



## ORIGINAL ARTICLE

# Injecting without pressing a button: An exploratory study of a shield-triggered injection mechanism

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## Funding information

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**Aims:** To evaluate the injection success and user perception of a shield-triggered pen-injector mechanism.

**Methods:** The trial (ClinicalTrials.gov NCT02627287) was an exploratory, two-centre, one-visit, open-label, randomized controlled trial conducted in Germany in 150 injection-experienced individuals with type 1 or type 2 diabetes. Participants self-administered subcutaneous injections of a placebo solution using a prototype shield-triggered pen-injector, DV3316 (Novo Nordisk, Bagsvaerd, Denmark), and FlexPen (Novo Nordisk, Bagsvaerd, Denmark). Injection success was evaluated on a yes/no basis by the investigator. Participant confidence, leakage of fluid and pain were evaluated after each injection. Pain and device experience were assessed after completion of all injections with each pen-injector. Overall preference was assessed after completion of all injections with both pen-injectors.

**Results:** Injection success was high with both pen-injectors (97.0%, DV3316 vs 99.7%, FlexPen). Participant confidence in dose delivery was similar for the two devices (88% of injections with DV3316 vs 81% with FlexPen were scored as “extremely confident”). The median injection pain score on a visual analogue scale (0-100) was 3 with DV3316 vs 4 with FlexPen after each injection, and 4 with DV3316 vs 5 with FlexPen after all injections with each device. After all injections were completed, 55% of participants reported an overall preference for DV3316 vs 21% for FlexPen.

**Conclusion:** This study demonstrates that injection-experienced individuals can achieve a high injection success rate with a shield-triggered pen-injector, with similar patient confidence and injection pain compared with FlexPen.

## KEYWORDS

confidence, FlexPen, pain, pen-injector, subcutaneous injections

## 1 | INTRODUCTION

Pen-injectors are the predominant device for insulin delivery for people with type 1 (T1D) or type 2 diabetes (T2D) in many countries worldwide, including in Europe and Japan.<sup>1,2</sup> By contrast, the traditional vial and syringe method is still widely used in the USA.<sup>3</sup> Compared with a vial and syringe, pen-injectors offer improved patient satisfaction and adherence, greater ease of use, superior dose

accuracy, greater social acceptability, better confidence in glycaemic control and lower injection pain.<sup>4-8</sup>

Correct insulin injection technique and adherence to treatment is a crucial aspect of diabetes management. Most available prefilled pen-injectors, such as SoloSTAR (Sanofi, Paris, France), KwikPen (Eli Lilly, Indianapolis, Indiana), and FlexPen (Novo Nordisk, Bagsvaerd, Denmark), require users to set the dose using an extended-dose button and to perform “air shots” before each injection. After inserting

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the needle into the skin, users must fully depress the dose button and wait for several seconds after the end-of-dose click or until the dose counter has returned to zero before withdrawing the needle from the skin. Issues associated with most pen-injectors include difficulty depressing the extended-dose button, especially among young patients or patients with impaired manual dexterity, strength or nerve function,<sup>9,10</sup> and premature needle withdrawal, leading to under-delivery of dose.<sup>11,12</sup>

DV3316 is a prototype multiple-use pen-injector with a shield-triggered injection mechanism developed by Novo Nordisk A/S. The aim of the new injection mechanism is to simplify insulin delivery and improve user experience compared with other available pen-injectors. The needle mounted on the DV3316 is covered by a shield, which triggers dose activation when pushed against the skin, and thus eliminates the need for the user to depress an extended-dose button (Figure 1). Additional features of DV3316 mean that users are not required to perform initial priming or “air shots” before injection, and there is no waiting time after the dose counter has returned to zero. Before injection, the dose is dialled into the prototype using a dose counter, in a similar manner to FlexPen.

The aim of the present randomized controlled trial was to evaluate injection success with a shield-triggered prototype pen-injector

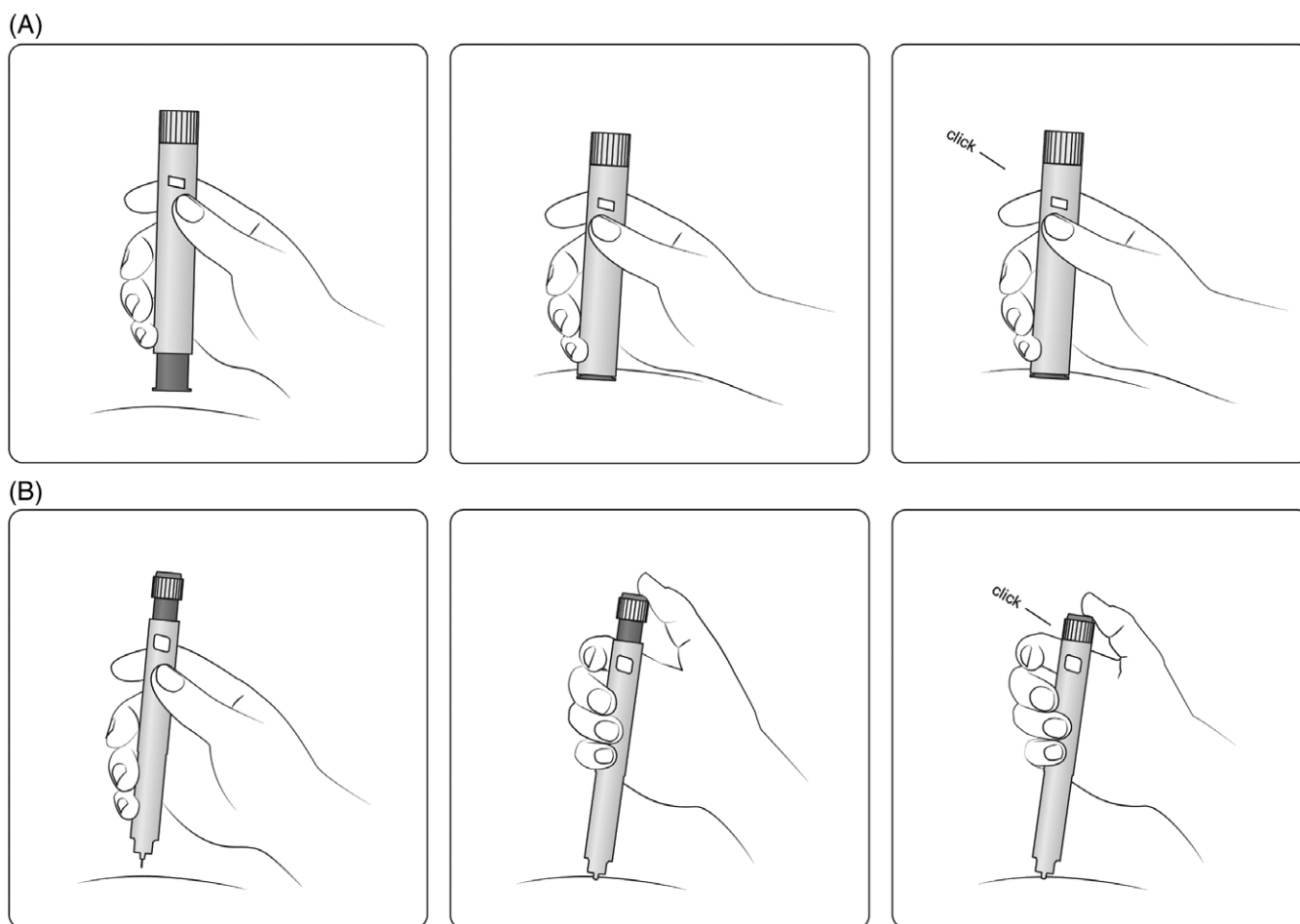
compared with FlexPen, and to assess how injection-experienced patients with diabetes perceive the new mechanism.

## 2 | MATERIALS AND METHODS

### 2.1 | Study design and participants

This study was an exploratory, two-centre, one-visit, open-label, randomized trial conducted in Germany in patients with diabetes (ClinicalTrials.gov NCT02627287). The study consisted of a 1-day visit, during which each participant performed injections with both DV3316 and FlexPen. All participants signed informed consent forms prior to any study-related activities. The study was approved by a local ethics committee (Ärztchamber Nordrhein, Ethikkommission, Düsseldorf, Germany) and was conducted in accordance with the Declaration of Helsinki and International Conference on Harmonization Good Clinical Practice.

The study population consisted of white men and women aged 18 to 74 years, with a diagnosis of T1D or T2D for at least 12 months, and self-injection experience with daily antidiabetic drugs (including insulin) administered via pen-injector or vial and syringe.



**FIGURE 1** Injection procedure with A, DV3316 and B, FlexPen. DV3316 has a shield concealing the needle. After setting the dose using the dose counter, users are required to press the shield against the skin to trigger the dose delivery mechanism. There is no need to wait after the dose counter has returned to zero. FlexPen users set the required dose using the extending dose button. After inserting the needle into the skin, users are required to fully depress the dose button to deliver the insulin dose and wait for 6 seconds after the “end-of-dose” click before withdrawing the needle

Participants were required to have normal vision (with or without correction) to a point where the participant was able to read the letters in a newspaper or device instructions. Exclusion criteria included: known or suspected hypersensitivity to placebo solution or related products; known urticaria factitia or abnormal reactions to mechanical trauma; haemophilia and any diseases affecting blood coagulation; anti-coagulant or inhibitors of platelet aggregation treatment within the last month; intake of any pain-relieving or analgesic drugs on the day of the site visit; self-reported intake of alcohol within the last 24 hours or a positive result of alcohol breath test; lipodystrophy, skin diseases or infections of the skin in the injection site areas; and severe neuropathy.

## 2.2 | Study procedures

Subcutaneous injections were performed with a 3-mL prototype DV3316 device and a 3-mL FlexPen. For each pen-injector, participants received training on the correct injection procedure from the device instructions for use and the study investigators, and practised injecting into a cushion. For FlexPen, training included instruction that the needle must remain under the skin for at least 6 seconds after the dose counter reached zero. For each injection, dose setting, and needle mounting and removal were performed by the investigators. Both pen-injectors were used with single-use 32-gauge 4-mm needles (NovoFine Plus; Novo Nordisk, Bagsvaerd, Denmark). During a 3- to 5-hour period, participants self-administered 20 injections of a placebo solution (Novo Nordisk, Bagsvaerd, Denmark) containing disodium phosphate dehydrate (1.42 mg/mL), propylene glycol (14.0 mg/mL) and phenol (5.5 mg/mL). Participants performed 10 injections with each device in alternate body regions, with at least 7 minutes between each injection. Five different volumes of placebo solution were injected by each participant (40, 100, 200, 400, 600  $\mu$ L). The volumes were equivalent to 4-, 10-, 20-, 40- and 60-unit (U) doses of 100 U/mL insulin. All injections with the first pen-injector were completed before switching to the second pen-injector. Participants were observed throughout the study by the investigators.

## 2.3 | Randomization

The sequence of pen-injector (DV3316 or FlexPen), body region (abdomen or thigh), body side (left or right) and volume was varied according to randomization procedures. Not all conceivable sequences were permissible. A pre-selected set of 320 sequences was generated beforehand and each participant was randomly assigned a sequence at randomization.

## 2.4 | Assessments

The primary endpoint of the study was injection success, as evaluated on a yes/no basis by the investigator. For DV3316, an injection was defined as successful if the dose counter returned to zero before removing the needle from the skin. For FlexPen, an injection was defined as successful if the needle was held in the skin for at least 6 seconds after the dose counter reached zero, according to the instructions for use.

Reaction time, the time from end-of-dose click until the pen-injector was removed from the injection site, was determined for DV3316. The time was measured between two distinct click sounds from the dose activation mechanism using audio analysis.

Leakage at the injection site was assessed by the amount of fluid absorbed onto a filter paper 2 minutes after each injection. The size of the wet spot on the filter paper was visually compared with a leakage reference scale and roughly translated into a volume of leakage.

After each injection, participant confidence in the delivery of a full dose was assessed on a 5-point scale (1 = "not at all confident", 5 = "extremely confident"), and pain was recorded on an electronic visual analogue scale (VAS) ranging from 0 to 100 (0 = "no pain" and 100 = "pain as bad as it could be").

Participant-reported experience and preference was assessed using a selection of questions from the validated Treatment-Related Impact Measure-Diabetes (TRIM-D) device on ease of learning to use, burden of size and physical discomfort, and confidence in correct use and correct dose delivery,<sup>13</sup> as well as study-specific device preference questionnaires. To evaluate both pen-injectors independently of each other, participants were asked to complete the modified TRIM-D device and a questionnaire assessing pain by electronic VAS (0 = "no pain" to 100 = "pain as bad as it could be") after completion of all injections with the first pen-injector (10 injections) and again after completion of all injections with the second pen-injector (10 injections). Participants were asked to complete a second questionnaire assessing device preference after completion of all injections with both pen-injectors (20 injections).

Local injection-site reactions (ISRs; subcutaneous bleeding, haemorrhage, bruising, erythema formation and oedema formation) were assessed by investigators approximately 10 minutes and 1 hour after each injection. ISRs were graded from 0 to 4 (0 = none, 1 = very mild, 2 = well-defined, 3 = moderate, 4 = severe). All adverse events or adverse device events observed by the investigator or reported spontaneously by the participants were to be recorded.

## 2.5 | Data analysis

All endpoints were analysed using descriptive statistics only. As DV3316 is an early prototype pen-injector, data associated with technical complaints were excluded from the analysis of performance endpoints assessed after each injection, but were included in the analysis of safety endpoints. No values were altered, imputed, inserted or excluded for other reasons.

The full analysis set (FAS) included all randomized participants who performed at least one injection attempt with either pen-injector. The safety analysis set (SAS) included all participants who performed at least one injection attempt with either pen-injector.

## 3 | RESULTS

### 3.1 | Baseline characteristics

Of the 169 screened participants, 150 with T1D (50.7%) or T2D (49.3%) were randomized and exposed to both pen-injectors. All

injections performed by one participant with DV3316 were associated with a technical complaint related to the dosing mechanism and were removed from the analyses of injection success, participant confidence, leakage, and pain assessed after each injection (injection success, subject confidence, and leakage: DV3316,  $N = 149$ ; FlexPen,  $N = 150$ ; pain assessed after each injection: DV3316,  $N = 149$ ; FlexPen,  $N = 149$ ). For pain assessed after each injection, VAS scores from one participant with FlexPen were not recorded because of investigator error (DV3316,  $N = 149$ ; FlexPen,  $N = 149$ ). One participant did not respond to the TRIM-D device for FlexPen, and one participant did not respond to the pain electronic VAS performed for each pen-injector for FlexPen (TRIM-D device and pain for each pen-injector: DV3316,  $N = 150$ ; FlexPen,  $N = 149$ ).

The mean participant age was 52 years and the mean duration of diabetes was 16 years. Diabetic retinopathy was reported in 4.7% of participants ( $N = 7$ ), and diabetic neuropathy was reported in 1.3% of participants ( $N = 2$ ). No participant reported diabetic nephropathy, macroangiopathy (including peripheral vascular disease) or lipodystrophy. All randomized participants were using pen-injectors to deliver their daily antidiabetic drugs, and 24% were currently using FlexPen (Table 1).

### 3.2 | Injection success

Injection success was high with both pen-injectors, with a success rate of 97.0% with DV3316 (1424 successful injections out of 1468 attempts,  $N = 149$ ) and 99.7% (1493 successful injections out of 1497 attempts,  $N = 150$ ) with FlexPen (Table 2). With each pen-injector, injection success was similar between all five injection volumes (40–600  $\mu\text{L}$ ) and between all injections in the abdomen and in the thigh. The observed mean reaction time for successful injection attempts with DV3316 was 1338 milliseconds (median [min.; max.] 1074 [202; 21452]; 1105 successful injection attempts,  $N = 146$ ).

### 3.3 | Leakage

Among successful injection attempts, fewer leakage episodes were observed with DV3316 (112 of 1424 successful injections [7.9%],  $N = 149$ ) than with FlexPen (323 of 1493 successful injections [21.6%],  $N = 150$ ). With both pen-injectors, the number of leakage episodes increased with injection volume. Geometric mean leakage volume among successful injections with non-zero leakage was similar with both pen-injectors (0.4 vs 0.5  $\mu\text{L}$  for DV3316 and FlexPen, respectively). Between the 40 and 600- $\mu\text{L}$  dose volumes, the percentage of successful injections with non-zero leakage increased from 3.2% to 13.1% with DV3316 and from 12.3% to 36.3% with FlexPen.

### 3.4 | Participant confidence

Overall, participants were “extremely confident” (the highest reportable score of confidence) with full dose delivery in 88% of all successful injections with DV3316 (1298 out of 1467 injections,  $N = 149$ ) and in 81% of all successful injections with FlexPen (1218 out of 1497 injections,  $N = 150$ ) (Figure 2A). Participant confidence with DV3316 vs FlexPen was similar, comparing participants who were

currently using FlexPen (307 out of 355 injections [86%],  $N = 36$  vs 280 out of 360 injections [78%],  $N = 36$  scored as “extremely confident”) with participants who were not using FlexPen (991 out of 1112 injections [89%],  $N = 113$  vs 938 out of 1137 injections [82%],  $N = 114$  scored as “extremely confident”). When injecting into the abdomen and thigh, 89% (654 out of 733 injections,  $N = 149$ ) and 88% of successful injections (644 out of 734 injections,  $N = 149$ ) with DV3316 were scored as “extremely confident,” compared with 85% (635 out of 748 injections,  $N = 150$ ) and 78% (582 out of 748 injections,  $N = 150$ ) with FlexPen, respectively.

**TABLE 1** Baseline characteristics

	All participants $N = 150$
Age, years	52 (14) [18;74]
Male, $n$ (%)	101 (67.3)
Female, $n$ (%)	49 (32.7)
Body weight, kg	92.5 (19.1) [54.0;145.0]
BMI, $\text{kg}/\text{m}^2$	30.3 (5.5) [20.3;44.4]
BMI category, $n$ (%)	
Normal: $\geq 18.5$ to $< 25$ $\text{kg}/\text{m}^2$	24 (16.0)
Overweight: $\geq 25$ to $< 30$ $\text{kg}/\text{m}^2$	55 (36.7)
Obese: $\geq 30$ $\text{kg}/\text{m}^2$	71 (47.3)
Duration of diabetes, years	16.3 (11.4) [1.1;53.4]
Diabetes type, $n$ (%)	
Type 1	76 (50.7)
Type 2	74 (49.3)
Current diabetes treatment device, $n$ (%) <sup>a</sup>	
FlexPen (Novo Nordisk)	36 (24.0)
FlexTouch (Novo Nordisk)	6 (4.0)
Byetta pen (AstraZeneca)	2 (1.3)
HumaPen Luxura (Eli Lilly)	18 (12.0)
HumaPen (other) (Eli Lilly)	16 (10.7)
KwikPen (Eli Lilly)	9 (6.0)
NovoPen 3 (Novo Nordisk)	8 (5.3)
NovoPen 4 (Novo Nordisk)	27 (18.0)
NovoPen (other) (Novo Nordisk)	19 (12.7)
SoloStar (Sanofi)	51 (34.0)
BerliPen (Berlin-Chemie)	8 (5.3)
CliKSTAR (Sanofi)	10 (6.7)
DIAPEN (Haselmeier)	2 (1.3)
InnoLet (Novo Nordisk)	1 (0.7)
JuniorSTAR (Sanofi)	2 (1.3)
TactiPen (Sanofi)	8 (5.3)
Unknown pen-injector type (Eli Lilly)	3 (2.0)
Vial and syringe	0 (0.0)

Abbreviations: BMI, body mass index; FAS, full analysis set;  $N$ , number of participants. Data are mean (sd) [min;max], unless otherwise stated.

<sup>a</sup> Some participants were using more than one pen-injector device to administer their diabetes treatment.

### 3.5 | Pain perception

Most pain scores assessed after each injection were at the lower end of the electronic VAS scale (90th percentiles were 14 and 17 with DV3316 and FlexPen, respectively; Figure 2B). The median pain score assessed after each injection was 3 with DV3316 and 4 with FlexPen. The median pain score assessed after all injections were completed with each device was 4 for DV3316 and 5 for FlexPen (90th percentiles were 14 and 28 with DV3316 and FlexPen, respectively).

### 3.6 | Device preference questionnaires

After using each pen-injector, participants were asked to score their experience using selected questions from the TRIM-D device on "ease of learning to use," "burden of size," "burden of physical discomfort," "confidence in correct delivery of insulin dose" and "confidence in proper use" (Table 3A). Overall, 87% of participants responded that DV3316 was either "extremely" or "very" easy to learn to use, vs 95% for FlexPen. These respondents included those currently using FlexPen. While 77% of participants were "not at all bothered" by the size of FlexPen, 44% answered the same regarding DV3316. The majority of participants were "not at all bothered" with the physical discomfort related to DV3316 (71%) or FlexPen (70%). After all injections with DV3316, 89% of participants responded that they were either "extremely" or "very" confident the correct dose had been delivered, vs 81% for FlexPen. Overall, 87% of participants responded that they were either "extremely" or "very" confident they were using DV3316 properly compared with 95% with FlexPen.

After all injections were completed, 55% of participants stated an overall preference for DV3316 and 21% stated a preference for FlexPen (18% of participants responded "either" and 6% responded "neither" to the overall device preference questionnaire; Table 3B). A preference for DV3316 over FlexPen was reported by both those currently using FlexPen (47% vs 28%,  $N = 36$ ) and those not using FlexPen (58% vs 18%,  $N = 114$ ).

**TABLE 2** Injection success as evaluated by the investigator

	DV3316				FlexPen			
	N	n	s	%	N	n	s	%
Volume of injection <sup>a</sup> (all body regions)								
40 µL	149	293	284	96.9	150	300	300	100.0
100 µL	149	295	289	98.0	150	300	299	99.7
200 µL	149	295	286	96.9	150	300	298	99.3
400 µL	149	292	275	94.2	150	297	296	99.7
600 µL	149	293	290	99.0	150	300	300	100.0
Abdomen (all volumes)	149	734	711	96.9	150	748	745	99.6
Thigh (all volumes)	149	734	713	97.1	150	748	747	99.9
Total (all regions, all volumes)	149	1468	1424	97.0	150	1497	1493	99.7

Abbreviations: %, percentage of successful injection attempts =  $100 \times (s/n)$ ; N, number of participants contributing to the success evaluation; n, number of injection attempts contributing to the success evaluation; s, number of injection attempts evaluated as successful. For DV3316, an injection was defined as successful if the dose counter returned to zero before removing the needle from the skin. For FlexPen, an injection was defined as successful if the needle was held in the skin for at least 6 seconds after the dose counter reached zero. All injections performed by one participant with DV3316 were associated with a technical complaint, and were removed from the analyses (DV3316,  $N = 149$ ; FlexPen,  $N = 150$ ).

<sup>a</sup> Ten microliters volume is equal to 1 unit of 100 units/mL insulin.

### 3.7 | Safety assessments and technical complaints

For injection attempts assessed after 10 minutes, 217 ISRs were observed with DV3316 ( $n = 1499$ ) and 358 with FlexPen ( $n = 1500$ ). Of these, 10 ISRs with DV3316 and 15 ISRs with FlexPen were assessed as grade 2 ("well-defined"), with the remainder assessed as grade 1 ("very mild"). No grade 3 or 4 ("moderate" or "severe") ISRs were observed. The majority of ISRs were classed as haemorrhage and erythema formation. For DV3316, 135 episodes of haemorrhage were observed in 73 participants and 66 episodes of erythema were observed in 31 participants. For FlexPen, 213 episodes of haemorrhage were observed in 83 participants and 109 episodes of erythema were observed in 48 participants. Most haemorrhage and erythema ISRs had resolved after 1 hour. No adverse events or adverse device effects were observed.

A total of 24 technical complaints were reported by 22 participants: 20 related to DV3316, two related to FlexPen and two related to the needle. The majority of the complaints related to DV3316 and the two complaints related to FlexPen were attributable to issues with the dosing mechanism. Of the 20 technical complaints related to DV3316, five were determined to be related to a minor assembly fault. For the remaining 15 complaints, no irregularities were detected with the device and they were ascribed to use error. The technical complaints related to the needle were attributable to bent needles.

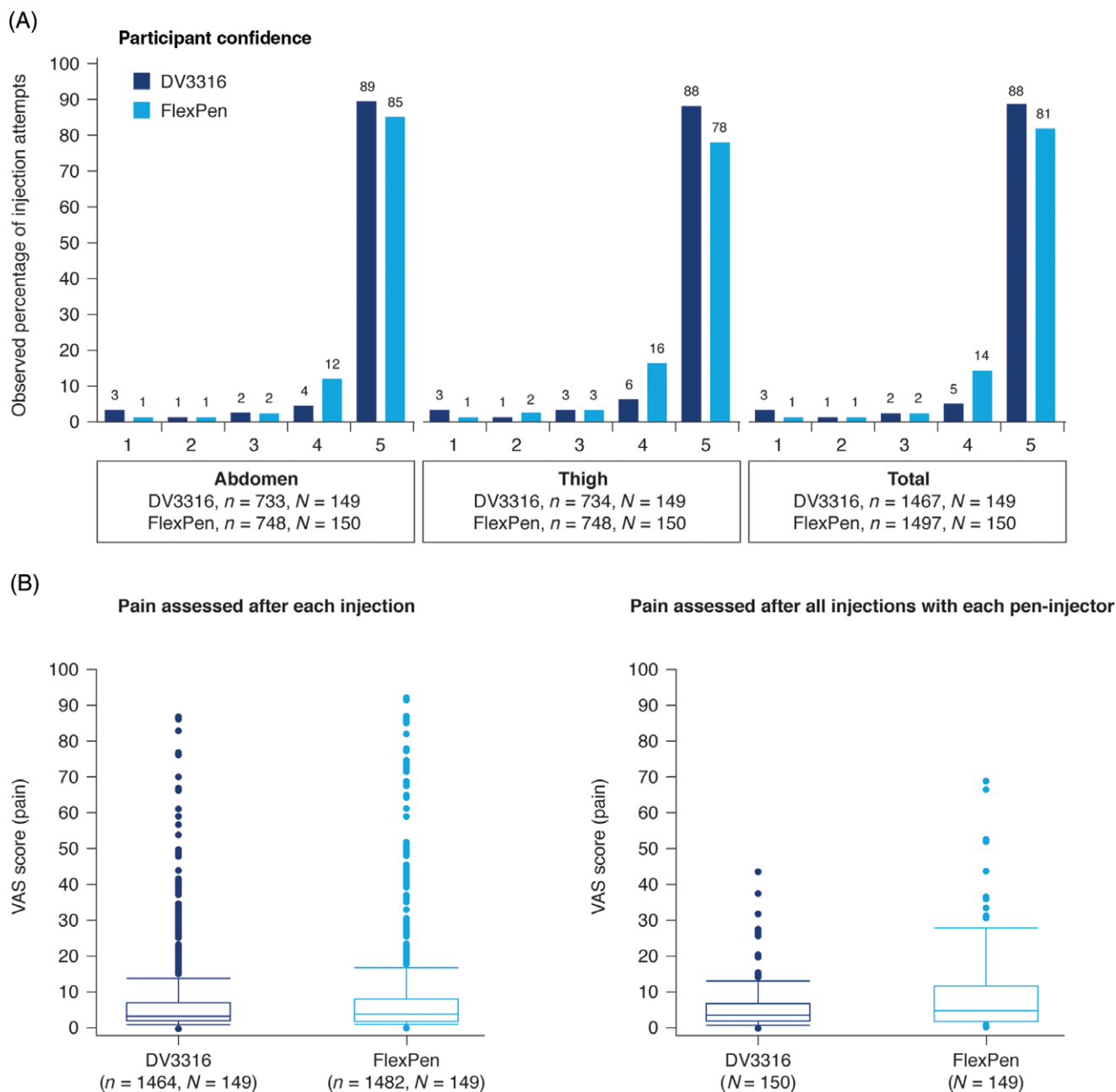
## 4 | DISCUSSION

In the present randomized clinical trial we assessed injection success and user perception of DV3316, a prototype, multiple-use, pen-injector with a shield-triggered injection mechanism. Injection success rate with DV3316 was 97.0%. This high success rate was achieved despite the participants' unfamiliarity with the new mechanism and injection procedure, but was lower than the 99.7% success rate achieved with the widely used FlexPen pen-injector.

The majority of participants experienced no leakage of fluid out of the skin after successful injection with either pen-injector. With both pen-injectors, the mean volume of any leakage was small ( $\sim 0.5 \mu\text{L}$ ) and within an expected range.<sup>14</sup> It is therefore unlikely that the small volume of leakage would have a meaningful pharmacological impact in a clinical setting. Interestingly, fewer instances of leakage were experienced with DV3316 than with FlexPen. Differences in needle dwelling time between the devices may affect the number of instances of leakage. After the counter reached zero, participants were required to hold the FlexPen needle in the skin for 6 seconds, whereas participants were not required to wait with DV3316. The observed mean time between the end-of-dose click and removal of DV3316 from the injection site was 1.3 seconds; however, this value

should be interpreted with caution because of technical difficulties interpreting the audio recordings of the end-of-dose clicks, especially after injection of small doses. Differences in injection pressure and activation force may also influence leakage; however, this trial was not designed to assess these factors and the reasons for this observation require further investigation.

Despite participants using the new shield-triggered mechanism for the first time, confidence in full dose delivery after each injection with DV3316 was as high as it was with FlexPen. DV3316 is an early prototype device and thus the higher number of technical complaints reported with DV3316 was not unexpected. The technical complaints may, however, have had an impact on confidence in the new injection mechanism.



**FIGURE 2** A, Subject's confidence in the delivery of a correct dose was assessed after each injection using a scale from 1 to 5, where 1 was 'not at all confident' and 5 was 'extremely confident'. B, assessment of pain with DV3316 and FlexPen. The outer ends of the whiskers of the box plots represent the 10th and the 90th percentiles, respectively, and the dots represent reported visual analogue scale (VAS) scores at each end of the range. Abbreviations: N, number of participants contributing to the evaluation; n, number of injection attempts contributing to the evaluation

The majority of the technical complaints for DV3316 were related to the dosing mechanism; some were attributable to minor assembly faults, and others were ascribed to use error. Use error complaints may be attributable to the participants' unfamiliarity with the DV3316 injection mechanism, and lack of understanding of the training materials.

Pain was assessed by electronic VAS after each injection and once after all injections were completed with each pen-injector. The median pain scores were low, similar in the two electronic VAS assessments and similar between the two pen-injectors. As the same gauge and length of needle were used with both pen-injectors, this similarity in perceived pain is related to the two dosing mechanisms. A number of injections with both pen-injectors were rated as "very painful" on the electronic VAS scale. Similarly, high ratings have been reported in a previous study of injection pain perception<sup>14</sup> and may depend on the location where the needle is inserted into the skin, as well as each participant's frame of reference.

Since the introduction of pen-injectors almost 30 years ago,<sup>15</sup> studies on patient-reported experiences and preferences, measured by questionnaires, have guided improvements in pen-injector technology. The TRIM-D device is a reliable and validated instrument used to assess treatment-related impact in people with T1D or

T2D,<sup>13,16</sup> and key questions from the TRIM-D device were selected for this study. Results of the questionnaires showed that participants considered DV3316 easy to learn how to use, and were confident using it to perform injections. When asked which of the two pen-injectors they preferred overall, more than half of the participants preferred DV3316 to FlexPen. This highlights that participants had a positive perception of the shield-triggered mechanism. Previous design modifications aimed at improving the ease of pen-injector handling and use have had a positive impact on patient confidence and preference, especially among those with impaired manual dexterity.<sup>10,17,18</sup> In addition, the shield of the DV3316 hides the needle during injection, which in a similar manner to contact-activated figure puncture lancets, may help alleviate anxiety in some people and enhance user acceptability.<sup>19</sup> Overall, a positive perception of a new pen-injector with a shield-triggered mechanism may contribute toward enhanced treatment satisfaction and adherence in patients with diabetes. However, it should be noted that all participants enrolled in this trial had experience in injecting insulin pens and the reasons for the positive perception of DV3316 require further investigation.

No adverse events or adverse device events were observed during this study. Fewer cases of haemorrhage and erythema were

**TABLE 3** Participant-reported experience assessed using A, selected questions from the Treatment-Related Impact Measure-Diabetes device after completion of 10 injections with the first pen-injector and again after completion of 10 injections with the second pen-injector and B, an overall device preference questionnaire after completion of all 20 injections

A, Modified TRIM-D device		Not at all	A little	Somewhat	Very	Extremely
How easy is it to learn how to use your device?	DV3316 (N = 150)	0 (0)	5 (3)	14 (9)	62 (41)	69 (46)
	FlexPen (N = 149)	0 (0)	2 (1)	6 (4)	55 (37)	86 (58)
How bothered are you by the:						
size of your device?	DV3316 (N = 150)	66 (44)	34 (23)	32 (21)	12 (8)	6 (4)
	FlexPen (N = 149)	115 (77)	21 (14)	9 (6)	4 (3)	0 (0)
physical discomfort related to using your device?	DV3316 (N = 150)	106 (71)	23 (15)	14 (9)	6 (4)	1 (1)
	FlexPen (N = 149)	105 (70)	30 (20)	9 (6)	5 (3)	0 (0)
How confident are you that:						
your device delivers the correct, full dose of your medication?	DV3316 (N = 150)	2 (1)	3 (2)	12 (8)	48 (32)	85 (57)
	FlexPen (N = 149)	3 (2)	5 (3)	21 (14)	48 (32)	72 (48)
you are using the device properly?	DV3316 (N = 150)	1 (1)	3 (2)	15 (10)	49 (33)	82 (55)
	FlexPen (N = 149)	2 (1)	2 (1)	3 (2)	42 (28)	100 (67)
B, Device preference questionnaire			DV3316	FlexPen	Either	Neither
Overall, which of the two pen-injectors do you prefer?	All participants (N = 150)	83 (55)	31 (21)	27 (18)	9 (6)	
	Participants currently using FlexPen (N = 36)	17 (47)	10 (28)	9 (25)	0 (0)	
	Participants currently NOT using FlexPen (N = 114)	66 (58)	21 (18)	18 (16)	9 (8)	

Abbreviations: N, number of participants contributing to the evaluation; TRIM-D, Treatment-Related Impact Measure-Diabetes. Data are reported as number of participants (%). One participant did not respond to the TRIM-D device for FlexPen (DV3316, N = 150; FlexPen, N = 149).

observed after injection with DV3316 than with FlexPen. Further research is needed to confirm this finding, and to investigate if it is a consequence of the different injection mechanisms.

A limitation of the present study was the artificial setting, as the shield-triggered pen-injector was used under the supervision of study investigators. This may have positively influenced the injection success rate and participant confidence. Additionally, participants may have preferred the shield-triggered pen-injector just because it is a new concept. The study was of an unblinded, open-label design by necessity because of the distinctly different devices.

This exploratory study shows that injection-experienced patients can achieve a high injection success rate with a shield-triggered pen-injector. The study participants reported an overall preference for the shield-triggered mechanism compared with FlexPen, with a similar confidence in full dose delivery and perception of injection pain.

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## Conflict of interest

E.Z. has received travel grants and speaker fees from Dance Bio-pharm, Novo Nordisk and Roche Diabetes Care. T.H. is shareholder of Profil, a private research institute that received research funds from Adocia, Biocon, Dance Pharmaceuticals, Eli Lilly, Johnson & Johnson, Julphar, Medimmune, Mylan, Nordic Bioscience, Novo Nordisk, Poxel, Roche Diagnostics, Saniona, Sanofi, Senseonics, Sky-Pharma and Zealand Pharma. In addition, T.H. received speaker honoraria from Eli Lilly, Novo Nordisk and Sanofi and fees for the participation in advisory boards from Novo Nordisk. H.-V.C. has no disclosures to report. L.P.-M. has received travel grants and speaker fees from Novo Nordisk. O.R., T.S., T.R., M.Q. and L.P. are employees of and hold shares in Novo Nordisk.

## Author contributions

All authors made a substantial contribution to the analysis and interpretation of the data and to the writing and revising of the manuscript. All authors reviewed the final version of the manuscript and gave permission to submit. Statistical analysis was provided by T.R.

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