

# Continuous Subcutaneous Insulin Infusion in Italy: Third National Survey

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## Abstract

**Background:** Continuous subcutaneous insulin infusion (CSII) is increasing worldwide, mostly because of improved technology. The aim of this study was to evaluate the current status of CSII in Italy.

**Materials and Methods:** Physicians from 272 diabetes centers received a questionnaire investigating clinical features, pump technology, and management of patients on CSII.

**Results:** Two hundred seventeen centers (79.8%) joined the study and, by the end of April 2013, gave information about 10,152 patients treated with CSII: 98.2% with type 1 diabetes mellitus, 81.4% adults, 57% female, and 61% with a conventional pump versus 39% with a sensor-augmented pump. CSII advanced functions were used by 68% of patients, and glucose sensors were used 12 days per month on average. Fifty-eight percent of diabetes centers had more than 20 patients on CSII, but there were differences among centers and among regions. The main indication for CSII was poor glucose control. Dropout was mainly due to pump wearability or nonoptimal glycemic control. Twenty-four hour assistance was guaranteed in 81% of centers. A full diabetes team (physician + nurse + dietician + psychologist) was available in 23% of adult-care diabetes centers and in 53% of pediatric diabetes units.

**Conclusions:** CSII keeps increasing in Italy. More work is needed to ensure uniform treatment strategies throughout the country and to improve pump use.

## Introduction

**I**N AGREEMENT WITH WHAT was happening worldwide, a 2005 survey showed that continuous subcutaneous insulin infusion (CSII) was spreading in Italy, especially among pediatric patients.<sup>1,2</sup>

The publication of national guidelines,<sup>3,4</sup> the introduction of smart pumps, and the integration of pump and glucose

sensor (sensor-augmented pump [SAP]) are all expected to increase the dissemination of CSII, even though budgetary constraints may have an adverse effect.

Because a national registry of patients on CSII is at present not available, a new national survey has been conducted to gain knowledge on the present use of CSII, on the type of patients using it, and on the characteristics of centers involved.

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## Materials and Methods

### Data collection

Data were collected through a questionnaire sent by e-mail to the chiefs of diabetes centers, both adult and pediatric, in which CSII is used. Centers were identified from previous surveys and through information from companies that sell CSII devices in Italy (Medtronic Italia [Milan, Italy], Movi-Animas SpA [Milan], and Roche Diagnostics [Basel, Switzerland]). The questionnaire explored CSII dissemination in Italy, patient characteristics, pump characteristics, and centers (Table 1).

Partial responses were integrated or corrected through phone calls or by e-mail.

The present data reflect CSII in Italy as it was on April 30, 2013.

### Statistical analysis

Data are presented as mean  $\pm$  SD values. Student's *t* test for unpaired data and analysis of variance were used. Differences

in frequency were analyzed with the  $\chi^2$  test. SPSS version 18 software (SPSS Inc., Chicago, IL) was used.  $P < 0.05$  was considered significant.

## Results

### Prevalence and distribution of CSII in Italy

By the end of April 2013, CSII was practiced in 272 diabetes centers throughout Italy. All of the centers received by e-mail the purpose of the present survey, a questionnaire, an invitation to participate, and instructions. Two hundred seventeen centers (79.8%), 39 centers more than in the 2005 survey, returned the questionnaire.

Among the participating centers, 51 (23.5%) dealt with pediatric patients (a 112.5% increase with respect to 2005), and 166 dealt with adult patients (37% more than in 2005).

As of April 30, 2013, the total number of CSII-treated patients in Italy was 10,152, a fourfold increase over 8 years (Fig. 1A). The yearly number of new people starting CSII increased by 19% in 2006, 24% in 2007–2008, and 5.5% in 2009–2010, decreased by 16% in 2011, and increased by 26% in 2012.

TABLE 1. QUESTIONNAIRE

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#### Information concerning centers

##### Diffusion of CSII

1. How many patients with type 1 diabetes mellitus are presently followed in your center?
2. How many patients use CSII?
3. How many of your patients with type 2 diabetes mellitus are on CSII?

##### Center organization

1. Start of CSII practice
2. Number of physicians, nurses, dieticians, and psychologists following patients on CSII
3. How many of the staff care full-time for patients on CSII?
4. How many of the staff were educated to CSII and how (informants from pump producers, scientific society, other staff)?
5. How do you start CSII? Choose among hospital stay, day-hospital, outpatient. Do you have a service dedicated to CSII?
6. Do you use a Web-based data download system?
7. Do you use other forms of telemedicine (fax, phone, short message service, e-mail, social network)?
8. Is there a specific phone address for CSII? Does it connect the patient to a diabetologist, a nurse, or other personnel?
9. What are the reasons to start CSII? Choose among HbA1c level above recommended target (i.e., HbA1c  $\geq 7.5\%$  or  $6.1\%$  in pregnant patients or patients planning pregnancy), recurrent or severe hypoglycemias, dawn phenomenon, low insulin need, pregnancy planning, desire of greater flexibility, desire for a better lifestyle.
10. Reasons limiting the implementation of CSII. Choose among cost, time spent for patient education or patient follow-up, unavailability of adequately prepared personnel, staff limitations.
11. How many patients stopped CSII?
12. Which were the reasons for stopping CSII? Choose among pump wearability, excess of hypoglycemias, end of pregnancy, missed glycemic target, other reasons.

#### Information concerning patients and devices

##### Patient characteristics

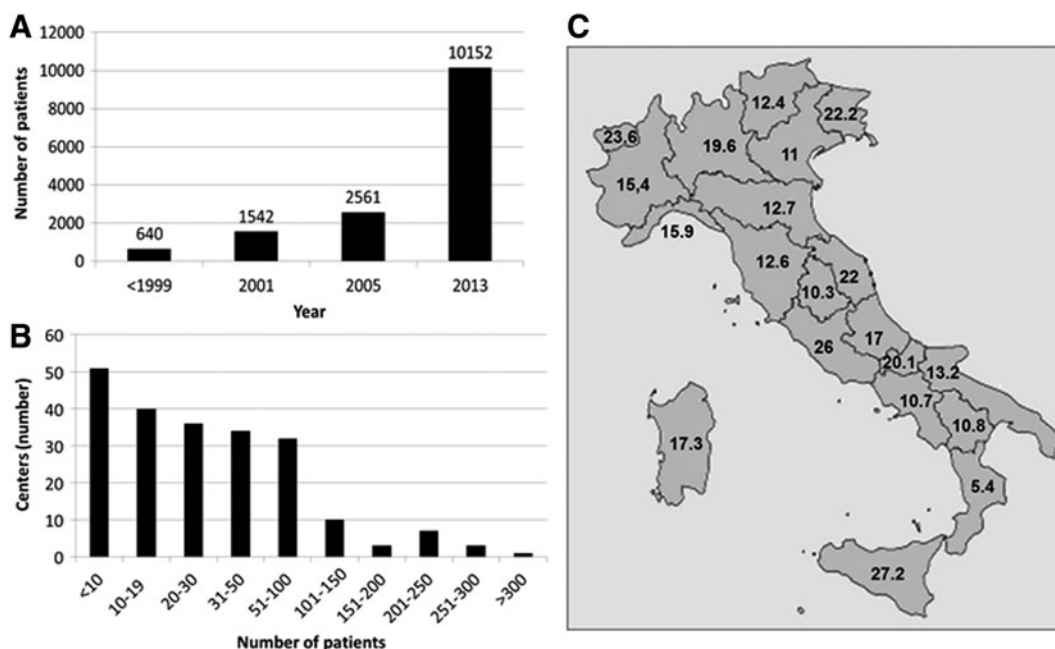
1. Birth date
2. Sex
3. Date of diagnosis of diabetes
4. Date of CSII start

##### Pump characteristics

1. Specify pump type. Choose among conventional pump, conventional pump associated with a dedicated CGM device, pump integrated with CGM.
2. Specify number of days per month of CGM use.
3. Does patient use temporary basal insulin infusion?
4. Does patient use different bolus options?
5. Does patient perform carbohydrate counting?
6. Does patient use bolus calculator?

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CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; HbA1c, glycosylated hemoglobin.



**FIG. 1.** Continuous subcutaneous insulin infusion in Italy: (A) patients treated with continuous subcutaneous insulin infusion, (B) patients on continuous subcutaneous insulin infusion per center, and (C) prevalence of continuous subcutaneous insulin infusion among different regions (number/100,000 inhabitants).

The distribution of CSII among the 20 Italian regions was uneven (Fig. 1C); with a national prevalence of 16.9 CSII patients/100,000 inhabitants, the regional prevalence went from 27.2 (in Sicily) to 5.4 (in Calabria).

The number of patients per diabetes unit was also unevenly distributed (Fig. 1B), even though the centers following more than 30 patients increased from 17% to 42%, and those following more than 50 patients increased from 10% to 26%.

#### Patients and devices

**Patients.** Patient characteristics are reported in Table 2.

Most patients on CSII had type 1 diabetes mellitus (98.2%) and were older than 18 years of age (81.4%). Patients followed in pediatric units comprised 24.9% of the total, indicating that some pediatric centers follow patients well into adulthood. All patients were on multiple daily injections (MDI) before CSII. Patients on CSII represented 16% of the whole population of patients with type 1 diabetes mellitus (this value was 5% in 2005). Specifically, patients on CSII represented 27% of the total population with type 1 diabetes

mellitus in pediatric units and 15% in adult diabetes centers ( $P < 0.05$ ).

The average number of daily blood glucose tests was four to six in 81% of diabetes units. In 12.5% of centers self-monitoring of blood glucose (SMBG) tests were more than seven per day (particularly among adult patients), whereas in 6.5% of units the average test number was two to three per day.

**Indications for CSII.** Patients started CSII for several reasons. High glycosylated hemoglobin (HbA1c) level despite intensive MDI therapy was the most common cause (90%) in both adult and pediatric patients. Recurrent hypoglycemia episodes came next (70% vs. 46% in the 2005 survey). Additional reasons were pregnancy planning (44%) and the hope for a better quality of life (43%). By contrast, the dawn phenomenon was a less important factor for starting CSII (17% vs. 51% in 2005). Greater flexibility in daily life and the low insulin need were minor reasons to use the pump. Reasons for MDI-to-CSII transition were similar among pediatric and adult patients, except for the hope for a better quality of life (68% in pediatric units vs. 36.5% in adults;  $P < 0.05$ ) and pregnancy planning (54.2% in adults vs. 8.5% in pediatric units;  $P < 0.001$ ).

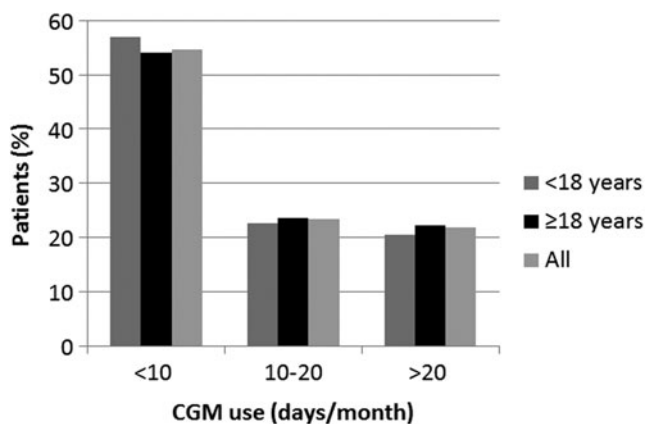
**Stopping CSII.** CSII was stopped in 962 patients (8.65%), a 50% reduction with respect to 2005. Reasons were pump wearability in 42% of cases, missed glycemic target in 38%, injection site reactions in 21%, and end of pregnancy in 17%. No specific reason was apparent in 38% of cases. Only in 3% of cases CSII was stopped because of hypoglycemic episodes (similarly to the previous surveys). In pediatric patients CSII was abandoned more often for pump wearability (48.9% vs. 33.3% in adults;  $P < 0.05$ ) or site reactions (29.7% vs. 15.1%;  $P < 0.05$ ).

**TABLE 2. CHARACTERISTICS OF PATIENTS ON CONTINUOUS SUBCUTANEOUS INSULIN INFUSION IN ITALY**

Variable	Adults	Pediatric	Total
Patients (number)	8,264	1,888	10,152
Age (years)	40.3 ± 13	12.6 ± 4	34.8 ± 16
Sex (% M/F)	42/58	50/50	43/57
Disease duration (years)	20.8 ± 11	6.7 ± 4.1	11.2 ± 9.5
Duration of CSII (years)	5.2 ± 4	3.9 ± 3	5 ± 4

Data are mean ± SD values.

CSII, continuous subcutaneous insulin infusion; F, female; M, male.



**FIG. 2.** Use (days per month) of continuous glucose monitoring (CGM) in patients wearing a sensor-augmented pump, grouped by age bracket (pediatric or adult) and total.

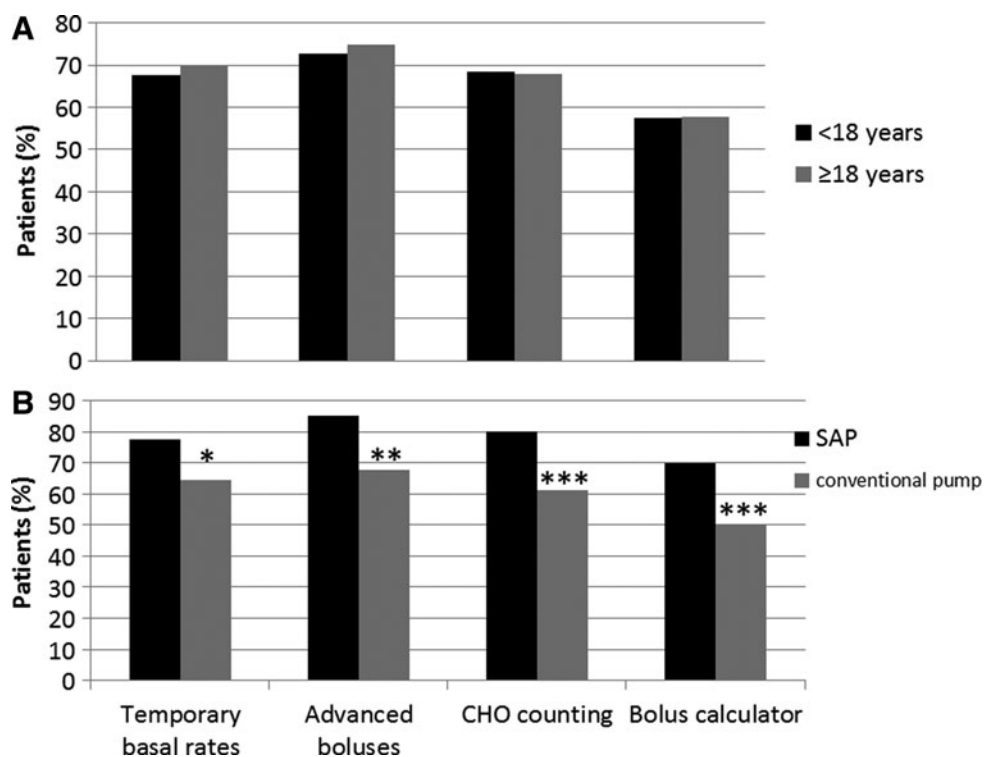
**Devices.** A conventional pump was used by 61% of patients, 32% used a pump with an integrated continuous glucose monitoring (CGM) system, and 7% used a pump associated with a dedicated CGM device. However, the glucose sensor was not used in 30% of patients wearing an integrated or associated system. Patients, both pediatric and adult, using the glucose sensor used it for 12 days/month on average, but more than half did so far less than 10 days/month, and only 21.9% for more than 20 days/month (Fig. 2). Sensor use varied widely among regions, ranging between 5.8 and 26.1 days/month.

Only 68% of CSII patients (both pediatric and adult subjects) exploited advanced pump features (Fig. 3). Advanced pump features were used significantly more by SAP-using patients as compared with diabetes patients wearing a conventional pump (Fig. 3). Only 68.5% of CSII patients usually did carbohydrate counting. Again, the prevalence was higher among SAP-using patients than conventional pump-wearing subjects ( $P=0.003$ ).

#### Diabetes centers

CSII therapy was started in an outpatient setting in 63% of centers (65% adult, 45% pediatric), in a day-hospital in 33% (32% adult, 39% pediatric), and in a regular hospital setting in 5.5% (3% adult, 16% pediatric).

Fifty-eight percent of adult units versus 28% of pediatric centers declared they had a CSII-dedicated outpatient unit. In most structures, the CSII-expert hospital team was also in charge of other diabetes patients, similarly to what was observed in the previous Italian survey.<sup>2</sup> However, the team composition in adult-caring structures has changed. The units with a physician as the only CSII-dedicated personnel decreased from 22% to 5%. Centers having a physician + a nurse in the team decreased from 21% to 12%. Conversely, teams including a physician + a dietician grew from 7% to 12%, those including a physician + a nurse + a dietician grew from 36% to 40%, and units with a physician + a nurse + a dietician + a psychologist almost doubled (from 12% to 23%). In pediatric centers, 53% of teams were made up of a physician + a nurse + a dietician + a psychologist. Eighty-one percent of centers (78% adult, 86% pediatric) provided a



**FIG. 3.** Use of pump advanced functions: comparison between (A) pediatric and adult patients and (B) patients treated with a sensor-augmented pump (SAP) and patients treated with a conventional pump. \* $P<0.05$ , \*\* $P<0.01$ , \*\*\* $P<0.005$  versus SAP. CHO, carbohydrate.

24-h, 7 days/week availability, as compared with 72% in 2005. The availability of an attending diabetologist was guaranteed in 97% of centers. Remote real-time or delayed patient counseling was also available in all centers through e-mail contacts (87.3%), phone calls (85.4%), short message service (40.2%), fax (35.9%), or social networks (8.7%).

The average CSII expertise was less than 5 years in 23%, 5–10 years in 35%, and more than 10 years in 42% of centers. Centers with less than 5 years of expertise had a lower number of CSII-dedicated physicians (1.8 vs. 2.3;  $P < 0.05$ ) and dieticians (0.7 vs. 1.0;  $P < 0.05$ ). Training for CSII-dedicated personnel took place through specific programs (56%), teaching from already trained colleagues (82%), counseling from employees of pump industries (76%), or just by working in the hospital (32%).

No specific issues about promoting CSII therapy could be identified by CSII-dedicated physicians in 31% of diabetes centers, as long as patient selection was accurate. However, in the remaining 69%, concerns limiting CSII dissemination included high costs (57%), lack of dedicated personnel (40%), time and effort required for patient training (27%), or patient follow-up (17%). The scarcity of properly trained staff was perceived as a CSII-limiting factor in only 7% of units.

## Discussion

As of April 30, 2013, 10,152 CSII patients were cared for in the 217 Italian diabetes centers, a fourfold increase from 2005.<sup>2</sup> Considering that 55 units did not respond to the questionnaire, the number of patients on CSII in Italy may be estimated as around 11,000. Thus, from 2005 to 2013 there has been in Italy a steady increase of CSII use and of centers offering it. The availability of official guidelines, with indications for patient selection,<sup>3,4</sup> and a nationwide effort in promoting CSII-oriented training programs for diabetes teams have both contributed to the change.

Nevertheless, the prevalence of CSII therapy in the Italian diabetes population remains low. The total number of type 1 diabetes mellitus patients in the country has been estimated at 250,000–300,000.<sup>5,6</sup> Thus, the 10,152 CSII-treated patients represent 3.5–4% of all Italian type 1 diabetes mellitus patients, a value markedly lower than the 40% in the United States and the almost 20% in other European countries, including Norway, Austria, The Netherlands, and Switzerland.<sup>1</sup> In Italy all patients are initiated to CSII in public institutions, not by private practice. This might be one of the reasons for the low dissemination of CSII.

Similarly to other European countries, the most common indications for CSII therapy are nonoptimal glycemic control despite intensive MDI therapy and recurrent hypoglycemia episodes.<sup>3,4</sup> According to the 2012 AMD Annals,<sup>7</sup> >40% of type 1 diabetes mellitus patients in Italy have an HbA1c level of >8%. Thus, the number of diabetes patients who could take advantage of CSII therapy is quite large. High device cost and scarcity of trained personnel are perceived as the main limitations to a wider CSII dissemination.

At present, even though the national health system completely covers the cost of devices and consumables, regional regulations vary widely in terms of prescription rules and requirements, limiting patient access to some tools (i.e., glucose sensors).<sup>8</sup> This could account for the marked differences in CSII use among different regions (Fig. 1).

It is interesting that pediatric centers show a higher penetration of CSII therapy in the total diabetes population than the adult-oriented units, in line with other European countries. Thus, in the future, the greater increase in CSII dissemination can be expected in the adult population of both type 1 and type 2 diabetes mellitus patients, particularly after the recent publication of the OpT2mise Trial, which showed an improvement of glycometabolic control in CSII-treated type 2 diabetes mellitus patients.<sup>9</sup>

The ideal setting for a unit in charge of CSII patients would require a dedicated outpatient clinic with a specifically trained team, including a physician, a nurse, a dietician, and a psychologist, and a minimum of CSII patients. Data of the present survey highlight that only a minority of centers fulfills these requirements. Approximately half of adult and 72% of pediatric centers have no CSII-dedicated unit, and most centers do not provide an integrated multidisciplinary team. Even though these figures have improved since 2005, units offering patients a coordinated group including a physician, a nurse, and a dietician are just 32% of the total (40% in adult and 6% in pediatric centers), and teams with a physician, a nurse, a dietician, and a psychologist are only 30% (53% in pediatric and 23% in adult centers).

In contrast, the numbers of units caring for fewer than 10 patients have significantly decreased, whereas the numbers of centers with more than 30 or more than 50 patients have more than doubled. This suggests a more solid expertise and a more updated know-how in patient care throughout the country. The empowerment of specialized, fully equipped, adequately organized, CSII-dedicated diabetes centers is critical for combining optimally resources and quality of care.

SMBG testing remains suboptimal in 6% of participating centers, with patients taking two to three blood glucose tests per day, even though Italian guidelines indicate four tests per day as the minimum requirement for SMBG.<sup>3</sup> Promoting a more frequent blood testing is essential because the SMBG rate correlates inversely with HbA1c in type 1 diabetes mellitus.<sup>10</sup>

The main reasons for switching from MDI to CSII are in line with Italian current guidelines. A wider dissemination of scientific recommendations, leading to more accurate patient selection, is at the basis of the significant reduction in CSII dropouts (8.65% vs. the previous 2005 value of 17.5%).

Approximately 39% of CSII patients use SAP. Randomized clinical trials have found that SAP improves metabolic control with respect to conventional pump therapy, even though this happens only when CGM is used >70% of the time.<sup>11,12</sup> This is probably due to both the glycemic variability that is commonly seen in type 1 diabetes mellitus patients and the time and expertise required to effectively manage CGM-derived data. In line with these results, clinical guidelines strongly encourage the continuous use of glucose sensors.<sup>13–15</sup> However, CGM use in Italy covers only 12 days/month, with wide regional fluctuations. The questionnaire did not specifically investigate the reasons for suboptimal CGM use; however, one important qualification could be that the health system does not completely cover sensor costs. In addition, because CGM technology is relatively recent, patient training and data interpretation may be insufficient. Finally, some patients may limit sensor wearing for skin reactions, personal discomfort due to frequent alarms, and/or the feeling of machine intrusion. These issues have been shown to be particularly relevant among teens.<sup>16</sup>

Modern pumps offer multiple “advanced” features (including bolus options, bolus calculator, and temporary basal infusion), which have been shown to improve patient life. Bolus options improve glucose excursions after meals with different nutrient composition.<sup>17–19</sup> A bolus calculator may help to precisely target prandial insulin administration and to effectively compute interprandial correction boluses, thus improving quality of life and treatment adherence.<sup>20–22</sup> The basal temporary profile provides a better control of glucose excursions during physical activity<sup>23</sup> and hypoglycemia, in particular when CSII is coupled to CGM. In this survey, barely 70% of patients exploited the advanced pump features, even though this percentage rises to >80% when considering SAP-treated patients. This suggests that CGM-derived information on the actual glucose profile may help patients to recognize meal- and exercise-associated glucose excursions more effectively. On the other hand, some CSII-treated patients are unwilling or unable to use advanced pump features, but can still take advantage of the continuous infusion strategy. A traditional “basic” pump, with only the essential features, would probably best suit the needs of these patients and be cost-effective at the same time.

In conclusion, CSII prevalence has increased in Italy between 2005 and 2013, even though significant regional differences still persist. The numbers of centers with adequate patient populations have also increased. High costs and lack of multidisciplinary teams are perceived as limiting factors for CSII dissemination. Significant numbers of patients do not fully exploit the opportunities offered by technology. However, a 50% reduction in CSII dropouts and the progressive dissemination of SAP are promising indicators for the future. Ongoing studies about the clinical characteristics of CSII-treated diabetes patients could provide valuable information on the impact of CSII on relevant clinical outcomes.

#### Author Disclosure Statement

D.B. has received lecture fees from Eli Lilly, LifeScan, Roche Diagnostics, and Sanofi Aventis and has provided advisory services to Abbott. L.L. has received speaker fees from Abbott, Astra Zeneca, Bayer, Eli Lilly, MSD, Novartis, Novo Nordisk, Roche Diagnostics, Sanofi Aventis, and Takeda and has provided advisory services to Astra Zeneca, Eli Lilly, Novartis, Novo Nordisk, Roche Diagnostics, Sanofi Aventis, and Takeda. G.L. has received speaker fees from Medtronic, Sanofi Aventis, and Eli Lilly and has provided advisory services to Novo Nordisk. R.B. has received fees for consulting from Roche Diagnostics, Eli Lilly, and Sanofi Aventis and a travel grant from Animas and has provided advisory services to Medtronic. A.C. has received speaker fees from Medtronic. V.D.B. has received speaker fees from Eli Lilly, Menarini, and Sanofi Aventis. A.G. has attended conferences organized by Eli Lilly as a contributor. G.G. has provided advisory services to Eli Lilly, Abbott, and Becton Dickinson and received speaker fees from Menarini, Roche Diagnostics, and Medtronic. I.R. has received speaker fees from Eli Lilly, Roche Diagnostics, and Sanofi Aventis. R.S. has received speaker fees from Eli Lilly and has provided advisory services to Roche Diagnostics and Abbott. L.B. and D.I. declare no competing financial interests exist.

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#### **Appendix. Members of the Italian Study Group on Diffusion of CSII**

All the following primary investigators and clinical centers, listed by region or city (affiliation), participated in this study:

##### *Abruzzo*

Atri (TE), V. Montani and P. Colleluori; Avezzano (AQ), V. Paciotti and P. Alfidì; Castel di Sangro (AQ), J. Grosso; Chieti, S. Tumini and P. Cipriano (Diabetologia Pediatrica) and E. Vitacolonna and G. Di Vieste (Diabetologia Universitaria Policlinico); Lanciano (CH), A. Minnucci and D. Antenucci; Pescara, G. La Penna and M. Taraborrelli; Sulmona (AQ), B. Macerata.

##### *Basilicata*

Potenza, G. Citro.

##### *Calabria*

Cosenza, G. De Morelli; Catanzaro, A. Gnasso and C. Irace (Malattie del Metabolismo, Università degli Studi Magna Graecia) and F. Citriniti (Diabetologia); Crotona, N. Lazzaro; Locri (RC), M. Bruzzese and F. Mammi; Paola (CS), F. De Berardinis and E. Santoro.

##### *Campania*

Avellino, G. Corigliano and M. Corigliano; Caserta, M. Parillo (Diabetologia UOC Geriatria ed Endocrinologia e Malattie del Ricambio AORN “S. Anna e S. Sebastiano”) and M. Schettino (Diabetologia UOC Medicina Interna AORN “S. Anna e S. Sebastiano”); Cava de’Tirreni (SA), V. Di Blasi and R. Fresa; Napoli, G. Annuzzi and L. Bozzetto

(Diabetologia Università Federico II), V. Bassi and C. Santinelli (PO S.G. Bosco, ASL Na1-Centro), P. Buono and E. Mozzillo (Diabetologia Pediatrica Università Federico II), G. Corigliano and V. Russo (Diabetologia AID), E. De Feo (Diabetologia AORN A. Cardarelli), K. Esposito and M. Petrizzo (Seconda Università), A. Foglia (Ospedale dei Pellegrini), A. Gatti (Diabetologia Ospedale San Gennaro), S. Gentile and G. Guarino (Dipartimento di Medicina Clinica e Sperimentale, Seconda Università), and D. Iafusco and A. Zanfardino (Diabetologia Pediatrica “G. Stoppoloni” Seconda Università); Salerno, C. Lambiase and A. Vitale.

##### *Emilia Romagna*

Bologna, S. Zucchini and G. Maltoni (Pediatría AOU di Bologna S. Orsola-Malpighi), G. Forlani and S. Moscatiello (Policlinico S. Orsola-Malpighi); Cesena, T. Suprani and M. Bensa; Ferrara, F. Tomasi and M. Monesi; Forlì, M. Nizzoli and S. Acquati; Guastalla-Correggio (RE), G. Chierici and B. Milli; Modena, L. Iughetti and B. Predieri (UO Pediatría Università Modena-Reggio Emilia) and R. Cavani and S. Romano (Servizio Diabetologico Azienda USL); Montecchio (RE), V. Manicardi and M. Michelini; Parma, M.C. Cimicchi and D. Ugolotti (Ambulatori Diabetologici Distretto), I. Zavaroni and A. Dei Cas (SS Endocrino-Metabolica, AOU Parma), E. Dall’Aglío and M. Papi (Malattie del Ricambio e Diabetologia, AOU Parma), and S.M. Tardio and M.C. Calderini (Trattamento intensivo del diabete, AOU Parma); Piacenza, S. Riboni and L. d’Amato (Pediatría) and D. Zavaroni and L. Gastaldi (Az. USL); Ravenna, A. Cirillo and V. Graziani (Pediatría) and P. Di Bartolo and F. Pellicano (Diabetologia AULS); Reggio Emilia, C. Di Seclì and V. Manicardi (AUSL) and S. Amarri and A. Lasagni (Pediatría, AO Santa Maria Nuova); Rimini, A. Marsciani and A. Pedini; Scandiano (RE), U. Pagliani and C. Rossi.

### *Friuli-Venezia Giulia*

Monfalcone (GO), C. Tortul, B. Brunato, and R. Assaloni; Pordenone (PN), G. Zanette; Sacile (PN), P. Livolsi; Trieste, A. Petrucco and K. Terceelj (SO Distretto 1), E. Manca (ASS1 Triestina, Distretto 2), R. Candido and E. Tommasi (ASS 1 Triestina, Distretto 3), and G. Tornese and E. Faleschini (UCO Clinica Pediatrica, IRCCS Burlo); Udine, L. Tonutti and S. Agus (SOC Endocrinologia e Metabolismo), M. Zannatta and A. Rosolen (AOU S. Maria della Misericordia), and A. Comici (SOC Pediatria, Ospedale San Antonio).

### *Lazio*

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#### *Veneto*

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