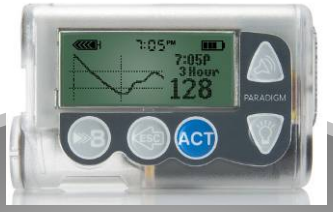
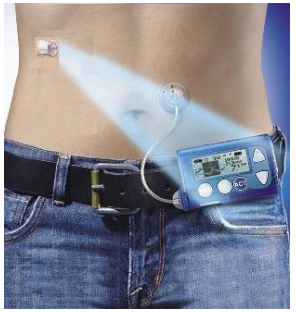
# Important key studies and rationale for CSII, SaPT* and CGM

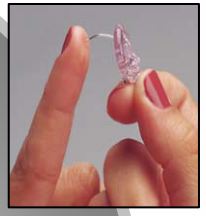



**MiniMed Paradigm REAL-Time System**

**Insulinpumpen MiniMed Paradigm 522 und 722**

**Continuous glucose monitoring (CGM)**



**Infusionssets & Reservoire**

**Glukosesensor Sof-sensor**



**BZ-Messgerät Bayer Contour Link**

**MiniLink Transmitter**

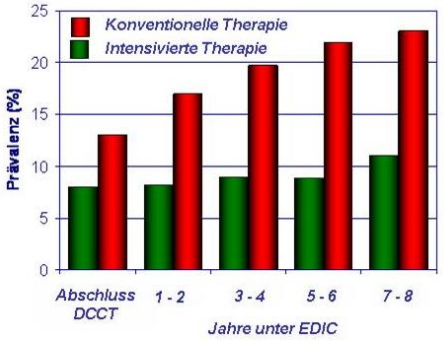

**Software CareLink Personal & PRO**



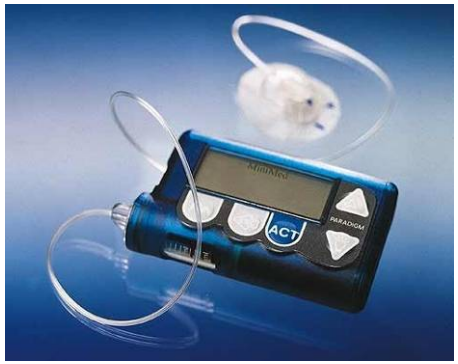
**SaPT – sensor augmented pump therapy*

Medtronic

# Important studies and rationale for CSII and CGM




**Rationale for glycemic control in accordance with DCCT/EDIC**




**Insulin pump therapy (CSII)**

**Accuracy of glucose sensors**

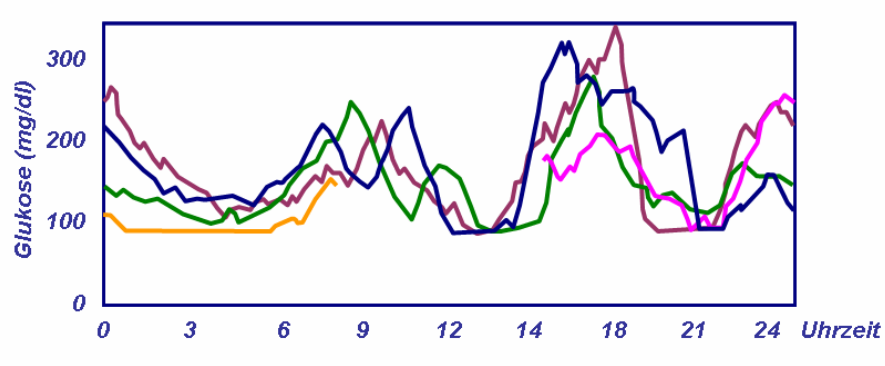

**Continuous glucose monitoring (CGM)**


**Sensor augmented pump therapy (SaPT)**

**Click on the picture to get to the contents of the chapter in which the studies are listed.**

Medtronic

# General statements on the success of treatment in patients with type 1 diabetes




Back

*Note: The information on glucose values (mg/dl or mmol/l) corresponds to the accounts in the original contributions*

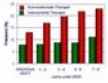
Medtronic

# General statements on success of treatment

## Claims (1):

- The better the blood sugar control as shown by the $HbA_{1c}$ value, the lesser the risk of diabetic complications, however:
- Even with the same $HbA_{1c}$ achieved with different therapies (intensive vs. conventional therapy) the risk is different.
- It is obvious that the risk of diseases resulting from the diabetes is less the more physiological the therapy.
- The lower the $HbA_{1c}$ value, the higher the risk of hypoglycemia – this is a frequently limiting factor for attaining near-normal control.

*Back*



# General statements on success of treatment

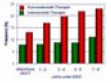
## Claims (2):

- The vascular damage caused by permanent hyperglycemia is irreversible.
- However, subsequent improvement in glycemia can moderate the progression of diabetic complications, but:
- Compared to patients where control has been near-normal in the long term, this progression is still definitely higher.

## Supporting documentary evidence:

- Diabetes Control and Complication Trial (DCCT)
- Epidemiology of Diabetes Interventions and Complications (EDIC) (follow-up study DCCT)

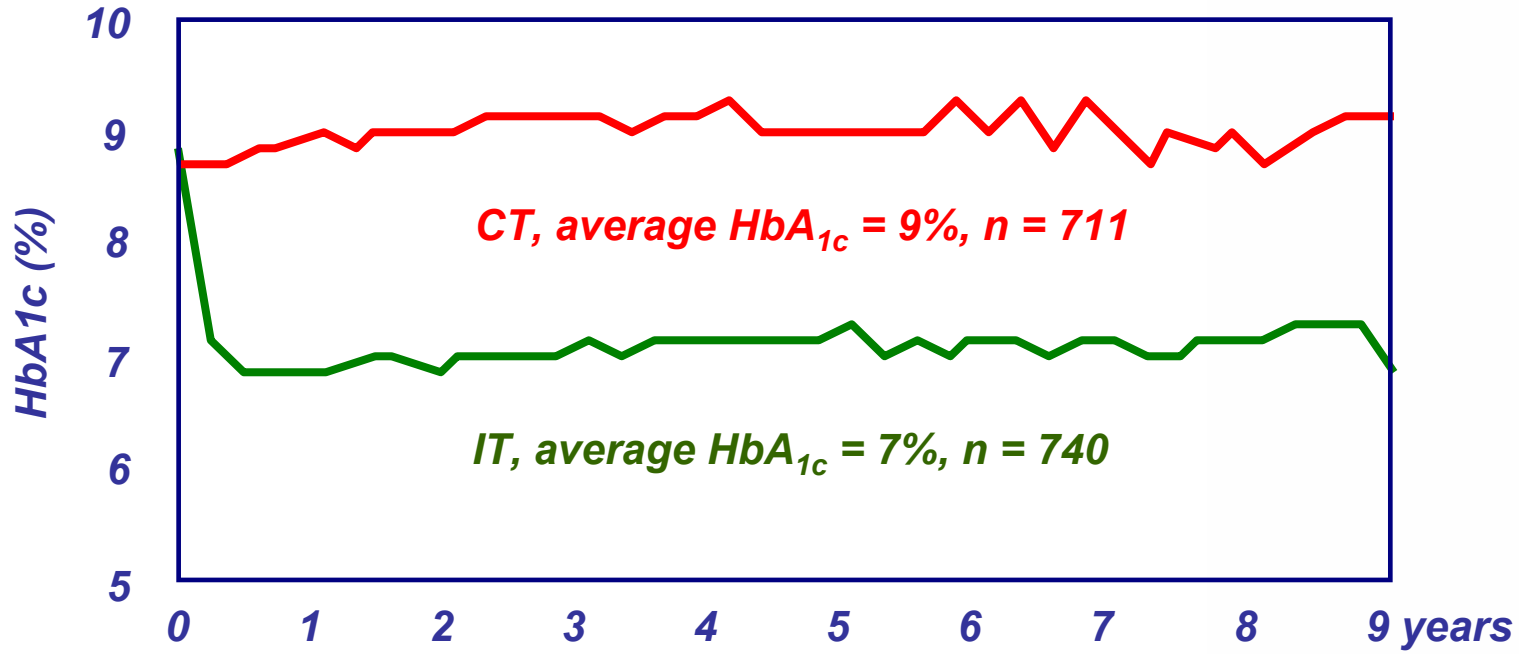
*Back*



Medtronic

# Connection between $HbA_{1c}$ and the development of diseases resulting from diabetes according to DCCT

$HbA_{1c}$ value achieved using different forms of insulin therapy over a period of 9 years:




***CT – conventional therapy***

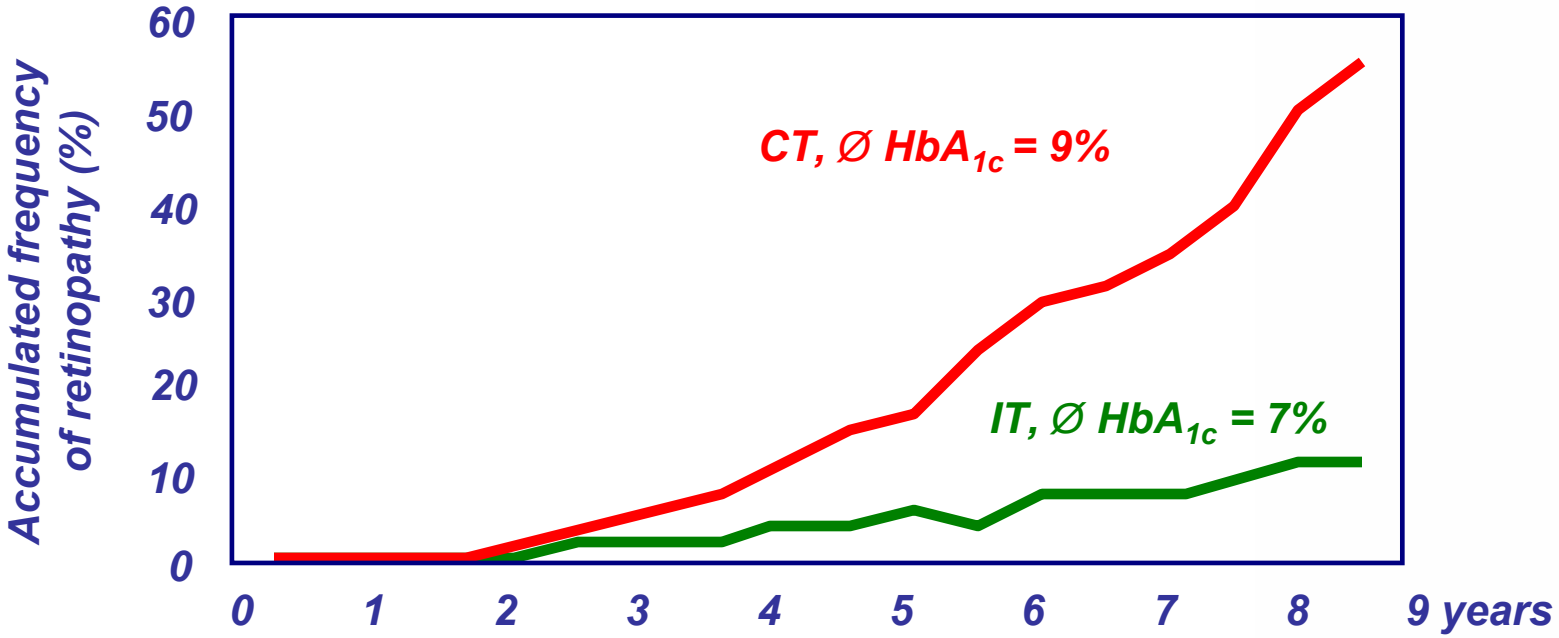
***IT – intensive therapy: MDI – multiple dose injection (n = 616), CSII (n = 124)***

*From: DCCT-Group: NEJM Vol.14 (Sept.1993), 977 – 986*

Medtronic

# Connection between $HbA_{1c}$ and the development of diseases resulting from diabetes according to DCCT

Accumulated frequency of retinopathy in type 1 diabetics over 9 years depending on therapy and $HbA_{1c}$ value achieved:




***CT – conventional therapy***

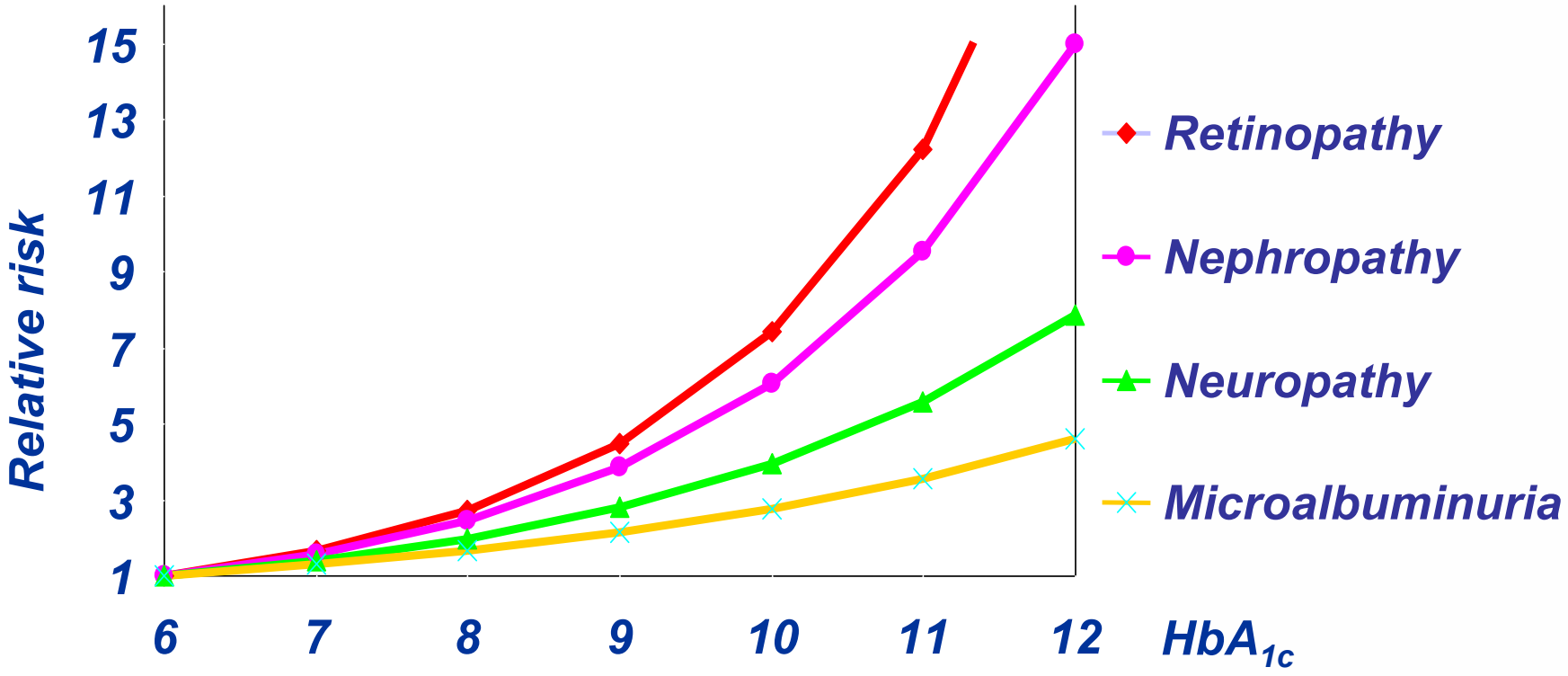
***IT – intensive therapy: MDI – multiple dose injection (n = 616), CSII (n = 124)***

*From: DCCT-Group: NEJM Vol.14 (Sept.1993), 977 – 986*

Medtronic

# Relative risk of progression of diabetic complications according to DCCT

Complications rate for various microvascular diseases dependent on $HbA_{1c}$ value:



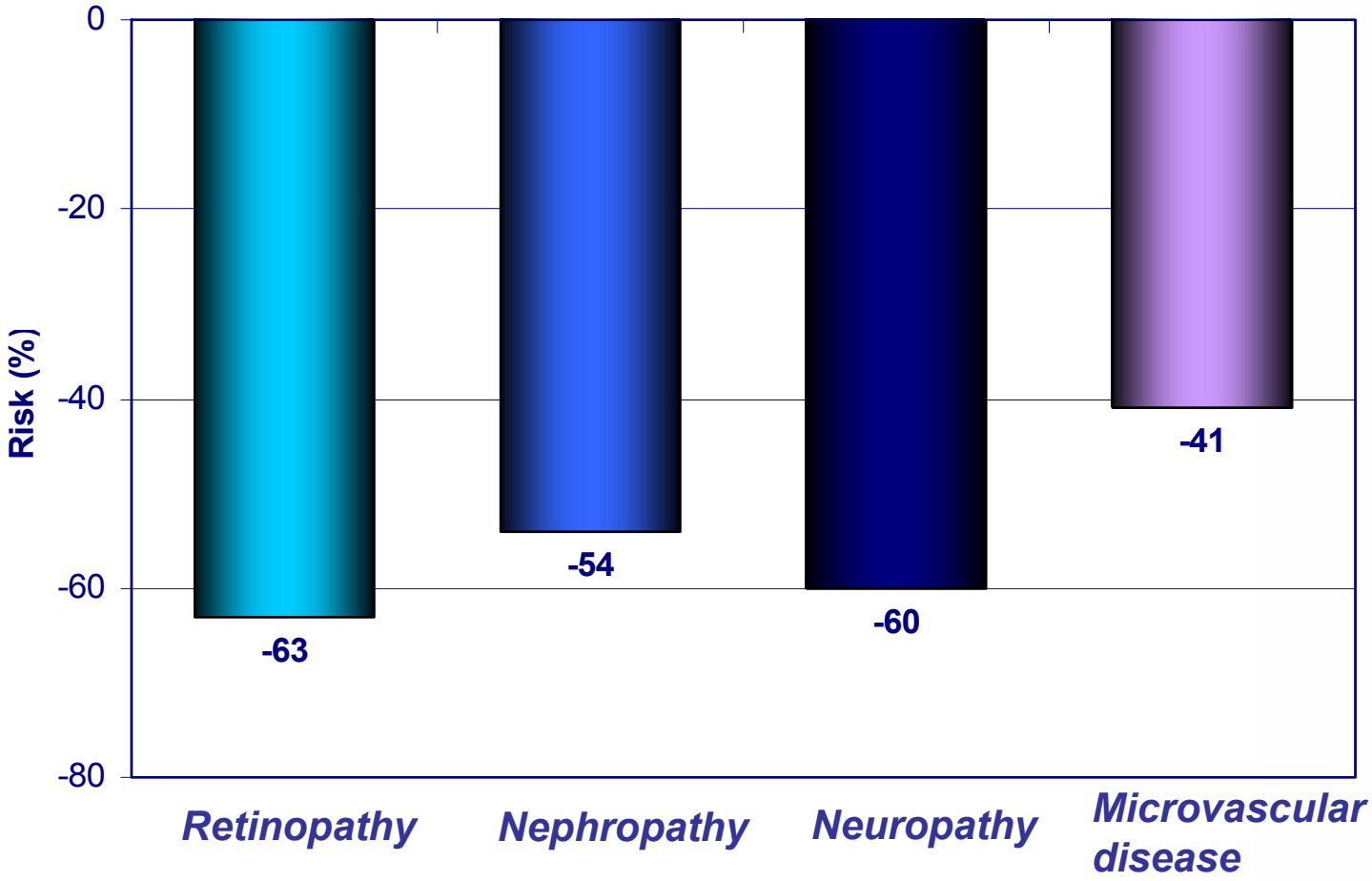

Reduction in risk with improved glycemic control is dependent on initial $HbA_{1c}$ value.

*From: Skyler, Endo Met Cl N Am 1996*

Medtronic

# Relative risk of progression of diabetic complications according to DCCT

Reduced risk of diabetic complications in relation to mean $HbA_{1c}$ value in both groups: 9.0 -> 7.0 %

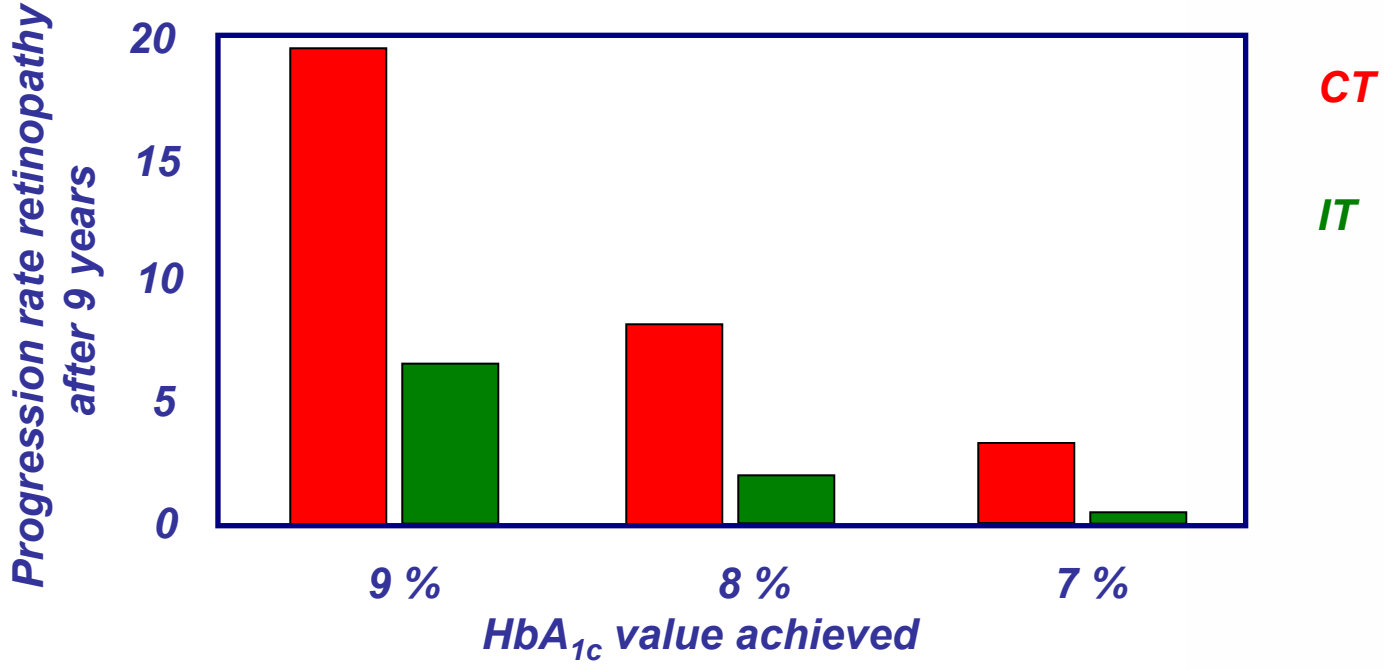



*From: Skyler, Endo Met Cl N Am 1996*

Medtronic

# Connection between $HbA_{1c}$ and the development of diabetic complications according to DCCT

**However:** With the same $HbA_{1c}$ values (subgroup analysis) the rate of retinopathy progression in the IT groups was lower than in the group treated with CT!




***CT – conventional therapy***

***IT – intensive therapy: MDI – multiple dose injection (n = 616), CSII (n = 124)***

*From: DCCT-Group: Diabetes Vol. 44 (1995), 968 – 983*

# *Connection between $HbA_{1c}$ and the development of diabetic complications according to DCCT*

**Possible causes for the differing risk of diabetic complications with the same $HbA_{1c}$:**

- Glucose fluctuations (glycemic amplitudes)
- Postprandial glucose excursions

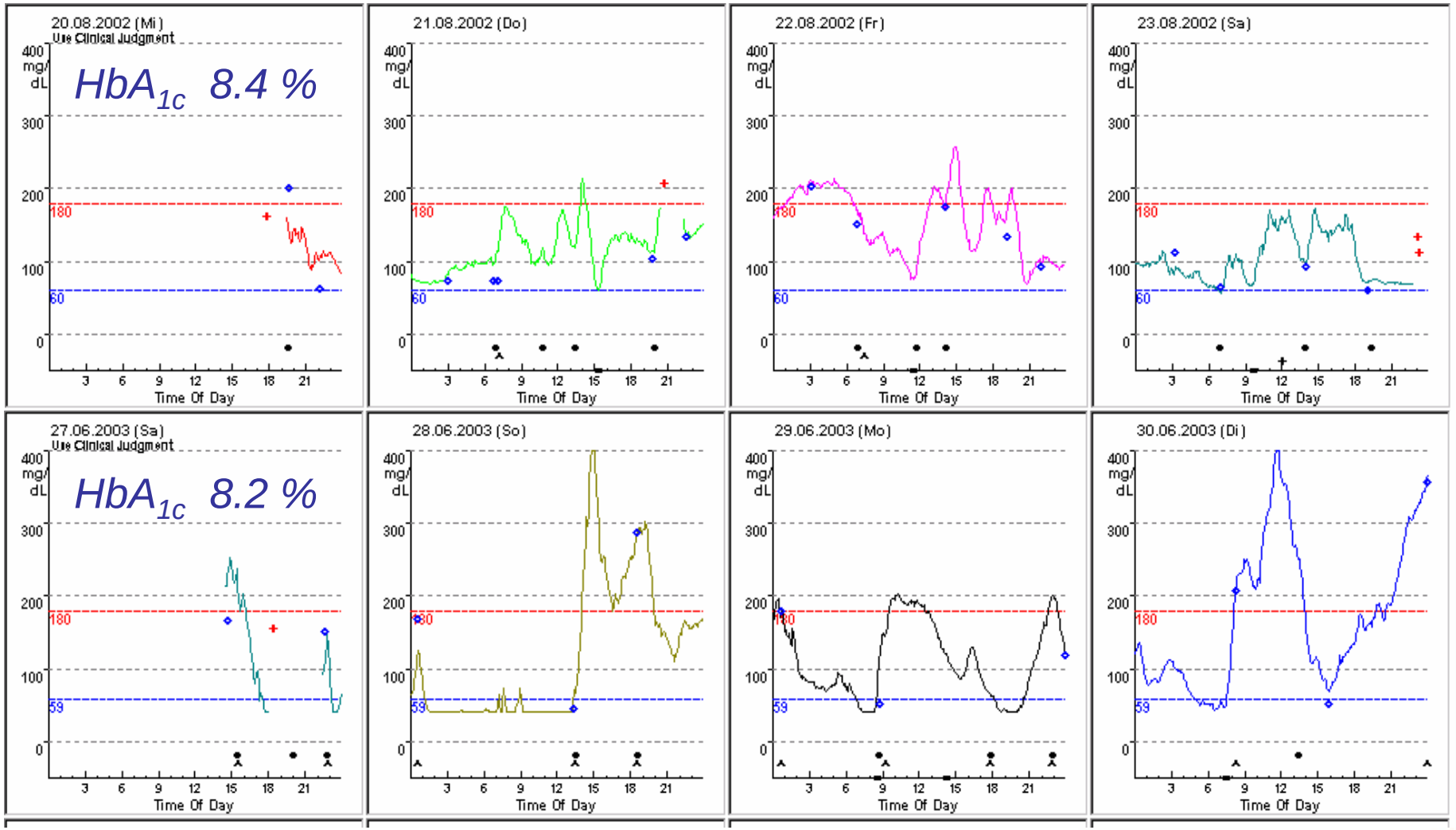
**Possible evidence:**

- Examinations with CGM
- This was not yet possible in DCCT
- A follow-up analysis would not be sensible or successful with the currently available data

*From: Kilpatrick ES et al.: Diabetes Care 2007, Vol. 29 (7), 1486-1490*
*Monnier L et al.: Diabetes Care 2007, Vol. 30 (1), 185-186*

Medtronic

# Glucose fluctuations and $HbA_{1c}$ value




*From Deiss D.: ISPAD 2007*

CHARITÉ KINDERDIABETOLOGIE BERLIN

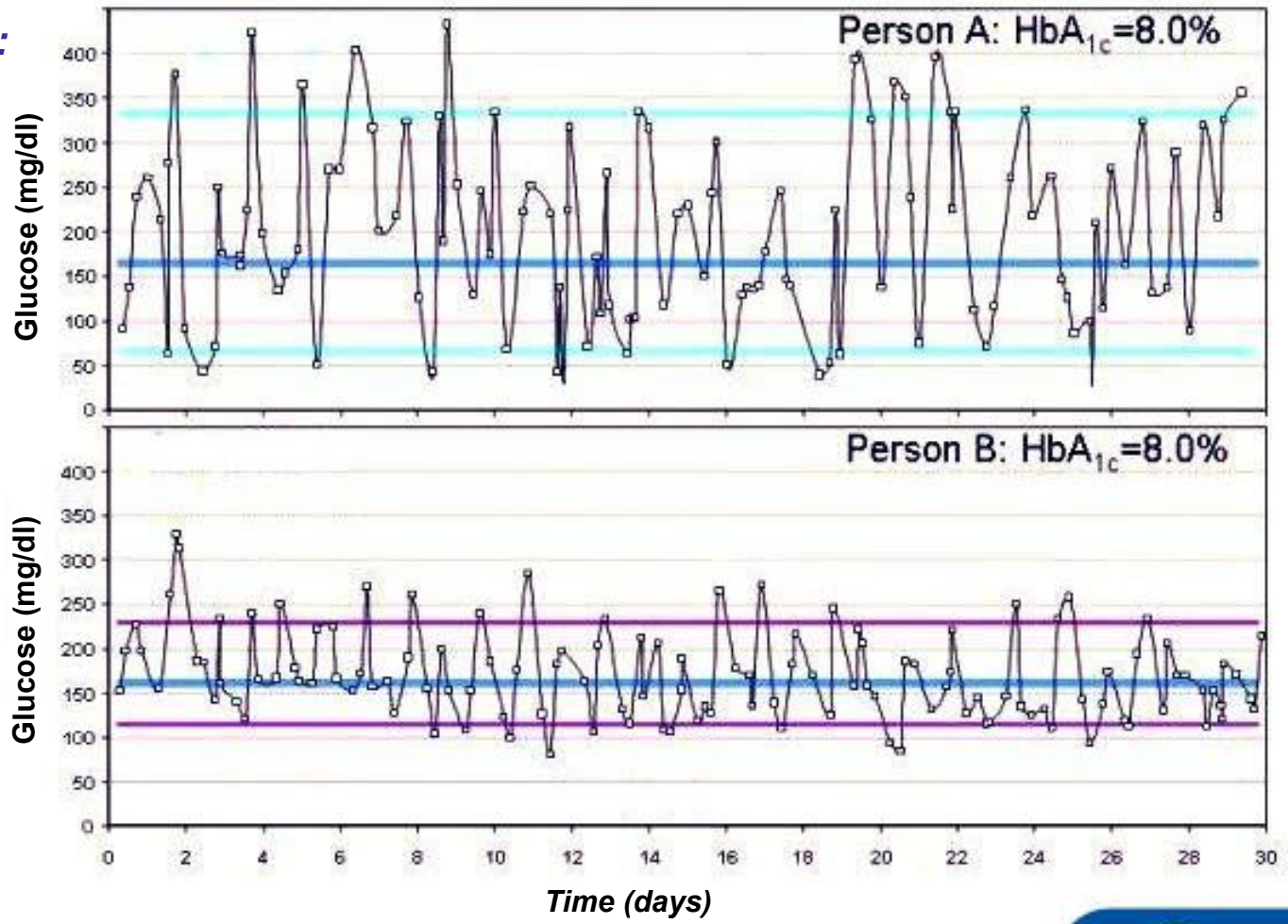
Medtronic

# Glucose fluctuations and $HbA_{1c}$ value

With the same $HbA_{1c}$ value the risk for development of associated illnesses grows with non-physiological glucose fluctuations

***High risk:***

***Low risk:***

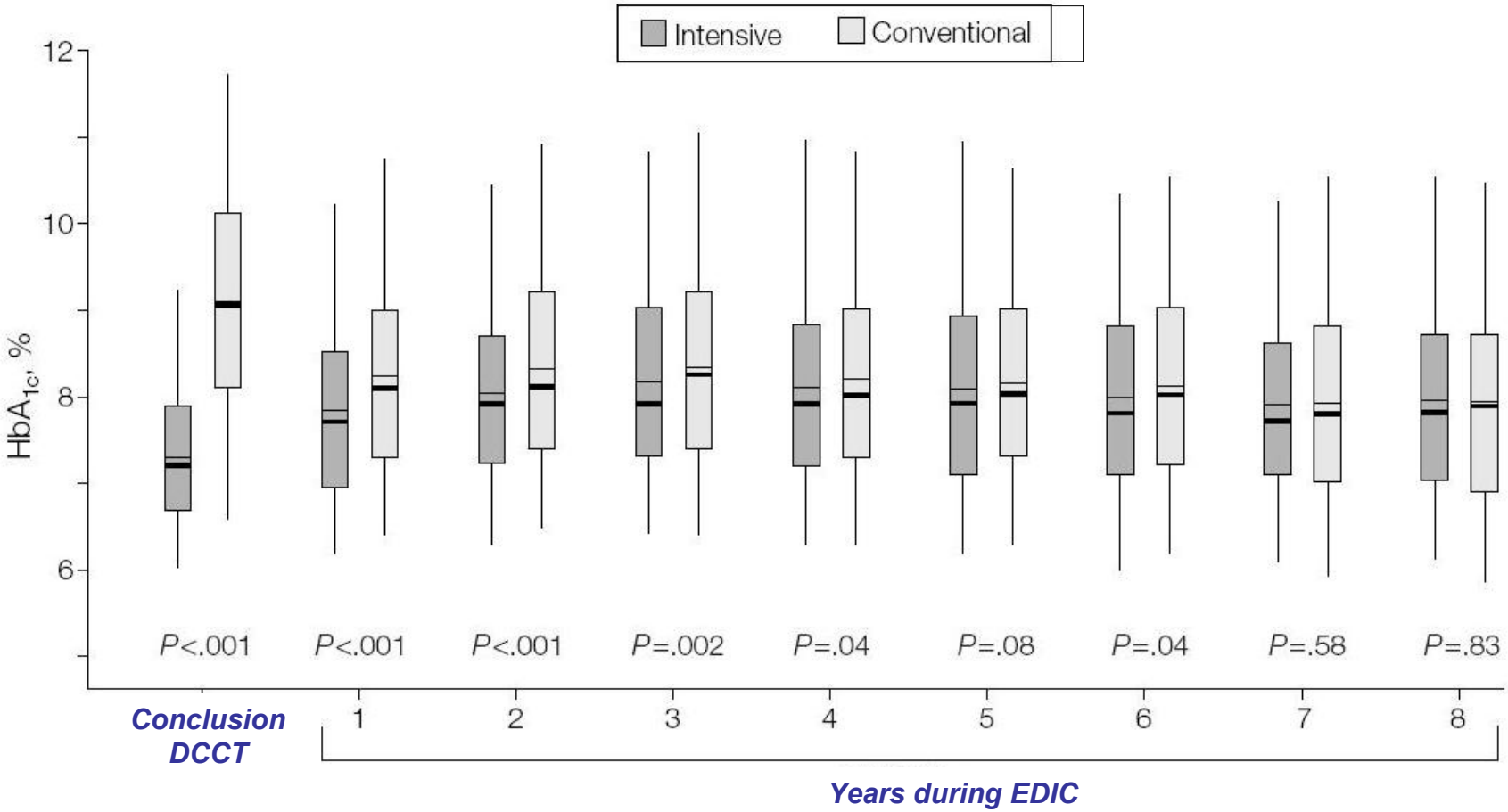



*From: Kovatchev B et al.: Diabetes 2007; 56 (Suppl. 1), A23*

Medtronic

# Connection between $HbA_{1c}$ and the development of diabetic complications according to DCCT /EDIC

Development of $HbA_{1c}$ value after conclusion of DCCT and during EDIC:

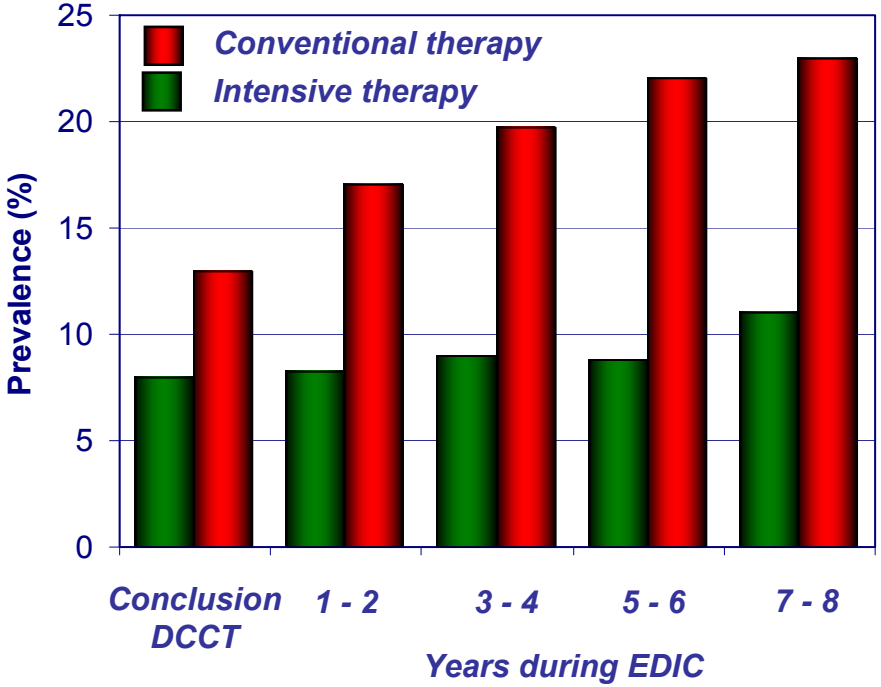


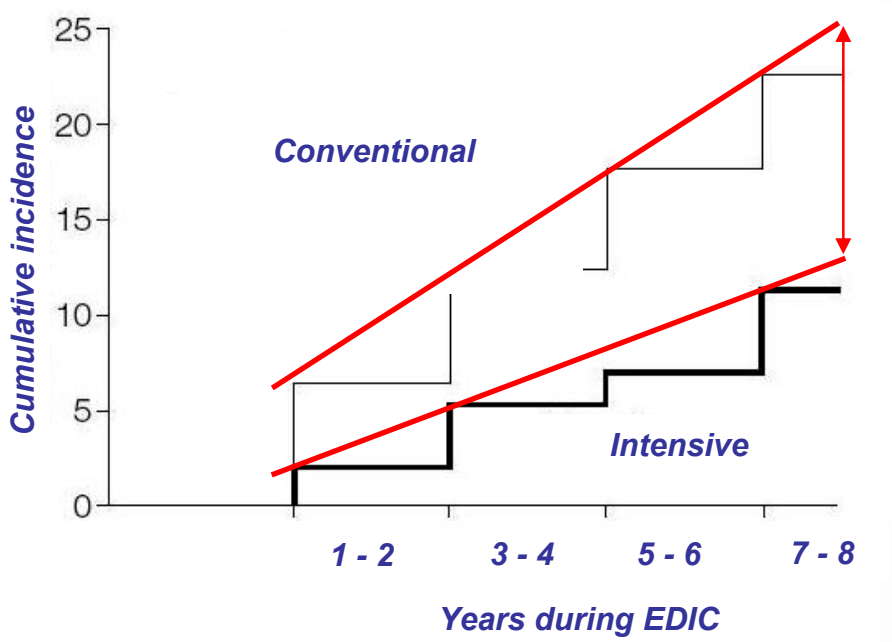

*From: DCCT and EDIC Group: JAMA 2003; Vol. 290 (16), 2160-2167*

Medtronic

# Connection between $HbA_{1c}$ and the development of diabetic complications according to DCCT /EDIC

Prevalence and cumulative incidence of microalbuminuria following conclusion of DCCT and during EDIC:




*From: DCCT and EDIC Group: JAMA 2003; Vol. 290 (16), 2160-2167*

Medtronic

# Cardiovascular risk in patients with type 1 diabetes?

## EARLY ONSET OF SUBCLINICAL ATHEROSCLEROSIS IN YOUNG PERSONS WITH TYPE 1 DIABETES

JODY S. KRANTZ, MD, WENDY J. MACK, PHD, HOWARD N. HODIS, MD, CHAO-RAN LIU, MD, CHI-HUA LIU, MD, AND FRANCINE R. KAUFMAN, MD

**Objective** To evaluate the degree of atherosclerosis and its risk factors in adolescents and young adults with type 1 diabetes.

**Study design** We measured carotid artery intima-media thickness (IMT) in 142 subjects with type 1 diabetes (mean [SD] age = 16.0 [2.6] years) and 87 control subjects (18.8 [3.1] years). Fasting lipid and homocysteine levels, degree of glycemic control, blood pressure, and body mass index were measured in persons with diabetes.

**Results** The mean carotid IMT was greater in persons with diabetes ($P$ = .002). Among subjects with type 1 diabetes, lipid levels were significantly higher in female subjects compared with male subjects. The mean carotid IMT was significantly higher in persons with a diabetic complication (including hypertension, retinopathy, or microalbuminuria). In male subjects but not female subjects, HDL cholesterol and the LDL/HDL ratio were correlated with carotid IMT.

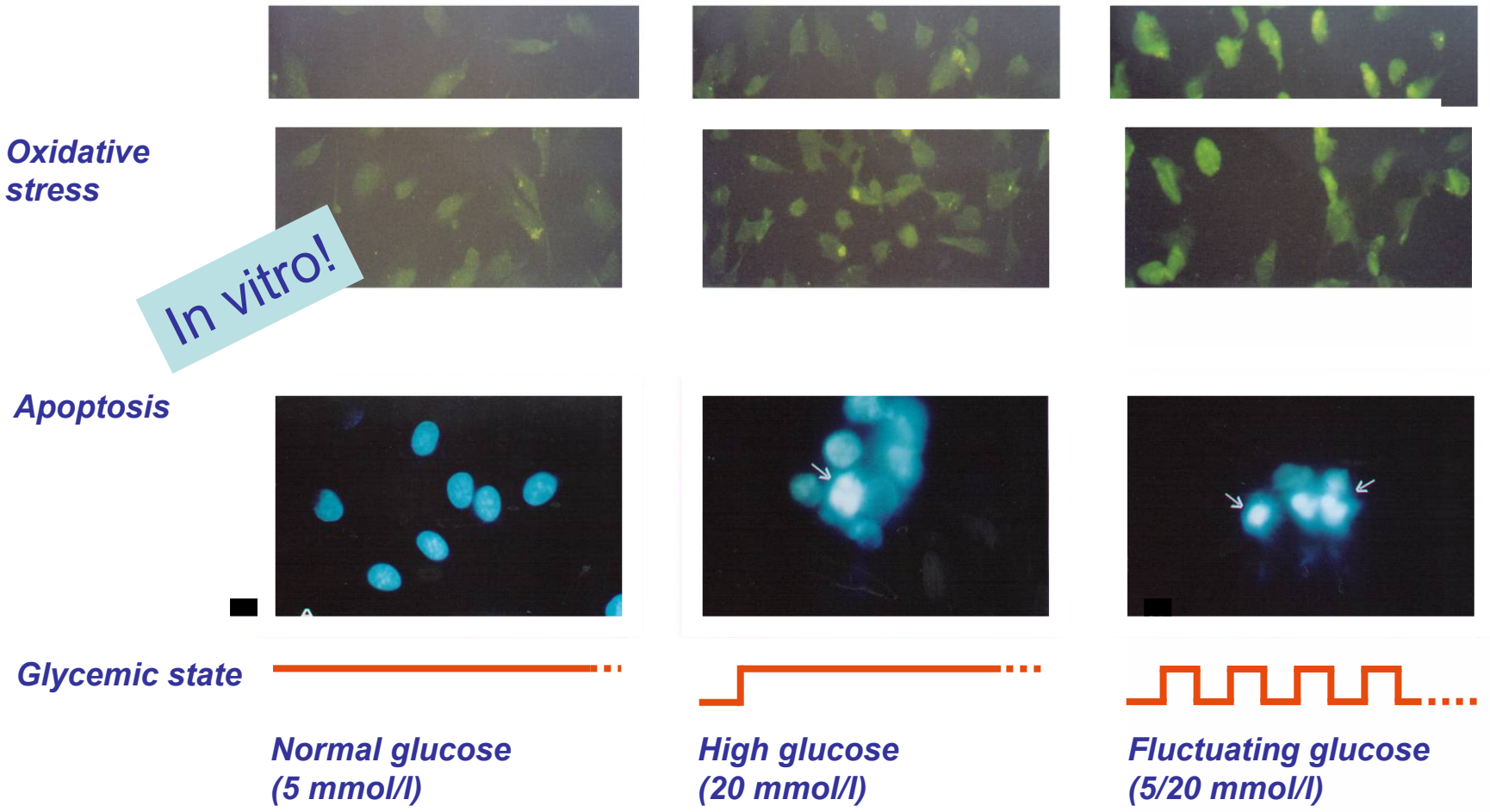
**Conclusions** Adolescents with type 1 diabetes have increased atherosclerosis compared with control subjects. Risk factors for increased carotid IMT in these younger patients include diabetic complications and HDL cholesterol and the LDL/HDL ratio, which may be sex-specific. *(J Pediatr 2004;145:452-7)*

**Conclusion:** Young people with type 1 diabetes have a higher risk of arteriosclerosis than comparable people. ….

Medtronic

# Oxidative stress[1] and cell apoptosis[2] dependent on glucose level

Oxidative stress[1] and the rate of cell apoptosis[2] are highest in alternating glucose levels i.e. glucose fluctuations

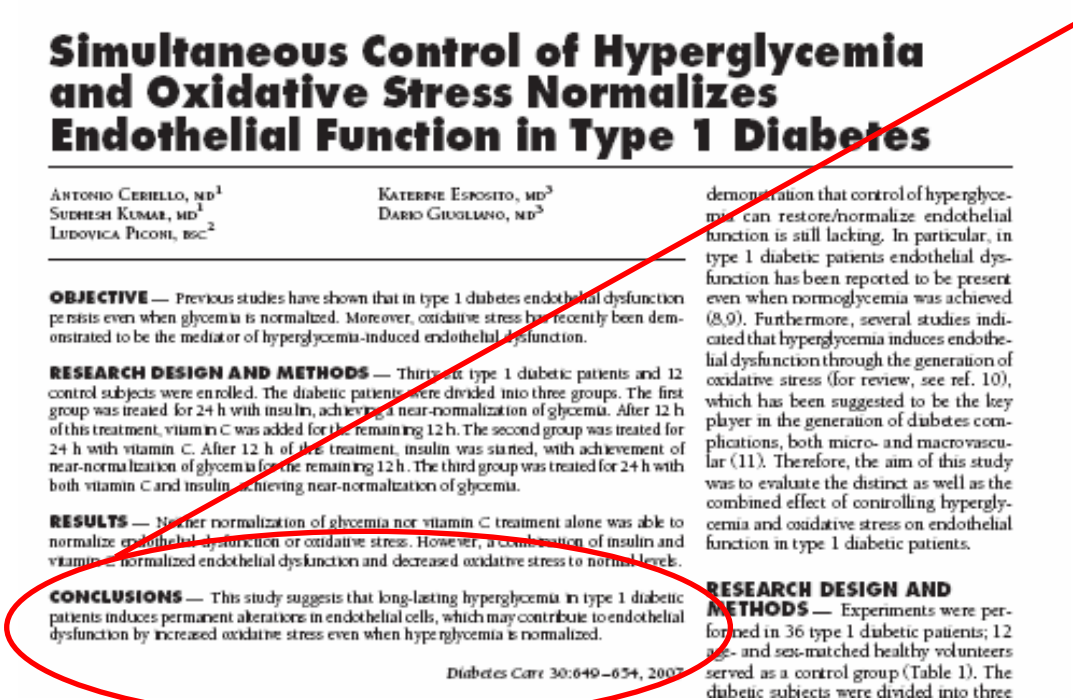




1. Piconi L et al. J Thromb Haemost 2004;2:1453-1459– .
2. Risso A et al. Am J Physiol Endocrinol Metab 2001;281:E924–E930.


Medtronic

# Cardiovascular risk in patients with type 1 diabetes?



## Simultaneous Control of Hyperglycemia and Oxidative Stress Normalizes Endothelial Function in Type 1 Diabetes


ANTONIO CERIELLO, MD[1]
SUDHESH KUMAR, MD[1]
LUDOVICA PICONI, BSC[2]
KATERINE ESPOSITO, MD[3]
DARIO GIUGLIANO, MD[3]



**OBJECTIVE** — Previous studies have shown that in type 1 diabetes endothelial dysfunction persists even when glycemia is normalized. Moreover, oxidative stress has recently been demonstrated to be the mediator of hyperglycemia-induced endothelial dysfunction.

**RESEARCH DESIGN AND METHODS** — Thirty-six type 1 diabetic patients and 12 control subjects were enrolled. The diabetic patients were divided into three groups. The first group was treated for 24 h with insulin, achieving a near-normalization of glycemia. After 12 h of this treatment, vitamin C was added for the remaining 12 h. The second group was treated for 24 h with vitamin C. After 12 h of this treatment, insulin was started, with achievement of near-normalization of glycemia for the remaining 12 h. The third group was treated for 24 h with both vitamin C and insulin, achieving near-normalization of glycemia.

**RESULTS** — Neither normalization of glycemia nor vitamin C treatment alone was able to normalize endothelial dysfunction or oxidative stress. However, a combination of insulin and vitamin C normalized endothelial dysfunction and decreased oxidative stress to normal levels.

**CONCLUSIONS** — This study suggests that long-lasting hyperglycemia in type 1 diabetic patients induces permanent alterations in endothelial cells, which may contribute to endothelial dysfunction by increased oxidative stress even when hyperglycemia is normalized.



*Diabetes Care* 30:649–654, 2007


demonstration that control of hyperglycemia can restore/normalize endothelial function is still lacking. In particular, in type 1 diabetic patients endothelial dysfunction has been reported to be present even when normoglycemia was achieved (8,9). Furthermore, several studies indicated that hyperglycemia induces endothelial dysfunction through the generation of oxidative stress (for review, see ref. 10), which has been suggested to be the key player in the generation of diabetes complications, both micro- and macrovascular (11). Therefore, the aim of this study was to evaluate the distinct as well as the combined effect of controlling hyperglycemia and oxidative stress on endothelial function in type 1 diabetic patients.

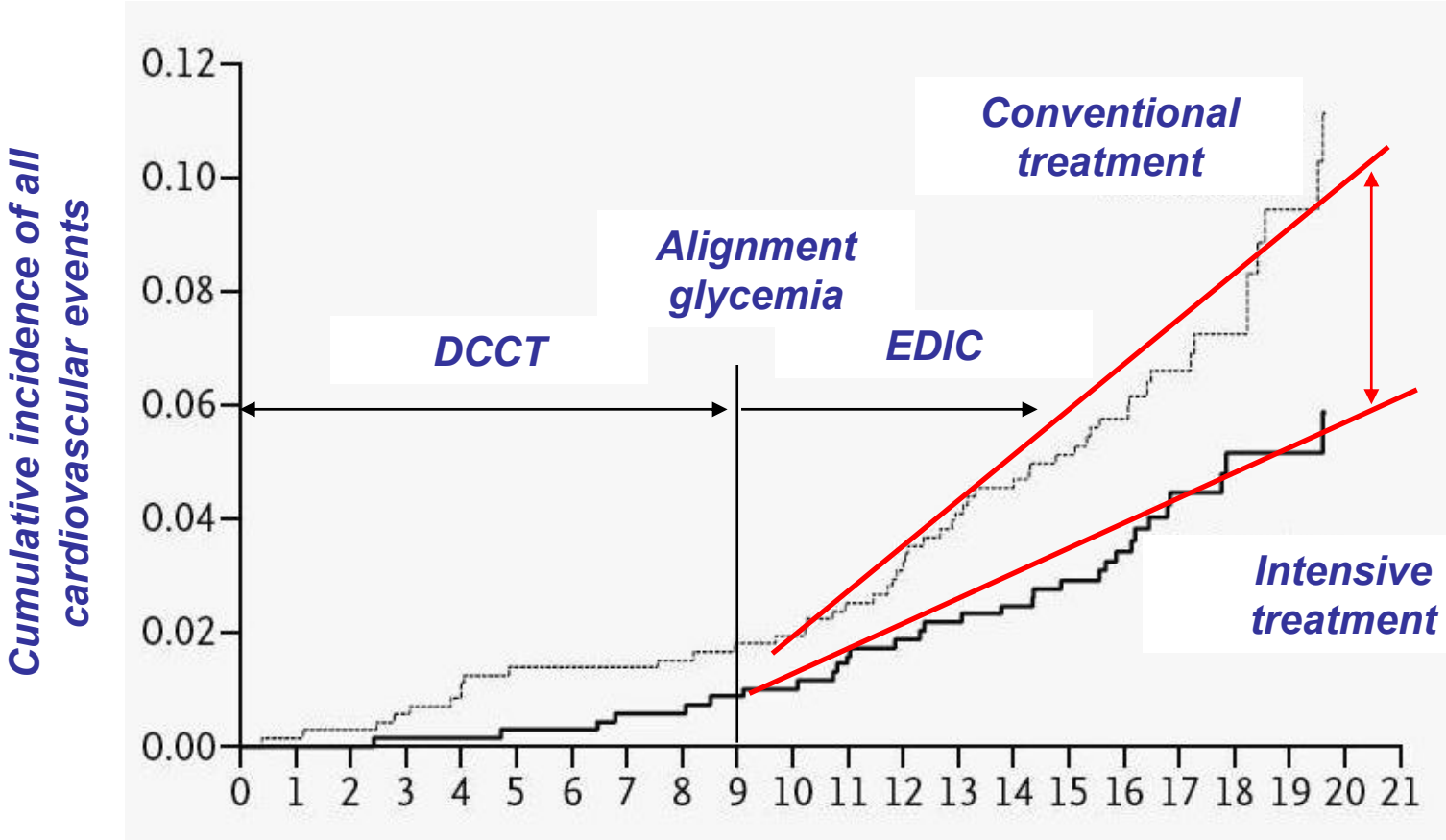
**RESEARCH DESIGN AND METHODS** — Experiments were performed in 36 type 1 diabetic patients; 12 age- and sex-matched healthy volunteers served as a control group (Table 1). The diabetic subjects were divided into three

**CONCLUSIONS:** This study suggests that long-lasting hyperglycemia in type 1 diabetic patients induces permanent alterations in endothelial cells, which may contribute to endothelial dysfunction by increased oxidative stress even when hyperglycemia is normalized.

Medtronic

# Connection between $HbA_{1c}$ and the development of diseases resulting from diabetes according to DCCT /EDIC

Prevalence and cumulative evidence of cardiovascular events according to DCCT/EDIC:




*From: DCCT and EDIC Group: NEJM 2005; Vol. 352 (25), 2643-2653*

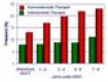
Medtronic

# Connection between $HbA_{1c}$ and the development of diabetic complications according to DCCT /EDIC

## Conclusion:

Whatever damage has been caused by poor glycemic control continues after metabolic improvement with accelerated progression!

*Back*



Medtronic

# Results during CSII


Back

# Results of CSII (1)

Important statements on the status and success of CSII

## CSII improves the $HbA_{1c}$ value

- Meta-analysis of diabetes control during CSII in adult patients with type 1 diabetes

- Meta-analysis of insulin pump therapy in children and adolescents with type 1 diabetes

- Further studies for comparison: Improvement in $HbA_{1c}$ value during CSII

- Improvement in glycemic control during CSII compared to MDI with analogue insulin

- Comparison of CSII and MDI with Aspart/Glargine in paediatric patients

- Metabolic control during CSII and MDI in a cross-over study
- Long term results of the treatment of type 2 diabetic patients with CSII



# Results of CSII (2)

## CSII reduces the rate of hypoglycemia

- Decrease in hypoglycemia during CSII

- Other studies for comparison: Decrease in hypoglycemia during CSII

- Effectiveness of CSII in type 1 diabetics with frequent severe hypoglycemia

## CSII increases the number of values in the normal glycemic range

- Glucose level during MDI with long-acting insulin analogue and during CSII

- Comparison of CSII and MDI with Glargine at night using continuous glucose monitoring

- Comparison of insulin and glucose variability of BOT* and CSII in patients with type 2 diabetes

- Arguments for CSII vs. Glargine

**BOT – basis oriented therapy, type 2 diabetics use only insulin Glargine for the insulin treatment*

Back

# Results of CSII (3)

## Glucose fluctuations are fewer during CSII than during MDI

- Glucose fluctuations during MDI and CSII

- Comparison: Smaller glucose fluctuations after change from MDI to CSII

## During CSII the risk of diabetic complications is reduced. It can even lead to regression in some cases

- Decrease in progression and regression of retinopathy during CSII

- Decrease in risk of renal failure in patients with type 1 diabetes during CSII

- Long term results for CSII compared to MDI in terms of diabetic complications

## CSII is cost-effective because it avoids stays in hospital

- Improvement in glycemia and reduction of clinical emergencies with CSII

Back

Medtronic

# Results of CSII (4)

## With CSII, quality of life and psychological factors tend to improve

- Assessment of quality of life and psychological parameters during CSII

## With the short-acting insulin used exclusively during CSII, insulin absorption is more defined than during MDI

- Smaller glucose fluctuations as a result of uniform absorption of short-acting insulin
  - Insulin absorption variability of different insulins
  - Intra-individual variability of different insulins
  - Pharmacodynamics of long-acting insulins and CSII

## Summary

- Summary: Results of CSII vs. Multiple injection therapy (MDI)

Back

# Important statements on status and success of CSII (1)

## Analysis of CSII studies shows that

- Control of diabetes is improved, evidenced by a reduction in $HbA_{1c}$ and by a reduction of severe hypoglycemia (if this was unsatisfactory during the previous therapy)
- There is definitely less fluctuation in glucose levels than during other therapy options
- Insulin levels are lower than during MDI when glycemic control is just as good or better
- Lower insulin doses are required to achieve good control of blood sugar than during MDI



# Important statements on status and success of CSII (2)

## Analysis of CSII studies shows that

- The basal insulin level is better adjusted to physiological requirements than with long-acting insulin or insulin analogues
- Postprandial glycemia is maintained at a low level by the application of different bolus options with pumps
- Improved postprandial glycemia reduces the risk of macrovascular complications
- The progression of diabetic complications is reduced
- Pregnant diabetics can be better adjusted and controlled
- Patient capability and quality of life are improved

Back

# Meta-analysis of diabetic control during CSII in adult patients with type 1 diabetes

## Statement:

In many observational studies on the comparison of CSII and MDI there is improved glycemic control during CSII with lower $HbA_{1c}$ values and a reduced rate of hypoglycemia.

## Evidence:

Meta-analysis of randomised controlled studies with the aid of the Medline, ENBASE and CENTRAL databases (update: March 2007) using the criteria: Adults with CSII $\geq$ 4 weeks and including at least 10 patients in the study.

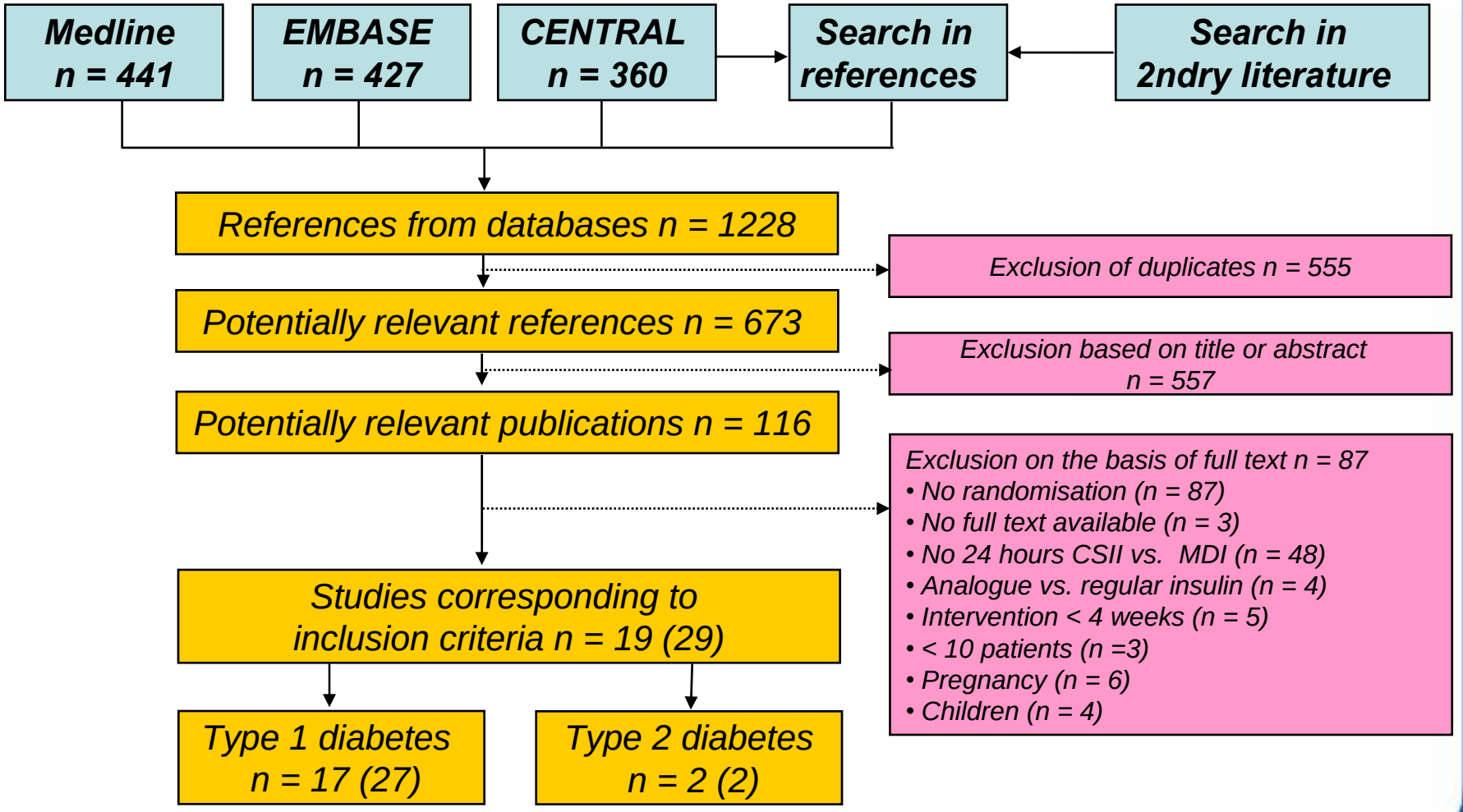
Back

*From: Horvath K et al.: Diabetes 2007; 56 (Suppl. 1), A123*

CSII

# Meta-analysis of diabetic control during CSII in adult patients with type 1 diabetes

## Work already done in accordance with criteria & classifications:




*From: Horvath K et al.: Diabetes 2007; 56 (Suppl. 1), A123*

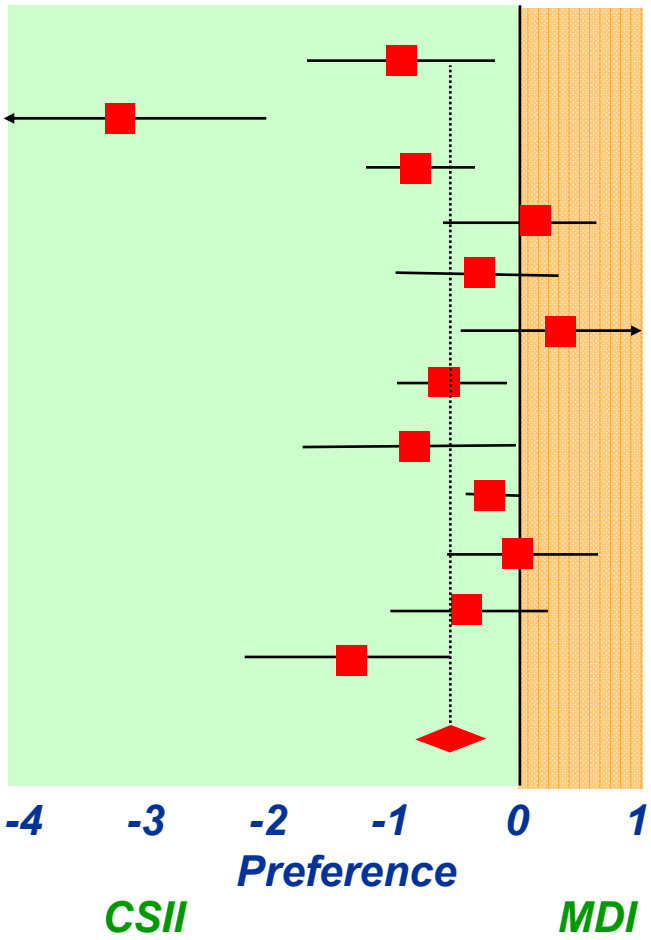
Medtronic

# Meta-analysis of diabetic control during CSII in adult patients with type 1 diabetes

Results for adult patients with type 1 diabetes:

- Change in $HbA_{1c}$ values in 12 selected studies:

| Study | Weight (%) | Difference (95% C.I.) |
|---|---|---|
| Berg 1998 | 7.90 | -0.92 (-1.64; -0.20) |
| Ciavarella 1985 | 4.46 | -3.19 (-4.43; -1.93) |
| DeVries 2002 | 10.17 | -0.81 (-1.28; -0.35) |
| Ziegler 1990 | 9.67 | 0.16 (-0.35; 0.68) |
| Oslo-Study 1987 | 7.90 | -0.29 (-1.01; 0.43) |
| Chiasson 1984 | 7.21 | 0.33 (-0.47; 1.13) |
| Hanaire-Broutin 2000 | 10.41 | -0.56 (-1.00; -0.12) |
| Home 1982 | 6.62 | -0.84 (-1.72; 0.04) |
| Hoogma 2006 | 12.35 | -0.22 (-0.40; 0.04) |
| Saurbrey 1987 | 8.60 | 0.00 (-0.64; 0.64) |
| Schiffrin 1982 | 8.10 | -0.41 (-1.10; 0.28) |
| Schmitz 1989 | 6.62 | -1.35 (-2.24; 0.48) |
| **Total (95% conf. Inter.):** | | **-0.55 (-0.87; 0.22)** |




**-0.63% (standardised)**

From: Horvath K et al.: Diabetes 2007; 56 (Suppl. 1), A123

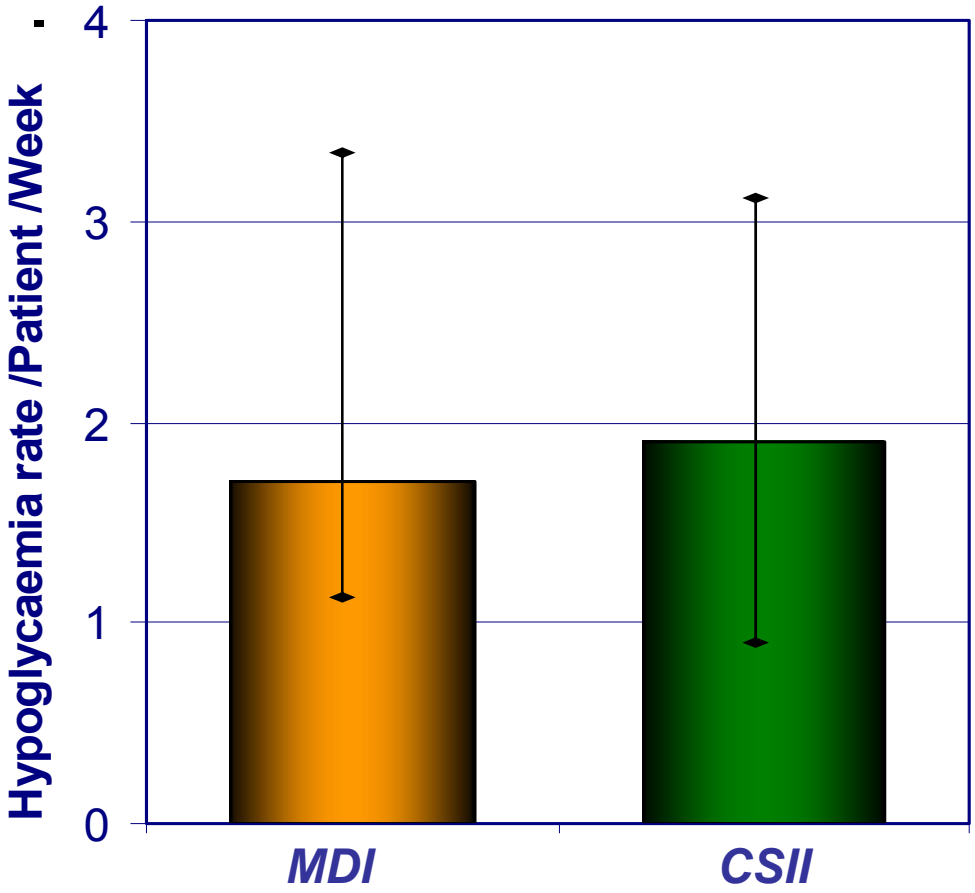
Medtronic

CSII

# *Meta-analysis of diabetic control during CSII in adult patients with type 1 diabetes*

Results for adult patients with type 1 diabetes:

- *Rate of moderate hypoglycemia:*




*From: Horvath K et al.: Diabetes 2007; 56 (Suppl. 1), A123*

Medtronic

# Meta-analysis of diabetic control during CSII in adult patients with type 1 diabetes

## Statement:

Besides improved glycemic control, CSII therapy leads to further benefits such as reduction of insulin dose and improvement to quality of life.

## Evidence:

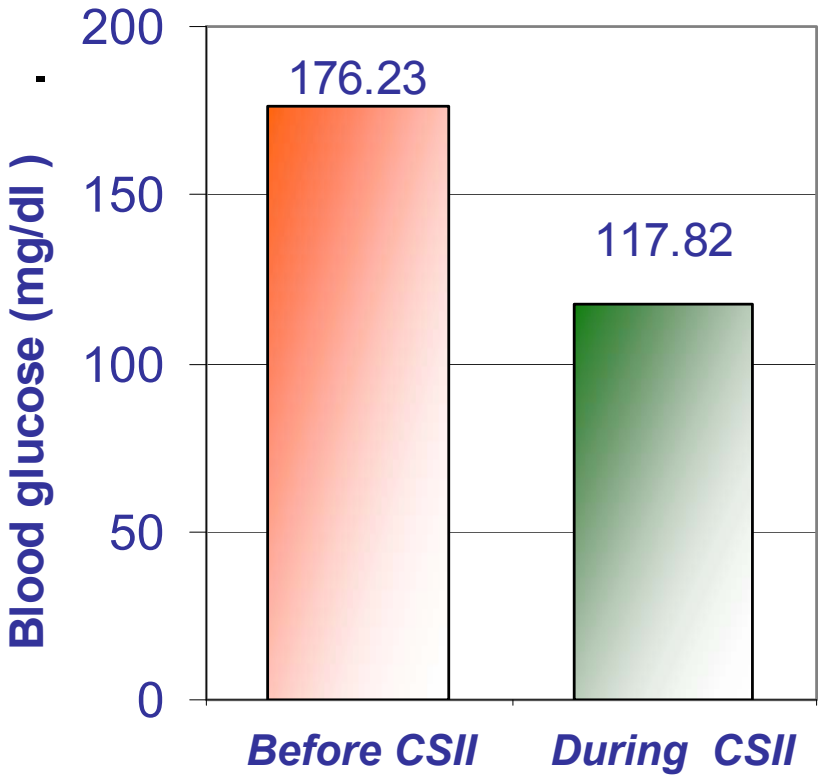
Meta-analysis on CSII over 52 studies with a total of 1,547 patients (11 parallel studies, 41 studies on the transition from MDI to CSII).

*From: Weinsberg-Benchell J et al.: Diabetes Care 26(4) (2003), 1079-1087*

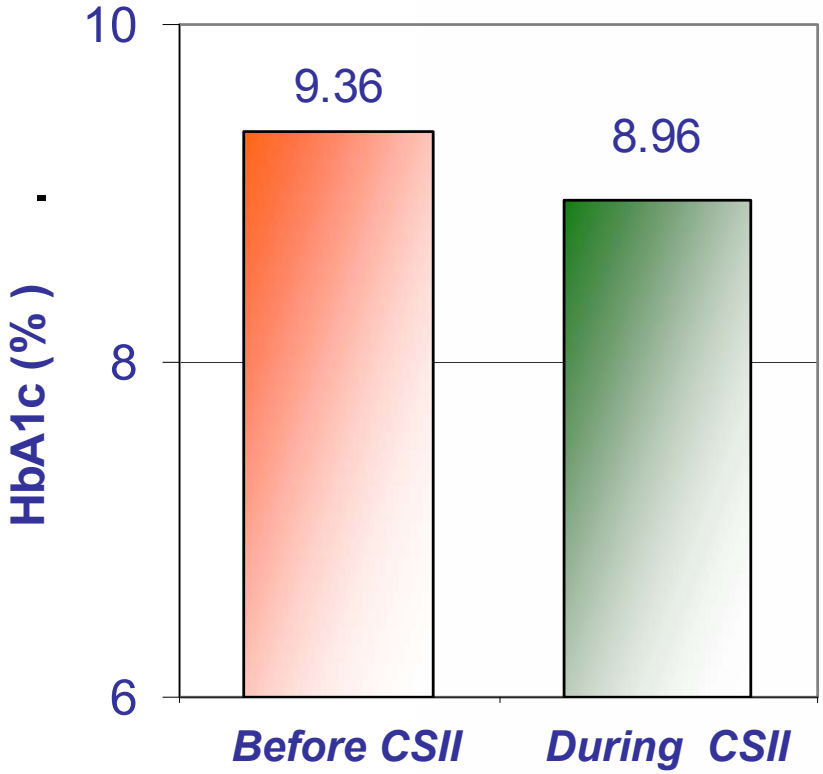
# Meta-analysis of diabetic control during CSII in adult patients with type 1 diabetes

Results before and during CSII:

- *Mean blood glucose:*




- *$HbA_{1c}$ values:*



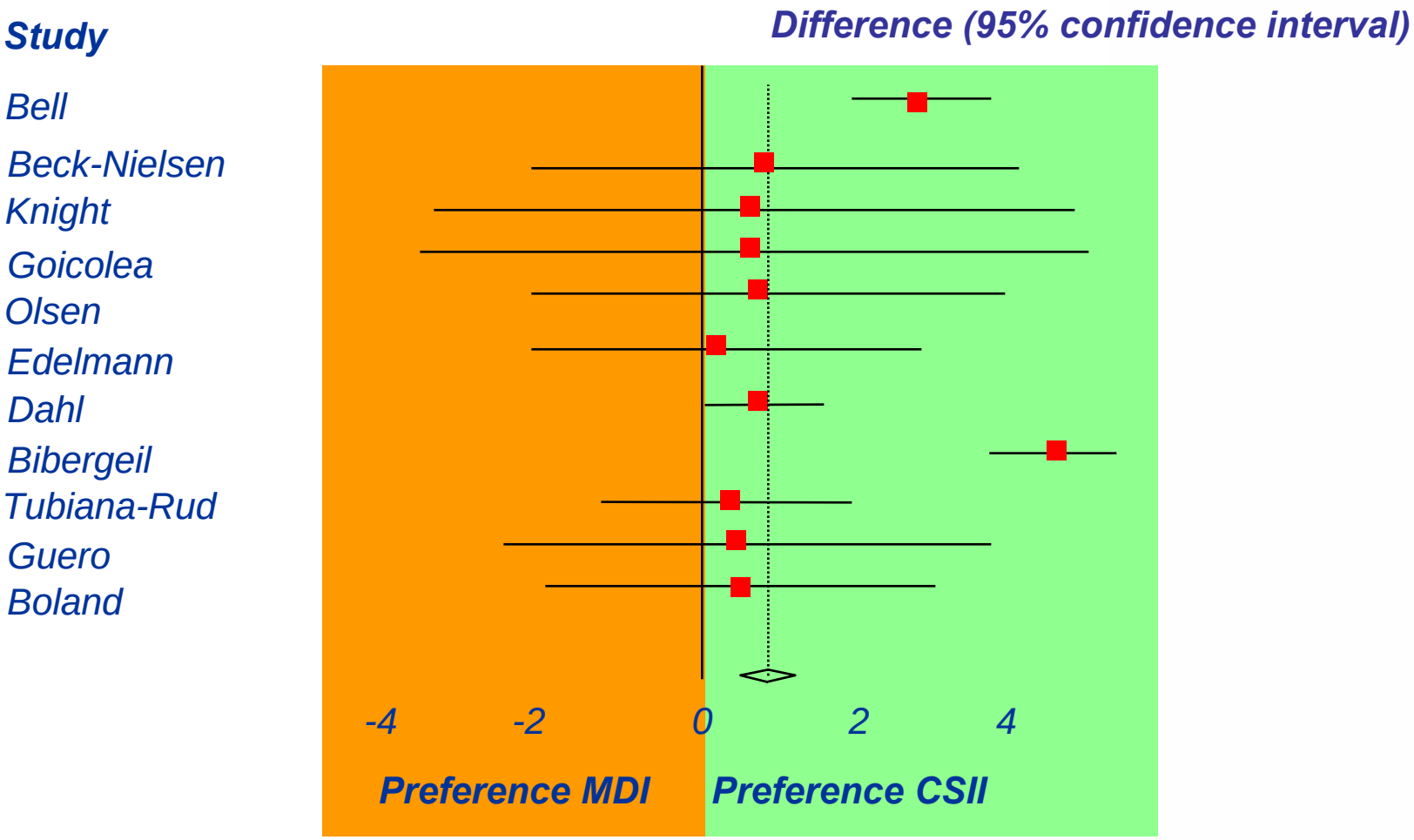

*From: Weinsberg-Benchell J et al.: Diabetes Care 26(4) (2003), 1079-1087*

Medtronic

CSII

# Meta-analysis of diabetic control during CSII in adult patients with type 1 diabetes

- Change in $HbA_{1c}$ values in 11 parallel studies:




*From: Weinsberg-Benchell J et al.: Diabetes Care 26(4) (2003), 1079-1087*

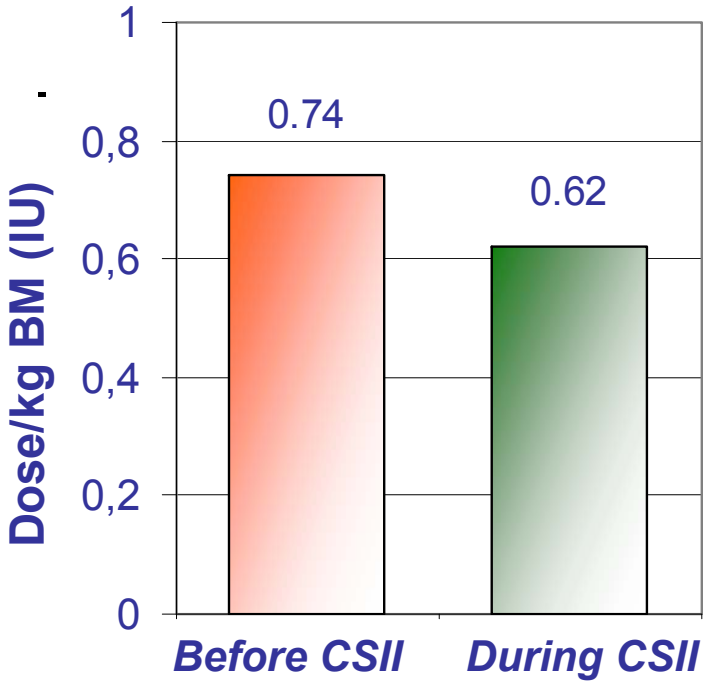
Medtronic

CSII

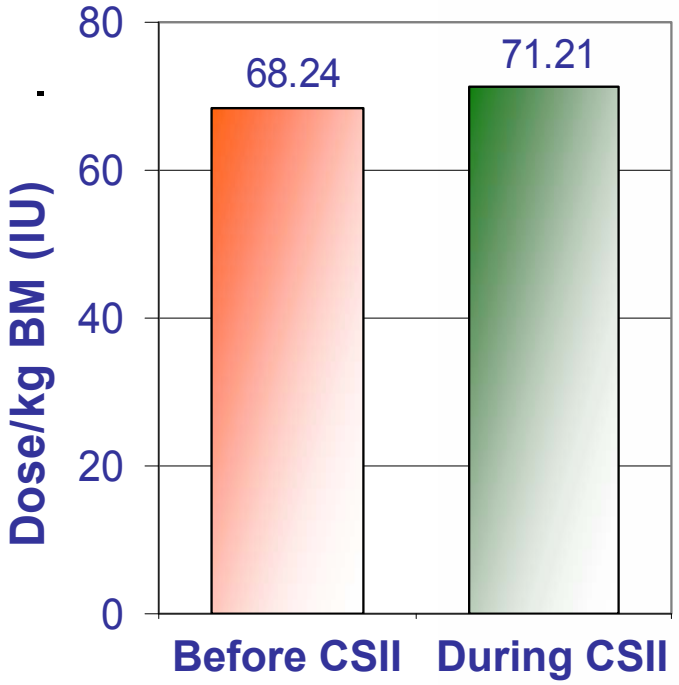
# Meta-analysis of diabetic control during CSII in adult patients with type 1 diabetes

Results before and during CSII:

- Insulin dose/kg body weight:




- Body weight:




*From: Weinsberg-Benchell J et al.: Diabetes Care 26(4) (2003), 1079-1087*

Medtronic

# Meta-analysis of diabetic control during CSII in adult patients with type 1 diabetes

- 16 of the 52 studies described the psychological effects of the pump therapy. Number of studies with result:

| Parameters | No change | Improvement |
|---|---|---|
| Depression | 4 | 1 |
| Quality of life | 3 | 2 |
| Anxiety/Agitation | 3 | 1 |
| Self esteem | 1 | 1 |
| Family situation | 1 | 1 |

- There were no reports of a deterioration in psychological state.

*From: Weinsberg-Benchell J et al.: Diabetes Care 26(4) (2003), 1079-1087*

CSII

# Meta-analysis of diabetic control during CSII in adult patients with type 1 diabetes

## Conclusion:

In almost all the meta-analysis studies looked at covering the assessment of CSII in adult type 1 diabetic patients there was an improvement in $HbA_{1c}$ values, mostly linked with a lower rate of hypoglycemia. On average, one can reckon on an improvement of 0.6% - 0.7% in the $HbA_{1c}$ value after transfer from MDI to CSII. There is also less blood sugar fluctuation, the required insulin dose is lower and an improvement in quality of life can be detected.

.

*Note:*
*These results were also confirmed in another meta-analysis from John Pickup.*
*(Pickup J et al.: BMJ 2002, Mar 23; 324(7339): 705)*

*From: Horvath K et al.: Diabetes 2007; 56 (Suppl. 1), A123*
*and: Weinsberg-Benchell J et al.: Diabetes Care 26(4) (2003), 1079-1087*

Back

Medtronic

# Meta-analysis of insulin pump therapy in children and adolescents with type 1 diabetes

## Statement:

Better glycemic control with lower HbA1c values and a lower rate of hypoglycemia may be expected when children and young people with type 1 diabetes change from MDI to CSII.

## Evidence:

Analysis of three identified randomised controlled studies from the Medline, EMBASE and CENTRAL databases with the criteria: Children and young people with type 1 diabetes, CSII 24h/day, duration of CSII $\geq$ 4 weeks and at least 10 patients included.

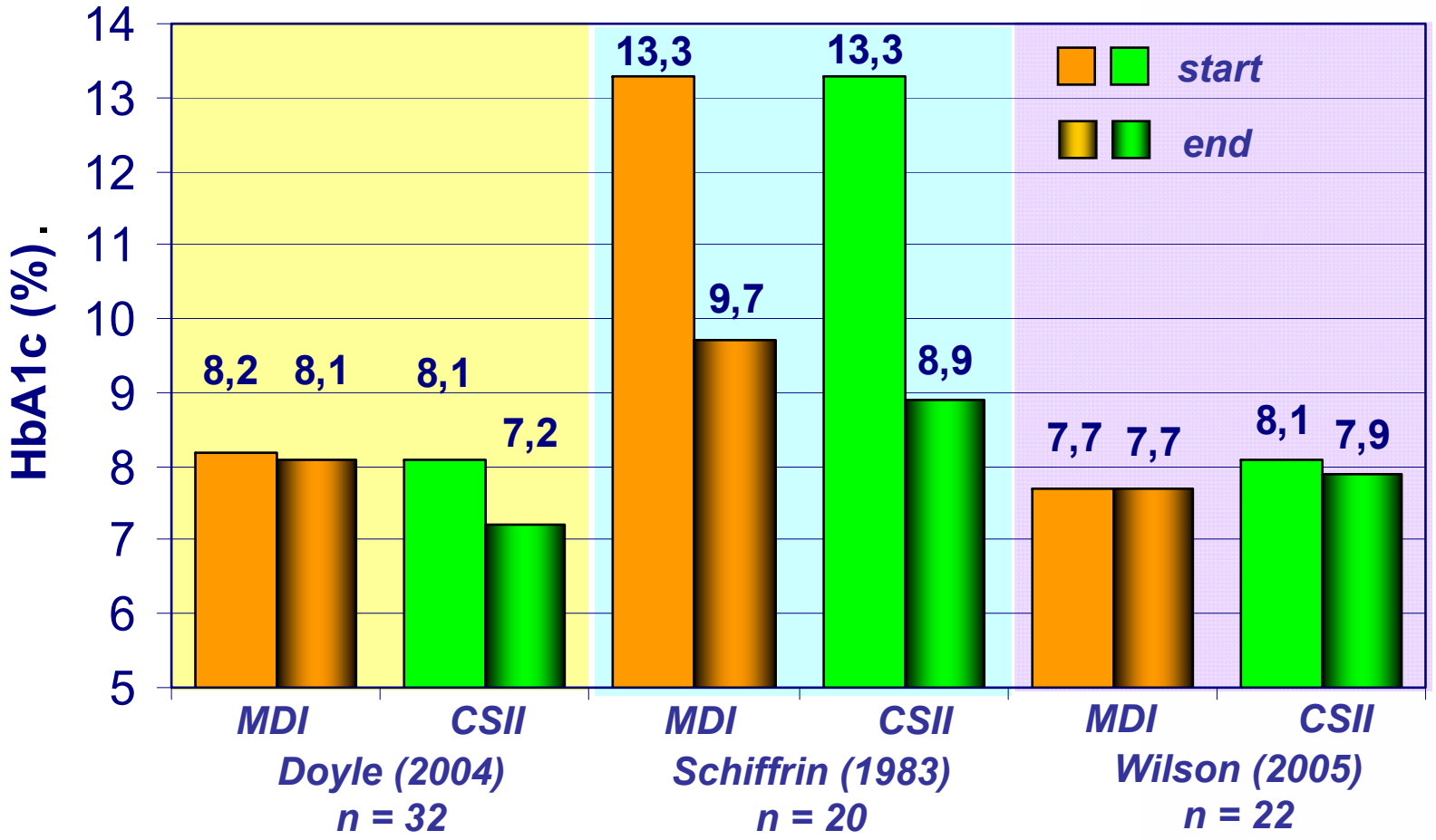
Back

*From: Gratzer TW et al.: Pediatric Diabetes 2007; 8 (Suppl. 7), 45-46.*

CSII

# Meta-analysis of insulin pump therapy in children and adolescents with type 1 diabetes

- Change to $HbA_{1c}$ values:

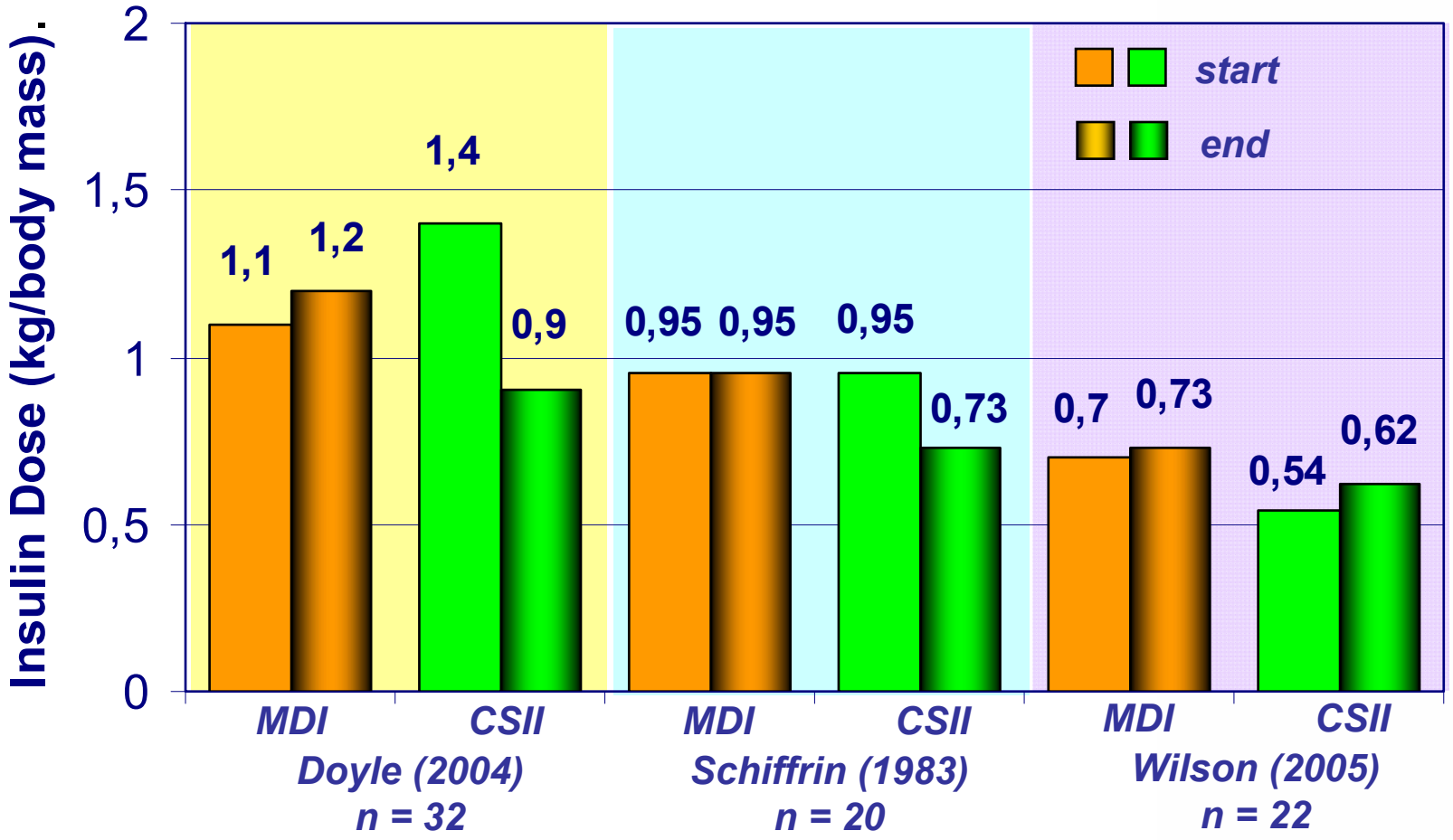



*From: Gratzer TW et al.: Pediatric Diabetes 2007; 8 (Suppl. 7), 45-46.*

Medtronic

# Meta-analysis of insulin pump therapy in children and adolescents with type 1 diabetes

- Change to insulin dose:




*From: Gratzer TW et al.: Pediatric Diabetes 2007; 8 (Suppl. 7), 45-46.*

Medtronic

CSII

# Meta-analysis of insulin pump therapy in children and adolescents with type 1 diabetes

## Conclusion:

CSII leads to improved glycemia compared to MDI in children and adolescents with type 1 diabetes, without increasing the rate of hypoglycemic events or diabetic ketoacidosis. It is linked with the need for a lower dose of insulin.

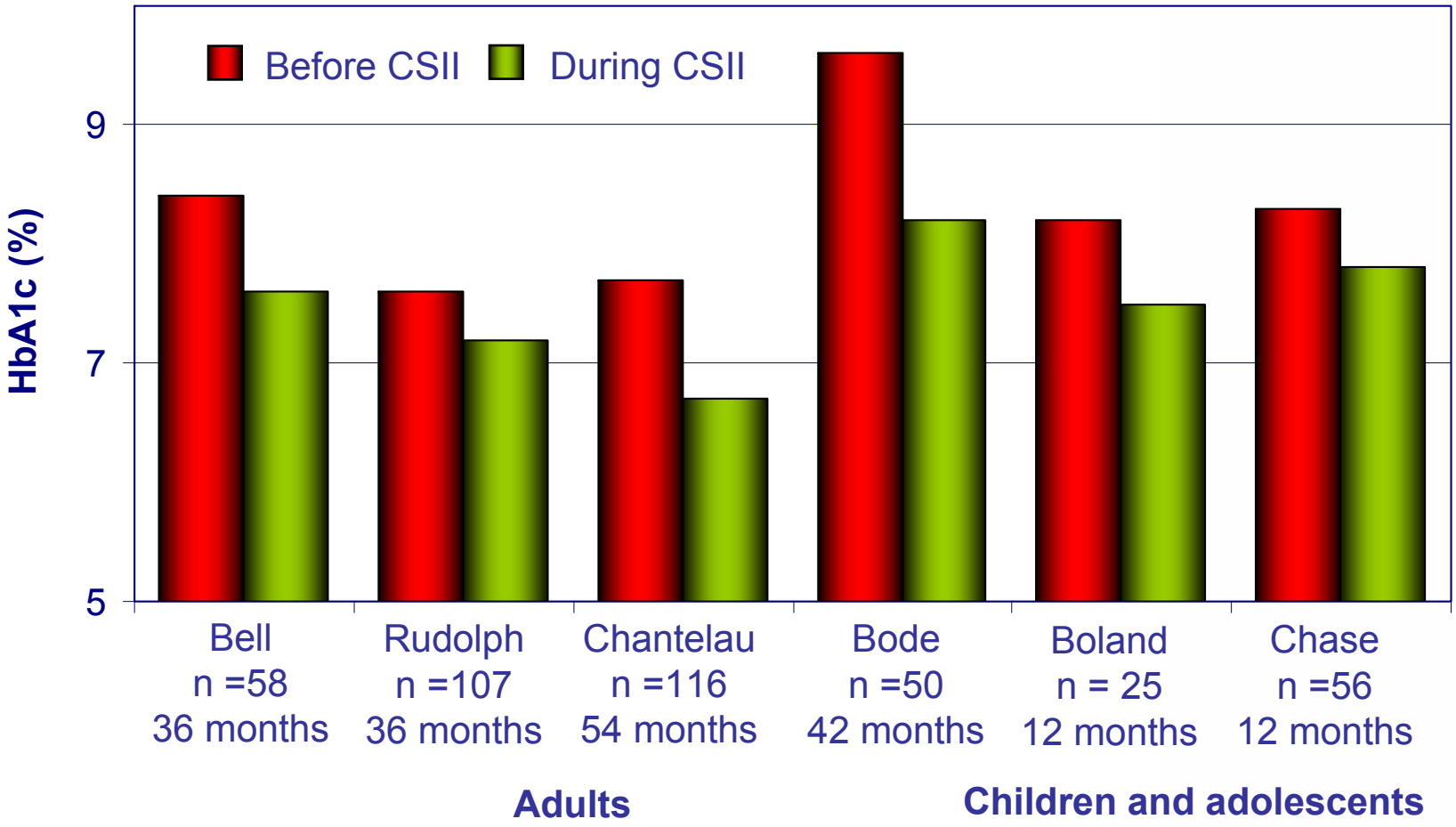
The data on randomised, controlled studies needs to be expanded.

*From: Gratzer TW et al.: Pediatric Diabetes 2007; 8 (Suppl. 7), 45-46.*

Medtronic

# Comparison: Improvement in $HbA_{1c}$ values during CSII

*$HbA_{1c}$ values in several studies before and during CSII:*




*From: Chantelau E, et al. Diabetologia. 1989;32:421–426; Bode BW, et al. Diabetes Care. 1996;19:324–327; Boland EA, et al. Diabetes Care. 1999;22:1779–1784; Bell DSH, et al. Endocrine Practice. 2000;6:357–360; Chase HP, et al. Paediatrics. 2001;107:351–356.*

*Back*

Medtronic

# Improvement in glycemic control during CSII compared to MDI with analogue insulin

## Statement:

During CSII with short-acting insulin analogue, glycemia improves in comparison with MDI with insulin analogue (short-acting and long-acting). There are also less glucose fluctuations.

## Supporting documentary evidence:

- Randomised cross-over study with 100 patients (comparable in both groups: age, time since onset of diabetes; $HbA_{1c}$ value: 7.5 $\pm$ 0.8 %): MDI with Aspart/Glargine vs. CSII with Aspart for 5 weeks in each case in each group. Determination of fructosamine and glucose profiles with continuous glucose monitoring*.
- Comparison of the same therapeutic options in 32 children and adolescents**.

Back

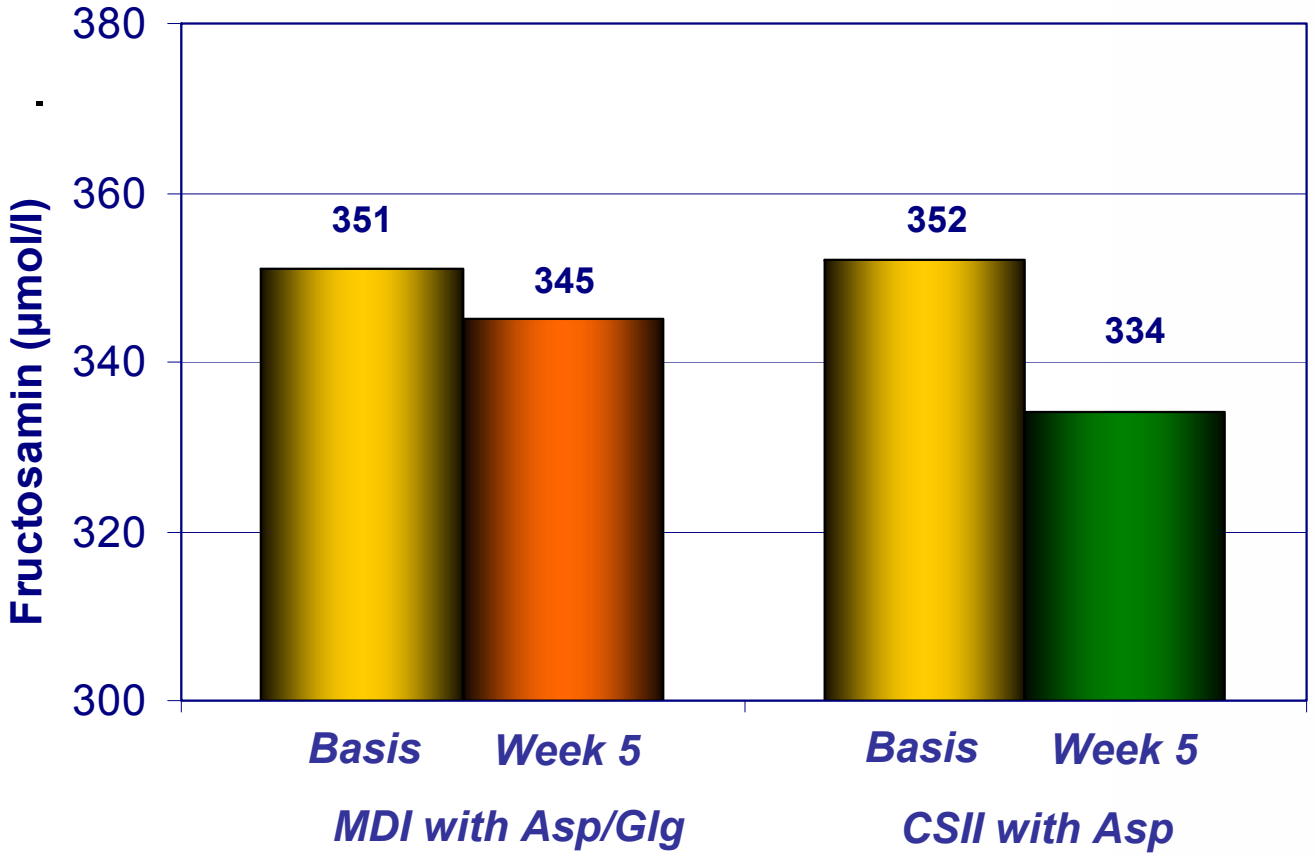
* *From: Hirsch IB et al. Diabetes Care 2005; 28(3):533-538*

** *From: Doyle-Boland EA et al.: Diabetes Care 2004; 27(7):1554-1558*

CSII

# Improvement in glycemic control during CSII compared to MDI with analogue insulin

- Change in fructosamine level after 5 weeks in each case:

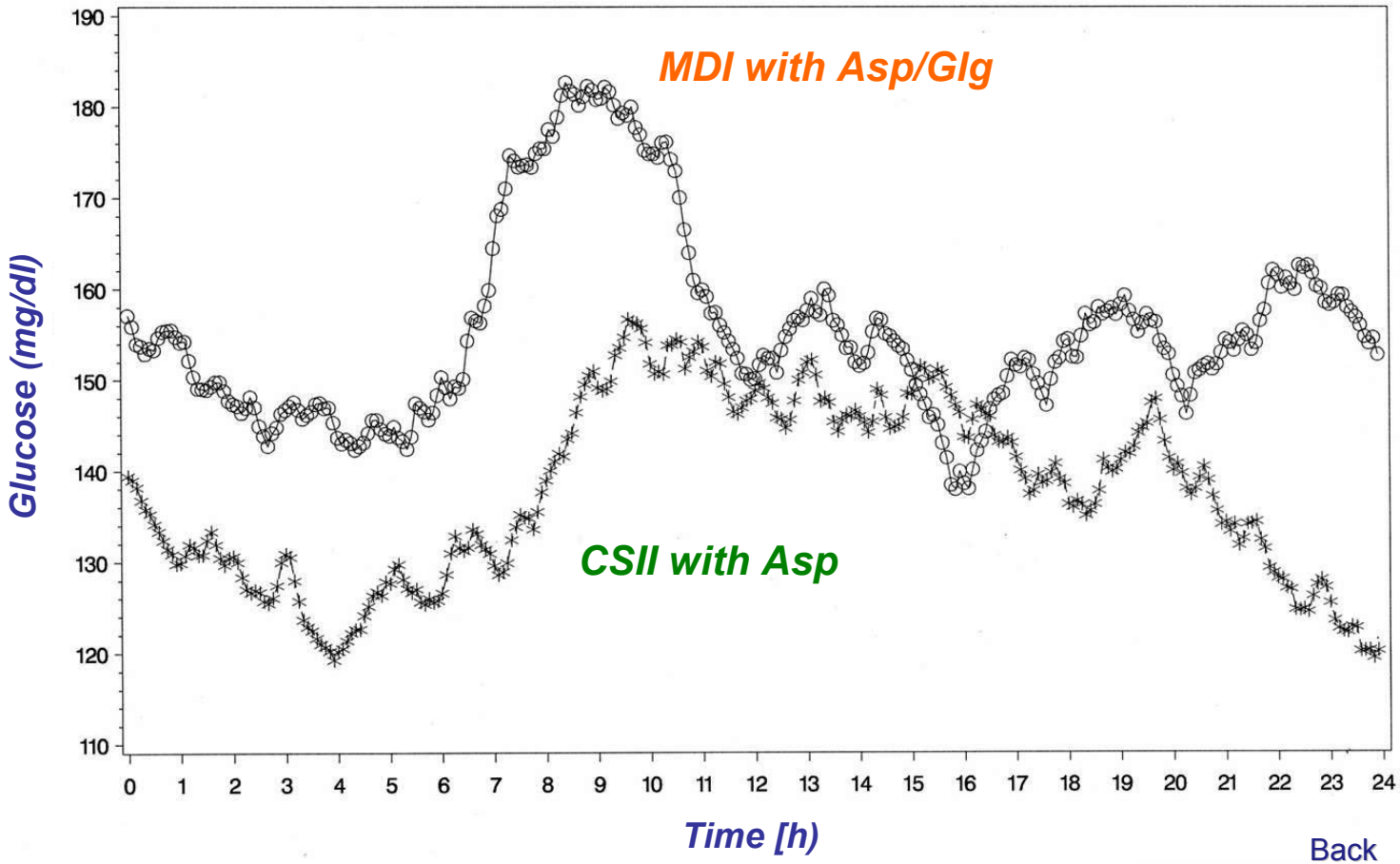



*From: Hirsch IB et al. Diabetes Care 2005; 28(3):533-538*

Medtronic

# Improvement in glycemic control during CSII compared to MDI with analogue insulin

CGM profile in the last week of treatment during MDI with Aspart/Glargine before and during CSII with Aspart:




Back

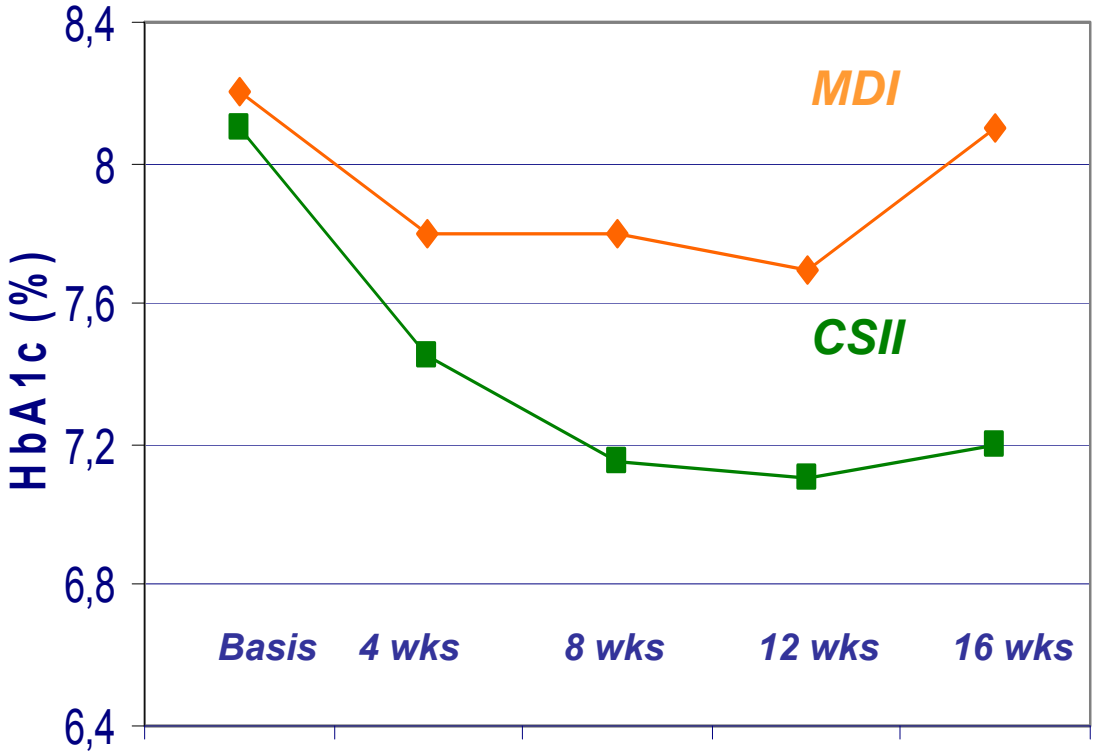
*From: Hirsch IB et al. Diabetes Care 2005; 28(3):533-538*

Medtronic

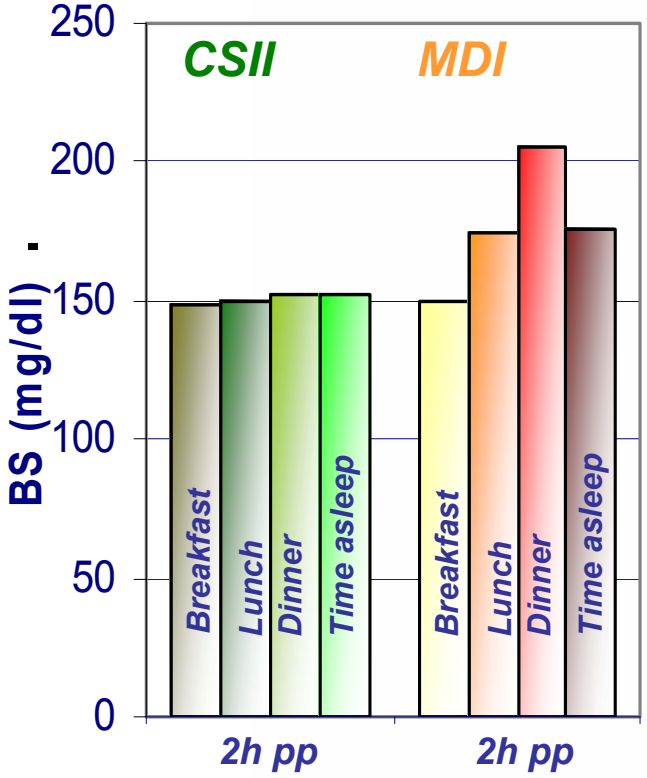
# Comparison of CSII and MDI with Aspart/Glargine in paediatric patients

Comparison of CSII and MDI with insulin analogue (Aspart/Glargine) in 32 type 1 paediatric diabetics who had previously carried out MDI with normal insulin/NPH insulin

- *Change in $HbA_{1c}$ values:*




- *pp blood sugar values:*




*From: Doyle EA et al.: Diabetes Care 2004; 27(7):1554-1558*



Medtronic

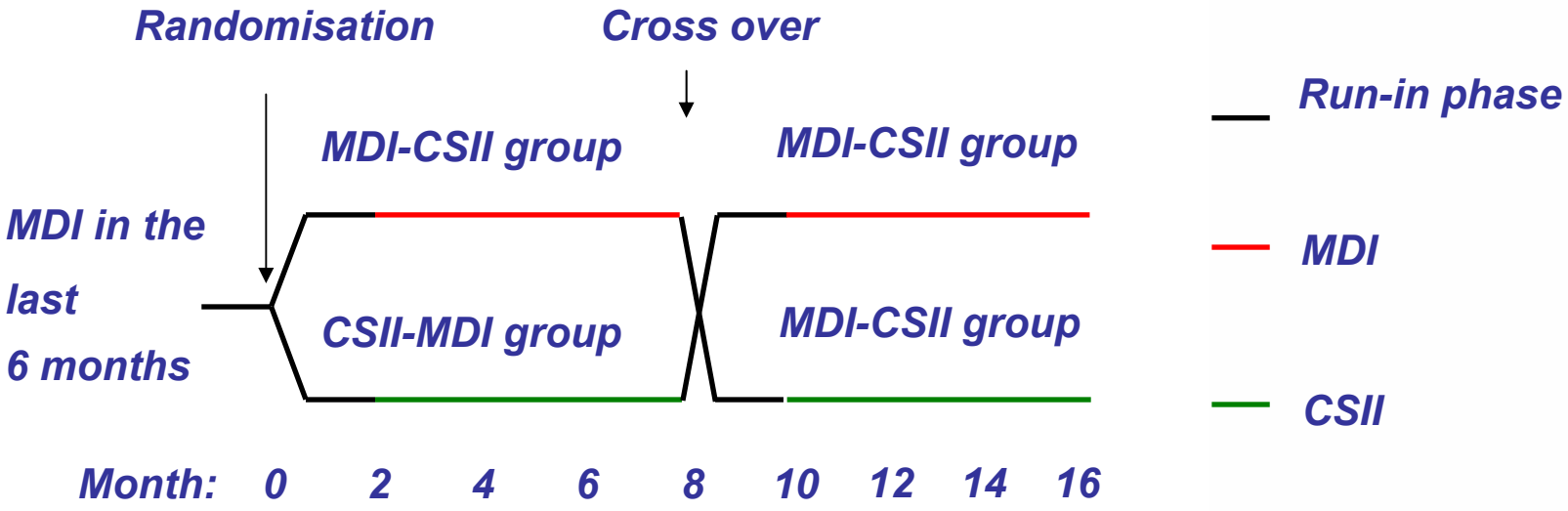
# Metabolic control during CSII and MDI

## Statement:

During CSII glycemia is improved in the long term with less glucose fluctuation and less hypoglycemia.

## Evidence:

Randomised, controlled, open, cross-over study (11 centres in 5 countries: D, NL, UK, ESP, I) for 16 months with 261 type 1 diabetic patients:



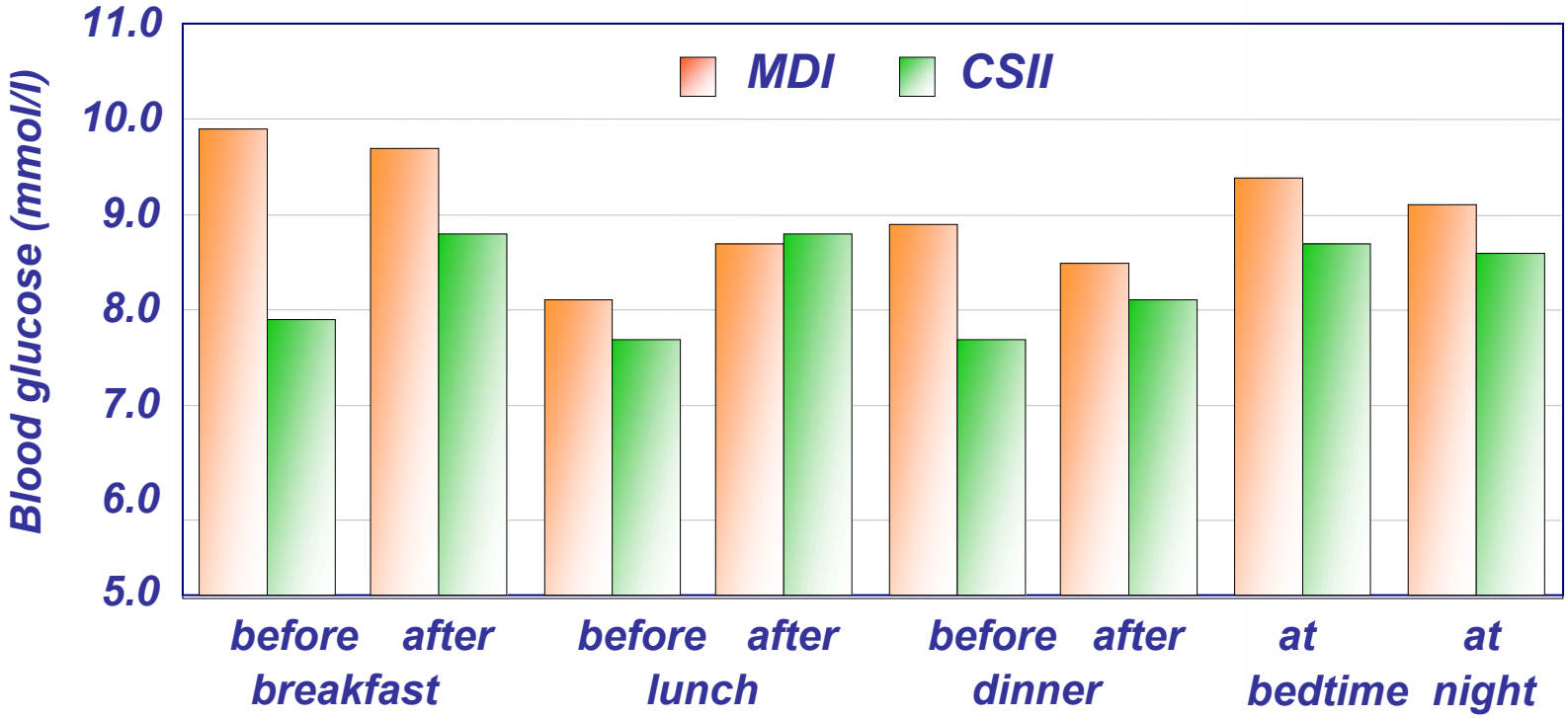

*From: Hoogma RPL et al.: Diabetic Medicine 2006; 23:141*

Back

Medtronic

# Metabolic control during CSII and MDI

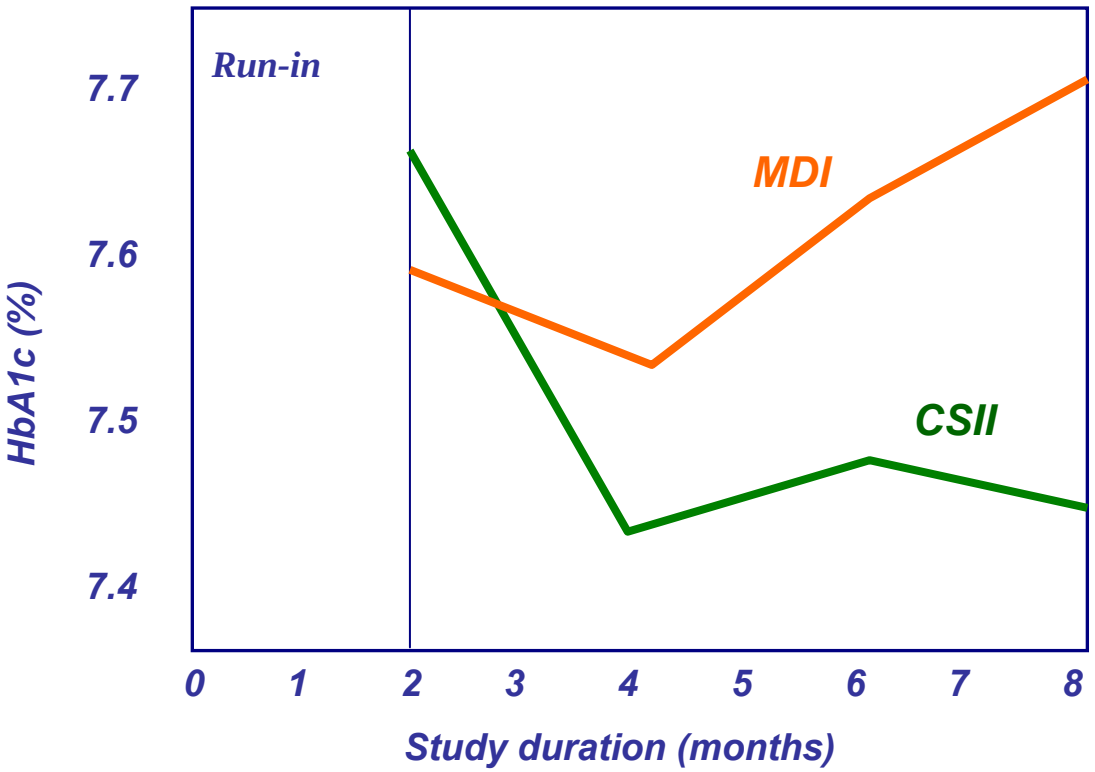
- Blood glucose profile over the course of a day:



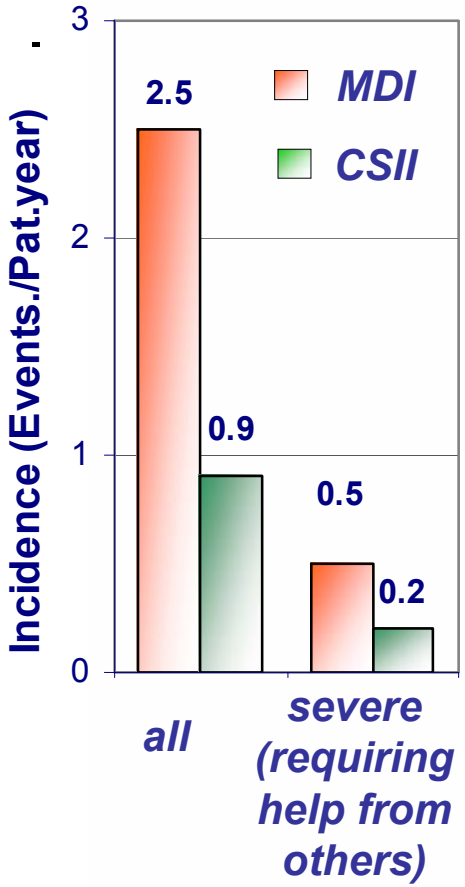

*From: Hoogma RPL et al..: Diabetic Medicine 2006; 23:141*

# Metabolic control during CSII and MDI

- Development $HbA_{1c}$:




- Hypoglycemic events:




*From: Hoogma RPL et al..: Diabetic Medicine 2006; 23:141*

Medtronic

# Metabolic control during CSII and MDI

**Conclusion:**

During CSII compared to MDI

- Glycemia is improved in the long term
- Glucose fluctuations are less frequent
- Less hypoglycemia was observed
- Required insulin doses are lower.

All metabolic processes deteriorate significantly during the transition from CSII to MDI.

Back

*From: Hoogma RPL et al..: Diabetic Medicine 2006; 23:141*

# Long term results of the treatment of type 2 diabetic patients with CSII

## Statement:

CSII also leads to good blood sugar control and a long term improvement in lipid parameters in patients with type 2 diabetes.

## Evidence:

Retrospective data analysis over a period of 10 years with data from 17 patients with type 2 diabetes (53% female, age: 55.9± 8.0 years, duration of CSII: 10.2 ± 2.5 years, duration of diabetes with adjustment to CSII: 8.5 ± 6.0 years).

*From: Soobong C et al.: Diabetes 2007; 56 (Suppl. 1), A533-A534.*

Back

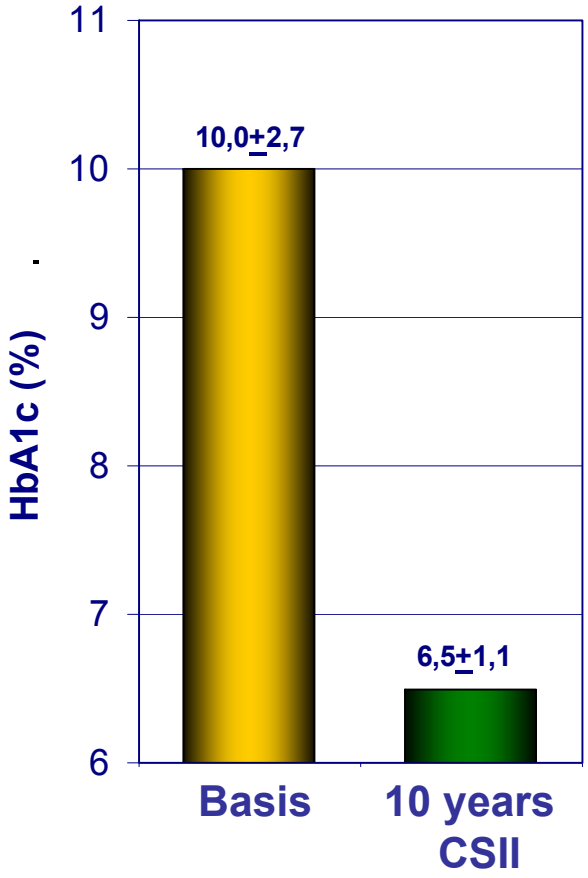
Medtronic

CSII

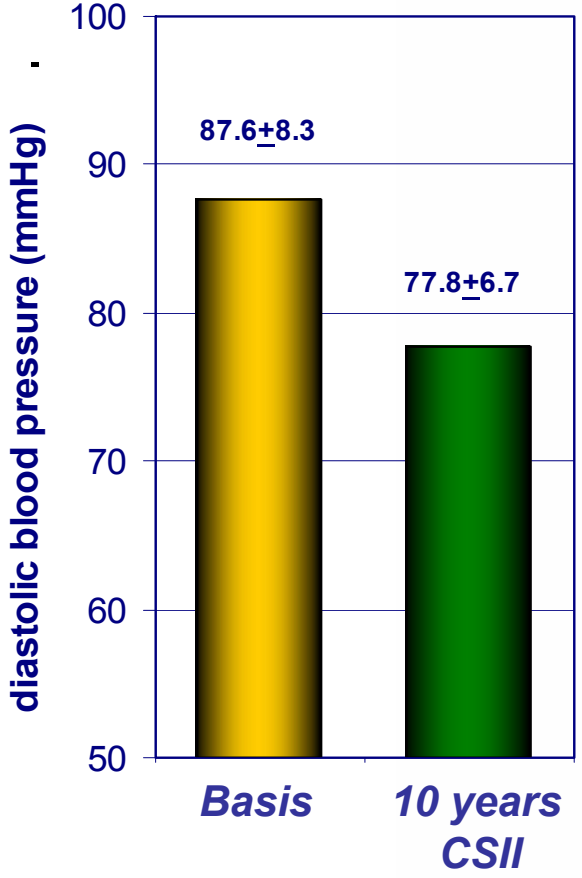
# Long term results of the treatment of type 2 diabetic patients with CSII

Change in glycemia and diastolic blood pressure:

- *$HbA_{1c}$:*




- *Diastolic blood pressure:*




*From: Soobong C et al.: Diabetes 2007; 56 (Suppl. 1), A533-A534.*

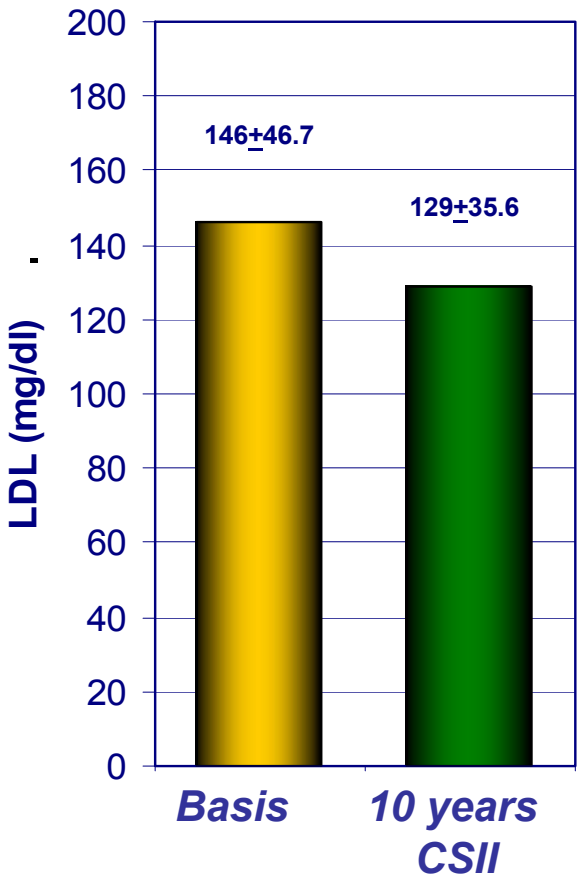
Medtronic

CSII

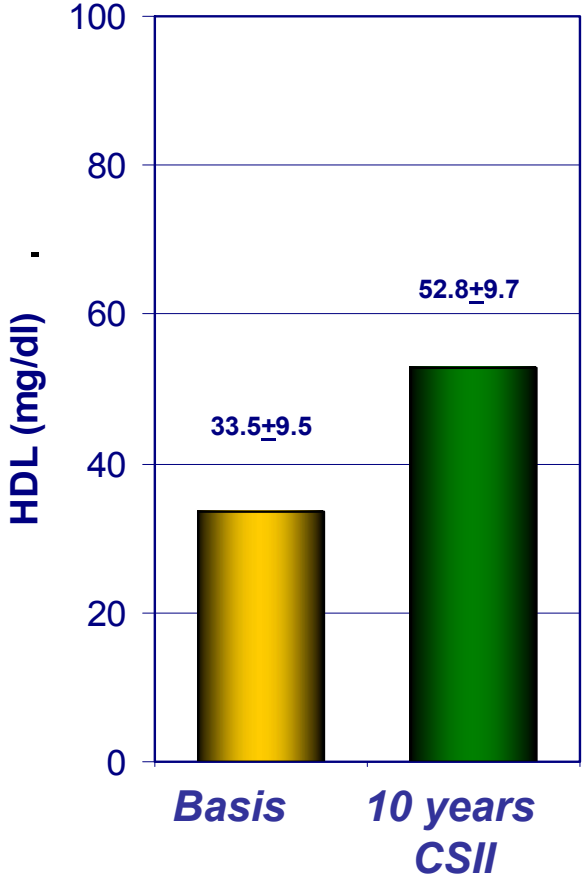
# Long term results of the treatment of type 2 diabetic patients with CSII

Change in lipid parameters (without lipid reducing therapy):

- *LDL:*




- *HDL:*




- Serum creatinine: No increase
- BMI: No increase

*From: Soobong C et al.: Diabetes 2007; 56 (Suppl. 1), A533-A534.*

Medtronic

CSII

# Long term results of the treatment of type 2 diabetic patients with CSII

## Conclusion:

The use of CSII over a long period also leads to euglycemic blood sugar control with concomitant improvement in cardiovascular risk factors in patients with type 2 diabetes. This evidence should be taken into account when selecting therapy.

**Note:**

CSII has another significant aspect that has not been taken into account in the few studies with this clientele, namely the high risk of macrovascular disease. This is associated with glycemic fluctuations, which are especially significant in the postprandial phase. These can only be properly controlled with the aid of the bolus options of an insulin pump

*From: Soobong C et al.: Diabetes 2007; 56 (Suppl. 1), A533-A534.*

Medtronic

# Decrease in hypoglycemia during CSII

## Statement:

After switching from MDI to CSII, blood sugar values (and $HbA_{1c}$) improve, especially in patients with high $HbA_{1c}$ values. The rate of hypoglycemia is also reduced, especially in patients with low $HbA_{1c}$ values (and therefore frequent hypoglycemia). In many patients, both improve.

## Evidence:

Study of 55 type 1 diabetics who were switched to CSII after frequent severe hypoglycemia.

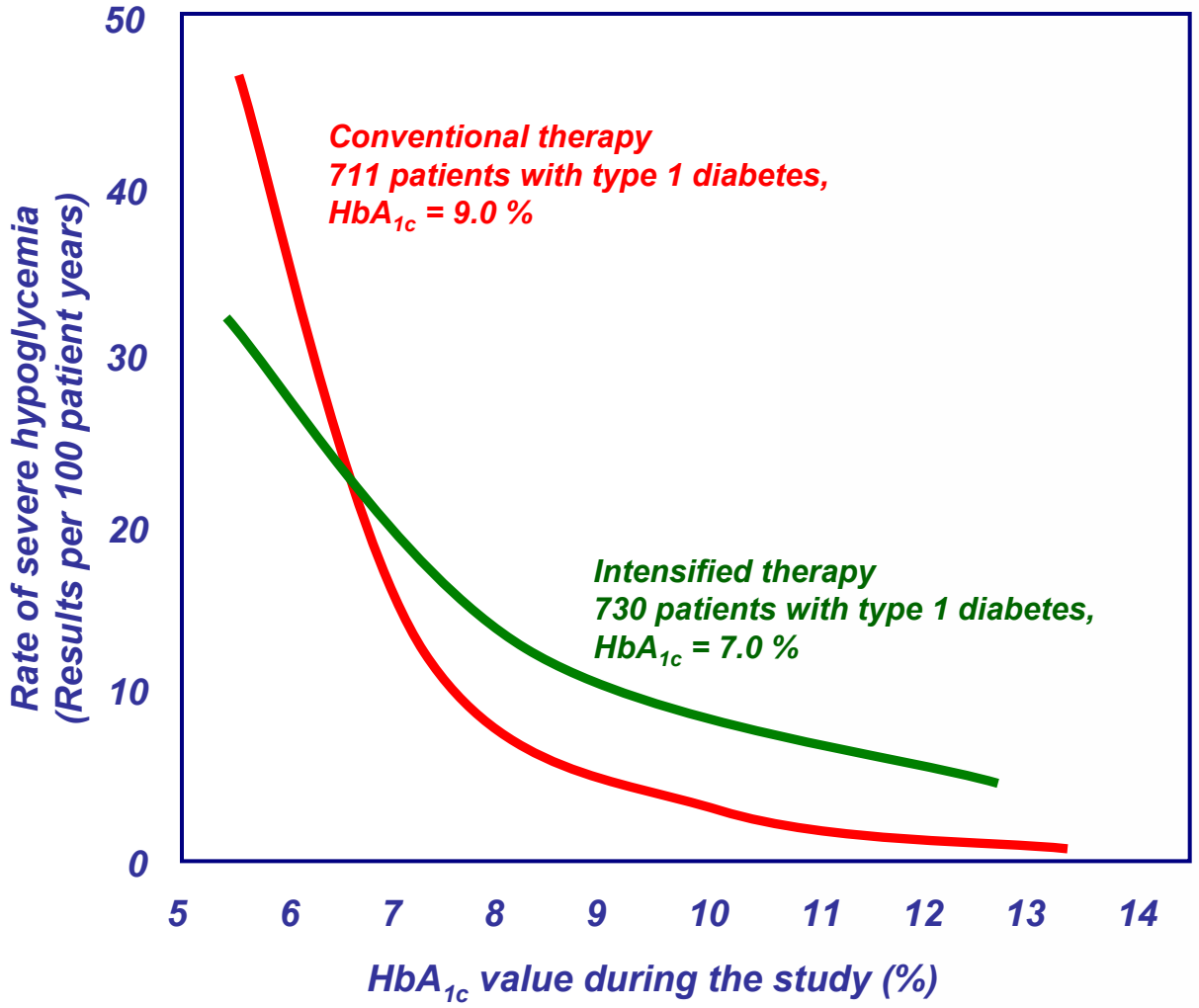
Back

*From: Bode B et al.: Diabetes Care 1996; 19(4): 324-327*

CSII

# Access: Connection between hypoglycemia and insufficient glycemic control according to DCCT

The worry about severe hypoglycemia obviously prevents better glycemic control!

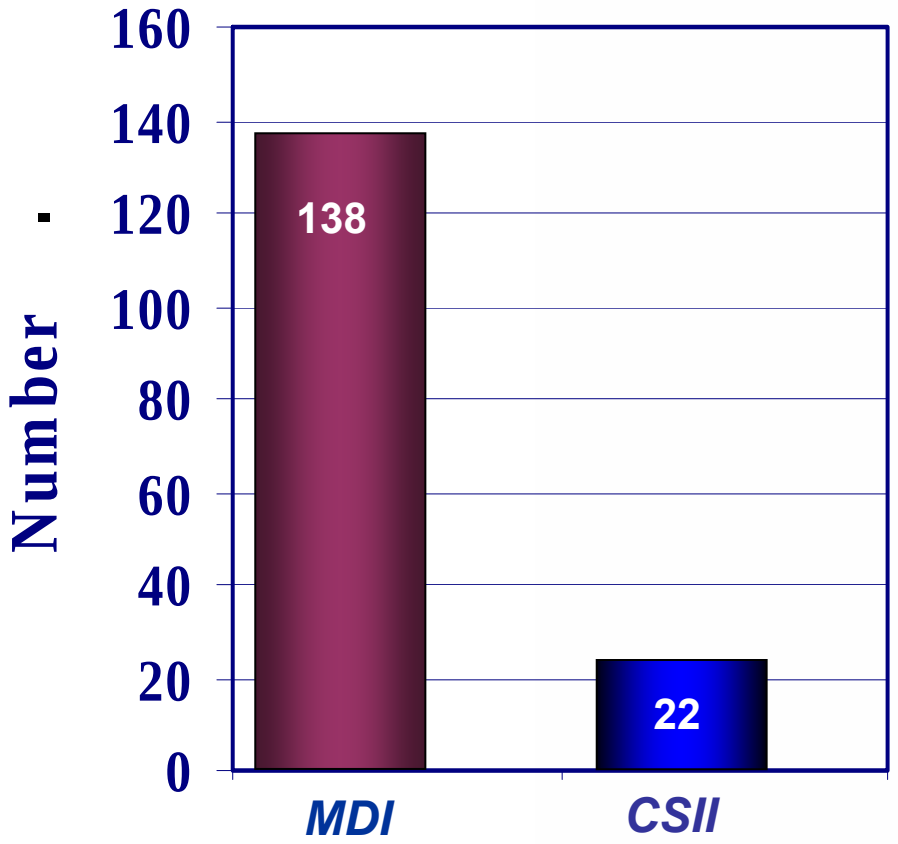



*From: DCCT Research Group; Diabetes (1997); 46: 271-286*

Medtronic

# Decrease in hypoglycemia during CSII

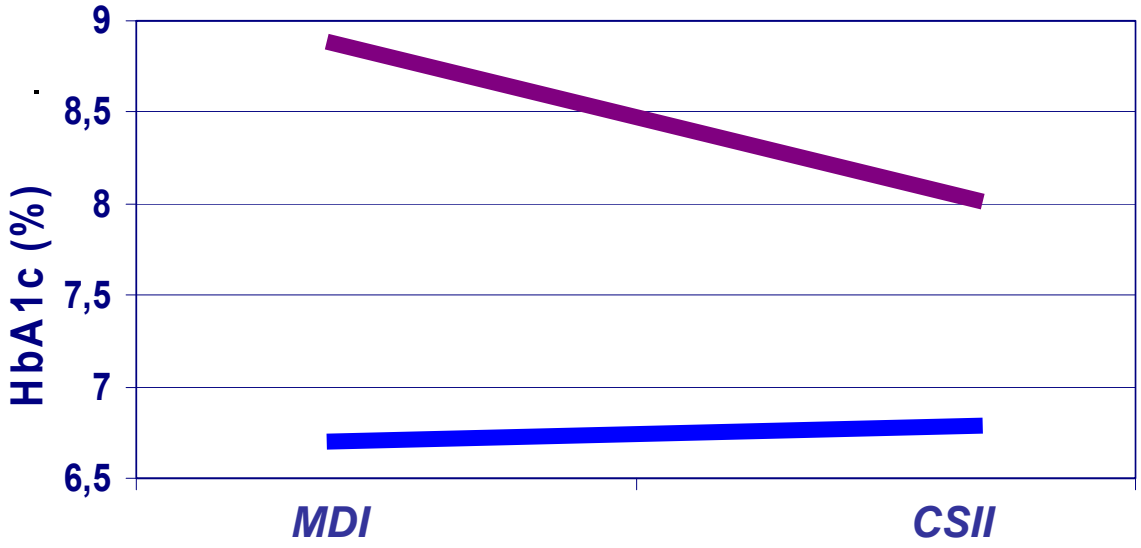
- Number of severe hypoglycemia events per 100 patient years after 12 months treatment with MDI and CSII:




*From: Bode B et al.: Diabetes Care 1996; 19(4): 324-327*

# Decrease in hypoglycemia during CSII

- Development of $HbA_{1c}$ values in patients with good and bad values during MDI



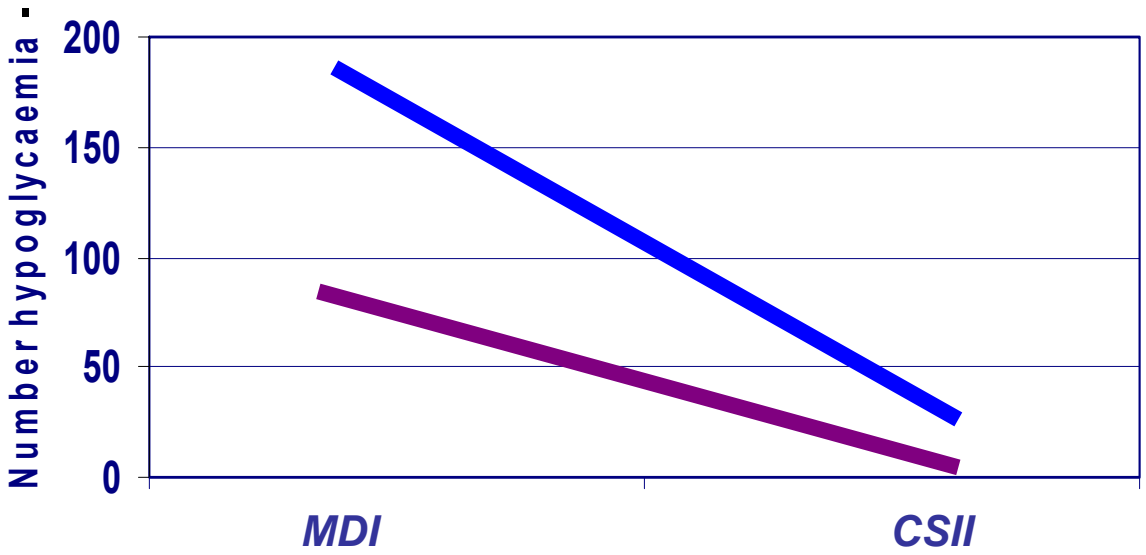

***Patients with poor $HbA_{1c}$ values during MDI***

***Patients with good $HbA_{1c}$ values during MDI***

*From: Bode B et al.: Diabetes Care 1996; 19(4): 324-327*

# Decrease in hypoglycemia during CSII

- Development of rate of hypoglycemia (events per 100 patient years patients with good and poor values during MDI




***Patients with good $HbA_{1c}$ values during MDI***

***Patients with poor $HbA_{1c}$ values during MDI***

*From: Bode B et al.: Diabetes Care 1996; 19(4): 324-327*

# Decrease in hypoglycemia during CSII

## Conclusion:

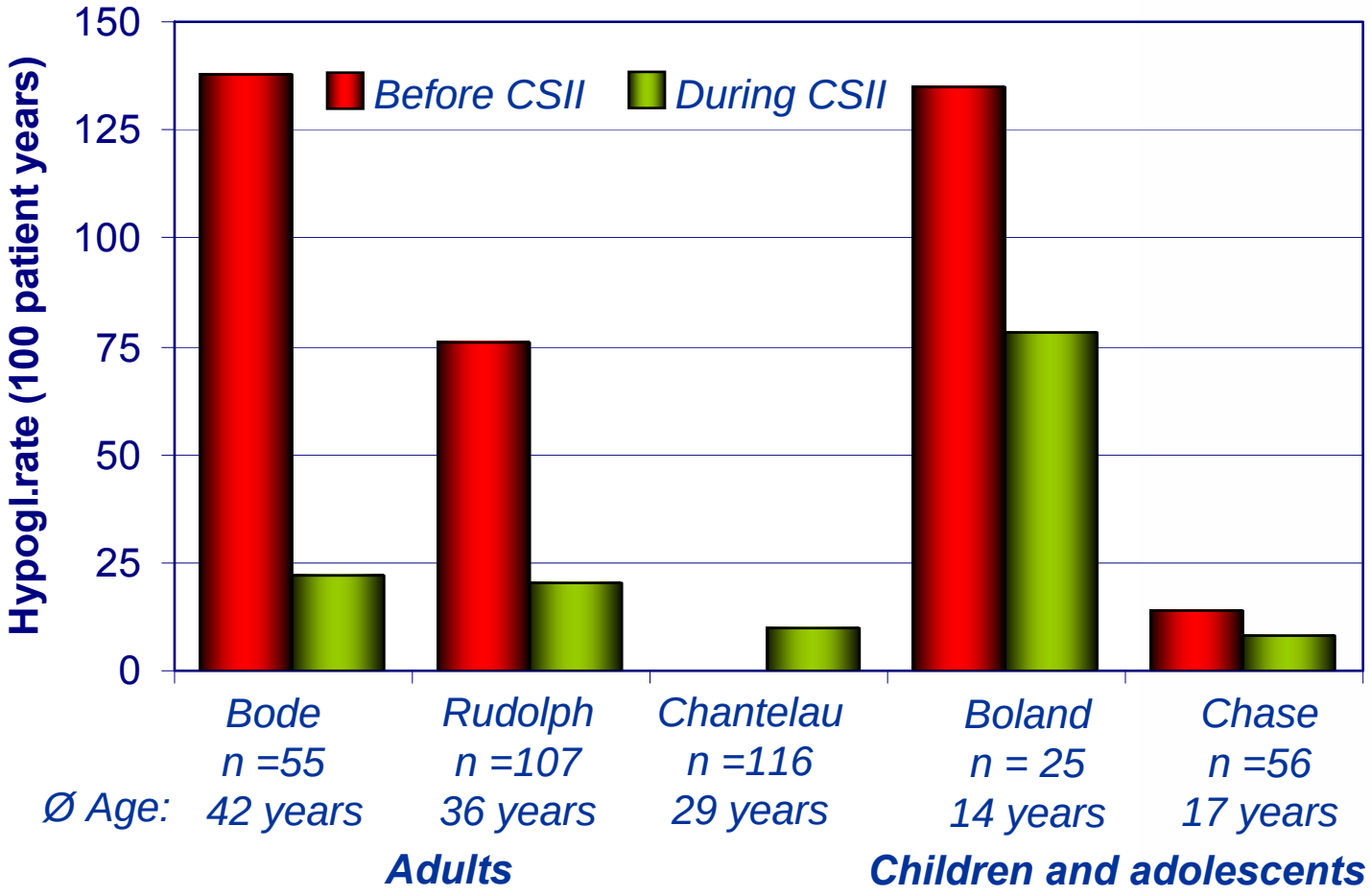
Patients with initially high blood sugar values benefit from CSII, especially with regard to the improvement in $HbA_{1c}$. Patients with good blood sugar values during MDI, however, often have a high rate of hypoglycemia and therefore also benefit from the reduction during CSII.

Back

*From: Bode B et al.: Diabetes Care 1996; 19(4): 324-327*

# Comparison:
# Decrease in hypoglycemia during CSII

Hypoglycemia rate before and during CSII in several studies:




Back

*From: Chantelau E, et al. Diabetologia. 1989;32:421–426; Bode BW, et al. Diabetes Care. 1996;19:324–327; Boland EA, et al. Diabetes Care. 1999;22:1779–1784; Chase HP, et al. Paediatrics. 2001;107:351–356.*

Medtronic

# Effectiveness of CSII in type 1 diabetics with frequent severe hypoglycemia

## Statement:

Not all patients insufficiently controlled during MDI with normal insulin benefit from the switch to MDI with insulin analogue. However, there is a definite improvement in the glycemia of these patients with a switch to CSII.

## Evidence:

Switching of patients with type 1 diabetes and frequent hypoglycemia from optimised MDI with Glargine to CSII.

Back

*From: Pickup JC et al.: Practical Diabetes International, 22 (1), 2005: 10-14*

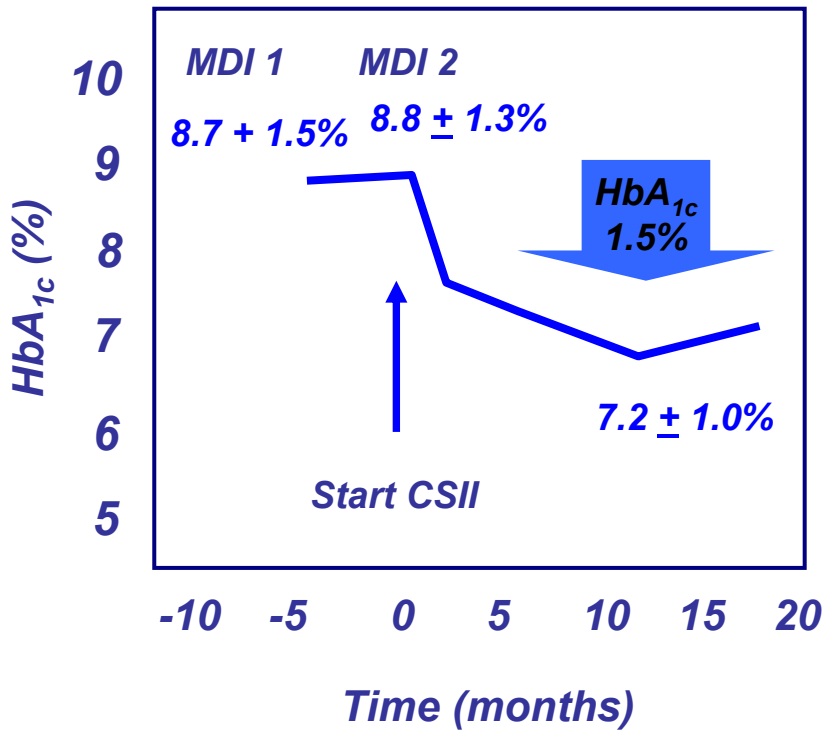
Medtronic

CSII

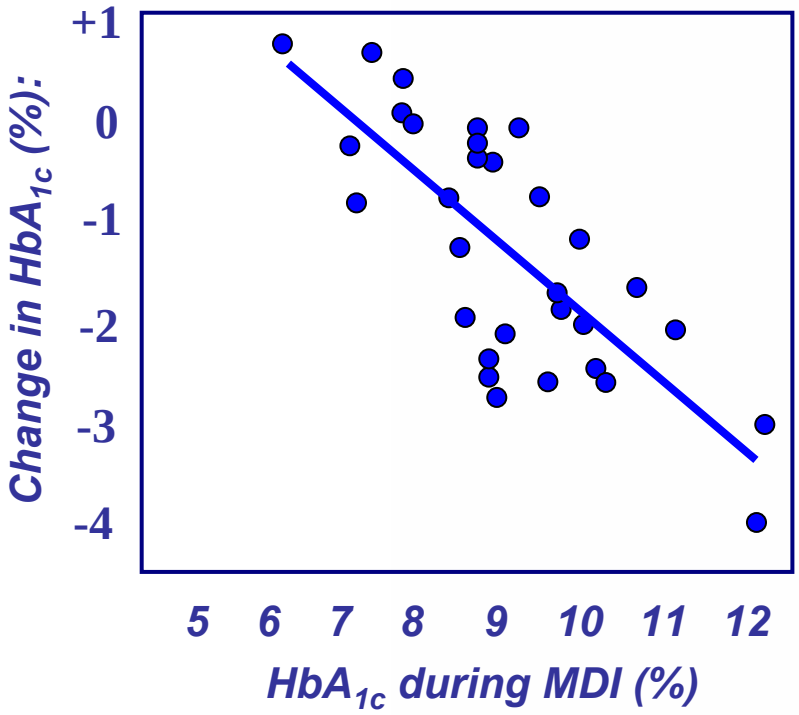
# Effectiveness of CSII in type 1 diabetics with frequent severe hypoglycemia

1. Optimisation of MDI (with NPH insulin) for patients with frequent hypoglycemia by switching to MDI with Glargine
2. Change to CSII and 17 months monitoring

• Development $HbA_{1c}$ value:




• Change to $HbA_{1c}$ value:



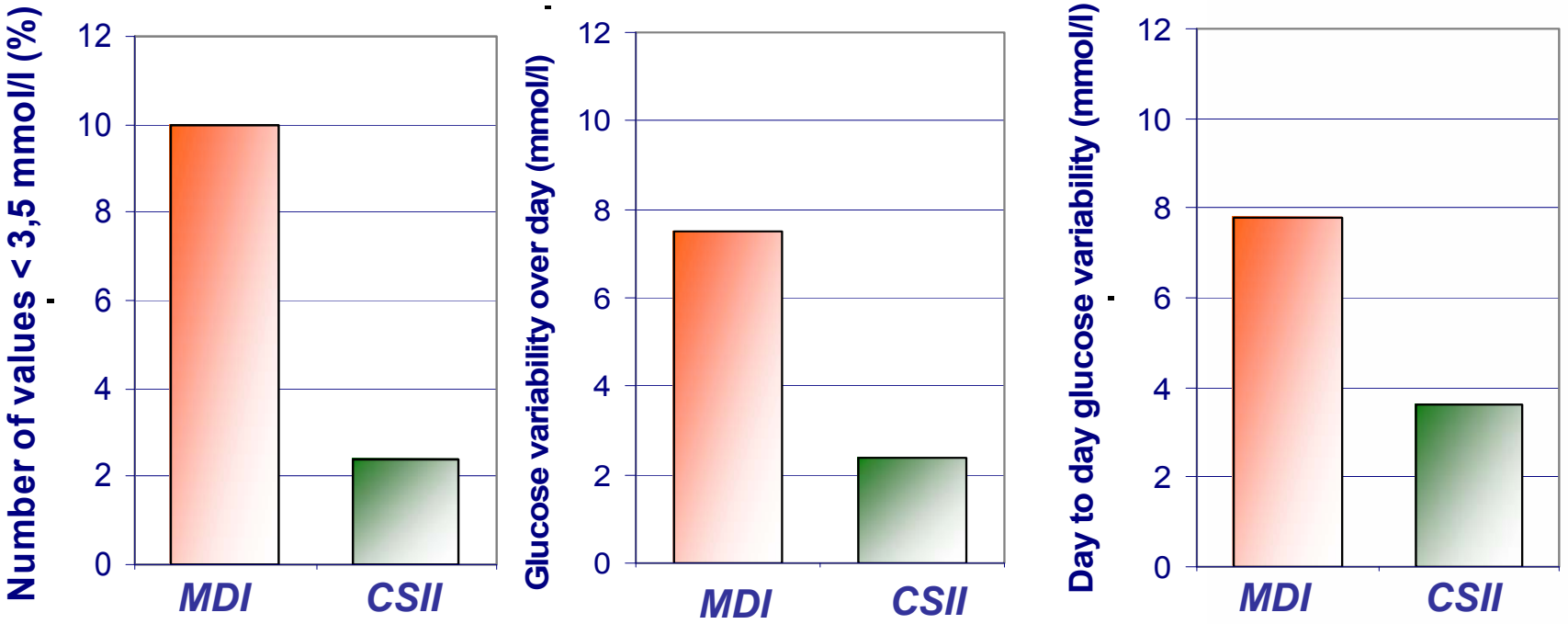

*From: Pickup JC et al.: Practical Diabetes International, 22 (1), 2005: 10-14*

Medtronic

CSII

# Effectiveness of CSII in type 1 diabetics with frequent severe hypoglycemia

- Amount of hypoglycemic values and glucose variability:




- Patients experiencing control difficulties, and with a disposition to hypoglycemia experience less improvement from the MDI change to Glargine, but improvement is significant with a change to CSII

*From: Pickup JC et al.: Practical Diabetes International, 22 (1), 2005: 10-14*

Medtronic

# Effectiveness of CSII in type 1 diabetics with frequent severe hypoglycemia

## Conclusion:

The glycemia of difficult to control patients is sometimes also not improved when MDI is optimised with insulin analogue. However, it is improved with a switch to CSII.

Back

From: Pickup JC et al.: Practical Diabetes International, 22 (1), 2005: 10-14

# Glucose level during MDI with long-acting insulin analogue and during CSII

## Statement:

Only with a continuous insulin infusion is an insulin level achieved which corresponds to almost the physiological condition of the organism. It leads to more stable glycemia with less values in hypoglycemic or hyperglycemic ranges.

## Evidence:

Comparison of glucose values with continuous glucose monitoring (CGMS) during the night in patients with type 1 diabetes, treated with Glargine or with CSII (comparable age, duration of diabetes, $HbA_{1c}$ and BMI).

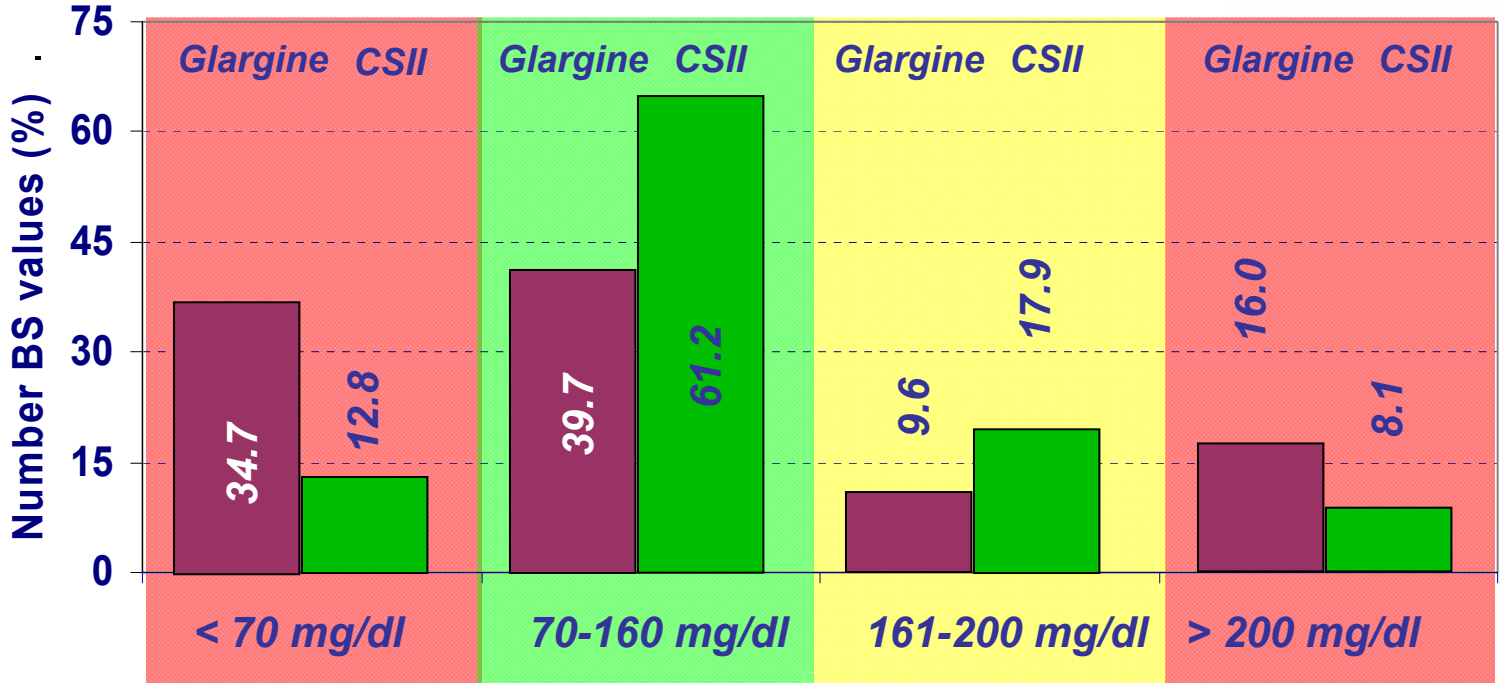
Back

*From: Armstrong DU et. al.: Diabetes 51 Suppl.2 (2002), A92*

CSII

# Glucose level during MDI with long-acting insulin analogue and during CSII

Comparison of CGMS values during the night in patients with type 1 diabetes, treated with Glargine or with CSII (comparable age, duration of diabetes, $HbA_{1c}$ and BMI).




- There were significantly more values within the normal glycemic range at night during CSII

*From: Armstrong DU et. al.: Diabetes 51 Suppl.2 (2002), A92*

Medtronic

# Glucose level during MDI with long-acting insulin analogue and during CSII

## Conclusion:

During CSII the glycemia is definitely more stable than with MDI using Glargine. There were significantly more values recorded within the normal glycemic range during CSII, particularly at night.

Back

*From: Armstrong DU et. al.: Diabetes 51 Suppl.2 (2002), A92*

# Comparison of CSII and MDI with Glargine at night using continuous glucose monitoring

## Statement:

Compared to MDI with long-acting insulin analogue, the glycemia during CSII is in the hypoglycemic or hyperglycemic ranges considerably less often. That also applies to the night-time hours, when postprandial glycemia recedes into the background.

## Evidence:

Comparison of night-time profiles measured with continuous glucose monitoring in 11 patients with CSII (Lispro) and 8 patients with MDI (Lispro and Glargine). The groups were comparable with regard to the $HbA_{1c}$ value (CSII - $HbA_{1c}$: 7.3±0.6 %, MDI - $HbA_{1c}$: 7.1±1.0 %).

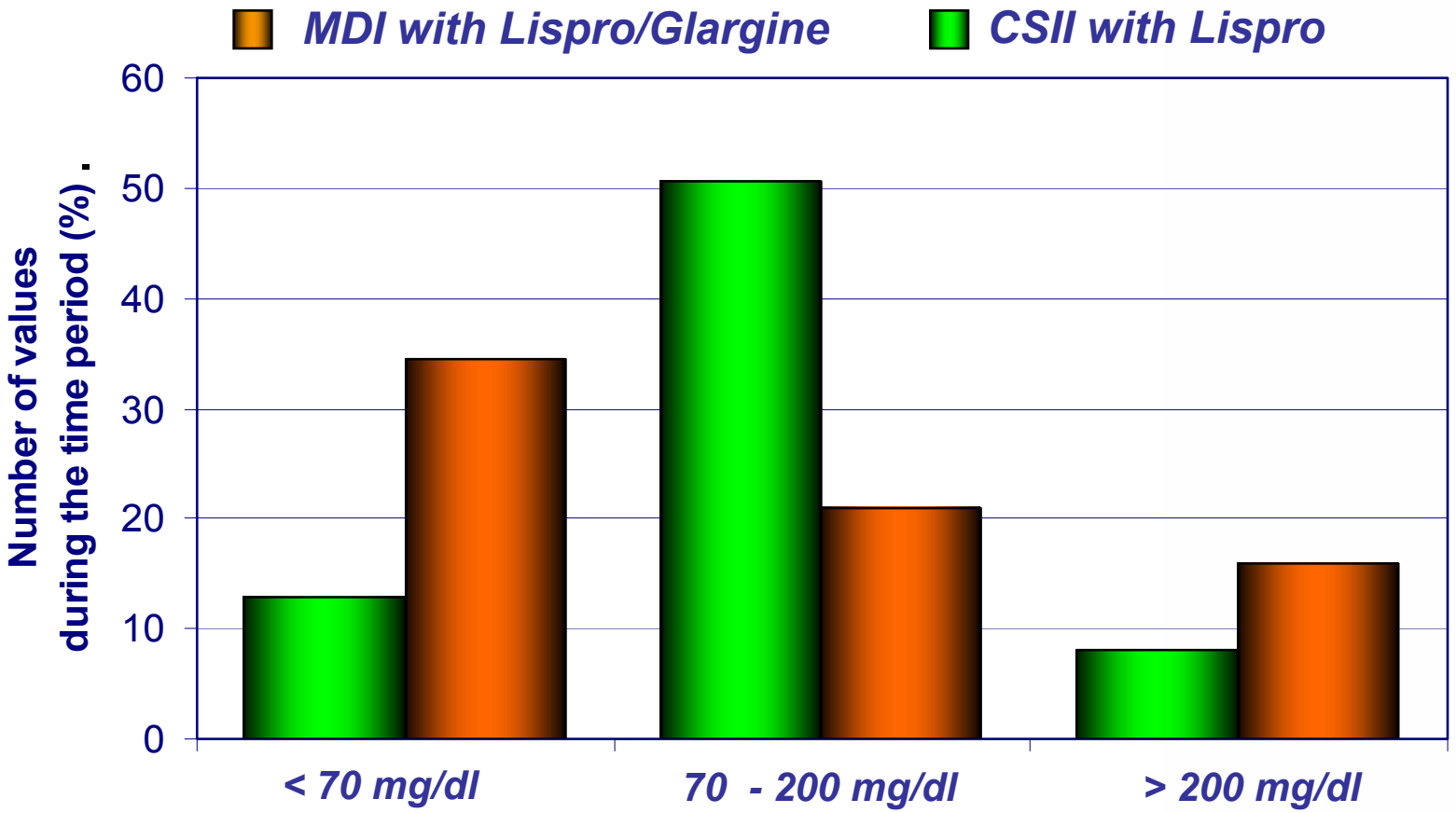
Back

*From: King AB et al. Diabetes Care 2003; 26(4): 1322*

CSII

# Comparison of CSII and MDI with Glargine at night using continuous glucose monitoring

- Amount of values in the various glucose ranges before and during the night:




*From: King AB et al. Diabetes Care 2003; 26(4): 1322*

Medtronic

CSII

# Comparison of CSII and MDI with Glargine at night using continuous glucose monitoring

## Conclusion:

In spite of comparable $HbA_{1c}$ values, there were significantly more values in the normal glycemic range during CSII than during MDI with long-acting insulin analogue. This considerably more balanced glycemia has been proved to also apply at night when glucose fluctuation caused by meals/activity has scarcely any influence.

Back

*From: King AB et al. Diabetes Care 2003; 26(4): 1322*

Medtronic

CSII

# Comparison of insulin and glucose variability during BOT* and CSII in patients with type 2 diabetes

## Statement:

In comparison to MDI with long-acting insulin analogue, the intra-individual insulin and glucose variability during CSII is significantly lower and therefore enables better and more foreseeable therapy management with better glycemic regulation.

## Evidence:

Comparison of intra-individual insulin and glucose variability during CSII with constant basal rate (insulin Aspart) and base oriented insulin therapy (insulin Glargine) in a cross-over study of 21 patients with type 2 diabetes and secondary failure of oral therapy.

**BOT – basis oriented therapy, type 2 diabetics use only insulin Glargine for the insulin treatment*

Back

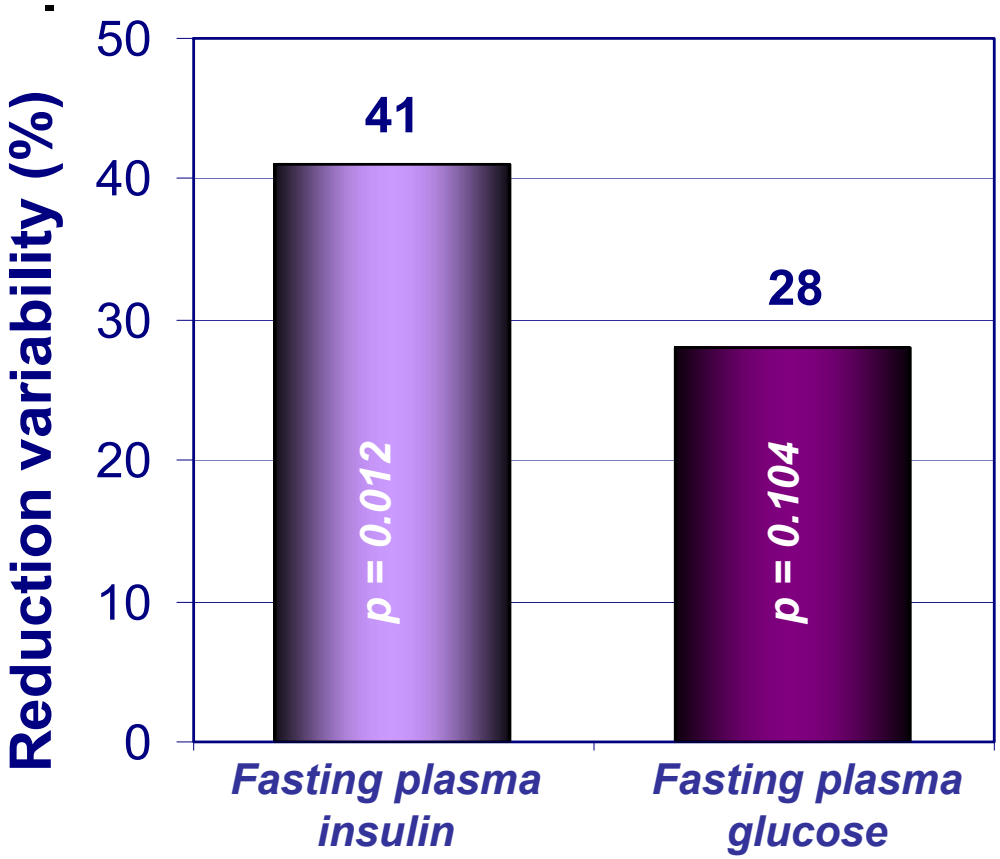
*From: Parkner T et al.: Diabetes 2007; 56 (Suppl. 1), A551.*

Medtronic

CSII

# Comparison of insulin and glucose variability during BOT and CSII in patients with type 2 diabetes

- Reduction in intra-individual variability from CSII with Aspart compared to BOT with Glargine:




- Glycemia:
  - Plasma glucose concentration CSII vs. BOT: Reduction by 11% (p = 0.001)
  - Rate of hypoglycemia: No significant difference

*From: Parkner T et al.: Diabetes 2007; 56 (Suppl. 1), A551.*

Medtronic

CSII

# Comparison of insulin and glucose variability during BOT and CSII in patients with type 2 diabetes

## Conclusion:

The constant infusion of short-acting insulin realised with CSII provides a significant reduction in insulin and glucose variability at low glucose levels, compared to injection of Glargine. There were also no maxima in the insulin profile during CSII. Overall, CSII increases the predictability and safety of therapy in patients with type 2 diabetes.

Back

*From: Parkner T et al.: Diabetes 2007; 56 (Suppl. 1), A551.*

Medtronic

# Arguments for CSII vs. Glargine

- In contrast to delayed action insulin, CSII enables modelling of the physiological insulin requirements.
- Only CSII ensures an even effect profile over 24 hours.
- The metabolic effect of a continuous supply of insulin is more effective than with Glargine (higher insulin level at the same dose in the Clamp trial*).
- During CSII there is less glucose fluctuation.
- Hypoglycemic and hyperglycemic values occur less often during CSII** (more normal glycemic values).
- The avoidance of non-physiological fluctuation of blood sugar prevents the development of macrovascular disease.

Back

** see M.Lepore etc.: Diabetes 49 Suppl.1 (5/2000), 436-OR*

*** see: D.U.Armstrong u.a., Diabetes 51 Suppl.2 (2002), A92*

# Glucose fluctuations during MDI and CSII

## Statement:

By optimising use of normal insulin MDI to MDI with insulin analogue, metabolic control can be achieved that is comparable to a switch to CSII, if glycemic control is assessed only by means of the $HbA_{1c}$ value. With continuous glucose monitoring, however, there is evidence that glucose levels are also subject to less fluctuations during CSII.

## Evidence:

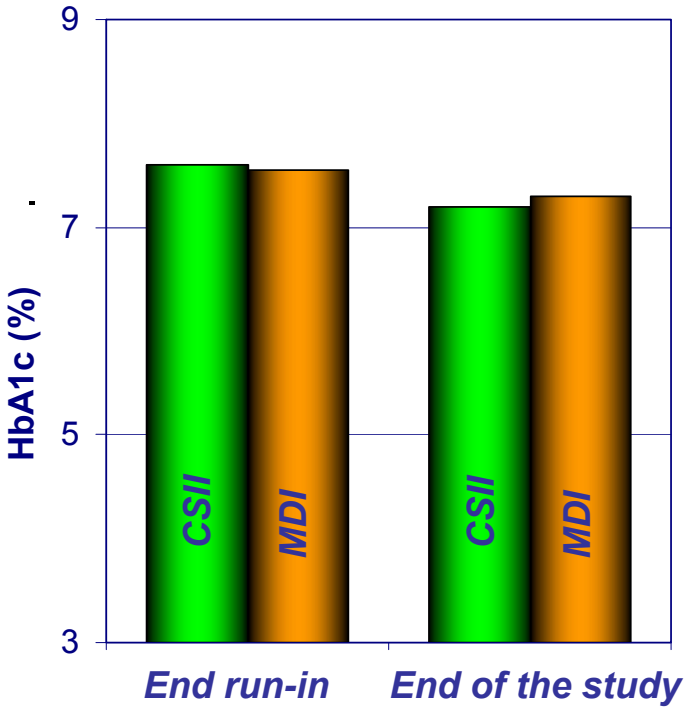
Randomised, controlled cross-over study over 8 months with 39 type 1 diabetics to compare the effectiveness of MDI with Lispro and Glargine and CSII with Lispro (age: 38.1±9.3 years, $HbA_{1c}$: 7.6±0.8 %).

Back

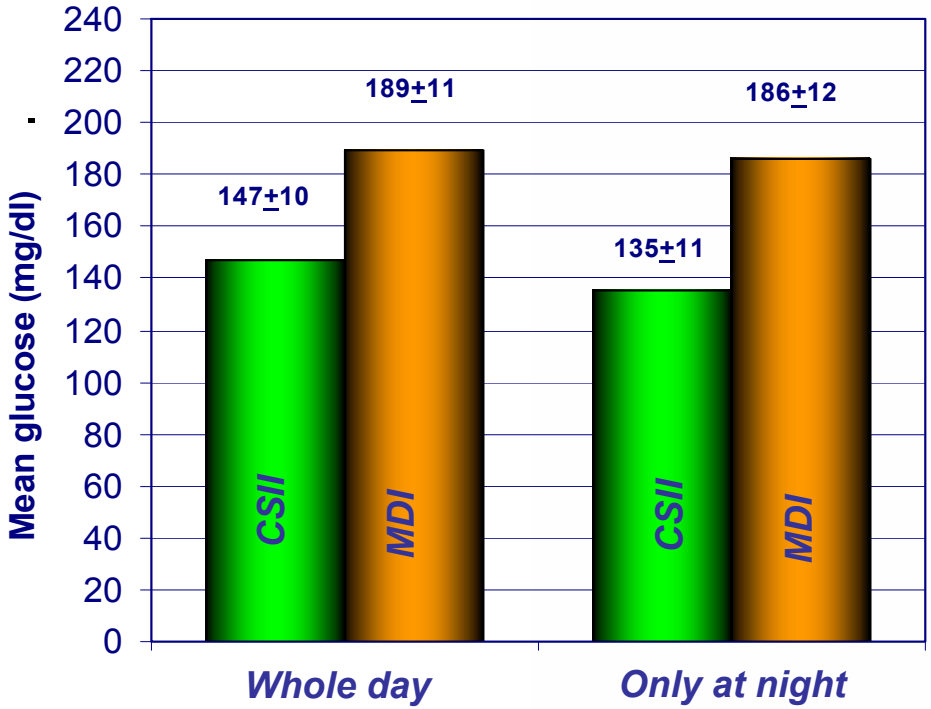
*From: Bruttomesso D et al.: Diabetologia 2006, 49 (Suppl. 1); 590*

# Glucose fluctuations during MDI and CSII

- Changes to $HbA_{1c}$:




- Change to the mean glucose values, measured with CGM:

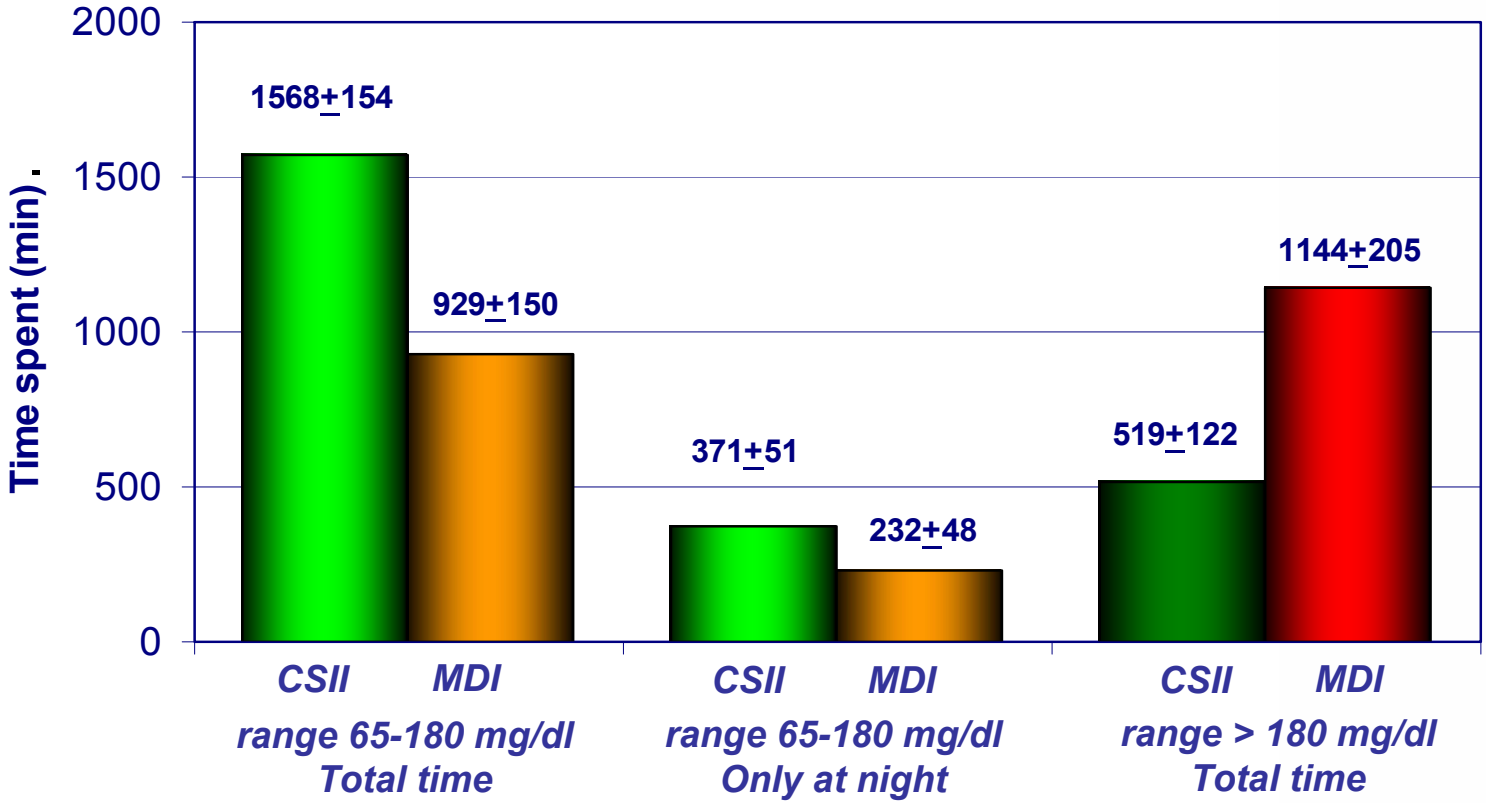



*From: Bruttomesso D et al.: Diabetologia 2006, 49 (Suppl. 1); 590*

Medtronic

# Glucose fluctuations during MDI and CSII

- Time spent in various glycemic conditions (average duration of sensor measurement 34 ± 3 hours):




*From: Bruttomesso D et al.: Diabetologia 2006, 49 (Suppl. 1); 590*

Medtronic

# Glucose fluctuations during MDI and CSII

## Conclusion:

Even when $HbA_{1c}$ values during MDI and CSII are comparable

- there are less glucose fluctuations during CSII
- the time spent in the hyperglycemic range is significantly shorter (in the example it is more than one halved)
- the risk of the development of diabetic complications is reduced by CSII

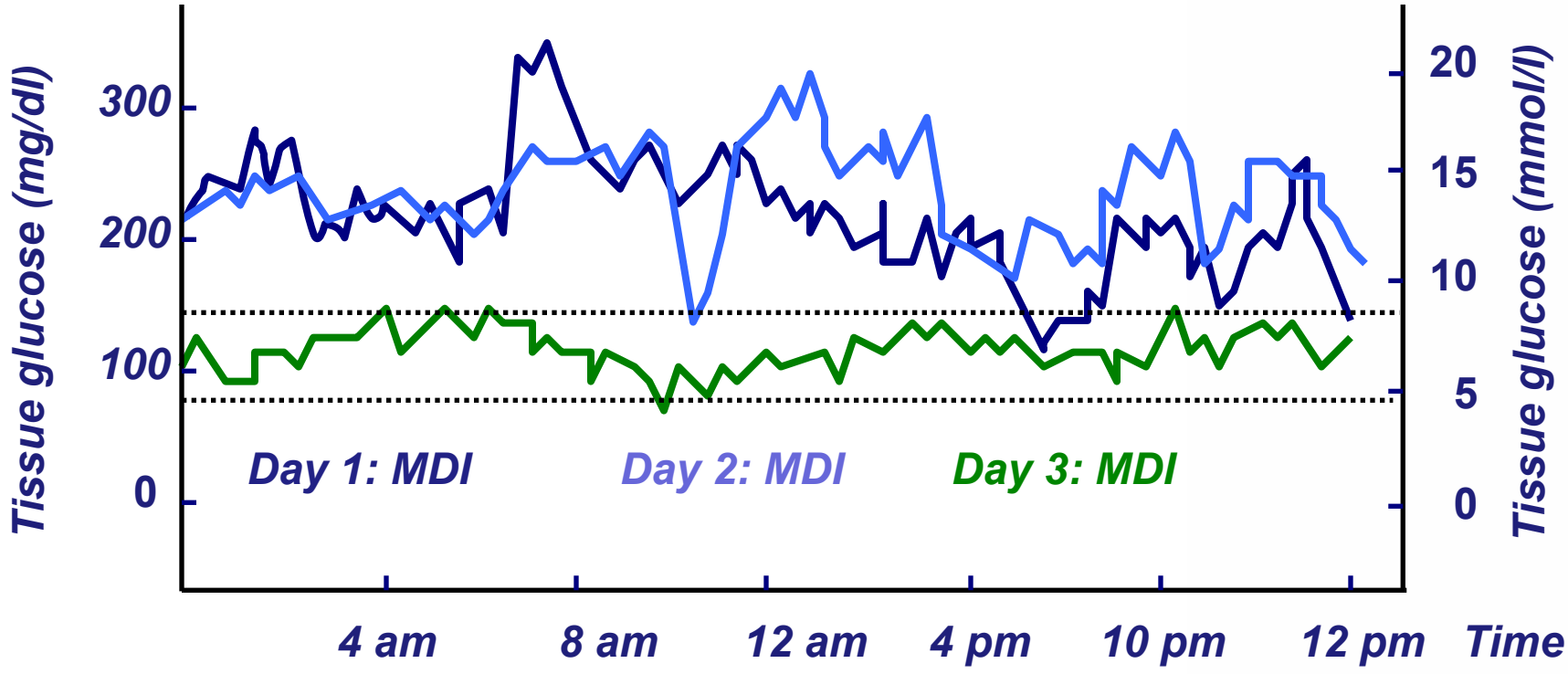
Back

*From: Bruttomesso D et al.: Diabetologia 2006, 49 (Suppl. 1); 590*

CSII

# Comparison: Fewer glucose fluctuations after change from MDI to CSII

- Evidence of glucose fluctuations with CGMS over 72 hours before CSII and during the CSII transfer phase:




Back

*From: Behre A et al: Diabetes und Stoffw. [Diabetes and metabolism] 10 Suppl.1 (2001), 126*

Medtronic

# Decrease in progression and regression of retinopathy during CSII

## Statement:

During CSII the progression of diabetic complications is not just delayed, it can even be reversed.

## Evidence:

Examination of the retina in 20 patients with type 1 diabetes (mean age: 37 years, diabetic for: 8 years) using fundoscopy for a period of 2 years after switching to CSII. Initial findings: 30% without retinopathy, 50% with non-proliferative retinopathy and 20% with proliferative retinopathy.

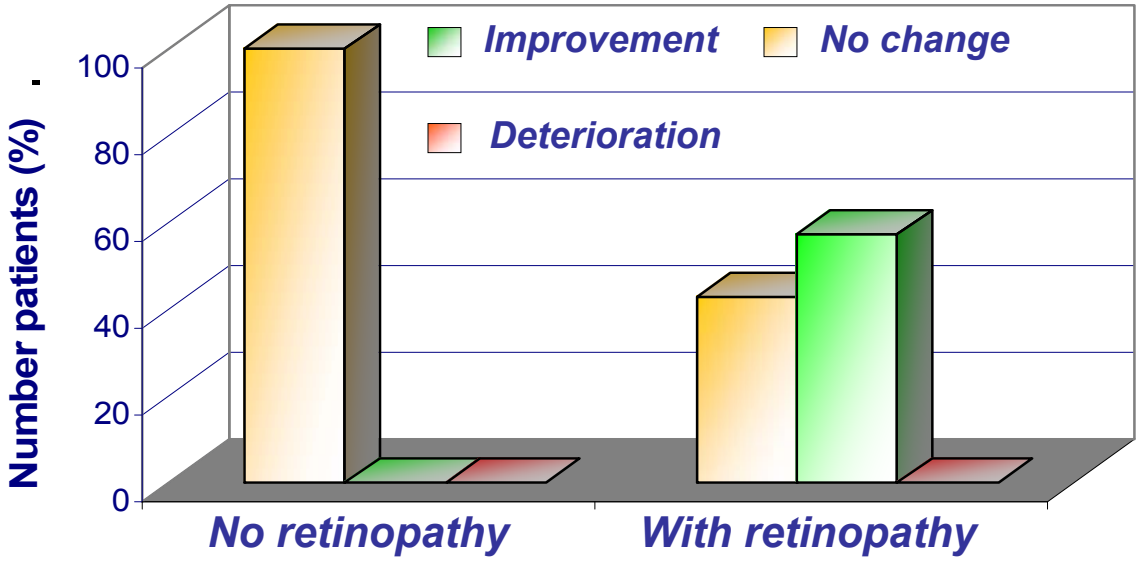
Back

*From: Aragona M et al: Diabetes Metabol. 29 (2003), 4S235*

CSII

# Decrease in progression and regression of retinopathy during CSII

- Improvement in $HbA_{1c}$ values after 2 years CSII compared to initial value: 9.1% -> 7.5%
- Changes in the state of retinopathy after two years compared to the state when CSII was initiated:




| Degree | Patient number | |
|---|---|---|
| RP | Beg. | After 2 yrs |
| 0 | 6 | 10 |
| 1 | 4 | 2 |
| 2 | 5 | 3 |
| 3 | 1 | 3 |
| 4-5 | 4 | 2 |

4 → 10
2 → 3
2 → 3

From: Aragona M et al:: Diabetes Metabol. 29 (2003), 4S235

Medtronic

CSII

# Decrease in progression and regression of retinopathy during CSII

## Conclusion:

During CSII there is significant regression in retinopathy, if present.

Back

*From: Aragona M et al:: Diabetes Metabol. 29 (2003), 4S235*

Medtronic

CSII

# Decrease in risk of renal failure in patients with type 1 diabetes during CSII

## Statement:

During CSII there is not only less progression of diabetic nephropathy, there is even regression of microalbuminuria, compared to a progression with MDI.

## Evidence:

Verification in a prospective, controlled observational study over 3 years involving 110 patients with type 1 diabetes (58 female / 52 male), of whom 90 with normal albumin excretion (age: 40 ± 10 years, diabetic for: 19 ± 9 years) compared to an adjusted MDI group.

Back

*From: Lepore G et al.: Diabetologia 2007, 50 (Suppl. 1), S94.*

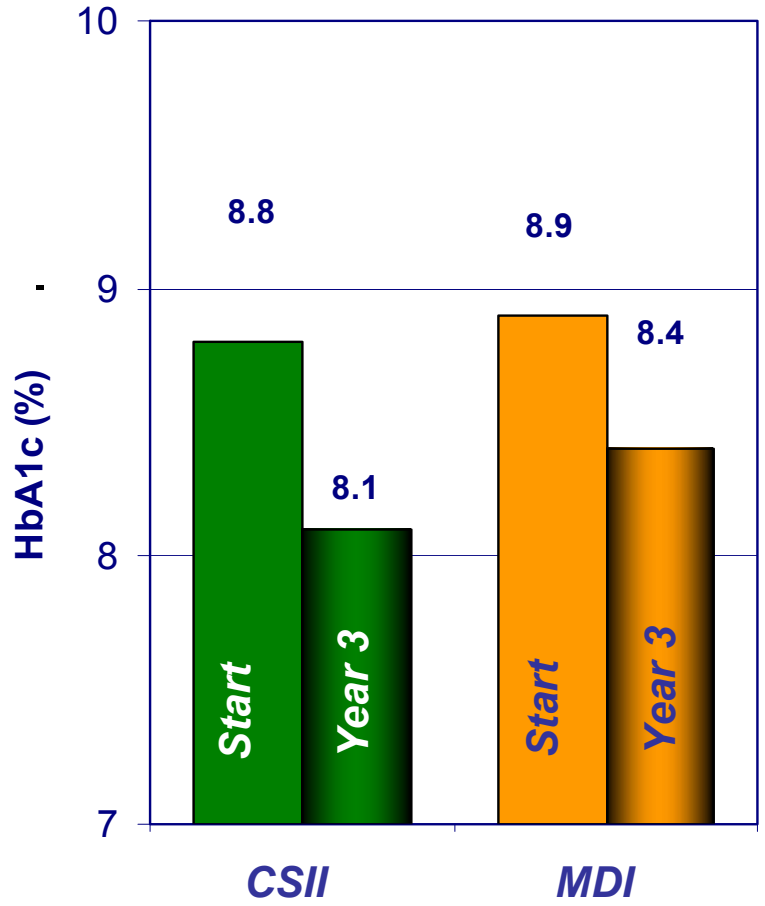
Medtronic

CSII

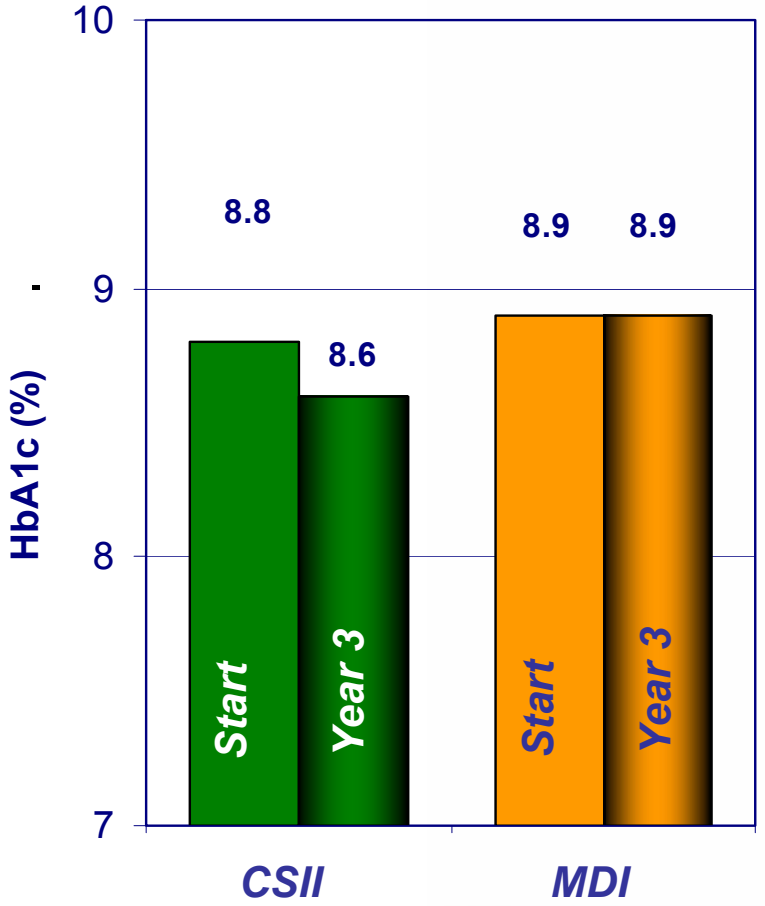
# Decrease in risk of renal failure in patients with type 1 diabetes during CSII

$HbA_{1c}$ values at the start and after 3 years:

- *All patients:*




- *Subgroup with albuminuria:*




*From: Lepore G et al.: Diabetologia 2007, 50 (Suppl. 1), S94.*

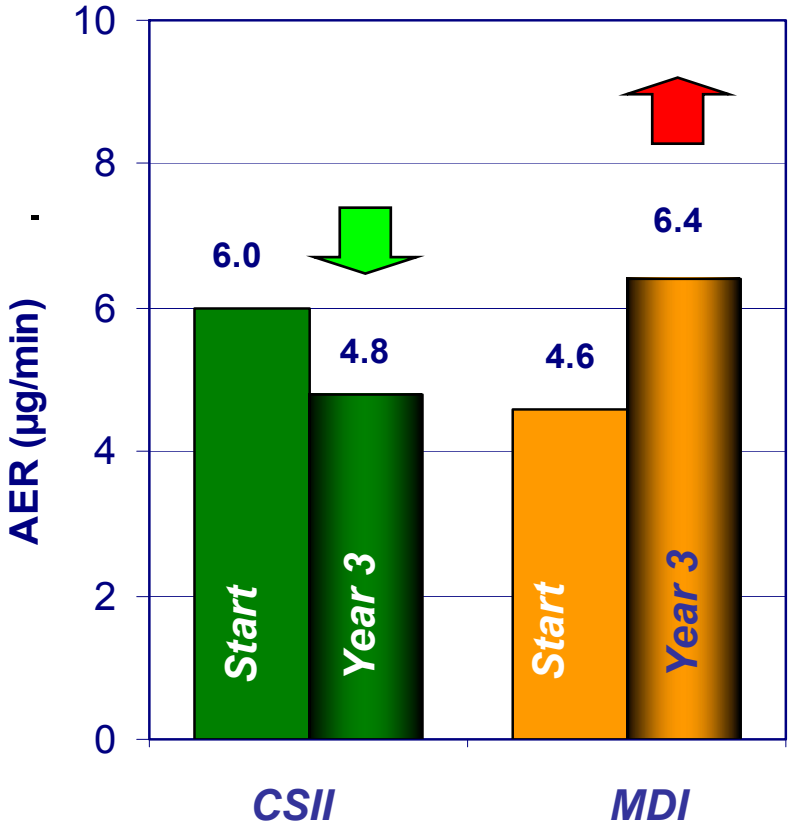
Medtronic

CSII

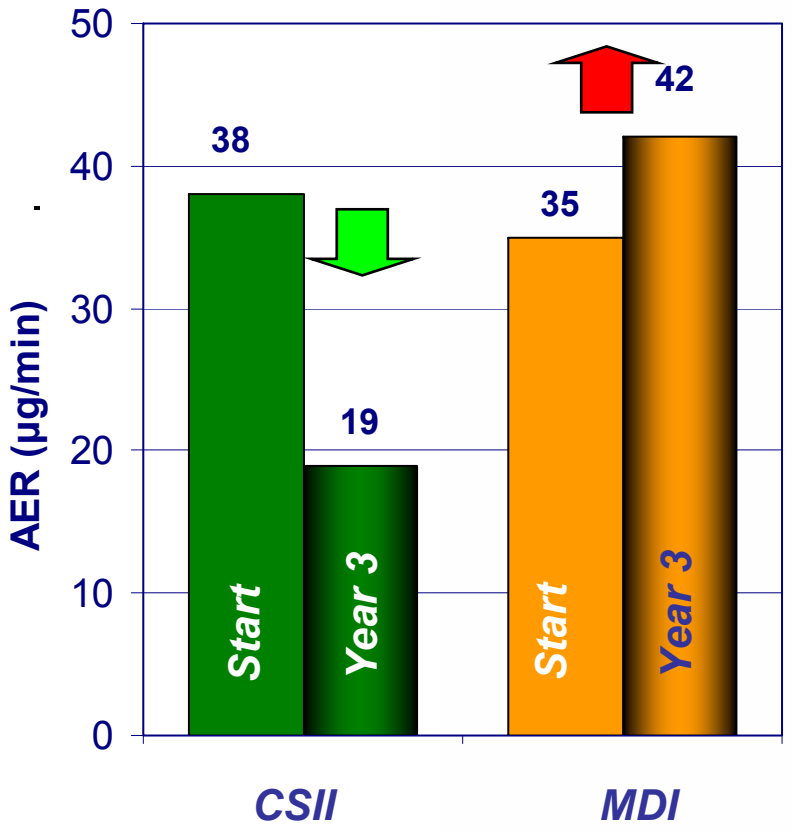
# Decrease in risk of renal failure in patients with type 1 diabetes during CSII

Albumin excretion rate (AER) at the start and after 3 years:

- All patients:




- Subgroup with albuminuria:




*From: Lepore G et al.: Diabetologia 2007, 50 (Suppl. 1), S94.*

Medtronic

CSII

# Decrease in risk of renal failure in patients with type 1 diabetes during CSII

## Conclusion:

The data show that during CSII the progression of nephropathy is not just reduced but even regression of albuminuria may also occur. In contrast, there is progression of renal damage during MDI, although the difference in $HbA_{1c}$ values in the subgroup with pre-existing albumin excretion was not significant.

Back

*From: Lepore G et al.: Diabetologia 2007, 50 (Suppl. 1), S94.*

Medtronic

# Long term results for CSII compared to MDI in terms of diabetic complications

## Statement:

CSII significantly delays the occurrence of diabetic complications in the long term, even though there are no significant differences in $HbA_{1c}$ values compared to MDI.

## Evidence:

Analysis of the long term data of 472 patients with type 1 diabetes and 29 patients with type 2 diabetes subjected to CSII for an average of 7 years, compared to 410 patients with type 1 diabetes and 252 patients with type 2 diabetes using MDI.

Back

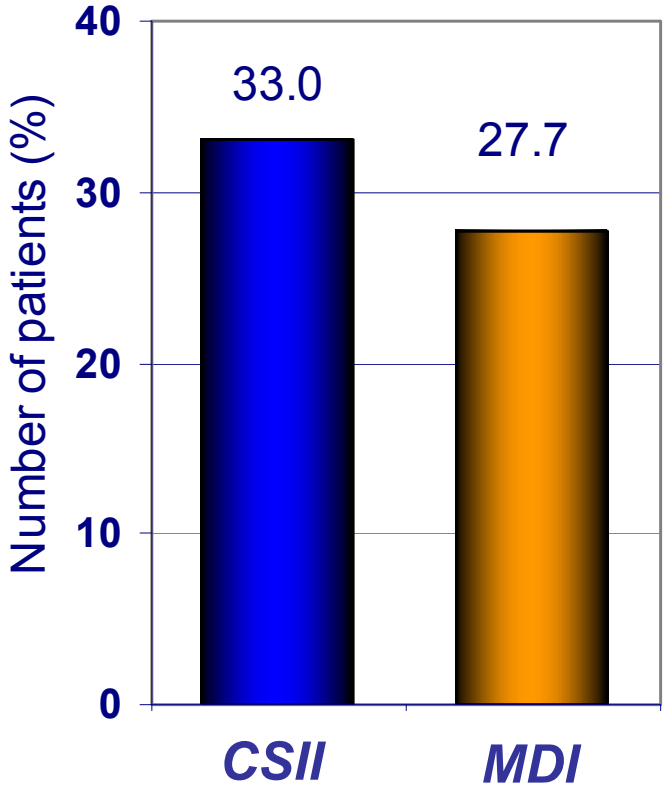
*From: Austenat E et al.: Diabetes 2006; 55 (Suppl. 1), A459.*

# Long term results for CSII compared to MDI in terms of diabetic complications

## Differences CSII vs. MDI:

- The average $HbA_{1c}$ value does not differ significantly in either group: 7.6 % (CSII) vs.. 7.7 % (MDI)

- Share of patients with $HbA_{1c}$ < 7%:



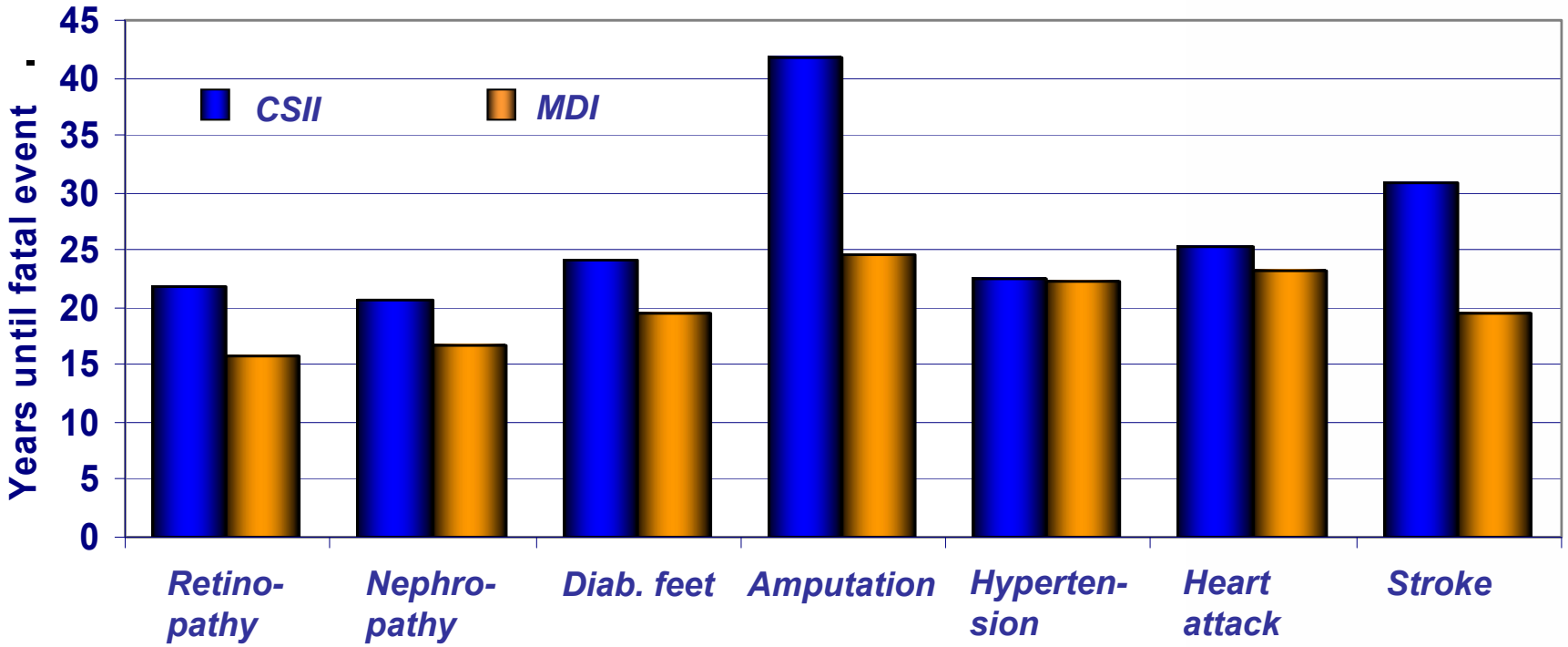

- BMI: n.s.
- Blood pressure control: n.s.

*From: Austenat E et al.: Diabetes 2006; 55 (Suppl. 1), A459.*

Medtronic

# Long term results for CSII compared to MDI in terms of diabetic complications

- Period of time until the occurrence of fatal event during CSII or MDI:




*From: Austenat E et al.: Diabetes 2006; 55 (Suppl. 1), A459.*

Medtronic

# Long term results for CSII compared to MDI in terms of diabetic complications

## Conclusion:

During CSII there is a delay in the onset of diabetic complications of sometimes years compared to MDI, even when there are no significant differences in the $HbA_{1c}$ values.

Back

*From: Austenat E et al.: Diabetes 2006; 55 (Suppl. 1), A459.*

# Improvement in glycemia and reduction of clinical emergencies with CSII

## Statement:

CSII leads to improved glycemia, with less acute complications and less stays in hospital or emergency admissions. CSII is therefore cost-efficient.

## Evidence:

Comparison of metabolic results and the number of emergency admissions and stays in hospital during CSII (n = 35) and MDI (n = 50) (both after training with evaluated programmes) over a period of 2 years (average age of patient: 37 years).

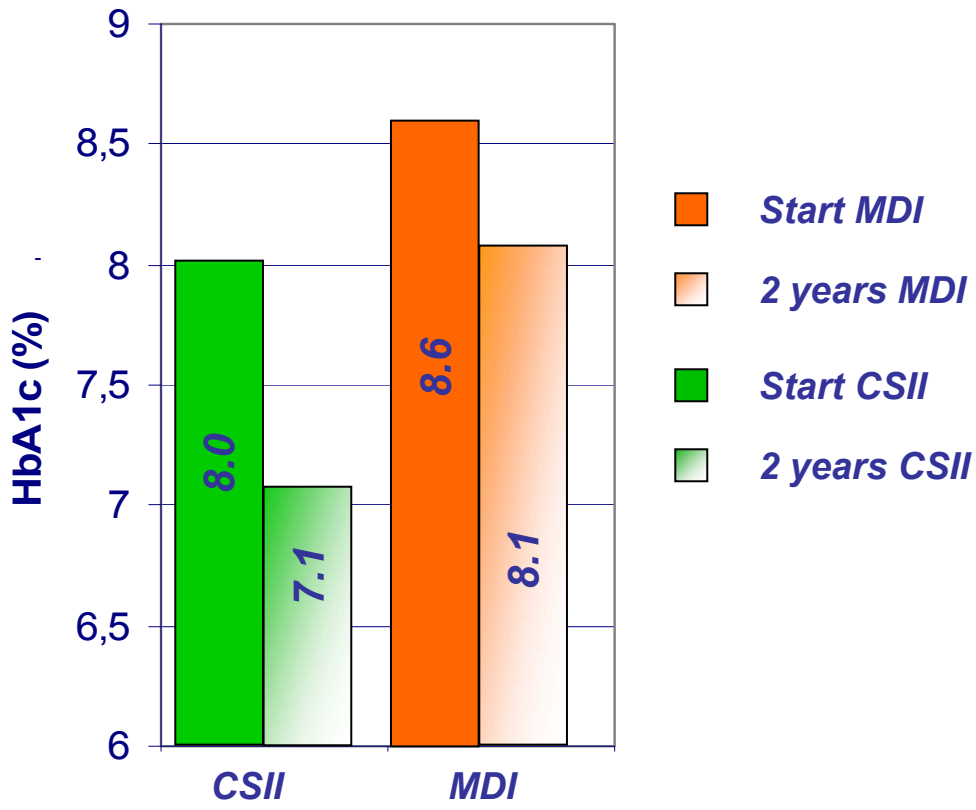
Back

*From: Cersosimo E et. al.: Diabetes 51 Suppl.2 (2002), A128*

CSII

# Improvement in glycemia and reduction of clinical emergencies with CSII

- Change to $HbA_{1c}$ values during CSII and MDI:



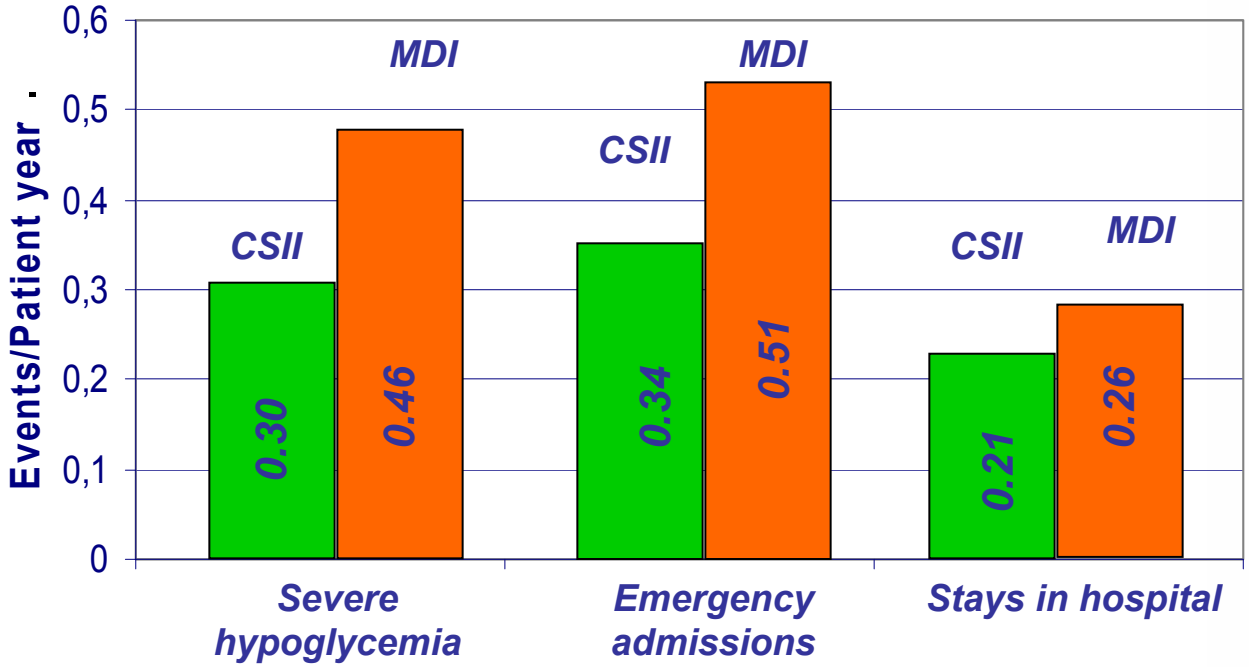

*From: Cersosimo E et. al.: Diabetes 51 Suppl.2 (2002), A128*

Medtronic

CSII

# Improvement in glycemia and reduction of clinical emergencies with CSII

- Number of acute complications, emergency admissions and stays in hospital with CSII and MDI:




- Ketoacidosis: No significant difference
- Complications: No significant change of amount in either group during the monitoring period

*From: Cersosimo E et. al.: Diabetes 51 Suppl.2 (2002), A128*

Medtronic

CSII

# Improvement in glycemia and reduction of clinical emergencies with CSII

## Conclusion:

Besides a definite improvement in $HbA_{1c}$ values during CSII compared to MDI, the rate of acute complications is also less; Stays in hospital and emergency admission are therefore less common. This reduces the cost of diabetes therapy in spite of higher initial costs for the pump and disposable materials.

Back

*From: Cersosimo E et. al.: Diabetes 51 Suppl.2 (2002), A128*

Medtronic

CSII

# Assessment of quality of life and psychological parameters during CSII

## Statement:

CSII provides not just better glycemic control but also leads to an improvement in quality of life and psychological parameters.

## Evidence:

Prospective study over 24 months involving 39 patients with type 1 diabetes (age 33 ± 11 years, diabetic for: 14.6 ± 7.8 years, $HbA_{1c}$: 8.0 ± 1.55 %) to determine the changes in glycemic and psychological characteristics and quality of life (in accordance with the DQOL score).

Back

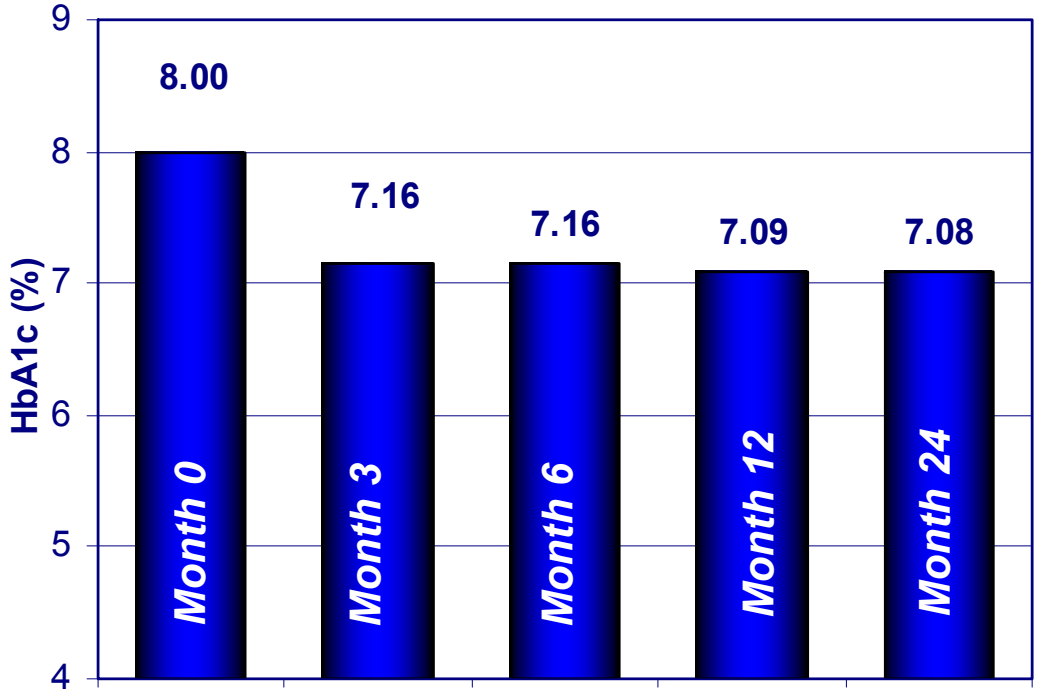
*From: Dominguez-Lopez M et al.: Diabetic Medicine 23 (Suppl. 4) 2006; 323*

Medtronic

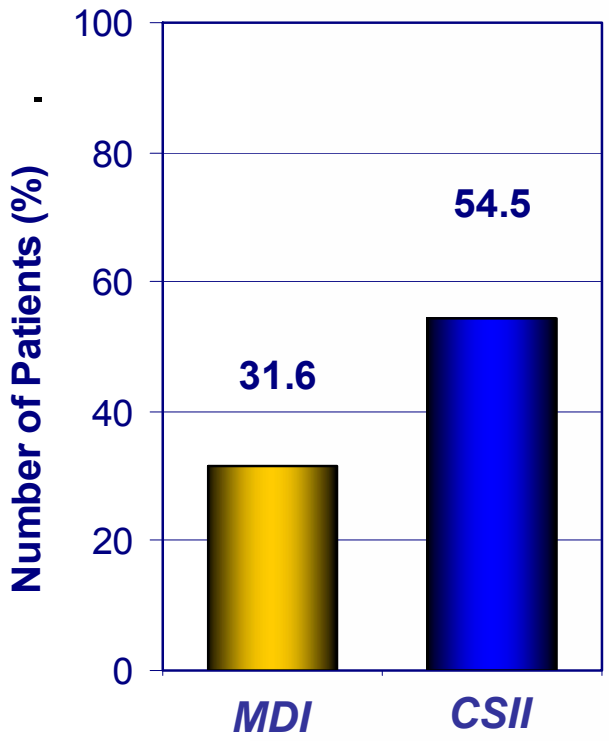
CSII

# Assessment of quality of life and psychological parameters during CSII

- Changes to $HbA_{1c}$ values during CSII:




- Number of CSII patients with $HbA_{1c}$< 7%:



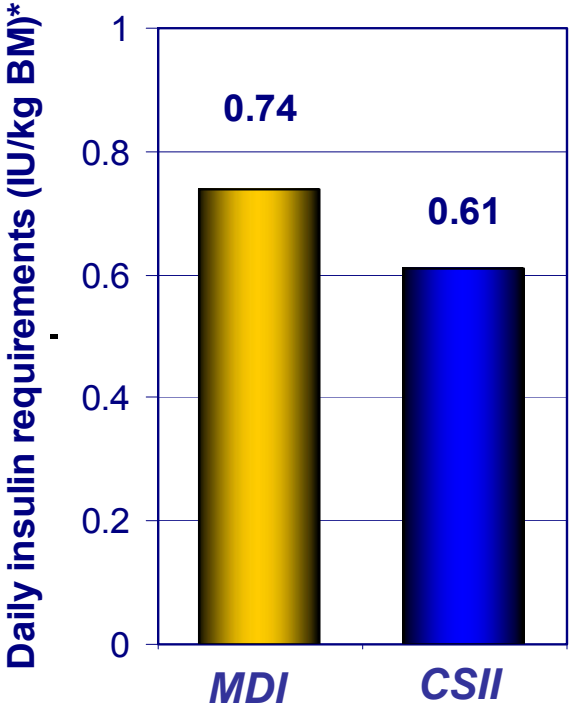

*From: Dominguez-Lopez M et al.: Diabetic Medicine 23 (Suppl. 4) 2006; 323*

Medtronic

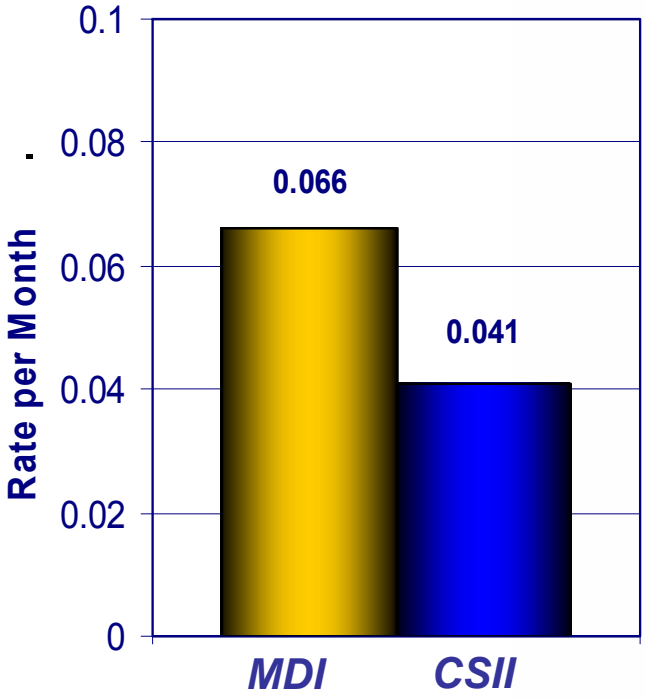
CSII

# Assessment of quality of life and psychological parameters during CSII

- Changes to daily insulin requirements:




- Rate of severe hypoglycemia:




- No significant difference in the rate of mild hypoglycemia and ketoacidosis

**IU/ kg BM – Insulin units per kg body mass*

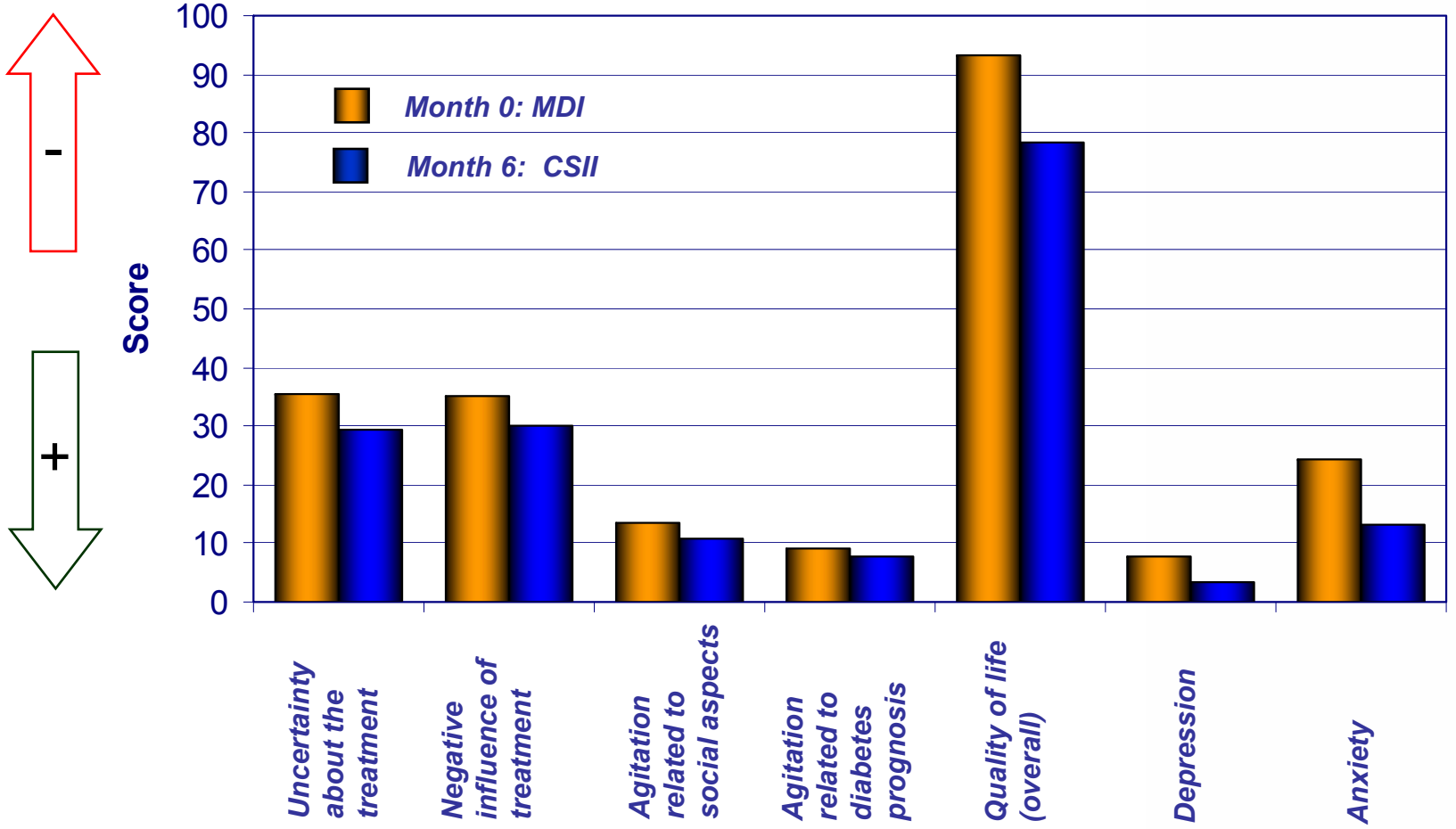
*From: Dominguez-Lopez M et al.: Diabetic Medicine 23 (Suppl. 4) 2006; 323*

Medtronic

CSII

# Assessment of quality of life and psychological parameters during CSII

- Changes in quality of life and psychological parameters:




*From: Dominguez-Lopez M et al.: Diabetic Medicine 23 (Suppl. 4) 2006; 323*

Medtronic

CSII

# Assessment of quality of life and psychological parameters during CSII

## Conclusion:

CSII provides insulin supply security and contributes thereby to better glycemic control with less insulin and a lower rate of severe hypoglycemia. All psychological parameters and factors relating to quality of life show a corresponding improvement.

Back

*From: Dominguez-Lopez M et al.: Diabetic Medicine 23 (Suppl. 4) 2006; 323*

Medtronic

CSII

# Smaller glucose fluctuations as a result of uniform resorption of short-acting insulin

## Statement:

One reason for smaller glucose fluctuations during CSII is the exclusive use of short-acting insulin / insulin analogue, which exhibit only small intra-individual differences in comparison with long-acting insulins.

## Evidence:

Various studies investigating intra-individual variability using the glucose clamp technique or with radioactive markers.

*From: Lauritzen et.al: Diabetologia. 1983;24:326–329.*

*From Heise T et al. Diabetes 2004; 53: 1614–1620*

*From: Lepore M et.al.: Diabetes 49 Suppl.1 (5/2000), 436-OR*

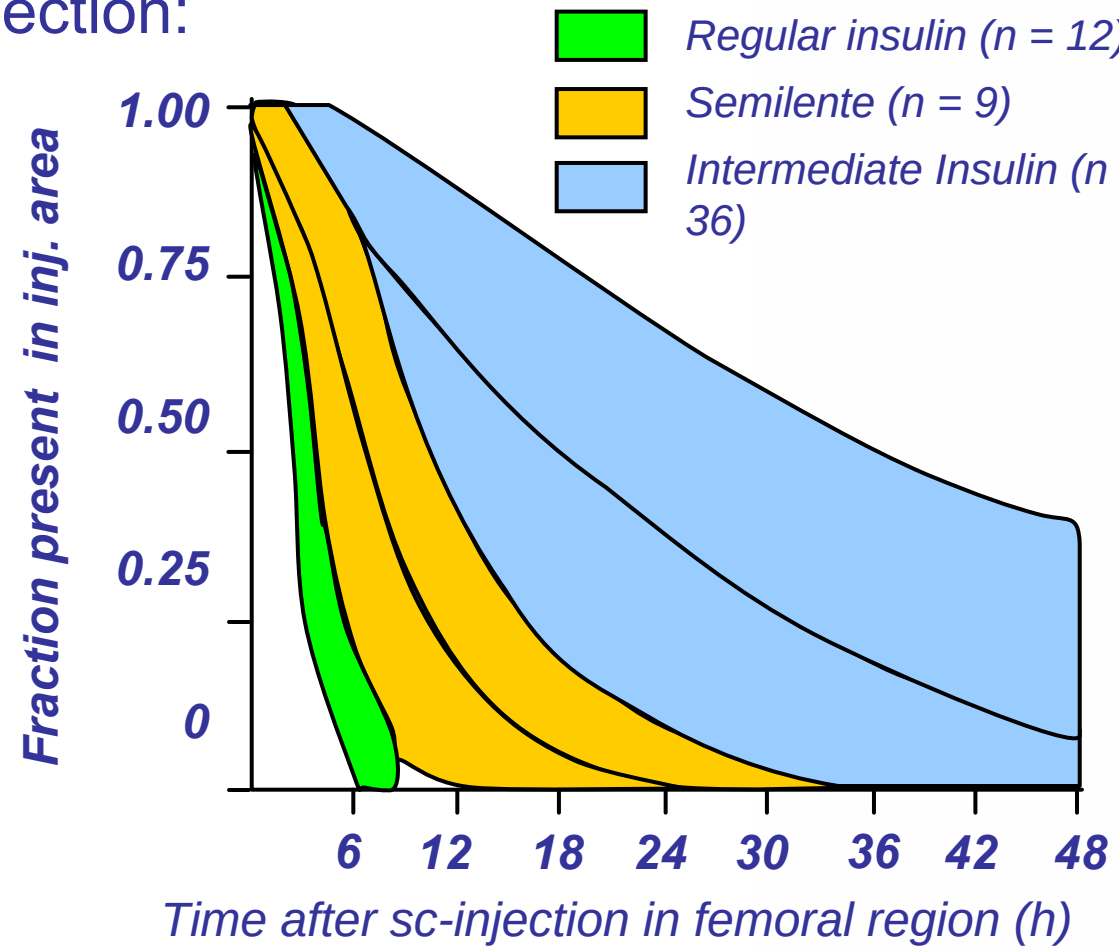
Back

Medtronic

# Insulin absorption variability for different types of insulin

## Insulin absorption variability:

- Subcutaneous injection: 10% to 52%
- CSII < 2.8%

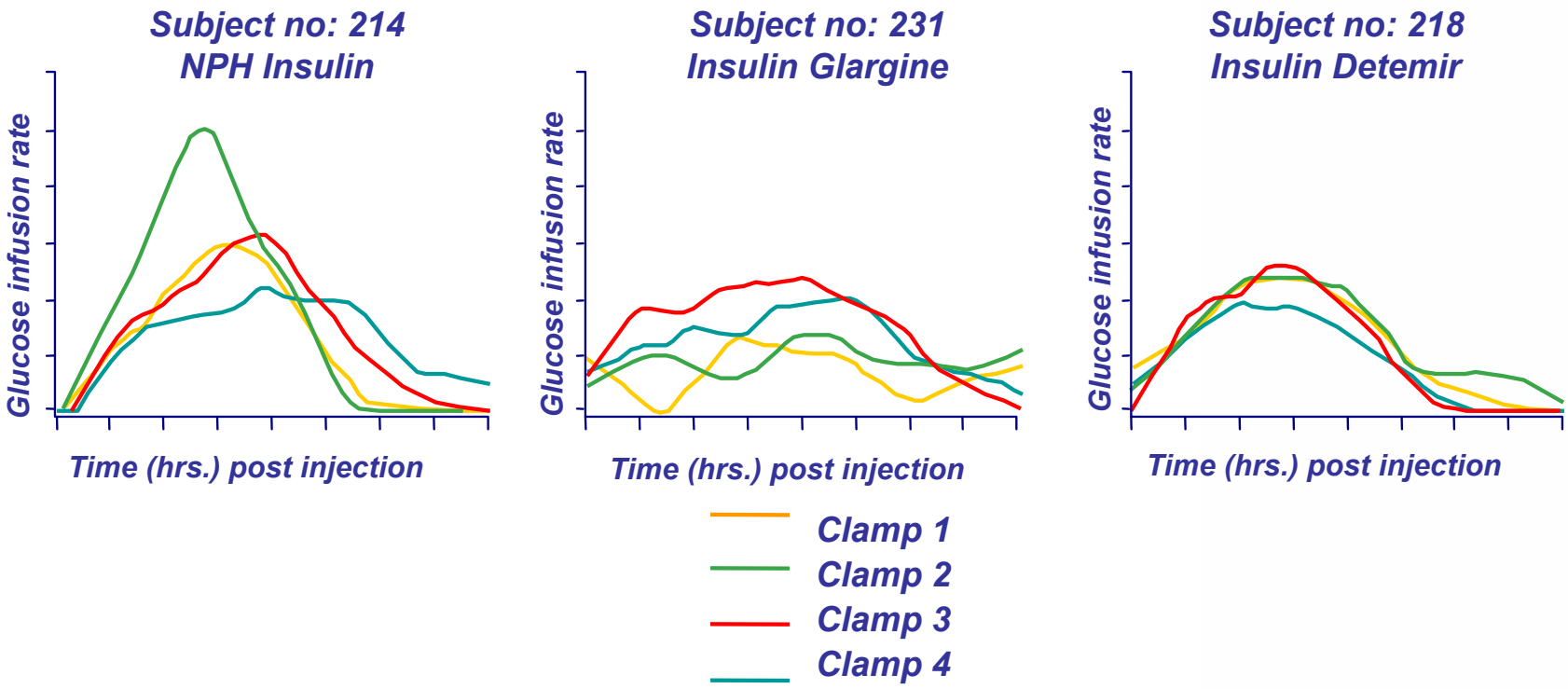



*From: Lauritzen et.al: Diabetologia. 1983;24:326–329.*



# Intra-individual variability of different insulins

Examples of intra-individual variability of different insulins used by respective patients:



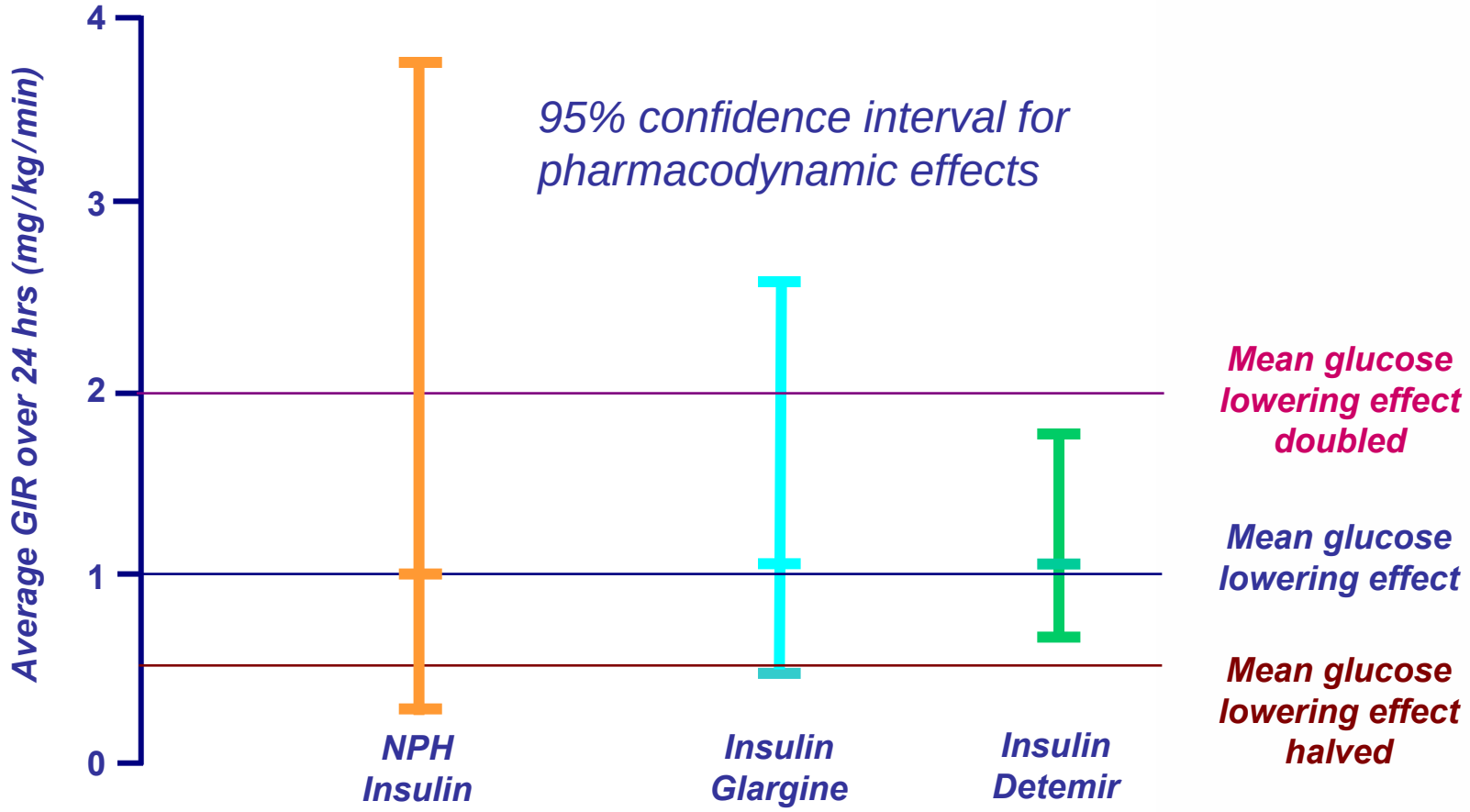

*From Heise T et al. Diabetes 2004; 53: 1614–1620*

Back

Medtronic

# Intra-individual variability of different insulins

## Pharmacodynamic variability of different long-acting insulins: even with Detemir this is higher than with short-acting insulins



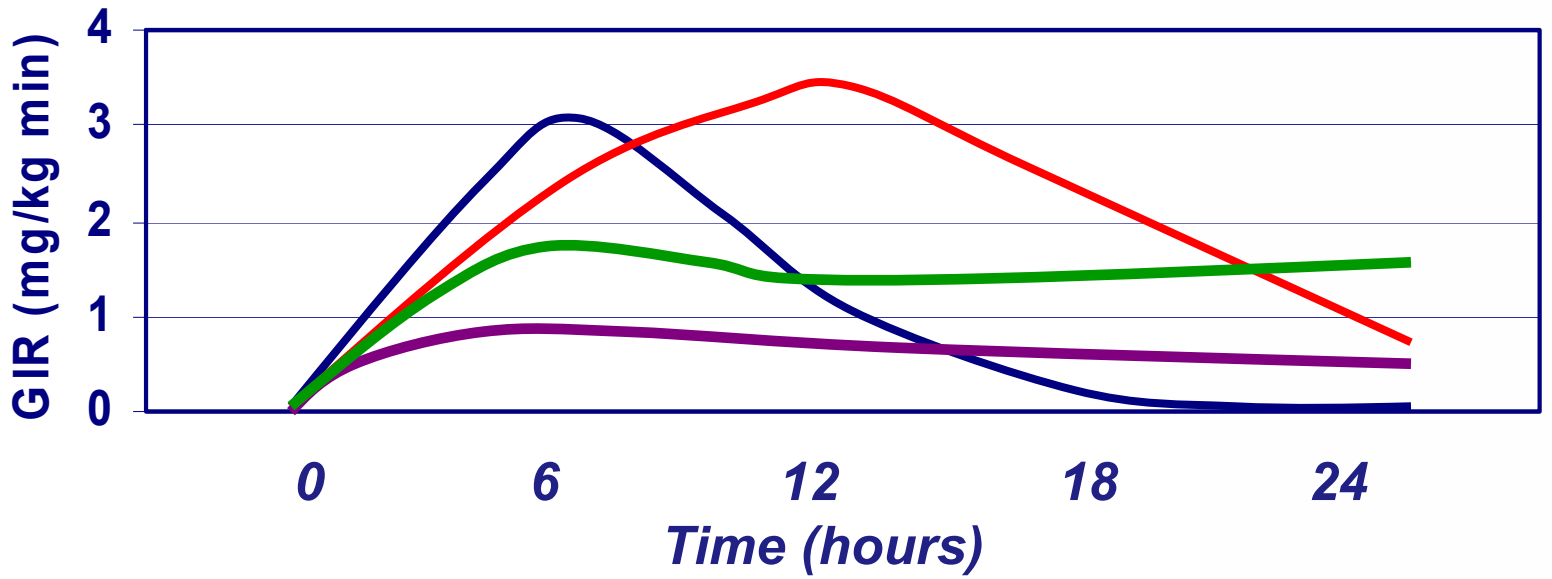

From Heise T et al. Diabetes 2004; 53: 1614–1620

Back

Medtronic

# Pharmacodynamics of long-acting insulins and CSII

Comparison of the glucose infusion rates of 20 patients with type 1 diabetes after identically dosed insulin injections and CSII in a euglycemic clamp experiment:




Back

*Lepore M et.al.: Diabetes 49 Suppl.1 (5/2000), 436-OR*

Medtronic

CSII

# Smaller glucose fluctuations as a result of uniform resorption of short-acting insulin

## Conclusion:

Short-acting insulins / insulin analogues exhibit, in comparison to long-acting insulins, a more uniform resorption and thereby a lower intra-individual variability. The basal insulin supply during CSII consists of short-acting insulins, thus resulting in a more predictable glycemia.

Zurück

Medtronic

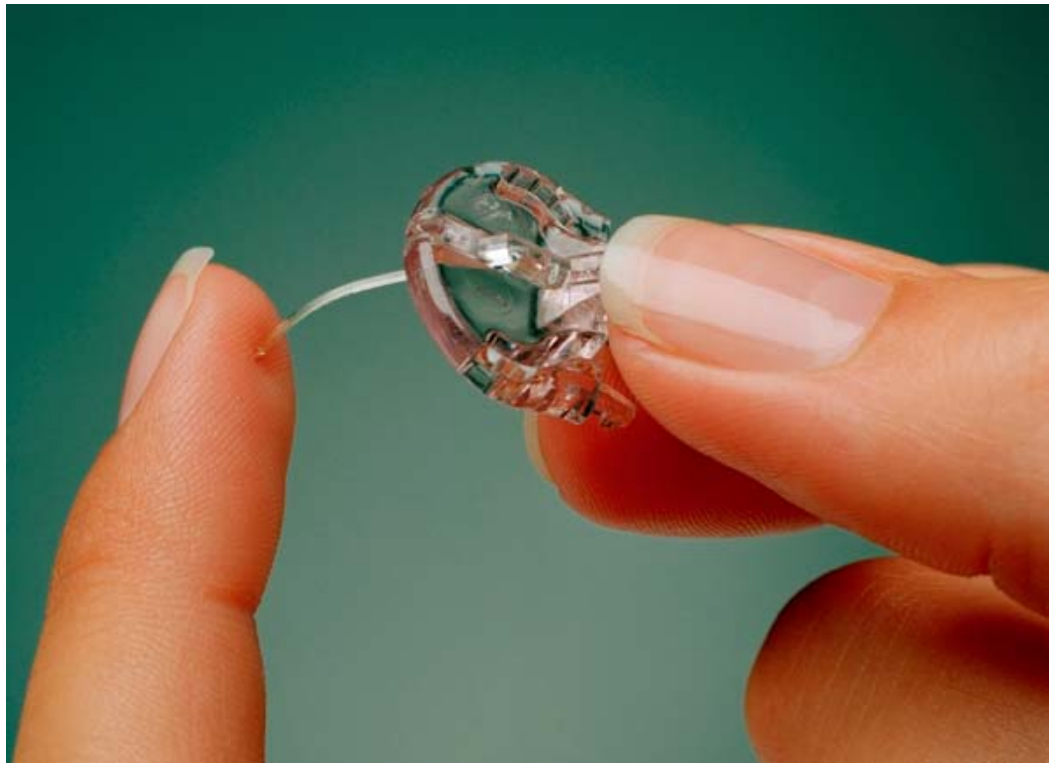
# Summary: Results of CSII vs. MDI

| CSII compared to: | MDI fixed RI/NPH insulin | MDT flexible RI/NPH insulin | MDI flexible insulin analogues |
|---|---|---|---|
| $HbA_{1c}$ (Type 1-D.m.) | better | better | same or better |
| $HbA_{1c}$ (Type 2-D.m.) | better | better | about the same |
| Blood sugar fluctuations | significantly less | | |
| pp Blood sugar (BS) rise | less | less | same or less |
| Alignment to meal times | practical only during CSII because of various bolus options | | |
| Reaction to high BS value | simpler via bolus provision at the press of a button | | |
| Insulin resorption | more defined due to exclusive use of short-acting insulins | | |
| Rate hypoglycemia | significantly less | significantly less | less |
| Rate ketoacidosis | higher or the same (raised risk demands structured training) | | |
| Insulin dose | less | less | mostly less |
| Adaption to sport | significantly easier | easier | easier |
| Adjustment to living conditions (travel etc.) | significantly easier due to use of temporary basal rate increase/decrease and various basal rate profiles | | |
| Reduction complications | documented with CSII (physiological insulin infusion?) | | |
| Wearing comfort | same or worse | | |

RI - regular insulin



# Accuracy of Glucose Sensors



Zurück

# Accuracy of Glucose Sensors

- Accuracy of Glucose Sensors: history and current situation
- Error tolerances with CGM in comparison to blood glucose self-monitoring spot-tests

Zurück

# Accuracy of Glucose Sensors

## Statement:

The accuracy and reproducibility of continuous glucose monitoring has progressively improved since the introduction of Medtronic diabetes sensor technology was initiated in 1999.

## Evidence:

Various investigations into the accuracy of sensors.

*From: Ford T et al.: Diabetes 51 Suppl.2 (2002), A11*

*From: Hoss U et al. Second Lajolla Conference on Glucose Monitoring and Control. 2003: 15 and Gross T et.al.:, in Diabetes 52 Suppl.1 (2003), A95*

*From: Armstrong D et.al.: Diabetes 52 (Suppl.1): A89, 2003*

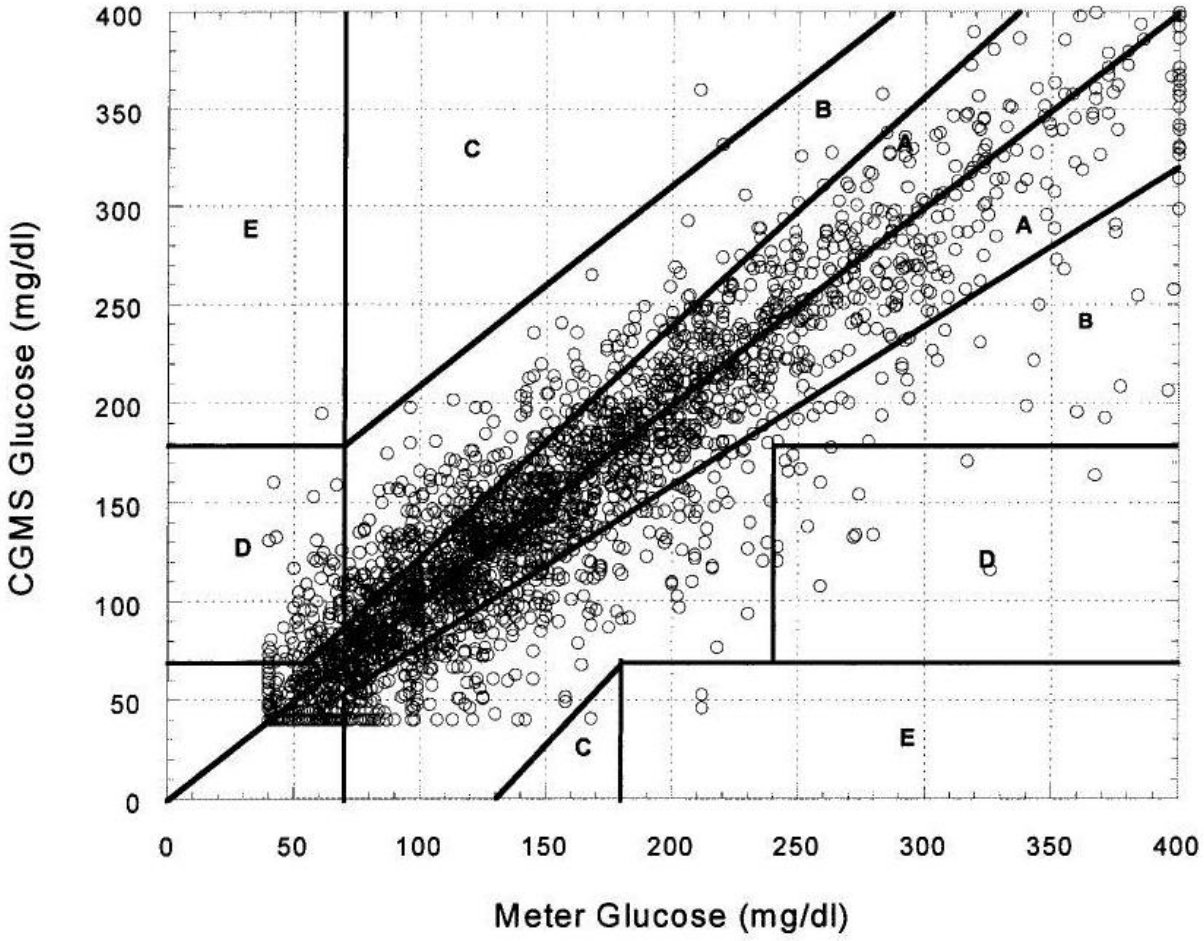
Back

# Accuracy of sensors: history and current situation

- CGMS – first generation sensors sometimes displayed measurement accuracy deficiencies.
- This was evident from the spread of results obtained when simultaneously employing multiple sensors in test subjects (e.g. Ford T et al.: Diabetes 51 (Suppl.2) A11, 2002).
- The reasons for this were, amongst others, lack of technological experience.
- Increasing experience led to improved quality in the sensors and thereby in the measurements.
- Reliable sensors have been available since as early as 2002.
- Such a development cycle is not untypical for new and innovative products.
- The effect is often described in the world of microelectronics as the “technological learning curve“.

# Accuracy of the first continuous glucose monitoring sensors

Error-Grid-Plot using 2,477 pairs of measurements taken from 135 patients: 96.2% of the values fall in areas A or B



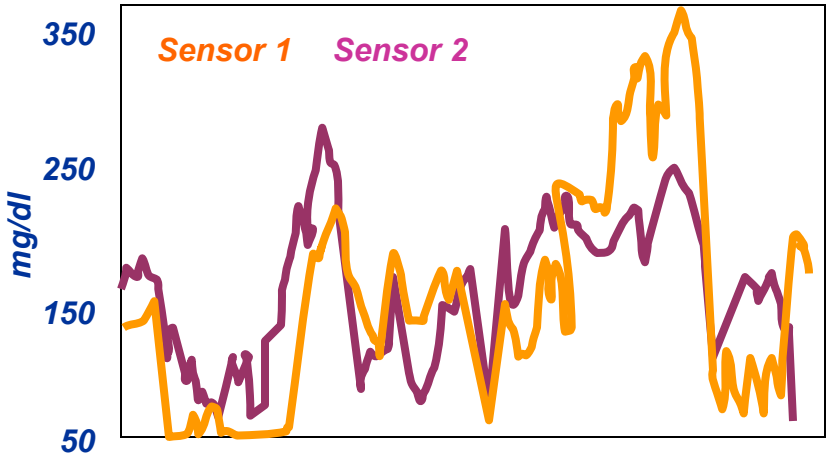

*From: Gross TM, et al. DiabetesTechnol Ther. 2000;2(Suppl 1):S19-26*

CGM

# Simultaneous use of first-generation CGMS sensors on type 1 diabetics and non-diabetics

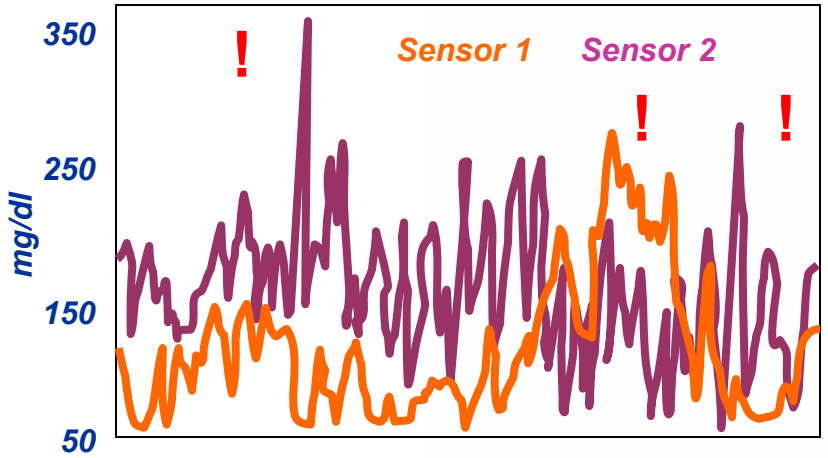
**Example of the deviations of "historical" sensors:**
Glucose curves during simultaneous recording with 2 sensors in test subjects over the course of 3 days:

- Subject with type 1 diabetes:




Standard deviation of the curves: 27%

- Subject without diabetes:




Standard deviation of the curves : 28% with illogical glucose profiles

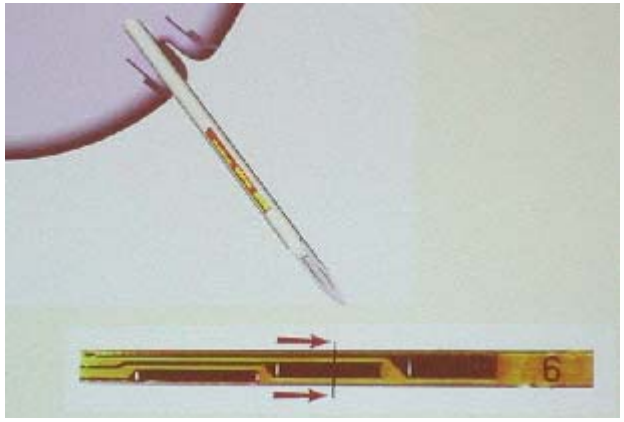
*From: Ford T et al.: Diabetes 51 Suppl.2 (2002), A11*

Medtronic

CGM

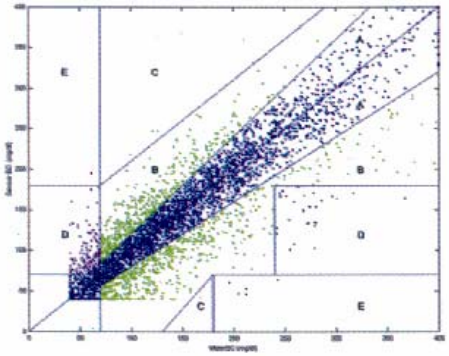
# Comparison of improved sensors with first-generation sensors in terms of recording accuracy

- Reason: improvement in technology

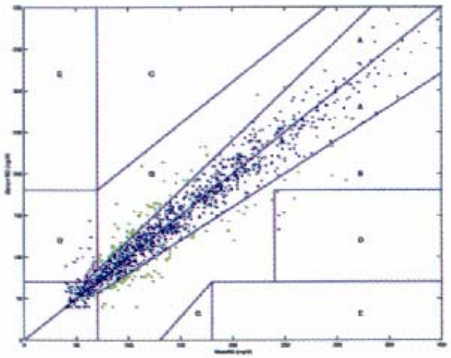



- Comparison of old and new sensors with an Error-Grid-Plot:

| Region in EG-Plot | Old Sensor | New Sensor |
|---|---|---|
| A | 71.5%, | 86.8%, |
| B | 25.7% | 11.0% |
| C,D or E | 2.8% | 2.2% |



Old sensor (n=4.015)



New sensor (n=1.165)

*From: Hoss U et al. Second Lajolla Conference on Glucose Monitoring and Control. 2003: 15 and Gross T et.al.:, in Diabetes 52 Suppl.1 (2003), A95*

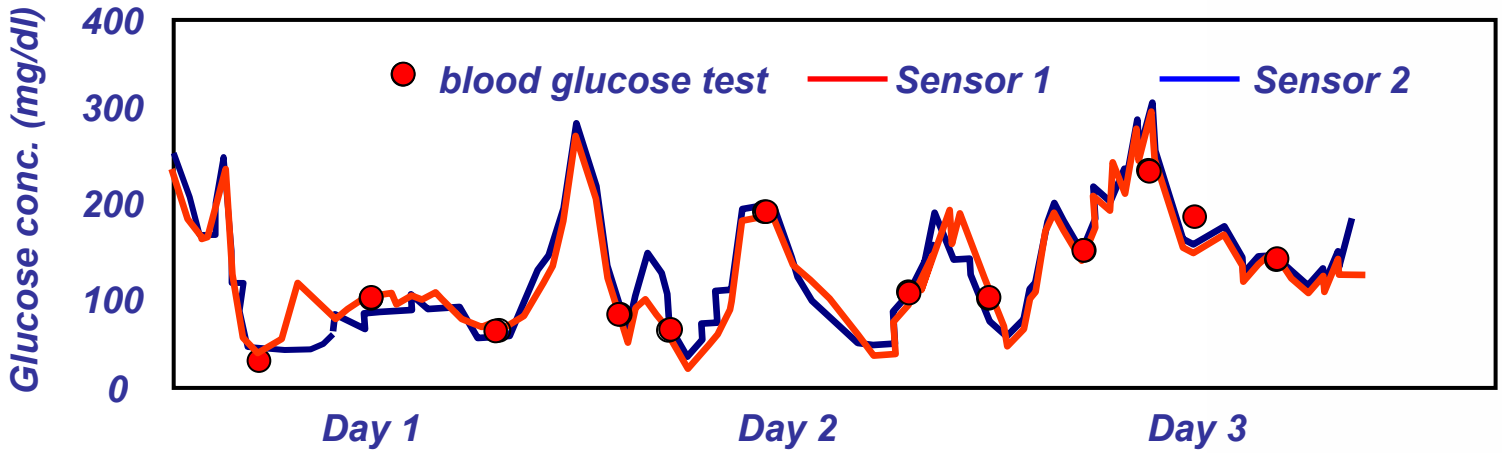
Medtronic

CGM

# Simultaneous use of improved CGMS sensors with type 1 diabetics

## Example of the deviations of improved sensors:

Glucose curves during simultaneous recording with 2 sensors in a test subject over the course of 3 days:




- Readings Sensor - Sensor (8,736):
  Error-Grid-Plot: 99.6% in A&B, mean dev.*:12.3%
- Readings Sensor - blood glucose monitoring device (531):
  Error-Grid-Plot: 98.0% in A&B, mean dev.*:13.8%

** Mean deviation of all pairs of recorded values from each other*

*From: Armstrong D et.al.: Diabetes 52 (Suppl.1): A89, 2003*

Medtronic

# Accuracy of Glucose Sensors

## Conclusion:

- The international guidelines allow an upper limit of 20% for blood glucose spot-test measurements.
- No such norms yet exist for continuous glucose monitoring.
- A suitable indicator can be considered to be the median absolute deviation (MAD) of the recordings.
- In contrast to individual measurements the MAD is based on the complete set of recorded values.
- The MAD values displayed in a range of studies lie between 11% and 16%.
- This is an acceptable tolerance within the context of diabetes treatment.

Back

* *Recommendation German Medical Association: 16%*

# Error tolerances with CGM in comparison to spot-check blood glucose self-monitoring

## Statement:

The recording of the glucose trend during continuous monitoring provides considerably more information. This means that higher tolerances and measurement error margins are clinically acceptable in comparison with spot-check blood glucose self-monitoring (BGSM).

## Evidence:

Simulation and determination of clinically acceptable error margins in the glucose region from 30 - 330 mg/dl with the aid of a modified diabetes error test model. Carbohydrate absorption, insulin effects and the glucose rate of change are taken into account.

Back

*From: Koschinsky T et. al.: Diabetologie & Stoffwechsel 2007; 2: S134 and Diabetes 2007; 56 (Suppl. 1), A109*

CGM

# Error tolerances with CGM in comparison to spot-check blood glucose self-monitoring

- Classification and definition of glucose rate of change (GRC):
  - large rise (↑↑): + 3.0 ± 0.9 mg/dl/min
  - slight rise (↑): + 1.5 ± 0.5 mg/dl/min
  - unchanged (↔ ): ± 0.0 ± 0.9 mg/dl/min
  - slight fall (↓): - 1.5 ± 0.9 mg/dl/min
  - large fall (↓↓): - 3.0 ± 0.5 mg/dl/min

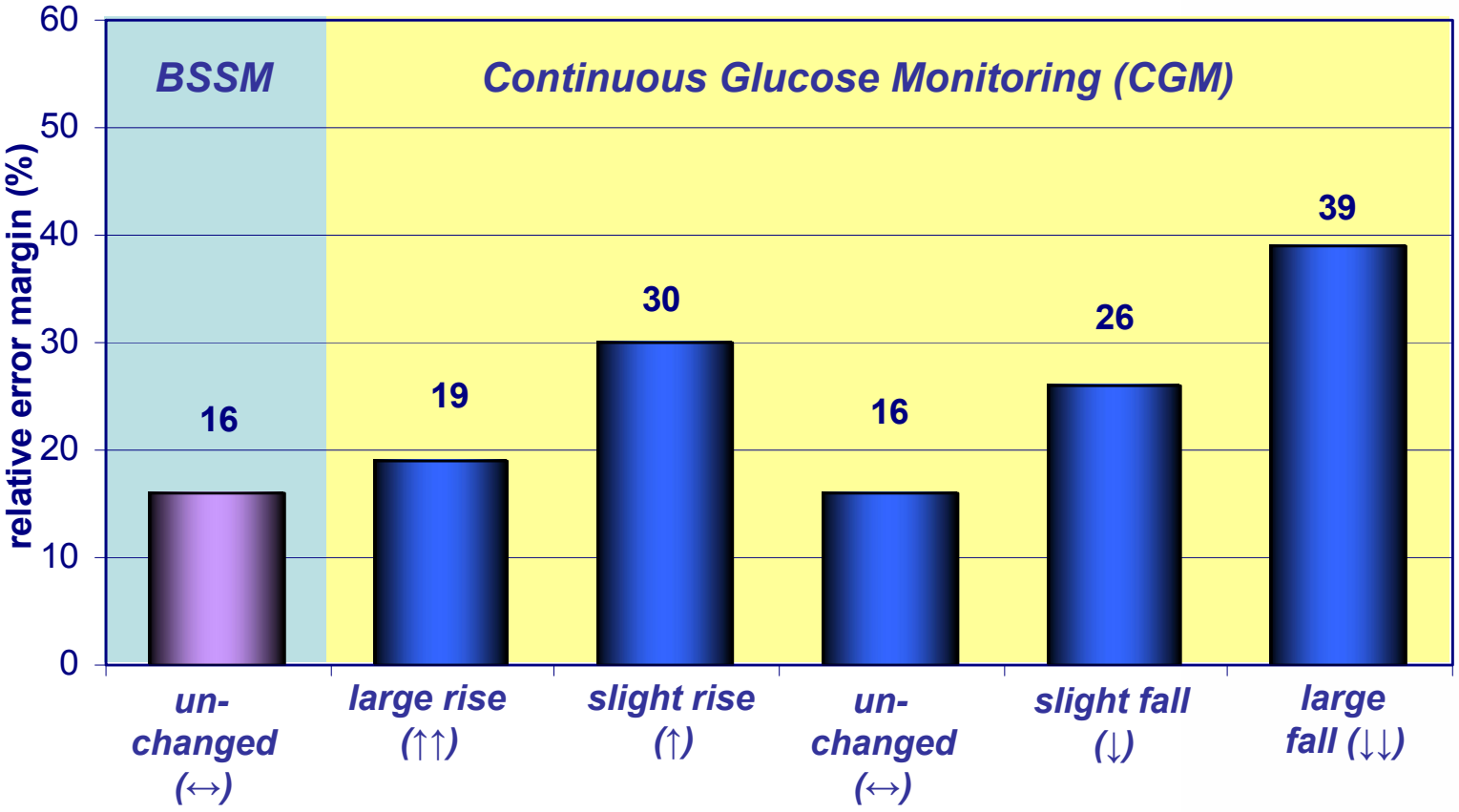
*From: Koschinsky T et. al.: Diabetologie & Stoffwechsel 2007; 2: S134 and Diabetes 2007; 56 (Suppl. 1), A109*

Medtronic

CGM

# Error tolerances with CGM in comparison to spot-check blood glucose self-monitoring

- Lowest clinically acceptable margins of error for hypoglycemia from an initially near-normal value:



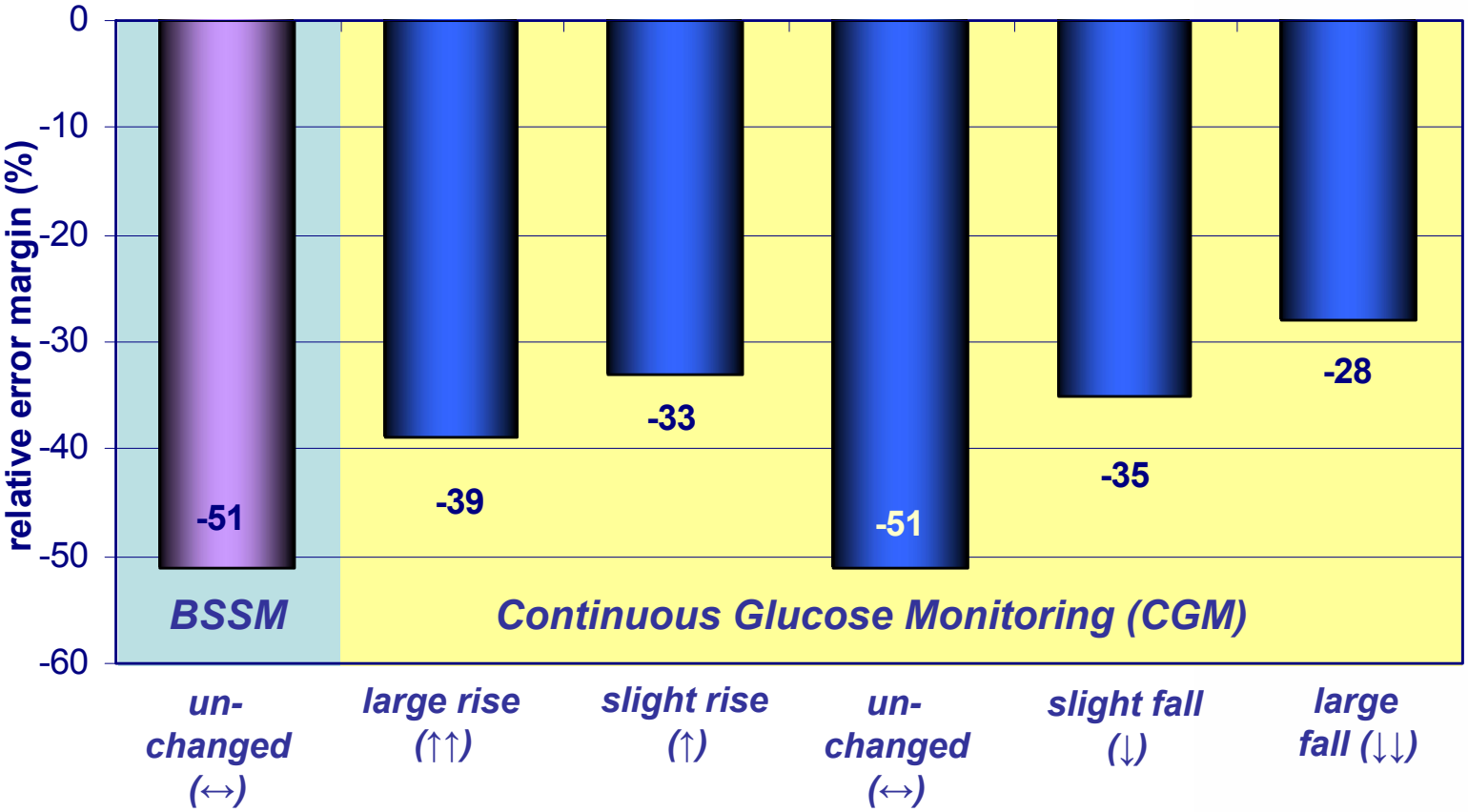

*From: Koschinsky T et. al.: Diabetologie & Stoffwechsel 2007; 2: S134 and Diabetes 2007; 56 (Suppl. 1), A109*

Medtronic

CGM

# Error tolerances with CGM in comparison to spot-check blood glucose self-monitoring

- Lowest clinically acceptable margins of error for hyperglycemia from an initially near-normal value:




*From: Koschinsky T et. al.: Diabetologie & Stoffwechsel 2007; 2: S134 and Diabetes 2007; 56 (Suppl. 1), A109*

Medtronic

# Error tolerances with CGM in comparison to spot-check blood glucose self-monitoring

## Conclusion:

Due to the additional information available about the glucose rate of change and its trend, continuous glucose monitoring allows higher margins of recording error than blood glucose self-monitoring, with respect to unacceptable postprandial hypoglycemia. Together with the results for possible error margins for postprandial hyperglycemias, this analysis supports the hypothesis that CGM systems can be used, within the stated error margins, for pre-prandial treatment decisions such as the insulin dose to be used.

Back

*From: Koschinsky T et. al.: Diabetologie & Stoffwechsel 2007; 2: S134 and Diabetes 2007; 56 (Suppl. 1), A109*

# Results of CGM Use



Back

# Results with CGM (1)

***CGM provides a detailed glycemia assessment and enables better adjustment of diabetes treatment control***

- Assessment of glycemic control using continuous glucose monitoring parameters

- Comprehensive assessment of glycemic control via continuous glucose monitoring

- Improved metabolic control using continuous glucose monitoring

**CGM enables comprehensive detection of glucose deviations and hypoglycemia**

- Evidence of hypoglycemia via continuous glucose monitoring

- Detection of otherwise unnoticed hypoglycemia using continuous glucose monitoring

- Hypoglycemic frequency documented with continuous glucose monitoring

Back

# Results with CGM (2)

**By displaying current glucose values CGM can lead to better adjustment of diabetes treatment control**

- Improved glycemic control by use of current glucose values from glucose monitoring

- Impact on glycemia of using glucose values from continuous glucose monitoring

**CGM, in combination with an alarm system based on current glucose values, can reduce the hypoglycemia and hyperglycemias rate**

- Deployment of the Guardian® glucose sensor as an alarm system for excessive glucose deviations

- Reduction in the hypoglycemia rate due to use of current glucose values from glucose monitoring

**CGM has a great and wide future potential**

- Potential and opportunities for continuous glucose monitoring

Back

# Assessment of glycemic control using continuous glucose monitoring parameters

## Statement:

CGM provides new parameters which can be used for the assessment of glycemic control, such as AUC's* and glucose amplitude. This allows improved glycemic control using CGM.

## Evidence:

An investigation of 28 young patients (aged 5 - 25 years) with type 1 diabetes and inadequate glycemic control (values 8.7 ± 1.3%) subjected to CGMS for 6 months. Determination of the correlation between CGMS data with $HbA_{1c}$ values.

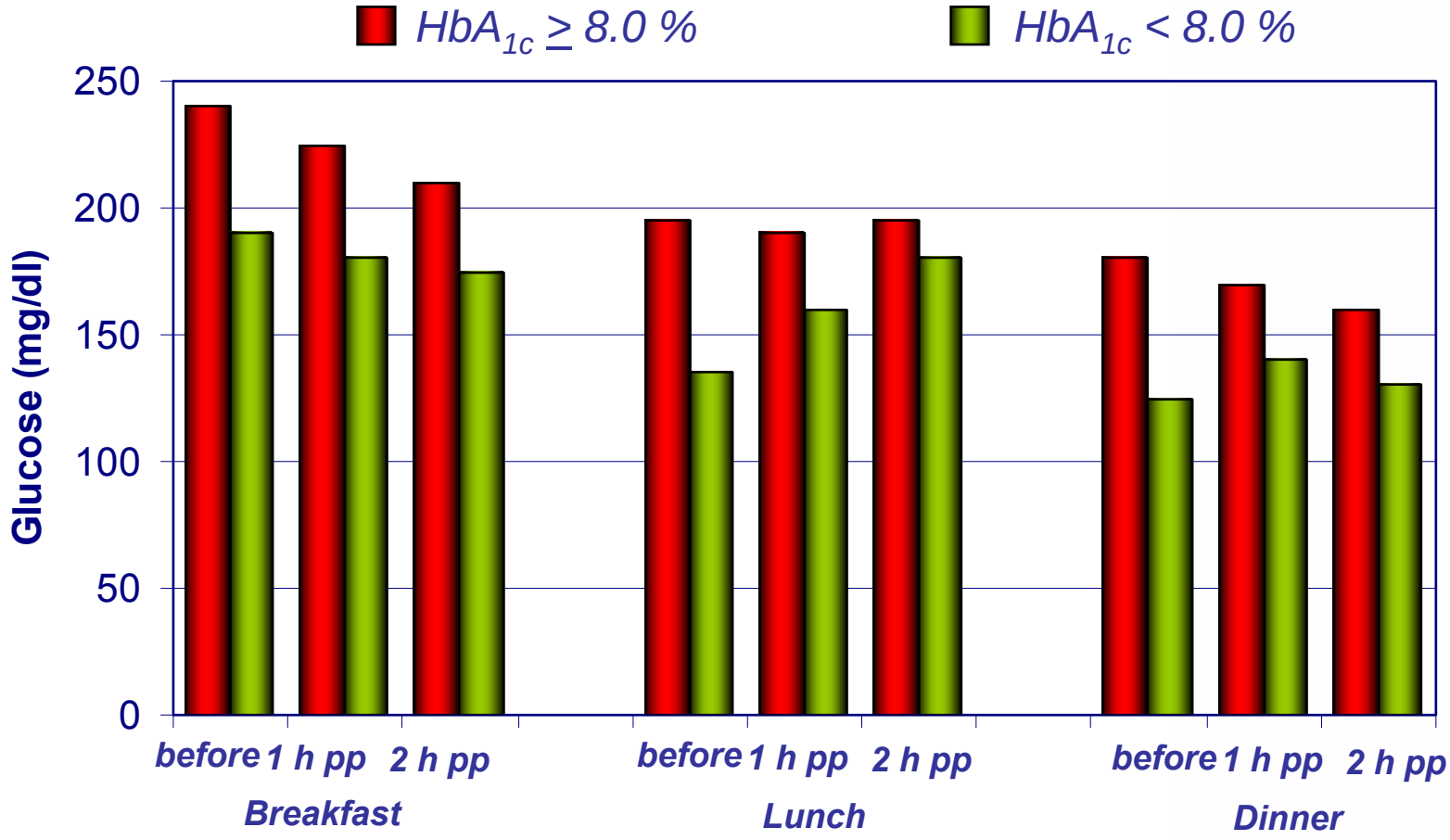
**AUC – area under curve, the area characterizes the glucose values falling within a certain glucose range over a defined period of time*

*From: Salardi S et al.: Diabetes Care 2002; 25:1840-1844*

Back

# Assessment of glycemic control using continuous glucose monitoring parameters

- Pre-prandial and post-prandial glucose values for various meals in conjunction with $HbA_{1c}$.values:



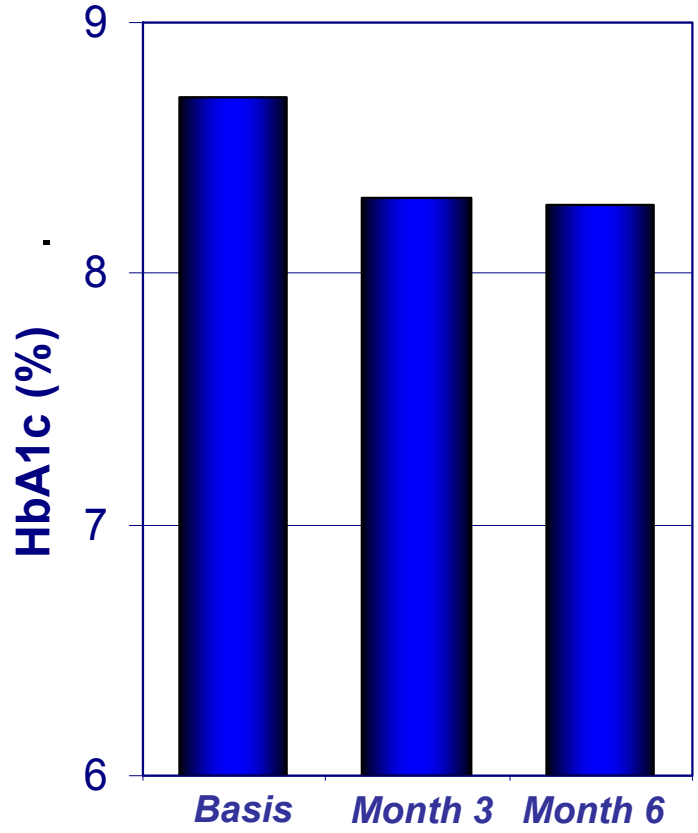

*From: Salardi S et al.: Diabetes Care 2002; 25:1840-1844*

Medtronic

CGM

# Assessment of glycemic control using continuous glucose monitoring parameters

- Change in $HbA_{1c}$. before and during use of CGMS:




- Correlation between AUC and $HbA_{1c}$ and fructosamine for various glucose ranges:

| *AUC over 3 days* | *$HbA_{1c}$* | | *Fructosamine* | |
|---|---|---|---|---|
| | *r* | *p* | *r* | *p* |
| *40-90* | *0.27* | *ns* | *0.30* | *ns* |
| *40-150* | *0.47* | *0.007* | *0.56* | *0.001* |
| *40-200* | *0.49* | *0.004* | *0.57* | *0.001* |
| *40-250* | *0.55* | *0.001* | *0.61* | *0.0001* |
| *40-300* | *0.54* | *0.002* | *0.60* | *0.0001* |
| *40-400* | *0.53* | *0.002* | *0.64* | *0.0001* |

*From: Salardi S et al.: Diabetes Care 2002; 25:1840-1844*

Medtronic

# Assessment of glycemic control using continuous glucose monitoring parameters

## Conclusion:

The glucose profiles of 80% of patients demonstrate a high rate of hyperglycemia. Postprandial values correlate with the $HbA_{1c}$ values: for higher $HbA_{1c}$ these were also higher. The AUC's over the whole day also correlate with the $HbA_{1c}$ ($r = 0.53$ for the range 40 - 400 mg/dl).

Back

*From: Salardi S et al.: Diabetes Care 2002; 25:1840-1844*

# Comprehensive assessment of glycemic control via continuous glucose monitoring

## Statement:

Continuous glucose monitoring allows a far more comprehensive description of the glycemia than with the measurement of $HbA_{1c}$ values alone. Glycemic control can also be problematic even with good long-term parameters, due to distinct glycemic excursions.

## Evidence:

Use of the CGMS®Gold System over 72 hours for assessment of glycemia for patients with various $HbA_{1c}$ values ($HbA_{1c}$ < 7%, $HbA_{1c}$ > 9%). Sample: 104 type 1 diabetic patients (56 female / 48 male, age: 37.5 ± 16.4 y., $HbA_{1c}$: 8.3 ± 1.1 %)

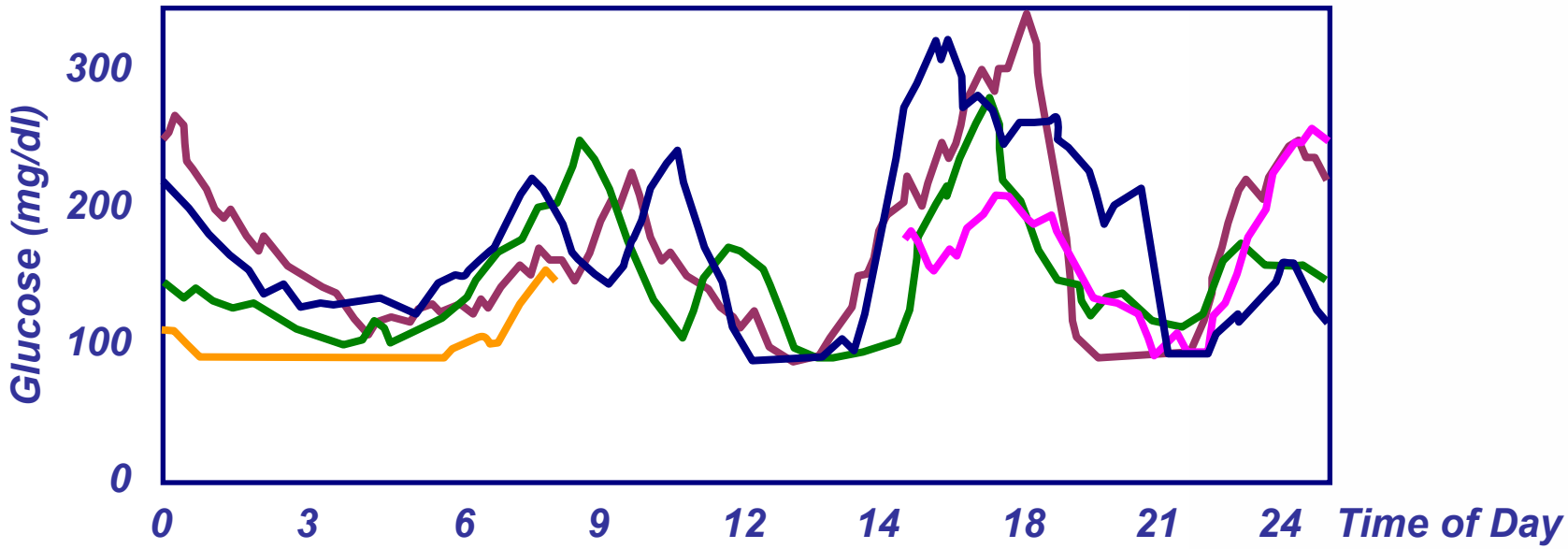
Back

*From: Gomez-Peralta et al.: Diabetes 2007; 56 (Suppl. 1), A117*

CGM

# *Comprehensive assessment of glycemic control via continuous glucose monitoring*

- Glucose profile (model day) from well to satisfactorily controlled patients (in terms of $HbA_{1c}$ values):
  - Example: $HbA_{1c}$ = 7.0% (Lispro + 2 x NPH)




*From: Gomez-Peralta et al.: Diabetes 2007; 56 (Suppl. 1), A117*

Medtronic

CGM

# Comprehensive assessment of glycemic control via continuous glucose monitoring

| *Data for patients (n=20) with $HbA_{1c}$ < 7,0%* | |
|---|---|
| *$HbA_{1c}$ (%)* | *6.5 ± 0.4* |
| *Mean glucose (mg/dl)* | *141.3 ± 30.0* |
| *Standard Deviation mean gluc. (mg/dl)* | *60 ± 15* |
| *Time in range > 180 mg/dl (%)* | *25 ± 17* |
| *Time in range 80-180 mg/dl (%)* | *55 ± 14* |
| *Time in range < 80 mg/dl (%)* | *19 ± 11* |
| *Glucose AUC >180 mg/dl* | *14.4 ± 12.0* |
| *Glucose AUC < 80 mg/dl* | *4.1 ± 3.0* |

*From: Gomez-Peralta et al.: Diabetes 2007; 56 (Suppl. 1), A117*

Medtronic

CGM

# Comprehensive assessment of glycemic control via continuous glucose monitoring

## Conclusion:

Glucose monitoring shows that glycemic deviations can vary tremendously even with comparable $HbA_{1c}$ values. An $HbA_{1c}$ value under 7% is no guarantee of good metabolic control. The CGMS data showed that these patients were outside the 80-180 mg/dl range for 45% of the time, and were even below 80 mg/dl for 20% of the time (4.8 hours).

Back

*From: Gomez-Peralta et al.: Diabetes 2007; 56 (Suppl. 1), A117*

Medtronic

CGM

# Improved metabolic control using continuous glucose monitoring

## Statement:

Continuous glucose monitoring enables improved glycemic control by utilising the glucose values to adapt treatment accordingly.

## Evidence:

Cross-over study with 27 children and adolescents (age: 12.5 ± 3.3 years) over 6 weeks in order to compare the impact of continuous monitoring of glucose (CGMS®Gold) and blood glucose self-monitoring (7-points-daily profile) on glycemic control. CGM was used for adaptation of the treatment of one group, and the blood glucose profiles for the other group.

Back

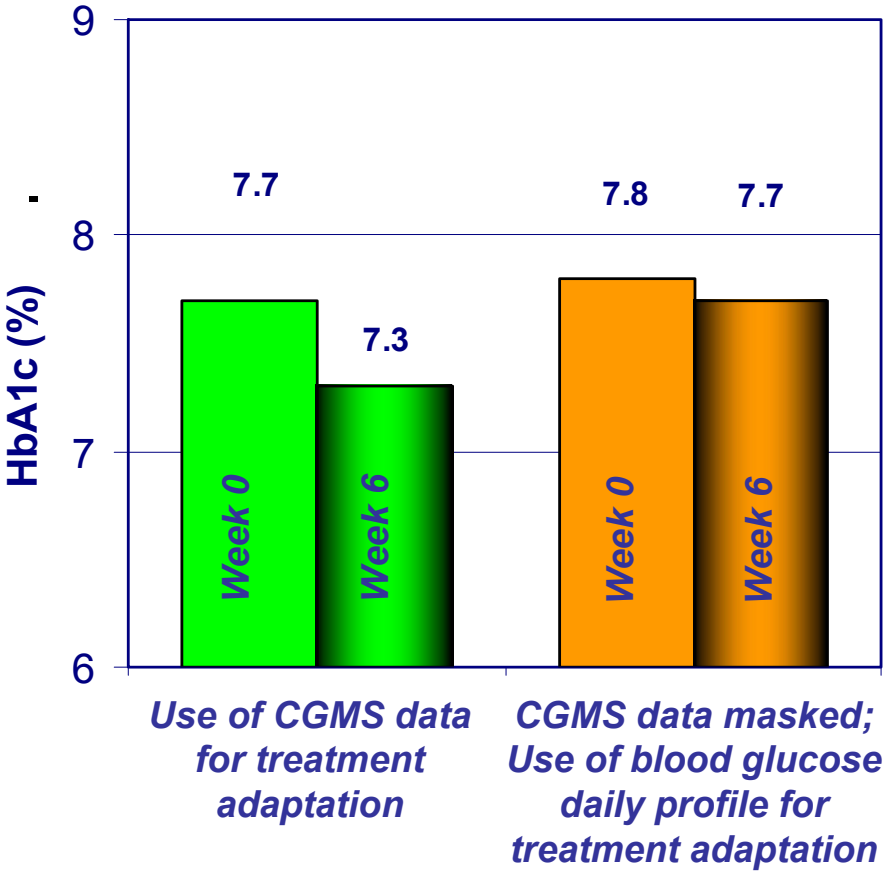
*From: Ludvigsson J et al.: Pediatrics 2003, 111; 933-938*

Medtronic

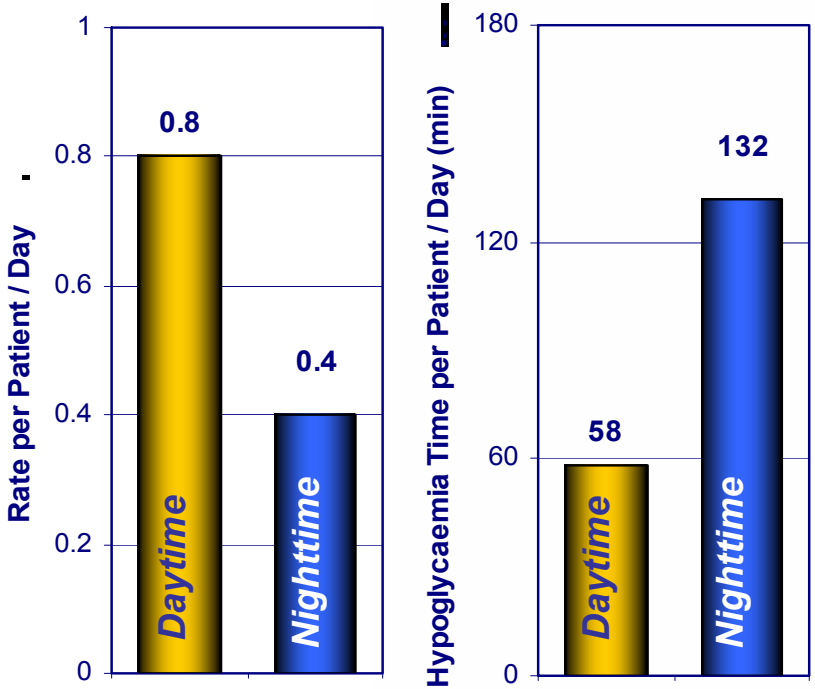
CGM

# Improved metabolic control using continuous glucose monitoring

- Changes in $HbA_{1c}$ values:




- Hypoglycemia rate and time detected with CGMS:




*From: Ludvigsson J et al.: Pediatrics 2003, 111; 933-938*

Medtronic

CGM

# Improved metabolic control using continuous glucose monitoring

## Conclusion:

Glucose profiles resulting from continuous glucose monitoring allow a detailed insight into the glycemia and can be used for improving the diabetes control (reduction of the $HbA_{1c}$ values and abatement of hypoglycemia). This potential can already be seen from the retrospective data analysis with the CGMS®Gold. blood glucose self-monitoring does not share this potential to the same extent.

**Remark:**

Displaying current glucose values further increases this potential ability to influence the situation due to the almost simultaneous reaction (see GuardControl study).

Back

*From: Ludvigsson J et al.: Pediatrics 2003, 111; 933-938*

Medtronic

# Evidence of hypoglycemia using continuous glucose monitoring (CGM)

## Statement:

CGMS provides a more sustainable way of verifying treatment deficits in diabetics than intensified blood glucose self-monitoring, thus leading to a more effective optimization of treatment.

## Evidence:

Randomized investigation involving 128 type 1 diabetics (age: 43 years, diabetic for 19 years) using blood glucose self-monitoring and CGMS for determining the hypoglycemia rate.

Back

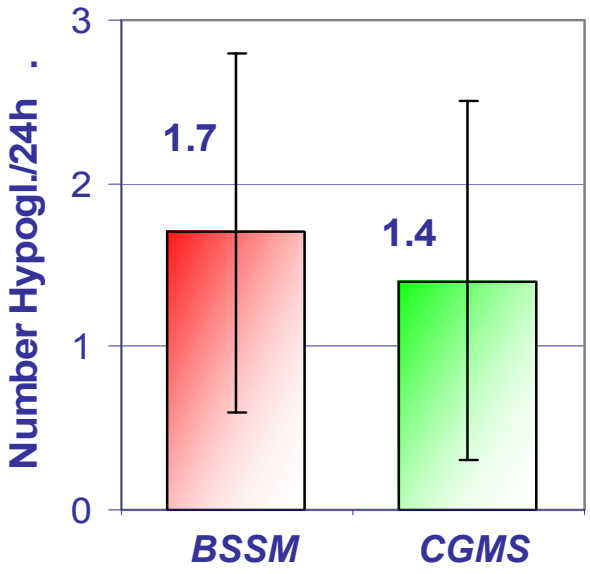
*From: Mastrototaro JJ et al.: Diabetologia 46, Suppl.2 (2003), A45*

CGM

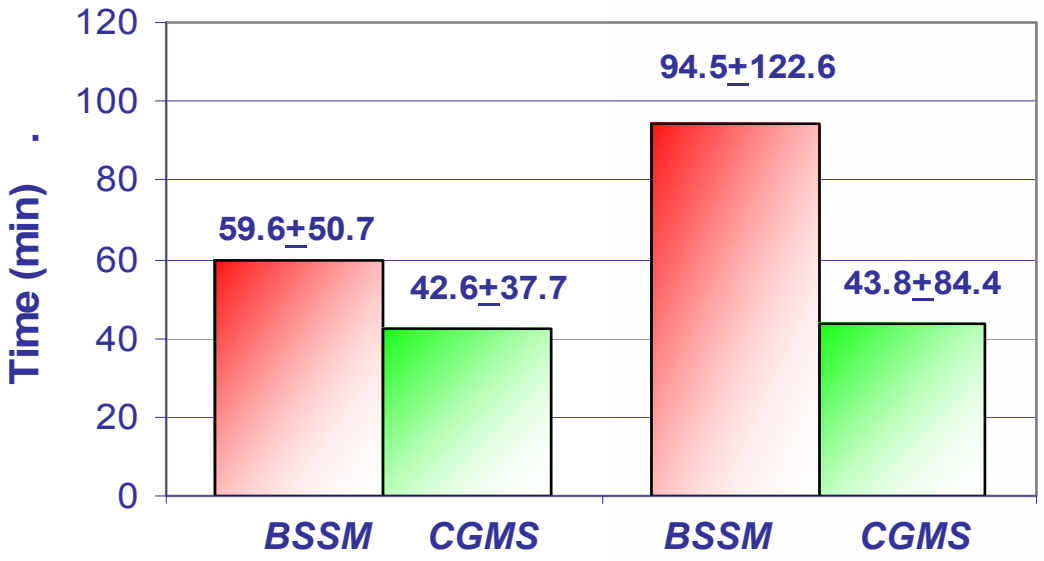
# Evidence of hypoglycemia using continuous glucose monitoring (CGM)

- $HbA_{1c}$ development: both groups improved to 8.3±1.0% after 8 and 12 weeks (initial value: 9.0% (CGMS group), 9.1% (blood glucose self monitoring (BGSM) group))

- Incidence of hypoglycemia:




- Duration of hypoglycemia:




*From: Mastrototaro JJ et al.: Diabetologia 46, Suppl.2 (2003), A45*

Medtronic

# Evidence of hypoglycemia using continuous glucose monitoring (CGM)

## Conclusion:

Despite similar improvements in $HbA_{1c}$ values in both groups, the study discovered a considerably higher rate of hypoglycemia when using CGMS, which led to a significant reduction of the time spent in such a state.

Back

*From: Mastrototaro JJ et al.: Diabetologia 46, Suppl.2 (2003), A45*

CGM

# Detection of otherwise unnoticed hypoglycemia using continuous glucose monitoring

## Statement:

Use of continuous glucose monitoring enables significantly more hypoglycemia to be verified than with spot-check blood glucose self-monitoring (BGSM).

## Evidence:

Determination using CGMS of hypoglycemia rate and duration for 45 type 1 diabetic patients (age: 45.4±12.6 y., diabetic for: 23.2±9.5 years, $HbA_{1c}$: 7.26±1.51%) compared to conventional blood glucose self-monitoring.

Back

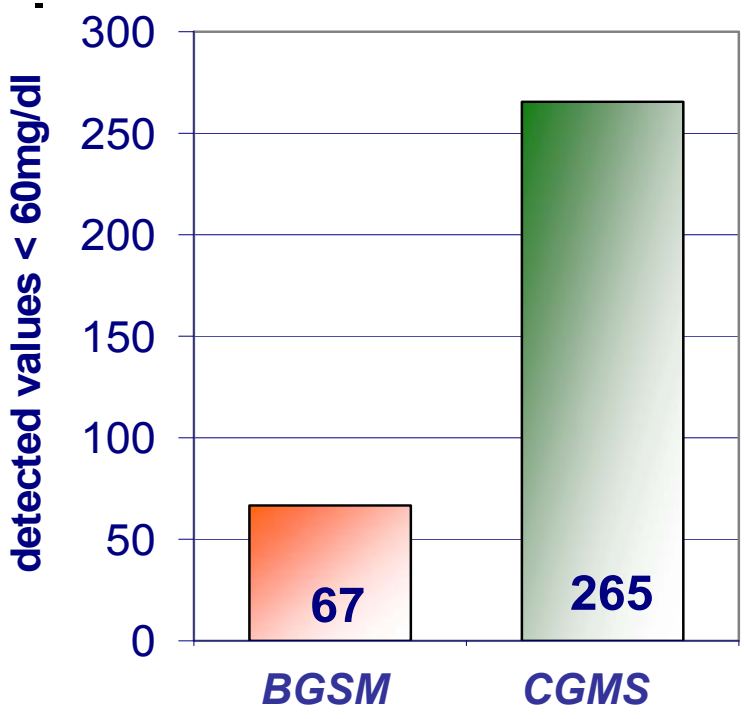
*From: Sibenaler A. et.al.: Diabetes 52 Suppl.2 (2003), A99*

Medtronic

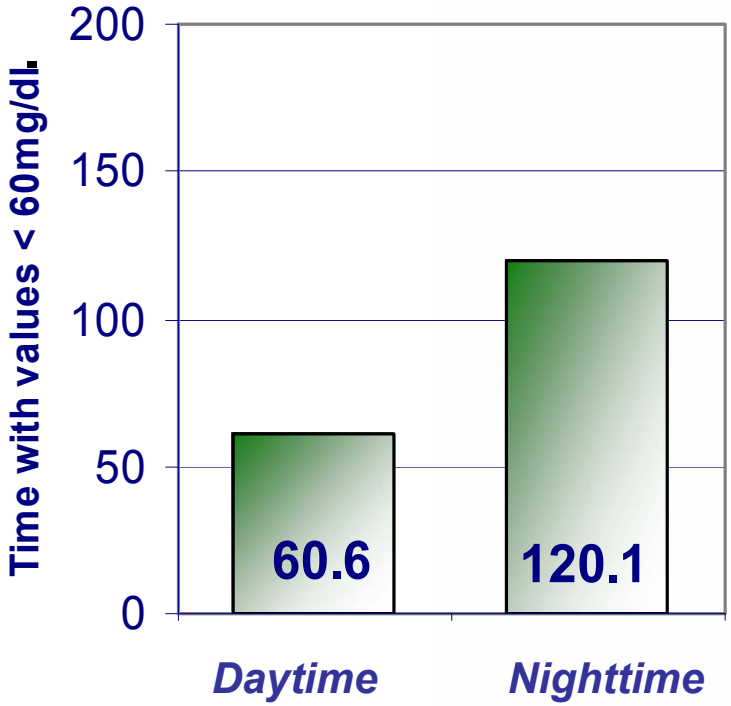
CGM

# Detection of otherwise unnoticed hypoglycemia using continuous glucose monitoring

- Number of detected values of < 60 mg/dl over 6 days:




- Duration of hypoglycemic values < 60 mg/dl, recorded with CGM:




82.2% of hypoglycemic events show no visible symptoms (!)

*From: Sibenaler A. et.al.: Diabetes 52 Suppl.2 (2003), A99*

Medtronic

# Detection of otherwise unnoticed hypoglycemia using continuous glucose monitoring

## Conclusion:

A greater number of hypoglycemic events can be verified with continuous glucose monitoring than with blood glucose self-monitoring. This confirms the fact that a large number of hypoglycemic events occur with no obvious symptoms.

Back

*From: Sibenaler A. et.al.: Diabetes 52 Suppl.2 (2003), A99*

CGM

# Hypoglycemic frequency documented with continuous glucose monitoring

## Statement:

The actual degree and frequency of hypoglycemia can be more accurately documented with continuous glucose monitoring than with blood glucose self-monitoring.

## Evidence:

Determination of hypoglycemia using 4 daily blood glucose self-monitoring checks (Hemo-Cue 201+) and using continuous glucose monitoring (CGMS®Gold). Determination of the degree of hypoglycemia was done in accordance with the ADA criteria for 119 diabetic patients (age: 46 ± 12 y., diabetic for: 21 ± 12 years, $HbA_{1c}$: 8.5 ± 1.0 %).

Back

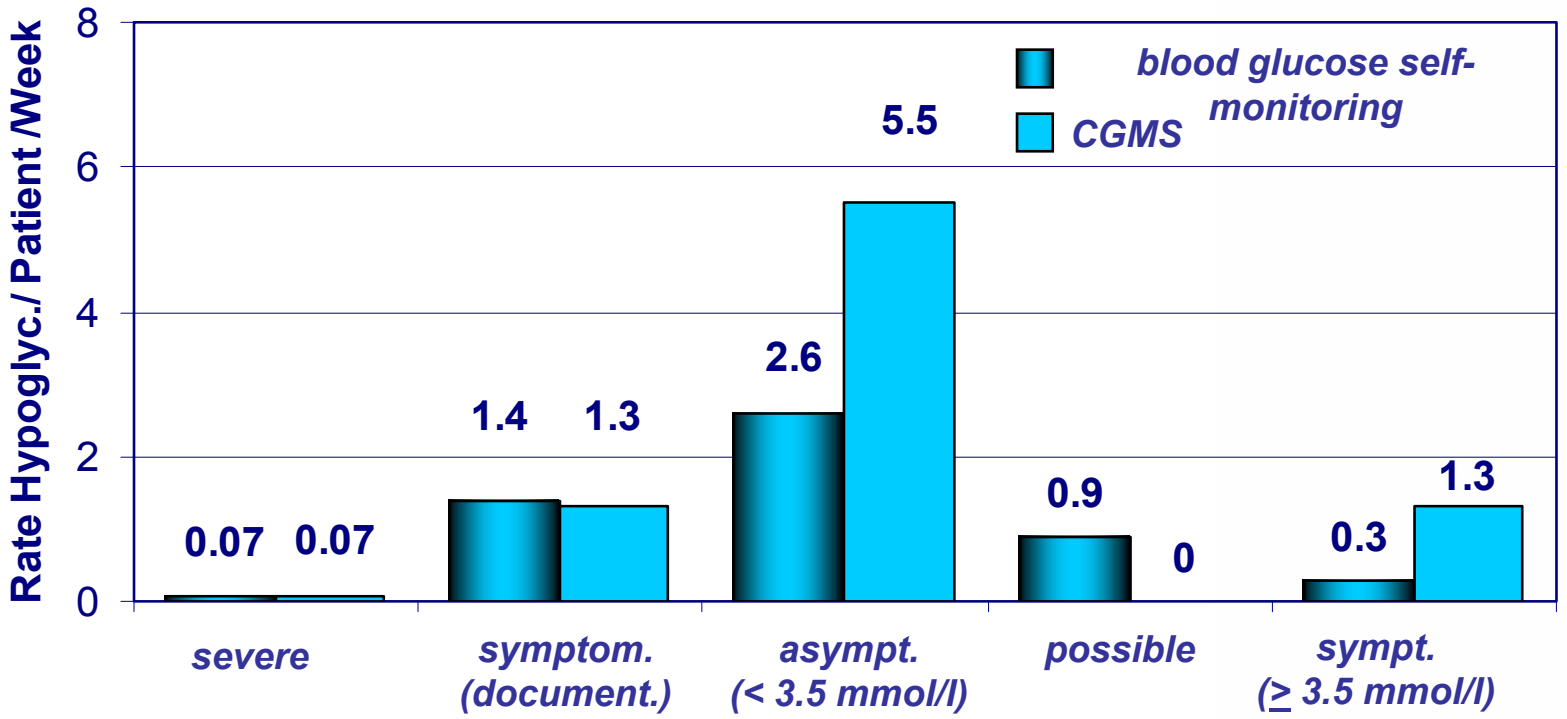
*From: Pedersen-Bjergaard U et al.: Diabetic Medicine 23 (Suppl. 4) 2006; 140-141*

Medtronic

CGM

# Hypoglycemic frequency documented with continuous glucose monitoring

- Frequency and distribution of hypoglycemia, determined using CGMS and blood glucose self-monitoring




*From: Pedersen-Bjergaard U et al.: Diabetic Medicine 23 (Suppl. 4) 2006; 140-141*

Medtronic

# Hypoglycemic frequency documented with continuous glucose monitoring

## Conclusion:

While both BSSM and CGMS detected hypoglycemia that also resulted in noticeable symptoms, a significantly greater number of asymptomatic hypoglycemic events were documented by CGMS. This clearly demonstrates the advantages of continuous glucose monitoring.

Back

*From: Pedersen-Bjergaard U et al.: Diabetic Medicine 23 (Suppl. 4) 2006; 140-141*

CGM

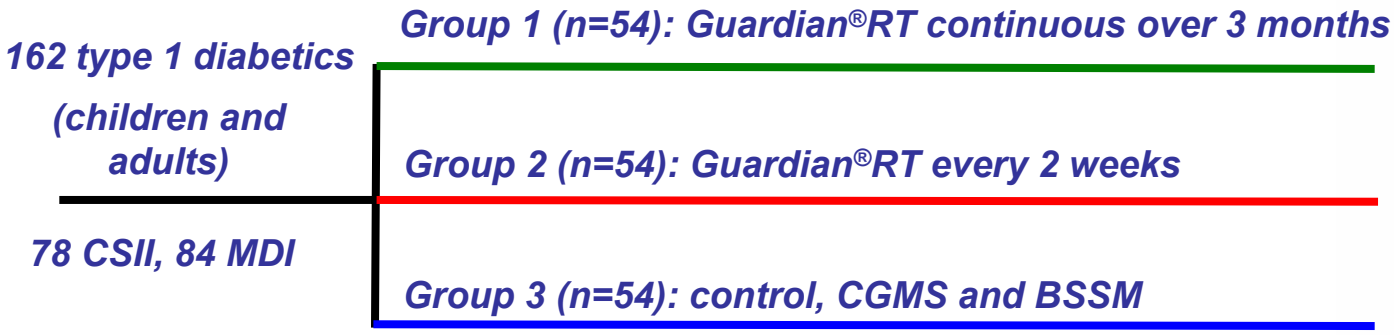
# Improved glycemic control by use of current glucose values from glucose monitoring

## Statement:

Glycemic control is improved by having current glucose values available. Patients can use the data to adapt and optimise treatment.

## Evidence:

Randomized control study to determine the impact of continuous glucose monitoring on the glycemia of type 1 diabetics.




*Recordings:*
- *$HbA_{1c}$ values*
- *Glucose profiles with the Guardian®RT or CGMS®Gold*

*From: Deiss D et al.: Diabetes Care 2006, 29 (12), 2730-2732*

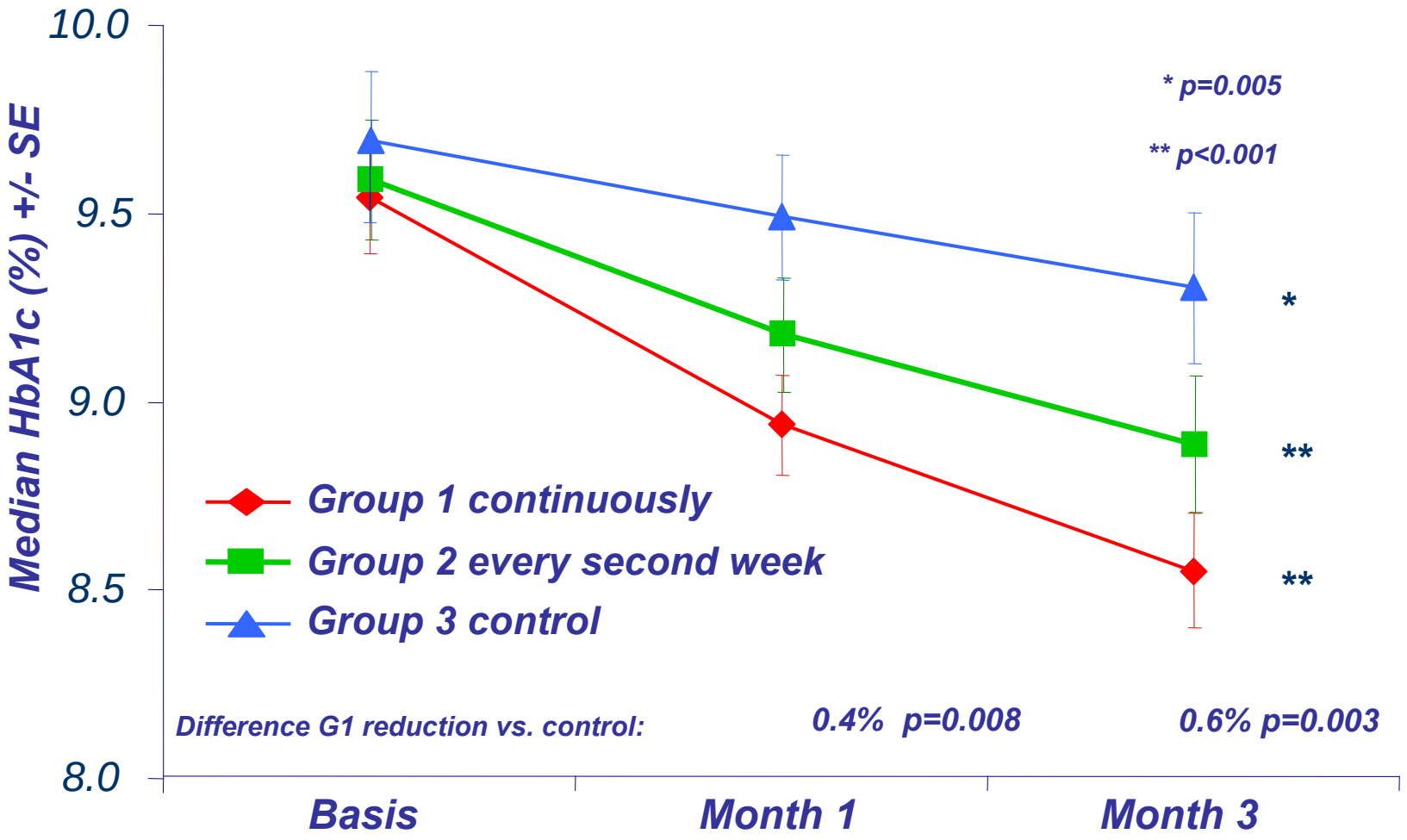
Back

Medtronic

CGM

# Improved glycemic control by use of current glucose values from glucose monitoring

- Changes to $HbA_{1c}$ values:




From: Deiss D et al.: Diabetes Care 2006, 29 (12), 2730-2732

Medtronic

CGM

# Improved glycemic control by use of current glucose values from glucose monitoring

- **50% of the group 1 patients achieved an $HbA_{1c}$ reduction ≥ 1%**
- **26% of the patients achieved an $HbA_{1c}$ reduction ≥ 2%**
- **Use of fresh glucose data:**
  - 82% (in month 1) and 95% (in month 3) of the patients actively used the glucose data to adapt their treatment regimes.
- **Adaptation of treatment by the patients:**
  - Insulin
  - Nutrition (supply of carbohydrates)
  - Lifestyle

*From: Deiss D et al.: Diabetes Care 2006, 29 (12), 2730-2732*

Medtronic

CGM

# Improved glycemic control by use of current glucose values from glucose monitoring

## Conclusion:

A continuous monitoring of glucose with associated display of current glucose values provides support for the patients‘ treatment and significantly facilitates the improvement of glycemic adjustment. The considerably improved control for diabetics who usually experience great difficulty with control has a great potential with respect to reducing the risks of developing secondary diabetic conditions.

Back

*From: Deiss D et al.: Diabetes Care 2006, 29 (12), 2730-2732*

Medtronic

CGM

# Impact on glycemia of using glucose values from continuous glucose monitoring

## Statement:

A continuous monitoring of glucose with associated display of current values improves diabetic control for type 1 patients during intensified insulin therapy and insulin pump therapy.

## Evidence:

Assessment of glycemic control by means of glucose profiles, $HbA_{1c}$ values and the hypoglycemia rate for 34 patients (25 female / 9 male) with type 1 diabetes (age: 42 $\pm$ 16 years, diabetic for: 23.7 $\pm$ 16.2 years).

Back

*From: Ellis SL et al.: Diabetes 2007; 56 (Suppl. 1), A119-A120 and Diabetologia 2007; 50 (Suppl. 1), S418*

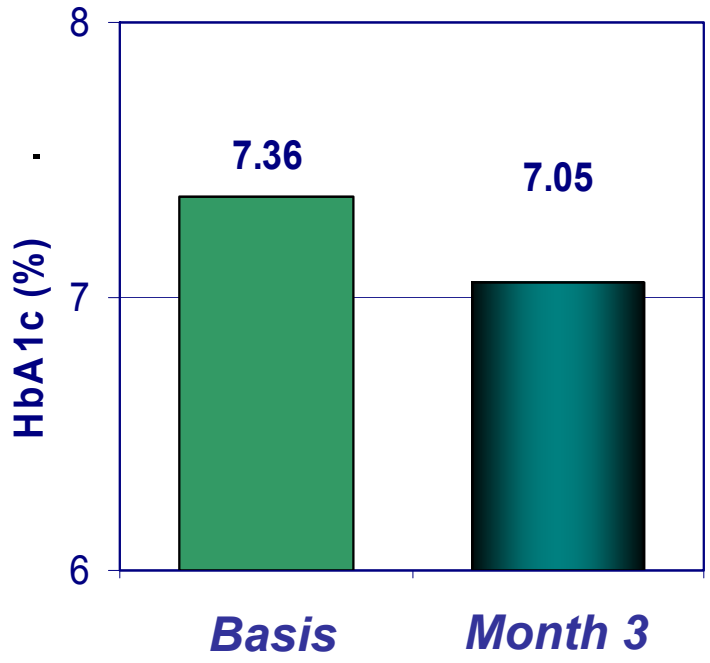
Medtronic

CGM

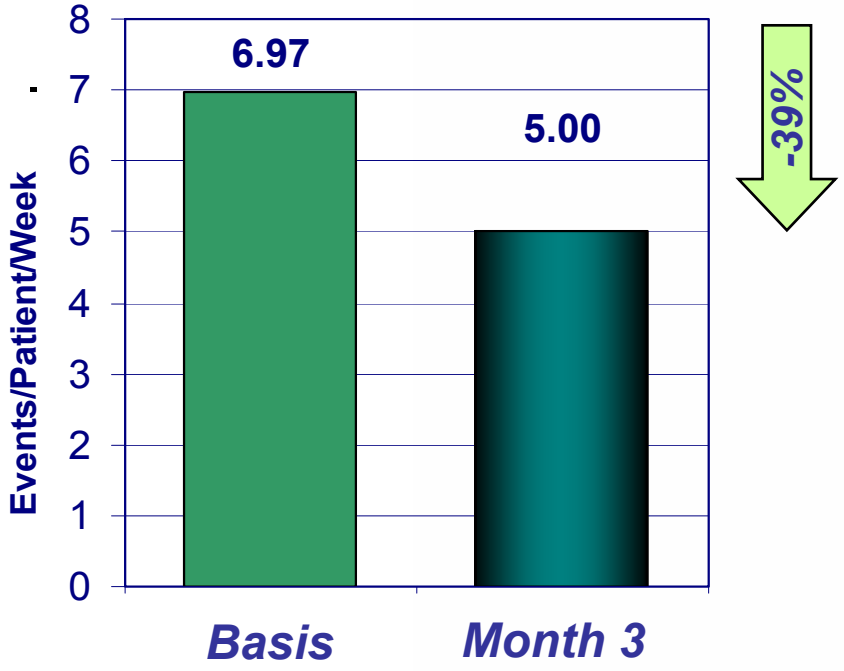
# Impact on glycemia of using glucose values from continuous glucose monitoring

*Results after average CGM use of 17 ± 9 (range 1 - 30) days / month*

- $HbA_{1c}$ development:




- Rate of hypoglycemia:




*From: Ellis SL et al.: Diabetes 2007; 56 (Suppl. 1), A119-A120 and Diabetologia 2007; 50 (Suppl. 1), S418*

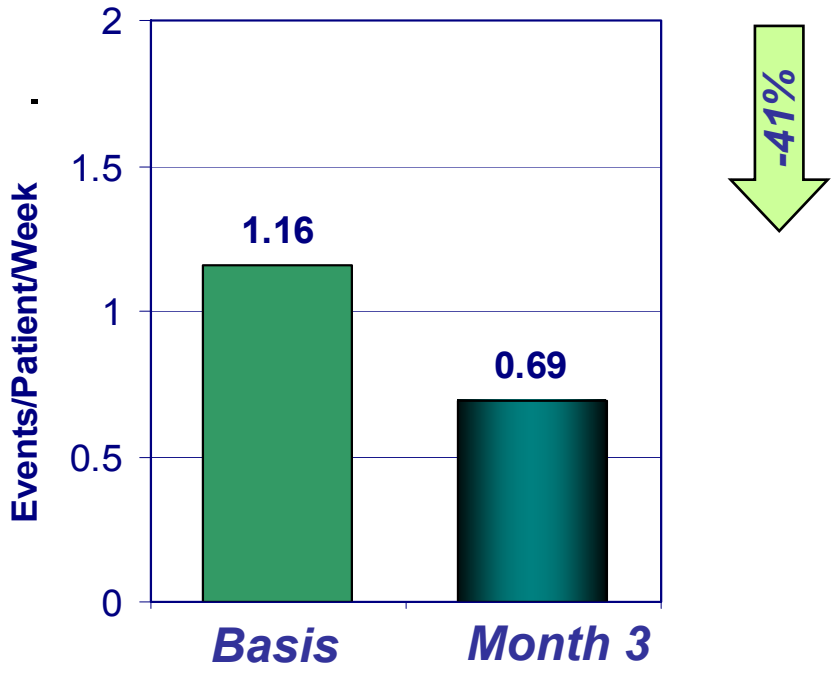
Medtronic

CGM

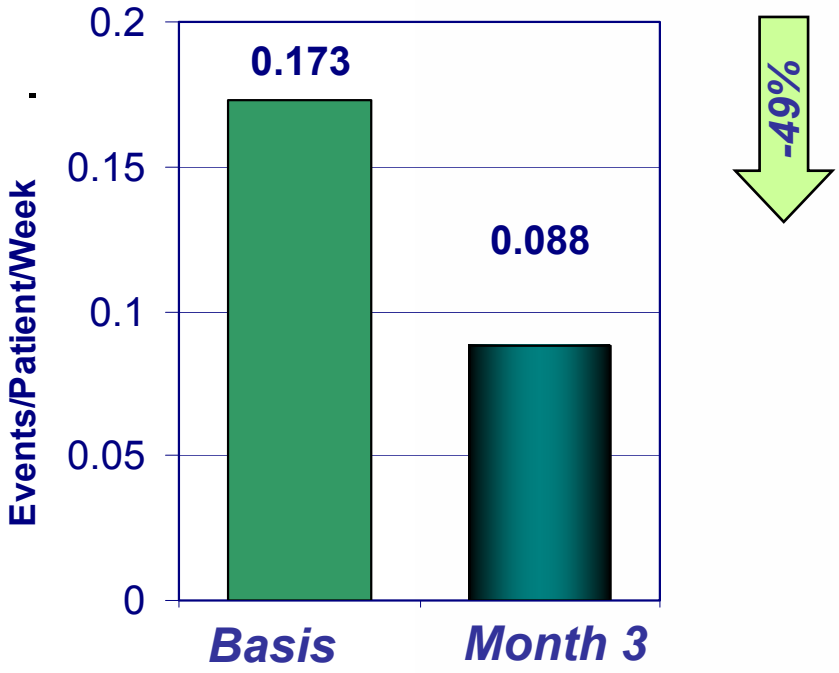
# Impact on glycemia of using glucose values from continuous glucose monitoring

Results after average CGM use of
17 ± 9 (range 1 - 30) days / month

- Rate of nocturnal hypoglycemia :




- Rate of severe hypoglycemia:




*From: Ellis SL et al.: Diabetes 2007; 56 (Suppl. 1), A119-A120 and Diabetologia 2007; 50 (Suppl. 1), S418*

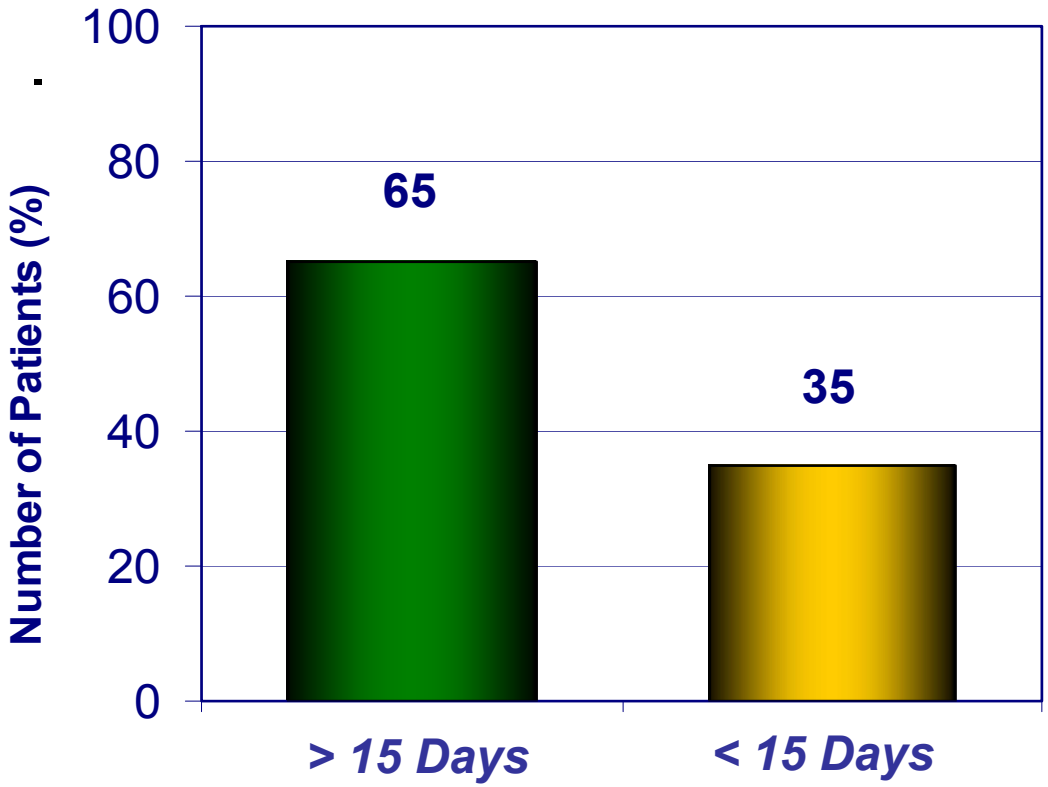
Medtronic

CGM

# Impact on glycemia of using glucose values from continuous glucose monitoring

Relationship between the period of wearing the sensor and the reaching of an $HbA_{1c}$ target value of 7.0%:

- Number of Patients with $HbA_{1c} \leq 7.0\%$:




*From: Ellis SL et al.: Diabetes 2007; 56 (Suppl. 1), A119-A120 and Diabetologia 2007; 50 (Suppl. 1), S418*

Medtronic

# Impact on glycemia of using glucose values from continuous glucose monitoring

## Conclusion:

The glycemia improves significantly when utilising fresh glucose readings from continuous glucose monitoring. There is a particularly significant reduction in hypglycemiia. Furthermore, the relationship between the success of the treatment and the length of time the sensor is used is substantiated.

Back

*From: Ellis SL et al.: Diabetes 2007; 56 (Suppl. 1), A119-A120 and Diabetologia 2007; 50 (Suppl. 1), S418*

CGM

# Deployment of the Guardian® glucose sensor as an alarm system for excessive glucose deviations

## Statement:

The use of a current-glucose-value based alarm system can reduce hypoglycemic and hyperglycemic deviations and their duration.

## Evidence:

Randomized, controlled, parallel study over 16 days with two groups. Group 1 (n=35): wear the sensor for 8 days without an alarm and 8 days with an alarm; group 2 (control, n=36): wear the sensor the whole time without an alarm. Age, time as diabetic, BMI and $HbA_{1c}$ (7.5%) were comparable.

Back

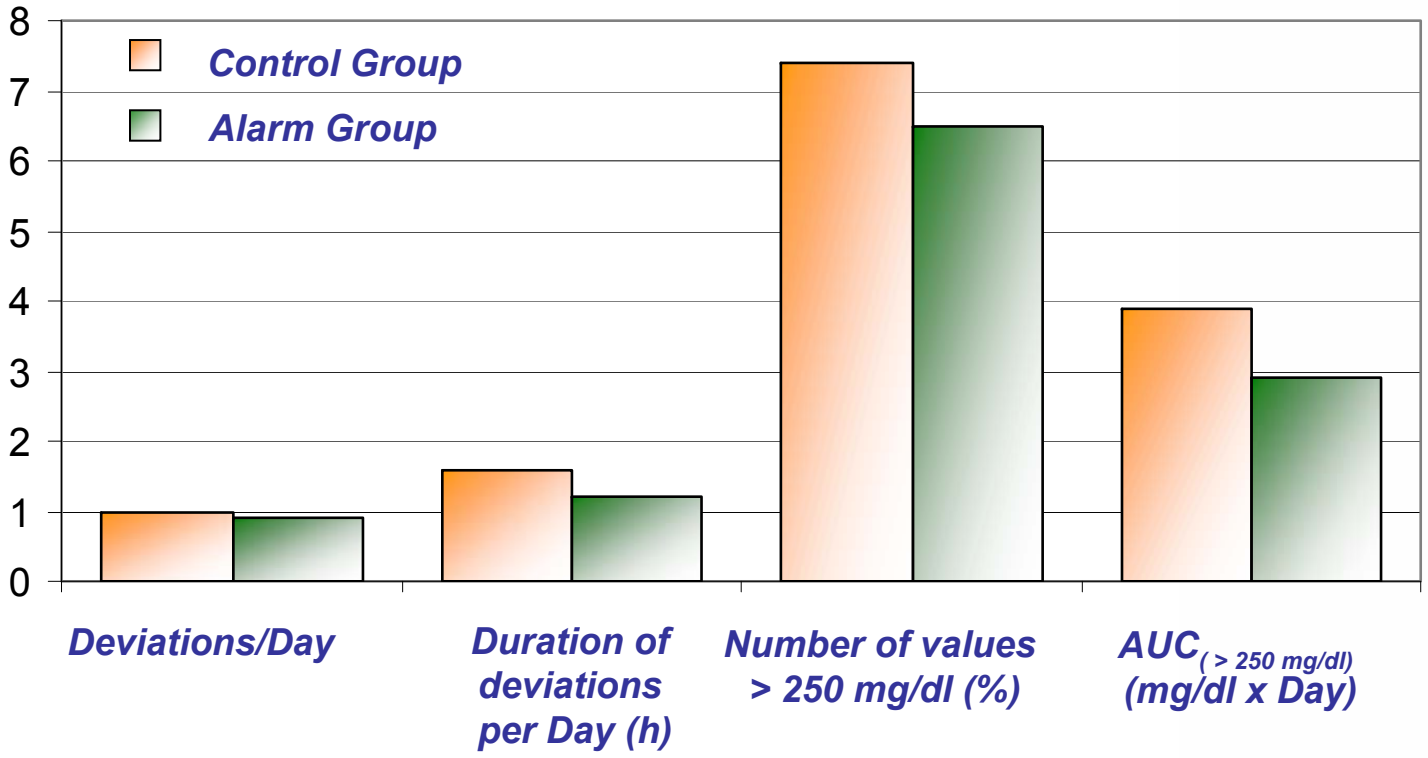
*From: J. Mastrototaro J et al.: Diabetes 53, Suppl.2 (2004), A3 and Diabetologia 47, Suppl.1 (2004), A93*

Medtronic

CGM

# Deployment of the Guardian® glucose sensor as an alarm system for excessive glucose deviations

- Comparison of hyperglycemic deviations between the alarm group and the control group:



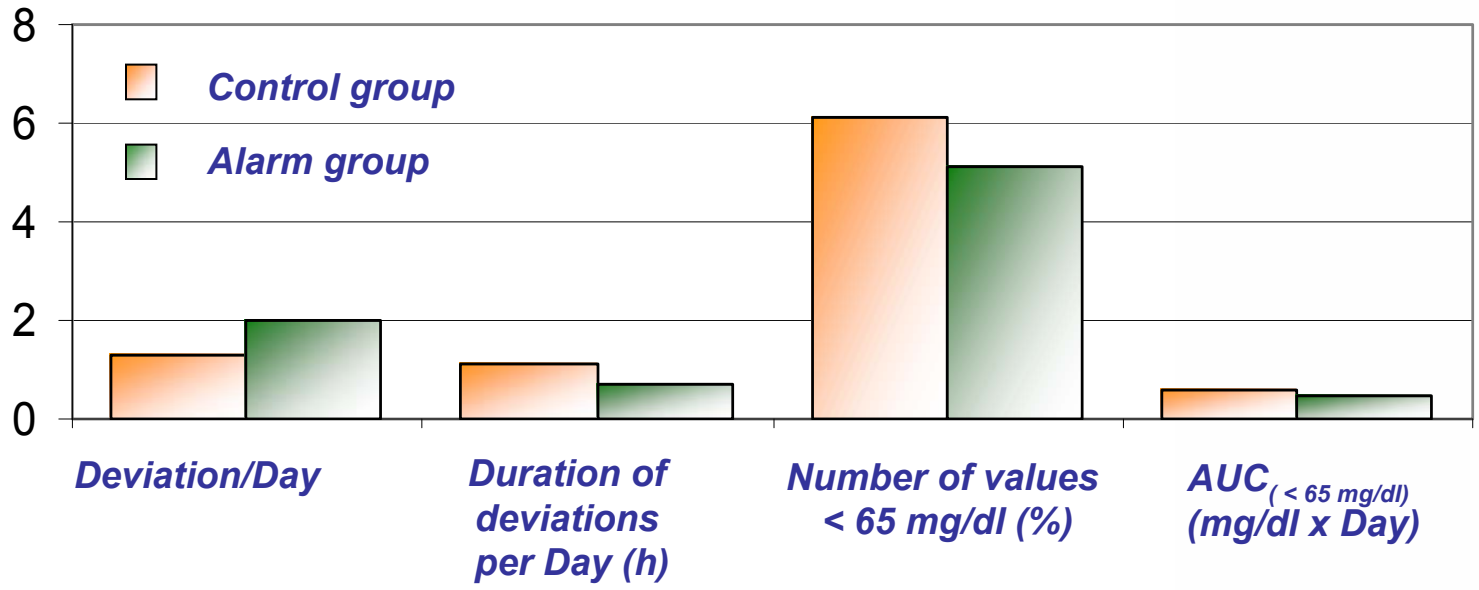

*From: J. Mastrototaro J et al.: Diabetes 53, Suppl.2 (2004), A3 and Diabetologia 47, Suppl.1 (2004), A93*

Medtronic

CGM

# Deployment of the Guardian® glucose sensor as an alarm system for excessive glucose deviations

- Comparison of hypoglycemic deviations between the alarm group and the control group:




*From: J. Mastrototaro J et al.: Diabetes 53, Suppl.2 (2004), A3 and Diabetologia 47, Suppl.1 (2004), A93*

Medtronic

CGM

# Deployment of the Guardian® glucose sensor as an alarm system for excessive glucose deviations

## Conclusion:

Deployment of the Guardian® as an alarm system allows reliable detection of hypoglycemic and hyperglycemic values. The duration of deviations is significantly reduced, thus improving the glycemia and lowering the risk for microvascular and macrovascular illnesses.

*From: J. Mastrototaro J et al.: Diabetes 53, Suppl.2 (2004), A3 and Diabetologia 47, Suppl.1 (2004), A93*

Back

Medtronic

CGM

# Reduction in the hypoglycemia rate due to use of current glucose values from glucose monitoring

## Statement:

The use of an alarm based on current glucose values reduces the rate of hypoglycemia and the time during which patients are subjected to too low glucose values.

## Evidence:

Randomized, controlled multi-centre study with 71 patients (age 44.0 ± 11.4 years) to investigate the influence of activated and deactivated alarms, without visual display of the current values (in order to obviate pro-active influences).

Back

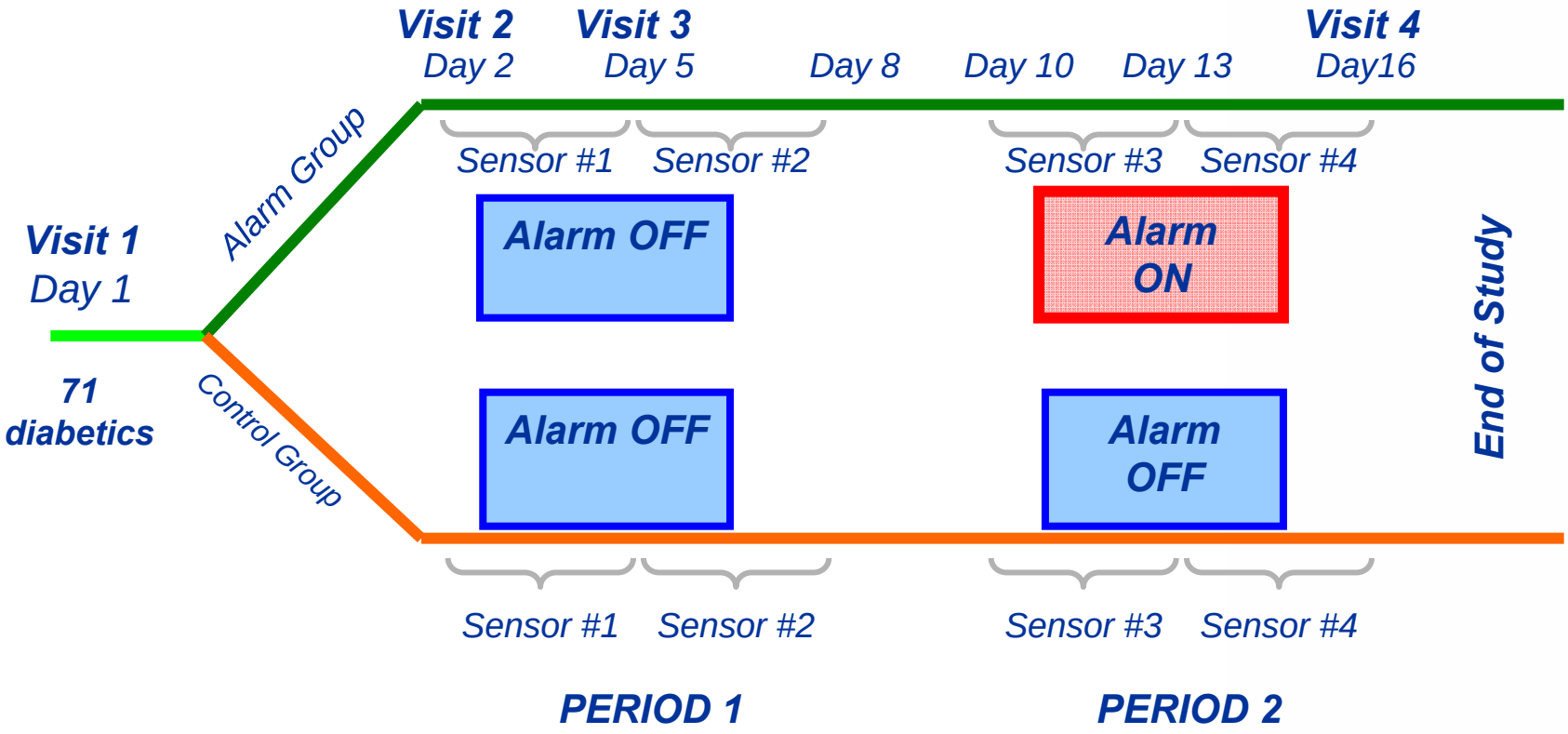
*From: Bode B. et al. Diabetes Technol Ther. 2004 Apr;6(2):105-13*

Medtronic

CGM

# Reduction in the hypoglycemia rate due to use of current glucose values from glucose monitoring

## Design of the randomized multi-centre study



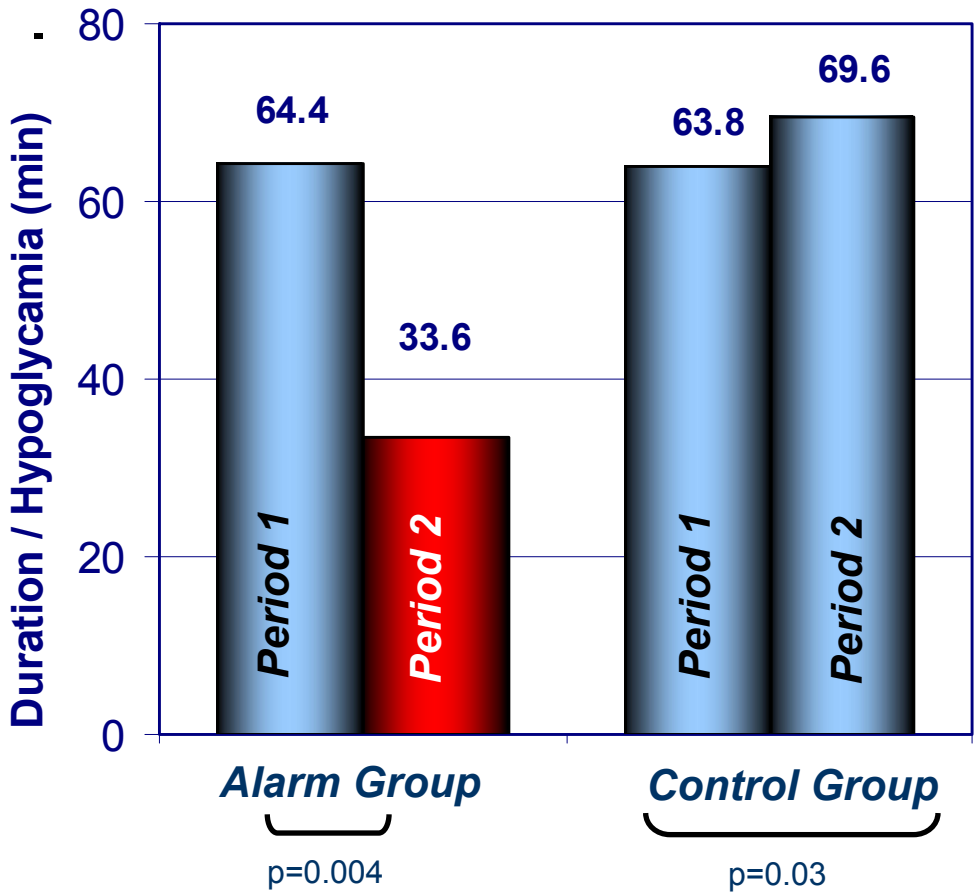

*From: Bode B. et al. Diabetes Technol Ther. 2004 Apr;6(2):105-13*

Medtronic

CGM

# Reduction in the hypoglycemia rate due to use of current glucose values from glucose monitoring

- Duration of each hypoglycemic event (values < 65 mg/dl) with and without activated alarm:




*Alarm OFF*

*Alarm ON*

- Use of the Guardian® alarm system reduced the hypoglycemia by 27 min (48%)

*From: Bode B. et al. Diabetes Technol Ther. 2004 Apr;6(2):105-13*

Medtronic

# Reduction in the hypoglycemia rate due to use of current glucose values from glucose monitoring

## Conclusion:

Alarms based on current glucose readings allow patients to react quickly to the occurrence of hypoglycemia, thereby reducing the duration of hypoglycemic episodes and avoiding the continued development of potentially serious situations (e.g. necessity for help from others).

Back

*From: Bode B. et al. Diabetes Technol Ther. 2004 Apr;6(2):105-13*

# *Potential and opportunities for continuous glucose monitoring*

- New assessment of glycemia?
- Treatment support?
- New opportunities with respect to providing patient care (Telemedicine etc.)?
- Closed system?



Reviews/Commentaries/ADA Statements
REVIEW ARTICLE

# Continuous Glucose Monitoring

## Roadmap for 21st century diabetes therapy

DAVID C. KLONOFF, MD, FACP

Continuous glucose monitoring provides maximal information about shifting blood glucose levels throughout the day and facilitates the making of optimal treatment decisions for the diabetic patient. This report discusses continuous glucose monitoring in terms of its purposes, technologies, target populations, accuracy, clinical indications, outcomes, and problems. In this context, the medical literature on continuous glucose monitoring available through the end of 2004 is reviewed.

**PURPOSES**— Continuous glucose monitoring provides information about the direction, magnitude, duration, frequency, and causes of fluctuations in blood glucose levels. Compared with conventional intensified glucose monitoring, era, on the other hand, takes multiple, poorly focused frames; displays a sequential array of frames whose trend predicts the future; produces too much information for each frame to be studied carefully; and operates automatically after it is turned on. The two types of blood glucose monitors differ in much the same way: *1*) an intermittent blood glucose monitor measures discrete glucose levels extremely accurately, whereas a continuous monitor provides multiple glucose levels of fair accuracy; *2*) with an intermittent monitor, current blood glucose levels do not predict future glucose levels, but with a continuous monitor, trends in glucose levels do have this predictive capability; *3*) with an intermittent monitor, it is easy to study every measured blood glucose value over most time periods, but with a

toring System Gold (CGMS Gold; Medtronic MiniMed, Northridge, CA) (1), the GlucoWatch G2 Biographer (GW2B; Cygnus, Redwood City, CA) (2), the Guardian Telemetered Glucose Monitoring System (Medtronic MiniMed) (3), the GlucoDay (A. Menarini Diagnostics, Florence, Italy) (4), and the Pendra (Pendragon Medical, Zurich, Switzerland) (5). A sixth monitor, whose premarket approval application has been submitted to the FDA, is the FreeStyle Navigator Continuous Glucose Monitor (Abbott Laboratories, Alameda, CA) (6).

The currently available CGMs measure blood glucose either with minimal invasiveness through continuous measurement of interstitial fluid (ISF) or with the noninvasive method of applying electromagnetic radiation through the skin to blood vessels in the body. The technologies for bringing a sensor into contact with ISF include inserting an indwelling sensor subcutaneously (into the abdomi-

From: Klonoff D: Diabetes Care 2005, 28 (5), 1231-1239

Back

device shown to be
he meal-related glu-
asured using eight-
as calculated by
from postmeal glu-
s glucose excursion
inuous glucose self-
was calculated as the
the premeal CGMS
g to the time of the
nd the peak value
premeal eight-point
cursions were two to
hen measured by the
-point testing. These
rising as it is unlikely
surement would co-
neal peak. Moreover,
t cannot measure the
neal glucose rise.
se profiles based on
postprandial mea-
optimal measure of
we believe it is pre-
the potential clinical
ng glycemic variabil-

# The Effect of Glucose Variability on the Risk of Microvascular Complications in Type 1 Diabetes

Response to Kilpatrick et al.

In an analysis of the datasets collected in the Diabetes Control and Complications Trial, Kilpatrick et al. (1) reported that mean blood glucose was predictive of microvascular complications in patients with type 1 diabetes, while glucose variability did not appear to be a factor in their development. We question their methodology and thereby also the conclusions. They calculated the variability of within-day blood glucose as the SD around the mean of a seven-point glycemic profile measured at each patient's quarterly visit. With such a methodology,



$P = 0.05$) was observed when SDs of seven-point glycemic profiles were substituted for MAGE values.

Even though the MAGE determination requires continuous glucose monitoring, we believe that this parameter should be the "gold standard" for assessing glucose fluctuations in all prospective interventional studies designed to estimate glucose variability. We therefore believe that additional studies are required to definitively determine the role of glycemic variability in the pathogenesis of the micro- and macrovascular complications of diabetes. Even though the technology of continuous measurements of glucose in interstitial fluid remains a subject of debate, the use of continuous glucose sensors might be useful for conducting such trials.

LOUIS MONNIER, MD[1]
CLAUDE COLETTE, PHD[2]
LAWRENCE LEITER, MD[3]
ANTONIO CERIELLO, MD[4]
MARKOLF HANEFELD, MD[5]

**Even though the MAGE determination requires continuous glucose monitoring, we believe that this parameter should be the "gold standard" for assessing glucose fluctuations in all prospective international studies designed to estimate glucose variability. We therefore believe that additional studies are required to definitively determine the role of glycemic variability in the pathogenesis of the microvascular and macrovascular complications of diabetes.**

*From: Monnier L et al.: Diabetes Care 2007, Vol. 30 (1), 185-186*



# Sensor Augmented Pump Therapy (SaPT) with the MiniMed Paradigm® REAL-Time System

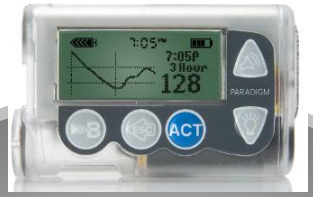

Back

Medtronic

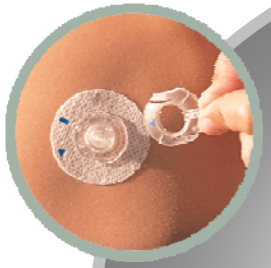
SaPT

# Status 2007: SaPT with MiniMed Paradigm®REAL-Time

***Insulin pump***
***MiniMed Paradigm 522/722***



***Infusions sets***
***& Reservoirs***



***Glucose sensor***
***Sof-sensor***

***BGM***
***Bayer ContourLink***

***MiniLink***
***Transmitter***

***Software***
***CareLink Personal & PRO***
***Therapy management system***

- real-time display of recorded values
- Trend indicator with arrows
- Alarm
- Pre-alarm
- Transfer to the Bolus Wizard possible
- Proposed insulin dose after confirmation by blood glucose measurement
- Memory for 3 months of recordings

Medtronic

SaPT

# Sensor Augmented Pump Therapy with the MiniMed Paradigm®REAL-Time System

**SaPT improves glycemic control, facilitates training of patients and is well-accepted by them**

- Sensor augmented pump therapy for adult type 1 diabetics
- Results and treatment security for type 1 diabetics using SaPT
- Use and experience with the MiniMed Paradigm®REAL-Time System during training
- Fewer glycemic excursions when using the MiniMed Paradigm®REAL-Time System
- Sensor augmented pump therapy for children and adolescents

Back

Medtronic

# Sensor Augmented Pump Therapy with the Paradigm®REAL-Time System

## SaPT extends treatment options

- Pyramid of therapy since 2007

- Diabetes mellitus treatment and associated diagnostic impact

*Zurück*

SaPT

# Sensor augmented pump therapy for adult type 1 diabetics

## Statement:

Sensor augmented pump therapy is an effective treatment option and improves glycemia in adult patients who have already been treated with CSII.

## Evidence:

Improvement of glycemic control in a sensor augmented pump therapy pilot study with and without CSII over 7 months using 9 type 1 diabetic patients already treated with CSII (age: 32.9 ± 11.2 years, diabetic for : 16.7 ± 9.1 years)

Back

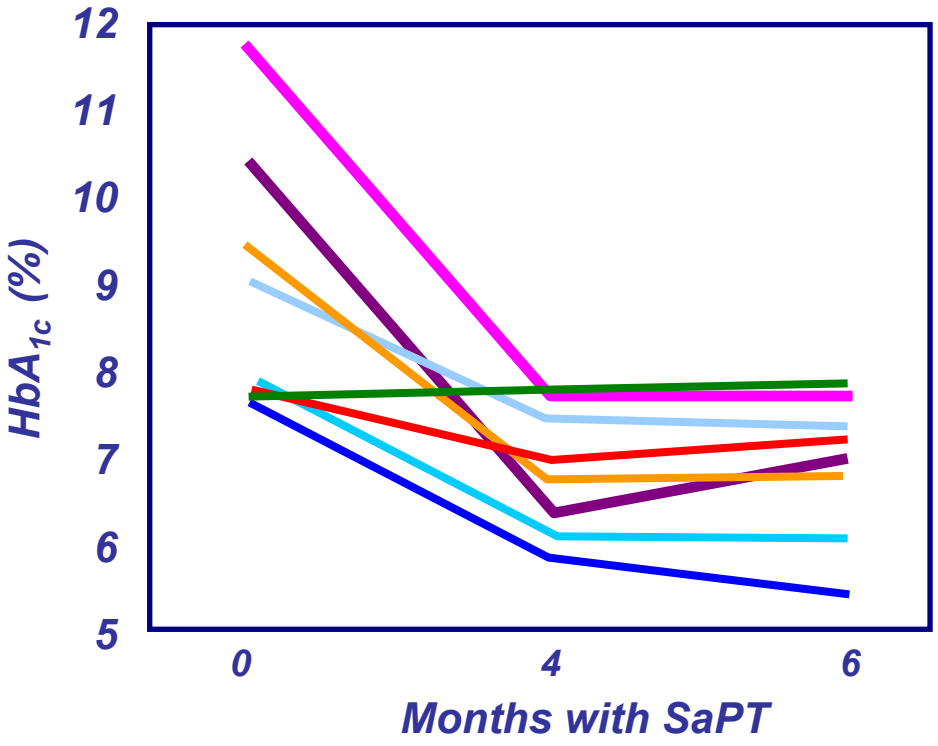
*From: Zoubas CS: Diabetologia 2007; 50 (Suppl. 1), S418*

Medtronic

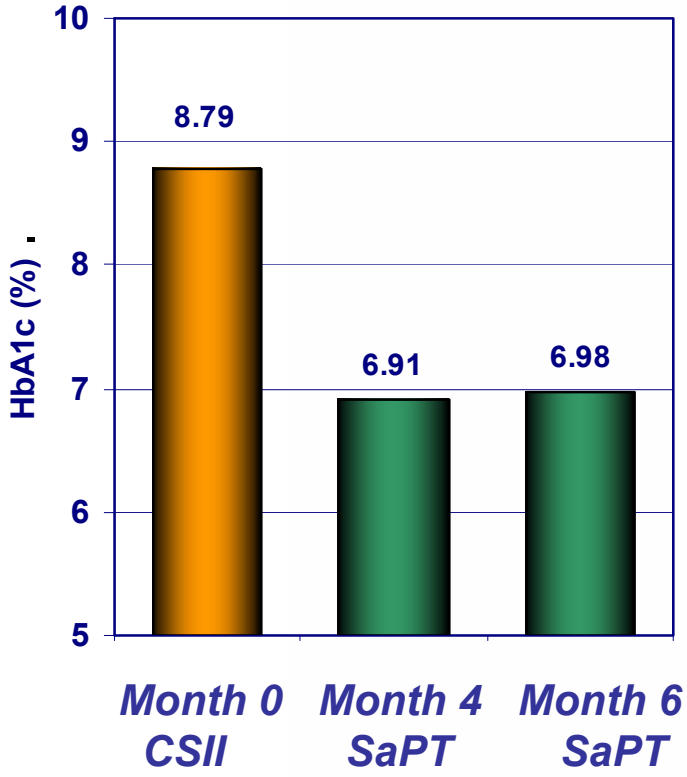
SaPT

# Sensor augmented pump therapy for adult type 1 diabetics

- Development of $HbA_{1c}$ values of individual patients:




- Development of $HbA_{1c}$ values overall:



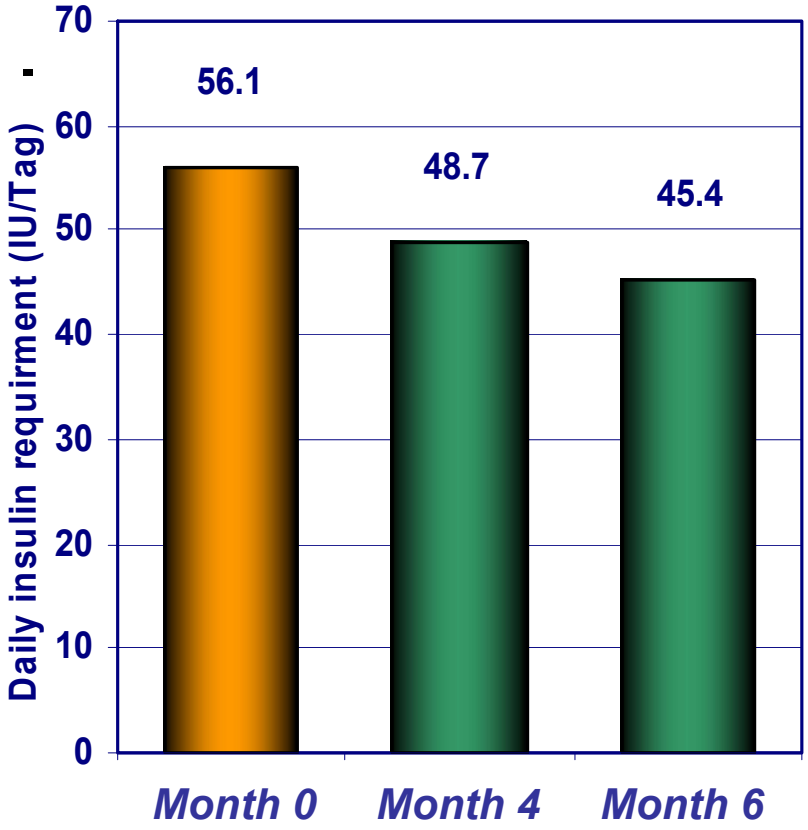

*From: Zoubas CS: Diabetologia 2007; 50 (Suppl. 1), S418*

Medtronic

SaPT

# Sensor augmented pump therapy for adult type 1 diabetics

- Change in daily insulin requirements:




- Development with reference to the AUC in the individual glycemic ranges:
  - Number AUC 70-180 mg/dl: 71% - 72%; ns
  - Number AUC < 70 mg/dl: 5 - 6 %; ns
  - Number AUC > 180 mg/dl: 22 - 24 %; ns

*AUC Area under curve*

*From: Zoubas CS: Diabetologia 2007; 50 (Suppl. 1), S418*

Medtronic

SaPT

# Sensor augmented pump therapy for adult type 1 diabetics

## Conclusion:

The long-term use of glucose sensors displaying the current glucose values optimizes metabolic control with both MDI and CSII. Within the context of sensor augmented pump therapy (SaPT), the insulin application rate and number of insulin boli also decrease. Due to the greater control provided by continuously updated and displayed glucose values, considerably fewer hyperglycemic deviations occur.

Back

*From: Zoubas CS: Diabetologia 2007; 50 (Suppl. 1), S418*

Medtronic

SaPT

# Results and treatment security for type 1 diabetics using SaPT

## Statement:

The treatment effectiveness and security for type 1 diabetics is significantly improved by the use of sensor augmented pump therapy (SaPT) when compared to the use of intensified insulin therapy (MDI).

## Evidence:

Improvement in glycemic control in a randomized, controlled study over 16 weeks using the Paradigm®REAL-Time system with 28 type 1 diabetic patients with previously insufficent diabetic control ($HbA_{1c}$ = 8.6 %).

Back

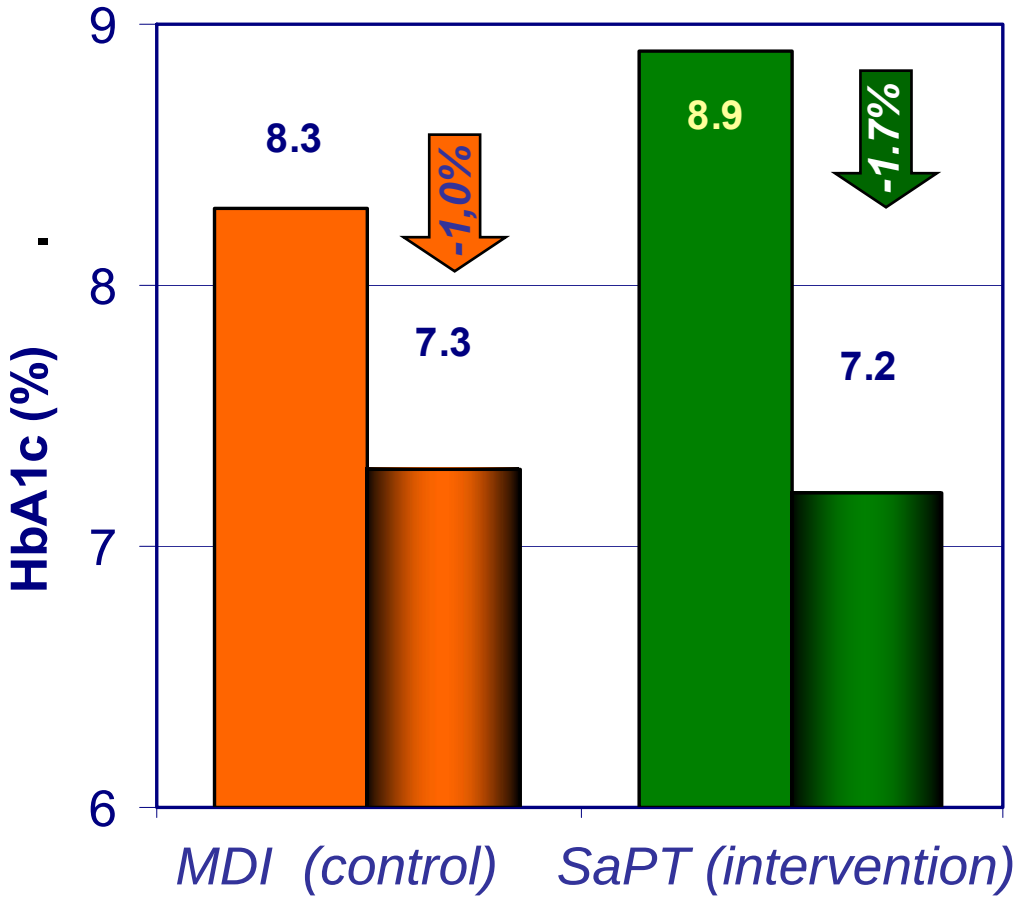
*From: Peyrot M et al.: Diabetes 2007; 56 (Suppl. 1), A122-A123*

Medtronic

SaPT

# Results and treatment security for type 1 diabetics using SaPT

- Changes in $HbA_{1c}$ values:




- Rate of severe hypoglycemia: only one event in the control group

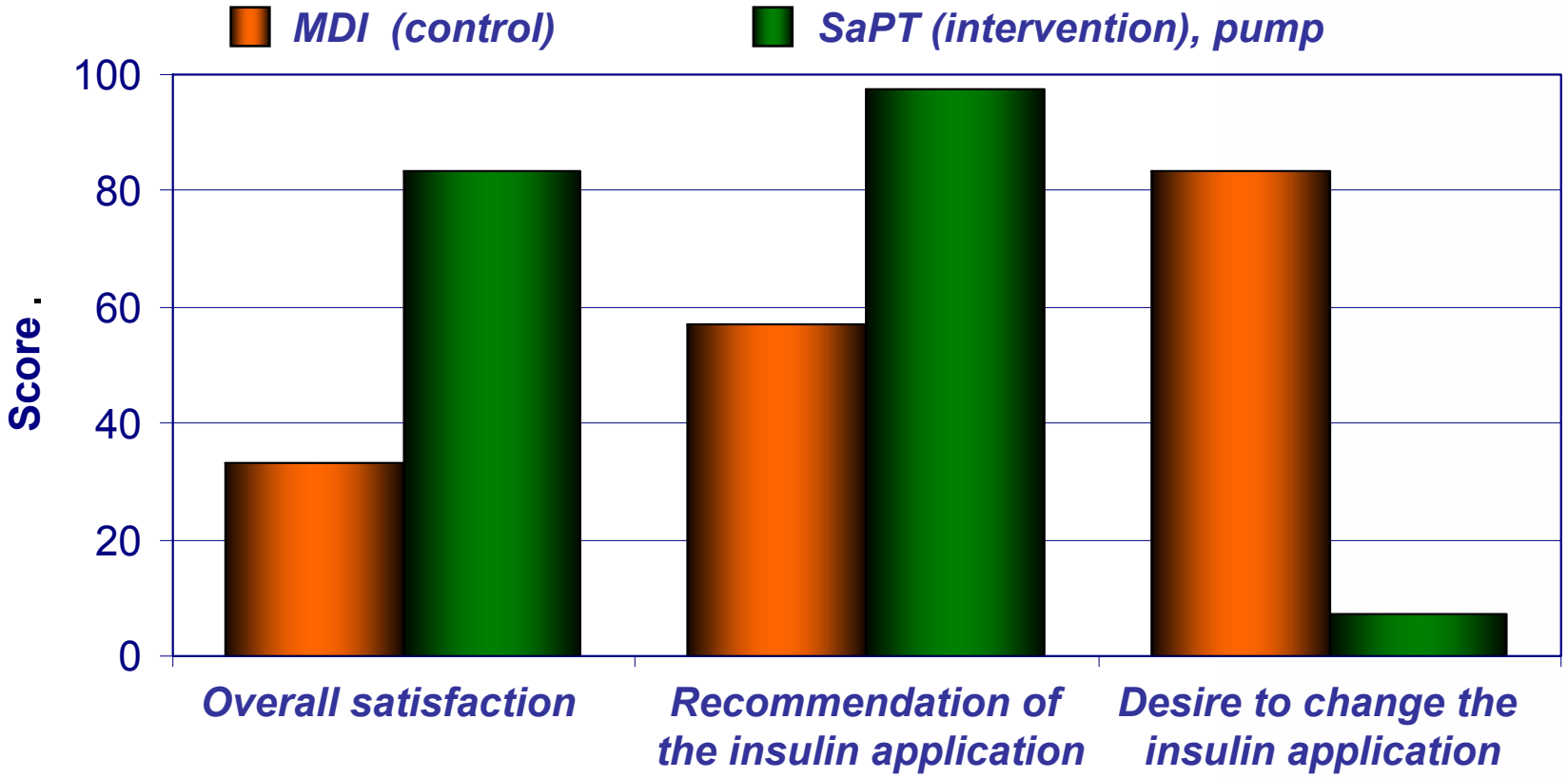
*From: Peyrot M et al.: Diabetes 2007; 56 (Suppl. 1), A122-A123*

Medtronic

SaPT

# Results and treatment security for type 1 diabetics using SaPT

- Results of the survey regarding insulin application: IDSRQ (Score from 0-100, higher values = more agreement)



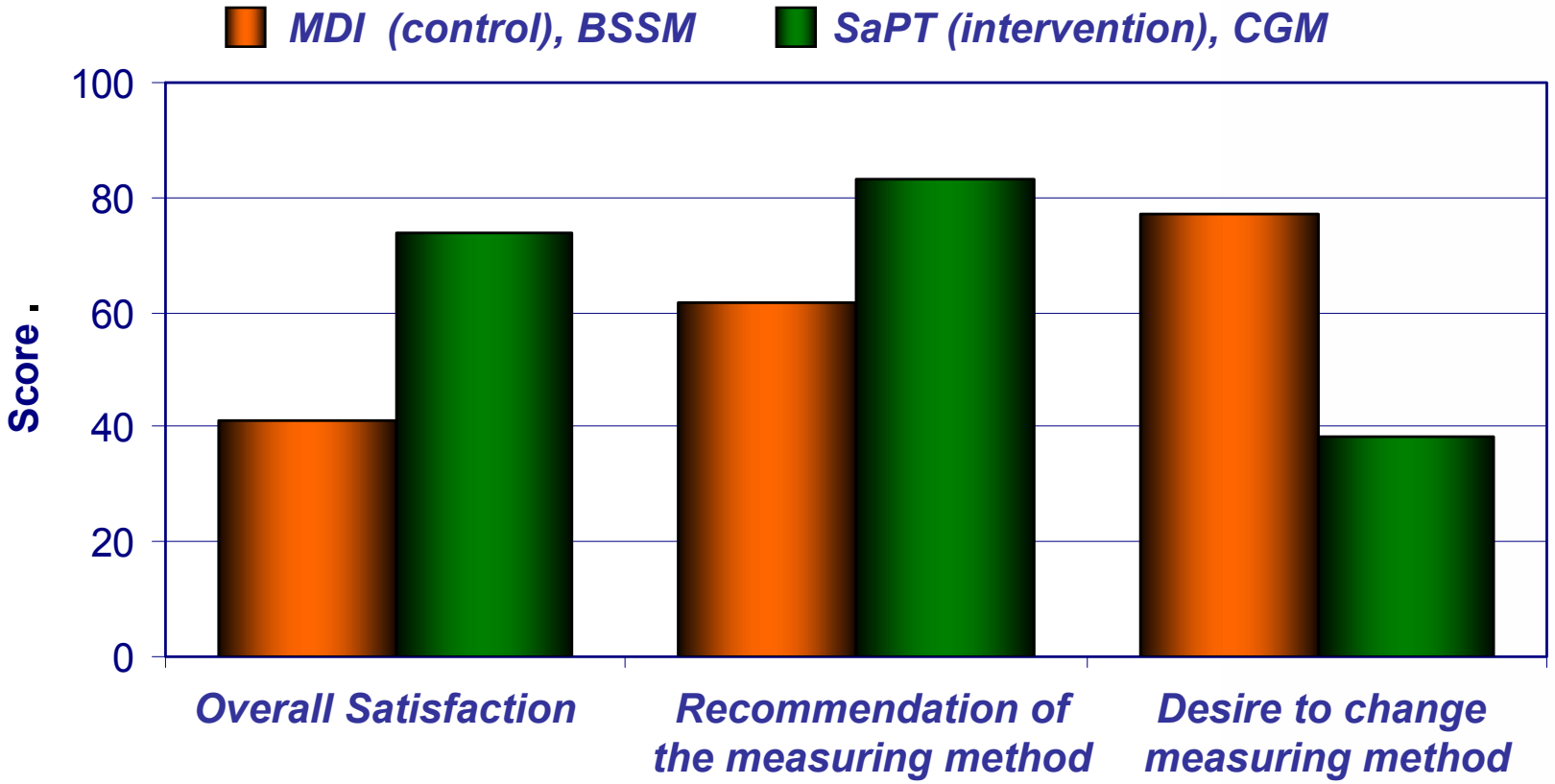

*From: Peyrot M et al.: Diabetes 2007; 56 (Suppl. 1), A122-A123*

Medtronic

SaPT

# Results and treatment security for type 1 diabetics using SaPT

- Results of the glucose measurement survey: BGMSRQ (Score from 0-100, higher values = more agreement)




*From: Peyrot M et al.: Diabetes 2007; 56 (Suppl. 1), A122-A123*

Medtronic

SaPT

# Results and treatment security for type 1 diabetics using SaPT

## Conclusion:

The use of sensor augmented pump therapy shows not just considerable improvements in glycemic control when compared to optimized MDI, but also a greater feeling of safety amongst patients with regard to the treatment – as documented in all questionnaires. This also has an impact on the acceptance of insulin pumps and glucose sensors.

Back

*From: Peyrot M et al.: Diabetes 2007; 56 (Suppl. 1), A122-A123*

Medtronic

SaPT

# Use and experience with the MiniMed Paradigm®REAL-Time system for education

## Statement:

Use of the Paradigm®REAL-Time system increases the effectiveness of diabetes education in various age groups and contributes thereby to adjustment of glucose values and hence better metabolic control.

## Evidence:

Prospective multi-centre study of the use of Paradigm® REAL-Time in everyday conditions with CSII-experienced type 1 diabetic patients for a month
(23 children: age 10.5 (3.3-15.3) years, CSII: 0.8 (0.2-3.0) y.,
12 adults: age 35 (24-48) years, CSII: 2.5 (0.5-13.3) years)

*Back*

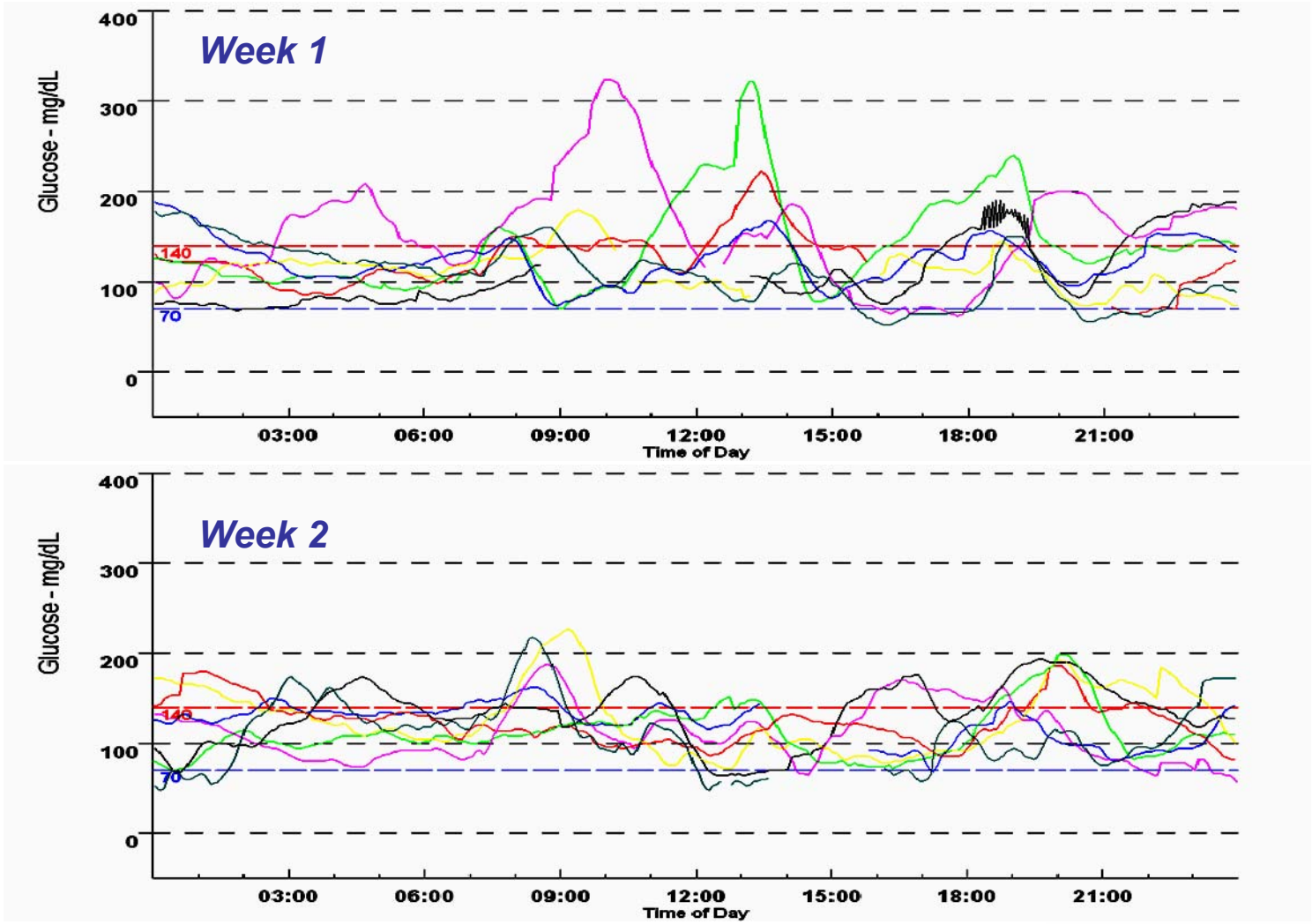
*From: Danne T et al.: Diabetologie 2006; 1: S93*
*and: Diabetes 2006; 55 (Suppl. 1), A194-A195*

Medtronic

SaPT

# Use and experience with the MiniMed Paradigm®REAL-Time system for education

## Improvement in glycemia with current glucose values displayed

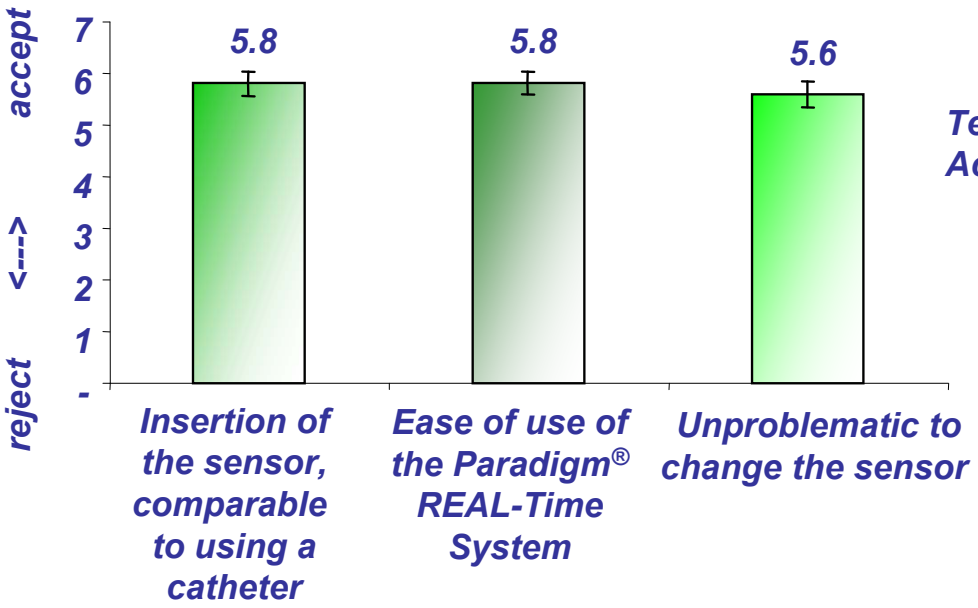



*From: Danne T et al.: Diabetologie 2006; 1: S93*
*and: Diabetes 2006; 55 (Suppl. 1), A194-A195*

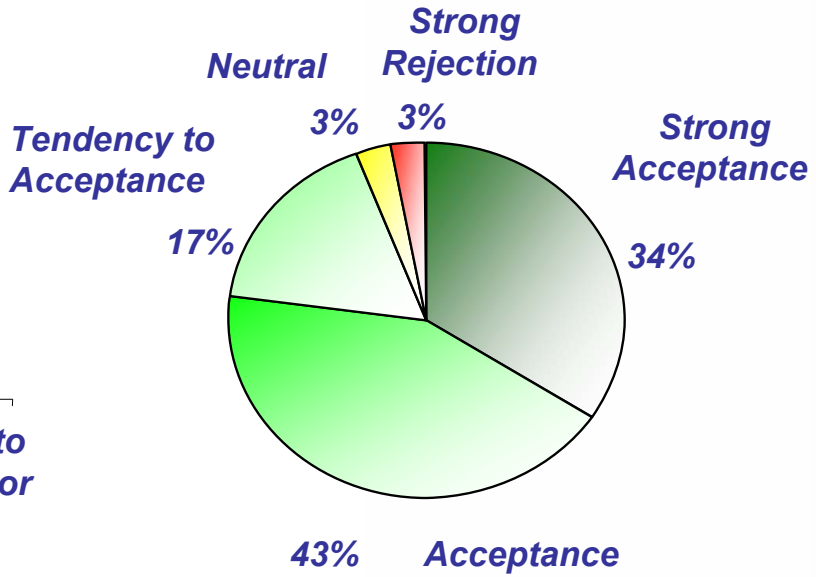
SaPT

# Use and experience with the Paradigm®REAL-Time system for education

- Evaluation of application / Overall acceptance:




- Overall satisfaction with the system:




- Average value for evaluation of all criteria: 6.0

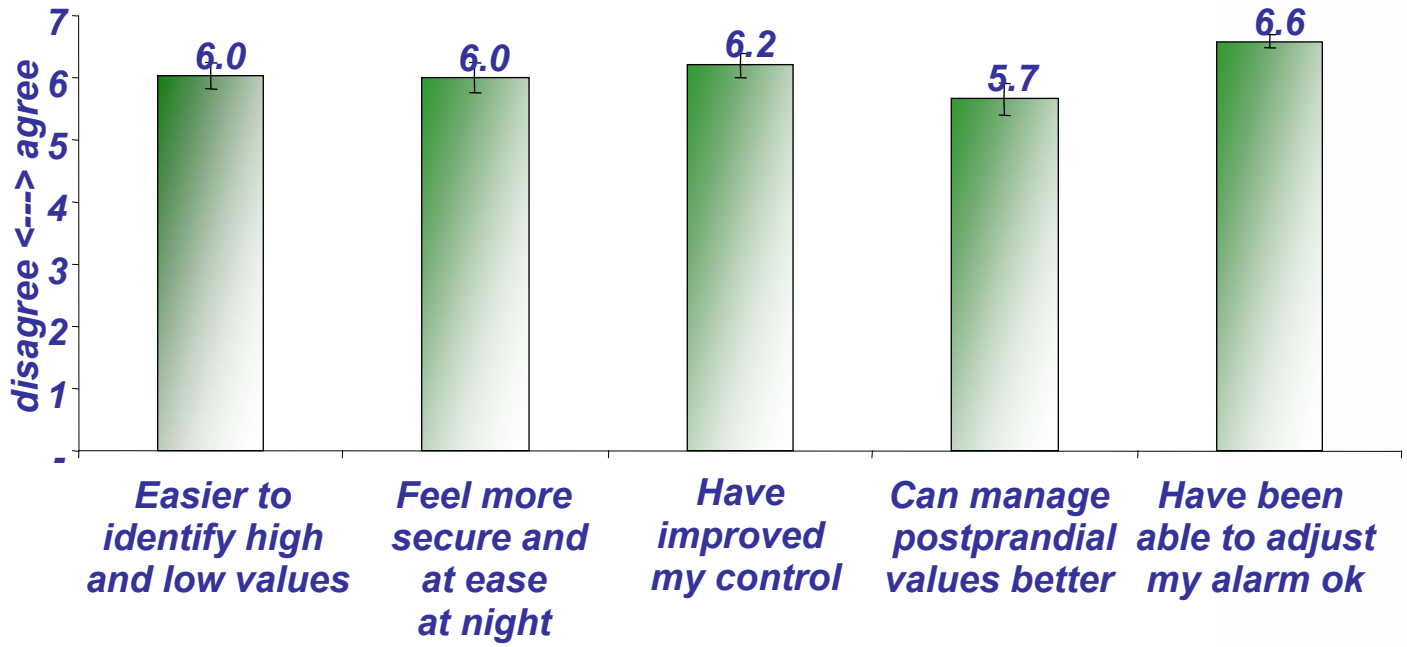
*From: Danne T et al.: Diabetologie 2006; 1: S93*
*and: Diabetes 2006; 55 (Suppl. 1), A194-A195*

Medtronic

SaPT

# Use and experience with the Paradigm®REAL-Time system for education

- Appraisal of diabetes management using the Paradigm®REAL-Time System




*From: Danne T et al.: Diabetologie 2006; 1: S93*
*and: Diabetes 2006; 55 (Suppl. 1), A194-A195*

Medtronic

SaPT

# Use and experience with the Paradigm®REAL-Time system for education

## Conclusion:

Type 1 diabetics from various age groups give a very positive judgment of their experience with the Paradigm®REAL-Time system for displaying current glucose values. 86% of the patients stated that the system would fundamentally change their diabetes management, was of considerable informative value and that a continuous use would improve their diabetic control.

Back

*From: Danne T et al.: Diabetologie 2006; 1: S93*
*and: Diabetes 2006; 55 (Suppl. 1), A194-A195*

Medtronic

SaPT

# Fewer glycemic excursions when using the Paradigm®REAL-Time System

## Statement:

Use of the Paradigm®REAL-Time system provides further improvements to the metabolic adjustment achieved with CSII. The glycemia improvement is particularly noticeable in the reduction of glycemic deviations and a diminished rate of hypoglycemia.

## Evidence:

Prospective pilot study comparing “conventional“ CSII (blind glucose monitoring with CGMS®Gold) with sensor augmented CSII after readjustment to the Paradigm® REAL-Time system with 7 type 1 diabetic patients (time frame: 1 week each).

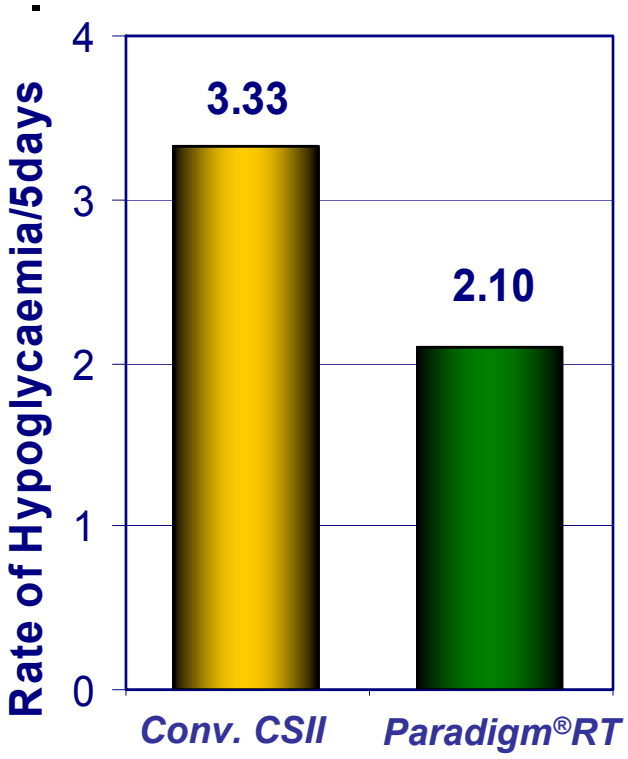
*From: Broz J et al.: Diabetologia 2006, 49 (Suppl. 1); 591-592 and Diabetic Medicine 23 (Suppl. 4) 2006; 292*



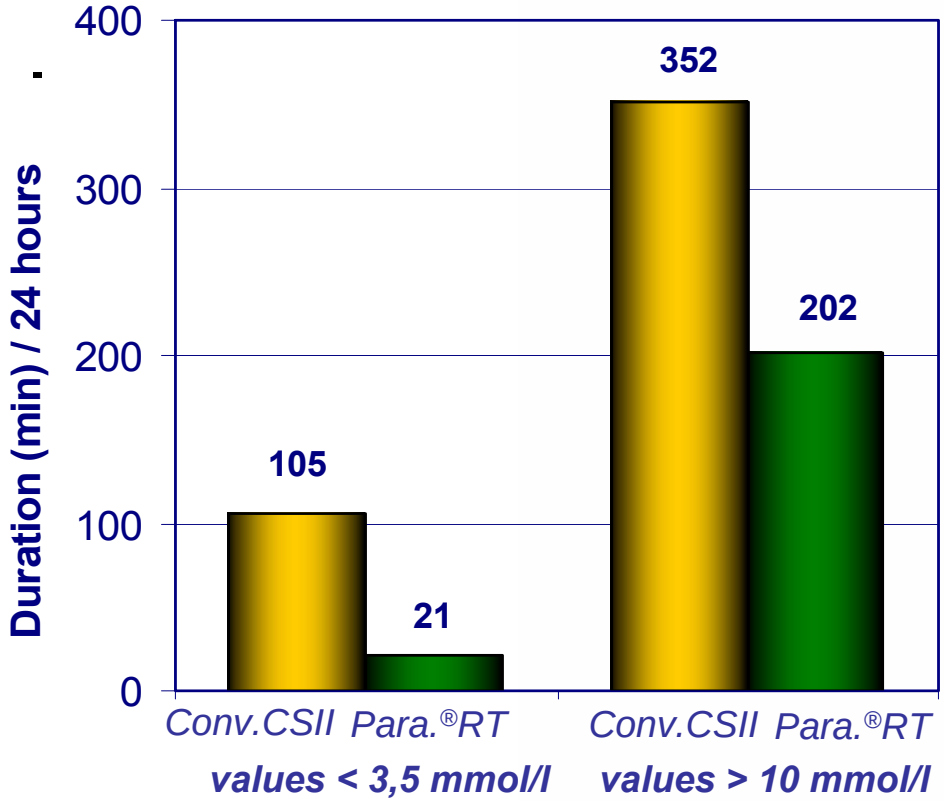
SaPT

# Fewer glycemic excursions when using the Paradigm®REAL-Time System

- Symptomatic hypoglycemia rate over 5 days:




- Duration of glycemic excursions per day:




*From: Broz J et al.: Diabetologia 2006, 49 (Suppl. 1); 591-592 and Diabetic Medicine 23 (Suppl. 4) 2006; 292*

Medtronic

SaPT

# Fewer glycemic excursions when using the Paradigm®REAL-Time System

## Conclusion:

Initial experiences with the Paradigm®REAL-Time system show the contribution of near real-time display of glucose recordings to glycemia improvements during CSII. The time spent in hypoglycemic and hyperglycemic conditions is also reduced as well as the rate of symptomatic hypoglycemia.

Back

*From: Broz J et al.: Diabetologia 2006, 49 (Suppl. 1); 591-592 and Diabetic Medicine 23 (Suppl. 4) 2006; 292*

Medtronic

SaPT

# Sensor augmented pump therapy (SaPT) for children and adolescents

## Statement:

The use of an alarm system based on current glucose values enables the number and duration of hypoglycemic and hyperglycemic deviations to be reduced for younger CSII patients as well. Furthermore, the glucose data can be used for adapting treatment and activities (after confirmation with blood glucose self monitoring).

## Evidence:

Pilot study with 10 children/adolescents (age: 14.1 ± 2.6 years, diabetic for: 9.1 ± 3.3 years, CSII used > 1 year, $HbA_{1c}$: 8.1 ± 0.9 %) over 6 weeks with the Paradigm®REAL-Time system.

Back

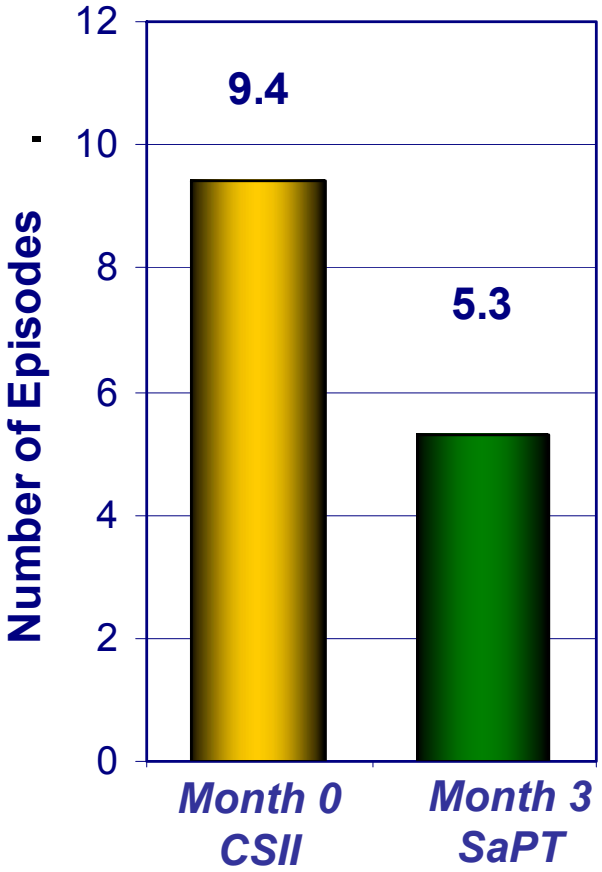
*From: Halvorson RN et al.: Journal of Pediatrics 2007: 103 - 105*

Medtronic

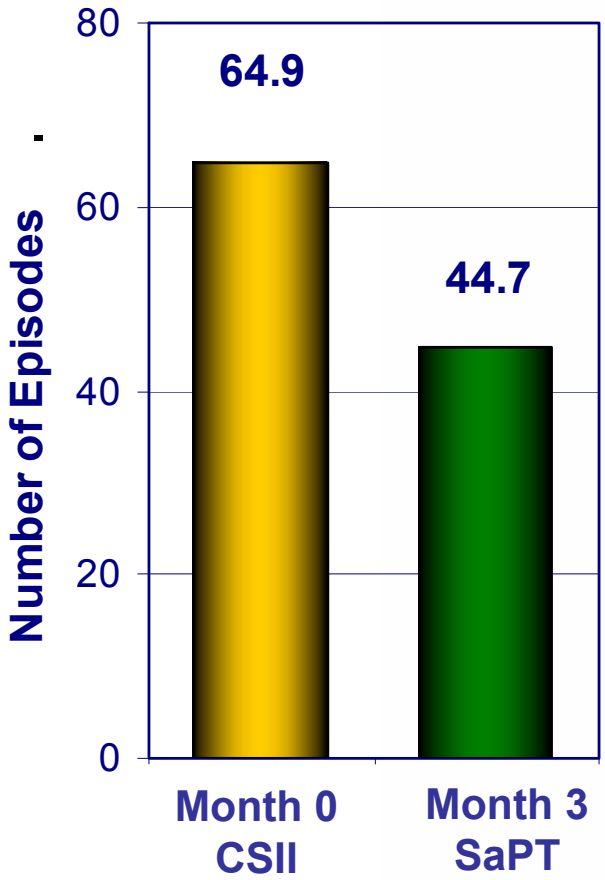
SaPT

# Sensor augmented pump therapy (SaPT) for children and adolescents

- Number detected values < 50 mg/dl over 72 hours:




- Number of detected values >250 mg/dl over 72 hours:



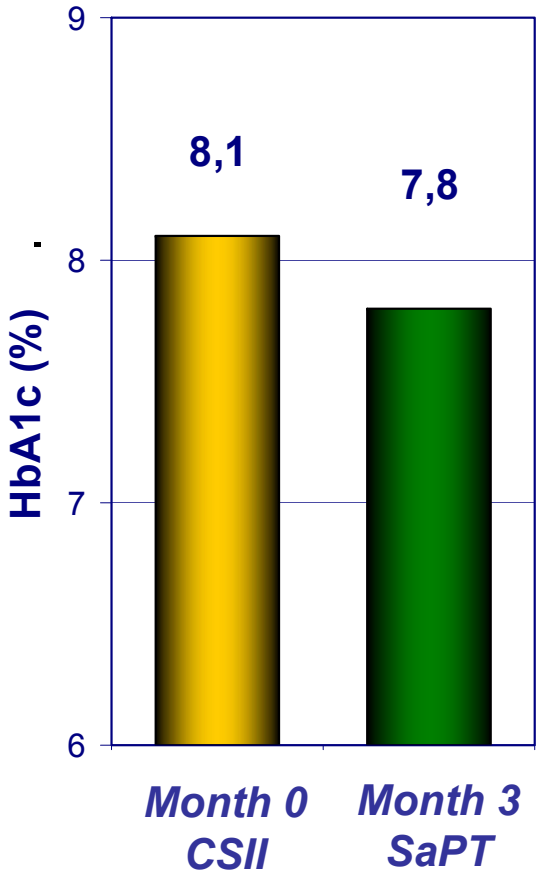

*From: Halvorson RN et al.: Journal of Pediatrics 2007: 103 - 105*

Medtronic

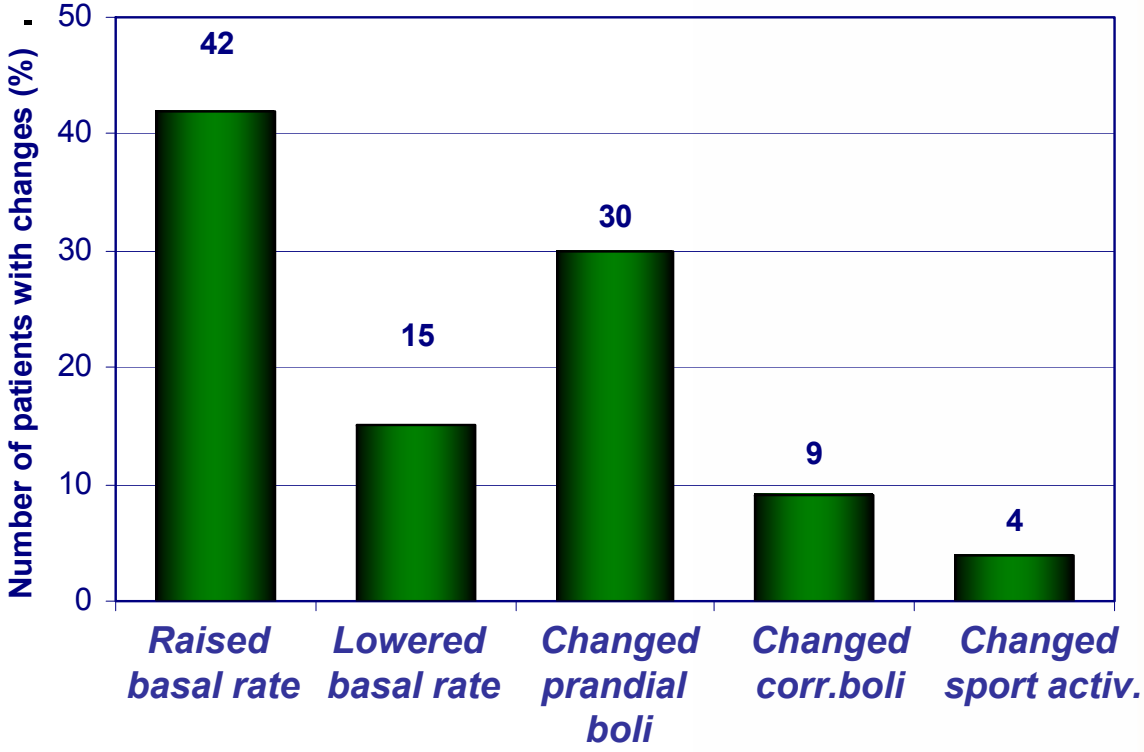
SaPT

# Sensor augmented pump therapy (SaPT) for children and adolescents

- Changes to $HbA_{1c}$ values over 3 months:




- Number of patients with adapted therapy with SaPT:




- The patients made on average 3.2 adjustments

*From: Halvorson RN et al.: Journal of Pediatrics 2007: 103 - 105*

Medtronic

SaPT

# Sensor augmented pump therapy (SaPT) for children and adolescents

## Conclusion:

Patients use current glucose values in order to adapt their therapy. The number of hypoglycemic and hyperglycemic deviations is significantly reduced .

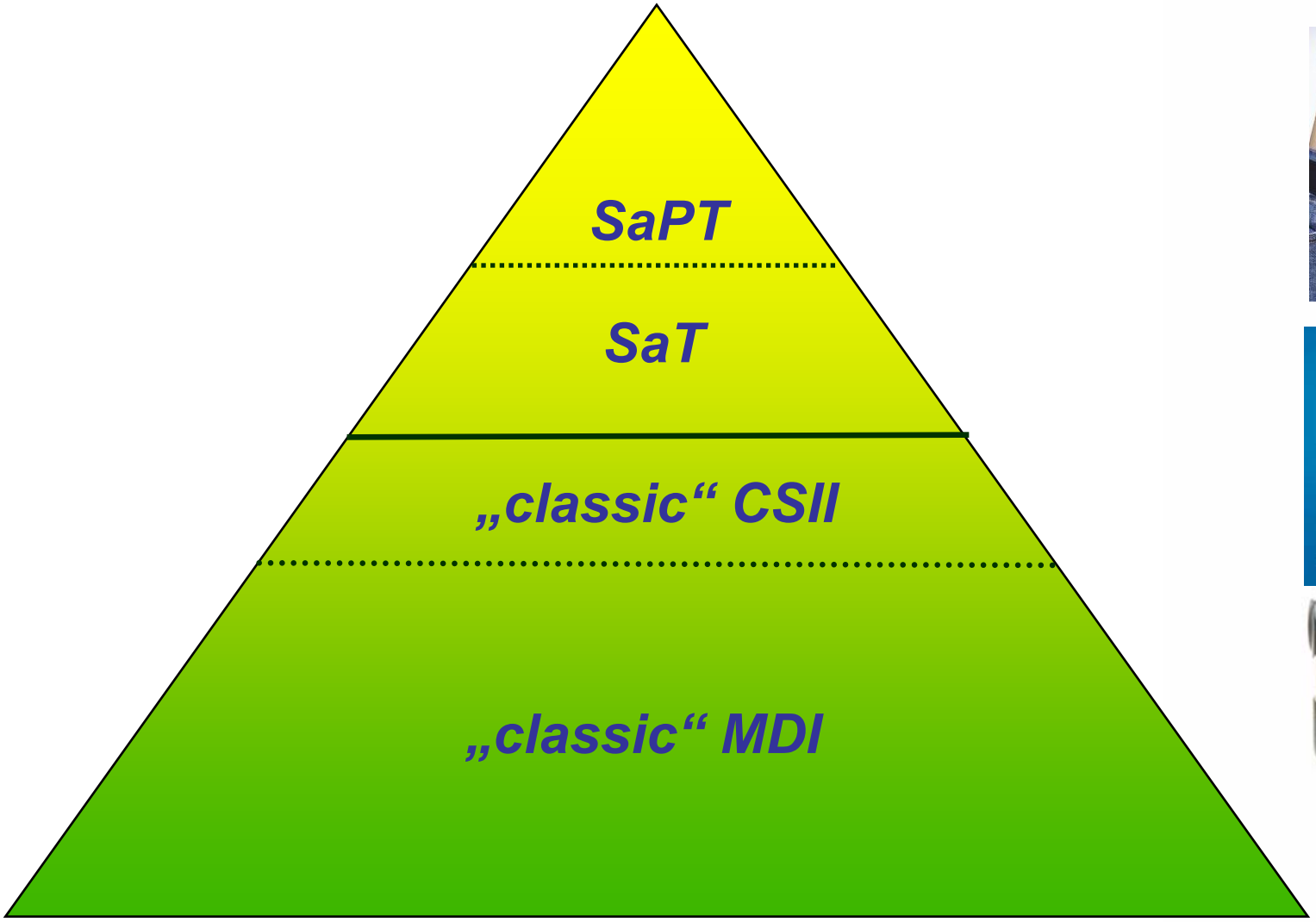
Back

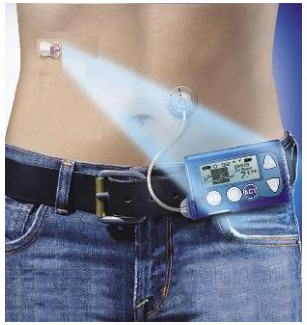
*From: Halvorson RN et al.: Journal of Pediatrics 2007: 103 - 105*

Medtronic

SaPT

# Pyramid of therapy since 2007





*SaT: Sensor augmented (intensified conventional) therapy*

*SaPT: Sensor augmented pump therapy*

Medtronic

SaPT

# Diabetes mellitus treatment and associated diagnostic impacts

| Form of Therapy | BGSM | CGM |
|---|---|---|
| *Non-drug based treatment:* / *Diet / Exercise* | | |
| *Drug based treatment:* / *Therapy with oral antidiabetica* | | |
| *Insulin therapy:* / *Conventional insulin therapy( CT)* | | |
| *Multiple dose injection therapy (MDI)* | | |
| *Insulin pump therapy (CSII)* | | |

*Impact on Treatment*

*Impact on Treatment*

**The more complex the treatment:**

- the greater the opportunity for refined settings
- the more subtle the diagnostic methods must be

*Back*

*BGSM – blood glucose self measurement*

Medtronic


The future has begun, and we will help to shape it.
Medtronic
Schmerzen lindern · Heilung fördern · Leben verlängern