CLINICAL GUIDING PRINCIPLES FOR SUBCUTANEOUS INJECTION TECHNIQUE

Technical Guidelines

Clinical Guiding Principles for Subcutaneous Injection Technique

Technical guidelines

Version	Date	Name(s)	Notes
1	2011	ADEA	Created and approved
2	2015	ADEA	Revised and approved
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4.1	6 Aug 2019	Dr Kate Marsh and Member consultation	Edits according to literature and member consultation
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Sponsors

This 2019 revision follows a review of the current evidence and feedback from ADEA members and is a revised version of the 2017 “Clinical Guiding Principles for Subcutaneous Injection Technique”.

The Guiding Principles have been revised with financial support from BD Diabetes Care.

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Disclaimer:

These clinical guiding principles form an acceptable basis for working with children and adults with diabetes mellitus who require injectable medicines, however there may be sound clinical reasons for different strategies initiated for an individual. The complexity of clinical practice requires that, in all cases, users understand the individual clinical situation, and exercise independent professional judgment within the scope of practice of their specific discipline when basing therapeutic intervention on this document. The information set out in this publication is current at the date of first publication. It is not exhaustive of this subject matter. Compliance with any recommendations cannot by itself guarantee discharge of duty of care owed to people with diabetes and their support people.

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Dr Kate Marsh APD CDE.

The ADEA Clinical Practice Review Committee.

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About ADEA

The Australian Diabetes Educators Association (ADEA) is the peak national organisation for multidisciplinary health professionals who are committed to the provision and excellence of quality, evidence-based diabetes education, care and management with over 2,300 members working in all sectors and across all locations.

ADEA aims to improve the health and wellbeing of people with diabetes by:

1. Assessing diabetes educators based on their qualifications, skills, knowledge and experience through the credentialling program
2. Supporting multidiscipline health professionals through its various programs, including mentoring, education and research
3. Developing and updating relevant policies, standards of practice and clinical guidelines

For more information, visit our website at www.adea.com.au.

Contents

Glossary

Continuous subcutaneous insulin infusion (CSII). The use of a portable electromechanical pump to deliver rapid-acting insulin into the subcutaneous tissue at preselected rates, via a needle or soft cannula under the skin.

Dermis + Subcutis. Describes the depth of the tissue from skin surface to muscle, i.e. epidermis, dermis and subcutaneous. This term is used to estimate the risk of intramuscular injections and the importance of choosing the correct needle length.

GLP-1 Receptor Agonists: GLP-1 receptor agonists are injectable medications for use in type 2 diabetes and include exenatide (Byetta® and Bydureon®), liraglutide (Saxenda®) and dulaglutide (Trulicity®).

Intradermal (ID): The skin layer: used to describe the action of injecting into skin (dermis).

Intramuscular (IM): The layer under the subcutis: used to describe the action of injecting into muscle.

Lifted skin fold. A lifted skin fold is made using the thumb and index or middle finger to gently lift subcutaneous tissue away from the muscle layer[1] . It is used to reduce the risk of intramuscular injection. Care should be taken not to pinch the skin and inadvertently also lift muscle tissue.

Lipoatrophy (LA) is a breakdown (atrophy) of the subcutaneous fat tissue. It is thought to be immunological in nature and probably results from impurities or other components in some insulin preparations. Due to the availability of purified human and analogue insulins, it is now less commonly seen, estimated to affect only 1-2% of those injecting insulin[2].

Lipodystrophy is one of the most common complications of subcutaneous insulin injection and may present as either lipoatrophy or lipohypertrophy[2].

Lipohypertrophy (LH) is an area of thickened subcutaneous tissue which may be hard or scar like, or soft like a rubber ball[3]. LH is common and is associated with repeated injection into the same sites, inadequate site rotation and the reuse of needles, and incidence is increased with duration of diabetes, duration of insulin use and number of injections per day[2,4–8].

Subcutaneous (SC). The layer between the skin (epidermis + dermis) and muscle which contains the fatty tissue which is ideal for the absorption of insulin and GLP-1 receptor agonists. Also called the subcutis.

Background

The Australian Diabetes Educators Association (ADEA) promotes evidence-based practice in all aspects of diabetes education and care. The teaching of subcutaneous injection technique (SCIT) is a fundamental role of the diabetes educator[1,9]. As such, ADEA recognises the need for diabetes educators to possess evidence-based knowledge and skills in relation to SCIT. This ensures the correct instruction and education regarding injectable medicines for people with diabetes, including the self-administration of insulin and GLP-1 receptor agonists.

These clinical guiding principles were first developed by ADEA in 2011 and were expanded and updated in 2016 and again in 2019, following a literature search and review, and a stakeholder consultation period to ensure current evidence is included and the guideline is relevant for diabetes educators and other health care professionals responsible for administering or teaching SCIT.

The guiding principles provide an evidence base for the injection of SC diabetes medicines for health care professionals involved in the administration and teaching of SCIT for diabetes therapies in various clinical settings. They include information about the principles of SCIT, education of individuals in safe and accurate injection technique (IT), evaluation of IT, and specific issues for health care settings and carers.

This document does not address the administration of glucagon, an injectable medicine for the treatment of severe hypoglycaemia, nor technical issues associated with continuous subcutaneous infusion devices (insulin pumps), however it does include a small section on CSII where principles of SCIT apply.

Introduction

An increasing number of Australians are injecting diabetes medicines. This is due to an increasing prevalence of diabetes, the move to earlier insulin use in type 2 diabetes (T2D) and the newer classes of non-insulin injectable medicines for T2D.

Insulin therapy is essential for the management of type 1 diabetes (T1D). It is also increasingly being used in those with T2D to achieve optimal glycaemic management. It is estimated that around 50% of people with type 2 diabetes will require insulin within 10 years of diagnosis and this increases with duration of diabetes[10]. Insulin may also be required for women with gestational diabetes (GDM) who are unable to maintain blood glucose levels in the recommended range for pregnancy with dietary modification and exercise alone[11]. According to the National Diabetes Services Scheme (NDSS), in June 2019 there were 416,269 Australians with diabetes registered as requiring insulin, representing 32% of all people registered with diabetes[12]. Of these, 29% were identified as having T1D, 66% as having T2D and 4% as having GDM[12].

Proper IT by individuals using injectable diabetes medicines is essential to reduce absorption variability, optimise the drug effect and in turn achieve target glycaemic goals[1,3]. Health care professionals, and particularly diabetes educators, play a crucial role in the education of individuals with diabetes regarding correct IT[1].

Despite the availability of IT guidelines, large studies of individuals with diabetes have found that many are not following evidence-based recommendations for the administration of insulin[13,14]. The most recent survey (Injection Technique Questionnaire [ITQ]) was conducted in 2014-2015 and sought more clinical and diabetes self-management information from respondents compared to the previous ITQ 2009. The survey included 13, 289 individuals with diabetes injecting insulin from 423 centres in 42 countries, including Australia for the first time[15]. The survey findings have been used to develop a set of recommendations, titled the Forum for Injection Technique and Therapy: Expert Recommendations (FITTER)[1]. The FITTER recommendations were published in 2016, with two additional publications focusing on the ITQ data and implications for health care professionals[15,16].

Summary of Recommendations:

- People with diabetes, their carers and health care professionals require high quality education and training from diabetes educators that encompasses current evidence and consensus-based principles of SCIT.
- Diabetes health care professionals require knowledge of the factors affecting the efficacy of injectable diabetes medicines.
- The choice of injection site should take into consideration the requirements of different injectable medicines. However, the abdomen is the preferred injection site for most people due to its convenience, consistency and reproducible rates of absorption of injectable medicines.
- Shorter length pen needles (4 and 5mm) are recommended for the initiation of SC injectable medicines in children, adolescents and adults of all sizes. There is no medical rationale for use of longer needles for SC diabetes medications.
- When using a syringe, needle length no longer than 6mm is recommended.
- The size and angle of insertion of the needle used for injection, and the need for a lifted skinfold, should be determined according to clinical examination and consideration of the likely composition of skin and SC tissue.
- Injections should not be administered through clothing.
- Regular review of SCIT and inspection of sites used for injection is an integral part of the education of SCIT.
- Review of SCIT should be completed at least annually for adults and at each visit for children and adolescents, or when lipodystrophy has been identified.
- Diabetes educators must document all components of the assessment and education for the administration of injectable diabetes medicines, including a review of technique and injection sites.

Objectives:

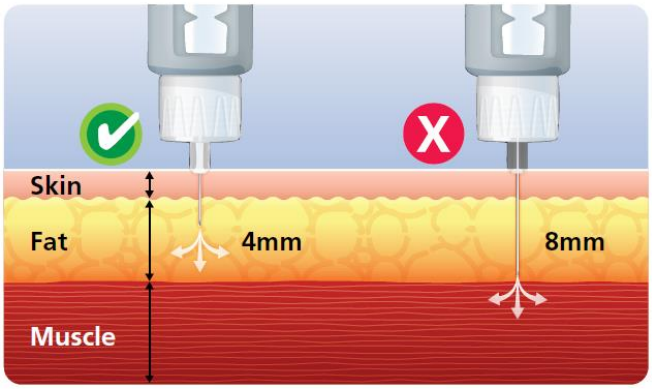
The objectives of these clinical guiding principles are to:

1. Identify and promote the quality framework required for the safe delivery of injectable diabetes medications.
2. Support evidence-based decision making for clinicians providing education for people who require injectable diabetes medicines.
3. Identify the appropriate injection sites, needle length, insertion angle, and need for a lifted skin fold for the administration of diabetes medicines to adults and children/adolescents.
4. Outline the principles required for the teaching, review and evaluation of the injection of insulin and GLP-1 receptor agonists for people with diabetes, carers and health professionals.
5. Highlight the potential impact of incorrect IT on blood glucose variability in those injecting diabetes medications.
6. Articulate and reinforce requirements for documentation of teaching of IT and review.
7. Minimise adverse outcomes caused by incorrect SCIT.
8. Reduce the risk of needle stick injury to family members, carers and healthcare professionals.

Guidelines

Principles of subcutaneous injection technique for insulin and GLP-1 receptor agonists

Correct SCIT can be defined as one that consistently delivers injected medicine into the SC space with minimal discomfort. The SC tissue has relatively poor blood supply, prolonging the absorption time of injected medicines, resulting in a more consistent absorption rate. This is advantageous for drugs that cannot be ingested, such as insulin, or drugs which require a slower, more predictable absorption rate. A network of blood vessels lie between the dermis and subcutaneous layer and serve as the site of absorption for medicines[17].



Correct SC administration of diabetes injectable medications requires consideration of the following:

- Injection site.
- Needle length.
- Use of a lifted skinfold.
- Angle of injection.

Choice of injection site

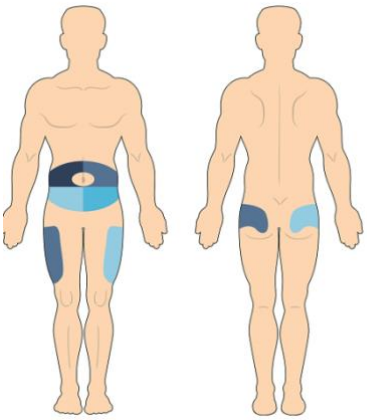
The most commonly recommended site for SC injections is the abdomen due to its convenience and tendency to more rapid and reproducible insulin uptake[1,18,19]. The buttocks, thigh and upper arms may also be used, however the risk of IM injection is higher with the thighs and arms[1]. The difference in absorption between sites needs also needs to be considered for some types of insulin (older human insulins, e.g. Regular and Neutral Protamine Hagedorn (NPH))[1,18]. When using the abdomen, injections should be given at least 1cm above the symphysis pubis, 1cm below the lowest rib and 1cm away from the umbilicus[1].

The posterior lateral aspects of the buttocks offer the slowest rate of absorption, and have a higher SC tissue depth, so injecting with a skin fold is generally not required[19]. If the person is able to reach this area for self-injection, SC injections can be safely performed with the correct needle length using a single handed technique[3,17].

Injection into the upper third anterior lateral aspects of both thighs is the preferred region to reduce inadvertently injecting IM[1]. The risk of IM injections into the thigh increases significantly with longer needles and in slimmer individuals[20]. Due to vascularisation of the area, there is also a risk of rapid absorption of insulin from the thigh where exercise is performed shortly after injection[21,22].

Use of the arms should be discouraged due to a reduced depth of subcutis, increasing the risk of IM injection, even with very short (4mm) needles. If used, injections should be given in the middle third posterior aspect of the arm and a lifted skin fold is recommend for children and slim adults[17,20,23–25]. However it is almost impossible to perform this

technique properly in those who are self-injecting[3].



Modern insulins/Insulin analogues

Modern analogue insulin including rapid (lispro, aspart and glulisine), long-acting (– (glargine, detemir and degludec) and premix (insulin aspart + aspart protamine, insulin lispro + lispro protamine and insulin aspart + degludec) can be given SC at any site as absorption rates do not appear to be site-specific[3]. However long-acting analogues can cause severe hypoglycaemia if inadvertently injected IM[26].

Human insulins

Human insulin is more variable in its absorption and pharmacodynamics. The abdomen is the preferred injection site for soluble human insulin (regular), due to the faster absorption from this area[1]. It is also the preferred site for morning doses of mixed human insulin due to increased absorption of the short-acting insulin to cover glycaemic excursions with breakfast[1]. IM administration of NPH should be absolutely avoided due to the increased risk of hypoglycaemia[1]. It is preferable that NPH (when given alone) be injected at bedtime rather than earlier in the evening in order to reduce the risk of nocturnal hypoglycaemia[1]. The thigh and buttocks are the preferred injection sites for NPH due to slower absorption from these sites which can help to reduce the risk of nocturnal hypoglycaemia[1]. Similarly, an injection of mixed insulin containing NPH should be given in the thigh or buttocks in the evening if there is a risk of nocturnal hypoglycaemia[1].

GLP-1 Receptor Agonists

There are few studies investigating the optimal IT for GLP-1 receptor agonists but their absorption does not appear to be site specific and injections into the abdomen, thigh or upper arm are recommended[3,27]. Pending further studies, individuals using non-insulin injectable therapy should follow the established recommendations for insulin injections regarding needle length, site selection and rotation[1].

Injection sites during pregnancy

During pregnancy women with GDM or pre-existing T2D may require insulin therapy to achieve glycaemic targets. Women with T1D will continue to inject but may require different insulin preparations. GLP-1 receptor agonists are not currently approved or indicated for use in pregnancy.

While there is a lack of research into the optimal IT during pregnancy, the following recommendations are made[1]:

- Shorter needles are preferred (pen: 4 or 5mm length, syringe: 6mm) when injecting into the abdomen due to the thinning of abdominal fat from uterine expansion.
- First trimester: Women should be reassured that no change in insulin site or technique is needed.
- Second trimester: Insulin can be injected over the entire abdomen as long as properly raised skinfolds are used. Lateral aspects of the abdomen can also be used when not using a skinfold.
- Third trimester: Injections can be given into the lateral abdomen using a correct skinfold technique. Apprehensive clients may use their thigh, upper arm or buttock instead of the abdomen.

Women can be reassured that insulin needles are not long enough to penetrate the uterine wall if insulin is injected abdominally.

Injections should not be given through clothing.

Injecting through clothing is discouraged as the person is unable to inspect the site, or properly use a lifted skin fold if required[3]. Further the advent of shorter needles means that the injection may not penetrate the skin sufficiently for correct administration of medicine into the SC space.

Choice of needle length

The choice of needle length should be one which will reliably deliver the medicine into the SC space without leakage or discomfort[3].

Various options for pen and syringe needles are available to users of insulin and GLP-1 receptor agonists in Australia. Pen needles from 4mm to 12.7mm in length are currently available and syringes with needles from 6mm to 8mm.

However needles longer than 6mm are no longer recommended due to the high risk of IM injection[1], so while they are still available on the NDSS, their use should be discouraged.

Studies examining the effect of shorter (4-6mm) needle lengths on glycaemic management, pain, insulin leakage, and other issues have found that shorter needles are safe, effective, and usually better tolerated[1]. Furthermore, the use of 4mm needles for overweight and obese people is efficacious, with no loss of safety, efficacy or tolerability, and no evidence of worsening metabolic management[1,28–30]. Studies have found no statistically significant difference between the efficacy of injections delivered into deep or shallow subcutis, supporting the fact that longer needles are not necessary for those with a greater amount of SCT[31–33].

Injections delivered at 90 degrees with a 4mm needle were estimated to deliver insulin to the subcutaneous tissue > 99.5% of the time

with minimal risk of intradermal (ID) injections. Inadvertent intramuscular injections occur more often using longer needles, in slimmer and younger people, males and in those who use limbs rather than truncal injection sites[1].

Until recently skin thickness (ST) was thought to depend on the weight or race of the individual. Recent studies have demonstrated that there is minimal difference in ST between adults of different age, gender and BMI. A variety of studies show the skin varies in thickness from approximately 1.25mm to 3.25mm in 90% of individuals[15]. Children have been shown to have a smaller ST, which increases gradually from birth to adulthood[1,24,34].

The thickness of the SC adipose layer (subcutis), on the other hand, is widely variable and women have approximately 5mm extra SC fat compared with men of the same BMI. In both children and adults, even the shortest needles (4mm) reliably transverse the skin and enter the subcutaneous (SC) fat[1].

In a studying comparing skin and SC adipose tissue thickness in 388 US adults of varying BMI and ethnicities, when measurements of ST and SCT were combined, it was estimated that the majority of injections across the four commonly-used injection sites with a 5mm needle at 90 degrees would be delivered into the SCT, with less than 2% estimated to be IM[35]. For 6mm, 8mm and 12.7mm needles, 6%, 15% and 45% of injections were estimated to be delivered IM[35]. Even when injected at 45 degrees, 21% of injections with a 12.7mm needle were estimated to be IM when injected at 90 degrees[35].

The use of shorter needles is particularly important in children. The distance from the skin surface to muscle has been estimated to be less than 4mm in 10% of children, particularly in the 2-6 age group[24]. Without a skinfold lift, it is estimated that 20% of injections would be given IM in this group, even with 4mm needles[24]. This doubles with 5mm and triples with 6mm needles.

Very young children (<6 years old) should use 4mm needles by lifting a skinfold and inserting the needle perpendicularly into it. Older children may inject without a skin fold using a 4mm needle[1].

The shortest syringe needle length available in Australia is 6mm at the time of publication. Therefore the use of syringes for very young children (<6 years old) is not recommended due to the higher risk of IM injection[1].

Current guidelines suggest there is no medical reason to recommend pen needles longer than 4-5mm for children and adults[1]. It is recommended that initial therapy should commence with shorter (4-5mm) pen needle lengths or 6mm syringe needle lengths[1].

In the 2008-2009 ITQ survey it was found that 63% of participants had used the same needle length since commencing an injectable medicine[14]. This highlights the importance of accurate initial education on appropriate needle length, and regular evaluation of IT in those administering injectable diabetes medicines.

Recommendations for adults include[1]:

- Use of shorter pen needles (4mm or 5mm) for all adults, including those who are overweight or obese.
- If 4mm needles are used they should be injected at 90 degrees to the skin surface.
- Very slim adults may need a lifted skin fold at all sites, even with a 4mm needle.
- Injections into the arm or thigh will require a lifted skin fold with any needle length and are known to increase the risk of unintentional IM injections.
- If needles ≥ 6mm are used, they should be used with a lifted skin fold or injected at 45 degrees to decrease the risk of unintentional IM injections.

Recommendations for children include[1]:

- Use of shorter pen needles (4mm or 5mm) for all children commencing insulin therapy although 4mm needles are the safest option, particularly for those aged 2-6 years.
- Children aged under 6 years must use a 4mm needle with a lifted skin fold.
- The use of syringes in very young children (<6 years old) is not recommended.
- Children using a 5mm pen needle or longer should be switched to a 4mm needle if possible and if not should always use a lifted skinfold.
- For children using syringes, the shortest available needle (6mm) must be used and injected using a lifted skinfold and 45 degree injection angle.
- The need to use a lifted skin fold should be reviewed as the child grows.

GLP-1 receptor agonist devices:

All of the **GLP-1 receptor agonists** currently available in Australia are supplied in disposable injection devices and have specific instructions for their preparation and administration. The recommended needle length is the same as that required to deliver a SC injection of insulin[1], except for Bydureon® and Trulicity®, which have their own specific needle devices. Refer to the manufacturer's specific instructions for more information.

Recommended sites for injection are the abdomen, thigh and arms, however the same principles apply for reducing the risk of IM injection as they do for insulin injections[1].

Table 1: A guide to needle length

Children	**Needle size**	**Angle of injection (degrees)**	**Use of skin fold**
	4 mm	90	May, in 2-6 year olds
	5 mm	45 or 90	Yes, may
	6 mm	45 or 90	Yes
	8 mm	Use not recommended with pen needles but may be used with syringes. If used, inject at 45 degree angle with a lifted skin fold	
	12 mm	Use not recommended	
Very slim adults	**Needle size**	**Angle of injection**	**Use of skin fold**
	4 mm	90	May
	5 mm	45 or 90	Yes
	6 mm	45 or 90	Yes
	8 mm	45	Yes
	12 mm	Use not recommended	
Adults of Normal Weight	**Needle size**	**Angle of injection**	**Use of skin fold**
	4 mm	90	No
	5 mm	90	May
	6 mm	90	Yes
	8 mm	45	Yes
	12 mm	Use not recommended	
Adults who are overweight or obese	**Needle size**	**Angle of injection**	**Use of skin fold**
	4 mm	90	No
	5 mm	90	No
	6 mm	90	May
	8 mm	45 – 90	Yes
	12 mm	Use not recommended	

Choice of injection device

Insulin pens

Insulin pen devices first became available in 1985 and are now the standard choice for most people with diabetes who inject insulin. GLP-1 receptor agonists only come in a prefilled pen device.

Studies have shown a number of benefits of insulin pens over syringes, including[36–38]:

- Convenience and ease of use.
- Greater accuracy, particularly at low doses.
- Greater adherence.
- Greater perceived social acceptance.
- Reduced fear of needles.
- User preference over syringes.

There is also evidence that they are safe to use in those with visual impairment[39].

There are a number of different brands and models of insulin pens available in Australia (Table 2) and the choice of pen device will depend on a number of factors including:

- Insulin type.
- The maximum dose of insulin that can be given (important for those taking large doses).
- Availability of 0.5 unit or 1.0 unit dosing increments (0.5 unit dosing may be helpful for children and/or those on smaller doses).
- Readability of the numbers for those who are vision impaired.
- Audible sound for dialing the dose for those who are vision impaired.
- Dexterity in dialing the dose.
- The ease of use of the pen.
- Choice of colour.
- Preference for disposable versus non-disposable.
- Additional features such as an inbuilt electronic memory of previous doses and administration times.

Syringes

Insulin syringes were the only method available for the administration of insulin until the 1980's. While they have largely been replaced by insulin pens and insulin pump therapy, some people still choose to use syringes.

They are also still commonly used by healthcare professionals for the administration of insulin. With this method, insulin is drawn up into the syringe from a vial or cartridge, and then injected. Insulin syringes are available in 0.3, 0.5 or 1.0ml sizes depending on the dose of insulin required, and needle lengths of 6mm and 8mm. The main advantage of a syringe is the ability to mix two different types of insulin in the one syringe, reducing the number of injections for those who take two different types of insulin at the same time (where the insulin types are compatible). However, the drawing up of the insulin is more time consuming and can be difficult when injecting away from home. There is also increased potential for insulin contamination and dose errors if the incorrect syringe size is inadvertently used. Where retractable insulin pen needles are not available in the health care setting, the use of syringes with non-capping technique after use, markedly reduce the incidence of needle stick injuries.

Note: Higher concentrated insulins (Toujeo, Humalog U200 and Humulin R-U) are in a pen device and should NOT ever be used to draw insulin from, nor should dose conversions be used – hence if required to give in a health care setting the Safety Pen Needle is required otherwise Medical review is needed to prescribe an alternative insulin type.

Table 2: A guide to insulin pen devices

Pen	Insulin types	Disposable or reusable	Dosing increments	Maximum dose	Colours /other features
Novo Nordisk					
NovoPen® 4	NovoMix® 30; NovoRapid®; Levemir®;Actrapid®; Protaphane®; Mixtard® 30/70; Mixtard® 50/50	Reusable	1.0	60	Silver or Blue
NovoPen Echo®	NovoMix® 30; NovoRapid®; Levemir®; Actrapid®; Protaphane®; Mixtard® 30/70; Mixtard® 50/50	Reusable	0.5	30	Red or Blue Memory function for last dose
InnoLet®	Protaphane®; Mixtard® 30/70	Disposable	1.0	50	Beige Large easy to read dial
FlexPen ®	NovoMix® 30; NovoRapid®; Levemir®	Disposable	1.0	60	Blue (NovoMix® 30) Orange (NovoRapid®) Green (Levemir®)
Lilly					
Humapen® Savvio™	Humalog®; Humalog® Mix 25®; Humalog® Mix 50®; Humulin® R; Humulin® NPH; Humulin® 30/70	Reusable	1.0	60	Grey, Blue, Green, Pink, Red and Graphite
Humapen® Luxura HD™	Humalog®; Humalog® Mix 25®; Humalog® Mix 50®; Humulin® R; Humulin® NPH; Humulin® 30/70	Reusable	0.5	30	Green
Kwikpen®	Humalog®; Humalog® Mix 25®;Humalog® Mix 50®; Humalog U200®, Humulin R-U500®	Disposable	1.0	60	Grey
Sanofi					
SoloSTAR®	Apidra®; Lantus®; Toujeo®	Disposable	1.0	80	Grey (Lantus®); Blue (Apidra®); Grey and Green (Toujeo®)
Allstar Pro®	Apidra®; Lantus®	Reusable	1.0	80	Silver, Blue
JuniorSTAR®	Apidra®; Lantus®	Reusable	0.5	30	Blue, Red, Silver

Use of pen devices

Steps for injecting with an insulin pen[1,19]:

1. Always follow the manufacturer's instructions to ensure the correct technique.

2. Fit a new needle to the top of the pen.

3. Resuspend cloudy insulin if applicable by gently rolling and tipping. Confirm visually that the resuspended insulin is sufficiently mixed. Avoid vigorous shaking as this produces air bubbles that may affect accurate dosing.

4. 'Prime' the pen to ensure it is working correctly and there are no air bubbles and that pen needle is correctly secured.

5. Dial up the required dose of insulin.

6. Insert the needle and push down the plunger along the axis of the pen to administer the insulin dose.

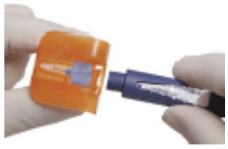
7. Leave the pen needle *in situ* after injecting the medicine for 10 seconds (or as per the manufacturer's instructions) to allow the medicine to fully inject. Counting past 10 seconds may be needed for higher doses.

8. Remove the pen needle and discard safely. Replace cap on the pen.

Note:

- Pen devices are for individual use only and should not be shared. "Think: One pen, one person" Pens and their cartridges can be contaminated with epithelial cells and blood after a single injection – leading to possible transmission of blood-borne illnesses if a pen is used in more than one person[40].
- Durable (reusable) injection devices must be matched with their complimentary insulin cartridge to ensure the injection and dosing is accurate. Each type of insulin cartridge requires a designated pen device.
- Manufacturers of pen devices for insulin and GLP-1 receptor agonists have different recommendations regarding the priming of a device at the commencement of use, and before each injection. It is generally advised to prime the insulin delivery device prior to each injection by dialling up 1-2 units, inverting the pen so that the needle is facing upwards and pressing the plunger. This is repeated until a few drops of insulin are seen, to check that the pen is working.
- During needle insertion the thumb button should be touched only after the pen needle is inserted to reduce accidental leakage.
- Pressure should be maintained on the thumb button until the needle is withdrawn from the skin to prevent aspiration of subcutaneous tissue into the cartridge.
- The pen needle should be removed from the injection device immediately after administration of the medicine to prevent the entry of air, or other contaminants, into the cartridge and to prevent the leaking of medication, which can affect subsequent dose accuracy. A new needle should be attached just prior to the subsequent injection.

- Syringes and pen needles are sterile, single-use devices. After one use they lose their sterility and can collect bacteria, posing an increased risk of infection. Repeated use of needles can also adversely affect needle integrity, resulting in needle bending, blockage or breakage. Attempts to cleanse the needle with alcohol are not recommended, as alcohol can strip the needle of the silicone lubricant which allows for less painful skin puncture.
- If there are patients with active lifestyles, dexterity or visual impairments that find change their needles after each use is difficult, then there are devices designed to prevent pen needle reuse and encourage frequent needle change which could be discussed which may help, such as:
    - safety pen needles
    - pen needles with a secure removal system
    - pen needle remover accessories.



Use of syringes

Steps for injecting with a syringe[1,19]:

1. Prepare syringe - choose the correct size syringe and remove from packaging (e.g. 0.3ml if taking less than 30 units, 0.5ml if taking less than 50 units and 1.0ml if taking less than 100 units).

2. Resuspend cloudy insulin if applicable by gently rolling vial.

3. For a single insulin dose:
    a. Inject air at a dose equal to or slightly greater than the desired dose of insulin into the vial
    b. Draw insulin dose into syringe
    c. Check for correct number of units and that there are no air bubbles.

4. For a mixed insulin dose:
    a. Inject air at a dose equal to or slightly greater than the desired dose of cloudy insulin into the vial
    b. Inject air equal to the dose of clear insulin into the clear vial
    c. Draw out clear insulin dose
    d. Check for correct amount and no air bubbles
    e. Insert needle into cloudy vial and withdraw correct dose
    f. Ensure total dose is correct
    g. If the incorrect dose(s) are drawn up the syringe should be discarded and the procedure started again with a fresh syringe.

Note:

- Long-acting insulin analogues (insulin detemir and insulin glargine) should not be mixed with rapid-acting insulin due to the blunting of the onset of action of the rapid-acting insulin[19,41,42].
- Short-acting and NPH insulins may be mixed and used immediately or stored for future use.
- Rapid-acting insulin can be mixed with NPH. The mixture should be injected within 15 minutes before a meal[19].
- If administering a dose greater than 100 units, two separate injections are required.

Other considerations when injecting diabetes medicines

Volume of medicine

There is no consensus regarding the largest volume of medicine that can be delivered subcutaneously in a single injection. Insulin absorption is prolonged with larger doses of insulin and there is also evidence of increased pain and leakage with higher doses[43]. It may therefore be desirable to divide large doses into smaller doses once the insulin dose reaches over 50 units (0.5ml). Studies into GLP-1 receptor agonists typically use smaller volumes for injection and have not focussed on the issue of maximum volume for injection.

Use of concentrated insulin

Over the past few years, several new concentrated insulins (more than 100U/ml) have become available. These include both basal and prandial insulins, ranging from 2 to 5-fold concentrations (200U/mL to 500U/mL). Potential benefits, particularly for those taking larger insulin doses, include reduced volumes, reduced number of injections, reduced injection pain, less frequent pen changes and easier delivery[44]. Studies have shown a reduced risk of nocturnal hypoglycemia compared to U-100, although a higher dose may be needed[44,45]. Diabetes educators should be aware that the onset, peak and duration of action of a concentrated insulin preparation may be different than 100 unit/ml preparations.

Leakage

Leakage of insulin may be reported from the injection site, from the tip of the needle or from the pen due to a poor seal between the needle and pen cartridge following injection[1]. If leakage occurs following injection of medicine it is recommended to increase the time the needle is left *in situ* following injection[1]. The most recent global review of IT indicated that less than one in three people with diabetes were waiting ten seconds (or longer) from fully depressing the device plunger to removal from the tissue[16]. However there is agreement in the literature that the percentage of medicine lost to leakage is minimal and not clinically significant relative to overall glycaemic management when the correct IT is used; there is also little difference between different needle lengths[28,46–51]. Leakage can be minimised by[1]:

- Ensuring the pen needle is correctly attached to the pen device.
- Counting ten seconds after the plunger is fully depressed before removing the needle from the skin allows enough time for the injected medicine to spread out through the tissue plains resulting in tissue expansion and stretch – however by trial and error, individuals with diabetes may learn how long they need to hold the device insitu prior to removing.
- Using needles that have a wider inner diameter (extra-thin-walled needles) can reduce dripping from the needle and skin leakage.
- Splitting larger doses of insulin.
- Pressure should be maintained on the thumb button of the pen device until it is withdrawn from the skin to prevent aspiration of subcutaneous tissue into the cartridge.

Bleeding and bruising

People with diabetes and caregivers should be reassured that local bruising and bleeding does not adversely affect the clinical outcomes or the absorption of insulin[1]. However if bleeding and bruising are frequent or excessive, IT should be carefully assessed, particularly if anticoagulants or antiplatelet agents are currently prescribed[1]. Needle

length does not alter the frequency of bleeding or bruising[1].

Storage of injectable medicines

Injectable medicines should be stored according to the manufacturer's instructions, considering the required temperature for used and unused medicine, length of time the medicine can be stored when open, requirements for protection from light, and the expiry date of the medicine. Insulin should be discarded if[19]:

- It is past the expiry date on the bottle or if the vial or cartridge/pen has been open for more than a month.
- The insulin is discoloured, lumps or flakes are seen, or clear insulin has turned cloudy.
- Uniform resuspension cannot be achieved.
- The insulin has been frozen or exposed to high temperatures.

Resuspension of insulin

Cloudy insulin (isophane and mixed insulin) must be resuspended according to individual manufacturers' instructions before each injection. The insulin should be gently rolled and tipped until the solution becomes milky white. This can be achieved by rolling the insulin cartridge between the palms 10 times for 5 seconds, and then tipping 10 times for 10 seconds[1]. Vigorous shaking of the preparation is discouraged because it can affect the kinetics of the preparation. Correct mixing of insulin suspensions reduces the risk of hypoglycaemia and variability in the action of the injected medicine[52]. In the ITQ survey, of those using a cloudy insulin 35% did not resuspend their insulin prior to injection, and 44 % rolled their insulin less than 10 times[14].

Reducing painful injections

While most insulin injections are not painful, some individuals complain of pain on injecting. The risk of painful injections can be minimised by[1,19]:

- Injecting insulin at room temperature rather than when cold.
- If using alcohol to clean the skin (although not necessary), injecting only after this has dried.
- Using a new needle for each injection.
- Using needles of shorter length and smaller diameter.
- Penetrating the skin quickly with the needle.
- Injecting the insulin slowly.
- Not changing the direction of the needle during insertion and withdrawal.

Preparation of the skin

If the site requires cleaning, soap and water is adequate. Use of alcohol swabs to cleanse the skin prior to injection is usually not required apart from in institutional settings such as hospitals and aged care facilities[1]. While cleansing with alcohol does reduce bacterial counts, a study in which 13 participants with T1D gave more than 1700 injections without skin preparation over a three to five month period found no evidence of local or systemic infections[53].

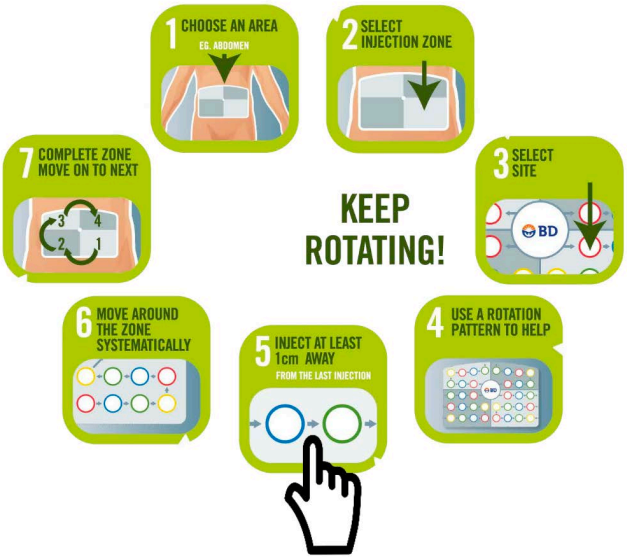
Disposal of sharps

It is essential that people with diabetes are taught about the safe disposal of their used sharps. Evidence suggests that only 33% of needle users dispose of their sharps in a designated waste unit[14]. Programs for the disposal of sharps vary between states/territories within Australia as well as within various local council areas and both health care professionals and people with diabetes should be aware of their local regulations. Links to current recommendations for each state and territory can be found in Appendix 3.

Site rotation

Site rotation is important for reducing the risk of lipodystrophy[1]. People with diabetes, their carers and health care professionals should be taught an easy-to-follow structured process for site rotation[1]. The rotation regimen used by the individual with diabetes needs to be documented by the diabetes educator. This should also be encouraged in health care facilities and documentation in the drug chart at time of administration will facilitate rotation of sites when injections are given by different staff.

One effective method of rotation is to divide the injection site into quadrants (abdomen) or halves (buttock or thigh), using one quadrant per week and moving clockwise around this area[3]. Injections within each area should be spaced at least 1cm apart[3]. Site rotation grids can be useful for people with diabetes who have difficulty remembering where they have injected. However, where different sites are used, variations in absorption between sites must be considered, where applicable[19].



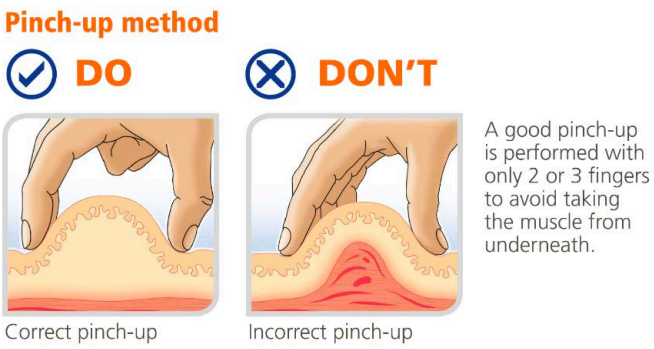
Angle of injection and use of lifted skinfold

Angle of injection

The angle of insertion of the needle used for injection should be determined according to the needle length, injection site and anticipated thickness of SC tissue, and use of a skinfold lift1,18. Needles 8mm or longer should usually be inserted at 45 degrees with a skinfold to reduce the risk of IM injection1,18. Shorter needles can usually be injected at 90 degrees in adults, however for children, slim adults and when injecting into the arms or thigh, a 45 degree angle and/or lifted skinfold may be required to avoid IM injections with 5mm and 6mm needles. A 4mm needle should be injected at 90 degrees[16,18].

Use of lifted skin fold

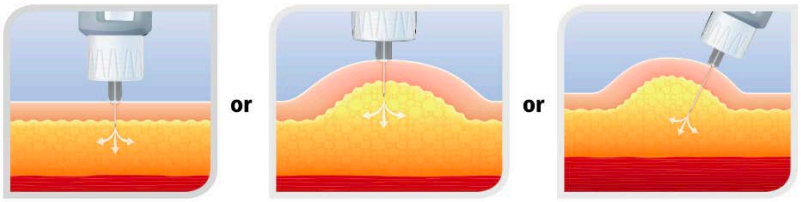
The purpose of using a lifted skin fold is to reduce the risk of IM injection by increasing the space between the skin and muscle fascia. The decision to use a lifted skin fold should be assessed individually, taking into account the likely composition of skin and subcutis relative to needle length, injection site, age, size and body composition. Some individuals (particularly young children and lean adults) may require a lifted skinfold for all injection sites and needle lengths, while for others this will only be needed at injection sites with less SC tissue (e.g. thighs and arms) and with longer (≥6mm) needle lengths[1].



All people injecting diabetes medicines should be taught the correct technique for lifting a skin fold. Two fingers should be used to lift the skin away from the muscle fascia. Ideally this should be the thumb and first or second finger[1].

Technique for lifting a skin fold:

1. Use thumb and index finger (or middle finger) to gently lift (not grab) the skin fold and avoid lifting accompanying muscle.
2. Inject into the raised tissue at 90 degrees.
3. Keep the skin fold raised as the medicine is administered.
4. Hold the needle *in situ* for 10 seconds, or as per the manufacturer's instructions (for insulin pens).
5. Withdraw the needle.
6. Release the skin fold.



90°, no pinch-up 90°, with pinch-up 45°, with pinch-up

Teaching subcutaneous injection technique

People with diabetes, family members, carers and health care professionals require detailed education on SCIT from a diabetes educator which reflects evidence-based practice. Consideration is also needed of the many psychological hurdles the person with diabetes, their family, and carers may face, to commencing insulin treatment[54]. Anxiety and the perception that injections will be painful are two major factors that often need to be addressed during education of IT[1].

Teaching IT is a dynamic process. It requires an individualised approach which takes into account the needs of the person with diabetes and/or their carer. Consideration must be given to multiple factors including:

- The person's readiness and ability to learn.
- The person's anxiety around self-injecting.
- Their understanding of diabetes and the reasons injectable medicines are needed.
- Physical or psychosocial factors affecting their ability to safely inject and the availability of support if needed.
- The learning environment, e.g., noise level, the presence of other people, anxieties of the healthcare professional and family members. The more apprehensive the family members are, the greater the pain and anxiety felt by the person with diabetes.
- Level of confidence and mastery in performing injections with correct technique.
- The type of device and needle length best suited to the individual.
- Willingness to perform other aspects of diabetes self-management related to injectable diabetes medicines (e.g. blood glucose monitoring).
- Management and prevention of hypoglycaemia.

Support for commencement of an injectable therapy

Initiation of injectable medicines can be overwhelming for many people. People with T1D, including children, adolescents and adults, will be required to commence insulin at the time of diagnosis. Those with T2D are likely to have had their condition for some time and are often aware of the need to begin insulin treatment for a period of time prior to its commencement. Healthcare professionals should prepare those with T2D for the likely future need for insulin treatment, explaining the progressive nature of the condition and making it clear that insulin treatment is not a sign of failure in managing their diabetes[16].

People of any age can struggle with injections and may require support and assistance to develop the skills required for improved diabetes management. Others may need support on an ongoing basis to achieve optimal glycaemic management.

Recommendations to support the education process include[1]:

- Showing empathy by addressing the individuals' emotional concerns first by exploring worries and barriers to treatment and acknowledging that anxiety is normal when beginning any new medication, especially insulin.
- Using distraction techniques or play therapy for children (e.g. injecting into a stuffed animal).
- Using cognitive behaviour therapy techniques for older children (e.g. guided imagery, incentive scheduling).

- Health care professionals or parents/carers demonstrating and self-injecting saline to help alleviate anxiety.
- Always using positive language to discuss injection of diabetes medicines. It is important to explain that insulin is not a punishment or failure and that improving blood glucose levels will make them feel better.
- Allowing the person with diabetes to be open and honest regarding their feelings and emotions towards injections, including their frustrations and struggles.
- Including caregivers and family members in the planning and education of the person with diabetes and tailoring education to the therapeutic needs of the individual.
- Considering that pen therapy may have psychological advantages over syringe therapy.
- Understanding that children have a lower pain threshold than adults, and therefore asking questions regarding pain at each diabetes education review.
- Referring to a psychologist for input if the person with diabetes has significant fear around injections.
- Considering use of devices that hide the needle.
- Fear and anxiety may be substantially reduced by having the person with diabetes or their care giver by having a 'dry run', placing the needle under the skin but not delivering any medication.
- Considering use of insulin ports, which may help to reduce anxiety and fear of injections and its associated pain.

Where other carers are involved in the administration of insulin, their involvement in the education process is essential. They should be offered the same education as the person with diabetes and this also requires documentation.

Examples of those who may be involved in the administration of an injectable medicine include:

- Family (spouse, children, partners).
- Health care professionals (diabetes educators, general practitioners, practice nurses, domiciliary nurses and community care workers).

Key topics for education

Research has shown that people with diabetes do not always receive education about the injection of diabetes medications, and when they do, not all essential topics are covered[13,14]. In the 2008-2009 ITQ survey, 25% of participants reported wanting more education regarding IT[14]. While there was some variation between countries, many participants did not recall a number of key topics being adequately covered during their education and training. An earlier study revealed that almost 70% of participants wantedto learn more about insulin IT[13].

Education in correct IT should cover the following essential topics[1]:

- The injection regimen including the timing and action of prescribed medicines and dose(s) required.
- The choice, and training in use of insulin pen device and/or syringe:
    - Assembly of the device including loading of insulin cartridge if applicable.
    - Preparation of the device for injection, including attaching pen needle and priming.
    - Drawing up of insulin for syringes.
- Choice of injection site(s) and importance of site rotation. Note that different sites can illicit different rates of insulin absorption.
- Care and self-examination of injection sites.
- Choice of optimal needle length. The recommended needle length should be recorded for the person with diabetes or carer to eliminate confusion when obtaining supplies from NDSS outlets.
- The importance of single use of pen needles and syringes.
- IT including angle of injection and use of a lifted skin fold, where required.
- Injection complications and how to avoid these.
- Storage of injectable medicines according to the manufacturers' instructions.
- Troubleshooting and a back-up plan for injection device malfunction.
- Safe disposal of sharps.
- Preparation of skin prior to injecting. Hands should be washed prior to preparing the device and injecting.
- Structured self-blood glucose monitoring, including appropriate frequency and timing in relation to injection regimen and documentation in a diary/logbook or meter download.
- Hypoglycaemia, including symptoms, prevention and treatment.
- Where required, discussion of the considerations for flying and travelling when taking injectable medicines.
- Sick day management.

If not already submitted, it is also important to complete or update the person's NDSS registration for the use of insulin or injectable therapies, to enable them to access subsidised pen needles and/or syringes.

Evaluation of injection technique

SCIT requires assessment by qualified and experienced healthcare professionals (e.g. a diabetes educator or endocrinologist) at least annually and ideally at each visit[1]. Review and documentation of injection or infusion insertion technique is pivotal to best practice. Studies have demonstrated that after 12 months the theoretical and practical information taught when initiating injections is not retained. Practical knowledge is more likely to be retained than theoretical knowledge[55]. One study found a significant decrease in glycosylated haemoglobin (HbA1c) in individuals with insulin-treated diabetes who underwent re-education in IT once a month for 4 months[56]. Those who had a poor understanding of IT initially had a higher HbA1c and experienced the greatest reductions in HbA1c with re-education[56].

Review of injection/insertion sites

Along with revision of IT, review of injection sites should occur at least annually and preferably at every diabetes visit[1]. The assessment should include the visual inspection and palpation of injection sites to check for problems related to injections, choice of sites and use of sites[1]. This not only enables the healthcare professional to discover and address injection site problems, but also reinforces to the person with diabetes the importance of correct IT to avoid such problems[14]. Of concern, in the 2014–2015 ITQ survey, 39% of participants could never remember having their injection sites checked[15].

Variable blood glucose levels without obvious explanation should provide the catalyst for sound clinical enquiry to review IT and sites.

Documenting education and evaluation of injection/insertion technique

Teaching of IT and regular review of IT and sites of injection requires documentation reflecting evidence-based recommendations

The entire process of education, including knowledge and competency, must be documented including regular review and assessment of any pre-existing knowledge and self-care practices related to IT[3]. Where family members, carers or other health care professionals are involved in the process, these details should also be recorded.

Documentation should include:

- Understanding of insulin action and the timing of injections.
- Recommended site(s) for injection.
- Recommended site rotation patterns.
- The needle length recommended.
- The angle of insertion recommended.
- Whether use of lifted skin fold is required.
- Demonstration of correct device assembly, following manufacturer's instructions for the device.
- Demonstration of IT.
- Correct dose selection.
- Evidence of damage to injection sites (lipohypertrophy or lipoatrophy), with a description of the size and location of damage, and advice on avoiding these areas for injection.
- Additional issues/barriers to correct IT including physical deficits, psychosocial issues.

Checklists for initial education and review of education on injectable therapies are provided in Appendix 1 and 2, to assist with documentation. However, these are a guide only, and teaching should be person-centred and tailored to the needs of each individual.

Continuous subcutaneous insulin infusion (CSII)

The uptake of continuous subcutaneous insulin infusion (CSII) is increasing in the management of diabetes. The same aims of administering insulin via SC tissue exist for CSII as they do for an insulin pen device or syringe. Similar criteria for choosing needle length for pen needles should apply for choosing optimal insulin infusion set cannula length[1].

Recommendations[1]:

- Cannulation sites should be changed every 48 – 72 hours.
- All people using CSII should be taught to rotate infusion sites along the same principles as people using pen devices and syringes.
- Use of the shortest needle/cannula available should be considered in line with the same principles of people with diabetes using multiple daily injections in order to minimise risk of IM infusion.
- Young children and very thin individuals my need to insert into a lifted skinfold to avoid IM insertion of the cannula.
- The smallest diameter needle/cannula should be considered to reduce pain and occurrence of insertion failure.
- Angled insertion should be considered in people who experience infusion site complications using a 90 degree insertion technique. Individuals who are lean, muscular or very active have a higher probability of the cannula being dislodged and may benefit from angled (30 – 45 degree) insertion of infusion set.
- Use of alternate infusion sets, tapes or skin barriers should be considered if hypersensitive reactions occur to the cannula material or adhesive.
- Unexplained glucose variability that includes frequent hypo/hyperglycaemia should have their infusion sites checked for LH, nodules, scarring, inflammation or other skin and SC conditions that could affect insulin flow or absorption.
- All people using CSII should have their infusion sites checked regularly (at least annually) for LH by a health care professional.
- If LH is suspected, the individual should be instructed to stop infusing into these areas and to insert the cannula into healthy tissue.
- Silent occlusion or interruption of insulin flow should be suspected in any person with unexplained glucose variability, unexplained hyperglycaemia, or frequent hypo/hyperglycaemia. If silent occlusion is suspected, an alternative cannula may need to be considered.
- Individuals who experience difficulty inserting their infusion sets manually may benefit using a mechanical insertion device.
- Women who become pregnant may need to adjust the type of infusion sets used, infusion site locations and frequency of site changes.

Problems with injection sites

Lipodystrophy

Lipodystrophy is one of the most common complications of SC insulin injection and may present as either lipoatrophy (LA) or lipohypertrophy (LH).

LA is a breakdown (atrophy) of the subcutaneous fat tissue. It is thought to be immunological in nature and probably results from impurities or other components in some insulin preparations[2]. Due to the availability of purified human and analogue insulins, it is now less commonly seen, estimated to affect only 1-2% of those injecting insulin[2].

LH is an area of thickened SC tissue which may be hard or scar like, or soft like a rubber ball[3]. Detection requires both visualisation and palpation of injection sites, as some lesions can be more easily felt than seen[1]. LH is associated with repeated injection into the same sites, poor site rotation and reuse of needles[2,4–8]. The incidence of LH is also increased with duration of diabetes, duration of insulin use and number of injections per day[2,4–8]. Unlike LA, LH is commonly seen. A 2017 meta-analysis of 26 studies involving close to 12500 people with diabetes using insulin found a pooled prevalence of LH of 38% [57]. There was a wide range in prevalence between studies (1.9 to 73.4%) and it has been suggested by other authors that this may relate to a number of factors including the lack of routine LH examination in some clinics and the level of training of health professionals to detect LH[58].

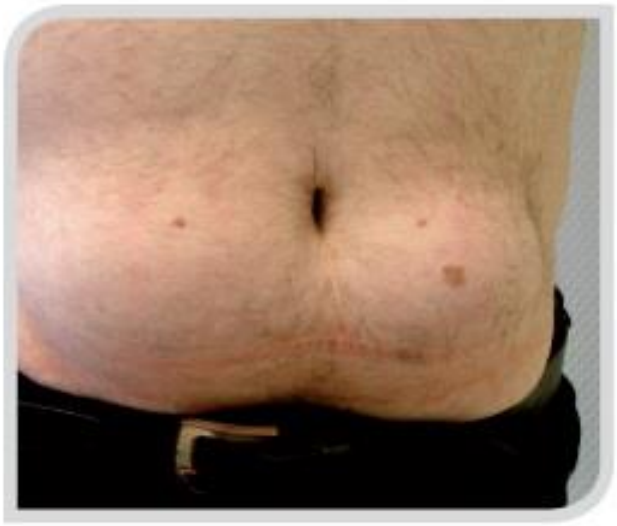
Injecting into LH-affected sites may lead to greater variability in blood glucose levels due to delayed or erratic insulin absorption[59–61].

Signs of lipohypertrophy include:

- Variable blood glucose levels and hyperglycaemia that does not appear to be explained by factors such as dietary intake, insulin dosing, stress, infection, or use of certain medicines known to increase blood glucose levels.
- Unexplained hypoglycaemia.
- Upon inspection and palpation, a thickened rubbery lesion/nodule that appears in the SC tissue of injection sites.
- Sites which cannot be tightly pinched.

Monitoring for lipodystrophy[1]:

- Visually inspect and palpate injection sites for nodules. Palpation is ideally performed with the person lying down and on bare skin, however if not possible, it is acceptable with the person sitting or standing, and being partially clothed.
- Look for multiple needle pricks from injections administered over a small area.
- Ask about the frequency and method of site rotation and reuse of needles.
- Inspect sites for signs of atrophied or hypertrophied skin at least annually and ideally at each visit. If LH is detected, sites require visual inspection and palpation at each visit.
- Be aware that longer duration of diabetes and insulin use and frequency of injecting are associated with a higher risk of LH.
- Documentation should also include location and size of LH and LA. Using a marker pen, two ink marks at the extreme edges of the affected area can be made to allow for accurate measurement and ongoing future assessment. Clinical photography stored on the client's medical record is also valuable.



Management of lipodystrophy:

- Rest affected sites until tissue changes have returned to normal. This can take months to years[1].
- The person administering the injectable medicines should firstly gently palpate the desired injection area, to identify and thus avoid injecting into areas of lipodystrophy.
- If changing from an affected site, doses of insulin need to be reviewed prior to administration in the new site. Change in insulin needs vary from one individual to another and should be guided by frequent blood glucose monitoring. Dose reductions of 20% are commonly recommended but in more serious cases may require a 50% insulin dose reduction when changing to a non-affected site[1].

Prevention of lipodystrophy:

The risk of developing lipodystrophy can be reduced by teaching people with diabetes and/or their family member or carers to[1]:

- Rotate injection sites using an easy-to-follow structured process.
- Use a new needle for each injection.
- Inspect their own injection sites and know how to detect LH.

Problems with injection technique

Intramuscular (IM) injections

. It has been noted that Injections into the IM tissue hasten the absorption of injected medicine by up to 50% due to the vascular nature of muscular tissue, and/or as a result of exercising the relevant muscle tissue[21,62]. Studies with insulin showed an increased rate of absorption with IM injection and this is thought to increase the risk and severity of hypoglycaemia[22,26,62,63].

Problems caused by IM injection of insulin:

- Hypoglycaemia with rapid onset and/or longer duration.
- Variable insulin uptake and duration - bioavailability of insulin can be double the expected time and duration of action, leading to faster onset and shorter duration of action.
- Unwanted fluctuations in blood glucose levels.
- Variable insulin absorption between injections.

Clinical Signs of IM injection of insulin:

- Pain occurring while injecting.
- Unexplained hypoglycaemia, often in the person who is slim and complains of pain on injection.
- Variable blood glucose levels.
- Bleeding and/or bruising.

Prevention of IM injection of insulin:

- Inject into the abdomen or buttocks.
- Avoid sites with little SC tissue such as arms and thighs.
- Consider the use of different techniques according to sites chosen including:
  - shorter needle lengths
  - lifted skin fold
  - insertion of the needle at 45 degree angle.

Intradermal (ID) Injections

Much of the research on the ID administration of insulin is with the use of micro-needles for developing alternative methods of insulin administration including an insulin patch[64]. Micro-needles have hollow cannulae with total lengths of less than 2mm and are commonly used in dermatology settings. Studies of ID insulin administration using micro-needles show increased bioavailability, more rapid absorption and reduced post-prandial glucose levels[65–69]. However insulin administration using micro-needles is not the same as an ID injection made accidentally using an incorrect SC technique. There is some evidence that this may lead to insulin leakage, higher dose requirements, and increased pain caused by direct nerve stimulation. More rapid absorption of insulin may lead to hypoglycaemia. There have also been case studies reporting localised site reactions, attributed to immunological response[70].

Considerations for healthcare settings and carers

People with diabetes may require additional support in administering their injectable diabetes medicines. This can occur in a range of settings that include their own home, school, camp settings, aged and disability care accommodation and support services and during hospitalisation. Those providing this support may include family members or close friends, paid carers, support workers, enrolled and registered nurses.

Organisations providing this support require comprehensive policies and procedures to guide staff in their responsibilities and the processes they are to follow in administering injectable diabetes medications. It is recommended that comprehensive training and evaluation of health and disability care workers knowledge and skills in this area be

undertaken by diabetes educators. This includes the development and ongoing review of appropriate policies and procedures for health care facilities and education programs that are implemented and evaluated to ensure effective care.

Organisations providing support with injectable medicines to individuals with diabetes should have:

- A comprehensive education program.
- IT skills training and evaluation of knowledge and skills.
- Education on safe sharps disposal and occupational health and safety.
- Education on identification, treatment and prevention of hypoglycaemia.
- An individualised written health care plan to guide the expected care for each individual with diabetes being supported, which includes specific requirements such as needle length, administration procedures and additional monitoring required.

Safety considerations for injectable diabetes medicines include:

- Syringes and pen needles are for single use only[1].
- Pen devices and cartridges or vials are for single person use only, and must never be shared due to the risk of cross contamination[40]. This applies even if a new needle is used for each injection.
- Safe disposal of sharps should be taught to people with diabetes and caregivers from the beginning of injection or infusion therapy and be regularly reinforced[1]. Potential adverse events of needle stick injuries should be emphasised to the person and family/caregivers, i.e. safe sharps disposal.
- Needle stick injuries are common among health care professionals[71]. One study of nurses in an Australian hospital found that insulin needles were the second most common causative device resulting in needle stick injuries[72]. Recapping of needles should be discouraged and only undertaken by the person with diabetes. Healthcare services should encourage reporting of needle stick injuries and near misses and should establish a blame-free culture[1]. Review of all needle stick injuries and near misses should take place regularly to assess educational needs and allow for policy change[1]. Safety Pen Needles should be used with insulin pen devices.
- Organisations are responsible for protecting the person with diabetes, other individuals being supported within the organisation, the public and staff from blood-borne pathogens by ensuring their specific infection control policies reflect current

evidence and best practice. Employees require access to training that supports best practice, and consideration should be given to the use of insulin pen needles and syringes with inbuilt safety mechanisms[71]. Campaigns to increase needle stick injury awareness should be conducted regularly.

- If the person with diabetes is unable to remove the pen device needle without help, health care professionals should instead administer injections using pen needles and syringes with inbuilt safety mechanisms[1,71].
- To minimise the risk of a needle stick injury through a skin fold, the use of a 4 or 5mm pen needle or 6 or 8mm insulin syringe needle without a skinfold is recommended[1]. If a lifted skinfold is used, the finger and thumb are approximately 25mm apart and the injection should occur in the centre of the fold.
- Pen device needles and syringes must be disposed of into an approved sharps container and be easily accessible at the point of care or beside the person with diabetes[1].

While the management of needlestick injuries is beyond the scope of this document, the review article *Management of sharps injuries in the healthcare setting (*Riddell et al, 2015) provides a good summary of the immediate management and risk assessment and management strategies to prevent the transmission of blood-borne viruses[73]. CDEs should also be familiar with their local policies and procedures.

Appendix 1: Checklist for Education of Initiation of Injectable Therapies

Date:	
Name of person with diabetes:	
Name of parent/carer (if applicable):	
Name of educator:	
Task	**Note**
☐ Timing and action of prescribed medicines	
☐ Dose of medicine(s) required	
☐ Assembly of the pen device including loading insulin cartridge if applicable	
☐ Preparation of the device for injection, including attaching pen needle and priming	
☐ Drawing up of insulin for syringes	
☐ Need for insulin resuspension (where relevant)	
☐ Choice of injection site(s) specify	
☐ Importance of and guidelines for site rotation	
☐ Preparation of skin prior to injecting	
☐ Importance of washing hands prior to preparing the device and injecting	
☐ Choice of optimal needle length	
☐ Recommended needle length recorded for obtaining supplies from NDSS outlets	
☐ Importance of single use of needles and syringe	
☐ Injection technique including angle of injection and use of a lifted skin fold, where required	
☐ Storage of injectable medicines according to the manufacturers' instructions	
☐ When to discard medicines	
☐ Safe disposal of sharps	
☐ SBGM, including appropriate frequency and timing in relation to injection regimen	
☐ Hypoglycaemia, including symptoms, prevention and treatment	
☐ Sick day management	
☐ Complete/update NDSS registration for insulin/injectable therapies	
☐ Other	

Appendix 2: Checklist for Review of Education of Injectable Therapies

Date:	
Name of person with diabetes:	
Name of parent/carer (if applicable):	
Name of educator:	

Task	Note
☐ Timing and action of prescribed medicines	
☐ Dose of medicine(s) required	
☐ Assembly of the pen device including loading insulin cartridge if applicable	
☐ Preparation of the device for injection, including attaching pen needle and priming	
☐ Drawing up of insulin for syringes	
☐ Need for insulin resuspension (where relevant)	
☐ Choice of injection site(s) specify	
☐ Importance of and guidelines for site rotation	
☐ Preparation of skin prior to injecting	
☐ Importance of washing hands prior to preparing the device and injecting	
☐ Choice of optimal needle length	
☐ Recommended needle length recorded for obtaining supplies from NDSS outlets	
☐ Importance of single use of needles and syringe	
☐ Injection technique including angle of injection and use of a lifted skin fold, where required	
☐ Storage of injectable medicines according to the manufacturers' instructions	
☐ When to discard medicines	
☐ Safe disposal of sharps	
☐ SBGM, including appropriate frequency and timing in relation to injection regimen	
☐ Hypoglycaemia, including symptoms, prevention and treatment	
☐ Check injection sites for signs of lipohypertrophy (LH)	
☐ Advice on avoiding injecting in areas of LH, if applicable	
☐ Potential impact on BGLs of moving injection sites away from areas of LH and need for regular monitoring	
☐ Sick day management	
☐ Other	

Appendix 3: Sharps Disposal

Programs for disposal of sharps vary between states/territories within Australia as well as within the various local council areas. Links to current recommendations for each state and territory can be found below.

NSW	https://www.safesharps.org.au/
QLD	https://www.health.qld.gov.au/public-health/topics/atod/queensland-needle-syringe-program
VIC	http://www.health.vic.gov.au/aod/about/needle.htm
SA	https://www.diabetessa.com.au/Web/Media/News/Safe_Sharps_Disposal.aspx
WA	https://healthywa.wa.gov.au/Articles/N_R/Needle-and-syringe-programs-in-WA
ACT	https://www.accesscanberra.act.gov.au/app/answers/detail/a_id/16/~/needle-or-syringe-collection-and-disposal%2Csharps#!tabs-2
TAS	http://www.dhhs.tas.gov.au/__data/assets/pdf_file/0017/109232/Safe_Sharps_Disposal_DL_Draft_1.0CH.pdf
NT	https://healthylivingnt.org.au/our-services/diabetes/frequently-asked-questions

Appendix 4: Resources

Astra Zeneca

Contact: 1800 805 342

- Byetta Clinicians Guide
- Bydureon Pen Getting Started (Booklet)
- Bydureon Pen Patient Booklet
- Bydureon Pen Instruction Video https://www.azhealth.com.au/ (Registration required)

BD Diabetes Care

Contact: 1800 656 100

https://www.bd.com/dc-anz/healthcare-professionals

- How to inject your diabetes medication: The 5 Golden Rules (booklet)
- Injection Technique Recommendations (Flyer)
- Injecting your Diabetes Medication (Flyer)
- Detecting, Treating and Preventing Lipohypertrophy (Booklet)
- Injection Site Rotation Grid
- Golden Rules posters

Lilly Diabetes

Contact: 1800 023 764

- Lilly Insulin Range (Flyer – tear-off pad)
- KwikPen: A how-to-use guide (Flyer – tear-off pad)
- Humapen Savvio Instructions for Use (Flyer – tear-off pad)
- Starting premixed insulin therapy for Humalog Mix 25 or Humalog Mix 50 (Booklet)
- Starting Humalog booklet
- Know your insulin resources, poster and flip chart
- Trulicity
  - Trulicity Patient Tear Sheet
  - Trulicity Patient Booklet
  - Trulicity Instructions for Use

Product Information and Consumer Medicine Information can be accessed via: www.lilly.com.au/en/products

Novo Nordisk

Contact 1800 668 626

- Product information can be found at www.novonordisk.com.au
- Changing Diabetes Website - https://www.changingdiabetes.com.au/resources (information guides, videos and other resources)
- Type 1 Diabetes (Booklet)
- Type 2 Diabetes (Booklet)
- Gestational Diabetes (Booklet)
- Quick Guides for Novopen Echo, Novopen 4, Innolet, FlexPen and FlexTouch (Flyers)
- Novorapid Patient User Guide in English, Chinese, Arabic, Greek, Vietnamese (Booklet)
- Novomix 30 Patient User Guide in English, Chinese, Arabic, Greek, Vietnamese (booklet)
- Ryzodeg 70/30 Patient User Guide, Carb Guide, Patient Conversion Tool and Time Action Profile Pad
- Levemir Patient User Guide in English, Chinese, Arabic (Booklet)
- Victoza Patient User Guide (Booklet)
- Glucogen Hypokit User Guide (Booklet)

Ascensia Diabetes Care

Owen Mumford

Contact: 1800 289 312
www.unifinepentips.com.au

www.unifinepentipsplus.com.au

www.diabetes.ascensia.com.au

• Impact of Unifine® Pentips® Plus on pen needle changing behaviour among patients injecting with cartridge therapy devices.

Sanofi

Contact: 1800 818 806

- Product Information www.sanofi.com.au
- Toujeo SoloSTAR® Instructions for Use Leaflet
- Apidra SoloSTAR® Instructions for Use Leaflet
- Lantus SoloSTAR® Instructions for Use Leaflet
- JuniorSTAR® User Guide
- SoloSTAR®& AllStar Pro® Guide
- Toujeo "How to inject video" http://videos.sanofi.com.au/howtoinjectvideo
- Toujeo online education resources https://www.toujeo.com.au/login

References:

1. Frid AH, Kreugel G, Grassi G, et al. New Insulin Delivery Recommendations. *Mayo Clin Proc*. 2016;91(9):1231-1255. doi:10.1016/j.mayocp.2016.06.010
2. Blanco M, Hernández MT, Strauss KW, Amaya M. Prevalence and risk factors of lipohypertrophy in insulin-injecting patients with diabetes. *Diabetes Metab*. 2013;39(5):445-453. doi:10.1016/j.diabet.2013.05.006
3. Frid A, Hirsch L, Gaspar R, et al. New injection recommendations for patients with diabetes. *Diabetes Metab*. 2010;36:S3-S18. doi:10.1016/S1262-3636(10)70002-1
4. Al Hayek AA, Robert AA, Braham RB, Al Dawish MA. Frequency of Lipohypertrophy and Associated Risk Factors in Young Patients with Type 1 Diabetes: A Cross-Sectional Study. *Diabetes Ther*. 2016;7(2):259-267. doi:10.1007/s13300-016-0161-3
5. Barola A, Tiwari P, Bhansali A, Grover S, Dayal D. Insulin-Related Lipohypertrophy: Lipogenic Action or Tissue Trauma? *Front Endocrinol (Lausanne)*. 2018;9:638. doi:10.3389/fendo.2018.00638
6. Al Ajlouni M, Abujbara M, Batieha A, Ajlouni K. Prevalence of lipohypertrophy and associated risk factors in insulin-treated patients with type 2 diabetes mellitus. *Int J Endocrinol Metab*. 2015;13(2):e20776. doi:10.5812/ijem.20776
7. Vardar B, Kızılcı S. Incidence of lipohypertrophy in diabetic patients and a study of influencing factors. *Diabetes Res Clin Pract*. 2007;77(2):231-236. doi:10.1016/j.diabres.2006.12.023
8. Pozzuoli GM, Laudato M, Barone M, Crisci F, Pozzuoli B. Errors in insulin treatment management and risk of lipohypertrophy. *Acta Diabetol*. 2018;55(1):67-73. doi:10.1007/s00592-017-1066-y
9. Spollett G, Edelman S V., Mehner P, Walter C, Penfornis A. Improvement of Insulin Injection Technique. *Diabetes Educ*. 2016;42(4):379-394. doi:10.1177/0145721716648017
10. Turner RC, Cull CA, Frighi V, Holman RR. Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). UK Prospective Diabetes Study (UKPDS) Group. *JAMA*. 1999;281(21):2005-2012. http://www.ncbi.nlm.nih.gov/pubmed/10359389. Accessed June 3, 2019.
11. (UK) NCC for W and CH. *Diabetes in Pregnancy*. National Institute for Health and Care Excellence (UK); 2015. http://www.ncbi.nlm.nih.gov/pubmed/25950069. Accessed June 3, 2019.
12. National Diabetes Services Scheme. *NDSS National Diabetes Data Snapshots: Insulin Therapy*.; 2019. https://static.diabetesaustralia.com.au/s/fileassets/diabetes-australia/6cb8d70d-c7ca-4713-a5ec-b79ae6d4385a.pdf. Accessed June 4, 2019.
13. Strauss K, De Gols H, Hannet I, Partanen T-M, Frid A. *A Pan-European Epidemiologic Study of Insulin Injection Technique in Patients with Diabetes*. Vol 19.; 2002. https://onlinelibrary.wiley.com/doi/pdf/10.1002/pdi.314. Accessed May 28, 2019.
14. DE CONINCK C, FRID A, GASPAR R, et al. Results and analysis of the 2008-2009 Insulin Injection Technique Questionnaire survey. *J Diabetes*. 2010;2(3):168-179. doi:10.1111/j.1753-0407.2010.00077.x
15. Frid AH, Hirsch LJ, Menchior AR, Morel DR, Strauss KW. Worldwide Injection Technique Questionnaire Study: Injecting Complications and the Role of the Professional. *Mayo Clin Proc*. 2016;91(9):1224-1230. doi:10.1016/j.mayocp.2016.06.012
16. Frid AH, Hirsch LJ, Menchior AR, Morel DR, Strauss KW. Worldwide Injection Technique Questionnaire Study: Population Parameters and Injection

Practices. *Mayo Clin Proc*. 2016;91(9):1212-1223. doi:10.1016/j.mayocp.2016.06.011
17. Saltiel-Berzin R, Cypress M, Gibney M. Translating the Research in Insulin Injection Technique. *Diabetes Educ*. 2012;38(5):635-643. doi:10.1177/0145721712455107
18. Hansen B, Matytsina I. Insulin administration: selecting the appropriate needle and individualizing the injection technique. *Expert Opin Drug Deliv*. 2011;8(10):1395-1406. doi:10.1517/17425247.2011.614229
19. American Diabetes Association. Insulin administration. *Diabetes Care*. 2004;27 Suppl 1(suppl 1):S106-9. doi:10.2337/diacare.27.2007.s106
20. Hirsch L, Byron K, Gibney M. Intramuscular Risk at Insulin Injection Sites—Measurement of the Distance from Skin to Muscle and Rationale for Shorter-Length Needles for Subcutaneous Insulin Therapy. *Diabetes Technol Ther*. 2014;16(12):867-873. doi:10.1089/dia.2014.0111
21. Frid A, Ostman J, Linde B. Hypoglycemia Risk During Exercise After Intramuscular Injection of Insulin in Thigh in IDDM. *Diabetes Care*. 1990;13(5):473-477. doi:10.2337/diacare.13.5.473
22. Vaag A, Handberg A, Lauritzen M, Henriksen JE, Pedersen KD, Beck-Nielsen H. Variation in absorption of NPH insulin due to intramuscular injection. *Diabetes Care*. 1990;13(1):74-76. doi:10.2337/diacare.13.1.74
23. Gin H, Hanaire-Broutin H. Reproducibility and variability in the action of injected insulin. *Diabetes Metab*. 2005;31(1):7-13. http://www.ncbi.nlm.nih.gov/pubmed/15803107. Accessed May 28, 2019.
24. Lo Presti D, Ingegnosi C, Strauss K. Skin and subcutaneous thickness at injecting sites in children with diabetes: ultrasound findings and recommendations for giving injection. *Pediatr Diabetes*. 2012;13(7):525-533. doi:10.1111/j.1399-5448.2012.00865.x
25. Frid AH, Kreugel G, Grassi G, et al. New Insulin Delivery Recommendations. *Mayo Clin Proc*. 2016;91(9):1231-1255. doi:10.1016/j.mayocp.2016.06.010
26. Karges B, Boehm BO, Karges W. Early hypoglycaemia after accidental intramuscular injection of insulin glargine. *Diabet Med*. 2005;22(10):1444-1445. doi:10.1111/j.1464-5491.2005.01654.x
27. Bond A. Exenatide (Byetta) as a novel treatment option for type 2 diabetes mellitus. *Proc (Bayl Univ Med Cent)*. 2006;19(3):281-284. http://www.ncbi.nlm.nih.gov/pubmed/17252050. Accessed June 3, 2019.
28. Bergenstal RM, Strock ES, Peremislov D, Gibney MA, Parvu V, Hirsch LJ. Safety and Efficacy of Insulin Therapy Delivered via a 4mm Pen Needle in Obese Patients With Diabetes. *Mayo Clin Proc*. 2015;90(3):329-338. doi:10.1016/j.mayocp.2014.12.014
29. Kreugel G, Keers JC, Kerstens MN, Wolffenbuttel BHR. Randomized Trial on the Influence of the Length of Two Insulin Pen Needles on Glycemic Control and Patient Preference in Obese Patients with Diabetes. *Diabetes Technol Ther*. 2011;13(7):737-741. doi:10.1089/dia.2011.0010
30. SCHWARTZ S, HASSMAN D, SHELMET J, et al. A multicenter, open-label, randomized, two-period crossovertrial comparing glycemic control, satisfaction, and preference achieved with a 31 gauge × 6 mm needle versus a 29 gauge × 12.7 mm needle in obese patients with diabetes mellitus. *Clin Ther*. 2004;26(10):1663-1678. doi:10.1016/j.clinthera.2004.10.007
31. Frid A, Linde B. Intraregional differences in the absorption of unmodified insulin from the abdominal wall. *Diabet Med*. 1992;9(3):236-239. http://www.ncbi.nlm.nih.gov/pubmed/1533580. Accessed June 3, 2019.
32. de la Pena A, Riddle M, Morrow LA, et al. Pharmacokinetics and

Pharmacodynamics of High-Dose Human Regular U-500 Insulin Versus Human Regular U-100 Insulin in Healthy Obese Subjects. *Diabetes Care*. 2011;34(12):2496-2501. doi:10.2337/dc11-0721
33. Hirose T, Ogihara T, Tozaka S, Kanderian S, Watada H. Identification and comparison of insulin pharmacokinetics injected with a new 4-mm needle vs 6- and 8-mm needles accounting for endogenous insulin and C-peptide secretion kinetics in non-diabetic adult males. *J Diabetes Investig*. 2013;4(3):287-296. doi:10.1111/jdi.12035
34. Seidenari S, Giusti G, Bertoni L, Magnoni C, Pellacani G. Thickness and Echogenicity of the Skin in Children as Assessed by 20-MHz Ultrasound. *Dermatology*. 2000;201(3):218-222. doi:10.1159/000018491
35. Gibney MA, Arce CH, Byron KJ, Hirsch LJ. 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):1519-1530. doi:10.1185/03007995.2010.481203
36. Selam J-L. Evolution of Diabetes Insulin Delivery Devices. *J Diabetes Sci Technol*. 2010;4(3):505-513. doi:10.1177/193229681000400302
37. Anderson BJ, Redondo MJ. What Can We Learn from Patient-Reported Outcomes of Insulin Pen Devices? *J Diabetes Sci Technol*. 2011;5(6):1563-1571. doi:10.1177/193229681100500633
38. Baruah MP. Insulin pens: the modern delivery devices. *J Assoc Physicians India*. 2011;59 Suppl:38-40. http://www.ncbi.nlm.nih.gov/pubmed/21823254. Accessed June 4, 2019.
39. Williams AS, Schnarrenberger PA. A comparison of dosing accuracy: visually impaired and sighted people using insulin pens. *J Diabetes Sci Technol*. 2010;4(3):514-521. doi:10.1177/193229681000400303
40. Herdman ML, Larck C, Schliesser SH, Jelic TM. Biological contamination of insulin pens in a hospital setting. *Am J Health Syst Pharm*. 2013;70(14):1244-1248. doi:10.2146/ajhp120728
41. Cengiz E, Swan KL, Tamborlane W V., Sherr JL, Martin M, Weinzimer SA. The Alteration of Aspart Insulin Pharmacodynamics When Mixed With Detemir Insulin. *Diabetes Care*. 2012;35(4):690-692. doi:10.2337/dc11-0732
42. Cengiz E, Tamborlane W V, Martin-Fredericksen M, Dziura J, Weinzimer SA. Early pharmacokinetic and pharmacodynamic effects of mixing lispro with glargine insulin: results of glucose clamp studies in youth with type 1 diabetes. *Diabetes Care*. 2010;33(5):1009-1012. doi:10.2337/dc09-2118
43. Heise T, Nosek L, Dellweg S, et al. Impact of injection speed and volume on perceived pain during subcutaneous injections into the abdomen and thigh: a single-centre, randomized controlled trial. *Diabetes, Obes Metab*. 2014;16(10):971-976. doi:10.1111/dom.12304
44. Schloot NC, Hood RC, Corrigan SM, Panek RL, Heise T. Concentrated insulins in current clinical practice. *Diabetes Res Clin Pract*. 2019;148:93-101. doi:10.1016/j.diabres.2018.12.007
45. Painter NA, Sisson E. An Overview of Concentrated Insulin Products. *Diabetes Spectr*. 2016;29(3):136-140. doi:10.2337/diaspect.29.3.136
46. Birkebaek NH, Solvig J, Hansen B, Jorgensen C, Smedegaard J, Christiansen JS. A 4-mm Needle Reduces the Risk of Intramuscular Injections Without Increasing Backflow to Skin Surface in Lean Diabetic Children and Adults. *Diabetes Care*. 2008;31(9):e65-e65. doi:10.2337/dc08-0977
47. Hirsch LJ, Gibney MA, Albanese J, et al. Comparative glycemic control, safety and patient ratings for a new 4 mm ×

32G insulin pen needle in adults with diabetes. *Curr Med Res Opin*. 2010;26(6):1531-1541. doi:10.1185/03007995.2010.482499
48. Hofman PL, Derraik JGB, Pinto TE, et al. Defining the Ideal Injection Techniques When Using 5-mm Needles in Children and Adults. *Diabetes Care*. 2010;33(9):1940-1944. doi:10.2337/dc10-0871
49. Miwa T, Itoh R, Kobayashi T, et al. Comparison of the Effects of a New 32-Gauge×4-mm Pen Needle and a 32-Gauge×6-mm Pen Needle on Glycemic Control, Safety, and Patient Ratings in Japanese Adults with Diabetes. *Diabetes Technol Ther*. 2012;14(12):1084-1090. doi:10.1089/dia.2012.0170
50. Wittmann A, Köver J, Kralj N, et al. Insulin Leakage Value in Relation to Pen Needle Length and Administered Dose After Subcutaneous Injection. *Diabetes Technol Ther*. 2010;12(8):587-590. doi:10.1089/dia.2010.0050
51. Ignaut DA, Fu H. Comparison of Insulin Diluent Leakage Postinjection Using Two Different Needle Lengths and Injection Volumes in Obese Patients with Type 1 or Type 2 Diabetes Mellitus. *J Diabetes Sci Technol*. 2012;6(2):389-393. doi:10.1177/193229681200600226
52. Kaiser P, Maxeiner S, Weise A, et al. Assessment of the Mixing Efficiency of Neutral Protamine Hagedorn Cartridges. *J Diabetes Sci Technol*. 2010;4(3):652-657. doi:10.1177/193229681000400320
53. Koivisto VA, Felig P. Is skin preparation necessary before insulin injection? *Lancet (London, England)*. 1978;1(8073):1072-1075. http://www.ncbi.nlm.nih.gov/pubmed/77369. Accessed June 3, 2019.
54. Frid A, Hirsch L, Gaspar R, et al. The Third Injection Technique Workshop In Athens (TITAN). *Diabetes Metab*. 2010;36:S19-S29. doi:10.1016/S1262-3636(10)70003-3
55. Bruttomesso D, Costa S, Dal Pos M, et al. Educating diabetic patients about insulin use: changes over time in certainty and correctness of knowledge. *Diabetes Metab*. 2006;32(3):256-261. http://www.ncbi.nlm.nih.gov/pubmed/16799403. Accessed June 3, 2019.
56. Nakatani Y, Matsumura M, Monden T, Aso Y, Nakamoto T. Improvement of Glycemic Control by Re-education in Insulin Injection Technique in Patients with Diabetes Mellitus. *Adv Ther*. 2013;30(10):897-906. doi:10.1007/s12325-013-0066-8
57. Deng N, Zhang X, Zhao F, Wang Y, He H. Prevalence of lipohypertrophy in insulin-treated diabetes patients: A systematic review and meta-analysis. *J Diabetes Investig*. 2018;9(3):536-543. doi:10.1111/jdi.12742
58. Gentile S, Strollo F, Guarino G, et al. Why are so huge differences reported in the occurrence rate of skin lipohypertrophy? Does it depend on method defects or on lack of interest? *Diabetes Metab Syndr Clin Res Rev*. 2019;13(1):682-686. doi:10.1016/j.dsx.2018.11.042
59. Gupta SS, Gupta KS, Gathe SS, Bamrah P, Gupta SS. Clinical Implications of Lipohypertrophy Among People with Type 1 Diabetes in India. *Diabetes Technol Ther*. 2018;20(7):483-491. doi:10.1089/dia.2018.0074
60. Deeb A, Abdelrahman L, Tomy M, et al. Impact of Insulin Injection and Infusion Routines on Lipohypertrophy and Glycemic Control in Children and Adults with Diabetes. *Diabetes Ther*. 2019;10(1):259-267. doi:10.1007/s13300-018-0561-7
61. Famulla S, Hövelmann U, Fischer A, et al. Insulin Injection Into Lipohypertrophic Tissue: Blunted and More Variable Insulin Absorption and Action and Impaired Postprandial Glucose Control. *Diabetes Care*. 2016;39(9):1486-1492. doi:10.2337/dc16-0610
62. Frid A, Gunnarsson R, Güntner P, Linde B. Effects of accidental intramuscular

injection on insulin absorption in IDDM. *Diabetes Care*. 1988;11(1):41-45. doi:10.2337/diacare.11.1.41
63. Thow JC, Johnson AB, Fulcher G, Home PD. Different absorption of isophane (NPH) insulin from subcutaneous and intramuscular sites suggests a need to reassess recommended insulin injection technique. *Diabet Med*. 1990;7(7):600-602. http://www.ncbi.nlm.nih.gov/pubmed/2146067. Accessed June 3, 2019.
64. Hultström M, Roxhed N, Nordquist L. Intradermal Insulin Delivery. *J Diabetes Sci Technol*. 2014;8(3):453-457. doi:10.1177/1932296814530060
65. Ita KB. Transdermal drug delivery: progress and challenges. *J Drug Deliv Sci Technol*. 2014;24(3):245-250. doi:10.1016/S1773-2247(14)50041-X
66. Nordquist L, Roxhed N, Griss P, Stemme G. Novel Microneedle Patches for Active Insulin Delivery are Efficient in Maintaining Glycaemic Control: An Initial Comparison with Subcutaneous Administration. *Pharm Res*. 2007;24(7):1381-1388. doi:10.1007/s11095-007-9256-x
67. Pettis RJ, Hirsch L, Kapitza C, et al. Microneedle-Based Intradermal Versus Subcutaneous Administration of Regular Human Insulin or Insulin Lispro: Pharmacokinetics and Postprandial Glycemic Excursions in Patients with Type 1 Diabetes. *Diabetes Technol Ther*. 2011;13(4):443-450. doi:10.1089/dia.2010.0183
68. Pettis RJ, Ginsberg B, Hirsch L, et al. Intradermal Microneedle Delivery of Insulin Lispro Achieves Faster Insulin Absorption and Insulin Action than Subcutaneous Injection. *Diabetes Technol Ther*. 2011;13(4):435-442. doi:10.1089/dia.2010.0184
69. Kochba E, Levin Y, Raz I, Cahn A. Improved Insulin Pharmacokinetics Using a Novel Microneedle Device for Intradermal Delivery in Patients with Type 2 Diabetes. *Diabetes Technol Ther*. 2016;18(9):525-531. doi:10.1089/dia.2016.0156
70. Sanyal T, Ghosh S, Chowdhury S, Mukherjee S. Can a faulty injection technique lead to a localized insulin allergy? *Indian J Endocrinol Metab*. 2013;17(Suppl 1):S358-9. doi:10.4103/2230-8210.119621
71. Trim JC, Elliott TSJ. A review of sharps injuries and preventative strategies. *J Hosp Infect*. 2003;53(4):237-242. http://www.ncbi.nlm.nih.gov/pubmed/12660120. Accessed June 3, 2019.
72. Smith DR, Smyth W, Leggat PA, Wang R-S. Needlestick and sharps injuries among nurses in a tropical Australian hospital. *Int J Nurs Pract*. 2006;12(2):71-77. doi:10.1111/j.1440-172X.2006.00553.x
73. Riddell A, Kennedy I, Tong CYW. Management of sharps injuries in the healthcare setting. *BMJ*. 2015;351:h3733. doi:10.1136/bmj.h3733