

Practical Aspects of Insulin Pen Devices

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Abstract

Insulin pen devices have several advantages over the traditional vial-and-syringe method of insulin delivery, including improved patient satisfaction and adherence, greater ease of use, superior accuracy for delivering small doses of insulin, greater social acceptability, and less reported injection pain. In recent years, pens have become increasingly user-friendly, and some models are highly intuitive to use, requiring little or no instruction. Despite this progress, uptake of these devices in the United States has not matched that in many other areas of the world. There is a need for improved awareness of the current characteristics of insulin pen devices among United States health care professionals. Knowledge of the design improvements that have been incorporated into pens, both to address patient needs and as a result of the improved technology behind the device mechanics, is essential to promoting the use of insulin pen devices. This review highlights some of the practical aspects of pen use and discusses the factors to be considered when selecting among different insulin pens.

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Introduction

Numerous studies have shown that insulin pen devices have several advantages over the traditional vial-and-syringe method of insulin delivery, including improved patient satisfaction and adherence, greater ease of use, and superior dosing accuracy.¹⁻⁷ Despite these advantages, the use of insulin pen devices in the United States remains low compared with other developed countries.⁸ About two-thirds of insulin prescriptions in Europe and about three-quarters in Japan are for pen devices.⁹ In contrast, in the United States, only 15% of patients are thought to use insulin pens.¹⁰

Possible reasons for the low adoption rates in the United States include lack of awareness among health care providers of the advantages of pens compared with the vial and syringe.^{8,11} An additional issue is the greater

prescription cost of insulin cartridges and prefilled insulin pens compared with insulin vials, although the cost to the patient may be the same depending on their coverage; in fact, if they have one copay per box of pens, the cost to the patient may actually be less per unit of insulin. It should be noted, however, that despite the higher unit cost of insulin in pen devices versus vials, several studies have found that overall diabetes-related treatment costs are lower with pen devices than with vial and syringe.^{1,2,12} In addition, most pen devices have good formulary coverage. For example, the FlexPen[®] prefilled pen is covered on more than 90% of managed care plans.¹³ Therefore, in theory, costs should not prevent the use of these devices.¹⁴ However, many smaller health maintenance organizations and state Medicaid plans may require prior authorization for insulin pens.

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Given the clinical, practical, and potential health economic advantages of insulin pens, there is a need for improved awareness of insulin pen devices among U.S. health care professionals. A study of patients with type 2 diabetes in the United States found that the physician's role in presenting the pen as an option and recommending pen use was a critical factor in patients' use of pens.¹⁵ Physicians, nurses, and diabetes educators should therefore become familiar with the various insulin delivery devices available so that they can discuss the potential benefits of these devices with patients and offer advice on which device best meets an individual patient's needs. Nurses, diabetes educators, and pharmacists have a particularly important role in educating patients on how to use insulin pens because incorrect use can affect pen performance and thus the accuracy of the administered dose.¹⁶ This review describes the practical aspects of insulin pen devices, including considerations when selecting among different insulin pens.

Advantages of Pen Devices Compared with Vial and Syringes

The traditional route of subcutaneous insulin administration has been the vial and syringe. However, this method of administration has many disadvantages, including fear of injections, poor dose accuracy, lack of social acceptance, lengthy training time, and difficulty of transportation. These factors can all act as barriers to insulin therapy, impacting on lifestyle flexibility and negatively influencing treatment adherence, patient self-management behavior, and achievement of euglycemia.^{17,18} Insulin pens have been developed to help address these issues, with resulting improvements in portability, dosing accuracy, mealtime flexibility, and convenience of delivery.^{4-6,19} Increased patient preference, treatment satisfaction, and quality of life have been reported for pen devices compared with the vial and syringe,^{3,7,20,21} these benefits may be particularly important due to their demonstrated impact on patient adherence. Other studies have shown that pen devices are associated with improved costs of care, less reported injection pain, and improved patient self-management behaviors, including adherence to treatment, compared with the vial and syringe.^{1,22-24} Because of the greater ease of use of insulin pens, people with visual impairment or reduced dexterity may especially benefit from using an insulin pen rather than a vial and syringe.

Once in use, most insulin analog vials, cartridges, and prefilled pens must be discarded after 28 days. This means that many patients who use a 10-ml vial end up either wasting insulin or using insulin beyond its

recommended discard date. This is rarely a problem for patients using either a 3-ml prefilled pen or a reusable pen containing a 3-ml insulin cartridge. Exceptions to the 28-day discard date are insulin detemir (vials and pens), which can be kept for up to 42 days once in use; biphasic insulin aspart 70/30 prefilled pens, which must be discarded after 14 days; and cartridges and prefilled pens containing biphasic insulin lispro premixes, which must be discarded after 10 days.

Two open-label, randomized, crossover studies have examined whether patients have greater dose confidence with a prefilled insulin pen or with a vial and syringe; both studies found that patients preferred the pen over the vial and syringe in this regard.^{3,25} In the first of these studies, 73% of patients felt more confident in the accuracy of the insulin dose delivered with the pen (original FlexPen) compared with 19% for the vial/syringe.³ In the other study, 88% of patients had greater confidence that they were taking the right dose with the pen (KwikPen[®]) than with the vial and syringe.²⁵ A more detailed discussion on the benefits of pen devices over vial and syringe can be found in the article by Selam²⁶ in this issue of *Journal of Diabetes Science and Technology*.

Available Insulin Pen Devices

Two types of insulin pen are available: prefilled disposable pens and refillable pens (**Table 1**).²⁷⁻⁴⁴ Most insulin pens are proprietary devices, manufactured by Eli Lilly, Novo Nordisk, and sanofi-aventis, and are designed to work with specific insulins from the same manufacturer. All currently available pens either are prefilled with 3 ml (300 units) of insulin or are refillable pens designed for use with 3-ml insulin cartridges (pens taking 1.5 ml insulin were formerly available). Insulin cartridges or prefilled disposable pens are available for all insulin analogs (rapid-acting, long-acting, and premixed) and for most human insulins (**Table 1**).

For all insulin pen devices, a separate prescription for pen needles is required. Pen needles are available from various manufacturers (Allison Medical, BD, Can-Am Care, Delta Hi-Tech, Medical Plastic Devices, Novo Nordisk, Owen Mumford, UltiMed) and come in gauges ranging from 29 to 32 gauge and in lengths from 5 to 12.7 mm.⁴⁵ More recent developments have resulted in the introduction of safety needles with protective shields that not only reduce needle-stick injuries but may also allay patient anxieties about needle use.⁴⁶ These are discussed in more detail in the section entitled "Individualizing Insulin Treatment with Pen Devices."

Table 1.
Insulin Pen Devices Currently Available in the United States.^{a, 27-44}

Product name	Insulin type	Dose range (unit)	Increment (unit)	Recommended needle type ^b	Dialing feature	Other features
Prefilled disposable insulin pens						
Humalog [®] KwikPen [®]	Insulin lispro and insulin lispro protamine suspension	Maximum dose 60 units	1	BD Ultra-Fine [™] needles	Dial-back feature Cannot dial more than the amount of insulin remaining	Light and portable
Original Humalog [®] pen Humalog [®] Mix75/25 [™] pen Humalog [®] Mix50/50 [™] pen	Insulin lispro Insulin lispro protamine suspension/insulin lispro injection	Maximum dose 60 units	1	BD Ultra-Fine needles	Dial-back feature After full dose is delivered, an arrow or diamond is centered in dose window Cannot dial more than the amount of insulin remaining	
Humulin [®] N pen Humulin [®] 70/30 pen	Human insulin isophane suspension Human insulin isophane suspension/human insulin injection	Maximum dose 60 units	1	BD Ultra-Fine needles	Dial-back feature After full dose is delivered an arrow or diamond is centered in the dose window Cannot dial more than the amount of insulin remaining	
Lantus [®] SoloSTAR [®] Apidra [®] SoloSTAR [®]	Insulin glargine Insulin glulisine	Maximum dose 80 units	1	BD Ultra-Fine needles	Dial-back feature Cannot dial more than the amount of insulin remaining	The two pens are distinguished by color, and the Apidra SoloSTAR has a raised dot on the push button
Levemir [®] FlexPen ^{®c} Novolog [®] FlexPen ^{®c} Novolog [®] Mix 70/30 FlexPen ^{®c}	Insulin levemir Insulin aspart Insulin aspart protamine suspension/insulin aspart	Maximum dose 60 units	1	NovoFine or NovoTwist needles	Dial-back feature Cannot dial more than the amount of insulin remaining	Little force required, dose delivery is confirmed by audible click, different insulins color coded, only pen with all three types of insulin analogs Raised dot on push button
Refillable pens						
Autopen [®] classic	Insulin lispro protamine suspension/insulin lispro injection	Maximum dose 21 or 42 units	1 or 2 unit models available	Compatible with all pen needles	Dial back not possible	Side-mounted release button that is pushed the same minimal distance to inject, regardless of the dose size and the needle gauge
Autopen 24 [®]	Insulin glargine Insulin glulisine	Maximum dose 21 or 42 units	1 or 2 unit models available	Compatible with all pen needles	Dial back not possible	The two dosing models are distinguished by color
HumaPen [®] LUXURA [™] and LUXURA [™] HD ^d	Insulin lispro Insulin lispro protamine suspension/insulin lispro injection	Maximum dose 60 units or 30 units (HD)	1 or 0.5 (HD) (minimum dose 1 unit)	BD Ultra-Fine needles	Dial-back feature	Relatively heavy; long reach needed for large doses
<i>Continued →</i>						

Table 1. Continued

Product name	Insulin type	Dose range (unit)	Increment (unit)	Recommended needle type ^b	Dialing feature	Other features
Refillable pens						
HumaPen® Memoir™	As HumaPen LUXURA	Maximum dose 60 units	1	BD Ultra-Fine needles	Dial-back feature	Digital display and memory of last 16 doses, including priming doses (i.e., eight injections) Relatively heavy; long reach needed for large doses
NovoPen® 3	Insulin aspart Insulin levemir Insulin aspart protamine suspension/insulin aspart Human insulin isophane suspension	Maximum dose 70 units	1	NovoFine needles	NovoPen 3 dial back requires partial disassembly	
NovoPen® 4	As NovoPen 3	Maximum dose 60 units	1	NovoFine needles	NovoPen 4 has easy dial back and cannot dial more than the amount of insulin remaining	Large easier-to-read numbers, reduced dose force, dose delivery confirmed by audible click
NovoPen® Junior	As NovoPen 3	Maximum dose 35 units	0.5 (minimum dose 1 unit)	NovoFine needles	Dial back requires partial disassembly	Distinguished from NovoPen 3 by raised circle on push button
OptiClik®	Insulin glargine Insulin glulisine	Maximum dose, 80 units	1	Ypsomed Clickfine™ needles or BD Ultra-Fine needles	Dial-back feature Cannot dial more than the amount of insulin remaining	Dose displayed for 2 minutes
^a Cartridge delivery capacity is 300 units, unless otherwise stated. ^b Needle types shown are recommended by the insulin pen device manufacturer. BD Ultra-Fine and Ypsomed Clickfine needles also fit all current insulin pens. ^c Also known as the improved FlexPen. ^d Half dose.						

How to Use an Insulin Pen

In a study assessing patient and physician acceptability of the prefilled Humulin®/Humalog® insulin pen device, 88% of the 33 physicians who completed questionnaires at the end of the study thought that it took less time to teach patients to use the pen and 73% thought that it took less time to initiate insulin therapy with the pen compared with a vial and syringe.⁴⁷ Teaching patients how to use an insulin pen can be summarized in the five main steps shown in **Figure 1**. It should be noted that because of the mechanics of pen devices, insulin can still be flowing out of the pen for several seconds after the button is fully depressed.¹¹ Patients must therefore keep the device in place with the button pressed in for 5–10 seconds (the stipulated time varies between

package inserts of the various insulin pens). For example, SoloSTAR® recommends a longer *in situ* time (10 seconds) compared with the FlexPen (6 seconds).^{37,38,41,42} The easiest way to ensure this is to instruct the patient to count to 5 (or 10, if using the SoloSTAR) before removing the needle. If the patient is using more than 50 units of insulin per dose, a good rule of thumb might be to instruct them to count to 10 regardless of the pen they are using to ensure complete absorption of the insulin.

If patients are using a pen that contains an insulin suspension (neutral protamine Hagedorn insulin or an insulin premix), they must carefully roll or tip the pen for the recommended number of times according to the

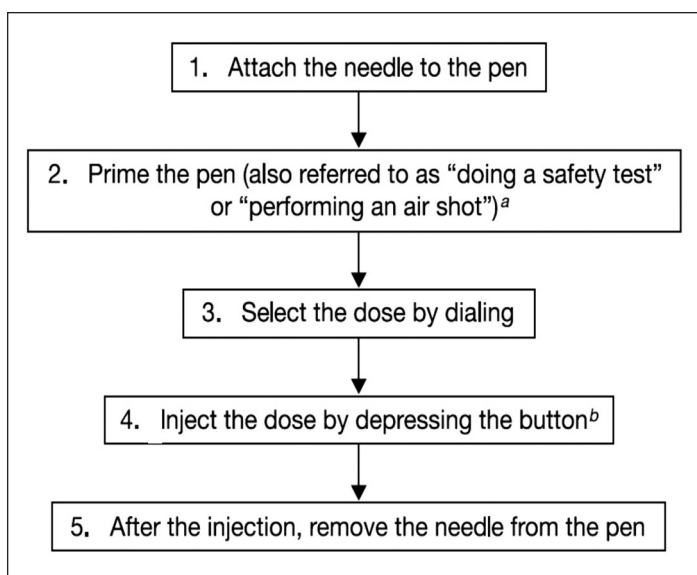


Figure 1. The five steps of insulin pen use. ^aThis is performed by instructing the patient to dial up 2 units and to inject these units into the air. ^bThe button needs to be pressed and the needle held in the skin for 5–10 seconds to ensure complete delivery of insulin dose. The easiest way to ensure this is to instruct the patient to count to 5 (or 10, if using the SoloSTAR[®]) before removing the needle.

package insert to ensure even mixing of the insulin suspension before attaching the needle. This issue may be especially important for patients who have used the vial-and-syringe method, as vials have a greater diameter than cartridges and so need to be tipped less often.⁴⁸

Pens must be primed before each injection, and the needle removed immediately after each use.¹¹ This is performed by instructing the patient to dial up 2 units and inject these units into the air (also called an “air shot”). This will displace any air in the needle and ensure an accurate injection. This air shot may need to be repeated when using a new pen or cartridge until a steady stream of insulin is observed. Insulin pens are manufactured with enough extra insulin to account for this air shot. An insulin pen must never be used by more than one individual, even if the pen needle is changed, because sharing of insulin pens can result in the transmission of hepatitis viruses, human immunodeficiency virus, or other blood-borne pathogens.⁴⁹

Patients and health care workers also need to be aware of the different procedures associated with insulin pens in case of accidentally dialing a dose larger than required. In the case of the Autopen[®], the side push-button design makes it impossible to dial back, and care should be taken not to dial past the required dose. With older versions of NovoPen[®] and NovoPen[®] Junior, the dose can be adjusted back down by partial disassembly of

the pen. This involves pulling the mechanical section and the cartridge holder apart and pressing the dial-up button back to zero. With other pens, namely the SoloSTAR, the improved FlexPen, Humalog KwikPen, original Humalog/Humulin pens, HumaPen[®] LUXURA[™], HumaPen[®] LUXURA[™] HD, HumaPen[®] Memoir[™], OptiClik[®], and NovoPen 4, easy dial back is possible by simply reversing the dial-up action.

Prior to first use, the insulin cartridge or pen should be stored in the refrigerator. The pen should be warmed to room temperature [below 86°F (30°C) for most insulin analogs] before use. After use, the pen should remain at room temperature below 86°F (30°C) in order to avoid producing air bubbles, which can form when the pen mechanism and the insulin expand/contract during a temperature change. As with all types of insulin, pens in use should be kept from extremes in temperature, keeping them as close as possible to room temperature below 86°F (30°C) at all times. Insulin glulisine has a narrower temperature range for storage than the other insulin analogs: Once in use, insulin glulisine must be stored below 77°F (25°C). In some buildings, for example, schools, the air conditioning is turned off at night, which may result in the room temperature rising above 77°F (25°C) or 86°F (30°C). Insulated storage packs are recommended in such conditions.

If a patient is switching from one type of insulin pen to another, it is important to check whether the procedure used for the previous pen also applies to the new pen.⁵⁰

Individualizing Insulin Treatment with Pen Devices

Health care practitioners should work with the patient to select insulin delivery devices that are compatible with their insulin regimen, lifestyle, and personal preferences. A regimen that causes the least disruption to the patient’s day-to-day life is much more likely to be used. Pens are more than just a matter of convenience, though; their ease of use allows patients to take better care of their own condition.¹⁵ As discussed by Selam²⁶ and summarized earlier, insulin pens can provide many potential benefits over vial-and-syringe delivery.

Patients across all age groups often have concerns regarding insulin therapy, and many of these concerns can be addressed effectively through choosing an insulin pen device rather than a vial and syringe.⁵¹ In particular, adolescents and children may find insulin pens more socially acceptable because of the pens’ greater portability

and discreetness. The NovoPen Junior, for example, has been developed specifically for use by children and teenagers or others requiring the ability to adjust their insulin in half-unit increments.³³ The HumaPen LUXURA HD can also deliver insulin in half-unit increments. However, both these pens administer a minimum dose of 1 unit, meaning that no pen is yet available that can deliver a dose of one-half unit. This can be problematic for young children, especially at school. With proper training, loading insulin and attaching the needle should be simple enough for grade school-aged kids.

Numbers on insulin pen dials are also larger than those on syringes, making it easier for those with visual impairment to select the correct dose. Some devices also incorporate audible clicks that notify the user of the number of units injected. Patients with impaired manual dexterity may find an insulin pen easier to use because it eliminates a step in the injection procedure, i.e., filling the syringe with insulin from the vial.

Advances in pen devices have also been made to improve needle safety and potentially reduce any needle anxiety. Needle-stick injuries are a common occupational hazard for health care professionals, particularly nurses. Use of the NovoFine[®] Autocover[®] safety pen needle has been shown to reduce the incidence of needle-stick injuries among nurses.⁴⁶ Although safety needles are not readily available outside the hospital setting, they may be a consideration for secondary caregivers to avoid needle-stick injuries. The other currently available safety pen needle is the BD AutoShield[™]. Both the NovoFine Autocover and the BD AutoShield conceal the needle, thus also potentially reducing needle anxiety. Two injection aids for insulin pens are available that also conceal the needle: NeedleAid[™] and NovoPen 3 PenMate[®].⁴⁵ Concealing the needle using the NovoPen 3 PenMate has been shown to reduce pain perception.⁵² The NeedleAid is an attachment designed to help visually impaired patients self-administer insulin.

Insulin pens are not without their limitations, and it is important that patients and health care workers are aware of these to ensure maximal outcomes. The maximum dose with most insulin pens is 60 to 80 units, but with a syringe it is 100 units. Patients cannot mix their own insulin formulations for use in a single injection given by an insulin pen. Despite their ease of use, pens are mechanically more complex than syringes, and some cases of malfunction have been reported in the literature.^{53,54} Therefore, patients using an insulin pen should have a backup pen available if traveling.

In terms of costs, there should be few reimbursement issues with most private health plans,⁹ although coverage by third-party payers may be under a tier that does not pay out in full.¹¹ However, costs to the patient for prefilled pens are minimized, as the pack dispensed by the pharmacy under one copayment contains five pens.¹¹ Most pens are now covered by Medicare.^{9,14} Some pens are associated with specific reimbursement issues.¹¹

Considerations When Choosing among Insulin Pens

In U.S. medical practice, the choice of insulin pen will be, to a large extent, determined by the choice of insulin, as particular insulins are specific to certain makes of insulin pen. Anecdotal reports suggest that many patients prefer prefilled disposable pens to refillable pens because disposable pens are typically lighter and smaller and are also simpler to use, as there is no requirement to load new insulin cartridges.⁵⁵ However, certain refillable pens have features, such as a memory function or the ability to dial in half-unit increments, that are not available with prefilled pens (**Table 1**). For example, the HumaPen LUXURA HD and NovoPen Junior are the only pens that allow the dose to be selected in half-unit increments. This may be important in children or in those sensitive to insulin. The OptiClik and SoloSTAR pens have a larger maximum dose (80 units) than the other insulin pens and therefore may be preferable in patients who take large doses of insulin.

The recently introduced improved FlexPen has a push-button mechanism that has been modified to reduce injection force while maintaining dose accuracy^{56,57} and retaining the ability to dial back. It therefore provides significantly less discomfort when injecting, which may be particularly suitable for patients with impaired manual dexterity or conditions such as arthritis. The improved FlexPen also has color-coded cartridges and packaging that clearly differentiate among insulin types.¹⁹ Color coding has also been incorporated into the SoloSTAR Lantus and Apidra pens to distinguish among insulin types.

Another initiative is for pens to supply auditory feedback, particularly since patients with type 2 diabetes often suffer from impairments in vision as well as manual dexterity.⁵⁸ The OptiClik, NovoPen 4, and improved FlexPen provide a confirmatory click when the correct dose has been delivered. In addition, the recently introduced NovoTwist[®] needle, for use with the improved FlexPen, has an easy twist-on action with an audible click when the needle is in place.

Both the OptiClik and the HumaPen Memoir devices have liquid crystal display screens powered by non-replaceable batteries. Therefore, when the battery runs out, patients have no visual confirmation of the dose selected, and the pen must be replaced. However, the OptiClik pen can be obtained only through a physician's office, making replacement more difficult. According to the manufacturers, the expected battery life for each of these pens is 3 years.

Clinical Studies Comparing Insulin Pens

Several studies have investigated dosing accuracy among pens. Generally, dosing accuracy is good, but the OptiClik pen can be subject to underdosing.^{59,60} One study found that, because of underdosing, 6.8% of 10-unit doses and 13.9% of 30-unit doses with the OptiClik pen were outside the International Organization for Standardization limits (± 1 unit for a 10-unit dose, and ± 1.5 units for a 30-unit dose).⁵⁹ Another separate study found that OptiClik underdosed for 17.1% of doses at 10 units and for 28.9% of doses at 30 units.⁶⁰ To avoid this, it may be necessary to carry out multiple priming before injecting with the OptiClik pen. Other studies have examined the dosing accuracy of SoloSTAR compared with FlexPen (improved and original), Humulin/Humalog pen, and OptiClik pen^{59,61-64} (Table 2). The largest of these comparative studies investigated 2280 doses of the SoloSTAR and the original FlexPen devices and showed that pens had comparable accuracy over the standard doses of 5, 10, and 30 units.⁵³

Another study also found that SoloSTAR and the original FlexPen were similarly accurate when used by device-naive individuals to deliver 20-unit doses of insulin.⁶⁵ One study compared the improved FlexPen with SoloSTAR: both pens showed very good accuracy, and the improved FlexPen was even more accurate than the SoloSTAR ($p < 0.05$)⁶⁴(Table 2).

Insulin pens also differ in the force required to inject an insulin dose, and this feature has been investigated in several studies,^{56,63,66-68} with results summarized in Table 3. In general, differences in the injection force among insulin pens are relatively small; however, the improved FlexPen does seem to show benefits when compared with SoloSTAR and OptiClik pens.^{56,67}

Data on ease of use and patient preference for different types of pen have been assessed in a number of clinical studies and in clinical practice. Many open-label studies have obtained information on patient preference, and results show that newer designs of pens are increasingly user-friendly and intuitive to use, requiring little or no instruction.^{54,69-71} For example, an open-label, crossover study showed that the improved FlexPen was faster to teach, simpler to use, and more trusted by patients compared with OptiClik.⁶⁹ Similarly, in an open-label, crossover study, the Novolog[®] Mix 70/30 FlexPen was associated with significantly greater intuitiveness and a shorter injection time compared with the HumaPen LUXURA device.⁷⁰ A separate study also showed a

Table 2.
Studies of Dose Accuracy of Insulin Pens with Comparable End Points

	Original FlexPen ^a	Improved FlexPen	HumaPen LUXURA	SoloSTAR	OptiClik	Reference
Deviation from 10-IU dose (mean)	1.64 ± 0.84%	NA ^b	1.10 ± 0.20%	2.61 ± 0.92%	4.78 ± 3.31%	59
	NA	1.63 ± 0.84% ^c	NA	2.11 ± 0.92%	NA	64
Deviation from 30-IU dose (mean)	0.83 ± 0.26%	NA	0.62 ± 0.19%	1.70 ± 0.84%	2.97 ± 2.48%	59
	NA	1.23 ± 0.76% ^d	NA	1.54 ± 0.84%	NA	64
Mean delivered dose of 5 IU	5.07 ± 0.15	NA	NA	5.03 ± 0.21	NA	61
	4.95 ± 0.19	NA	NA	4.86 ± 0.39	NA	62
Mean delivered dose of 10 IU	9.87 ± 0.16	NA	NA	9.83 ± 0.14	NA	61
	9.61 ± 0.27	NA	NA	9.27 ± 0.52	NA	62
Mean delivered dose of 30 IU	29.70 ± 0.38	NA	NA	29.45 ± 0.25	NA	61
	29.70 ± 0.34	NA	NA	28.73 ± 0.47	NA	62

^a No longer available commercially.

^b Not assessed.

^c $p < 0.001$

^d $p < 0.05$ for improved FlexPen vs SoloSTAR.

Table 3.
Studies of Injection Force of Insulin Pen Devices: FlexPen, Lilly Pen, SoloSTAR, and KwikPen

	Injection speed mm/s and insulin	Original FlexPen ^a	Improved FlexPen	Lilly Pen	SoloSTAR	KwikPen	Reference
Injection force using BD Micro-Fine 31-gauge needle (N)	3.3		8.1 ± 0.7 ^c		9.2 ± 0.5	12.5 ± 1.6	56
	5		10.7 ± 1.4 ^c		13.3 ± 0.8	16.9 ± 1.2	
	8.3		15.6 ± 0.9 ^c		20.7 ± 2.4	24.5 ± 2.6	
	4				12.9 ± 0.8		67
	6				20.5 ± 1.3		
	8				29.6 ± 1.9		
Injection force using NovoFine 32-gauge tip	3.3		5.7 ± 0.4 ^c		6.7 ± 0.3	9.1 ± 1.3	56
	5		8.2 ± 0.7 ^c		10.4 ± 2.1	13.1 ± 0.8	
	8.3		12.7 ± 0.5 ^c		16.3 ± 1.1	21.6 ± 2.0	
	4		8.3 ± 0.6		10.2 ± 1.1		67
	6		12.0 ± 0.9		15.7 ± 1.5		
	8		16.2 ± 1.3		22.3 ± 1.1		
	40 units rapid-acting insulin analog in 4 seconds	17.2		25.3	10.3		63
	40 units basal insulin analog in 4 seconds	16.3			11.3		
	40 units NPH ^b insulin in 4 seconds	17.7		24.2			
Maximum glide force (lb)	30 units	5.36				3.42 ^d	66
	60 units	5.62				3.61 ^d	

^a No longer available commercially.

^b Neutral protamine Hagedorn.

^c $p < 0.05$ for the improved FlexPen versus SoloSTAR or KwikPen.

^d $p < 0.0001$ for KwikPen versus original FlexPen.

greater patient preference with fewer problems for the Novolog Mix 70/30 FlexPen compared with the Humalog Mix75/25 Pen.⁷¹ Results of other studies have shown an overall preference for SoloSTAR (53%) rather than for the original FlexPen (31%) or Humulin/Humalog pen (15%),⁷² with the SoloSTAR and original FlexPen found to be more user-friendly than the Eli Lilly disposable pen.⁷³ To date, there are no studies comparing patient preference for the improved FlexPen compared with the SoloSTAR or Humulin/Humalog Pen.

Yakushiji and colleagues⁷⁴ assessed the preferences of 22 Japanese men and women for various insulin pens when self-injecting and when administering an injection to another person. Insulin injections were administered into prosthetic skin attached either to the participant or to a mock patient. The FlexPen was rated as the best

device for self-injection, whereas the OptiClik, perhaps because of its larger size, was rated as the best device for administration of an injection to another person.

Conclusions

In conclusion, the use of insulin pens offers many options to allow insulin delivery to be tailored to the individual patient. Newer designs of pens are increasingly user-friendly and are intuitive to use, requiring little or no instruction. This means that patients can quickly be taught how to use an insulin pen, which should go hand in hand with educating the patient on the importance of achieving accurate dosing. Thorough training of patients in the practical aspects and aims of insulin injection remains important, as errors in insulin delivery can result in incorrect dose administration and thus affect clinical

outcomes adversely. Health care providers need to ensure that they are updated on the latest developments in pen devices and teaching approaches in order to provide informed, individualized advice for their patients.

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References:

- Cobden D, Lee WC, Balu S, Joshi AV, Pashos CL. Health outcomes and economic impact of therapy conversion to a biphasic insulin analog pen among privately insured patients with type 2 diabetes mellitus. *Pharmacotherapy*. 2007;27(7):948-62.
- Lee WC, Balu S, Cobden D, Joshi AV, Pashos CL. Medication adherence and the associated health-economic impact among patients with type 2 diabetes mellitus converting to insulin pen therapy: an analysis of third-party managed care claims data. *Clin Ther*. 2006;28(10):1712-25; discussion 1710-1.
- Korytkowski M, Bell D, Jacobsen C, Suwannasari R; FlexPen Study Team. A multicenter, randomized, open-label, comparative, two-period crossover trial of preference, efficacy, and safety profiles of a prefilled, disposable pen and conventional vial/syringe for insulin injection in patients with type 1 or 2 diabetes mellitus. *Clin Ther*. 2003;25(11):2836-48.
- Keith K, Nicholson D, Rogers D. Accuracy and precision of low-dose insulin administration using syringes, pen injectors, and a pump. *Clin Pediatr (Phila)*. 2004;43(1):69-74.
- Lteif AN, Schwenk WF. Accuracy of pen injectors versus insulin syringes in children with type 1 diabetes. *Diabetes Care*. 1999;22(1):137-40.
- Graff MR, McClanahan MA. Assessment by patients with diabetes mellitus of two insulin pen delivery systems versus a vial and syringe. *Clin Ther*. 1998;20(3):486-96.
- Kadiri A, Chraibi A, Marouan F, Ababou MR, el Guermai N, Adjiny A, Kerfati A, Douiri M, Bensouda JD, Belkhadir J, Arvanitis Y. Comparison of NovoPen 3 and syringes/vials in the acceptance of insulin therapy in NIDDM patients with secondary failure to oral hypoglycaemic agents. *Diabetes Res Clin Pract*. 1998;41(1):15-23.
- Da Costa S, Brackenridge B, Hicks D. A comparison of insulin pen use in the United States and the United Kingdom. *Diabetes Educ*. 2002;28(1):52-6, 59-60.
- Bhargava A. Insulin therapy: the question this issue. *Insulin*. 2007;2(2):92-4.
- Marcus A. Diabetes care: insulin delivery in a changing world. *Medscape J Med*. 2008;10(5):120.
- Magnotti MA, Rayfield EJ. An update on insulin injection devices. *Insulin*. 2007;2(4):173-81.
- Pawaskar MD, Camacho FT, Andersen RT, Cobden D, Joshi AV, Balkrishnan R. Health care costs and medication adherence associated with initiation of insulin pen therapy in medicaid-enrolled patients with type 2 diabetes: a retrospective database analysis. *Clin Ther*. 2007;29 Spec No:1294-305.
- Novo Nordisk (2010) FlexPen insulin pen [cited 2010 Mar 23]. Available from: <http://www.novonordiskcare.com/flexpen/>.
- Medicare: the official US government site for people with Medicare July 9, 2009 [cited 2009 Sept 16]. Available from: <http://formularyfinder.medicare.gov/formularyfinder>.
- Rubin RR, Peyrot M. Factors affecting use of insulin pens by patients with type 2 diabetes. *Diabetes Care*. 2008;31(3):430-2.
- Thurman JE. Insulin pen injection devices for management of patients with type 2 diabetes: considerations based on an endocrinologist's practical experience in the United States. *Endocr Pract*. 2007;13(6):672-8.
- Peyrot M, Rubin RR, Lauritzen T, Skovlund S, Snok FJ, Matthews DR, Landgraf R, Kleibreil L; International DAWN Advisory Board. Resistance to insulin therapy among patients and providers: results of the cross-national Diabetes Attitudes, Wishes, and Needs (DAWN) study. *Diabetes Care*. 2005;28(11):2673-9.
- Summers KH, Szeinbach SL, Lenox SM. Preference for insulin delivery systems among current insulin users and nonusers. *Clin Ther*. 2004;26(9):1498-505.
- Sommavilla B, Jorgensen C, Jensen K. Safety, simplicity and convenience of a modified prefilled insulin pen. *Expert Opin Pharmacother*. 2008;9(13):2223-32.
- Lee IT, Liu HC, Liao YJ, Lee WJ, Huang CN, Sheu WH. Improvement in health-related quality of life, independent of fasting glucose concentration, via insulin pen device in diabetic patients. *J Eval Clin Pract*. 2009;15(4):699-703.
- Hörnquist JO, Wikby A, Andersson PO, Dufva AM. Insulin-pen treatment, quality of life and metabolic control: retrospective intra-group evaluations. *Diabetes Res Clin Pract*. 1990;10(3):221-30.
- Davis EM, Bebee A, Crawford L, Destache C. Nurse satisfaction using insulin pens in hospitalized patients. *Diabetes Educ*. 2009;35(5):799-809.
- McKay M, Compion G, Lytzen L. A comparison of insulin injection needles on patients' perceptions of pain, handling, and acceptability: a randomized, open-label, crossover study in subjects with diabetes. *Diabetes Technol Ther*. 2009;11(3):195-201.
- Davis EM, Christensen CM, Nystrom KK, Foral PA, Destache C. Patient satisfaction and costs associated with insulin administered by pen device or syringe during hospitalization. *Am J Health Syst Pharm*. 2008;65(14):1347-57.
- Ignaut DA, Schwartz SL, Sarwat S, Murphy HL. Comparative device assessments: Humalog KwikPen compared with vial and syringe and FlexPen. *Diabetes Educ*. 2009;35(5):789-98.
- Selam JL. Evolution of diabetes insulin delivery devices. *J Diabetes Sci Technol*. 2010;4(3):505-13.
- Eli Lilly (2006) HumaPen LUXURA HD insulin delivery device user manual (November 11, 2006).
- Eli Lilly (2006) HumaPen MEMOIR user manual (revised November 20, 2006).
- Eli Lilly (2007) KwikPen disposable insulin delivery device user manual (September 6, 2007).
- Eli Lilly (2009) Insulin pens [cited 2009 Jul 31]. Available from: <http://www.humalog.com/humalog-insulin-pens/humalog-insulin-pens.jsp>.
- Eli Lilly (2009) Prefilled insulin delivery device user manual (revised April 17, 2009).
- Novo Nordisk (1998) NovoPen 3 instructions for use.

33. Novo Nordisk (2002) NovoPen Junior instructions for use.
34. Novo Nordisk (2006) NovoLog Mix 70/30 FlexPen simple instructions for use (September 2006).
35. Novo Nordisk (2009) Insulin pens [cited 2009 Jul 31]. Available from: <http://www.novonordiskcare.com/insulin-pens>.
36. Novo Nordisk (2009) NovoLog Mix 70/30 FlexPen [cited 2009 Jul 31]. Available from: <http://www.novologmix70-30.com/novolog-mix-FlexPen.asp>.
37. Novo Nordisk (2009) NovoLog FlexPen [cited 2009 Jul 31]. Available from: <http://www.novolog.com/devices-flexpen.asp?s=ds&h=150>.
38. Novo Nordisk (2009) Levemir FlexPen [cited 2009 Jul 31]. Available from: <http://www.levemir-us.com/about-levemir-FlexPen-demo.asp?WT.ac=LevemirFlexPen>.
39. Owen Mumford (2006) Autopen 24 instructions for use (revised April 2006).
40. Owen Mumford (2009) Autopen [cited 2009 Jul 31]. Available from: <http://www.owenmumford.com/us/range/24/autopen.html>.
41. Sanofi-Aventis (2009) Lantus SoloSTAR pen [cited 2009 Jul 31]. Available from: http://www.lantus.com/solostar/solostar_insulin_pen.aspx.
42. Sanofi-Aventis (2009) Your guide to the Lantus SoloStar pen.
43. Sanofi-Aventis (2009) OptiClik [cited 2009 Jul 31]. Available from: <http://www.opticlik.com/>.
44. BD (2009) BD pen needles fit these pens [cited 2009 Jul 31]. Available from: <http://www.bd.com/us/diabetes/page.aspx?cat=7002&id=10257>.
45. American Diabetes Association. 2009 resource guide. Diabetes Forecast. 2009;62.
46. Lautier O, Mosnier-Pudar H, Durain D, Gonbert S, Spinu L, Faure P. Risk of needlestick injuries among nurses using NovoFine Autocover safety needles and nurses' satisfaction with the needles: the NOVAC study. *Insulin*. 2008;3(4):232-7.
47. Bohannon NJ, Ohannesian JP, Burdan AL, Holcombe JH, Zagar A. Patient and physician satisfaction with the Humulin/Humalog pen, a new 3.0-mL prefilled pen device for insulin delivery. *Clin Ther*. 2000;22(9):1049-67.
48. Korytkowski M, Niskanen L, Asakura T. FlexPen: addressing issues of confidence and convenience in insulin delivery. *Clin Ther*. 2005;27 Suppl B:S89-100.
49. US Food and Drug Administration. Risk of transmission of blood-borne pathogens from shared use of insulin pens. Information for healthcare professionals. March 19, 2009 [cited 2009 Jul 31]. Available from: <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHealthcareProfessionals/ucm133352.htm>.
50. Bhardwaj VR, Metcalfe N, Innes E, Harrison E, Jenkins D. Recurrent diabetic ketoacidosis after changing pen devices for insulin injection. *BMJ*. 2006;332(7552):1259-60.
51. Funnell MM. Overcoming barriers to the initiation of insulin therapy. *Clin Diabetes*. 2007;25(1):36-8.
52. Diglas J, Feinböck C, Irsigler K, Winkler F, Egger T, Weitgasser R, Pieber T, Lytzen, L. Reduced pain perception with Pen Mate, an automatic needle insertion device for use with an insulin pen. *Practical Diabetes Int*. 1999;16(2):39-41.
53. Boronat M, García-Delgado Y, Pérez-Martin N, Nóvoa FJ. Severe deterioration of metabolic control caused by malfunction of a disposable insulin pen device. *J Am Board Fam Med*. 2008;21(6):575-6.
54. Venekamp WJ, Kerr L, Dowsett SA, Johnson PA, Wimberley D, McKenzie C, Malone J, Milicevic Z. Functionality and acceptability of a new electronic insulin injection pen with a memory feature. *Curr Med Res Opin*. 2006;22(2):315-25.
55. Shaefer CF. The pen is mightier than the sword. *Insulin*. 2009;4(3):132-5.
56. Asakura T, Seino H, Kageyama M, Yohkoh N. Evaluation of injection force of three insulin delivery pens. *Expert Opin Pharmacother*. 2009;10(9):1389-93.
57. Pfützner A, Reimer T, Hohberg C, Frøkjær LP, Jørgensen C. Prefilled insulin device with reduced injection force: patient perception and accuracy. *Curr Med Res Opin*. 2008;24(9):2545-9.
58. Asakura T, Seino H. Assessment of dose selection attributes with audible notification in insulin pen devices. *Diabetes Technol Ther*. 2005;7(4):620-6.
59. Hänel H, Weise A, Sun W, Pfützner JW, Thomé N, Pfützner A. Differences in the dose accuracy of insulin pens. *J Diabetes Sci Technol*. 2008;2(3):478-81.
60. Asakura T. Comparison of the dosing accuracy of two insulin injection device. *J Clin Res*. 2005;8:33-40.
61. Penfornis A, Horvat K. Dose accuracy comparison between SoloSTAR and FlexPen at three different dose levels. *Diabetes Technol Ther*. 2008;10(5):359-62.
62. Asakura T, Seino H, Kageyama M, Yohkoh N. Dosing accuracy of two insulin pre-filled pens. *Curr Med Res Opin*. 2008;24(5):1429-34.
63. Clarke A, Spollett G. Dose accuracy and injection force dynamics of a novel disposable insulin pen. *Expert Opin Drug Deliv*. 2007;4(2):165-74.
64. Weise A, Pfützner JW, Borig J, Pfützner AM, Safinowski M, Hänel H, Musholt PB, Pfützner A. Comparison of the dose accuracy of prefilled insulin pens. *J Diabetes Sci Technol*. 2009;3(1):149-53.
65. Friedrichs A. Dose accuracy of SoloSTAR and FlexPen as assessed in a clinical setting. *Diabetes Technol Ther*. 2009;11(9):609-13.
66. Ignaut DA, Opincar M, Lenox S. FlexPen and KwikPen prefilled insulin devices: a laboratory evaluation of ergonomic and injection force characteristics. *J Diabetes Sci Technol*. 2008;2(3):533-7.
67. Rissler J, Jørgensen C, Rye Hansen M, Hansen NA. Evaluation of the injection force dynamics of a modified prefilled insulin pen. *Expert Opin Pharmacother*. 2008;9(13):2217-22.
68. Toraishi K, Yuizono Y, Nakamura N, Kato S, Aoki T, Ashida K, Sako Y. Force requirements and insulin delivery profiles of four injection devices. *Diabetes Technol Ther*. 2005;7(4):629-35.
69. Asakura T, Jensen KH. Comparison of intuitiveness, ease of use, and preference in two insulin pens. *J Diabetes Sci Technol*. 2009;3(2):312-9.
70. Reimer T, Hohberg C, Pfützner AH, Jørgensen C, Jensen KH, Pfützner A. Intuitiveness, instruction time, and patient acceptance of a prefilled insulin delivery device and a reusable insulin delivery device in a randomized, open-label, crossover handling study in patients with type 2 diabetes. *Clin Ther*. 2008;30(12):2252-62.
71. Niskanen L, Jensen LE, Råstam J, Nygaard-Pedersen L, Erichsen K, Vora JP. Randomized, multinational, open-label, 2-period, crossover comparison of biphasic insulin aspart 30 and biphasic insulin lispro 25 and pen devices in adult patients with type 2 diabetes mellitus. *Clin Ther*. 2004;26(4):531-40.
72. Haak T, Edelman S, Walter C, Lecointre B, Spollett G. Comparison of usability and patient preference for the new disposable insulin device Solostar versus FlexPen, Lilly disposable pen, and a prototype pen: an open-label study. *Clin Ther*. 2007;29(4):650-60.
73. Fischer JS, Edelman SV, Schwartz SL. United States patient preference and usability for the new disposable insulin device Solostar versus other disposable pens. *J Diabetes Sci Technol*. 2008;2(6):1157-60.
74. Yakushiji F, Fujita H, Terayama Y, Yasuda M, Nagasawa K, Shimojo M, Taniguchi K, Fujiki K, Tomiyama J, Kinoshita H. The best insulin injection pen device for caregivers: results of injection trials using five insulin injection devices. *Diabetes Technol Ther*. 2010;12(2):143-8.