Practical implementation of automated closed-loop insulin delivery: A French position statement

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Practical implementation of automated closed-loop insulin delivery: a French position statement

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Abstract

Automated closed-loop (CL) insulin therapy has come of age. This major technological advance is expected to significantly improve the quality of care for adults, adolescents and children with type 1 diabetes. To improve access to this innovation for both patients and healthcare professionals (HCPs), and to promote adherence to its requirements in terms of safety, regulations, ethics and practice, the French Diabetes Society (SFD) brought together a French Working Group of experts to discuss the current practical consensus. The result is the present statement describing the indications for CL therapy with emphasis on the idea that treatment expectations must be clearly defined in advance. Specifications for expert care centres in charge of initiating the treatment were also proposed. Great importance was also attached to the crucial place of high-quality training for patients and healthcare professionals. Long-term follow-up should collect not only metabolic and clinical results, but also indicators related to psychosocial and human factors. Overall, this national consensus statement aims to promote the introduction of marketed CL devices into standard clinical practice.

Keywords: Adolescents; Adults; Artificial pancreas; Automated closed-loop insulin delivery; Children; Closed-loop; Organization of care; Position statement; SFD; Therapeutic education; Type 1 diabetes

Abbreviations

AJD: Help Association for Youth with Diabetes

CGM: continuous glucose monitoring

CL: closed-loop

CNP-EDN: National Professional Council of Endocrinology, Diabetology and Nutrition

FENAREDIAM: National Federation of Regional Associations of Endocrinology, Diabetology and Metabolism

FFD: French Diabetes Federation

HCC: home care company

HCL: hybrid closed-loop

HCP: healthcare professional

OL: open-loop

PTE: patient therapeutic education

PWD: patient with diabetes

SFD: French-Speaking Diabetes Society

SFE: French Society of Endocrinology

SFEDP: French Society of Paediatric Endocrinology and Diabetology

T1D: type 1 diabetes

T2D: type 2 diabetes

TAR: time above range

TBR: time below range

TIR: time in range

Introduction

Over the last decade, semi-automated or hybrid closed-loop (CL) insulin therapy has made significant progress. This technological breakthrough constitutes a major innovation affecting the daily life of patients with type 1 diabetes (T1D) by contributing towards better medical care and improved quality of life. The practices of health professionals involved in the care of T1D patients will also be profoundly modified. For these reasons, an expert Working Group was brought together by the *Société Francophone du Diabète* (SFD, French-Speaking Diabetes Society) to prepare for the imminent arrival of CL technology and to elaborate this position statement.

The Working Group comprised 35 experts representing French hospital and university hospital diabetology, including: the SFD; French Society of Endocrinology (*Société française d'endocrinologie*, SFE); French Society of Paediatric Endocrinology (*Société française d'endocrinologie pédiatrique*, SFEDP); independent diabetology (*Fédération Nationale des Associations Régionales d'Endocrinologie Diabétologie et Métabolisme*, FENAREDIAM); therapeutic education nurses (paramedical SFD); patient associations (French Diabetes Federation, *Fédération française des diabétiques,* FFD); Help Association for Youth with Diabetes (*Aide aux Jeunes Diabétiques*, AJD); and a professional association (National Professional Council of Endocrinology, Diabetology and Nutrition, *Conseil national professionnel d'Endocrinologie, Diabétologie et Nutrition*, CNP-EDN).

The expert Working Group met between November 2019 and June 2020. Their general objective was to produce an expert consensus to guarantee the safety, regulatory, ethical and professional practice requirements generated by CL systems. Specific objectives were: (*i*) to summarize the main clinical studies documenting the efficacy of CL and describing the characteristics of the main systems available in 2020; (*ii*) to specify the current indications for CL therapy and anticipate future indications; (*iii*) to specify the goals incumbent upon a

diabetology centre investing in the initiation of patients to CL; (*iv*) to describe the requirements and methods of training of healthcare professionals (HCPs), as well as the main stages of therapeutic education for patient candidates on CL; (*v*) to determine long-term evaluation criteria for CL use; and (*vi*) to identify the long-term follow-up procedures for these patients.

1. Current industrial achievements in closed-loop systems

Four manufacturers (Medtronic, Diabeloop, Tandem Diabetes Care, CamDiab) have developed monohormonal hybrid CL systems (Table S1; see supplementary materials associated with this article online) that have gone through pivotal trials, thus allowing them to obtain approval from US and European regulatory authorities [1–4]. (A pivotal trial of the Insulet Omnipod 5 system is currently ongoing.) The Diabeloop DBLG1® and CamDiab CamAPS FX® [both *Conformité Européenne* (CE)-marked], Tandem Control-IQ® [US Food and Drug Administration (FDA)-approved] and Medtronic MiniMed 780G (FDA- and CE-marked) have been examined in randomized controlled trials (RCTs), whereas the Medtronic MiniMed 670G (FDA- and CE-marked) and Insulet Omnipod-5® have gone through before–after studies. The main characteristics of these systems, and the results of their pivotal trials in adults and as reported in children are summarized in Table S1, Table S2 and Table S3 (see supplementary materials associated with this article online). The above-mentioned pivotal trials and three meta-analyses (one including paediatric populations) [5–7] have all demonstrated the metabolic efficacy and safety of these systems under real-life conditions. All of these devices increased the time spent in the optimal sensor glucose range [time in range (TIR) 70–180 mg/dL] by 10–11% in absolute values, reduced the time spent in the hypoglycaemic range [time below range (TBR) < 70 mg/dL] by 50%, nearly suppressed risk

of major hypoglycaemia (< 54 mg/dL) and did not expose patients to severe metabolic events (ketoacidosis, severe hypoglycaemia).

The paediatric meta-analysis [7] and subsequent published studies of larger populations of children over longer durations of time (up to 4 months; Table S3) [1, 8–11], including those with insufficiently controlled diabetes [1], were highly conclusive as regards the feasibility of CL in children. Indeed, these studies showed an increase in TIR of 11 points in absolute value, with significant reductions in glycaemic mean values and in TBR < 70 mg/dL and, in at least two studies, significant reductions in HbA1c levels [1, 8]. Thus, CL systems make it possible to: (*i*) achieve the TIR objectives recommended by international paediatric diabetes societies, such as the International Society for Pediatric and Adolescent Diabetes (ISPAD) [12] and International Consensus on TIR [13], at night; (*ii*) very closely approach these goals over 24 h; and (*iii*) achieve TBR objectives.

Questions regarding its long-term impacts on HbA1c, glycaemic control, risk of chronic complications, and quality of life and satisfaction are still open to discussion. However, the currently available results were considered sufficiently convincing for social insurance policies to start covering the reimbursement of at least one of these systems in France [14].

2. Indications for closed-loop therapy in clinical practice

The indications for CL systems proposed by our Working Group were based on the results of real-life studies (see above) as well as the experience gained by investigators. However, it is likely that these indications will evolve over the years to come as more and more upcoming findings accumulate. In addition, the opinions and attitudes of HCPs will be instrumental in the adoption of such new technologies by patients of all ages [15].

Delivering clear and complete information to patients, and investigating their representations ahead of the initiation of CL delivery are crucial steps towards allowing

patients to make up their own minds, thereby promoting long-term adherence. It is equally important to explain the expected benefits of CL—for instance, better quality of life—as well as to delineate the stress its use may cause to limit stoppages. In addition, patients should be informed of the three main constraints of CL use: the presence of alarms; the physical and material constraint of wearing the devices; and the limitations brought about by the essential adherence to good practices for use of a hybrid system (a 'responsibility' of patients). In paediatric cases, the prerequisites and indications for CL are similar to those for adults living with diabetes (PWDs). However, in paediatrics, the CL technology has a more urgent indication because of the prominent instability of diabetes in children, its psychosocial consequences (for both children and parents), the often suboptimal glycaemic control and increased risk of long-term complications [16–22].

Table I presents a summary of recommendations based on the: (*i*) prerequisites established from studies published to date; (*ii*) objectives of metabolic control based on the recommendations of international expert panels [12, 13, 23]; and (*iii*) diabetes-related alterations in quality of life. These recommendations include a 3-month initial probationary period with the CL system. As with any intensified insulin therapy, there are precautions that must be taken with CL use in addition to points of vigilance for which the benefit/risk ratio must be evaluated [24] and discussed at the end of the initiation period (Table I). The motivation of patients (both adults and children with their parents) is essential for successful CL therapy. Any prescription of CL should therefore be conditional, after sufficient information has been provided, upon the patients' commitment to respect good practices, and their specific educational and care processes.

However, the indications for CL are likely to evolve based on the results of ongoing CL studies, some of which should be available as soon as 2021. These upcoming indications are relevant for several groups of patients with T1D. First, concerning patients at high risk of

hypoglycaemia, studies show that CL significantly reduces time spent in hypoglycaemia [5–7]. One study of the DBLHU system (Diabeloop SA, Grenoble, France) compared CL with a system using predictive discontinuation before the onset of hypoglycaemia (predictive low-glucose suspend system, PLGS) in patients at high risk of hypoglycaemia due to undetected hypoglycaemia or a history of severe hypoglycaemia. The DBLHU system *vs* PLGS was associated with a highly significant increase in TIR 70–180 mg/dL (73.3 ± 1.7% *vs* 43.5 ± 1.7%, respectively; $P < 0.0001$) and a reduction in TBR < 70 mg/dL (0.9 ± 0.4% *vs* 3.7 ± 0.4%, respectively; $P < 0.0001$). These results made it possible to obtain the CE mark for the Diabeloop DBLHU CL system for the indication of unstable diabetes [25]. Similar studies are now underway or planned for other systems, such as Control-IQ (Tandem Diabetes Care, San Diego, CA, USA) and MiniMed 670G (Medtronic, Minneapolis, MN, USA). Second, in very young children (aged 1–6 years) with T1D, the initial studies were indeed highly encouraging in terms of feasibility and metabolic outcomes, and hopefully will be confirmed in ongoing RCTs [16, 26–28]. Of note, the results with the use of non-diluted insulin showed no inferiority [26]. Third, in children and adults with T1D, the currently ongoing Closed Loop From Onset in Type 1 Diabetes (CLOuD) study aims to assess the effectiveness of CL from the time of diagnosis in preserving β-cell function and therefore maintaining optimal glycaemic control from the start, thereby limiting the risk of hypoglycaemia [29]. Fourth, CL should be indicated for patients treated with multiple injections and who are naïve to pump treatment and, fifth, for pregnant woman. Two randomized crossover studies comparing CL and open-loop (OL) systems during pregnancy were carried out in a small number of women with T1D. One study showed the efficacy of CL, used only at night, in increasing TIR (63–140 mg/dL) at night with no increase in hypoglycaemia [30]. In the other study, CL was used day and night, and reduced the time spent in hypoglycaemia (< 63 mg/dL) [31]. However,

additional and more powerful studies are still needed for a better understanding of the contribution of CL to glycaemic control during pregnancy.

Nevertheless, CL systems are pushing T1D therapy into a new era starting in 2020. The position of our Working Group is to retain indications for CL therapy in situations where glycaemic control is less than optimal (HbA1c and/or TIR not on target, frequent/severe hypoglycaemia) despite optimalized treatment with subcutaneous (SC) pumps and continuous glucose monitoring (CGM), and/or where quality of life of patients and/or their relatives is clearly impaired. With simpler devices such as pumps and CGM systems, the need for repeated decision-making by patients (or parents) concerning insulin dosages remains a limitation for treatment effectiveness. CL systems, on the other hand, can truly shape a novel treatment featuring automated insulin delivery as the major innovation. Thanks to the optimalization of insulin dose adjustment, CL systems should help to achieve therapeutic objectives that have still not been reached by a large proportion of patients with T1D.

3. Initiation of closed-loop therapy at expert care centres

The organization proposed for CL systems is based on the model used in France for 20 years for insulin pump treatment [32] and, more recently, sensor-augmented pump therapy [33]. This structure involves four main actors: treating diabetologists; initiation centres; home care providers (home care companies, HCCs); and device manufacturers. The objective is to provide accessibility to CL treatment all across the country. The expert Working Group recommends an initial CL probationary period of 3 months for the initiation of care, and therapeutic education of adult and adolescent patients and children.

The initiation and follow-up of CL treatment should be managed by a multiprofessional team in the broadest sense of the term, associating physicians specializing in endocrinology–diabetology and paediatricians, nurses and dietitians experienced in diabetology with pump

initiating centres, HCCs and device manufacturers. Such an organization would involve both hospital-based and 'liberal' (independent) diabetologists who wish to support their patients with this new treatment development and to also refine their practices. To participate in establishing and monitoring CL treatment, the specifications include, beyond treatment management knowledge and skills, a structured and organized system of implementation, patient support and capacity for emergency responses. The concept of an initiating centre is based on the possibility of deploying a multiprofessional team trained in therapeutic education (doctors specializing in endocrinology–diabetology, paediatricians, educational nurses, dietitians) with at least two physicians specializing in endocrinology–diabetology or paediatricians experienced in diabetology trained in the use of CL systems. In addition, the initiating centre must be able to provide 24/7 on-call medical help. This initiating centre concept can be applied to both hospital-based and independent teams as well as to mixed public/private organizations with multiple coordinated and structured sites as per predetermined criteria. This structure should also take into account any regional specificities and organizations. The goals of CL initiation and monitoring centres are presented in Table II.

To provide high-level expertise and high-quality CL treatment, the labelling and approval of care providers must be based on well-defined criteria for both initiation and monitoring centres. Among these criteria, it is necessary to emphasize the importance of: (*i*) expertise in pump treatment (sufficiently large pump initiating centres and cohorts); (*ii*) training of every worker in automated CL insulin therapy under the supervision of institutional boards (such as the SFD and SFEDP) as well as training and certification in the techniques required for every system by its manufacturer (see section 4 below); and (*iii*) specific therapeutic education for adult patients, and children and parents in paediatric centres (see section 5 below).

4. Training of healthcare professionals

The success of automated CL insulin therapy in adult and paediatric PWDs requires specific, comprehensive and structured training of the HCPs involved. The advent of different hybrid CL systems in the marketplace, and the increasingly pressing demands from patients to be equipped with them, place caregivers on the front line to inform PWDs, to train them in the use of the CL system and to ensure their dedicated follow-up. The objectives of HCP training are dual: the first includes general objectives aimed at supporting the setting up of CL in patients likely to benefit from it; while the second, more specific, objectives include taking into account the type of centre and type of care to be provided. The end goal of HCP training in CL systems is to ensure patients' (and their families) empowerment and autonomy together with the long-term efficacy of their CL therapy. This will translate into patients having the power to act and react appropriately with no stress both as regards their chosen devices and, more importantly, in their everyday life as PWDs.

The training of CL-related aspects should involve all HCPs who provide patient care and patient therapeutic education (PTE) for the initiation and follow-up of patients receiving CL therapy systems. In practice, this includes: doctors specializing in endocrinology–diabetology; paediatricians experienced in diabetology; advanced practice nurses, nurses and dietitians experienced in diabetology; and caregivers within HCCs.

The training programme for HCPs will be developed and operated by the SFD in partnership with the SFEDP and associations/federations of adult and paediatric PWDs, whereas the specific and technical parts of training required by each given CL system will be provided by the relevant manufacturers. Caregiver training will be provided in a practical, interactive form by addressing clinical cases, case studies and the interpretation of traces produced by CL systems related to interstitial glucose levels as well as the delivery of insulin doses and intervention of patient resources. Caregivers will be encouraged to handle the

demonstration equipment themselves and, if desired, to actually wear the systems too. Training should provide guidance concerning the available systems, as informed knowledge of the different CL systems will allow caregivers to offer them to patients in an appropriate and individualized way.

More important, optimalization of system settings will be covered during this training. Trained HCPs will be responsible for establishing, based on recommendations, a specific step-by-step PTE programme intended for patient training, including psychosocial assessment (see section 5 below). The skills to be acquired by HCPs during their training to allow them to introduce patients to CL systems and follow them were established by our expert Working Group and are presented in Table III. Continuing medical education (CME) for HCPs will complement and update their initial training as part of their accreditation for this new technology. Our recommendations are in line with those recently issued in the UK [34].

5. Patient therapeutic education

The forthcoming availability of CL systems is a tremendous therapeutic breakthrough in clinical practice that will transform the lives of adults, adolescents and children with diabetes, as well as the people around them. However, individualized and successful education of the patient in how CL systems work is a prerequisite for therapeutic success. The PTE guide developed in the present position paper summarized here should foster its conduct by labelled initiation and monitoring centres, thereby promoting the required PTE. Indeed, careful observation of a specific educational process, structured in stages, should ease appropriation of the CL system by patients and support them towards integrated autonomy. To this end, the following points must be considered.

Listen to the needs, expectations and representations of PWDs

To date, CL systems are not as autonomous as the term 'artificial pancreas' would suggest. The automation is still partial, and these so-called hybrid CL (HCL) systems require the intervention of patients in certain situations, such as the correct determination of insulin doses for meals (carbohydrate-counting and size in relation to typical meals, or some other method, depending on the system). Similarly, patients are expected to announce any upcoming physical activity, and to carry out the calibration of capillary glycaemia for proper functioning of certain systems (MiniMed 670G and 780G, Medtronic). Such information should be provided by HCPs interacting with patients upstream of their decisions. In addition, exploration of the expectations and representations of PWDs (and parents in paediatric cases) is a prerequisite that may require several interviews. More important, the caregiver's attitude can either promote or hinder expression of this information. As the realistic or unrealistic nature of these expectations with respect to CL is a predictor of its short- and medium-term success, any explanations and precise information given upstream will inform patients' decisions. It is especially important that patients play an active role from the outset, so that their expectations are met and that they willingly and fully commit to respecting good practice rules and care as well as the education process.

CL therapeutic education process for PWDs

For whom and by whom?

Subsequent to the patients' preparation time and shared decisions of the PWD–HCP, detailed information about the initiation education course, in compliance with prerequisites and indications, are to be given. In paediatric cases, such education is intended for the child and immediate family (at best, both parents), as well as the child's caregivers (for example, grandparents). Nurses caring for the child when at school should also be trained in the use of

the CL device and its monitoring. In addition, particular attention should be paid to specific documents intended for school and extracurricular stakeholders concerning the management of alerts issued by the CL system. Caregivers of adult PWDs would also be invited to attend training sessions to give them an understanding of the important changes in treatment, and to prepare and accompany them in their new roles as caregivers.

Which course?

PTE is a process integrated into the CL care pathway; it includes the initial PTE up to the end of the 3-month probationary period and follow-up PTE (see Fig. 1 for flowchart and Table IV for PTE stages).

Process and phases of patient and entourage training programme

The CL PTE process

This educational process (Fig. 2) must be read from bottom to top, from the 'base' level of PTE up to the CL system, with reinforcement of the mastery of pump and CGM handling through PTE up to the optimal objective of PWD success with the chosen CL system.

Initial PTE

In the first phase, the pump and sensor have to be set up in an OL configuration (no CL algorithm) to allow patients to become familiar with the technical manipulations and to master manual operation of the pump, and to understand and interpret sensor data (Table IV). This initial period of 1–2 weeks for the pump (especially in cases of a change in pump model) and at least 2 weeks for CGM will allow assessment of the patient's acceptance of the device, adherence to good use practices and safety points.

In the second phase, the algorithm, after explanation of its operation, will then be activated and configured. As the algorithm varies across different CL systems, the patient's education should be specific to the chosen CL model [35]. Moreover, with a CL system, a number of other practices will also change for patients compared with the OL situation.

Basal rates

With CL systems, the pump automatically determines the basal rate, which is continuously adjusted by an algorithm based on (*i*) glucose values detected by the sensor and (*ii*) history of insulin delivery. CL delivers a basal flow that may be higher than OL in some cases due to the shutdown function in cases of a predicted hypoglycaemic risk. Care must therefore be taken in programming the baseline reference rate in the event of a return to OL.

Pump disconnections

With CL systems, disconnecting the pump or cannula for > 15 min (for instance, to take a shower) affects the learning algorithm and estimation of active insulin. It is recommended, in this case, to stop the pump.

Management of hyperglycaemia

Depending on the CL system, a hyperglycaemia correction bolus is delivered either manually or automatically, or both. In the event of an automated corrective bolus, it is advisable to let the system perform its programmed actions and avoid manual correction, as the latter entails a risk of insulin overdose and will affect the learning algorithm.

Management of hypoglycaemia

Compared with an OL system, the use of CL requires a lower sugar intake to prevent or treat hypoglycaemia.

Data from the glucose sensor

The on-screen algorithm's instructions eliminate the need for patients to constantly review their interstitial glucose measurement (CGM) data and to follow prompts. For some patients, this 'letting go' can be difficult and will require support for the first few months.

For all of the above reasons, a period of appropriation of the CL device is required for patients to feel they can trust the system, and allow the algorithm to perform its tasks and use it properly. Indeed, the first few weeks or months after initiation are critical to the success of CL delivery. The keys to this success are based on the follow-up and support of PWDs during this initial period, when the objectives are: (*i*) to strengthen and resume the initial education; (*ii*) to analyze target TIR and, with consultations or phone calls with HCPs and based on downloaded data, to refine the adjustment of CL parameters (for example, depending on the system: blood glucose targets; insulin/carbohydrate meal ratios, often modified in paediatric cases [36]; duration of active insulin; and insulin sensitivity); (*iii*) to check patients' best practices for making calibrations (MiniMed 670G or 780G); (*iv*) to help patients understand the importance of boluses taken before meals [37], proper compliance with the recommendations of various systems, treatment and corrective measures for hyperglycaemia, and available options for physical activity; (*v*) to check the wearing time of glucose sensors and CL operating time, and analyze the reasons for exits from CL mode and malfunctions; (*vi*) to minimize alarms as much as possible; (*vii*) to detect misuse or failure to 'let go'; and (*viii*) to assess patients' experience and support their progress towards autonomy, which requires *trusting the system* and using it properly.

Consultations (face-to-face or phone calls) are offered with data downloads at 3 and 7 days, 2 and 4 weeks, and 2 and 3 months after CL activation to: (*i*) continue patients' education; (*ii*) maintain and strengthen patients' skill over time; (*iii*) make early assessments of patients' experience and CL effectiveness; (*iv*) support patients towards greater autonomy by interpreting downloaded CL data; and (*v*) adjust any editable parameters.

Educational follow-up

Beyond the initial 3-month trial period, and provided that safety and efficacy conditions are met, if patients are independent and so desire it, then personalized care tailored to their individual needs can be continued by their monitoring centre (see section 6 below). Table IV specifies the pathway and stages of patients' educational follow-up.

Patients' skills by stage of PTE

The skills to be acquired by patients are listed in Table IV. This step-by-step process splits the information load, allowing their gradual acquisition and better quality of educational sessions for patients. Regular assessments should focus on both metabolic and psychosocial indicators to allow individualized adaptation of stages of training.

Closing the loop in the care relationship

After a learning phase with a rapid progression curve, PWDs should be able to benefit from a reduction in their daily burden of treatment and a marked decrease in the mental load it causes. Indeed, even though CL systems are as yet not completely automated and still require patients' inputs for meals and physical activities, for the rest of the time, dose adjustments are made automatically with results that are unmatched thus far. In addition, those results are quickly apparent initially at night, allowing patients and their caregivers to regain their sleep

and serenity. As all this is highly motivating, even previously divested and/or discouraged patients regain their motivation to take care of themselves. Nevertheless, patients will always have a 'job' to do: it would be wrong to believe that a button can be activated and everything will be done on its own, although the job can be made markedly easier and more efficient than usual, thereby explaining patients' enthusiastic satisfaction with CL treatment.

For patients, it is a matter of ensuring the correct functioning of these devices (which, over time, will progress ergonomically and become more user-friendly), the correct bolus doses for meals, announcing physical activities, and allowing the algorithm to bring about the optimal benefits of CL treatment and technology. For caregivers, their job is to support these changes and new practices, and to help patients mobilize their newly acquired knowledge and know-how.

The new autonomy of PWDs, made uniquely possible by CL systems, is an opportunity that disrupts the usual care relationships. CL offers PWDs the potential to use their power positively in the treatment of their own disease and, thus, their own lives, thereby offering a new role for patients in relation to their disease by putting diabetes in a different place in their lives instead of having to adapt their lives to diabetes as a priority. Symbolically, it could be said that, at all levels, the patient is now 'in the loop'.

These changes need to be made on both sides of the care and education relationship. HCPs will have to prepare for a new paradigm of patient empowerment, for which some caregivers have already trained and incorporated into their practices. Changes in professional identity, particularly with new representations by caregivers of the respective roles of HCPs and PWDs, should therefore be supported during CL training. In addition, the new conceptual framework for the role of caregivers requires more reflection, work and training, while a change in the place of caregivers will make it possible to offer patients a new care relationship by pursuing the process of therapeutic education—with patients' autonomy as the goal—

towards an empowerment approach that supports and mobilizes their capacity to make decisions and take action.

6. Long-term follow-up

With a CL device, this will begin after the first 3 months of use during the initiation and probationary period, and be carried out by doctors specializing in endocrinology–diabetology or by paediatricians with experience in diabetology, all qualified in the use of CL systems and most often working in multiprofessional teams. Throughout the long-term follow-up, HCPs can contact the initiating centre should the patient's objectives not be reached and/or thorough re-evaluation (or even discontinuation) of the CL treatment be required.

The place of remote monitoring

The benefits of CL therapy with or without remote monitoring have yet to be evaluated in dedicated RCTs. However, one meta-analysis has shown a significant superiority of CL treatments associated with telemonitoring in terms of time spent in hypoglycaemia [5]. One prominent advantage of remote monitoring is that it allows for continuing optimalization of CL system settings based on patients' downloaded data. In addition, remote monitoring constitutes a substantial support tool for patients as it helps to remove obstacles, whether felt or real, thereby increasing patients' adherence as well as proficiency with the device [38]. It also makes it possible to quickly identify any possible misuse of the CL system that might affect its efficacy and/or safety. In fact, in well-defined cases, remote monitoring may even allow patients' relatives to access real-time blood sugar data and alerts and, thus, help them to manage their situations and devices. Whatever the purpose, remote monitoring requires CL systems to be connected to a platform that hosts and analyzes data with an organization of dedicated HCPs at specialized centres.

Criteria for metabolic evaluation of patients using CL devices

HbA1c levels remain the gold standard of long-term metabolic assessment, but they can neither assess glycaemic variability *per se* nor exposure to hypoglycaemia [23]. In 2016, a consensus statement listed the CGM parameters required to evaluate a CL system in a clinical study [39]. Definition of the objectives to be achieved was recently the subject of an international consensus of experts [13], and those objectives are now considered the main criteria for metabolic monitoring of patients equipped with CL systems.

Criteria for clinical evaluation of patients equipped with CL devices

In addition to metabolic parameters, it is important to assess how CL systems are used and tolerated (Table V), including: management and tolerability of alarms; wearing of devices; skin condition; adherence to good system-use practices; and management of meals, hypoglycaemia, hypoglycaemia treatment and implementation of adaptive behaviours.

Assessment of psychosocial factors

Other factors relating to patients' expectations should be taken into account to promote improved device acceptance and optimal benefits from CL system use. First, during follow-up, overall PWD satisfaction will depend on the ease of use and perceived effectiveness of the device in managing diabetes control [40], both of which may change with levels of adoption and 'domestication' of devices. In fact, what was once an important satisfaction item might fade with use and become trivial or, conversely, become even more important. Second, different indicators may be used to assess patients' trust in their devices, such as: (*i*) the patient's own assessment of risk associated with the device; (*ii*) correct positioning of what the patient lets the system do while maintaining relevant control; and (*iii*) the patient's

appreciation of the 'benefits/constraints' balance. Third, body acceptance must be contextualized through possible adaptations considering real-life circumstances, such as the patient's love life or professional situation, or seasonality (time of the year). Fourth, the patient's management of CL system data must be taken into account for two possible pitfalls: (*i*) risk of being overwhelmed by the quantity of data produced and the patient's subsequent dropping out; and (*ii*) risk of discouragement due to no longer sufficiently increasing in skill, with subsequent misuse of the system.

Table V presents a checklist of questions aimed at assessing psychosocial factors. To date, although no study has evaluated caregivers' perceptions of CL devices, it is clear that the patient/doctor relationship will be transformed. The expertise of HCPs will shift from diabetes expertise to technical expertise, including thorough knowledge of the different available systems that are constantly evolving. HCPs will therefore need to spend a great deal of time keeping abreast of any new systems, whereas the PWDs who use them on a daily basis may often master these devices much better than do caregivers, which could become the source of a technological divide between patients and caregivers and so disrupt the usual relationship. However, once the effort has been made and the technical skills acquired, the automated insulin delivery by CL systems will free consultations of numerous technical aspects and make it possible to strengthen the quality of the care relationship, which is the key that lies at the very heart of the health professions.

Safety and malfunctions: materiovigilance

The development of CL devices has to meet very specific safety standards. Patients equipped with CL devices may, however, in a small number of cases be confronted by a possible malfunction of one of its three components (pump, CGM, control system) or loss of connectivity between them, thereby exposing patients to either under- or overdelivery of

insulin (Table VI). Most of these risks are known, expected and identical to those receiving the usual pump and CGM treatment [1–3]. Nevertheless, patients should be educated in the use of CL to allow optimal functioning of the system and adequate coping with metabolic emergencies. Finally, the essential post-marketing follow-up of CL devices should make it possible to assess the security of these systems in real-life situations.

7. Future perspectives

A key perspective of CL insulin therapy is complete automation of the system. Various strategies are how being considered to free patients from any compulsory participation, including the use of fast- and shorter-acting insulin formulations [16], alternatives to the SC route of insulin administration such as the intraperitoneal route [41], automated detection of food intakes or physical activities through specific signals [42, 43], and automated detection of insulin delivery faults by abnormalities of the infusion site [44].

Other avenues of research concern the development of bihormonal CL systems combining insulin and glucagon infusions. Meta-analyses evaluating the performances of monohormonal and bihormonal CL systems have indicated superiority of the latter in terms of improvement in TIR 70–180 mg/dL over 24 h and reductions in TBR [5, 6]. However, the number of bihormonal system studies are limited and, in most of them, there was no direct comparison between monohormonal and bihormonal systems. Bihormonal insulin–glucagon systems involve increased complexity in the management of the CL system, with additional cannulae and manipulations for glucagon infusion. The instability of glucagon in solution requires daily replacement from a dedicated reservoir, so studies are also underway to obtain more stable glucagon in solution with a unique two-chamber infusion device for administration of both hormones. Longer-term directly comparative studies are still a necessary priority to define the target population that should benefit from CL devices, such as patients exposed to severe

hypoglycaemia and/or lacking awareness of hypoglycaemia, those with frequent, repeated or intense physical activity, and even young children. The long-term tolerability of glucagon also needs to be assessed.

Another bihormonal approach has recently been developed involving the co-administration *via* two separate pumps of insulin and pramlintide, an amylin analogue physiologically secreted by β cells. Amylin administered at mealtime delays gastric-emptying, slows glucagon secretion, stimulates satiety and ultimately reduces post-meal glycaemic excursions [45].

Finally, while most experimental studies of CL insulin therapy systems have been proposed for the treatment of T1D, a clinical research domain has been developing in recent years in the field of type 2 diabetes (T2D). Preliminary work [46–51] has thus far shown the potential metabolic impact of CL technology to treat T2D, albeit still with unresolved questions of the feasibility and medicoeconomic relevance of its use as well as the target population that could use and most likely benefit from it.

Conclusion

To the best of our knowledge, recommendations for the training and support of users of commercially available HCL systems are the sole result of individual initiatives with no endorsement by professional associations [52, 53]. The present position statement was written by T1D experts in France, the first country to allow full nationwide coverage of CL treatment through its social insurance programme [14], and has been endorsed by the main professional associations in the country. Most of the experts in our Working Group have had previous experience with CL therapy through their involvement in numerous clinical trials.

Overall, the present consensus emphasizes the crucial impact of both PWD and HCP training on any future success with this new technology. These experts also agree on the

formidable perspectives offered by CL therapy, and are now calling for the further extension of the current indications to keep up with confirmation trials. As this new technology is expected to make deep changes in the metabolic and qualitative outcomes for PWDs and their caregivers, and to disrupt the organization of diabetes care, CL systems should now be seen as the next frontier in diabetology. The challenge is not an easy one, but it will be successful.

Appendix supplementary material

Supplementary materials (Tables S1–S3) associated with this article can be found at http://www.scincedirect.com at doi . . .

Figure legends

Fig. 1. Horizontal flow diagram of patient therapeutic education (PTE) when integrated into a closed-loop (CL) course of treatment. CGM, continuous glucose monitoring.

Fig. 2. Closed-loop (CL) patient therapeutic education (PTE) process for adults and paediatric cases rises from bottom to top: from base level skills to success. TIR, time in range; TBR, time below range; QoL, quality of life; CGM, continuous glucose monitoring.

References

1. Tauschmann M, Thabit H, Bally L, Allen JM, Hartnell S, Wilinska ME et al. APCam11 Consortium. Closed-loop insulin delivery in suboptimally controlled type 1 diabetes: a multicentre, 12-week randomised trial. Lancet 2018; 392:1321-9.
2. Benhamou PY, Franc S, Reznik Y, Thivolet C, Schaepelynck P, Renard E et al. on behalf of Diabeloop WP7 trial investigators. Closed loop insulin delivery in adults with type 1 diabetes in real life conditions: a multicentre, 12-week randomised crossover trial. On behalf of diabeloop trial investigators. Lancet Digit Health 2019; 1: e17-25.
3. Brown SA, Kovatchev BP, Raghinaru D, Lum JW, Buckingham BA, Kudva YC, et al. iDCL Trial Research Group. Six-month randomized, multicenter trial of closed-loop control in type 1 diabetes. N Engl J Med 2019; 381: 1707-17.
4. Garg SK, Weinzimer SA, Tamborlane WV, Buckingham BA, Bode BW, Bailey TS, et al. Glucose outcomes with the in-home use of a hybrid closed-loop insulin delivery system in adolescents and adults with type 1 diabetes. Diabetes Technol Ther 2017; 19: 155–63.
5. Weisman A, Bai JW, Cardinez M, Kramer CK, Perkins BA. Effect of artificial pancreas systems on glycaemic control in patients with type 1 diabetes: a systematic review and meta-analysis of outpatient randomised controlled trials. Lancet Diabetes Endocrinol 2017; 5:501-12.
6. Bekiari E, Kitsios K, Thabit H, Tauschmann M, Athanasiadou E, Karagiannis T et al. Artificial pancreas treatment for outpatients with type 1 diabetes: systematic review and meta-analysis. BMJ 2018; 361:k1310. doi: 10.1136/bmj.k1310.
7. Karageorgiou V, Papaioannou TG, Bellos I, Alexandraki K, Tentolouris N, Stefanadis C et al. effectiveness of artificial pancreas in the non-adult population: a systematic review and network meta-analysis. Metabolism 2019; 90:20-30.
8. Forlenza GP, Pinhas-Hamiel O, Liljenquist DR, Shulman DI, Bailey TS, Bode BW et al. Safety evaluation of the MiniMed 670G system in children 7-13 years of age with type 1 diabetes. Diabetes Technol Ther 2019; 21:11–9.
9. Renard E. Invited communication. The artificial pancreas in 2019: first reports of new, large-scale trials and the path forward. ADA 2019.
10. Tubiana-Rufi N, Bismuth E, Dalla-Valle F, Bonnemaison E, Coutant R, Farret A et al. for the Free-Life Kid AP Study Group. Closed-loop insulin therapy in free-life shows better glucose control when used 24/7 versus overnight only in pre-pubertal children with type 1 diabetes: interim analysis of the Free-life Kid AP Study. ISPAD 2019, Boston. Pediatric Diabetes 2019;20 (Suppl.28):15 (O20).
11. Breton MD, Kanapka LG, Beck RW, Ekhlaspour L, Forlenza GP, Cengiz E et al; iDCL Trial Research Group. A Randomized Trial of Closed-Loop Control in Children with Type 1 Diabetes. N Engl J Med 2020; 383: 836-45.
12. DiMeglio LA, Acerini CL, Codner E, Craig ME, Hofer SE, Pillay K et al. ISPAD Clinical Practice Consensus Guidelines 2018: Glycemic control targets and glucose monitoring for children, adolescents and young adults with diabetes. Pediatr Diabetes 2018;19 (Suppl. 27):105–14.

13. Battelino T, Danne T, Bergenstal RM, Amiel SA, Beck R, Biester T, et al. clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range. Diabetes Care 2019; 42:1593-603.
14. Statement for reimbursement of DBLG1 by French regulatory authority. https://www.has-sante.fr/upload/docs/evamed/CNEDIMTS-5998_DBLG1%205998_occultation.pdf (accessed August 28, 2020).
15. Farrington C, Hovorka R, Murphy HR. Who should access closed-loop technology? A qualitative study of clinician attitudes in England. Diabetes Technol Ther 2020; 5: 404-10.
16. Dovc K, Boughton C, Tauschmann M, Thabit H, Bally L, Allen JM, et al. APCam11, AP@Home, and KidsAP Consortia. Young children have higher variability of insulin requirements: observations during hybrid closed-loop insulin delivery. Diabetes Care 2019; 42: 1344-7.
17. Commissariat PV, Harrington KR, Whitehouse AL, Miller KM, Hilliard ME, Van Name M et al. "I'm essentially his pancreas": Parent perceptions of diabetes burden and opportunities to reduce burden in the care of children <8 years old with type 1 diabetes. Pediatr Diabetes 2020;21: 377-83.
18. Van Name MA, Hilliard ME, Boyle CT, Miller KM, DeSalvo DJ, Anderson BJet al Nighttime is the worst time: parental fear of hypoglycemia in young children with type 1 diabetes. Pediatr Diabetes 2018;19: 114–20.
19. Musolino G, Dovc K, Boughton CK, Tauschmann M, Allen JM, Nagl K et al. Consortium. Reduced burden of diabetes and improved quality of life: Experiences from unrestricted day-and-night hybrid closed-loop use in very young children with type 1 diabetes. Pediatr Diabetes 2019;20: 794-9.
20. Sánchez-Rodríguez R, Perier S, Callahan S, Séjourné N. Revue de la littérature relative au burnout parental. Canadian Psychology/Psychologie canadienne 2019; *60*: 77–89.
21. Foster NC, Beck RW, Miller KM, Clements MA, Rickels MR, DiMeglio LAet al. State of Type 1 Diabetes management and outcomes from the T1D exchange in 2016-2018. Diabetes Technol Ther 2019;21: 66-72.
22. Rawshani A, Sattar N, Franzén S, Rawshani A, Hattersley AT, Svensson AMet al. Excess mortality and cardiovascular disease in young adults with type 1 diabetes in relation to age at onset: a nationwide, register-based cohort study. Lancet 2018; 392: 477–86.
23. American Diabetes Association. Standards of Medical Care in Diabetes. Diabetes Care 2020; 43: 566-76.
24. Messer LH, Tanenbaum ML, Cook PF, Wong JJ, Hanes SJ, Driscoll KA et al. Cost, hassle, and on-body experience: barriers to diabetes device use in adolescents and potential intervention targets. Diabetes Technol Ther 2020 Mar 27. doi: 10.1089/dia.2019.0509. Online ahead of print.
25. Benhamou PY, Lablanche S, Vambergue A, Doron M, Franc S, Charpentier G. Highly unstable type 1 diabetes, indicating for islet transplantation, can be addressed by closed-loop insulin delivery: a 16-week randomised crossover trial. Diabetes Obes Metab 2020 Oct 1. doi: 10.1111/dom.14214.

26. Tauschmann M, Allen JM, Nagl K, Fritsch M, Yong J, Metcalfe E et al; KidsAP Consortium. home use of day-and-night hybrid closed-loop insulin delivery in very young children: a multicenter, 3-week, randomized trial. Diabetes Care 2019; 42:594-600.

27. Salehi P, Roberts AJ, Kim GJ. Efficacy and safety of real-life usage of MiniMed 670G automode in children with type 1 diabetes less than 7 years old. Diabetes Technol Ther 2019; 21:448-51.

28. Buckingham B, Forlenza G, Jennifer S, Galderisi A, Ekhlaspour L, Lee JB et al. Safety and performance of the Omnipod Hybrid in young children aged 2-6 yrs with Type 1 diabetes. ISPAD 2019, Boston. Pediatric Diabetes 2019; 20 (Suppl.28): 15 (O21).

29. Boughton C, Allen JM, Tauschmann M, Hartnell S, Wilinska ME, Musolino G et al. CLOuD Consortium. assessing the effect of closed-loop insulin delivery from onset of type 1 diabetes in youth on residual beta-cell function compared to standard insulin therapy (CLOuD Study): a randomised parallel study protocol. BMJ open 2020;10: e033500.

30. Stewart ZA, Wilinska ME, Hartnell S, Temple RC, Rayman G, Stanley KP et al. Closed-loop insulin delivery during pregnancy in women with type 1 diabetes. N Engl J Med 2016; 375:644-54.

31. Stewart ZA, Wilinska ME, Hartnell S, O'Neil LK, Rayman G, Scott EM et al. Day-and-night closed-loop insulin delivery in a broad population of pregnant women with type 1 diabetes: a randomized controlled crossover trial. Diabetes Care 2018; 41: 1391-9.

32. Lassmann-Vague V, Clavel S, Guerci B, Hanaire H, Leroy R, Loeuille GA, et al; Société francophone du diabète. When to treat a diabetic patient using an external insulin pump. Expert consensus. Société francophone du diabète (ex ALFEDIAM) 2009. Diabetes Metab. 2010;36:79-85. doi: 10.1016/j.diabet.2009.09.002. Epub 2010 Jan 13. PMID: 20074990

33. Borot S, Benhamou PY, Atlan C, Bismuth E, Bonnemaison E, Catargi B et al. Practical implementation, education and interpretation guidelines for continuous glucose monitoring: A French position statement. Diabetes Metab 2018;44: 61-72. doi:10.1016/j.diabet.2017.10.009

34. Kimbell B, Rankin D, Ashcroft NL, Varghese L, Allen JM, Boughton CK et al. What training, support, and resourcing do health professionals need to support people using a closed-loop system? Diabetes Technol Ther 2020; 22:468-75.

35. Messer LH, Berget C, Forlenza GP. A clinical guide to advanced diabetes device and closed-loop systems using the CARES paradigm. Diabetes Technol Ther. 2019 Aug;21(8):462-469. doi: 10.1089/dia.2019.0105. Epub 2019 May 29

36. Berget C, Thomas SE, Messer LH, Thivener K, Slover RH, Wadwa RP, Alonso GT. A clinical training program for hybrid closed loop therapy in a pediatric diabetes clinic. J Diabetes Sci Technol 2020;14:290-6. doi: 10.1177/1932296819835183. Epub 2019 Mar 12.

37. Boughton CK, Hartnell S, Allen JM, Hovorka R. The importance of prandial insulin bolus timing with hybrid closed-loop systems. Diabet Med 2019;36: 1716-7. doi:10.1111/dme.14116

38. Forlenza GP, Messer LH, Berget C, Wadwa RP, Driscoll KA. biopsychosocial factors associated with satisfaction and sustained use of artificial pancreas technology and its components: a call to the technology field. Curr Diab Rep 2018;18: 114.
39. Maahs DM, Buckingham BA, Castle JR, Cinar A, Damiano ER, Dassau E et al. Outcome measures for artificial pancreas clinical trials: a consensus report. Diabetes Care 2016; 39: 1175-9.
40. Liberman A, Buckingham B, Phillip M. diabetes technology and the human factor. Diabetes Technol Ther 2014;16: S110-8.
41. Dassau E, Renard E, Place J, Farret A, Pelletier MJ, Lee J et al. intraperitoneal insulin delivery provides superior glycemic regulation to subcutaneous insulin delivery in model predictive control-based fully-automated artificial pancreas in patients with type 1 diabetes: a pilot study. Diabetes Obes Metab 2017; 19: 1698-705.
42. Samadi S, Rashid M, Turksoy K, Feng J, Hajizadeh I, Hobbs N et alAutomatic Detection and estimation of unannounced meals for multivariable artificial pancreas system. Diabetes Technol Ther 2018; 20: 235-46.
43. Turksoy K, Monforti C, Park M, Griffith G, Quinn L, Cinar A. Use of wearable sensors and biometric variables in an artificial pancreas system. Sensors 2017; 17: 532.
44. Howsmon DP, Baysal N, Buckingham BA, Forlenza GP, Ly TT, Maahs DM et al. Real-time detection of infusion site failures in a closed-loop artificial pancreas. J Diabetes Sci Technol 2018; 12: 599-607.
45. Haidar A, Tsoukas MA, Bernier-Twardy S, Yale JF, Rutkowski J, Bossy A et al. a novel dual-hormone insulin-and-pramlintide artificial pancreas for type 1 diabetes: a randomized controlled crossover trial. Diabetes Care 2020;43: 597-606.
46. Kumareswaran K, Thabit H, Leelarathna L, Caldwell K, Elleri D, Allen JM et al. Feasibility of closed-loop insulin delivery in type 2 diabetes: a randomized controlled study. Diabetes Care 2014;37: 1198–203.
47. Thabit H. Closed-loop insulin delivery in inpatients with type 2 diabetes: a randomised, parallel-group trial. Lancet Diabetes Endocrinol 2017;5: 117-24.
48. Taleb N, André C. Carpentier AC, Messier V, Ladouceur M, Haidar A et al. efficacy of artificial pancreas use in patients with type 2 diabetes using intensive insulin therapy: a randomized crossover pilot trial. Diabetes Care 2019;42: e107–9.
49. Bally L. fully closed-loop insulin delivery improves glucose control of inpatients with type 2 diabetes receiving hemodialysis. Kidney Int 2019;96: 593-6.
50. Bally L, Thabit H, Hovorka R. Closed-loop insulin for glycemic control in noncritical care. N Engl J Med 2018; 379:1970-1.
51. Schliess F, Heise T, Benesch C, Mianowska B, Stegbauer C, Broge B et al. Artificial pancreas systems for people with type 2 diabetes: conception and design of the european CLOSE Project. J Diab Sci Technol 2019; 13: 261–7.
52. Boughton C, Hartnell S, Allen J, Fuchs J, & Hovorka, R. Training and support for hybrid closed-loop therapy. J Diabetes Sci Technol 2020 ; sept 11. https://doi.org/10.17863/CAM.56437
53. Bally L, Thabit H, Hovorka R. Closed-loop for type 1 diabetes–an introduction and appraisal for the generalist. BMC Medicine 2017;15: 14.

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NTR has received congress invitations, honoraria and consultancy fees from Abbott, Eli Lilly and Tandem Diabetes Care.

PS declares congress invitations, honoraria and consultancies from Abbott Diabetes Care, Roche and Ypsomed, and has served on advisory board panels for Diabeloop.

SF declares congress invitations from Sanofi, Eli Lilly, MSD, Novo Nordisk, Roche, Abbott and Boehringer Ingelheim, and has received speaker honoraria from Eli Lilly and Novo Nordisk, and served on advisory board panels for Novo Nordisk, Roche, Sanofi, Janssen and LifeScan. She owns shares in Diabeloop SA.

LC reports congress invitations, honoraria and consultancies from Abbott, Air Liquide SI, Diabeloop, Medtronic, Eli Lilly, Novo Nordisk and Sanofi.

MJ discloses congress accommodations, honoraria and participation in advisory board panels from Abbott, Diabeloop, Medtronic, Sanofi, Eli Lilly, Novo Nordisk, AstraZeneca, MSD, BMS, Boehringer Ingelheim, Amgen, Air Liquide SI and LifeScan.

ER has received research support from Abbott, Dexcom Inc., Insulet Inc., Roche and Tandem Diabetes Care, and has been a consultant for Menarini Diagnostics, Abbott, Air Liquide SI, Becton, Dickinson and Company, Cellnovo, Dexcom Inc., Diabeloop, Eli Lilly, Hillo, Insulet Inc., Johnson & Johnson (Animas, LifeScan), Medtronic, Medrio, Novo Nordisk, Roche and Sanofi-Aventis.

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CA declares no conflicts of interest.

EBi has received congress invitations, honoraria and consultancy fees from Abbott, Eli Lilly, Novo Nordisk, Insulet Inc. and Medtronic.

JB was a clinical investigator for Diabeloop and Medtronic, and served on advisory board panels for Medtronic and Insulet.

EBo has received congress invitations, honoraria and consultancy fees from Abbott, Novo Nordisk, Medtronic and Air Liquide SI.

SB discloses congress invitations, honoraria and consultancies from Abbott, Animas/Johnson & Johnson, Medtronic and Roche, and has served on advisory board panels for Diabeloop.

GC has received congress invitations, honoraria and consultancy fees from Abbott, Dexcom and Medtronic, and owns shares in Diabeloop SA.

BD reports congress invitations from Novo Nordisk, Sanofi, Eli Lilly and Novartis, board fees and speaker honoraria from Sanofi, Eli Lilly, Novo Nordisk and Abbott, and has served on advisory board panels for Diabeloop.

AD declares no conflicts of interest.

DD reports honoraria for congress, formation and conferences from Abbott, Eli Lilly, Becton, Dickinson and Company, Roche and Asten-Santé.

AF declares conference honoraria from Novo Nordisk.

NF served on an advisory board panel for Ypsomed.

BG reports congress invitations, honoraria and consultancies from Abbott, Medtronic, Eli Lilly, Dexcom and Roche, and has served on advisory board panels for Diabeloop.

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RL has received speaker honoraria and congress invitations from Abbott, Novo Nordisk, Insulet and Eli Lilly.

VM received speaker honoraria from Abbott and Novo Nordisk.

MM declares no conflicts of interest.

AP discloses congress invitations, speaker honoraria and consultancies from Abbott, Eli Lilly, LifeScan, Medtronic, Novo Nordisk and Sanofi, and has served on advisory board panels for Abbott, Diabeloop, Insulet, Novo Nordisk and Sanofi.

SP discloses consulting and/or speaker fees from Abbott, Air Liquide, AstraZeneca, Eli Lilly, Novo Nordisk, Sanofi and VitalAire.

JP declares no conflicts of interest.

JPR discloses speaker honoraria from Abbott, Novo Nordisk, Eli Lilly, Sanofi, MSD, Novartis, Orkyn and Johnson & Johnson, has served on advisory board panels for Abbott and Eli Lilly, and was clinical investigator for Roche, Eli Lilly, Novo Nordisk, Orkyn and Medtronic.

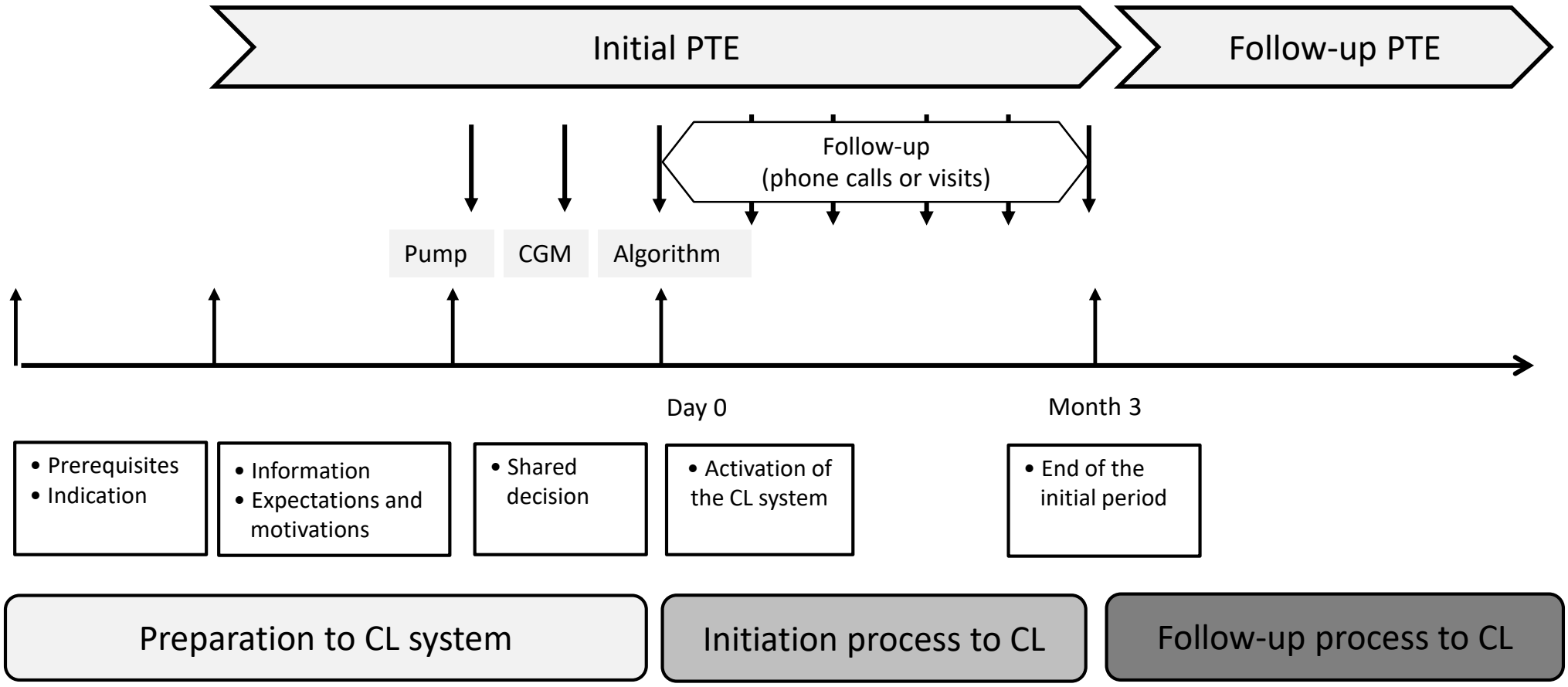
PS reports congress invitations, honoraria and consultancies from Abbott, Medtronic, Eli Lilly, Novo Nordisk and Sanofi.

ASG reports speaker honoraria from Abbott, Novo Nordisk and Johnson & Johnson, has served on advisory board panels for Abbott and Eli Lilly, and was an investigator for Roche, Eversense, Eli Lilly and Medtronic.

CT has received speaker honoraria from Abbott, Eli Lilly and Sanofi, and served on advisory board panels for Abbott, Diabeloop, Roche and Medtronic.

HH has received congress invitations, honoraria and consultancy fees from Abbott, Animas/Johnson & Johnson, Medtronic, Roche, Eli Lilly, Novo Nordisk and MSD, and served on advisory board panels for Diabeloop and Insulet.

PYB has received speaker honoraria from Abbott, Roche, Eli Lilly, Novo Nordisk and Sanofi, and served on advisory board panels for Abbott, Diabeloop, Roche, Medtronic, Dexcom, Insulet, LifeScan, Eli Lilly, Novo Nordisk and Sanofi.


Initial PTE
Follow-up PTE
Follow-up
(phone calls or visits)
Pump
CGM
Algorithm
Day 0
Month 3
• Prerequisites
• Indication
• Information
• Expectations and motivations
• Shared decision
• Activation of the CL system
• End of the initial period
Preparation to CL system
Initiation process to CL
Follow-up process to CL

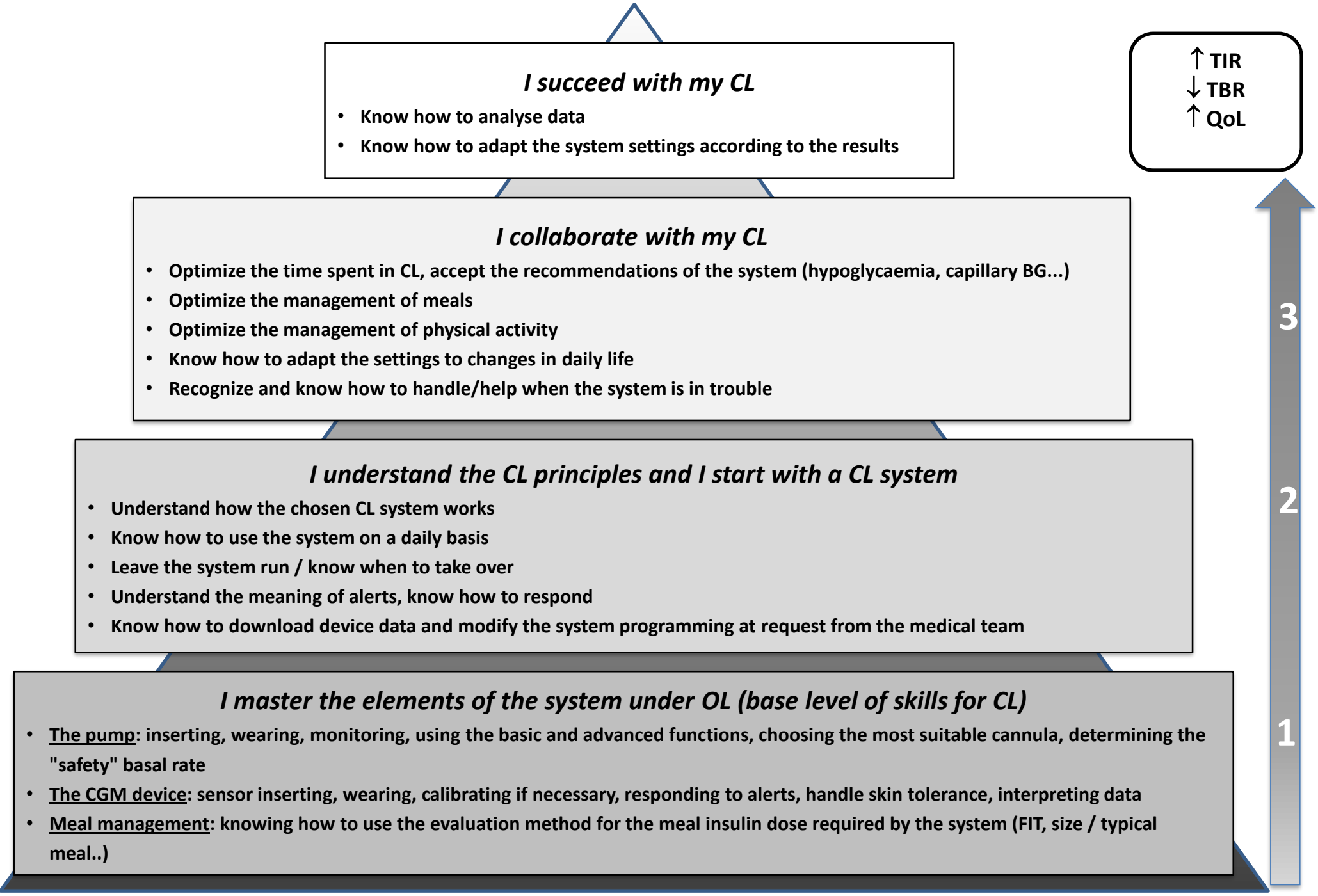

I succeed with my CL
• Know how to analyse data
• Know how to adapt the system settings according to the results
↑ TIR
↓ TBR
↑ QoL
I collaborate with my CL
• Optimize the time spent in CL, accept the recommendations of the system (hypoglycaemia, capillary BG...)
• Optimize the management of meals
• Optimize the management of physical activity
• Know how to adapt the settings to changes in daily life
• Recognize and know how to handle/help when the system is in trouble
I understand the CL principles and I start with a CL system
• Understand how the chosen CL system works
• Know how to use the system on a daily basis
• Leave the system run / know when to take over
• Understand the meaning of alerts, know how to respond
• Know how to download device data and modify the system programming at request from the medical team
I master the elements of the system under OL (base level of skills for CL)
• The pump: inserting, wearing, monitoring, using the basic and advanced functions, choosing the most suitable cannula, determining the "safety" basal rate
• The CGM device: sensor inserting, wearing, calibrating if necessary, responding to alerts, handle skin tolerance, interpreting data
• Meal management: knowing how to use the evaluation method for the meal insulin dose required by the system (FIT, size / typical meal..)
3
2
1

Table I
Summary of recommendations for use of closed-loop (CL) insulin therapy systems in 2020 in adult and paediatric* patients with diabetes (PWDs)

Prerequisite	
Type of diabetes	Type 1
Age	≥ 6 years
Current treatment	Insulin pump
Patient training	Carbohydrate-counting
Patient commitment	Compliance with good practices and participation in dedicated patient therapeutic education (PTE) programmes delivering clear and detailed information on CL systems after a 3-month initiation period.
Indications	
Non-achievement of metabolic goals set by international panels [American Diabetes Association (ADA), International Consensus on TIR (time in range), International Society for Pediatric and Adolescent Diabetes (ISPAD)]: Objectives: HbA1c < 7% and/or TIR 70–180 mg/dL > 70% and/or time below range (TBR) < 70 mg/dL < 4% *and/or* Quality of life of patients altered by constraints of daily diabetes management *and/or* by mental burden of diabetes *and/or* by consequences of diabetes on social and professional integration.	
Precautions for use and elements of vigilance	
Risks associated with rapid glycaemic normalization (retinopathy, neuropathy); Vigilance against possible misuse of CL systems by patients if some constraints are refused *and/or* in cases of poor acceptance of wearing external devices *and/or* insufficient previous compliance with monitoring and treatment of diabetes.	

* Children and their parents

Table II
Goals of initiating and monitoring centres for closed-loop (CL) insulin treatment in adults, adolescents and children with type 1 diabetes (T1D)

Mission	**Initiating centre[a]**	**Monitoring centre[b]**
To place CL indication	✓	✓
To validate CL indication	✓	
To support patients in choosing a more adapted CL system	✓	
To initiate treatment with CL	✓	
To provide initial PTE training (0–3 months) for patients/entourage or caregivers	✓	
To begin patient monitoring during initial probationary period (0–3 months)	✓	
To ensure early reassessment of patients at 3 months after initiation of CL therapy	✓	
To ensure daily follow-ups of patients using CL after 3-month probationary period	✓	✓
To write prescriptions	✓	✓ after 3 months
To give expert opinion if poor glucose control persists despite CL (tele-expertise, MPCM …)	✓	
To ensure annual reassessment	✓	
To reassess CL indication at request of diabetologist from monitoring centre	✓	
To provide training for HCP stakeholders	✓	contributory
To ensure on-call 24/7 responses	✓ up to 3 months	✓ after 3 months
To take responsibility for treatment	✓ up to 3 months	✓ after 3 months

[a] Multiprofessional team for adult or paediatric patients; [b] multiprofessional adult or paediatric team, or independent specialists for adults;
PTE, patient therapeutic education; MPCM, multiprofessional consultation meeting; HCP, healthcare professional

Table III
Skills checklist expected of healthcare professionals (HCPs) to initiate and/or monitor patients using closed-loop (CL) insulin therapy systems

HCP skills required to initiate and/or monitor patients using CL		**Specific training objectives**
Psychosocial skills		How to suggest CL free of preconceived ideas to all patients who wish it (impact of HCP attitude); How to explore and manage patients' expectations and representations
Specific technical skills	Know specificities and options offered by different CL systems	How to support patients in choosing CL devices; How to ensure initial technical training of patients/entourage (algorithm function, adjustable settings, alerts, good technical and safety practices, reasons for exiting CL ...)
Specific medical and educational skills	Know indications of CL systems	How to offer CL to patients who can benefit from it and prepare them (prerequisite)
	Confirm indication of CL system and choice of device; Supervise implementation and ensure initial follow-up; Initiate remote monitoring during initial period; Manage end of initial period	How to take into account patients' specific needs and expectations, motivations; How to optimalize transition to CL (key points of education: announcement of meals/physical activities, calibrations, all aspects changed by CL ...); How to analyze remote monitoring data and modify initial settings if necessary; How to ensure evaluation at end of initial period
	Ensure long-term patient follow-up and annual assessment; Renew CL prescription	How to support patients to optimalize CL in the long term in most possible autonomous way (settings to be modified by patients and/or doctors, data downloading and analysis); How to check appropriate patient practices
	Ensure medical on-call responses	How to manage emergency situations and ensure safety
Medical expertise	Ensure expertise function *via* MPCM between initiating and monitoring centres	Analysis of specific cases (discussions on indications, maintenance or stopping device use); Continuing medical education (CME) of HCPs
Skills for technical follow-up of CL at patient's home	Ensure continuing technical training of patients to support independence in data downloading; Ensure technical on-call responses.	How to check patients' best practices for pump and CGM use (interval between cannula changes, which affects CL effectiveness ...); Interventions in cases of system malfunction/failure and to ensure materiovigilance.

Note: 'Patients' refers to either adults or children and parent(s); 'initial period' refers to the 3 months following the start of CL device use;
MPCM, multiprofessional consultation meeting; CGM, continuous glucose monitoring

Table IV
Closed-loop (CL) therapeutic education for adults and children/parents with diabetes: course, stages and skills to be acquired

Therapeutic education	**Skills to be acquired by patient/child's parent(s)**
PTE initiation course (after informed patient/child–parent decision-making)	
Information on PTE course	
Shared educational assessment: guidance on choice and suitability of CL system	• Benefits and limitations of CL systems • Prerequisites and personal motivation
Reinforcement of PTE in daily management of diabetes with pump therapy	• Insulin therapy, carbohydrate-counting, flexible insulin treatment (FIT) parameters according to system • Treatment of hypoglycaemia • Pump safety: correction of hyperglycaemia with/without ketones • Pump efficiency: boluses before meals, cannula change
Change of insulin pump model (if applicable)	• Programming basic pump functions • Mastery of infusion settings
Control of continuous glucose monitoring (CGM) device with alerts	• Mastery of different components and installation of sensor • Knowing and understanding concept of interstitial glucose • How to respond to alerts
Downloading and transmission of data	• Knowing objectives for time in range (TIR) and time spent in hypoglycaemia • How to transmit data and how to contact team
Summary and assessment of core competencies	• Mastery of all components of CL system (ensured by team)
Activation of CL system: Learning how to collaborate with system	• Understanding how algorithm works • How to use CL on a daily basis and to manage alerts • When and how to take over the system • Adaptation of hypoglycaemia treatment/optimalization of meal announcements • How to trust the system
PTE process for CL system follow-up	
Data analysis: Adjustment of settings	• Management of downloads and contact with healthcare team • What metabolic goals to achieve • How to perform retrospective data analysis • What settings in CL system are adjustable • How to adjust settings, particularly meal insulin-to-carbohydrate ratios • How to use device manual and other provided documents
Reinforcement PTE for daily management of CL system	• Meal announcement • Treatment of hypoglycaemia • Responses to system alerts • Detection and management of infusion setting failure • Management and announcement of physical exercise
CL optimalization	• Time spent in CL • Time spent in target range • Time spent in hypoglycaemia

Note: ‘Initial patient therapeutic education (PTE)’ (first 3 months) and ‘follow-up PTE’ are provided by multiprofessional teams from institutions labelled ‘initiation centres’; follow-up PTE may be provided by teams from follow-up centres in collaboration with other healthcare professionals

Table V
Main clinical factors to explore when monitoring patients equipped with closed-loop (CL) systems

Parameters	**Questions to ask (or to ask oneself)**
Technique	*Questions to patients*: Do you have: problems with pump cannula? at insertion site? technical problems with sensor? communication problems between devices?
	Questions HCPs should ask themselves: In the event of frequent or prolonged out-of-control periods: is technical compliance involved (change of cannula or sensor, pump-filling, low battery, missing or postponed calibrations, false calibrations …)?
Alarms	Do you often have alarms? If so, at what frequency, what type, at what times and does it bother you?
Compliance with good system practices	Do you announce: meals, and if so, how long before? physical activity, and if so, how long before? How often are pump cannulae changed?
Carbohydrates and preventative or curative treatment of hypoglycaemia	How many times a week do you take carbohydrates to treat or prevent hypoglycaemia, at what times and with what effects? Have you observed any weight changes?
Adaptive behaviours	Do you manually inject insulin by yourself? Do you ever 'cheat' with the system? If so, why and with what results?*
Psychosocial factors	What has this device brought you to date (sleep, fear of hypoglycaemia, stress …)? What bothers you about using it today (bulk of device, alarms, continuous wearing, liability)? Do you feel you have learned more about your disease since using it?

* Voluntary declaration of wrongdoing or non-declaration of carbohydrate intake or activity

Table VI
Main malfunctions, risks and safety issues of closed-loop (CL) therapy systems

Component	Dysfunction	Risk	Internal safety	External safety
Pump and infusion line	Cannula obstruction	Insulin underdelivery	Overpressure sensor	Patient education: cannula change
	Electronic or mechanical component failure	Insulin under-/overdelivery	Autocheck of integrity of system, alarms, alerts	Patient education: insulin injection replacement protocol
Sensor	Missing data; Loss of signal	Interruption of CL system	Alarm/automatic switch to open-loop (OL) system	Switch to OL system
	Erroneous data	Insulin under-/overdelivery; no hypo- or hyperglycaemia alarms	Autodetection of outliers/automatic switch to OL system	Patient education: capillary blood glucose control/sensor change
Algorithm	Unknown 'bug' in system	Insulin under-/overdelivery	Supervisor, safety module	Patient vigilance