How technology has changed diabetes management and what it has failed to achieve

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Abstract

Tremendous improvements have modified diabetes management from pure clinical diagnosis and the discovery of insulin to continuous subcutaneous insulin infusion (CSII) coupled with continuous glucose monitoring (CGM) to allow patients to adapt insulin delivery to glycaemia on a virtually “real-time” basis. Insulin was first discovered in 1923 and, in less than a century, it has been purified, humanized and now synthesized by genetically modified microorganisms. Insulin analogue, kinetics and reproducibility now allow near-normal glycaemia to be targeted without increasing hypoglycaemia, thus allowing greater flexibility in the patient’s day-to-day life. In addition, advances have been made over the past few decades in the development of the necessary and complementary technologies for insulin infusion, glucose measurement, glucose insulin interaction and telemedicine. The major remaining limitations are the lack of glycaemic regulation on insulin administration and the burden of parenteral delivery. Thus, the dream of both patients and diabetologists is to close the loop and to build an artificial pancreas.

Keywords: Type 1 diabetes; Diabetes technology evolution; Continuous insulin infusion; Continuous glucose monitoring; Sensors; Review

1. Introduction

Diabetes was first described by the Ancient Greek physician Aretaeus of Cappadocia, who first coined the term “diabetes”. In Ancient India, diabetes was called “sweet urine disease”; they had observed that ants were attracted to the patients’ urine, and this became a positive test for the disease. Later, European physicians would taste urine samples to identify whether or not it had a “sweet” taste.

The big step for physicians in this field was dosing of glucose in venous glycaemia coupled with urine strips. This “security glycosuria” to avoid hypoglycaemia was, at the time, the admitted dogma; it impressed upon diabetic patients the notion of insulin dose adaptation, hypoglycaemia preservation...

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and microangiopathic complications. A significant correlation between long-term metabolic control and fewer chronic diabetes complications was shown in the Diabetes Control and Complications Trial (DCCT) [1], which involved modifying diabetes management and aimed for “near-normal glycaemia” coupled with a low frequency of hypoglycaemia. To achieve this goal, new tools were developed.

2. The first technical tool: Urine-testing

The first method for assessing glycaemic status was the urine strip, which measures glucose and ketones; however, results were delayed depending on vesical repletion [2]. Urine was tested regularly to allow adaptation of insulin doses, and glycosuria without ketones was the goal to achieve at bedtime [2]. Ketonuria associated to glycosuria indicates a catabolic state and the breakdown of fat; in this case, the patient was advised to take measures to keep well-hydrated, to take extra insulin and to test again every 2h.

The measurement of ketonaemia was a huge improvement to day-to-day diabetes management, as patients were more compliant with testing blood than urine; ketonaemia is also more reliable, has no delay and responds quickly, thereby immediately demonstrating the efficacy of any therapeutic decisions made. Furthermore, this tool is easier to use as the patient can use the same blood drop to measure ketonaemia. Few glucometers provide this function. The strips are reimbursed in France for type 1 diabetes (T1D) patients for continuous subcutaneous insulin infusion (CSII) and during pregnancy.

3. Self-monitoring of blood glucose: A revolution for patients and physicians

In 1969, the first glucose monitoring device (Ames Reflectance Meter) appeared. It was based on glucose oxidase and assessed glucose levels in a 50 μL blood sample. In the 1970s, self-monitoring of diabetes became available with the creation of the personal glucose monitor (Fig. 1A), which allowed multiple capillary blood glucose tests, insulin dose adaptation and, thus, better glucose control in terms of both hyper- and hypoglycaemia.

Self-monitoring of blood glucose (SMBG) devices were widely introduced in the early 1980s and became commonplace in the 1990s as a replacement for urine testing to allow diabetic patients to assess their current level of glycaemia. Patients were taught how to use these SMBG readings to guide their decisions for immediate treatment. It has been shown to be an essential component in the intensive management of T1D patients.

Compared with the older devices, SMBG instruments are now smaller, with design improvements: most of them no longer require changing codes when switching strip batches (no coding feature), and they now give their results in <5s from only 0.5 μL of blood. Haematocrit, peritoneal dialysis and blood oxygenation, as well as alternative puncture sites (arm, ear), are also less likely to interfere with the dosage.

Analytical or statistical accuracy of SMBG systems is necessary between reference and SMBG values to prevent the possibility of serious errors in treatment decision-making. The American Diabetes Association (ADA) has suggested

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Fig. 1. Improvements in glucose monitoring and insulin syringes: A) the first portable glucose monitors were heavy, required large blood samples and were highly variable in performance; and B) some old-fashioned insulin injection systems
that systems should achieve an analytical plus user error of < 10% with blood glucose levels between 30 and 400 mg/dL. This means that, for a reference value of 74 mg/dL, an SMBG value would be considered accurate if it were between 59 and 89 mg/dL. However, these two values lead to entirely different clinical responses. The term “accuracy” as applied to analytical performance is defined by the International Organization for Standardization (ISO) as “the difference between the expectation of measurement results and the true value of the measured quantity” – in other words, the assessment of the difference between obtained results (by the blood glucose monitor) and the true value (determined by a reference method that remains undetermined) [3]. Precision and reproducibility may still be improved, and the error grid assessed, in most SMBG devices. Altitude and temperature remain additional sources of error.

Thus, the overall performance of an SMBG system is a combination of the analytical performance of the device, quality of the test strips and performance of the user. Improving the accuracy of glucose monitoring systems emphasizes technical improvements and better patients’ education to reduce user errors, such as failure to correctly calibrate the meter, dirty meters, inadequate hand-washing and improper storage of the test strips [4].

Despite these limitations, SMBG is now essential for intensive T1D patients’ management to achieve and maintain the tight levels of glucose necessary to avoid macro- and microangiopathy [1]. Virtually all intensive insulin-therapy programmes depend on the measurement of glucose levels at least four times a day to determine the appropriate basal and prandial doses [5]. The ADA also recommends that patients with T1D monitor their blood glucose at least three times a day [6]. For most patients with T1D, testing blood sugar levels before and at intervals after meals; before, during and after exercise; and occasionally during the night will provide useful information for adjusting insulin and carbohydrate intakes. With “conventional” insulin therapy, oral agents and glucagon-like peptide-1 (GLP-1) analogue regimens, SMBG may be less frequent, but remains mandatory to avoid hypoglycaemia during changes in treatment or lifestyle [5].

However, the efficacy of SMBG in improving glycaemic control in type 2 diabetes (T2D) patients is more controversial. Multiple observational studies have evaluated SMBG in T2D, with some showing benefit [7,8] and others not [9-11]. Meta-analyses of randomized trials report conflicting results, with one reporting no benefit [12], and two subsequent analyses, limited to trials evaluating SMBG in non-insulin users, reporting a modest decrease in HbA1c in the SMBG group compared with the controls (pooled mean difference: -0.24%) [13,14]. In one study of newly diagnosed patients, SMBG was associated with higher scores on a depression scale [15].

To improve diabetes control, monitoring blood glucose also needs to be considered a tool for modifying treatment and behaviour; indeed, it should drive any therapeutic decisions. SMBG provides important information with which motivated educated patients can safely modify their behaviour and improve their HbA1c levels. SMBG means collecting glycaemia and treatment in a logbook, and changing the therapy, food and/or exercise patterns according to glycaemic variations.

As the use of SMBG grows, it has to become cost-effective. In an economic analysis of SMBG alone or with additional training on how to incorporate the results into self-care, SMBG proved unlikely to be cost-effective in addition to the usual standardized care [16]. In France, strip reimbursement has recently been limited to 200/year for patients treated with oral antidiabetic agents (OADs).

At present, the use of computerized glucose monitoring with memory meters is expanding. This allows the analysis of hundreds of data, and the calculation of mean blood glucose levels, daily fluctuations and hypoglycaemia frequency. It is a useful tool for clinical trials, but also for patients’ clinical management and education when data are discussed with caregivers.

Nevertheless, one of the main limitations of SMBG is the small amount of data provided: four to six capillary blood glucose values a day are often the best a patient can perform on a routine basis, considering the burden, pain and time involved with the technique. Moreover, glycaemic variations may be missed (Fig. 2), particularly at night-time, thereby leading to wrong therapeutic decisions. One recently developed solution is the continuous glucose monitoring (CGM) system.

4. Continuous glucose monitoring: Identification of undetected glycaemic fluctuations

The first CGM system was approved by the US Food and Drug Administration (FDA) in 1999 and was rather like a “glycaemic Holter” device, with the patient remaining unaware of the glycaemic data until they were downloaded, analyzed by the healthcare provider and discussed with the patient. However, it allowed treatment changes and has remained a useful educational tool.

CGM can also display glucose values continuously on a screen, and alarm limits can be set to allow immediate therapeutic
adjustments on the basis of real-time glucose results, thus avoiding glycaemic variability ("open loop"). Also, low-blood-glucose alarms can prevent hypoglycaemia, especially at night. Mandatory requirements include accuracy without too-frequent recalibration by the user [5,17]. However, interstitial glucose fluctuations and levels are not perfectly correlated with capillary glycaemia. Increased glycaemia may be observed with a delay at the interstitial glucose level. On the other hand, when sugar is decreasing, interstitial glucose decreases more rapidly, yet the technical delay can slow the results by up to around 10 min. For this reason, the ADA recommends verification of capillary glycaemia before each treatment modification (insulin correction, snacks) and in cases of "weird" results [18].

CGM technology provides a basis for insulin administration at more appropriate dosages and timing for patients using real-time monitoring. At present, a reduction of 0.3-0.6% in HbA1c can be expected with CGM in the patients considered "responders" [17]. Benefits have been shown at 3 months [17,19] and confirmed at 6 months [20-22], and appear to be higher in compliant, previously well-controlled, pump patients [23]. In a study comparing CSII with and without CGM [20], the benefits were found to be significantly greater in patients wearing the sensor for > 70% of the time and modifying their diabetes management (real trend) accordingly. These observations may explain in part the greater benefits seen in adult patients aged > 25 years compared with adolescents [21,24]. Also, adherence to CGM over the first 3 or 4 weeks is predictive of compliance ultimately [24], so a 1-month CGM trial should perhaps be proposed for all patients who wish to try it.

One study showed a significant decrease in hypoglycaemia frequency coupled with HbA1c improvement with CGM [23]. However, no difference in quality of life was noted, although some parameters, such as “fear of hypoglycaemia”, were improved [25]. Patients’ education and, thus, care-provider training is mandatory to teach the most appropriate reactions to “real-time data” to avoid overreactions that can lead to wide glycaemic fluctuations and increased anxiety [26].

5. Insulin administration: from injections to perfusion?

After the discovery of insulin and its synthesis, diabetes therapy began to use several insulin injections of regular non-modified insulin. The addition of zinc and protamine led to long-acting insulins that allowed a reduction in the number of insulin shots. Injections were given using needles and syringes that had to be boiled prior to use (Fig. 1B), but these materials have become more and more user-friendly over time such that, nowadays, most insulin pens are prefilled devices needing limited manipulation, and use very small needles (5-8 mm) that are almost painless. This comfort for the patient, coupled with the use of insulin analogues, has allowed the development of intensive treatments such as the "basal-bolus" regimen.

CSII begun in the 1970s [27, 28], and enables treatment to mimic physiological insulin basal secretion by adapting infusions to 24-h circadian needs, which are generally lower between midnight to 4AM, and the dawn phenomenon.

Insulin pumps are small devices programmed to infuse insulin through a catheter inserted under the skin. Insulin injections, even with rapid-acting analogues, often induce glycaemic fluctuations due to variations in injection sites and depths. CSII ameliorates these parameters. The constancy of basal delivery allows a near-flat blood insulin profile and is adjustable at preset times to suit the changing needs of the patient throughout the day [29]; it also allows good reproducibility in the same patient. With CSII and the other technologies, patients can adapt to near real-time modifications (so-called “open loop”) [30]. Insulin infusions can be modified at any time – in case of, for example, unexpected exercise – with a secondary transient basal rate. Different studies have demonstrated the superiority of CSII coupled with analogues in terms of HbA1c and hypoglycaemia compared with multiple injections. Insulin pump therapy is now the "gold standard" for T1D intensive insulin therapy [29].

The frequency of severe hypoglycaemia is reduced by about 75% with CSII [29]. Two meta-analyses [31,32], involving 600 and 1547 patients, respectively, confirmed a -0.5% improvement of HbA1c with CSII in association with a decrease in insulin doses. Also, programmable pumps have led to improved preprandial glycaemic control and fewer episodes of overnight hypoglycaemia [33]. In addition, studies evaluating depression and quality of life have shown either benefits or neutral effects with CSII [31,32].

The main risk of CSII is ketoadicosis due to the lack of a subcutaneous insulin depot. Undetected insulin infusion interruption due to catheter obstruction, needle displacement or pump dysfunction is another cause for concern, especially at night or during pregnancy [5]. However, studies have shown a lower number of ketoadicosis episodes in CSII-treated patients [34,35].

Nevertheless, CSII remains a complex therapy: some patients are reluctant to wear a pump at all times as it reminds them of their disease; blood glucose measurements have to be performed at least four times a day to adapt basal rates and boluses; and ketonaemia has to be checked before going to bed to detect any pump malfunctions. Another limitation of CSII is the complexity of device usage, especially for older and blind patients. Nowadays, however, pumps are more user-friendly and more like cell-phone devices.

CSII has also been considered in recent years as a potential treatment for improving blood glucose control in uncontrolled T2D patients using basal-bolus regimens, as it can reduce HbA1c levels and daily insulin requirements [36,37]. Quality-of-life scales are also improved, in particular, the anxiety and burden scales. However, it still remains more controversial.

In children and particularly in neonates, CSII compared with multiple daily insulin injections (MDI) results in better metabolic control [37]. CSII allows very low-dose insulin delivery and, in adolescents, quality of life is improved by permitting more flexibility in meals and physical activities. The dawn phenomenon, frequently seen in adolescents, is also easily compensated for. The insulin-delivery history function allows clinicians and parents to verify whether insulin delivery
has been properly done and no bolus omitted, and an alarm reminds users that it is “bolus time” [38, 39].

Others indications of CSII include pregnancy in T1D patients, insulin allergy and lipoatrophy. In addition, CSII has also proven its efficacy in transitory indications such as hyperalgesia in neuropathy, infections and wound-healing. It can also help to rapidly decrease glucotoxicity in uncontrolled diabetic patients.

In general, pumps are now safer, their alarms can alert users to electronic failure or increased catheter pressure, basal rates can be changed every few hours, and boluses can be normal or square wave, or a combination of the two, to adapt to different types of meals.

A new feature, a bolus calculator called “Bolus Wizard”, determines bolus doses based on data input from the wearer, such as the patient’s current blood glucose, target blood glucose, evaluated amount of carbohydrate consumed, insulin sensitivity and insulin-to-carbohydrate ratio, as well as insulin action duration (“insulin on board”) [40]. In 2008, Shashaj et al. [41] showed that, in paediatric patients, the bolus insulin dose calculated by Bolus Wizard was effective for improving pre- and postprandial glycaemic control, with fewer correction boluses, no differences in prandial insulin requirements and no restriction in the carbohydrate content of meals. Also, patients reported that using Bolus Wizard was easy and associated with a high level of satisfaction.

CSII limitations are essentially its cost and the education necessary for its proper use. Patients’ motivation and skills also need to be regularly evaluated, for example, by an annual therapeutic efficacy evaluation for every patient. Recent cost–benefit analyses have concluded that CSII is cost-effective when it induces improvements in both glycaemic control and chronic complications [42–44].

Contraindications to CSII are essentially severe psychiatric disorders, patients’ inability to use the device, and activities involving extreme conditions such as cold, heat, scuba diving or exposure to magnetic fields such as magnetic resonance imaging.

Nevertheless, despite these technological improvements, the fear of hypoglycaemia is one of the main limitations for intensive insulin therapy to achieve HbA1c goals in diabetic patients [45]. The Paradigm® Veo™ pump is linked to a glucose sensor that shuts down when glycaemia is under a certain limit, and restarts after 2h. This may be the beginning of a solution for patients with hypoglycaemia unawareness, especially at night. However, no randomized study has been carried out with this device. Its limitations could include the risk of very high glycaemia when insulin is stopped after a hypoglycaemic episode, and the risk of restarting the pump when no capillary blood glucose has been performed.

6. Continuous peritoneal insulin infusion

This route of insulin infusion allows insulin to be absorbed by the physiological portal route. This means that insulin absorption is rapid compared with subcutaneously administered insulin analogues, and more reproducible [5]. Insulin first absorbed in the liver normalizes a number of proteins synthesized by the liver through insulin regulation, such as lipoproteins, plasminogen activator inhibitor-1 (PAI-1) and insulin-like growth factor-1 (IGF-1). Thus, glycogen storage is increased in the liver, and peripheral insulin levels are lower, thereby reducing the frequency of glucose variations and, consequently, severe hypoglycaemia. Implantable devices are used to avoid peritoneal infections; these are composed of a casing containing the pump system, a negative-pressure insulin reservoir and a two-layer silicone catheter. An external communicator enables remote control of the device by telemetry [5]. The use of a specific insulin stabilizer is mandatory, however, to avoid insulin aggregation and pump blockages [46].

Indications for this insulin delivery system are limited to T1D patients who remain uncontrolled despite well-managed CSII and certain, rare, cases of subcutaneous insulin resistance.

Pumps are implanted during a surgical procedure and need to be replaced every 7 years (the average lifetime of the battery). The main complications are telemetry disconnection, catheter blockages, electronic pump dysfunction and pump blockages due to insulin aggregates; however, such accumulations are unusual and are usually solved by rinsing the pump in vivo, using a basic solution.

This mode of insulin administration may be one of the steps towards closing the loop.

7. Closing the loop: advances in pump therapy and continuous glucose monitoring

On the basis of insulin administration regulated by real-time glucose levels determined by a glucose sensor using mathematical algorithms, the first artificial endocrine pancreas [47] involved a double-lumen catheter that allowed continuous glucose measurement of venous blood, using a microcomputer and an intravenous insulin infusion. The Biostator GCIIS [48] became commercially available and was used for hospitalized fasting patients in numerous clinical studies to determine insulin sensitivity and circadian needs using a glucose clamp technique. The technology was highly effective but was, of course, never used for clinical diabetes management.

Many factors need to be taken into account when creating mathematical algorithms adapted to ambulatory, meal-taking patients, including insulin pharmacokinetics and pharmacodynamics, glucose metabolism, glucose concentrations in blood interstitial fluid and insulin resistance. Some studies have shown good responses in basal situations, but results have been less satisfactory at mealtimes [49]. Different sites have also been evaluated, such as intraperitoneal or subcutaneous insulin infusions combined with a subcutaneous or intravenous sensor [49, 50]. Indeed, the feasibility of a closed-loop system of insulin delivery using a subcutaneous glucose sensor and intraperitoneal insulin delivery, vs an open-loop system in T1D patients has been evaluated [49].
In hospitalized patients, significantly higher postprandial glycaemia, but lower average glycaemia, were observed; improvements in glucose control were also noted during extraprandial periods and in interindividual postprandial or nocturnal variations. Hypoglycaemia rates were low and comparable between the two groups. This study suggests that better glycaemic control with closed-loop insulin delivery is feasible. In addition, nocturnal closed-loop insulin delivery would clearly be clinically relevant for preventing nocturnal hypoglycaemia.

In most studies, glycaemic between-meal results are usually satisfactory, whereas postprandial periods have failed to fulfill requirements despite the use of various algorithms and insulin infusion routes [51, 52]. This might be explained by the cephalic phase of insulin secretion, the incretin effect, and the variability of intestinal absorption and the glycaemic index. Given the prandial-state limitations, a “partial open loop” was proposed by Weinzimer et al. [51] to control postprandial hyperglycaemia, and demonstrated significantly lower postprandial glucose levels with the hybridized system (manual bolus plus automatic bolus) compared with the fully automated system.

8. Can the development of telemedicine replace the human healthcare provider?

Health authorities have high expectations for telemedicine (TM), as it addresses several major challenges, such as improving access to healthcare, especially in underserved or remote areas; overcoming the lack of specialists facing the diabetes epidemic; and reducing the costs of healthcare while improving its quality. The aims of TM in diabetes, however, differ according to the type of diabetes [53].

In T1D, despite optimized insulin treatment, proper follow-up, education and compliance, many patients’ HbA1c values remain persistently > 8% [54]. Leaving aside the relatively rare cases of authentic instability, these poor results may be explained, at least in part, by the difficulties faced by patients in coping with the burden and complexity of the disease, such as properly applying the complex rules of calculation of their prandial and basal insulin doses, keeping a logbook and having regular consultations with their physician [53]. Physicians themselves often face a lack of information during the consultation, with no data on which to base their advice regarding the patient’s insulin dose adjustments.

In T1D, the goal of TM is to help patients to achieve better control of their blood glucose levels through accurate adjustments of their insulin doses. Teletransmission of glycaemic data to a care provider, who sends feedback to the patient, is one of the main tools of TM. Several studies [55-57] have shown conflicting outcomes, with improvements in diabetes control not always being significant. One limitation of the method is the possible lack of the different parameters needed to adjust insulin doses (meals, previous insulin doses, activities). Thus, an active electronic diary kept on a smartphone that allows automatic teletransmission of data such as blood glucose, insulin doses, dietary data and details of physical activity may be more attractive than a traditional diary [53]. Data stored on a mobile phone can be periodically sent as short messages and reviewed by physicians on their computers, and new prescriptions may then be sent back. Alarms set up by physicians can be incorporated such that, when high or low blood glucose is detected, the data and alarm will be automatically sent to the physician [53]. The Diabeo system [58, 59] produced good results in terms of blood glucose improvement and patients’ satisfaction. At the end of the study, a large majority of patients wished to continue using the system, even at their own expense, rather than returning to a traditional passive diary.

The same tools may be used in T2D, although the impact of SMBG on glucose control is more controversial in this considerably larger diabetic population. T2D requires not only treatment adjustments, but also behavioural changes (control of calorie intakes and regular physical activity) that appear to be best established through regular coaching from caregivers. One study [60] has shown that educational messages were as efficient for individual consultations as video-conferencing, with an HbA1c of 7.8 ± 1.5% in both groups immediately after the educational programme that remained comparable 3 months later.

Many TM studies focusing on the management of blood glucose levels have been published, but the majority have failed to demonstrate any superiority of TM vs traditional care. Three prerequisites are needed for success [53]. First, systems need to be easy to use on readily available, pocket-sized, electronic devices. Also, patients’ questions have to be answered quickly, as feedback delay has accounted for the poor performance of many systems. In addition, easy interactivity with a known caregiver is important, as it explains both the good results achieved with TM systems using teleconsultations, and the poorer results when human contact consists of only texting or e-mails and when the patient is unknown to the care provider.

Active electronic diaries could replace traditional logbooks, and could allow insulin doses to be proposed based on the automatic application of algorithms coupled with automatic alarms sent to physicians in case of major glucose variations. Glucose readings could then be automatically transferred to a smartphone, pending a direct connection with the glucose sensor and a return of control of the insulin pump, thus forming a closed loop [53].

However, effective TM programmes are expensive and time-consuming, and require reorganization of the healthcare system. It would also be useful to involve nurses and other caregivers specialized in diabetes to ensure adequate education and TM system management under the control of the referring physician. Also, because of the growing number of T2D patients, it will be necessary to identify the most distressed patients likely to benefit the most from targeted interventions.

Thus, TM is a valuable tool, but it cannot completely replace human care providers and physicians. Moreover, the technology is not accessible to all patients, as elderly people are often incapable of coping with such systems.
9. Conclusion

The treatment and follow-up of diabetes have dramatically improved over the past century. Changes have tended to improve glucose management towards achieving near-normal glycaemia while avoiding chronic complications, and have also tended to improve patients’ quality of life. All devices comprise one of the steps towards the concept of “closed-loop insulin delivery”, which will free patients of glucose control and parenteral self-monitored insulin administration. However, at present, around 30% of T1D and T2D patients are far from achieving their defined glycaemic goals. Diabetes still remains a complex chronic disease that makes it a true burden for patients in their day-to-day lives. Attention, empathy and personal involvement are still the main tools for motivating and supporting the patients who suffer from this chronic disease. Nevertheless, these innovative technologies are to be considered only tools, and not replacements for human skills.

Conflicts of interest statement

N. Jeandidier: investigator (Abbott, Lilly, Medtronic, Novo) ; investigator and expert (Sanofi Aventis) ; board (Novo Nordisk).
M. Pinget: advisory services (Medtronic, Roche Diagnostic et Ypsomed) ; participation, for the past twelve months, to national and international boards (MSD, Medtronic, NovoNordisk, Sanofi-Aventis) ; Conferences: attendance as contributor for the past twelve months to national and international symposiums (Astra-Zeneca, BMS, Medtronic, MSD, Novartis, NovoNordisk, Pfizer).
F. Moreau: investigator (Medtronic, Abbott) ; expert (Lilly, Lifescan) ; consultant (BMS) ; attendance (congress) (Lilly)

References


