Pro e contro in tema di microinfusori: microinfusore stand alone vs SAP

Pro CSII STAND ALONE

Dott.ssa Ilaria Barchetta
Dipartimento di Medicina Sperimentale
Università Sapienza, Roma

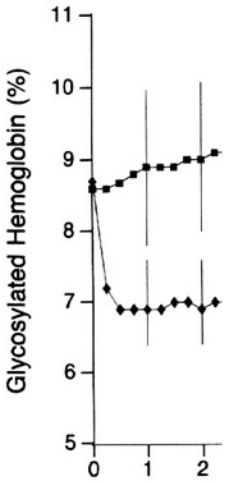
VENERDÌ 21 Giugno 2019
ROMA || Starhotels Metropole

La Dr.ssa Ilaria Barchetta dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

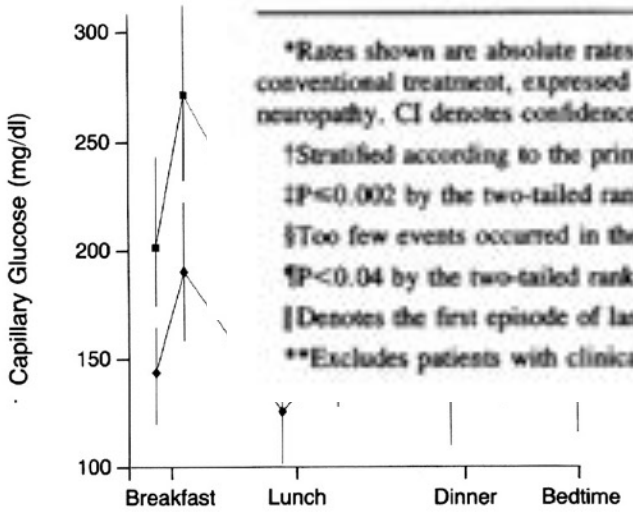
- Eli Lilly
- Menarini
- Astra Zeneca
- MSD
- Sanofi
- Roche
- Novo Nordisk

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, etc.)

Intensive therapy effectively delays the onset and slows the progression of diabetic complications



A



Complications	Primary Prevention			Secondary Intervention			Both Cohorts†
	Conventional Therapy	Intensive Therapy	Risk Reduction	Conventional Therapy	Intensive Therapy	Risk Reduction	Risk Reduction
	rate/100 patient-yr		*% (95% CI)*	*rate/100 patient-yr*		*% (95% CI)*	*% (95% CI)*
≥3-Step sustained retinopathy	4.7	1.2	76 (62–85)‡	7.8	3.7	54 (39–66)‡	63 (52–71)‡
Macular edema§	—	—	—	3.0	2.0	23 (−13–48)	26 (−8–50)
Severe nonproliferative or proliferative retinopathy§	—	—	—	2.4	1.1	47 (14–67)¶	47 (15–67)¶
Laser treatment§‖	—	—	—	2.3	0.9	56 (26–74)‡	51 (21–70)¶
Urinary albumin excretion (mg/24 hr)							
≥40	3.4	2.2	34 (2–56)¶	5.7	3.6	43 (21–58)‡	39 (21–52)‡
≥300	0.3	0.2	44 (−124–86)	1.4	0.6	56 (18–76)¶	54 (19–74)¶
Clinical neuropathy at 5 yr**	9.8	3.1	69 (24–87)¶	16.1	7.0	57 (29–73)‡	60 (38–74)‡

*Rates shown are absolute rates of the development and progression of complications per 100 patient-years. Risk reductions represent the comparison of intensive with conventional treatment, expressed as a percentage and calculated from the proportional-hazards model with adjustment for base-line values as noted, except in the case of neuropathy. CI denotes confidence interval.

†Stratified according to the primary-prevention and secondary-prevention cohorts.

‡$P \leq 0.002$ by the two-tailed rank-sum test.

§Too few events occurred in the primary-prevention cohort to allow meaningful analysis of this variable.

¶$P < 0.04$ by the two-tailed rank-sum test.

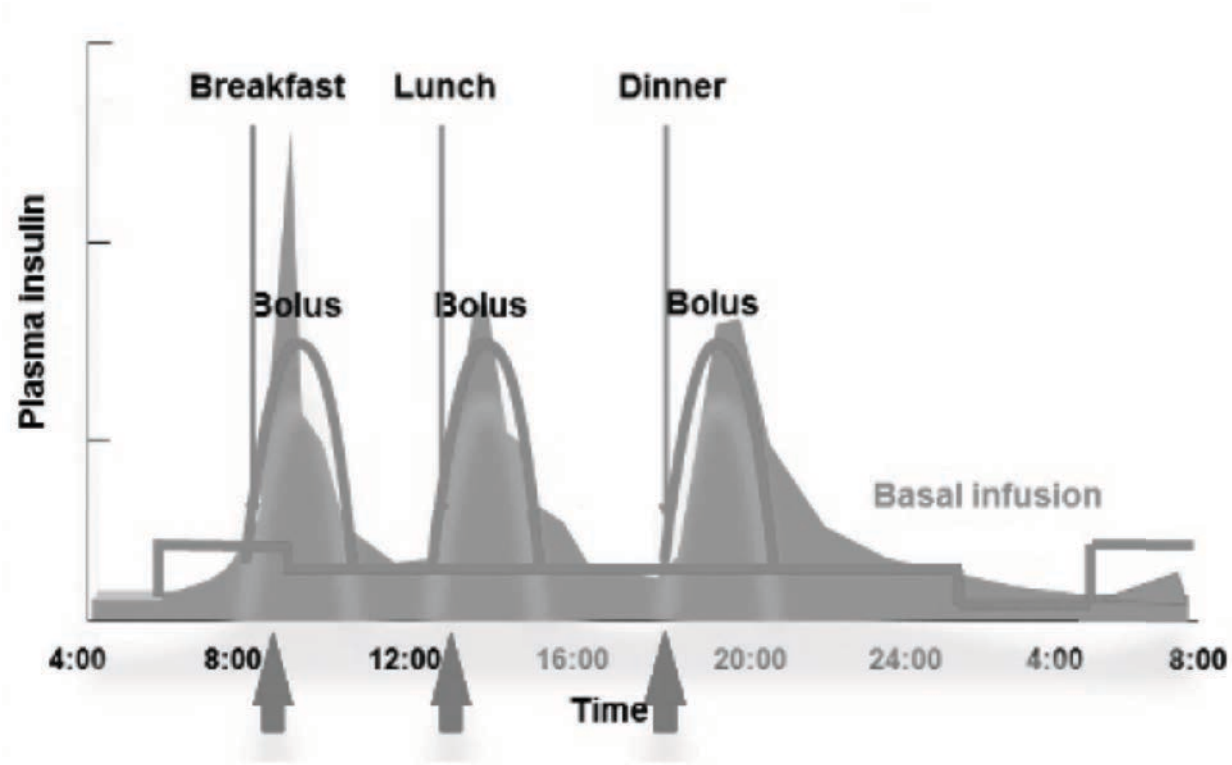
‖Denotes the first episode of laser therapy for macular edema or proliferative retinopathy.

**Excludes patients with clinical neuropathy at base line.

The Diabetes Control and Complications Trial Research Group. N Engl J Med 1993;329:977-986

Continuous subcutaneous insulin infusion (CSII)

La terapia insulinica sottocutanea continua con microinfusore rappresenta il **gold standard della terapia insulinica intensiva**, in quanto in grado di mimare più fisiologicamente la secrezione insulinica pancreatica e di permettere aggiustamenti più accurati della dose insulinica.



DIABETICMedicine

DOI: 10.1111/j.1464-5491.2007.02365.x

Original Article: Clinical Care

In Type 1 diabetic patients with good glycaemic control, blood glucose variability is lower during continuous subcutaneous insulin infusion than during multiple daily injections with insulin glargine

D. Bruttomesso, D. Crazzolara, A. Maran, S. Costa, M. Dal Pos, A. Girelli*, G. Lepore†, M. Aragona‡, E. Iori, U. Valentini*, S. Del Prato‡, A. Tiengo, A. Buhr§, R. Trevisan† and A. Baritussio¶

Multicentre, open-label, randomized, cross-over trial
RCT performed on 39 pts treated with CSII
in good glycaemic control and randomized at CSII or MDI

Primary end-point: **blood glucose variability**
Secondary end-points: blood glucose concentrations, number and severity of hypo/hyperglycaemic episodes, number of episodes of ketoacidosis, insulin requirement, body weight, HbA1c, lipid profile, serum FFA and hGH, and treatment satisfaction.

Table 1 Baseline characteristics of participants

Variable	MDI to CSII (N = 15)	CSII to MDI (N = 24)
Sex (F/M)	8/7	12/12
Age (years)	35.5 ± 10.2	39.8 ± 8.4
Weight (kg)	66.8 ± 11.7	71.0 ± 12.9
BMI (kg/m^2)	22.9 ± 2.1	24.1 ± 3.2
Duration of diabetes (years)	15.7 ± 9.6	17.2 ± 7.3
Duration of CSII (years)	3.2 ± 2.6	3.6 ± 2.9
Daily insulin dose (IU/kg)	0.49 ± 0.14	0.52 ± 0.12
Basal (IU/kg)	0.28 ± 0.08	0.30 ± 0.08
Bolus (IU/kg)	0.23 ± 0.08	0.24 ± 0.09
HbA_{1c} (%):		
at screening (week −4)	7.5 ± 0.7	7.6 ± 0.9
at randomization (week 0)	7.4 ± 0.7	7.4 ± 0.7

Data are means ± SD. N = number of patients. None of the differences between the two sequence groups was significant. BMI, Body mass index; MDI, multiple daily injections; CSII, continuous subcutaneous insulin infusion.

Bruttomesso D et al, Diabetic Medicine 2008

During CSII, glucose variability was 5–12% lower than during MDI with glargine.
Although HbA 1c was similar during both treatments, during CSII blood glucose levels were significantly lower, hyperglycaemic episodes were fewer, daily insulin dose was less, and treatment satisfaction was greater than during MDI with glargine.
The frequency of hypoglycaemic episodes was similar during both treatments.

Variable	Unit	CSII (M ± SD)	MDI with glargine (M ± SD)	Mean difference (CSII-MDI)	Mean difference (95% CI)	*P*-value
Self-monitored blood glucose						
Morning	mmol/l	8.4 ± 3.8	8.8 ± 4.1	–0.49	–1.07, 0.08	0.087
Before lunch	mmol/l	7.4 ± 3.1	8.0 ± 3.4	–0.59	–1.06, –0.14	0.011
Before evening meal	mmol/l	7.9 ± 3.7	8.7 ± 4.0	–0.66	–1.17, –0.13	0.014
All day measurements	mmol/l	8.2 ± 3.8	8.5 ± 3.9	–0.35	–0.62, –0.08	0.012
Blood glucose standard deviation						
Morning	mmol/l	3.3 ± 0.9	3.7 ± 0.8	–0.40	–0.71, –0.10	0.011
Before lunch	mmol/l	2.8 ± 0.8	3.0 ± 0.9	–0.20	–0.48, 0.08	0.152
Before evening meal	mmol/l	3.4 ± 1.1	3.5 ± 1.0	–0.06	–0.33, 0.21	0.678
All day measurements	mmol/l	3.5 ± 0.8	3.7 ± 0.7	–0.18	–0.37, 0.004	0.054
MAGE	mmol/l	7.1 ± 2.0	7.7 ± 1.9	–0.54	–0.99, –0.11	0.016
Lability index	$[(mmol/l)^2/h] \times week$	310.5 ± 89.2	331.3 ± 94.2	–20.8	–35.06, –6.56	0.005
ADRR	BG risk*	25.52 ± 7.95	26.93 ± 6.88	–1.40	–3.35, 0.55	0.153

Measurements taken during the last month of CSII or MDI with glargine.
MAGE, Mean amplitude of glycaemic excursions; ADRR, average daily risk range; MDI, multiple daily injections; CSII, continuous subcutaneous insulin infusion.
*BG Risk calculated according to reference 21. $n = 39$. Paired *t*-test.

Bruttomesso D et al, Diabetic Medicine 2008

Continuous Subcutaneous Insulin Infusion Is Better Than Multiple Daily Insulin Injections in Reducing Glucose Variability Only in Type 1 Diabetes With Good Metabolic Control

The aim of this study was to evaluate whether CSII reduces glucose variability with respect to MDI, in patients with comparable A1C levels

- *36 type 1 diabetic patients, treated with CSII (15 male and 21 female subjects, aged 35 ± 12 years, duration of diabetes 16 ± 11 years, A1C 8.3 ± 1.5%)*
- *77 patients treated with MDI (35 male and 42 female subject, aged 40 ± 15 years, duration of diabetes 17 ± 12 years, A1C 8.5 ± 1.4%)*

The patients in the CSII quartile with the best metabolic control (A1C < 7.5%) showed a significantly lower glucose variability than the MDI group.

The indexes of glucose variability of the two groups were similar when mean HbA1c was between 7.5 and 9.2%.

In the quartile with the worst metabolic control (A1C > 9.2%), the CSII group showed higher glucose variability than the MDI group.

CSII particolarmante vantaggioso quando si vuol mantenere un controllo glicemico ottimale

Lepore G et al, Diabetes Care 2010

The Effects of Subcutaneous Insulin Infusion Versus Multiple Insulin Injections on Glucose Variability in Young Adults with Type 1 Diabetes: The 2-Year Follow-Up of the Observational METRO Study

Maria Ida Maiorino, MD, PhD,[1,*] Giuseppe Bellastella, MD, PhD,[1,*] Ofelia Casciano, MD, PhD,[1] Paolo Cirillo, BS,[1] Vittorio Simeon, MSc, PhD,[2] Paolo Chiodini, MSc,[2] Michela Petrizzo, MD, PhD,[3] Maurizio Gicchino, MD, PhD,[3] Ornella Romano, MD,[1] Paola Caruso, MD,[1] Dario Giugliano, MD, PhD,[1] and Katherine Esposito, MD, PhD[1,3]

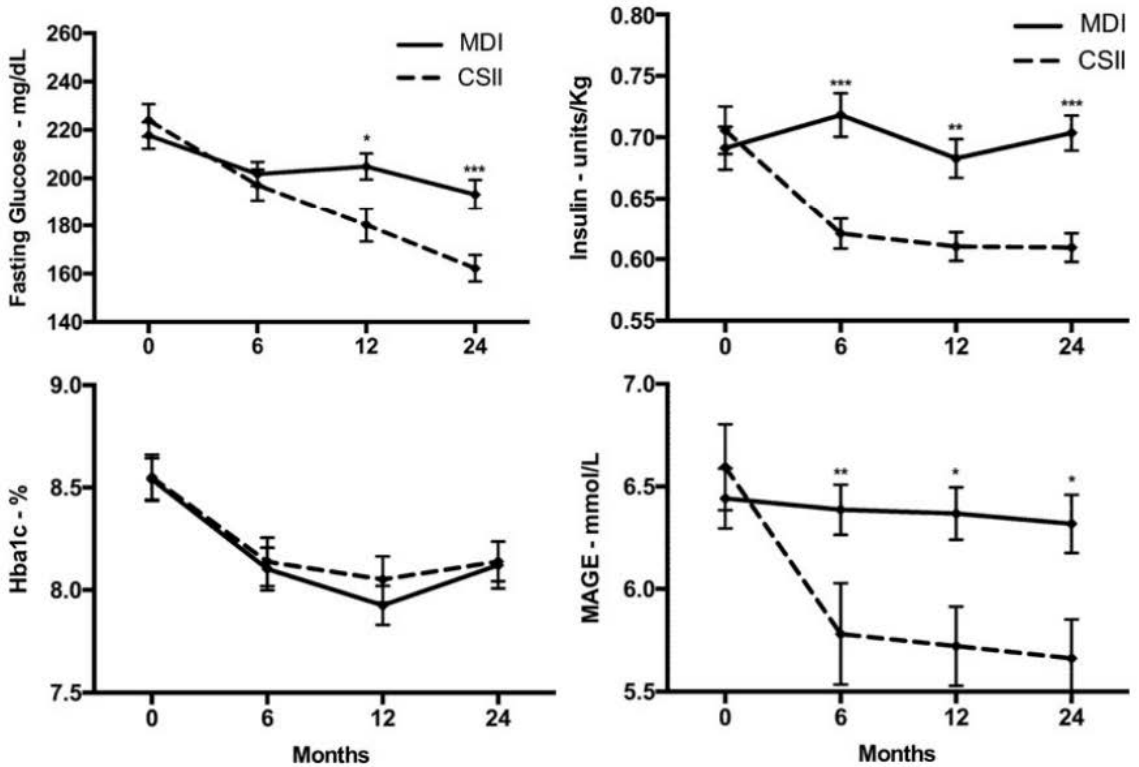


FIG. 2. HbA1c levels, MAGE, fasting glucose, and insulin dose at 6, 12, and 24 months in all the study patients according to insulin regimen. Values are mean ± SE. Asterisks denote significant differences for all comparisons between pump therapy and injection therapy at each time point. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$. MAGE, mean amplitude of glycemic excursion.

DIABETES TECHNOLOGY & THERAPEUTICS
Volume 20, Number 2, 2018
© Mary Ann Liebert, Inc.
DOI: 10.1089/dia.2017.0334

Table 3. Main Outcomes at 2 Years

Parameter	CSII (n=98)			MDI (n=125)			Adjusted difference[a] (95% CI)	P value
	Baseline	End point	Difference	Baseline	End point	Difference		
Weight, Kg	70.7±10.7	71.6±10.7	0.85±3.73	69.9±9.5	70.3±10.0	0.45±4.48	0.63 (−2.11, 3.42)	0.65
BMI, kg/m^2	24.8±3.3	25.1±3.2	0.32±1.49	24.2±2.9	24.4±2.7	0.23±1.75	0.12 (−0.65, 0.93)	0.75
Fasting glucose, mg/dL	224.1±67.1	162.3±54.5	−61.73±72.4	217.8±61.7	193.3±67.5	−24.5±74.6	−31.2 (−47.91, −14.42)	<0.001
Fasting glucose, mM	12.4±3.7	9.0±3.0	−3.4±4.0	12.1±3.4	10.7±3.8	−1.4±4.1	−1.7 (−2.7, −0.8)	<0.001
HbA1c,%	8.6±1.1	8.1±1.0	−0.41±1.07	8.5±1.2	8.1±1.3	−0.42±1.0	0.05 (−0.26, 0.35)	0.77
HbA1c, mmol/mol	70.5	65.0	—	69.4	65.0	—	—	0.77
Insulin dose, UI/kg	0.73±0.2	0.63±0.1	−0.10±0.14	0.72±0.2	0.73±0.2	0.01±0.14	−0.1 (−0.15, −0.06)	<0.001
Prandial	0.36±0.1	0.31±0.2	−0.05±0.15	0.35±0.2	0.35±0.1	0.01±0.12	−0.06 (−0.14, 0.02)	0.13
Basal	0.37±0.2	0.32±0.1	−0.05±0.13	0.37±0.1	0.38±0.1	0.01±0.14	−0.06 (−0.13, 0.01)	0.09
MAGE, mM	6.6±2.1	5.7±1.9	−0.93±2.55	6.4±1.6	6.3±1.6	−0.12±1.03	−0.74 (−1.22, −0.26)	<0.01
CONGA-2 h, mM	6.6±1.6	6.3±1.7	−0.31±1.47	6.6±1.8	6.4±1.8	−0.19±0.92	−0.01 (−0.48, 0.46)	0.97
SD, mM	3.3±0.8	3.2±0.8	−0.17±0.79	3.6±0.8	3.5±0.8	−0.06±0.54	−0.3 (−0.52, −0.10)	<0.01
HBGI	8.5±3.4	7.6±3.0	−0.87±3.28	8.9±3.9	8.4±3.3	−0.53±2.16	−0.9 (−1.8, 0.05)	0.06
LBGI	5.5±1.7	5.0±1.9	−0.56±1.3	5.5±1.2	5.2±1.4	−0.29±1.06	−0.15 (−0.56, 0.26)	0.47
ADRR	31.9±8.6	30.3±8.0	−1.61±5.22	32.1±7.5	30.5±6.8	−1.56±2.61	−0.05 (−2.10, 2.05)	0.97
Total cholesterol	167.3±27.8	167.8±30.2	0.58±23.54	163.5±28.3	159.3±28.3	−4.19±23.2	4.5 (−3.01, 12.01)	0.24
LDL cholesterol	96.5 (75, 115)	86.0 (71.0, 114.0)	−2 (−12, 9)	88.4 (76, 104)	88.6 (72, 102)	−5 (−15, 5)	1.7 (−5.63, 8.91)	0.65
HDL cholesterol	57.6±12.4	58.6±14.4	1.1±10.4	57.1±13.1	58.7±14.7	1.6±9.6	−0.7 (−4.42, 3.04)	0.70
Triglycerides	74.5 (53, 97)	75.5 (56, 90)	2 (−15, 9)	71.4 (54, 85)	69.7 (58, 88)	0 (−10, 9)	0.14 (−7.21, 7.53)	0.97
SBP	120 (90, 140)	115 (110, 120)	0 (−10, 0)	120 (90, 140)	115 (110, 120)	0 (0, 0)	−1.5 (−4.03, 1.10)	0.26
DBP	75 (60, 90)	70 (70, 80)	0 (−10, 0)	70 (60, 90)	70 (70, 80)	0 (−5, 0)	−1.15 (−3.13, 0.81)	0.25
DTSQ total score	27.5±3.5	29.1±3.7	1 (0, 3)	27.4±3.7	28.2±3.4	1 (−1, 2)	0.5 (−0.42, 1.52)	0.27
Perceived hypoglycemia	3 (2, 4)	2 (1, 3)	−1 (−2,0)	3 (2, 4)	3 (2, 3)	−1 (−1, 0)	−0.5 (−0.83, −0.21)	<0.01
Perceived hyperglycemia	2 (2, 3)	2 (1, 3)	0 (−1, 1)	2 (2, 3)	2 (1, 3)	−0.5 (−1, 0)	−0.02 (−0.35, 0.30)	0.93

[a]Difference between groups adjusted with the propensity score.
For definition of abbreviations, refer to Table 1 footnotes.

Table 4. Frequency of Hypoglycemic Events According to the Treatment Regimen

Events, n	Baseline			2 years		
	CSII (n=98)	MDI (n=125)	P	CSII (n=98)	MDI (n=125)	P
Daily hypoglycemia, *n* (%)						
0	0 (0.00)	1 (0.80)		10 (10.20)	1 (0.80)	
≥1	98 (100.0)	124 (99.20)	0.37	88 (89.80)	124 (99.20)	<0.01
Nocturnal hypoglycemia, *n* (%)						
0	53 (54.08)	69 (55.20)		71 (72.45)	64 (51.20)	
≥1	45 (45.92)	56 (44.80)	0.87	27 (27.55)	61 (48.80)	<0.01
Severe hypoglycemia, *n* (%)						
0	69 (70.41)	84 (67.20)		88 (89.80)	99 (79.20)	
≥1	29 (29.59)	41 (32.80)	0.61	10 (10.20)	26 (20.80)	<0.05

DIABETES TECHNOLOGY & THERAPEUTICS
Volume 20, Number 2, 2018
© Mary Ann Liebert, Inc.
DOI: 10.1089/dia.2017.0334

Relative effectiveness of insulin pump treatment over multiple daily injections and structured education during flexible intensive insulin treatment for type 1 diabetes: cluster randomised trial (REPOSE)

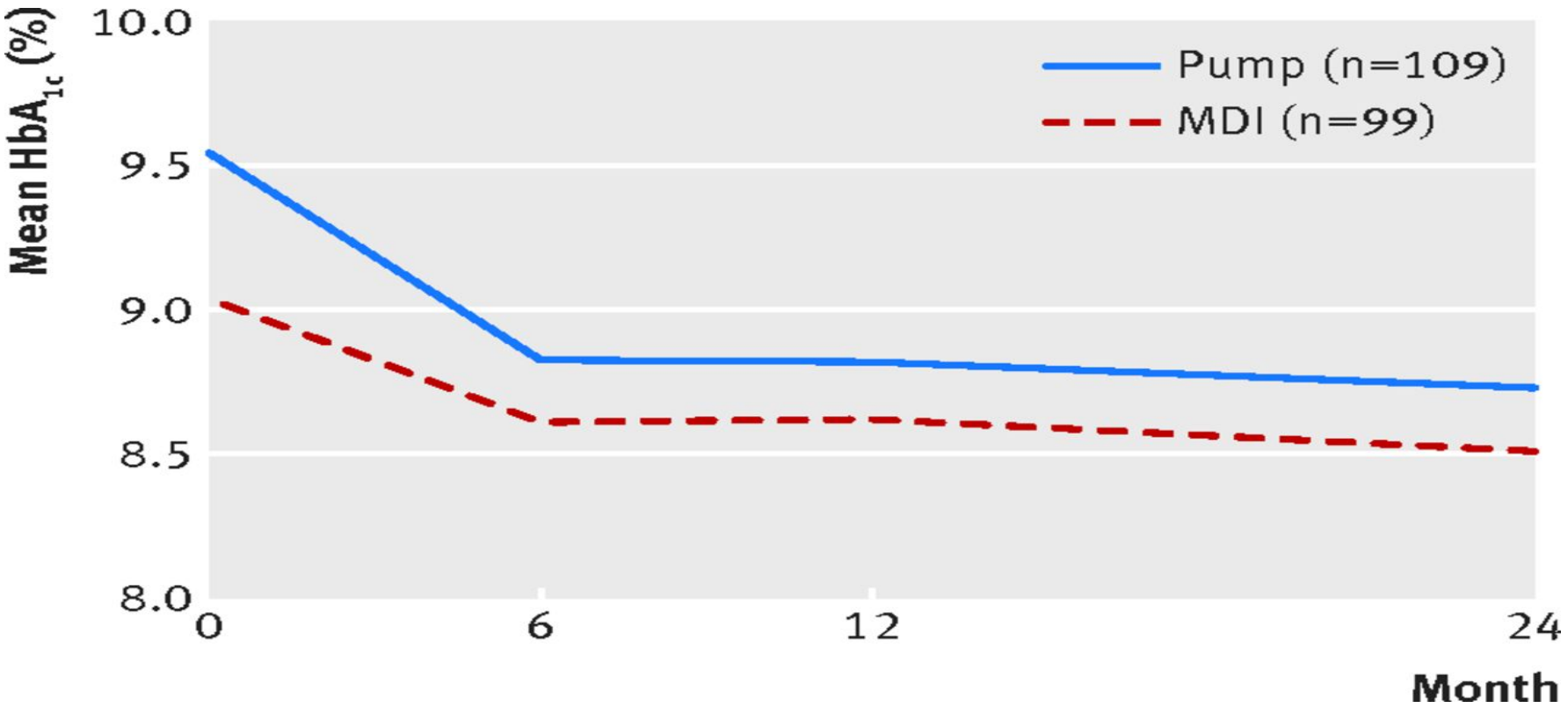
thebmj

Pragmatic, multicentre, open label, parallel group, cluster randomised controlled trial
to compare the effectiveness of insulin pumps with multiple daily injections for adults with type 1 diabetes,
with both groups receiving **equivalent training in flexible insulin treatment.**

Table 1 | Baseline demographics of trial population. Values are numbers (percentages) unless stated otherwise

Characteristics	Pump treatment (n=132)	Multiple daily injections (n=135)	Total (n=267)
Mean (SD) age (years), range	41.5 (14.2), 18.5-77.6	39.9 (12.5), 18.5-73.1	40.7 (13.4), 18.5-77.6
Men	78 (59)	82 (61)	160 (60)
White British	125 (95)	119 (88)	244 (91)
Mean (SD) body mass index, range	27.4 (5.0), 17.4-47.9	27.0 (5.0), 17.2-45.9	27.2 (5.0), 17.2-47.9
Mean (SD) duration of diabetes (years), range	18.5 (12.9), 1.1-56.9	17.5 (12.1), 1.1-51.9	18.0 (12.5), 1.1-56.9
Any macrovascular complication	68 (52)	79 (59)	147 (55)
Retinopathy	51 (39)	65 (48)	116 (43)
Neuropathy	13 (10)	6 (4)	19 (7)
Nephropathy:			
Present	26 (20)	24 (18)	50 (19)
Not calculable	24 (18)	26 (19)	50 (19)
≥1 episodes of severe hypoglycaemia within past year	16 (12)	15 (11)	31 (12)
HbA1c 7.5%	119 (90)	123 (91)	242 (91)
Mean (SD) HbA1c (%), range	9.3 (1.9), 5.7-16.7	9.0 (1.4), 6.1-14.1	9.1(1.7), 5.7-16.7
Mean (SD) HbA1c (mmol/mol), range	77.9 (21.0), 39.0-159.0	74.8 (15.6), 43.0-131.0	76.3 (18.5), 39.0-159.0
Total insulin dose (IU/weight)	128 (97)	133 (99)	261 (98)
Mean (SD) total insulin dose (IU/weight), range	0.72 (0.28), 0.20-1.53	0.75 (0.29), 0.28-1.99	0.74 (0.28), 0.20-1.99

Mean change (%) in glycated haemoglobin (HbA1c) over time in participants with baseline HbA1c ≥7.5% (58 mmol/mol)



The REPOSE Study Group BMJ 2017;356:bmj.j1285

Mean difference in quantitative psychosocial outcomes from baseline to 24 month

Outcomes	Pump treatment		Multiple daily injections		Adjusted difference* (95% CI)	P value
	No	Mean (SD) change (SD)	No	Mean (SD) change		
SF-12 physical component summary†	122	0.3 (7.9)	112	1.0 (8.3)	−0.4 (−2.1 to 1.3)	0.66
SF-12 mental component summary	123	2.1(11.2)	114	0.5 (10.3)	1.6 (−0.7 to 4.0)	0.18
DSQOL:						
Total score†	123	−8.2 (13.1)	114	−4.2 (13.2)	−3.8 (−6.5 to −1.1)	0.01
Social relations	123	−5.7 (12.9)	113	−2.7 (14.8)	−2.5 (−5.4 to 0.4)	0.09
Leisure time restrictions and flexibility	123	−8.1 (17.0)	113	−3.6 (19.7)	−4.6 (−8.4 to −0.9)	0.02
Physical complaints	123	−8.7 (17.2)	113	−4.8 (16.6)	−3.6 (−7.3 to −0.0)	0.05
Worries about the future	123	−11.9 (23.3)	113	−7.8 (21.2)	−4.8 (−9.7 to 0.2)	0.06
Daily hassle of functions	123	−9.6 (21.2)	113	−3.6 (21.5)	−6.3 (−10.9 to −1.8)	0.01
Diet restrictions	123	−12.8 (19.5)	113	−6.9 (19.3)	−5.1 (−8.6 to −1.6)	0.004
Treatment satisfaction (PWTSS) †	113	1.9 (4.5)	108	1.5 (5.4)	0.5 (−0.5 to 1.4)	0.32
WHOQOL-BREF:						
Physical health†	123	0.5 (2.4)	114	−0.1 (2.2)	0.5 (−0.0 to 1.0)	0.07
Psychological	123	0.5 (2.5)	114	0.3 (2.4)	0.2 (−0.4 to 0.7)	0.57
Social relationships	123	0.0 (3.3)	114	0.1 (2.9)	−0.2 (−0.9 to 0.5)	0.63
Environment	122	0.4 (2.2)	114	0.3 (2.0)	0.3 (−0.2 to 0.8)	0.21
HFS behaviour score‡	122	−1.4 (5.6)	114	−0.6 (5.1)	−0.4 (−1.5 to 0.7)	0.44
HFS worry score§	123	−6.7 (13.0)	114	−2.9 (12.5)	−3.4 (−6.0 to −0.8)	0.01
HADS anxiety score¶	123	−1.0 (4.0)	114	−0.5 (3.5)	−0.5 (−1.3 to 0.4)	0.26
HADS depression score	123	−1.0 (3.8)	114	−0.2 (3.3)	−0.7 (−1.5 to 0.1)	0.11
EQ-5D**	123	−0.00 (0.18)	113	−0.02 (0.18)	0.02 (−0.03 to 0.06)	0.46

SF12=12 item short form health survey; DSQOL=diabetes specific quality of life; PWTSS=preference weighted treatment satisfaction score; WHOQOL-BREF=World Health Organization quality of life-BREF; HFS=hypoglycaemia fear survey; HADS=hospital anxiety and depression scale; EQ-5D=EuroQ five dimensions questionnaire.

The REPOSE Study Group BMJ 2017;356:bmj.j1285

CSII (stand alone)

Dati su miglioramento della variabilità glicemica

Dati su riduzione rischio ipoglicemico

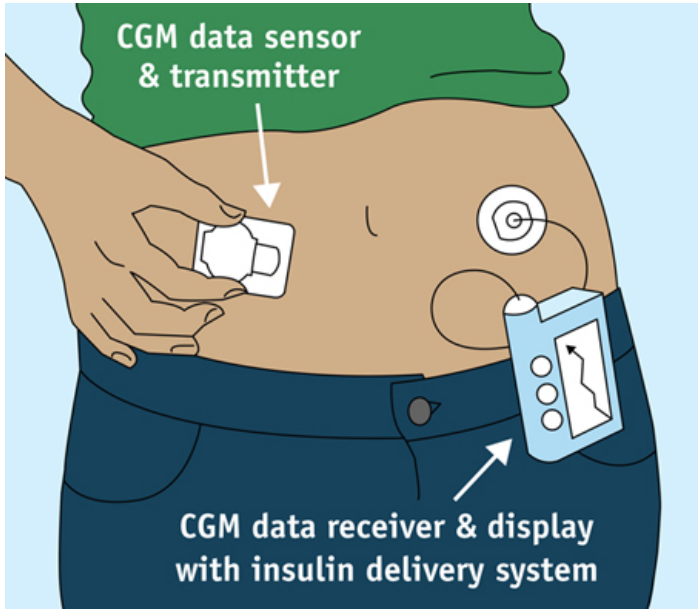
Performance migliore per range di HbA1c più ambiziosi

Miglioramento della qualità della vita: flessibilità

CSII + CGM (continuum glucose monitoring)

- SAP: sensor augmented insulin pump, microinfusore integrato con sensore per monitoraggio glicemico in tempo reale (RT-CGM)
  il paziente visualizza i valori glicemici real-time
  può adoperare correzioni in base ai valori/trend

- Holter type: con valutazione retrospettiva delle misure glicemiche
  Il sistema è di esclusivo uso del medico e consente di valutare l'andamento glicemico di un paziente "in cieco".
  Le informazioni fornite dal monitoraggio retrospettivo possono essere utilizzate a fine didattico e terapeutico

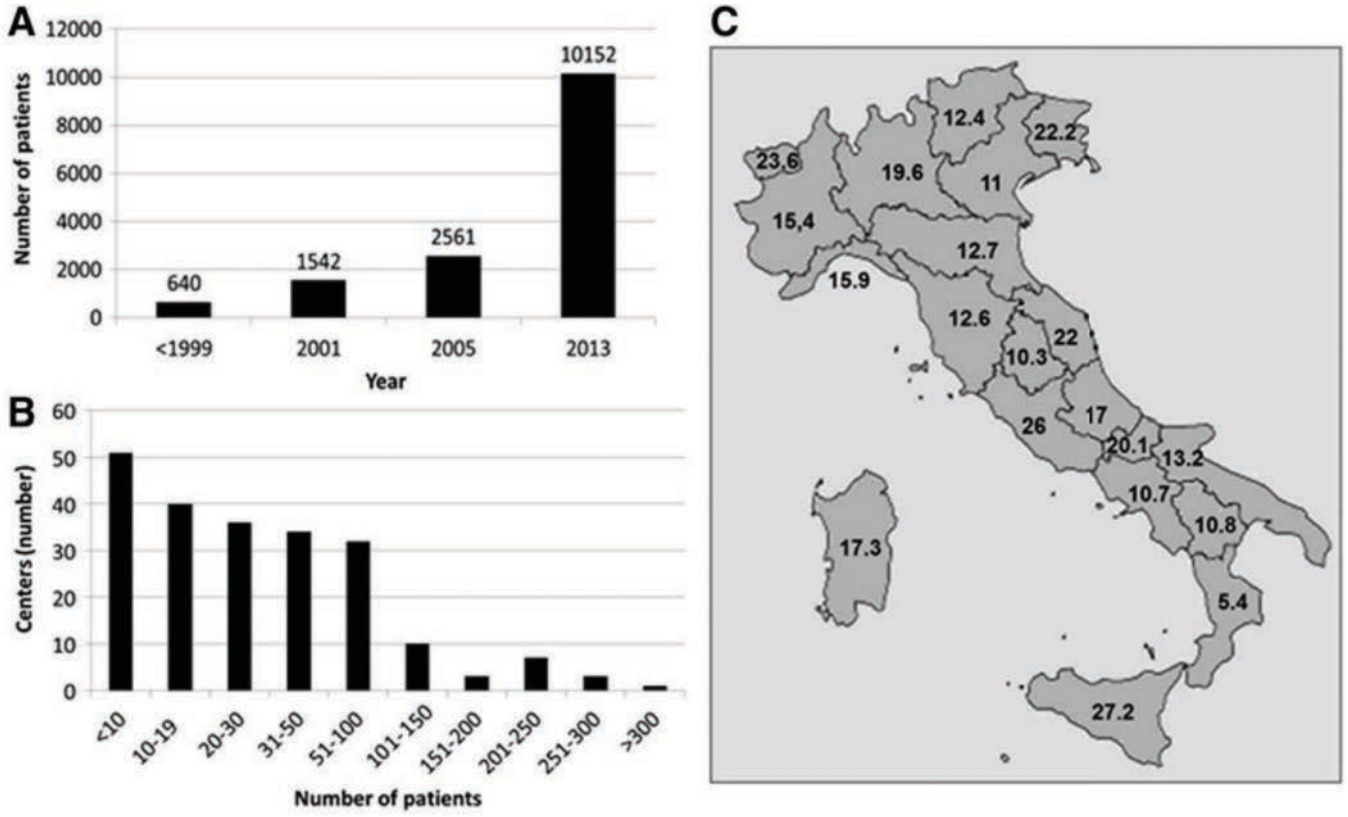


Continuous Subcutaneous Insulin Infusion in Italy: Third National Survey

Daniela Bruttomesso, MD, PhD,[1,*] Luigi Laviola, MD, PhD,[2,*] Giuseppe Lepore, MD,[3,*] Riccardo Bonfanti, MD,[4] Lutgarda Bozzetto, MD, PhD,[5] Andrea Corsi, MD,[6] Vincenzo Di Blasi, MD,[7] Angela Girelli, MD,[8] Giorgio Grassi, MD,[9] Dario Iafusco, MD,[10] Ivana Rabbone, MD, PhD,[11] Riccardo Schiaffini, MD,[12] and the Italian Study Group on Diffusion of CSII[†]

10.152 patients treated with CSII

- 98.2% diabete di tipo 1
- 81.4% adulti



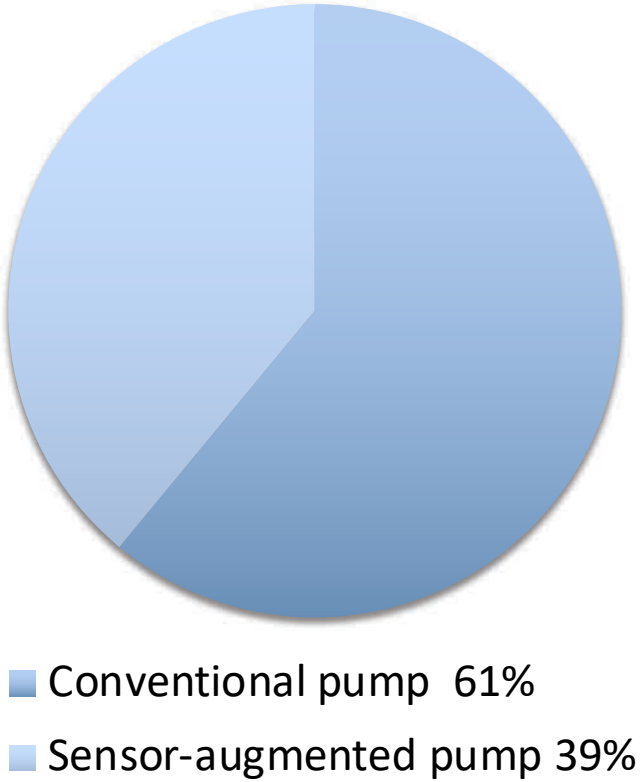
Patients (number)	8,264	1,888	10,152
Age (years)	40.3±13	12.6±4	34.8±16
Sex (% M/F)	42/58	50/50	43/57
Disease duration (years)	20.8±11	6.7±4.1	11.2±9.5
Duration of CSII (years)	5.2±4	3.9±3	5±4

FIG. 1. Continuous subcutaneous insulin infusion in Italy: **(A)** patients treated with continuous subcutaneous insulin infusion, **(B)** patients on continuous subcutaneous insulin infusion per center, and **(C)** prevalence of continuous subcutaneous insulin infusion among different regions (number/100,000 inhabitants).

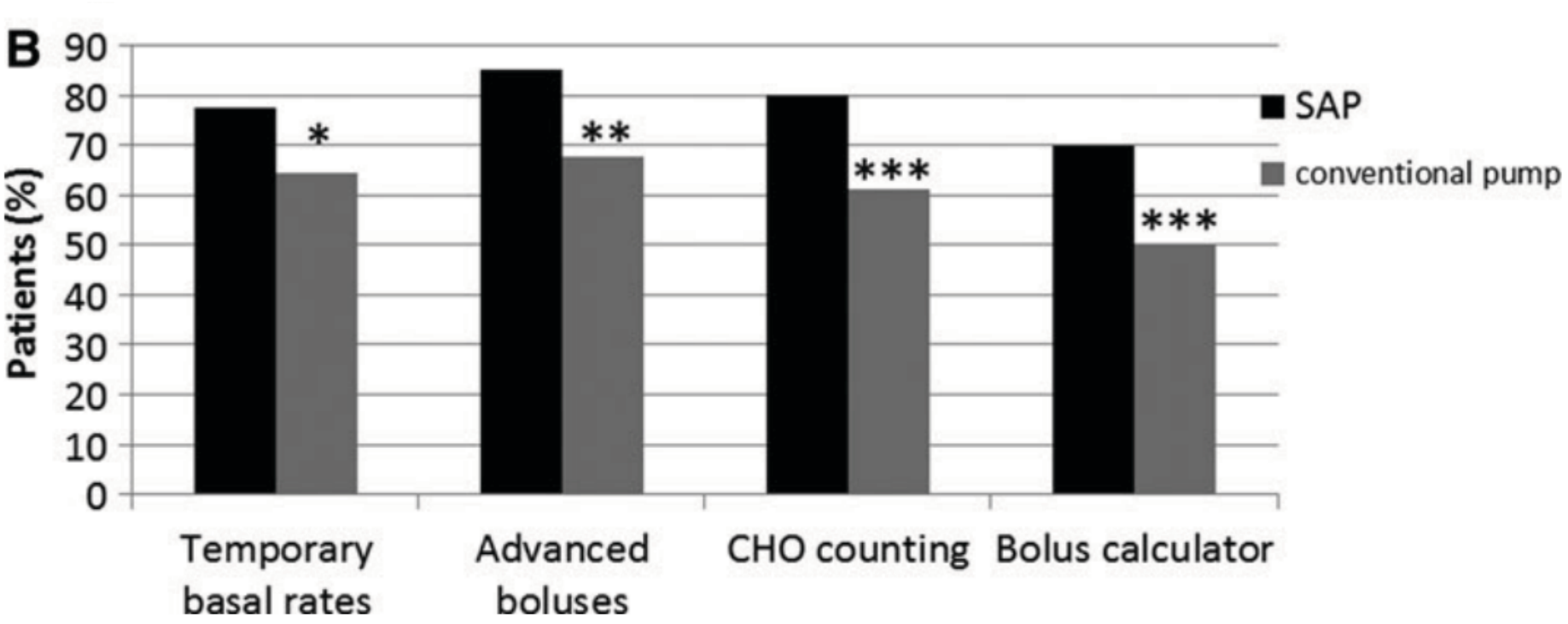
DIABETES TECHNOLOGY & THERAPEUTICS
Volume 17, Number 2, 2015
© Mary Ann Liebert, Inc.
DOI: 10.1089/dia.2014.0242

CSII IN ITALY: THIRD NATIONAL SURVEY

61% con pompa convenzionale versus 39% CSII+SAP



Funzioni avanzate del CSII usate dal 68% dei pazienti



Sensori usati per una media di 12 giorni/mese

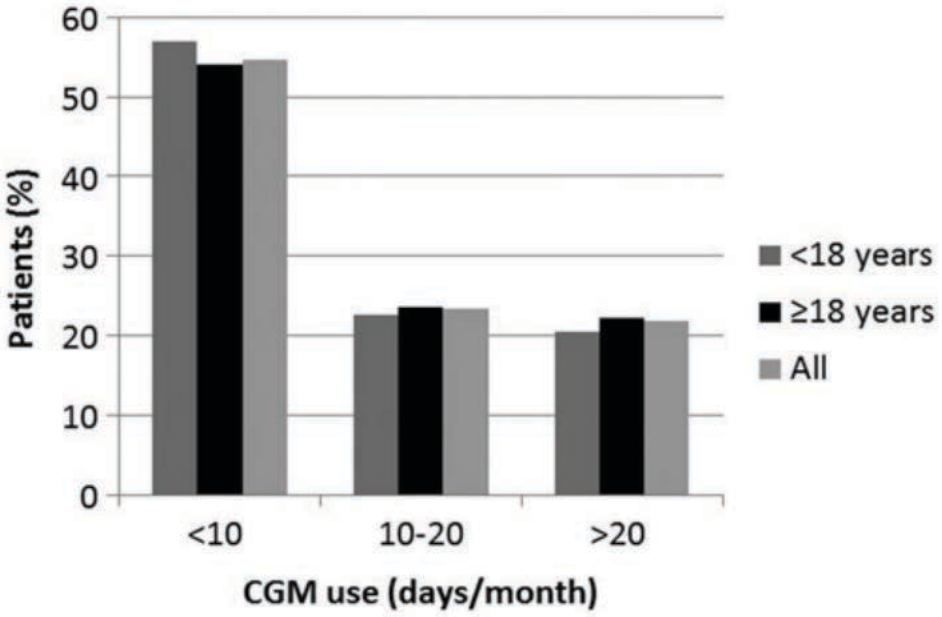


FIG. 2. Use (days per month) of continuous glucose monitoring (CGM) in patients wearing a sensor-augmented pump, grouped by age bracket (pediatric or adult) and total.

Devices. A conventional pump was used by 61% of patients, 32% used a pump with a integrated continuous glucose monitoring (CGM) system, and 7% used a pump associated with a dedicated CGM device. However, the glucose sensor was not used in 30% of patients wearing an integrated or associated system. Patients, both pediatric and adult, using the glucose sensor used it for 12 days/month on average, but more than half did so far less than 10 days/month, and only 21.9% for more than 20 days/month (Fig. 2). Sensor use varied widely among regions, ranging between 5.8 and 26.1 days/month.

ORIGINAL ARTICLE

Incremental Value of Continuous Glucose Monitoring When Starting Pump Therapy in Patients With Poorly Controlled Type 1 Diabetes

The RealTrend study*

–*Baseline and demographic characteristics*

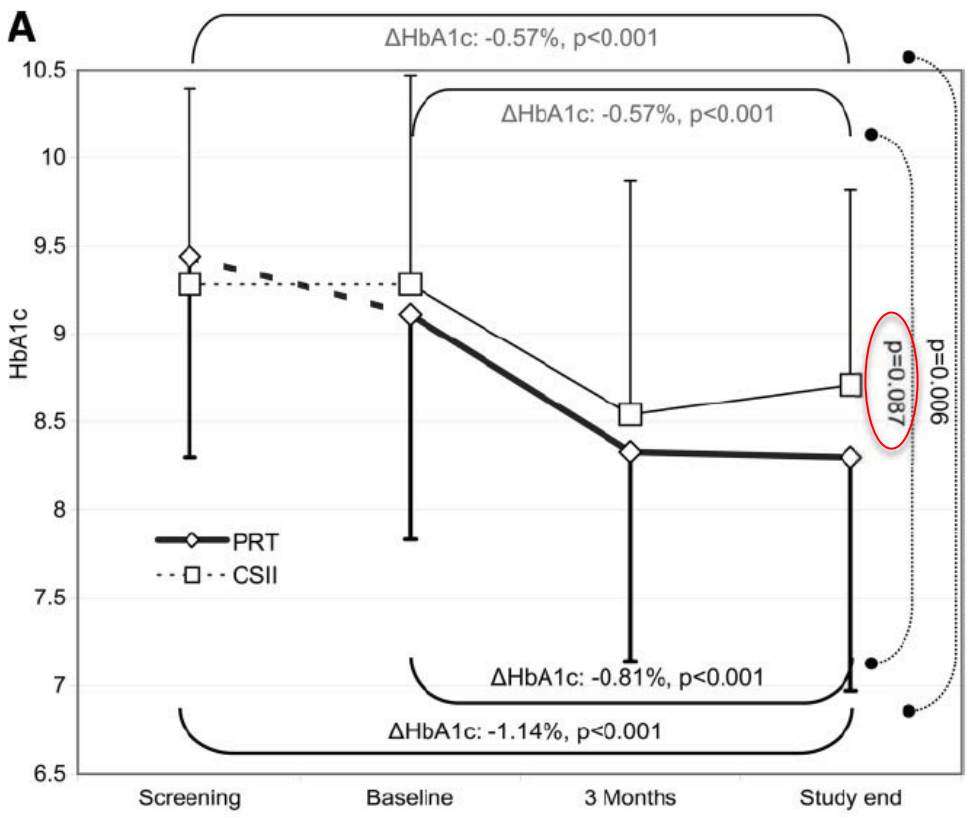
	FAS		Per protocol	
	PRT	CSII	PRT	CSII
n	55	60	32	59
Age (years)	28.1 ± 15.1	28.8 ± 16.7	30.9 ± 16.2	28.1 ± 15.7
Age ≥19 years	33 (60.0)	36 (60.0)	21 (65.6)	35 (59.3)
Male sex	30 (54.5)	34 (56.7)	19 (59.4)	33 (55.9)
Weight (kg)	65.7 ± 17.4	62.6 ± 18.6	66.8 ± 19.9	62.3 ± 18.7
Height (cm)	166.0 ± 12.3	164.6 ± 14.4	166 ± 13.6	164.5 ± 14.5
BMI (kg/m^2)	23.5 ± 4.1	22.5 ± 4.4	23.8 ± 4.7	22.5 ± 4.4
Screening A1C (%)	9.4 ± 1.1	9.3 ± 1.1	9.2 ± 1.0	9.3 ± 1.1
Baseline A1C (%)	9.11 ± 1.28	9.28 ± 1.19	8.9 ± 1.12	9.25 ± 1.19
Baseline MAGE (mg/dl)	188.5	192.9	194.4	192.2
Baseline SD (mg/dl)	74.4	75.1	72.1	75.1
Type 1 diabetes duration (years)	11.2 ± 9.0	12.3 ± 8.8	13.7 ± 10.2	12.2 ± 8.9
Daily insulin doses (units/day)	42.9 ± 17.5	42.2 ± 17.0	40.2 ± 14.8	42.8 ± 16.5

Data are means ± SD, *n* (%), or mean.

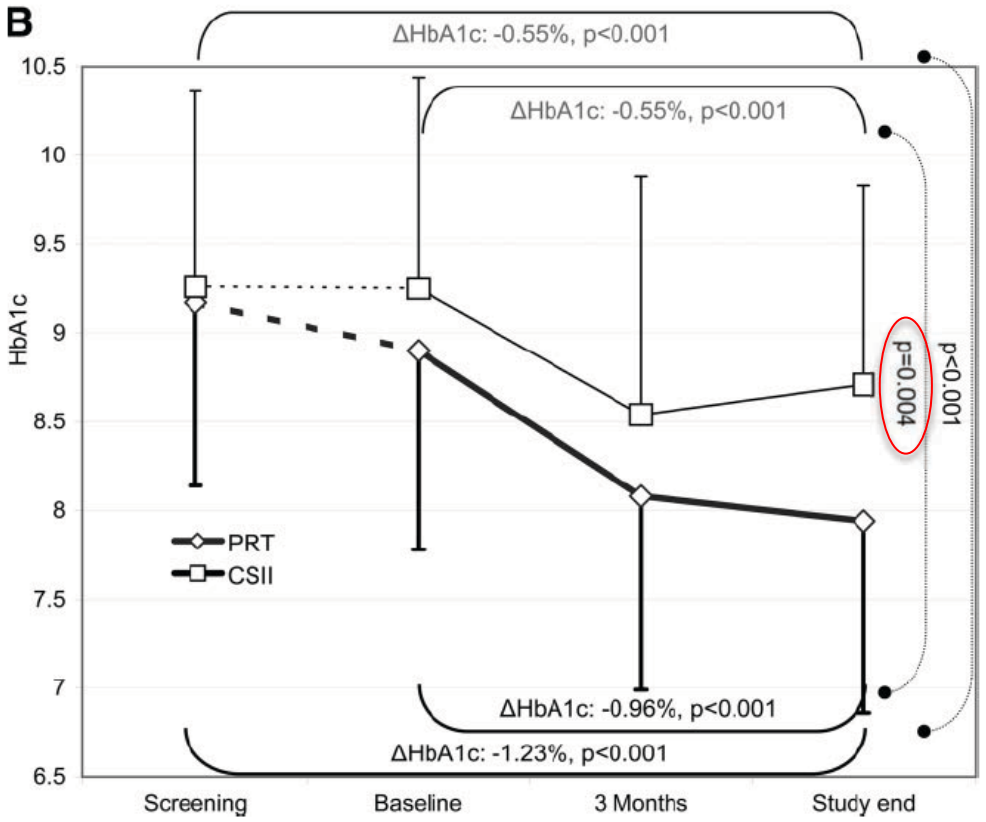
23 patients in the PRT group failed to wear glucose sensors at least 70% of the time (mainly in pts 15-25 years old).

Raccah D et al, Diabetes Care 2009

Full analysis set population



Per protocol population



A 6 mesi dal passaggio MDI a CSII miglioramento significativo della HbA1c in tutta la popolazione
Il vantaggio di SAP vs CSII *stand alone* è apprezzabile solamente con un utilizzo del CGM > 70%

Raccah Det al, Diabetes Care 2009

Table 2—*Measured A1C, glycemic, and insulin parameter changes, baseline to end of study*

	FAS		Per protocol	
	PRT	CSII	PRT	CSII
n	46	54	30	53
Δ Blood glucose (mg/dl)	−30.6 ± 54.0*	−10.8 ± 39.6	−39.6 ± 55.8*	−9.0 ± 39.6
Δ Hyperglycemia >190 mg/dl (h/day)	−3.5 ± 4.8*	−0.7 ± 3.8	−4.1 ± 5.1*	−0.6 ± 3.8
Δ Hyperglycemia AUC (mg · dl^{-1} · day^{-1})	−17.1 ± 31.7†	−5.8 ± 26.7	−19.1 ± 35.5†	−5.2 ± 26.5
Δ Hyperglycemia (episodes/day)	−0.2 ± 0.7	−0.2 ± 0.7	−0.2 ± 0.7	−0.2 ± 0.7
Δ Hypoglycemia <70 mg/dl (h/day)	0.3 ± 1.4	0 ± 1.2	0.6 ± 1.3	0.0 ± 1.2
Δ Hypoglycemia AUC (mg · dl^{-1} · day^{-1})	0.4 ± 1.3	0.0 ± 1.8	0.7 ± 1.3	0.0 ± 1.8
Δ Hypoglycemia (episodes/day)	0.1 ± 0.9	0.1 ± 0.7	0.2 ± 1.0	0.1 ± 0.7
Δ MAGE (mg/dl)	−27.5*	−16.2	−20.4	−16.2
Δ SD	−15.8*	−5.7	−11.3	−5.7
Δ Daily insulin doses (units/day)	6.8 ± 17.3†	1.5 ± 9.1	6.2 ± 14.8	1.1 ± 8.4
Bolus insulin (%/day)	53.8 ± 10.0	49.8 ± 15.8	53.3 ± 9.3	49.7 ± 15.9
Number of boluses/day	4.7 ± 1.4	3.9 ± 1.4	4.9 ± 1.4	3.9 ± 1.4

Data are means ± SD or means. *$P \leq 0.005$ vs. CSII group. †$P \leq 0.05$ vs. CSII group.

Raccah D et al, Diabetes Care 2009

DIABETES TECHNOLOGY & THERAPEUTICS
Volume 10, Number 5, 2008
© Mary Ann Liebert, Inc.
DOI: 10.1089/dia.2008.0068

Sensor-Augmented Insulin Pump Therapy: Results of the First Randomized Treat-to-Target Study

Irl B. Hirsch, M.D.,[1] Jill Abelseth, M.D.,[2] Bruce W. Bode, M.D.,[3] Jerome S. Fischer, M.D.,[4] Francine R. Kaufman, M.D.,[5] John Mastrototaro, Ph.D.,[6] Christopher G. Parkin, M.S.,[7] Howard A. Wolpert, M.D.,[8] and Bruce A. Buckingham, M.D.[9]

6-month, randomized, multicenter, treat-to-target study 146 subjects treated with CSII between the ages of 12 and 72 years with type 1 diabetes and initial A1C levels of 7.5%.
Subjects were randomized to pump therapy with real-time CGM (sensor group) or to pump therapy and self-monitoring of blood glucose only (control group).

Greater than 60% sensor utilization was associated with A1C reduction (p= 0.0456)

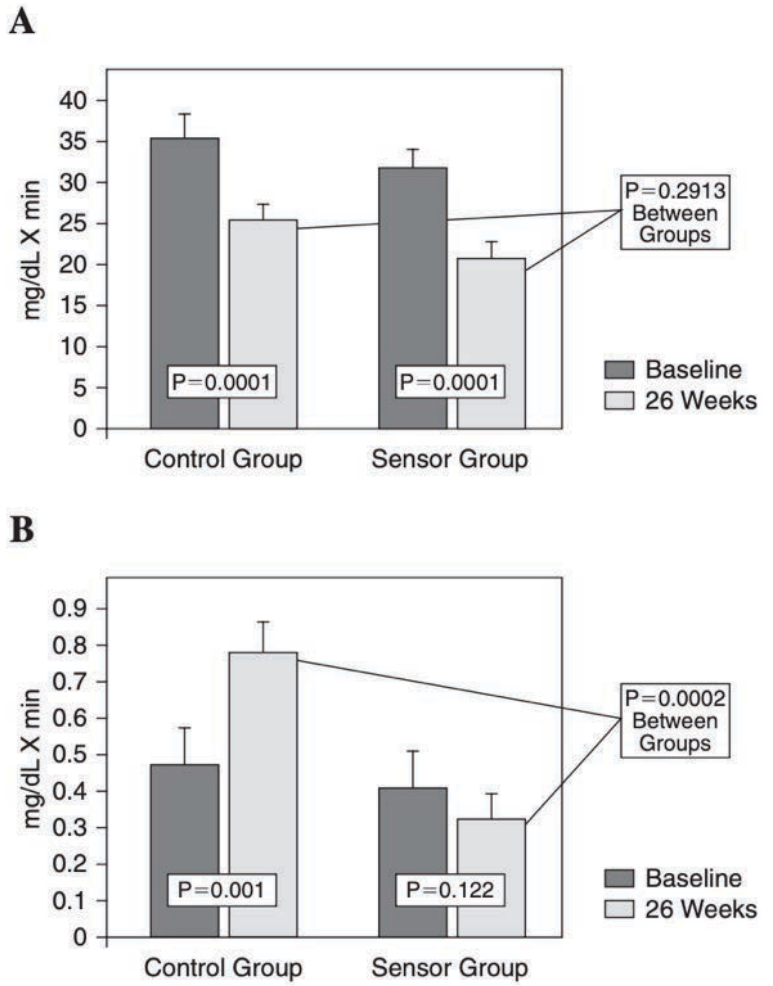


FIG. 1. (**A**) Mean hyperglycemia AUC, time, and amplitude >180 mg/dL. (**B**) Mean hypoglycemia AUC, time, and amplitude <70 mg/dL.

Diabetologia (2012) 55:3155–3162
DOI 10.1007/s00125-012-2708-9

ARTICLE

The use and efficacy of continuous glucose monitoring in type 1 diabetes treated with insulin pump therapy: a randomised controlled trial

T. Battelino · I. Conget · B. Olsen · I. Schütz-Fuhrmann · E. Hommel · R. Hoogma · U. Schierloh · N. Sulli · J. Bolinder · the SWITCH Study Group

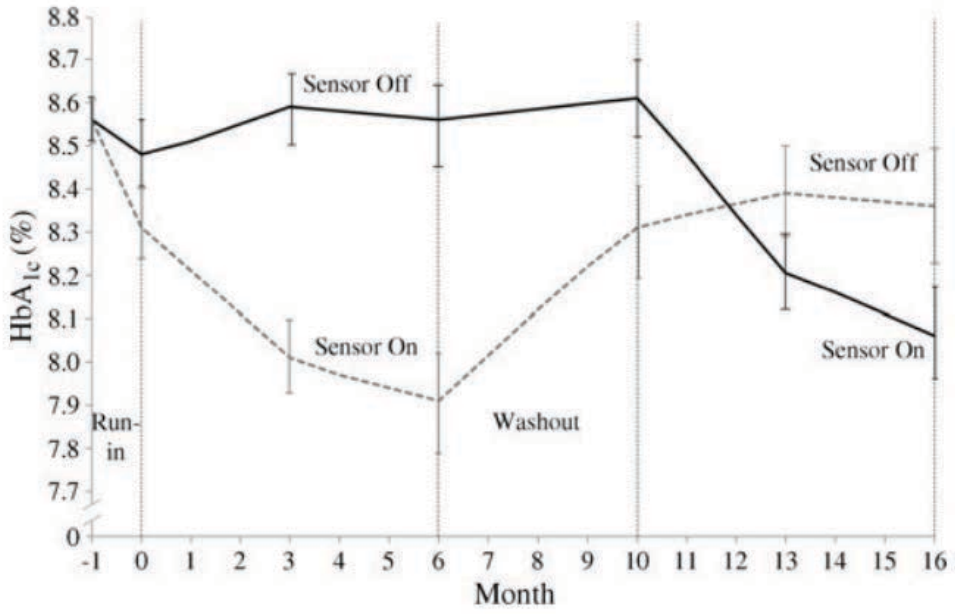


Fig. 2 Mean (±SEM) HbA_{1c} in participants randomised to Off/On (solid line) and On/Off (dashed line) sequences (all available observations): months −1 to 0: run in period; months 1 to 6: first period; months 7 to 10: washout; months 11–16: second period. To convert values for HbA_{1c} in % into mmol/mol, subtract 2.15 and multiply by 10.929

- **Mean sensor use was 80% (median 84%) of the required time.**
- In the paediatric group, mean sensor use was 73% (median 78%) of the required time.
- In the adult group mean sensor use was 86% (median 89%) of the required time (mean 87% over the final 4 weeks).
- The decrease in HbA1c was smaller in the group that used the sensor <70% of the required time than in the group that used it ≥70% of the required time.

Uso subottimale del CGM riduce significativamente i vantaggi del suo impiego

Possibili spiegazioni:

- Costi
- Scarsa aderenza del paziente al training e alla interpretazione dei dati -> poca motivazione?
- Reazioni cutanee
- Sensazione di fastidio
- “Intrusione”

Nutrition, Metabolism & Cardiovascular Diseases (2018) **28**, 335–342

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

journal homepage: www.elsevier.com/locate/nmcd

Metabolic control and complications in Italian people with diabetes treated with continuous subcutaneous insulin infusion

Giuseppe Lepore [a], Riccardo Bonfanti [b], Lutgarda Bozzetto [c], Vincenzo Di Blasi [d], Angela Girelli [e], Giorgio Grassi [f], Dario Iafusco [g], Luigi Laviola [h], Ivana Rabbone [i], Riccardo Schiaffini [j], Daniela Bruttomesso [k,*], Italian Study Group on the Diffusion of CSII[1]

Cross-sectional study to evaluate the degree of glycaemic control and the frequency of diabetic complications in Italian people with diabetes who were treated with continuous subcutaneous insulin infusion (CSII)

- 6623 pazienti in trattamento da >1 anno con CSII
- 93 centri
- 98.8% diabete di tipo 1
- 57.2% sesso femminile
- HbA1c mediana: 7.6%

Informazioni su qualità del controllo glicemico e complicanze del diabete

64% CSII stand alone vs 36% SAP

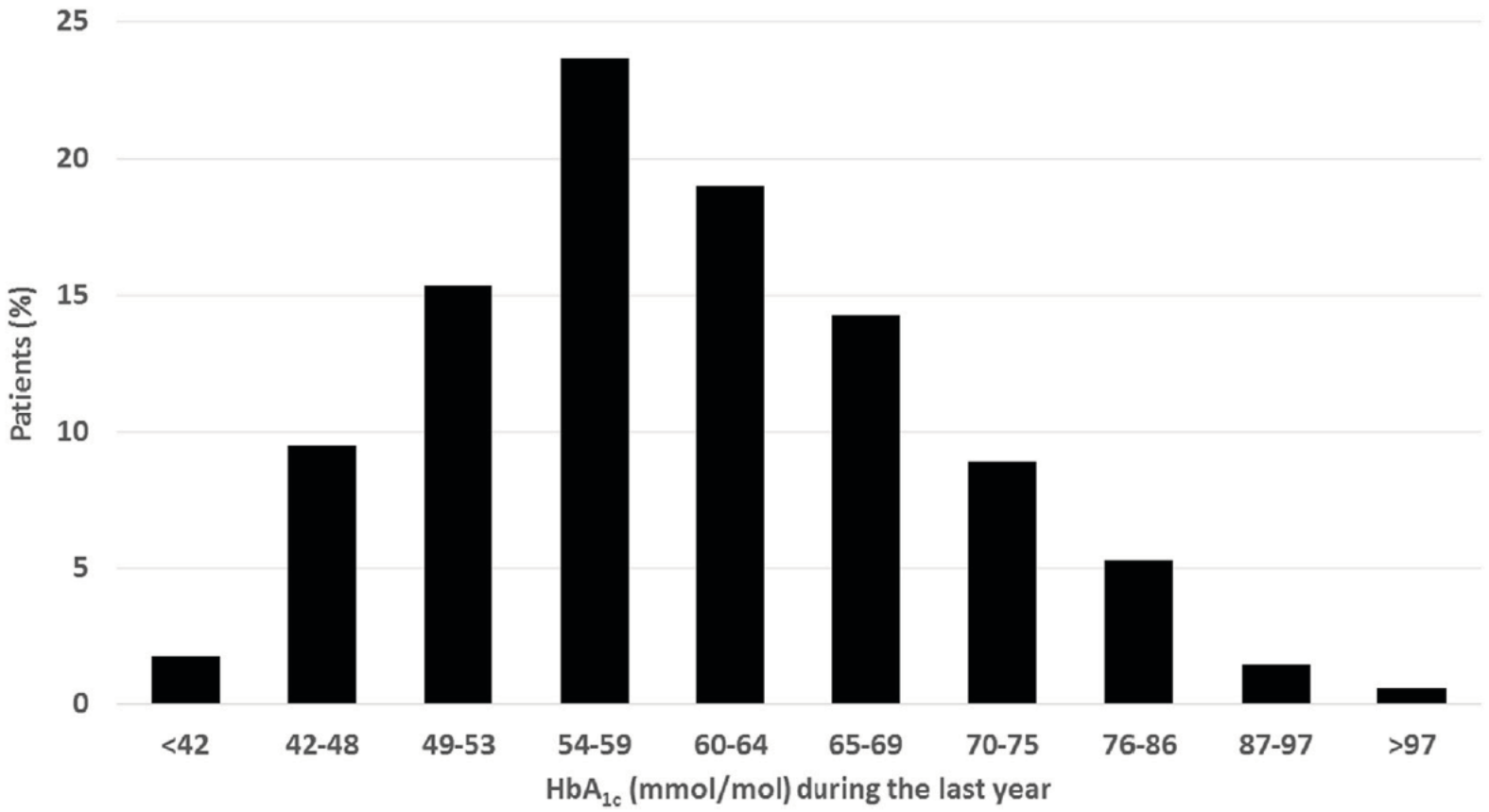
Table 1 Clinical characteristics of study participants.

Variable	Total	<18 years	≥18 years
Number of participants	6623	1025	5598
Type of diabetes:			
type 1	6543 (98.8)	1025 (100)	5518 (98.6)
type 2	80 (1.2)	0 (0)	80 (1.4)
Age, years[a]	37 (22–49)	14 (11–16)	41 (29–51)
Sex:			
Male	2796 (42.2)	497 (48.5)	2299 (41.1)*
Female	3827 (57.8)	528 (51.5)	3299 (58.9)
Duration of diabetes, years[a]	16 (9–26)	5 (3–8)	19 (12–28)*
Duration of diabetes at CSII start, years[a]	10 (4–19)	2 (1–4)	12 (6–21)*
Duration of CSII, years[a]	5 (2–8)	2 (1–4)	5 (3–8)*
Blood glucose tests, n/day[a]	5.2 (4.0–6.0)	6.1 (6.0–7.0)	5.0 (4.0–6.0)**
Type of device:[b]			
CSII	4206 (64.1)	606 (59.1)	3600 (65.0)***
SAP	2360 (35.9)	419 (40.9)	1941 (35.0)
SAP: sensor use, days/month[a,c]	15 (7–24)	21 (10–30)	15 (7–21)*

Data are presented as n (%) or [a]median (IQR), where appropriate.
Data not available for. [b]57 patients and. [c]84 patients.
*$p < 0.0001$ for <18 years.
**$p < 0.05$ for <18 years.
***$p < 0.0005$ for <18 years.

Media giorni con CGM: 15
1/3 dei pazienti < 10 giorni
35% > 20 giorni

Distribution of mean glycated haemoglobin levels during the year before the study



Participants who used SAP had a lower HbA1c level than those who used the conventional pump 7.5% [IQR: 6.9%-8.2%] vs 7.6% [IQR: 7.1%-8.3%]; p < 0.0001).

Participants who used a sensor more than 20 days per month had a lower HbA1c level than those who used it less than 20 days per month.

Uso funzioni avanzate CSII e controllo glicemico

81.2% basale temporanea
82.2% opzioni di bolo,
56.5% calcolatore di bolo 75.9% conta CHO

SAP CSII stand alone

84.2% vs 79.1% basale temporanea
89.2% vs 77.8% opzioni di bolo,
72.5% vs 64.3% calcolatore di bolo 81.8% vs 72.2% conta CHO

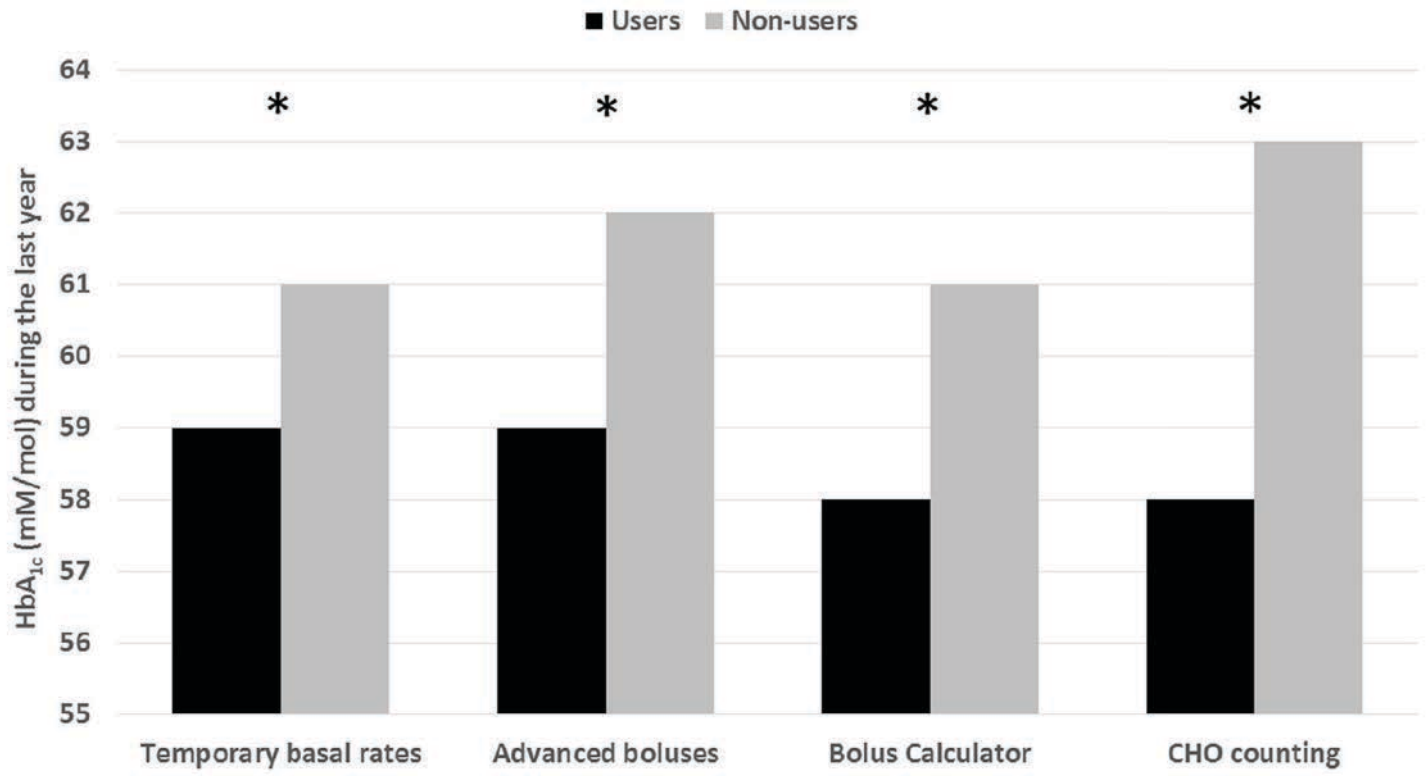


Figure 2 Median glycated haemoglobin levels during the year before the study according to the use of advanced pump functions and CHO counting (*$p < 0.0001$). Non-users of the bolus calculator include only participants who count carbohydrates.

SAP:

Efficace → SI!

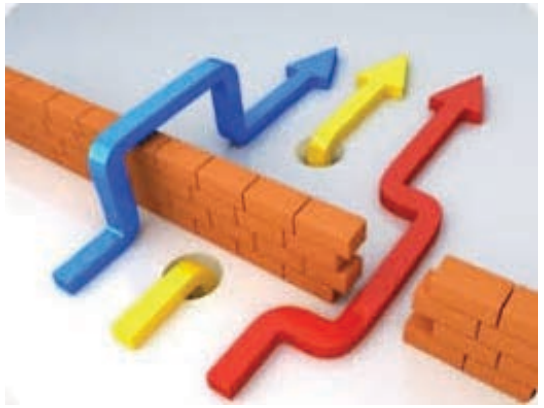
Efficacia *tout court*? **NI**

- Tempo di utilizzo
- Utilizzo finalizzato all'impiego delle funzioni avanzate del CSII
- …sostenibilità?

Identificare il paziente adatto al SAP

- ipoglicemie inavvertite
- presumibile ridotta capacità di segnalare l'ipoglicemia (ad es. bambini di età inferiore a 6 anni)
- ipoglicemie severe
- pazienti con non meno di 2 ipoglicemie notturne nell'arco di 6 mesi
- età inferiore a 18 anni con diabete instabile che richiede più di 10 controlli glicemici al giorno
- in preparazione all'impianto del microinfusore
- categorie particolari di pazienti (sportivi, musicisti, lavori e professioni con esposizione a pericolo e che rendano complicato garantire la regolarità dei pasti e/o dell'attività fisica in situazioni di rischio)
- età inferiore a 18 anni con difficoltà all'inserimento sociale a causa del diabete
- persistente scompenso glico-metabolico continuativo (HbA1c 10 mmol/mol oltre il target, per almeno 6 mesi)
- diabete pre-gravidico e programmazione alla gravidanza
- pazienti di età inferiore a 18 anni con paura dell'ipoglicemia (documentata con questionario Fear of Hypo e PAID)
- pazienti con diabete noto con episodi di ricovero per chetoacidosi (DKA)

In alternativa…



SBGM – automonitoraggio glicemico su sangue capillare

- Ottimizzando frequenza e timing dell'autocontrollo
- Impiego di sistemi innovativi: app per scarico dati
- Integrazione con sistemi di CHO counting

CGM *holter type*

con valutazione retrospettiva delle misure glicemiche

- a scopo didattico per il paziente
- in caso di sospetta falsificazione delle misure glicemiche
- per un aggiustamento fine della terapia insulinica
- ai fini di verifica dell'indicazione all'uso del microinfusore

Grazie per l'attenzione!

Dott.ssa Ilaria Barchetta
Dipartimento di Medicina Sperimentale
Università Sapienza, Roma

VENERDÌ 21 Giugno 2019
ROMA || Starhotels Metropole