



# A Coloured Pen Needle Education System Improves Insulin Site Rotation Habits: Results of a Randomized Study

Lori D. Berard · Sherri A. Pockett · Robert S. Roscoe ·  
Rick L. Siemens

Received: July 24, 2020 / Accepted: October 1, 2020 / Published online: October 16, 2020  
© The Author(s) 2020

## ABSTRACT

**Introduction:** Needle reuse and repeated injection of insulin into the same site encourage lipohypertrophy. We explored the potential of coupling a novel pen needle strategy with community pharmacists to improve injection site rotation.

**Methods:** Between October 2018 and January 2019, adult insulin users with type 1 or 2 diabetes were enrolled by 16 community pharmacists across 7 Canadian provinces and randomized to their usual pen needles (control) or coloured pen needles packaged with education materials in boxes with reminder sound chips (intervention [mCPN]). A total of 203 individuals completed all requirements of the 30-day study. The primary outcome was a composite of the number of zones injected, the

use of new injection zones if the number of zones equaled that at baseline, and the change in size of the injection area from baseline. The pharmacists completed two questionnaires, which provided insights into whether study participation elevated their comfort and confidence in providing injection site rotation counselling.

**Results:** Compared to the control group, more participants in the mCPN arm improved their site rotation practices (54.1% vs. 33.7%;  $P = 0.005$ ), 15 more increased the number of injection zones used ( $P = 0.03$ ), and there was less needle reuse (25% vs. 12% reduction). The pharmacists reported improved knowledge of the consequences of lipohypertrophy and the proportion who were “very comfortable” with pen needle tip selection and use rose from 31.3% pre-study to 93.8% post-study.

**Conclusion:** The coloured pen needles with their education materials are a novel means of encouraging injection site rotation. Community pharmacists represent an untapped resource for improving injection self-care practices.

**Keywords:** Diabetes mellitus; Education; Insulin; Injection site rotation; Lipohypertrophy; Pen needles; Pharmacists

---

L. D. Berard (✉)  
Nurse Consultant, Winnipeg, Manitoba, Canada  
e-mail: ldberard@gmail.com

S. A. Pockett  
St. Boniface General Hospital, Winnipeg, Manitoba,  
Canada

R. S. Roscoe  
R2 Consulting Ltd, Diabetes Education Centre, Saint  
John Regional Hospital, Saint John, New Brunswick,  
Canada

R. L. Siemens  
London Drugs Pharmacy, Lethbridge, Alberta,  
Canada

### Key Summary Points

#### Why carry out this study?

Lipohypertrophy is a persistent and major complication among individuals who use insulin to manage their diabetes.

The study sought to determine if coloured pen needles, dispensed with colour-associated injection zone maps in boxes with in-built reminder sound chips, would promote injection site and zone rotation among insulin users.

#### What was learned from the study?

The study demonstrated that the coloured pen needles, with their associated educational material and reminder mechanisms, were associated with significantly improved injection site rotation and reduced needle reuse.

The study intervention represents a novel and pragmatic means of promoting injection site rotation and limiting needle reuse to reduce the occurrence of lipohypertrophy.

The study also revealed that community pharmacists are an untapped source for educating on and encouraging proper injection site rotation habits.

## DIGITAL FEATURES

This article is published with digital features to facilitate understanding of the article. You can access the digital features on the article's associated Figshare page. To view digital features for this article go to <https://doi.org/10.6084/m9.figshare.13020683>.

## INTRODUCTION

Despite advances in insulin therapy and new strategies to educate on good injection self-care practices, many insulin users have poor injection site rotation habits and favour the same few injection sites [1–9]. Many insulin users also use their pen needles more than once to reduce expenses or perhaps for convenience [1]. The repeated local insult with or without a dulled pen needle encourages lipohypertrophy [10, 11]. Administration of insulin in areas of lipohypertrophy can impede insulin absorption and trigger undesirable glycaemic excursions [2], which can in turn increase the need for higher doses of insulin [2], cause greater overall hypoglycaemia [12], heighten the risks of severe hypoglycaemia and all-cause mortality [13], and elevate the risk for developing heart failure with preserved fraction in type 2 diabetes [14, 15].

Although it is recommended that new insulin users be counselled on the importance of rotating their injection sites to make their injections easier, safer, and more comfortable [16], many may not recall being instructed on the importance of site rotation and using a new needle for each injection. That said, it is also possible that while supporting insulin-using patients, the importance of teaching and reinforcing proper insulin injection habits tends to be ignored with the assumption of competence in proper injection technique among experienced insulin users.

In response to the escalating incidence of lipohypertrophy [1–9], the Canadian Forum for Injection Technique (FIT) has been proactive in increasing awareness of proper site rotation [16] in part by expanding the range of educational tools available to insulin users and their healthcare teams. FIT Canada recommends that all new users of insulin be provided with individualized education on the importance of injection site and zone rotation. FIT Canada also encourages reinforcing self-care practices of routine site and zone rotation with every insulin user at all follow-up visits.

Given that insulin users arguably see their pharmacists more frequently than they do their physicians or diabetes educators, community

pharmacists are uniquely poised to partner with their insulin-using clients to help optimize their diabetes management. The primary objective of this pharmacist-facilitated study was to determine if coloured pen needles, dispensed at community pharmacies with colour-associated injection zone maps in boxes with in-built reminder sound chips, would promote injection site and zone rotation among insulin users who live with type 1 or type 2 diabetes. Recognizing that pharmacists often multitask among patient care, service delivery, and business management, the participating pharmacists were specifically instructed not to offer counselling on pen needle use beyond standard practice and to only respond to queries about study participation. This afforded the opportunity to also evaluate the effectiveness the coloured pen needles and accompanying education materials in the absence of active pharmacist intervention. Given that pharmacists do not typically have advanced training in the nuances of diabetes management, pharmacists who do not have specialized diabetes practices were specifically targeted to facilitate this study. In that vein, we also report herein the predefined analysis that sought to determine whether participation in this initiative would alter the knowledge and perspectives community pharmacists have on injection site rotation and whether their confidence and comfort related to identifying and educating insulin users on recommended injection self-care practices would improve over the course of the study. This trial is registered at ClinicalTrials.gov (Identifier: NCT03914183).

## METHODS

### Pharmacist and Patient Participants

All pharmacists based in Canadian community pharmacies that provide services to individuals with diabetes who use injectable insulin therapy were eligible to participate in this study. Patient eligibility criteria included age  $\geq$  18 years, a diagnosis of type 1 or type 2 diabetes mellitus, daily use of insulin therapy for at least 1 year, and the ability to read the English or

French text on the boxes encasing the pen needles. Individuals were excluded if they were on a glucagon-like peptide 1 receptor agonist, currently using or had previously used the intervention coloured pen needles, unable to understand or communicate in English or French, pregnant, or living with a serious mental illness (e.g. dementia, schizophrenia disorders, bipolar disorders, major depression, etc.).

### Study Design and Conduct

The protocol, study materials, and participating pharmacists of this 30-day, two-arm, randomized, controlled trial were approved prior to study initiation by Advarra, an independent central ethics review board. This study was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments. To standardize the study conduct process, sites were only activated after the onsite study pharmacist had been trained by the lead investigator (L.D. Berard). Each pharmacist was asked to recruit up to 24 individuals who routinely obtained their insulin pen needles from their pharmacy. To ensure that individuals with both type 1 and type 2 diabetes were represented in the final analysis cohort, each pharmacist was asked to enroll an equal number of patients who required  $\leq$  2 injections and  $\geq$  3 injections of insulin each day.

Every enrolled patient was required to answer a questionnaire prior to randomization and another at the follow-up visit. The questionnaires captured details on the demography, number of daily insulin injections, length of the needle, injection zones used (upper right abdomen, upper left abdomen, lower right abdomen, lower left abdomen, right thigh, left thigh, right back of the arm, left back of the arm, left buttock, and right buttock), size of the injection area (i.e. dimensions of a postage stamp, credit card, playing card, or postcard), and participants' injection site rotation practices at the baseline and follow-up visits. Randomization codes were scrambled and provided to the sites to be opened after consent was obtained. Participants were assigned in a 1:1 fashion to either

**site smart**  
CHANGER DE COULEUR, CHANGER DE SITE™  
CHANGE COLOUR, CHANGE SITE™

**Option 1**  
Abdomen and thighs  
**IMPORTANT:** Spread your injections evenly throughout the entire area of the site, as shown in the examples below.

**Option 2**  
Abdomen only  
**IMPORTANT:** Répétez les injections uniformément sur toute la surface du site tel qu'il est indiqué dans les exemples ci-dessus.

**Option 3**  
Create your own plan  
Place a coloured sticker (included in box) on any of the recommended injection sites.  
Pick any pen needle, and simply inject in the injection site associated to the colour of the pen needle.

**Créer votre propre plan**  
Placez un autocollant de couleur (inclus dans la boîte) sur l'un des sites d'injection recommandés ci-dessus.  
Choisissez n'importe quelle aiguille pour stylo, et injectez tout simplement dans le site d'injection associé à la couleur de l'aiguille.

**Questions?**  
1-866-695-1222  
www.montmed.ca

**32G 4mm**  
**mont méd**  
**site smart**  
coloured pen needles • aiguilles colorées pour stylo

**CHANGE COULEUR, CHANGE SITE™**  
**CHANGER DE COULEUR, CHANGER DE SITE™**

**100 pcs/box**  
Includes 4 colours of pen needles  
Inclus 4 couleurs d'aiguille  
Patent Pending/Brevet en instance

**REFERENCES**  
(1) FIT Canada (Forum for Injection Techniques) <http://www.fit4diabetes.com/canada-english/>  
(2) Johansson UB, et al. Impaired absorption of insulin as part from lipohypertrophic injection sites. Diabetes Care 2005;28(6):2025-7  
(3) Frid AH, Hirsch LJ, Menchior AR, et al. Worldwide injection technique questionnaire study. Mayo Clin Proc. 2016;91:1212-1223.  
(4) Chowdhury TA, Escudélier V. Poor glycaemic control caused by insulin induced lipohypertrophy. BMJ. 2003; 327:365-364.

**mont méd**  
Expertise Médicale Canadienne  
Canadian Medical Expertise

**Questions?**  
1-866-695-1222  
www.montmed.ca

TM Trademarks of montmed inc.  
© Copyright 2017 montmed inc., all rights reserved

Getting the most out of your insulin treatment requires regular injection site rotation

**site smart**  
coloured pen needles

The only pen needle that seamlessly reminds you to do so!

**32G 4mm**

**Why should you regularly rotate your injection site?**

- leads to better blood glucose control<sup>1,2,3,4</sup>
- helps to reduce some unexplained blood sugar variation<sup>1,2,3,4</sup>
- may also help you to reduce the amount of insulin you are taking<sup>1,2,3,4</sup>



**REFERENCES**  
(1) FIT Canada (Forum for Injection Techniques) <http://www.fit4diabetes.com/canada-english/>  
(2) Johansson UB, et al. Impaired absorption of insulin as part from lipohypertrophic injection sites. Diabetes Care 2005;28(6):2025-7  
(3) Frid AH, Hirsch LJ, Menchior AR, et al. Worldwide injection technique questionnaire study. Mayo Clin Proc. 2016;91:1212-1223.  
(4) Chowdhury TA, Escudélier V. Poor glycaemic control caused by insulin induced lipohypertrophy. BMJ. 2003; 327:365-364.



Expertise Médicale Canadienne  
Canadian Medical Expertise

**Questions?**  
1-866-695-1222  
www.montmed.ca

TM Trademarks of montmed inc.  
© Copyright 2017 montmed inc., all rights reserved

◀ **Fig. 1** Packaging of the study intervention (mCPN)

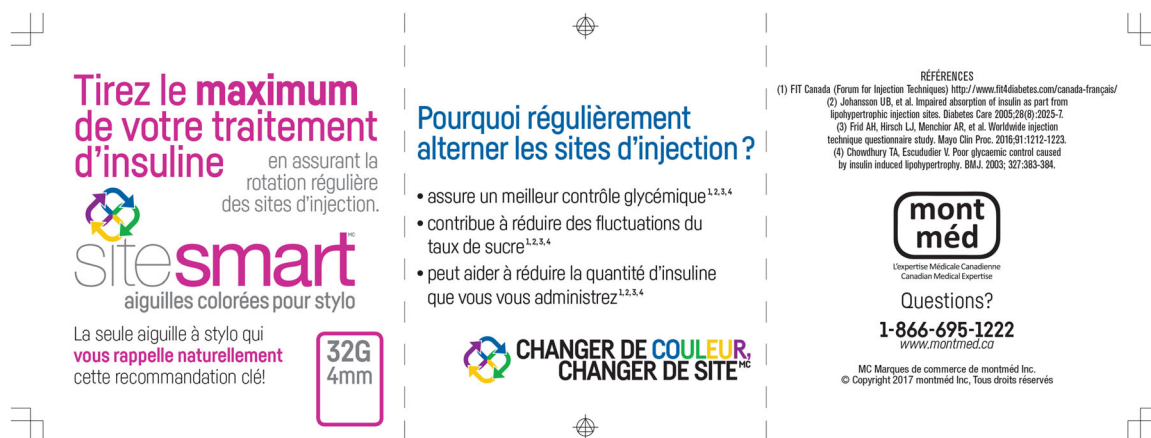
the control or intervention (mCPN) group. Participants in the former were provided boxes of their usual insulin pen needles while those in the latter were dispensed boxes of montméd Coloured Pen Needles that incorporated site rotation education on the packaging (Fig. 1) and through embedded sound chips (Fig. 2).

Pharmacists were required to answer two questionnaires. The first had to be submitted ahead of enrolling their first participant. The second was to be submitted after the last participant enrolled at their site had completed the final follow-up visit. These questionnaires captured information on the pharmacists’ perception and knowledge related to injection site rotation and lipohypertrophy as well as their comfort level with pen needle selections and providing counselling on injection site rotation. The pharmacists were also asked to estimate the proportion of their insulin-using clients whom they believed followed good injection self-care practices (i.e. rotating injection sites and not reusing pen needles) and whether they believed that participation in the study had altered their enrollees’ injection behaviours.

**Study Outcomes**

The primary outcome, injection site rotation, was a composite of the number of zones injected,

the use of new injection zones if the number of injection zones had not changed from that at baseline, and the size of the injection area relative to that at baseline. An improvement in injection site rotation was defined as an increase in the number of zones used over the past 7 days, use of new injection zones if the number of zones injected was the same as that at baseline, or an expansion of the injection area relative to that at baseline. Secondary quantitative outcomes determined at the follow-up visit were the change from baseline in the frequency at which pen needles were replaced, the average number of daily insulin injections required, total insulin used the day before answering the questionnaire, and the incidence of hypoglycaemic episodes over the last 30 days. Those randomized to the intervention (mCPN) arm were also asked to rate their experience with the coloured pen needles relative to their usual pen needles. The pharmacist sub-study evaluated the changes, from pre-study initiation to study end, in the level of knowledge about lipohypertrophy and its relation to poor injection practices, confidence in providing injection site rotation counselling, and time invested to provide education on good injection habits. Answer options for all the questionnaires were in the format of dichotomous scales, 5-point Likert scales, and nominal clusters, as appropriate.



**Fig. 1** continued

**Message 1**

Site Rotation matters!

Did you know that always injecting into the same place can damage the tissues?

This can affect your blood sugar levels.

It can increase your risk of low blood sugars and it can even increase how much insulin you take.

Unique color coding of SiteSmart pen needles reminds you to rotate injection site.

Change color, Change Site.

For more information ask your pharmacist.

**Message 2**

Change color, change site.

Check your SiteSmart packaging.

Use of the 2 readymade popular injection plans or develop your own plan that works for you by assigning a color to each of the recommended injection site. Every time you grab a needle simply inject it to the site matching the color of the pen needle.

It is as simple as that.

**Message 3**

Injection Technique Best Practice Tip

In addition to performing regular site rotation, Canadian injection technique experts recommend using a pen needle once, discarding it, and using a new one for each injection to keep your tissues healthy.

**Message 4**

Congratulations!

I hope you have appreciated these few educational sound bites, and that by now SiteSmart has helped you to adopt a healthy injection site rotation routine that easily fits into your daily life.

Keep going!

**Fig. 2** Reminder messages embedded in the sound chips. The messages play one at a time each time the box is opened followed by 15 silent box openings. The cycle repeats thereafter

## Data Management and Statistical Analyses

Data from the patient and pharmacist surveys were entered into independent Microsoft Access databases and extracted to a CSV file format for analysis. Categorical variables were evaluated and are presented as *n* (percentage); continuous variables were evaluated and are presented as mean (standard deviation). Statistical analyses were conducted with R.

A generalized linear regression model was used to determine whether the outcome measures in the intervention (mCPN) group were significantly different from those of the control group; these evaluations were adjusted for the patients' baseline age, daily number of injections, duration of diabetes, and period of insulin use. Given that the number of zones injected over a 7-day period may be influenced by the number of injections needed, the analyses for

the “number of zones injected” outcome were based on the proportional number of zones used (number of zones injected over the 7 days divided by the number of injections required that week). If the number of zones injected at baseline and at the follow-up visit were the same, the locations of the study zones at each time point were reviewed to determine if new zones had been used during the study.

## RESULTS

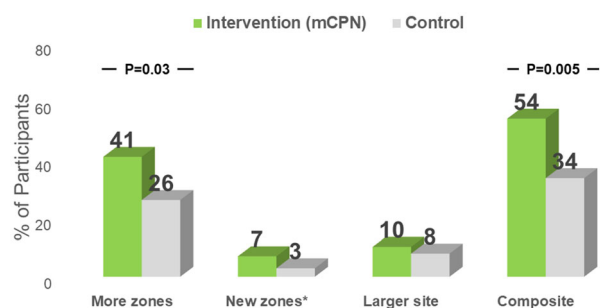
### Final Patient Analysis Group

Between October 2018 and January 2019, a total of 16 pharmacists from 14 community pharmacies in 7 Canadian provinces enrolled 208 patients. Five patients were excluded from the final analysis group because they had only

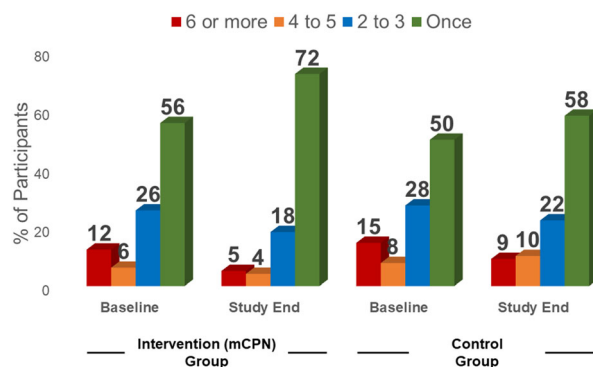
**Table 1** Baseline characteristics of the patient cohort

	All (N = 203)	Intervention (mCPN) group (n = 100)	Control group (n = 103)
Age, years	62 (15.1)	60 (17.3)	65 (12.3)
Female	73 (35.9)	33 (33.0)	40 (38.8)
Type of diabetes mellitus			
Type 1	39 (19.2)	27 (27.2%)	12 (11.7%)
Type 2	163 (80.3)	72 (72.7)	91 (88.3)
Duration of diabetes, years	18 (10.9)	19.7 (11.8)	18.0 (10.0)
Duration of insulin use, years	11.8 (11.4)	12.3 (12.7)	11.2 (10.0)

Categorical variables are presented as *n* (percentage); continuous variables are presented as mean (standard deviation)



**Fig. 3** Summary of the occurrence of the primary outcome (improved injection site rotation) and the individual components—number of zones injected; \*new zones injected (if the number of zones were the same as that at the baseline visit) and the size of the injection zone



**Fig. 4** Summary of the number of times a needle was used on average before it was replaced with a new needle at baseline and at the follow-up visit

completed one of the two mandatory study questionnaires. The key baseline characteristics of the entire cohort as well as the intervention and control sub-groups are detailed in Table 1. None of the patients reported issues with any of the pen needle types dispensed.

**Patient and Pharmacist Responses Regarding Injection Site Rotation Habits**

As summarized in Fig. 3, the patient-reported outcomes indicate that there were significant differences in the change in injection site rotation habits between the two study groups for the duration of the study. Specifically, 15 more

participants in the intervention (mCPN) group than the control group reported, at the follow-up visit, that they had increased the number of injection zones they used, and this yielded a statistical difference of  $P = 0.03$ . Of those who stayed with the same number of zones they routinely injected in, more individuals in the intervention (mCPN) group than in the control group injected into new zones. Of note, although more patients in the intervention (mCPN) group expanded the size of their injection zone, the between-group difference for this parameter did not achieve statistical significance. Importantly, the proportion of participants in the intervention (mCPN) group who demonstrated an overall improvement in

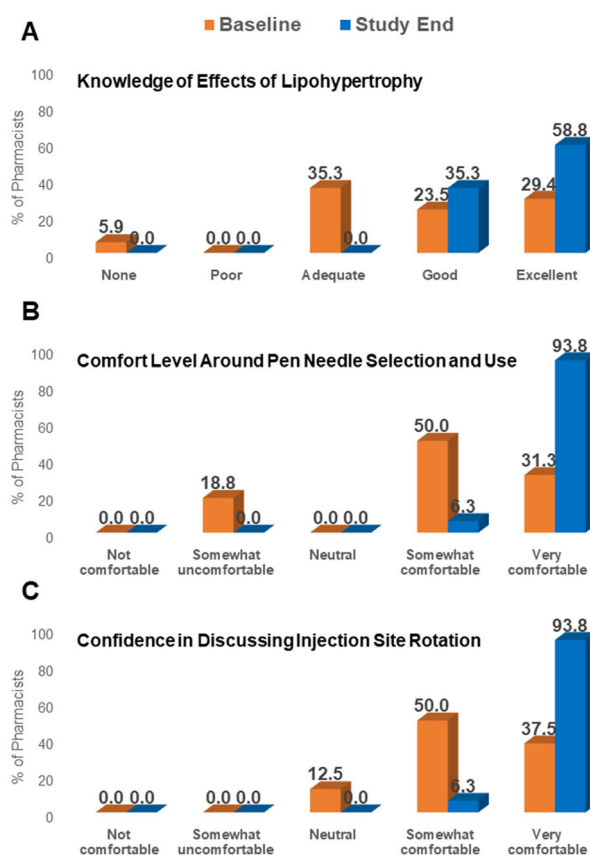
site rotation practices was significantly greater than that in the control group (54.1% vs. 33.7%;  $P = 0.005$ ).

Prior to study initiation, 56.3% of the pharmacists believed that 41 to 60% of the patients practised proper injection site rotation. At the end of the study, 50.0% believed that 61 to 80% of the patients properly rotated their injection sites while 31.3% believed that over 81% of their patients were correctly rotating their injection sites.

### Patient and Pharmacist Responses to Secondary Patient-related Outcomes (Needle Reuse, Daily Insulin Doses, and Hypoglycaemic Events)

Figure 4 summarizes the number of times the patients reported that a needle was used on average before it was replaced at baseline and at the follow-up visit. At the follow-up visit, 17% more of the overall cohort used their pen needles only once during the study. Between the baseline and follow-up visits, the control group demonstrated a 12% reduction in the average number of times a needle was used (2.5–2.2 times) while a 25% decrease was documented for the intervention (mCPN) group (2.3–1.7 times). It is notable that whereas 19% of the control group was still using a needle at least four times at the follow-up visit, this practise was only reported by 9% of the intervention (mCPN) group. Prior to study initiation, 31.3% of the pharmacists believed that 81–100% of the patients routinely used their pen needles more than once. At the end of the study, 6.3% of the pharmacists believed that 81–100% of the patients used their pen needles more than once.

The number of daily insulin injections administered did not change over the 30-day study window in either group (4.1 [1.4] for the intervention (mCPN) group and 3.7 [1.5] for the control group;  $P = 0.73$ ). There was no significant change in the total insulin used the day before the questionnaires were answered at baseline and at the follow-up visit (76.1 units at baseline and 73.8 units at follow-up for the intervention (mCPN) group; 64.0 units and 64.1



**Fig. 5** Educational impact of the study on the pharmacists was determined via their **a** knowledge of the effects of lipohypertrophy, **b** comfort level around pen needle selection and use, and **c** confidence in discussing proper injection site rotation practices

units correspondingly for the control group;  $P = 0.24$ ).

At the follow-up visit, 44% of the intervention (mCPN) group and 50% of the control group stated that they had not had a hypoglycaemic episode over the 30-day study window; 39% of the intervention (mCPN) group and 29% of the control group had experienced 1–3 events; 12% of both groups indicated that they had endured 4–7 occurrences. Relative to the control group, the intervention (mCPN) group had proportionally fewer participants reporting 8–13 and 14–28 hypoglycaemic episodes during the study although 2% of each group had experienced > 1 hypoglycaemic event per day over the same period.



## Educational Impact of the Study on the Patients and Pharmacists

At the baseline visit, none of the participants believed that lack of proper injection site rotation may account for why they experienced episodes of higher glucose readings. At the follow-up visit, 39% of the intervention (mCPN) group and 16% of the control group responded that they believe poor injection site rotation likely contributed to their higher glucose measurements. At the baseline visit, 56% of the intervention (mCPN) group and almost 70% of the control group reported no knowledge of the potential clinical impact of repeatedly injecting insulin into the same spot for a long period of time. At the follow-up visit, these numbers were reduced to 44% for the intervention (mCPN) group and 48% for the control group.

The pre-study survey responses indicated that although 87.5% of the pharmacists had heard about lipohypertrophy, only half rated their knowledge about the consequences of lipohypertrophy to be either good or excellent (Fig. 5a). At the end of the study, almost all considered themselves to have a good or excellent understanding of the downstream effects of lipohypertrophy (Fig. 5a).

The percentage of pharmacists who considered injection site rotation education to be “very important” in insulin therapy rose from 68.8% pre-study to 93.8% post-study. When asked about their comfort level around pen needle selection and use, less than one-third indicated that they were “very comfortable” prior to study initiation, while at the end of the study, most responded that they were “very comfortable” (Fig. 5b). As illustrated in Fig. 5c, study participation dramatically promoted the pharmacists’ confidence in reviewing injection site rotation practices, which likely contributed, at least in part, to the reported increase in time spent counselling on proper injection site rotation—from one-quarter pre-study to almost all post-study reporting having discussions for > 61% of the time they see their insulin-using clients.

## Patients’ and Pharmacists’ Perceived Impact of the Coloured Pen Needles on Site Rotation and Needle Change

Approximately 48% of those in the intervention (mCPN) arm believed they changed their pen needles more often. Over 68% of the same group believed that they varied their injection sites more frequently and 70% stated that they found it easier during the study to remember to rotate their injection sites. More than 63% of those assigned the coloured pen needles thought that the phrase “Change colour, change site” was a helpful reminder to consider changing injection sites more frequently while 67% believed the coloured pen needles helped remind them to consider other injection sites. At the end of the study, approximately 71% of those in the intervention (mCPN) arm indicated that they were either “very satisfied” or “satisfied” with the coloured pen needles and the additional education tools; 66% were either “very satisfied” or “satisfied” with the utility of the coloured pen needles relative to their usual pen needles. Furthermore, post-intervention, participants in the intervention (mCPN) group were asked if they would consider switching to the coloured pen needle if its cost were comparable to and not more expensive than the current pen needles. More than one-half of them (57%) said they would consider switching, 19% were not sure, and the rest (25%) said they would not consider switching to the coloured pen needle.

There was a consensus amongst the pharmacists that the mCPN intervention improved injection habits. All believed that it promoted site rotation, 93.8% believed that it led to the use of more injection zones, 93.8% believed that injection areas were expanded, and 81.8% believed that there was less needle re-use. Most believed the act of simply providing insulin users with coloured pen needles with educational tools may improve injection behaviours (93.8%), proper site rotation (87.5%), and needle re-use (68.8%).

## DISCUSSION

The current study demonstrated that the combination of coloured pen needles with supportive education and reminder tools (colour-associated injection zone maps and reminder sound chips built into the dispensing box) significantly improved injection site and zone rotation among insulin users. While the practice of reusing pen needles was still evident in the group assigned the coloured pen needles, there was an overall trend towards less reuse with 72% reporting at the end of the study that they only used each pen needle once. Importantly, these positive findings arose from dispensing actions initiated with no additional verbal education in community pharmacies and support the translational potential of this practical approach to enhance self-care injection practices among individuals who use insulin to manage their type 1 or type 2 diabetes.

Lipohypertrophy is the most significant complication of poor injection technique [1–4, 6, 9, 17, 18]. While convenience, habitual behaviour, and “less pain” may partially account for why areas of lipohypertrophy are repeatedly accessed over prolonged periods, the growing prevalence of lipohypertrophy [1–9] appears to be at least in part due to a poor understanding of why it is important to rotate injection sites [4, 7] and how to go about maximizing injection zones to optimize site rotation and minimize lipohypertrophy.

Despite significant attempts to raise awareness among diabetes care providers about the importance and impact of incorporating site rotation education into diabetes-focused visits [16, 19], uptake has been inconsistent. Indeed, patient load and the need to address more pressing clinical concerns may also limit the opportunities to review site rotation practices. Notably, insulin users who do not have regular access to diabetes care providers would likely not have had their injection practices and sites assessed or participated in discussions about the significance of site rotation.

Insulin users do, however, routinely visit their pharmacies to collect prescriptions and injection-related supplies. The pharmacists who

participated in this study were explicitly instructed to not provide counselling on pen needle use beyond standard practice. It is therefore notable that despite the lack of additional explanation, none of the participants randomized to the intervention (mCPN) group indicated any issues with using the coloured pen needles suggesting therefore that the participants encountered few, if any, challenges transitioning from their usual pen needles to the intervention (mCPN) needles. Furthermore, most of these participants expressed satisfaction with the utility of the intervention (mCPN) needles and over two-thirds believed that the coloured intervention (mCPN) needles together with the accompanying education and reminder tools helped improve their injection site rotation practices.

Approximately three-quarters of the pharmacists in Canada work in community pharmacies [20, 21] where they often serve as the first point of engagement that patients have with the healthcare system [22]. Most individuals with diabetes may not think twice about regularly visiting their community pharmacy to obtain products and services beyond prescription medications but many likely do not intuitively perceive their community pharmacists as a support source for their diabetes care. Notably, two systematic reports and meta-analyses have suggested that diabetes circles of care that include pharmacists with active intervention roles are associated with better glycaemic control, improved risk factor modification (e.g. lower blood pressure, favourable lipid changes, and weight loss), better medication adherence, and improved patient-reported quality of life [23, 24].

Pharmacists are not traditionally educated on the importance of injection site rotation with injectable therapy and this likely accounted, at least in part, for the variable knowledge documented in the pre-study initiation questionnaire administered as well as the wide range in comfort and confidence in providing injection site rotation counselling. A key finding was that the participating pharmacists believed their involvement in this study not only enhanced their knowledge of the downstream effects of lipohypertrophy but also elevated

their comfort in providing counselling on pen needle tip selection and the importance of routinely rotating injection sites. Taken together with the available literature, these data highlight the opportunity to expand the scope of diabetes-care services community pharmacists can offer to their local communities. Community pharmacists are highly accessible, and because of the already established familiarity, insulin users may be more inclined to cooperate with their community pharmacists to work towards improving injection practices and, in so doing, lower the risk of lipohypertrophy. A potential ripple effect of this personalized approach may be less frequent and shorter consultations with time-constrained family physicians and diabetes educators, thereby reducing imposition on healthcare costs [25].

This study has several strengths. First, it included patients with both type 1 and type 2 diabetes. Second, the pharmacists were based in pharmacies located in suburban areas and metropolitan cities of seven Canadian provinces, thus providing geographical diversity. Third, the study followed a randomized controlled design. Fourth, the questionnaire format allowed the authors to capture insights on patient and pharmacist attitudes and beliefs about injection site rotation, as well as the clinical and educational impact, and patients' and pharmacists' perspectives of the utility of the coloured pen needles. There are also limitations that should be noted. First, given the patient cohort size of 203, the patient data may not necessarily be generalizable to the entire Canadian population or globally. Second, this was a short 30-day-long study and whether the improved injection site rotation habits would have eventually translated into definitive reductions in lipohypertrophy is unknown. Third, there may have been some participating bias since the study pharmacists actively chose to contribute to the study. Fourth, it is likely that despite the randomized design, it was the most motivated patients who signed up. It is therefore probable that the increased understanding of proper injection site habits detected in the control group stemmed from acquisition of knowledge from sources outside of the study

(e.g. other members of the Circle of care, literature search, etc.). Fifth, we cannot discount the possibility that the open-label design may have influenced the outcomes to some degree.

## CONCLUSION

The growing armamentarium of antihyperglycaemic agents with benefits beyond glycaemic control has of late been at the forefront of diabetes management. However, it is a given that for many people living with diabetes, insulin therapy will likely become a reality as their condition progresses. Accordingly, novel approaches like that described herein, which promote consistent and proper injection technique to ensure complete delivery of every dose of insulin, and can be reinforced by community pharmacists, are useful tools that should not be relegated to the background of diabetes care.

## ACKNOWLEDGEMENTS

The authors thank the patient participants, participating pharmacists—Nadine Abou Kheir (Calgary, AB), Randeep Birdi (Edmonton, AB), Anita Brown (Okotoks, AB), Rob Caravan (Kamloops, BC), Rebecca Dunn (Cornwall, ON), Mohamed Hemeda (Niagara Falls, ON), Richard Kelch (Sarnia, ON), Dean Mercer (Rothesay, NB), Noura Nakhla (Milton, ON), Vincent Ouellet (Laval, QC), Tiffany Pankratz (Winnipeg, MB), Monique Prévost (Montréal, QC), Roger Tam (Winnipeg, MB), Jérôme Tousignant (Montréal, QC), and Paul Zemlak (Claresholm, Alberta), Selam Mequanint of Mequanint Consulting for conducting the statistical analyses, Hwee Teoh of HTaq Biomedical Editorial and Education Services Inc. for writing and editorial support in the preparation of this manuscript, and Kristin Canart for assistance with data entry.

**Funding.** This investigator-initiated study was supported by an unrestricted research grant from Montméd Inc. The funder had no role in the design and conduct of the study; collection,

management, analysis, and interpretation of the data; preparation or decision to submit the manuscript for publication. No funding or sponsorship was received for the publication of this article.

**Authorship.** All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

**Authorship contributions.** Lori Berard took the lead in designing the methodology, collecting and interpreting the data, and took the lead in writing, revising and reviewing the final manuscript. S.A. Pockett, R.S. Roscoe, and R.L. Siemens assisted with designing the methodology, interpreting the data, and writing, revising, and reviewing the final manuscript.

**Disclosures.** Lori D. Berard reports receiving consulting fees and/or speaker honoraria from Abbott, AstraZeneca Canada, Bayer, BD Canada, Boehringer Ingelheim, Eli Lilly, HLS Therapeutics, Janssen, MontMed, QUANTA, Novo-Nordisk, and Sanofi. Sherri.A. Pockett reports no relevant conflicts of interests. Robert S. Roscoe reports receiving consulting fees and/or speaker honoraria from Abbott, API (Allied Pharmacists Inc.), AstraZeneca Canada, BD Canada (Becton Dickinson), Bayer Healthcare, Bausch Health (Valeant (Bio-Vail) Pharmaceuticals), Boehringer-Ingelheim Canada, the Canadian Pharmacists Association, Diabetes Care Canada, Eli Lilly Canada, HLS Therapeutics, Janssen Canada, Medtronic-Canada, Merck Canada, montmed Canada, NB Pharmacists Association, New Brunswick Government—Department of Health—(Diabetes Task), Novo-Nordisk Canada, Roche Diagnostics, Sanofi Canada, and Top Guns Conference. Rick L. Siemens reports receiving honoraria from Abbott, Lilly, Janssen, Novo Nordisk, and Sanofi.

**Compliance with ethics guidelines.** Ethics approval was obtained from Advarra and all subjects provided written informed consent to participate in the study. This study was

conducted in accordance with the declaration of Helsinki 1964 and its later amendments

**Data availability.** The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Open Access.** This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc/4.0/>.

## REFERENCES

1. 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;7:259–67.
2. Blanco M, Hernandez MT, Strauss KW, Amaya M. Prevalence and risk factors of lipohypertrophy in insulin-injecting patients with diabetes. *Diabetes Metab.* 2013;39:445–53.
3. 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.* 2017;9:536–43.
4. 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;91:1224–300 **PubMed PMID: 27594186.**

5. Frid AH, Hirsch LJ, Menchior AR, Morel DR, Strauss KW. Worldwide injection technique questionnaire study: population parameters and injection practices. *Mayo Clin Proc.* 2016;91:1212–23.
6. Ji L, Sun Z, Li Q, Qin G, Wei Z, Liu J, et al. Lipohypertrophy in China: prevalence, risk factors, insulin consumption, and clinical impact. *Diabetes Technol Ther.* 2017;19:61–7.
7. Kalra S, Mithal A, Sahay R, John M, Unnikrishnan AG, Saboo B, et al. Indian injection technique study: injecting complications, education, and the health care professional. *Diabetes Ther.* 2017;8:659–72.
8. Kalra S, Mithal A, Sahay R, John M, Unnikrishnan AG, Saboo B, et al. Indian injection technique study: population characteristics and injection practices. *Diabetes Ther.* 2017;8:637–57.
9. Pozzuoli GM, Laudato M, Barone M, Crisci F, Pozzuoli B. Errors in insulin treatment management and risk of lipohypertrophy. *Acta Diabetol.* 2018;55:67–73.
10. Richardson T, Kerr D. Skin-related complications of insulin therapy: epidemiology and emerging management strategies. *Am J Clin Dermatol.* 2003;4:661–7.
11. Thow JC, Johnson AB, Marsden S, Taylor R, Home PD. Morphology of palpably abnormal injection sites and effects on absorption of isophane (NPH) insulin. *Diabet Med.* 1990;7:795–9.
12. Ceriello A, Monnier L, Owens D. Glycaemic variability in diabetes: clinical and therapeutic implications. *Lancet Diabetes Endocrinol.* 2019;7:221–30.
13. Zinman B, Marso SP, Poulter NR, Emerson SS, Pieber TR, Pratley RE, et al. Day-to-day fasting glycaemic variability in DEVOTE: associations with severe hypoglycaemia and cardiovascular outcomes (DEVOTE 2). *Diabetologia.* 2018;61:48–57.
14. Gu J, Fan YQ, Zhang JF, Wang CQ. Association of hemoglobin A1c variability and the incidence of heart failure with preserved ejection fraction in patients with type 2 diabetes mellitus and arterial hypertension. *Hellenic J Cardiol.* 2018;59:91–7.
15. Yokota S, Tanaka H, Mochizuki Y, Soga F, Yamashita K, Tanaka Y, et al. Association of glycemic variability with left ventricular diastolic function in type 2 diabetes mellitus. *Cardiovasc Diabetol.* 2019;18:166.
16. Berard L, Desrochers F, Hagerty D, MacNeill G, Roscoe R. FIT forum for injection technique Canada. Becton: Dickinson and Company; 2016.
17. 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:e20776.
18. Baruah MP, Kalra S, Bose S, Deka J. An audit of insulin usage and insulin injection practices in a large indian cohort. *Indian J Endocrinol Metab.* 2017;21:443–52.
19. Hicks D, Berard L, Twamley H. Forum for Injection Technique (FIT): FIT International; <https://www.fit4diabetes.com/canada-1/>. Accessed 17 Mar 2018.
20. Canadian Institute for Health Information (CIHI). Pharmacists. 2016. <https://secure.cihi.ca/estore/productFamily.htm?pf=PFC3363&lang=en&media=0>. Accessed 20 Apr 2020.
21. Canadian Pharmacists Association. Pharmacy in Canada. 2016. <https://www.pharmacists.ca/cpha-ca/assets/File/pharmacy-in-canada/Pharmacy%2520in%2520Canada.pdf>. Accessed 29 Apr 2020.
22. National Association of Chain Drug Stores (NACDS) Economics Department. National Council for Prescription Drug Programs (NCPDP) Pharmacy File. Arlington: NACDS; 2013.
23. Jokanovic N, Tan EC, Sudhakaran S, Kirkpatrick CM, Dooley MJ, Ryan-Atwood TE, et al. Pharmacist-led medication review in community settings: An overview of systematic reviews. *Res Social Adm Pharm.* 2017;13:661–85.
24. Pousinho S, Morgado M, Falcao A, Alves G. Pharmacist interventions in the management of type 2 diabetes mellitus: a systematic review of randomized controlled trials. *J Manag Care Spec Pharm.* 2016;22:493–515.
25. Gagnon-Arpin I, Dobrescu A, Sutherland G, Stonebridge C, Dinh T. The value of expanded pharmacy services in Canada. Ottawa: The Conference Board of Canada; 2017.