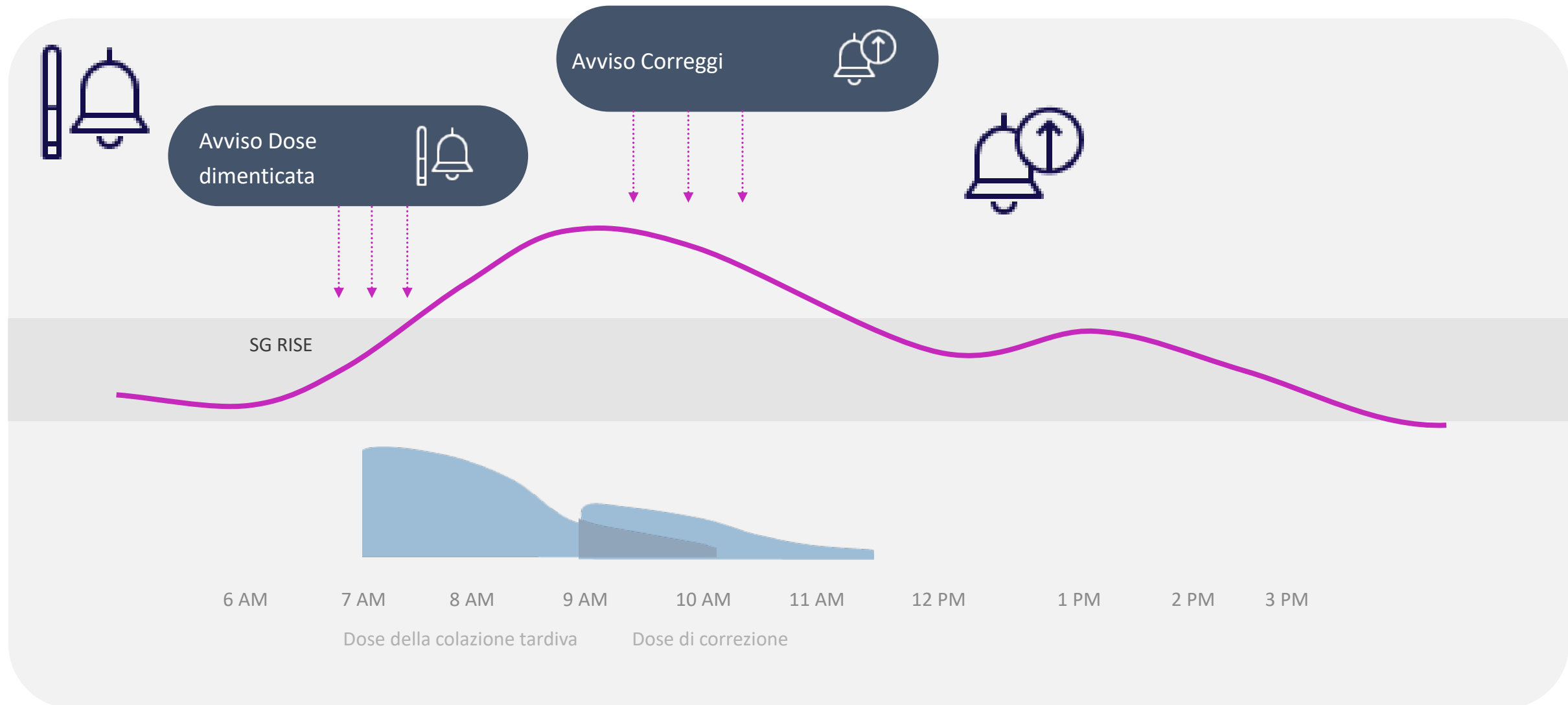


Target glicemico	130	130	130	130	mg/dL
Rapp. carb./ins.	14	12	18	14	g/U
Sensib. insulina	70	70	70	70	mg/dL/U

Dose massima: 10 U Durata azione insulina: 3 h



Avvisi



Real World

InPen alert settings

Missed dose alerts enabled^a

Daytime (06:00–00:00) 1617 (87.3)

Nighttime (00:00–06:00) 710 (38.3)

Correct high glucose alerts enabled^a

Daytime (06:00–0:00) 1732 (93.5)

Nighttime (00:00–06:00) 857 (46.3)

InPen alert response interactions

Daily number of missed dose alerts (MDA) 0.93 ± 0.63

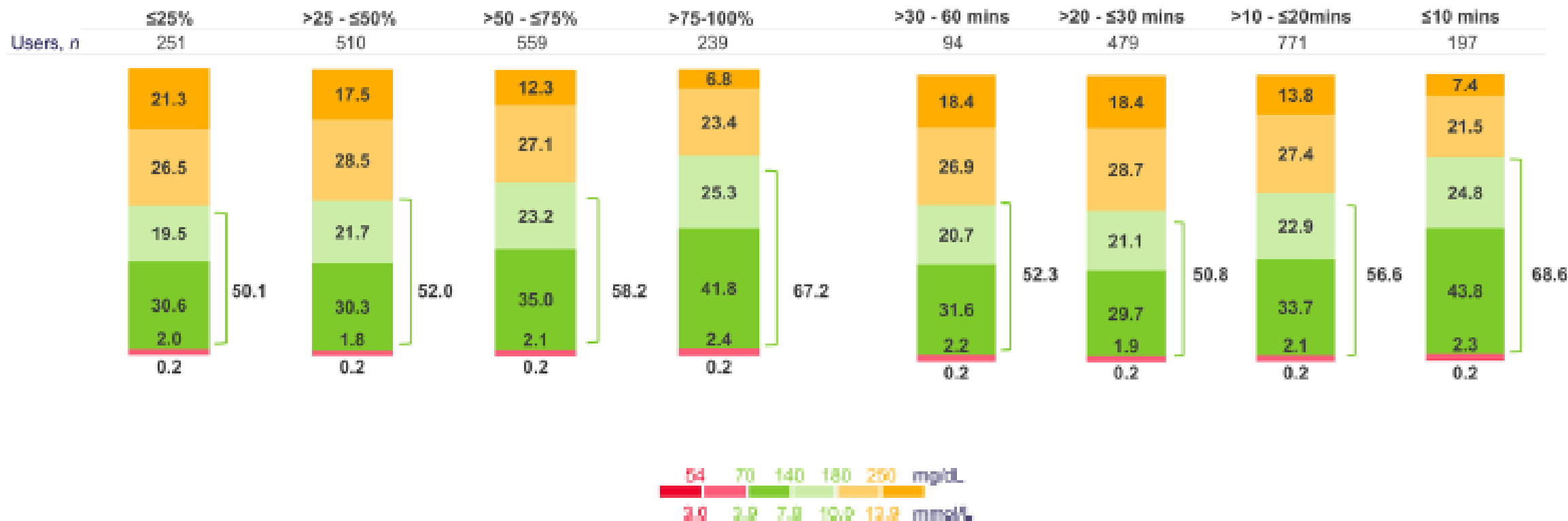
Daily number of correct high glucose alerts (CHGA) 3.12 ± 2.35

Real World

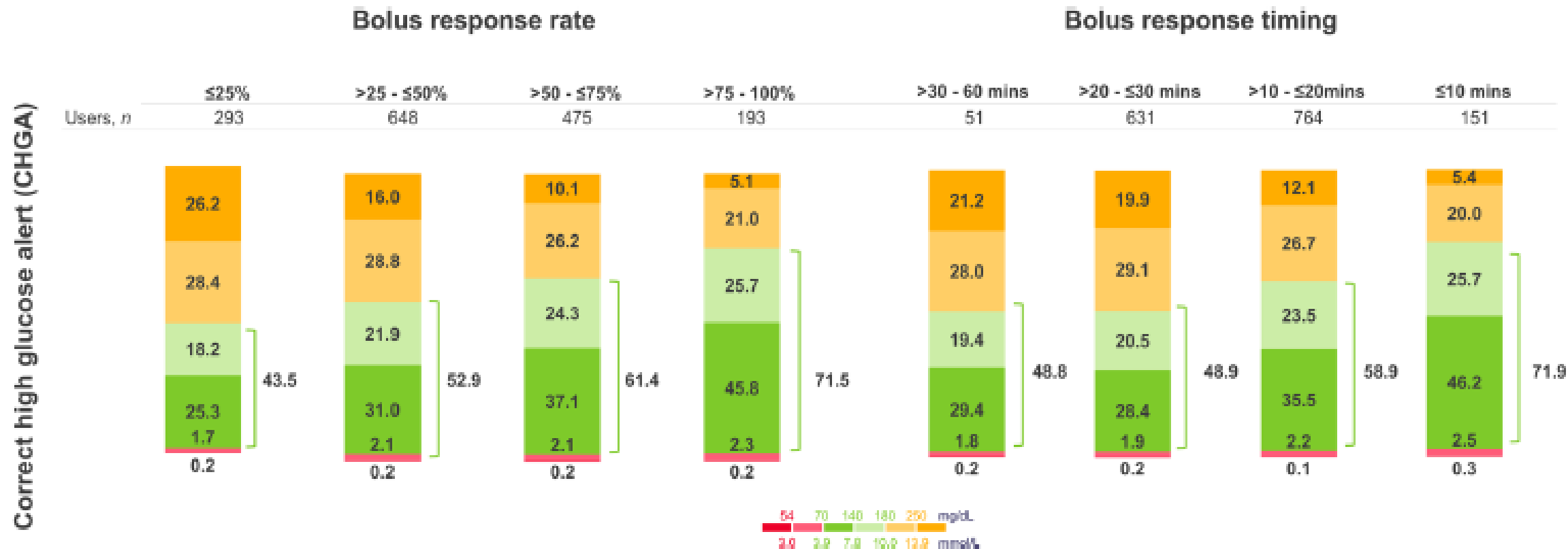
Bolus response rate

Bolus response timing

Missed dose alert (MDA)



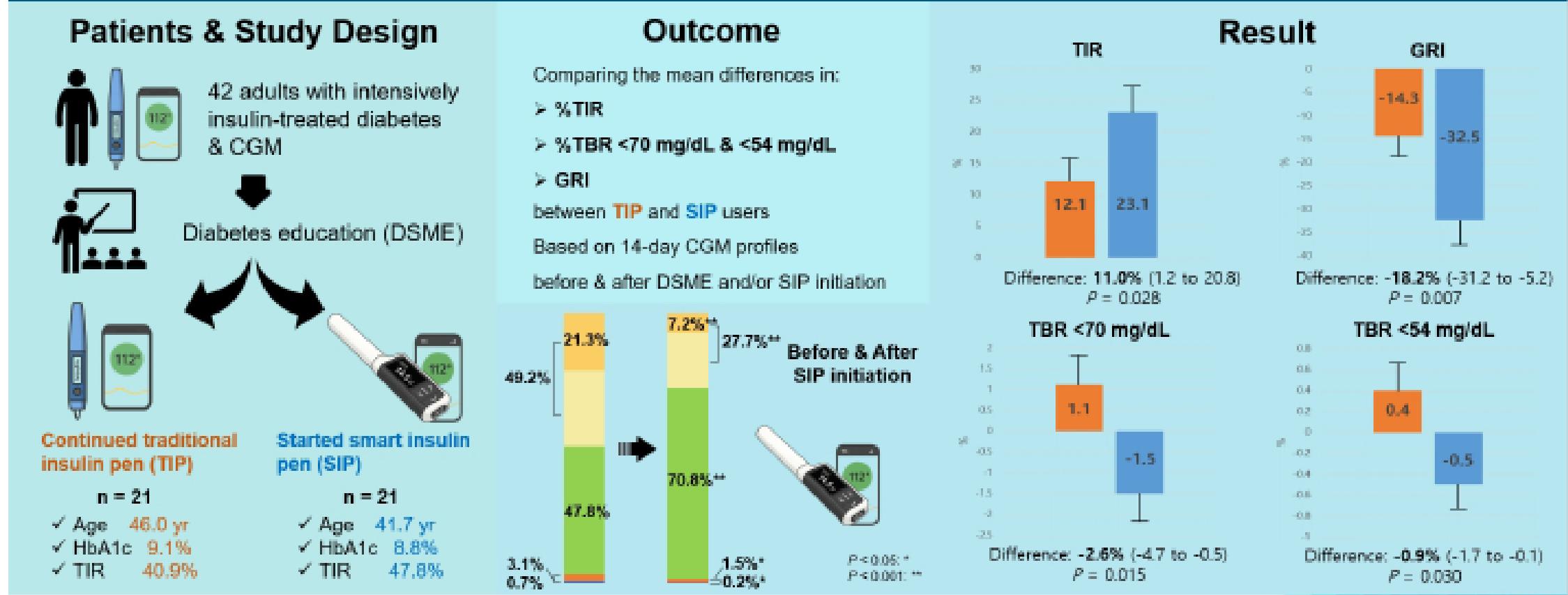
Real World



Laurenzi A, Edd SN, Adolfsson P, Di Piazza F, Voelker B, Im G, van den Heuvel T, Cohen O. Insights into the effective use of the Smart MDI system: Data from the first 1852 type 1 diabetes users. Diabet Med. 2025 Oct 13:e70161. doi: 10.1111/dme.70161. Epub ahead of print. PMID: 41084119.

Efficacia

Effectiveness of the Stage 4 Smart Insulin Pen DIA:CONN P8 for Glycemic Control in a Real-World Setting



Penne intelligenti...Vantaggi

- Miglioramento controllo metabolico
- Riduzione ipoglicemie
- Miglioramento soddisfazione terapia
- Efficacia visite (finalmente dati...)

Penne intelligenti...Limiti

- Educazione paziente
- Cooperazione paziente

Real World

InPen alert response interactions	
Daily number of missed dose alerts (MDA)	0.93 ± 0.63
Proportion MDA acknowledged by user (any response ^{b)})	$55.9 \pm 23.9\%$
Proportion MDA responded as <i>Calculate Dose</i>	$27.7 \pm 23.1\%$
Proportion MDA followed by insulin bolus within 1 h	$49.3 \pm 22.8\%$
Mean post-MDA time to bolus	18.2 ± 7.7 min
Daily number of correct high glucose alerts (CHGA)	3.12 ± 2.35
Proportion CHGA acknowledged by user (any response ^{c)})	$60.4 \pm 23.1\%$
Proportion CHGA responded as <i>Calculate Dose</i>	$26.5 \pm 21.8\%$
Proportion CHGA followed by insulin bolus within 1 h	$46.6 \pm 22.4\%$
Mean post-CHGA time to bolus	18.7 ± 6.4 min

Laurenzi A, Edd SN, Adolfsson P, Di Piazza F, Voelker B, Im G, van den Heuvel T, Cohen O. Insights into the effective use of the Smart MDI system: Data from the first 1852 type 1 diabetes users. *Diabet Med*. 2025 Oct 13:e70161. doi: 10.1111/dme.70161. Epub ahead of print. PMID: 41084119.

Penne intelligenti...Limiti

- Educazione paziente
- Cooperazione paziente
- Costo???

Ruolo Penne intelligenti

- Miglioramento controllo in MDI
- Coinvolgimento-responsabilizzazione paziente
- Stimolo CHO counting
- Spinta telemedicina
- Passaggio MDI-AID

Why not?



Why not?

