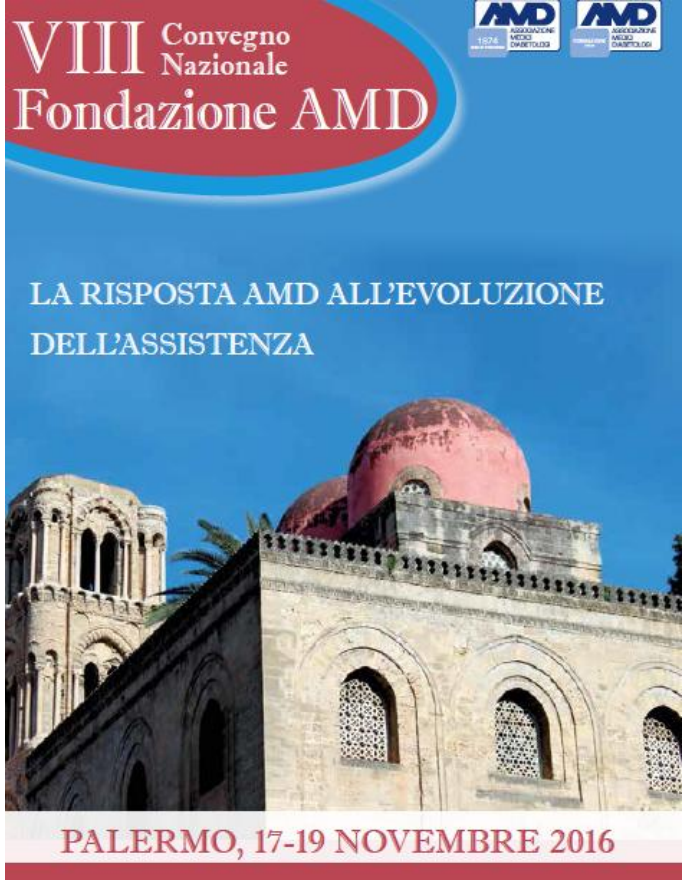

Appropriatezza e Sostenibilità delle Tecnologie per i Centri di Diabetologia

Paolo Di Bartolo

UO Diabetologia Ravenna

Rete Clinica di Diabetologia AUSL della Romagna

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Paolo Di Bartolo Disclosure

Board Member/Advisory Board

Abbott Diagnostic Italy, Boehringer Ingelheim Italy, Eli Lilly International, Novartis Italy, Novo Nordisk Italy

Speaker's Bureau

Abbott Diagnostic Italy, Astra Zeneca BMS Italy, Eli Lilly Italy, Novartis Italy, Novo Nordisk Italy, Sanofi Aventis Italy, Sigma-Tau Italy, Ypsomed Italy.

Ai sensi dell'art. 3.3 del Regolamento applicativo dell'Accordo Stato-Regioni 05.11.2009, dichiaro che negli ultimi due anni ho avuto i seguenti rapporti anche di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:

Appropriatezza e Sostenibilità un Difficile Equilibrio

SOSTENIBILITA'

Il concetto di sostenibilità di una società organizzata nasce alla fine degli anni ottanta, con il rapporto Brundtland all'ONU, in cui veniva così definito: **"equilibrio fra il soddisfacimento delle esigenze presenti senza compromettere la possibilità delle future generazioni di sopperire alle proprie".**

Report of the World Commission on Environment and Development - Our Common Future. United Nations 1987 – Brutland Report. –
-Available at "*conspect.nl/pdf/Our_Common_Future*
-Brundtland_Report_1987.pdf

Programma Synthesis: http://www.uvetgbt.com/media/115564/programma_syn_thesis_sifo.pdf

Dal 1969 al 2012……

Are new technolgies for insulin delivery and glucose monitoring the best solutions for everybody?

REVIEW | Annals of Internal Medicine

Comparative Effectiveness and Safety of Methods of Insulin Delivery and Glucose Monitoring for Diabetes Mellitus

A Systematic Review and Meta-analysis

Hsin-Chieh Yeh, PhD; Todd T. Brown, MD, PhD; Nisa Maruthur, MD, MHS; Padmini Ranasinghe, MD, MPH; Zackary Berger, MD, PhD; Yong D. Suh, MBA, MSc; Lisa M. Wilson, ScM; Elisabeth B. Haberl, BA; Jessica Brick, MD; Eric B. Bass, MD, MPH; and Sherita Hill Golden, MD, MHS

Ann Intern Med. 2012;157:336-347.

Innovations in insulin delivery and glucose monitoring are designed to improve glycemic control and quality of life (QOL) while limiting adverse effects, such as hypoglycemia and weight gain. These advances include continuous subcutaneous insulin infusion (CSII) and real-time continuous glucose monitoring (rt-CGM).

…….their effectiveness has not been consistently demonstrated and the populations most likely to benefit are unclear. Health professionals and their diabetic patients need objective information when making decisions about these technologies, which may be expensive or heavily marketed. Such information is important to persons who decide on reimbursement policies …..

Agency for Healthcare Research and Quality. (AHRQ)

Ann Intern Med. 2012;157(5):336-347. doi:10.7326/0003-4819-157-5-201209040-00508

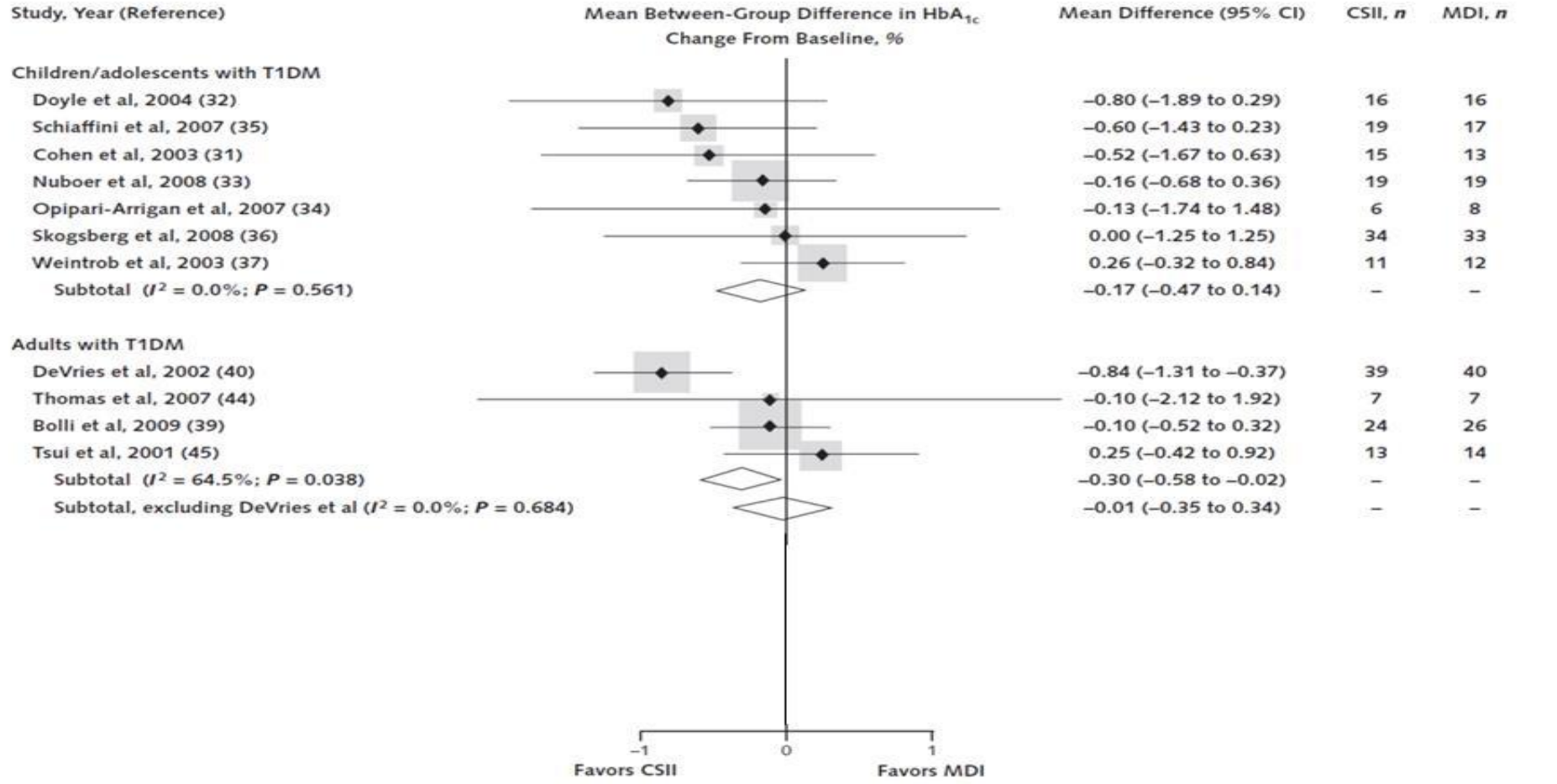
Annals of Internal Medicine

Comparat and Gluc

A Systematic R

Hsin-Chieh Yeh, P
Yong D. Suh, MBA
and Sherita Hill Go

Figure 1. Mean between-group difference in the change from baseline HbA_{1c} comparing CSII with MDI among children and adolescents with T1DM, adults with T1DM, and adults with T2DM.



Error bars represent 95% CIs. Shaded boxes represent individual study point estimates. Box size corresponds to weight of study. CSII = continuous subcutaneous insulin infusion; HbA_{1c} = hemoglobin A_{1c}; MDI = multiple daily injections; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus.

Ann Intern Med. 2012;157(5):336-347. doi:10.7326/0003-4819-157-5-201209040-00508

Journal of Diabetes Science and Technology
Volume 7, Issue 6, November 2013

REVIEW ARTICLE

The Evidence Base for Diabetes Technology: Appropriate and Inappropriate Meta-Analysis

John C. Pickup, B.M., D.Phil.

RCTs of CSII Vs MDI have usually been conducted in volunteers with T1DM without specific clinical problems and not in those with persistent poor control on MDI.

It is known [...] that the greatest effect of insulin pump therapy in improving HbA1c or reducing severe hypoglycemia is in those patients with the highest baseline HbA1c or hypoglycemia frequency.

People with type 1 diabetes already well controlled on MDI may not improve further by switching to insulin pump therapy

Journal of Diabetes Science and Technology
Volume 7, Issue 6, November 2013

REVIEW ARTICLE

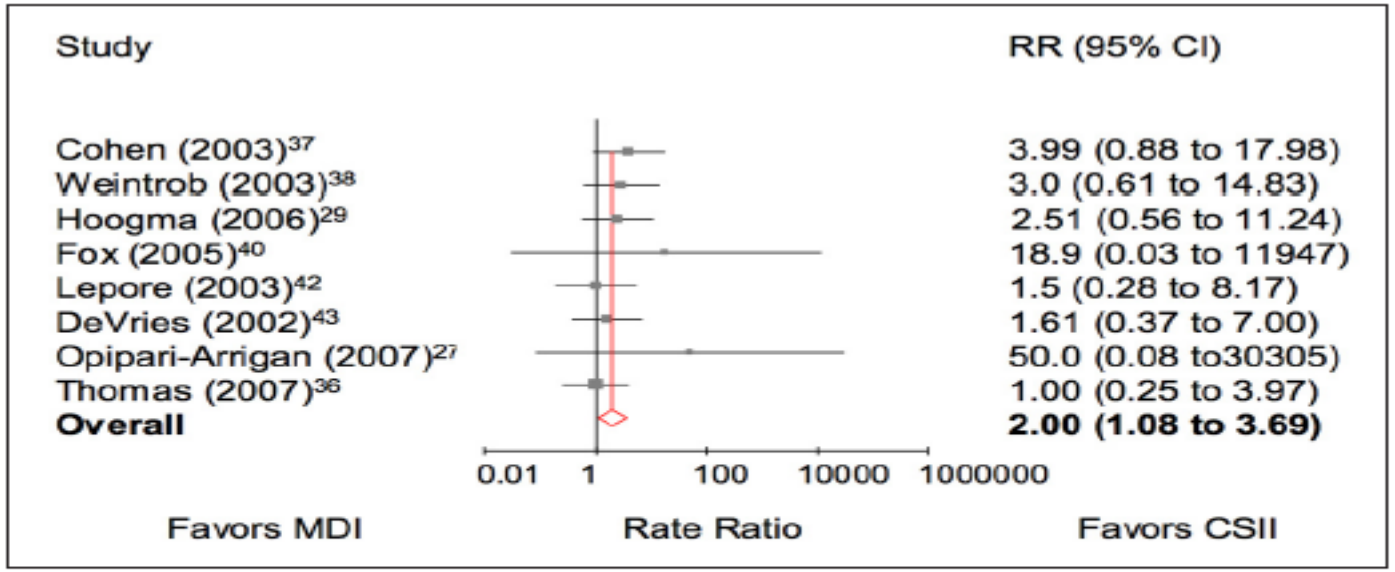


Figure 3. Decision-making random-effects meta-analysis of severe hypoglycemia RRs on MDI versus CSII. Only RCTs where the baseline population (MDI) rate of severe hypoglycemia was elevated (>18 episodes/100 patient-years) were included. CI, confidence interval.

REVIEW | Annals of Internal Medicine

Comparative Effectiveness and Safety of Methods of Insulin Delivery and Glucose Monitoring for Diabetes Mellitus

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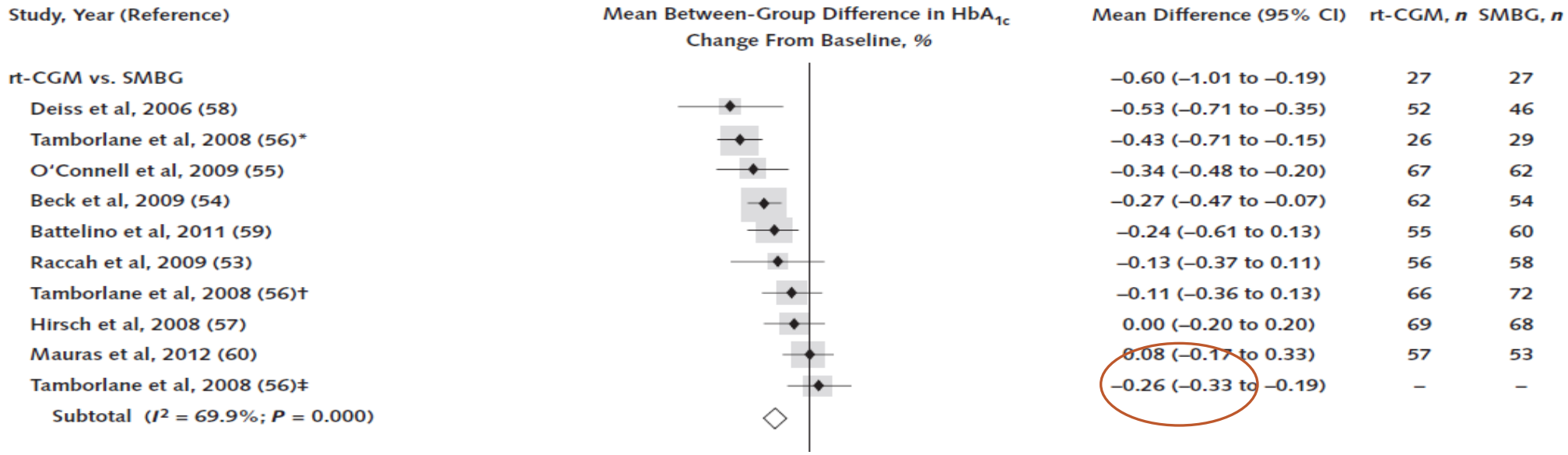
Hsin-Chieh Yeh, PhD; Todd T. Brown, MD, PhD; Nisa Maruthur, MD, MHS; Padmini Ranasinghe, MD, MPH; Zackary Berger, MD, PhD; Yong D. Suh, MBA, MSc; Lisa M. Wilson, ScM; Elisabeth B. Haberl, BA; Jessica Brick, MD; Eric B. Bass, MD, MPH; and Sherita Hill Golden, MD, MHS

Ann Intern Med. 2012;157:336-347.

Figure 4. Comparison of rt-CGM with SMBG and SAP use with MDI plus SMBG among patients with T1DM.



Comparative Effectiveness and Safety of Methods of Insulin Delivery and Glucose Monitoring for Diabetes Mellitus

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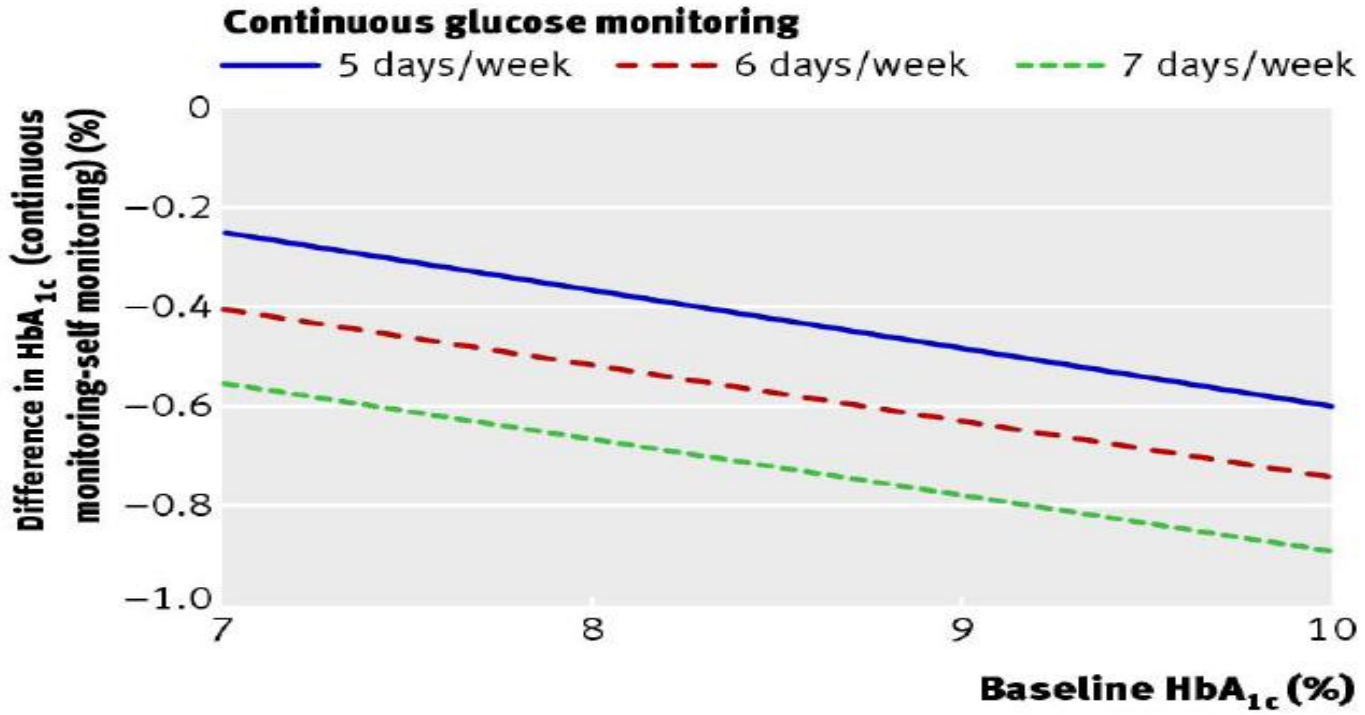
Ann Intern Med. 2012;157:336-347.

Table 2. Summary of the Subgroup Analyses in the Between-Group Change From Baseline HbA_{1c} Among Patients With T1DM Comparing rt-CGM with SMBG

Analysis	Studies Included (Participants Included), *n* (*n*)	Mean Difference in HbA_{1c} (95% CI), %	I^2, %
All studies*	8 (1066)†	−0.26 (−0.33 to −0.19)	66.6
Adults ≥18 y‡	3 (312)§	−0.38 (−0.53 to −0.23)	77.3
Children <18 y‖	5 (434)¶	−0.13 (−0.27 to 0.01)	46.0
Adherence >60%	7 (705)**	−0.36 (−0.44 to −0.27)	40.8

Glycaemic control in type 1 diabetes during real time continuous glucose monitoring compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data

John C Pickup *professor of diabetes and metabolism*[1], Suzanne C Freeman *medical statistics student*[2 3], Alex J Sutton *professor of medical statistics*[2]



CGM shows that for frequent sensor usage (7 days per week) and a high baseline HbA1c of 10% (86 mmol/mol), CGM is predicted to lower HbA1c by approximately 0.9% (9 mmol/mol) compared with SMBG

BMJ

BMJ 2011;343:d3805 doi: 10.1136/bmj.d3805

Novel glucos
type 1 diabet
controlled tr

Jan Bolinder, Ramiro Antuna,

Background Tight control o
complications; however, gl
whether a factory-calibrate
testing reduced exposure t

Method In this multicentr
well controlled type 1 diabe
participants wearing the bl
(1:1) to flash sensor-based
capillary strips (control gr
dependent on study centre
masked to group allocation
between baseline and 6 m
positive pregnancy test dur

	Intervention (n=119)	Control (n=120)
Men	77 (65%)*	59 (49%)*
Women	42 (35%)	61 (51%)
Race		
White	119 (100%)	119 (99%)
Black	0	1 (1%)
Age (years)	42 (33-51)	45 (33-57)
BMI (kg/m²)	25·2 (3·6)	24·8 (3·5)
Duration of diabetes (years)	20 (13-27)	20 (12-32)
Screening HbA_{1c} (%; mmol/mol)	6·7 (0·5); 50·1 (5·7)	6·7(0·6); 50·2 (6·5)
Self-reported blood glucose frequency per day	5·4 (2·0)	5·6 (2·3)
Insulin administration method		
Multiple daily injections	81 (68%)	80 (67%)
Continuous subcutaneous insulin infusion	38 (32%)	40 (33%)
Insulin, total daily dose		
Basal (units)	25·7 (13·9)	20·9 (10·0)
Bolus (units)	24·2 (13·5)	22·2 (13·4)
Continuous subcutaneous insulin infusion (units)	41·4 (17·1)	35·9 (15·6)

Data are n (%), median (IQR), or mean (SD). *p=0·0153.

Table 1: **Baseline characteristics**

www.thelancet.com Published online September 12, 2016

	Baseline		Study end		Difference in adjusted means in intervention vs control	Difference in intervention vs control (%)	p value
	Intervention (n=119)	Control (n=119)	Intervention (n=119)	Control (n=119)			
HbA_{1c} (mmol/mol)	50·7 (5·7)	50·6 (7·0)	52·4 (7·2)	52·4 (7·2)	0·0 (0·65)	NA	0·9543
HbA_{1c} (%)	6·79 (0·52)	6·78 (0·64)	6·94 (0·65)	6·95 (0·66)	0·00 (0·059)	NA	0·9556
Time with glucose 3·9–10·0 mmol/L (70–180 mg/dL) in h	15·0 (2·5)	14·8 (2·8)	15·8 (2·9)	14·6 (2·9)	1·0 (0·30)	NA	0·0006
Glucose <3·9 mmol/L (70 mg/dL) within 24 h							
Events	1·81 (0·90)	1·67 (0·80)	1·32 (0·81)	1·69 (0·83)	−0·45 (0·089)	−25·8%	<0·0001
Time in h	3·38 (2·31)	3·44 (2·62)	2·03 (1·93)	3·27 (2·58)	−1·24 (0·239)	−38·0%	<0·0001
AUC (hxmg/dL)	53·42 (43·46)	58·34 (57·22)	28·58 (31·15)	54·67 (60·08)	−25·14 (5·32)	−46·7	<0·0001
Glucose <3·9 mmol/L (70 mg/dL) at night (2300–0600 h) within 7 h							
Events	0·47 (0·32)	0·46 (0·29)	0·27 (0·23)	0·40 (0·29)	−0·14 (0·029)	−33·2%	<0·0001
Time in h	1·32 (1·07)	1·48 (1·29)	0·68 (0·97)	1·23 (1·10)	−0·47 (0·118)	−39·8%	<0·0001
Glucose <3·1 mmol/L (55 mg/dL) within 24 h							
Events	0·96 (0·65)	0·92 (0·73)	0·56 (0·55)	0·92 (0·74)	−0·38 (0·074)	−41·3%	<0·0001
Time in h	1·59 (1·42)	1·77 (1·86)	0·80 (0·96)	1·65 (1·97)	−0·82 (0·175)	−50·3%	<0·0001
AUC (hxmg/dL)	16·04 (17·46)	18·94 (23·22)	7·59 (10·25)	17·69 (26·34)	−9·67 (2·29)	−56·1%	<0·0001
Glucose <3·1 mmol/L (55 mg/dL) at night (2300–0600 h) within 7 h							
Events	0·34 (0·27)	0·36 (0·34)	0·19 (0·24)	0·30 (0·28)	−0·11 (0·03)	−34·9%	0·0005
Time in h	0·62 (0·60)	0·75 (0·83)	0·31 (0·43)	0·66 (0·080)	−0·32 (0·07)	−48·9%	<0·0001

BACKGROUND

The threshold-suspend feature of sensor-augmented insulin pumps is designed to minimize the risk of hypoglycemia by interrupting insulin delivery at a preset sensor glucose value. We evaluated sensor-augmented insulin-pump therapy with and without the threshold-suspend feature in patients with nocturnal hypoglycemia.

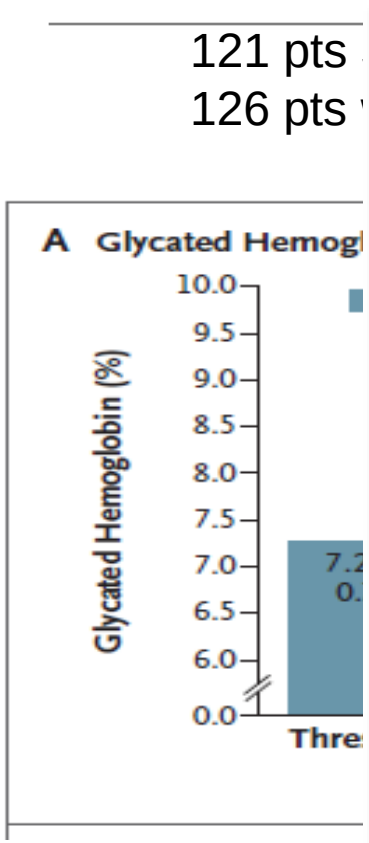
METHODS

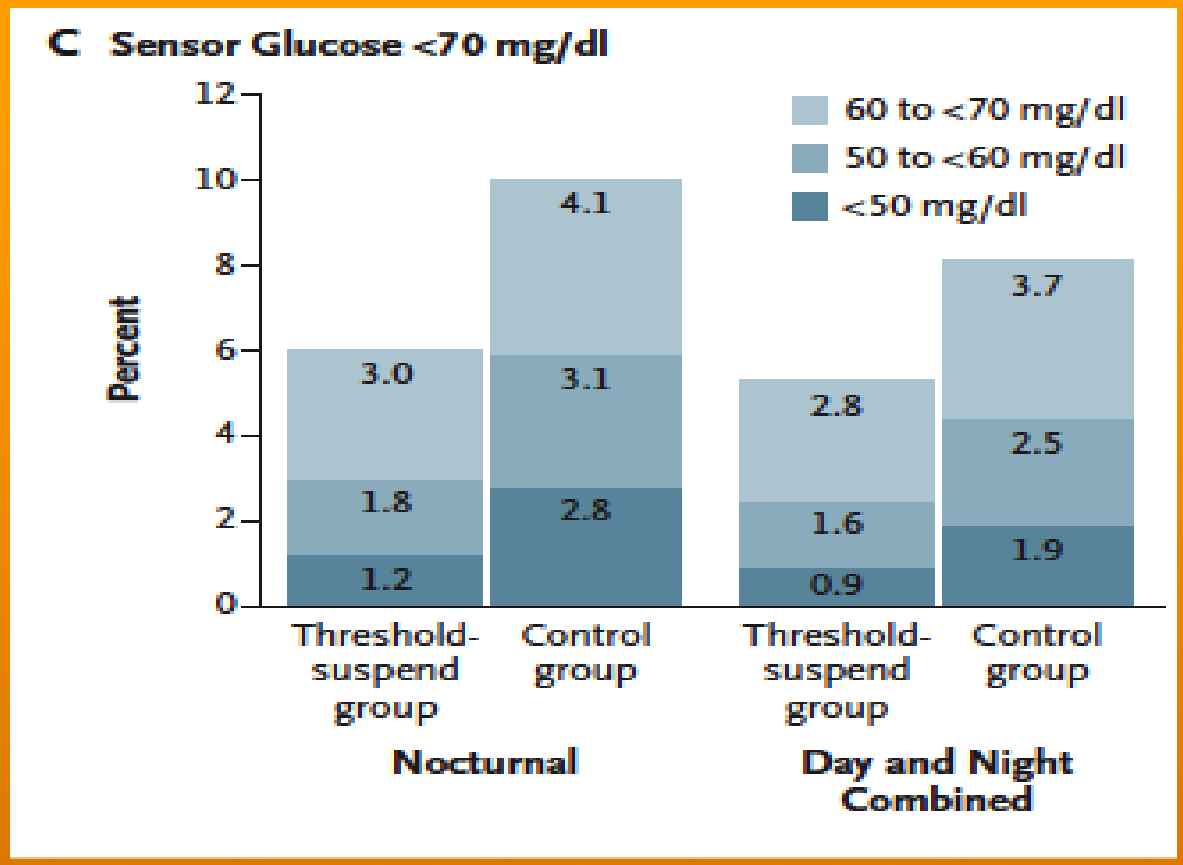
We randomly assigned patients with type 1 diabetes and documented nocturnal hypoglycemia to receive sensor-augmented insulin-pump therapy with or without the threshold-suspend feature for 3 months. The primary safety outcome was the change in the glycated hemoglobin level. The primary efficacy outcome was the area under the curve (AUC) for nocturnal hypoglycemic events. Two-hour threshold-suspend events were analyzed with respect to subsequent sensor glucose values.

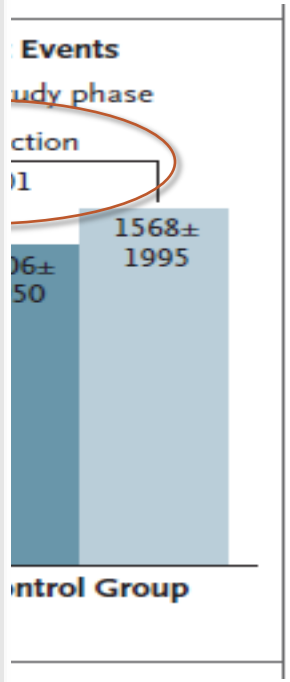
The NEW ENGLAND JOURNAL of MEDICINE

Threshold-Based Insulin-Pump Interruption for Reduction of Hypoglycemia

121 pts
126 pts







Bergenstal RM et al, N Eng J Med 2013, DOI: 10.1056/NEJMoa1303576

Original Investigation

Effect of Sensor-Augmented Insulin Pump Therapy and Automated Insulin Suspension vs Standard Insulin Pump Therapy on Hypoglycemia in Patients With Type 1 Diabetes

A Randomized Clinical Trial

Tran
Adar
Timo

Eligible patients included those aged 4 to 50 years with type 1 diabetes receiving insulin pump therapy, having been diagnosed with diabetes for at least a year, being treated with an insulin pump for at least 6 months, having a glycated hemoglobin level of 8.5% or lower, **and having impaired awareness of hypoglycemia.**

Original Investigation

Effect of Sensor-Augmented Insulin Pump Therapy and Automated Insulin Suspension vs Standard Insulin Pump Therapy on Hypoglycemia in Patients With Type 1 Diabetes
A Ra

Trang T. Ly
Adam Rett
Timothy W

Table 2. Clinical Outcomes

	Insulin Pump (n = 49)	Sensor-Augmented Pump With Low-Glucose Suspension (n = 46)
Sum of Severe and Moderate Hypoglycemia		
Baseline		
Rate per 100 patient-months (95% CI)[a]	20.7 (13.8 to 30)	129.6 (111.1 to 150.3)
No. of events (total No. of patients)	28 (45)	175 (45)
End point		
6-Month rate per 100 patient-months (95% CI)[a]	11.9 (6.8 to 19.3)	28.4 (19.8 to 39.6)
No. of events (total No. of patients)	13 (45)	35 (41)
Incidence rate per 100 patient-months (95% CI)[b]	34.2 (22.0 to 53.3)	9.5 (5.2 to 17.4)
Patients modeled	45	41
Incidence rate ratio per 100 patient-months (95% CI)[b]		3.6 (1.7 to 7.5)
P value		<.001

JAMA. 2013;310(12):1240-1247. doi:10.1001/jama.2013.277818

Effect of Sensor-Augmented Insulin Pump Therapy and Au Th A

Trang
Adam
Timot

Severe hypoglycemia[a]		
Baseline		
Rate per 100 patient-months (95% CI)	2.1 (0.8 to 4.6)	1.8 (0.6 to 4.3)
No. of events (total No. of patients)	6 (49)	5 (46)
End point		
6-Month rate per 100 patient-months (95% CI)	2.2 (0.5 to 6.5)	0 (0 to 2.4)
No. of events (total No. of patients)	6 (45)	0 (41)
Incidence rate difference from baseline to end point (95% CI)		1.5 (0.3 to 2.7)
P value		.02

JAMA. 2013;310(12):1240-1247. doi:10.1001/jama.2013.277818

Analisi di costo efficacia nel trattamento dei pazienti diabetici T1 in Italia

La costo-efficacia delle terapie per il DM in Italia

ANALISI COSTO-EFFICACIA CSII VS MDI

Cost-Effectiveness Analysis of Continuous Subcutaneous Insulin Injection vs. Multiple Daily Injections in Type 1 Diabetes Patients: An Italian Perspective

Peter Lynch[1]; Stefano Giardina[2]; Antonio Nicolucci[3]; Natalie L. Papo[4]; Marco Orsini Federici[2]; Michael E. Minshall[5]

[1]Medtronic Diabetes, USA; [2]Medtronic Italy, IT; [3]Mario Negri Sud, IT; [4]Medtronic International, CH; [5]IMS Health, USA

ims | INTELLIGENCE. APPLIED.

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Background and Objectives

Due to burgeoning healthcare costs and multiple effective treatment options for type 1 diabetes mellitus (T1DM), it is becoming more important that decision makers identify cost-effective interventions for use in treating T1DM. Two recent studies have found that continuous subcutaneous insulin injection (CSII) represents good value for money in the UK and Australia.[1,2] The objective of this study was to project long term costs and outcomes of CSII compared with multiple daily injections (MDI) of insulin in adult T1DM patients in Italy.

Methods

- A validated health economic model (CORE Diabetes Model)[3,4] was used to determine the incremental cost effectiveness ratio (ICER) of CSII compared with MDI using published clinical and Italian cost data
- The model is based on a series of Markov-based sub-models that simulate all major complications of diabetes.
- The primary input variable was change in HbA_{1c} and was assumed to be an improvement of -1.2% for CSII compared with MDI in the base case.[5] The base case also assumed a 50% reduction in severe hypoglycemia events for CSII compared to MDI[6], and no disutility associated with the fear of hypoglycemia.
- The average annual costs for CSII compared with MDI and diabetes complications were taken from published sources with an 8-year pump life assumed in the base case.
- A 60-year time horizon and an annual discount rate of 3.0% on costs and outcomes were used.
- Adult cohort baseline characteristics used for both CSII and MDI included mean age, 27.0 years; duration of diabetes, 9.0 years; 53.5% male; 90% Caucasian, 5% African-American, 5% Hispanic; body mass index, 23.75 kg/m^2; mean HbA_{1c}, 8.95%.[7]
- Annual treatment costs were €5699 for CSII and €2734 for MDI including costs for insulin pump (CSII), disposables, insulin, SMBG, and outpatient visits.

References:

[1]Cohen N *et al. Pharmacoeconomics*, 2007;25(10):881-897. [2]Roze S *et al. Diabetic Medicine*, 2005;22:1239-1245
[3]Palmer *et al. Current Medical Research and Opinion* 2004;20(Supplement 1):S5-S26.
[4]Palmer *et al. Current Medical Research and Opinion* 2004;20(Supplement 1):S27-S40.
[5]Weissberg-Benchell J *et al. Diabetes Care*, 2003;26(4):1079-1087.
[6]Bruttomesso D *et al. Diabetic Medicine*, 2002;19(8):628-634. [7](DCCT). *New England Journal of Medicine*, 2005;353(25):2643-53.
[8]Pickup J *et al. Diabetic Medicine*, 2008;25:765-774. [9]Currie C. *Current Medical Research and Opinion* 2006;22(8):1523-34.
[10]NICE technology appraisal guidance 151 (2008). Available from: www.nice.org.uk/TA151
[11]Scroccaro *et al. Pharmacoeconomics Italian Research Articles* 2005;7(3):195-206

This study was funded by Medtronic Diabetes, Northridge, CA, USA

Email to: peter.m.lynch@medtronic.com

Results-Base Case

Table 1. Incremental Cost-Effectiveness Ratios (ICERs)*

Effectiveness Measure	Incremental Costs	Incremental Effectiveness	ICER
Based on QALYs	€33,874	1.063 QALYs	€31,879/QALY
Based on Life Expectancy	€33,874	0.981 years	€34,541/LYG

*Incremental value=CSII value-MDI value; LYG=life-year gained; QALY=quality-adjusted life year; Costs are €2007.

Table 2. Direct Medical Costs over Patient's Lifetimes*

Costs (per patient over lifetime)	CSII	MDI	Difference (CSII-MDI)
Total Direct Costs	254,871	220,997	33,874
Treatment and Management Costs	134,037	73,261	60,776
Complication Costs	120,834	147,736	-26,902

*Costs are €2007.

Table 3. Risk of Selected Diabetes-Related Complications

Diabetes-Related Complication	% Reduction in Selected Complications
Proliferative Diabetic Retinopathy	-29%
End-Stage Renal Disease (ESRD)	-20%
Nephropathy Death	-24%
Peripheral Vascular Disease	-15%

Results-Sensitivity Analyses

Table 4. Incremental Cost-Effectiveness Ratios (ICERs)*

Variable Changes from Base Case (Univariate)	ICER (Cost/QALY)
Alternate HbA_{1c} Setting #1 (-0.95%±0.15% HbA_{1c})[3]	€40,545
Alternate HbA_{1c} Setting #2 (-0.62%±0.15% HbA_{1c})[8]	€61,345
No Difference in Hypoglycemia rates	€53,483
75% Reduction in Hypoglycemia rates	€20,167
Fear of Hypoglycemia Setting #1 (QOL disutility -0.023)[9,10]	€19,796
Fear of Hypoglycemia Setting #2 (QOL disutility -0.05)[10]	€13,694
6-Year Insulin Pump Life before Replacement	€34,906
4-Year Insulin Pump Life before Replacement	€40,943
Variable Changes from Base Case (Multivariate)	**ICER (Cost/QALY)**
4-Yr Pump Life + Fear of Hypoglycemia #1 + HbA_{1c} Setting #1	€29,351
4-Yr Pump Life + Fear of Hypoglycemia #1 + HbA_{1c} Setting #2	€36,341
4-Yr Pump Life + Fear of Hypoglycemia #1 + No Difference in Hypo rates	€38,088
4-Yr Pump Life + Fear of Hypoglycemia #2 + HbA_{1c} Setting #1	€19,450
4-Yr Pump Life + Fear of Hypoglycemia #2 + HbA_{1c} Setting #2	€22,333
4-Yr Pump Life + Fear of Hypoglycemia #2 + No Difference in Hypo rates	€25,936

*Costs are €2007.

Summary:

- CSII was associated with a QALY gain of 1.063 and demonstrated an ICER of €31,879/QALY compared to MDI in adult T1DM patients in Italy (Table 1).
- CSII was associated with increased treatment and management costs that were partially offset by a reduction in diabetes complication costs (Table 2).
- Improved glycemic control with CSII led to a lower projected incidence of diabetes complications (Table 3).
- Sensitivity analyses demonstrated findings were most sensitive to changes in HbA_{1c}, hypoglycemia rates, fear of hypoglycemia and pump life (Table 4).
- Probabilistic sensitivity analysis demonstrated a 84.9% chance of the true cost/QALY being ≤€40,000/QALY for adult T1DM patients in Italy.

Conclusion: Given a willingness to pay of €40,000/QALY[11] in Italy, the analysis demonstrated that CSII is a cost-effective treatment option when compared to MDI for adult patients with T1DM in Italy.

ISPOR 2010

La costo-efficacia delle terapie per il DM in Italia

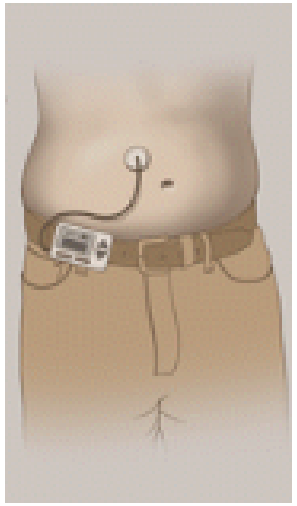
ANALISI COSTO-EFFICACIA CSII VS MDI

PRINCIPALI CARATTERISTICHE ANALISI

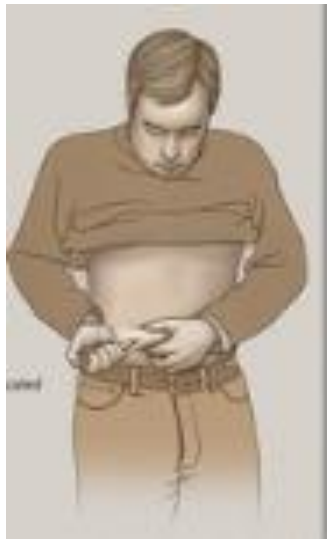
- ✓ Utilizzo Core Diabetes Model[1]
- ✓ Prospettiva: SSN
- ✓ Orizzonte temporale: lifetime

COORTE PAZIENTI ADULTI CON DMT1

Emoglobina glicata (HbA1c): 8,95%



CSII vs MDI
nei pazienti con diabete di tipo 1[2]



PRINCIPALI DATI INPUT

- ✓ Riduzione di **1,2%** della HbA1c
- ✓ Riduzione del **50%** degli eventi di ipoglicemia severa per CSII
- ✓ Costo annuale di trattamento per la terapia CSII pari a **€5.699**
- ✓ Costo annuale di trattamento per la terapia MDI pari a **€2.734**

[2]Peter Lynch et al. Cost-Effectiveness Analysis of Continuous Subcutaneous Insulin Injection vs. Multiple Daily Injections in Type 1 Diabetes Patients: An Italian Perspective.

La costo-efficacia delle terapie per il DM in Italia

ANALISI COSTO-EFFICACIA CSII VS MDI

Misura dell'efficacia	Costo incrementale	Efficacia incrementale	ICER
QALY	33.874€	1,063 QALYs	**31.879€/QALY**
Anni di vita guadagnati	33.874€	0,981 anni	**34.541€/LYG**

Data la soglia di costo-efficacia in Italia pari a 60.000 €/QALY[1], la terapia CSII è **costo-efficace** rispetto alla MDI in pazienti adulti con DMT1

[2]eter Lynch et al. Cost-Effectiveness Analysis of Continuous Subcutaneous Insulin Injection vs. Multiple Daily Injections in Type 1 Diabetes Patients: An Italian Perspective.

La costo-efficacia delle terapie per il DM in Italia

ANALISI COSTO-EFFICACIA SAP VS CSII

HEALTH-ECONOMIC EVALUATION OF SENSOR-AUGMENTED PUMP (SAP) VERSUS INSULIN PUMP THERAPY ALONE (CSII), IN TYPE 1 DIABETES PATIENTS, IN ITALY

STÉPHANE ROZE[1], ELSA DUTEIL[1], MARIANTONIETTA NACLERIO[2], DANIELA D'OSTILIO[2], SIMONA DE PORTU[3]

1: HEVA HEOR Sarl, Lyon, France. 2: Medtronic, Milano, Italy. 3: Medtronic International Trading Sarl, Tolochenaz, Switzerland.

HEVA HEOR

OBJECTIVES

The objective of the study was to estimate the cost-effectiveness and to project the clinical benefits of sensor augmented pump (SAP) versus continuous subcutaneous insulin infusion therapy alone (CSII) in type 1 diabetes patients (T1D) in the Italian setting.

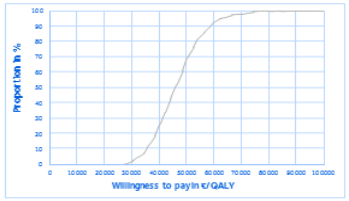
TABLE 1: Cohort characteristics

	Hyperglycemic population	hypoglycemia-prone population
Mean baseline age	27 years	18.6 years
Diabetes duration	13 years	11 years
Mean baseline HbA1c	64 mmol/mol (8.1%)	58 mmol/mol (7.5%)

RESULTS

In the hyperglycemic population, the incremental cost-effectiveness ratio (ICER) was 44,982 per Quality Adjusted Life Year gained (QALY) based on a societal perspective. The improvement in discounted QALY was 1.448 in favour of SAP. Undiscounted life expectancy was increased by 0.476 year for SAP versus CSII alone. Additional SAP related costs were partially offset by the savings due to the reduction in diabetes related complications and the lower frequency of SMBG tests.

Figure 1: Acceptability curve (hyper population)



CONCLUSIONS

According to commonly accepted thresholds, SAP vs. CSII can be considered good value for money in the Italian setting both in the hyperglycemic and hypoglycemia-prone patients. Extensive sensitivity analysis on key drivers confirmed the robustness of results.

MATERIAL AND METHODS

The health-economic modelling was based on the Core Diabetes Model (CDM) 4.5. The CDM is a published and well-accepted diabetes model, which covers both type 1 and type 2 diabetes. It allows the comparison of several treatment strategies, based on clinical parameters. The simulation includes all major diabetes related complication as well as non-specific mortality.

Two separate analyses were conducted on a) a population with hypoglycemic concerns and b) a population with hyperglycemia.

The first analysis was based on the study reported by Ly et al (1,2). The second one was based on the meta-analysis performed by Pickup et al.(3) This allowed us to use some baseline characteristics of patients and to derive the effect on clinical parameters for the 2 arms: CSII alone and SAP for various scenario.

Intervention effects

- Cohort with increased risk for hypoglycemia

The key efficacy data used for this analysis also came from Ly et al (2). After 6 months using SAP, no severe hypoglycemic events (SHE) were reported (0) for these patients versus 2.2 per 100 patients month in the CSII arm. In the base-case analysis, these reductions in SHE rates were assumed to be transferable to the Italian setting.

- Hyperglycemic population

Intervention effects were directly derived from the formulae published by Pickup et al 2011 (3) meta-analysis, for both patients on CSII alone and patients on SAP. Effects have been evaluated for a baseline HbA1c level of 64 mmol/mol in IFCC units (8.1% in DCCT unit) and a frequency of use of SAP per week of 5.64 days/week (49 sensors per year).

Costs of complications, interventions and related to loss of productivity were derived from Italian published sources.

RESULTS

The acceptability curve showed that the likelihood to be cost-effective at a willingness to pay of 84,000 €/QALY was 100% and for a probability of 69.2% this willingness to pay was 50,000 €/QALY.

In the population with hypoglycemia concerns, due to the reduction in SHE, the increase in discounted life expectancy was 0.189 years in favour of SAP. When quality of life is taken into account, this difference was 1.877 QALY. This led to an ICER of 33,692 €/QALY. Additional SAP related costs were partially offset by the savings due to the lower frequency of SMBG tests and the indirect costs.

1. Ly et al. Diabetes Care. 2012;35(7):1462-3.
2. Ly et al. JAMA. 2013;310(12):1240-7.
3. Pickup et al BMJ. 2011;343:d3805.
4,5. Palmer AJ, Roze S, et al. The CORE Diabetes Model. Curr Med Res Opin. 2004;20 Suppl 1:S5-26.

Medtronic

La costo-efficacia delle terapie per il DM in Italia

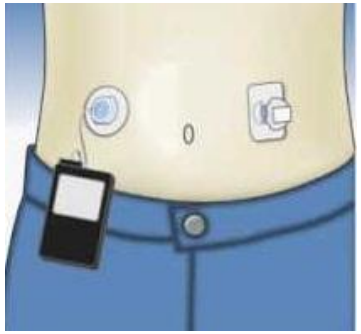
ANALISI COSTO-EFFICACIA SAP VS CSII

PRINCIPALI CARATTERISTICHE ANALISI

- ✓ Utilizzo Core Diabetes Model[1]
- ✓ Prospettive : SSN e società
- ✓ Orizzonte temporale: lifetime

PAZIENTI ADULTI CON DMT1

- ✓ Coorte con rischio di ipoglicemia - coorte IPO
- ✓ Coorte con emoglobina glicata oltre target (media 8,1%) - coorte IPER



SAP vs CSII
nei pazienti con diabete tipo 1[2]

PRINCIPALI DATI INPUT

Coorte IPO

- ✓ Eventi di ipoglicemie severe :
  - CSII: **2,2 episodi/100 pazienti anno**
  - SAP: 0
- ✓ Δ costo trattamento annuale SAP vs CSII: **3.951,25€**

Coorte IPER

- ✓ **2,6 episodi/100 pazienti anno** di ipoglicemie severe in entrambi i bracci di trattamento
- ✓ Δ costo trattamento annuale SAP vs CSII: **3.951,25€**
- ✓ Riduzione della HbA1c:
  - SAP: **0,6%**
  - CSII: **0,1%**

Roze S et al. Health-economic evaluation of sensor-augmented pum (SAP) vs insulin pump therapy alone (CSII) in type 1diabetes patients, in Italy. Presented at ATTD 2016

La costo-efficacia delle terapie per il DM in Italia

ANALISI COSTO-EFFICACIA SAP VS CSII

Coorte	Prospettiva	Costo incrementale	Efficacia incrementale	ICER
IPER	SSN (solo costi diretti)	1,448	77.075€	**53.225€/QALY**
	Società (costi diretti + indiretti)	1,448	65.139€	**44.982€/QALY**
IPO	SSN (solo costi diretti)	1,877	71.796€	**38.250€/QALY**
	Società (costi diretti + indiretti)	1,877	63.240€	**33.692€/QALY**

Data la soglia di costo-efficacia in Italia pari a 60.000 €/QALY[1], la terapia SAP è **costo-efficace** rispetto alla CSII in pazienti adulti con DMT1

Roze S et al. Health-economic evaluation of sensor-augmented pum (SAP) vs insulin pump therapy alone (CSII) in type 1diabetes patients, in Italy. Presented at ATTD 2016

Le analisi di costo-efficacia nel trattamento dei pazienti diabetici T1 nel contesto internazionale

Il contesto internazionale

RACCOMANDAZIONI UK E GERMANIA

NUOVE LINEE GUIDA SUL TRATTAMENTO DEL DIABETE (2015)

Il NICE raccomanda il CGM in:

- ✓ particolari sottogruppi di pazienti adulti con DMT1
- ✓ sottogruppi di bambini e giovani con DMT1 e DMT2 (elemento prioritario nell'implementazione)
- ✓ sottogruppi di donne con diabete pre-gestazionale

NUOVO DIAGNOSTIC ASSESSMENT PATHWAY (DAP) DEL SISTEMA PARADIGM VEO (draft 2015)

Il NICE raccomanda l'utilizzo del **MiniMed Paradigm Veo** nei casi con:

- ✓ episodi ripetuti e inavvertiti di ipoglicemia disabilitante
- ✓ eventi di ipoglicemie nonostante la gestione ottimale con CSII
- ✓ ansia a causa della paura di eventi ipoglicemici

ULTIMO REPORT IQWIG PUBBLICATO NEL 2015

- ✓ Il **CGM** ha un **comprovato vantaggio** vs **SMBG** negli adulti (>18 anni) e dimostra un certo beneficio anche nei bambini
- ✓ La **Federal Joint Committee** (GBA) sta lavorando alla decisione finale in materia di rimborso

Il contesto internazionale

EVIDENZE ECONOMICHE IN EUROPA

- ✓ **Analisi di costo-efficacia SAP vs CSII nei pazienti con DMT1**

SVEZIA: pubblicazione - Diabetic Medicine 2015

UK: pubblicazione - JME 2015

Francia: pubblicazione - DTT 2015

Olanda: presentazione a ISPOR 2015

Danimarca: poster presentato all'ATTD 2016

Italia: poster presentato all'ATTD 2016

- ✓ **Analisi di costo- efficacia CSII vs MDI nei pazienti con DMT1: revisione sistematica della letteratura** Diabetic Medicine 2015
- ✓ **Analisi economica delle complicanze relative al livello di HbA1c nei pazienti DMT1 in Italia –** pubblicazione Acta Diabetologica 2015

"Short-term cost analysis of complications related to glaycated hemoglobin in patients with type 1 diabetes in the Italian setting" - Acta Diabetologica 2015

S Roze et al. Systematic Review or Meta-analysis Cost-effectiveness of continuous subcutaneous insulin infusion versus multiple daily injections of insulin in Type 1 diabetes: a systematic review Diabet Med. 2015 May 11

Cost-Effectiveness CSII Vs MDI, SAP Vs CSII

Published cost-effectiveness analyses show that in Type 1 diabetes CSII is cost-effective vs. MDI and SAP Vs CSII across a number of settings for patients who have poor glycaemic control and/or problematic hypoglycaemia, with cost-effectiveness highly sensitive to the reduction in HbA1c and hypoglycaemia frequency

S Roze et al. Diabet Med. 2015
S Roze et al. Diabet Tech Ther 2016
Rob Riemsma. NHS HTA 2016

Regione Emilia-Romagna

SERVIZIO ASSISTENZA TERRITORIALE

DIREZIONE GENERALE SANITÀ E POLITICHE SOCIALI E PER L'INTEGRAZIONE

Linee di indirizzo regionali per un uso appropriato dei dispositivi medici per l'autocontrollo e l'autogestione nel Diabete Mellito

Ottobre 2015

Appropriatezza Prescittiva FGM

Sulla base di quanto sopra esposto il gruppo ha definito appropriata la prescrizione nei pazienti con diabete di tipo 1 in terapia insulinica intensiva e precedentemente avviati a programmi di educazione terapeutica quando fossero state documentate almeno una delle seguenti condizioni:

- inadeguato compenso glicemico: HbA1c>64 mmol/mol (HbA1c>8%);
- sindrome da ipoglicemie inavvertite (“hypoglycemia unawareness”).;
- documentati episodi di ipoglicemia ricorrente che interferiscano negativamente con la qualità di vita e/o episodi di ipoglicemia severa (>1 episodio/anno).

Criteri Clinici di Appropriatezza e

- So
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700 soggetti con T1DM
(350 pediatrici e 350 Adulti)

Costo Incementale 671.000 €

Conclusion

Are New Technology Worth the Expense?