

CONGRESSO REGIONALE
CONGIUNTO **SID-AMD**
PIEMONTE | VALLE D'AOSTA 2023



SINFONIA 2.0 PER IL DIABETE: *prove d'orchestra*

TORINO | Centro Congressi Unione Industriali Torino
27-28 ottobre 2023

Focus 2 Diabete 3C
S. Bertaina

la Dr.ssa Silvana Bertaina dichiara di NON aver ricevuto negli ultimi due anni compensi o finanziamenti da Aziende Farmaceutiche e/o Diagnostiche

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.)

Prevalence (9%) and causes of type 3c diabetes mellitus

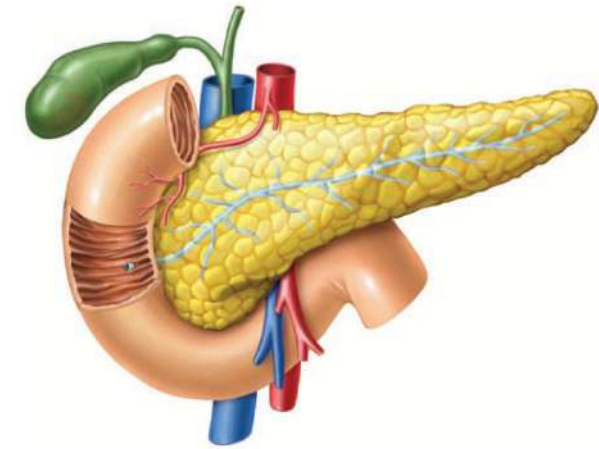
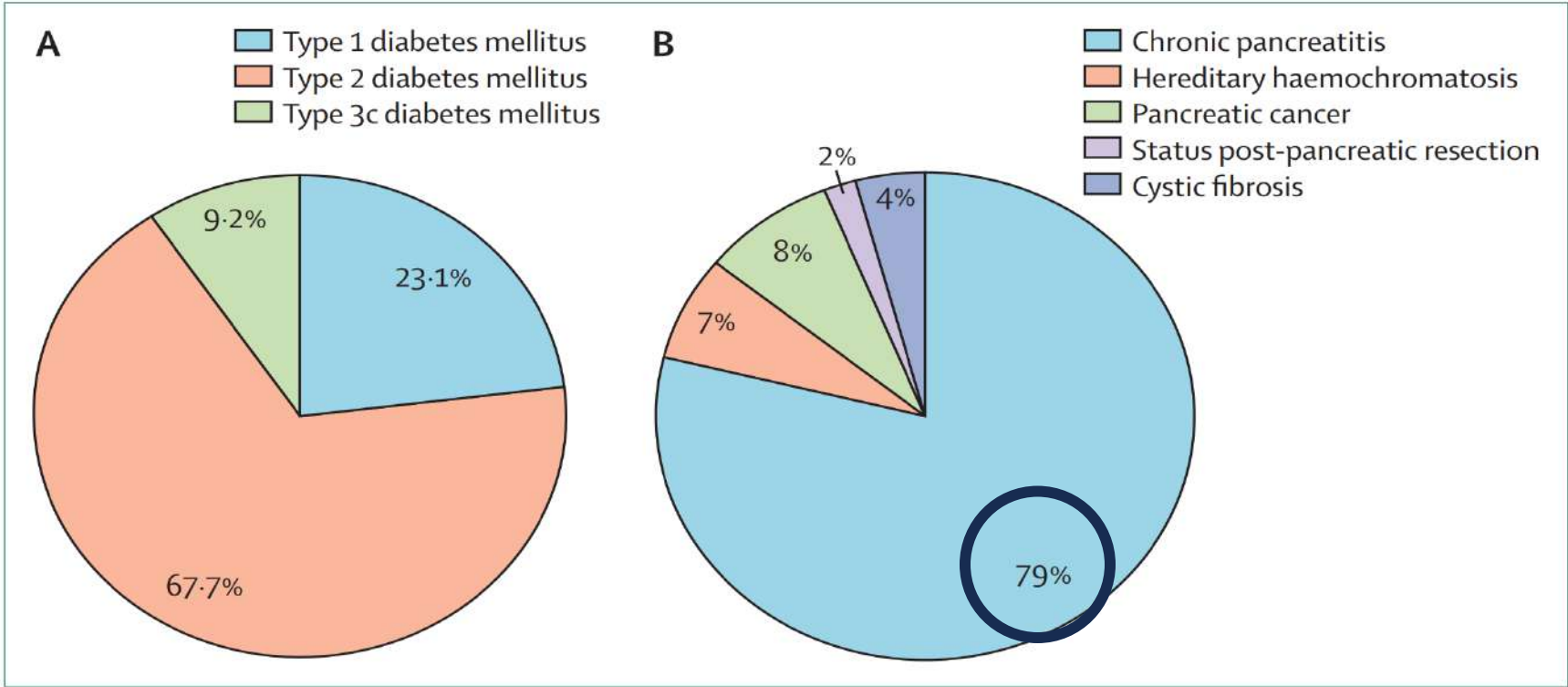


Figure: Prevalence and causes of type 3c diabetes mellitus

(A) Prevalence of type 3c diabetes in a cohort of 1868 participants with diabetes. (B) Frequency of different causes in the 117 participants with type 3c diabetes. Reproduced from Ewald and colleagues,³ by permission of John Wiley and Sons.

Meccanismi fisiopatologici dell'iperglicemia nel DM tipo 3c

Panel: Subclassifications of causes of type 3c diabetes grouped according to their potential mechanisms

Congenital or acquired complete absence of islets

- Pancreatic agenesis
- Pancreatectomy (total)

Acquired partial absence of functional islets

- Chronic pancreatitis*
- Pancreatectomy (partial)
- Severe acute pancreatitis
- Cystic fibrosis
- Haemochromatosis

Paraneoplastic

- Pancreatic ductal adenocarcinoma

Other

- Transient† hyperglycaemia of acute pancreatitis

*Includes tropical pancreatitis, which was previously referred to as fibrocalculous pancreatopathy. †Hyperglycaemia secondary to acute pancreatitis can persist for weeks.

DMT2 vs DMT3c : trova la differenza

TABLE 2. - Diagnostic features of diabetes by type^{3,7}

Parameter	Type 1	Type 2	Type 3c
A1C	>6.5%	>6.5%	>6.5%
Fasting glucose	>126 mg/dL	>126 mg/dL	>126 mg/dL
Fasting C-peptide (0.5 to 2.0 ng/mL)	Very low: <0.2 ng/mL	Normal to high	Low to normal
Ketoacidosis	Common	Rare	Rare
Hypoglycemia (glucose <69 mg/dL)	Common	Rare	Frequent
Islet autoantibodies	Positive	Negative	Negative
Exocrine insufficiency (fecal elastase <200 mcg/g)	Negative	Negative	Positive
CGM	Hyperglycemia and reactive hypoglycemia	Hyperglycemia	Alternate hyperglycemia and hypoglycemia

Secondo ADA ,in aggiunta ai criteri diagnostici per diabete,la diagnosi di DMT3c richiede :

Table 3. Criteria for diagnosing T3cDM proposed by Ewald and Bretzel [32,54,56].

Major Criteria (All Must Be Fulfilled):	
1	Evidence of exocrine pancreatic insufficiency (faeces elastase 1 (FE1) < 200 µg/g or incorrect direct function testing)
2	Pathological pancreatic imaging (endoscopic ultrasound, magnetic resonance imaging, and computed tomography)
3	Absence of type 1 diabetes mellitus-associated autoimmune markers.
Minor Criteria:	
1	Impaired beta cell function (e.g., HOMA-B, C-peptide/glucose-ratio)
2	No excessive insulin resistance (e.g., HOMA-IR)
3	Impaired incretin secretion (e.g., GLP-1, pancreatic polypeptide)
4	Low serum levels of lipid soluble vitamins (A, D, E, and K)

Attenti a quei due : associazione tra diabete e carcinoma del pancreas

Il diabete è un fattore di rischio per carcinoma pancreatico

e

un potenziale precoce segnale di allerta di un tumore che sta crescendo (attenzione a new onset diabetes)



Linee guida NICE

For people aged 60 and over presenting with weight loss and new-onset diabetes, follow recommendations on assessing for pancreatic cancer in the section on pancreatic cancer in the NICE guideline on suspected cancer: recognition and referral. [2022]

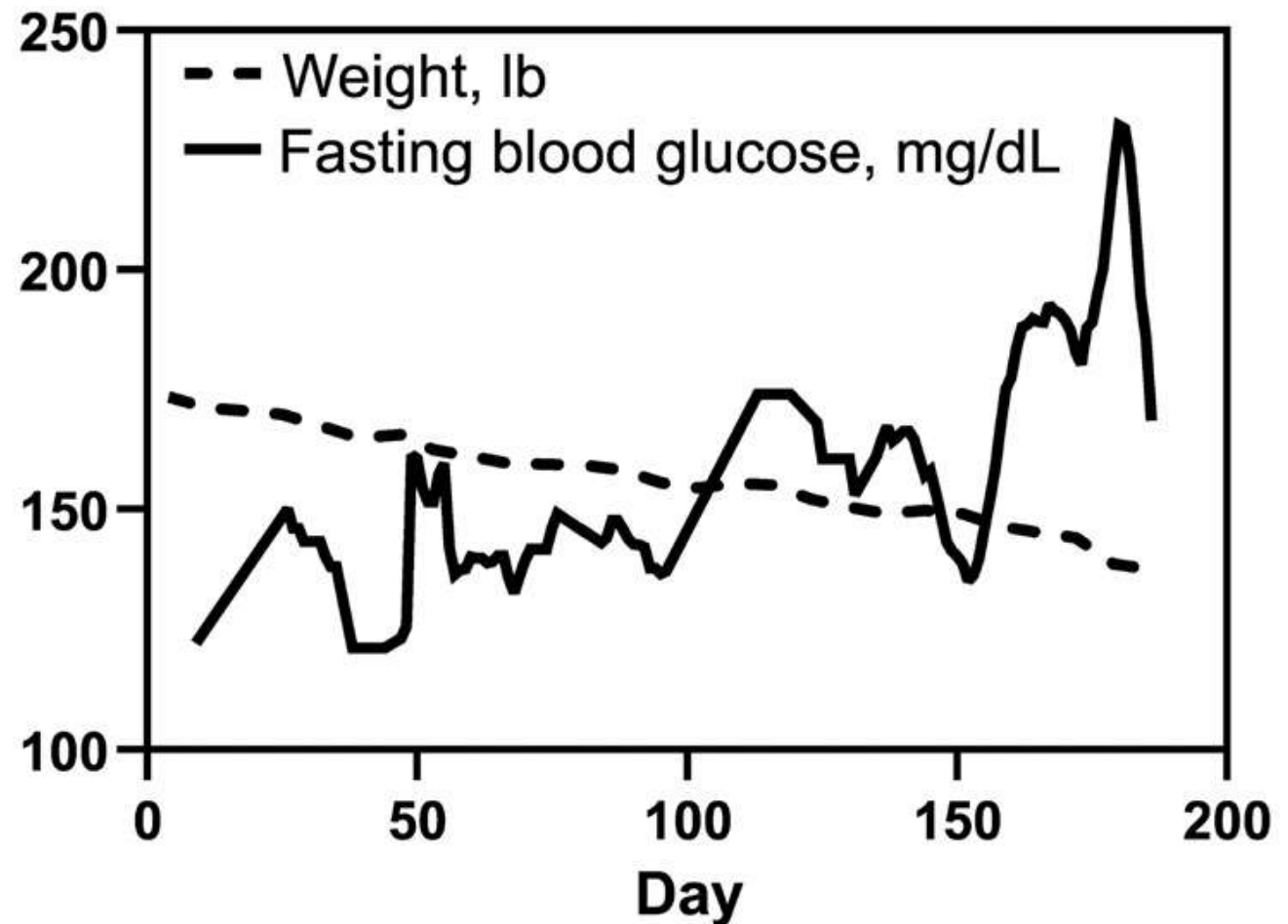
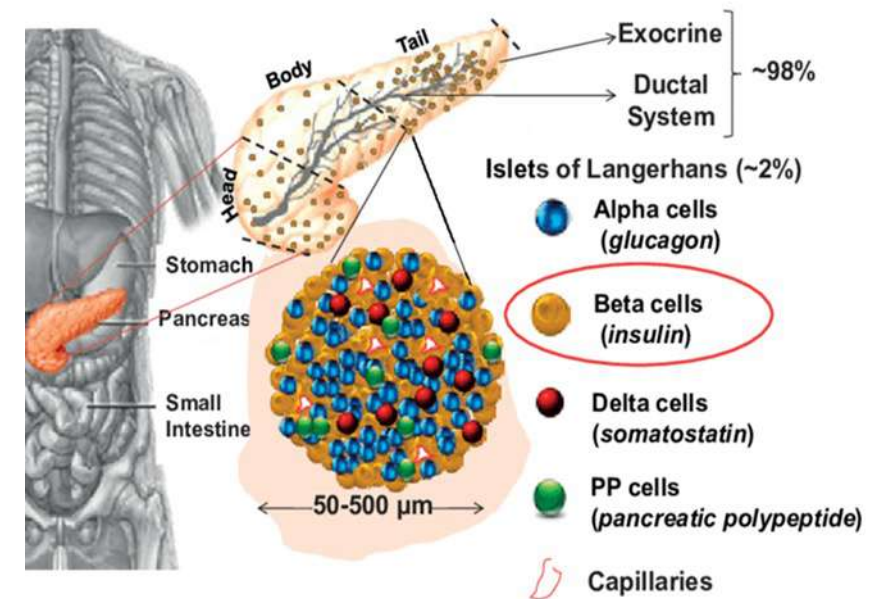


FIGURE 1 Weight and fasting blood glucose trends from day of initial presentation (day 0). Blood glucose trendline represents 7-day running average.

Pancreasectomy e incidenza di DM T3c

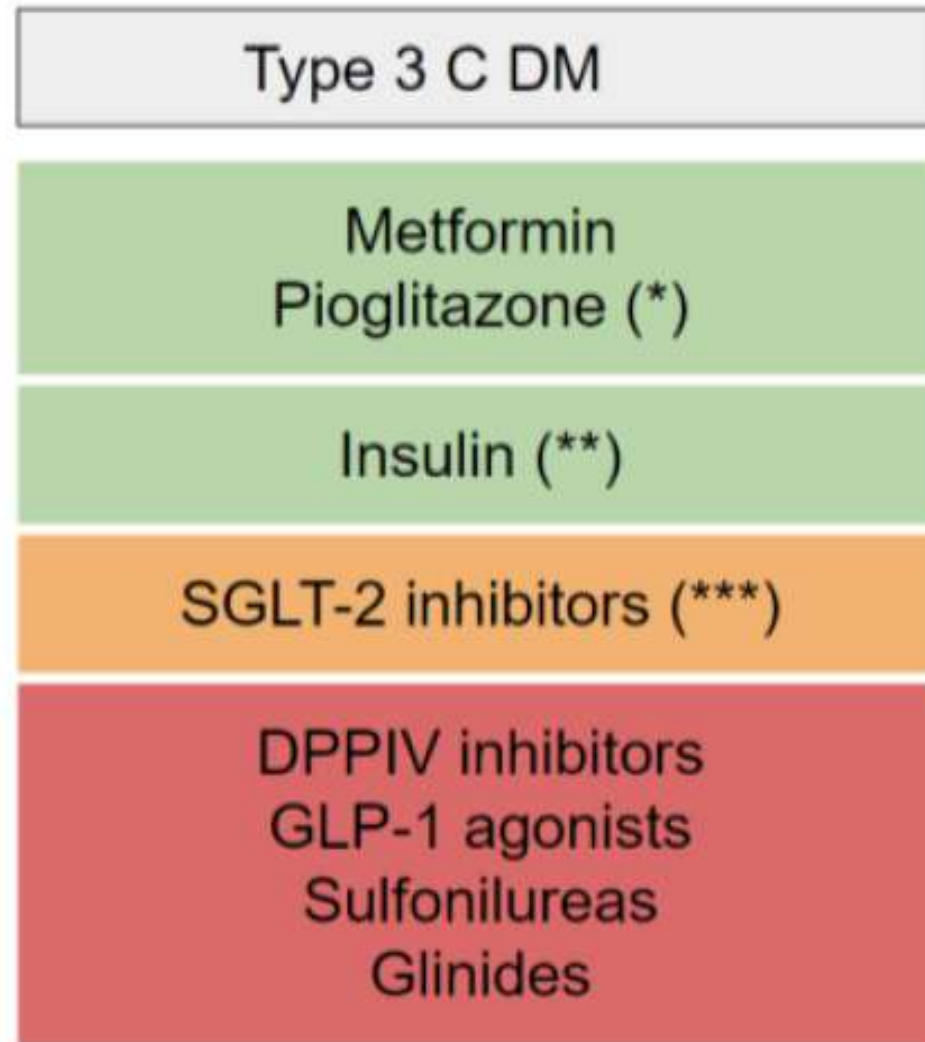
Distal pancreatectomy resulted in the highest incidence of new-onset DM (21%), followed by pancreaticoduodenectomy (16%) while central pancreatectomy presented the lowest incidence of DM (6%). In one study, the median time to develop diabetes was up to 15 months, indicating the need for ongoing screening for T3CDM. Higher preoperative HbA1C (>5.7%), lower remnant pancreatic volume, and fasting plasma glucose were the risk factors with the strongest associations with the onset of T3CDM [25].



Differenze cliniche tra DMT1 e DM secondario a pancreasectomia

	DMT1	Diabete apancreatico
Instabilità glicemica	++	+++
Fabbisogno insulinico	+++	+
ipoglicemia	++	+++
chetoacidosi	+++	+
Complicanze vascolari	+++	+
Livelli ormonali		
Insulina	Bassa	Bassa/assente
Glucagone	Normale/alto	Basso /assente
PP	Normale/basso	Basso
GIP	Normale/basso	Basso
		(duodenectomia)
GLP1	Normale	Normale/alto

Trattamento



Treatment includes both management of hyperglycemia and exocrine pancreatic insufficiency.

The aim of treatment is not only to control hypoglycemia and hyperglycemia but also malabsorption, malnutrition, and chronic DM complications

Basso fabbisogno insulinico (media 0.50 UI/KG body weight)

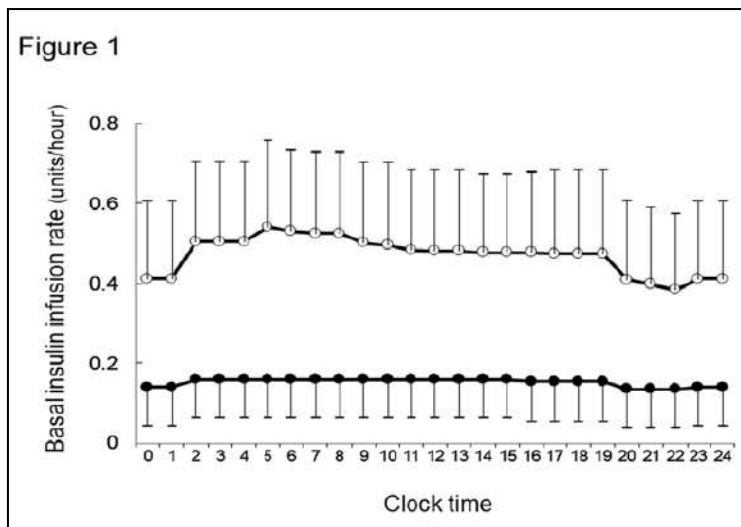


Figure 1. Basal insulin requirements (units/h) in patients with total pancreatectomy (closed circle) and type 1 diabetes (open circle), whose glycemic control was optimized by using an insulin pump.

Data are expressed as the means \pm SD.

Author	Number	Episodes of hypoglycemia	HbA1c levels (%)	Median insulin requirement, U/day (range)
Crippa et al. [78]	65	0–5/week	56% between 7 and 9% 11% > 9%	32 (18–52)
Billings et al. [73]	99	–	5.0–11.3%	32 (2–66)
Casadei et al. [80]	20	1–10/week	5.2–10.3%	25 (20–52)
Muller et al. [25]	147	–	6.7–7.5%	–
Barbier et al. [79]	56	1–36/month	6.3–10.3%	16 (7–48) long acting and 21 (7–70) rapid acting
Watanabe et al. [81]	44	12/week	6.2–11.2%	6 (0–16) long acting and 17 (10–28) rapid acting

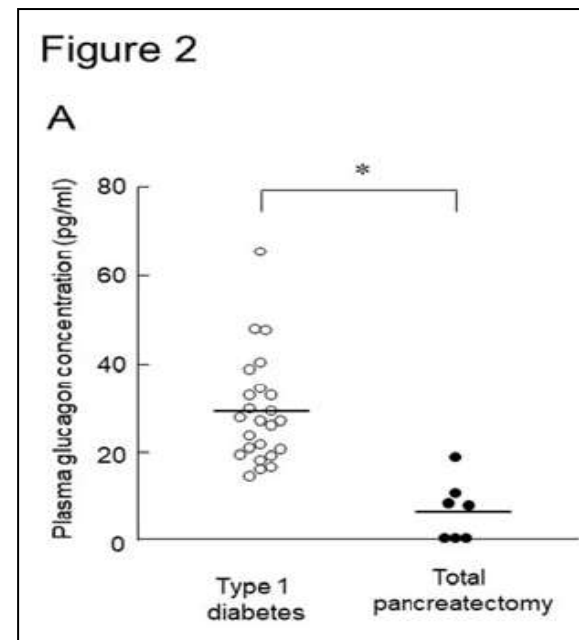


Figure 2.

A. Plasma glucagon concentration (pg/ml) in patients with total pancreatectomy (closed circle) and type 1 diabetes (open circle). Shown are all individual data points and means. The plasma glucagon concentration in the total pancreatectomy group was significantly lower than that in the type 1 diabetes group (6.3 ± 6.9 vs. 28.7 ± 12.2 pg/ml, $P=0.00007$)* $p=0.00007$ vs. type 1 diabetes

B. Correlation between the fasting plasma glucagon concentration and basal insulin dose in patients with total pancreatectomy (closed circle) and type 1 diabetes (open circle). The basal insulin requirement was positively associated with the fasting plasma glucagon concentration ($R=0.38$, $p=0.038$). However, the correlation was not statistically significant within each group (total pancreatectomy: $R=0.43$, NS; type 1 diabetes: $R=0.02$, NS).

Linee guida NICE

Some people have insulin insufficiency because of other conditions. The committee noted that these people would get the same care as people with type 1 diabetes, so they should have access to CGM in the same way.

Due to the increased risk of hypoglycemia in these patients when they are on intensive insulin therapy (basal-bolus regimen), **a continuous interstitial glucose monitoring system should be considered**



Glucose metrics	
Average glucose <i>Goal < 154 mg/dL</i>	156 mg/dL
Glucose management indicator (GMI) <i>Goal < 7%</i>	7%
Glucose variability <i>Defined as percent of coefficient variation Goal < 36%</i>	46%

Ambulatory glucose profile

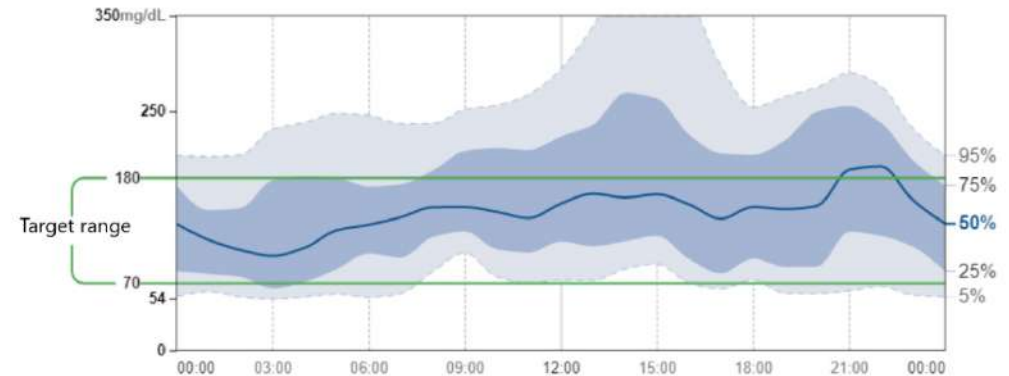


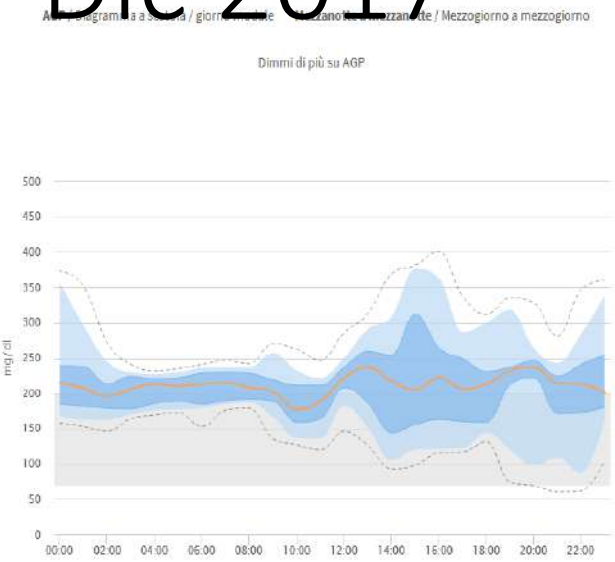
Figure 2. Ambulatory glucose profile (AGP) report of continuous glucose monitoring (CGMS) in a patient with total pancreatectomy due to an 8 × 6 × 7.5 cm pNET.

Donna di 66 aa
 7/2017 Pancreasectomia totale (radicalizzazione della pancreasectomia per sanguinamento dell'anastomosi pancreatico-digiunale in paziente sottoposta ad exeresi di massa addominale , emicolectomia dx ,nefrectomia dx e DCP in data 6/2017. liposarcoma retroperitoneale)

Da dic 2017 inizia CGM



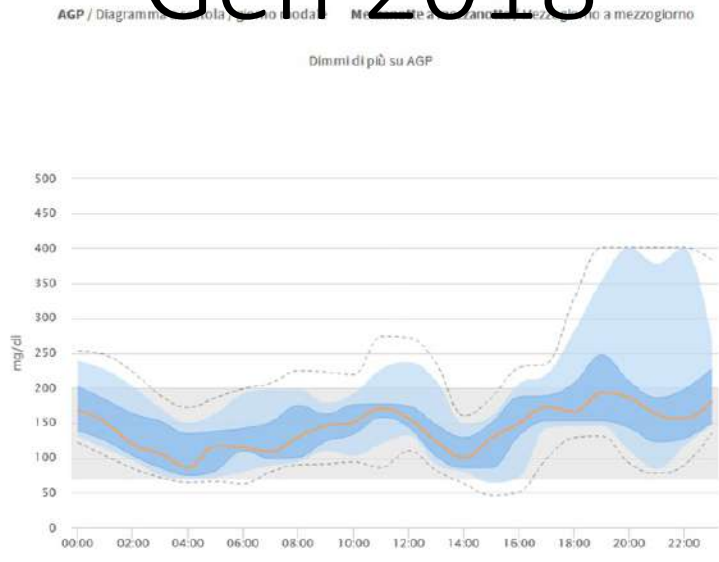
Dic 2017



Mostra profilo basale attivo:

Numero valori: 2206	Valori sopra target (200 mg/dl): 1318	Valore massimo (mg/dl): 401
Valori/giorno: 275.8	Valori entro target (70-200 mg/dl): 876	Valore minimo (mg/dl): 61
Media periodo (mg/dl): 211	Valori sotto target (70 mg/dl): 12	Deviazione standard: 52

Gen 2018



Mostra profilo basale attivo:

Numero valori: 2166	Valori sopra target (200 mg/dl): 305	Valore massimo (mg/dl): 401
Valori/giorno: 270.8	Valori entro target (70-200 mg/dl): 1819	Valore minimo (mg/dl): 46
Media periodo (mg/dl): 153	Valori sotto target (70 mg/dl): 42	Deviazione standard: 60

Da 11.2018 SAP CSII+ CGM



Glucometri SM74413192
PL90404772
Periodo: 28/02/2021 - 13/03/2021, 14 giorni

Pompa per insulina

130441418

CGM 🕒 Tempo CGM attivo: 88%



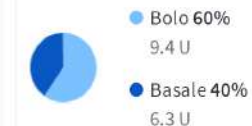
Intervallo impostato: 70-200 mg/dL

Tempo entro target ● 53%

Media 199 mg/dL

Deviazione standard 62 mg/dL

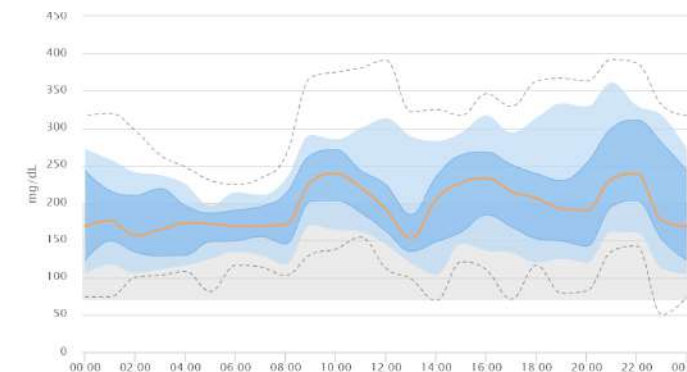
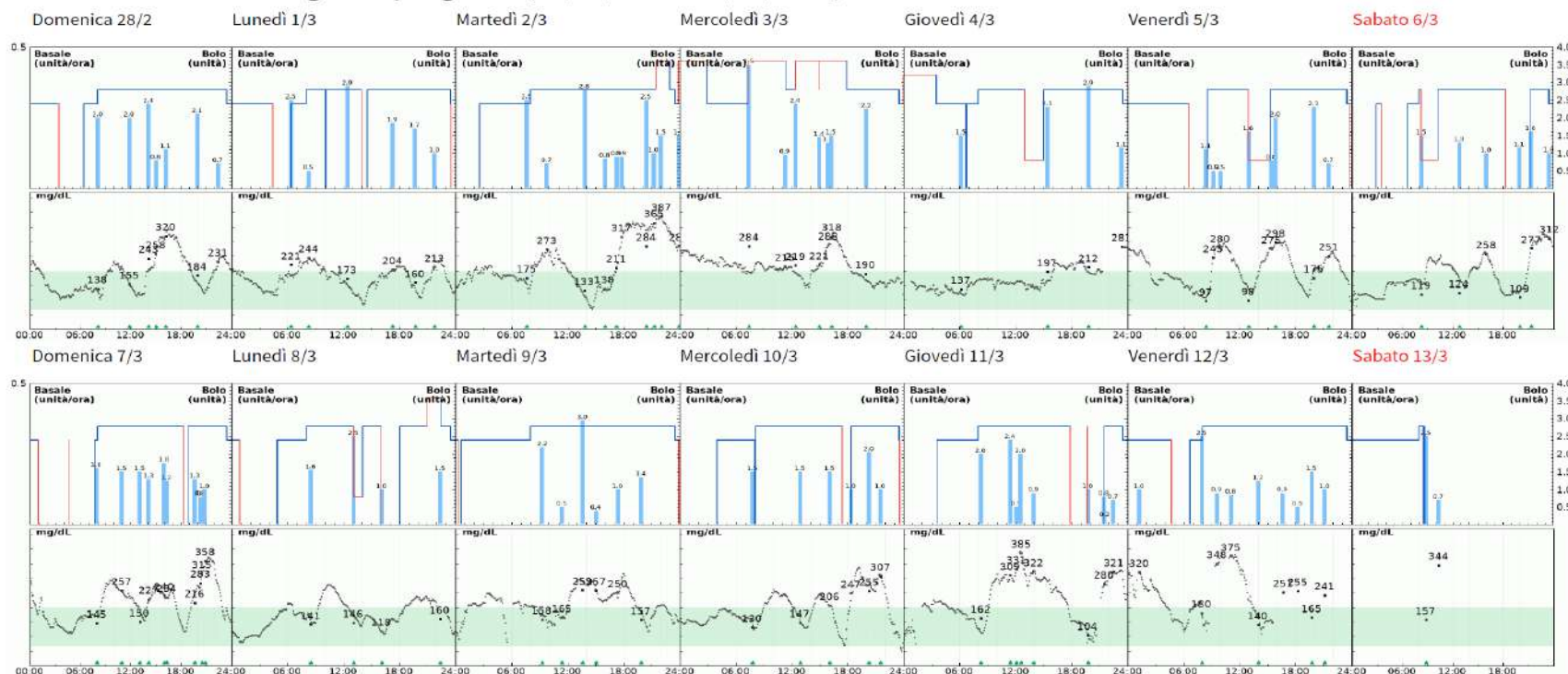
Insulina



Dose Giornaliera Media 15.8 unità

Deviazione standard 5.3

Confronto : Panoramica giorno per giorno (28/02/2021 - 13/03/2021)



Molto basso < 54 mg/dL	Basso 54 - 70 mg/dL	Tempo entro target 70 - 200 mg/dL	Alto 200 - 250 mg/dL	Molto alta > 250 mg/dL	Tempo CGM attivo
0%	0%	54%	26%	20%	88%

Media periodo: 199 mg/dL

Valore massimo: 392 mg/dL (02/03/2021 21:36)

Valore minimo: 50 mg/dL (10/03/2021 23:45)

Deviazione standard (SD): 62 mg/dL

Coefficiente di variazione (CV): 31%

Glucose management indicator (GMI): 64.8 mmol/mol - 8.1%



Advanced hybrid closed-loop system: first successful clinical case after total pancreatectomy

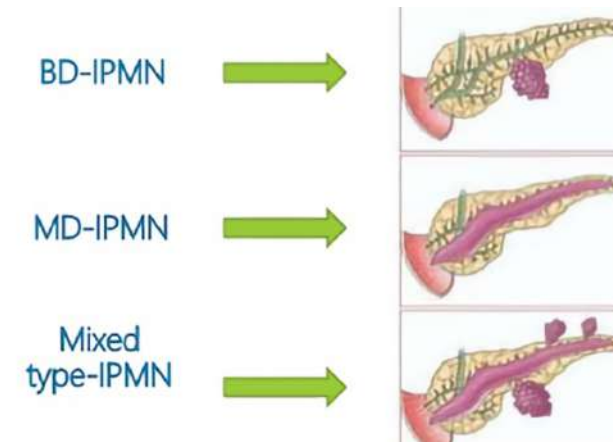
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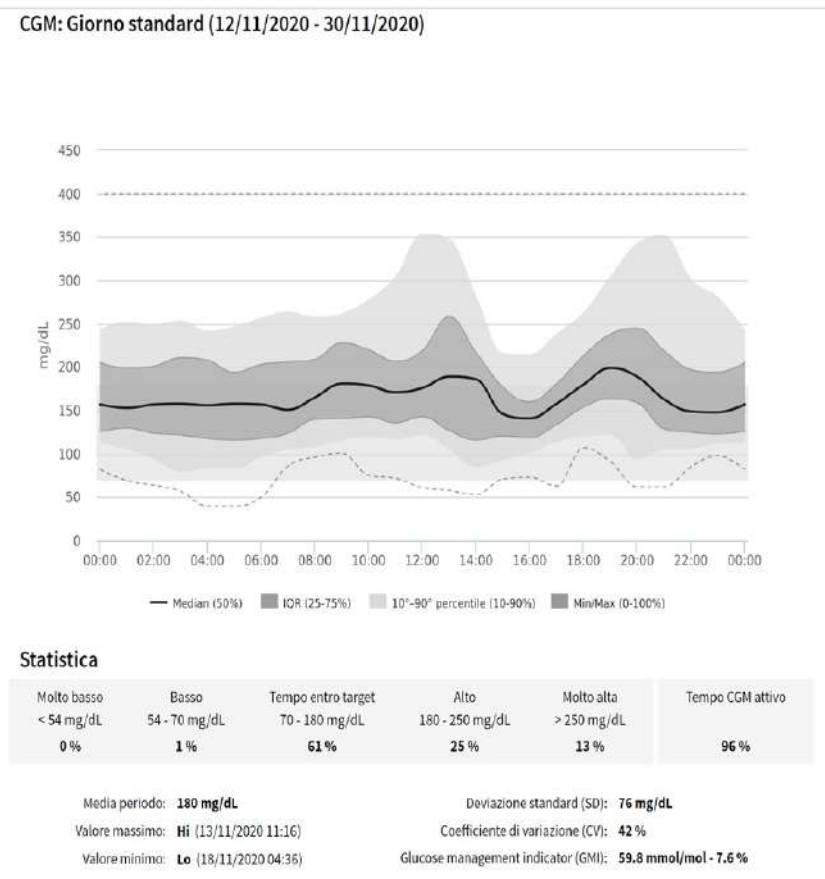
Ci siamo anche noi (sabaudamente)



Uomo 64 aa
 familiarità per IPMN degenerate
 10/11/2020 pancreasectomia totale spleen
 preserving per IPMN multifocale



In corso di ricovero inizia
 utilizzo di MDI+ CGM



Dal 1 dicembre 2020 Microinfusore PLGS e poi HCLS

DdN: 22 apr, 1956 Diabete: Tipo 1

13 ott, 2023 - 26 ott, 2023 (14 giorni)

Oggi: 26 ottobre 2023

Glicemia - Tempo in target



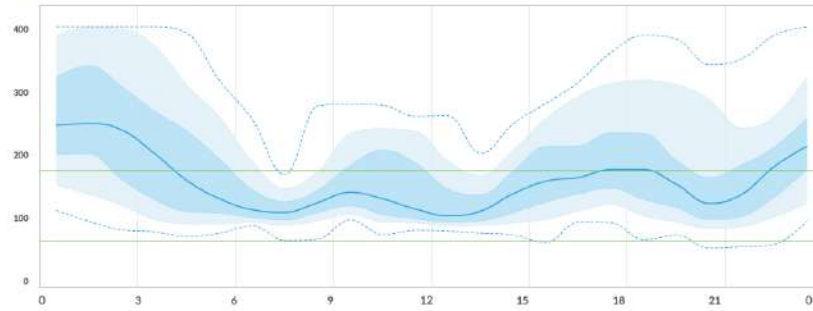
Riepilogo

GMI: **7.5% (58,9 mmol/mol)**
 Media: **177 mg/dl**
 % di tempo CGM attivo: **94,3% (13,2 giorni)**

DS: **78mg/dl**
 CV: **44.2%**
 Mediana: **155mg/dl**
 Più alta: **HI mg/dl**
 Più bassa: **60mg/dl**

Profilo Glicemico Ambulatoriale (AGP)

Intervallo target (70-180 mg/dl) 25-75% Infioreso-superiore
 Mediana 10-90%



Insulina - Dispositivo

Dal microinfusore per insulina



Dettagli del sistema

Tandem tslim X2 (13gg 7h)

- Control-IQ: **98% (13gg)**
- Attività - Sonno: **35% (4gg 15h)**
- Attività - Esercizio: **0%**
- Manuale: **2% (7h)**

LGS/PLGS

Tempo di sospensione/giorno: **2h 22m**
 Media sospensioni/giorno: **6,5**
 Media sospensione/ora del giorno

- Mattino: **27%**
- Pomeriggio: **31%**
- Sera: **19%**
- Notte: **24%**

Dieta

Carboidrati/Giorno: **285,6g**
 Dati/Giorno: **4,4**

Fitness

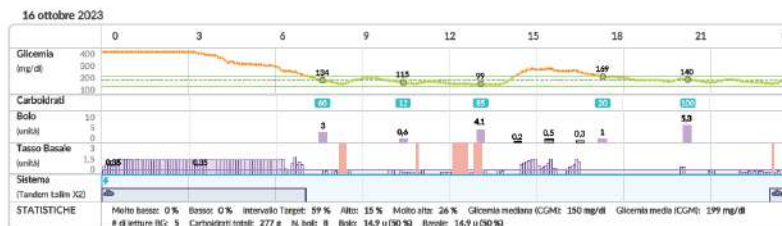
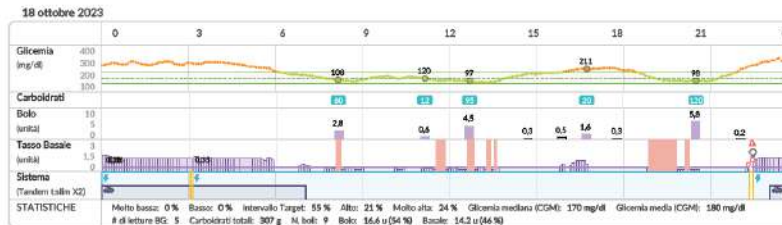
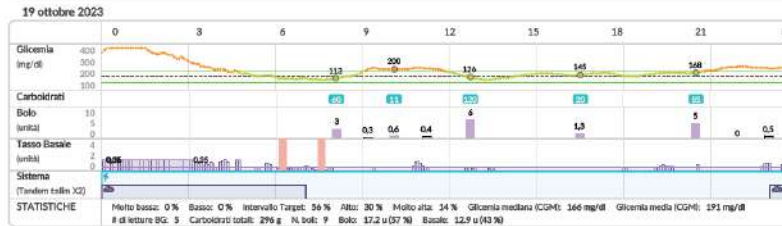
Neosun indicatore di fitness collegato

Commenti

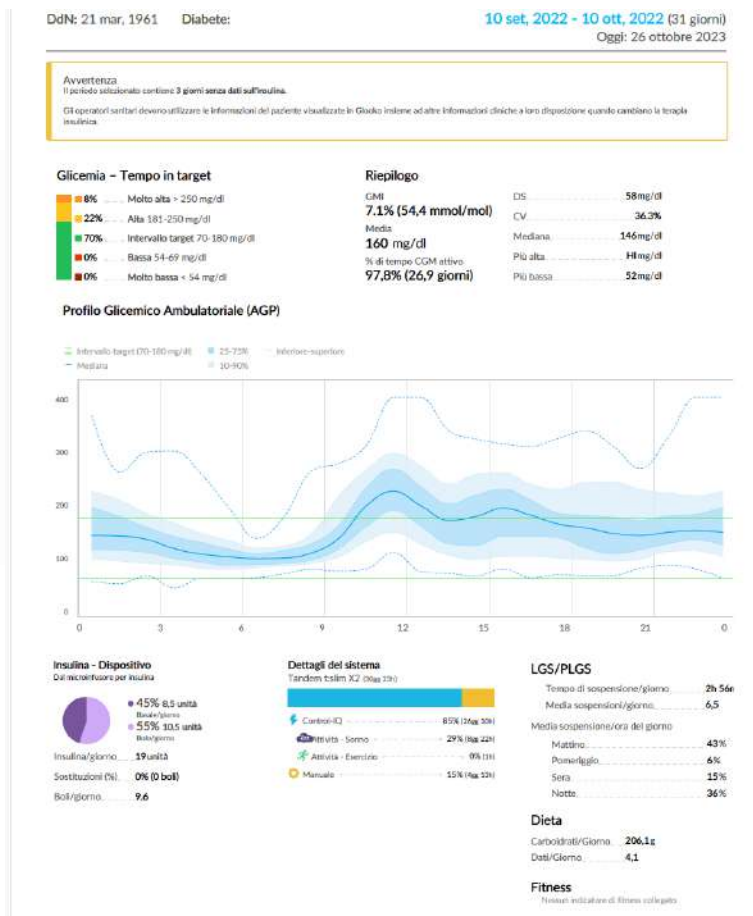
DdN: 22 apr, 1956 Diabete: Tipo 1

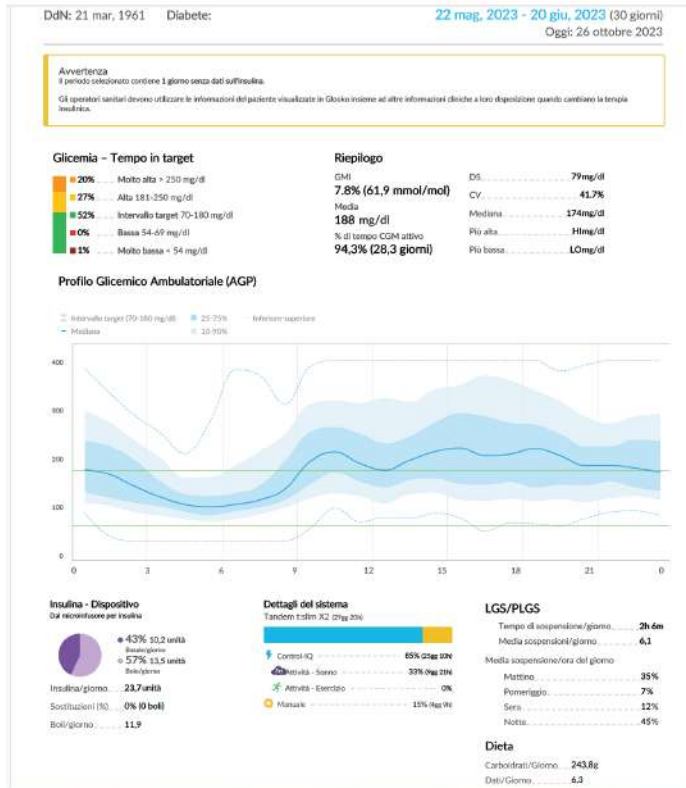
13 ott, 2023 - 26 ott, 2023 (14 giorni)

Oggi: 26 ottobre 2023



Donna di 60 aa
 DMT2 dal 2013 (non complicanze) con valori in peggioramento dal 6.2021
 2.2022 pancreasectomia totale per NET
 Dal 13.09.22 utilizza HCLS

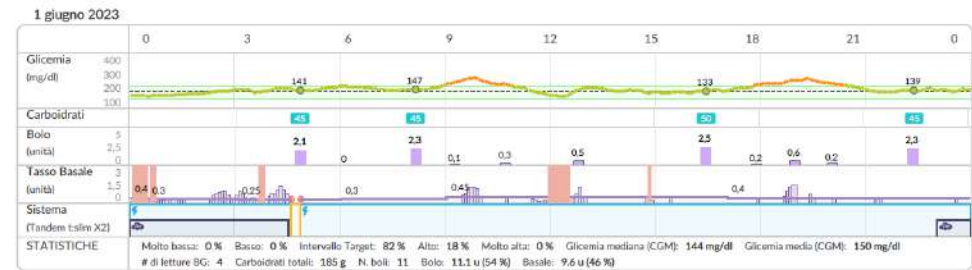
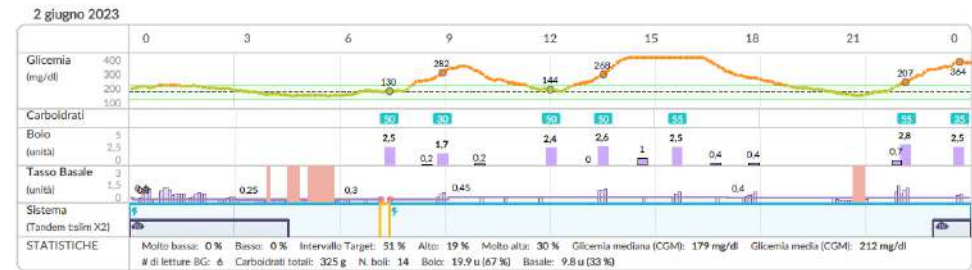




DdN: 21 mar, 1961 Diabete:

22 mag, 2023 - 20 giu, 2023 (30 giorni)

Oggi: 26 ottobre 2023



Grazie,continue le prove

