

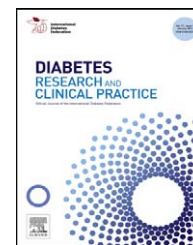


Contents available at Sciverse ScienceDirect

## Diabetes Research and Clinical Practice

journal homepage: [www.elsevier.com/locate/diabres](http://www.elsevier.com/locate/diabres)

International  
Diabetes  
Federation



### Review

# Personal continuous glucose monitoring (CGM) in diabetes management: Review of the literature and implementation for practical use

M. Joubert<sup>a,\*</sup>, Y. Reznik<sup>a,b</sup>

<sup>a</sup> Caen University Hospital, Department of Endocrinology, Caen F-14000, France

<sup>b</sup> Univ Caen, Medical School, Caen F-14000, France

#### ARTICLE INFO

##### Article history:

Received 9 September 2011

Received in revised form

2 December 2011

Accepted 6 December 2011

Published on line 28 December 2011

##### Keywords:

Continuous glucose monitoring

Type 1 diabetes

Type 2 diabetes

Gestational diabetes

Therapeutic education

#### ABSTRACT

**Aim:** Despite recent advances in diabetes therapy including the new long- and rapid-insulin analogs, insulin intensification strategies such as basal/bolus or pump therapy and sophisticated methods for insulin titration derived from the principles of functional insulin therapy, many patients fail to reach or maintain target glycosylated hemoglobin (HbA1c) values, putting them at increased risk for vascular complications. Continuous glucose monitoring (CGM) systems represent an important advance in diabetes technology that can facilitate optimal glucose control in type 1 diabetes.

**Method:** This review focuses on the efficacy and safety of CGM systems in diabetes management. The different CGM devices available are also described, as the way to use them and the educational approach to the patient in a step-by-step progression toward optimal glycemic control.

**Results:** In type 1 diabetes, CGM systems are associated with 0.5–1% reduction in HbA1c without increased risk of hypoglycemia. CGM efficacy correlates with compliance to sensor wear, whatever the patient's age range.

**Conclusion:** Efficacy of CGM systems is now proven but indications, terms of use and educational issues of this new technology still need to be specified.

© 2011 Elsevier Ireland Ltd. All rights reserved.

#### Contents

1. CGM in the management of type 1 diabetes in adults . . . . .	295
1.1. Impact on HbA1c. . . . .	295
1.2. Impact on the incidence, duration and severity of hypoglycemia . . . . .	295
1.3. Impact on glycemic variability . . . . .	298
1.4. Impact of CGM on quality of life. . . . .	298
2. CGM in the management of type 1 diabetic children and adolescents . . . . .	298
3. CGM use in the management of gestational or pre-gestational diabetes . . . . .	298
4. CGM in diabetic patients hospitalized in intensive care. . . . .	299
5. CGM in the management of type 2 diabetes. . . . .	299

\* Corresponding author at: CHU de Caen, service d'endocrinologie, 14033 Caen, France. Tel.: +33 2 31 06 45 75; fax: +33 2 31 06 48 54.

E-mail address: [joubert-m@chu-caen.fr](mailto:joubert-m@chu-caen.fr) (M. Joubert).

0168-8227/\$ – see front matter © 2011 Elsevier Ireland Ltd. All rights reserved.

doi:10.1016/j.diabres.2011.12.010

6.	CGM in practice . . . . .	299
6.1.	Availability of devices . . . . .	299
6.2.	Indications . . . . .	301
6.3.	Terms of use and patient education . . . . .	301
7.	Conclusion . . . . .	303
	Acknowledgements . . . . .	303
	References . . . . .	304

Achieving optimal glycemic control remains a challenge in type 1 diabetes, and about 30% patients exhibit poor glycemic control despite an intensification of insulin therapy using multiple daily injections (MDI) or continuous subcutaneous insulin infusion (CSII) [1]. Observational studies have clearly demonstrated the relationship between the daily number of self-monitored blood glucose (SMBG) tests and glycemic control as expressed by HbA1c. Continuous glucose monitoring (CGM) is a major technological advance, since for the first time in the history of glucose measurement, the patient receives first-order information illustrated by the ball-sports metaphor: “I know the position of the ball in space” together with information of 2nd or 3rd order: “I can appreciate and forecast the motion of the ball”. This paradigm gives the patient and the professional who assists in the educational process the opportunity to achieve a qualitative leap in the understanding of glycemic control.

First, this review will point on the state of the art about the use of CGM in otherwise-healthy adults, children and adolescents with type 1 diabetes patients, and then will consider specific indications such as pregnancy, type 2 diabetes, and hospitalization. Then, various devices for measuring glucose continuously will be described with their terms of use and appropriate education to help patients make optimal use of this new technology.

## 1. CGM in the management of type 1 diabetes in adults

### 1.1. Impact on HbA1c

SMBG has allowed improving glycemic control but many patients fail to lower HbA1c below 7% threshold as recommended by scientific societies [2]. Observational studies have clearly linked the quality of glycemic control with the frequency of daily SMBG in patients treated with insulin [3]. In recent years, several randomized controlled trials clarified the benefits of CGM (Table 1). In 2006, the Guard Control Study conducted in 161 patients including 81 adults with poor metabolic control (HbA1c > 8.1%) evaluated the impact of CGM worn intermittently (3 days every 2 weeks) or permanently. Compared with the control group, the group with permanent CGM monitoring obtained a 0.6% HbA1c decrease after 3 months, while no benefit was obtained by the group wearing sensors intermittently [4]. In 2008, a large JDRF-sponsored study evaluated the impact of CGM compared to SMBG in 322 patients including 98 adults with HbA1c values between 7 and 10%. The study showed in adult subjects (mostly treated with an external insulin pump) an HbA1c decrease of 0.5% ( $p < 0.001$ ), and confirmed that compliance with the device (i.e.  $\geq 6$  days/week) correlated with its effectiveness [5]. In 2009, the ASAP (Australian Sensor

Augmented Pump) study compared in 62 patients (50% adults) with an HbA1c < 8.5% the efficacy of the sensor augmented pump (SAP) in comparison with the sole external pump on metabolic control over a 3-month period. The SAP group realized a 0.43% HbA1c decrease, compared to the CSII group ( $p < 0.01$ ). The wearing of CGM sensors for >70% of the time was also crucial in this study [6]. The same year, the RealTrend study, conducted in 8 French centers and enrolling 132 patients (69 adults), evaluated the contribution of the CGM in uncontrolled type 1 diabetes patients (HbA1c  $\geq 8\%$ ) with multiple daily injections who were switched to insulin pump therapy at the beginning of the study. Over a period of 6 months, an additional  $-0.68\%$  decrease in HbA1c ( $p < 0.001$ ) was observed in 91 patients who wore the device > 70% of the time in comparison with the sole insulin pump, while the analysis of the whole cohort showed that HbA1c decrease was not different between those with or without CGM, due to a lack of compliance in a substantial proportion of patients [7]. In 2010, the STAR 3 study confirmed the advantage for using the sensor augmented pump (SAP) in comparison with MDI. The authors compared the device to MDI treatment in 485 children, adolescents, and adults with type 1 diabetes. In all age groups, a decrease of  $-0.6\%$  HbA1c was shown after 3 months in the SAP group compared to the MDI group ( $p < 0.001$ ), an advantage maintained after 1 year. Moreover, the percentage of patients reaching an HbA1c target < 7% (as recommended by ADA) was significantly higher in the SAP group compared to the MDI group (27% vs. 10% respectively) [8].

The JDRF study confirmed the long term effectiveness of continuous CGM use with visits at 3-month intervals. After 12 months, the mean change in HbA1c level from baseline remained  $-0.4\%$  in adult type 1 patients with a baseline HbA1c > 7% ( $p < 0.001$ ), the median CGM use being 6.8 days per week [12]. The STAR 3 study also showed the long term beneficial effect of SAP compared to MDI over a 12 months study period [8].

Recently, a meta-analysis performed on the individual patient data from six major randomized prospective trials evaluating CGM impact on glucose control showed a mean overall HbA1c decrease of 0.30% for CGM users ( $n = 449$ ) in comparison with patients using SMBG ( $n = 443$ ). This meta-analysis also confirmed that the frequency of sensor usage is a crucial parameter for efficacy of CGM with an additional 0.15% decrease of HbA1c for every one day increase of sensor usage per week [9].

### 1.2. Impact on the incidence, duration and severity of hypoglycemia

The impact of CGM on the occurrence of hypoglycemia has been clarified in randomized trials. In contrast with the DCCT

**Table 1 – Main prospective randomized trials evaluating the impact of CGM on HbA1c in patients with type 1 diabetes.**

Reference	Population (n)	Design	Measures	Glycemic control findings	Detection and reduction of hypoglycemia
O'Connell [6]	62 patients randomized Intention to treat analysis PRT group: 26 CSII group: 29 Open RCT DTI > yr Age: 13-40 yrs CSII+ dose calculator > 3 months HbA1c ≤ 8.5% Sensor wear ≥ 70% SMBG: 4/day Study period: 3 months Mean baseline HbA1c: 7.3%	Assess the impact of patient-led sensor-guided pump management on glycemic control, and compare the effect with standard insulin pump therapy	<i>Primary outcome:</i> Proportion of time in the target (target ranges 4–10 mmol/l). <i>Secondary outcomes</i> HbA1c, time in hypoglycemic (<3.9 mmol/l) and hyperglycemic (≥10.1 mmol/l) glycemic variability	HbA1c was 0.43% lower in the PRT group compared with the CSII group No difference in CGM-derived time in target hypoglycemic or hyperglycemic range or in glycemic variability Within the intervention group, HbA1c was 0.51% lower in participants with sensor use ≥70% compared with participants with sensor use <70%	An apparent effect of sensor usage was noted
Deiss [4]	Type 1 162 adults and children (8–60 years) CSII = 78, MDI = 84 3 groups of 54 pts Guardian RT Continuously 3 days every 2 weeks SMBG	To determine whether patients with poor glycemic control as evidenced by HbA1c ≥ 8.1% can achieve improved metabolic control using the real-time blood glucose values of the Guardian TM RT compared to conventional Self-Monitoring Blood Glucose finger-sticks (control group) after 12 weeks of continuous use	<i>Primary outcome</i> HbA1c at 3, 6 months <i>Secondary outcomes:</i> Fructosamine 3-day Mean Blood Glucose Hypoglycemic and Hyperglycemic excursions AUC	HbA1c significantly lower (0.4% at 3 months and 0.6 at 6 months) between continuous and control groups in the whole population	AUC reduction at 3 and 6 months for values >190 mg/dl and <70 mg/dl
Raccach [7]	Type 1 (≥1 year) Treated with basal/bolus MDI 132 patients (51 children, 81 adults) 2–65 years HbA1c ≥ 8% CGM worn > 70% of study duration n = 55 treatment group (sensor augmented pump) PRT n = 60 control group (insulin pump) CSII Per protocol population: (Sensor worn ≥ 70%) n = 32 PRT n = 59 CSII	To assess whether type 1 diabetic patients treated with Multiple Daily Injections and in poor metabolic control can improve using the Paradigm <sup>®</sup> Real Time system compared to conventional Self-Monitoring Blood Glucose and Continuous Subcutaneous Insulin Infusion	<i>Primary outcome</i> HbA1c at 3 and 6 months <i>Secondary outcome</i> Blood glucose variability (mean, AUC above and below target, MAGE, SD), insulin dos	Total population: HbA1c, no significant difference Pre protocol population: significant improvement in favor of treated group From beginning of study to end: 1.23% (PRT group) vs. 0.57% (CSII group) in the per protocol population Significant improvement in hyperglycemic parameters in the PRT group	Treatment with sensors works if patient wear sensors ≥ 70% of the time without any increase in hypoglycemic parameters

JDRF [5]	Type 1 diabetes ≥8 years of age A1C ≤ 10% with no lower limit Naïve to sensor use up to 6 months Intensive treatment (pump or MDI) Age brackets: 98 patients ≥ 25 years 110 patients 15–24 years 114 patients 8–14 years	To assess the safety and efficacy of continuous glucose monitoring in adults and children with type 1 diabetes	<i>Primary outcome</i> HbA1c at 6 months <i>Secondary endpoints:</i> Reduction in glucose variability Frequency of sensor use	HbA1C: Adults (≥25 years) –0.50, significant difference treated group vs. control group Adolescents (15–24 years) no SD Children (8–14 years) no SD Sensor use (more than 6 days/week during 6 months): adults 83%, adolescents: 30%, children: 50% Time spent within target: significantly greater in the CGM group than in the control group ( $p < 0.0001$ ) for adults, no significant changes in any of the secondary outcomes in the children and adolescents groups	Use of sensors was greater in patients who were in the ≥ 25 years of age group and correlated with an HbA1c improvement Sensor use declined over time in the 8–14, and 15–24 age groups
Star 3 [8]	Type 1 diabetes Treated with MDI Age: 18–65 years HbA1c average 8.3% 2 groups randomized: Pump + CGM Multi-injections Study period: 12 months	To assess efficacy of pump coupled to continuous glucose monitoring compared to MDI and SMBG	<i>Primary outcome</i> HbA1c at 52 weeks <i>Secondary endpoints:</i> % of patients obtaining an HbA1c < 7.0% Impact on hypoglycemia	HbA1c after 3, 6, 12 months: PRT group –0.8% vs. –0.2% compared with the control group, $p < 0.001$ Benefit for adults, children and adolescents % of patients with HbA1c < 7.0%: 27% in the CGM group vs. 10% in MDI group ( $p < 0.001$ ). No difference on hypoglycemia	Superiority of the system pump + CGM compared to conventional therapy by multiple injections in type 1 diabetics poorly controlled, regardless of age
JDRF hypo [13]	Type 1 diabetes Multiple injections Age 18–65 HbA1c < 7% Randomization: Pump + CGM Pump only Study period: 6 months	Evaluate the benefit of CGM in type 1 diabetes children or adults with good glycemic control	<i>Primary endpoint:</i> Time variation in hypoglycemia (<70 mg/dl) <i>Secondary endpoints:</i> HbA1c at 26 weeks % of patients with hypoglycemia	Reduced frequency of hypoglycemia (<70 mg/dl) (54 vs. 91 mn (difference NS), Significant decrease in blood glucose <60 mg/dl ( $p = 0.05$ ) Significant reduction in time away from the goal (70–180 mg/dl): 377 mn CGM group vs. 491 mn control group, $p = 0.003$ HbA1c < 7% in 88% CGM group vs. 63% control group, $p < 0.001$	CGM is useful in type 1 diabetes well balanced to reduce the impact of hypoglycemia and improve glycemic control

CGM: continuous glucose monitoring, AUC: area under the curve, MAGE: mean amplitude of glucose excursion.

study showing that intensification of glycemic control was accompanied by an increased incidence of hypoglycemia [10], improvements of glycemic control with the use of CGM seen in the JDRF, ASAP, RealTrend, and STAR 3 studies were not accompanied by increases in the number of hypoglycemic episodes [5–8]. In a study including 71 patients, Bode et al. observed that subjects using a CGM system (with an alarm for hypoglycemic episodes) spent less time in hypoglycemia (–23.8 min/day) [11]. These data were confirmed in another study with a similar methodology: 14 patients with type 1 diabetes consecutively used a CGM system with or without hypoglycemic alarm (threshold 80 mg/dl). The set alarm group reduced the incidence of hypoglycemia (CGM readings  $\leq 65$  mg/dl) by 44% as well as the time spent below this hypoglycemic threshold by 64% without increasing average BG levels. However, the alarm status – i.e. set or unset – had no effect on the incidence of symptomatic hypoglycemia [12]. The JDRF study group conducted a study in 129 (50% adults) patients with fair metabolic control (HbA1c  $< 7\%$ ), under intensified insulin therapy, in order to evaluate the benefit of CGM on hypoglycemia. The study concluded that the time spent in hypoglycemia ( $< 0.60$  g/l) was reduced by CGM use (18 min vs. 35 min per day,  $p = 0.05$ ). Nevertheless, the rate of severe hypoglycemia was not influenced by CGM use [13]. Battelino et al. recently reported a study questioning the impact of CGM on hypoglycemia in type 1 diabetes with a basal HbA1c below 7.5%. Among the 120 patients (67% CSII, 33% MDI) enrolled, 58 used CGM (vs. 62 SMBG) for a period of 26 weeks. The primary outcome, time spent in hypoglycemia ( $< 63$  mg/dl), was reduced in the CGM group by 41% (mean 0.48 h/day vs. 0.81 h/day) in pump users and by 59% (0.49 vs. 1.20) in subjects on multiple daily injections ( $p = 0.03$ ). In this study, no severe hypoglycemia was reported in each group [14].

### 1.3. Impact on glycemic variability

The level of oxidative stress correlates fairly with glycemic variability in preclinical studies but less consistently in experimental settings performed in type 2 diabetic patients. The relation between glycemic variability and micro- and macrovascular complications is more controversial [15]. However, glycemic variability is associated with severe hypoglycemia in insulin treated patients [16,17]. A study from Garg et al. showed that CGM use resulted in a 23% decrease in the incidence of postprandial hyperglycemia [18]. In the RealTrend study, glucose variability indices calculated from retrospective CGM data analysis in both groups of patients (with and without access to real-time CGM data) were favorably modified in the group with real-time data access as evidenced by daily SD (standard deviation) and MAGE (Mean Amplitude of Glucose Excursion) index lowering [7].

### 1.4. Impact of CGM on quality of life

Quality of life (QoL) was assessed in the JDRF study by general health-related and diabetes-specific questionnaires. After 26 weeks of CGM use, most QoL parameters remained unchanged. However, questions designed to evaluate anxiety or ability to avoid hypoglycemic events improved significantly in

the CGM group ( $p < 0.05$ ) [19]. An “online” Internet study about medical devices was conducted in 311 type 1 diabetics patients treated with SAP ( $n = 162$ ) or SMBG ( $n = 149$ ). Its aim was to assess the level of satisfaction, the impact of the devices on daily life, social events and psychological well-being. CGM users reported a feeling of improved efficiency and a greater satisfaction with the medical device, while QoL parameters were not significantly affected by the use of CGM [20].

## 2. CGM in the management of type 1 diabetic children and adolescents

Use of an ambulatory glucose monitoring system in children has shown that almost all children experienced asymptomatic postprandial and nocturnal hypoglycemia [21]. The long-term use of CGM in children has been evaluated in several studies, all concluding that the favorable effect of the device on glucose control was critically dependent on appropriate use of the device and especially on adequate compliance. The study using the DirecNet GlucoWatch showed no benefit of CGM, but device compliance was low [22]. The JDRF study examined the impact of CGM in 114 children over 8 years and in 110 adolescents with poor glycemic control (HbA1c  $> 7\%$ ). After 6 months of use, the reduction in HbA1c was modest (–0.2 to –0.3%) in those children wearing the CGM device in comparison to the control group. Compliance was poor among these subjects – the device was carried more than 70% of the time respectively in only 50% and 30% – but compliant children and adolescents obtained an HbA1c decrease of –0.8% without any increase in hypoglycemia [5]. This beneficial effect was maintained after 12 months in the compliant pediatric subgroup [23]. In the STAR 3 study, the same degree of glycemic improvement was observed among children and adolescents compared with adults [8]. In the JDRF study, the frequency of severe hypoglycemia was 11.2 events per 100 patient-years among the whole pediatric cohort, much lower than the 86 events per 100 patient-years reported in the historical DCCT cohort [5,24]. The Onset study [25] analyzed the impact of initiating SAP vs. pump-only therapy at the onset of diabetes in 160 children age 1–16 years. After 1 year, an improvement in HbA1c (–0.5%,  $p < 0.05$ ) was observed in the subgroup of children wearing the CGM device regularly, whatever the patient’s age. This study also showed a decrease frequency of severe hypoglycemic events and a decrease of glycemic variability, in comparison to the control group. In addition, basal C-peptide was preserved, but only in the adolescent subgroup. This study is the first to demonstrate the efficacy of a regular use of CGM (at least one sensor per week) in young children upon discovery of the disease.

## 3. CGM use in the management of gestational or pre-gestational diabetes

Strict glycemic control is of paramount importance during pregnancy to reduce the risk of fetal or obstetrical complications [26–28]. In a pilot study performed in 6 women with type



1 diabetes using CGM compared to matched patients using SMBG, CGM resulted in a decrease of HbA1c while it worsened in the SMBG group. Furthermore, fetal macrosomia did not occur in the CGM group in contrast with 2/6 in the SMBG group [29]. Yogeve et al. have described the normal glucose profile in normal-weight pregnant non-diabetic women, and observed a fasting glucose level of  $75 \pm 12$  mg/dl and mean daily glucose of  $110 \pm 16$  mg/dl. In contrast, non-diabetic obese women exhibited an abnormal glucose profile characterized by relative post-prandial hyperglycemia and lower nocturnal blood glucose levels [30]. Normal glucose levels measured by CGM have to be defined in women during pregnancy in order to allow more stringent control of blood glucose and hence reduce the obstetrical risk associated with minor abnormalities of glucose. Large studies are needed during pregnancy (type 1 or type 2 diabetes, gestational diabetes), to explore the effect of real time CGM on pregnancy and fetal prognosis.

#### 4. CGM in diabetic patients hospitalized in intensive care

Reaching a normal glucose target is an important issue for the treatment of different medical and surgical conditions in the intensive care unit (ICU) that may influence both morbidity and mortality. In 2001, Van De Berghe showed a mortality reduction in surgical ICU patients as a result of intensified blood glucose management, but later studies and a meta-analysis failed to confirm these results [31–33]. Several authors have drawn attention to the potential risk associated with unrecognized hypoglycemia in the setting of intensive insulin therapy [32,34]. The measurement of glucose in the ICU raises methodological problems since the accuracy of conventional devices for capillary blood glucose measurement may be compromised by several confounding factors including intensive oxygen therapy, acidosis, hypotension, hypothermia, electrolyte or protein imbalances, or vasoactive drugs. An Austrian study recently explored the effect of CGM in the ICU: 124 subjects receiving mechanical ventilation and intensive insulin therapy were randomly assigned to classical capillary blood glucose monitoring or real time CGM. In each group, on the basis of glucose values (capillary or interstitial), ICU nurses guided insulin therapy according to an insulin titration algorithm. Rate of hypoglycemia was significantly lower in the real-time CGM group than in the control group (1.6% vs. 11.5%,  $p = 0.0312$ ). Relative risk reduction for severe hypoglycemia was 86% using real-time CGM. However, percentage of time at a glucose level  $< 110$  mg/dl ( $59.0 \pm 20\%$  vs.  $55.0 \pm 18\%$  in the control group,  $p = 0.245$ ) and the mean glucose level ( $106 \pm 18$  mg/dl vs.  $111 \pm 10$  mg/dl in the control group,  $p = 0.076$ ) could not be improved using real-time CGM [35]. The same group also evaluated the accuracy and reliability of CGM in critically ill patients: they compared two thousand forty-five CGM sensor glucose values from 174 critically ill patients on intensive insulin therapy, with arterial reference blood glucose levels. They showed a strong correlation between the two methods (Pearson correlation coefficient: 0.92) with a mean difference between CGM and reference values of  $-2$  mg/dl (confidence interval:  $-2$  to  $-1$ ) [36].

#### 5. CGM in the management of type 2 diabetes

In contrast with type 1 diabetes, CGM has been incompletely evaluated in the management of type 2 diabetes. Most studies were performed on small patient samples and evaluated the ability of 3-day blinded, retrospective CGM recordings to identify abnormal glycemic excursions. However, Yoo et al. evaluated whether real-time CGM helps to induce a behavioral change in patients' diet and exercise habits; the authors conducted a randomized controlled trial in 65 poorly controlled patients treated with oral anti-diabetic drugs, insulin, or both. All patients received lifestyle and dietary advice. Patients from the intervention and control group were trained for CGM or SMBG respectively. The CGM device was worn 3 days per month for 3 consecutive months, and patients in the CGM group were instructed to adjust their physical exercise and carbohydrate intake in case of hyperglycemia. The use of CGM had a favorable impact on HbA1c in the intervention group ( $-1.1\%$  vs.  $-0.4\%$  for the control group,  $p = 0.004$ ) and was associated with weight loss, increased physical activity, and reduction of calorie intake [37]. Another study recently conducted has shown similar results on HbA1c in a population of 100 patients with type 2 diabetes treated with oral antidiabetic drugs and/or basal insulin. They were randomized to SMBG or intermittent real-time CGM during 12 weeks: at the end of this study, decline in A1C was  $1.0\%$  ( $\pm 1.1\%$ ) in the CGM group and  $0.5\%$  ( $\pm 0.8\%$ ) in the SMBG group ( $p = .006$ ). Compliance to the device seems once again a major point, even in type 2 diabetic patients, because those who used the CGM for  $\geq 48$  days (per protocol) reduced their A1C by  $1.2\%$  ( $\pm 1.1\%$ ) vs.  $0.6\%$  ( $\pm 1.1\%$ ) in those who used it  $< 48$  days ( $p = 0.003$ ) [38]. Medico-economic studies integrating all modifiable parameters should be conducted to validate the use of CGM as a self-monitoring and educational tool in type 2 diabetes.

#### 6. CGM in practice

##### 6.1. Availability of devices

Five CGM devices are currently available in the EU countries: Paradigm Real-Time (Medtronic), Paradigm Veo (Medtronic), Freestyle Navigator (Abbott), Seven Plus (Dexcom) and Gluco-Day (Menarini).

For the Menarini device, the sensor is not inserted in the body and operates on the principle of micro-dialysis. All other CGM devices operate on the same principle: an electrochemical sensor is inserted into the subcutaneous tissue where it measures interstitial glucose levels continuously. This sensor is physically connected to a transmitter that sends data to a receiver via telemetry. The system needs to be calibrated with capillary glucose tests. For Paradigm systems, it is possible to use a glucose meter that automatically transmits the blood glucose value to the receiver by telemetry (Contour Link, Bayer). If calibrations are performed according to manufacturers' recommendations, data regarding interstitial glucose value, curves representing the evolution of this rate over the last few hours, as well as arrows showing the direction and

**Table 2 – Main technical characteristics and use of CGMperso available in European countries (data from manufacturers).**

	Paradigm Real Time	Paradigm Veo	Navigator	Seven Plus	GlucoDay S
Company	Medtronic		Abbott	Dexcom/Novalab	A. Menarini Diagnostics
Sensor					
Technology	Glucose-oxidase/bovine serum albumin		Glucose-oxidase/osmium	Glucose-oxidase	Glucose-oxidase
Length (mm)	20		5	13	20 (Microdialysis Probe)
Insertion	45°		90°	45°	Disposable Inserter
Life (days)	6		5	7	2
Transmitter					
Technology	Radio frequency		Radio frequency	Radio frequency	NA
Size	3.5 × 3		5.2 × 3.1 × 1.1	3.8 × 1.5 × 1	7.5 × 11 × 2.5
Weight (g)	10		13.6 (battery included)	6.7	245
Energy	Internal battery rechargeable		Battery	Internal battery non-rechargeable	Battery
Autonomy	14 days		30 days	18 months	2 days
Life (months)	6–9		24	18	NA
Receiver					
Perimeter	2		3	1.7	NA
Reception (m)					
Size (cm)	Pump 522: 7.1 × 5.1 × 2.0 Pump 722: 8.9 × 5.1 × 2.0	Pump 554: 7.1 × 5.1 × 2.0 Pump 754: 8.9 × 5.1 × 2.0	8.2 × 6.3 × 2.2	11.4 × 5.8 × 2.2	NA
Coupled pump	Yes		No	No	No
Integrated blood glucose monitor	No		Yes (automatic calibration)	No	No
Integrated blood glucose monitor	Yes (Contour Link - Bayer)		NA	No	No
Calibration					
Initial calibration period without results	2 h		1 h	2 h	2–6 h
Number of calibration	1/12 h minimum 3/day recommended		5 in 5 days (1 h, 2 h, 10 h, 24 h, 72 h)	1/12 h minimum	1/day
Optimal conditions for calibration	No arrow on the screen		Automatic detection of optimal conditions	No cons-indication to the calibration	No cons-indication to the calibration
Interstitial glucose					
Unit	mg/dl		mg/dl	mg/dl	mg/dl and mmol/L
Frequency of updating (min)	5		1	5	3
Maximum lag in hyperglycemia (min)	10		ND	ND	ND
Maximum lag in hypoglycemia (min)	4		ND	ND	ND
Average lag (min)	ND		10–15	5	ND
Glucose curves in real time					
Retrospective consultation of glucose values on the receiver	Yes		No	No	Yes
Retrospectively analyzing time range (h)	3–24	3–6–12–24	2–4–6–12–24	1–3–6–12–24	NA
Trend arrows					
Pictograms and meaning (mg/dl/min)	↑↑: >+2 ↑: +1 to +2 No arrow: –1 to +1 ↓: –1 to –2 ↓↓: <–2		↑: > +2 ↗: +1 to +2 →: –1 to +1 ↘: –1 to –2 ↓: <–2	↑↑: >+3 ↑: +2 to +3 ↗: +1 to +2 →: –1 to +1 ↘: –1 to –2 ↓: –2 to –3	NA NA NA NA NA

Alarms			↓↓: <−3	NA
Hypo/hyperglycemia	Yes		Yes	Yes
Predictive hypo/hyperglycemia	No		No	No
Rate of glycemic progression	No	Yes (5–30 min before)	Yes (10, 20 or 30 min before)	No
Stop basal rate if hypo	No	Yes (adjustable from 1.1 to 5 mg/dl/min)	Yes (>2 or 3 mg/dl/min)	No
Exploiting of historical data			NA	NA
Memory (days)	90		30	NA
Medical Software	Care Link Pro		Data Manager 3	GlucoDay S
Patient Software	Care Link Personal		Data Manager 3	NA

ND: not determined and NA: not applicable.

speed of change of the rate are available to the patient. Changes in the rate of interstitial glucose values are not quite in real time: there is a lag of between 4 and 15 min on the glycemic variability, because of technical limitations of current technology. All systems also have alarms for hypo- or hyperglycemia that alerts the patient when the glucose concentration crosses below or above a configured threshold. The Freestyle Navigator device also has predictive alarms, indicating to the patient a high probability of occurrence of hypo- or hyperglycemia 10, 20 or 30 min in the future. For the Seven Plus, there are trend alarms, indicating a high rate of change of interstitial glucose levels. The Paradigm Veo allows for all types of alarms (hypo-/hyperglycemia, predictive, and trends).

Paradigm systems are unique in that they combine an insulin pump with CGM technology. In addition, the Paradigm Veo allows for automatic shut-off of basal insulin delivery in case low levels of interstitial glucose are detected.

All data on interstitial glucose (and data concerning the functioning of the insulin pump for Paradigm devices) are stored in the memory of the receiver, allowing patients and/or physicians to download and review data at a later time.

The main technical characteristics and use of these devices are presented in Table 2.

## 6.2. Indications

Therapeutic indications for the use of CGM are not yet clearly codified. However, three recent expert recommendation statements list the clinical situations where the use of CGM is recommended: the update of the ADA recommendations for the management of diabetes [39], the AACE (American Association of Clinical Endocrinologists) consensus on the use of CGM [40] and the Endocrine Society clinical practice guidelines for the use of CGM [41].

According to these publications, personal CGM may be recommended (i) to type 1 diabetes patients who do not reach the recommended target HbA1c; (ii) for patients with repeated episodes of hypoglycemia and/or hypoglycemia unawareness, or for subjects who need better glycemic control without increased risk of hypoglycemia; (iii) to maintain an HbA1c < 7% while decreasing the frequency of hypoglycemia [42]; (iv) to achieve an optimal glycemic control in women (diabetes type 1 or 2) for pre-conception and during pregnancy; and (v) finally, to improve unstable – brittle – diabetes. Apart from “high HbA1c level” and “high frequency of hypoglycemia” indications, scientific evidence is lacking for other indications. It is important to mention that the endocrine society recommend against the use of CGM alone for glucose management in the intensive care unit [41].

## 6.3. Terms of use and patient education

Whatever the study population, the main interventional prospective trials have shown a correlation between the improvement in HbA1c and adherence to the use of the sensor [4,5,7,22,42,43]. Unfortunately, there are no reliable criteria predicting a good adherence to the use of the CGM sensor. However, one study has shown that compliance to CGM in children was positively correlated with the number of daily



capillary blood glucose performed previously [44]. Moreover, even if it is difficult to assess across studies, we believe that the understanding and interpretation of data from CGM as well as the relevance of therapeutic interventions are all key elements for effectiveness of these devices. A study also recently showed that, for the initiation of CGM in patients with type 1 diabetes, an algorithm guiding therapeutic responses to this device improved quality of life [45]. This emphasizes the importance of initial guidance for the use of CGM.

There is a repository of training and procedures regarding the use of CGM in the pediatric population but not in adults to our knowledge [46].

In general terms, when prescribing such a device, it is necessary (i) to determine the patient needs and the expected goals of the CGM, (ii) to provide an education adapted to the objective and abilities of the patient and (iii) to accompany the patient in his “first steps” with this technology.

The potential uses of CGM are multiple and still not completely formalized given the recent emergence of this technology. They can be listed in a terminology that reflects the attitude and/or involvement of the patient relative to the device. Here we distinguish (from the most basic to most advanced stage) “passive”, “reactive”, “active”, “proactive” and “educational” use (see below). This didactic classification is not frozen; a patient may change from one use to another over time. Whatever the proposed use, some technical training is mandatory to optimize the reliability of results and safety of use, and includes (i) how to insert a sensor, (ii) the overall functioning of the system, the minimal handling of the receiver and (iii) the provision of blood glucose measurements for calibration of the system. The patient must know optimal conditions for implementing the calibration, especially with Paradigm systems for which the calibration must be performed, if possible, within a period of stable blood glucose.

*Passive use* is the most basic use of CGM and requires minimal patient engagement. For this use, basic technical education is sufficient for obtaining prolonged glucose profiles of 10–15 days (2–3 sensors). Such long-duration studies are often more informative than profiles covering 3–6 days because of large inter-day variability observed in type 1 diabetes patients.

*Reactive use:* In this case, patients are asked to respond to CGM system-generated alarms. Besides minimum technical education, the patient should be trained to understand the lag time between interstitial glucose and blood glucose. The patient should also adjust alarm thresholds to find the best compromise between actionable and so-called “nuisance” alarms. Thus, for example, we may initially set the threshold “hypoglycemia” at 70 mg/dl and ask the patient to progressively increase the threshold in case of authentic hypoglycemia without triggering an alarm (due to the delay or lag). The use of predictive alarms can theoretically mitigate the delay between vascular and interstitial glucose concentrations and thereby improve the performance of the CGM to forecast hypoglycemia. As part of that reactive use, it is possible to provide the patient a protocol to correct hypo- or hyperglycemia according to the alarm.

*Active use* requires regular observation of the device screen by the patient. This use corresponds to the principles of functional insulin therapy (insulin-to-carbohydrate ratios,

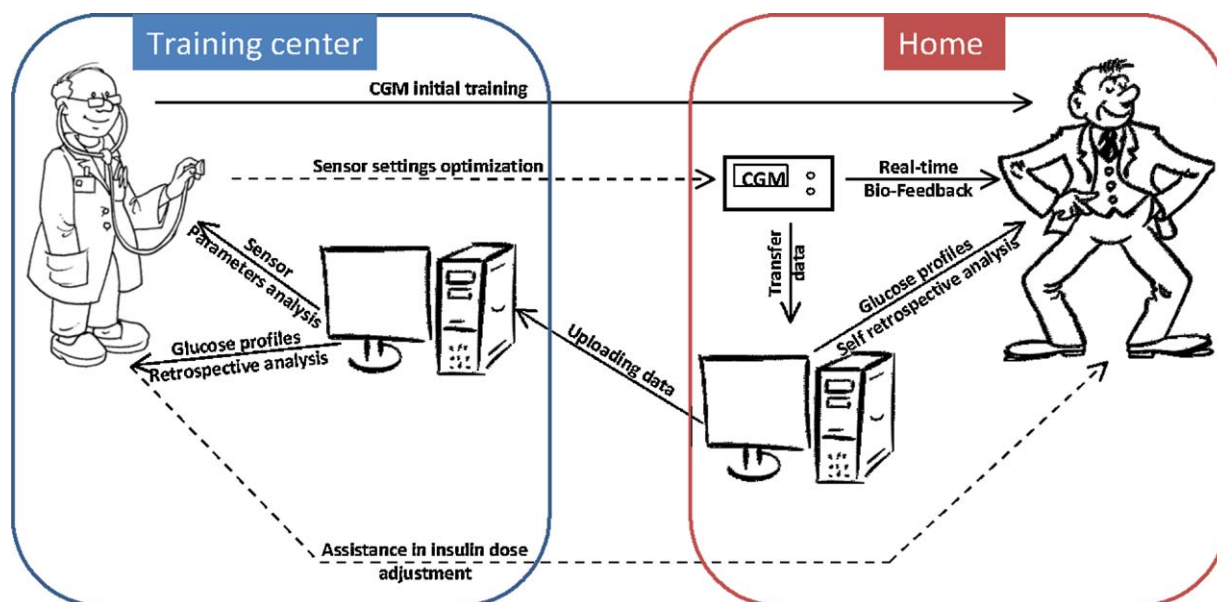
insulin sensitivity estimates for correction boluses, etc.) which are supported by regular reading of the device screen, allowing insulin dose adaptations that will greatly accelerate the improvement of glycemic parameters. Training must integrate the understanding of available data on the screen (interstitial glucose value, tendency arrow, retrospective curve, alarms, symbols, etc.). As part of this active use, the patient will have to master knowledge of functional insulin therapy, necessary for an optimal adjustment of insulin doses. Depending on the diversity of situations and CGM data, patients should take the initiative to adjust insulin, diet and/or physical activity. It is impractical for the caregiver to provide a precise protocol that summarizes appropriate responses in all of these situations.

*Proactive use* will require a different perception by the patient that will use more than static data to anticipate glucose drift: trend information combines the instant value, the arrow (up or down) and the glucose curve of the last hours. Most patients understand intuitively how to use trends but for others, the interpretation of this information can be complex. Simulation through a simple clinical case will identify patients who intuitively perceive the potential uses of trends information to optimize their management. For example, we can ask: “If you do one hour of running with a glycemia at 113 mg/dl, what will you do?” According to their habits, patients will decide to take a snack or to start a temporary basal rate. Then if we ask: “Now, with the technology of continuous glucose monitoring, if you go to one hour of running with a blood glucose level starting at 113 mg/dl and a strong tendency to rise, what will you do?”. Most patients will integrate the interpretation of trends in their glucose value to avoid a systematic attitude (making a snack, start a temporary basal rate) that may prove to be counterproductive. In our experience, this type of reasoning is difficult for patients who do not intuitively understand.

Finally, the *educational use* of this technology with all glucose information in real time, completely transforms the device into a real therapeutic educational tool. In fact, repeated interviews between physician and patient on stored data will target the therapeutic adaptations to be then tested and validated in an iterative process. An analysis plan of glucose profiles with a methodology for treatment adjustments will be needed to focus the patient on different therapeutic changes to be made. In practice, patients will be asked to use CGM data to analyze several scenarios:

- (1) Adjustment of the nocturnal dose of long-acting insulin (or basal during the night if treated by pump).
- (2) Adjustment of rapid analogs insulin (or bolus) for meals.
- (3) Effect of carbohydrates taken in response to hypoglycemia to calibrate sugar intake.
- (4) Kinetics of rapid analog dose (or bolus) in case of hyperglycemia to titrate the right insulin correction.
- (5) Impact of the trend for treatment decisions in different situations.

Prior education to functional insulin therapy before CGM data analysis is, of course, greatly beneficial for an optimal educational use of the device. The devices integrating pump and CGM appear to be most suited to this educational use:



**Fig. 1 – Example of possible use of CGM data when patient and doctor are equipped with software to analyze these data. Dotted arrows indicate actions achievable through telemedicine.**

indeed, they allow parallel analysis of glucose profiles and therapeutic actions taken by patients.

Patients starting with CGM require regular visits with healthcare providers, especially in the first weeks, to optimize the use of the tool. In addition, each contact is an opportunity for the physician to do a retrospective analysis of glucose profiles stored by the device, and to refine the parameters of insulin therapy. Finally, the setting and the progressive adjustment of the various sensor alarms, according to the experiences of the patient, can improve the utility of the system. By contrast, an improper setting of the sensor can increase the number of false alarms and alter the patient's motivation to use the device regularly. Each CGM device can be downloaded with specific software for self retrospective analysis of the glucose data. A software includes a feature that allows the physician to view the patient's glucose profiles remotely via a secure Internet portal, opening prospects of telemedicine for patient support (Fig. 1).

CGM training programs have not yet been standardized. However, given the technical aspects (implementation of the sensor, the transmitter, the receiver) and therapeutic aspects from results of the CGM, it seems essential that education must be done jointly by a nurse, a diabetologist and possibly a dietician and can be achieved during a lengthy outpatient visit. In our experience, excluding special circumstances, recourse to traditional hospitalization is not necessary for initiation of CGM. Optimizing glycemic control with CGM frequently requires pump therapy and/or functional insulin therapy. A trained team specialized in diabetology is preferable to help patients using long term CGM.

The lack of support for CGM by health insurance is of course the main limitation to the current widespread use of these devices: only few countries have partial reimbursement (like Sweden, Nederland, Slovenia, Israel) and several requests for support are being evaluated around the world.

## 7. Conclusion

In type 1 diabetes patients, CGM systems have now clearly proven to be of clinical value in terms of improvement of HbA1c with no increase in hypoglycemia with long-term use. Precise indications for these devices need to be established. Indications will probably be guided first by the reimbursement when applied. Optimal training regimens for these new tools remain unclear, but must emphasize the need for routine use of the sensors to optimize glycemic control. Together with CGM, pump therapy and educational efforts will allow patients to operate appropriately with real time glucose data. It is possible to imagine, once the methodological aspects and the effectiveness of continuous glucose measurement proved by randomized controlled trials, that these systems may, in the future, progressively supplant and replace conventional blood glucose monitoring. Moreover, the development of CGM devices opens the prospect of systems that could automatically adjust insulin delivery according to the interstitial glucose levels in a close-loop fashion.

## Conflict of interest

The authors have a competing interest to declare. M.J. declares advisory services and research fees with Medtronic; Y.R. declares advisory services, research fees and study coordination with Medtronic.

## Acknowledgement

The authors acknowledge Charlotte CAVE (Medtronic, France) for her technical support and Elisabeth ANDRIEUX (Medtronic, France) for her help for translating this manuscript.

## REFERENCES

- [1] Petitti DB, Klingensmith GJ, Bell RA, Andrews JS, Dabelea D, Imperatore G, et al.; for the SEARCH for Diabetes in Youth Study Group. Glycemic control in youth with diabetes: the SEARCH for diabetes in Youth Study. *J Pediatr* 2009;155:668–72.
- [2] Ong KL, Cheung BM, Wong LY, Wat NM, Tan KC, Lam KS. Prevalence, treatment, and control of diagnosed diabetes in the U.S. National Health and Nutrition Examination Survey 1999–2004. *Ann Epidemiol* 2008;18:222–9.
- [3] Haller MJ, Stalvey MS, Silverstein JH. Predictors of control of diabetes: monitoring may be the key. *J Pediatr* 2004;144:660–1.
- [4] Deiss D, Bolinder J, Riveline JP, Battelino T, Bosi E, Tubiana-Rufi N, et al. Improved glycemic control in poorly controlled patients with type 1 diabetes using real-time continuous glucose monitoring. *Diabetes Care* 2006;29:2730–2.
- [5] Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Tamborlane WV, Beck RW, Bode BW, Buckingham B, Chase HP, et al. Continuous glucose monitoring and intensive treatment of type 1 diabetes. *N Engl J Med* 2008;359:1464–76.
- [6] O'Connell MA, Donath S, O'Neal DN, Colman PG, Ambler GR, Jones TW, et al. Glycaemic impact of patient-led use of sensor-guided pump therapy in type 1 diabetes: a randomised controlled trial. *Diabetologia* 2009;52:1250–7.
- [7] Raccach D, Sulmont V, Reznik Y, Guerci B, Renard E, Hanaire H, et al. Incremental value of continuous glucose monitoring when starting pump therapy in patients with poorly controlled type 1 diabetes: the RealTrend study. *Diabetes Care* 2009;32:2245–50.
- [8] Bergenstal RM, Tamborlane WV, Ahmann A, Buse JB, Dailey G, Davis SN, et al. Effectiveness of sensor-augmented insulin-pump in type 1 diabetes. *N Engl J Med* 2010;363:311–20.
- [9] Pickup JC, Freeman SC, Sutton AJ. Glycaemic control in type 1 diabetes during real time continuous glucose monitoring compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data. *BMJ* 2011;343:d3805.
- [10] Diabetes Control and Complications Trial (DCCT) Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;329:977–86.
- [11] Bode B, Gross K, Rikalo N, Schwartz S, Wahl T, Page C, et al. Alarms based on real-time sensor glucose values alert patients to hypo- and hyperglycemia: the guardian continuous monitoring system. *Diabetes Technol Ther* 2004;6:105–11.
- [12] Davey RJ, Jones TW, Fournier PA. Effect of short-term use of a continuous glucose monitoring system with a real-time glucose display and a low glucose alarm on incidence and duration of hypoglycemia in a home setting in type 1 diabetes mellitus. *J Diabetes Sci Technol* 2010;4:1457–64.
- [13] Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Beck RW, Hirsch IB, Laffel L, Tamborlane WV, Bode BW, et al. The effect of continuous glucose monitoring in well-controlled type 1 diabetes. *Diabetes Care* 2009;32:1378–83.
- [14] Battelino T, Phillip M, Bratina N, Nimri R, Oskarsson P, Bolinder J. Effect of continuous glucose monitoring on hypoglycemia in type 1 diabetes. *Diabetes Care* 2011;34:795–800.
- [15] Siegelaar SE, Holleman F, Hoekstra JBL, DeVries JH. Glucose variability; does it matter? *Endocr Rev* 2010;31:171–82.
- [16] Cox DJ, Gonder-Frederick L, Ritterband L, Clarke W, Kovatchev BP. Prediction of severe hypoglycemia. *Diabetes Care* 2007;30:1370–3.
- [17] Kilpatrick ES, Rigby AS, Goode K, Atkin SL. Relating mean blood glucose and glucose variability to the risk of multiple episodes of hypoglycemia in type 1 diabetes. *Diabetologia* 2007;50:2553–61.
- [18] Garg S, Zisser H, Schwartz S, Bailey T, Kaplan R, Ellis S, et al. Improvement in glycemic excursions with a transcutaneous, real-time continuous glucose sensor. *Diabetes Care* 2006;29:44–50.
- [19] Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Beck RW, Lawrence JM, Laffel L, Wysocki T, Xing D, et al. Quality-of-life measures in children and adults with type 1 diabetes: Juvenile Diabetes Research Foundation Continuous Glucose Monitoring randomized trial. *Diabetes Care* 2010;33:2175–7.
- [20] Rubin RR, Peyrot M. Treatment satisfaction and quality of life for an integrated continuous glucose monitoring/insulin pump system compared to self-monitoring plus an insulin pump. *J Diabetes Sci Technol* 2009;3:1402–10.
- [21] Chase HP, Kim LM, Owen SL, MacKenzie TA, Klingensmith GJ, Murtfeldt R, et al. Continuous subcutaneous glucose monitoring in children with type 1 diabetes. *Pediatrics* 2001;107:222–6.
- [22] Chase HP, Beck R, Tamborlane W, Buckingham B, Mauras N, Tsalikian E, et al. A randomized multicenter trial comparing the GlucoWatch Biographer with standard glucose monitoring in children with type 1 diabetes. *Diabetes Care* 2005;28:1101–6.
- [23] Chase HP, Beck RW, Xing D, Tamborlane WV, Coffey J, Fox LA, et al. Continuous glucose monitoring in youth with type 1 diabetes: 12-month follow-up of the Juvenile Diabetes Research Foundation continuous glucose monitoring randomized trial. *Diabetes Technol Ther* 2010;12:507–15.
- [24] DCCT Research Group. The effect of intensive diabetes treatment on the development and progression of long-term complications in adolescents with insulin-dependent diabetes mellitus: the Diabetes Control and Complications Trial. *J Pediatr* 1994;125:177–88.
- [25] Kordonouri O, Pankowska E, Rami B, Kapellen T, Coutant R, Hartmann R, et al. Sensor-augmented pump therapy from the diagnosis of childhood type 1 diabetes: results of the Paediatric Onset Study (ONSET) after 12 months of treatment. *Diabetologia* 2010;53:2487–95.
- [26] Lauenborg J, Mathiesen E, Ovesen P, Westergaard JG, Ekbohm P, Moelsted-Pedersen L, et al. Audit on stillbirths in women with pregestational type 1 diabetes. *Diabetes Care* 2003;26:1385–9.
- [27] Jensen DM, Damm P, Moelsted-Pedersen L, Ovesen P, Westergaard JG, Moeller M, et al. Outcomes in type 1 diabetic pregnancies: a nationwide, population-based study. *Diabetes Care* 2004;27:2819–23.
- [28] Clausen TD, Mathiesen E, Ekbohm P, Hellmuth E, Mandrup-Poulsen T, Damm P. Poor pregnancy outcome in women with type 2 diabetes. *Diabetes Care* 2005;28:323–8.
- [29] Voelmlle M, Gottlieb P, Ellis S, Wallace A, Gerard L. Fetal outcomes and improved A1c values in pregnant women with type 1 diabetes using real-time continuous glucose sensors. *Diabetes* 2007;56(Suppl.). 0440-P [Abstract].
- [30] Yogev Y, Ben-Haroush A, Chen R, Rosenn B, Hod M, Langer O. Diurnal glycemic profile in obese and normal weight nondiabetic pregnant women. *Am J Obstet Gynecol* 2004;191:949–53.
- [31] Van de Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med* 2001;345:1359–67.
- [32] NICE-SUGAR Study Investigators, Finfer S, Chittock DR, Su SY, Blair D, Foster D, et al. Intensive versus conventional

- glucose control in critically ill patients. *N Engl J Med* 2009;360:1283–97.
- [33] Wiener RS, Wiener DC, Larson RJ. Benefits and risks of tight glucose control in critically ill adults: a meta-analysis. *JAMA* 2008;300:933–44.
- [34] Krinsley JS, Grover A. Severe hypoglycemia in critically ill patients: risk factors and outcomes. *Crit Care Med* 2007;35:2262–7.
- [35] Holzinger U, Warszawska J, Kitzberger R, Wewalka M, Miehsler W, Herkner H, et al. Real-time continuous glucose monitoring in critically ill patients: a prospective randomized trial. *Diabetes Care* 2010;33:467–72.
- [36] Brunner R, Kitzberger R, Miehsler W, Herkner H, Madl C, Holzinger U. Accuracy and reliability of a subcutaneous continuous glucose-monitoring system in critically ill patients. *Crit Care Med* 2011;39:659–64.
- [37] Yoo HJ, An HG, Park SY, Ryu OH, Kim HY, Seo JA, et al. Use of real time continuous glucose monitoring system as a motivational device for poorly controlled type 2 diabetes. *Diabetes Res Clin Pract* 2008;82:73–9.
- [38] Ehrhardt NM, Chellappa M, Walker MS, Fonda SJ, Vigersky RA. The effect of real-time continuous glucose monitoring on glycemic control in patients with type 2 diabetes mellitus. *J Diabetes Sci Technol* 2011;5:668–75.
- [39] American Diabetes Association. Standards of medical care in diabetes-2011. *Diabetes Care* 2011;34(Suppl. 1):S11–61.
- [40] Blevins TC, Bode BW, Garg SK, Grunberger G, Hirsch IB, Jovanović L, et al. Statement of the American Association of Clinical Endocrinologists consensus panel on continuous glucose monitoring. *Endocr Pract* 2010;16:730–45.
- [41] Klonoff DC, Buckingham B, Christiansen JS, Montori VM, Tamborlane WV, Vigersky RA, et al. Continuous glucose monitoring: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2011;96:2968–79.
- [42] Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Bode B, Beck RW, Xing D, Gilliam L, Hirsch I, et al. Sustained benefit of continuous glucose monitoring on A1C, glucose profiles, and hypoglycemia in adults with type 1 diabetes. *Diabetes Care* 2009;32:2047–9.
- [43] Hirsch IB, Abelson J, Bode BW, Fischer JS, Kaufman FR, Mastroianni J, et al. Sensor-augmented insulin pump therapy: results of the first randomized treat-to-target study. *Diab Technol Ther* 2008;10:377–83.
- [44] Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Beck RW, Buckingham B, Miller K, Wolpert H, Xing D, et al. Factors predictive of use and of benefit from continuous glucose monitoring in type 1 diabetes. *Diabetes Care* 2009;32:1947–53.
- [45] Jenkins AJ, Krishnamurthy B, Best JD, Cameron FJ, Colman PG, Hamblin PS, et al. An algorithm guiding patient responses to real-time-continuous glucose monitoring improves quality of life. *Diabetes Technol Ther* 2011;13:105–9.
- [46] Diabetes Research in Children Network (DirecNet) Study Group, Buckingham B, Xing D, Weinzimer S, Fiallo-Scharer R, Kollman C, et al. Use of the DirecNet Applied Treatment Algorithm (DATA) for diabetes management with a real-time continuous glucose monitor (the FreeStyle Navigator). *Pediatr Diabetes* 2008;9:142–7.