Hormones
https://doi.org/10.1007/s42000-022-00412-8

ORIGINAL ARTICLE

Monitoring of continuous subcutaneous insulin infusion treatment in Portugal and its implications for diabetes management

Ana Rita Figueiredo[1] · **Tânia Matos**[2] · **Sónia do Vale**[1,2,3]

Received: 16 June 2022 / Accepted: 12 October 2022

Abstract

Aims/hypothesis Intensive insulin therapy in the treatment of type 1 diabetes can, in place of multiple daily injections of subcutaneous insulin (MDI), be performed with continuous subcutaneous insulin infusion (CSII) systems. This method allows for better glycemic control and thus reduces the risk of complications of the disease. The aim of this study was to evaluate the results of treatment with CSII in Portugal**.**

Methods A retrospective analysis of the records on the national CSII platform was carried out between January 2010 and August 2021. All the registered patients are followed in certified CSII treatment centers in Portugal. Of the 7135 registered patients, 3807 were excluded due to absence of monitoring data. The reasons for treatment were analyzed and a comparison was made between patients with and without CSII. The statistical significance considered was $\alpha < 0.05$.

Results A total of 3328 patients were included in the study, 1136 under MDI and 2192 under CSII. The main reasons for CSII use were marked glycemic variability (25%) and HbA1c greater than 7% (23%). Patients under CSII had a lower HbA1c ($7.7 \pm 1.0\%$ vs. $8.0 \pm 1.5\%$, $p < 0.001$), as well as a lower frequency of episodes of severe hypoglycemia (1.4 vs. 3.3 per 100 patient-years, $p < 0.001$), and ketoacidosis (1 vs. 2.4 per 100 patient-years, $p < 0.001$).

Conclusions The present analysis validates the advantage of using CSII in metabolic control and reduction of acute complications of type 1 diabetes, both severe hypoglycemia and ketoacidosis, in the Portuguese population. CSII therapy is classically associated with an increased risk of ketoacidosis; however, in experienced centers and adequate patient education, the opposite is found.

Keywords Continuous subcutaneous insulin infusion · CSII · HbA1c · Hypoglycemia · Portugal · Ketoacidosis · Type 1 diabetes

Abbreviations

CSII Continuous subcutaneous insulin infusion
DGS *Direção-Geral da Saúde (Directorate-General of Health)*
MDI Multiple daily injections of subcutaneous insulin
PND *Programa Nacional para a Diabetes (National Program for Diabetes)*

Introduction

Type 1 diabetes is a chronic immune-mediated disease characterized by the destruction of insulin-producing pancreatic β cells [1]. Although it can appear at any age, it is classically more common in the pediatric age group, with its highest incidence among young people between the ages 10 and 14, being the most frequent chronic disease in this population group [2]. When it is diagnosed in the first years of life, it accompanies children into adulthood. The longer the course of the disease and the worse the glycemic control, the greater the risk for complications [3, 4], so that type 1 diabetes, as a disease with a predominant incidence in childhood, in the long term presents a risk for the health of this population.

The complications of diabetes affect several organs and systems and are a consequence of metabolic imbalance and persistent hyperglycemia. The mortality and morbidity of diabetes mainly result from its micro- and macrovascular

✉ Ana Rita Figueiredo
arfigueiredo@campus.ul.pt

1 Endocrinology Department, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal

2 Endocrinology Diabetes and Metabolism Department, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal

3 National Program for Diabetes, Directorate-General of Health, Lisbon, Portugal

Published online: 07 November 2022

complications and, in developed countries, it is currently the leading cause of blindness in adults, end-stage renal disease, and non-traumatic lower extremity amputation [2, 4–8]. The publication of the pioneering Diabetes Control and Complications Trial (DCCT) in 1993 changed the way in which type 1 diabetes is controlled, showing that by seeking to achieve glucose concentrations closer to those among non-diabetic individuals, it would be possible to reduce the microvascular and macrovascular complications of type 1 diabetes [3, 9].

In type 1 diabetes, current treatment with insulin therapy simulates, as closely as possible, the physiological secretion of insulin. This functional insulin therapy can be administered in multiple dose regimens (multiple daily injections—MDI) by insulin pens, or alternatively, by continuous subcutaneous insulin infusion (CSII) systems. The intensive regimen of insulin therapy that is required to prevent the microvascular and cardiovascular complications of diabetes improves glycemic control; however, it may increase the frequency of hypoglycemic events when performed using MDI. CSII therapy attempts to more accurately reproduce physiological insulin secretion by administering small amounts of basal insulin throughout the day overlapping with smaller prandial boluses, by using rapid-acting insulin. Thus, it allows an adjustment that takes into account the daily variations of insulin needs according to the periods of the day and the individual's variations of insulin sensitivity [10]. CSII therefore allows for better control of fasting and pre- and postprandial glycemia, with a lower risk of hypoglycemia and with less need for daily injections, thereby enabling greater flexibility in lifestyle without negatively impacting the quality of life of individuals with type 1 diabetes and their families [11–14].

The administration of rapid-acting insulin is continuous throughout the day, in contrast to a combination with a dose of long-acting insulin; however, with the CSII systems, the risk of ketoacidosis due to system failure would likely be greater. Although malfunction problems with infusion devices are possible, incidence of diabetic ketoacidosis with CSII therapy has been disputed in past studies [10, 13, 15].

With the technological evolution of insulin pumps and interstitial glucose monitoring devices, it is now possible to achieve better glycemic control with less need for daily interventions considered "invasive" (injections and capillary punctures). This has a significant positive impact not only by preventing the complications of diabetes but also by enhancing the individual's well-being through minimizing the possible limitations of daily life inherent to a rigorous and demanding therapy [11].

In Portugal, patients with type 1 diabetes who use CSII under the *National Program for Diabetes* (PND) are enrolled in the Directorate-General of Health (DGS) CSII device management platform [16]. It is, however, important to evaluate the results of treatment with CSII in the Portuguese population for the purpose of determining what its benefits have been in order to consolidate or redefine the criteria and indications which support the decision on how to continue this treatment program.

The objective of this study was to analyze the results of treatment with CSII with regard to the following: motives for starting this type of treatment, impact of therapy on glycemic control, and impact on diabetes complications.

Methodology

A retrospective collection of data from patients who are enrolled in the CSII device management platform of the DGS was carried out. Data were collected for the period between January 2010 and August 2021. This platform includes the register of the vast majority of patients being treated with CSII in the country. All the patients are annually monitored at certified treatment centers.

Data from the platform were downloaded to an original database with 8080 records. A total of 945 records were eliminated due to errors in entry of the data. After excluding these, the database had records from 7135 patients, 3328 of whom had monitoring data and were included in the present study. The variables included were gender, date of birth, date of diagnosis, reasons for insertion of CSII, discontinuation (yes/no), reason for discontinuation, replacement (yes/no), and annual monitoring data, as follows: HbA1c value, number of severe hypoglycemia events, number of ketoacidosis events, and whether or not CSII was used during monitoring. To avoid an incoherent comparison between patient data, only one record per patient in each treatment group was considered. That is, the first record of monitoring data without CSII and the first record of monitoring data with CSII therapy for at least 3 months were considered.

A descriptive analysis of the population was performed and subsequently a comparative analysis was carried out between patients without CSII and patients with CSII at the time of the first monitoring on the platform.

Quantitative variables were presented as mean and standard deviation and qualitative variables as absolute frequency and percentage. Quantitative variables were tested for normal distribution with the Kolmogorov–Smirnov test. When they followed a normal distribution, the parametric Student t-test for independent or paired samples was used to test for differences between variables. When they did not follow a normal distribution, the nonparametric Mann–Whitney *U* test or the Wilcoxon test was used. Chi-square test was implemented to investigate the relationship between qualitative variables. A two-tailed p-value < 0.05 was considered statistically significant.

Table 1 Demographic characteristics

Demographic characteristics	Without CSII ($n=1136$)	With CSII ($n=2192$)	p-value	Total ($n=3328$)
Sex (n,%)				
Male	550 (48.4%)	1013 (46.2%)	0.194	1563 (47%)
Female	582 (51.2%)	1179 (53.7%)		1761 (52.9%)
N/A	4 (0.1%)			4 (0.1%)
Age (years)*	27.8 ± 13.9 ($n=1136$)	25.1 ± 14.6 ($n=2146$)	< 0.001	26.1 ± 14.4 ($n=3282$)
Age at diagnosis (years)*	13.3 ± 9.3 ($n=961$)	10.4 ± 8.8 ($n=1760$)	< 0.001	11.4 ± 9.1 ($n=2721$)

P-values were determined by Mann–Whitney *U* test and chi-square test

CSII continuous subcutaneous insulin infusion, *N/A* not available

*Data shown are represented as means ± SD

Table 2 Motives for CSII therapy (n, %)

	Total ($n=2578$)
"Marked daily variability in blood glucose levels"	632 (24.5%)
"HbA1c > 7% despite intensive therapy"	603 (23.4%)
"Need for lifestyle flexibility"	460 (17.8%)
"Need for small doses of insulin"	307 (11.9%)
"History of hypoglycemia unawareness"	236 (9.2%)
"Dawn phenomenon"	97 (3.8%)
"Child ≤ 5 years old"	34 (1.3%)
"Pregnant or woman trying to conceive"	21 (0.8%)

CSII continuous subcutaneous insulin infusion

Table 3 Motives for CSII discontinuation (n, %)

	Total ($n=165$)
"Withdrawal of the treatment method"	66 (40%)
"Patient maladjustment"	22 (13.3%)
"Failure to comply with the therapeutic regimen"	9 (5.5%)
"Patient's refusal"	7 (4.2%)
"Emigration"	5 (3%)
"Failure to resolve the problem that led to the insertion of CSII"	3 (1.8%)
"Other"	52 (31.5%)

CSII continuous subcutaneous insulin infusion

Results

Characteristics of the participants

Demographic characteristics of the 3328 patients are summarized in Table 1. The mean age was 26.1 ± 14.4 years and age at diagnosis 11.4 ± 9.1 years. The patients under treatment with CSII were younger than patients under MDI (25.1 ± 14.6 vs. 27.8 ± 13.9 years, $p < 0.001$) and were diagnosed at a younger age (10.4 ± 8.8 vs. 13.3 ± 9.3 years, $p < 0.001$).

Motives for treatment with CSII

The main motive reported to initiate treatment was "severe daily variability in blood glucose levels" (24.5%), followed by "HbA1c > 7% despite intensive therapy" (23.4%) (Table 2).

Discontinuation of treatment

In total, 143 patients (5.5%) had their devices replaced and 165 patients (6.4%) discontinued therapy with CSII. The most frequently reported motives were "withdrawal of the treatment method" (40%), "maladjustment of the patient" (13.3%), and "Other" (31.5%) (Table 3).

Metabolic control and complications in patients with or without CSII

A comparison was made between the CSII patient group and the group without CSII (Table 4).

In the group of patients with CSII, the mean HbA1c was lower compared to that in patients without CSII (7.7 ± 1.0% vs. 8.0 ± 1.5%, $p < 0.001$). The difference in HbA1c was significant in patients who started therapy due to marked glycemic variability, HbA1c > 7% despite intensive control, need for lifestyle flexibility, and a history of hypoglycemia unawareness (Table 5). The difference in HbA1c between groups remained significant independently of age group (< 18, 18–39, and ≥ 40 years, $p = 0.106$) (Table 6).

The group of patients treated with CSII also had a lower number of severe hypoglycemia events (1.4 vs. 3.3 per 100 patient-years, $p < 0.001$) and ketoacidosis (1 vs. 2.4 per 100 patient-years, $p < 0.001$) compared with the group of patients without CSII. These differences were independent of age and age at diagnosis.

Table 4 Metabolic control and acute complications

	Without CSII ($n=1136$)	With CSII ($n=2192$)	p-value
HbA1c (%)*	8.0 ± 1.5	7.7 ± 1.0	< 0.001
Male	7.9 ± 1.3	7.7 ± 1.0	< 0.001
Female	8.2 ± 1.6	7.7 ± 1.1	< 0.001
HbA1c > 7% (n, %)	843 (74.7%)	1562 (71.4%)	< 0.043
HbA1c > 7.5% (n, %)	679 (60.2%)	1114 (50.9%)	< 0.001
Daily dose of insulin (insulin units)*	42.7 ± 19.2	41.6 ± 19.5	0.120
Severe hypoglycemia (n, %)	38 (3.3%)	31 (1.4%)	< 0.001
Ketoacidosis (n, %)	27 (2.4%)	22 (1.0%)	0.002
Hospitalizations (n, %)	35 (3.3%)	63 (3%)	0.659

P-values were determined by Mann–Whitney *U* test and chi-square test

CSII continuous subcutaneous insulin infusion

*Data shown are represented as means ± SD

Table 5 HbA1c comparison by PSCI therapy motives

	Without CSII	With CSII	p-value
"Marked daily variability in blood glucose levels"	8.2 ± 1.5 ($n=197$)	7.8 ± 1 ($n=521$)	0.001
"HbA1c > 7% despite intensive therapy"	8.2 ± 1.3 ($n=198$)	7.8 ± 1 ($n=490$)	< 0.001
"Need for lifestyle flexibility"	8.2 ± 1.4 ($n=133$)	7.6 ± 1 ($n=390$)	< 0.001
"Need for small doses of insulin"	8.0 ± 1.5 ($n=63$)	7.6 ± 1 ($n=269$)	0.057
"History of hypoglycemia unawareness"	8.1 ± 1.5 ($n=46$)	7.4 ± 0.9 ($n=208$)	0.009
"Dawn phenomenon"	7.7 ± 1.4 ($n=39$)	7.7 ± 1.1 ($n=73$)	0.586
"Child ≤ 5 years old"	8.1 ± 1.8 ($n=5$)	7.7 ± 0.8 ($n=32$)	0.848
"Pregnant or woman trying to conceive"	8.4 ± 2.2 ($n=14$)	7.2 ± 0.6 ($n=15$)	0.158

P-values were determined by Mann–Whitney *U* test

CSII continuous subcutaneous insulin infusion

*Data shown are represented as means ± SD

Table 6 HbA1c comparison by age groups

	Without CSII	With CSII	p-value
< 18 years	7.9 ± 1.3 ($n=316$)	7.7 ± 0.9 ($n=881$)	< 0.001
18–39 years	8.2 ± 1.7 ($n=577$)	7.8 ± 1.2 ($n=851$)	< 0.001
≥ 40 years	7.9 ± 1.1 ($n=234$)	7.5 ± 0.9 ($n=411$)	< 0.001

P-values were determined using the ANOVA test

CSII continuous subcutaneous insulin infusion

*Data shown are represented as means ± SD

Discussion

The results of this study enabled us to verify the advantage of CSII therapy, which is in agreement with previous studies. To our knowledge, it was the first study of type 1 diabetes to be conducted at a population level in Portugal.

In the general characterization of the study population, the mean age at diagnosis (11 years) coincides with the highest incidence of type 1 diabetes in the age group from 10 to 14 years [2] and, in Portugal, on average, among pediatric age (under 19 years) at 10 ± 5 years [17]. The age difference

between treatments with and without CSII can be explained by the fact that the insertion of the CSII device until 2019 was reimbursed under the PND for all eligible children and young people up to the age of 18, but only for a limited number of adults [18].

Regarding the reasons for starting CSII therapy, the most frequently reported reason was "Accentuated glycemic variability" (25%), which can be broadly defined by large daily glycemic excursions, including hypoglycemic and hyperglycemic episodes [19]. With the popularization of continuous glucose monitoring (CGM) systems, the main reason for initiating the therapy is observed to be high glucose variability when the daily coefficient of variation is above > 36%, calculated within the monitoring system [20, 21]. This is one of the eligibility indications to start CSII in Portugal [16], even though it is not classically described as one of the reasons associated with the insertion of CSII in the literature [22], the results of this therapy on glycemic variability not having been evaluated. Nonetheless, since this is one of the metabolic control variables to be taken into account, in addition to HbA1c [23], it would be advisable to assess the benefit of CSII therapy on glycemic variability, especially in the subgroup of patients who reported marked variability as one of the reasons to start treatment. The data available on the platform did not allow for the assessment of the impact of the CSII on this parameter since it is not registered. In the future, the inclusion of this monitoring parameter in the platform may be important. However, in the subgroup of patients who reported marked glycemic variability as a reason for initiating CSII therapy, HbA1c was significantly lower with treatment, even though HbA1c does not correlate linearly with variability; the CSII group also had a significantly lower frequency of severe hypoglycemia, which is related to greater glycemic variability [10, 13].

The second most frequently reported reason, "HbA1c > 7% despite intensive therapy," is in the literature one of the main reasons for CSII therapy, applied for the purpose of achieving better metabolic control via the approach of physiological endogenous insulin release. The difference in HbA1c was significant in the subgroup of patients who started therapy due to lack of control despite intensive therapy. However, as observed in this study, the goal of < 7% HbA1c was not achieved in 71.4% of cases, being higher in those without CSII (74.7%). This percentage is in agreement with that published in the literature, which reports that in intensive insulin therapy regimens, a therapeutic target of HbA1c < 7% is still not achieved in more than 70% of cases [24], or is achieved but at the cost of a higher frequency of hypoglycemia. Considering an HbA1c target < 7.5% to be adequate for metabolic control, in the present study it was determined that if there is a high risk of hypoglycemia [5], this objective is achieved in half of the patients treated with CSII (Table 4).

Hypoglycemia is the main acute complication of diabetes as well as the main obstacle to therapeutic management, especially in younger children who have little ability to recognize their symptoms, or when it appears without prodromes. Only 9.2% of patients who started treatment with CSII reported hypoglycemia unawareness as a reason to start therapy. Notwithstanding, there is no option to record a "history of severe or frequent hypoglycemia," as is the procedure in other centers [5, 22]. On the other hand, reporting of hypoglycemia unawareness is associated with a higher frequency of hypoglycemia and increased risk of severe hypoglycemia; therefore, this subgroup would benefit from the reduction of severe hypoglycemic episodes observed in CSII therapy.

When CSII therapy is evaluated, objective outcomes such as HbA1c reduction and frequency of complications are classically measured; however, quality of life and treatment satisfaction are equally important measures to assess. Although these outcomes were not measured, the "need for lifestyle flexibility" was the third most commonly reported motive for CSII therapy (17.8%) and reflects the need to improve the convenience of insulin administration [11, 14] by avoiding multiple daily administrations with subcutaneous injections, which can be uncomfortable, and thus allowing via the CSII device continuous infusion. In this group, the difference in HbA1c with CSII was also significant, which underlines the benefit of therapy in addition to quality of life.

The motive "small doses of insulin" was the fourth most frequently reported reason (11.9%), which may be due to the fact that CSII devices allow infusions and boluses of smaller amounts of insulin (0.05–0.1 units), which are not possible with the insulin pens available on the market (0.5–1 units) [25]. The subgroup of patients requiring lower doses of insulin tends to be younger [10, 11], which was observed in our study in patients with CSII who were on average younger than the others (25.1 ± 14.6 vs. 27.8 ± 13.9 years, $p < 0.001$).

Dawn phenomenon is one of the reasons for starting therapy reported in previous studies [22] and in 3.8% of patients who started therapy with CSII. It consists of the presence of morning hyperglycemia, triggered by the normal secretion of hyperglycemic hormones, such as cortisol, growth hormone, and catecholamines. Management of significant morning hyperglycemia is a challenge in MDI therapy, as increasing insulin the night before to take effect the next morning carries a risk of nocturnal hypoglycemia. Thus, although there may be a high day-to-day variability, the CSII device can be a useful resource because of its ability to program and change the insulin dose for the morning and morning periods, reducing the risk of hypoglycemia in the early evening.

Difficulty with insulin administration due to lack of autonomy in younger children and fear of needles and pain during multiple injections is one of the commonly reported reasons for initiating CSII therapy in children [10, 12,

14], the current study noting that 5 years of age or below accounts for 1.3% of reasons for this mode of treatment. Children in this age group depend on third parties to manage their illness, which implies a unique effort from their caregivers and also on the part of the school communities they attend. The flexibility that CSII devices provide to children and young people should also be taken into account for the treatment of this age group, even in the absence of therapeutic failure with intensive MDI therapy [1, 5, 6, 15].

During pregnancy, due to the need for strict metabolic control conditioned by the risk that hyperglycemia poses to the fetus and pregnant woman, CSII is a therapeutic option of particular interest as it reduces the level of HbA1c without increasing the risk of hypoglycemia, which is also harmful to the fetus [26]. Only 0.8% of patients reported pregnancy or preconception as a reason to initiate therapy. Since CSII therapy is started early, i.e., in adolescence and early adulthood, many women may already be on CSII treatment when they decide to become pregnant. There may also be fear of starting a therapy that requires training and greater control, in addition to a need for learning concomitantly with the beginning of a pregnancy.

The demands of this type of treatment can initially be tiring and excessive if the individual is not motivated to learn and comply with the therapy. The discontinuation rate of 6.4% is consistent with that described in previous studies which reported rates between 3 and 5% for new generation devices and 11 to 15% for older devices [10, 27], this corresponding to those patients reimbursed in Portugal until 2021. The reasons reported for the discontinuation (Table 3) were mainly related to withdrawal of the treatment method (40%), inadaptation (13.3%), therapeutic non-compliance (5.5%), or refusal due to patient preference (4.2%), with only 1.8% of the cases failing to resolve the problem that led to the insertion of CSII. The most frequent reasons seem to be those related to problems with use and lack of comfort of the device [27], which, with the development of increasingly advanced devices of smaller size and closer to closed-loop circuits, may be overcome in the future as they are reported to be easier and more comfortable for the user. Further possible problems with the infusion site (infection, lipodystrophy, and dislocation), cannula problems (obstruction, kink, and leak), and device malfunction can be the cause of hyperglycemia [11] and are side effects that have been reported, some of which may lead to replacement or even discontinuation of the device.

Overall, the group treated with CSII had a lower level of HbA1c and a lower frequency of severe hypoglycemia than the group without CSII, which is consistent with the results in previous studies showing better control of blood glucose with the CSII device. In this analysis, the CSII group also had a lower frequency of ketoacidosis, which has been classically described as a potential and significant risk of CSII therapy in previous studies: this, however, has been refuted by more recent studies and reviews due to better conditions and experience levels of CSII centers as well as patient education regarding alarm signals and device malfunctions [13, 23]. In previous studies, CSII therapy led to an average HbA1c reduction of 0.3% (0.1–0.4%) in both pediatric and adult groups [11, 13]. CSII therapy was also associated in previous studies with a lower frequency of severe hypoglycemia (9.55 vs. 13.97 per 100 patient-years, $p < 0.001$) and ketoacidosis (3.64 vs. 4.26 per 100 patient-years, $p = 0.04$) [10]. These results are also in line with an earlier Portuguese study that compared the cost of the two therapy modalities. It showed an expected annual saving of around 3000€ per patient in the short term and 25,000€ in the long term, reporting an investment of up to 3500€ per patient per year, justifying the use of CSII therapy given the estimated savings [28].

It is important to note that the quality of the records is crucial for the adequate analysis of the results. Although 7135 patients were registered on the platform, only 3328 had adequate records of monitoring data, which limits the conclusions of this study. It would also be helpful to assess, in addition to HbA1c and acute complications, also glycemic variability, which was not possible in the current study. Furthermore, other ambulatory glucose profile data could be collected through the generalized use of glucose monitoring devices, although the present CSII platform does not support their registration. The CSII devices reimbursed in Portugal are also not the new generation devices. The future introduction of adhesive devices and devices integrated with real-time CGM within the national CSII treatment program is expected to further improve treatment results. Nevertheless, this study is the first, to our knowledge, to be conducted at a population level in Portugal to address the impact of CSII treatment in the control of diabetes and its complications.

In conclusion, the analysis of the results of the CSII platform validates the advantage of using CSII devices in the metabolic control and reduction of acute complications of type 1 diabetes, achieving a significant reduction in HbA1c as well as a reduction in the number of episodes of severe hypoglycemia and ketoacidosis. The treatment program should be reformulated in order to keep up with technological developments so as to make it accessible to all patients with DM1 in Portugal.

Acknowledgements We would like to thank the coordinators and all the professionals of the Treatment Centers for CSII for all the excellent work they did, and continue to do, managing the large volume of platform data on the treatment and monitoring of patients with DM1, namely, Ana Maia Silva, Anneke Joosten, Catarina Silvestre, Celestino Neves, Cristina Valadas, Edite Nascimento, Ester Gama, Francisco Sousa Santos, Goreti Lobarinhas, Helena Cardoso, Isabel Joaquim, Isabel Ramoa, Luísa Barros, Luísa Raimundo, Manuela Calha, Maria João Oliveira, Marta Alves, Nelson Cunha, Rosa Príncipe, Sérgio Borges, Sofia Castro, Susana Lira, Susana Parente, and Teresa Azevedo. We

also thank Dr. Cristina Portugal for the support of the platform in the development of this study and Dr. Isabel Dinis for the critical revision of the paper.

Declarations

Ethics approval The study protocol was approved by the direction of the *Directorate-General of Health* (DGS) and by the Ethical Committee of the Lisbon Academic Medical Center (*Centro Académico de Medicina de Lisboa, CAML*).

Informed consent This study design did not require informed consent as patients had already consented to data usage when being introduced to the DGS CSII platform.

Conflict of interest The authors declare no competing interests.

References

1. Daneman D (2006) Type 1 diabetes. Lancet 367(9513):847–858. https://doi.org/10.1016/S0140-6736(06)68341-4
2. Maahs DM, West NA, Lawrence JM, Mayer-Davis EJ (2010) Epidemiology of type 1 diabetes. Endocrinol Metab Clin North Am 39(3):481–497. https://doi.org/10.1016/j.ecl.2010.05.011
3. Diabetes Control and Complications Trial Research Group, Nathan DM, Genuth S et al (1993) The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 329(14):977–986. https://doi.org/10.1056/NEJM199309303291401
4. Rawshani A, Sattar N, Franzén S et al (2018) 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 392(10146):477–486. https://doi.org/10.1016/S0140-6736(18)31506-X
5. Jameson LJ, Fauci A, Kasper D, Hauser S, Longo D, Loscalzo J (2018) Harrison's principles of internal medicine, 20th ed. McGraw-Hill Education/Medical. https://accessmedicine.mhmedical.com/book.aspx?bookid=2129. Accessed 7 Dec 2021
6. Norris JM, Johnson RK, Stene LC (2020) Type 1 diabetes—early life origins and changing epidemiology. Lancet Diabetes Endocrinol 8(3):226–238. https://doi.org/10.1016/S2213-8587(19)30412-7
7. World Health Organization (2016) Global report on diabetes. Retrieved December 7, 2021, from https://www.who.int/publications/i/item/9789241565257
8. International Diabetes Federation (2021) IDF Diabetes Atlas, 10th edn. Belgium, Brussels
9. Nathan DM (2014) The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study at 30 years: overview. Diabetes Care 37(1):9–16. https://doi.org/10.2337/dc13-2112
10. Nimri R, Nir J, Phillip M (2020) Insulin pump therapy. Am J Ther 27(1):e30–e41. https://doi.org/10.1097/MJT.0000000000001097
11. Pickup JC (2012) Insulin-pump therapy for type 1 diabetes mellitus. N Engl J Med 366(17):1616–1624. https://doi.org/10.1056/NEJMct1113948
12. Hussain T, Akle M, Nagelkerke N, Deeb A (2017) Comparative study on treatment satisfaction and health perception in children and adolescents with type 1 diabetes mellitus on multiple daily injection of insulin, insulin pump and sensor-augmented pump therapy. SAGE Open Med 5:205031211769493. https://doi.org/10.1177/2050312117694938
13. Karges B, Schwandt A, Heidtmann B et al (2017) Association of insulin pump therapy vs insulin injection therapy with severe hypoglycemia, ketoacidosis, and glycemic control among children, adolescents, and young adults with type 1 diabetes. JAMA 318(14):1358. https://doi.org/10.1001/jama.2017.13994
14. Maiorino MI, Bellastella G, Petrizzo M et al (2014) Treatment satisfaction and glycemic control in young type 1 diabetic patients in transition from pediatric health care: CSII versus MDI. Endocrine 46(2):256–262. https://doi.org/10.1007/s12020-013-0060-6
15. DiMeglio LA, Evans-Molina C, Oram RA (2018) Type 1 diabetes. Lancet 391(10138):2449–2462. https://doi.org/10.1016/S0140-6736(18)31320-5
16. Direção-Geral da Saúde (2008) Circular normativa nº17/DSCS/DGID. Gestão integrada de diabetes - elegibilidade dos doentes para tratamento através de perfusão subcutânea contínua de insulina. Lisboa. Retrieved December 7, 2021, from http://nocs.pt/wp-content/uploads/2016/04/circularnormativan17de4808.pdf
17. Programa Nacional para a Diabetes (PND), do Vale S, Martins F, Cruz D, Freitas G (2020) PROGRAMA NACIONAL PARA A DIABETES 2019. Desafios e Estratégias. Lisboa. Retrieved December 7, 2021, from https://www.dgs.pt/programa-nacional-para-a-diabetes/ficheiros-upload/arquivo/programa-nacional-para-a-diabetes-desafios-e-estrategias-2019-pdf.aspx
18. Gabinete do Secretário de Estado Adjunto e da Saúde (2016) Despacho nº 13277/2016. Diário da República 2(213). https://dre.pt/dre/detalhe/despacho/13277-2016-75676511. Accessed 7 Dec 2021
19. Suh S, Kim JH (2015) Glycemic variability: how do we measure it and why is it important? Diabetes Metab J 39(4):273. https://doi.org/10.4093/dmj.2015.39.4.273
20. Marchand L, Reffet S, Vouillarmet J, Cugnet-Anceau C, Disse E, Thivolet C (2019) The 36% coefficient of variation for glucose proposed for separating stable and labile diabetes is clinically relevant: a continuous glucose monitoring-based study in a large population of type 1 diabetes patients. Diabetes Metab 45(6):598–600. https://doi.org/10.1016/j.diabet.2018.05.009
21. Battelino T, Danne T, Bergenstal RM et al (2019) Clinical targets for continuous glucose monitoring data interpretation: recommendations from the International Consensus on Time in Range. Diabetes Care 42(8):1593–1603. https://doi.org/10.2337/dci19-0028
22. Jendle JH, Rawshani A, Svensson A-M, Avdic T, Gudbjörnsdóttir S (2016) Indications for insulin pump therapy in type 1 diabetes and associations with glycemic control. J Diabetes Sci Technol 10(5):1027–1033. https://doi.org/10.1177/1932296816650209
23. Beck RW, Riddlesworth TD, Ruedy KJ et al (2017) Effect of initiating use of an insulin pump in adults with type 1 diabetes using multiple daily insulin injections and continuous glucose monitoring (DIAMOND): a multicentre, randomised controlled trial. Lancet Diabetes Endocrinol 5(9):700–708. https://doi.org/10.1016/S2213-8587(17)30217-6
24. Wan W, Skandari MR, Minc A et al (2018) Cost-effectiveness of initiating an insulin pump in T1D adults using continuous glucose monitoring compared with multiple daily insulin injections: The DIAMOND Randomized Trial. Med Decis Making 38(8):942–953. https://doi.org/10.1177/0272989X18803109
25. Wilmot E, Hammond P, Choudhary P et al (2018) BEST PRACTICE GUIDE: continuous subcutaneous insulin infusion (CSII): a clinical guide for adult diabetes services. Retrieved January 23, 2022, from https://abcd.care/sites/abcd.care/files/BP_DTN_v13%20FINAL.pdf
26. Alexopoulos A-S, Blair R, Peters AL (2019) Management of preexisting diabetes in pregnancy. JAMA 321(18):1811–1819. https://doi.org/10.1001/jama.2019.4981
27. Wong JC, Boyle C, DiMeglio LA et al (2017) Evaluation of pump discontinuation and associated factors in the T1D Exchange Clinic

Registry. J Diabetes Sci Technol 11(2):224–232. https://doi.org/10.1177/1932296816663963
28. Joaquim I, Vilaverde J, Barros L et al (2016) Economic impact on the use of insulin pumps in diabetes type I – analysis on Portuguese real life results. Endocr Abstr. https://doi.org/10.1530/endoabs.41.EP554