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Advance Insulin Injection Technique and Education With FITTER Forward Expert Recommendations

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Abstract

Injectable insulin therapy is a valuable therapeutic option for millions of people with diabetes worldwide. However, many people with diabetes undergoing insulin therapy experience suboptimal outcomes and/or have complications because of inadequate injection technique and training. Practical, current, evidence-based recommendations are mandatory for primary care practitioners and diabetes specialists alike to address unmet needs in insulin injection technique, education, and consequent outcomes. The most recent global insulin injection technique best practices were published in 2016 by the Forum for Injection Technique and Therapy Expert Recommendations (FITTER). While injection technique efforts in different regions have reflected some developments since 2016, a global effort was warranted to comprehensively capture new evidence and modern expert perspectives. In this article, we share the output of the "FITTER Forward" initiative, authored by 16 diabetes specialists from 13 countries who met virtually in 2023-2024. FITTER Forward provides an updated rationale for the importance of proper injection technique training and its impact on diabetes management. The FITTER Forward recommendations are organized for use in clinical practice and include 4 sections describing (1) the foundational science informing injection device design, experiences, and outcomes, (2) proper injection technique procedures for insulin pens and syringes from insulin storage to needle disposal, (3) lipodystrophy risk reduction, with a focus on lipohypertrophy, and (4) structured injection technique training programs for people with diabetes. Overall, FITTER Forward aims to better equip health care professionals to advance diabetes care by empowering people with diabetes and their caregivers to correctly and safely deliver insulin.

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One hundred years after its initial therapeutic use, insulin remains critical to diabetes care, with approximately 150 to 200 million people with diabetes (PWD) worldwide requiring insulin treatment.[1,2] Insulin should be delivered to the subcutaneous (SC) tissue by injection or infusion for best absorption into the bloodstream and subsequent glucose-lowering activity.[3,4] People with diabetes and/or their caregivers are therefore tasked to learn optimal, evidence-based techniques to deliver insulin as part of daily life.[5] Unfortunately, insulin delivery technique education is often neglected. In the 2015 Injection Technique Questionnaire (ITQ) surveying more than 13,000 PWD from 42 countries, less than 40% of respondents reported receiving injection instructions from their health care professionals (HCPs)

within the preceding 6 months.[6,7] In the ITQ, inadequate injection technique was common, and multiple recent reports revealed that all surveyed PWD made at least one insulin injection technique error.[6-9] Technique errors may lead to undesirable glycemic outcomes, excess pain, or skin complications such as lipodystrophy.[5-7,10] Fortunately, injection technique educational programs can improve patient satisfaction and reduce insulin requirements as well as the frequency of hypoglycemic events, glucose variability, and risk of lipodystrophy.[11-17]

The Forum for Injection Technique and Therapy Expert Recommendations (FITTER) group, comprised of physicians, nurses, diabetes educators/certified diabetes care and education specialists, and allied HCPs, previously created an evidence-based resource (referred to herein as FITTER) for insulin delivery technique via a workshop in 2015, which expanded on prior workshops and incorporated the aforementioned ITQ results (Supplemental Figure 1, available online at http://www.mayoclinicproceedings.org).[5,18,19] FITTER became a landmark reference for insulin delivery technique and is cited in the American Diabetes Association Standards of Care as best practice.[5,20] Since 2015, regional-specific iterations of FITTER and other initiatives such as the Forum for Injection Technique have emerged as valuable resources.[21-23] These regional efforts serve to adapt recommendations to unique local needs (eg, highlighting challenges for low- or middle-income countries). Now, nearly a decade since FITTER was published, an update is warranted to reflect the latest technological and research advancements.

Our new group, known as FITTER Forward, convened virtually in 2023-2024 to create an updated reference for HCPs, PWD, and their caregivers on optimal insulin delivery, with a focus on injection technique. This effort revises prior recommendations and shares new insights on injection education program design. We also sought to improve the practical utility of the recommendations with a new organization of content and new figures/tables. Overall, our goal was to highlight the measurable value of proper insulin delivery technique for improving clinical outcomes and reducing unwanted adverse effects.

METHODS

Sixteen diabetes experts from 13 countries (list in Supplemental Table 1, available online at http://www.mayoclinicproceedings.org) held 4 virtual sessions from September 26, 2023, to June 28, 2024, to review (1) the recommendations from the last FITTER[5]; (2) recent literature on injection technology (eg, new pen needle designs/lengths) and educational programs; and (3) practical teaching tools for injection technique. Meeting virtually offered ease of scheduling, reduced carbon footprint, and improved ability to share references/photos digitally. The output of the virtual meetings combined with literature reviews of the aforementioned topics have informed the FITTER Forward recommendations. The present recommendations pertain largely to injection technique for adults, with adaptation specific to children/adolescents. A brief summary of insulin infusion considerations has been included in Supplemental Table 2 (available online at http://www.mayoclinicproceedings.org).

FITTER FORWARD INSULIN DELIVERY RECOMMENDATIONS

Section 1: Understand How Characteristics of Physiology, Devices, and Injection Technique Impact Injection Experiences

Human skin consists of the epidermis, dermis, and SC fat layers above the muscle layer (Figure 1). Based on its pharmacokinetics and pharmacodynamics, insulin should be administered into the SC layer for optimal absorption rate into the bloodstream. Intramuscular (IM) injections increase hypoglycemia risk because of a faster absorption rate.[4] Delivery device, injection technique, and physiology contribute to the likelihood of correct insulin delivery to the SC tissue with minimization of pain (Figure 2). Health care professionals should understand how the design of insulin delivery devices (especially needles) interplays

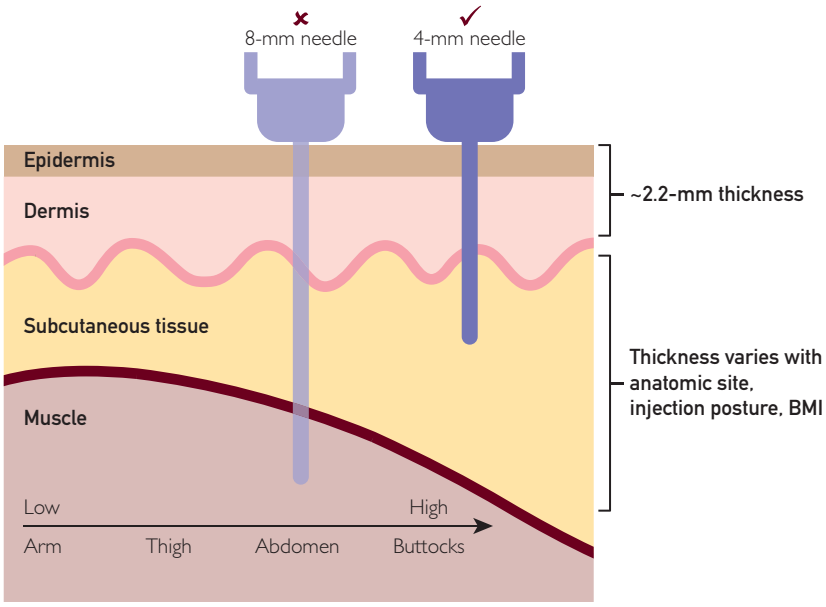

FIGURE 1. Successful insulin injection into the subcutaneous tissue can be achieved with a 4-mm pen needle inserted at 90° for most individuals. Insulin is best absorbed from the subcutaneous tissue. The thickness of subcutaneous tissue varies by the body mass index of the person with diabetes and by anatomic location.[24] Typically, the subcutaneous layer is thinnest in the arm and increases in the thigh, abdomen, and buttocks.[24] Long needles (eg, 8 mm) injected perpendicular to the skin risk painful intramuscular injection and are not recommended. BMI, body mass index; PWD, people with diabetes. Adapted from *Diabetes Ther*,[25] in accordance with the Creative Commons license (CC BY-NC 4.0).

with technique and physiology to affect injection force/pain/outcomes.

Early devices for insulin administration were syringes made of breakable glass with long, manually sharpened needles.[3] Thankfully, innovation over the past century has led to new devices offering improved experiences for PWD (Supplemental Figure 1).[3] Options for insulin injection now include vial-and-syringes, prefilled syringes, autoinjectors, injection pens/pen needles (disposable pens, refillable pens, and connected or smart pens), and safety needles for hospital/clinical settings (Supplemental Figure 1).[26,32–34] The device factors (of pen needles and syringes) that HCPs should understand to appropriately educate PWD in their care on injection technique are described in the following text.

Needle Length Should Be Adequate to Reliably Administer Insulin to the Subcutaneous Adipose Tissue. All needles for insulin delivery have to be long enough to traverse the skin and reliably deliver insulin to the SC tissue but short enough to avoid accidental IM injection.[35] While characteristics of the individual may influence the thickness of the skin and/or the SC adipose tissue layer, 4 mm is an appropriate pen needle length/penetration depth for all adults and children with diabetes (Figures 1 and 2).[5] Differences in skin layer thickness proportionate to body mass index (BMI) have been observed, but reports conflict as to whether skin thickness is increased or decreased with high BMI and if these differences are clinically meaningful.[24,36] Meanwhile, it is established that the SC adipose tissue layer does vary with BMI, putting individuals with lean body mass at greater risk of IM injection (Figure 1).[24] Therefore, individuals with high or low BMI can use a 4-mm needle; however, those with reduced adiposity or thinner skin layers (eg, low BMI, older adults, or pregnant women) using standard injection sites may need a skin lift/skinfold/skin "pinch

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up" technique to accumulate sufficient SC tissue for injections (Table).[37-43] Recommended skin lift technique is described in Supplemental Figure 2 (available online at http://www.mayoclinicproceedings.org).

If 4-mm pen needles are unavailable, then 5-mm needles are a backup/alternative option. Longer pen needle lengths of 6 to 8 mm should be discouraged because of the higher risk of IM injection and greater preference by PWD for 4-mm pen needles.[44-46] In some countries, 3.5-mm length pen needles are emerging as an option with initial evidence indicating they are noninferior to 4-mm pen needles, although the currently available 3.5-mm pen needles have a high gauge number (34G; see Section 2), contributing to reports of increased manual effort during injection.[47]

Health care professionals should discuss the pros and cons of various needle lengths with the individual PWD or their caregiver to arrive at an appropriate personalized decision. Experienced PWD may still be using 5- or 6-mm needles prescribed in the past; discuss if 4-mm would be preferable for them. Note that not all needle lengths are available in every country, and HCPs should be aware of their locally available options. Health care professionals should advise PWD on what to do when their preferred length is unavailable (eg, at what length should they implement a skin lift).

Thin and Sharp Needles With Increased Flow Rate Reduce Injection Pain. Needle penetration force is correlated with pain perceived by the individual, with the gauge size (exterior diameter of the needle) being directly linked to needle penetration force (Figure 2).[26,27] Gauge number and exterior diameter are inversely related—as the gauge number increases, the external needle diameter decreases (Supplemental Table 3, available online at http://www.mayoclinicproceedings.org).[26] The inner diameter of the needle influences the flow rate of insulin, which contributes to the pressure required to press the injection dose button of the pen or the plunger of a syringe and the time needed to administer an insulin dose.[48] High-gauge needles with thinner walls require less needle penetration force and offer increased flow rate through the needle.[3,48,49] While higher-gauge needles are less painful[50] and may cause less fear of injection, they may pose an increased risk of bending or breaking; current evidence suggests that 32G reduces pain without being too fragile.[51,52]

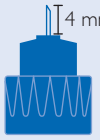
Needle sharpness can also affect the pain of SC insulin application, with sharper generally being less painful because of reduced injection force (both penetration and extraction force) (Figure 2).[49,53,54] Sharpness is achieved through the design of the needle tip and by avoiding needle reuse. More "bevels" or cuts in the tip geometry improve the sharpness. Health care professionals can consult with local health agencies, pharmacists, or needle manufacturers to learn the available needle tip designs in their country/region and may consider advocating for better options.

Lubrication of the steel surface of the needle with silicone oil by manufacturers, a common practice for all hypodermic needles, also reduces the force required for skin penetration.[49,55] Needle reuse reduces the lubrication on the steel surface and the sharpness, part of why single-use needles should not be reused.[49] Although needle lubrication is not directly linked to skin irritation/inflammation/allergy, the loss of lubrication through needle reuse could potentially lead to increased discomfort or tissue damage. The lubrication on new needles is generally considered beneficial for reducing injection discomfort.

Pen Base Design Can Influence the Impact of Excess Force. In a survey of 230 PWD, the use of excessive force on a pen needle was the most common injection technique error (76% of users).[8] Force applied with a pen has a different impact on the skin surface if the pen needle is posted (a cylindrical feature surrounds the metal needle) or contoured, which may be amplified in persons with hand dexterity challenges such as arthritis (Figure 2).[3,8,56] The base of a pen needle should not indent the skin during injection. With a posted base, pressure applied onto the insulin pen is focused to a small skin area,

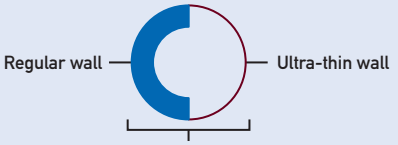
Device characteristics

Needle length should be long enough to traverse the skin but short enough to avoid intramuscular injection



4-mm pen needles are recommended for all people (adults and children)

Needle width (gauge) should be thin to reduce injection pain; higher gauge number indicates a thinner needle



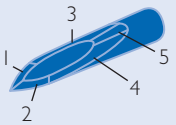
(needle cross-section, not to scale)

32G is recommended for most adults with diabetes

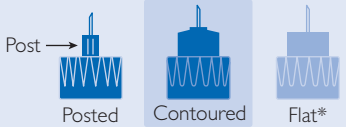
Needle wall thickness should be thin to create larger lumen to enable higher flow rate

Needle sharpness (tip geometry) should minimize skin penetration force

5 bevels, the angles that create the needle tip, are preferred to 3 bevels



Needle base design can influence the way pressure is concentrated at the injection site



A posted base pen needle concentrates pressure at the insertion site to a small area.

A contoured base pen needle has a larger surface area in contact with skin; therefore, pressure is more widely distributed for reduced overall force.

Other factors that contribute to injection force/pain/experience include:

- Injection **volume** and **flow rate**
- Device ergonomics (button or plunger force, grip shape, etc.)
- Needle **lubrication** to reduce penetration force

Physiology considerations

Skin/subcutaneous (SC) layer thickness

- The thickness of skin is relatively consistent between individuals; however, the SC layer is highly variable
- Age, BMI, sex, and pregnancy status influence SC thickness
- SC layer thickness may vary by anatomic location

Delivery site selection

- Injection into lipohypertrophy hinders insulin absorption
- The presence of scars, tattoos, or skin lesions may alter insulin absorption should be avoided if possible

Dexterity/movement abilities

- For self-injection, all people with diabetes will need sufficient dexterity to assemble and use an injection device
- People with diabetes will also require ability to comfortably reach multiple injection sites or access to assistance

Technique characteristics

Needle reuse

Avoid needle reuse to prevent infection pain from dull needles

Temperature of insulin when delivered

Injection of cold insulin should be avoided; room temperature is preferred

Device angle skin lift

- 90°is recommended for most adults using 4 to 5-mm pen needles
- For conventional syringes, a 6-mm needle should be injected into a skin lift at 90°

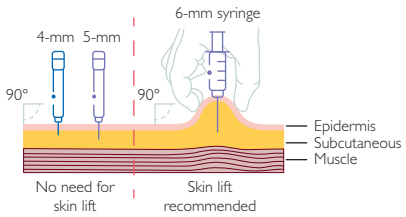


FIGURE 2. Characteristics of insulin delivery devices, physiology, and characteristics of injection technique all contribute to minimizing injection force/pain and maximizing delivery to the intended subcutaneous adipose tissue.[3,26–30] BMI, body mass index. *A flat-base pen needle is also available,[31] but there is currently no evidence documenting the impact of flat bases on injection pressure.

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TABLE. Subpopulations of People With Diabetes Who May Benefit From a Skin Lift to Avoid IM Injection[a,b]

Population	Considerations regarding skin lift
Older adults	Skin from older individuals, compared with younger individuals, is often thinner and more fragile .[37] The distribution of SC fat can also change with age.[38] That said, these skin changes are more clinically meaningful for predisposition to lipohypertrophy or bleeding/bruising than for needing to perform a skin lift technique, which may be difficult for older adults with dexterity challenges.[22,39,40] The need to implementa skin lift should be assessed on an individualized basis
Low BMI (<19 kg/m^2)/lean body mass	Risk of unintentional IM injections is especially high in people with low BMI/lean body mass, who have shorter distance between skin and muscle. This group should inject using a 4-mm pen needle perpendicularly into a skin lift[41]
Pregnant women	No differences in needle length recommendations are required for pregnant women, and standard injection sites including the abdomen may be used throughout pregnancy (although the thigh, upper arm, or buttock may be more comfortable). In the 1st trimester, no change in site/technique is needed; 2nd trimester, use lateral abdominal areas or implement skin lift in central areas overlying fetus; 3rd trimester, use lateral parts of the abdomen with skin lift[42]
Children	4-mm pen needles are the safest for children to prevent IM injection. Injecting the 4-mm pen needle perpendicularly into a skin lift is recommended for children ≤6 years old.[5,43] Syringe needle use in very young children (≤6 years) is not recommended since the risk of IM injection remains high even with a correctly raised skin lift.[5] If using a syringe for children >6 years old, then injections should always be given into a skin lift[5]

[a]BMI, body mass index; IM, intramuscular; SC, subcutaneous.

[b]If there is concern that the distance from the skin surface to the muscle is shorter than the available needle length, then a skin lift can reduce the risk of IM injection. Health care professionals should have the person with diabetes demonstrate a proper skin lift to check understanding.

which may increase the risk of indentation, bruising, or unintended IM injection.[57,58] While bruising does not appear to impede insulin absorption, it is an uncomfortable cosmetic issue and may be a lipohypertrophy precursor.[56] A contoured-base pen needle has a larger surface area in contact with skin; therefore, pressure is more widely distributed for reduced overall force and less bruising/reduced risk of IM injection.[57,58] A flat-base pen needle is also available,[31] but there is currently no evidence describing the impact of flat bases on injection pressure.

Section 2: Evidence-Based Injection Technique Procedure

Insulin Storage and Handling. Proper insulin storage has recently been expertly reviewed.[59] In brief, insulin is temperature-sensitive and requires specific conditions throughout the supply chain to maintain adequate quality.[59] Storage and expiration guidelines for insulin products vary by product and by regional practices/professional guidelines.[59] Therefore, HCPs should personalize the instructions per the relevant manufacturer's guidelines. A summary of insulin storage guidelines in the United States and European Union is available in Heinemann et al[59] and from diabetes education resources such as Diabetes Education Services (diabetesed.net).[60] Most guidelines will advise that unopened insulin vials/pens be stored in a refrigerator at 2 to 8 °C (36 to 46 °F), without freezing or contamination by food. HCPs may advise PWD to check the temperature of the refrigerator where they store their unopened insulin since household refrigerators are commonly outside this range.[59,61] PWD should also use cooler packs/insulated bags if bringing insulin outside in hot or cold/freezing conditions.[59,61]

Once opened, insulin vials/pens should be stored at ambient temperatures (15 to 30 °C or 59 to 86 °F) away from direct sunlight exposure until the expiration date designated by the manufacturer (often 28 days).[5,59] Removing insulin from a prefilled disposable insulin pen using a syringe to fill another device should be avoided unless absolutely necessary because of possible insulin concentration differences.

Before injection, PWD should check that their insulin is not expired and/or cloudy. The rationale and procedure for cloudy

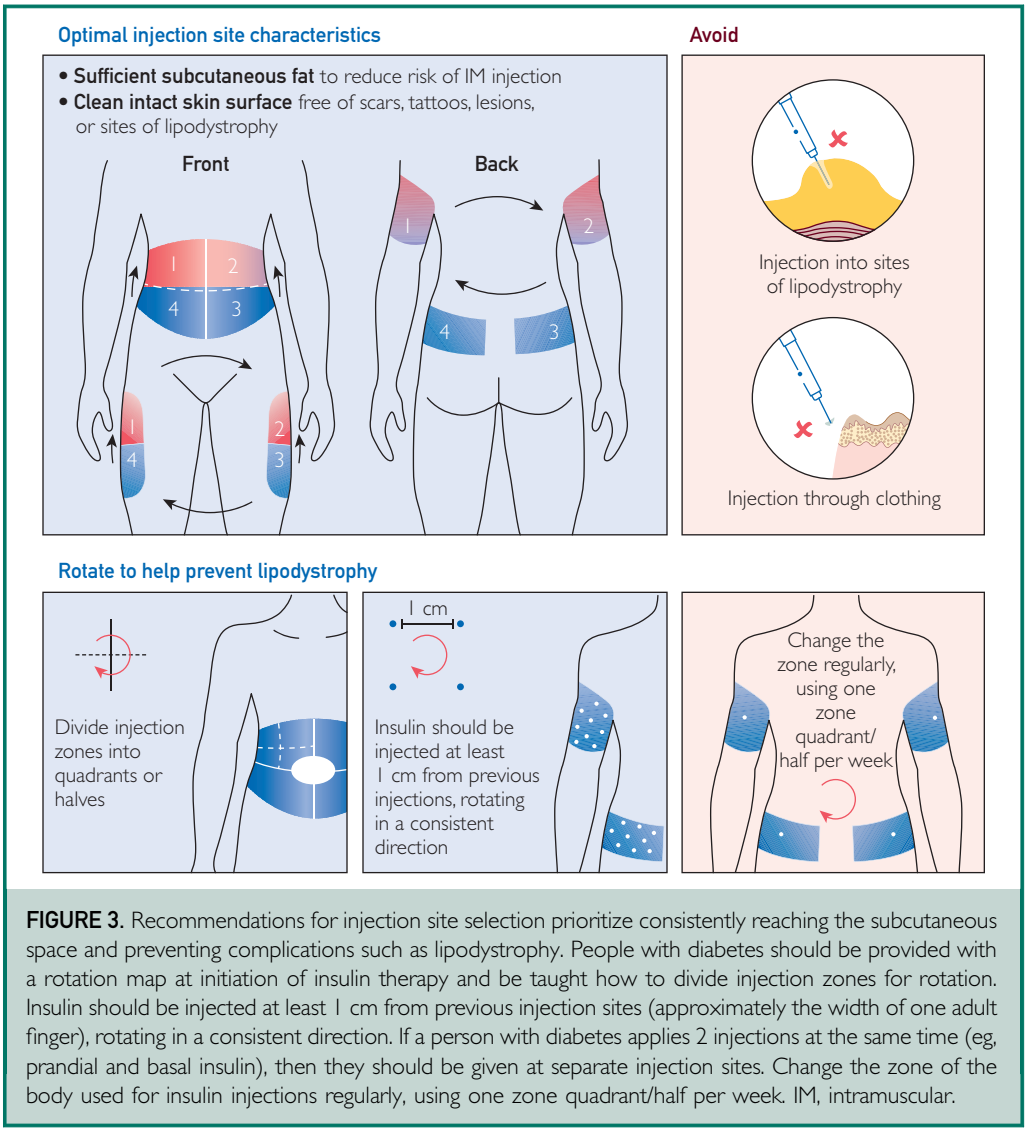

FIGURE 3. Recommendations for injection site selection prioritize consistently reaching the subcutaneous space and preventing complications such as lipodystrophy. People with diabetes should be provided with a rotation map at initiation of insulin therapy and be taught how to divide injection zones for rotation. Insulin should be injected at least 1 cm from previous injection sites (approximately the width of one adult finger), rotating in a consistent direction. If a person with diabetes applies 2 injections at the same time (eg, prandial and basal insulin), then they should be given at separate injection sites. Change the zone of the body used for insulin injections regularly, using one zone quadrant/half per week. IM, intramuscular.

insulin resuspension (like neutral protamine Hagedorn [NPH] insulin) remains the same as the previous FITTER; gently roll/tip the vial/pen until crystals dissolve because vigorous shaking may introduce air bubbles.[5] Crucially, before injecting, insulin should be allowed to come to room temperature by leaving it out of the refrigerator for 30 to 60 minutes because injecting cold insulin can be painful and contribute to lipodystrophy development.[17,62]

Selection, Preparation, and Rotation of Injection Sites. Skin sites used for insulin injection must have sufficient SC fat to reduce the risk of IM injection; therefore, recommended sites include the abdomen, thighs, buttocks, and upper arms (Figure 3).[5] The arm is the least preferred site for self-injection, as it may be difficult to ensure the optimal 90° angle of injection or independently perform a skin lift; assistance may be needed to use this site optimally. People with diabetes should use only these recommended body areas for consistent insulin absorption and will need to systematically rotate both the area used and within the area to avoid insulin injection into skin areas with known lipodystrophy (see Section 3). Systematic rotation of injection sites reduces

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the risk of lipodystrophy and minimizes skin thickening at overused sites; see Figure 3 for suggested systematic rotation practices.[63] Health care professionals should review rotation practices at least annually or if warning signs of poor injection technique arise (discussed in Sections 3 and 4). In some cases, injecting into lipodystrophy areas is painless, which may contribute to incorrect preferential use of these sites.[62]

The skin surface should also be inspected prior to injection to ensure that it is clean and intact. Disinfect with an alcohol swab and allow the alcohol to evaporate on its own. Disinfection is particularly important in group care settings, such as hospitals and nursing homes. If possible, avoid injecting into scars, stretch marks, or tattoos as their impact on administering insulin correctly to the SC layer or altering insulin absorption rates is unknown. Insulin should never be injected into skin areas that show signs of edema, infection, inflammation, or ulceration. People with diabetes should not inject through clothing because doing so prevents the examination of the injection site, proper skin lift technique, and needle penetration verification.[64]

Proper Injection Technique for Pens. Health care professionals should educate PWD on step-by-step utilization of the selected device for insulin administration and perform a follow-up assessment to check their understanding. Discuss the components of the pen, their names, and important notes pertaining to safety/efficacy, such as noting not to use expired needles or insulin. Importantly, pen needles often have an inner needle cover that must be removed prior to injection. Failure to remove this inner needle cover is a common mistake that can lead to failure to deliver intended insulin doses followed by hyperglycemia or diabetic ketoacidosis.[65,66] Never assume that PWD will know to remove the inner needle cover unless instructed/supervised.

After correct assembly of the insulin pen with the needle, manufacturer instructions to prime the needle should be followed. Instruct PWD to see at least one drop of insulin at the tip of the needle to confirm priming. Afterward, the individual should check that their pen has sufficient insulin volume, dial the desired insulin dose, and inject. For the majority of adults using a 4-mm needle, the pen should be held perpendicular to the skin surface for injection (90° angle), regardless of whether a skin lift is performed (see the Table and Supplemental Figure 2 for skin lift recommendations). A 5-mm needle length may also be used if a 4-mm needle is not available or if 5 mm is preferred. Select a needle with a diameter of 32G (or thinnest available under 32G if resources are limited) and a sharp tip design to minimize insertion pain. After the pen needle is fully inserted into the skin, the injection dose button of the pen should be pressed completely with even, steady pressure in the same direction as the pen (perpendicular to the skin surface), generally using the thumb. Inject insulin slowly, observe cues for successful injection tailored to the injection device (eg, dose dial returning to zero), and wait approximately 10 seconds before removing the needle from the skin to reduce the chance of insulin leakage; recommendations vary on how long to wait, but even just 3 to 10 seconds can reduce leakage.[67] Individuals with low vision can pay attention to auditory feedback from their pens. People with diabetes should also be coached to recognize unsuccessful injection signs such as insulin leakage (droplets at the tip of the pen needle or wetness at injection site) and intradermal injection (bump on the skin, swelling at injection site).

Proper Injection Technique for Syringes. Although insulin pens are generally simpler, safer, and more convenient to use than syringes, syringes remain a viable option for insulin injection for many with diabetes and have the advantage of being more affordable than insulin pens.[32,68] Syringe needles are often longer than pen needles because syringe needles need to be sufficiently long/sturdy to pierce the rubber of the vial cap; available syringe needle lengths

range from 6.0 to 12.7 mm.[3,27] The anatomically appropriate syringe needle length for most adults and adolescents with diabetes is 6 mm if it is used.[5] This length requires a skin lift with 90° injection angle for those with a BMI of 19 to 25 kg/m^2 to prevent IM injection.[5] Syringe needle use in those with little SC fat (BMI <19 kg/m^2) or those less than 6 years of age is not recommended since the risk of IM injections remains high even with a correctly raised skin lift.[5]

Recommendations for insulin injection technique using a syringe have not changed since the previous version of FITTER.[5] In brief, PWD should first understand all the parts of their syringe, confirm the needle and insulin are not expired, and use the optimal syringe size for the insulin dose to be administered (syringe sizes include 1 mL, 0.5 mL, and 0.3 mL for U100 insulin doses of 100 units or less, 50 units, and 30 units, respectively).[69] Health care professionals should ensure that the available syringes have the appropriate markings for the prescribed insulin concentration.[69] Notably, U500 insulin is available in both pens and vials, and when vials are used, a prescription for specific U500 syringes is necessary to minimize dosing errors.[20]

People with diabetes using syringes will need to draw the insulin from a vial and should be instructed on how to apply air to the vial to avoid a vacuum forming. The individual should first draw air into the syringe at a volume equal to or slightly greater than the intended dose.[5] This air is then injected into the vial to facilitate withdrawal of insulin. Then the insulin vial should be inverted, keeping the needle aligned with the vial while transferring insulin from the vial to the syringe. Once the individual has removed insulin from the vial into the syringe, it is critical to check the syringe for air bubbles. Air bubbles can be removed by holding the syringe vertically with needle up, tapping on the barrel to bring bubbles to the top, and then pushing the plunger up to clear the air bubbles. All PWD using a syringe should use the shortest available syringe needle, 6 mm, following appropriate recommendations regarding skin lift (Table), and should ensure that all insulin drawn up into the syringe is administered.

Postinjection Best Practices. Educate the PWD to remove the pen needle from their pen after each use. This practice prevents air seepage into the cartridge, which could impact dosing accuracy.[70] Avoid reusing needles because they are no longer sterile after being used and may become blunted or misshapen over time, which can increase injection force/pain and contribute to elevated risk of lipohypertrophy development.[28] However, needle reuse is a common practice globally, with surveys from various countries reporting that 40% to 96% of respondents reuse their pen needles.[6,71] Practical limitations may lead to situations in which needle reuse may be needed, for example, if a PWD does not have a new needle available, then reusing one of their own needles may be preferable to missing an injection. There is insufficient evidence on the maximum allowable number of injections with one needle in one individual; however, one study suggested pen needles could be used 4 to 5 times without increasing pain intensity.[72,73] Health care professionals should educate PWD on the possible consequences of needle reuse and recommend carrying extra injection supplies to mitigate the need to reuse needles. Crucially, needles should never be shared/reused between individuals to prevent the transmission of bloodborne infectious diseases.[74] Insulin pens/cartridges/vials should be clearly labeled with individual names in group health care facilities to ensure "1 Person/1 Pen" practices are followed.[5]

Needles must be disposed of safely to avoid accidental needlesticks or environmental contamination. Always use a certified waste receptacle for needles and syringes and return it to an official site for medical waste disposal, following local guidelines even when traveling.[75] Do not use unofficial plastic bottles/boxes because needles can puncture the plastic.

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Considerations for Injectable Treatments for Diabetes (Noninsulin). Understanding proper insulin injection technique is also relevant for other injectable antidiabetic drugs that are applied into the SC adipose tissue. Since the previous FITTER recommendations were released, the landscape of pharmacotherapy for type 2 diabetes has significantly changed to include therapies based on incretins (hormones that stimulate endogenous insulin secretion). These include glucagon-like peptide 1 (GLP-1) receptor agonists and dual- or triple-agonists acting via GLP-1, glucose-dependent insulinotropic polypeptide, and/or glucagon.[76,77] Some PWD may learn injection practices from these therapies before starting insulin therapy and may be undergoing both therapies concurrently.[20] Noninsulin injectable use should follow the same recommendations as those used for insulin injections regarding needle length, site selection, and rotation schemes. The risk of lipohypertrophy is considerably less with noninsulin injectables compared with insulin, although palpable injection site SC nodules have been reported following delivery of once-weekly exenatide and semaglutide (both GLP-1 receptor agonists).[78–80] Coformulations of premixed insulin and GLP-1 receptor agonists in the same pen device are also available and use should follow the recommendations for insulin delivery.[81]

Section 3: Implement Proactive Risk Reduction and Detection of Lipodystrophy

Lipodystrophy is a class of fat tissue disorders that can arise from repeated insulin injection or infusion into one skin site.[10,82] Lipodystrophy includes lipohypertrophy (enlargement of adipocytes, presenting as swelling/nodules), lipoatrophy (loss of adipocytes, presenting as indents/cratering), and amyloidosis (accumulation of amyloid deposits).[5,10,78,82] Injection into sites of lipodystrophy may cause erratic insulin absorption, increasing the risk of hypoglycemia, hyperglycemia, and glucose variability.[29,82,83] Even subclinical lipodystrophy can negatively influence glycemic outcomes.[84] Lipohypertrophy is the most common lipodystrophy, occurring in approximately 37% to 64% of adults with diabetes undergoing insulin therapy, and is therefore the focus of FITTER Forward.[5,13,62,82] In a meta-analysis of 37 studies, glycosylated hemoglobin, overall/unexplained hypoglycemia, and glycemic variability were significantly worse in PWD with lipohypertrophy than in those without, and with higher total daily insulin doses as well.[82] Therefore, it is critical that HCPs explain the importance of lipohypertrophy risk reduction and encourage PWD to take an active role in self-detection.

Lipohypertrophy detection should be a routine part of diabetes-related complication assessment. Lipohypertrophy is often underdiagnosed and can be challenging to identify in subclinical stages in which it is difficult to detect by visual/palpation examination.[83,84] Ultrasound detection has emerged as a sensitive and objective detection method, superior to palpation (especially for flat skin areas), and is recommended where available.[84] If availability and cost constraints are a concern, then it is recommended that lipohypertrophy detection methods include structured and periodic palpation and visual examination of all injection sites routinely, either as self-examination by the individual or conducted by an HCP. Simply asking whether an individual rotates their sites is insufficient. Images of lipohypertrophy and detailed palpation/visual examination recommendations can be found in Gentile et al.[85] Considerations for monitoring lipohypertrophy via telehealth are described in Supplemental Figure 3 (available online at http://www.mayoclinicproceedings.org).

Once lipohypertrophy has been detected, instruct PWD to cease injecting into these sites and discuss how the risk of lipohypertrophy can be reduced by regular, systematic rotation of insulin delivery sites, avoiding delivery of cold insulin, and avoiding needle reuse. Documenting lipohypertrophy with visuals to show site and size can be helpful for tracking improvements over time. Injection site map handouts or injection rotation apps can encourage regular rotation both between sites and within sites, with sufficient

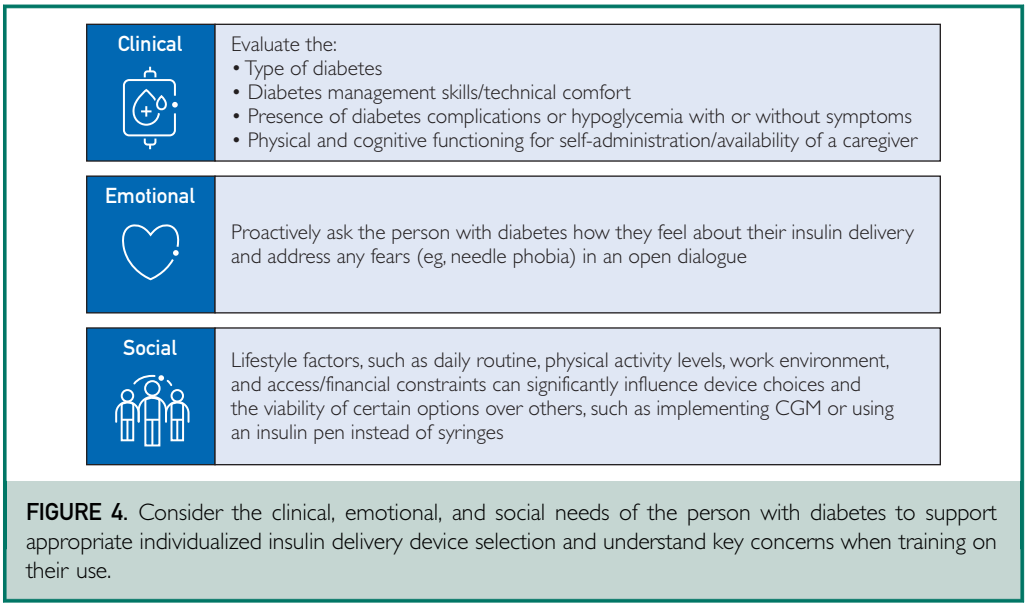

FIGURE 4. Consider the clinical, emotional, and social needs of the person with diabetes to support appropriate individualized insulin delivery device selection and understand key concerns when training on their use.

distance from prior injection sites (Figure 3). The use of site documentation by HCPs in skilled nursing facilities is recommended to assist with regular rotation. Skin sites with lipohypertrophy will tend to decrease in size after insulin delivery technique is corrected and affected sites are avoided for future injections.[83] In severe cases, liposuction may be considered as treatment.[86] Lipoatrophy can also be treated by improving site rotation practices, and case reports suggest that anti-inflammatory approaches (eg, glucocorticoid injections,[87] low-dose oral prednisone,[88] or cromolyn sodium[89]) or laser treatment[90] may have value. Further research on lipodystrophy treatment is warranted alongside a focus on prevention and early detection.

Notably, there is a risk for hypoglycemia in PWD who begin injecting insulin into other skin areas[62]; glucose values should be monitored closely after changing injection technique, and HCPs should adjust insulin dose as appropriate. Selecting rapid-acting analogues for prandial insulin therapy may be advantageous; their usage appears to be associated with a reduced risk of lipohypertrophy relative to regular insulin, possibly because of their faster absorption from the insulin depot reducing the local interaction of insulin with adipocytes.[5,91]

Section 4: Utilize Structured Injection Technique Training for Optimal Outcomes

The HCP Role as a Guide/Educator for PWD. The biological effect of insulin is not only driven by its pharmacokinetic and pharmacodynamic properties but also by its "pharmacoadherence"; is the drug applied appropriately?[92] Only then will PWD gain the full intended benefit. Health care professionals should therefore ensure that PWD receive education and support when starting insulin therapy or other injectable therapies. When discussing initiation of insulin therapy with a PWD/caregiver, identify clinical, emotional, and social needs and offer appropriate personalized insulin delivery device choices (Figure 4). By meaningfully discussing concerns, HCPs can help reduce anxiety and facilitate a smoother training process. Recommendations for educational strategies to achieve appropriate insulin delivery technique are presented in the next section, and resources aligned with these recommendations can be accessed at fitterdiabetes.com.[93] For details on insulin prescribing, refer to local resources because insulin types, concentrations, and brand names vary by country. For example, insulins currently available in the United States (December 2024) include ultrarapid-acting, rapid-acting, short-acting, intermediate-acting, and long-acting types, as well as

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premixed products.[94,95] While not yet approved in the United States, once-weekly insulin is available in some countries and holds potential to reduce treatment burden.[96]

Evidence-Based Educational Strategies. Many studies have found that structured, intensive educational programs for insulin injection technique improve clinical outcomes by using visual aids, simulated injection tools, or instructional videos. Examples of impactful protocols are summarized in Supplemental Table 4 (available online at http://www.mayoclinicproceedings.org) to highlight the clinical outcomes of proper training. Synthesizing these studies and our expert perspectives, the following key actions emerge to:

- Provide early education on insulin injection/devices in new or recently diagnosed PWD to support familiarity with insulin, whether they may need insulin later or not
- Involve PWD/caregivers in insulin delivery device choices and take time to understand their treatment needs, insulin delivery device preferences, concerns around usage/motivation, and cost/access barriers (Figure 4)
- Discuss the "why" behind recommendations and use apps/visuals throughout all aspects of injection education for meaningful education
- Explain warning signs/symptoms that should be brought to their HCP's attention to empower PWD to handle disease management concerns that may arise
- Assess understanding by having the individual demonstrate/explain correct technique after initial instruction
- Implement ongoing assessment, frequent refresher education, and clinician accessibility to positively influence treatment adherence[66]
- Ensure that all HCPs, including nurse practitioners, physician assistants, diabetes educators, pharmacists, and junior clinicians keep abreast of new insulin delivery technology and educational tactics

Warning Signs That an Injection Technique Review Is Warranted. An important component of injection technique training is conveying which warning signs indicate that insulin injection technique may be suboptimal. People with diabetes should report to their HCP any unusual pain (or unusual lack of pain), leaking, bleeding, or bruising, as well as a need for increased force when pressing an injection dose button or syringe plunger. These signs could be related to injection into sites of lipohypertrophy or signs of a faulty device. If an individual reports these signs, then examine their injection sites and revisit their technique. Reviewing sites in person when possible is important given the increased use of telehealth. Health care professionals should also review reports from systems for continuous glucose monitoring, if possible, and continuous glucose monitoring—derived parameters such as time-in-range. If glucose levels become unstable, unpredictable, or inconsistent with the individual's usual insulin regimen, then it may indicate the development of lipohypertrophy and insulin injections into affected tissue areas. Health care professionals may also take note if insulin or needle refills do not occur as scheduled and use this information as a proxy for practices like needle reuse.[97]

FUTURE PERSPECTIVES

A challenge when drafting these recommendations has been ensuring that they are practical globally regardless of available resources. It is crucial that injection technique education programs are accessible regardless of socioeconomic status or geographic location. We encourage HCPs, health care authorities, payers, and manufacturers to take action to support equitable resource allocation and access to evidence-based injection education.

With respect to the future of insulin delivery, it can be anticipated that the development of novel insulin delivery devices (such as patch pumps) or alternative routes of

administration (such as needle-free injectors and inhaled insulin, which are available but not in widespread use[98]), will continue. Insulin administration technologies with systems for automated insulin delivery are growing in popularity and sophistication. The 2015 FITTER recommendations covered only conventional tubed insulin pumps with infusion sets—the landscape is now complex enough to require a separate set of recommendations for various types of insulin pumps.

Awareness around the importance of "Green Diabetes" is also increasing, although all stakeholders can do more to reduce the environmental impact of devices used for insulin injection.[99,100] Manufacturers should be encouraged to design insulin delivery devices that have minimal environmental impact, and HCPs should promote recycling programs for nonsharp diabetes care waste, such as insulin pen bodies and parts of insulin pumps.[101,102] Government/regulatory agencies can establish high standards of sustainable device manufacturing and disposal. Health care professionals can encourage PWD to choose options with minimal waste and advocate for legislation that promotes sustainable and safe medical waste practices.[100] Everyone can support community involvement and awareness campaigns that promote proper disposal practices, recycling, and sustainable choices that support the environment.

Hopefully, our work will inspire more research on optimal injection technique education. Multiple stakeholders can play a part in developing engaging educational programs, eg, manufacturers can add key educational points to the instructions for use and websites of their products. People with diabetes can tell their HCPs the types of educational programs they find most useful, and HCPs can tailor their practices appropriately. There is great opportunity to improve diabetes management through responsive collaboration and optimizing the basics of injection technique using the FITTER Forward recommendations. Equipped with these updated insulin injection technique recommendations and strategies for education, HCPs can improve the likelihood that their patients optimally use insulin with minimal complications.

CONCLUSION

Insulin therapy will have limited/unpredictable effects if not delivered properly; therefore, time spent by HCPs and PWD/caregivers on injection technique education is essential for improving clinical outcomes and reducing health care costs. FITTER Forward outlines how state-of-the-art injection technology impacts clinical outcomes. All steps in the injection process are described, with evidence-based recommendations to correctly and safely deliver insulin to the SC tissue. Reducing the risk for development of lipodystrophy is stressed, including strategies for detection and management of such skin lesions. Finally, FITTER Forward summarizes new evidence on structured education programs for injection technique to aid HCPs in their practices.

POTENTIAL COMPETING INTERESTS

The Forum for Injection Technique and Therapy: Expert Recommendations (FITTER) Forward advisory board was funded by embecta, a manufacturer of injecting devices. FITTER Forward members received an honorarium from embecta for their participation in the advisory board but not for manuscript development. One advisor, Miae Yoon, was unavailable to serve as an author but is acknowledged for her participation in the advisory board.

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SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mayoclinicproceedings.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **BMI,** body mass index; **FITTER,** The Forum for Injection Technique and Therapy Expert Recommendations; **GLP-1,** glucagon-like peptide 1; **HCP,** health care professional; **IM,** intramuscular; **ITQ,** Injection Technique Questionnaire; **PWD,** people with diabetes; **SC,** subcutaneous

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