SAP
THERAPY
aspetti educazionali
e psicologici

SEMINARIO

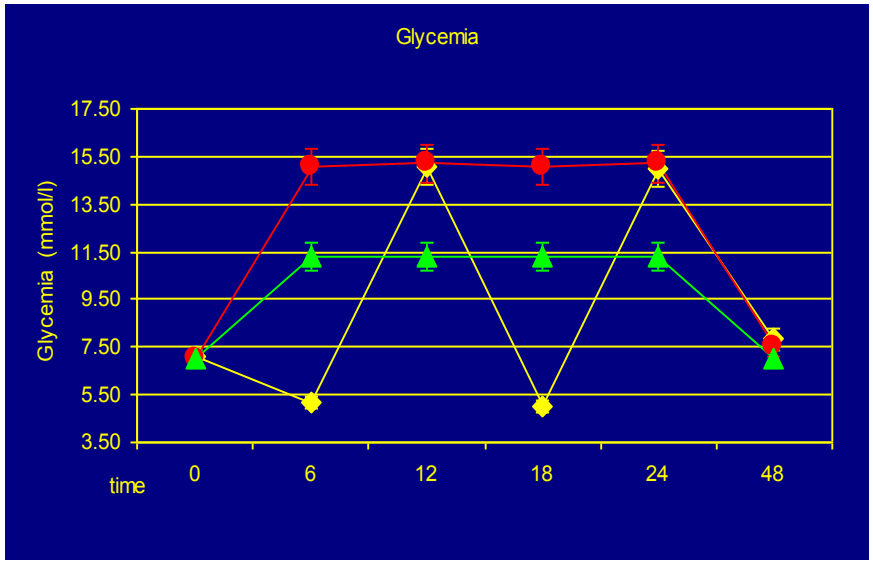
12 dicembre
2014

Hotel Scapolatiello
Cava de' Tirreni (Sa)

Angela Girelli e Giorgio Grassi

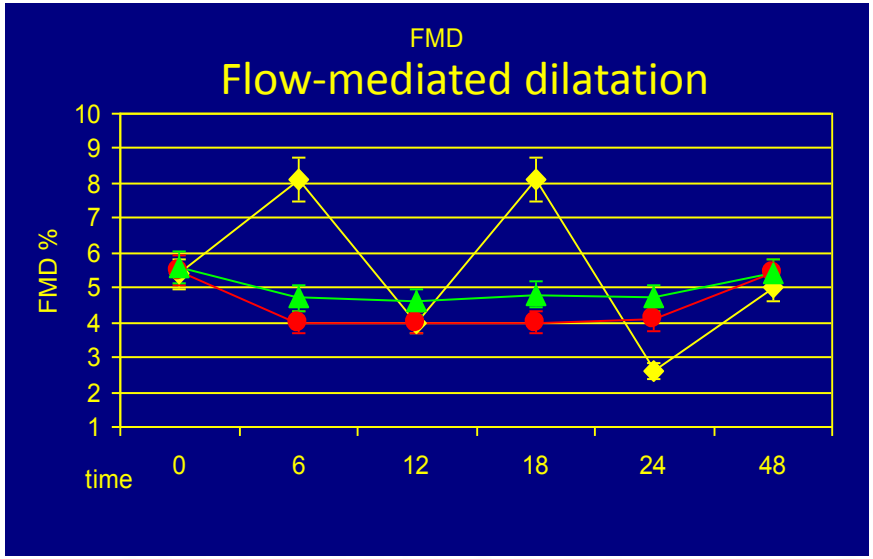
Stato dell' arte del paziente in SAP
Ipoglicemia e variabilità glicemica

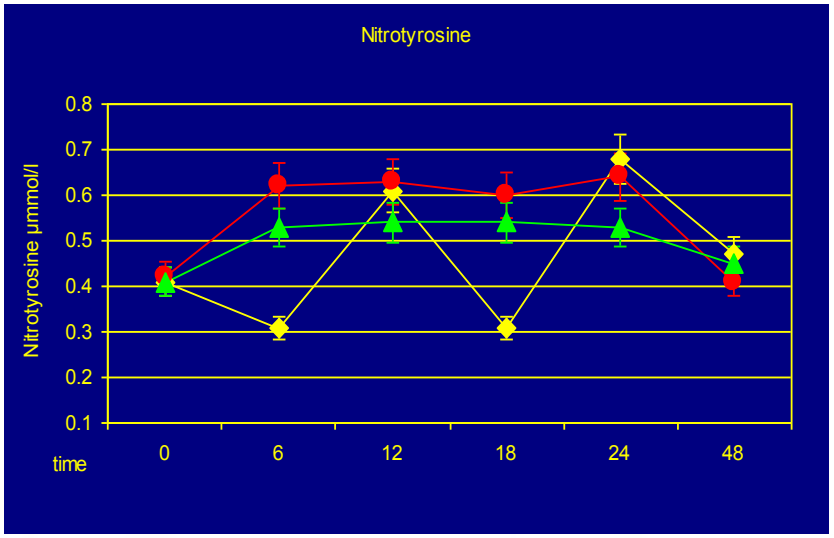
Le basi sperimentali



Ceriello A:Diabetes 2008: 57: **1349–1354**

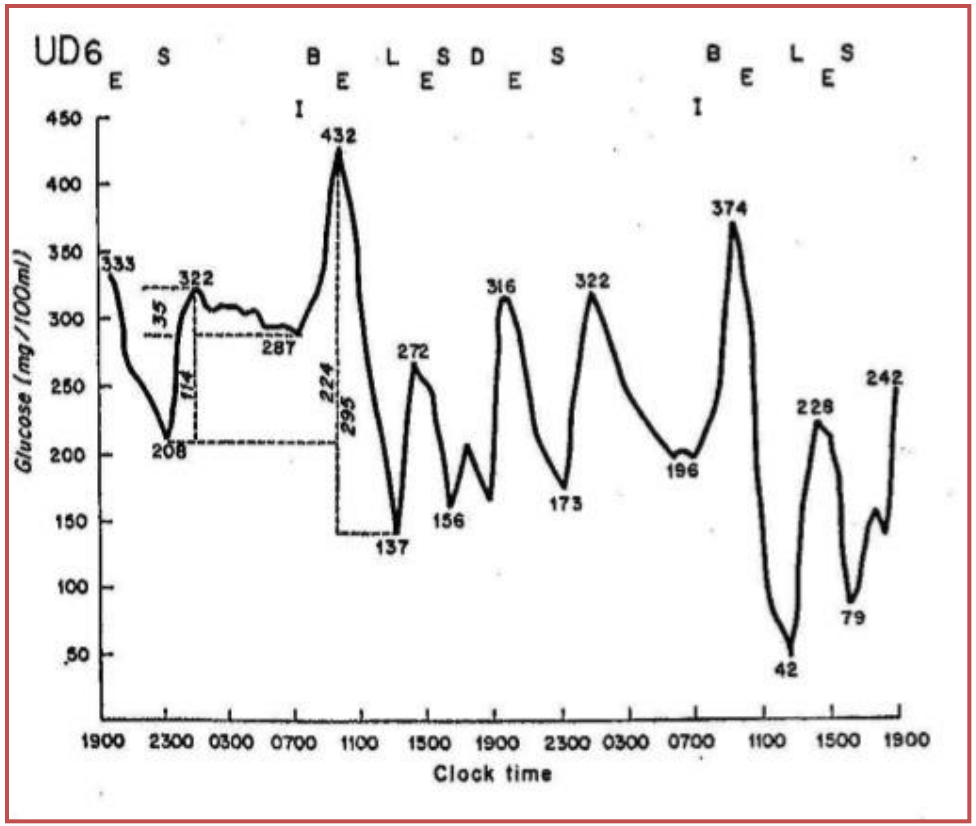
- 15 mmol/l every six h and normalized for the further six h
- maintained at 15 mmol/l; Peak Glycemia
- maintained at 10 mmol/l; Mean Glycemia/24 h





Mean **A**mplitude of **G**lycemic **E**xcursion

Service et al. Diabetes 1970,19(9):644-655



Calculation of MAGE for subject UD6 on intermediate-acting insulin regimen

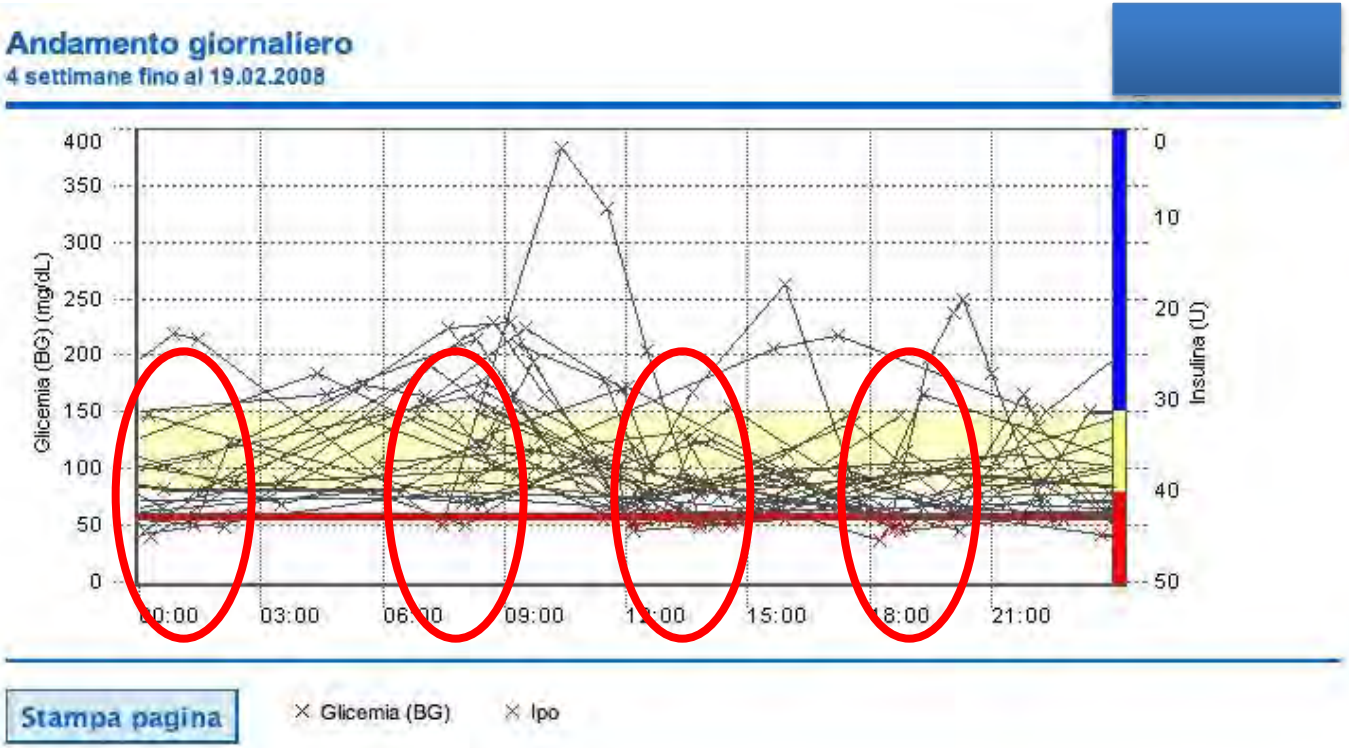
Day	BG peak, P (mg./100 ml.)	BG nadir, N (mg./100 ml.)	Amplitude of glycemic excursion, P-N (mg./100 ml.)	Standard deviation of respective BG
1	333	208	125	62
	432	137	295	
	272	156	116	
2	316	173	143	74
	322	196	126	
	374	42	332	
	228	79	149	

Total = 1,286
MAGE = 1,286/7 = 184

HbA_{1c} = 6,2 %

MBG = 102 mg/dl
SD = 58 mg/dl

Profili Glicemici Giornalieri



Nocturnal hypoglycaemia

- Approximately 30% of non-severe nocturnal hypoglycaemic events result in work absenteeism and lost productivity[1]
- Affects functioning the following day

Function	Effect
Mood, subjective wellbeing	Impaired[2–5]
Physical fatigue	Increased[5]
Memory (from before event)	Reduced[4]
Morning food intake	Increased[6]
Neuroendocrine hypoglycaemia counter-regulation	Reduced[7,8]
Hypoglycaemia awareness	Reduced[7,8]
Neurocognitive function during hypoglycaemia	Reduced[7,8]

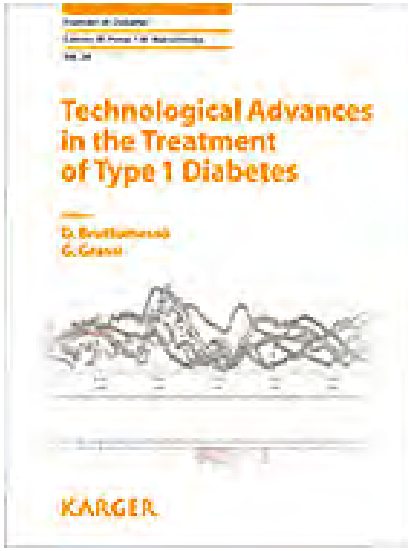
Adapted from Jauch-Chara *et al*. *Best Pract Res Clin Endocrinol Metab* 2010;24:801–15.
[1]Brod *et al. Diabetes* 2011;60(Suppl. 1):A329(1197-P);
[2]Bendtson *et al. Diabetologia* 1992;35:898–903; [3]Matyka *et al. Arch Dis Child* 1999;81:138–142;
[4]Jauch-Chara *et al. Diabetes Care* 2007;30:2040–5; [5]King *et al. Diabetes Care* 1998;21:341–5;
[6]Schmid *et al. Diabet Med* 2008;25:232–5; [7]Veneman *et al. Diabetes* 1993;42:1233–7;
[8]Fanelli *et al*. *Diabetes* 1998;47:1920–7

Continuous Glucose Monitoring

- Continuous Glucose Monitoring (CGM) is an innovative technology with diagnostic and therapeutic applications. It is typically used with an insulin pump to improve glycaemic control both in Diabetes care and in other conditions associated with altered glycaemic homeostasis.

SAP

- Sensor-augmented pump therapy (SAP) is represented by the contemporary use of CSII and CGMS in order to further improve glucose control by employing both technologies. While with self-monitoring of blood glucose (SMBG) it is only possible to assess single instantaneous glucose values, by using SAP it is feasible for the patient to also evaluate glucose trends and adjust insulin administration accordingly.



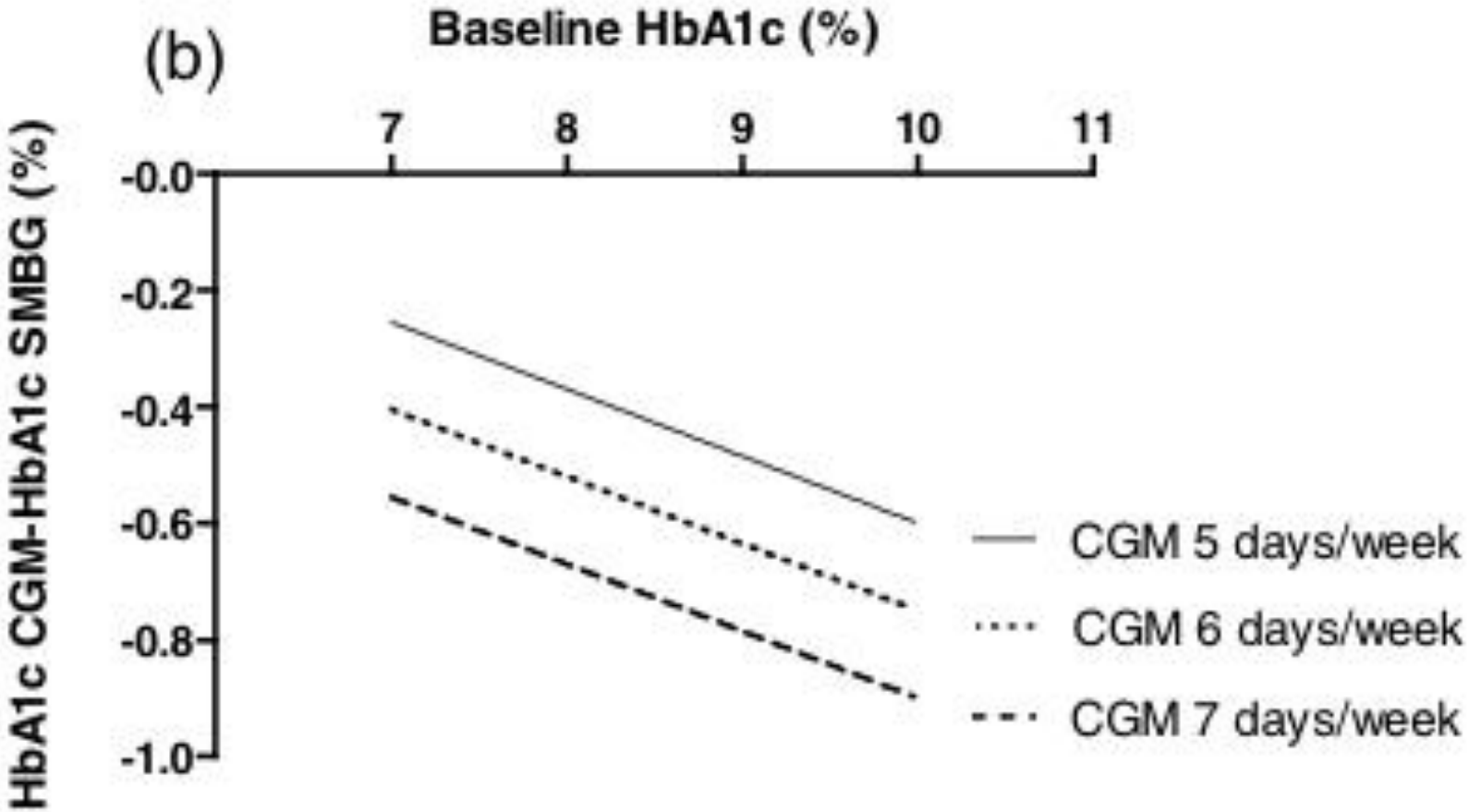
- Rabbone, Bonfanti in Technology Advances In the Treatmento of type 1 diabete 2014

- In contrast to these positive views and evidence of the value of CGM, Yeh et al.
- ‘CGM achieved a lower HbA1c level but below the difference that was clinically significant’
- ‘The incidence of severe hypoglycemia did not differ between RT [real time]-CGM and SMBG’.
- Ann Intern Med 2012; 157: 336–347.

HBa1c and Hypoglycemia

- In a Meta- analysis of six RCTs comparing CGM with SMBG, the mean difference in HbA1c level depended both on sensor usage and baseline HbA1c. (. *BMJ* 2011; **343**: d3805)
- When sensors are used frequently, the mean difference in HbA1c across all patients is substantial, at ~7.7 mmol/mol (0.7%), and when both the baseline HbA1c on MDI is high (say 75 mmol/mol or 9%) and sensor use is frequent, the mean difference in HbA1c between CGM and SMBG increases to ~9.9 mmol/mol (0.9%).
- Several studies have also shown that exposure to mild-to-moderate hypoglycaemia and the frequency of severe hypoglycaemia are reduced on CGM. (*Diabetes Care* 2011; **34**: 795–800 Diabetes Care 2013; 36: 4160–4162.)

Banting Memorial Lecture 2014. Technology and diabetes care: appropriate and personalized
J.C. Pickup



Children Adolescents

- Children: compared to SMBG, RT-CGM allows a higher number of patients to reduce HbA1c of at least 0.5% after three months. Moreover, HbA1c reduction is more visible with higher compliance to continuous monitoring; in fact, after twelve months patients highly compliant obtain HbA1c reduction greater than that observed in patients with an intermittent use of sensors
- Adolescents: in patients with experience in insulin-pump use, RT-CGM allows a reduction of HbA1c of 0.4% higher than SMBG in 6 months

Langendam M, Luijf YM, Hooft L, Devries JH, Mudde AH, Scholten RJ (2012) Continuous glucose monitoring systems for type 1 diabetes mellitus. Cochrane Database Syst Rev. Review

Adults

- Adults: compared to SMBG, both in short and long-term, RT-CGM demonstrates an improvement in HbA1c significantly higher; even in this case improvement is related to compliance.
- After six months a significant larger decline in HbA1c level for real-time CGM users starting insulin pump therapy compared to patients using MDI and SMBG (mean difference (MD) in change in HbA1c level -0.7%, 95% confidence interval (CI) -0.8% to -0.5%)

Langendam M, Luijf YM, Hooft L, Devries JH, Mudde AH, Scholten RJ (2012) Continuous glucose monitoring systems for type 1 diabetes mellitus. Cochrane Database Syst Rev. Review

Major clinical studies on RT-CGM

- In Type 1 Diabetes patients with poor glycaemic control, RT-CGM improves metabolic control reducing HbA1c and therefore time spent in hyperglycaemia
- HbA1c reduction is obtained without increasing hypoglycaemia risk: patients using RT-CGM experience the same frequency of moderate-severe hypoglycaemia episodes of patients in the control group using SMBG but they have a significantly lower HbA1c
- HbA1c reduction is achieved in all patients, both with baseline HbA1c higher and lower than 7%
- **HbA1c reduction is strongly associated with sensor compliance, i.e. frequency of sensor usage**

- Efficacy is sustained over time.

SAP THERAPY

	SWEDEN (46, 47)	AUSTRIA (48)	GERMANY (49)	The NETHERLANDS (50)	UNITED KINGDOM (51)		SPAIN (52)		FRANCE (53)
Adults	Metabolic control: HbA1c > 9% Hypoglycemia: ≥2 severe episodes/year that require help from other person	Metabolic control: HbA1c > 7,5% Hypoglycemia: Severe episodes, nocturnal hypoglycemia, hypoglycemia unawareness	Metabolic control: insufficiente Hypoglycemia: Frequent, severe or nocturnal, hypoglycemia unawareness	Metabolic control: Long term poor glycemic control (frequent hypo- and hyperglycemia) despite intensive training, good adherence and at least 4 SMBG/day in the last 3 months Hypoglycemia: hypo unawareness (based on SMBG tests) Other indications: rapid development of ketoacidosis, or regular need of hospitalization (> 2 in last year); documented and inexplicable glycemic fluctuations	No distinction based on age	Metabolic control: HbA1c > 7,5% Hypoglycemia: Recurrent, disabling, hypo unawareness, fear of hypo	No distinction based on age	Metabolic control: Discrepancies between HbA1c and SMBG tests Hypoglycemia: hypo unawareness. Nocturnal hypos and in non-diabetic patients	Metabolic control: HbA1c above the threshold defined by the Haute Autorite de Sante (≥ 8,1%) despite good insulin therapy management, including CSII or MDI Hypoglycemia: moderate unperceived hypos or frequent hypos, nocturnal episodes; frequent severe hypos
Children	>10 SMBG/day, clinically non justifiable, in order to attempt to achieve acceptable HbA1c values and avoid severe hypo episodes	Limited hypo perception, highly sensitive to glucidic intake, often unable to autonomously react	No indication	Below 6 years of age					Metabolic control: HbA1c above the threshold defined by the Haute Autorite de Sante Hypoglycemia: moderate unperceived hypos or frequent hypos, nocturnal episodes; frequent severe hypos
	No indication	No indication	Pregnancies with unsatisfactory glycaemia and more than 10 SMBG/day needed	Preconception (DM T1,2): HbA1c out of target, frequent and/or severe hypos, unperceived hypo, unpredictable	HbA1c > 6,1%		Gestational diabetes and preparation for pregnancy		**During pregnancy or preconception in case HbA1c target is not achieved or in case HbA1c controlled but with frequent**

Summary of reimbursement indications in Europe

	SWEDEN	The NETHERLANDS	SLOVENIA	ESTONIA	SLOVAKIA	SWITZERLAND	IRELAND	AUSTRIA
Adults	Metabolic control: HbA1c> 8,5% Hypoglycemia: ≥2 severe episodes/year	Metabolic control: HbA1c> 8%	Hypoglycemia: unperceived, severe			No distinction based on age Metabolic control: HbA1c≥8% Hypoglycemia: severe Other indications: Unstable diabetes with need of emergency visits or hospitalizations	Reimbursed with no special restrictions.	DMT1; hypoglycaemia unawareness; severe hypoglycaemia; undergoing intensive insulin treatment
Children	>10 SMBG/day	DMT1	DMT1 ≤7 years of age	0-4 years: 48 sensors/year 5-18 years: 12 sensors/year if HbA1c≥10%	DMT1 < 15 years of age on CSII Metabolic control: HbA1c>8% Hypoglycemia: severe			< 7 years of age;
Pregnancy and preconception		DMT1 and DMT2	DMT1 and DMT2 Intensive insulin treatment					Pregnant women with DMT1 and DMT2

Patients with Type 1 Diabetes younger than 18 years

- pump-user
- hypoglycaemia
  - severe episodes: highly recommended
  - frequent, recurrent, unawareness: recommended
- with more than 10 finger-sticks a day
- with high glycaemic variability, independently from HbA1c values
- with HbA1c < 7% (< 53 mmol/mol) who need to minimize the risk of hypoglycaemia

Adults with Type 1 Diabetes:

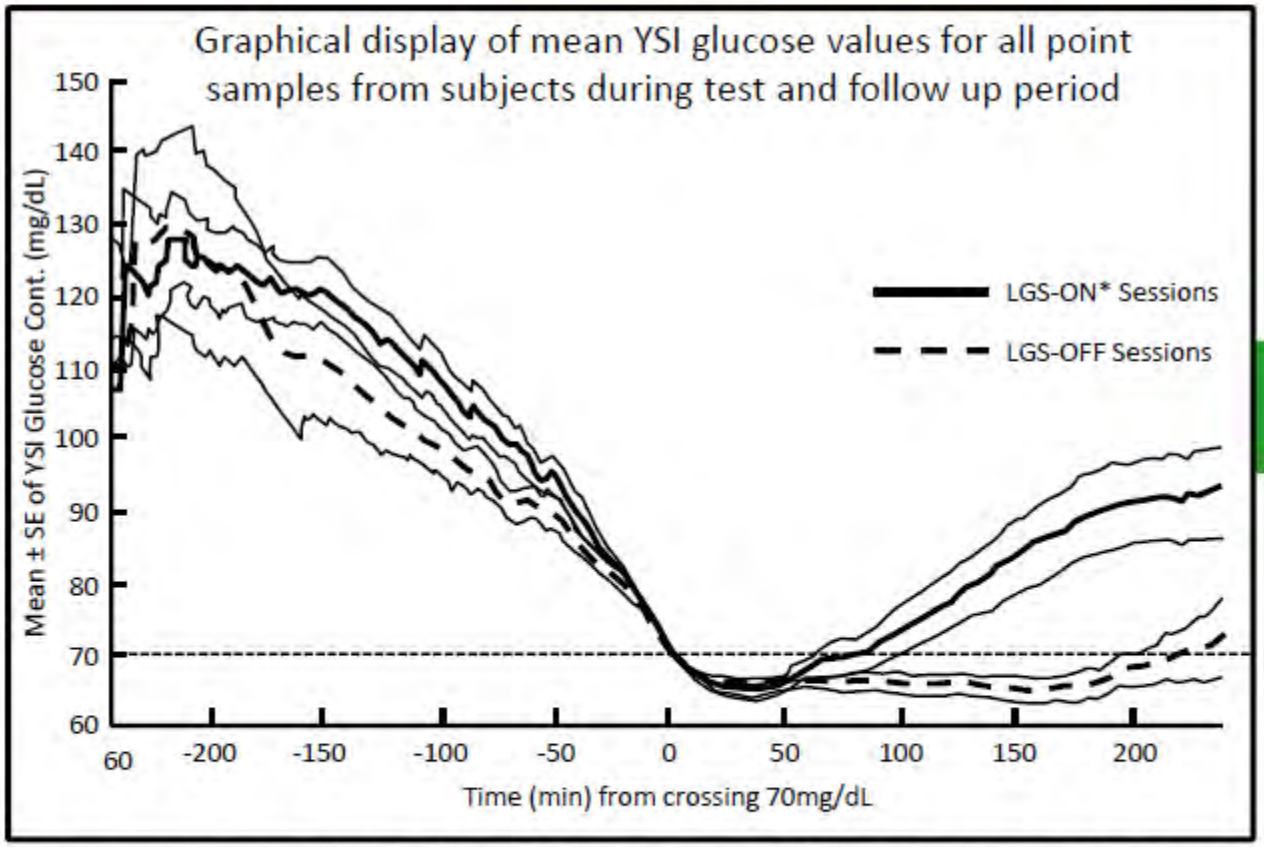
- in CSII regimen and HbA1c>8% (> 64 mmol/mol), or
- **hypoglycaemia**
  - **severe episodes: highly recommended**
  - **frequent, recurrent, unawareness: recommended**
- instable diabetes causing emergency care visits and hospitalisation
- when SMBG tests reveal discrepancies with HbA1.

Automatic suspension of insulin delivery: the in-clinic ASPIRE study

A multi-centre randomised cross-over study assessing the efficacy of the low glucose suspend (LGS) feature of the sensor-augmented pump (SAP) to stop insulin delivery in induced hypoglycaemia among adult subjects (n=50) with Type 1 diabetes

Garg S et al. *Diabetes Technol Ther* 2012;14:205–209

PRIMARY END POINT: COMPARISON OF THE DURATION AND SEVERITY OF HYPOGLYCAEMIA MEASURED BY PLASMA GLUCOSE DURING SUCCESSFUL LGS-ON AND LGS-OFF SESSIONS

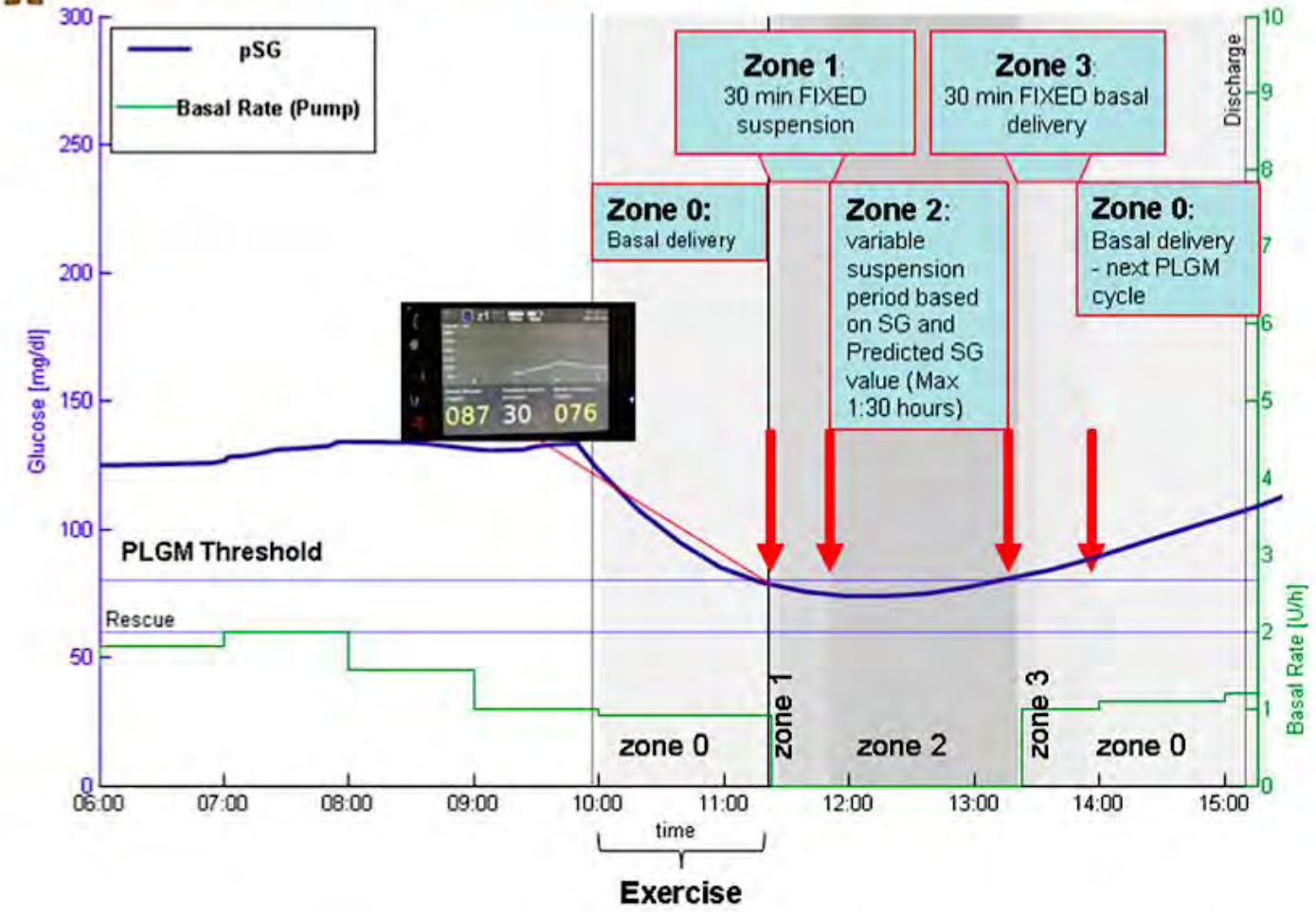


The LGS feature can significantly reduce the duration and severity of hypoglycaemia without causing significant rebound hyperglycaemia

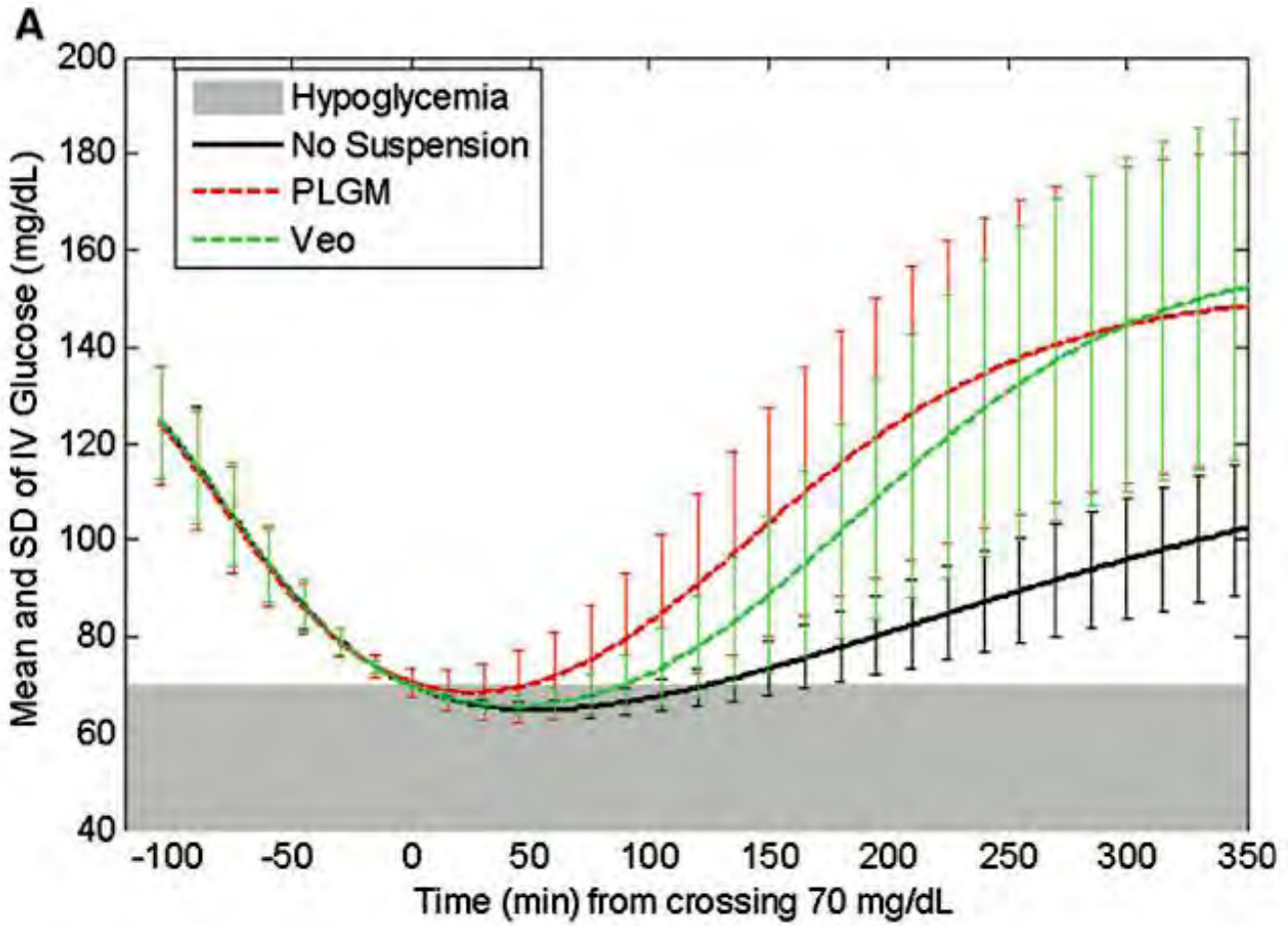
PLGS

PILGRIM

PredIctive Low Glucose Management in Realtime Sensing Insulin PuMp Therapy



DIABETES TECHNOLOGY & THERAPEUTICS Volume 16, Number 6, 2014

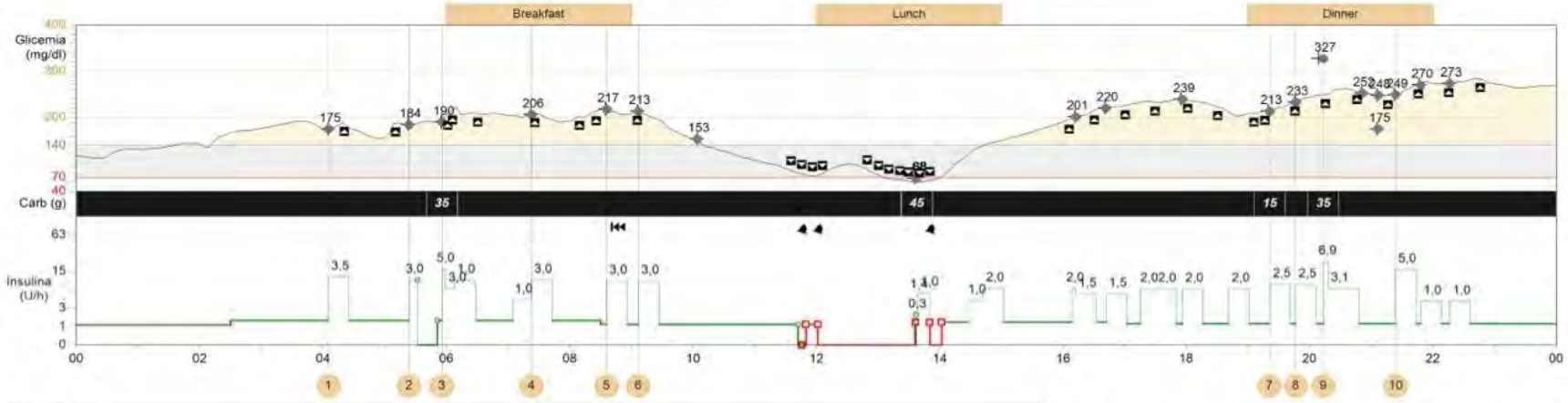


PLGS

The mean (–SD) sensor glucose at predictive suspension was 92–7mg/dL, resulting in a post-suspension nadir (by HemoCue) of 77–22mg/dL. The suspension lasted for 90–35 (range, 30–120) min, resulting in a sensor glucose level at insulin resumption of 97 – 19 mg/dL.

DIABETES TECHNOLOGY & THERAPEUTICS Volume 16, Number 6, 2014

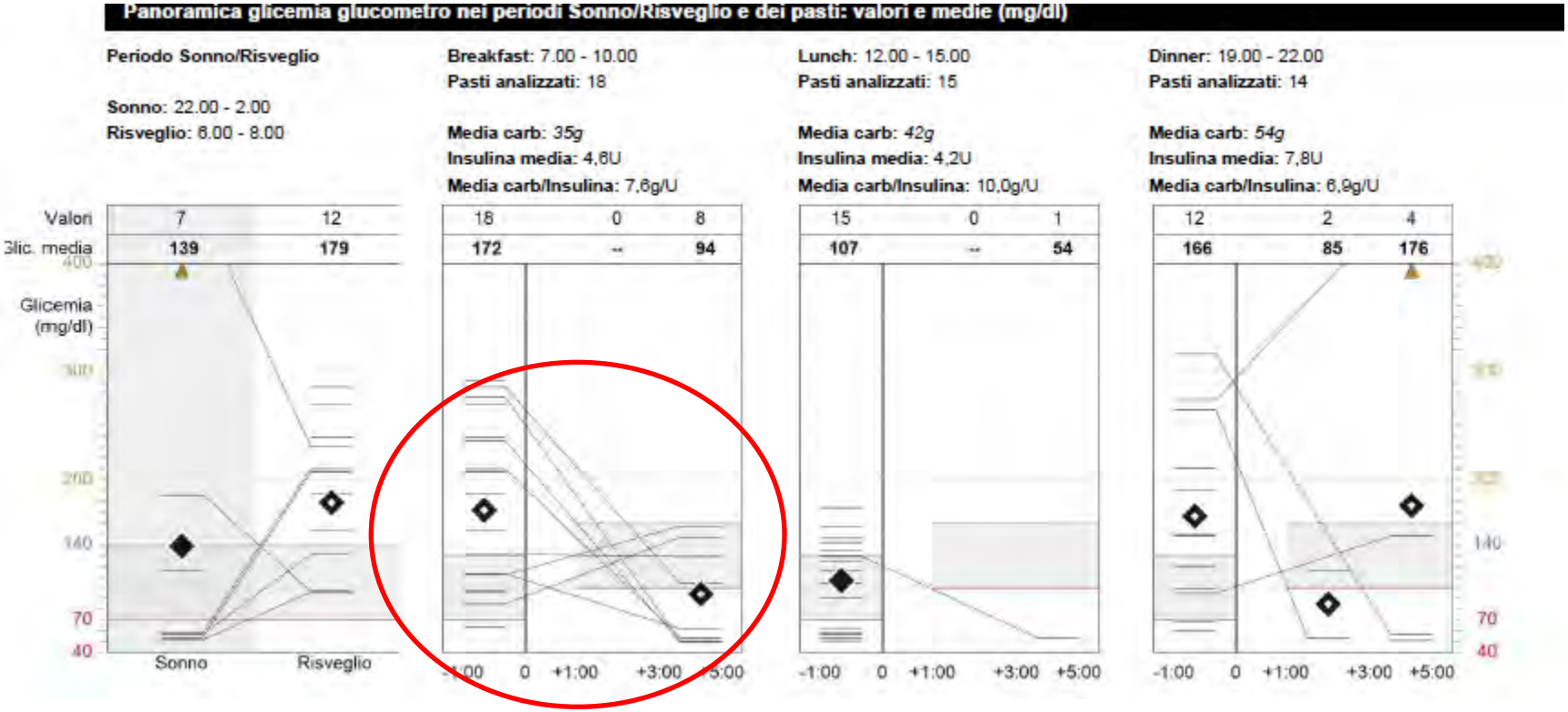
Il Pancreas “Mentale”



Eventi di bolo										
Evento di bolo	1	2	3	4	5	6	7	8	9	10
Ora	04:05	05:23	05:55	07:22	08:35	09:06	19:21	19:46	20:13	21:23
Tipo di bolo	Normale	Normale	Doppia	Normale	Normale	Normale	Normale	Normale	Doppia	Normale
Bolo normale erogato (U)	3,5	3,0	5,0	3,0	3,0	3,0	2,5	2,5	6,9	5,0
+ quantità quadra (U, h:mm)	--	--	3,0, 0:30	--	--	--	--	--	3,1, 0:30	--
Bolo consigliato (U)	3,5	1,2	6,0	--	--	--	2,5	--	7,5	--
Differenza (U)	--	1,8	2,0	3,0	3,0	3,0	--	2,5	2,5	5,0
Carb (g)	--	--	*35*	--	--	--	*15*	--	*35*	--

Statistiche	09/02		09/02 - 26/02	
Glicemia media (mg/dl)	208		203 ± 63	
Valori glicemia	21		308	18,7/giorno
Valori superiori al target	19	90%	260	84%
Valori inferiori al target	2	10%	5	2%
Glic. sens. media (mg/dl)	182 ± 59		178 ± 57	
AUC media > 140 (mg/dl)	52,1	1d 0h	46,4	15d 18h
AUC media < 70 (mg/dl)	0,2	1d 0h	0,2	15d 18h

Ipercorrezione? FSI – I/CHO modificabili?



Eventi di bolo										
Evento di bolo	1	2	3	4	5	6	7	8	9	10
Ora	5.16	5.50	12.50	14.16	14.50	15.39	16.14	21.41	22.44	23.31
Tipo di bolo	Normale	Normale	Normale	Normale	Normale	Normale	Normale	Normale	Normale	Normale
Bolo normale erogato (U)	3,10	3,00	1,00	8,50	2,90	2,50	2,50	3,70	4,50	4,50
+ quantità quadra (U, h:mm)	--	--	--	--	--	--	--	--	--	--
Bolo consigliato (U)	--	--	0,400	--	--	--	--	--	--	--
Differenza (U)	--	--	0,600	--	--	--	--	--	--	--
Carb (g)	--	--	--	--	--	--	--	--	--	--
Imp. rapp. carboidrati (g/U)	--	--	8,0	--	--	--	--	--	--	--
Bolo prandiale (U)	--	--	--	--	--	--	--	--	--	--
Glicemia (mg/dl)	--	--	149	--	--	--	--	--	--	--
Imp. targ glicemico (mg/dl)	--	--	120 - 130	--	--	--	--	--	--	--
Impost. sensibilità insulina (mg/dl per U)	--	--	47	--	--	--	--	--	--	--
Bolo correttivo (U)	--	--	0,400	--	--	--	--	--	--	--
Insulina attiva (U)	0,900	3,40	--	0,700	8,40	8,60	8,40	--	3,00	5,80

*Nota: sono stati rilevati più di 10 boli. Vengono mostrati i 10 boli più grandi.

Aspetti educazionali e psicologici

ALGORITMI DECISIONALI : DirectNet

Tabella 1 Algoritmo per la titolazione del bolo insulinico	
Glicemia stabile	dose del bolo usuale
Glicemia in moderato incremento	↑ bolo 10%
Glicemia in moderato incremento	↑ bolo 20%
Glicemia in moderata discesa	↓bolo 10%
Glicemia in rapida discesa	↓bolo 20%

ALGORITMI DECISIONALI : ALGOS

TREND ARROW	LOW (Below 4.0 pre-meal or below 6.0 after meal or bed-time)	TARGET (4.0-8.0 pre-meal or 6.0-10.0 after meal or bed-time)	HIGH (more than 8.0 pre-meal or more than 10.0 after meal or bed-time)
↑↑	**Recheck** in 10-15 min	**Recheck** in 1 hour. **Confirm meal bolus given**	**Line check Ketone check Correction bolus** and **Recheck in 1-2 hours**
↑	**Eat, Recheck** in 10-15 min	No action	**Line check Ketone check Correction bolus** and **Recheck in 1-2 hours**
No arrows	**EAT.** Set **temp basal. Recheck** in 10-15 min.	No action	**Correction bolus. Recheck in 1-2 hours**
↓	**EAT.** Set **temp basal. Recheck** in 10-15 min.	**6.0-8.0** at **bedtime temp basal** and **recheck** in 1 hr	**Recheck** in 2 hrs. Consider Correction Bolus.
↓↓	**EAT.** Set **temp basal. Recheck** in 10-15 min.	**6.0-8.0 (Bedtime below 10): EAT** (Consider temp basal) and **recheck In 30 min. 4.0-6.0: EAT + temp basal** and **recheck In 15 min.**	**Recheck** in 2 hrs.

Alarms <4.5 and >11.0
Bolus Wizard Target Range 5.0 – 9.0

Insulin Sensitivity: _____
(100/Total raily Insulin Dose = glucose drop for 1 unit insulin)

O'Neal D. EASD 2008

If your blood sugar is 3.9mmol/L or lower: take 15g of simple carbohydrate, and once your glucose is above 3.9mmol/L, then begin to eat your meal, and take your usual insulin bolus to cover all of the carbohydrates in the meal.

If your blood sugar is above 3.9mmol/L: do your usual calculation of the amount of rapid-acting insulin needed to cover the carbohydrates in the meal and the correction for high blood sugar if present

Now look at the receiver screen on your RT-CGM. See if there are any up or down arrows adjacent to your glucose reading. Make the following adjustment to the amount of rapid acting insulin that you just calculated for your meal:

Glucose rising >2.2mmol/L (↑↑) two up arrows	Increase meal dose by 20%
Glucose rising by 1.1-2.2mmol/L (↑) one up arrow	Increase meal dose by 10%
Glucose rising or falling by <1.1mmol/L, no arrows	No change in meal dose of rapid acting insulin
Glucose falling by 1.1-2.2mmol/L (↓) one down arrow	Decrease meal dose by 10%
Glucose falling by >2.2mmol/L (↓↓) two down arrows	Decrease meal dose by 20%

NHS | HEART of ENGLAND NHS Foundation Trust

Insulin Dose Adjustment REAL-Time CGMS Guidelines for Subjects on Pump Therapy

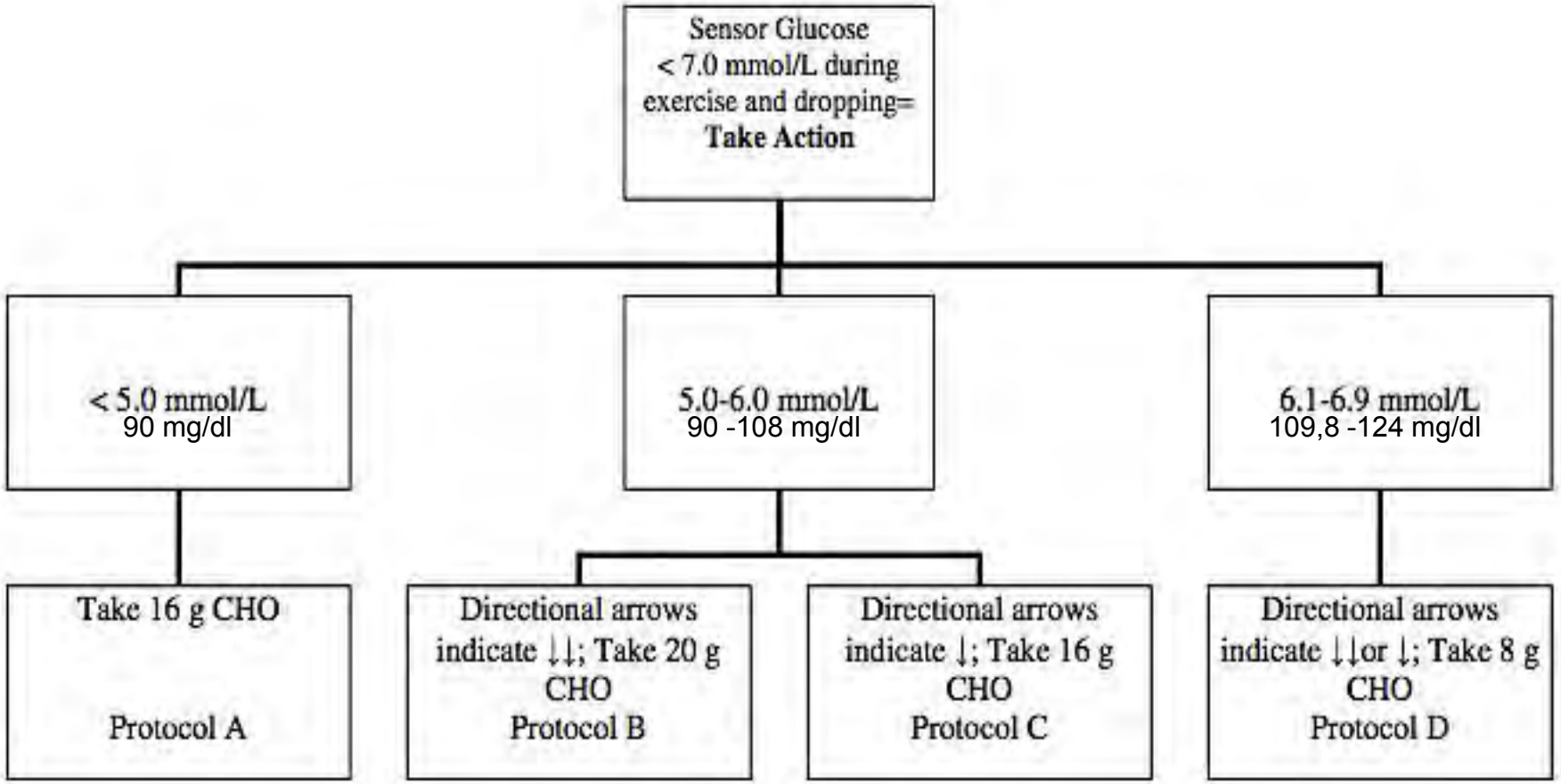
SUGGESTED INSULIN DOSE ADJUSTMENT

Glucose pattern (2-3 days)	Suggested changes
Bedtime	
High	Dinner ICR: increase ratio by 5g (example: if 1:15, change to 1:10).
	Increase the basal rate by 0.05-0.1 units/h between dinner and 8 p.m.
Low	Dinner ICR: decrease ratio by 5g (example: if 1:15, change to 1:20).
	Decrease the basal rate by 0.05-0.1 units/h between dinner and 8 p.m.

When to check your blood sugar with the blood glucose meter:

1. Whenever the RT-CGM calls for a calibration to be entered.
2. When you are going to make an insulin management decision.
3. You have symptoms that are not consistent with the RT-CGM values (for example, you feel low, but the RT-CGM do not show that you are low).
4. Anytime a high or low alarm/event goes off (high or low event is considered first alarm in a 1-h period).

Preventing Exercise-Induced Hypoglycemia in Type 1 Diabetes Using Real-Time Continuous Glucose Monitoring and a New Carbohydrate Intake Algorithm: An Observational Field Study



DIABETES TECHNOLOGY & THERAPEUTICS Volume 13, Number 8, 2011

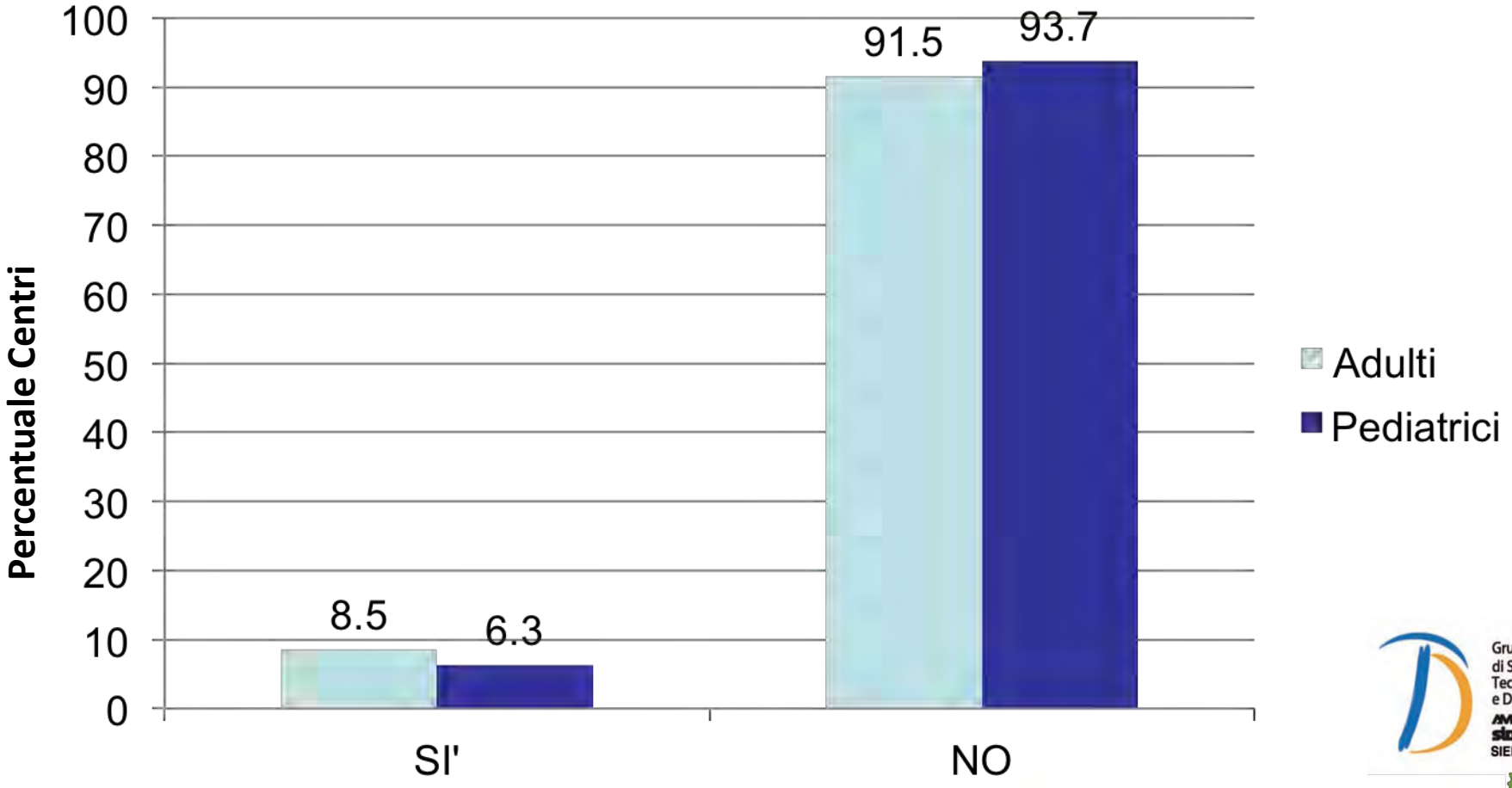
Utilizzo del sensore

Età pazienti	N.pazienti con sistema integrato	N.pazienti che utilizzano sensore	Giorni/mese utilizzo sensore
Adulti (>18 anni)	3202	2246	12,1±8,8
Pediatrici (<18 anni)	753	536	11,8±8,6
Tutti	3955	2782	12,0±8,8

Gruppo di Studio Tecnologie e Diabete
AMD SID SIEDP

I.M.ITA
Indagine Microinfusori

Presenza di Personale dedicato alla CSII: Centri dell'Adulto vs Centri Pediatrici



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I.M.ITA
Indagine Microinfusori

Quello che spesso le persone mi dicono della loro esperienza con Il micro e d il sensore: “Se lo avessi SAPuto prima …….”

Una Tecnologia che aumenta il gradi di “partecipazione” attiva del Paziente alla gestione della terapia