Worldwide Injection Technique Study: Population Surveyed

Introduction

From February, 2014 until June, 2015 the Insulin Injection Technique Questionnaire (ITQ) survey was conducted among 13,264 patients from 425 centers in 42 countries. This is the largest survey of its kind ever done in diabetes, in fact in all of medicine. All survey patients had diabetes and had been injecting insulin for at least 6 months. The various language versions of the questionnaire (nurse and patient forms) can be found at **www.fitter4diabetes.com**. Twelve different languages were used, but the content of each questionnaire was identical across languages. Table 1 lists the countries which participated, along with the number of centers and patients from each.

Table 1

COUNTRY	NUMBER CENTERS	NUMBER SUBJECTS	% SUBJECTS
Argentina	3	75	0.6
Australia	7	95	0.7
Austria	6	116	0.9
Belgium	9	165	1.2
Brazil	5	255	1.9
Canada	14	329	2.5
Chile	1	21	0.1
China	21	3853	29
Colombia	1	25	0.4
Czech Republic	11	163	1.2
Denmark	1	36	0.3
Ecuador	1	23	0.1
Finland	4	103	0.8
France	21	254	1.9
Germany	26	480	3.6
Greece	2	30	0.2
India	20	1011	7.6
Indonesia	7	144	1.1
Ireland	3	45	0.3
Italy	15	358	2.7
Japan	N/A*	1342	10.1
Malaysia	2	51	0.4
Mexico	5	138	1
Netherlands	4	83	0.6
Nicaragua	1	16	0.1
Perú	1	25	0.2
Philippines	3	77	0.6
Poland	4	111	0.8

Russia	7	173	1.3
S. Korea	9	180	1.4
Saudi Arabia	11	515	3.9
Singapore	2	25	0.2
South Africa	4	162	1.2
Spain	9	203	1.5
Sweden	3	104	0.8
Switzerland	7	84	0.6
Taïwan	1	100	0.8
Turkey	56	1376	10.4
UK	61	499	3.8
United Arab Emirates	5	115	0.9
USA	49	304	2.3
Venezuela	1	25	0.2
TOTAL	**423**	**13,264**	**100.0**

*In Japan the ITQ was not administered center by center. Instead it was Internet-based. Patients from many centers all over the country participated.

Methods

The questionnaire consisted of an initial participant section (administered by an experienced diabetes nurse) followed by a section completed by the nurse after an injection was observed and a meticulous examination made of all injection sites.

The objectives of this questionnaire were:

- to understand the epidemiologic profiles for the major insulin injection parameters
- to determine the major causes of variability in injection technique, their ranking and their interactions, and
- to query the participants perception of the injection process, the psychological barriers and aids.

Besides participant demographic information, the key insulin injection parameters queried by the questionnaire were:
Current Practice: injection device and needle length, number of injections/day, choice of injection site, use and characteristics of skin folds (pinch-up), needle entry angle, size of injecting zone, site rotation, disinfecting prior to injecting, dwell time of needle under the skin, site inspection by health care professional, needle reuse, sharps disposal, injection through clothing;
Observed Anomalies at Injection Sites: insulin leakage, bruising, lipoatrophy, lipohypertrophy, inflammation, pain;
Knowledge about Injections: identity of teacher, themes covered in education, adequacy of the coverage of these themes, desire for more knowledge (4, 5).
Blood Glucose Anomalies: episodes of hypo- and hyperglycemia, hospitalizations for hypoglycemia, DKA, glucose variability and unexpected hypoglycemia.

Safety: needle-stick injuries, risk factors for blood-borne infections, disposal habits for used sharps.

There were also several questions which were asked in an open way giving the participants and nurses the chance to write out their opinions in free hand. These answers were also carefully studied by the authors and a summary is included in these reports wherever relevant.

Three previous ITQs have been done, in 1995, 2000 and 2009. This ITQ (2014-15) was one of the largest multi-center studies of its kind. Centers were required to understand and agree with the questions posed in the questionnaire and to recruit approximately twenty-five subjects/center within the allotted timeframe. Subjects were not placed at any risk by the study, therapy decisions were not based on it and no financial compensation was offered for participation. For these reasons signed informed consent was not sought.

Subject identify was kept confidential at all times and the study was conducted according to GCP and the Helsinki accords. No participant identifying information was made available to the sponsor and participants were informed that their care would not be affected in any way by their participation. They were not put at risk in any way by the study and were not paid to participate. Ethics committee approval was therefore not generally required but was obtained whenever specifically requested by a center and/or by local regulations.

Centers were selected to be, as much as possible, representative of diabetes care in the countries involved. Approximately a third were specialist diabetes clinics, a third were community care centers and a third were general practice centers. All participating centers did so willingly and without financial incentive.

Participants were required to have used insulin for at least 6 months. In order to eliminate selection bias subjects were recruited into the study on a sequential basis, i.e. consecutive eligible and consenting participants entering the clinic were accessioned. Injections were performed with an insulin pen or syringe or both and participants gave verbal consent to participate. A total of 13,264 participants with diabetes who had both patient and nurse forms filled out were included in the database.

SPSS software was used to perform the data analysis. Descriptive statistics, frequencies and rankings were obtained. Chi-squared analysis was performed where appropriate for contingency tables. Log linear analysis and ANOVA were used for the analysis of individual parameters and multiple regression and correlation analysis were used for multi-parametric analysis. Two-tailed tests were used in all analyses. Initially results from each of the 42 countries were analyzed independently and only when the distributions of key demographic parameters (age, sex, BMI and duration of diabetes) were shown to be comparable were all the data pooled into an overall database.

Population Descriptors

Table 2 gives the population statistics for the participants accessioned to the study.

Table 2: Population descriptive statistics

	N	Mean	Std. Deviation	Minimum	Maximum
AGE	13225	**51.9**	18.1	1	95
BMI*	12806	**26.6**	6.2	11.1	70.4
YEARS with DM	9197	**13.2**	9.7	1	78
AGE DM DIAGNOSED	12737	**39.9**	17.2	0	90
YEARS ON PILLS	6607	**8.3**	7.2	0	76
YEARS ON INSULIN	8242	**8.7**	8.9	0	78
DAILY DOSE RAPID INSULIN	1422	**27.0**	20.7	1	200
DAILY DOSE FAST ANALOGUE	3467	**31.9**	21.6	1	240
DAILY DOSE NPH	1134	**31.6**	24.4	1	180
DAILY DOSE BASAL ANALOGUE	4709	**27.6**	19.5	1	260
DAILY DOSE PRE-MIXES	1796	**43.0**	25.3	1	252
TOTAL DAILY DOSE INSULINS	7756	**48.5**	32.4	0	340
HbA1c	7663	**8.47**	2.139	4	19

*BMI =body mass index calculated as height (in meters)/(weight in kg)2

Overall 90.5% of participants were adults, 4.9% were adolescents, 2.4% were children and 2.2% were parents giving injections to children. Regarding gender 51.3% were female and 49.7% were male. Regarding diabetes type 33.8% had type 1 (T1DM), 65.2% type 2 (T2DM) and 1.0% gestational (GDM).

Medications and Devices

Participants were required to be taking a medication by injection (insulin, GLP-1 or both) to be eligible for the study. 56.5% of participants took insulin only for diabetes treatment while 40.5% of participants took both insulin and pills and 2.0% took GLP-1 alone or in combination with other treatments.

Regarding devices, 85.6% of participants used an insulin pen alone to inject insulin while 9.6% used a syringe alone, 2.8% used both and 1.4% used a pen as well as another device (such as insulin pump).

Needle Length

Patients were asked what needle length they used. Table 2 lists their answers for this ITQ and for the last ITQ done in 2009. The evolution away from 12.7 and 8 mm and towards the 5 and especially 4 mm is evident.

Table 2

NEEDLE LENGTH	**% 2014**	**% 2009**
12.7 mm	**1.0**	**5.3**
8 mm	**16.0**	**48.6**
6 mm	**15.1**	**15.8**
5 mm	**28.6**	**21.6**
4mm	**20.9**	**0**
Don't know	**13.2**	**7.0**

As an additional check, nurses were asked to examine the devices that the patients used and to report the length of the needle that was attached. Their observations are listed in Table 3.

Table 3

NEEDLE LENGTH	% as per Nurse
12.7 mm	**0.9**
8 mm	**27.1**
6 mm	**20.1**
5 mm	**20.3**
4mm	**28.1**
Don't know	N/A

If we eliminate the 12.7mm needle and the 'Don't know' responses, we have very good agreement between the patient and nurse responses, as shown in Table 4.

Table 4

		Patient-Reported				
		4	**8**	**6**	**8**	**TOTAL**
Nurse Observed	**4**					
	%					28.7%
	5					
	%					21.8%
	6					
	%					20.3%
	8					
	%					29.2%
	TOTAL					
	%	28.0%	21.7%	21.1%	29.2%	100.0%

In summary, for the 5826 subjects for which we have both a patient report and a nurse observation we have almost complete agreement on the percentages of needle lengths currently on the market in the world: just under 30% for both the 4 and 8 mm and just over 20% for both the 5 and 6 mm. However there are very large differences country to country in these percentages.

When viewed by age category (Table 5) it was evident that longer needles use was more prevalent in the adult groups, while adolescents, children and parents injecting children used the shorter needles more frequently.

Table 5

		Needle Length			
		4	**5**	**6**	**8**
Respondent	**Adult**	1680	1407	1325	1942
	%	26.4%	22.1%	20.9%	30.6%
	Adolescent	187	97	84	48
	%	45.0%	23.3%	20.2%	11.5%
	Child	107	29	43	23
	%	53.0%	14.4%	21.3%	11.4%
	3rd Party	122	11	42	16
	%	63.9%	5.8%	22.0%	8.4%

P<0.000

Table 6 shows the use of different needle lengths by injection sites. Considerable percentages of patients (see circled high risk area) continue to use the 6 and 8mm needle in the limbs despite recent evidence that the IM injection risk is very high there (Table 7)

Table 6

		Needle Length				
		4	**5**	**6**	**8**	**TOTAL (n)**
Site of Injection	**Abdomen alone**	26.6	23.3	22.3	27.8	1995
	Thigh alone	29.5	19.4	26.5	24.6	268
	Arm alone	22.6	21.9	20.5	34.9	146
	Abdomen/Thigh	29.8	20.4	20.3	29.5	1510
	Abdomen/Arm	22.8	25.3	19.4	32.4	438
	Thigh/Arm	28.2	16.8	21.5	33.6	298
	Abd/Thigh/Arm	31.3	18.7	19.1	31.0	1253
	All 4	37.5	19.4	20.0	23.0	664

Table 7: Estimated IM Injection Risk, by Body Site*

Needle Length	Combined	Thigh	Arm	Abdomen	Buttock
4 mm	0.4%	1.6%	1.0%	0.3%	0.1%
5 mm	1.8%	4.7%	3.1%	1.1%	0.5%
6 mm	5.7%	10.0%	7.0%	2.8%	1.3%
8 mm	15.3%	25.0%	19.5%	9.7%	5.5%
12.7 mm	45.0%	63.0%	55.0%	38.0%	26.9%

***Assumes injection straight in [90°] without pinch-up (Table adapted from Hirsch [1])**

[1] 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 Dec;16(12):867-73.

Comparative analysis revealed that the 4 mm needle was associated with lower BMI, fewer years on insulin, younger age, lower total daily doses (TDD) of insulin, more fingersticks/day, less hyperglycemia and hospitalization for hypoglycemia, less needle reuse and less LH (all difference with $p < 0.05$ by multivariate analysis). Needle length was not associated with differences in HbA1c, DKA or the frequency of hypoglycemia.

Needle Gauge

In the same way that needle length has trended shorter, the gauge (diameter) of needles has trended towards thinner and thinner (i.e. higher number G) needles. Table 8 shows the gauge as observed by the nurses on inspection of the needles. Over 9500 subjects had their needles inspected.

Table 8

GAUGE	% as per Nurse
29	**2.9**
30	**13.1**
31	**46.1**
32	**34.7**
33	**0.2**

Table 9 shows the relationship of needle length to gauge. In general, the shorter the needle the more frequent it is associated with a thin gauge (higher G number).

Table 9: Percentages (by row) of needle gauge as a function of length

	Gauge (% of total)			
NEEDLE LENGTH	**29**	**30**	**31**	**32**
4 mm	0	1.0	10.6	88.4
5 mm	.5	3.2	80.6	15.6
6 mm	3.0	7.1	69.8	20.1
8mm	1.2	41.5	51.6	5.7

There is still a great deal of country variation in the distribution of different needle gauges. Adolescents and children use the thinnest gauge (32G) more frequently than adults. For unknown reasons, lipohypertrophy (LH) seems to be less frequent with 32G than the other gauges. Correspondingly, needle reuse seems to be lower with this gauge,

while correct rotation seems to increase in frequency as the gauge thins. 32G needles are associated with less bleeding, but there are no apparent differences in injection pain, hypoglycemia or leaking from the site as a function of needle gauge (data not shown for all statements but for all differences $p<0.05$).

Insulin Usage

The average total daily dose (TDD) of insulin is approximately the same between T1DM and T2DM, with greater variability of dosage in patients with T2DM (Table 10).

Table 10

		TDD		
		Mean	**SD**	**N**
DM type	**T1DM**	48	25	2512
	T2DM	49	35	5030
	GDM	22	23	81

There is huge variability in mean TDD and SD country to country. Lowest TDD is associated with use of 4 mm needles and highest with 8mm (Table 11).

Table 11

Needle Length	**Mean TDD**	**SD**	**N**
4	44.9	31.6	2031
5	47.6	31.6	1454
6	47.0	29.6	1466
8	54.0	33.6	1993
Total	48.5	32.0	6944

$p < 0.000$

TDD is also lower for syringe use, use of limbs as sole injection sites and correct rotation of injections (for all differences $p<0.05$). Higher TDD are associated with leakage from the site, failing to reconstitute cloudy insulin, skipping injections, hypo- and

hyperglycemia, injection pain, the presence of LH and injecting into LH (for all differences $p<0.05$).

Glucose Control

We defined 'Hypoglycemia' as the occurrence of ≥1 symptom of low sugar (e.g., palpitations, tiredness, sweating, strong hunger, dizziness, tremor) and a confirmed blood glucose meter reading ≤60 mg/dL (3.3 mM/L). We defined 'Frequent unexplained hypoglycemia' as hypoglycemia occurring one or more times weekly in the absence of a definable precipitating event such as a change in medication, diet or activity. We defined 'Glycemic variability' as the presence of blood glucose oscillations from less than 60 mg/dL (3.3 mM/L) to more than 250 mg/dL (13.9 mM/L) at least 3 times a week in an unpredictable and unexplained fashion and evidence of such a pattern for at least the previous 6 months.

Nurses were asked to review the records of each subject in the ITQ and assess how many qualified as having 'frequent unexplained hypoglycemia' and 'glucose variability'. Approximately 1 out of 4 insulin injectors has frequent unexpected hypoglycemia and more than 1 out of 3 has glucose variability (Table 12).

Table 12

HYPOS?	N	%
Yes	1580	**19.4**
No	6558	**80.6**
VARIABILITY?	N	%
Yes	2872	**35.4**
No	5251	**64.6**

An overlap between those with unexpected hypos and glucose variability exists but there are still 24% of patients with variability who don't have hypos and 18% of those with hypos who don't have variability (Table 13).

Table 13

	Unexpected Hypos	
Glucose Variability	**Yes**	**No**
Yes	1282	1558
%	81.8%	24.0%
No	286	4929
%	18.2%	76.0%

$p < 0.000$

HbA1c values did not differ between T1DM and T2DM injectors, but T1DM patients have significantly higher frequencies of unexpected hypoglycemia and glucose variability. HbA1c values do not differ amongst the different needle lengths, but injectors using the 6mm needle have somewhat higher frequencies of unexpected hypoglycemia and glucose variability for unknown reasons. HbA1c values are approximately 0.5 higher in injectors with LH (in both T1DM and T2DM) and are significantly higher with incorrect rotation of sites and with needle reuse. HbA1c values are lower in subjects who use larger injection areas and whose sites are inspected routinely. The frequency of unexpected hypoglycemia and glucose variability are significantly higher with LH, with injecting into LH, with incorrect rotation of sites and with needle reuse. Rates of unexpected hypoglycemia and glucose variability are lower when the abdomen is used exclusively as an injection site, but as one adds the use of the limbs the rates of both disorders increase. Receiving injection training from a diabetes nurse is associated with significantly lower HbA1c levels as well as less frequent unexpected hypoglycemia and glucose variability (data not shown for above paragraph but for all differences $p<0.05$).

Discussion

Our questionnaire covered all the major aspects of injections, including demographics, all important injecting practices and parameters, complications of injections and the patient's education on, feelings about and psychological hurdles over injecting.

With such a large number of subjects in this survey (n= 13,264) even slight differences between groups generally reach statistical significance, often with p values as low as <0.000. Hence we accompany our comments about p values with assessments of the clinical and practical significance of each of our findings. Time and again common sense and medical experience are called in to temper purely mathematical probabilities.

This latest ITQ showed that needle length over the last 5-6 years has shifted dramatically, away from the 8 mm and towards the 4 and 5 mm. This follows a trend towards shorter needles that began 2 decades ago. But in the last 5-6 years, a sea-change has occurred with a much faster conversion to 4 mm than seen with other needle length changes. Currently just less than 30% of patients use 4 and 8 mm respectively. Just over 20% use the 5 and 6 mm respectively. There is considerable variability, however, country to country worldwide. Considerable percentages of patients continue to use the 8mm needle in high-risk sites (e.g. in the limbs, especially in males).

The shorter needles tend to have smaller diameters and have newer geometry (e.g. ultra-thin walls and 5-bevel tips). According to our study, the 4 mm needle was used more frequently in T1DM, children and adolescents and was associated with lower BMI, fewer years on insulin, younger age, lower total daily doses (TDD) of insulin, more fingersticks/day, less hyperglycemia and hospitalization for hypoglycemia, less needle reuse and less LH. Needle length was not associated with differences in HbA1c, DKA or the frequency of hypoglycemia. It is clear that the use of the shortest needles can be protective against IM injections.

Recent studies have shown that skin thickness at injection sites in a diverse population of adults with diabetes varies minimally by demographic characteristics, including BMI (e.g., obese patients have similar skin dimensions as normal-weight and thin patients).[2] However the same study showed that fat thickness (SC space) varied widely from one individual to another based on gender, BMI and injection zone of the body. It highlighted the risk of IM injections and showed that they were lowest with 4 mm needles.

The 4mm32G pen needles were shown to provide equivalent glycemic control (HbA1c) to 8mm31G and 12.7 mm29G pen needles, in a large, prospective, randomized controlled crossover study of obese patients taking large insulin doses, with two separate arms (4 vs 8mm, and 4 vs 12.7mm) [3]. There was no increase in backflow or skin leakage with the 4mm needles. Additionally patients reported less injection pain with the 4mm needles. There is no consistent evidence to date of increases in leakage of insulin, pain, or lipohypertrophy, nor worsened diabetes management or other complications in patient populations using shorter (4, 5, 6 mm) needles. [4 5 6 7 8 9 10]

[2] 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 ResOpin 2010;26:1519–1530.

[3] Bergenstal RM et al. 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.

[4] Birkebaek N, Solvig J, Hansen B, Jorgensen C, Smedegaard J, Christiansen J. 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;22: e65.

[5] Jamal R, Ross SA, Parkes JL, Pardo S, Ginsberg BH. Role of injection technique in use of insulin pens: prospective evaluation of a 31-gauge, 8mm insulin pen needle. Endocr Pract 1999;5:245-50.

[6] Kreugel G, Keers JC, Jongbloed A, Verweij-Gjaltema AH, Wolffenbuttel BHR. The influence of needle length on glycemic control and patient preference in obese diabetic patients. Diabetes 2009;58:A117.

[7] Schwartz S, Hassman D, Shelmet J, Sievers R, Weinstein R, Liang J, Lyness W. A multicenter, open-label, randomized, two-period crossover trial comparing glycemic control, satisfaction, and preference achieved with a 31

Additional studies have recently been performed using the 4 mm needle, with identical results. Miwa[11] compared 4mm32G with 6mm32G have and showed equivalent safety and efficacious results. The 4mm was judged by Japanese patients to be less painful and easier to use. Nagai[12] compared 4mm32G to 5mm33G (tapered), and found similar results. Hirose[13] performed PK/PD studies which showed bioequivalent maximum concentration and area under the curve for the 4mm32G needle relative to the 6mm32G and the 8mm31G needles. A PK/PD crossover study using the euglycemic clamp in both normal-weight and in obese, healthy adults showed equivalent insulin uptake and action for insulin lispro, injected one day with a 5mm needle, and another day with an 8mm needle[14].

Birkebaek[15] compared the 4 mm with the 6 mm pen needle in lean subjects, both children and adults, with diabetes. The 4 mm led to fewer IM injections with equivalent levels of leakage compared to the 6 mm needle. The probability of IM injection with the 6mm vs the 4mm was considerably higher when comparing percentages in adults, and was dramatic higher in children and adolescents. Hirsch[16] has shown equivalence between 4mm, 5mm and 8mm pen needles in regards to glucose control, with no difference between obese and non-obese subjects.

Lo Presti[17] has studied the skin and SC thickness at various injecting sites in children and adolescents with diabetes (ages 2-17) and has concluded that the safest injecting alternative for all ages is the 4 mm needle. A 4 mm needle is long enough to penetrate the skin but sufficiently short to avoid reaching the muscle in the vast majority of children. However, all pediatric groups exhibit some values at the lower range of skin + SC thickness which are at or below the threshold of 4 mm. These findings raise concerns that injections, especially in very young patients, may go into the IM space when they are

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gauge x 6mm needle versus a 29 gauge x 12.7mm needle in obese patients with diabetes mellitus. Clin Ther 2004;26:1663-78.

[8] Kreugel G, Beijer HJM, Kerstens MN, ter Maaten JC, Sluiter WJ, Boot BS. Influence of needle size for SC insulin administration on metabolic control and patient acceptance. Europ Diab Nursing 2007;4:1-5.

[9] Van Doorn LG, Alberda A, Lytzen L. Insulin leakage and pain perception with NovoFine 6 mm and NovoFine 12 mm needle lengths in patients with type 1 or type 2 diabetes. Diabetic Medicine 1998;1:S50.

[10] Bergenstal RM et al. 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.

[11] Miwa T, Itoh R, Kobayashi T, Tanabe T, Shikuma J, Takahashi T, Odawara M. 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 Dec;14(12):1084-90.

[12] Nagai Y, Ohshige T, Arai K, Kobayashi H, Sada Y, Ohmori S. Comparison between shorter straight and thinner microtapered insulin injection needles. Diab Tech Ther 2013;15(7):550-555.

[13] 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 May 6;4(3):287-96.

[14] de la Peña A, Yeo KP, Linnebjerg H, Catton E, Reddy S, et al. Subcutaneous Injection Depth Does Not Affect the Pharmacokinetics or Glucodynamics of Insulin Lispro in Normal Weight or Healthy Obese Subjects. J Diabetes Sci Technol. 2015;9 :1-7.

[15] 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 Sep;31(9):e65.

[16] Hirsch LJ, Gibney MA, Li L, Bérubé J. Glycemic control, reported pain and leakage with a 4 mm × 32 G pen needle in obese and non-obese adults with diabetes: a post hoc analysis. Curr Med Res Opin. 2012 Aug;28(8):1305-11.

[17] 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 Nov;13(7):525-33.

given perpendicularly without a lifted skin fold, even with the 4 mm needle.

Hofman[18] has done similar studies using the 5 mm needle. He found that 5mm needles gave equivalent glucose control to 8mm ones in both children and adults, and no substantial back flow or leakage was seen from 5mm compared to 8mm in doses up to 60 IU. Children prefer the 5mm to longer needles and generally have less pain with 5mm. HbA1c improvements on the 5mm needle are sometimes seen and are probably a result of fewer IM injections. Hirsch[19] has shown equivalence between 4mm, 5mm and 8mm pen needles in regards to glucose control, with no difference between obese and non-obese subjects.

Strock[20] performed a subgroup analysis of a large study comparing 4mm32G pen needles with 8mm31G and 12.7mm29G ones in obese subjects, among those taking relatively high doses of glargine (>40 IU). No significant differences in glucose control (as measured by HbA1c), number of hypo- or hyperglycemic events or insulin leakage were seen in obese subjects (BMI $\geq$ 30 kg/m^2) amongst the three needle lengths. The 4 mm needle was judged to be less painful, easier to insert, easier to use and less anxiety-provoking than the other two lengths (all at $p < 0.05$).

In a cross-over trial involving obese adults with DM, Ignaut[21] compared the 5mm to the 8mm pen needle. They found minimal leakage overall with no difference between needle lengths, no difference by injection volume (20 and 60 IU compared) and no difference in bruising, bleeding or pain between the needle lengths. They concluded that the 5mm needle is acceptable for obese patients at low and high insulin volumes.

In a crossover trial involving obese adults (BMI $\geq$30 kg/m) with DM, Kreugel[22] compared the 5mm to the 8mm pen needle. No within-group changes were observed using 3 different integrated measures of glucose control: HbA1C, serum fructosamine and 1,5-anhydroglucitol. Furthermore, there were no differences in hypoglycemic events, bruising or pain. Authors concluded that the 5 mm needle may be used safely in obese patients. Several other authors[23] [24] [25] have shown equivalence between 4mm, 5mm and

[18] Hofman PL, Derraik JG, Pinto TE, Tregurtha S, Faherty A, et al. Defining the Ideal Injection Techniques When Using 5-mm Needles in Children and Adults. Diab Care. 2010 Sep;33(9):1940-4.
[19] Hirsch LJ, Gibney MA, Albanese J, Qu S, Kassler-Taub K, Klaff LJ, Bailey TS. Comparative glycemic control, safety and patient ratings for a new 4 mm x 32G insulin pen needle in adults with diabetes. Curr Med Res Opin. 2010 Jun;26(6):1531-41.
[20] Strock E et.al. Glycemic control, Pain and Leakage with 4 mm vs Larger Pen Needles in Obese Patients treated with Lantus or Higher Insulin Doses: Prespecified Subgroup Analyses. 2013. Poster 997-P. EASD, Barcelona, Spain.
[21] Ignuat D, 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: 389-393.
[22] Kreugel G, Keers JC, Kerstens MN, Wolffenbuttel BH. 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 Jul;13(7):737-41.
[23] Hirsch LJ, Gibney MA, Albanese J, Qu S, Kassler-Taub K, Klaff LJ, Bailey TS. Comparative glycemic control, safety and patient ratings for a new 4 mm x 32G insulin pen needle in adults with diabetes. Curr Med Res Opin. 2010 Jun;26(6):1531-41.
[24] Hirsch LJ, Gibney MA, Li L, Bérubé J. Glycemic control, reported pain and leakage with a 4 mm × 32 G pen needle in obese and non-obese adults with diabetes: a post hoc analysis. Curr Med Res Opin. 2012 Aug;28(8):1305-11.
[25] Bergenstal RM et al. 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.

8mm pen needles in regards to glucose control, with no difference between obese and non-obese subjects.

As this ITQ has shown, needle gauge over the last decade has shifted significantly towards lower diameters (31 and 32G). This shift has tracked the move to shorter needle lengths, although not as dramatically. It may be that at or near 29G we reach the threshold for pain detection in the majority of patients.

The association of lower TDD with the 4 mm pen needle in the ITQ is probably explained by the fact that such needles are used more frequently in younger patients who use lower doses of insulin. LH rates are also lower with 4 mm needles (for various reasons, not necessarily causative) and insulin use in LH- subjects is lower. Finally 4mm pen needles are used more frequently in intensively-treated patients (both T1DM and T2DM), who may require less insulin overall.

A new set of international injecting recommendations has been developed and is being published. A number of these have been incorporated in the text above. It may be appropriate for the local countries and regions to revise their own guidelines in the light of the new recommendations and the ITQ survey data reported above.

This paper will be followed by three others:

- Worldwide Injection Technique Study: Injecting Practices
- Worldwide Injection Technique Study: Injecting Complications
- Worldwide Injection Technique Study: Education and the Health Care Professional

Duality of interest:

Kenneth Strauss is employed by BD, a manufacturer of injecting devices.

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