CONSENSUS STATEMENT BY THE AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/ AMERICAN COLLEGE OF ENDOCRINOLOGY INSULIN PUMP MANAGEMENT TASK FORCE

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This document represents the official position of the American Association of Clinical Endocrinologists and the American College of Endocrinology. Where there were no randomized controlled trials or specific U.S. FDA labeling for issues in clinical practice, the participating clinical experts utilized their judgment and experience. Every effort was made to achieve consensus among the committee members. Guidelines are meant to provide guidance, but they are not to be considered prescriptive for any individual patient and cannot replace the judgment of a clinician.

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Task Force for Insulin Pump Management

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Abbreviations
AACE = American Association of Clinical Endocrinologists; **CMS** = Centers for Medicare & Medicaid Services; **CGM** = continuous glucose monitoring; **CSII** = continuous subcutaneous insulin infusion; **DKA** = diabetic ketoacidosis; **FDA** = U.S. Food and Drug Administration; **GDM** = gestational diabetes mellitus; **HbA_{1c}** = hemoglobin A_{1c}; **ICR** = insulin-to-carbohydrate ratio; **ISF** = insulin sensitivity factor; **MDI** = multiple daily injections; **RCT** = randomized controlled trial; **SAP** = sensor-augmented pump; **SMBG** = self-monitored blood glucose; **T1DM** = type 1 diabetes mellitus; **T2DM** = type 2 diabetes mellitus

EXECUTIVE SUMMARY

Insulin pumps have come of age. With their proliferation in medical practice, some guidance is necessary for prospective and current prescribers to ensure their optimal and safe use. This document summarizes the current state-of-the-art of continuous subcutaneous insulin infusion (CSII) options available to patients who are using basal-bolus insulin management to control their diabetes mellitus. The American Association of Clinical Endocrinologists (AACE) published its first Consensus Statement on Insulin Pump Management in 2010 (1). This document provides an update to that statement and attempts to avoid the repetition of some general but still valid information.

The current version includes extensive updates regarding the State of Insulin Pump Technology (Section 1). This section includes a discussion of improvements to the functional features of pumps and insulin action acceleration technology. Additionally, new devices are discussed, including the first pump with a low-glucose "threshold suspend" system (MiniMed 530G with Enlite; Medtronic, Minneapolis, MN) and a new disposable insulin delivery system for type 2 diabetes (V-Go; Valeritas, Inc., Bridgewater, NJ).

The section on Insulin Pump Use in Various Patient Populations (Section 5) includes an expanded discussion of CSII in pediatric patients and offers specific guidelines for selecting pediatric candidates, including recommendations from an international consensus conference of leading pediatric diabetes specialists. Data on the use of concentrated regular U-500 insulin in CSII, a potentially effective option for patients with type 2 diabetes mellitus (T2DM), is also covered in the patient populations section.

Section 6 on Training and Education has been substantially expanded to discuss the need to develop uniform training and also suggests what this training should cover. This section now addresses training patients and their families to handle emergency situations, retraining when pumps are upgraded, and recommended training for medical professionals and school personnel.

Section 7 on Patient Safety Issues has been revised to discuss both pump problems related to the devices themselves, as well as the effects of patient selection and education on safe CSII use.

The recommendations made in this Consensus Statement are summarized below:

- Based on currently available data, CSII is justified for basal-bolus insulin therapy in patients with type 1 diabetes mellitus (T1DM)
- Only providers whose practice can assume full responsibility for a comprehensive pump management program should offer this technology
- Appropriate patient selection is necessary and must include a thorough assessment of the patient's knowledge of diabetes management principles
- The ideal CSII candidate is:
  - A patient with T1DM or intensively managed insulin-dependent T2DM
  - Currently performing ≥4 insulin injections and ≥4 self-monitored blood glucose (SMBG) measurements daily
  - Motivated to achieve optimal blood glucose control
  - Willing and able to carry out the tasks that are required to use this complex and time-consuming therapy safely and effectively
  - Willing to maintain frequent contact with their health care team
- Adult patients
  - At CSII initiation, the patient should have daily contact with the pump trainer
  - A return visit with the endocrinologist/diabetologists/advanced practice nurse is advised within 3 to 7 days of initiation
  - Educational consults should be scheduled weekly or biweekly at first, then periodically as needed
  - Specialist follow-up visits should be scheduled at least monthly until the pump regimen is stabilized, then at least once every 3 months
- Pediatric patients
  - An international consensus conference of leading pediatric diabetes specialists agreed that CSII was indicated for pediatric patients with:
    - Elevated hemoglobin A_{1c} (HbA_{1c}) levels on injection therapy
    - Frequent, severe hypoglycemia
    - Widely fluctuating glucose levels

        - A treatment regimen that compromises lifestyle
        - Microvascular complications and/or risk factors for macrovascular complications
    - Ideal pediatric candidates are those with motivated families who are committed to monitoring blood glucose ≥4 times/day and have a working understanding of basic diabetes management
    - Patient age and duration of diabetes should not be factors in determining the transition from injections to CSII
- Pregnant women with diabetes
    - The literature does not provide clear evidence that CSII is necessary for optimal treatment of pregnant women with T1DM
    - Intensive education and surveillance of the infusion site and sets are required during pregnancy
    - Insulin pump therapy seems to be safe and effective for maintaining glycemic control in pregnancies complicated by gestational diabetes mellitus (GDM)/T2DM and requiring large insulin doses
    - After delivery, the insulin pump infusion should be stopped temporarily to avoid hypoglycemia; once the blood glucose is >100 mg/dL, infusion should be resumed at the prepregnancy settings
- Pump use in hospital settings
    - At emergency room or hospital admission, should the patient not be able to manage his/her own pump, the specialist(s) responsible for the patient's ambulatory pump management should be contacted promptly to make decisions about infusion adjustments
    - Hospitalized patients and their admitting physicians should be encouraged to not discontinue the pump infusion and should consult a specialist as needed
- Patient diabetes education and pump training should be implemented by a multidisciplinary team under the direction of an experienced endocrinologist/diabetologist
    - Patients must be educated on the meaning of pump alarms, particularly those that may signal a potential interruption to insulin delivery
    - Patients must be taught to keep backup supplies on hand in the event of a pump or infusion set failure
    - Patients/families should undergo periodic retesting of skills to maximize the effectiveness of pump therapy and maintain patient safety
    - Patients should have the knowledge and technical ability to make recommended pump setting changes at home
    - Patients/families should be trained to handle emergency situations
    - Patients should be retrained when switching to a new pump model
- All patients should have periodic re-education and retraining to address knowledge gaps, as well as to troubleshoot any issues with the pump system and glycemic control
- The health care team should periodically re-evaluate whether pump therapy is appropriate for the patient
- Schools and hospitals should be provided with manufacturers' information describing insulin pump use, along with a contact to answer questions and provide further training
- Providers should have on-call systems available 24 hours/day to handle patient questions; patients should also be periodically reminded of the pump manufacturer's emergency number

This document summarizes available peer-reviewed publications and provides data that compare pumps with multiple insulin injections, address pump safety issues, and document the available cost-effectiveness analyses of insulin pump use. Essential issues related to the economic feasibility of pump use in medical practice are also addressed.

1. PREAMBLE

Insulin pumps have been used for more than 35 years (2). In the U.S. in 2005, the level of insulin pump penetration was estimated at 20 to 30% in patients with type 1 diabetes mellitus (T1DM) and <1% in insulin-treated patients with T2DM (3). The U.S. Food and Drug Administration (FDA) estimated that the number of U.S. patients with T1DM using continuous subcutaneous insulin infusion (CSII) was approximately 375,000 in 2007, up from approximately 130,000 in 2002 (4). The actual number of patients using insulin pumps in the U.S. is difficult to ascertain, but has been reported to range from 350,000 to 515,000 (5-7).

It has been estimated that by 2050, up to one-third of U.S. residents may have T2DM (8), and many of these individuals will require insulin. Therefore, it is increasingly important for more clinicians to develop a comprehensive understanding of these devices. The American Association of Clinical Endocrinologists (AACE) published its first Consensus Statement on Insulin Pump Management in 2010 (1). This document updates that statement and attempts to avoid repetition of some general but still valid information.

In the U.S., there is currently no official requirement for medical supervision of this complex diabetes therapy.

In addition, no certifying process exists to guide community physicians, patients and their families, payers, or regulators to qualified clinical settings for the initiation of insulin pump therapy.

Many knowledge gaps hamper truly evidence-driven decisions regarding insulin pump use. Some of these include the influence of CSII on hemoglobin A_{1c} (HbA_{1c}) levels, daily glucose levels, and glycemic variability; effect on weight control and/or hypoglycemia; reductions in emergency department visits and hospitalizations for acute events; effect on quality of life (e.g., easier travel across time zones and working various shifts); improved work habits and/or productivity; and liberalization of diet timing and composition.

2. STATE OF INSULIN PUMP TECHNOLOGY

Insulin pumps are advancing in form as well as function. For many years, they were simply miniature syringe pumps, with all of the pitfalls associated with these devices (9). Although complex, insulin pumps are now easier and safer to use. Insulin dose calculators ("wizards") are standard features of all current pumps; these improve dosing consistency and may decrease the frequency of insulin "stacking" (i.e., administering an insulin bolus while a recent prior bolus is still active). However, it is important to recognize device-specific recommendations may differ among patient scenarios. Therefore, prescribers should be familiar with these differences and train patients appropriately.

In the past, innovations in pump therapy were primarily cosmetic (e.g., availability in multiple colors) or incremental (e.g., allowing the storage of a customized series of basal rates or "profiles" to assist the user in adjusting pump settings to different life conditions). Insulin pumps are now following the lead of consumer electronics and have introduced features such as color touch screens, USB-rechargeable batteries, prefilled insulin cartridges, and disposability.

The availability of multiple infusion set types, various catheter tubing lengths, and tubeless pumps (where the infusion set and reservoir are integrated) have enhanced the acceptability of pump therapy and led to increased pump usage. Clinical trials are underway to validate methods that accelerate insulin action. These include the addition of hyaluronidase to the tubing, heating of the injection site, intradermal insulin injection, and new formulations of rapid-acting insulin (10-13). Data that support the feasibility of locating infusion sets and continuous glucose monitoring (CGM) catheters in close proximity make it likely that combination sensor and infusion sets will be developed (14), which will further increase patient convenience.

Improved connectivity to other devices is another area of rapid improvement. For many years, insulin pumps have received data transmitted from glucose meters. Insulin pumps can now display data from a CGM on the same screen and share data for display on other remote devices. This feature is likely to become more common in the next few years. Ultimately, insulin pumps may send data continuously to the "Cloud." However, currently most require a computer connection.

In 2013, the FDA approved Medtronic's MiniMed 530G with Enlite, under its new Artificial Pancreas Device System-Threshold Suspend guidelines, as the first device that alters insulin delivery in response to CGM sensor data (15-18). The pump features "threshold suspend," meaning that when CGM sensor glucose levels decline below a specified threshold, the pump alarms and suspends insulin delivery for 2 hours (or until the suspension is manually overridden). The use of this device has been shown to reduce nocturnal hypoglycemia (19). Table 1 shows a comparison of major insulin pumps, and Table 2 shows the characteristics of V-Go, a new type of disposable insulin delivery device for T2DM.

3. CLINICAL EVIDENCE T1DM

Table 3 provides a summary of clinical research findings on CSII efficacy and safety in patients with T1DM; included in this table are the results of selected meta-analyses covering clinical research on insulin pump therapy published after 2003. The goal of this section is not to provide an exhaustive summary of available CSII literature, but to provide a representative sample of available outcomes data as reported in a series of rigorous meta-analyses.

In addition to these meta-analyses, 2 publications provide more evidence. First, a 2010 Cochrane review compared CSII use with multiple daily injection (MDI) insulin regimens. This review included 23 randomized studies (duration, 6 days to 4 years) involving 976 patients with T1DM. A significant difference was documented in HbA_{1c} response favoring CSII (weighted mean difference –0.3% [95% confidence interval (CI), –0.1 to –0.4%]). In addition, CSII users demonstrated greater improvements in quality of life measures. No difference in body weight was observed between the 2 treatments. Severe hypoglycemia appeared to be reduced in CSII users, although no difference was observed in the frequency of nonsevere hypoglycemia (20). This report has been criticized because it included data from very short studies conducted in the 1980s, using less reliable technology in an era before monomeric rapid-acting insulin analogs were universally used in pumps (21). Furthermore, many of the patients had no prior problems with hypoglycemia at baseline (20).

Additionally, the Sensor-Augmented Pump Therapy for A1C Reduction (STAR-3) study showed significantly greater HbA_{1c} reductions in patients with T1DM (adults and children) randomly assigned to sensor-augmented insulin pump therapy versus MDI with conventional self-monitored blood glucose (SMBG; final HbA_{1c} 7.5%

Table 1
Comparison of Features of Major Insulin Pump Models

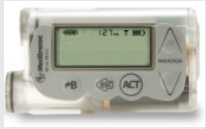
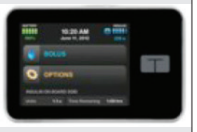
	Model (Manufacturer)							
	Accu-Chek Combo System (Roche Health Solutions)	**Accu-Chek Spirit System (Roche Health Solutions)**	**Asante Snap Insulin Pump System (Asante Solutions)**	**MiniMed Paradigm Real-Time Revel System (523/723) (Medtronic MiniMed)**	**MiniMed 530G with Enlite (551/751) (Medtronic MiniMed)**	**OmniPod Insulin Management System (Insulet Corporation)**	**OneTouch Ping (Animas)**	**t:slim Insulin Pump (Tandem Diabetes Care)**
Description								
Basal increments	0.05-25.0 U/h increments of 0.01 U (available up to 1.00 U/h)	0.1 U increments from 0.1-25.0 U/h	0.05 U; 0-4 U/h range	0.025-35.0 U/h	0.025 to 35.0 U/h	0.05-30 U/h	0.025 U/h	0.001 U at programmed rates ≥0.1 U/h; maximum basal rate of 15 U/h
Temp basal	Increase to 250% for up to 24 h; decrease to 0% for up to 24 h	10% increments from 0 to 200%; 15-min increments from 15 min to 24 h	0 to 500%, up to 24 h	± 0.1 u increment as single basal rate for 0.5 to 24 h or as % of current basal (from 0-200%, with max being current max basal)	± 0.1 u increment as single basal rate for 0.5 to 24 h or as % of current basal (from 0-200% with max being current max basal)	30 min to 12 h, in 30-min increments	–90% to 200% in increments of 10% for 0 to 24 h (30-min increments)	Range: 0 to 250%, from 15 min to 72 h
Bolus increments	0.1-25.0 U	Pre-programmable increments of 0.1, 0.2, 0.5, 1.0, 2.0 U	0.05 U	0.025 U (0.025-25.0 U)	0.025 U (0.025-25 U)	0.05, 0.1, 0.5, 1.0 U	0.05 visual, 0.1, 0.5, 1.0, 5.0 audio	0.01 U at volumes >0.05 U Quick bolus increments: 0.5, 1, 2, 5 U, or 2, 5, 10, or 15 g
Carb + correction factors	Yes, carb values, BG values, and patient health events can be communi-cated from Accu-Chek Aviva Combo meter-remote to Accu-Chek Spirit Combo insulin pump via Bluetooth	Yes, carb and BG values entered into bolus calculator program	Yes, carb, BG values entered via numeric keypad Option to apply IOB to Correction or All (correction plus food)	Yes, manual carb, BG direct from brand-name meter or manual entry	Yes, manual carb, BG direct from Contour Next Link Meter or manual entry	Yes, manual carb, BG value from Abbott Freestyle meter or manual entry	Yes, carb and BG values can be entered into the pump or meter/ remote	Yes, carb, BG values entered via numeric keypad
1-U bolus duration	5 s	5 s	20 s	20 s	20 s	40 s	1 s for normal bolus and 3 s for slow bolus	30 s
Dimensions (inches)	3.2 × 2.2 × 0.8 (for Accu-Chek Spirit Combo insulin pump)	3.2 × 2.2 × 0.8	3.88 × 1.72 × 0.75	2.0 × 3.3 (2.8 at the battery cap) × 0.82 (523) 2.0 × 3.7 (3.5 at the battery cap) × 0.84 (723)	2.0 × 3.3 (2.8 at the battery cap) × 0.82 (551) 2.0 × 3.7 (3.5 at the battery cap) × 0.84 (751)	OmniPod: 1.53 × 2.05 × 0.57 Personal diabetes manager: 2.4 × 4.4 × 0.98	3.25 × 2.00 × 0.86	2.0 × 3.13 × 0.6
Weight (ounces)	3.9 (empty)	2.8 (empty); 4.0 (with battery, full cartridge, and infusion set)	2.6 (full, with battery)	3.4 (523, empty) 3.6 (723, empty)	3.4 (551, empty) 3.6 (751, empty)	OmniPod: 0.88 (empty) Personal diabetes manager: 4.4 with batteries	3.43 (empty)	3.95 (with battery and full 300 U cartridge)

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Table 1 *(Continued)*
Comparison of Features of Major Insulin Pump Models

	Model (Manufacturer)							
	Accu-Chek Combo System (Roche Health Solutions)	**Accu-Chek Spirit System (Roche Health Solutions)**	**Asante Snap Insulin Pump System (Asante Solutions)**	**MiniMed Paradigm Real-Time Revel System (523/723) (Medtronic MiniMed)**	**MiniMed 530G with Enlite (551/751) (Medtronic MiniMed)**	**OmniPod Insulin Management System (Insulet Corporation)**	**OneTouch Ping (Animas)**	**t:slim Insulin Pump (Tandem Diabetes Care)**
Basal patterns	5 patterns	5 profiles	4 patterns	3 patterns	3 patterns	7 patterns	4 patterns	6 customizable personal profiles with 16 timed settings per profile
IOB calculations	Yes	Yes	Yes, shown in status screen	Yes	Yes	Yes	Yes	Yes, shown on home screen
Special features	Bluetooth wireless communi-cation between Accu-Chek Aviva Combo meter-remote and Accu-Chek Spirit Combo insulin pump Accu-Chek Aviva Combo meter-remote can remotely control nearly all of the pump's other functions Customized bolus recommen-dations based on health status/events Adjusts basal rates in increments as precise as 0.01 U ICR and ISF program-mable in 0.1 U increments 315-U cartridge Full-color, on-screen BG and bolus data graphs on Accu-Chek Aviva Combo meter-remote Delivers a confirmed bolus even if user moves out of the 6.5-foot wireless communi-cation range Choice of 3 menus (standard, advanced, custom) Child lock	Backlight available to display in low lighting Screen display is 180° reversible (no upside-down) Selectable user menus: Standard, Advanced or Custom Bolus customization 30 most recent results are viewable for boluses, alerts and errors, insulin totals, and temporary basal rates Standard AA battery for easy and convenient replacement Programming retained with battery changes 315 U cartridge Automatic prime Audible or vibrating bolus confirmation and alerts Display in 12 languages including English, French, and Spanish Standard luer-lock connections for infusion set flexibility Infrared port for wireless data transfer	Prefilled insulin cartridge Auto-priming Enhanced occlusion detection Replaceable drive system No-fuss battery (never change or charge it) Alarm capable of >56 dBa at 1 m Automatic backlight Flashlight Water ingress alarm Major impact alarm Missed insulin notification Integrated bolus calculator with flexible IOB application High-contrast screen readable in direct sunlight	Real-time trend graphs (3, 6, 12, 24 h) Predictive alerts 8 customizable high/low threshold alerts Alert-directed navigation Rate of change alerts 1:1 ICR Missed meal bolus alert Linking brand meters Child lock Remote control capabilities 2 pump sizes (180 and 300 U)	Threshold Suspend function will shut off the pump for 2 h if sensor glucose levels fall below the threshold values and the patient doesn't respond to alarms 6-day sensor clock Real-time trend graphs (3, 6, 12, 24 h) Predictive alerts 8 customizable high/low threshold alerts Alert-directed navigation Rate of change alerts 1:1 ICR Missed meal bolus alert Linking meter (Bayer Contour Next Link Meter) Child lock Remote control capabilities 2 pump sizes (180 and 300 U)	No tubing to catch or snag and disrupt insulin activity Waterproof and body-worn, so no need to disconnect Auto insertion of cannula reduces user error Fully integrated FreeStyle BG meter Large, easy-to-read LCD Child lock-out feature Carbohydrate and bolus presets	Remote bolus from OneTouch Meter High-contrast color screen Waterproof up to 12 feet for 24 h 500-food database 4 basal insulin profiles, each with up to 12 insulin requirements based on time of day 12 ICR, ISF, and BG target ranges based on time of day Ability to lock pump and meter remote from unintended use Tunes for alarms and warnings	Smallest available pump with up to 300 U capacity Bright color touch screen Integrated rechargeable lithium polymer battery Micro-delivery technology Integrated bolus calculator with carb-adding capabilities 25 U max bolus with option for another 25 U

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Table 1 *(Continued)*
Comparison of Features of Major Insulin Pump Models

	Model (Manufacturer)							
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Pump programming	Accu-Chek 360° Insulin Pump Configuration Software	ACCU-CHEK Pocket Compass software with bolus calculator v3.0 Software	Intuitive user interface with smart buttons Compatible with Diasend and Glooko applications for pump and BG reporting	CareLink available through CareLink USB or through the Contour Next Link Meter USB	CareLink available through CareLink USB or through the Contour Next Link Meter USB	CoPilot software to download personal diabetes manager data; supported by multiple data management platforms	Diasend web-based software or EZ Manager Max software to download pump and meter data Mac- and PC-Compatible	Intuitive user interface with direct keypad entry t:connect Diabetes Management Application for pump and BG reporting
Bolus "types"	Quick Standard Extended Multiwave	Quick Scroll Extended Multiwave	Bolus entry: Manual Smart bolus Audio Bolus delivery: Now Timed (square wave) Combo (dual wave)	Normal Square wave (extended) Dual wave (combination) Correction	Normal Square wave (extended) Dual wave (combination) Correction	Meal Correction Meal and correction Extended Manual	Carb Smart EZ Bolus Combination Correction	Standard Correction Extended Quick

Abbreviations: BG = blood glucose; ICR = insulin-to-carbohydrate ratio; IOB = insulin on board; ISF = insulin sensitivity factor; max = maximum

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vs. 8.1%, respectively, compared with a baseline of 8.3%; *P*<.001). A higher proportion of patients randomly assigned to pump therapy achieved an HbA_{1c} level <7%; without any increase in the severe hypoglycemia rate or weight gain compared to the MDI group. This study did not assess the effect of sensor-augmented pump therapy versus the effect of insulin pump therapy alone (22).

On the basis of this evidence and other currently available data, CSII appears to be justified for basal-bolus insulin therapy in patients with T1DM.

T2DM

Fewer clinical investigations have examined CSII in patients with T2DM. In a published analysis of 4 randomized controlled trials (RCTs), no significant HbA_{1c} improvements, differences in hypoglycemic risk, or weight differences were observed with CSII versus MDI over 12 to 52 weeks (Table 4). However, a nonsignificant trend toward decreased insulin requirements was observed among CSII patients (23-25). Additional published studies of CSII in patients with T2DM are summarized in Table 5. A large, randomized multicenter trial comparing CSII to MDI in 50+ T2DM patients failing MDI is ongoing in Europe and North America, with results expected in 2014 (26).

4. PATIENT AND PROVIDER SELECTION

Successful CSII implementation depends to a large extent on patient and clinician selection because both insulin pump candidates and providers must have the knowledge, skills, and resources to use this complex and time-consuming therapy safely and effectively.

Patient Selection

The selection of optimal candidates for CSII therapy has been debated since insulin pumps became available

Table 2
V-Go Disposable Insulin Delivery Device

Characteristic	V-Go Disposable Insulin Delivery Device (Valeritas, Inc.)
Description	
Basal increments	3 preset basal rates: 20 U/24 h 30 U/24 h 40 U/24 h
Carb + correction factors	N/A
1-U bolus duration	Bolus delivered in 2 U increments; up to 18 clicks of 2 u per day
Dimensions (inches)	2.4 × 1.3 × 0.5
Empty weight (ounces)	0.7 to 1.8
Basal patterns	3 preset basal rates/fixed
Insulin-on-board calculations	N/A
Special features	V-Go designed for the T2DM population Accessible for the T2DM population Simplification of basal-bolus therapy No electronics, batteries Simple filling accessory – EZ Fill
Pump programming	N/A
Bolus types	Bolus delivered in 2-U increments (36 U/24 h in 2-U increments)

Abbreviations: T2DM = type 2 diabetes mellitus

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Table 3
Key Findings From CSII Meta-analyses Published since 2003

Author, Year	Meta-analyses objectives	No./types of studies included in meta-analyses	Clinical findings	Notes
Weissberg-Benchell et al, 2003 (102)	Investigation of metabolic and psychosocial impact of CSII therapy vs. other treatment modalities (e.g., MDI, conventional therapy) in children, adolescents, and adults (N = 1,547)	2,483 studies identified; 61 met initial criteria; final review consisted of 52 studies (37 paired, 4 randomized crossover, and 11 parallel) published between 1979 and 2001	Compared with MDI, CSII therapy was associated with significant improvements in glycemic control based on decreases in HbA_{1c} and mean blood glucose levels Analysis of CSII complications before 1993 revealed decreased risk of hypoglycemic events with insulin pump therapy but a potential increase in DKA risk	Changes in insulin requirements and body weight not included in analysis due to insufficient data CSII did not appear to be associated with increased risk of poor psychosocial outcomes, although effects on patient perspectives and psychosocial functioning were difficult to assess due to inconsistencies in study design and methodology
Jeitler et al, 2008 (103)	Comparison of effects of CSII vs. MDI on glycemic control, hypoglycemic risk, insulin requirements, and adverse events in adults with T1DM (n = 908), children with T1DM (n = 74), and patients with T2DM (n = 234)	673 studies identified; final review consisted of 22 RCTs (17 T1DM, 2 T2DM, 3 pediatric) published through March 2007	HbA_{1c} reduction greater and insulin requirements lower with CSII than with MDI in adults and adolescents with T1DM; risk of hypoglycemia comparable among adult patients (data unavailable for adolescent subjects) No conclusive CSII benefits for patients with T2DM	
Fatourechi et al, 2009 (104)	Comparison of effects of CSII and MDI on glycemic control and hypoglycemia in adults and children with T1DM (n = 669) or T2DM (n = 239)	107 studies identified; final review consisted of 15 RCTs published between 2002 and March 2008	In patients with T1DM, HbA_{1c} was mildly decreased with CSII vs. MDI; CSII affect on hypoglycemia unclear CSII and MDI outcomes were similar among patients with T2DM	CSII efficacy in patients with hypoglycemia unawareness or recurrent severe hypoglycemia inconclusive due to lack of data
Pickup and Sutton, 2008 (105)	Examination of CSII and MDI effects on glycemic control and incidence of severe hypoglycemia in patients with T1DM (N = 1,414); focused on studies with ≥6 months of CSII therapy and >10 episodes of severe hypoglycemia per 100 patient-years with MDI therapy	61 studies identified; final review consisted of 22 RCTs and before/after studies published between 1996 and 2006	Risk of severe hypoglycemia was decreased with CSII vs. MDI; greatest reduction observed in patients with diabetes of longest duration and in those with highest baseline rates of severe hypoglycemia with MDI therapy HbA_{1c} was lower for CSII than for MDI, with greatest improvement seen in patients with highest initial HbA_{1c} values on MDI	
Monami et al, 2009 (23)	Comparison of glycemic control and hypoglycemic incidence with short-acting analog-based CSII (n = 444) vs. MDI (n = 439) therapy of ≥12 weeks' duration in patients with T1DM	177 studies identified; final review consisted of 11 RCTs published between 2000 and 2008	HbA_{1c} was significantly lower with CSII vs. MDI; HbA_{1c} reduction was only evident for studies with mean patient age >10 years Severe hypoglycemia occurred at a comparable rate with CSII and MDI therapy	

Abbreviations: CSII = continuous subcutaneous insulin infusion; DKA = diabetic ketoacidosis; HbA_{1c} = hemoglobin A_{1c}; MDI = multiple daily injections; RCT = randomized controlled trial; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus

Table 4
RCTs Comparing CSII and MDI for Patients With T2DM

				HbA_{1c} (%) (SD)			
Reference	**n[a]**	**Design**	**Follow-up**	**Baseline**	**CSII**	**MDI**	***P* value**
Noh et al, 2008 (106)	15	Observational	30 weeks	7.9 (1.9)	5.0 (0.9)	NA	<.001
Parkner et al, 2008 (109)	10	Observational	3 successive nights	FPG: 209 (52.3) mg/dL	99.1 (28.8) mg/dL	NA	<.0001
Berthe et al, 2007 (107)	17	Crossover	2 periods of 12 weeks	9 (1.6)	7.7 (0.8)	8.6 (1.6)	<.03
Herman et al, 2005 (25)	107	Parallel	1 year	CSII: 8.4 (1.1) MDI: 8.1 (1.2)	6.6 (0.8)	6.4 (0.8)	.19
Wainstein et al, 2005 (108)	40	Crossover	2 periods of 18 weeks	CSII-MDI: 10.1 (1.6) MDI-CSII 10.2 (1.4)	–0.8 (1.5)[b]	+0.4 (1.3)[b]	.007
Raskin et al, 2003 (24)	132	Parallel	24 weeks	CSII: 8.2 (1.4) MDI: 8.0 (1.1)	7.6 (1.2)	7.5 (1.2)	NS

Abbreviations: CSII = continuous subcutaneous insulin infusion; FPG = fasting plasma glucose; HbA_{1c} = hemoglobin A_{1c}; MDI = multiple daily injections; NS = not significant; T2DM = type 2 diabetes mellitus
[a] Subjects randomized
[b] HbA_{1c} values for CSII and MDI are presented by Wainstein et al as a direct treatment effect in the completers' cohort.

for use in clinical practice during the late 1970s (27,28). Clearly, CSII is not appropriate for every patient with insulin-requiring diabetes. Box 1 provides a summary of the characteristics that may make a patient ill suited for this form of therapy, based on the AACE Insulin Pump Task Force Expert Consensus.

The ideal CSII candidate would be a patient with T1DM or intensively managed insulin-dependent T2DM who currently performs ≥4 insulin injections and ≥4 SMBG measurements daily, is motivated to achieve optimal blood glucose control, and is willing and able to carry out the tasks required to use this complex and time-consuming therapy safely and effectively. Patients who tend to be most successful are those who are taking all the steps required to manage their glucose levels but are unable to achieve their HbA_{1c} target despite their best efforts, are having difficulty with hypoglycemia, and/or are seeking a means to maintain target glucose and HbA_{1c} levels with greater ease and flexibility. Eligible patients should be capable of self-management through frequent SMBG measurements and/or the use of a CGM device. Furthermore, candidates should have training in carbohydrate counting and/or matching food with insulin action, as well as knowledge of how to calculate insulin correction doses using the pump's computer. Patients should also be willing to maintain frequent contact with members of their health care team, in particular their pump-supervising physician.

On the basis of the AACE Insulin Pump Task Force's comprehensive research and decades of clinical experience with CSII, the proposed clinical characteristics, or profiles, of suitable insulin pump candidates are summarized in Table 6.

Should insulin pump therapy fail to provide a patient with the expected benefits or if there are safety issues, clinicians must be willing to terminate pump therapy and offer suitable alternatives. This would be relevant, for example, in pump users who enjoy their pump experience but are not dosing correctly and thus have chronically and seriously uncontrolled glucose levels.

Provider Selection

Less attention has been devoted to defining selection criteria for insulin pump providers than for patients, and no standardized guidelines have been established for this purpose in the U.S. As suggested by Skyler and colleagues, insulin pumps should only be prescribed by clinicians who possess the necessary knowledge, skills, and resources to provide effective and safe initiation and maintenance of this complex and time-consuming therapy (29). Furthermore, the availability of adequate patient education, training, and follow-up are mandatory to ensure optimal usage of this technology. Unfortunately, given the need for a multidisciplinary team to implement insulin pump therapy and the poor level of reimbursement available, relatively few clinicians have the resources to incorporate this sophisticated treatment modality into their practice. It has been estimated that about 2,000 U.S. physicians prescribe insulin pumps (5).

5. INSULIN PUMP USE IN VARIOUS PATIENT POPULATIONS

It is not the purpose of this document to detail the specific therapeutic decisions required to design personalized

insulin pump programs. Several existing publications provide the information required to establish basal and bolus insulin calculations in adults and in special populations (29-33). Instead, this section will summarize the therapeutic challenges associated with insulin pump use in specific patient populations and describe strategies for successful CSII implementation in each of these groups. A brief outline of specific suggestions for initial pump settings for adult and pregnant patients is shown in Tables 7 and 8.

Adults

After a clinician has determined that a patient is eligible for insulin pump therapy (see Box 1 and Table 6), he/she must ensure that the patient has a multidisciplinary CSII health care team in place before therapeutic initiation. Although the precise composition of this team depends on the clinical practice setting, its members should include an endocrinologist/diabetologist with demonstrated expertise in insulin pump therapy, a diabetes specialist nurse/diabetes educator, and a dietitian.

The health care team's initial task is to assess the patient's level of expertise in the following areas:

- Ability to check capillary glucose levels and maintain glucose meter
- Knowledge of premeal, postmeal, and bedtime target glucose values
- Knowledge of steps for hypoglycemia detection, prevention, and treatment
- Sick-day management and diabetic ketoacidosis (DKA) prevention strategies
- Ability to maintain food and physical activity records
- Basic and advanced carbohydrate-counting skills

Following this assessment, an education and training plan can be designed to address gaps in the patient's knowledge and to provide information about insulin pump and infusion set operation, maintenance, and troubleshooting; infusion site preparation; and the calculation and configuration of basal insulin infusion rates, initial insulin-to-carbohydrate ratios (ICRs), boluses, and insulin sensitivity factor (ISF) (more details are provided in Section 6).

A simplified scheme for initiating insulin pump therapy is presented in Table 7. Initial basal rates and bolus settings are calculated from the available knowledge of a patient's previous basal and bolus insulin doses and weights, as well as considerations based on individual lifestyles.

Once the patient is successfully transitioned from MDI to CSII, frequent (i.e., daily) contact with the pump trainer is mandatory. A return visit with the endocrinologist/diabetologist/nurse specialist is advised within 3 to 7 days to begin fine-tuning the insulin infusion parameters using the initial glucose data provided by the patient. Educational consults (e.g., clinic visits, phone calls, e-mail communication) should be scheduled weekly or biweekly at first and then periodically as necessary. Initially, some patients may require daily contact. Often, patients can take advantage of

Table 5
Additional Studies of CSII in Patients With T2DM

Reference	n[a]	Design	Therapy	Follow-up	Primary end point	Primary result
Edelman et al, 2010 (110)	58	Longitudinal	CSII simple dosing	4 months	HbA_{1c}	Significant reduction in HbA_{1c}
Parkner et al, 2008 (114)	21	Crossover	Basal CSII or insulin glargine	2 periods of 8 days	Insulin and glycemic profiles	Improved insulin and glycemic profiles favoring CSII
Kapitza et al, 2008 (112)	6	Feasibility	CSII with simple insulin pump	7 days	Glycemic profiles	Stable or improved glycemic profiles
Labrousee-Lhermine et al, 2007 (113)	59	Longitudinal	CSII simple dosing, 2 regimens	3 years	HbA_{1c}	Significant reduction in HbA_{1c} for 2 CSII regimens
Lane et al, 2006 (69)	9	Feasibility	CSII with U-500 insulin	3 months	HbA_{1c}	Significant reduction in HbA_{1c}
Testa et al, 2001 (115)	126	RCT	CSII or MDI	24 weeks	Treatment satisfaction	Improved treatment satisfaction favoring CSII
Jennings et al, 1991 (111)	20	RCT	CSII or conventional insulin	4 months	HbA_{1c}	Significant reduction in HbA_{1c} favoring CSII

[a] Patients randomized
Abbreviations: CSII = continuous subcutaneous insulin infusion; HbA_{1c} = hemoglobin A_{1c}; MDI = multiple daily injections; RCT = randomized controlled trial; T2DM = type 2 diabetes mellitus

Box 1
Specific Characteristics of Patients Who Are Not Good Candidates for Insulin Pump Use

- Unable or unwilling to perform MDI injections (≥3-4 daily), frequent SMBG (≥4 daily), and carbohydrate counting
- Lack of motivation to achieve tighter glucose control and/or a history of non-adherence to insulin injection protocols
- History of serious psychological or psychiatric condition(s) (e.g., psychosis, severe anxiety, or depression)
- Substantial reservations about pump usage interfering with lifestyle (e.g., contact sports or sexual activity)
- Unrealistic expectations of pump therapy (e.g., belief that it eliminates the need to be responsible for diabetes management)

Abbreviations: MDI = multiple daily injections; SMBG = self-monitored blood glucose

experienced Certified Diabetes Educators employed by a pump company, provided they follow the clinician's orders for pump therapy. Specialist follow-up visits are recommended at least monthly until the pump regimen is stabilized and at least once every 3 months thereafter.

As with any sophisticated device, the ability to use more complex pump features (e.g., adjusting bolus "wizard" settings, configuring different basal settings depending on expected daily routine, and exploring different modes of bolus delivery, temporary as-needed basal settings, and/or adjustments for periods of physical activity) depends on each patient's knowledge, skills, motivation, and ability to obtain sufficient data related to glucose levels, carbohydrate intake, insulin administration, and physical activity levels. This individualized, incremental approach is an ongoing process, as the patient and health care team work together to optimize glycemic control.

All patients will require periodic re-education and retraining to improve diabetes management, and the health care team should regularly re-evaluate whether pump therapy should be withdrawn for those patients who are not benefiting from this form of insulin delivery.

Children

The first successful studies of CSII effectiveness were carried out more than 30 years ago in children (34), but it was not until the last 15 years that pediatric CSII use took off. Since then, randomized and nonrandomized pediatric

Table 6
Proposed Clinical Characteristics of Suitable Insulin Pump Candidates

Patient clinical characteristics	
T1DM	**T2DM**
Patients with T1DM who do not reach glycemic goals despite adherence to maximum MDI, especially if they have: • Very labile diabetes (erratic and wide glycemic excursions, including recurrent DKA) • Frequent severe hypoglycemia and/or hypoglycemia unawareness • Significant "dawn phenomenon," extreme insulin sensitivity Special populations (e.g., preconception, pregnancy, children, adolescents, competitive athletes) Patients with T1DM who, after investigation and careful consideration, feel that CSII would be helpful in achieving and maintaining treatment targets and improve their ability to cope with the challenges of managing their diabetes	Selected patients with insulin-requiring T2DM who satisfy any or all of the following: • C-peptide positive, but with suboptimal control on a maximal program of basal/bolus injections (Note: CMS will not reimburse for pumps or pump supplies in T2DM patients who are not C-peptide deficient) • Substantial "dawn phenomenon" • Erratic lifestyle (e.g., frequent long-distance travel, shift work, unpredictable schedules leading to difficulty maintaining meal timing) • Severe insulin resistance, candidate for U500 insulin by CSII Selected patients with other DM types (e.g., postpancreatectomy)

Abbreviations: CMS = Centers for Medicare & Medicaid Services CSII = continuous subcutaneous insulin infusion; DKA = diabetic ketoacidosis; DM = diabetes mellitus; MDI = multiple daily injections; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus

Table 7
Calculations for Insulin Pump Settings (116)

Pump TDD calculation	
Method 1 **Pre-pump TDD**	**Method 2** **Patient weight**
Pre-pump TDD × 0.75	Weight: kg × 0.5 or lb × 0.23
Clinical considerations on pump TDD: • Average values from methods 1 and 2 • Hypoglycemic patients → start at lower value • Hyperglycemic, elevated HbA_{1c}, or pregnant → start at higher value	

Pump dose adjustment		
Basal Rate	**Carbohydrate Ratio**	**Insulin Sensitivity Factor/ Correction**
(Pump TDD × 0.5)/24 h	450/TDD	1700/Pump TDD

Clinical Guidelines
• Start with one basal rate, adjust according to glucose trends over 2-3 days
• Adjust to maintain stability in fasting state (between meals and during sleep)
• Add additional basal according to diurnal variations (dawn phenomenon)
	Clinical Guidelines
	• Adjust based on low-fat meals with known carbohydrate content
	• Acceptable 2-hr postprandial rise is ~60 mg/dL above preprandial BG
	• Adjust CR in 10%-20% increments based on post-prandial BG
	• Alternate Methods
	  • CR (6 × weight in kg/TDD) or (2.8 × weight [lb]/TDD)
	  • Fixed Meal Bolus = (TDD × 0.5)/ 3 equal meals (when not carb counting)
	  • Continue existing CR approach from MDI regimen
		Clinical Guidelines
		• To assess sensitivity factor, BG should be checked 2 h after correction; if BG is within 30 mg/dL of target range, sensitivity is correct
		• Make adjustments in 10-20% increments if 2-h post correction BGs are consistently above or below target

Abbreviations: BG = blood glucose; CR = carbohydrate ratio; HbA_{1c} = hemoglobin A_{1c}; ISF = insulin sensitivity factor; MDI = multiple daily injection; TDD = total daily dose

studies have shown CSII to be more effective in lowering HbA_{1c} than injection therapy (35,36). CSII has also been associated with improved patient satisfaction and reduced hypoglycemia frequency (37).

Some practical benefits of CSII compared to MDI include: the ability to program temporary basal rates, needing only 1 insertion site every 2 to 3 days, use of the dose calculator to adjust premeal bolus doses, customizable square- and dual-wave boluses, and programmable alternate basal rate patterns for weekends and nights following afternoon exercise. For the pediatric practitioner, the memory functions that record all pump-related activities are especially important because failure to administer premeal boluses is a prime cause of elevated HbA_{1c} levels in adolescents (38).

A specific risk of pump therapy for all patients is that prolonged accidental or purposeful interruption of insulin delivery over several hours can lead to increases in blood ketones and the subsequent development of diabetic ketoacidosis (DKA) because patients are only receiving rapid-acting insulin. This risk can be reduced or eliminated by regular blood glucose testing and standard patient protocols for hyperglycemia management. In addition, many pumps have alarms that can be set to indicate if no active bolus is provided within a specified time range. Recent data from the T1D Exchange Clinic Registry Group (39) indicate that HbA_{1c} levels and the annual rate of DKA events are lower in pediatric patients receiving CSII than those receiving MDI.

In 2006, an international consensus conference of leading pediatric diabetes specialists was convened in Berlin (37) to develop treatment guidelines for the use of CSII in children and adolescents. These experts agreed that CSII was indicated for pediatric patients with:

- Elevated HbA_{1c} levels on injection therapy
- Frequent, severe hypoglycemia
- Widely fluctuating glucose levels
- A treatment regimen that compromises lifestyle
- Microvascular complications and/or risk factors for macrovascular complications

CSII was also identified as beneficial for athletes, very young children, adolescents with eating disorders, patients with a pronounced dawn effect, ketosis-prone patients, pregnant teens (ideally, with pump use initiated before conception), and children with pronounced needle phobia. The consensus conference also recommended that a pediatric multidisciplinary diabetes team experienced in insulin pump therapy should initiate and supervise the ongoing management of children on CSII (37).

Ideal candidates for pediatric CSII include patients with motivated families who are committed to monitoring blood glucose at least 4 times per day and have a working understanding of basic diabetes management, especially carbohydrate counting and the use of ICR and ISF to calculate bolus insulin doses. HbA_{1c} level also plays a role in determining CSII readiness, although it is less important than the factors listed above. Patient age and duration

Table 8
Suggested Protocol for Insulin Pump Use during Pregnancy

Insulin infusion rates for women with T1DM: Total basal insulin requirement calculated for 24 h	
Gestation	**Units × weight (kg)**
Prepregnancy	0.3
First trimester	0.35
Second trimester	0.4
Third trimester	0.45
Term pregnancy (>38 weeks' gestation)	0.5
Hourly infusion rate changes based on time of day (divide the total basal U by 24)	
Time of Day	**Infusion rate**
12 - 4 AM	0.5 × calculated basal/24
4 - 10 AM	1.5 × calculated basal/24
10 - 6 PM	1.0 × calculated basal/24 (may need adjustment based on stress and exercise in the time period)
6 PM - 12 AM	Calculated (may need adjustment based on stress and exercise in the time period)
Meal-related insulin bolus[a]	
Gestation	**U × weight (kg) (divided into thirds for a dose before each meal)**
Prepregnancy	0.3
First trimester	0.35
Second trimester	0.4
Third trimester	0.45
Term pregnancy (>38 weeks' gestation)	0.5
After second trimester, in case of dislodgment at infusion site	
Dose of NPH 0.1 × weight (in kg) before bed, then a lower early morning insulin infusion rate	

Abbreviations: NPH = neutral protamine Hagedorn; T1DM = type 1 diabetes mellitus
[a] Use only rapid-acting insulin analog.

of diabetes should not be factors in determining when patients will transition from injections to CSII. In fact, it is increasingly clear that infants, toddlers, and preschoolers are probably the ideal pediatric CSII patients, because it lowers HbA_{1c}, reduces the frequency of severe hypoglycemic episodes, and improves parents' quality of life (40,41). Immediately starting newly diagnosed patients on pump therapy is an increasingly common and effective approach to initiating insulin therapy in children with new-onset diabetes.

The use of CGM in combination with insulin pump therapy has been shown to lower HbA_{1c} levels by 0.5 to 0.8% in youth and adults with T1DM who frequently wear CGM devices (42). In the STAR 3 Study, treatment with an integrated sensor-augmented pump system (SAPS) was more effective than MDI in lowering HbA_{1c} levels. The FDA recently approved a SAPS that represents the first step toward an automatic or semiautomatic closed-loop insulin delivery device. This pump features a "threshold suspend" function that suspends insulin delivery for 2 hours (or until the suspension is manually overridden) when the CGM sensor glucose level declines below a specified threshold. Moreover, SAPS that prevent hypoglycemia by suspending insulin delivery using an algorithm based on the rate of glucose fall may be available soon (22).

Pregnant Women With Diabetes

T1DM and Pregnancy

Macrosomia (infants in the >90th percentile of weight for gestational age or sex, or >2 SD above the mean of a normal population of newborns) is the most common neonatal complication associated with diabetes during pregnancy. However, macrosomia is secondary to hyperglycemia; therefore, while insulin pumps are an effective insulin delivery system, inadequate blood glucose control, regardless of treatment modality, is the real culprit in macrosomia (43,44). Insulin pump therapy has not been shown to be superior to MDI for maintaining HbA_{1c} levels in pregnant women (45).

A 2007 Cochrane Library review, assessed as current in 2011, analyzed 5 RCTs (153 women with 154 pregnancies) comparing CSII with MDI in pregnant women with diabetes (46). No significant differences were found in any outcomes measured; however, the number of trials and participants was small. The available evidence does not support the use of 1 intensive insulin approach over another in pregnancy complicated by diabetes. In addition, a study of 42 women with pre-existing diabetes visiting a joint obstetric-diabetic clinic demonstrated that insulin pump therapy was equivalent to MDI for HbA_{1c} control and fetal outcomes (47).

Thus, the literature does not contain clear evidence that insulin pumps are necessary for the optimal treatment of women with T1DM during pregnancy. A robust randomized trial that is adequately powered to assess efficacy outcomes for CSII versus MDI in pregnant women with diabetes is needed. However, in many specialized diabetes practices it is customary to switch to CSII pre- or postconception if the patient is not at their glycemic goal (typically fasting plasma glucose >90 mg/dL and/or 1-hour postmeal glucose >120 mg/dL).

Treatment Protocol: Insulin Pump Therapy for T1DM During Pregnancy

Because pregnancy is a state of accelerated ketosis (48), just a few hours of insulin interruption can lead to hyperglycemia and ketosis. As diabetic ketosis is associated with fetal demise (49), intensive education and surveillance of the infusion site and sets are required with insulin pump use during pregnancy (50-53).

As the abdominal skin stretches and the subcutaneous tissue thins, the pump infusion set must be moved to other sites that offer a more secure and predictable absorption pattern. Usually, this transition occurs after the second trimester. As a safety feature, and because there is no long-acting insulin in the pump infusion, a low dose of neutral protamine Hagedorn (NPH) or insulin detemir may be given at bedtime to ensure that there will never be a lack of insulin in circulation if the needle dislodges. Practical guidance for the use of insulin pumps in diabetes-complicated pregnancy is outlined in Table 8.

Insulin Pump Therapy for T2DM During Pregnancy

One study assessed the use of CSII in women with insulin-requiring GDM or T2DM in pregnancy with persistent hyperglycemia (1991-1994 data) (54). However, this nested case-control study used older insulin pumps and regular insulin. Insulin pump therapy seems to be safe and effective for maintaining glycemic control in pregnancies complicated by GDM/T2DM and requiring large insulin doses.

Insulin Pump Therapy During Labor and Delivery

Few studies have investigated insulin and glucose requirements during labor and delivery (55). It may be prudent to discontinue insulin pump use at labor onset. Physiologically, labor can be considered as the equivalent of prolonged exercise (56). Before the implementation of management protocols to normalize blood glucose in women with T1DM during pregnancy, women starting their labor in the hyperglycemic state required large insulin doses (57-60).

To prevent the complete depletion of hepatic glycogen stores during labor, the glucose substrate need is similar to that of a trained marathon runner (2.55 mg/kg/min). This infusion rate is equivalent to 10 g glucose/hour for a 60-kg woman. This protocol has been applied to women with

T1DM during labor and delivery with excellent outcomes (61). Protocols for labor and delivery have been published on the basis of this experience (52).

In addition, upon delivery, insulin pump infusion should be temporarily stopped to avoid hypoglycemia. Once the blood glucose is >100 mg/dL and the patient or medical professional caring for the patient can safely assume responsibility for pump function, infusion should be resumed at the prepregnancy settings for the basal rate, bolus dose or ICR, and correction dose or ISF.

Insulin Pump Use During Lactation/Breastfeeding

Only 1 publication has evaluated insulin requirements for T1DM specifically related to basal and bolus insulin distribution when women utilize CSII. This case report showed the optimal insulin doses for a woman with T1DM using CSII treatment (62). Based on their findings, the authors recommended that the starting basal insulin dose for breastfeeding women with T1DM should be 0.21 × weight (kg). This regimen results in normoglycemia and minimizes the risk of severe hypoglycemia associated with lactation (63). Further studies are necessary to validate this hypothesis.

Use of Pumps in Inpatient Settings

When CSII users are evaluated in emergency departments or are admitted to medical or surgical units for nonacute hyper- or hypoglycemic crisis, they typically have more knowledge and expertise with this form of insulin delivery than the medical professionals handling their hospital stay. It is imperative that the specialist(s) responsible for the patient's ambulatory pump management is contacted promptly to make decisions about appropriate infusion adjustments during the hospital stay. If the facility does not have an internal insulin pump specialist, the patient's managing practitioner or an external expert should be consulted. In addition, patients should be encouraged to not discontinue pump infusion unless directed by their diabetes specialist (64). With the increased utilization of insulin pumps by patients with both T1DM and T2DM, hospitals are encouraged to have pump experts on staff. As stated in the American Diabetes Association's 2014 Standards of Medical Care and supported by others (64-66), "Patients who use CSII pump therapy in the outpatient setting can be candidates for diabetes self-management in the hospital, provided that they have the mental and physical capacity to do so. [The] availability of hospital personnel with expertise in CSII therapy is essential. It is important that nursing personnel document basal rates and bolus doses on a regular basis (at least daily)."

U-500 Insulin Use in CSII

The global obesity epidemic has given rise to a population of obese patients with T2DM with high insulin requirements (>200 U/day) due to insulin resistance. In this population, several small retrospective case report series (67-71) and 1 uncontrolled prospective trial (72) have shown that concentrated regular (R) U-500 insulin delivered by CSII is safe and effective. A recent meta-analysis found that patients with mean baseline HbA_{1c} levels of 8.6 to 10.8% and mean total daily insulin doses of 172 to 410 U/ day experienced a significant HbA_{1c} reduction of 1.64% (95% CI, 1.14-2.14) after conversion to R U-500 insulin delivered by CSII (73). Overall, weight increased by 2.99 kg (95% CI, –1.83-7.81), but this change did not reach statistical significance. Hypoglycemia was not common with R U-500 insulin via CSII.

A 12-month prospective trial of R U-500 insulin delivered by OmniPod (Insulet) revealed a 70% increase in the time spent in the target blood glucose range (70-180 mg/dL) without a significant increase in hypoglycemia, as assessed by 72-hour glucose monitoring (72). A retrospective case series of 59 patients showed that insulin pump therapy with R U-500 resulted in a sustained 1% reduction in HbA_{1c} ($P = .003$) for up to 72 months without significant weight gain (74). Although R U-500 insulin is not FDA-approved for CSII use, this treatment appears to be effective in delivering insulin to patients with T2DM who have high insulin requirements and are failing other treatment regimens. An RCT using this concentrated insulin is currently being prepared (75).

6. EDUCATION AND TRAINING

In contrast to the highly structured insulin pump programs available in countries such as France and the United Kingdom, where patient education and training are a high priority, many U.S. patients report that their initial pump training took less than 3 hours. A Swedish study reported that new CSII users experienced a higher frequency of DKA shortly after pump therapy was initiated, suggesting that a failure of education can affect patient safety (76,77).

Need for Training

To reduce the risk of adverse events, it is recommended that patients receive extensive education regarding the technical aspects of insulin pump use. Preventive measures, such as training in proper catheter insertion technique are important, and frequent glucose monitoring (≥4 or 5 times daily) is also critical. Patients must be educated on the meaning of pump alarms, particularly those that may signal a potential interruption in insulin delivery (e.g., battery failure, empty syringe). In addition, patients must be reminded that backup supplies (e.g., additional insulin infusion sets, pump batteries, and insulin syringes or pens) should be kept on hand in the event of a pump or infusion set failure. Providers should have on-call systems available 24 hours a day to handle patient questions. Patients should also be periodically reminded of the pump manufacturer's emergency number. In addition, even patients who have

been using insulin pumps for many years are prone to mistakes when they change from an older pump to a newer model, and serious morbidity can result (78). Following the initial patient education and training phase, periodic retesting of patients and their families is necessary to maximize the value of pump therapy for CSII and to maintain patient safety.

Since the publication of the AACE Insulin Pump Consensus Statement in 2010 (1), there has been little progress in developing uniform, comprehensive, and structured training programs in the use of insulin pump therapy. Similarly, there is a lack of consensus regarding the best training methods (group or private, use of multidisciplinary teams, educational materials) and the timing of training and follow-up.

A systematic review conducted by Jayasekara and colleagues focused on pump education strategies offered to adults with T1DM who were using CSII as their primary mode of insulin delivery (79). An initial literature review identified 142 studies; of these, only 5 provided descriptive information on the educational methods used, and none compared the benefits of 1 training method over another.

Developing Uniform Training

Insulin pump therapy training is essential for successful device use. An introduction to insulin pump therapy should include a description of the different devices available and a demonstration of the benefits of each (to determine which device best accommodates the patient's needs). Once an insulin pump has been selected, training should be provided by either the diabetes program or by clinical representatives of the device company. Group training has been used more frequently in the hope that patients will receive support and guidance from each other, while decreasing the burden for professionals.

This training should cover the technical aspects of using the device, including filling the reservoir and tubing, priming, button pushing, and the mechanics of insulin delivery. The choice of infusion sets and their correct insertion and use must also be covered, as should the use of injectable glucagon for hypoglycemia. One of the greatest challenges facing patients is the best area to place the infusion set. This is particularly important in patients with many years of use, because overuse of skin sites increases insulin absorption variability and scar tissue risk. Education on preventing infusion site and infection site reactions should be discussed at pump initiation, with the appropriate infusion site preparation and tape selected to minimize allergic reactions and improve adherence.

Additionally, good hand-washing techniques should be emphasized to minimize infections. Antistaph soap is often needed when infections do occur, along with retraining in appropriate sterile techniques. If an allergic reaction occurs at the site, a change in the tape adhesive or infusion site type may be required. In addition, the need to change the infusion site every 2 to 3 days to prevent glucose control deterioration has been documented (80).

Upon initiation, all pump setting changes should be made under the guidance of the diabetes team, based on the patient's individualized glycemic goals. Optimally, patients should be trained to adjust settings based on a review of SMBG and CGM results. Access to the diabetes team is essential for successful pump therapy, and many changes can be made over the phone after uploading pump, SMBG, and/or CGM information to the "Cloud" or diabetes team office. The diabetes specialist often makes these adjustments at patient visits, but patients may need changes between visits. Therefore, it is important that patients have the knowledge and technical ability to make recommended pump setting changes at home.

Training Patients and Their Families

It is essential to train patients and their families to handle emergency situations. Patients must understand that hyperglycemia, vomiting, and ketosis can be caused by an infusion site failure or pump malfunction, and they must know how to respond. If unexplained hyperglycemia (blood glucose >250 mg/dL to 300 mg/dL) occurs, troubleshooting should be implemented immediately to ensure the pump is in place, the prior bolus dose was delivered, and that the infusion set is in place without leaks or crimps in the system. If the blood glucose does not correct with a correction bolus within a specified timeframe, the entire infusion set and reservoir should be replaced with new insulin. In the event of pump failure or patient illness, a backup plan to start injection therapy is required (i.e., having basal insulin or an active prescription available), as is access to emergency help (for example, a 24-hour phone line covered by pump therapy specialists). In the case of pump failure, patients should have a backup, written copy of their pump settings and/or should understand how to adjust their insulin requirements for basal injection therapy.

When acute events occur months after initial training, many patients complain that they have forgotten their emergency plan. It is helpful to provide patients and their families with a written summary of responses to different situations that can be placed prominently at home, work, or school. Reminding patients of their backup plan and what to do in the event of illness should be part of a routine office visit. Ideally, patients should be offered ongoing review classes that discuss emergency situations and offer more advanced pump training.

The Importance of Retraining When Insulin Pumps are Upgraded

Even patients who have been successfully using insulin pumps for many years are prone to mistakes when switching from an older to a newer pump, and serious morbidity can occur as a result (78). Therefore, when switching to a new pump model, it is essential for the health care team to

emphasize to patients the clinical and safety importance of professional training.

Educating Medical Professionals and School Personnel

The increasing popularity of insulin pump therapy has placed more responsibility on medical professionals who do not specialize in diabetes, such as emergency room and hospital staff, as well as those without medical training, such as teachers and other school personnel. This change requires that these professionals familiarize themselves with this form of insulin delivery. In response to increased patient demand to remain on their devices while hospitalized, several publications now describe efforts to teach hospital staff about insulin pump therapy (81).

There are no published reports of training programs for school personnel, and this has been frustrating to children, parents, and other school staff, particularly if a school nurse is not available. In many situations, it is the children's parents who are responsible for educating the school staff on basic and emergency procedures related to their child's insulin delivery. Many guidebooks are available from manufacturers describing insulin pump use, and these should be provided to schools and hospitals, along with a contact to answer questions and provide further training.

As the use of insulin pumps increases, there is a greater need to develop better and more standardized training and assessment programs for patients, diabetes specialists, nondiabetes practitioners, and nonmedical personnel. To promote improved patient outcomes, these training programs need to effectively share the knowledge base of insulin pump experts.

7. PATIENT SAFETY ISSUES

In the past 3 years, technological advances have resulted in more sophisticated insulin pumps, with new features of great promise and complexity. However, concurrent with these advancements is an increased awareness of patient safety concerns. Specifically, the complexity of current insulin pumps creates diagnostic dilemmas for patients in the event of unexplained hyperglycemia, hypoglycemia, or unexpected pump error messages or alarms. The AACE has been recognized by the FDA for bringing this problem to its attention (82). In March 2012, the FDA stated that current data showed the value of insulin pump use in properly selected, well-trained patients, but they also showed the hazards when patients were not selected appropriately or had inadequate education on pump use. The FDA also drew attention to the "Medical Devices" page of the FDA website (http://www.fda.gov/MedicalDevices/default.htm), which provides information on both adverse event reporting for insulin pumps and recalls of insulin pumps and infusion sets.

In 2010, the FDA convened an expert panel and issued an Infusion Pump Improvement Initiative and recommendations that affected all pump manufacturers, including insulin infusion pumps (4,83-85). The FDA also added requirements for infusion pump manufacturers and began a dialogue with each manufacturer. The FDA noted that, historically, even when serious design flaws were the root cause of adverse events, the initial response of some manufacturers was denial and blaming the adverse event on user error (86).

Judging by the number of adverse device events reported on the FDA website and the continued occurrence of both Class II and Class I recalls (Class I is likely to cause patient injury) of insulin pumps, tubing, and reservoirs, problems persist in insulin pump and infusion set design and manufacture (9).

Infusion pumps in general and insulin infusion pumps in particular are complex devices. They may fail due to a variety of causes, including software deficits, user interface issues, or mechanical or electrical failure. Pump design deficiencies are not uncommon and may lead either to repetitive failures or latent flaws that become problematic under certain circumstances (e.g., an alarm that should alert the user to a tubing blockage but does not sound if the reservoir is also defective). Because design flaws may lead to human error, human factors and usability should also be used as criteria to judge new insulin pumps. It is hoped that open-source insulin pump software will make it easier for manufacturers to correct product software issues.

Patient selection also affects CSII therapy success, and expert experience suggests that outcomes differ widely between groups of highly motivated, well-educated patients with few comorbidities and poorer, sicker patients with limited financial means who lack access to highly trained pump personnel. Although several pump manufacturers have online and phone help resources, an experienced, pump-knowledgeable diabetes care team is optimal.

Furthermore, patient mental status is key to safe insulin pump use. The patient selection process should include an evaluation of comorbidities, such as depression, mood disorders, and cognitive dysfunction, which are commonly associated with severe hyper- or hypoglycemia. Comorbid conditions such as chronic renal failure, recent chemotherapy, or excessive sedation due to medication may also lead to diminished mental acuity, which may increase the risk of adverse events with CSII therapy. For example, a June 22, 2009 report on the AACE Patient Safety Exchange website (87) discusses the effect of stage IV renal failure on cognitive function and the resultant reduction in the patient's ability to use a pump that was previously used safely. Even with increased support, the presence of cognitive dysfunction or severe psychological distress may affect the patient's ability to continue to safely use an insulin pump. In addition, because individual circumstances may change,

patient suitability for pump use must be re-examined over time.

There is little question that insulin pump therapy, particularly with the addition of CGM and an appropriate educational program and medical support, has enormous potential benefit for the right patients. However, pumps can and do malfunction, and patients need to be given information to help them in the event of pump failure or malfunction. For the powerful tool of CSII to be safely implemented, it is the role of the prescribing endocrinologist/diabetologist to evaluate the appropriateness of pump use for individual patients and to oversee an appropriate educational program and monitor the patient's progress.

8. INSULIN PUMPS: CODING AND REIMBURSEMENT ISSUES IN PRACTICE

Standardized payment for existing codes for diabetes education has not been established across the private and public sectors. Accordingly, existing evaluation and management (E/M) codes for office encounters are typically used (Table 9). These involve initial or follow-up use dependent on the complexity of the visit (99203-99205 and 99213-99215). If the physician time involved exceeds the appropriate visit time for the code used, prolonged visit codes are used. However, these are only used after an additional 30 minutes have elapsed at the end of the office visit.

Most private insurers provide reimbursement for insulin pumps for patients with T1DM and T2DM, although benefits verification is recommended before pump purchase. The Centers for Medicare & Medicaid Services (CMS) also covers CSII. The patient must be insulinopenic, defined as having a fasting C-peptide level ≤110% of the laboratory's lower limit of normal, with a concurrently obtained fasting glucose ≤225 mg/dL, or they must be beta-cell autoantibody positive. In addition, patients must meet the criteria outlined in Box 2. Continued CMS insulin pump coverage requires evaluation by the treating physician at least every 3 months (88).

Many prescribing physicians, professional societies, and industry partners believe that requiring patients on intensive insulin regimens with basal/bolus therapy to be C-peptide negative or have other markers of islet autoimmunity is not justified. Insulin pump therapy can be an effective regimen to deliver basal/bolus therapy in a segment of T2DM patients who should not be denied access by CMS. Additionally, the requirement to undergo these blood tests upon entry to the CMS program can exclude patients with T2DM already successfully using CSII. It is inappropriate for any payer to cease coverage for a therapy that has been beneficial, or to force that patient back to a

Table 9
Insulin Pump E/M Codes for Office Encounters

Code	Typical Time for Code	Threshold Time to Bill Code 99354 (min)
99203	30	60
99204	45	75
99205	60	90
99213	15	45
99214	25	55
99215	40	70

Abbreviation: E/M = evaluation and management.

Box 2
U.S. Centers for Medicare & Medicaid Services (CMS) Insulin Pump Patient Eligibility Criteria (88)

To be eligible for CMS insulin pump coverage, patients must meet 1 of the following criteria:

(A) Patient has completed a comprehensive diabetes education program and has been receiving MDI insulin with frequent self-adjustments for at least 6 months before pump initiation. Patient has documented SMBG frequency an average of ≥4 times per day during the previous 2 months. Patient must also meet ≥1 of the following criteria:

- HbA_{1c} >7.0%
- History of recurrent hypoglycemia
- Wide fluctuations in blood glucose before mealtime
- "Dawn phenomenon" with FPG frequently >200 mg/dL or a history of severe glycemic excursions

(B) Patient on pump therapy before enrollment with a documented SMBG an average of ≥4 times per day during the month before enrollment.

(C) Fasting C-peptide ≤110% lower limit of normal or ≤200% lower limit of normal if CrCl ≤50 mL/min with concurrent FPG ≤225 mg/dL; or beta-cell autoantibody positive (+ICA or +GAD antibodies)

Abbreviations: CrCl = creatinine clearance; FPG = fasting plasma glucose; GAD = glutamate decarboxylase, HbA_{1c} = hemoglobin A_{1c}; ICA = islet cell antibodies; MDI = multiple daily injections; SMBG = self-monitored blood glucose

Table 10
Summary Data of Cost-effectiveness Analyses Comparing Continuous Subcutaneous Insulin Infusion versus Multiple Daily Injection in Adults and Children with T1DM

Study	Study objective, perspective, and data source	QALYs gained	Cost per QALY (ICER)	Additional key findings
Kamble et al, 2012 (98)	To estimate the long-term cost-effectiveness of SAPT compared to MDI in T1DM	QALY gains for SAPT vs. MDI were 0.376	Lifetime cost: SAPT: $253,493 MDI: $167,170 ICER = $(c_1-c_2)/q_1-q_2$ = $229,582	Despite superior clinical benefits of SAPT compared to MDI, SAPT did not appear to be economically attractive in the US for adults with T1DM in its current state of development Further clinical development to reduce disposable costs of the system could improve this
Nørgaard et al, 2010	To project the long-term clinical and economic outcomes of CSII treatment compared to MDI in T1DM in Denmark Meta-analysis of CSII treatment from over 50 studies	CSII was associated with improved quality-adjusted life expectancy compared to MDI (QALY not calculated)	Lifetime costs were higher for CSII than for MDI with ICERs in terms of cost per QALY within the range considered good value for money	CSII led to improved long-term clinical outcomes due to improved glycemic control vs. MDI Economic impact of CSII vs. MDI would likely represent good value for cost
Cummins et al, 2010 (96)	Assessment report to examine the clinical and cost-effectiveness of using CSII to treat DM (T1DM and during pregnancy) United Kingdom, NICE Systematic review and economic evaluation (74 studies included)	N/A	N/A	CSII is cost-effective for T1DM in both children and adults
Cohen et al, 2007 (44)	To project long-term (lifetime horizon) costs and outcomes of CSII vs. MDI in adults and adolescents with T1DM Australian perspective Computer simulation model (CORE Diabetes Model)	QALY gains for CSII vs. MDI were 0.467 (adults) and 0.560 (adolescents)	CSII: $74,147 (adults); $74,661 (adolescents)	Authors indicated that CSII represents good value for most scenarios studied
St Charles et al, 2009 (94)	To estimate long-term (60-year) cost-effectiveness of CSII compared with MDI in adults/children with T1DM U.S. third-party payer perspective Computer simulation model (CORE Diabetes Model)	QALY gains for CSII vs. MDI were 0.262	CSII: $16,992 MDI: $27,195	Improved glycemic control from CSII reduced incidence of DM complications including PDR, ESRD, and PVD The NNT for PDR was 9, (i.e., only 9 patients need to be treated with CSII to avoid 1 case of PDR)
St Charles et al, 2009 (95)	To evaluate the long-term (60-year) cost-effectiveness of CSII compared with MDI in adult patients with T1DM Canadian payer perspective Computer simulation model (CORE Diabetes Model)	QALY gains for CSII vs. MDI were 0.655	CSII: $27,265 MDI: $23,797 (Canadian dollars)	
Roze et al, 2005 (97)	To project the long-term (60-year) costs and outcomes of CSII vs. MDI in patients with T1DM United Kingdom; third-party National Health Services perspective Computer simulation model (CORE Diabetes Model)	QALY gains for CSII vs. MDI were 0.76	CSII: £80,511 MDI: £61,104 (variance = £25,648/QALY gained with CSII)	Improvements in glycemic control with CSII vs. MDI led to a reduced incidence of DM-related complications For patients with T1DM, CSII represents good value based on current United Kingdom standards

Abbreviations: CSII = continuous subcutaneous insulin infusion; DM = diabetes mellitus; ESRD = end-stage renal disease; ICER = incremental cost-effectiveness ratio; MDI = multiple daily injections; NICE = National Institute for Health and Clinical Excellence; NNT = number needed to treat; PDR = proliferative diabetic retinopathy; PVD = peripheral vascular disease; QALY = quality-adjusted life year; SAPT = sensor-augmented pump therapy; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus

management strategy that was ineffective in the past.

Since the last AACE statement publication in 2010, there has been movement by physicians and payers to recognize the clinical value of CSII therapy for some non-type 1a insulin-dependent patients (mainly T2DM) (89-93). This trend is a reflection of the increased recognition that intensification of insulin regimens for a select subset of non-type 1a diabetic patients can yield significant improvements in glycemic control.

Nearly all private payers now reimburse CSII therapy for qualified insulin-dependent diabetes patients, regardless of diabetes type. The clinical criteria are typically focused on insulin administration frequency (3-4 injections per day), SMBG adherence (≥4 times per day), and lack of glycemic control despite continued efforts. This approach has created a group of patients who are typically older (often covered by Medicare) than average pump cohorts and presents an additional reimbursement challenge to practitioners and patients.

9. ECONOMICS OF INSULIN PUMP THERAPY

Concerns have been raised about the costs incurred by insulin pump therapy. However, recent evidence indicates that CSII is a cost-effective treatment option, both in general and compared with MDI, for children and adults with T1DM (94-97). Tables 10 and 11 summarize the key assumptions and findings of 8 recent, representative cost-effectiveness analyses comparing CSII with MDI in specific patient populations with T1DM and T2DM (44,94-96,98-100).

10. FUTURE NEEDS AND CONCLUSIONS

Despite many new capabilities, further enhancements are needed to improve the configurability and safety of insulin pumps. For example, in most models, the ICR can only be set to integer values, so dosing precision may be compromised with lower value settings (e.g., <10). In addition, pump settings may be compromised over time (e.g., carbohydrate factors, correction factors, and duration of insulin action are frequently set at initiation and then never adjusted or optimized). Thus, clinical practices should conduct standardized periodic audits of pump settings in the context of current glucose dynamics. To help with this, practitioners may want to use online registries (e.g., CareLink). Making the downloading process easier for patients to perform will be critical to the success of any such initiative. Currently, the time-consuming nature of this task, along with low reimbursement rates, makes it challenging to complete during an office visit. Unfortunately, recent data from the T1D Exchange indicate that most patients with and parents of children with T1DM are not retrospectively reviewing stored insulin pump data (39).

Beyond improvements in the pump-user interface, there is a clear need for educational programs administered

Table 11
Summary Data of Cost-effectiveness Analysis Comparing CSII versus Multiple Daily Injection in Patients with T2DM

Study	Study objective, perspective, and data source	Key findings
David et al, 2012 (100)	To capture the fixed and variable costs associated with insulin pumps in T2DM versus injection Break-even analysis used administrative claims data to compare the cost of care among T2DM patients using an insulin pump versus alternate delivery methods (in particular, MDIs)	Durable insulin pumps required an upfront investment of approximately $4,200, plus additional pump supply costs. Insulin pump users, however, required less insulin and other drugs compared with MDI patients, resulting in decreased associated costs. Breakeven analysis revealed that patients at the top 10th percentile of insulin plus other drug expenditures generated cost savings through lower use of insulin, which offset the pump cost in 1,071 days (<3 years). The lifespan for a durable insulin pump was stated as 4 years. Thus, the authors concluded that although durable pumps have an upfront cost, they are better able to control insulin delivery than MDI, and the reduced insulin and drug–related expenditures offset initial pump investment within 3 years for the most costly cohort of insulin users (i.e., top 10th percentile of insulin usage and other drug usage).

Abbreviations: CSII = continuous subcutaneous insulin injection; MDI = multiple daily injection; T2DM = type 2 diabetes mellitus

by qualified, experienced physicians to provide patients with initial and follow-up pump use training.

Research continues toward a fully closed-loop "artificial pancreas" that will integrate CGM and insulin pumps with an algorithm that doses the correct amount of insulin at the right time with the ultimate goal of normalizing glucose levels automatically (control to target).

The next step in the development of the artificial pancreas is predictive low-glucose suspend, which will be launched in 2014 in Europe (101), followed by normalization of overnight blood glucose (overnight closed loop). Another expected stage is a system that will automatically administer or withhold insulin if glucose levels pass beyond set limits (control to range). The technology and regulatory support required to accomplish these ambitious goals are progressing rapidly.

It is clear that even after more than 3 decades of clinical insulin pump use, many critical questions remain. High-quality, peer-reviewed research studies must be conducted to provide timely answers. In addition, because insulin pump technology is advancing at a rapid pace, clinicians need more knowledge about the best and safest means to translate research findings to clinical practice.

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REFERENCES

1. **Grunberger G, Bailey TS, Cohen AJ, et al.** Statement by the American Association of Clinical Endocrinologists Consensus Panel on insulin pump management. *Endocr Pract*. 2010;16:746-762.
2. **Bruttomesso D, Costa S, Baritussio A.** Continuous subcutaneous insulin infusion (CSII) 30 years later: still the best option for insulin therapy. *Diabetes Metab Res Rev.* 2009;25:99-111.
3. **HSBC Global Research.** Diabetes: Proprietary survey on insulin pumps and continuous blood glucose monitoring. *Healthcare US Equipment & Supplies*. 2005.

4. **U.S. Food and Drug Administration.** General Hospital and Personal Use Medical Devices Panel. Insulin infusion pumps panel information. Available at: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/GeneralHospitalandPersonalUseDevicesPanel/UCM203749.pdf. 2010.
5. **Chait J.** Insulin pumps: not just for type 1. Diabetes Self-Management website. Available at: http://www.diabetesselfmanagement.com/articles/insulin/insulin_pumps/1/. Accessed April 19, 2013.
6. **JMP Securities L.** US medical devices-update. March 17, 2009.
7. **Millennium Research Group I.** US Markets for Infusion Pumps 2013. Available at: http://mrg.net/products-and-services/syndicated-report.aspx?r=rpus60ip12. October 2012.
8. **U.S. Centers for Disease Control and Prevention.** CDC Media Relations - Press Release: October 22, 2010. Available at: http://www.cdc.gov/media/pressrel/2010/r101022.html. Accessed December 14, 2013.
9. **U.S. Food and Drug Administration.** Medical devices: Infusion pumps. Available at: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/GeneralHospitalDevicesandSupplies/InfusionPumps/default.htm. 2013.
10. **Cengiz E, Weinzimer SA, Sherr JL, et al.** Acceleration of insulin pharmacodynamic profile by a novel insulin infusion site warming device. *Pediatr Diabetes*. 2013;14:168-173.
11. **Vaughn DE, Muchmore DB.** Use of recombinant human hyaluronidase to accelerate rapid insulin analogue absorption: experience with subcutaneous injection and continuous infusion. *Endocr Pract*. 2011;17:914-921.
12. **Hanaire H.** External insulin pump treatment in the day-to-day management of diabetes: benefits and future prospectives. *Diabetes Metab*. 2011;37 Suppl 4:S40-47.
13. **Pettis RJ, Harvey AJ.** Microneedle delivery: clinical studies and emerging medical applications. *Ther Deliv.* 2012; 3:357-371.
14. **O'Neal DN, Adhya S, Jenkins A, Ward G, Welsh JB, Voskanyan G.** Feasibility of adjacent insulin infusion and continuous glucose monitoring via the Medtronic Combo-Set. *J Diabetes Sci Technol*. 2013;7:381-388.
15. U**.S. Food and Drug Administration.** MiniMed 530G FDA Approval Letter. Available at: http://www.accessdata.fda.gov/cdrh_docs/pdf12/p120010a.pdf2013.
16. **U.S. Food and Drug Administration, Center for Devices and Radiological Health.** Guidance for industry and food and drug administration staff: The content of investigational device exemption (IDE) and premarket approval (PMA) applications for artificial pancreas device systems. Available at: http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM259305.pdf. 2012.
17. **U.S. Food and Drug Administration.** Medical devices: MiniMed 530G System - P120010. Available at: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm372176.htm. 2013.
18. **American Journal of Managed Care (AJMC).** With MiniMed 530G, Medtronic Seeks New CMS Code. Available at: http://www.ajmc.com/newsroom/With-MiniMed-530G-Medtronic-Seeks-New-CMS-Code-2014.
19. **Bergenstal RM, Klonoff DC, Garg SK, et al.** Threshold-based insulin-pump interruption for reduction of hypoglycemia. *N Engl J Med*. 2013;369:224-232.
20. **Misso ML, Egberts KJ, Page M, O'Connor D, Shaw J.** Continuous subcutaneous insulin infusion (CSII) versus multiple insulin injections for type 1 diabetes mellitus. *Cochrane Database Syst Rev.* 2010:CD005103.
21. **Pickup JC.** Insulin pumps. *Int J Clin Pract*. 2012;66 Suppl s175:15-19.
22. **Bergenstal RM, Tamborlane WV, Ahmann A, et al.** Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes. *N Engl J Med*. 2010;363:311-320.
23. **Monami M, Lamanna C, Marchionni N, Mannucci E.** Continuous subcutaneous insulin infusion versus multiple daily insulin injections in type 2 diabetes: A meta-analysis. *Exp Clin Endocrinol Diabetes*. 2009;117:220-222.
24. **Raskin P, Bode BW, Marks JB, et al.** Continuous subcutaneous insulin infusion and multiple daily injection therapy are equally effective in type 2 diabetes: A randomized, parallel-group, 24-week study. *Diabetes Care*. 2003;26:2598-2603.
25. **Herman WH, Ilag LL, Johnson SL, et al.** A clinical trial of continuous subcutaneous insulin infusion versus multiple daily injections in older adults with type 2 diabetes. *Diabetes Care*. 2005;28:1568-1573.
26. **ClinicalTrials.gov.** Efficacy of continuous subcutaneous insulin infusion versus basal-bolus multiple daily injections regimen in Type 2 diabetes. Available at: http://clinicaltrials.gov/ct2/show/NCT00942318?term=NCT00942318&rank=1. Accessed December 14, 2013.
27. **Pickup JC, Keen H, Parsons JA, Alberti KG.** Continuous subcutaneous insulin infusion: An approach to achieving normoglycaemia. *Br Med J*. 1978;1:204-207.
28. **Pickup J, Keen H.** Continuous subcutaneous insulin infusion at 25 years: Evidence base for the expanding use of insulin pump therapy in type 1 diabetes. *Diabetes Care*. 2002;25:593-598.
29. **Skyler JS, Ponder S, Kruger D, Matheson D, Parkin C.** Is there a place for insulin pump in your practice? *Clin Diabetes*. 2007;32:50-56.
30. **Tomky DM, Kulkarni K.** Intensifying insulin therapy: Multiple daily injections to pump therapy. In: Mensing C, ed. *The Art and Science of Diabetes Self-Management Education: A Desk Reference for Healthcare Professionals*. Washington, DC: American Association of Diabetes Educators; 2006: 371-398.
31. **Bode BW, Tamborlane WV, Davidson PC.** Insulin pump therapy in the 21st century. Strategies for successful use in adults, adolescents, and children with diabetes. *Postgrad Med*. 2002;111:69-77.
32. **Wolpert H.** *Smart Pumping: A Practical Approach to Mastering the Insulin Pump*. Alexandria, VA: American Diabetes Association; 2002.
33. **Walsh J, Roberts R.** *Pumping Insulin: Everything You Need for Success on an Insulin Pump*. 5th ed. San Diego, CA: Torrey Pines Press; 2013.
34. **Tamborlane WV, Sherwin RS, Genel M, Felig P.** Reduction to normal of plasma glucose in juvenile diabetes by subcutaneous administration of insulin with a portable infusion pump. *N Engl J Med*. 1979;300:573-578.
35. **Ahern JA, Boland EA, Doane R, et al.** Insulin pump therapy in pediatrics: a therapeutic alternative to safely lower HbA1c levels across all age groups. *Pediatr Diabetes*. 2002;3:10-15.
36. **Doyle EA, Weinzimer SA, Steffen AT, Ahearn JA, Vincent M, Tamborlane WV.** A randomized, prospective trial comparing the efficacy of continuous subcutaneous insulin infusion with multiple daily injections using insulin glargine. *Diabetes Care*. 2004;27:1554-1558.

37. **Phillip M, Battelino T, Rodriguez H, et al.** Use of insulin pump therapy in the pediatric age-group: Consensus statement from the European Society for Paediatric Endocrinology, the Lawson Wilkins Pediatric Endocrine Society, and the International Society for Pediatric and Adolescent Diabetes, endorsed by the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2007;30:1653-1662.
38. **Danne T, Battelino T, Jarosz-Chobot P, et al.** Establishing glycaemic control with continuous subcutaneous insulin infusion in children and adolescents with type 1 diabetes: experience of the PedPump Study in 17 countries. *Diabetologia*. 2008;51:1594-1601.
39. **Beck RW, Tamborlane WV, Bergenstal RM, et al.** The T1D exchange clinic registry: overview of the project and characteristics of initial 20,119 participants. *J Clin Endocrinol Metab*. 2012;97:4383-4389.
40. **Weinzimer SA, Ahern JH, Doyle EA, et al.** Persistence of benefits of continuous subcutaneous insulin infusion in very young children with type 1 diabetes: A follow-up report. *Pediatrics*. 2004;114:1601-1605.
41. **Sullivan-Bolyai S, Knafl K, Tamborlane W, Grey M.** Parents' reflections on managing their children's diabetes with insulin pumps. *J Nurs Scholarsh*. 2004;36:316-323.
42. **Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Tamborlane WV, Beck RW, et al.** Continuous glucose monitoring and intensive treatment of type 1 diabetes. *N Engl J Med*. 2008;359: 1464-1476.
43. **Langer O, Mazze R.** The relationship between large-for-gestational-age infants and glycemic control in women with gestational diabetes. *Am J Obstet Gynecol*. 1988;159:1478-1483.
44. **Cohen N, Minshall ME, Sharon-Nash L, Zakrzewska K, Valentine WJ, Palmer AJ.** Continuous subcutaneous insulin infusion versus multiple daily injections of insulin: Economic comparison in adult and adolescent type 1 diabetes mellitus in Australia. *Pharmacoeconomics*. 2007; 25:881-897.
45. **Cohen O, Keidar N, Simchen M, Weisz B, Dolitsky M, Sivan E.** Macrosomia in well controlled CSII treated Type I diabetic pregnancy. *Gynecol Endocrinol*. 2008;24:611-613.
46. **Farrar D, Tuffnell DJ, West J.** Continuous subcutaneous insulin infusion versus multiple daily injections of insulin for pregnant women with diabetes. *Cochrane Database Syst Rev.* 2007:CD005542.
47. **Kernaghan D, Farrell T, Hammond P, Owen P.** Fetal growth in women managed with insulin pump therapy compared to conventional insulin. *Eur J Obstet Gynecol Reprod Biol*. 2008;137:47-49.
48. **Buchanan TA, Metzger BE, Freinkel N.** Accelerated starvation in late pregnancy: a comparison between obese women with and without gestational diabetes mellitus. *Am J Obstet Gynecol*. 1990;162:1015-1020.
49. **Jovanovic L, Druzin M, Peterson CM.** Effect of euglycemia on the outcome of pregnancy in insulin-dependent diabetic women as compared with normal control subjects. *Am J Med*. 1981;71:921-927.
50. **Jovanovic L, Peterson CM, Saxena BB, Dawood MY, Saudek CD.** Feasibility of maintaining normal glucose profiles in insulin-dependent pregnant diabetic women. *Am J Med*. 1980;68:105-112.
51. **Jovanovic-Peterson L, Peterson CM.** The art and science of maintenance of normoglycemia in pregnancies complicated by insulin-dependent diabetes mellitus. *Endocr Pract*. 1996;2:130-143.
52. **Jovanovic L, ed.** *Medical management of pregnancy complicated by diabetes*. 4th ed. Alexandria, VA: American Diabetes Association; 2009.
53. **Jovanovic L, Pettitt DJ.** Treatment with insulin and its analogs in pregnancies complicated by diabetes. *Diabetes Care*. 2007;30 Suppl 2:S220-224.
54. **Simmons D, Thompson CF, Conroy C, Scott DJ.** Use of insulin pumps in pregnancies complicated by type 2 diabetes and gestational diabetes in a multiethnic community. *Diabetes Care*. 2001;24:2078-2082.
55. **Jovanovic L**. Glucose and insulin requirements during labor and delivery: The case for normoglycemia in pregnancies complicated by diabetes. *Endocr Pract*. 2004;10 Suppl 2:40-45.
56. **Jovanovic L, Peterson CM.** Insulin and glucose requirements during the first stage of labor in insulin-dependent diabetic women. *Am J Med*. 1983;75:607-612.
57. **Lepercq J, Abbou H, Agostini C, et al.** A standardized protocol to achieve normoglycaemia during labour and delivery in women with type 1 diabetes. *Diabetes Metab*. 2008;34:33-37.
58. **Alberti KG, Thomas DJ, Thomas JM.** Control of blood glucose in labour. *Br Med J*. 1977;2:266-267.
59. **Grylack LJ, Chu SS, Scanlon JW.** Use of intravenous fluids before cesarean section: effects on perinatal glucose, insulin, and sodium homeostasis. *Obstet Gynecol*. 1984;63:654-658.
60. **Barnardo PD, Patel M.** Eating in labour. *Anaesthesia*. 1999;54:1017-1019.
61. **Caplan RH, Pagliara AS, Beguin EA, et al.** Constant intravenous insulin infusion during labor and delivery in diabetes mellitus. *Diabetes Care*. 1982;5:6-10.
62. **Riviello C, Mello G, Jovanovic LG.** Breastfeeding and the basal insulin requirement in type 1 diabetic women. *Endocr Pract*. 2009;15:187-193.
63. **Rogers LM, Jovanovic L, Becker DJ.** Should she or shouldn't she? The relationship between infant feeding practices and type 1 diabetes in the genetically at risk. *Diabetes Care*. 2005;28:2809.
64. **Moghissi ES, Korytkowski MT, DiNardo M, et al.** American Association of Clinical Endocrinologists and American Diabetes Association Consensus Statement on Inpatient Diabetes Control. *Endocr Pract*. 2009;15:1-17.
65. **American Diabetes Association.** Standards of Medical Care in Diabetes - 2014. *Diabetes Care*. 2014;37 Suppl 1:S14-S80.
66. **Funnell MM, Brown TL, Childs BP, et al.** National standards for diabetes self-management education. *Diabetes Care*. 2010;33 Suppl 1:S89-S96.
67. **Knee TS, Seidensticker DF, Walton JL, Solberg LM, Lasseter DH.** A novel use of U-500 insulin for continuous subcutaneous insulin infusion in patients with insulin resistance: a case series. *Endocr Pract*. 2003;9:181-186.
68. **Schwartz FL.** A caution regarding U-500 insulin by continuous subcutaneous infusion. *Endocr Pract*. 2004;10: 163-164.
69. **Lane WS.** Use of U-500 regular insulin by continuous subcutaneous insulin infusion in patients with type 2 diabetes and severe insulin resistance. *Endocr Pract*. 2006; 12:251-256.
70. **Bulchandani DG, Konrady T, Hamburg MS.** Clinical efficacy and patient satisfaction with U-500 insulin pump therapy in patients with type 2 diabetes. *Endocr Pract*. 2007;13:721-725.

71. **Reutrakul S, Brown RL, Koh CK, Hor TK, Baldwin D.** Use of U-500 regular insulin via continuous subcutaneous insulin infusion: clinical practice experience. *J Diabetes Sci Technol*. 2011;5:1025-1026.
72. **Lane WS, Weinrib SL, Rappaport JM, Przestrzelski T.** A prospective trial of U-500 insulin delivered by OmniPod in patients with type 2 diabetes mellitus and severe insulin resistance. *Endocr Pract*. 2010;16:778-784.
73. **Reutrakul S, Wroblewski K, Brown RL.** Clinical use of U-500 regular insulin: Review and meta-analysis. *J Diabetes Sci Technol*. 2012;6:412-420.
74. **Lane WS, Weinrib SL, Rappaport JM, Hale CB, Farmer LK, Lane RS.** The effect of long-term use of u-500 insulin via continuous subcutaneous infusion on durability of glycemic control and weight in obese, insulin-resistant patients with type 2 diabetes. *Endocr Pract*. 2013;19:196-201.
75. **ClinicalTrials.gov.** Study of human regular U-500 insulin in adult participants with type 2 diabetes. Available at: http://clinicaltrials.gov/show/NCT01774968. Accessed November 19, 2013.
76. **Hanas R, Ludvigsson J.** Hypoglycemia and ketoacidosis with insulin pump therapy in children and adolescents. *Pediatr Diabetes*. 2006;7 Suppl 4:32-38.
77. **Hanas R, Lindgren F, Lindblad B.** A 2-yr national population study of pediatric ketoacidosis in Sweden: predisposing conditions and insulin pump use. *Pediatr Diabetes*. 2009;10:33-37.
78. **Rule AM, Drincic A, Galt KA.** New technology, new errors: How to prime an upgrade of an insulin infusion pump. *Jt Comm J Qual Patient Saf*. 2007;33:155-162.
79. **Jayasekara RS, Munn Z, Lockwood C.** Effect of educational components and strategies associated with insulin pump therapy: a systematic review. *Int J Evid Based Healthc*. 2011;9:346-361.
80. **Schmid V, Hohberg C, Borchert M, Forst T, Pfutzner A.** Pilot study for assessment of optimal frequency for changing catheters in insulin pump therapy--trouble starts on day 3. *J Diabetes Sci Technol*. 2010;4:976-982.
81. **Boyle ME, Seifert KM, Beer KA, et al.** Guidelines for application of continuous subcutaneous insulin infusion (insulin pump) therapy in the perioperative period. *J Diabetes Sci Technol*. 2012;6:184-190.
82. **Clayton-Jeter H.** U.S. Food and Drug Administration. Contributing Factors to Insulin Pump Errors in Children, Adolescents and Adults. Available at: http://www.fda.gov/ForHealthProfessionals/ArticlesofInterest/ucm295562.htm. March 2012.
83. **U.S. Food and Drug Administration.** Workshops & Conferences (Medical Devices). Infusion Pump Workshop: Transcript for May 25th, 2010 (Part 1). Available at: http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm214408.htm. 2010.
84. **U.S. Food and Drug Administration.** Workshops & Conferences (Medical Devices). Infusion Pump Workshop: Transcript for May 26th, 2010. Available at: http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm214410.htm.
85. **U.S. Food and Drug Administration, Center for Devices and Radiological Health.** White Paper: Infusion Pump Improvement Initiative. Available at: http://www.fda.gov/medicaldevices/productsandmedicalprocedures/GeneralHospitalDevicesandSupplies/InfusionPumps/ucm205424.htm. April 2010.
86. **Taylor A.** U.S. Food and Drug Administration. Infusion pump design deficiencies and their impact on users and caregivers. Available at: http://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM219687.pdf. 2010.
87. **Hellman R.** Patient safety, insulin pumps, and cognitive dysfunction. AACE Patient Safety Exchange Editorials. Available at: http://www.aacepatientsafetyexchange.com/editorial/index.php?id=32. 2009.
88. Centers for Medicare & Medicaid Services. Publication #100-03 Medicare National Coverage Determinations. Available at: https://www.cms.gov/manuals/iom/list.asp. 2010.
89. **Bode BW.** Insulin pump use in type 2 diabetes. *Diabetes Technol Ther.* 2010;12 Suppl 1:S17-S21.
90. **Wolff-McDonagh P, Kaufmann J, Foreman S, Wisotsky S, Wisotsky JA, Wexlar C.** Using insulin pump therapy in poorly controlled type 2 diabetes. *Diabetes Educ*. 2010;36:657-665.
91. **Frias JP, Bode BW, Bailey TS, Kipnes MS, Brunelle R, Edelman SV.** A 16-week open-label, multicenter pilot study assessing insulin pump therapy in patients with type 2 diabetes suboptimally controlled with multiple daily injections. *J Diabetes Sci Technol*. 2011;5:887-893.
92. **Lynch PM, Riedel AA, Samant N, et al.** Resource utilization with insulin pump therapy for type 2 diabetes mellitus. *Am J Manag Care*. 2010;16:892-896.
93. **Reznik Y, Cohen O.** Insulin pump for type 2 diabetes: use and misuse of continuous subcutaneous insulin infusion in type 2 diabetes. *Diabetes Care*. 2013;36 Suppl 2:S219-225.
94. **St Charles M, Lynch P, Graham C, Minshall ME.** A cost-effectiveness analysis of continuous subcutaneous insulin injection versus multiple daily injections in type 1 diabetes patients: A third-party US payer perspective. *Value Health*. 2009;12:674-686.
95. **St Charles ME, Sadri H, Minshall ME, Tunis SL.** Health economic comparison between continuous subcutaneous insulin infusion and multiple daily injections of insulin for the treatment of adult type 1 diabetes in Canada. *Clin Ther.* 2009;31:657-667.
96. **Cummins E, Royle P, Snaith A, et al.** Clinical effectiveness and cost-effectiveness of continuous subcutaneous insulin infusion for diabetes: Systematic review and economic evaluation. *Health Technol Assess*. 2010;14:iii-iv, xi-xvi, 1-181.
97. **Roze S, Valentine WJ, Zakrzewska KE, Palmer AJ.** Health-economic comparison of continuous subcutaneous insulin infusion with multiple daily injection for the treatment of Type 1 diabetes in the UK. *Diabet Med*. 2005;22:1239-1245.
98. **Kamble S, Schulman KA, Reed SD.** Cost-effectiveness of sensor-augmented pump therapy in adults with type 1 diabetes in the United States. *Value Health*. 2012;15:632-638.
99. **Nørgaard K, Sohlberg A, Goodall G.** Cost-effectiveness of continuous subcutaneous insulin infusion therapy for type 1 diabetes. *Ugeskr Laeger.* 2010;172:2020-2025.
100. **David G, Shafiroff J, Saulnier A, Gunnarsson C.** Multiple daily injection therapy (MDI) versus durable insulin pump therapy in Type II diabetics: a breakeven analysis. *Value Health* 2012;15:A65.
101. Workshop on Innovation Towards an Artificial Pancreas | diaTribe. Available at: http://diatribe.us/issues/54/conference-pearls/1. Accessed December 14, 2013.
102. **Weissberg-Benchell J, Antisdel-Lomaglio J, Seshadri R.** Insulin pump therapy: A meta-analysis. *Diabetes Care*. 2003;26:1079-1087.

103. **Jeitler K, Horvath K, Berghold A, et al.** Continuous subcutaneous insulin infusion versus multiple daily insulin injections in patients with diabetes mellitus: Systematic review and meta-analysis. *Diabetologia*. 2008;51:941-951.
104. **Fatourechi MM, Kudva YC, Murad MH, Elamin MB, Tabini CC, Montori VM.** Clinical review: Hypoglycemia with intensive insulin therapy: A systematic review and meta-analyses of randomized trials of continuous subcutaneous insulin infusion versus multiple daily injections. *J Clin Endocrinol Metab*. 2009;94:729-740.
105. **Pickup JC, Sutton AJ.** Severe hypoglycaemia and glycaemic control in Type 1 diabetes: Meta-analysis of multiple daily insulin injections compared with continuous subcutaneous insulin infusion. *Diabet Med*. 2008;25:765-774.
106. **Noh YH, Lee SM, Kim EJ, et al.** Improvement of cardiovascular risk factors in patients with type 2 diabetes after long-term continuous subcutaneous insulin infusion. *Diabetes Metab Res Rev.* 2008;24:384-391.
107. **Berthe E, Lireux B, Coffin C, et al.** Effectiveness of intensive insulin therapy by multiple daily injections and continuous subcutaneous infusion: a comparison study in type 2 diabetes with conventional insulin regimen failure. *Horm Metab Res*. 2007;39:224-229.
108. **Wainstein J, Metzger M, Boaz M, et al.** Insulin pump therapy vs. multiple daily injections in obese type 2 diabetic patients. *Diabet Med*. 2005;22:1037-1046.
109. **Parkner T, Møller MK, Chen JW, et al.** Overnight CSII as supplement to oral antidiabetic drugs in type 2 diabetes. *Diabetes Obes Metab*. 2008;10:556-563.
110. **Edelman SV, Bode BW, Bailey TS, et al.** Insulin pump therapy in patients with type 2 diabetes safely improved glycemic control using a simple insulin dosing regimen. *Diabetes Technol Ther.* 2010;12:627-633.
111. **Jennings AM, Lewis KS, Murdoch S, Talbot JF, Bradley C, Ward JD.** Randomized trial comparing continuous subcutaneous insulin infusion and conventional insulin therapy in type II diabetic patients poorly controlled with sulfonylureas. *Diabetes Care*. 1991;14:738-744.
112. **Kapitza C, Fein S, Heinemann L, Schleusener D, Levesque S, Strange P.** Basal-prandial insulin delivery in type 2 diabetes mellitus via the V-Go: A novel continuous subcutaneous infusion device. *J Diabetes Sci Technol*. 2008;2:40-46.
113. **Labrousse-Lhermine F, Cazals L, Ruidavets JB, Hanaire H.** GEDEC Study Group. Long-term treatment combining continuous subcutaneous insulin infusion with oral hypoglycaemic agents is effective in type 2 diabetes. *Diabetes Metab*. 2007;33:253-260.
114. **Parkner T, Laursen T, Vestergaard ET, et al.** Insulin and glucose profiles during continuous subcutaneous insulin infusion compared with injection of a long-acting insulin in type 2 diabetes. *Diabet Med*. 2008;25:585-591.
115. **Testa MA, Hayes JF, Turner RR, Simonson DC.** Patient acceptance and satisfaction with intensive insulin therapy in type 2 diabetes: a randomized trial of the insulin pen vs. pump. *Diabetes*. 2001;50 Suppl 2:A428.
116. **Bode BW, Kyllo J, Kaufman FR.** Pumping Protocol: A Guide to Insulin Pump Initiation. Medical Education Academia. 2013. Medtronic.