

A PRACTICAL REVIEW OF INSULIN PEN DEVICES

*Teresa L. Pearson

Director, Clinical Services at Innovative Health Care Designs, LLC, Minneapolis, Minnesota, USA

*Correspondence to tpearson9@comcast.net

Disclosure: No potential conflict of interest.

Received: 06.05.14 **Accepted:** 21.07.14

Citation: EMJ Diabet. 2014;2:58-64.

ABSTRACT

Since the advent of insulin pens in 1985, there have been ongoing improvements providing several advantages over the traditional vial and syringe method of insulin delivery. 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, there remains to be disparity in access to insulin pens to people with diabetes in various countries. There is a need for improved awareness of the benefits of insulin pens among healthcare professionals. Continual advances have been made to address patient needs such as improved technology to make them easier to use; less painful; more discreet and convenient; and more accuracy for small doses of insulin, as well as the incorporation of a memory function, all contribute to an insulin delivery device that allows the patient to better manage their diabetes anytime and anyplace, without the bulk and challenge of carrying a vial and syringe. These advances have resulted in increased patient satisfaction with insulin pens and most importantly, all of these benefits improve adherence and result in improved clinical outcomes. This review highlights these benefits of insulin pen use and presents the issues to be considered when helping patients decide on the insulin pen that will best suit their needs.

Keywords: Type 2 diabetes, insulin, insulin pen, practical use.

INTRODUCTION

For over 50 years, vial and syringe was the only method of delivering insulin. While life-saving, it was crude at best, and ever since its discovery much effort has gone into improving the insulin. Initially, insulin was used primarily for people with Type 1 diabetes mellitus (T1DM), but research has shown that most people with Type 2 diabetes mellitus (T2DM) will also require insulin to maintain HbA1c at levels recommended by the American Diabetes Association/European Association for the Study of Diabetes.^{1,2} While insulins have improved, they still require an injection. Additional effort has gone into finding an adequate delivery method; in the 1970s insulin pumps became available, and in 1985, the first insulin pen was introduced.³ This review will focus on insulin pens.

Insulin pens have been shown to 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.⁴⁻¹⁰ About two-thirds of insulin prescriptions in Europe and about three-quarters in Japan are for pen devices⁹ while only 15% of patients are thought to use insulin pens in the US.¹¹ According to the recent report, *Access to Quality Medicines and Medical Devices for Diabetes Care in Europe*,¹² there remains a great disparity in access to insulin pens across Europe. While insulin seems to be a covered benefit in most countries, use of insulin pens varies more widely and may, in some cases, be restricted to people with T1DM and/or to children under the age of 18 years.

In spite of the convenience and greater ease of use, cost may be an issue. The greater cost of insulin cartridges and prefilled insulin pens, compared with insulin vials, can impact the acceptance of insulin pens as a viable option for people with T2DM. For some patients, the cost may be the same depending on coverage, and in fact, if they have

one co-payment per box of pens, the cost to the patient may actually be less per unit of insulin. If this seems to be an issue it is important to consider 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.^{3,4,11} Increased adherence with the use of insulin pens has been demonstrated and further emphasises the need to consider them as an option when initiating insulin.^{5,11,13} Therefore, in theory, costs should not prevent the use of these devices.

PERSPECTIVES

Healthcare Providers

Despite the many advantages of insulin pens, there is a lack of awareness among healthcare providers of those advantages which have been cited as a possible reason for low adoption rates in some countries.^{14,15} It has been shown that the physician plays a significant role in the patient's acceptance of the insulin pen as an option.¹⁶ In fact, the most powerful predictor of pen use was found to be physician recommendation. This emphasises the importance of the role of the physician in this self-care practice. It also emphasises the need to ensure that physicians are aware of insulin pens and how they can benefit patient adherence resulting in better outcomes. Nurses and diabetes educators should also become familiar with the various insulin pens available so they can discuss the potential benefits with their patients and offer advice on which device best meets their patients' needs. Nurses, diabetes educators, and pharmacists have particularly important roles in educating patients on how to use insulin pens. Incorrect use can affect pen performance, and thus, the accuracy of the administered dose.¹⁷ Healthcare professionals have been found to be strongly supportive of the use of insulin pens and they find them to be easier to handle, preferable to use, and more accurate in delivering insulin doses as compared to vial and syringe.^{18,19}

Patients

Patient perception has also been found to be an important predictor of pen use. A vial and syringe is clumsy to say the least but, over time, most people adapt to it quite well. The insulin pen, on the other hand, can easily fit into a pocket or purse, is durable, and much more discreet to use. In an open-label, randomised, multicentre study, patient

preference for insulin pens versus vial and syringe was statistically significant¹⁸ citing convenience, ease of use - including assembly - injection, and confidence in the dosage. The visual and auditory cues from the pen contribute to the increased level of confidence. Two open-label, randomised, crossover studies found that patients have greater dose confidence with a prefilled insulin pen over a vial and syringe.^{6,20} In the first of these studies, 73% of patients felt more confident in the accuracy of the insulin dose delivered with the pen, compared with 19% for the vial/syringe.⁶ In the other study, 88% of patients had greater confidence that they were taking the right dose with the pen than with the vial and syringe.²⁰ The vial and syringe do not offer this level of confidence and, as eyesight and dexterity decrease with age, the vial and syringe become much more challenging to handle.

The vial and syringe has many disadvantages including fear of injections, poor dose accuracy, lack of social acceptance, lengthy training time, and difficulty of transportation.²¹ These are potential barriers to insulin therapy, impacting flexibility, and affecting adherence to treatment, thus negatively impacting the achievement of euglycaemia.^{22,23} Insulin pens were designed to help address these issues, with resulting improvements in portability, dosing accuracy, mealtime flexibility, and convenience of delivery.^{7-9,24} Increased patient preference, treatment satisfaction, and quality of life have been reported for pen devices compared with the vial and syringe.^{6,10,25,26} Other studies have shown that pen devices are associated with improved costs of care, less reported injection pain, and improved patient self-management behaviours, including adherence to treatment, compared with the vial and syringe.^{4,27-29} Many of these benefits make insulin pens especially beneficial to people with visual impairment or reduced dexterity.

USING AN INSULIN PEN

Once in use, most insulin analogue vials, cartridges, and prefilled pens must be discarded after 28 days. The exceptions to the 28-day discard date is insulin detemir (Levemir®), which can be kept for up to 42 days once in use. Two types of insulin pens are available: prefilled disposable pens and refillable pens.³⁰⁻⁴⁶ Most insulin pens are proprietary devices, and are designed to work with specific insulins from the same manufacturer.

Insulin cartridges or prefilled disposable pens are available for all insulin analogues (rapid-acting, long-acting, ultra-long-acting, and premixed) and for most human insulins. Most currently-available pens are either prefilled with 3 ml of insulin or are refillable pens that are designed for use with 3 ml insulin cartridges. U100 insulin is used in most devices providing 300 units of insulin per cartridge or prefilled device. However, insulin degludec (Tresiba®) is also available in U200 strength, providing 600 units of insulin per device. The dose counter window for degludec will show the number of units, irrespective of the strength, so no dose conversion is required.⁴⁷

For all insulin pen devices, pen needles are purchased separately and may require a separate prescription. Pen needles are available from various manufacturers and come in gauges ranging from 29 G to 32 G, and in lengths from 4 to 12.7 mm.⁴⁶ 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.⁴⁸ Health professionals are also being advised to use these safety needles in accordance with the safety recommendations of the EU Council Directive 2010/32/EU.⁴⁹ As shorter needles have become available, the question of how to select the appropriate needle length has come up. For the average adult, 4, 5, and 6 mm needles are appropriate and can be injected at a 90-degree angle. For the overweight or obese patient, research shows that needle length should not be a concern.⁵⁰⁻⁵² According to the First Injection Technique (FIT) Guidelines,⁵² there really is no reason, even for very obese patients, to use a needle longer than 8 mm.

For very lean patients, it is recommended to raise a fold of skin and inject at an angle to prevent a possible intramuscular (IM) injection, especially if using an 8 mm needle or greater.^{50,52,53} For children, 6 mm or shorter needles are recommended. A 4 mm needle may be injected at a 90-degree angle while a 5 or 6 mm needle will require a lifted skin-fold to avoid possible IM injection. If an 8 mm needle is all that is available for a child it is essential to do a lifted skin-fold. Therefore, needle length should not be a concern but proper injection technique should be a part of the training for both insulin pens and vial and syringe use.^{50,54} The use of the FIT Guidelines is an excellent resource if any questions remain.

Healthcare practitioners should work with the patient to select the insulin pen that is most suited to their insulin regimen, lifestyle, and personal preferences. A regimen that causes the least disruption to the patient's lifestyle 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.¹⁶ Patients across all age groups often have concerns regarding insulin therapy, and many of these concerns can be effectively addressed through choosing an insulin pen.⁵⁵ In particular, adolescents and children may find insulin pens more socially acceptable because of the pens' greater portability and discreetness. The NovoPen® Junior, the HumaPen® Luxura™ HD, and the NovoPenEcho®, have been developed specifically for use in children and others requiring the ability to adjust their insulin in half-unit increments.³⁶

For people with visual impairment there are some advantages to using an insulin pen over a vial and syringe. For example, the numbers on insulin pens are larger than those on syringes, making it easier to select the correct dose. The audible clicks notify the user of the number of units injected, as well as when the insulin has been fully injected. And patients with impaired manual dexterity may find insulin pens easier to use because it eliminates the process of drawing up the insulin from the vial with the syringe. There have also been advances to improve needle safety and potentially reduce any anxiety about needles. The use of safety needles has been shown to reduce the incidence of needle-stick injuries among nurses, a common occupational hazard.^{48,49} While the safety needles are not readily available outside the hospital setting, they may be a consideration for secondary caregivers to avoid needle-stick injuries. The safety pen needles conceal the needle, so could potentially be used to reduce needle anxiety. There are injection aids for insulin pens that also conceal the needle: NeedleAid™ and NovoPen® 3 PenMate®. Concealing the needle using the NovoPen 3 PenMate has been shown to reduce pain perception.⁵³ The NeedleAid is an attachment designed to help visually impaired patients self-administer insulin.

Limitations of Insulin Pens

Insulin pens are not without their limitations and it is important that patients and healthcare workers

are aware of these to ensure the best outcomes. The maximum dose with most insulin pens is 60-80 units, but with a syringe it is 100 units. Patients cannot mix their own insulin formulations for use in a single injection given by insulin pen. Despite their ease of use, there have been some cases of malfunction reported in the literature.⁵⁷ Therefore, patients using an insulin pen should have a backup pen with them at all times.

Choosing Between Insulin Pens

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. Anecdotally, 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. However, some 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. This may be important in children or in those sensitive to insulin. Some insulin 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.⁵⁸

Newer technologies have improved the push-button mechanisms to reduce injection force while

maintaining dose accuracy^{59,60} and still retaining the ability to dial back. This may be particularly suitable for patients with impaired manual dexterity or conditions such as arthritis. Colour coding has also been incorporated into several of the pens to distinguish between insulin types. Some pens now supply auditory feedback to assist patients with T2DM who may suffer from visual impairments and/or manual dexterity.⁶¹ Several insulin pens provide a confirmatory click when the correct dose has been delivered. Memory is an added feature that is now available. In a study comparing an insulin pen with memory function to a pen without memory function it was found that significantly more patients preferred the memory function, indicating that it gave them more confidence about when they last injected, how much insulin they injected, and in improving their diabetes management.⁶²

How to Use an Insulin Pen

In a study assessing the patient and physician acceptability of a prefilled insulin pen device, 88% of the 33 physicians who completed questionnaires at the end of the study said it took less time to teach patients to use a pen, and 73% thought that it took less time to initiate insulin therapy with the pen, compared with a vial and syringe.⁶³ The basic steps in teaching patients how to use an insulin pen are shown in **Figure 1**.

1. Ensure insulin is at room temperature.
2. If using a pre-mixed insulin, first gently roll the insulin pen ten times and then gently invert ten times (not shaken) to resuspend the insulin. The solution should be a milky white.
3. Attach the needle to the pen.
4. Prime the insulin pen (also referred to as 'doing a safety test' or 'doing an air shot'^a).
5. Select the dose by dialling.
6. Hold the pen gently against the skin.
7. Inject the dose by depressing the button, holding it in position in the skin for at least 10 seconds.^b
8. After the injection, remove the needle from the pen and replace the cover on the pen.

Figure 1: The eight steps of insulin pen use.

^a This is performed by instructing the patient to dial up 2 units and to inject these units into the air.

^b The 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 five (or ten if using the SoloSTAR[®]) before removing the needle.

Because it is possible for insulin to still be flowing out of the pen for several seconds after the button has been fully depressed,¹⁵ to prevent any leakage of insulin, it is important to instruct patients to hold the pen in place with the button pressed in for 5-10 seconds (the exact time varies between the various insulin pens and is described in their respective package inserts).^{38,39,41,43} The easiest way to ensure this is to instruct the patient to count to five (or ten, if using the SoloSTAR®) before removing the needle. If the patient is using >50 units of insulin per dose, a good rule of thumb might be to instruct them to count to ten regardless of the pen they are using to ensure complete absorption of the insulin.

If patients are using a pen that contains neutral protamine Hagedorn insulin, or an insulin premix, it is important that they gently mix the insulin by carefully rolling or tipping the pen for the recommended number of times according to the package insert to ensure even mixing of the insulin suspension before attaching the needle. Emphasise this even 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.⁶⁴ Pens must be primed before each injection, and the needle removed immediately after each use.¹⁵ This is performed by instructing the patient to dial up 2 units and inject these units into the air (also called an 'airshot'). This will displace any air in the needle and ensure an accurate injection.

Insulin pens should never be used by more than one individual, even if the pen needle is changed, because sharing of insulin pens can result in transmission of hepatitis viruses, HIV, or other blood-borne pathogens. Prior to first use, the insulin cartridge or pen should be stored in the refrigerator. The pen should be warmed to room temperature (30 °C) for most insulin analogues before use. After the first use, the pen should remain at room temperature (<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; keep them as close as possible to room temperature (<30 °C) at all times. Insulin glulisine (Apidra®) has a narrower temperature range for storage than the other insulin analogues;

once in use, insulin glulisine must be stored <25 °C. In some buildings, for example schools, air conditioning is turned off at night, which may result in the room temperature rising above 25 °C or 30 °C. If a change in temperature is anticipated, insulated storage packs are recommended. 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.

Clinical Studies Comparing Insulin Pens

Several studies have investigated dosing accuracy between pens. Generally, dosing accuracy is good.^{56,65-70} Insulin pens also differ in the force required to inject an insulin dose, and this feature has been investigated in several studies.^{56,68,71-73} In general, differences in the injection force between insulin pens are relatively small.^{59,72} 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 the results show that newer designs of pens are increasingly user-friendly, and are intuitive to use, requiring little or no instruction.^{57,74-80}

CONCLUSIONS

In conclusion, insulin pens offer many benefits to people with diabetes who use insulin. They provide an opportunity to select a delivery device that will meet the specific needs of the patient. Insulin pens are increasingly more user-friendly requiring little or no instruction. For the healthcare professional, this means that teaching a patient how to use an insulin pen, along with the importance of accurate dosing, can be done quickly and efficiently in a busy clinical setting. In spite of the ease of use with insulin pens, educating patients about the practical aspects and purpose of insulin in general remains important. It is important that healthcare providers are aware of the benefits of insulin pens and the role they play in increasing adherence. It is important for healthcare professionals to keep up-to-date on the latest developments in pen devices and teaching approaches in order to assist their patients in making informed, individualised decisions.

REFERENCES

1. Inzucchi SE et al. Management of hyperglycemia in type 2 diabetes: a patient-centered approach: position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care*. 2012;35(6):1364-79.
2. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet*. 1998;352(9131):837-53.
3. Rex J et al. A review of 20 years' experience with the NovoPen family of insulin injection devices. *Clin Drug Investig*. 2006;26(7):367-401.
4. Cobden D et al. 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.
5. Lee WC et al. 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.
6. Korytkowski M et al. 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.
7. Keith K et al. Accuracy and precision of low-dose insulin administration using syringes, pen injectors, and a pump. *Clin Pediatr (Phila)*. 2004;43(1):69-74.
8. Lteif AN, Schwenk WF. Accuracy of pen injectors versus insulin syringes in children with type 1 diabetes. *Diabetes Care*. 1999;22(1):137-40.
9. 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.
10. Kadiri A et al. 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.
11. Pawaskar MD et al. 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.
12. Access to quality medicines and medical devices for diabetes care in Europe. International Diabetes Federation Europe. August 2013.
13. Shelmet J et al. Preference and resource utilization in elderly patients: InnoLet versus vial/syringe. *Diabetes Res Clin Pract*. 2004;63(1):27-35.
14. Da Costa S et al. A comparison of insulin pen use in the United States and the United Kingdom. *Diabetes Educ*. 2002;28(1):52-6, 59-60.
15. Magnotti MA, Rayfield EJ. An update on insulin injection devices. *Insulin*. 2007;2(4):173-81.
16. Rubin RR, Peyrot M. Factors affecting use of insulin pens by patients with type 2 diabetes. *Diabetes Care*. 2008;31(3):430-2.
17. 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.
18. Ahmann A et al. Comparing patient preferences and healthcare provider recommendations with the pen versus vial-and-syringe insulin delivery in patients with type 2 diabetes. *Diabetes Technol Ther*. 2014;16(2):76-83.
19. Asakura T. Comparison of clinically relevant technical attributes of five insulin injection pens. *J Diabetes Sci Technol*. 2011;5(5):1203-9.
20. Ignaut DA et al. Comparative device assessments: Humalog KwikPen compared with vial and syringe and FlexPen. *Diabetes Educ*. 2009;35(5):789-98.
21. Pearson TL. Practical aspects of insulin pen devices. *J Diabetes Sci Technol*. 2010;4(3):522-31.
22. Peyrot M et al. 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.
23. Summers KH et al. Preference for insulin delivery systems among current insulin users and nonusers. *Clin Ther*. 2004;26(9):1498-505.
24. Somavilla B et al. Safety, simplicity and convenience of a modified prefilled insulin pen. *Expert Opin Pharmacother*. 2008;9(13):2223-32.
25. Lee IT et al. 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.
26. Hörnquist JO et al. Insulin-pen treatment, quality of life and metabolic control: retrospective intra-group evaluations. *Diabetes Res Clin Pract*. 1990;10(3):221-30.
27. Davis EM et al. Nurse satisfaction using insulin pens in hospitalized patients. *Diabetes Educ*. 2009;35(5):799-809.
28. McKay M et al. 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.
29. Davis EM et al. 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.
30. Eli Lilly. HumaPen® LUXURA™ HD insulin delivery device user manual (11 November, 2006).
31. Eli Lilly. HumaPen® MEMOIR™ user manual (revised 20 November, 2006).
32. Eli Lilly. KwikPen™ disposable insulin delivery device user manual.
33. Eli Lilly. Humalog insulin lispro injection: insulin pens. <http://www.humalog.com/Pages/Results.aspx?k=Insulin%20pens&s=Humalog>. Accessed: 31 July, 2009.
34. Eli Lilly. Prefilled insulin delivery device user manual. Revised 17 April, 2009.
35. Novo Nordisk. NovoPen® 3 PenMate: instruction manual. 1999.
36. Novo Nordisk. NovoPen® Junior instructions for use. 2001.
37. Novo Nordisk. FlexPen®: insulin delivery that goes with you. 2014.
38. Novo Nordisk. Insulin pens. http://www.novonordisk.com/diabetes_care/insulin_pens_and_needles/default.asp. 2014.
39. Novo Nordisk. NovoLog® FlexPen®. <http://www.novolog.com/devices-flexpen.asp?s=ds&h=150>. 2014.
40. Novo Nordisk. Levemir® FlexPen®. <http://www.levemir.com/>. 2014.
41. Owen Mumford. Autopen: insulin delivery pens (revised April 2006).
42. Owen Mumford. Autopen®: simplifying insulin injections. 2009.
43. Sanofi-Aventis. Get to know the Lantus® SoloSTAR® pen. 2009.
44. Sanofi-Aventis. Your guide to the Lantus® SoloStar® insulin pen. 2009.
45. Sanofi-Aventis. OptiClik®. <http://www.opticlik.com/>. 2009.
46. BD. BD pen needles. <http://>

- www.bd.com/us/diabetes/page.aspx?cat=7002&id=10257. 2009.
47. National Institute for Health and Care Excellence. ESNM24: Type 1 diabetes: insulin degludec [http://publications.nice.org.uk/esnm24-type-1-diabetes-insulin-degludec-esnm24. 2013. Accessed: 18 July, 2014.
 48. American Diabetes Association. 2013 Resource Guide. Diabetes Forecast.
 49. European Agency for Safety and Health at Work. Directive 2010/32/EU - prevention from sharp injuries in the hospital and healthcare sector. 2010. Accessed: 17 July, 2014.
 50. The Forum for Injection Technique. Diabetes care in the UK: the first UK injection technique recommendations 2nd edition. 2011. Accessed: 18 July, 2014.
 51. Gibney MA et al. Skin and subcutaneous adipose layer thickness in adults with diabetes at sites used for insulin injections: implications for needle length recommendations. *Curr Med Res Opin.* 2010;26(6):1519-30.
 52. Hirsch LJ et al. Comparative glycemic control, safety and patient ratings for a new 4mm x 32G insulin pen needle in adults with diabetes. *Curr Med Res Opin.* 2010;26(6):1531-41.
 53. Hofman PL et al. Defining the ideal injection techniques when using 5-mm needles in children and adults. *Diabetes Care.* 2010;33(9):1940-4.
 54. Siminerio L et al. Strategies for insulin injection therapy in diabetes self-management. A White Paper of the American Association of Diabetes Educators (AADE). 2011.
 55. Funnell MM. Overcoming barriers to the initiation of insulin therapy. *Clin Diab.* 2007;25(1):36-8.
 56. Diglas J et al. Reduced pain perception with Pen Mate™ an automatic needle insertion device for use with an insulin pen. *Prac Diabetes Int.* 1999;16(2):39-41.
 57. Boronat M et al. Severe deterioration of metabolic control caused by malfunction of a disposable insulin pen device. *J Am Board Fam Med.* 2008;21(6):575-6.
 58. Venekamp WJ et al. Functionality and acceptability of a new electronic insulin injection pen with a memory feature. *Curr Med Res Opin.* 2006;22(2):315-25.
 59. Shaefer CF. The pen is mightier than the sword. *Insulin.* 2009;4(3):132-5.
 60. Asakura T et al. Evaluation of injection force of three insulin delivery pens. *Expert Opin Pharmacother.* 2009;10(9):1389-93.
 61. Pfützner A et al. Prefilled insulin device with reduced injection force: patient perception and accuracy. *Curr Med Res Opin.* 2008;24(9):2545-9.
 62. Klausmann G et al. Evaluation of preference for a novel durable insulin pen with memory function among patients with diabetes and health care professionals. *Patient Prefer Adherence.* 2013;7:285-92.
 63. Lautier O et al. 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.
 64. Bohannon NJ et al. 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.
 65. Asakura T, Seino H. Assessment of dose selection attributes with audible notification in insulin pen devices. *Diabetes Technol Ther.* 2005;7(4):620-6.
 66. Asakura T. Comparison of the dosing accuracy of two insulin injection device. *J Clin Res.* 2005;8:33-40.
 67. Penfornis A, Horvat K. Dose accuracy comparison between SoloSTAR and FlexPen at three different dose levels. *Diabetes Technol Ther.* 2008;10(5):359-62.
 68. Asakura T et al. Dosing accuracy of two insulin pre-filled pens. *Curr Med Res Opin.* 2008;24(5):1429-34.
 69. 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.
 70. Weise A et al. Comparison of the dose accuracy of prefilled insulin pens. *J Diabetes Sci Technol.* 2009;3(1):149-53.
 71. Friedrichs A. Dose accuracy of SoloSTAR and FlexPen as assessed in a clinical setting. *Diabetes Technol Ther.* 2009;11(9):609-13.
 72. Ignaut DA et al. FlexPen and KwikPen prefilled insulin devices: a laboratory evaluation of Ergonomic and Injection Force Characteristics. *J Diabetes Sci Technol.* 2008;2(3):533-7.
 73. Rissler J et al. Evaluation of the injection force dynamics of a modified prefilled insulin pen. *Expert Opin Pharmacother.* 2008;9(13):2217-22.
 74. Toraishi K et al. Force requirements and insulin delivery profiles of four injection devices. *Diabetes Technol Ther.* 2005;7(4):629-35.
 75. 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.
 76. Reimer T et al. 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.
 77. Niskanen L et al. 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.
 78. Haak T et al. 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.
 79. Fischer JS. 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.
 80. Yakushiji F et al. 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.