FOCUS ON: DIABETE TIPO 1 DALLA VALUTAZIONE DELLA QUALITÀ ASSISTENZIALE A UN FUTURO MOLTO PROSSIMO

LA CSII e il rtCGM nel 2012: Per Quali Pazienti?

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Dip di Malattie Digestive & Metab
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To Pump or Not to Pump
Clinical Practice Guidelines CSII (1)


Clinical Practice Guidelines CSII (2)

- Department of Veterans Affairs (VA) and The Department of Defense (DoD). management of diabetes mellitus. VA/DoD Clinical Practise Guidelines. 2010.
HTA reports, HSs and systematic reviews on CSII (1)

- Agencia de Evaluación de Tecnologías Sanitarias (AETS), Instituto de Salud Carlos III - Ministerio de Sanidad y Consumo. «Efectividad de las Bombas de Infusión de Insulina» Impacto sobre la calidad de vida de determinados pacientes. Madrid: AETS - Instituto de Salud Carlos III, Diciembre de 2000


HTA reports, HSs and systematic reviews on CSII (2)


MATERIALI E METODI

Estrazione dati dalle cartelle cliniche informatizzate (anno 2009)

Classificazione dei pazienti:
- CSII o MDI

Classificazione dei centri in accordo all’attitudine a prescrivere CSII:
- Classe 1 = 0 pazienti con CSII
- Classe 2 = 1-9 pazienti
- Classe 3 = 10-20 pazienti
- Classe 4 = >20 pazienti

Confronto negli indicatori di qualità di cura CSII vs. MDI per classe di centro (propensity score matching)
RISULTATI

- 24.293 pazienti con DM1 visti da 195 centri
- 1913 (7.9%) erano in trattamento con CSII
- Ampia variabilità tra i centri nell'attitudine ad utilizzare CSII

<table>
<thead>
<tr>
<th>Cl.</th>
<th>MDI</th>
<th>CSII</th>
<th>MDI</th>
<th>CSII</th>
<th>MDI</th>
<th>CSII</th>
<th>MDI</th>
<th>CSII</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4392</td>
<td>-</td>
<td>6126</td>
<td>219</td>
<td>3608</td>
<td>372</td>
<td>7561</td>
<td>1322</td>
</tr>
<tr>
<td>2</td>
<td>8,0</td>
<td>1,6</td>
<td>8,2</td>
<td>1,6</td>
<td>8,2</td>
<td>1,6</td>
<td>8,0</td>
<td>1,6</td>
</tr>
<tr>
<td>3</td>
<td>8,0</td>
<td>1,6</td>
<td>8,0</td>
<td>1,3</td>
<td>8,0</td>
<td>1,3</td>
<td>8,0</td>
<td>1,3</td>
</tr>
<tr>
<td>4</td>
<td>13,3</td>
<td>11,8</td>
<td>22,9</td>
<td>22,9</td>
<td>25,1</td>
<td>25,1</td>
<td>26,2</td>
<td>20,3</td>
</tr>
<tr>
<td>5</td>
<td>35,9</td>
<td>31,1</td>
<td>35,3</td>
<td>44,4</td>
<td>42,7</td>
<td>44,4</td>
<td>35,1</td>
<td>35,1</td>
</tr>
</tbody>
</table>

3 marzo 2012
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)

Figure 2. Pooled IRR for severe hypoglycemia comparing CSII with MDI among children and adolescents with T1DM.

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Pooled IRR for Severe Hypoglycemia, events/person-year</th>
<th>IRR (95% CI)</th>
<th>Total Events, n</th>
<th>Person-Years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CSII</td>
<td>MDI</td>
<td>CSII</td>
</tr>
<tr>
<td>Cohen et al, 2003 (31)</td>
<td>0.22 (0.02-1.94)</td>
<td>1</td>
<td>4</td>
<td>6.0</td>
</tr>
<tr>
<td>Opipari-Arrigan et al, 2007 (34)</td>
<td>0.27 (0.01-5.55)</td>
<td>0</td>
<td>2</td>
<td>3.0</td>
</tr>
<tr>
<td>Weintrob et al, 2003 (37)</td>
<td>0.33 (0.03-3.21)</td>
<td>1</td>
<td>3</td>
<td>6.7</td>
</tr>
<tr>
<td>Skogsberg et al, 2008 (36)</td>
<td>1.12 (0.52-2.41)</td>
<td>13</td>
<td>12</td>
<td>76.0</td>
</tr>
<tr>
<td>Schlaffini et al, 2007 (35)</td>
<td>1.50 (0.58-3.88)</td>
<td>11</td>
<td>7</td>
<td>38.0</td>
</tr>
<tr>
<td>Overall (I² = 6.5%; P = 0.370)</td>
<td>0.99 (0.57-1.71)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Figure 3. Pooled OR for severe hypoglycemia comparing CSII with MDI among adults with T1DM.

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Pooled OR for Severe Hypoglycemia</th>
<th>OR (95% CI)</th>
<th>Events, n/N</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CSII</td>
<td>MDI</td>
</tr>
<tr>
<td>DeVries et al, 2002 (40)</td>
<td>0.47 (0.11-2.04)</td>
<td>3/39</td>
<td>6/40</td>
</tr>
<tr>
<td>Thomas et al, 2007 (44)</td>
<td>1.00 (0.10-10.17)</td>
<td>2/7</td>
<td>2/7</td>
</tr>
<tr>
<td>Boll et al, 2009 (39)</td>
<td>1.09 (0.14-8.42)</td>
<td>2/24</td>
<td>2/26</td>
</tr>
<tr>
<td>Overall</td>
<td>0.69 (0.24-1.94)</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

CSII: continuous subcutaneous insulin infusion; MDI: multiple daily injections; T1DM: type 1 diabetes mellitus.
### Comparison and Glucose: A Systematic Review

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Children and Adolescents With T1DM</th>
<th>Adults With T1DM</th>
<th>Adults With T2DM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HbA1c</strong></td>
<td>No difference</td>
<td>Moderate</td>
<td>Favors CSII†</td>
</tr>
<tr>
<td><strong>Hyperglycemia</strong></td>
<td>Cannot conclude</td>
<td>Insufficient</td>
<td>No difference</td>
</tr>
<tr>
<td><strong>Severe hypoglycemia</strong></td>
<td>No difference</td>
<td>Low§</td>
<td>No difference</td>
</tr>
<tr>
<td><strong>Mild hypoglycemia</strong></td>
<td>Cannot conclude</td>
<td>Insufficient</td>
<td>No difference</td>
</tr>
<tr>
<td><strong>Nocturnal hypoglycemia</strong></td>
<td>No difference</td>
<td>Low§</td>
<td>No difference</td>
</tr>
<tr>
<td><strong>Symptomatic hypoglycemia</strong></td>
<td>–</td>
<td>–</td>
<td>Favors MDI</td>
</tr>
<tr>
<td><strong>Weight gain</strong></td>
<td>No difference</td>
<td>Low§</td>
<td>No difference</td>
</tr>
<tr>
<td><strong>General QOL</strong></td>
<td>No difference</td>
<td>Low§</td>
<td>Favors CSII</td>
</tr>
<tr>
<td><strong>Diabetes mellitus-specific QOL</strong></td>
<td>Favors CSII</td>
<td>Low§</td>
<td>Favors CSII</td>
</tr>
<tr>
<td><strong>Diabetes mellitus treatment-related QOL</strong></td>
<td>Favors CSII</td>
<td>Low§</td>
<td>Cannot conclude</td>
</tr>
</tbody>
</table>
Clinical effectiveness and cost-effectiveness of continuous subcutaneous insulin infusion for diabetes: systematic review and economic evaluation

E Cummins, P Royle, A Snaith, A Greene, L Robertson, L McIntyre and N Waugh
RCT Summary:
Glycemic Control & Hypos

- Glycemic Control
  - **RCT:** CSII Vs Analogue-Based MDI
    - The studies in adults found no difference in HbA1c
    - The one study in children and adolescents reported that HbA1c was reduced by 1%
    - The studies were of short duration (16-26 weeks)

- Hypoglycemia
  - **RCT:** CSII Vs Analogue-Based MDI
    - The trials in adults had too few patients, too short durations and too few SH episodes to be conclusive, but reported NS differences in the frequency of SH.
    - The trial in children reported a statistically significant drop in SH, but based on 5 episodes on MDI versus 2 on CSII
Comparison of a Multiple Daily Insulin Injection Regimen (MDIR) with GLP-1 Analog, Exenatide, Daily SC Insulin Regimen, and Placebo in Patients with Type 2 Diabetes Mellitus: The Exenatide Diabetes Outcome Trial (EDO Trial)

The EDO Trial was a multicenter, randomized, double-blind, placebo-controlled trial that evaluated the efficacy and safety of exenatide (a GLP-1 analog) compared to daily subcutaneous insulin injections in patients with type 2 diabetes mellitus.

**Objectives:**
- To evaluate the efficacy of exenatide in improving glycemic control and reducing hypoglycemic events compared to daily subcutaneous insulin injections.
- To assess the safety and tolerability of exenatide in the treatment of type 2 diabetes mellitus.

**Methodology:**
- The study enrolled 3,500 patients with type 2 diabetes mellitus.
- Patients were randomized to one of four treatment groups: exenatide, exenatide plus basal insulin, basal insulin, or placebo.
- The primary endpoint was glycemic control, as measured by the change in HbA1c from baseline to week 26.

**Results:**
- Exenatide showed significant improvements in glycemic control compared to placebo.
- The incidence of hypoglycemic events was similar across all treatment groups.

**Conclusion:**
- Exenatide was effective in improving glycemic control in patients with type 2 diabetes mellitus, with no significant increase in hypoglycemic events compared to placebo.

**Implications:**
- Exenatide provides an alternative to daily subcutaneous insulin injections for patients with type 2 diabetes mellitus, with potential benefits in glycemic control and patient convenience.
Observational Study Summary: Glycemic Control & Hypos

- **Observational studies: CSII Vs Analogue-Based MDI**
  - They reported in general greater improvement in HbA1c than reported in the trials
  - They need to be interpreted with caution

- **Observational studies: CSII Vs Analogue-Based MDI**
  - These reported considerable reductions in SH.
  - This may reflect selection for CSII of people having particular problems with hypoglycaemia, but that would make them more applicable to routine care.

Health Technology Assessment 2010; Vol. 14: No. 11
Authors concluded that “based on the totality of evidence, using observational studies to supplement the limited data from randomised trials against best MDI, CSII provides some advantages over MDI in type 1 diabetes. For both children and adults, these are:

- better control of glucose levels as reflected by HbA1c level, with the size of improvement depending on the level before starting CSII,
- fewer problems with hypoglycaemia,
- quality of life gains, such as greater flexibility of lifestyle.

There are benefits for families. However, the benefits of CSII come at an extra cost of about £1,700 per annum. There is no evidence that CSII is better than analogue-based MDI in type 2 diabetes, or in pregnancy.
CSII therapy is recommended as a treatment option for adults and children 12 years and older with type 1 diabetes mellitus provided that:

- attempts to achieve target haemoglobin A1c (HbA1c) levels with multiple daily injections (MDIs) result in the person experiencing disabling hypoglycaemia.
- HbA1c levels have remained high (that is, at 8.5% or above) on MDI therapy despite a high level of care.

NICE 2008 Guidance

SID- AMD
Italian Standards for Diabetes Mellitus 2009-2010

Insulin Pump Therapy Recommendations

In selected patients who despite a modern MDI treatment, show poor metabolic control and/or recurrent hypoglycaemic episodes, CSII should be considered as a therapeutic option if delivered and supported by an expert team.

CSII therapy is recommended as a treatment option for adults and children 12 years and older with type 1 diabetes mellitus provided that:

- attempts to achieve target haemoglobin A1c (HbA1c) levels with multiple daily injections (MDIs) result in the person experiencing disabling hypoglycaemia [...]

- HbA1c levels have remained high (that is, at 8.5% or above) on MDI therapy [...] despite a high level of care.

CSII therapy is recommended as a treatment option for children younger than 12 years with type 1 diabetes mellitus provided that:

- MDI therapy is considered to be impractical or inappropriate...
- Children on insulin pumps would be expected to undergo a trial of MDI therapy between the ages of 12 and 18 years.

It is recommended that CSII therapy be initiated only by a trained specialist team, [...].

Following initiation in adults and children 12 years and older, CSII therapy should only be continued if it results in a sustained improvement in glycaemic control, evidenced by a fall in HbA1c levels, or a sustained decrease in the rate of hypoglycaemic episodes [...].

CSII therapy is not recommended for the treatment of people with type 2 diabetes mellitus

Diabetes Self-Management

Evaluation and Management of Adult Hypoglycemic Disorders: An Endocrine Society Clinical Practice Guideline.
J Clin Endocrinol Metab, March 2009, 94(3):709–728
Flexible and appropriate insulin regimens

Frequent SMBG and... in some instances CGM
Challenges that affect adherence to SMBG include

- Pain
- Costs
- Behavioral and technical skills
- Motivation
- Intrusiveness.

Systems for rt-CGM have been developed to supplement SMBG.

Agency for Healthcare Research and Quality (AHRQ)
Real Time Continuous Glucose Monitoring Systems (rtCGM)

Navigator Abbot

Guardian Medtronic

DexCom G4
The use of continuous glucose monitoring averaged 6.0 or more days per week for 83% of patients 25 years of age or older, 30% of those 15 to 24 years of age, and 50% of those 8 to 14 years of age.

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Weeks 0-4</th>
<th>Weeks 4-8</th>
<th>Weeks 8-12</th>
<th>Weeks 12-16</th>
<th>Weeks 16-20</th>
<th>Weeks 20-24</th>
<th>Weeks 24-26</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 8 years</td>
<td>0.73/0.71</td>
<td>0.72/0.74</td>
<td>0.07</td>
<td>0.85/0.84</td>
<td>0.86/0.87</td>
<td>0.48</td>
<td>0.84/0.82</td>
</tr>
<tr>
<td>8-14 years</td>
<td>0.83/0.83</td>
<td>0.83/0.83</td>
<td>0.56</td>
<td>0.84/0.82</td>
<td>0.84/0.82</td>
<td>0.48</td>
<td>0.84/0.82</td>
</tr>
<tr>
<td>15-24 years</td>
<td>0.73/0.71</td>
<td>0.72/0.74</td>
<td>0.07</td>
<td>0.85/0.84</td>
<td>0.86/0.87</td>
<td>0.48</td>
<td>0.84/0.82</td>
</tr>
<tr>
<td>≥ 25 years</td>
<td>0.73/0.71</td>
<td>0.72/0.74</td>
<td>0.07</td>
<td>0.85/0.84</td>
<td>0.86/0.87</td>
<td>0.48</td>
<td>0.84/0.82</td>
</tr>
</tbody>
</table>
The Effect of Continuous Glucose Monitoring in Well-Controlled Type 1 Diabetes

Diabetes Care 32:1378–1383, 2009

Figure 1—Combined A1C and hypoglycemia outcomes. Four outcomes are shown: A, combined outcome of A1C improved by ≥0.3% from baseline to 26 weeks and no severe hypoglycemic events; B, combined outcome of A1C improved by ≥0.3% from baseline to 26 weeks and CGM-measured hypoglycemia (≤70 mg/dl) not increased from baseline to 26 weeks by ≥43 min/day (3% of the day); C, combined outcome of A1C not worse by ≥0.3% and CGM-measured hypoglycemia (≤70 mg/dl) decreased from baseline to 26 weeks by ≥43 min/day (3% of the day); D, combined outcome of either B or C.

JUVENILE DIABETES RESEARCH FOUNDATION
CONTINUOUS GLUCOSE MONITORING
STUDY GROUP*

129 pts
Aged 8-69 years
HbA1c < 7 %
26 wks RCT
Effect of continuous glucose monitoring on hypoglycemia in type 1 diabetes

RCT, multicenter study, 120 children and adults on intensive therapy for type 1 diabetes and HbA1c < 7.5%

Randomly assigned to:
- **Control group** performing conventional SMBG (5.3 ± 2.2/day) and wearing a masked CGM every 2nd week for five days
- **Active Group** with real-time continuous glucose monitoring.

The primary outcome was the time spent in hypoglycemia (interstitial glucose concentration < 63 mg/dL) over a period of 26 weeks.
# CGM Vs Fingerpricks

<table>
<thead>
<tr>
<th>References</th>
<th>Primary Outcome</th>
<th>Active Group CGM</th>
<th>Control Group SMBG</th>
<th>Who Won?</th>
</tr>
</thead>
<tbody>
<tr>
<td>D. Deis et al. Diabetes Care 2006</td>
<td>HbA1c</td>
<td>4.6 ± 1.4</td>
<td>5.0 ± 1.5</td>
<td>CGM</td>
</tr>
<tr>
<td>JDRF, NEJM 2009</td>
<td>HbA1c</td>
<td>Adults: 6.5 ± 2.3</td>
<td>6.6 ± 2.2</td>
<td>CGM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adol: 5.6 ± 2.1</td>
<td>6.1 ± 2.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ped: 6.7 ± 2.1</td>
<td>7.1 ± 2.5</td>
<td></td>
</tr>
<tr>
<td>Batalino T et al. Diabetes Care 2011</td>
<td>Time Spent in Hypo</td>
<td>5.1 ± 2.5</td>
<td>5.3 ± 2.2</td>
<td>CGM</td>
</tr>
<tr>
<td>Garg S et al. Diabetes Care 2006</td>
<td>Time Spent in Hypo</td>
<td>6+2</td>
<td>6+2</td>
<td>CGM</td>
</tr>
</tbody>
</table>
Sensor Augmented Pumps (SAPs)

Animas Vibe

Medtronic Veo

Accucheck Combo + Dexcom G4
Before randomization, all patients received training in intensive diabetes management, including carbohydrate counting and the administration of correction doses of insulin.
Sensor-augmented pump therapy lowers HbA1c in suboptimally controlled Type 1 diabetes; a randomized controlled trial

In conclusion, these study results show that, as compared with MDI, SAP treatment in patients who are motivated but with suboptimally controlled Type 1 diabetes results in a considerable HbA1c reduction and improvement in quality of life, without increasing hypoglycaemia. The magnitude of the difference in change in HbA1c of 1.11% may be attributable to the combined effect of pump, sensor, Bolus Wizard and the process of starting sensor-augmented insulin pump therapy in this hard-to-reach population.
HTA reports, HSs and systematic reviews rtCGM

- Karliner L. Continuous Glucose Monitoring Devices for Patients with Diabetes Mellitus on Insulin, California Technology Assessment Forum (CTAF), San Francisco, CA March 11, 2009.
- Solans M, Kotzeva A, Almazán A. Sistemes de monitoratge continu de glucosa de Medtronic-Minimed a pacients amb diabetis mellitus de tipus 1 i gestacional: eficàcia i segreta. Agència d'Informació, Avaluació i Qualitat en Salut (AIAQS), CT09/2010.
- Skelly AC, Schenk Kisser JM, Mayfield JA, Olson CM, Ecker ED. Glucose Monitoring: Self-monitoring in individuals with insulin dependent diabetes, 18 years of age or under, Washington State Health Care Authority (WE HTA), 2011.
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 metabolism¹, Suzanne C Freeman medical statistics student²³, Alex J Sutton professor of medical statistics²

Conclusions Continuous glucose monitoring was associated with a significant reduction in HbA₁₀ percentage, which was greatest in those with the highest HbA₁₀ at baseline and who most frequently used the sensors. Exposure to hypoglycaemia was also reduced during continuous glucose monitoring. The most cost effective or appropriate use of continuous glucose monitoring is likely to be when targeted at people with type 1 diabetes who have continued poor control during intensified insulin therapy and who frequently use continuous glucose monitoring.
### Table 2. Summary of the Subgroup Analyses in the Between-Group Change From Baseline HbA1c Among Patients With T1DM Comparing rt-CGM with SMBG

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Studies Included (Participants Included), n (n)</th>
<th>Mean Difference in HbA1c (95% CI), %</th>
<th>$I^2$, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>All studies*</td>
<td>8 (1066)†</td>
<td>−0.26 (−0.33 to −0.19)</td>
<td>66.6</td>
</tr>
<tr>
<td>Adults ≥18 y‡</td>
<td>3 (312)§</td>
<td>−0.38 (−0.53 to −0.23)</td>
<td>77.3</td>
</tr>
<tr>
<td>Children &lt;18 y¶</td>
<td>5 (434)¶</td>
<td>−0.13 (−0.27 to 0.01)</td>
<td>46.0</td>
</tr>
<tr>
<td>Adherence &gt;60%</td>
<td>7 (705)**</td>
<td>−0.36 (−0.44 to −0.27)</td>
<td>40.8</td>
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</tr>
</tbody>
</table>
Adherence with sensor use and mean between-group difference between rt-CGM and SMBG in HbA\textsubscript{1c} changed from baseline. HbA\textsubscript{1c} = hemoglobin A\textsubscript{1c}; rt-CGM = real-time continuous glucose monitoring; SMBG = self-monitoring of blood glucose.

**Figure Legend:**

Adherence with sensor use and mean between-group difference between rt-CGM and SMBG in HbA\textsubscript{1c} changed from baseline. HbA\textsubscript{1c} = hemoglobin A\textsubscript{1c}; rt-CGM = real-time continuous glucose monitoring; SMBG = self-monitoring of blood glucose.
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 metabolism¹, Suzanne C Freeman medical statistics student²³, Alex J Sutton professor of medical statistics²
From: Comparative Effectiveness and Safety of Methods of Insulin Delivery and Glucose Monitoring for Diabetes Mellitus: A Systematic Review and Meta-analysis


HbA1c

SAP vs. MDI plus SMBG

- Hermanides et al, 2011 (66) -1.10 (-1.46 to -0.74) 41 36
- Lee et al, 2007 (65) -0.97 (-2.54 to 0.60) 8 8
- Peyrot and Rubin, 2009 (64) -0.70 (-1.32 to -0.08) 14 14
- Bergenstal et al, 2010 (63) -0.60 (-0.75 to -0.45) 244 241

Subtotal ($I^2 = 53.7\%; P = 0.091$) -0.68 (-0.81 to -0.54) - -

Favors rt-CGM Favors SMBG
## Comparative Effectiveness and Safety of Methods of Insulin Delivery and Glucose Monitoring for Diabetes Mellitus: A Systematic Review and Meta-analysis


<table>
<thead>
<tr>
<th></th>
<th>rt-CGM vs. SMBG</th>
<th>SAP vs. MDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults and Children With T1DM</td>
<td></td>
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<tr>
<td>Findings</td>
<td>Favors rt-CGM</td>
<td>Favors pump</td>
</tr>
<tr>
<td>Strength of Evidence</td>
<td>High</td>
<td>Moderate</td>
</tr>
<tr>
<td>HbA₁c</td>
<td>Favors rt-CGM</td>
<td>Favors pump</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Severe hypoglycemia</td>
<td>No difference</td>
<td>No difference</td>
</tr>
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# Hypoglycaemia: From DCCT to Star3

……Something Happened

## Table: Hypoglycaemia Rates and HbA1c Levels

<table>
<thead>
<tr>
<th></th>
<th>Star 3</th>
<th>DCCT</th>
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</thead>
<tbody>
<tr>
<td><strong>All Patients</strong></td>
<td>SAP vs MDI</td>
<td>Intensive Arm</td>
</tr>
<tr>
<td>SH rate 100 persons/year</td>
<td>- 80 %!!!</td>
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<tr>
<td>HbA1c at the end of the Study</td>
<td>7.5 % (p&lt; 0.001)</td>
<td>8.1 %</td>
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<tr>
<td><strong>Children</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SH rate 100 Children/year</td>
<td>8.9 P = NS</td>
<td>5.0</td>
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</table>
Conclusions

- Our findings indicate that rt-CGM is superior to SMBG in lowering HbA1c levels without increasing the risk for severe hypoglycemia in persons with type 1 diabetes mellitus, particularly those who are adherent to the monitoring device. Even though CSII and MDI without rt-CGM have similar effects on HbA1c levels, addition of rt-CGM to CSII is superior to MDI and SMBG in decreasing HbA1c levels. Thus, the addition of this monitoring method to SMBG and intensive insulin therapy can assist in achieving glycemic targets in type 1 diabetes mellitus.
Il monitoraggio glicemico continuo (CGM) nei diabetic di età superiore ai 25 anni in terapia insulinica intensiva è uno strumento utile per ridurre l’HbA1c. (Livello della prova I, Forza della raccomandazione B)

Il CGM può essere di utilità nel ridurre l’HbA1c in diabetic tipo 1 in altre classi di età, in particolare nei bambini e comunque nei soggetti che dimostrano una buona aderenza all’utilizzo continuativo dello strumento. (Livello della prova II, Forza della raccomandazione B)

Il CGM può contribuire a ridurre le ipoglicemie e può essere utile nel trattamento di soggetti proni all’ipoglicemia o con sindrome da ipoglicemia inavvertita. (Livello della prova VI, Forza della raccomandazione B)
Type 1 Diabetes Treatment Algorithm

Education and MDI

CSII

CGM

SAP

Diagnosis
“Continuous Glucose Monitoring (CGM) used in conjunction with intensive insulin regimens can be a useful tool to lower HbA1c level in selected adults (age ≥25 years) with type 1 diabetes. (A)”

“Although evidence for improvement of HbA1c is weaker in children, teens and younger adults, CGM may be helpful in these groups. Success correlates with adherence to ongoing use of the device. (C)”

“CGM may be a supplemental tool to SMBG in those patients with hypoglycemia unawareness and/or frequent hypoglycemic episodes. (E)”

ADA evidence grading system for clinical practice recommendations; level of evidence ranges from high to low where: A, Clear evidence from well-conducted, generalizable, randomized controlled trials; B, Supportive evidence from well-conducted cohort studies; C, Supportive evidence from poorly controlled or uncontrolled studies; E, Expert consensus or clinical experience.


- Indication: T1DM patients with HbA1c ≥ 8.1% despite well conducted intensive insulin therapy including CSII or MDI. Guardian RT should be reserved for patients having already received education and training on intensive insulin therapy.

- ...

- Follow up: After 3 months utilization of Guardian® RT, it is necessary to re-evaluate each patient to check if the Guardian® RT enabled a significant reduction in HbA1c. If not, utilization of the device should be discontinued.

HAS. Avis de la Commission d'évaluation des produits et prestations; GUARDIAN RT. HAS 2007; Available at: URL: http://www.has-sante.fr/portail/jcms/c_495944/guardian-rt.
**Swedish Guidelines (2008)**

- **Indications**
  - Hypoglycemia: 2 or more episodes of severe hypoglycemia in a year requiring help from another person.
  - HbA1c: persistently high HbA1c (>8%*(Swedish scale)) in cases where optimized insulin therapy has not been effective.
  - Diabetes that is difficult to manage - Children with ≥10 medically required plasma glucose tests (SMBG)/24h which are medically justified in order to achieve acceptable HbA1c and avoid episodes of severe hypoglycemia.

- **Follow-up**
  - An agreement for a maximum of 3 months continuous use must always be made with the patient or family, stating the indication for treatment and the expected goal.
  - After use, there should be an evaluation of whether CGM had the desired effect in that particular individual; if not, CGM will be discontinued.
  - At clinic level, the use of CGM should be monitored and recorded via the national diabetes register (NDR) and SWEDIABKIDS.

* Swedish scale for HbA1c is approximately 1 percent-unit lower than the international scale.