Overview of Insulin Delivery Options

Overview of Insulin Delivery Options is supported by an educational grant from Novo Nordisk Inc. It has been accredited by the American Association of Diabetes Educators (AADE) for nurses, dietitians, and pharmacists.
The following program is a taped presentation by Jerry Meece.

Jerry Meece is owner and Director of Clinical Services of Plaza Pharmacy and Wellness Center in Gainesville, Texas, one of the first freestanding pharmacies in the country to achieve Provider Education Recognition from the American Diabetes Association.

In addition to serving on numerous consultant and advisory boards for health care and pharmaceutical companies, he has served on the Board of Directors for the American Association of Diabetes Educators and was elected to their Executive Board in the position of Vice President.

Mr. Meece speaks both nationally and internationally on the subject of diabetes, and clinician/patient behavior in the health care setting. He has also written many articles on diabetes care and insulin use in the patient with diabetes.

Mr. Meece has won many awards including the Innovative Practice Award by the Texas Pharmacy Association, the Legislative Leadership Award by the American Association of Diabetes Educators, and the Individual Educational Excellence Award by the Texas Pharmacy Association.

We will now join Mr. Meece.
This knowledge-based program will address the important role of insulin delivery systems in helping patients meet their individual therapeutic goals. By the end of this program you should be able to:

- Identify the benefits of insulin therapy for glycemic control and reduction of long-term complications and the major issues surrounding the initiation of insulin therapy in patients with type 2 diabetes
- Discuss evidence-based approaches for selecting the optimal insulin delivery system for a specific patient
- Describe how to select the most appropriate insulin delivery system for a specific patient
Glycemic control is fundamental to the management of diabetes. The Diabetes Control and Complications Trial (DCCT), Kumamoto study, and UK Prospective Diabetes Study (UKPDS) showed definitively that lowering the A1C to below or around 7% is associated with:

- Significantly decreased rates of microvascular and neuropathic complications
- Long-term decrease in macrovascular disease (as long as A1C reduction is implemented soon after diabetes diagnosis)

Therefore, reasonable goals for many nonpregnant adults with diabetes are <7% (ADA), ≤6.5% (AACE)†

† Goals for pregnant women: ADA, <6.0%; AACE, ≤6.0%

AACE = American Association of Clinical Endocrinologists; ADA = American Diabetes Association.

Glycemic control is fundamental to the management of diabetes. The Diabetes Control and Complications Trial (DCCT), Kumamoto study, and UK Prospective Diabetes Study (UKPDS) showed definitively that lowering the A1C to below or around 7% is associated with significantly decreased rates of microvascular and neuropathic complications.

Similarly, the DCCT/Epidemiology of Diabetes Interventions and Complications Study and the UKPDS demonstrated that lowering the A1C to around or below 7% is associated with a long-term decrease in macrovascular disease, as long as this A1C reduction is implemented soon after the diagnosis of diabetes.

Therefore, reasonable goals for many nonpregnant adults with diabetes are <7% according to the American Diabetes Association (ADA) and ≤6.5% according to the American Association of Clinical Endocrinologists (AACE). The AACE recommends an A1C goal of 7% to 8% for individuals with a history of severe hypoglycemia, limited life expectancy, advanced complications, extensive comorbid conditions, or long-standing diabetes in which the general goal has been difficult to attain despite intensive efforts.

(A1C goals for pregnant women are <6.0% according to the ADA and ≤6.0% according to the AACE.)
Despite the desirability of maintaining an A1C level below 7%, many US residents have not reached this goal. An analysis of National Health and Nutrition Survey data performed by Cheung and colleagues showed that overall glycemic control improved significantly among US adults with diagnosed diabetes between 1999 and 2006.

Nevertheless, nearly 43% of US residents continued to have an A1C level of 7% or greater, and the proportion of patients who were not at goal was considerably higher in some ethnic groups. For the period 2003 to 2006, nearly 56% of non-Hispanic blacks and over 59% of Mexican Americans had an A1C of at least 7%.

These statistics emphasize the urgency of adopting measures that will substantially improve glycemic control in the US.
The prevalence of diagnosed and undiagnosed diabetes in the US adult population is projected to increase from about 14% in 2010 to as much as 33% by 2050. This is of great concern, because diabetes imposes a heavy personal and economic burden.

After adjustment for potential risk factors and mediators, persons with diabetes are at increased risk for premature mortality due to vascular disease, several types of cancer, infectious diseases, external causes, intentional self-harm, and degenerative disorders. On average, a 50-year-old person with diabetes but no history of vascular disease is about 6 years younger at the time of death than a counterpart without diabetes. There are generally continuous associations between fasting BG levels above 100 mg/dL and risk of death, supporting the view that hyperglycemia may be directly relevant to increased and accelerated mortality.

Many studies have shown that diabetes has a pervasively negative impact on the quality of life (QoL) of persons with diabetes.

Direct costs for preventing and treating diabetes and its complications in the US are projected to rise from $198 billion in 2010 to $264 billion in 2030.

Collectively, these data indicate that there is an urgent need to prevent the onset of diabetes whenever possible, to ensure that persons with diabetes have appropriate screenings for associated disorders, and to reduce the development of diabetic complications through effective treatment.
In recent years there has been a paradigm shift in the treatment of type 2 diabetes. According to AACE Diabetes Care Plan Guidelines published in 2011, “the traditional postponement of insulin therapy for years after prolonged lifestyle and oral agent efforts to achieve glycemic control has been revised in the last decade to incorporate primarily basal insulin therapy much sooner.”

In the 2009 consensus algorithm for the management of type 2 diabetes that was developed by the ADA and the European Association for the Study of Diabetes (EASD), basal insulin is a tier 1, step 2 therapy that can be started within 2–3 months of beginning treatment with lifestyle modification + metformin (or even sooner if A1C remains elevated or patient is symptomatic).

The text accompanying the algorithm explains that basal insulin can be initiated even sooner if the target A1C level is not achieved with lifestyle modification and metformin.

The algorithm also specifies that insulin therapy in combination with lifestyle intervention is the initial treatment of choice for some patients. These include individuals with severely uncontrolled diabetes with catabolism, defined as fasting plasma levels greater than 250 mg/dL, random glucose levels consistently above 300 mg/dL, A1C above 10%, or the presence of ketonuria. Symptomatic patients with polyuria, polydipsia, and weight loss should also begin insulin therapy immediately.
Research has shown that treatment intensification improves glycemic control in patients with type 2 diabetes, with no worsening of overall health status or psychological problems, even in elderly patients. Nevertheless, clinical inertia remains widespread. In the context of diabetes, “clinical inertia” refers to the failure of health care providers to intensify a patient’s glucose-lowering therapy when doing so would clearly be beneficial. In one study, the mean A1C of patients receiving metformin monotherapy before intensification was 8.8%, and monotherapy was continued for a mean of 25.9 months after the A1C rose above 7%.

In another study, fewer than half of patients with elevated A1C levels during their visit to the diabetes clinic of an academic medical center had changes to their regimen. Although diabetes specialists are more likely than primary health care providers to intensify treatment and especially to initiate insulin, clinical inertia is also prevalent among specialists.

Clinical inertia also extends to the willingness to use devices that can facilitate insulin delivery, such as insulin pens and insulin pumps. Reluctance to use these devices is especially widespread among primary health care providers. Reasons for delaying insulin therapy include concerns about hypoglycemia and weight gain, reluctance to initiate a more complex regimen in patients who have been nonadherent to their existing regimen, concerns about the time required to titrate patients to the optimal insulin dose and follow their progress, and reluctance to alienate patients. Remedies for clinical inertia include professional education about implementing treatment algorithms, such as the ADA/EASD algorithm; computerized A1C tracking systems and alerts; and working collaboratively with a certified diabetes educator (CDE).
The term “psychological resistance to insulin” describes a patient’s reluctance to accept a prescription for insulin therapy, have an initial or subsequent insulin prescription filled, adhere to the complete insulin treatment regimen, or accept the addition of one or more insulin injections to the existing regimen. In one study of 708 patients with type 2 diabetes, for example, 28% reported being unwilling to take insulin if it was prescribed for them.

Studies have shown that health care providers often have little understanding of their patients’ psychological resistance to insulin and thus are not effective in preventing or reducing it.

A major reason for psychological resistance to insulin is misinformation, such as the belief that insulin causes blindness or the conviction that needing insulin is a sign of personal failure. Other reasons include fear of pain or bruising at the injection site, embarrassment about injecting insulin in public, concern about hypoglycemia or weight gain, reluctance to change one’s lifestyle or daily routines, and resistance to frequent self-monitoring of blood glucose (SMBG).
Health care providers can take several steps to reduce psychological insulin resistance in their patients with type 2 diabetes. The provider should prepare all newly diagnosed patients for future insulin therapy by discussing the progressive nature of the disease, explaining that most patients eventually require insulin therapy, and emphasizing that insulin treatment is not an indication of failure on the patient’s part. Both the short- and long-term advantages of tight glucose control should be stressed. Finding the right combination of therapies to bring the A1C within the target range, not minimizing the number of agents or injections used, should be the goal. Through culturally appropriate stories, metaphors, and pictures, the health care provider should show how insulin injections enhance both the duration and quality of life.

Clinicians should determine what the patient knows about insulin and gently correct any misinformation. Fears of insulin injections are often reduced when the health care provider shows the patient the devices currently used to administer insulin, including the very short, fine needles available today. A discussion about practical ways to reduce the risk of hypoglycemia and weight gain is also likely to be reassuring.

Health care providers should think about their own perceptions of insulin therapy and avoid any language implying that insulin therapy is a form of punishment or a sign of failure.
An accurate statement about diabetes is: __________.

a. lowering A1C to around 7% is associated with a decreased rate of microvascular disease but does not affect the development of macrovascular disease
b. in 2006, approximately 75% of US adults with diagnosed diabetes had an A1C of <7%
c. the US prevalence of diagnosed and undiagnosed diabetes is projected to be as high as 20% by 2050
d. according to the 2009 ADA/EASD treatment algorithm, basal insulin is a recommended treatment for patients with an inadequate response to lifestyle modification plus metformin
The correct answer is d.

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According to the 2009 ADA/EASD treatment algorithm, basal insulin is a recommended treatment for patients with an inadequate response to lifestyle modification plus metformin.
The vial and syringe is still the most widely used insulin delivery method in the US. Administering insulin with a vial and syringe has several advantages. Syringes are widely available and relatively inexpensive. Most importantly, this delivery method permits in-syringe mixing of some types of insulin that are not commercially available as premixed products. For example, a patient who uses NPH insulin could mix it with regular insulin or a rapid-acting insulin analog and administer both types of insulin with one injection. Another advantage is that, unless an injection aid that conceals the syringe is used, insulin can be seen leaving the syringe, providing reassurance that the dose has actually been delivered.

However, there are also many disadvantages to using vials and syringes. Because patients must draw up their own insulin doses, there is a risk of inaccurate dosing, especially if a small dose is needed. Some people find that it is more cumbersome to use a vial and syringe than an insulin pen. Using a syringe, which is traditionally associated with illness, is an unpleasant reminder to some patients that they have a chronic disease. Administering insulin with a syringe may be perceived as less discreet than using a pen, and considerable social stigma surrounds syringe use in the US. This may be particularly problematic for those who lead active lives or travel extensively. Although various assistive devices are available, many people with limited manual dexterity or vision find it difficult to use a vial and syringe. Unlike administration with an insulin pen, when needles as short as 4 mm can be used, syringe needles less than 8 mm in length are not available, due to compatibility issues with some vial stoppers.
Following the discovery of insulin in the 1920s, insulin was administered using a glass syringe with a removable needle, both of which had to be disinfected by boiling after each use. Today’s plastic syringes come with attached needles and should be used only once. This slide focuses on insulin syringes used to administer U-100 insulin, by far the most commonly used insulin in the US. To facilitate accurate reading of the marking scale, patients should use the smallest syringe that holds their entire insulin dose. Recommended syringe sizes are 3/10 mL for a dose of ≤30 units, 1/2 mL for a dose of ≤50 units, and 1 mL for a dose of ≤100 units. Syringes with a 3/10 mL capacity are available with 1/2-unit or 1-unit markings, 1/2 mL syringes have 1-unit markings, and 1 mL syringes have either 1-unit or 2-unit markings. Traditionally, a 12.7 mm- (1/2 inch) long needle was recommended for patients whose body mass index (BMI) was ≥27 kg/m², and an 8 mm (5/16 in) needle, sometimes called a “short needle,” was recommended for leaner patients. Recently, however, a panel of experts chaired by Anders Frid suggested that all patients who administer their insulin with a syringe should use an 8 mm needle to reduce the risk of injecting insulin into muscle. The needle length determines the injection angle that should be used. Injections with a needle of ≥8 mm are usually given at an angle of 45° or 60° to avoid intramuscular injection. SMBG frequency should be increased when a patient changes from a needle of one length to another to assess for variability of insulin absorption. Standard syringe needles range from 28 gauge (G) to 31G. (Note that larger gauges signify thinner needles, which generally cause less injection discomfort.)

U-500 insulin, which is 5 times more concentrated than U-100 insulin, is sometimes prescribed for highly insulin-resistant patients who would need to take a very high dose of U-100 insulin. To avoid potentially life-threatening dosing errors, U-500 insulin should be administered with a tuberculin syringe.

Used syringes, needles, lancets, and other medical waste must be disposed of properly, in accordance with local regulations.
Many administration aids have been developed to make giving insulin injections easier. They are particularly useful for patients with limited vision or dexterity, who might otherwise have difficulty drawing up accurate doses of insulin and administering them correctly. The Consumer Guide published annually in the January issue of *Diabetes Forecast* magazine is a valuable source of information about injection aids and other insulin delivery products. This information can be supplemented by going to the manufacturer’s website.

The BD Magni-Guide™ is a clear plastic tube that fits over a syringe barrel, magnifying markings 1.7 times. The needle end fits snugly with many types of insulin vials, increasing vial stability while insulin is drawn.

The Count-A-Dose® is a holder that securely positions 1 or 2 insulin vials. An audible click dial enables the patient to count out units of each type of insulin to be added to the syringe.

The Injection Safety Guard is an attachment that fits over the cap of an insulin vial, creating a barrier that protects the hand holding the vial from accidental needle sticks.
This slide shows some other examples of administration aids.

The **Phone Monocle®** (Magnifics) is a soft plastic band that wraps around an insulin pump display to increase type size up to 2×. An accessory called “Merlin’s Window” accessory further increases magnification. Originally developed for cell phones.

The **Safe Shot®** (AliMed) is a guide for a syringe plunger that can be preset so patient draws same insulin dose each time.

The **Securitee Blanket®** (Regato Enterprises, Ltd.) is a bright-colored insulin vial cover that makes vial less likely to break if dropped. Also makes vial easier to see and grip.
Needle insertion aids facilitate insertion of the needle into the skin while concealing the needle and most or all of the body of the insulin syringe or pen. The depth of the injection can be controlled. Many of these aids allow insulin to be inserted with one hand, simplifying the process of injecting insulin into hard-to-reach places.

The Autoject® 2, manufactured by Owen Mumford, is a spring-loaded device. The safety lock prevents accidental firing and the indicator changes color when the injection is complete. The Inject-Ease®, made by AmbiMedInc, is a spring-loaded device whose tip has been designed to reduce injection pain. The Instaject®, manufactured by Medicool, Inc., is spring-loaded and button-activated. It comes with a lancing attachment for gentle finger sticks. The NeedleAid™, made by NeedleAid, Ltd, is a bell-shaped device that provides stability during the injection process. It ensures consistent injection at the proper angle. The NovoPen® 3 PenMate®, manufactured by Novo Nordisk Inc., conceals the needles of NovoPen® 3 and NovoPen® Junior insulin pens. It accurately inserts the needle at 45° and 90° angles and is associated with reduced injection pain compared to manual insertion.
The I-Port® and Insuflon® are insulin infusers, serving as gateways for needles. A small, flexible tube called a cannula is inserted under the skin and remains in place for up to 3 days. When it is time to administer an insulin dose, the needle is inserted into the infuser, injecting insulin into the system but not into the subcutaneous space. Insulin infusers make insulin administration painless and are suitable for use in adults and children.

The I-Port® is a button-shaped device that is inserted into the skin at a 90-degree angle with the needle as the guide. The I-Port® is extremely small, with a diameter of 1.1 inches and a height of 0.4 inches after application. Up to 75 injections can be administered through the I-Port® membrane.

The Insuflon® is a patch-like device that is inserted into the skin at an angle of 20 to 45 degrees with the needle as the guide. The shallow angle of insertion makes this device suitable for children and others with little subcutaneous fat. Insuflon® has a small membrane through which medication can be injected painlessly. At least 75 injections can be made through this membrane. To allow visual inspection of the site, the Insuflon® has a built-in see-through window.

A potential disadvantage of these systems is that they can become displaced or occluded if the device is not removed on schedule or if the cannula crimps.
An insulin delivery option for patients who are reluctant to use needles is the jet injector. Jet injectors, which were introduced in the 1970s, are needleless devices that deliver insulin transcutaneously by an airjet mechanism. They release a fine, high-pressure stream of insulin that penetrates the skin. Some studies have shown that jet injectors are accurate and consistent in terms of the amount of insulin delivered, while others suggest that the depth of penetration, and thus the amount of insulin delivered, is unpredictable.

Although jet injectors may be the insulin system of choice for individuals with true needle phobia, many patients find them too complex and cumbersome to use. Unless they are cleaned at regular intervals, they can become blocked, preventing delivery of the full dose of insulin. They can also cause bruising and discoloration of the skin.

Jet injectors are more expensive than the vial and syringe or pen method of insulin delivery and are infrequently used today.

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Insulin pens are another type of insulin delivery system. The first manufactured insulin pen, the Novo Nordisk NovoPen®, was introduced in 1985. Today, insulin pens are used by about 15% of US patients with diabetes who treat their diabetes with insulin. This is in sharp contrast to the situation in Europe, where the majority of patients use a pen rather than a vial and syringe to administer insulin. The two basic types of insulin pens are reusable, or durable, pens and disposable pens. Reusable pens deliver insulin via cartridges that are purchased separately. Disposable pens come with an installed, non-removable insulin cartridge.

Currently available reusable insulin pens available in the United States are the:
- Autopen®, manufactured by Owen Mumford
- HumaPen® LUXURA™ HD, manufactured by Eli Lilly
- HumaPen® MEMOIR™, manufactured by Eli Lilly
- NovoPen® 3, manufactured by Novo Nordisk
- NovoPen® Junior, manufactured by Novo Nordisk

Available disposable pens are the:
- Humalog® KwikPen™, manufactured by Eli Lilly
- Original Prefilled (Humalog®) Pen, manufactured by Eli Lilly
- FlexPen®, manufactured by Novo Nordisk
- SoloSTAR®, manufactured by sanofi-aventis
Eli Lilly and Company manufactures 2 types of durable pen, the HumaPen® LUXURA™ HD and the HumaPen® MEMOIR™. Both are used with Humalog® cartridges. The HumaPen® LUXURA™ HD delivers insulin in half-unit increments, up to 30 units at a time. Since the pen can dispense half units of insulin, it is suitable for children and others who require small doses. The pen is green and made of metal. The HumaPen® MEMOIR™ delivers insulin in 1-unit increments, up to 60 units at a time. It has a digital display with memory, which allows users to see the time, date, and amount of the last 16 doses delivered. The nonreplaceable battery has a 3-year lifespan. The pen is burgundy and made of metal.

Novo Nordisk manufactures 2 types of durable pen, the NovoPen® 3 and the NovoPen® Junior. Both are used with NovoLog® (insulin aspart) cartridges. The NovoPen® 3 delivers insulin in 1-unit increments, up to 35 units at a time. It is available in silver, green, or blue and is made out of metal. The NovoPen® Junior is intended for children. The minimum dose of insulin is 1 unit. After that, it delivers insulin in half-unit increments, up to 35 units at a time. The pen, which is made of aluminum and plastic, is blue, with colorful detailing.
Owen Mumford manufactures the Autopen® Classic, which is used with Humalog® (insulin lispro) cartridges. Two models are available: a 1-unit increment version that dispenses up to 21 units at a time, and a 2-unit increment version, which can dispense up to 42 units at a time.

The Autopen® differs from other insulin pens in that the delivery button is on the side, not at the end of the pen. This arrangement allows the hand to hold the pen closer to the injection site, permitting a more stable injection process. Because insulin is delivered with a spring mechanism, the pressure needed to press the button is the same regardless of the dose size or needle gauge. The Autopen® Classic is available in blue or green.
Eli Lilly and Company manufactures 2 types of disposable pen, the Humalog® KwikPen™ and the Original Prefilled Pen.

Three kinds of insulin are available in the Humalog KwikPen™: Humalog® (insulin lispro), Humalog® Mix75/25™ (75% insulin lispro protamine suspension and 25% insulin lispro injection), and Humalog® Mix50/50™ (50% insulin lispro protamine suspension and 50% insulin lispro injection). The Humalog® KwikPen™ delivers insulin in 1-unit increments, up to 60 units at a time. The body of the pen is blue, with labels of different colors for different types of insulin. Label colors are burgundy and white for Humalog®, yellow and white for Humalog® Mix75/25™, and burgundy, red, and white for Humalog® Mix50/50™.

Two kinds of insulin are available in the Original Prefilled Pen: Humulin® N (NPH insulin) and Humulin® 70/30 (70% human insulin isophane suspension and 30% human insulin injection). Lilly is no longer manufacturing the Original Prefilled Pen with Humalog®, Humalog® Mix75/25™, or Humalog® Mix50/50™. The Original Prefilled Pen delivers insulin in 1-unit increments, up to 60 units at a time. The body of the pen is white, with different colored labels for different types of insulin. Label colors are blue, green, and white for Humulin® N and blue, brown, and white for Humulin® 70/30.
The FlexPen® is a disposable pen manufactured by Novo Nordisk. Three kinds of insulin are available in the FlexPen®: Levemir® (insulin detemir), NovoLog® (insulin aspart), and NovoLog® Mix 70/30™ (70% insulin protamine suspension and 30% insulin aspart injection). The FlexPen® delivers insulin in 1-unit increments, up to 60 units at a time. These pens are color-coded to reduce the risk of medication errors. Pens containing Levemir® are green and blue, with green and white labels. Pens containing NovoLog® are orange and blue, with orange and white labels. Pens containing NovoLog® Mix 70/30™ are blue and white, with blue and white labels.

Sanofi-Aventis manufactures the SoloSTAR® disposable pen. Two kinds of insulin are available in this pen: Apidra® (insulin glulisine) or Lantus® (insulin glargine). The SoloSTAR® delivers insulin in 1-unit increments, up to 80 units at a time. Pens containing Apidra® are blue and those containing Lantus® are gray.
Insulin pens have many advantages. They are portable, compact, and discreet, thereby encouraging lifestyle flexibility. They often improve dosing accuracy, especially for patients who are using low insulin doses. Their large dose display windows compensate for visual limitations, and their dosing buttons are easy to push, simplifying insulin delivery for patients with limited manual dexterity. Most participants in clinical studies preferred insulin pens to vials and syringes and reported that using insulin pens improved their quality of life. These findings suggest that using an insulin pen may promote patient’s adherence to their insulin regimen.

However, insulin pens also have some disadvantages. Different types of insulin cannot be mixed by the patient and then inserted into the pen. Therefore, persons who use more than one type of insulin are limited to the premixed formulations that are commercially available for use in pens. If multiple types of insulin are required, the patient must take another injection using a second pen. Another important disadvantage is that air and non-inert biological matter, such as epithelial cells, may enter the pen. To reduce the risk for contamination, the pen needle must be removed as soon as insulin has been administered, needles should never be reused, and insulin pens must never be shared. Although insulin pens are extremely reliable, they are also mechanically complex, so that there is a greater potential for malfunction than there is with a syringe. Furthermore, today’s insulin pens are rather large. Pens must be primed, insulin leakage may occur at the injection site, and there is no confirmation that a complete dose has been given. Additionally, the plastics used in insulin pens must be disposed of.

Many factors affect the cost of insulin pen therapy. Limited insurance coverage is available for insulin pens. For the patient without medical insurance or whose insurance does not cover their cost, pens are more expensive than vials and syringes unless the individual uses less than 1 insulin vial per month. Since insulin vials must be discarded within 1 month of being opened, using an insulin vial may result in substantial waste for some patients. While an insulin vial holds 1000 units of insulin, an insulin pen cartridge holds only 300 units. This lower capacity is often beneficial for patients treated with low doses of insulin.
The following are general instructions for insulin pen users.

- Become familiar with manufacturers’ instructions for the specific pen to be used, and take advantage of supplemental materials, including videos, at the manufacturer’s website. Follow all instructions about needle attachment, dose selection and correction, and, for durable pens, cartridge insertion.
- Keep insulin cartridges and disposable insulin pens in a part of the refrigerator where the insulin will not freeze. Never refrigerate a durable insulin pen and do not refrigerate a disposable pen once it has been used. Thirty days after its first use, discard a partially used insulin cartridge or disposable pen, following local regulations about disposal.
- NPH insulin and premixed insulin must be thoroughly resuspended before injection. Pens should be gently rolled and/or tipped, but not shaken, for 20 cycles until the crystals go back into suspension and the solution becomes milky white.
- Following the manufacturer’s instructions, prime the pen before each injection. Attach the needle to the pen, select the test dose specified by the manufacturer, hold the pen with the needle pointed upward, and push the button. Insulin should appear at the tip of the needle. If it does not, follow the manufacturer’s instructions about how often to repeat the procedure before changing the needle or taking other action.
- Keep fingers away from the injection button while inserting the pen into subcutaneous tissue.
- After pressing the injection button all the way in, keep the pen in place for at least 10 seconds to ensure complete insulin delivery.
- Remove the pen needle as soon as the injection has been given and replace the pen cap to reduce the risk of contamination and insulin leakage. Dispose of the needle according to local regulations.
- To prevent infection, never reuse needles or share your pen with anyone else.
Recently, many hospitals have begun to transition from the use of patient-specific insulin vials to patient-specific pens, mainly to reduce insulin waste. An estimated 30% of hospitals have completed the conversion. An 18-week study conducted in the medical cardiology units of 2 hospitals compared the use of vials and syringes equipped with safety needles to the use of pens with safety needles. The study found that 77% of nurses were either neutral to or favored replacing insulin vials with pens and 63% of nurses reported that patients liked the pens. Of 3 needle stick injuries, 2 were from syringes and 1 was from a pen needle. Glycemic control improved by 2% during the study. According to financial projections for the 2 hospitals, there would be cost savings of $12,000 per month per institution if pens were used throughout the hospitals.

Although, as this study suggests, hospitals can transition successfully to insulin pens, other studies have identified problems with pen use in hospitals and other health care institutions. Bloodborne infections can occur when a single insulin pen is used to administer insulin to more than one patient. Large pockets of air can develop in a cartridge when the cartridge is used as a vial and insulin is aspirated from the cartridge with a syringe. Labels with the patient’s name, location, and identification number are sometimes applied over the insulin pen label, concealing important information. Recently, pen manufacturers have introduced color-coding systems to help to differentiate various types of insulin and reduce the risk of medication errors related to administering the wrong type of insulin. Nevertheless, it is still important for the manufacturer’s label to remain visible.

Recommendations for using insulin pens in the inpatient health care setting are:

- Never use an insulin pen for more than one patient
- Never use an insulin pen cartridge as an insulin vial
- Do not cover the manufacturer’s label on an insulin pen with another label
- Always administer insulin with a safety needle
The health care provider should ask the following questions when helping a patient to select an insulin pen.

- Does the pen contain the type of insulin the patient will be using?
- How accurate is the pen?
- Does it administer insulin in the necessary increment?
- Does it administer a large enough dose in a single injection?
- Is it difficult to learn how to use the pen?
  - Removing and replacing cap
  - Removing and replacing needle
  - Setting, reading, and correcting dose
  - Effort needed to inject dose
- Does the patient prefer a durable or disposable pen?
- Are the pen’s design and aesthetics acceptable?
- Is the pen covered by the patient’s insurance?
In addition to the advantages we have already discussed, another advantage of administering insulin with a pen is that most patients can use extremely small and thin needles, potentially reducing injection discomfort. The table on this slide shows the sizes of needles made by 3 manufacturers: BD, Novo Nordisk, and Owen Mumford. The length of these needles ranges from 4 mm (5/32 in) to 12.7 (1/2 in) and their gauge ranges from 29 to 32.

Currently, the BD Ultra-Fine™ Nano is the shortest available pen needle, with a length of 4 mm (5/32 in) and a gauge of 32. In a study that compared this needle with a 5 mm × 31G needle and an 8 mm × 31G needle, the 4 mm needle was rated significantly less painful and was preferred by approximately two thirds of patients. Glycemic control and injection site leakage were similar with each type of needle. Studies in patients whose BMI ranged from 20 to 49 kg/m² have shown that the Nano needle is as effective as longer insulin pen needles, irrespective of body size. Another noteworthy pen needle is the Novo Nordisk NovoTwist®, which was launched in the US in April 2011. The NovoTwist® attaches to Novo Nordisk prefilled pens with a single twist, and is the first single-twist needle approved for use in the US. With this NovoTwist®, an audible and tactile click confirms that the needle is successfully attached to the pen.

Patients should receive education about the proper injection angle for the needle they will be using. In adults, injections with 4, 5, and 6 mm needles should be given at a 90° angle.
Hundreds of thousands of needle puncture wounds occur throughout the world each year, exposing patients, caregivers, health care providers, and sanitation workers to biological material. Today, needle stick injuries account for up to 80% of all accidental exposures to blood.

Insulin pen safety needles, including the BD Autoshield™ and the Novo Nordisk NovoFine® Autocover®, are designed to prevent needle stick injuries. These devices have sliding needle shields that retract only while an insulin injection is being given. Following the injection, the shield permanently locks into place so the needle cannot be reused. Another benefit of a safety needle is that the actual needle is concealed at all times, making it more acceptable than a conventional needle to many patients with needle phobia.

The BD Autoshield™ is a 29G needle that comes in 2 lengths: 5 mm (3/16 in) and 8 mm (5/16 in). Once the injection is given and the shield slides back over the needle, metal tabs appear, showing that the device is permanently locked. The NovoFine® Autocover® is a 30G, 8 mm (5/16 in) safety needle. After the injection has been given, a red indicator appears, showing that the device is locked.
A laboratory study compared the accuracy of 4 insulin pens. Two of the pens, the HumaPen® LUXURA™ and the OptiClik®, were durable and two, the FlexPen® and the SoloSTAR®, were disposable. (Note that sanofi-aventis has recently discontinued sales of the OptiClik® pen in the US.) Experienced investigators dispensed multiple 10- and 30- unit doses of insulin, following the manufacturers’ instructions for use. The insulin dispensed from the pen was then weighed on a pharmaceutical balance. The main outcome measure was the accuracy of dose delivery from the 4 types of pens compared with the specified doses.

The mean dosing accuracies of all pens were within the range specified in International Organization for Standardization (ISO) guidelines. As shown in this slide, the percentage of dosage deviations was significantly lower with the FlexPen® and the HumaPen® LUXURA™ than with the OptiClik® and the SoloSTAR®.
This slide summarizes results from a study that assessed patient satisfaction with the FlexPen® insulin pen or the InnoLet® doser compared with vial and syringe insulin delivery. (Note that the InnoLet® doser is a device that allows patients to select the correct dose of insulin using a large dial. It is no longer available for purchase in the US.)

Participants in this study were hospitalized patients with diabetes who were recruited from 2 general medical-surgical units. Prior to discharge, they completed a survey about their satisfaction with the insulin delivery method they used in the hospital. Thirteen percent of patients had type 1 diabetes and the others had type 2 diabetes, but responses were not analyzed by diabetes type.

The main differences between the responses of the pen or doser group and the vial and syringe group were that a significantly higher proportion of patients who had received insulin using a pen or doser wished to continue this method of insulin delivery at home, and a significantly greater proportion of patients in the pen or doser group would recommend the device they used to other people with diabetes.
Several studies have shown that using an insulin pen rather than a vial and syringe is associated with improved adherence and economic benefits. For example, Cobden and colleagues evaluated the impact of switching from vial and syringe to a prefilled insulin analog pen in patients with type 2 diabetes. This retrospective analysis of an integrated medical/pharmacy claims database covering greater than 40 million lives included 57 managed care plans across the US. The investigators identified 486 patients who had switched from insulin delivery with a vial and syringe to delivery with a biphasic insulin aspart 70/30 pen. Participants’ mean age was 45.1 years, and 56.4% were male.

As shown in this slide, overall treatment adherence as measured by the medication possession ratio (MPR) improved significantly after the switch. (The MPR, a common measure of compliance, was defined in this study as the number of days of drug supply divided by the number of days between the first and last prescription fill. Thus, a patient with a 30-day supply of medicine and a 30-day interval between the first and last fill would have an MPR of 1.0, while a patient with a 60-day interval would have an MPR of 0.5.)

Also during the study of Cobden et al, the percentage of patients with optimal adherence (MPR ≥ 80%) increased significantly after conversion from a vial and syringe to an insulin pen. Other significant differences following the switch were reductions in annual total healthcare costs, annual costs for oral antidiabetic agents per patient, and costs per hypoglycemic events per patient. The likelihood of experiencing hypoglycemia after conversion to an insulin pen also decreased significantly and was associated with significant reductions in emergency department and physician visits related to hypoglycemia.
To identify factors differentiating patients who use insulin pens from those who use vials and syringes, Rubin and Peyrot conducted a telephone survey of 300 insulin pen users and 300 vial and syringe users. Participants were 35 years of age or older, had taken insulin for at least 1 year, and had heard of insulin pens. Almost all participants had type 2 diabetes.

As shown on this slide, regression analysis showed that 6 factors were significantly associated with insulin pen use. These were: the patient performs SMBG frequently, the patient is currently employed, the patient believes that insulin pens are not costly, the physician identifies an insulin pen as a treatment option, the patient believes that insulin pens facilitate self-care, and the physician encourages pen use. By far the most important of these factors was encouragement of pen use by the physician. The patient whose physician encouraged insulin pen use was almost 136 times as likely to use an insulin pen as a patient whose physician did not discuss the pen as an insulin delivery option or discouraged pen use.

The investigators concluded that there is a need to increase physician awareness of the potential benefits of pen use, including improved health outcomes, treatment satisfaction, and adherence to the therapeutic regimen. Additionally, clinicians should talk to their patients about pen use to insure that they are aware of this potentially beneficial insulin delivery option.

### Factors Differentiating Insulin Pen Users From Non-Users

Patients ≥ 35 Years Who Had Been Taking Insulin for ≥ 1 Year, Had Heard of Insulin Pens, and Were Using (n = 300) or Not Using (n = 300) Insulin Pen

<table>
<thead>
<tr>
<th>Factor</th>
<th>Odds Ratio of Using (Versus Not Using) Insulin Pen</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient performs SMBG frequently</td>
<td>2.16</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Patient is currently employed</td>
<td>2.53</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Patient believes that pens are not costly</td>
<td>4.79</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Physician identifies pen as an option*</td>
<td>14.09</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Patient believes that pen facilitates self-care</td>
<td>20.15</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Physician encourages pen use†</td>
<td>135.63</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

*Nearly all patients had type 2 diabetes.
†Versus physician who did not discuss pen or discouraged pen use.

Virginia is a 72-year-old African American woman. She weighs 156 pounds, is 68 inches tall, and has a BMI of 23.7 kg/m². She is married and has 2 grown children. Until her retirement 5 years ago, she was a supervisor in the purchasing department of a large city. Now she and her husband watch their grandchildren 3 days per week and participate in many community activities.

Virginia was diagnosed with type 2 diabetes 12 years ago. Her A1C is 9.1% and her BG ranges from 160 to 220 mg/dL throughout the day. She has moderate nonproliferative diabetic retinopathy. She has used insulin, administered with a vial and syringe, for 7 years. Currently she uses 70/30 premixed insulin (20 units before breakfast and dinner).

Other medical issues are hyperlipidemia and osteoarthritis.

Virginia’s primary health care practitioner has referred her to the CDE for diabetes self-management education (DSME).
During her first meeting with the CDE, Virginia reports that her efforts to manage her diabetes are inconsistent. She says she is careful about food selection and portion control and walks for up to 30 minutes on days when her arthritis is not too painful.

She explains that most of her problems with diabetes management are related to taking insulin. She finds it challenging to draw up a dose of insulin because of difficulty manipulating the vial and syringe and reading the lines on the syringe. Even more annoying to her is the way that taking insulin governs when and how much she eats. Now that she is retired, she is unwilling to eat all of her meals at specified times and would like to be able to adjust her food intake based on her appetite.

She says she finds it too limiting to wait 30 minutes after taking her premixed insulin to eat breakfast or dinner. Instead, she usually takes insulin right before meals. She often forgets to take insulin when she dines away from home. Even when she remembers, she is reluctant to use a vial and syringe in public.

Case 1: Patient Concerns at First Visit With CDE

- Difficulty drawing up insulin dose due to problems with dexterity and vision
- Dislikes having to eat at specified times
- Wants to be able to adjust food intake based on appetite
- Finds it too limiting to wait 30 minutes after taking premixed insulin to eat; usually takes insulin right before breakfast and dinner
- Often forgets to take insulin when she dines away from home; if she remembers, reluctant to use vial and syringe in public
The CDE contacted the primary care physician and recommended that Virginia’s insulin delivery system be changed to an insulin pen. The CDE also recommended that basal and mealtime insulin be substituted for premixed insulin to allow flexibility in Virginia’s busy schedule.

The physician was amenable to the CDE’s recommendations and started Virginia on 15 units of a long-acting insulin analog at bedtime. The physician also asked the CDE to determine Virginia’s I:C ratio.

Virginia was started on a rapid-acting insulin analog at mealtime, using a 1:15 I:C ratio. She demonstrated a good understanding of how to dose mealtime insulin based on the carbohydrate content of her meals.

When she experienced an approximately 55-point rise in her BG level 2 hours after meals, her I:C ratio was changed to 1:10. Using this ratio, Virginia took 4 to 7 units of a rapid-acting insulin analog at each meal based on carbohydrate content.

Virginia’s BG log showed that her fasting BG levels ranged from the 130s through the 140s. However, since her bedtime BG values were at target, increasing her dinnertime dose of rapid-acting insulin analog to achieve tighter control was not a solution. Therefore, her dose of long-acting insulin analog was increased to a total of 28 units at bedtime over the next month.
The table on this slide shows Virginia’s BG log 3 months after her regimen change. The BG values recorded in the log suggest that her I:C ratio and bedtime dose of long-acting insulin analog are adequate. (Note that during the 8-day period when she kept this log, Virginia did not perform SMBG more than 4 times per day and usually performed it only twice daily. However, she always measured her BG before and after the same meal. This technique, called “bracketed testing,” is a practical way of providing the patient and health care provider with the necessary information, without placing onerous demands on the patient.)

Virginia reports that she is very pleased with her improved glycemic control, how she feels, and the greater mealtime flexibility. She finds it convenient to dial up a dose of insulin and carry an insulin pen in her purse. She also has an easier time remembering to take insulin when not eating at home, and is not embarrassed to use her pen in public.

Three months after changing her insulin regimen, her A1C is 7.2%.
An accurate statement about insulin pens is: __________.

a. all currently available insulin pens administer insulin in 1/2-unit increments
b. both durable and disposable pens should be refrigerated after each use
c. treatment adherence may increase when a patient switches from vial and syringe to a pen
d. today’s insulin pen needles are longer than those used with disposable syringes
The correct answer is c.

Treatment adherence may increase when a patient switches from vial and syringe to a pen.
Another insulin delivery option is continuous subcutaneous insulin infusion (CSII). CSII is also referred to as “insulin pump” therapy. The proportion of patients who use CSII has increased steadily since the first pump became available in 1974. Today, between 20% and 30% of patients with type 1 diabetes and less than 1% of those with type 2 diabetes use pumps.

CSII consists of the continuous delivery of short-acting insulin through a cannula (short flexible tube) inserted in the subcutaneous tissue. With most insulin pumps, insulin is transported from the reservoir in the pump to the body by flexible 24G to 31G tubing. With the OmniPod, however, the patient wears a “Pod” on the surface of the body and insulin enters the body from an insulin reservoir in the Pod through a cannula. A remote Personal Diabetes Monitor (PDM) wirelessly regulates insulin flow.

CSII therapy delivers basal insulin over a 24-hour period. Based on the individual patient’s needs, pumps can be programmed to deliver different basal rates throughout the day, reducing the risk of hypoglycemia and hyperglycemia. Premeal and snack bolus doses can be selected to cover the user’s estimated carbohydrate intake at mealtime and correct for out-of-range BG readings. Only regular human insulin and rapid-acting insulin analogs are approved and suitable for pump use. Intermediate- or long-acting insulins are not suitable for use in an insulin pump.

### Continuous Subcutaneous Insulin Infusion/“Insulin Pump” Therapy

- Used by 20–30% of patients with type 1 diabetes and <1% of those with type 2 diabetes
- Continuous delivery of short-acting insulin through cannula (short flexible tube) or needle inserted in subcutaneous tissue
- Insulin transported from insulin reservoir in pump or in “Pod” worn on body
- Delivers basal insulin over 24-hour period; bolus doses administered to cover meals and snacks
- Only regular human insulin and rapid-acting insulin analogs approved and suitable for pump use

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Five types of insulin pumps were available in the US in May 2011. These are:

- ACCU-CHEK® Spirit, manufactured by Roche Insulin Delivery Systems
- Dana Diabecare® IIS, manufactured by Sooil Development
- MiniMed Paradigm® REAL-Time Revel, manufactured by Medtronic Diabetes
- OmniPod®, manufactured by Insulet Corporation
- OneTouch® Ping®, manufactured by Animas Corporation

All of these devices are extremely small. Their main component is about 3 inches long, 2 inches wide, and 0.8 inch thick, and weighs about 4 ounces.

Major differences among these systems are whether they are used with infusion sets, their basal and bolus ranges, and whether they interact with BG meters and continuous glucose monitors (CGMs). Important features of each insulin pump are discussed in the next 5 slides.
# ACCU-CHEK® Spirit

<table>
<thead>
<tr>
<th>Feature</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin capacity</td>
<td>315 units</td>
</tr>
<tr>
<td>Infusion set</td>
<td>Compatible with all standard, Luer-lock connectors</td>
</tr>
<tr>
<td>Basal range</td>
<td>0.1 to 25 units/h, in 0.1-unit increments</td>
</tr>
<tr>
<td>Bolus range</td>
<td>0.1 to 25 units in increments of 0.1, 0.2, 0.5, and 2 units for standard boluses; extended boluses adjustable in 0.1-unit increments</td>
</tr>
<tr>
<td>Food database</td>
<td>900+ preloaded foods, room for 1200 items</td>
</tr>
<tr>
<td>BG meter interaction</td>
<td>No</td>
</tr>
<tr>
<td>CGM interaction</td>
<td>No</td>
</tr>
<tr>
<td>Special features</td>
<td>Includes a backup pump that operates for up to 180 days and PDA that calculates boluses. “Skins” available for customization. Works with ACCU-CHEK® 360° software, insulin pump configuration software, and Smart Pix® device reader. Software and reader compatible with Windows (except Windows 7), but not Mac</td>
</tr>
</tbody>
</table>

BG = blood glucose; CGM = continuous glucose monitor; PDA, personal digital assistant.


The ACCU-CHEK® Spirit has a 315-unit insulin cartridge. It is compatible with standard infusion sets with Luer-lock connectors. (Recall that Luer connection systems are the standard way of joining catheters, IV tubes, and other commonly used medical devices together. Luer connectors consist of round, male and female interlocking tubes. An outer rim of threading, called a Luer lock, securely holds different parts of the device together.)

The ACCU-CHEK® Spirit has a basal range of 0.1 to 25 units of insulin per hour in 0.1-unit increments. Its bolus range is 0.1 to 25 units in increments of 0.1, 0.2, 0.5, 1, and 2 units for standard boluses. Extended boluses are adjustable in increments of 0.1 units. By using ACCU-CHEK® Pocket Compass® software and personal digital assistant (PDA), the user can access a food database with over 900 preloaded foods. A total of 1200 items, including user-selected foods, can be stored. The ACCU-CHEK® Spirit does not interact with a BG meter or CGM.

The display can flip 180 degrees for easy reading on different parts of the body. The package includes a backup pump that operates for up to 180 days and a PDA that calculates boluses. “Skins” are available for customization.

The ACCU-CHEK® Spirit can send data to the PDA wirelessly. This insulin pump works with ACCU-CHEK® 360° software, insulin pump configuration software, and a Smart Pix® device reader for data management. The software and reader are compatible with Windows (except Windows 7), but not with the Mac operating system.
The Dana Diabecare® IIS has a 300-unit insulin cartridge. It is compatible only with Sooil infusion sets. It has a basal range of 0.01 to 16 units of insulin per hour in 0.1-unit increments. Its bolus range is 0.1 to 10 units in 0.1-unit increments, and from 10 to 87 units in 1-unit increments. It does not have a food database and does not interact with a BG meter or CGM.

The menu of the Dana Diabecare® IIS uses icons instead of words. This pump is available in a choice of 5 colors. It does not work with data management software.
The MiniMed Paradigm® REAL-Time Revel comes in two models. Model 523 has a 176-unit insulin reservoir and Model 723 can be ordered with either a 176- or a 300-unit reservoir. The REAL-Time Revel is compatible with Medtronic infusion sets and some other sets, as well. It has a basal range of 0.025 to 35 units of insulin per hour in 0.025-unit increments. Its bolus range is 0.025 to 25 units. It can be dosed in increments of 0.025 units up to 0.975 units and in increments of 0.05 units for amounts larger than 0.975 units. It does not have a food database.

Currently, the OneTouch® UltraLink™ meter can be used to wirelessly send test results to the REAL-Time Revel pump. Soon, however, the Revel will be linked to the Bayer Contour® USB meter and the UltraLink™ meter will be phased out. As of May 2011, patient software for the Contour® meter is compatible with both Windows and Macintosh, but its professional software is not Macintosh compatible.

The REAL-Time Revel is a combination pump and CGM, and uses a sensor to wirelessly transmit continuous glucose readings to the pump. Hundreds of “skins” are available to enable the owner to customize the pump. The REAL-Time Revel works with CareLink® Personal software to upload and manage pump and CGM data. This software is compatible with both Windows and Macintosh computers. The CareLink® Pro software is compatible with Windows computers only.
The OmniPod® is the world’s first tubing-free insulin pump. It includes 2 components, a Pod that is worn on the body and a Personal Diabetes Manager (PDM) that controls the Pod. The Pod, which holds 200 units of insulin, comes with a built-in infusion set, cannula, and automated inserter.

The OmniPod® has a basal range of 0.05 to 30 units of insulin per hour in 0.05-unit increments. Its bolus range is 0.05 to 30 units in increments of 0.05, 0.1, 0.5, or 1 unit. The PDM has a food database that includes more than 1000 common foods and their nutrition information. It also stores up to 36 preset carbohydrate values for user-selected foods. A FreeStyle® BG meter is built into the PDM. The OmniPod® does not interact with a CGM.

The Pod is waterproof to a depth of 8 feet. Seven “skins” are available for customization. The system works with Abbott’s CoPilot® data management software. This software is compatible with Windows (except Windows 7), but not with the Mac operating system.
The OneTouch® Ping® is a 2-part system consisting of an insulin pump and a meter remote. The meter remote controls pump functions from up to 10 feet away. The pump has a 200-unit insulin cartridge. It is compatible with all standard, Luer-lock infusion sets. It has a basal range of 0.025 to 25 units of insulin per hour in 0.025-unit increments. Its bolus range is 0.05 to 35 units in 0.05-unit increments. The meter remote stores nutrition information on up to 500 foods, and patients can add information about additional foods to the database. The system does not interact with a CGM.

The pump is waterproof up to a depth of 12 feet. Eight pump and meter “skins” are available for customization.

The OneTouch® Ping® works with ezManager® Max data management software. Software is compatible with Windows and Mac operating systems.

The OneTouch® Ping® also works with Diasend®, a diabetes management system that allows patients to store, review, and print their insulin pump and BG meter data on the Diasend® website. Once patients have uploaded their data at home, their health care provider can review it between or during appointments. Diasend® is compatible with Windows and Mac.

<table>
<thead>
<tr>
<th>Feature</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Insulin capacity</td>
<td>200 units</td>
</tr>
<tr>
<td>Infusion set</td>
<td>Compatible with all standard, Luer-lock systems</td>
</tr>
<tr>
<td>Basal range</td>
<td>0.025 to 25 units/h, in 0.025-unit increments</td>
</tr>
<tr>
<td>Bolus range</td>
<td>0.05 to 35 units in 0.05-unit increments</td>
</tr>
<tr>
<td>Food database</td>
<td>500 preloaded foods; users can customize database</td>
</tr>
<tr>
<td>BG meter interaction</td>
<td>Yes, meter sends results wirelessly to pump</td>
</tr>
<tr>
<td>CGM interaction</td>
<td>No</td>
</tr>
<tr>
<td>Special features</td>
<td>Includes pump and meter remote. Remote controls pump functions from up to 10 feet away. Pump is waterproof to depth of 12 feet. Eight pump and meter “skins” available. Works with ezManager® Max data management software, which is compatible with Windows and Mac. Also works with Diasend® web-based diabetes management system.</td>
</tr>
</tbody>
</table>
Among currently available insulin delivery systems, pumps most closely mimic the body’s physiologic release of insulin. Pumps deliver very precise doses of insulin throughout the day, and insulin absorption is stable and predictable. Flexible programming options permit increased lifestyle flexibility. Excellent glycemic control can be achieved without the need for multiple daily injections of insulin. Today’s equipment used for CSII therapy is small, lightweight, and discreet. In studies that included patients with type 1 and type 2 diabetes and adults, adolescents, and children, participants often preferred CSII therapy over MDI therapy. Furthermore, using an insulin pump may improve treatment adherence.

Despite these advantages, insulin pump therapy also has some disadvantages. It is technically demanding and requires an ongoing high level of motivation. Although insulin pumps have become increasingly dependable over the years, the potential remains for malfunction of the pumping mechanism or occlusion of the tubing or cannula. If mechanical problems of this type are not detected and corrected quickly, the potential exists for developing hypoglycemia or ketoacidosis. Some patients, particularly adolescents, may be self-conscious about being attached to what they perceive as a “foreign object.” The initial purchase of a pump is expensive, and patients’ insurance may not cover CSII therapy. Currently, few insurers offer CSII reimbursement for patients with type 2 diabetes.

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**Advantages and Disadvantages of CSII Therapy**

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Most closely mimics body’s physiologic insulin secretion</td>
<td>• Technically demanding</td>
</tr>
<tr>
<td>• Increased dosing accuracy</td>
<td>• Requires high degree of motivation</td>
</tr>
<tr>
<td>• Predictable insulin absorption</td>
<td>• Potential for occlusion of tubing or cannula and mechanical failure, possibly resulting in hypoglycemia or ketoacidosis</td>
</tr>
<tr>
<td>• Flexible programming, resulting in increased lifestyle flexibility</td>
<td>• Patients may be self-conscious about being attached to “foreign object”</td>
</tr>
<tr>
<td>• Multiple injections eliminated</td>
<td>• Initial purchase is expensive; limited insurance coverage</td>
</tr>
<tr>
<td>• Equipment is small, lightweight, discreet</td>
<td></td>
</tr>
<tr>
<td>• Preferred over MDI therapy by many patients</td>
<td></td>
</tr>
<tr>
<td>• May improve treatment adherence</td>
<td></td>
</tr>
</tbody>
</table>

The Consensus Panel on Insulin Pump Management of the AACE has identified the characteristics of candidates who are well suited for CSII therapy. These individuals have type 1 diabetes or type 2 diabetes with absolute insulin deficiency. They currently perform at least 4 insulin injections and 4 SMBG measurements daily. Suitable candidates are motivated to achieve tighter BG control. In addition, they are both willing and intellectually able to undergo training and perform ongoing maintenance and troubleshooting. They are willing to perform frequent SMBG or use CGM (at least initially). They are emotionally mature, stable life situation, willing to maintain regular contact with health care team. Suitable candidates also have adequate insurance or financial resources to cover the cost of pump and supplies.

The Consensus Panel on Insulin Pump Management of the AACE has identified the characteristics of candidates who are well suited for CSII therapy. These individuals have type 1 diabetes or type 2 diabetes with absolute insulin deficiency. They currently perform at least 4 insulin injections and 4 SMBG measurements daily. Suitable candidates are motivated to achieve tighter BG control. In addition, they are both willing and intellectually able to undergo intensive training and to perform ongoing maintenance and troubleshooting. They are willing to perform frequent SMBG and/or to use CGM, at least during the initial period of CSII therapy. They are emotionally mature and have a stable life situation. They are willing to maintain regular contact with the health care team, which typically consists of a physician, and CDEs including a registered nurse (RN) and registered dietitian (RD).

Suitable candidates also have adequate insurance or financial resources to cover the cost of the pump and related supplies.
The Consensus Panel on Insulin Pump Management of the AACE has identified 3 classes of patients who are suitable candidates for CSII therapy based on their clinical characteristics.

Patients in class 1, the highest priority group, are individuals with type 1 diabetes who do not reach glycemic goals despite adherence to a maximal MDI program, especially if they have very labile diabetes, frequent severe hypoglycemia and/or hypoglycemia unawareness, significant “dawn phenomenon,” or extreme insulin sensitivity. Other patients in class 1 are members of special populations, such as women with diabetes in the preconception period, pregnant women, children with eating problems, and competitive athletes.

Patients in class 2, the intermediate priority group, are individuals with type 1 diabetes who are on a maximized basal-bolus MDI insulin regimen, regardless of their level of glycemic control and who, after investigation and careful consideration, think CSII would be helpful or more appropriate for lifestyle reasons.

Patients in class 3, the lowest priority group, are selected patients with insulin-treated type 2 diabetes who have any of the following characteristics. They may be C-peptide positive but with suboptimal control on a maximal program of basal/bolus injections. These patients might also experience a substantial “dawn phenomenon,” have an erratic lifestyle, or have severe insulin resistance, making them candidates for U-500 insulin administered by CSII. Also in class 3 are selected patients with other types of diabetes, such as patients who have undergone pancreatectomy.
Successful use of an insulin pump requires basic diabetes self-management knowledge and skills. The health care team working with a candidate for insulin pump therapy should assess the following:

- Knowledge of premeal, postmeal, and bedtime target BG values
- Ability to check BG levels and monitor ketones
- Can treat hyperglycemia
- Knows steps for hypoglycemia detection, prevention, and treatment
- Familiar with management strategies for sick days, travel, holidays, and exercise
- Able to keep food and physical activity logs
- Demonstrates basic and advanced carbohydrate-counting skills

Patients with deficits in any of these areas should receive personalized education to remedy these deficits before proceeding with pump-specific training.
Many patients who have transitioned from MDI to insulin pump therapy report that they received inadequate initial training in using their pump. Insulin pump-specific education should be provided by the patient’s diabetes care team and supplemented with training provided by the pump manufacturer.

Basic topics should include pump and infusion set (or Pod) operation, maintenance, and troubleshooting; infusion site preparation and protection; and the calculation and configuration of basal insulin rates, initial insulin-carbohydrate ratios, correction boluses, and insulin sensitivity. They should also be reminded of the importance of always having access to an alternate insulin delivery system, such as an insulin pen.

Education should also include the treatment of pump related hyperglycemia, monitoring of ketones, insulin replacement when off pump, and alterations for travel, sick days, holidays, exercise etc.

Motivated patients may benefit from advanced training on topics such as adjusting bolus “wizard” settings, configuring different basal settings based on the expected level of physical activity on a specific day, and programming temporary basal settings. It may take patients months or even years to become proficient in using some of their pump’s advanced features.
Approximately 2500 published studies have investigated the efficacy and safety of CSII. Six meta-analyses published between 2003 and 2010 assessed the findings of the best-designed and best-reported of these studies.

With regard to efficacy, these analyses found that in adults, adolescents, and children with type 1 diabetes, CSII results in A1C levels that are lower than, or similar to, those achieved with MDI therapy. In adults with type 2 diabetes, on the other hand, A1C values are similar in patients treated with CSII or MDI therapy.

With regard to safety, many, but not all, analyses identified a reduced risk of hypoglycemia and severe hypoglycemia in patients treated with CSII compared to those treated with MDI therapy.

Although infusion-site infections are uncommon, some patients may experience irritation or inflammation at the infusion site. These local reactions can often be prevented by carefully following instructions about site preparation and cannula insertion techniques, changing the cannula as scheduled, and adhering to the site rotation schedule.
The Equality 1 Study was a case-control study that compared QoL and treatment satisfaction in adults with type 1 diabetes treated with either CSII or MDI therapy. During routine visits to an Italian diabetes clinic, consecutive patients aged 18 to 55 years completed 3 validated scales: the Diabetes-Specific Quality-of-Life Scale (DSQOLS), the Diabetes Treatment Satisfaction Questionnaire (DTSQ), and the SF-36 Health Survey (SF-36).

A total of 1341 patients were enrolled. On the DSQOLS, patients in the CSII group had significantly better (higher) scores than patients in the MDI group for diet restrictions, daily hassles, and fears about hypoglycemia. On the DTSQ, patients in the CSII group had a significantly better (higher) total score than those in the MDI group. There were no significant differences between groups on the SF-36, a QoL measure that is not specific to diabetes. MDI was not superior to CSII on any domain of any of the scales used in the study.
Ricardo is a 49-year-old Hispanic man who is referred by his primary health care provider to a CDE for evaluation. Ricardo weighs 207 pounds, is 72 inches tall, and has a BMI of 28.1 kg/m$^2$. He is married and has 3 children in high school and college. He owns a large landscaping company. Recently, the demands of his job have become more intense and unpredictable because he has added several large commercial clients and lost 2 long-time employees. Although he was accustomed to spending his days managing the company from his office and meeting with clients, he is now spending more time at job sites, digging and planting shrubs and trees. His mealtimes and the length of his work days have become extremely variable.

Ricardo was diagnosed with diabetes 18 years ago, and his most recent A1C was 7.9%. He complains of experiencing hyperglycemic episodes interspersed with hypoglycemia as often as 5 times per week. He demonstrates limited overall knowledge of diabetes self-management. His current insulin regimen includes 36 units of a long-acting insulin analog at 10 p.m. and 8–10 units of a rapid-acting insulin analog at mealtimes. When asked how he determines the dose of premeal insulin to be administered, he replies, “less if I eat a small meal and a little more if I eat a bigger one.”

Ricardo’s symptoms have become so severe that it has become almost impossible for him to handle his work. He tells his primary health care provider that he is willing to perform SMBG as often as necessary and learn new self-management skills to get his BG under control. He notes that his wife, who has always prepared meals that are nutritionally balanced and emphasize vegetables and whole grains, is very supportive of his efforts to stabilize his diabetes.
Ricardo keeps a detailed BG log for 10 days and then meets with the CDE to discuss the results. Recall that the ADA recommends that patients have a preprandial BG level within the range of 70 to 130 mg/dL and a peak postprandial BG level of less than 180 mg/dL. Hypoglycemia is defined as a BG value of less than 70 mg/dL. On Ricardo’s log, high values are indicated in red and low values in blue. Important patterns are shown with boxes.

Review of the log shows that about two thirds of Ricardo’s BG values are either above or below the target range, and that many of the other values are at an extreme end of the recommended range. The extremely high morning fasting BG values on all 10 days, marked on the log with a purple box, indicate that Ricardo experiences the dawn phenomenon.

Analysis of Ricardo’s values over the 10 days reveals 2 basic patterns. August 2 and 7, days when BG values are consistently high throughout the day, are marked with red boxes. Ricardo explains that those were days that he spent in the office and did little physical work. August 3 and 6, days with post-breakfast hypoglycemia and low BG values before dinner, are marked with blue boxes. Ricardo says that those were days on which employees called in sick and he did exceptionally heavy landscaping work.

After reviewing and discussing the BG log, the CDE tells Ricardo that he can achieve tighter BG control, despite his challenging situation, in either of two ways. He can continue to use an MDI regimen if he acquires the skills needed to match his premeal insulin doses to the content of his meals and performs SMBG frequently. It will also be necessary to fine-tune his bedtime dose of long-acting insulin analog to counteract the dawn phenomenon. Alternatively, Ricardo can begin insulin pump therapy if he is willing to make the commitment to mastering basic self-care skills, learn how to match his premeal insulin doses to the content of his meals, perform SMBG frequently, and learn how to use and troubleshoot an insulin pump. Overall, the CDE says that insulin pump therapy appears to be the better approach, for the reasons discussed on the next slide.
The CDE and Ricardo discuss the pros and cons of insulin pump therapy for Ricardo. As we learned earlier, the Consensus Panel on Insulin Pump Management of the AACE has identified the characteristics of suitable candidates for CSII therapy. One of these is “currently performs at least 4 insulin injections and at least 4 SMBG measurements daily.” Although Ricardo administers 4 daily insulin injections, he performed SMBG sporadically until the CDE asked him to keep a 10-day BG log. Furthermore, he lacks much of the basic knowledge and many of the skills required for insulin pump use. In addition, his medical insurance does not cover the costs of insulin pump therapy for patients with type 2 diabetes.

Nevertheless, there are many arguments in favor of CSII therapy for Ricardo. The strongest of these is that he experiences the dawn phenomenon. Although this is often hard to control with a bedtime injection of a long-acting insulin analog, it is easily controlled by increasing the basal rate from an insulin pump during the early morning hours (eg, between 4 a.m. and 9 a.m.). A secondary consideration is that he has an erratic schedule in terms of his level of physical activity and mealtimes. According to the AACE consensus guidelines, substantial dawn phenomenon and having an erratic schedule are both characteristics that warrant the use of insulin pump therapy in patients with type 2 diabetes.

Furthermore, Ricardo has a strong motivation to achieve tighter BG control, as evidenced by performing SMBG between 4 and 7 times a day for the 10 days during which he kept his BG log. In addition to performing SMBG as often as needed, he is open to learning new diabetes self-management skills. His wife appreciates the importance of a nutritionally sound meal plan and supports her husband’s desire to improve his health. Although his insurance does not cover insulin pump therapy, Ricardo has the financial resources to cover the costs of the pump, pump-related supplies, and pump-specific education.

After thorough discussions with the CDE and his wife, Ricardo decides that he would like to begin his preparation for insulin pump therapy.
Over the next 2 months, Ricardo works closely with the CDE to master basic diabetes self-management skills, including carbohydrate-counting; hypoglycemia detection, prevention, and treatment; and sick-day management strategies. He also meets with a registered dietitian to fine-tune his carbohydrate-counting skills.

After demonstrating that he has mastered those skills, Ricardo is referred to an outpatient class at the local hospital to learn how to use an insulin pump. The class is held over 3 days and focuses on day-to-day use of the pump and making adjustments for special situations, such as physical activity, delayed meals, sick days, and travel. Ricardo also meets with a representative of the manufacturer of his insulin pump to learn about the pump’s special features.

The first months after receiving his insulin pump are a process of learning and adjustment for Ricardo. He remains in frequent contact with his CDE and the representative of his pump manufacturer to learn how to customize the pump to meet his changing needs. For example, he learns how to program different temporary basal infusion rates based on the type of work he will be doing on a specific day.

Three months after beginning pump therapy, Ricardo’s A1C has decreased to 7.1% and his BG values are consistently within goal. He has experienced only 2 minor hypoglycemic episodes despite his hectic and unpredictable work schedule. He is feeling much better, and is very pleased by the way the pump accommodates his lifestyle.
An accurate statement about CSII therapy is: __________.

a. separate infusion sets are used with all currently available insulin pumps
b. today, patients with type 2 diabetes are not considered suitable candidates for CSII therapy
c. studies have consistently shown that mean A1C levels are lower with CSII therapy than with MDI therapy
d. many studies have found a lower risk of hypoglycemia with CSII therapy than with MDI therapy
The correct answer is d.

Many studies have found a lower risk of hypoglycemia with CSII therapy than with MDI therapy.
Summary

• Effective glycemic control in patients with diabetes is associated with reduced rates of microvascular and neuropathic complications and long-term decrease in macrovascular disease (as long as A1C reduction is implemented soon after diabetes diagnosis)
• Evidence-based guidelines recommend early treatment with insulin for many patients with type 2 diabetes, but clinical inertia and psychological resistance to insulin often delay insulin initiation
• Many insulin delivery systems are now available, and clinical studies have identified criteria that can be used to select the optimal insulin delivery system for a specific patient
• Prescribing the most appropriate insulin delivery system for a specific patient can result in greater adherence to the treatment regimen and increased glycemic control

In summary:

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