

**STATEMENT BY THE
AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS
CONSENSUS PANEL ON INSULIN PUMP MANAGEMENT**

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AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS INSULIN PUMP MANAGEMENT TASK FORCE

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Abbreviations:

CSII = continuous subcutaneous insulin infusion; **DKA** = diabetic ketoacidosis; **DM** = diabetes mellitus; **FDA** = US Food and Drug Administration; **HbA_{1c}** = hemoglobin A_{1c}; **MDI** = multiple daily injections

EXECUTIVE SUMMARY

Insulin pumps have come of age. With their proliferation in medical practices, 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 delivery available to patients requiring intensive insulin management to control their diabetes mellitus. Appropriate patient selection is critical and must be followed by thorough assessment of their knowledge of diabetes management principles. Likewise, selection of a provider is critical and only those whose practice can assume full responsibility for the comprehensive pump management program should offer it. Patient diabetes education and a pump training plan must be implemented by a multidisciplinary team under direction of an experienced endocrinologist/diabetologist to address gaps in patient knowledge. The importance of periodic reevaluation and retraining is stressed. Physicians prescribing insulin pumps for their patients should have a round-the-clock system in place to answer patients' concerns about pump problems.

We summarize available peer-reviewed publications providing data that compare pumps with multiple insulin injections, address pump safety issues, and document cost-effectiveness analyses of insulin pump use. We address the essential issue related to the economic feasibility of using pumps in medical practices. Gaps in our knowledge and research areas to be addressed conclude this statement.

1. PREAMBLE

Insulin pumps have been used for more than 30 years (1). In the United States, the level of insulin pump penetration has been estimated at 20% to 30% in patients with type 1 diabetes mellitus (DM) and less than 1% in insulin-treated patients with type 2 DM (2). The US Food and Drug Administration (FDA) estimates that the number of US patients with type 1 DM using continuous subcutaneous insulin infusion (CSII) was approximately 375 000 in 2007, up from approximately 130 000 in 2002 (3).

Despite their long history of use and the increasing number of patients using CSII, no recent document has been published by US-based endocrinologists regarding the appropriate and safe use of insulin pump therapy among adults in clinical practice. The American Diabetes Association published a position statement in 2004 (4). The

American Association of Diabetes Educators published its Guidelines for Successful Outcomes in 2009 (5) and an insulin pump position statement in 2002. The American Academy of Pediatrics published its position statement in 2006 (6), and the National Institute for Health and Clinical Excellence has thoroughly reviewed the topic of CSII several times for the United Kingdom (7,8). Last, the European Society for Paediatric Endocrinology, the Lawson Wilkins Pediatric Endocrine Society, and the International Society for Pediatric and Adolescent Diabetes have published a joint consensus statement regarding the use of insulin pumps in children (9).

In the United States, 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. As a result, any US clinician today can prescribe insulin pump therapy. Too often, patients have only support from the product manufacturer and their own efforts to initiate and advance this demanding therapy. Not surprisingly, because inappropriate candidates with inadequate training and without expert guidance have been allowed to manage their DM using CSII, some unfortunate outcomes have occurred.

Most available patient and professional resources for CSII have been published by device makers for lay users and focus only on the logistics of insulin pump use and DM self-management. "Hard-core" data from randomized clinical trials published in peer-reviewed journals that provide evidence for the benefits of insulin pump therapy are lacking. Posited benefits of CSII for which we need worthwhile research data include influence on hemoglobin A_{1c} (HbA_{1c}) levels, 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 (such as easier travel across time zones); improved work habits and/or productivity; and liberalization of diet timing and composition.

Type 1 DM

Table 1 presents a summary of clinical research findings on CSII efficacy and safety in patients with type 1 DM; included in the 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 on 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 this summary research, 2 very recent publications provide new evidence. First, a 2010 Cochrane review compares the use of CSII with multiple daily injection (MDI) insulin regimens. This review included 23

Table 1
Key Findings From Continuous Subcutaneous Insulin Infusion Meta-Analyses Published Since 2003

Author, year	Meta-analysis objectives	No./types of studies included in meta-analysis	Clinical findings	Notes
Weissberg-Benchell et al, 2003 (10)	Investigation of metabolic and psychosocial impact of CSII therapy vs other treatment modalities (eg, MDI, conventional therapy) in children, adolescents, and adults (n = 1547)	2483 studies identified; 61 met initial criteria; final review consisted of 52 studies (37 paired, 4 randomized cross-over, 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 risk of DKA	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 (11)	Comparison of effects of CSII vs MDI on glycemic control, hypoglycemic risk, insulin requirements, and adverse events in adults with type 1 DM (n = 908), children with type 1 DM (n = 74), and patients with type 2 DM (n = 234)	673 studies identified; final review consisted of 22 RCTs (17 type 1 DM, 2 type 2 DM, 3 pediatric) published through March 2007	HbA _{1c} reduction greater and insulin requirements lower with CSII than with MDI in adults and adolescents with type 1 DM; risk of hypoglycemia comparable among adult patients (data unavailable for adolescent subjects) No conclusive CSII benefits for patients with type 2 DM	...
Fatourechi et al, 2009 (12)	Comparison of effects of CSII and MDI on glycemic control and hypoglycemia in adults and children with type 1 DM (n = 669) or type 2 DM (n = 239)	107 studies identified; final review consisted of 15 RCTs published between 2002 and March 2008	In patients with type 1 DM, HbA _{1c} was mildly decreased with CSII vs MDI; CSII affect on hypoglycemia unclear CSII and MDI outcomes were similar among patients with type 2 DM	CSII efficacy in patients with hypoglycemia unawareness or recurrent severe hypoglycemia inconclusive due to lack of data
Pickup and Sutton, 2008 (13)	Examination of CSII and MDI effects on glycemic control and incidence of severe hypoglycemia in patients with type 1 DM (n = 1414); 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 DM 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 (14)	Comparison of glycemic control and hypoglycemic incidence with short-acting analogue-based CSII (n = 444) vs MDI (n = 439) therapy of ≥12 weeks' duration in patients with type 1 DM	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; DM, diabetes mellitus; HbA_{1c}, hemoglobin A_{1c}; MDI, multiple daily injections; RCT, randomized controlled trial.

randomized studies (duration, 6 days to 4 years) involving 976 participants with type 1 DM. A significant difference was documented in HbA_{1c} response favoring CSII (weighted mean difference -0.3% [95% confidence interval, -0.1 to -0.4%]). In addition, CSII users demonstrated greater improvements in quality-of-life measures. No differences were observed between the 2 treatments' effect on body weight. Severe hypoglycemia appeared to be reduced in users of CSII, although no difference between regimens was observed for the frequency of nonsevere hypoglycemia (15).

In addition, the Sensor-Augmented Pump Therapy for A1C Reduction (STAR-3) study showed significantly greater HbA_{1c} reduction in patients with type 1 DM patients (adults and children) randomly assigned to sensor-augmented insulin pump therapy vs MDI (mean HbA_{1c} decrease, 7.5% vs 8.1% vs baseline of 8.3% ; $P < .001$). A higher proportion of patients randomly assigned to pump therapy reached a HbA_{1c} level less than 7% ; however, no differences were observed between the groups for rates of severe hypoglycemia or weight gain. This study did not assess the effect of sensor augmentation of pump therapy vs the effect of insulin pump alone (16).

On the basis of this evidence and other currently available data, CSII appears to be justified for basal-bolus insulin therapy in patients with type 1 DM that is inadequately controlled with MDI.

Type 2 DM

Few clinical investigations have examined CSII use in patients with type 2 DM. In one analysis of 4 randomized controlled trials in patients with type 2 DM, Monami et al found no significant HbA_{1c} improvements and no significant differences in hypoglycemic risk with CSII vs MDI therapy over 12 weeks. However, a nonsignificant trend toward decreased insulin requirements was observed among CSII patients (17).

2. STATE OF INSULIN PUMP TECHNOLOGY

Table 2 documents key properties of currently available insulin pump models. Several newer capabilities have made insulin pumps easier to use and safer. The availability of insulin dose calculators, or "wizards," has provided benefits such as improved dosing consistency and decreased frequency of insulin "stacking." While calculator manufacturers' recommendations vary based on the specific device, consensus exists that the advice given is usually helpful. Products such as the OmniPod Insulin Management System have increased the accessibility and broadened the appeal of insulin pump technology by allowing patients to be free from infusion set tethering. Enhancements in meter-to-pump communication, remote control operation, and reminder/alarm features (eg, signals

to check glucose levels, change insulin infusion sets, or refill insulin reservoirs) offer further improvements in pump convenience and usability. Last, the introduction of "skins" for the personalization of insulin pumps is a "low-tech" approach intended to make these devices more acceptable to users.

Currently, available pump technology uses a semi-closed loop or hybrid system to provide prebolus insulin according to a computer algorithm (delivered by patient) before meal consumption to account for the lag time in insulin delivery by the "artificial pancreas" (JDRF Artificial Pancreas Project, with collaborations such as Johnson & Johnson's Animas, Roche with University of California in Santa Barbara and Sansum Diabetes Institute). An "artificial pancreas" aims to integrate 2 currently available technologies—continuous glucose monitors and insulin pumps—with an algorithm that provides the right amount of insulin at the right time. Its goal is achievement of blood glucose control while avoiding both high and dangerously low values. Such designs provide the best available approximation of a closed-loop system. Clinical trials of more autonomously functioning pumps are planned.

3. PATIENT AND PROVIDER SELECTION

Successful CSII implementation depends to a large extent on patient and clinician selection, since 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 an optimal candidate for this complex therapy has been debated since insulin pumps became available for use in clinical practice during the late 1970s (18,19). Clearly, CSII is not appropriate for every patient with insulin-requiring DM. Box 1 provides a summary of the characteristics, on the basis of the American Association of Clinical Endocrinologists Insulin Pump Task Force expert consensus, that may make a patient ill suited for this form of therapy. The ideal CSII candidate would be a patient with type 1 DM or absolutely insulin-deficient type 2 DM who currently performs 4 or more insulin injections and 4 or more self-monitored blood glucose measurements daily, is motivated to achieve tighter blood glucose control, and is willing and intellectually and physically able to undergo the rigors of insulin pump therapy initiation and maintenance. Eligible patients should be capable of self-management through frequent self-monitored blood glucose measurements (at least initially) and/or the use of a continuous glucose sensor device. Further, candidates must be able to master carbohydrate counting and insulin correction and adjustment formulas and must be prepared to troubleshoot problems related to pump operation and blood

Table 2
Comparison of Major Insulin Pump Models

Characteristics	Model (manufacturer)			
	Accu-Spirit (Roche-Disetronic)	One Touch Ping (Animas Johnson & Johnson)	Paradigm 522, 722, 523, 723 (Medtronic Minimed)	OmniPod (Insulet Corporation)
Description				
Basal increments	0.1-5 u/h	0.025 u/h	522/722: 0.05-36 u/h 523/723: 0.025 u/h	0.05-30 u/h
Temp basal	In 10% increments from 0% to 200%, and 15 min to 24 h	-90% to 200% in increments of 10% for 0.5 to 24 hours (30 min increments)	± 0.1 u increment as single basal rate for 0.5 to 24 hours or as % of current basal	% or u/h (1-12 h, in 30 min increments)
Bolus increments	0.1, 0.2, 0.5, 1.0, 2.0	0.05 visual or audio, 0.1, 1.0, 5.0 audio	0.1 visual, 0.5 or 1.0 visual or audio, remote extra	0.05, 0.1, 0.5, 1.0 u
Carb + correction factors	Yes, manual carb, blood glucose from Accu-Chek blood glucose monitor	Yes, carb and blood glucose values can be entered into the pump or meter-remote	Yes, manual carb, blood glucose direct from brand name meter or manual entry	Yes
1 unit bolus duration	5 s	1 or 3 s	30 s	40 s
Dimensions	3.2 × 2.2 × 0.8 in	2.9 × 2.0 × 0.76 in	522/722: 1.9 × 3 × 0.77 in 523: 2 × 3.0 × 0.8 in 723: 2.0 × 3.6 × 0.8 in	OmniPod: 1.6 × 2.4 × 0.7 in Personal diabetes manager: 2.6 × 4.3 × 1.0 in
Empty weight	2.8 oz	3.25 oz	522/722: 3.3 oz 523: 3.5 oz	OmniPod: 1.2 oz Personal diabetes manager: 4.0 oz w/ batteries
Basal patterns	5 patterns	4 patterns	3 patterns	7 patterns
Insulin on board calculations	Yes	Yes	Yes	Yes
Special features	<ul style="list-style-type: none"> • Personal digital assistant with Diabetes Management tool • 315-unit cartridge • Reversible display • Child lock 	<ul style="list-style-type: none"> • Multiple insulin to carb ratios • Child lock • Big screen • High-contrast color screen for readability • 500-food database • Tunes for alarms and warnings • Remote bolus from One Touch Meter 	<ul style="list-style-type: none"> • Real-time glucose sensor capabilities • Paradigm links to blood glucose monitor • Bolus wizard calculator • Child lock • Remote control • Two pump sizes (180 and 300 units) 	<ul style="list-style-type: none"> • No tubing to catch or snag and disrupt insulin activity • Fully integrated FreeStyle blood glucose meter • Intuitive setup wizard • Large, easy-to-read LCD • Food database • Programmable reminders and alerts • Child lock-out feature • Reservoir capacity: 200 deliverable units
Pump programming	Accu-Chek Insulin Pump Configuration Software™	EZ Manager Max™ software to download pump and blood glucose meter	Paradigm PAL™ software to download pump and meter; Carelink™ software cable	PathFinder™ software to download personal diabetes manager data
Bolus “types”	<ul style="list-style-type: none"> • Quick • Standard • Extended • Multiwave 	<ul style="list-style-type: none"> • Carb Smart • EZ Bolus • Combination • Correction 	<ul style="list-style-type: none"> • Normal • Square Wave • Dual Wave • Correction • Extended • Combination 	<ul style="list-style-type: none"> • Meal • Correction • Mean & Correction • Normal

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

- Unable or unwilling to perform multiple daily insulin injections (≥ 3 to 4 daily), frequent blood glucose monitoring (≥ 4 to 6 daily), and carbohydrate counting
- Lack motivation to achieve tighter glucose control and/or have a history of nonadherence to insulin injection protocols
- History of serious psychologic or psychiatric condition(s) (eg, psychosis, severe anxiety, or depression)
- Reservations about pump usage interfering with lifestyle (eg, contact sports or sexual activity)
- Unrealistic expectations of pump therapy (eg, belief that it eliminates the need to be responsible for diabetes management)

glucose levels. Last, patients should be emotionally mature, with a stable life situation, and willing to maintain frequent contact with members of their health care team, in particular their pump-supervising physician.

On the basis of the American Association of Clinical Endocrinologists 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 3.

Clinicians must be willing to terminate insulin pump therapy when it fails to provide a patient with the expected benefits; for example, in the rare case of "pump abusers" who love their pump, but 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. As suggested by Skyler et al and others, insulin pumps should only be prescribed by clinicians possessing the necessary knowledge, skills, and resources to provide effective and safe initiation and maintenance of this complex and time-consuming therapy (20). Further, the availability of adequate patient education, training, and follow-up is 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.

One way to promote the optimal and safe initiation and maintenance of insulin pump therapy would be to establish a standardized provider certification process. As with any advanced form of medical intervention, when practitioners have more experience with the tool, it becomes more likely that patients will experience improved outcomes. However, before formal efforts to investigate such a process can begin, several questions must be answered:

- What evidence of clinical endocrinologist/diabetologist training would be sufficient for initial certification?
- What documentation would be required to demonstrate advanced proficiency and/or a need for continuing education? Duration of expertise? Quality of resources or expertise at the clinical site? Number of insulin pumps initiated and maintained in the practice?
- What would constitute a successful outcome? Achieving glycemic targets? Avoidance of severe hypoglycemic episodes? Positive quality-of-life assessments?

4. INSULIN PUMP USE IN VARIOUS PATIENT POPULATIONS

It is not the purpose of this document to detail specific therapeutic decisions that must be made when designing personalized insulin pump programs. Several existing publications provide the information required to establish basal and bolus insulin calculations in adults and in special populations (20-23). Instead, the goal of this section is to summarize therapeutic challenges associated with insulin pump use in specific patient populations and to describe strategies for successful CSII implementation in each of these groups.

Adults

After a clinician has determined that a patient is eligible for insulin pump therapy (Box 1 and Table 3), 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.

Table 3
Proposed Clinical Characteristics of Suitable Insulin Pump Candidates

Clinical characteristics		
Class 1	Class 2	Class 3
Patients with type 1 DM who do not reach glycemic goals despite adherence to a maximum MDI, non-CSII program, especially if they have: <ul style="list-style-type: none"> • Very labile DM (erratic and wide glycemic excursions, including recurrent DKA) • Frequent severe hypoglycemia and/or hypoglycemia unawareness • Significant “dawn phenomenon,” extreme insulin sensitivity Special populations (eg, preconception, pregnancy, children, adolescents with eating problems, competitive athletes)	Patients with type 1 DM who are on a maximized basal-bolus MDI insulin regimen, regardless of their level of glycemic control and who, after investigation and careful consideration, feel that CSII would be helpful or more suitable for lifestyle reasons	Selected patients with insulin-requiring type 2 DM who satisfy any or all of the following: <ul style="list-style-type: none"> • C-peptide positive but with suboptimal control on a maximal program of basal/bolus injections • Substantial “dawn phenomenon” • Erratic lifestyle (eg, frequent long distance travel, shift-work, unpredictable schedules leading to difficulty maintaining timing of meals) • Severe insulin resistance, candidate for U500 insulin by CSII Selected patients with other DM types (eg, postpancreatectomy)
Abbreviations: CSII, continuous subcutaneous insulin infusion; DKA, diabetic ketoacidosis; DM, diabetes mellitus; MDI, multiple daily injections.		

The health care team’s initial task is to assess the patient’s level of expertise in the following: (a) ability to check capillary glucose levels; (b) knowledge of pre-meal, postmeal, and bedtime target glucose values; (c) ability to maintain and troubleshoot glucose meter; (d) knowledge of steps for hypoglycemia detection, prevention, and treatment; (e) sick day management strategies; (f) ability to keep food and physical activity records; and (g) basic and advanced carbohydrate-counting skills. Following completion of 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, troubleshooting, and infusion site preparation and the calculation and configuration of basal insulin infusion rates, initial insulin-carbohydrate ratios, correction boluses, and insulin sensitivity.

Once the patient is successfully transitioned from MDI to CSII, frequent (ie, daily) contact with the pump trainer is mandatory; a return visit with the endocrinologist/diabetologist is advised within 3 to 7 days to begin fine-tuning the insulin infusion parameters on the basis of initial glucose data provided by the patient. Educational consults (eg, clinic visits, phone calls, e-mail communication) should be scheduled weekly or biweekly at first and then periodically as necessary. One can often take advantage of the experienced Certified Diabetes Educators employed by a pump company provided they follow the physicians’ 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 (eg, adjustment of bolus “wizard” settings, configuration of different basal settings depending on expected daily routine, exploration of different modes of bolus delivery, temporary basal settings, 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 level of physical activity. This incremental process may take months or years, with the speed of progress depending on both the patient and health care team’s assessment of the overall benefits of pump therapy.

All patients should undergo periodic reevaluations to determine whether there is a need for further education and/or training; the importance of this assessment cannot be overemphasized. Inclusion of this reevaluation in the overall insulin pump program would also enable the specialist to make the sometimes difficult decision to withdraw CSII therapy from patients who do not benefit from this form of insulin delivery.

Children

In the early days of CSII therapy, children were not considered for this emerging technology; however, advances in other areas have made it possible to use insulin

pumps in children. Although little guidance exists for this topic in the peer-reviewed literature, specific recommendations for basal and bolus insulin rates, glucose monitoring, and pump and tubing selection in pediatric patients have been summarized by Phillip et al (9). While existing data suggest that the use of insulin pumps in pediatric patients does not necessarily lower HbA_{1c} levels, evidence does indicate that pump therapy is associated with a reduced risk of diabetic ketoacidosis (DKA)-related hospitalization in children with recurrent DKA.

Some fear that the publication of patient selection guidelines for CSII therapy in pediatric populations could lead parents to pressure clinicians to prescribe insulin pump use in cases where it might not be beneficial. Many endocrinologists prefer to use a common sense patient selection approach, particularly because CSII eligibility depends not only on a patient's capabilities, but also, to a large extent, on his/her family's psychological competence/fitness. This is of particular concern, since a substantial proportion of pediatric patients have only 1 caregiver or live with a blended family (A review of current literature indicates a tacit assumption on the part of investigators that both pediatric patients and their parents have been appropriately screened to identify those with unrealistic expectations or social/emotional issues that may preclude successful insulin pump use. Evidence also suggests that most patients receiving insulin pump therapy are assumed to have adequate education, training, and follow-up. In many current practice settings, however, these assumptions may be overly optimistic.

Physicians must consider the unique issues that may arise when implementing insulin pump therapy in pediatric patients. In particular, clinicians must be prepared to address concerns relating to puberty, menses, school and camp attendance, exercise variability, reliance on adults (eg, parents, caretakers) for input, age-specific constraints (eg, use of pumps in toddlers, teens, etc), patient reliability issues (eg, faking boluses, not checking glucose levels), divorce-related complications, and parental factors (eg, education, expectations, etc). Health care providers must also be prepared to discontinue pump therapy if either the parent or patient is unable or unwilling to perform minimal required tasks.

Pregnant Women With Diabetes

Type 1 DM and Pregnancy

Macrosomia (infants born at greater than the 90th percentile of weight for gestational age or sex or greater than 2 standard deviations above the norm) is the most common neonatal complication associated with DM during pregnancy. However, macrosomia is secondary to hyperglycemia; therefore, while insulin pumps are an effective insulin delivery system, inadequate control of blood glucose,

regardless of treatment modality, is the real culprit in macrosomia (25,26). Study findings suggest that maintaining HbA_{1c} levels in the normal range during pregnancy is essential to avoid malformations and macrosomia; however, insulin pump therapy has not been shown to be superior to MDI for maintaining HbA_{1c} levels in pregnant women (27).

A 2007 search of the Cochrane Pregnancy and Childbirth Group's Trials Register (28) indicates that 2 randomized controlled trials (n = 60 and n = 61) have compared CSII with MDI in pregnant women with diabetes. A significant increase in mean birth weight was associated with CSII. However, because of the lack of significantly different macrosomia rates observed in the population, this was not considered clinically significant. No significant differences were found in any other outcomes measured; however, the number of trials and participants was small. The authors concluded that there is a dearth of robust evidence to support the use of one intensive insulin approach over another in DM-complicated pregnancy.

A study of 42 women with preexisting DM attending a joint obstetric-diabetic clinic (29) found that insulin pump therapy was equivalent to MDI for HbA_{1c} control and fetal outcomes. In this prospective, nonrandomized study, women chose whether to commence insulin pump therapy (n = 18) or to remain on a conventional insulin regimen (n = 24). Estimated fetal weight and growth velocity were calculated from routinely collected third trimester ultrasonography biometry and expressed as standard deviation (Z) scores. There was no difference in preconception HbA_{1c} (7.62 vs 8.01%) or third trimester glycemic control (mean HbA_{1c} 6.63 vs 6.44%) among the groups studied. Women using pump therapy had similar mean growth velocity, fetal weight, and birth weight Z scores compared with those of women using conventional insulin therapy.

Thus, the literature does not suggest clear evidence that insulin pumps are necessary for optimal treatment of women with type 1 DM during pregnancy. A robust randomized trial, adequately powered to assess efficacy outcomes for CSII vs MDI in pregnant women with DM, is needed.

Treatment Protocol: Insulin Pump for Type 1 DM During Pregnancy

Because pregnancy is a state of accelerated ketosis (30), just a few hours of insulin interruption can lead to hyperglycemia and ketosis. Since diabetic ketosis is associated with fetal demise (31), intensive education and surveillance of the infusion site and sets (32-35) are required with insulin pump use during pregnancy.

As the abdominal skin stretches and the subcutaneous tissue thins, the pump infusion needle 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 insulin may be given before bed to ensure that if the needle dislodges there will never be a lack of insulin in the circulation. Therefore, some experts recommend that a dose of neutral protamine Hagedorn 0.1 times the weight in kilograms be given before bed and that the early morning insulin infusion rate be lowered (Table 4).

Insulin Pump for Type 2 DM During Pregnancy

One study assesses the use of insulin pump therapy in women with insulin-requiring gestational DM or type 2 DM in pregnancy with persistent hyperglycemia (36). This nested case-control study used 1991-1994 data from a single South Auckland hospital, comparing insulin pump and noninsulin pump therapy (matched for DM type) in pregnancies complicated by gestational DM/type 2 DM with peak insulin requirements of 100 to 199 units/day.

Thirty of 251 women used an insulin pump; an additional 2 women with high insulin requirements discontinued pump therapy. Overall, none of the women experienced severe hypoglycemia, and 79% had improved glycemic control within 1 to 4 weeks. Those using a pump had greater insulin requirements and greater weight gain. Their babies were more likely to be admitted to the special care baby unit, but were neither significantly heavier nor more likely to experience greater hypoglycemia than control patients' infants. Therefore, insulin pump therapy seems to be safe and effective for maintaining glycemic control in pregnancies complicated by gestational DM/type 2 DM requiring large doses of insulin.

Insulin Pump Therapy During Labor and Delivery

Few studies have investigated insulin and glucose requirements during labor (37). Now that women with type 1 DM are able to have normal pregnancies, including vaginal delivery, specific protocols for maintaining

Table 4
Suggested Protocol for Insulin Pump Use During Pregnancy

Insulin infusion rates for women with type 1 diabetes mellitus: total basal insulin requirement for 24 hours	
Gestation	Units × weight (in kg)
Prepregnant	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 units by 24)	
Time of day	Infusion rate
12-4 AM	½ calculated basal rate
4-10 AM	1½ calculated basal rate
10-6 PM	calculated (may need adjustment based on stress and exercise in the time period)
6-12 PM	calculated (may need adjustment based on stress and exercise in the time period)
Meal-related insulin bolus^a	
Gestation	Units × weight (in kg) (divided into thirds for a dose before each meal)
Prepregnant	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 lower early morning insulin infusion rate	

^a Use only rapid-acting insulin analogues.

normoglycemia during labor and delivery are required. Labor can be considered equivalent to prolonged exercise (38). When women with type 1 DM exercise while hyperglycemic, blood glucose levels may rise. In fact, exercise in the hyperglycemic state has been reported to cause ketosis (38-41). Before the implementation of management protocols to normalize blood glucose in women with type 1 DM during pregnancy, women starting their labor in the hyperglycemic state required large insulin doses (39-42).

To prevent complete depletion of hepatic glycogen stores during labor, the glucose substrate need is similar (2.55 mg/kg/min) to that of a trained marathon runner. This infusion rate is equivalent to 10 g of glucose per hour for a 60-kg woman. This protocol has been applied to women with type 1 DM during labor and delivery with excellent outcomes (43). Protocols for labor and delivery have been published on the basis of this experience (34).

Use of Pumps in Inpatient Settings

CSII use in the hospital setting presents additional challenges. When CSII users are evaluated in emergency departments or are admitted to medical or surgical units, 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 a patient's ambulatory pump management is contacted promptly to make decisions about appropriate infusion adjustments during the hospital stay. In addition, patients should be instructed not to discontinue the pump infusion unless directed by their diabetes specialist. As stated in the American Diabetes Association's 2010 Standards of Medical Care (44), "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. It is important that nursing personnel document basal rates and bolus doses on a regular basis (at least daily). The availability of hospital personnel with expertise in CSII therapy is essential."

5. INSULIN PUMPS: PATIENT SAFETY ISSUES

Current literature on insulin pump use has focused primarily on the benefits of CSII in patients with type 1 DM, with some attention to the role of CSII in patients with severely insulin-deficient type 2 DM. However, several recently published articles have examined CSII safety through investigations of adverse events in patients undergoing insulin pump therapy and analyses of factors that may increase morbidity and/or mortality risk with CSII.

Device-Related Problems

According to a March 5, 2010, report published by an FDA panel established to examine insulin pump problems,

the agency received 16 849 adverse event reports between October 1, 2006, and September 20, 2009, including 12 093 injuries (72%), 4294 pump malfunctions (25%), and 310 deaths (1.8%) (3). Analysis of the 16 640 discrete events reported for pumps made by the 5 top manufacturers revealed that the most commonly reported patient-related problems were hospitalization (21%), high blood glucose (17%), DKA (8%), hyperglycemia (8%), treatment with medication (6%), and low blood glucose (5%), while the most frequently identified device-related problems included "unknown" (20%), "replace" (9%), "audible alarm" (6%), "use of device issue" (5%), "device displays error message" (5%), and "failure to deliver" (3%).

Event reports for the 310 mortalities were frequently incomplete, but causes of death included diabetic coma, hypoglycemia, hyperglycemia, DKA, unresponsiveness, respiratory infection, alcohol consumption, and motor vehicle crash. For cases in which a device problem could be identified, reported malfunctions included infusion set failure, disconnection, device issue, pump alarming, overinfusion, bent cannulas, pump not working properly, failure to deliver, suspected electromagnetic interference, display failures, and issues with infusion sets.

A 2008 review of an FDA registry of adverse events involving insulin pump therapy specific to adolescents identified 1594 reports submitted between January 1, 1996, and December 31, 2005, including 1038 injuries (65%), 528 pump malfunctions (33%), and 13 deaths (0.8%). Ninety-two percent of these events resulted in hospitalization (45). Among the injuries reported were 987 cases (62%) of hyperglycemia (with DKA in 46.6%) and 167 cases (11%) of hypoglycemia and/or insulin overdosage. Mortality resulted from hyperglycemic or hypoglycemic complications (n = 5), DKA (n = 3), seizure (n = 1), coma (n = 1), or unknown causes (n = 3). Investigators concluded that adolescent-specific issues may have played a contributing role in 102 of these adverse events, including problems relating to education (47 events), noncompliance (19 events), sports/other activities (12 events), and device misuse (8 events). Clearly, in some adolescents, insulin pump use may be problematic because of the patients' lifestyle and/or psychosocial status.

In addition to the FDA analyses, a number of key studies from the French literature have contributed substantially to our understanding of the risks of CSII (46-48). One such study, a 2006 review of CSII safety by Guilhem et al (46), reported that the most common insulin pump problems involved infusion set failure, particularly due to infusion set obstruction or leakage, and infection/inflammation of the infusion site. Insulin precipitation or aggregation is believed to be an inciting factor for both obstruction- and infection-related failures. On the basis of an assessment of pump malfunction data for 376 new insulin pumps used in ambulatory diabetes treatment in France from 2001 to 2004, investigators found that failures occurred at a rate

of 23 per 100 pump-years, with a median time-to-failure of 28 months. The authors also noted that insulin delivery failure, particularly when insulin analogues are used, may rapidly lead to severe hyperglycemia and ketosis. In more than 85% of occlusion events, metabolic deterioration developed before the high-pressure alarm was activated.

In addition, the fact that most pump alarm systems do not detect leakage of insulin from the infusion set may be a major cause of DKA, which occurs more frequently in patients using CSII than in patients using MDI (49-51). As such, the occurrence of unexplained hyperglycemia or ketosis in patients using CSII should lead to replacement of the insulin infusion set.

Patient Selection

Patient selection affects the success of CSII therapy, and outcomes differ widely between groups of highly motivated, well-educated patients with few comorbidities and poorer, sicker patients with limited means who do not have access to highly trained pump personnel.

Furthermore, mental status has an important role in the patient's ability to use an insulin pump safely; the patient selection process should include an evaluation of comorbidities such as depression, mood disorders, and cognitive dysfunction, which are commonly seen in association with severe hyperglycemia or hypoglycemia in patients with DM. Comorbid conditions such as chronic renal failure, postchemotherapy, and excessive sedation from medication may also lead to diminished mental acuity, which may increase the risk of adverse events with CSII therapy. For example, the June 22, 2009, report on the AACE Patient Safety Exchange Web site (<http://www.aacepatientsafety-exchange.com/editorial/index.php?id=32>) discusses the effect of stage IV renal failure on cognitive function and the resultant reduction in the ability of a patient to use a pump they previously could use safely (51).

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 US patients report that their initial pump training took less than 3 hours and that the only health care professional likely to be helpful to them in an emergency is the voice on the insulin pump company's hotline, since neither their doctor nor the hospital staff understand how the pump works. Evidence such as that provided by a Swedish study (49,50), in which new CSII users experienced a higher frequency of DKA shortly after pump therapy was initiated, suggests that a failure of education can affect patient safety.

To reduce the risk of adverse events, it is recommended that patients receive extensive education regarding the technical aspects of insulin pump use (52). Preventive measures, such as training in proper catheter insertion

technique, are important, and frequent (≥ 4 or 5 times daily) glucose monitoring is also critical. Patients must be educated on the meaning of pump alarms, particularly those that may signal a potential interruption in insulin delivery (eg, battery failure, empty syringe). In addition, patients must be reminded that backup supplies (eg, 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 per day to handle patient questions. 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 (52).

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.

6. INSULIN PUMPS: CODING AND REIMBURSEMENT ISSUES IN PRACTICE

Payment for existing codes for DM education has not been established across the private and public sectors. Accordingly, existing E/M codes for office encounters are typically used (Table 5). 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 after the end of the office visit.

Most private insurers provide reimbursement for insulin pumps for patients with type 1 DM, although verification of benefits is recommended before pump purchase. In addition, the Center for Medicare and Medicaid Services covers CSII. The patient must be insulinopenic, defined as

Table 5
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

having a fasting C-peptide level $\leq 110\%$ of the laboratory's lower limit of normal, with a concurrently obtained fasting glucose ≤ 225 mg/dL, or they must be β -cell autoantibody positive. In addition, patients must meet the criteria outlined in Box 2. Continued Center for Medicare and Medicaid Services coverage of the insulin pump requires evaluation by the treating physician at least every 3 months (53).

7. ECONOMICS OF INSULIN PUMP THERAPY

Concerns have been raised about the costs incurred by this therapeutic modality. However, recent evidence indicates that CSII is a cost-effective treatment option, both in general and compared with MDI, for children and adults with type 1 DM (54-57). Table 6 summarizes the key assumptions and findings of 5 recent, representative cost-effectiveness analyses comparing CSII with MDI in specific patient populations.

8. 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, insulin-to-carbohydrate ratios can only be set to integer values; as such, dosing precision may be compromised with lower-value (eg, <10) settings. In addition, in clinical practice, insulin pumps are often suboptimally configured (eg, carbohydrate factors, correction factors, and duration of insulin action are frequently set and never changed). Thus, standardized periodic audits of pump settings in the context of current glucose dynamics, are required. To help

with this, practitioners may want to use online registries (eg, 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, alongside low reimbursement rates, makes it challenging to complete during an office visit.

Beyond improvements in the pump user interface, there is a clear need for educational programs administered by qualified experienced physicians, to provide patients with initial and follow-up training on pump use.

From the foregoing discussion, 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 for use in clinical practice.

Key questions that should be addressed in controlled research studies:

- How do we determine superiority (or noninferiority) of insulin pump vs MDI use? (Glycemic variability? Frequency and severity of hypoglycemia? Number of emergency department visits? Patient satisfaction? Productivity/absenteeism? Diabetic complications? Overall cost of DM care?)
- How do we define improvements in DM control in patients using insulin pumps?
- What objective criteria should be considered when selecting appropriate candidates for insulin pump use? Current intensive insulin

Box 2

Center for Medicare and Medicaid Services Insulin Pump Patient Eligibility Criteria

To be eligible for Center for Medicare and Medicaid Services insulin pump coverage, patients must meet 1 of the following criteria:

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

- Hemoglobin A_{1c} $>7.0\%$
- History of recurrent hypoglycemia
- Wide fluctuations in blood glucose before mealtime
- Dawn phenomenon with fasting plasma glucose concentration frequently >200 mg/dL *or* a history of severe glycemic excursions

(b) Patient on a pump therapy before enrollment and has documented self-monitored blood glucose an average of ≥ 4 times per day during the month before enrollment.

Table 6
Summary Data of Cost-effectiveness Analyses Comparing Continuous Subcutaneous Insulin Infusion vs Multiple Daily Injection in Adults and Children With Type 1 Diabetes Mellitus

Study	Study objective, perspective, and data source	QALYs gained	Cost per QALY (ICER)	Additional key findings
St. Charles et al (54)	To estimate long-term (60-year) cost-effectiveness of CSII compared with MDI in adults/children with type 1 DM US 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, PVD The NNT for PDR was 9, (ie, only 9 patients need to be treated with CSII to avoid 1 case of PDR)
St. Charles et al (55)	To evaluate the long-term (60-year) cost-effectiveness of CSII compared with MDI in adult patients with type 1 DM 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)	...
Cummins et al (56)	Assessment report to examine the clinical and cost-effectiveness of using CSII to treat DM (type 1 DM and during pregnancy) NICE, United Kingdom Systematic review and economic evaluation (74 studies included)	N/A	N/A	CSII is cost-effective for type 1 DM in both children and adults No evidence that CSII is better than MDI in pregnancy
Cohen N et al (26)	To project long-term (lifetime horizon) costs and outcomes of CSII vs MDI in adults and adolescents with type 1 DM Australian perspective Computer simulation model (CORE Diabetes Model)	QALY gains for CSII vs MDI were 0.467 (adults) and 0.560 (adolescents)	CSII: A\$74 147 (adults); A\$74 661 (adolescents)	Authors indicated that CSII represents good value for most scenarios studied
Roze et al (57)	To project the long-term (60-year) costs and outcomes of CSII vs MDI in patients with type 1 DM 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 type 1 DM, 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.

management should be a given, but beyond that, what else? (Age? Maturity? Home/family/workplace support? Motivation? Resources? Patient education? Number of daily glucose monitoring tests? Glycemic variability? Frequency and severity of hypoglycemic reactions? Hypoglycemia unawareness? Frequency of emergency department visits? History of hospital admissions? Type of DM?)

- Who is the best person to determine the patient's pump candidacy?
- Who should be in charge of initial training?
- Who should be in charge of reevaluating skills, continuing education, and reeducation?
- What is the role of specialist physician? The role of allied health professionals (physician assistant, nurse practitioner)? The role of DM nurse educators or dietitians?
- What is the role of the device maker and what professional support should they provide?
- How does one define an "insulin pump specialist"? (Length of training? Place of training? Number of patients managed on the pump? Number of years in practice? Patient satisfaction? Referring doctors' satisfaction? Patient outcomes [and if so, defined how]?)
- How will the expert insulin pump management be paid for or reimbursed? How can one be paid for downloading of devices during a standard office visit? Who should set up the criteria for reimbursement? (Insurance coverage for patient needs, and payment for physician services to deliver the optimum standard of care)
- What are the key components of insulin pump therapy reimbursement? (Each specific therapeutic component? Global payment to the health care team for successful implementation of insulin management?)
- What is the optimal way to integrate insulin pumps with continuous glucose monitoring systems?
- Can insulin pump therapy be successfully initiated and maintained in non-English-speaking patients in the United States?
- What modifications are necessary to accommodate successful insulin pump therapy in patients of varied ethnic/cultural backgrounds?

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