

# **Examining the Options for Insulin Delivery**

This program is supported by an  
educational grant from Novo Nordisk Inc.

Examining the Options for Insulin Delivery 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, pharmacists, and pharmacy technicians.

## **Jerry Meece, RPh, CDE**



**Owner and Director of Clinical Services**

**Plaza Pharmacy and Wellness Center  
Gainesville, Texas**

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.

## Objectives

- ❑ Identify the benefits of insulin therapy for glycemic control and reduction of long-term complications
- ❑ Discuss the issues surrounding insulin use in diabetes
- ❑ Describe the advantages and disadvantages of the currently available insulin delivery systems
- ❑ Apply the information presented in this activity to guide the selection of a patient's insulin delivery device

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
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## **Objectives - Pharmacy Technicians**

- Explain to patients the benefits of insulin therapy for glycemic control and reduction of long-term complications
- Discuss the issues surrounding insulin use in diabetes
- Describe to patients the advantages and disadvantages of the currently available insulin delivery systems
- Apply the information presented in this activity to guide the selection of a patient's insulin delivery device

The objectives for pharmacy technicians are slightly different and are as follows:

- Explain to patients the benefits of insulin therapy for glycemic control and reduction of long-term complications
- Discuss the issues surrounding insulin use in diabetes
- Describe to patients the advantages and disadvantages of the currently available insulin delivery systems
- Apply the information presented in this activity to guide the selection of a patient's insulin delivery device

## Diabetes: Scope of the Problem

- ❑ An estimated 23.6 million Americans (7.8% of the population) have diabetes mellitus
  - 17.8 million people with diagnosed diabetes
  - 5.7 million people with undiagnosed diabetes
- ❑ 57 million Americans over 20 years of age have prediabetes
- ❑ Diabetes-related healthcare costs reached \$174 billion in 2007
- ❑ Prevalence and costs continue to trend upward

National Diabetes Fact Sheet, United States, 2007. Available at [http://www.cdc.gov/diabetes/pubs/pdf/ndfs\\_2007.pdf](http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2007.pdf).

Healthcare professionals are well aware that diabetes is a debilitating and costly disease that is reaching epidemic proportions.

Estimates from 2007 indicate that 23.6 million people in the United States, or almost 8% of the population, have diabetes mellitus. While diabetes has been diagnosed in 17.8 million people, an additional 5.7 million people (or nearly one third) are unaware that they have the disease.

Of related concern is that 57 million Americans over 20 years of age have prediabetes, which is characterized by higher than normal blood glucose levels but not high enough to be classified as diabetes.

The cost for diabetes is of notable economic consequence. In 2007, costs for diabetes-related healthcare in the United States were estimated at \$174 billion. These included \$116 billion in direct medical care costs and \$68 billion related to lost productivity.

Previous estimates on diabetes trends and the most recent data from 2007 confirm that the prevalence of diabetes and the associated healthcare costs continue to increase.

## Diabetes: Scope of the Problem

### ☐ Minorities

- 15% of all non-Hispanic blacks aged  $\geq 20$  years have diabetes
- 10.4% of Hispanics aged  $\geq 20$  years have diabetes
- Minorities tend to develop diabetes earlier than whites

### ☐ Youth

- >186,000 have type 1 or type 2 diabetes
- 7% of 12–19 year olds have prediabetes
- Incidence of type 2 diabetes is increasing among minority youth (African Americans, Native American Indians, Hispanics)

National Diabetes Fact Sheet, United States, 2007. Available at [http://www.cdc.gov/diabetes/pubs/pdf/ndfs\\_2007.pdf](http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2007.pdf).

Estimates among certain populations (ie, minorities and youth) are particularly notable.

A total of 15% of all adult blacks and over 10% of all adult Hispanics in the United States have diabetes. Among Hispanics, the prevalence rates are 12.6% for Puerto Ricans, 12% for Mexican Americans, and 8.2% for Cubans. Importantly, minorities tend to develop diabetes at earlier ages than their white counterparts.

While the prevalence of type 1 and type 2 diabetes among children and adolescents remains much lower than in adults, data indicate that the prevalence of type 2 diabetes among American adolescents is increasing. Currently, 7% of all 12 to 19 year olds have impaired fasting glucose, a marker of prediabetes. The incidence of diagnosed diabetes is increasing particularly among minority groups (African Americans, Native Americans, and Hispanics).

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There are 3 main types of diabetes.

Type 1 diabetes often develops in children and young adults, but it can occur at any age. It results from the destruction of pancreatic  $\beta$ -cells, which produce insulin. Exogenous insulin is necessary for survival in patients affected with type 1 diabetes. Approximately 5% to 10% of diagnosed cases of diabetes are type 1.

In the United States, 90% to 95% of individuals with diabetes have type 2 diabetes. It is assumed that most of the estimated 6 million people who are undiagnosed have type 2 diabetes. Type 2 diabetes is a physiologic condition encompassing both insulin resistance (cells do not use insulin properly) and progressive failure of pancreatic  $\beta$ -cells, reducing their ability to produce insulin. Indeed, by the time of diagnosis, patients with type 2 diabetes have lost approximately 50% of  $\beta$ -cell function; consequently, many will eventually require insulin therapy. Obesity contributes to insulin resistance. The increased prevalence of type 2 diabetes and prediabetes among adolescents is attributed to increased rate of obesity in this population.

Gestational diabetes is defined as glucose intolerance occurring during pregnancy. If not treated, gestational diabetes can cause complications in both mother and fetus. Approximately 4% of pregnant women (135,000 cases in the United States annually) develop gestational diabetes. Women with a history of gestational diabetes have a 40% to 60% chance of developing type 2 diabetes 5 to 10 years after delivery; 5% to 10% of these women have diabetes (usually type 2) immediately following pregnancy.

## Diabetes Is Still Not Managed Properly in Many Patients

Percent of patients with the following:

A1C $\geq$ 7%	42%
BP >140/90 mm Hg	47%
Total cholesterol >200 mg/dL	49%
$\geq$ 2 A1C tests in last year	26%
No annual dilated eye exam	28%
No annual foot exam	30%

A1C = glycosylated hemoglobin; BP = blood pressure.

McWilliams JM et al. *Ann Intern Med* 2009;150:505–515.  
Data and trends. National Diabetes Surveillance System. Available at:  
<http://www.cdc.gov/diabetes/statistics/preventive/fAllPractices.htm>.

Despite the known risks of the complications of diabetes and the importance of identifying and treating risk factors early to reduce complications, many patients in the United States still do not meet disease treatment and management recommendations. According to data collected from survey participants in recent National Health and Nutritional Examination Surveys:

- 42% of adults with diabetes have higher than the American Diabetes Association (ADA) target A1C level of <7%. While this is better than what has been observed in previous years, it is still less than desirable.
- The treatment goal for blood pressure in diabetes is  $\leq$ 130/80 mm Hg, yet 47% of patients with diabetes have blood pressure measurements above 140/90 mm Hg. Almost half of patients with diabetes have high cholesterol (>200 mg/dL).
- 74% of adults with diabetes do not receive at least 2 glycosylated hemoglobin (A1C) tests per year, and one-third do not have the annual eye and foot examinations (these are recommended for the prevention and management of retinopathy and neuropathy).

## The Role of Insulin Therapy

- ❑ Required for type 1 diabetes from the time of diagnosis to sustain life
- ❑ Many patients with type 2 diabetes will ultimately require insulin
  - Progressive  $\beta$ -cell failure
  - Unable to achieve glycemic targets on other antidiabetic medications
  - Symptoms of hyperglycemia
  - Development of diabetes-related complications or other health problems

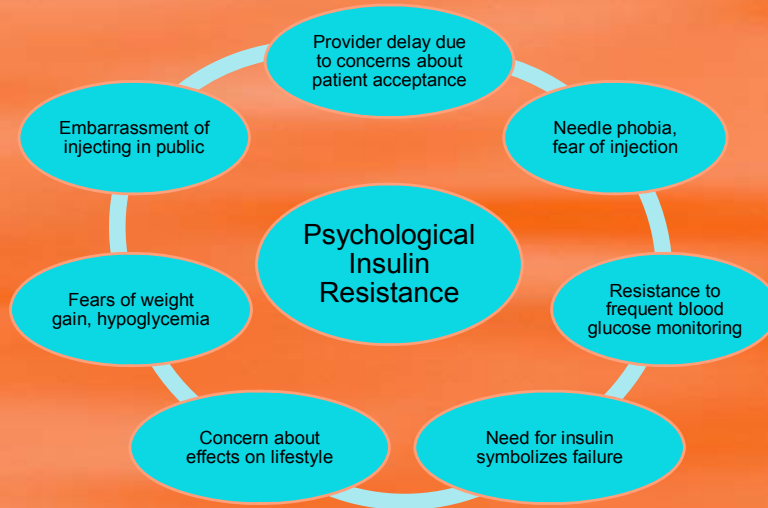
American Diabetes Association. *Diabetes Care*. 2009;32(Suppl 1):S62–S67.  
Wright A et al. *Diabetes Care*. 2002;25:330–336.  
Marrero DG. *Clinical Cornerstone*. 2007;8:33–43.

In type 1 diabetes, insulin is necessary to sustain life. Insulin also is an important therapeutic option for type 2 diabetes, as many patients with type 2 diabetes may ultimately require insulin therapy to achieve glycemic targets. Indeed, in the United Kingdom Prospective Diabetes Study (UKPDS), more than half of patients who were started on oral antidiabetic agents required the addition of insulin after 6 years because their fasting plasma glucose level was  $>108$  mg/dL despite maximal doses of sulfonylureas.

Factors that contribute to the need to make the transition from oral to insulin therapy include progressive  $\beta$ -cell failure, symptoms of hyperglycemia, and the development of complications or deteriorating health, which also signify a lack of glycemic control.

Insulin therapy is hormone replacement. Therefore, drug–drug interactions are less likely when prescribing insulin. Insulin can be used both as monotherapy and in combination with oral antidiabetic agents in patients with type 2 diabetes. Insulin therapy has the potential to have a significant impact on lowering A1C levels.

# Resistance to Initiating Insulin



Marrero DG. *Clinical Cornerstone*. 2007;8:33–43.  
Second International Dawn Summit. *Prac Diab Int*. 2004;21:201–208.

Ample data indicate that both providers and patients with type 2 diabetes are reluctant to initiate insulin therapy. Many physicians wait to prescribe insulin until absolutely necessary, mainly because they believe it will not be well received by patients and that patient adherence will be less than ideal. This is unfortunate, as complications are likely to have progressed by this time.

Patients do report worries about starting insulin therapy. This is often called psychological insulin resistance and may occur for various reasons including:

- Fear of needles or injection discomfort
- Embarrassment of injecting in public
- Fears about hypoglycemia
- Fear of weight gain
- Resistance to frequent blood glucose monitoring
- Concern about having to change lifestyle or daily routines
- Symbolism attached to insulin therapy. Some people associate insulin with personal failure, some fear that diabetes has become more serious, and others consider insulin therapy to be the “end of the road.” The symbolism attached to insulin therapy is a serious emotional burden that educators in diabetes strive to lift.

## Some Remedies for Psychological Resistance to Insulin

- ❑ Teach patients about progression and underlying pathophysiology of type 2 diabetes at the time of diagnosis, including deterioration of  $\beta$ -cell function and risk for complications
- ❑ Be honest and upfront about addressing the possible use of insulin at some point in therapy. Do this in the first or second meeting with the patient
- ❑ Provide information about modern insulin delivery systems and disposable needles
- ❑ Educate about prevention of hypoglycemia and weight gain
- ❑ Acknowledge patient's fear that diabetes is more serious or due to personal failure and clarify misconceptions
- ❑ Understand cultural issues and adapt management accordingly

Marrero DG. *Clinical Cornerstone*. 2007;8:33–43.  
Peragallo-Dittko V. *Diabetes Educ*. 2007;33(Suppl 3):60S–65S.

A patient's transition to insulin therapy can be eased by anticipating psychological resistance to insulin. Acknowledge that most people are hesitant to make the transition to insulin, offer common reactions shared by other patients, and ask the patient to describe his or her concerns. Based on the patient's response, consider the following:

- Modify your curriculum for type 2 diabetes to include teaching about the concept of  $\beta$ -cell failure so that patients learn that treatment with insulin is one of many therapies for diabetes and does not indicate personal failure.
- Be honest and upfront about addressing the possible use of insulin at some point in therapy. Do this in the first or second meeting with the patient.
- If a patient voices concern about discomfort or practical lifestyle issues, describe new insulin delivery systems with small needles and virtually no injection discomfort. These insulin delivery systems may help alleviate concerns regarding the use of insulin, including social stigmas. Indeed, many patients report that the use of insulin pens or dosers makes them more comfortable injecting in public.
- It is important to explore the patient's experience with hypoglycemia and reassure patients that while there is always some risk of hypoglycemia with insulin therapy, it can be minimized with prevention and treatment strategies.
- Sometimes, well-intentioned efforts encouraging patients to use lifestyle modification to lower blood glucose levels have included using insulin therapy as a threat (eg, "If you can't control your diabetes with these recommendations, I'll have to put you on insulin.") Clinicians must be sensitive to how insulin therapy is discussed. For many patients, the introduction of insulin therapy signifies that their diabetes has become more serious. Develop the skill of acknowledging the patient's fears while gently offering clarification.

## Check Point

The vast majority of patients with type 2 diabetes are able to maintain glycemic, blood pressure, and cholesterol goals.

- a. True
- b. False

And now it's time for a checkpoint question.

Most patients with diabetes are able to maintain glycemic, blood pressure, and cholesterol goals.

- a. True
- b. False

## Check Point

b. False

Over 40% of patients do not have the American Diabetes Association–recommended A1C values of <7%; half do not achieve blood pressure or cholesterol goals.

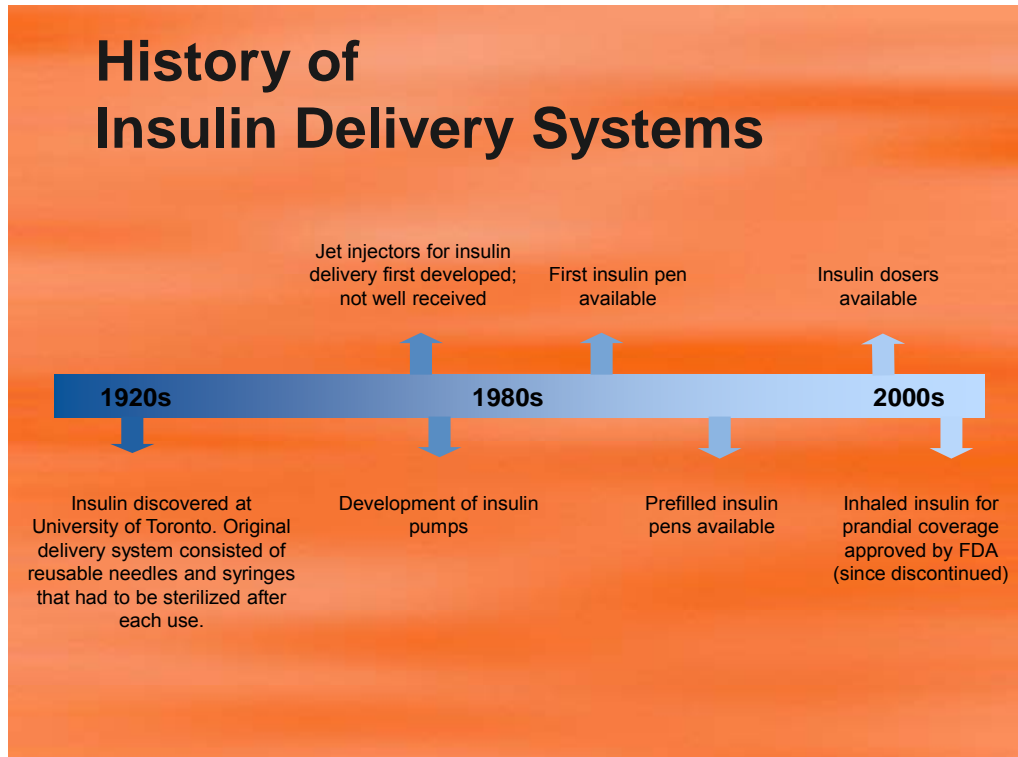
The answer is b—false.

Over 40% of patients do not have A1C values <7%, which is recommended by the ADA. Furthermore, the ADA recommends individualization of A1C goals; some may aim for an A1C <6%, providing hypoglycemia does not occur.

Achieving optimal glycemic targets is critically important for reducing the risk of complications from diabetes. Every 1 percentage point drop in A1C reduces the risk of microvascular complications by 40%. Similarly, the UKPDS established that microvascular complications could be reduced 25% by lowering A1C from a median of 7.9% to 7.0%.

Maintaining adequate blood pressure and lipid goals further reduce the macrovascular risk, a problem among patients with diabetes. For this reason, blood pressure goals are lower for patients with diabetes ( $\leq 130/80$  mm Hg) than for those without diabetes ( $\leq 140/90$  mm Hg). Despite this, only half of patients with type 2 diabetes even meet the non-diabetic blood pressure goal, and only half meet the total cholesterol goal.

# History of Insulin Delivery Systems



Although options for insulin delivery have changed over time, most preparations are still administered by injection. When insulin was first discovered in the 1920s, it was delivered via large glass syringes and reusable needles, both of which had to be boiled to sterilize after each use. Needles were sharpened with a pumice stone so they could be reused. For the next 60 years, vial and syringe remained the only delivery option. Jet injectors were then developed; the first one marketed in 1979 was considered cumbersome. Early insulin pumps also became available in the late 1970s, followed by prefilled pens in 1993, insulin dosers, and, most recently, inhaled insulin in 2006 (however, this product was discontinued due to lack of sales).

Advances in insulin delivery have had many benefits. A study by Rubin and Peyrot demonstrated that self-care behaviors have an effect on clinical outcomes. One particular self-care behavior that lowered A1C was improvement in insulin administration such as skipping fewer injections and improving dose adjustment. If patients have anxiety about the self-administration of insulin, simplifying the process is an important step in overcoming that barrier. Consider that if an insulin delivery device helps a patient skip fewer injections or eases anxiety, then the device becomes a valuable treatment tool.

# Vial and Syringe

## Advantages

- Widely available
- Inexpensive
- Permits self-mixing of different insulin types

## Disadvantages

- Risk of inaccurate dosing
- Difficult to measure small doses
- Cumbersome to carry/use
- Not discreet; possible social stigma
- Can be challenging for the physically or visually impaired

The traditional vial and syringe is still a viable delivery method for insulin, although insulin pens are becoming increasingly more popular.

There are many disposable syringe/needle options available with varying syringe characteristics, such as dosage lines or syringe capacity, and length and gauge of the needle. Syringes are relatively inexpensive and permit in-syringe mixing of different types of insulin. However, because users must measure their own doses, there is a risk of inaccurate dosing. Furthermore, they are more cumbersome to use and less discreet than insulin pens. This may be particularly problematic to those who travel extensively or lead active lives. Unfortunately, it may be difficult for visually and physically impaired patients to use a vial and syringe with ease.

For the patient using the vial and syringe method of insulin delivery, the diabetes educator must assess patient's choice of syringe, injection technique, and ability to draw up the correct dose. The syringe must match the insulin dose. If the dosage is less than 30 units of insulin, use a 3/10-cc syringe. For greater than 30 but less than 50 units of insulin, use a 1/2-cc syringe. If the dose is greater than 50 units, use a 1-cc syringe.

Needle choices include the length of the needle as well as the gauge—5-mm, 8-mm, or 12.7-mm needles may be prescribed. Since injection depth may change the absorption of insulin, consistency in the length of needle is important. Blood glucose should be monitored with needle size changes to assess variability in insulin absorption. Needle gauges vary from 29 to 31 gauge; the higher the gauge, the thinner the needle.

In the United States, U-100 is the predominant insulin; however, U-500 is also available. Patients traveling outside the United States should be aware that a U-40 strength insulin is available and requires use of U-40 syringes.

## Potential Medication Errors With Insulin

- ❑ Prescribing issues
  - Wrong dose or product
  - Order writing
    - “U” confused with “0”
    - “L” for “Lente” or “Lantus”
- ❑ Product and administration
  - Wrong syringe selected
  - Incorrect dose drawn into syringe
  - Wrong product selected
  - Inadequate mixing of suspensions
  - Patient’s inability to administer drug correctly

Grissinger M et al. *J Manag Care Pharm.* 2003;9(Suppl 3):2–13.  
Senthil MJ. *J Postgrad Med.* 2005;51:152–153.

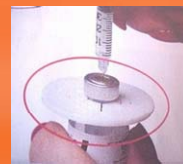
There are a number of potential medication errors that can occur with insulin injection. The wrong dose or type of insulin may be written or communicated. A potentially very serious error that involves order writing would be mistaking a “U” for unit with a zero at the end of a dose (eg, 140 instead of 14). Therefore, all insulin doses should be written using the word “units” and not the abbreviation letter U. When changing dosages with patients, the new dosage should be written down to avoid error. Over the telephone, always repeat the name and dosage for verification.

Part of the insulin delivery selection process includes assessing the safety needs of a patient. The potential errors surrounding the vial and syringe delivery system include:

- Wrong syringe selected
- Incorrect dose drawn into syringe
- Wrong product selected
- Inadequate mixing of suspensions
- The patient’s inability to administer insulin using a syringe

## Injection Aids

- ❑ Designed to make administering injections easier
- ❑ Aid patients with visual or physical impairment



Several aids have been developed to make giving injections easier. These are particularly applicable for patients with visual or physical impairment who might otherwise have difficulty drawing up accurate doses of insulin and administering them correctly.

## Aids for People With Visual or Physical Disabilities

Syringe magnifiers	BD Magni-Guide™ (BD) Tru-Hand (Whittier Medical) Syringe Magnifier (Apothecary Products)
Needle guides and vial stabilizers	Inject Assist™ (Apothecary Products) NeedleAid™ (NeedleAid, Ltd) Injection Safety Guard™ (Apothecary Products)
Vial syringe guides	Vial Syringe Guide (Apothecary Products)
Audible click devices	Count-a-Dose (Medicool, Inc)



*Diabetes Forecast*. 2009:62. Available at <http://www.forecast.diabetes.org/magazine/resource-guide/2009-resource-guide>.

This slide lists various aids available in the United States for patients with visual or physical difficulties in administering insulin therapy.

- Syringe magnifiers enlarge the calibration marks on the syringe.
- A needle guide and vial stabilizer help with needle insertion by holding the vial and syringe together while the syringe is being filled with insulin.
- Vial syringe guides allow patients to reconstitute or draw up medication using any syringe with a standard luer-style tip. They eliminate problems of broken needles by safely connecting the syringe to the insulin bottle.
- For nonvisual insulin measurement, there is a syringe-filling device that produces an audible click with each unit of insulin drawn into the syringe.

Some products can be used with any syringe; others are designed to work only with a specific brand.

## Insertion Aids




Manufacturer	Brand Name	Features	
Owen Mumford	Autoject® 2 Fixed Needle Autoject® 2 E1 Fixed Needle Autoject® 2 Removable Needle	Spring-loaded, hides needle from view Safety lock Window shows when injection complete	
Becton Dickinson	INJECT-EASE®	Spring-loaded, hides needle from view	

*Diabetes Forecast*. 2009:62. Available at <http://www.forecast.diabetes.org/magazine/resource-guide/2009-resource-guide>.

Insertion aids facilitate and accelerate insertion of the needle into the skin for patients who are reluctant to do it themselves or who have difficulty injecting insulin into hard-to-reach areas, such as the buttocks. Most are spring-loaded and hide the needle from view. Pushing the plunger automatically inserts the needle into the skin. In most models, the depth of skin penetration is adjustable for very thin or obese people.

Insertion aids can be used with 1-cc, ½-cc, or 3/10-cc syringes. The Autoject 2 is designed for 1-mL Becton Dickinson tuberculin syringes.

## Insertion Aids

Manufacturer	Brand Name	Features	
Medicoool, Inc	Instaject	Injector and lancet device	
NeedleAid, Ltd	NeedleAid™	Stabilizing guide, hides needle from view	
Novo Nordisk Inc.	NovoPen® 3 PenMate®	Works with NovoPen® 3 or NovoPen® Junior and hides needle from view	



*Diabetes Forecast*. 2009:62. Available at <http://www.forecast.diabetes.org/magazine/resource-guide/2009-resource-guide>.

Instaject is a combination syringe injector and lancet device that also is button-activated. This device also has adjustable depth settings for skin penetration.

NeedleAid hides the needle from view upon injecting and also acts as a stabilizing guide for the insulin syringe or pen. It ensures consistent injection at the proper angle and to the proper depth.

The NovoPen 3 PenMate is an attachment that conceals the needles of NovoPen Junior and NovoPen 3 insulin pens.

# Insulin Infusers

Manufacturer	Brand Name	
Patton Medical Devices LP	I-Port™ Injection Port	
IntraPump Infusion Systems	Insufion® Indwelling Cannula	

*Diabetes Forecast*. 2009;62. Available at <http://www.forecast.diabetes.org/magazine/resource-guide/2009-resource-guide>.

Insulin infusers serve as a gateway for needles. A cannula is inserted under the skin and remains in place for a certain period of time (3–7 days). Each time an insulin dose is needed, the needle is inserted directly into the infuser, not the skin, thereby avoiding multiple needle sticks.

## Jet Injectors

- ❑ Deliver insulin transcutaneously by an airjet mechanism
- ❑ Needleless
- ❑ Release a fine, high-pressure stream of insulin that penetrates skin



Pictured: Medi-Jector Vision® from Antares Pharma, Inc.

*Diabetes Forecast*. 2009:62. Available at <http://www.forecast.diabetes.org/magazine/resource-guide/2009-resource-guide>.

Another option for insulin delivery is the jet injector. Jet injectors deliver insulin transcutaneously by an airjet mechanism instead of using a needle. They release a fine, high-pressure stream of insulin that penetrates the skin.

There are several jet injectors available:

- Activa Brand Products, Inc. markets Advanta, Advanta Jet ES, and Gentle Jet
- Antares Pharma, Inc. markets Medi-Jector Vision

# Jet Injectors

## Advantages

- Portable
- Needleless
- Reduced risk of cross-contamination

## Disadvantages

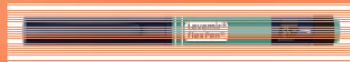
- Bruising or “tattooing” of skin is possible
- Mechanically complex
- Inconsistent depth of penetration
- Not well studied in trials
- Not widely used
- High cost

Ratner RE. *Practical Diabetology*. 2004;23:2–12.

*Diabetes Forecast*. 2009;62. Available at <http://www.forecast.diabetes.org/magazine/resource-guide/2009-resource-guide>.

Jet injectors may be the insulin delivery system of choice for those with a true needle phobia. They can cause bruising and some patients develop permanently discolored skin called tattooing. Some may find use of these systems complicated, cumbersome, and mechanically complex. The potential for inconsistent depth of penetration with each administration exists, which could affect the amount of insulin delivered. For others, the jet injector is the only way that they can administer insulin. Jet injectors are more costly than the vial and syringe method of insulin delivery, are not widely used, and have not been well studied in clinical trials.

## Insulin Pens and Dosers

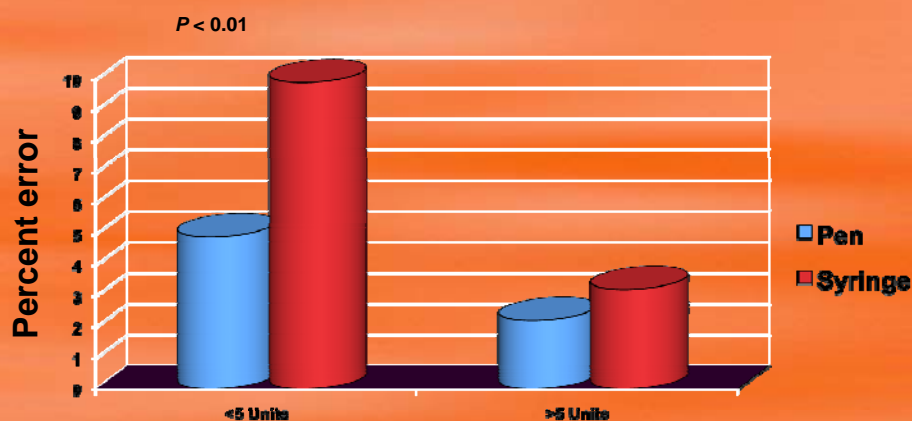


Another alternative to the vial and syringe is the insulin pen. As the name implies, these are compact, penlike devices that contain a supply of insulin.

Insulin pens are either multidose, prefilled, disposable, or durable pens. The disposable pens are used until the insulin supply is completely consumed and then the entire pen is discarded. The durable pens are reusable and contain replaceable insulin cartridges.

This slide shows some of the insulin pens and a doser that are available in the United States.

## Accuracy of Insulin Pens vs Vial and Syringe



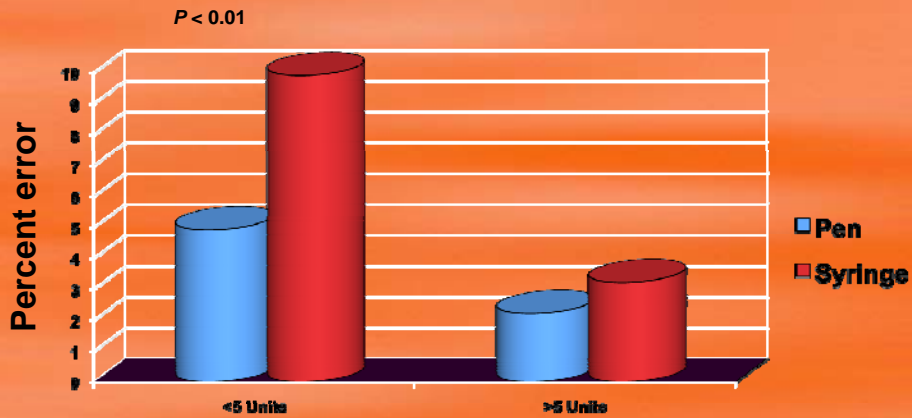
Lteif AN, Schwenk WF. *Diabetes Care*. 1999;22:137–140.

The primary advantages of insulin pens and dosers, compared with vial and syringe insulin delivery, are their portability and convenience. They are discreet, result in a consistent dose delivery, permit a more flexible lifestyle, and eliminate the need to draw up insulin. Compared with other countries, pens are not used as much in the United States, although their popularity is increasing. As the technology improves, newer generation pens also offer advantages over former versions, such as a need for less injection force.

The disadvantages of pens and dosers are that they are limited to premixed formulations available for pen use, and different types of insulin cannot be mixed. If multiple types of insulin are required, the patient must take another injection.

Cost can be either an advantage or disadvantage compared with vial and syringe delivery. This is dependent on many variables, including whether the pens are covered by insurance, the copayment set by insurance companies, and amount of insulin used. If the patient is paying out of pocket, pens are generally more expensive than vial and syringe, unless the patient ends up wasting insulin in vials because s/he uses less than 1 vial a month. Thus, it is important for diabetes educators and pharmacists to know the costs and insurance coverage for insulin delivery systems in their area. However, recent studies have found insulin pens to be more economical than vial and syringe in some populations.

# Accuracy of Insulin Pens vs Vial and Syringe



Lteif AN, Schwenk WF. *Diabetes Care*. 1999;22:137-140.

To compare the accuracy and precision of insulin pens and syringes, a study was conducted in 48 patients (32 children and 16 parent administrators representing an additional 16 children). The participants used a radiolabeled solution that patients measured out from vials and/or cartridges. The radiolabeled solution was measured by spectroscopy. For insulin doses less than 5 units, pens were significantly more accurate than vial and syringe, but for higher doses, accuracy was the same.

# Accuracy of Prefilled Insulin Pen

SoloSTAR® prefilled pen, N = 60 (360 doses)

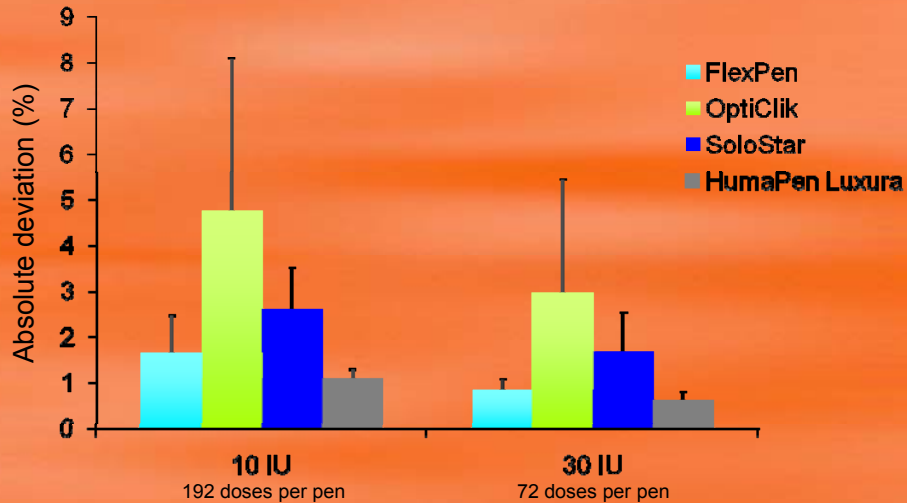
Target dose of insulin glargine	ISO limits	Mean (SD) dose delivered	Target dose of insulin glulisine	ISO limits	Mean (SD) dose delivered
10 U	9-11	9.87 (0.24)	5 U	4-6	4.98 (0.20)
40 U	38-42	39.54 (0.36)	15 U	14-16	14.87 (0.29)
80 U	76-84	79.02 (0.62)	30 U	28.5-31.5	29.67 (0.34)

ISO = International Organization for Standardization.  
Hermanns N et al. *Diab Technol Ther.* 2008;10:322–327.

Additional studies have confirmed the dosing accuracy of individual insulin pens. This slide shows the results of a prospective, open-label, single-center study in which 60 patients with either type 1 or type 2 diabetes (age range, 18-79 years), were evaluated for their dosing accuracy using a disposable insulin pen (SoloSTAR). Patients could have received prior insulin or were treatment-naïve. After a study nurse demonstrated the proper use of the SoloSTAR pen, each patient delivered 6 separate insulin injections into a sponge (3 different doses of insulin glargine and 3 doses of insulin glulisine; order of pen usage and dose delivery were randomized). Pens were weighed before and after injection using a precision balance. The dosing accuracy was assessed using International Organization for Standardization (ISO) criteria.

As shown, in the clinical setting the pen delivered accurate doses of 2 types of insulin over a range of doses.

## Dosing Accuracy of Various Pens



Hänel H et al. *J Diabetes Sci Technol.* 2008;2:478–481.

Another study compared the accuracy of 4 insulin pens (2 disposable, 2 durable) in the laboratory by having experienced investigators dispense 10 units and 30 units of insulin multiple times; the amount of insulin was emptied from the cartridge/pen and weighed on a pharmaceutical balance.

The mean dosing accuracies of all the pens were within ISO standards. As shown in this slide, FlexPen and HumaPen Luxura exhibited the lowest degree of dosing deviations among the 4 pens.

## Preparation Prior to Use of Insulin Pens and Dosers

- Review user instructions for each insulin delivery pen or doser (including cartridge insertion for durable pens)
- Patients should demonstrate ability to use device correctly
- Resuspend insulin before injection, if necessary
- Before each injection, patient should perform an “air shot” to ensure insulin delivery (durable or disposable)
- After injection, the pen or doser should remain in place for at least 10 seconds to ensure complete delivery
- Refer to the package insert for specific directions for each device

Before using any insulin delivery injection system, patients should demonstrate their ability to use it correctly. Manufacturers’ instruction materials should be followed for proper needle attachment, dose selection and correction, and, for durable pens and dosers, cartridge insertion.

Intermediate-acting insulin formulations, including premixed (cloudy), must be thoroughly resuspended before injection. Cartridges and prefilled pens must be turned end-over-end at least 10 times or until the insulin has been completely resuspended.

Following manufacturers’ instructions, patients should prime the device or perform an “air shot” before each injection. To ensure that the insulin in the pen or doser reaches the needle, attach a needle to the device, select the dose stated in the instructions, hold the device with the needle pointed upward, and push the button. Insulin should appear at the tip of the needle. If it does not, the procedure should be repeated until insulin appears.

After injection, the pen or doser should remain in place for at least 10 seconds to ensure complete delivery. Refer to the package insert for specific directions for each device.

# Disposable Insulin Pens

## Eli Lilly and Company

Name	Comments
Humulin® N Pen	Prefilled with 3 mL corresponding insulin 1-unit increments, 1–60 units Original Humalog Pens still available (audible clicks when dialing)
Humulin® 70/30 Pen	
Humalog® KwikPen™	
Humalog® Mix75/25™ KwikPen™	
Humalog® Mix50/50™ KwikPen™	

*Diabetes Forecast*. 2009:62. Available at <http://www.forecast.diabetes.org/magazine/resource-guide/2009-resource-guide>.

Insulin pens offer patients many options. When the patient chooses an insulin pen, assessment includes matching the products available to the patient's needs. Consider the formulation of insulin, disposable versus durable pens, whether the pen delivers insulin in 1- or half-unit increments, and the patient's total daily dose per injection.

Disposable pens are multidose pens prefilled with insulin that are discarded when empty. A new needle must be used for each injection. Several manufacturers market disposable insulin pens. Unused pens are to be refrigerated; in-use pens are stored at room temperature.

The Humulin and Humalog pens are manufactured by Eli Lilly. Each pen contains 3 mL of insulin and can deliver up to 60 units of insulin per injection. The dose window is magnified, and can be dialed backward and forward in single-unit increments. An audible click accompanies the turning of the dosing dial. If too much is dialed, the dial can be turned back to the correct dose.

The newest version of the Humalog pens is the KwikPen. The original Humalog pens also are available. The pens have varying dose-viewing areas, differences in how a dose is set, and differences in how much pressure it takes to deliver the dose. Diabetes educators and pharmacists should become familiar with each pen so they can assist their patients in selecting or using them. The KwikPen is text color coded (making it easier to read), smaller and less bulky than the original. Some patients may find it easier to dose because the pen is shorter and, therefore, the distance from the button to the needle is shorter.

Both Humulin N (neutral protamine Hagedorn [NPH]) and premixed 70/30 are available in prefilled, disposable Humulin pens. Humalog Pen contains 3 mL of Humalog, a rapid-acting insulin analog. Humalog Mix75/25 Pen contains 3 mL of Humalog Mix75/25. Humalog Mix50/50 Pen contains 3 mL of Humalog Mix50/50.

# Disposable Insulin Pens/Doser

## Novo Nordisk Inc.

Name	Comments
NovoLog® FlexPen®	Prefilled with 3 mL corresponding insulin, 1-unit increments, 1–60 units
NovoLog® Mix 70/30 FlexPen®	
Levemir® FlexPen®	Different pen colors for each New models use less injection force
Novolin® InnoLet®	Contains 3 mL of either Novolin R, Novolin NPH, or 70/30 human insulin, 1-unit increments, 1–50 units, large dial and easy to grip

NPH = neutral protamine Hagedorn.

*Diabetes Forecast*. 2009;62. Available at <http://www.forecast.diabetes.org/magazine/resource-guide/2009-resource-guide>.

The NovoLog FlexPen, NovoLog Mix 70/30 FlexPen, Levemir FlexPen, and Novolin InnoLet are marketed by Novo Nordisk. The NovoLog FlexPen contains 3 mL of NovoLog. NovoLog Mix 70/30 FlexPen contains 3 mL of NovoLog Mix. Levemir FlexPen contains 3 mL of Levemir, a long-acting basal insulin analog.

In 1 study with a sample of 105 participants, 74% preferred the FlexPen to the vial and syringe and considered it easier to use; another 85% believed the pen to be more discreet. The newest models of FlexPen released in 2009 require 30% less injection force than the previous model. This feature may be of particular benefit in patients with reduced grip strength or limited joint mobility of the hand. Another study of 64 patients found that significantly more patients found the newer FlexPen to be easier to identify the type of insulin and overall easier to use.

Novolin InnoLet is a prefilled, handheld injection device. It features a large kitchen timer–like dial that clicks audibly for each unit dialed. The scale is easy to read, and it has a support shoulder that provides stability. InnoLet is available prefilled with 3 mL of either Novolin R, Novolin N, or Novolin 70/30. Disposable needles are available separately. The device is disposed of when the cartridge is empty.

In a prospective study, 260 patients with type 1 or type 2 diabetes used both traditional vial and syringe and the InnoLet doser for 12 weeks. Patients reported significantly less fear of self-injection with the doser versus vial/syringe, and 71.5% of patients indicated a preference for InnoLet.

# Disposable Insulin Pens

sanofi-aventis

Name	Comments
SoloSTAR®	For use with Lantus® and Apidra® 1–80 units, 1-unit increments Different pen colors for the different insulin preparations

Diabetes Forecast. 2009;62. Available at <http://www.forecast.diabetes.org/magazine/resource-guide/2009-resource-guide>.

SoloSTAR is a disposable pen that has been available prefilled with Lantus or Apidra insulins in Europe; in the United States, the Lantus-filled SoloSTAR has been available since 2007 and in February 2009, Apidra SoloSTAR was approved by the US Food and Drug Administration.

Like the newest FlexPen, SoloSTAR also has been shown to reduce injection force compared with earlier pen models.

SoloSTAR is capable of delivering 1 to 80 units of insulin at 1-unit increments. The pens for Lantus and Apidra vary in color for correct identification, which may help visually impaired patients.

## Durable Insulin Pens

Manufacturer	Name	Comments
Eli Lilly	HumaPen <sup>®</sup> MEMOIR <sup>™</sup>	1-unit increments, 1–60 units Has memory for last 16 doses Overdial correction
	HumaPen <sup>®</sup> LUXURA <sup>™</sup> HD	1/2-unit increments after the 1st unit, 1–30 units, backward dial correction
Novo Nordisk	NovoPen <sup>®</sup> 3	1-unit increments, 2–70 units per injection
	NovoPen <sup>®</sup> Junior	1/2-unit increments, 1–35 units

*Diabetes Forecast*. 2009:62. Available at <http://www.forecast.diabetes.org/magazine/resource-guide/2009-resource-guide>.

The durable insulin pen is shaped like a traditional ink-cartridge writing pen. Instead of a writing point, there is a disposable needle, and instead of an ink cartridge, there is a cartridge containing one of several available insulin formulations. When the insulin cartridge is empty, it is discarded and a new cartridge is loaded into the pen. The pen itself is not disposable. The needles must be changed after each injection.

- The HumaPen MEMOIR is a durable pen for use with Humalog 3-mL insulin cartridges. It has a memory feature that includes up to the last 16 doses of insulin administered. Like all the Eli Lilly pens, the dose knob can be dialed backward to correct overdialing. The MEMOIR delivers from 1 to 60 units of insulin per injection.
- HumaPen LUXURA HD also uses Humalog 3-mL insulin cartridges. The user can administer insulin in half-unit doses with 1 to 30 units per injection.
- NovoPen 3 uses 3-mL cartridges of either Novolog or Novolin insulin and offers dosing in 1-unit increments with 2 to 70 units per injection.
- NovoPen Junior uses 3-mL cartridges of either Novolog or Novolin insulin and offers dosing in half-unit increments with 1 to 35 units per injection.
- PenMate is an accessory that conceals the needle on the NovoPen 3 and NovoPen Junior. In one study of 57 participants, it was shown to reduce perception of pain.

## Durable Insulin Pens

Manufacturer	Name	Comments
Owen Mumford	Autopen® Classic	2 models use 3-mL cartridges from Eli Lilly: 3800 (2–42 units in 2-unit increments) 3810 (1–21 units in 1-unit increments)
	Autopen® 24	2 models use 3-mL cartridges from sanofi-aventis: 4200 (2–42 units in 2-unit increments) 4210 (1–21 units in 1-unit increments)
sanofi-aventis	OptiClik®	Uses 3-mL (100 unit) Lantus® or Apidra® cartridges (different colored pens for each type of insulin) 1-unit increments, 1–80 units per injection

*Diabetes Forecast*. 2009:62. Available at <http://www.forecast.diabetes.org/magazine/resource-guide/2009-resource-guide>.

Several models of the durable-type Autopen multidose insulin injection systems are available in the United States. These pens are marketed by Owen Mumford and are compatible with Eli Lilly and sanofi-aventis cartridges.

The Autopen Classic uses 3-mL cartridges from Eli Lilly and is available in 2 models as follows:

Model 3800 offers dosing in 2-unit increments with 2 to 42 units per injection.

Model 3810 offers dosing in 1-unit increments with 1 to 21 units per injection.

The Autopen 24 uses 3-mL cartridges from sanofi-aventis and is available in the following 2 models:



Model 4200 offers dosing in 2-unit increments with 2 to 42 units per injection.

Model 4210 offers dosing in 1-unit increments with 1 to 21 units per injection.

The Autopen has a side button release. The dose indicator returns to the start line after injection.

OptiClik is a reusable insulin pen that is used with 3-mL cartridges of Lantus, a long-acting insulin analog, or Apidra, a rapid-acting insulin analog. Delivery is in 1-unit increments with up to 80 units per injection. The cartridge clicks into place to ensure proper setup. The dose is displayed digitally and the indicator returns to zero after injection. OptiClik, Lantus, and Apidra are marketed by sanofi-aventis.

## Durable Pens Designed for Children

Pen Name	Type of insulin	Features	Picture
HumaPen® LUXURA™ HD	Humalog	½-unit increments after the 1st unit, 1–30 units; backward dial correction	
NovoPen® Junior	Novolog Novolin	½-unit increments, 1–35 units; dose indicator returns to zero after injection PenMate® available to conceal needle and reduce pain perception	

This slide reiterates the 2 pens that are designed specifically for children with diabetes. The HumaPen LUXURA HD and the NovoPen Junior allow for accurate dosing of lower doses by utilizing ½-unit increments.

## Check Point

Traditional vial and syringe delivery of insulin is more accurate than using an insulin pen.

- a. True
- b. False

Traditional vial and syringe delivery of insulin is more accurate than using an insulin pen.

- a. True
- b. False

## Check Point

b. False

Insulin pens have been shown to be very accurate and are more accurate than vial and syringe delivery.

The answer is b—false.

Studies have proven the accuracy of insulin delivery via pen and found it to be better than vial and syringe delivery. This is important, particularly among older persons, as they may have visual and manual dexterity difficulties drawing up insulin into a syringe. In fact, insulin is one of the top medications leading to emergency department visits for adverse events among older persons (along with warfarin and digoxin).

# Patient Satisfaction With Insulin Delivery

Hospitalized patients completing patient satisfaction survey; responded "agree" or "strongly agree"

Survey item	Insulin pen group (N = 35)	Vial/syringe group (N = 40)
The method used to give me my insulin was convenient	33 (94%)	39 (98%)
The method used to give me my insulin was simple and easy	31 (89%)	38 (95%)
I would like to continue taking my insulin at home the same way	26 (74%)*	18 (45%)
I would recommend this method to other people with diabetes	33 (94%)*	29 (73%)
I was confident I was given the correct dose	34 (97%)	37 (93%)
Overall, I was satisfied with the method used to give me my insulin	34 (97%)	38 (95%)

\* $P < 0.05$ .

Davis EM. *Am J Health-Syst Pharm*. 2008;65:1347-1357.

This slide shows some results from a study comparing patient satisfaction with insulin pens (Innolet or FlexPens) versus vial and syringe insulin delivery in hospitalized patients with diabetes. Patients were recruited from 2 general medical-surgical units from July 2005 through May 2006; before discharge, patients completed a survey regarding satisfaction with the insulin delivery method.

The main differences between the delivery methods were that 1) significantly more patients receiving insulin via pen wanted to continue this method of insulin delivery when at home, and 2) significantly more patients would recommend insulin pens versus vial and syringe to other people with diabetes.

## Durable Insulin Pens: Patient Survey Results

Prefilled disposable pen containing a suspension of premixed insulin analog (70/30) vs vial and syringe (N = 372)

### Responses

- Efficacy benefits were greatest in those who had never used insulin
- Those new to an insulin pen reported greatest improvement in convenience and flexibility
- All 5 groups responded with an overall preference for pen

Rubin RR, Peyrot M. *Diabetes Care*. 2004;27:2495–2497.

In another study of 372 participants, patients with type 2 diabetes were divided into 5 treatment groups based on their prior treatment (those who had never used insulin; those who had never used mixed insulin; those who had used 70/30 insulin but not in a pen; those who had used 70/30 insulin in a pen; and all others). All groups overwhelmingly preferred a prefilled pen containing a premixed insulin analog (70/30) to vial and syringe.

Efficacy benefits were greatest in the group who had never used insulin, but those who had previously used only syringes to deliver unmixed insulin reported the greatest overall benefits on outcomes such as convenience, flexibility, and quality of life.

# Economic Impact of Insulin Pens

486 patients with type 2 diabetes in whom treatment was converted from vial/syringe to prefilled biphasic insulin aspart 70/30 pen

Outcome	Before pen	After pen	Significance
Treatment adherence (MPR)	59%	68%	$P < 0.01$
MPR $\geq$ 80%	35%	56%	$P < 0.01$
Annual associated healthcare costs per patient	\$16,004	\$14,256	$P < 0.01$
Annual cost of OADs	\$1790	\$1018	$P < 0.01$
Annual hypoglycemia costs/patient	\$1528	\$620	$P < 0.01$
Hypoglycemic events	<ul style="list-style-type: none"> <li>• 60% decrease in likelihood of hypoglycemic events after conversion to pen (<math>P &lt; 0.05</math>)</li> <li>• 64% decrease in ED visits and 61% reduction in physician visits related to hypoglycemic events</li> </ul>		

MPR = medication possession ratio; OADs = oral antidiabetic agents; ED = emergency department.

Cobden D et al. *Pharmacotherapy*. 2007;27:948–962.

Patient satisfaction and preference for insulin pens have been demonstrated repeatedly across all insulin formulations and manufacturers. But what about the cost issues related to insulin pens?

Cobden and colleagues recently evaluated the impact of switching from vial and syringe to a prefilled insulin analog pen using biphasic insulin aspart 70/30. This retrospective, longitudinal, pre–post analysis of an integrated medical/pharmacy claims database covering greater than 40 million lives included 57 managed care plans across the United States. A total of 486 patients with type 2 diabetes who had newly initiated treatment with the biphasic insulin aspart 70/30 pen device were identified. The mean age of the patient population was 45.1 years, and 56.4% were male.

As shown in this slide, overall treatment adherence measured by medication possession ratio (MPR), improved significantly after the switch. Similarly, the percentage of patients with optimal adherence (MPR  $\geq$ 80%) increased significantly after conversion from vial and syringe to the pen. Also significant 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 for experiencing hypoglycemia after conversion to an insulin pen also was reduced significantly and was associated with significant reductions in emergency department and physician visits related to hypoglycemia; hospitalizations and outpatient visits remained similar after conversion (data are not shown).

## Case #1

- FM is a 67-year-old male with type 2 diabetes for 12 years. Since he retired 2 years ago, his glycemic control is waning, with a recent A1C of 8.4% (3 years ago his A1C was 7%). His BP is 140/90 mm Hg and his LDL is 88 mg/dL. He appears to be less focused on healthy food choices and exercise than he use to be. He also reports that his arthritis is becoming more bothersome, further limiting his ability to exercise.

LDL = low-density lipoprotein.

Let's take a look at a case study. FM is a 67-year-old male with type 2 diabetes for 12 years. Since he retired 2 years ago, his glycemic control is waning, with a recent A1C of 8.4% compared with an earlier value of 7.0%. His BP is 140/90 mm Hg and his LDL is 88 mg/dL. He appears to be less focused on healthy food choices and exercise than he used to be. He also reports that his arthritis is becoming more bothersome, further limiting his ability to exercise.

## Case #1

- FM receives metformin 1000 mg BID and glyburide 10 mg QD.
- What are FM's options for improving glycemic control?

FM receives metformin 1000 mg BID and glyburide 10 mg QD.  
What are FM's options for improving glycemic control?

## Case #1

### □ Issues:

- FM lost focus in retirement
  - Expresses less interest in maintaining glycemic control
- Possible contributing factors
  - Disease progression
  - Increase in arthritis symptoms
  - Less structured lifestyle—possibly affecting meal schedule and food choices?
  - Boredom? Depression?
  - Hyperglycemia?
  - Financial issues leading to missed doses?

Let's take a look at some of the issues with FM. The loss of glycemic control appears to have started when he retired. There may be several reasons for this. It could be that his disease is progressing and residual  $\beta$ -cell function continues to deteriorate. FM notes that his arthritis symptoms are more bothersome, which makes it difficult or uncomfortable for him to exercise. In addition, in retirement his lifestyle became less structured; perhaps he is even bored with so much time on his hands versus working full days. This could be causing him to eat less healthily.

Frequent hyperglycemia could be compounding the problem of lack of energy, further potentiating his downward spiral. Another common concern among older patients with diabetes is depression. Additionally, he may have experienced a change in health-care insurance or finances that is causing him to miss doses of his oral antidiabetic agents. Clearly, a candid and thorough discussion with FM regarding these potential contributors is warranted. More information is needed to help FM get back in control.

## Case #1

- Workup reveals no depression or financial issues
- His primary care provider prescribes a long-acting basal insulin at bedtime and ACE inhibitor for blood pressure
- Discuss potential reasons for lack of glycemic control

ACE = angiotensin converting enzyme.

After a thorough workup, it does not appear FM has depression or financial concerns that could be causing medical nonadherence. Thus, it is likely that disease progression and reduced exercise, along with poorer nutrition, are likely culprits.

FM's primary care provider prescribes a long-acting basal insulin at night to help FM improve his glycemic control, and an angiotensin converting enzyme inhibitor as an antihypertensive. (Remember that the blood pressure goal for patients with diabetes is  $\leq 130/80$  mm Hg.)

As an educator, there are several things you can do to help FM follow this new treatment plan. These include discussing the possible confounding factors that could be contributing to the worsening of glycemic control (issues regarding nutrition, exercise, etc.).

## Case #1

- FM is resistant to insulin therapy
  - Unsure he can self-inject
  - Need for insulin suggests failure on his part
- Reassure/remind of risk of complications
- Show him various insulin delivery options
  - Suggest pen delivery due to arthritis

FM is very upset and hesitant to begin insulin therapy. He is unsure about his ability to self-inject, and is upset with himself that he has “failed” to take care of himself.

There are several things you can do to help FM feel better about beginning this new treatment plan. Remind him about the life cycle of diabetes—the progressive loss of  $\beta$ -cell function and risk of complications. Now that he is retired, FM should be enjoying life to the fullest—a major facilitator to enjoying life is maintaining good health. Show him how both vial and syringe and pen options are used so that he can make an informed decision about which would best suit his lifestyle. Suggest that, given his arthritis, an insulin pen might make administration easier.

## Case #1

### □ Outcome:

- FM selected a disposable pen for insulin delivery
- Began volunteering with a local boys and girls club
- Manages arthritis symptoms better with exercise and OTC analgesics
- Appears to be more motivated to manage diabetes; 6 months later, A1C 6.9%, BP 120/76 mm Hg, and LDL 70 mg/dL

OTC = over the counter.

FM experienced positive outcomes. He selected an insulin pen because he found the vial and syringe method of insulin delivery too difficult with his arthritis. FM reported that he began volunteering with a local boys and girls club. This helped him get back on a regular schedule. He also began managing his arthritis symptoms better through regular exercise and over-the-counter analgesics, as suggested by his primary care provider. Most importantly, FM appears motivated to regain control of his diabetes; 6 months after beginning insulin therapy, his A1C had decreased to 6.9%.

## Continuous Subcutaneous Insulin Infusion (CSII)

- ❑ Continuous short-acting insulin delivery via flexible tube with needle inserted subcutaneously
- ❑ Basal rate is continuous, so no peak concentration unless bolus dose administered to cover meals
- ❑ Regular human insulin or rapid-acting insulin analogs are approved for pump use. Intermediate- or long-acting insulin are not approved or suitable for pump use.

Continuous subcutaneous insulin delivery (CSII), or insulin pumps, are another option for insulin delivery.

The pumps are external; are roughly the size of a small cell phone; weigh less than 4 ounces; and are comprised of an insulin reservoir, a small battery-operated pump, and a computerized control mechanism. In most pumps, insulin reservoirs must be filled by the patient. Insulin is delivered through a flexible plastic tube (cannula), with or without a small needle, which is inserted subcutaneously and taped into place. One model (OmniPod®) does not have tubing; rather, it adheres to the skin, and insertion of the cannula into the skin is automatically directed via a wireless handheld personal diabetes manager (PDM).

The insulin pump can be programmed to deliver both basal and bolus doses. Basal insulin is provided by a slow, steady infusion of insulin over a 24-hour period. Pumps can be programmed to deliver different basal rates throughout the 24-hour period, reducing the risk of hypoglycemia or hyperglycemia. Premeal or snack bolus doses can be selected to cover the user's estimated carbohydrate intake at mealtime and correct for out-of-range blood glucose readings or patterns.

# Insulin Pumps—CSII

## Advantages

- Small, discreet
- Most closely mimics body's physiologic secretion of insulin
- Increased accuracy in insulin dosing
- Predictable absorption of insulin
- Increased flexibility in lifestyle
- Flexible programming
- No need for multiple injections

## Disadvantages

- Initial purchase expensive
- Potential for inflammation and infection at infusion site
- Potential for catheter occlusion/mechanical failure, increased risk of ketoacidosis, hypoglycemia
- Requires higher degree of patient motivation to manage indwelling catheter/potential problems

Insulin pumps use computerized systems to deliver continuous basal doses of insulin as well as bolus doses. Of all delivery systems, pumps most closely mimic the body's physiologic release of insulin and thus are most suited for achieving intensive treatment goals. Pumps deliver very precise insulin doses throughout the day. Insulin absorption is more stable and predictable than with a multiple-injection regimen; this may increase the potential for improved glycemic control. The pumps are discreet, and permit a flexible lifestyle.

Disadvantages to the pump include an initial high cost, which may not be feasible for all patients; the potential for inflammation and infection at the infusion site, which can be avoided by changing the site every 2 to 3 days; and a possibility of "kinking" of the catheter or mechanical failure, which could lead to ketoacidosis or hypo-hyperglycemia. However, all pumps have alarms to alert the patient when there is an interruption in the delivery of insulin.

Since mechanical problems can occur, such as leakage, battery problems, and the remote possibility of generalized mechanical failure, patients need to learn how to deal with these situations.

## Insulin Pumps—CSII

- ❑ Patient determines bolus dose before each meal, providing flexibility and convenience
- ❑ Requires frequent blood glucose monitoring ( $\geq 4$  times daily)
- ❑ Careful patient selection is crucial for best results
  - Highly motivated
  - Willing to assume substantial responsibility for their own care
  - Willing to check blood glucose levels 4 to 6 times daily
  - Able and willing to make adjustments in insulin, food intake, and exercise in response to blood glucose results

When using an insulin pump, the patient selects and delivers the bolus dose before each meal or snack to control rises in postprandial blood glucose. The dose is determined by the preprandial blood glucose concentration and the type and amount of food the patient will eat at that meal. Insulin doses are calculated by the pump based on carbohydrate intake and blood glucose readings.

All pumps have alarm systems to alert the user to catheter problems and low levels of insulin in the reservoir.

Patients who choose insulin pump therapy require sophisticated skills for diabetes self-management. They are willing to check their blood glucose levels frequently throughout the day and learn how to coordinate their blood glucose levels with adjustments in the basal and bolus infusion rates.

Newer pumps make all mathematical calculations for the patient, eliminating errors and helping those with limited numeracy skills.

# Efficacy and Safety of CSII

## □ Efficacy

- Studies have found that CSII effectively lowers A1C in adults and children/adolescents
- Effects  $\geq$  multiple daily injections of insulin

## □ Safety

- Fewer hypoglycemic events with CSII than prepump therapy

Herman WH et al. *Diabetes Care*. 2005;28:1568–1573.

Raskin P et al. *Diabetes Care*. 2003;26:2598–2603.

Litton J et al. *J Pediatr*. 2002;141:490–495.

Weintrob N et al. *Pediatrics*. 2003;112:559–564.

Ahern JA et al. *Pediatr Diabetes*. 2002;3:10–15.

Boland EA et al. *Diabetes Care*. 1999;22:1779–1784.

Several studies have evaluated the effectiveness of continuous subcutaneous insulin infusion or insulin pump therapy with prepump therapy, or more specifically, with multiple daily injections (MDIs) of insulin. In general, these studies have demonstrated that A1C is effectively lowered in all patient groups ranging from preschoolers with type 1 diabetes to adults with type 2 diabetes. Some studies have shown a significant advantage of insulin pumps over MDIs in lowering A1C, whereas other studies have shown that intensive control with MDIs is comparable to insulin pump therapy.

Particularly in children, insulin pump therapy is associated with a significant reduction in the number of hypoglycemic episodes.

## Various Models



This slide depicts some of the insulin pump models currently available with numerous, varied features. All include occlusion, overdelivery/safety, and near-empty alarms; are battery operated; and have 4-year warranties. All have memory features that store a number of readings (either by event or number of days).

## CSII Product Details

Manufacturer	Name	Comments
Animas Corporation	One Touch® Ping™	500-item database from CalorieKing; includes remote meter; waterproof
Insulet Corporation	OmniPod® Insulin Management System	Automated cannula insertion Personal diabetes manager wirelessly programs OmniPod; integrates with freestyle meter
Medtronic Diabetes	Paradigm® 522/722	Component of REAL-Time System with continuous glucose monitor; pediatric version available

*Diabetes Forecast*. 2009:62. Available at <http://www.forecast.diabetes.org/magazine/resource-guide/2009-resource-guide>.

The first 4 pump models listed (this and the next slide) all interact with blood glucose monitors.

The Animas One Touch Ping delivers up to 12 basal rates in 4 personalized programs, plus a temporary basal rate that can be adjusted from 30 minutes to 24 hours in 30-minute increments. Basal rates can be programmed from 0.025 to 25 units/hour, and the smallest bolus is 0.05 unit. The One Touch Ping can store the nutritional value of up to 500 food items from CalorieKing database on the pump. It interacts wirelessly with a remote meter that can perform functions such as calculating a bolus and instructing the pump to deliver it. The meter is waterproof to 12 feet so it can be worn during swimming.

Insulet Corporation manufactures the OmniPod Insulin Management System, which consists of the pump and a Personal Diabetes Manager (PDM). The PDM is a wireless, handheld device that is used to program the OmniPod with customized insulin delivery instructions, monitor the operation of the OmniPod, and monitor blood glucose levels. The pump has capacity for 7 basal programs with up to 24 rates per program. The basal rate range is 0.05 to 30 units/hour, and the smallest bolus dose is 0.05 unit. The PDM also has a food database of over 1000 common food items and a child lock-out feature. At 1.2 ounces, it is the lightest pump as well as the smallest.

Medtronic Diabetes markets the Paradigm pump which is part of the REAL-Time system. This is the only pump system that integrates with continuous blood glucose monitoring (glucose monitoring system sold separately). The paradigm offers 3 basal patterns and up to 48 basal rates per pattern, with a basal range of 0.05 to 35 units/hour, with the smallest bolus dose of 0.1 unit. There are 3 bolus delivery options and a bolus wizard that recommends a bolus based on personal settings, food intake, and amount of endogenous insulin. A downloadable memory includes a 90-day history that can be used to help the patient evaluate basal and bolus rates. A pediatric version is available.

## CSII Product Details (cont.)

Manufacturer	Name	Comments
Disetronic Medical Systems AG	Accu-Chek® Spirit	Palm device to chart progress and calculate boluses; interacts with blood glucose monitor via software; comes with 180-day backup pump
Sooil Development	DANA Diabecare® IIS	Watertight; available in 4 colors
Nipro Diabetes Systems	Amigo®	Shatter-resistant and waterproof casing

*Diabetes Forecast*. 2009:62. Available at <http://www.forecast.diabetes.org/magazine/resource-guide/2009-resource-guide>.

Disetronic Medical Systems markets the Accu-Chek Spirit in the United States. This pump accommodates a 315-unit cartridge and features 5 basal profiles with up to 24 rates each and a temporary basal rate in 10% increments from 0% to 200%, and 15-minute increments from 15 minutes to 24 hours. The basal range is 0.1 to 25.0 units/hour in 0.1-unit increments. It interacts with a blood glucose monitor via the Accu-Chek Pocket Compass Software. An interesting feature is that it comes with a 180-day backup pump. It also comes with a handheld palm device to chart progress and calculate boluses.

Sooil Development manufactures the DANA Diabecare IIS. This pump has a 300-unit insulin reservoir and features 4 basal profiles with 24 basal rates per profile, plus a temporary basal in 10% increments  $\pm$  100%. The basal rate range is 0.00 to 16 units/hour in 0.1-unit increments. The smallest bolus dose is 0.1 unit. It is available in 4 trendy colors. The unit also features icon-driven programming and is watertight.

The Nipro Amigo has been available in the United States since 2008. This pump features 4 basal profiles with 48 rates available per profile, and a temporary basal rate in 10% increments from 10% to 200% and 15-minute increments from 15 minutes to 24 hours. The basal range is 0 to 30 units in 0.05-unit increments. Three bolus delivery options are possible in increments programmable in 0.05 unit over the range of 0.05 up to 30.0 units. Its casing is shatter resistant and waterproof, and the screen uses icons and words during programming.

## Patient Preference for CSII

Patient group	N	Comments
Adults with type 2 diabetes	132, randomized to CSII or multiple daily injections (MDIs) for 24 weeks	93% CSII patients preferred it over MDI; reasons included flexibility, ease of use, and convenience
Children aged 9 to 14 years with type 1 diabetes	23, crossover study between CSII and MDI for 3.5 months	70% of children preferred CSII over MDI for continued therapy

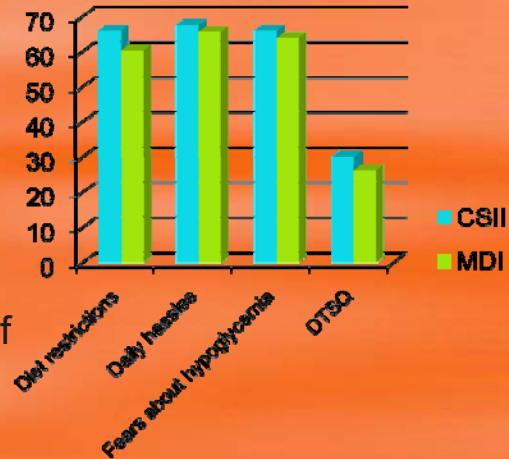
Raskin P et al. *Diabetes Care*. 2003;26:2598–2603.  
Weintrob N et al. *Pediatrics*. 2003;112:559–564.

Patient preference and satisfaction for insulin pumps has been evaluated in clinical trials. In one study of 132 adults with type 2 diabetes, patients were randomized to either insulin pump use or MDI of insulin for 24 weeks. At the end of the study, 93% of patients using insulin pumps preferred it over MDIs. The reasons they cited for the preference included flexibility, ease of use, and convenience.

In another study, 23 children aged 9 to 14 years of age were randomized to insulin pump use or MDIs for 3.5 months and then crossed over to the other delivery option for another 3.5 months. At the end of the study, 70% of study participants reported a preference for insulin pump therapy over MDIs.

## Quality of Life And Treatment Satisfaction With CSII

- N = 1341
- CSII vs MDI
- 3 separate QoL measures
- No negative impact of CSII vs MDI
- Some advantages of CSII over MDI



QoL = quality of life; DTSQ = Diabetes Treatment Satisfaction Questionnaire.

EQuality 1 Study Group. *Diabet. Med.* 2008;25:213–220.

The results of the largest study assessing quality of life (QoL) and treatment satisfaction between CSII and MDIs of insulin was recently published. A total of 1341 adult patients with type 1 diabetes recruited from 60 diabetes clinics who were receiving either CSII or MDI (90% glargine-based) completed 3 treatment measurements: The Diabetes Specific Quality of Life Scale (DSQOLS), which measures 4 main components of QoL (physical, emotional, social burdens, and daily functioning); the Diabetes Treatment Satisfaction Questionnaire (DTSQ), and the SF-36 Health Survey. Higher scores signify better outcomes on these scales.

On multivariate regression analysis of the DSQOLS (after adjusting for socioeconomic and clinical characteristics), patients receiving CSII reported significantly higher scores than those receiving MDIs for diet restrictions, daily hassles, and fears about hypoglycemia (higher scores mean better results). In addition, scores were significantly higher for CSII over MDI on the DTSQ by multiple regression analysis. On the SF-36, there were no differences between groups in the results when adjusted for confounders (data not shown).

## Case #2

- MB is a 47-year-old sales executive who has had type 2 diabetes for 7 years. Because of her concern for long-term complications, she began insulin therapy almost immediately following diagnosis and uses disposable pens for delivery and maintained an A1C between 6.8% and 7.0%. Her job now requires her to commute regularly between New York and Chicago. Given the irregularity in her travel and meal schedule, her A1C increased from 7% to 7.6% in the last 6 months, and she has gained 12 pounds.

Let's take a look at the case of patient MB, who is a 47-year-old sales executive with type 2 diabetes for 7 years. Because of her concern for long-term complications, she began insulin therapy almost immediately following diagnosis and uses disposable pens for delivery. She was able to maintain an A1C between 6.8% and 7.0% with this method. Her job now requires her to commute regularly between New York and Chicago. Given the irregularity in her travel and meal schedule, her A1C increased from 7% to 7.6% in the last 3 months, and she has gained 12 pounds.

## Case #2

- MB is worried about the loss of glycemic control. Since her work life has become more hectic, she wants to make her insulin delivery system as seamless as possible.
- She wants to learn more about an insulin pump but has concerns about using it while traveling and going through security at airports.
- Is MB a candidate for CSII?

MB is worried about the loss of glycemic control she has experienced and attributes it to her hectic work schedule. She wants to improve upon it while making insulin delivery as seamless as possible and reduce the risk of diabetes-related complications. As a result, she wants to learn more about an insulin pump, but has concerns about using it while traveling.

Is MB a candidate for CSII?

## Case #2

- While a CSII will deliver insulin more predictably, it will not improve MB's food choices or help her exercise
- She* needs to improve these aspects of her life as they relate to diabetes health
- A diabetes educator can help in this regard

While MB may want to change her method of insulin delivery, thinking that it will help her glycemic control, MB must understand that a pump will not improve her food choices or teach her how to estimate carbohydrates or calories when eating out, nor will a pump help her with her exercise regime. It will only provide the insulin more predictably. Thus, MB must understand that she needs to adjust her lifestyle accordingly. Nevertheless, the pump is an option for her.

## Case #2

### □ Patient-related factors

- Hectic lifestyle; irregularity in travel and meal schedule
- Patient is motivated

### □ Disease-related factors

- A1C beginning to increase
- Weight gain
- Patient concerned about developing complications

There are several factors that should be considered. MB is an executive with a hectic lifestyle, and she is extremely motivated to maintain glycemic control. Clearly, she is well informed about diabetes and wants to reduce the risk of diabetes-related complications.

Another consideration is MB's increasing A1C level and weight gain. A change in delivery systems may serve to motivate her to restore her glycemic control and improve her health and well-being.

## Case #2

- ❑ No travel/security-related issues specific to an insulin pump vs insulin pens
- ❑ Diabetes educator selects an appropriate pump for MB
- ❑ MB meets several times with diabetes educator to “get back on track”
- ❑ Outcome: MB successfully made the transition to pump
  - ❑ Glycemic control restored
  - ❑ MB is once again motivated to watch her food choices and weight

MB is concerned about traveling with an insulin pump and going through airport security. An insulin pump poses no difference than any other method of insulin delivery in this regard. Patients with diabetes are to notify the Transportation and Safety Administration security officer at airport security of the diabetes diagnosis and the need for insulin. The security officers are familiar with a number of medical conditions that travelers must declare, including diabetes. If MB is uncomfortable with walking through the metal detector at the airport, she may choose to have a visual inspection of the pump instead.

Her diabetes educator shows MB 2 pump options; MB chooses one of them. She meets with her educator for extensive instruction on pump programming and troubleshooting. MB also meets numerous times with her diabetes educator for “refresher courses” on carbohydrate-counting skills and calculating insulin doses based on blood glucose readings, meals, and activity level.

MB’s life became so busy that she let management of her diabetes slip. While switching to a pump per se did not necessarily help her achieve improved glycemic control, it did serve as a motivator to get her disease management back on track.

## Check Point

Involvement in their own diabetes management is not required when people use insulin pumps.

- a. True
- b. False

Involvement in their own diabetes management is not required when people use insulin pumps.

- a. True
- b. False

## Check Point

b. False.

Patients must *always* participate in their own management regardless of the insulin delivery system used; with pumps in particular, patients must be especially vigilant about their blood glucose levels as insulin delivery is relatively constant.

The correct answer is b—false.

Patients need to participate in their own management regardless of the insulin delivery system used. Patients using pumps must be especially vigilant about their blood glucose levels.

## Summary

- ❑ There are several options for insulin delivery
- ❑ Patients who require insulin should be made aware of the options so that they can assist in selecting the one that most fits their desires, needs, and lifestyles
- ❑ Tailoring the insulin delivery to the patient's needs may assist in improving outcomes

There are several options for insulin delivery. Patients who require insulin would benefit from knowing about these options so that they can assist in selecting the one that most fits their desires, needs, and lifestyles. Both patient input and healthcare professional recommendations are combined to determine the best fit.

Tailoring the mode of insulin delivery to the patient's needs may assist in improving outcomes. Pharmacists and nurses can supply easy-to-learn tools to reinforce learning. Educating patients in the use of today's wide range of insulin delivery systems can empower them to take an active role in the management of their diabetes. We are challenged to listen to patients' concerns about insulin therapy, address their needs, and offer the abundance of options provided through insulin delivery systems.