IL DIABETE IN GRAVIDANZA

Chieti, 19-20 aprile 2018

DALLA RICERCA ALLA PRATICA CLINICA



Tecnologia e Diabete tipo 2 in Gravidanza…

Quale contributo?

Raffaella Fresa

Struttura diabetologica di II° livello

Asl Salerno



introduzione

- Il parallelo aumento dell’obesità e del diabete tipo 2 nella popolazione, in particolare nelle fasce di età più giovani, si riflette in un incremento delle gravidanze complicate da diabete tipo 2



- E’ ancora da dimostrare con chiarezza se le gravidanze complicate da DMT2 abbiano outcome uguali o più seri** di quelle con DMT1.
- ipotesi: mancanza di informazione e quindi di ottimizzazione del compenso
- Scarsa abilità alla gestione della terapia insulinica intensiva
- Di certo la dimensione del problema è rilevante

- ** Murphy, Mathiensen; Corcoy

Poor Pregnancy Outcome in Women With Type 2 Diabetes

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DIABETES CARE, VOLUME 28, NUMBER 2, FEBRUARY 2005

before 24 weeks' gestation in 57 pregnancies in women with type 2 diabetes compared with pregnancies in women with type 1 diabetes (3,4). In 182 pregnancies

Table 2—*Complications in pregnancy and perinatal outcome*

	Type 2 diabetes	Type 1 diabetes	*P*
n	61	240	
Complications in pregnancy			
Pregnancy-induced hypertension	6 (10)	12 (5)	0.22
Preeclampsia	4 (7)	30 (13)	0.26
Caesarean delivery	22 (36)	123 (51)	0.04
Perinatal outcome			
Congenital malformations	4 (6.6)	7 (2.9)	0.24
Perinatal mortality	4 (6.7)	4 (1.7)	0.05
Gestational age (weeks)*	38.0 (37–39)	37.3 (36–38)	0.03
Birth <34 weeks' gestation*	8 (14)	17 (7)	0.19
Birth <37 weeks' gestation*	18 (31)	87 (38)	0.29
Birth weight (g)*	3,600 (3,095–3,990)	3,595 (3,064–3,925)	0.79
Large for gestational age*	33 (56)	117 (51)	0.54
Small for gestational age*	1 (2)	9 (4)	0.35
Birth weight >4,500 g*	5 (8)	11 (5)	0.27
Neonatal jaundice*	13 (22)	40 (18)	0.35
Respiratory difficulties*	12 (20)	52 (23)	0.79

Data are medians (interquartile range) or *n* (%). *The total of live-born singleton infants was 59 for type 2 diabetes and 228 for type 1 diabetes.

Glycemic control during pregnancy			
HbA_{1c} at admission (%)	6.8 (6.1–7.7)	7.0 (6.5–7.8)	0.41*
HbA_{1c} second trimester (%)	5.7 (5.2–6.2)	6.3 (5.8–6.8)	0.002*
HbA_{1c} third trimester (%)	5.9 (5.5–6.2)	6.3 (5.9–6.7)	0.005*

Maternal and Fetal Outcome in Women with Type 2 *Versus* Type 1 Diabetes Mellitus: A Systematic Review and Metaanalysis

Montserrat Balsells, A. García-Patterson, I. Gich, and R. Corcoy

J Clin Endocrinol Metab, November 2009, 94(11):4284–4291

33 studi in 20yr type 2 vs type 1
Main outcomes : Stillbirth; **perinatal mortality**
Neonatal mortality; congenital malformations
Gli altri outcome non sono inferiori rispetto al tipo 1

		tipo 2	tipo 1
HbA1c (%)			
At booking	9	7.20	8.06
Second trimester	4	5.70	6.23
Third trimester	7	5.69	6.00

n, Number of papers contributing to each characteristic

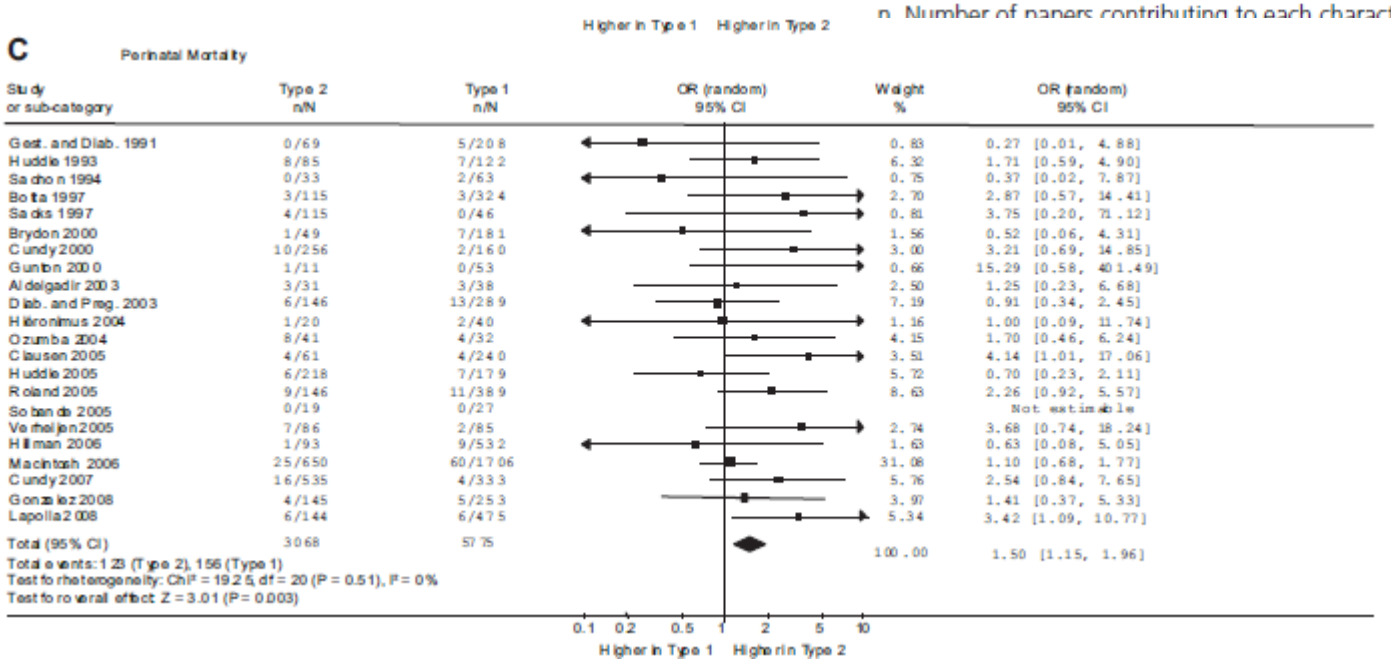


TABLE 3. Systematic review of type 2 *vs.* type 1 diabetic pregnancies: maternal and fetal secondary outcomes

Secondary outcomes	n	Heterogeneity (I^2) (%)	OR (95% CI)	*P* value
Maternal				
Pregnancy-induced-hypertension	9	48	0.87 (0.61–1.25)	NS
Preeclampsia	7	0	0.85 (0.61–1.17)	NS
Hypoglycemic coma	3	59.3	0.17 (0.03–1.11)	0.06
Diabetic ketoacidosis	5	0	0.09 (0.02–0.34)	<0.001
Cesarean section	18	33.0	0.80 (0.68–0.94)	<0.01
Fetal				
Miscarriages	7	0	1.36 (0.98–1.90)	0.07
Pregnancy terminations	6	0	1.02 (0.48–2.16)	NS
Preterm birth	17	23.6	0.85 (0.70–1.03)	NS
Small for gestational age newborns	10	27.6	1.30 (0.80–2.11)	NS
Large for gestational age newborns	14	14.5	0.98 (0.81–1.18)	NS
Macrosomia	6	23.0	1.02 (0.68–1.52)	NS
MCM	2	0	1.00 (0.27–3.70)	NS
Hypoglycemia	11	31.0	0.85 (0.62–1.16)	NS
Jaundice	7	0	0.82 (0.63–1.08)	NS
Respiratory distress	10	39.0	0.67 (0.41–1.09)	NS

n, Number of papers contributing to each outcome; NS, not significant.

Diabetologia (2017) 60:1668–1677
DOI 10.1007/s00125-017-4314-3

ARTICLE

Improved pregnancy outcomes in women with type 1 and type 2 diabetes but substantial clinic-to-clinic variations: a prospective nationwide study

Helen R. Murphy[1,2] · Ruth Bell[3] · Cher Cartwright[4] · Paula Curnow[4] · Michael Maresh[5] · Margery Morgan[6] · Catherine Sylvester[4] · Bob Young[4] · Nick Lewis-Barned[7]

Aims/hypothesis The aim of this prospective nationwide study was to examine antenatal pregnancy care and pregnancy outcomes in women with type 1 and type 2 diabetes, and to describe changes since 2002/2003.
Methods This national population-based cohort included 3036 pregnant women with diabetes from 155 maternity clinics in England and Wales who delivered during 2015. The main outcome measures were maternal glycaemic control, preterm delivery (before 37 weeks), infant large for gestational age (LGA), and rates of congenital anomaly, stillbirth and neonatal death.

	tipo 1	tipo 2	
Early pregnancy HbA_{1c}	*n* = 1306	*n* = 1024	
%	7.6 (6.8–8.7)	6.8 (6.2–8.0)	<0.001
mmol/mol	60.0 (51.0–72.0)	51.5 (44.0–64.3)	
HbA_{1c} < 6.5% (48 mmol/mol)	16.2%	38.3%	
Late pregnancy HbA_{1c}	*n* = 1210	*n* = 1017	
%	6.7 (6.1–7.5)	5.9 (5.5–6.5)	<0.001
mmol/mol	50 (43–58)	41 (37–47)	
HbA_{1c} < 6.5% (48 mmol/mol)	40.0%	76.0%	
Perinatal outcomes[c,d]			
Gestational age at delivery (weeks)	36.4 (2.0)	37.1 (2.0)	<0.001
Preterm delivery $<37^{+0}$ weeks	568 (39.7%)	278 (21.7%)	<0.05
LGA >90th percentile	667 (46.4%)	307 (23.9%)	<0.05
LGA >97.7th percentile	423 (29.4%)	180 (14.0%)	
Serious adverse pregnancy outcome[d]			
Congenital anomaly	69 (46.2/1000)	46 (34.6/1000)	NS
Stillbirth	16 (10.7/1000)	14 (10.5/1000)	NS
Neonatal death	12 (8.1/1000)	15 (11.4/1000)	NS



STUDIO ITALIANO MULTICENTRICO
Caratteristiche Materne

	DM Tipo 2 n. 164	DM Tipo 1 n. 504
Età (anni)	33.2*	29.9
Durata del Diabete (anni)	5.7 *	13.4
BMI pre-gravidico (Kg/m^2)	28.1*	23.3
Counselling Pre-gravidico (%)	29.1*	43.9

Lapolla A et al 2007 *Nutr Metab Cardiovasc Dis*

* $p<0.05$



- E’ a tutti noi nota la correlazione tra obesità e outcome avversi materno-fetali:
- cesarean section
- gestational diabetes
- hypertensive disorders
- birth defects and prematurity

- A ciò vanno aggiunti:
- Mancanza di programmazione
- Difficoltà ad ottenere uno stretto controllo metabolico nella fase precoce di gravidanza
- Condizioni socio-economiche



Diabete tipo 2 e CSII

- posizione delle NICE 2008:
- In DMT2 non raccomandata
- In DMT2 e gravidanza si raccomanda la terapia insulinica già in fase pregestazionale
- di raggiungere gli stessi obiettivi metabolici del DMT1
- ADA, NICE, Standard Italiani



Glycemic Control During Continuous Subcutaneous Insulin Infusion Versus Multiple Daily Insulin Injections in Type 2 Diabetes: Individual Patient Data Meta-analysis and Meta-regression of Randomized Controlled Trials

John C. Pickup,[1] Yves Reznik,[2] and Alex J. Sutton[3]

Diabetes Care 2017;40:715–722 | DOI: 10.2337/dc16-2201

CONCLUSIONS

CSII achieves better glycemic control than MDI in people with poorly controlled type 2 diabetes, with ~26% reduction in insulin requirements and no weight change. The best effect is in those worst controlled and with the highest insulin dose at baseline.

DIABETES TECHNOLOGY & THERAPEUTICS
Volume 20, Number 2, 2018
Mary Ann Liebert, Inc.
DOI: 10.1089/dia.2017.0283

DTT

ORIGINAL ARTICLE

Complex Assessment of Metabolic Effectiveness of Insulin Pump Therapy in Patients with Type 2 Diabetes Beyond HbA1c Reduction

Rudolf Chlup, MD,[1–3] Sarah Runzis, MSc,[4] Javier Castaneda, MSc,[5] Scott W. Lee, MD,[6] Xuan Nguyen,[6] and Ohad Cohen, MD[7]

Conclusion: CSII therapy safely and significantly improved metabolic control with less insulin usage, with no sustainable reduction of BM, blood pressure, and lipid profile, in insulin-resistant T2D patients. Treatment adherence and satisfaction in these patients were excellent.



Use of Insulin Pumps in Pregnancies Complicated by Type 2 Diabetes and Gestational Diabetes in a Multiethnic Community

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Diabetes Care 24:2078–2082, 2001

OBJECTIVE — To describe the use of insulin pump therapy in women with gestational diabetes mellitus (GDM) or type 2 diabetes in pregnancy and persistent hyperglycemia despite multiple injections of subcutaneous insulin.

RESULTS — A total of 30 of 251 Polynesian, European, and South Asian women with singleton pregnancies complicated by insulin-requiring GDM/type 2 diabetes used an insulin pump. An additional two women with high insulin requirements discontinued pump therapy. None of the women with GDM/type 2 diabetes experienced severe hypoglycemia, whereas 79% of the women had improved glycemic control within 1–4 weeks. Mothers using a pump had greater insulin requirements (median maximum 246 vs. 130 units per day) and greater weight gain (10.6 vs. 5.0 kg). Their babies were more likely to be admitted to the Special Care Baby Unit but were neither significantly heavier nor experienced greater hypoglycemia than control subjects.

CONCLUSIONS — Insulin pump therapy seems to be safe and effective for maintaining glycemic control in pregnancies complicated by GDM/type 2 diabetes and requiring large doses of insulin.



Insulin Pump for Type 2 Diabetes

Use and misuse of continuous subcutaneous insulin infusion in type 2 diabetes

DIABETES CARE, VOLUME 36, SUPPLEMENT 2, AUGUST 2013

YVES REZNIK, MD[1]
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Razionale alla CSII nel DMT2 e in gravidanza

- Non ci sono studi controllati sufficienti
- Miglior controllo glicemico rispetto a MDI
- Basale flessibile e basale temporanea
- Flessibilità nei boli
- Minori ipoglicemie
- Contenimento del peso corporeo
- Migliore qualità della vita

Vantaggi sovrapponibili al tipo 1

Lo scarico dati facilita l' **insight del paziente e del medico sul controllo metabolico, i comportamenti e le sue necessità educative**

Insulin pump therapy may be offered to pregnant women with gestational diabetes mellitus or type 2 diabetes who fail to obtain adequate glycemic control with a basal/bolus regimen, need very high insulin requirements, or experience persistent accelerated fetal growth despite optimal conventional MDI regimen.



Donna con diabete tipo 2 a 8 sett. BMI 39

At 6 weeks: HbA1c 6,8% and total daily dose (TDD) of 32 U/day with a ratio of 25% basal and 75% boluses and after one week the total daily dose increased to 54 U with no good control after lunch and dinner

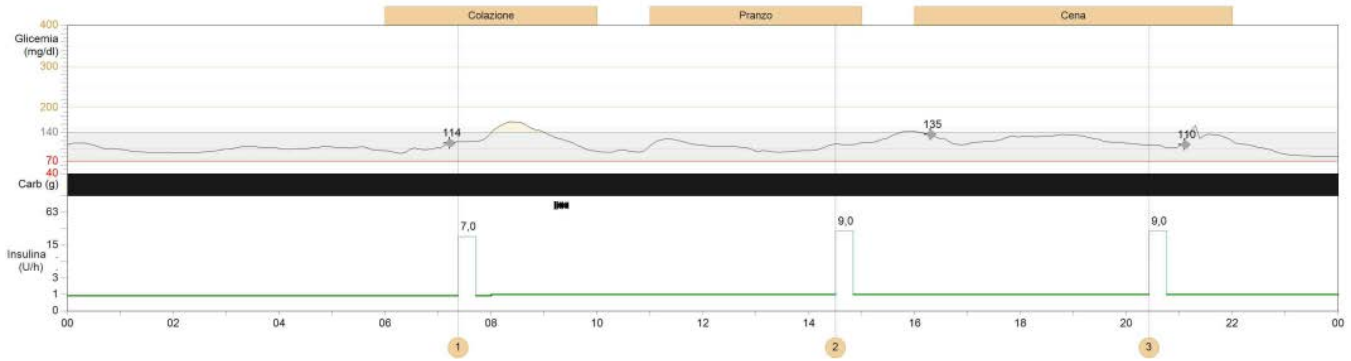
SAP →

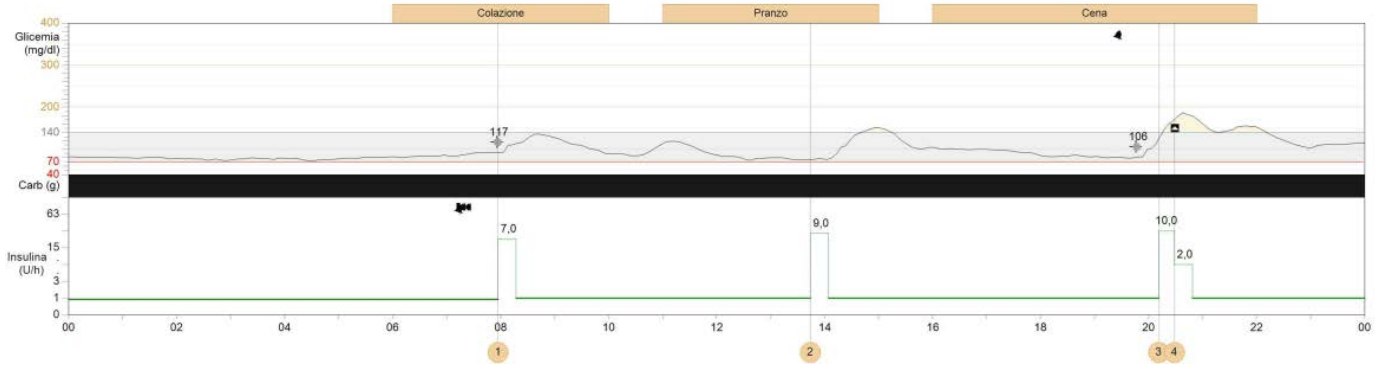
61 U/die in MDI 8°
55 U/die impianto 8°
60 U/die a 20 sett
65 a 28 sett
71 a 30 sett
85 U/die a 36 sett

	Mean CBG	Mean sensor values	Time on sensor (day/hours)	AUC>140	AUC<70	Total daily dose	Basal/bolus %
30 days Before SAP	140.8 ± 38					61 U	30/70
2 days After SAP	86 ± 20 (n=6)	94 ±30	1d 20h	1.6	2.4	52.1 U	54/46
30 days after SAP	100±19 (n=47)	103± 28	20d 8h	2.3	0.7	54.3± 3.6	44/55



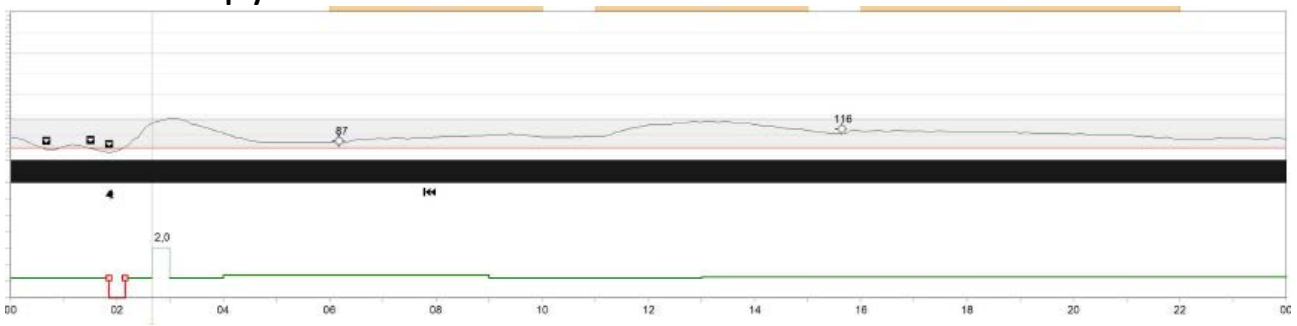
Donna con diabete tipo 2 a 8 sett. BMI 39





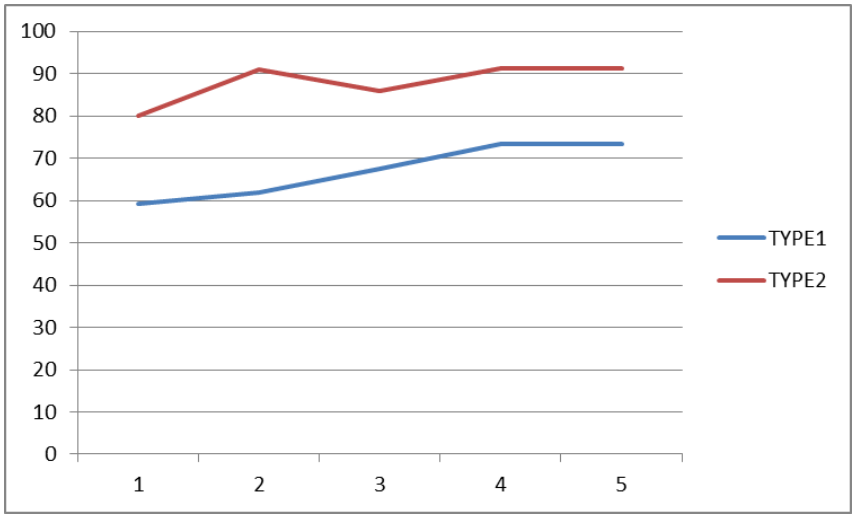
Weight (Kg)	90 a 6wk	93 a 28wk	99 a 36wk

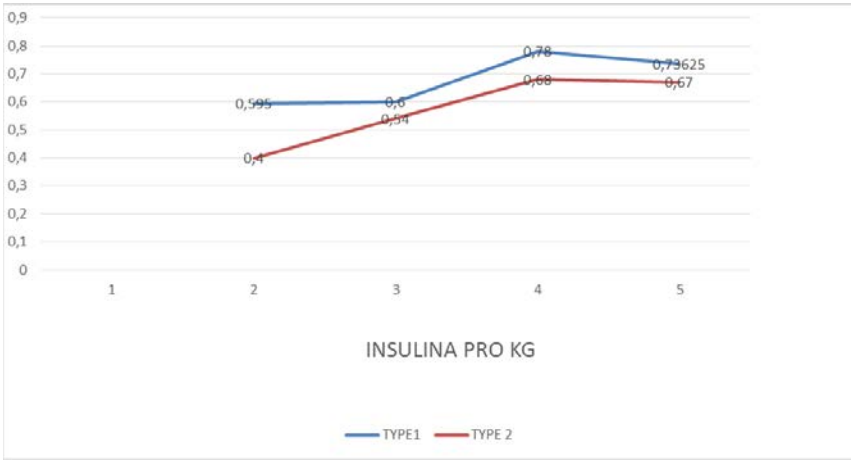
- At the 36th week (HbA1c 5,3%) we registered a repentine weight gain (4 Kg) in 15 days associated to an increase of blood pressure values and a worsening of glycemic control. According to the gynecologist, she delivered a female of 3.150 Kg with an elective c-section and with SAP therapy on



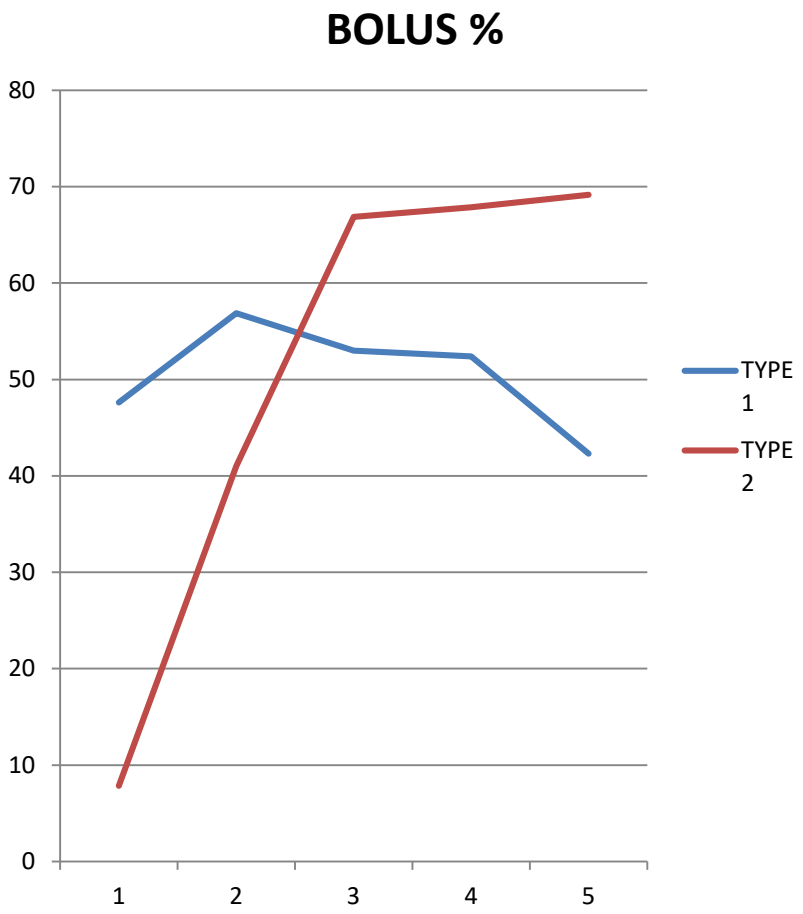
	CBG	Sensor values	AUC >140	AUC <70
36wk	104+16	116+25	2.9	0
1d bef	110	113+26	3	0
deliv	102	102+17	0	0,2
1° aft	95	96+15	0	0
2° aft	128	111+24	1,7	0,1

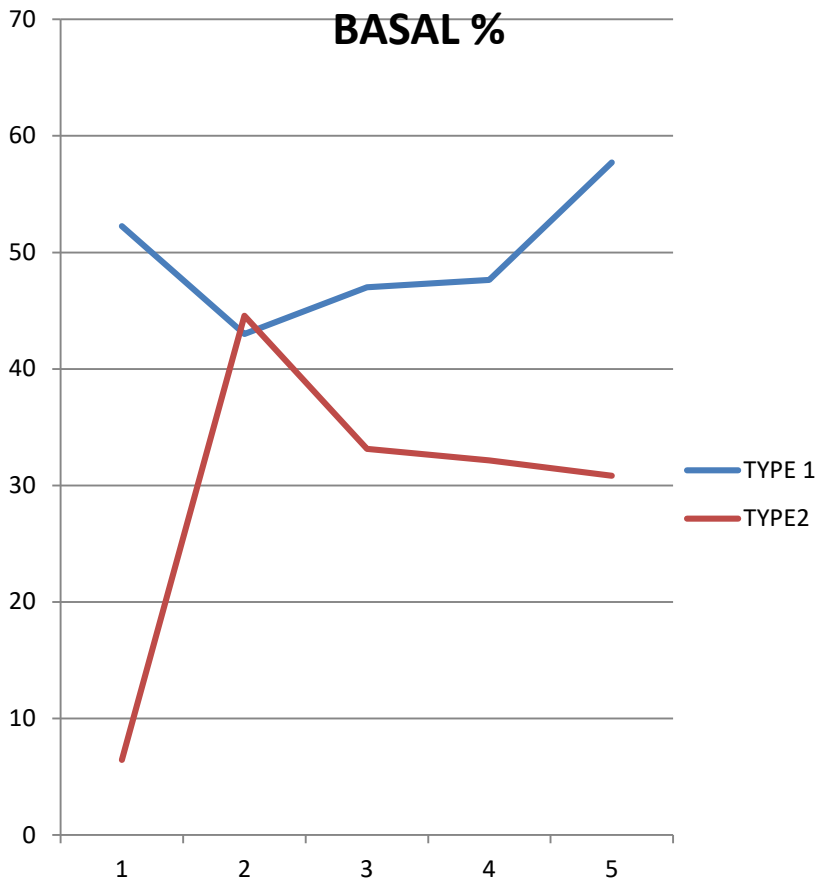
Peso e insulina type 1 vs type 2

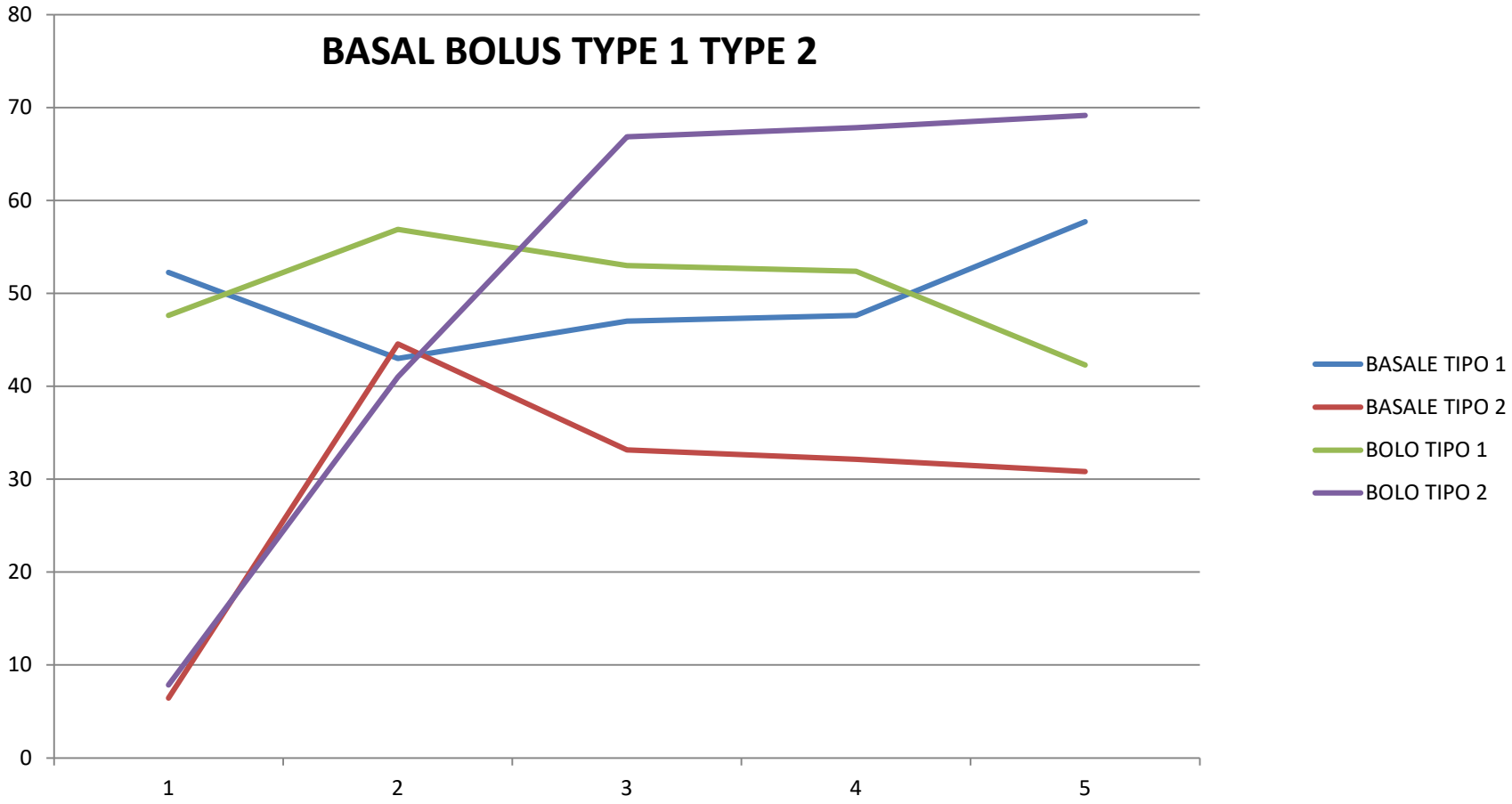




% Bolo Basale TYPE1 VS TYPE 2






BASAL BOLUS TYPE 1 TYPE 2
80
70
60
50
40
30
20
10
0
1
2
3
4
5
BASALE TIPO 1
BASALE TIPO 2
BOLO TIPO 1
BOLO TIPO 2



conclusioni

- Se in letteratura la CSII da sola non ha mostrato vantaggi….
- Importante può essere l’ ausilio del monitoraggio glicemico in tempo reale (sistema integrato) come strumento educativo per la paziente, grazie al quale è stato possibile contenere l’assunzione di cibo e quindi il peso finale, le glicemie e le dosi di insulina.