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ORIGINAL ARTICLE

A Randomized, Open-Label, Comparative Crossover Handling Trial between Two Durable Pens in Patients with Type 1 or 2 Diabetes Mellitus

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Abstract

Background:

This open-label, randomized, comparative crossover usability study investigated preference between durable insulin pens, NovoPen® 4 and NovoPen 3, among patients with types 1 and 2 diabetes.

Methods:

In a timed test, 82 current NovoPen 3 users (mean age, 48.5 years) assessed intuitiveness of NovoPen 4. After timed training, this group and 34 insulin-naïve patients (mean age, 61.8 years) were randomized to a handling evaluation of NovoPen 4 followed by NovoPen 3, or *vice versa*, in which participants made three injections into a foam cushion. A device-specific questionnaire was filled out for each pen. A third questionnaire asked participants to compare pens.

Results:

Current NovoPen 3 users completed the intuitive assessment of NovoPen 4 in an average time of 1.94 min (range, 0.57–4.98 min). The training of insulin-naïve patients occurred in slightly less time with NovoPen 4 than with NovoPen 3 but did not reach significance (9.9 versus 11.5 min; $p = .32$). Survey responses showed that both groups had less difficulty and were more confident in handling NovoPen 4 than NovoPen 3; 96.3% of the NovoPen 3 users and 100% of the insulin-naïve group preferred to use NovoPen 4 ($p < .0001$).

Conclusion:

Patients currently using NovoPen 3 or who were insulin naïve expressed a preference for NovoPen 4 in this study, reporting it to be simpler to learn and easier to use than NovoPen 3. NovoPen 4 may help facilitate insulin therapy among newly diagnosed patients and potentially improve adherence and treatment satisfaction among current NovoPen 3 users.

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Abbreviations: (DNE) diabetes nurse educator, (T1DM) type 1 diabetes mellitus, (T2DM) type 2 diabetes mellitus

Keywords: diabetes mellitus, insulin pen, NovoPen, preference

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Introduction

Insulin therapy is a standard treatment for diabetes, essential in patients with type 1 diabetes mellitus (T1DM) and frequently necessary in patients with type 2 diabetes mellitus (T2DM) as the condition of their disease progresses.[1]

Despite the confirmed benefits of insulin therapy for patients with T2DM,[2–10] there is a resistance on the part of both patients and physicians to begin insulin therapy for the treatment of T2DM.[11] This resistance has been termed "psychological insulin resistance," which is a general term encompassing many psychological factors, such as needle anxiety, social embarrassment, and fears of the risks of weight gain and hypoglycemia.[11] Even though the consequences can be negative, psychological insulin resistance appears also to affect adherence with insulin treatment plans. One study estimated that only 63% of patients with T2DM took their insulin doses as prescribed.[12] The Diabetes Attitudes, Wishes, and Needs (or DAWN) study has indicated that the way to overcome the patient's and physician's psychological barriers to initiating insulin therapy is through innovative management techniques and improving insulin delivery systems.[11]

Compared with conventional vial and syringe delivery, pen devices have simplified the administration of insulin, and patients express a preference for using them.[13–17] Users have reported an improved quality of life, greater ability to adhere to treatment regimens, and more accurate dosing when self-injecting insulin with a pen instead of a syringe.[18,19]

The durable insulin pen NovoPen® 4 (Novo Nordisk A/S, Bagsværd, Denmark) was designed to enhance the ease with which health care professionals instruct patients in its use and the ability of patients to handle it, compared with NovoPen 3. Both pens have been shown to deliver accurate doses of insulin over a period of 5 years under simulated testing conditions in which pens were also exposed to mechanical and temperature stresses that could occur in daily patient use.[20,21] The changes in NovoPen 4 compared with NovoPen 3 include ability for the selector dial to be turned backward and forward without wasting insulin when adjusting dosage; automatic zero positioning of the dosage scale after injection; inability to select more insulin than what remains in the cartridge; audible end-of-dose click; easy to push back piston rod; bayonet interface for the two parts of the pen that require only a quarter turn, simplifying cartridge replacement; easier-to-read dosage scale with numbers more than four times larger ($p < .001$);[22] reduced injection force of approximately 50% throughout the specified lifetime of the pen;[22] and, lastly, a noticeably smaller pen size.

The aim of this trial was to investigate which insulin pen, NovoPen 4 or NovoPen 3, was preferred by patients with T1DM or T2DM by comparing how much time was required to train participants in the use of either pen and how the participants assessed intuitiveness, performance, acceptance, and handling of the pens. A secondary goal was to determine any adverse device effects.

Methods

Ethics Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committees of the Prevention Center University Hospital in Salzburg and Servizio di Diabetologia Azienda USL in Reggio Emilia. All patients gave written consent before being enrolled in the study. They also gave verbal informed consent prior to each testing step.

Patients

A total of 117 patients with T1DM or T2DM were enrolled in this open-label, crossover handling test in two countries. They were recruited to study centers in either Austria or Italy. All patients were adults at least 18 years old, and they currently used NovoPen 3 ($n = 82$) or vial and syringe ($n = 1$) or were insulin naïve ($n = 34$). No NovoPen 3 user had previous experience with NovoPen 4. Fifty-one of the patients had T1DM and 65 had T2DM. Complete demographic information about the patients, with the exception of the sole vial and syringe user whose responses were not included in the study results, appears in **Table 1**.

Potential participants were excluded if they were suspected of abusing alcohol or drugs; were judged to have significant visual impairment, which was considered as having difficulty in reading and performing daily tasks due to lack of vision; were judged to have significant dexterity impairment, which was considered as difficulty in performing daily tasks due to motor dysfunction caused by conditions such as neuropathy, arthritis, familiar

tremor, Parkinson's disease, stroke-induced partial paralysis, or generalized lupus; were suffering from a serious chronic disease that made completion of the study unlikely; or had a mental incapacity, unwillingness, or language barrier that prevented adequate mutual understanding or cooperation.

Table 1.
Patient Demographics

	NovoPen 3 users	Insulin-naïve
Participants (*N*)	82	34
Gender		
Unknown (*n*)	2	1
Male (*n*)	46	14
Female (*n*)	34	19
Age group		
18 to <25 (*n*)	6	0
25 to <35 (*n*)	8	1
35 to <45 (*n*)	23	2
45 to <55 (*n*)	16	4
55 to <65 (*n*)	17	12
65 to <75 (*n*)	9	12
≥75 (*n*)	3	3
Mean age [years (standard deviation)]	48.5 (1.6)	61.8 (1.9)
Diabetes diagnosis		
T1DM (*n*)	51	0
T2DM (*n*)	31	34
Study center		
Austria (*n*)	63	34
Italy (*n*)	19	0

Study Design

In the first part of the study, all participants currently using NovoPen 3 (n = 82) were given a NovoPen 4 intuitiveness assessment with a maximum 5 min time limit by a diabetes nurse educator (DNE). Participants were handed a NovoPen 4 device containing an empty Penfill® (Novo Nordisk A/S) cartridge with no needle attached and then asked to replace the cartridge, attach a NovoFine® (Novo Nordisk A/S) 31 G needle, select 20 U, and deliver the selected dose into a foam cushion. The DNE recorded the amount of time needed if the patient successfully completed the sequence of tasks within 5 min. The patient's attempt was recorded as unsuccessful if the allotted time passed before completion of the tasks.

For the second part of the study, the two groups of patients—NovoPen 3 users and insulin-naïve patients—were each divided in half. One half of each group first evaluated NovoPen 3 then NovoPen 4, while the other half evaluated the pens in the reverse order (**Figure 1**). Patients were instructed in the use of each pen before completing a series of tasks unassisted. Current NovoPen 3 users, however, who were to test NovoPen 3 did not receive instruction on use of this pen. The amount of time required for training patients was recorded. To successfully perform the tasks, the patient had to insert a Penfill cartridge into the pen; attach a NovoFine 31 G needle; prime the pen; deliver three doses of 6, 25, and

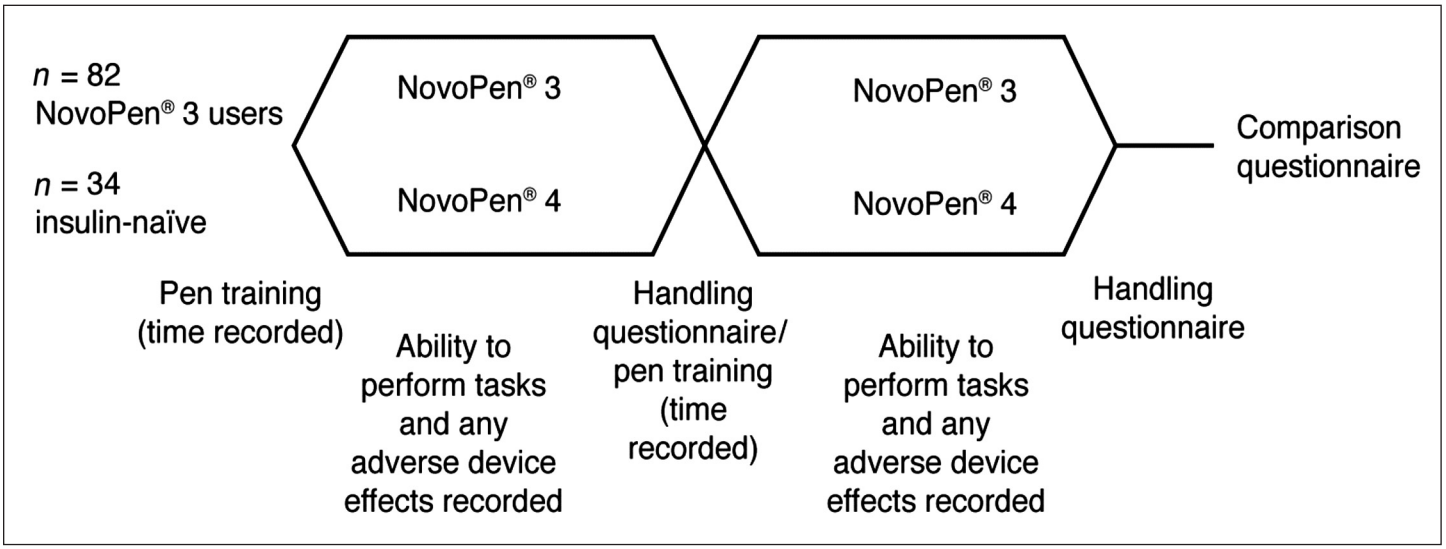

Figure 1. Flow chart of patient assessment of NovoPen 4 versus NovoPen 3.

60 U into a foam cushion; and correct a dosage amount from 30 to 25 U. The DNE recorded whether the patient completed the tasks successfully without assistance and if there were any adverse device effects. The patient then completed a questionnaire about that specific device before repeating the process with the other pen. After assessing that device, the patient completed a questionnaire comparing both devices.

The device-specific questionnaires were identical, except that the one for evaluating NovoPen 4 had three additional questions about the unique features of NovoPen 4 relating to its inability to have a dosage set higher than the amount remaining in the cartridge and the audible end-of-dose click. The 20 questions that the questionnaires had in common asked patients to rate various aspects of using the pens on a five-point scale, including how easy it was to set the required dose, press the injection button, change the Penfill cartridge, and learn how to use the device. Patients were also asked to assess the pens' appearance. **Table 2** contains all questions asked on the two device-specific questionnaires. In the comparative questionnaire at the end of the study, patients were asked to identify which pen was easiest to operate for a variety of handling characteristics and which pen they would prefer to use. Three answer choices were possible

Table 2.
Results of Device-Specific Questionnaires for NovoPen 3 and NovoPen 4.

		NovoPen 3 questionnaire responses		NovoPen 4 questionnaire responses	
		Current NovoPen 3 users, *N* (%)	Insulin-naïve patients, *N* (%)	Current NovoPen 3 users, *N* (%)	Insulin-naïve patients, *N* (%)
I. Setting the dose					
1. How easy/difficult is it to set up the required dose?	Very easy Easy Neither easy nor difficult Difficult Very difficult	25 (30.5) 40 (48.8) 12 (14.6) 5 (6.1) 0	1 (2.9) 13 (38.2) 16 (47.1) 4 (11.8) 0	72 (87.8) 10 (12.2) 0 0 0	19 (55.9) 15 (44.1) 0 0 0
2. How easy/difficult is it to turn the dose selector when choosing the right dose?	Very easy Easy Neither easy nor difficult Difficult Very difficult	33 (40.2) 31 (37.8) 15 (18.3) 2 (2.4) 0	2 (5.9) 14 (41.2) 13 (38.2) 5 (14.7) 0	72 (87.8) 10 (12.2) 0 0 0	16 (47.1) 16 (47.1) 2 (5.9) 0 0
3. How easy/difficult is it to read the dose scale (numbers in the dose window)?	Very easy Easy Neither easy nor difficult Difficult Very difficult	11 (13.4) 33 (40.2) 23 (28.0) 14 (17.1) 1 (1.2)	1 (2.9) 8 (23.5) 11 (32.4) 12 (35.3) 2 (5.9)	79 (96.3) 2 (2.4) 1 (1.2) 0 0	24 (70.6) 10 (29.4) 0 0 0
4. How easy/difficult is it to correct the dialed dose?	Very easy Easy Neither easy nor difficult Difficult Very difficult	9 (11.0) 28 (34.1) 22 (26.8) 19 (23.2) 4 (4.9)	0 6 (17.6) 9 (26.5) 12 (35.3) 7 (20.6)	67 (81.7) 14 (17.1) 1 (1.2) 0 0	24 (70.6) 9 (26.5) 1 (2.9) 0 0
5. How easy/difficult is it to feel clicks as dialing the dose?	Very easy Easy Neither easy nor difficult Difficult Very difficult	9 (11.0) 32 (39.0) 32 (39.0) 8 (9.8) 1 (1.2)	1 (2.9) 9 (26.5) 19 (55.9) 4 (11.8) 1 (2.9)	43 (52.4) 31 (37.8) 8 (9.8) 0 0	14 (41.2) 15 (44.1) 5 (14.7) 0 0
6. How easy/difficult is it to hear clicks as dialing the dose?	Very easy Easy Neither easy nor difficult Difficult Very difficult	31 (37.8) 11 (13.4) 26 (31.7) 10 (12.2) 3 (3.7)	6 (17.6) 3 (8.8) 17 (50.0) 7 (20.6) 1 (2.9)	59 (72.0) 21 (25.6) 1 (1.2) 1 (1.2) 0	15 (44.1) 13 (38.2) 6 (17.6) 0 0
7. How confident are you that you set the correct dose every time?	Very confident Pretty confident Moderately confident Slightly confident Not at all confident	35 (42.7) 38 (46.3) 8 (9.8) 1 (1.2) 0	3 (8.8) 16 (47.1) 12 (35.3) 3 (8.8) 0	66 (80.5) 16 (19.5) 0 0 0	15 (44.1) 18 (52.9) 1 (2.9) 0 0

(Continued) →

Table 2. Continued

		NovoPen 3 questionnaire responses		NovoPen 4 questionnaire responses	
		Current NovoPen 3 users, *N* (%)	Insulin-naïve patients, *N* (%)	Current NovoPen 3 users, *N* (%)	Insulin-naïve patients, *N* (%)
II. Injecting the dose					
8. How easy/difficult is it to push down the injection button?	Very easy Easy Neither easy nor difficult Difficult Very difficult	27 (32.9) 33 (40.2) 14 (17.1) 7 (8.5) 1 (1.2)	1 (2.9) 14 (41.2) 15 (44.1) 4 (11.8) 0	61 (74.4) 21 (25.6) 0 0 0	16 (47.1) 18 (52.9) 0 0 0
9. How easy/difficult is it to know if the push button has been pushed completely down?	Very easy Easy Neither easy nor difficult Difficult Very difficult	25 (30.5) 27 (32.9) 19 (23.2) 11 (13.4) 0	1 (2.9) 17 (50.0) 12 (35.3) 4 (11.8) 0	64 (78.0) 17 (20.7) 1 (1.2) 0 0	22 (64.7) 9 (26.5) 3 (8.8) 0 0
10. How easy/difficult is it to hold the pen when injecting?	Very easy Easy Neither easy nor difficult Difficult Very difficult	23 (28.0) 37 (45.1) 17 (20.7) 5 (6.1) 0	5 (14.7) 16 (47.1) 12 (35.3) 1 (2.9) 0	48 (58.5) 33 (40.2) 1 (1.2) 0 0	12 (35.3) 20 (58.8) 2 (5.9) 0 0
11. How confident are you that you injected the correct amount every time?	Very confident Pretty confident Moderately confident Slightly confident Not at all confident	28 (34.1) 45 (54.9) 8 (9.8) 1 (1.2) 0	3 (8.8) 18 (52.9) 12 (35.3) 1 (2.9) 0	62 (75.6) 20 (24.4) 0 0 0	15 (44.1) 18 (52.9) 1 (2.9) 0 0
III. Changing the Penfill cartridge					
12. How easy/difficult is it to change the Penfill cartridge in your pen (including resetting of the piston rod and screwing on the Penfill holder)?	Very easy Easy Neither easy nor difficult Difficult Very difficult	10 (12.2) 30 (36.6) 30 (36.6) 12 (14.6) 0	2 (5.9) 9 (26.5) 12 (35.3) 10 (29.4) 1 (2.9)	75 (91.5) 7 (8.5) 0 0 0	15 (44.1) 15 (44.1) 4 (11.8) 0 0
13. How easy/difficult is it to perform the air shot (priming) before the injection?	Very easy Easy Neither easy nor difficult Difficult Very difficult	16 (19.5) 37 (45.1) 24 (29.3) 4 (4.9) 1 (1.2)	6 (17.6) 17 (50.0) 10 (29.4) 1 (2.9) 0	58 (70.7) 19 (23.2) 4 (4.9) 1 (1.2) 0	17 (50.0) 13 (38.2) 4 (11.8) 0 0
14. How confident are you that you performed the air shot procedure (priming) correctly?	Very confident Pretty confident Moderately confident Slightly confident Not at all confident	21 (25.6) 46 (56.1) 13 (15.9) 2 (2.4) 0	3 (8.8) 26 (76.5) 5 (14.7) 0 0	45 (54.9) 32 (39.0) 5 (6.1) 0 0	13 (38.2) 21 (61.8) 0 0 0
IV. Overall ease of use—convenience—of the pen					
15. Overall, how convenient is the handling of NovoPen 3/ NovoPen 4 (e.g., is it easy to hold, does it fit nicely in the hand, etc.)?	Very convenient Pretty convenient Moderately convenient Slightly convenient Not at all convenient	26 (31.7) 41 (50.0) 13 (15.9) 2 (2.4) 0	4 (11.8) 25 (73.5) 4 (11.8) 1 (2.9) 0	59 (72.0) 23 (28.0) 0 0 0	18 (52.9) 16 (47.1) 0 0 0
VI. Appearance of the pen					
16. How appropriate do you find the appearance of NovoPen 3/NovoPen 4?	Very appropriate Pretty appropriate Moderately appropriate Slightly appropriate Not at all appropriate	24 (29.3) 46 (56.1) 10 (12.2) 2 (2.4) 0	6 (17.6) 25 (73.5) 3 (8.8) 0 0	59 (72.0) 21 (25.6) 2 (2.4) 0 0	23 (67.6) 11 (32.4) 0 0 0

(Continued) →

Table 2. Continued

		NovoPen 3 questionnaire responses		NovoPen 4 questionnaire responses	
		Current NovoPen 3 users, *N* (%)	Insulin-naïve patients, *N* (%)	Current NovoPen 3 users, *N* (%)	Insulin-naïve patients, *N* (%)
VI. Appearance of the pen					
17. How appropriate do you find the weight of NovoPen 3/ NovoPen 4?	Very appropriate Pretty appropriate Moderately appropriate Slightly appropriate Not at all appropriate	13 (15.9) 57 (69.5) 9 (11.0) 3 (3.7) 0	5 (14.7) 21 (61.8) 6 (17.6) 2 (5.9) 0	38 (46.3) 39 (47.6) 5 (6.1) 0 0	11 (32.4) 22 (64.7) 1 (2.9) 0 0
18. How appropriate do you find the size of NovoPen 3/ NovoPen 4?	Very appropriate Pretty appropriate Moderately appropriate Slightly appropriate Not at all appropriate	13 (15.9) 53 (64.6) 13 (15.9) 3 (3.7) 0	3 (8.8) 21 (61.8) 10 (29.4) 0 0	47 (57.3) 29 (35.4) 5 (6.1) 0 1 (1.2)	13 (38.2) 19 (55.9) 2 (5.9) 0 0
19. How suitable would NovoPen 3/NovoPen 4 be to use in public?	Very suitable Pretty suitable Moderately suitable Slightly suitable Not at all suitable	27 (32.9) 40 (48.8) 10 (12.2) 4 (4.9) 1 (1.2)	4 (11.8) 22 (64.7) 7 (20.6) 1 (2.9) 0	58 (70.7) 20 (24.4) 3 (3.7) 1 (1.2) 0	13 (38.2) 19 (55.9) 2 (5.9) 0 0
VI. Easiness of learning how to use the pen					
20. Overall, how easy/difficult is it to learn to use NovoPen 3/ NovoPen 4?	Very easy Easy Neither easy nor difficult Difficult Very difficult	31 (37.8) 31 (37.8) 19 (23.2) 0 1 (1.2)	3 (8.8) 8 (23.5) 21 (61.8) 2 (5.9) 0	70 (85.4) 12 (14.6) 0 0 0	12 (35.3) 16 (47.1) 6 (17.6) 0 0
VII. Additional questions					
21. It is not possible to set a dosage higher than what is left in the Penfill cartridge. How useful do you find this feature?	Very useful Pretty useful Moderately useful Slightly useful Not at all useful	n/a	n/a	77 (93.9) 5 (6.1) 0 0 0	24 (70.6) 10 (29.4) 0 0 0
22. How easy was it to hear and/or feel the end-of-dose confirmation “click” with NovoPen 4?	Very easy Easy Neither easy nor difficult Difficult Very difficult	n/a	n/a	51 (62.2) 29 (35.4) 2 (2.4) 0 0	18 (52.9) 15 (44.1) 1 (2.9) 0 0
23. With regards to the end of dose confirmation “click” on NovoPen 4, how useful do you find this feature?	Very useful Pretty useful Moderately useful Slightly useful Not at all useful	n/a	n/a	67 (81.7) 15 (18.3) 0 0 0	28 (82.4) 6 (17.6) 0 0 0

for this questionnaire: one for each pen device, plus one indicating no difference. All questionnaires were translated into the local language.

Test products (both pen devices and insulin cartridges) were provided by Novo Nordisk A/S, Hillerød, Denmark. Adverse device effects monitored during the study included any deficiencies related to the identity, quality, durability, reliability, safety, or performance of either NovoPen 4 or NovoPen 3 that resulted in, or could have resulted in, a serious injury.

Statistical Methods

The primary end point of the trial—preference for using either NovoPen 4 or NovoPen 3—was evaluated by a superiority test, where superiority was claimed if the lower limit of the two-sided 95% confidence interval for the difference in preference between NovoPen 4 and NovoPen 3 was above 0%. The test corresponded to performing a Wald’s test in which no difference in preference was equal to zero. A sample size of 60 patients previously using NovoPen 3 was determined to provide a statistical power of 86% for this test. Difference

in preference between NovoPen 4 and NovoPen 3 was considered significant if $p < .05$. All statistical calculations were performed with Statistical Analysis Software (SAS), version 8.2 (SAS Institute Inc., Cary, NC).

Results

Intuitive Assessment

All 82 current NovoPen 3 users were able to complete the intuitive test for using NovoPen 4 within the 5 min time limit. The average amount of time needed to complete the sequence of tasks that demonstrated the ability to load the newer pen with a cartridge and discharge a 20 U dose into a foam cushion was 1.94 min (range, 0.57–4.98 min).

Training Time and Device-Specific Responses

The average amount of time needed to instruct patients in the insulin-naïve group so that they could successfully complete the series of handling tasks with NovoPen 3 was 11.5 min (range, 4.1–31.8 min). On average, patients required 9.9 min (range, 3.5–22.3 min) to learn how to use NovoPen 4, but the difference in learning times was insignificant ($p = .32$). Current NovoPen 3 users needed an average of 4.9 min (range 2.2–12.6 min) of instruction time before starting the handling tasks with NovoPen 4.

The results of the device-specific questionnaires suggest that, in general, patients in the insulin-naïve group had more difficulty and were less confident in operating both pens than the group of NovoPen 3 users (**Table 2**). For every question from 1 to 20 on both questionnaires, a greater percentage of the NovoPen 3 users responded "very easy," "very confident," and "very appropriate/suitable" than patients in the insulin-naïve group.

Both groups claimed to have less difficulty and were more confident handling NovoPen 4 than NovoPen 3. When asked how easy it was to set the required dose for NovoPen 3, 79.3% of NovoPen 3 users and 41.1% of insulin-naïve patients responded "very easy" or "easy." However, 100% of both groups described setting the dose for NovoPen 4 as "very easy" or "easy." One hundred percent of both groups also considered it "very easy" or "easy" to push down the injection button on NovoPen 4 and thought that, overall, the ease of using this pen was "very convenient" or "pretty convenient." In comparison, 73.1% of NovoPen 3 users and 44.1% of insulin-naïve patients answered that it was "very easy" or "easy" to push down the NovoPen 3 injection button, and 81.7% and 85.3% of each group felt it was "very convenient" or "pretty convenient" to use NovoPen 3. NovoPen 4 was rated easier to learn how to use: 100% of current NovoPen 3 users and 82.4% of the other group claimed it as "very easy" or "easy" to learn, while only 75.6% and 32.3% of the respective groups gave NovoPen 3 such high marks. More than 85% of the subjects in both groups also found the appearance of NovoPen 4 to be "pretty appropriate" or "very appropriate." NovoPen 4 was viewed as having a "very appropriate" appearance by 72.0% and 67.6% by the current NovoPen 3 users and insulin-naïve group, respectively. The corresponding percentages for NovoPen 3 were 29.3% and 17.6%, respectively.

Comparative Responses

When asked to directly compare the two pens, both groups expressed a clear preference for NovoPen 4 (**Figure 2**). The preference in response to all questions was highly significant ($p < .0001$). One hundred percent of insulin-naïve patients and 96.3% of current NovoPen 3 users expressed a preference for NovoPen 4. No participant in this group preferred NovoPen 3 for any of the eight evaluative criteria, although for five criteria, a few participants thought there was no difference between the pens. When asked which device they would recommend to others, 97.6% of current NovoPen 3 users and 97.1% of insulin-naïve patients replied NovoPen 4; 96.3% and 100% of the groups, respectively, said they would prefer to use NovoPen 4.

No adverse effects for either pen were recorded during the handling tests. As only one vial and syringe user was enrolled in the study, responses from this patient were not included in the results.

Discussion

In this handling trial and patient preference evaluation of NovoPen 4 versus NovoPen 3, both current NovoPen 3 users and insulin-naïve patients ranked NovoPen 4 as easier to use and more suitable against a variety of handling criteria. Although the insulin-naïve group did not rate either pen as high as the current NovoPen 3 users did in their responses to the device-specific questions, this difference should be expected, because the insulin-naïve patients had no prior experience with insulin therapy and were less confident operating the pens than the other group. NovoPen 3 users quickly determined without assistance how to use the newer pen, completing the intuitive assessment test in an average of 1.94 min. It took less time for the insulin-naïve patients to be instructed in the sequence of handling tasks for NovoPen 4, compared with the amount of time for

NovoPen 3 (9.9 versus 11.5 min), although the difference did not reach statistical significance. No insulin-naïve patient identified NovoPen 3 as easier to use or preferable in the questionnaire comparing the two pen devices. The study met its primary end point of determining patient preference between the two pen devices by showing that 96.3% of NovoPen 3 users and 100% of insulin-naïve patients preferred to use NovoPen 4. Due to the patient selection criteria in this study, however, the ability to extrapolate results to a wider population is limited. The clinical usefulness of this study's results is also diminished by the use of nonvalidated patient questionnaires.

Although the experience of NovoPen 3 users with this pen device was not controlled for in the analysis of results, our study's main end point showing a preference for NovoPen 4 does not appear to be affected. In fact, the previous use of NovoPen 3 by these users probably explains why there were more "no difference" responses from this group than from insulin-naïve users in the answers to the comparative questionnaire. All insulin-naïve patients considered it easier to set the dose for and read the dosage scale of the NovoPen 4, but in the NovoPen 3 group, 17 and 6 people (20.7% and 7.3%), respectively, replied that there was no difference between the two pens (**Figure 2**, responses to questions 1 and 2). Most likely, the previous experience of NovoPen 3 users influenced their answers.

The results of our study are consistent with the findings of a randomized 12-week study in which 208 patients with diabetes who had been on insulin therapy for more than 1 year compared daily usage of NovoPen

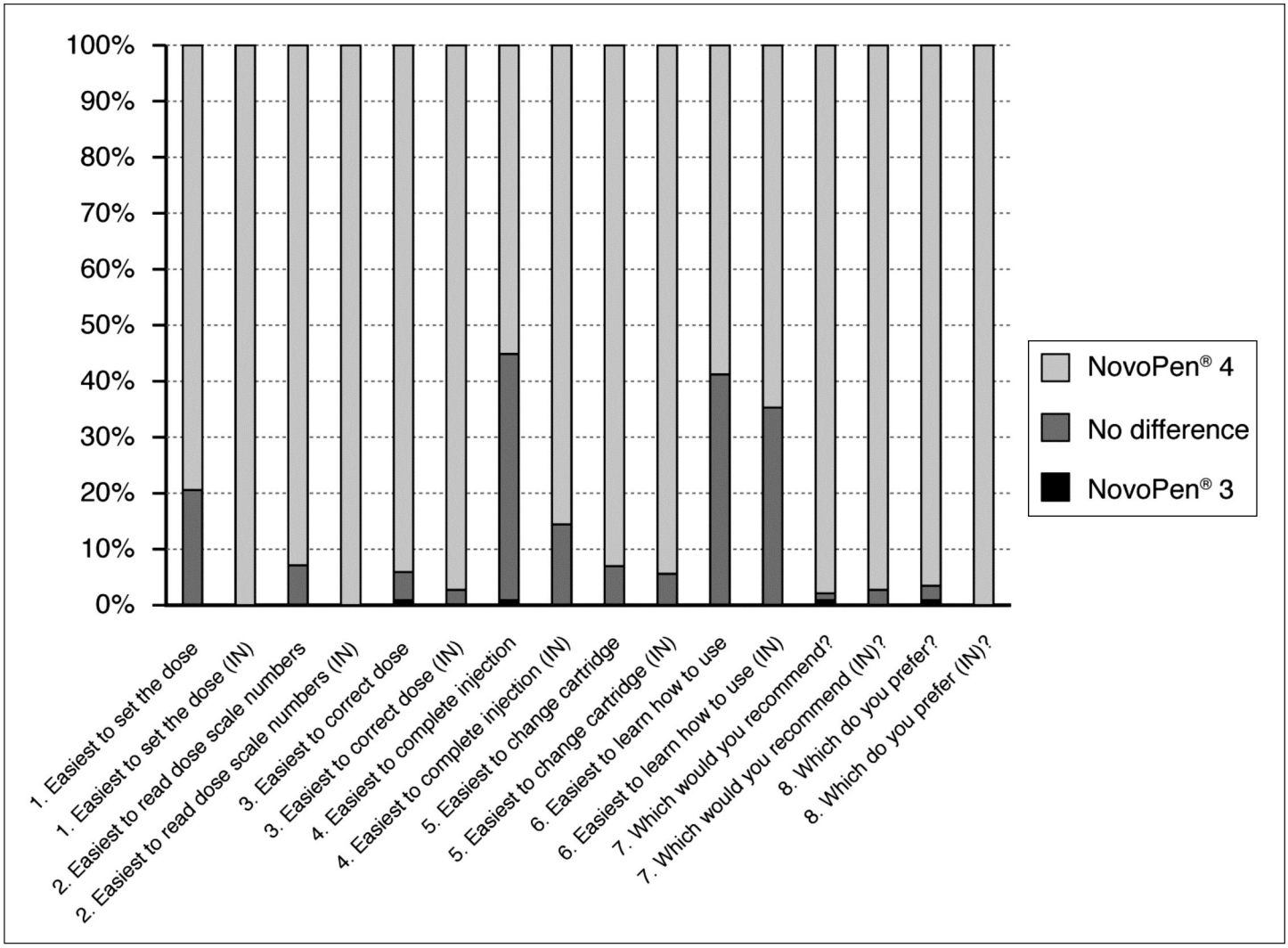

Figure 2. Results of comparative questionnaire for NovoPen 4 versus NovoPen 3 among current NovoPen 3 users and insulin-naïve patients. Within both groups, preference for NovoPen 4 in response to each question was highly significant ($p < .0001$). IN, insulin-naïve patients.

4 with NovoPen 3.[23] After using each pen for 6 weeks, 81% expressed an overall preference for NovoPen 4 ($p < .05$), 9% for NovoPen 3, and 10% had no preference. In another study evaluating patient preference for NovoPen 4 versus OptiClik® (sanofi-aventis, Bridgewater, NJ), after completing a randomized handling test with both pens, 32 of 35 patients with diabetes (91.4%; $p < .001$) responded on the questionnaire that they would prefer to use NovoPen 4.[24] Patients in this study also rated NovoPen 4 as more intuitive to use (83.3% versus 5.6%; $p < .001$) and identified NovoPen 4 as "very easy" or "easy" to learn more often than OptiClik (80% versus 22.9%; $p < .001$).[24] The preference shown for NovoPen 4 in these studies, including ours, cannot be explained by the presence of any one feature. NovoPen 4 has a number of design enhancements compared with previous versions of NovoPen, including a dosage scale selector that turns forward and backward, a more visible dosage scale, an audible end-of-dose click, and less injection force required to deliver insulin, which all have been seen to improve ease of use and increase preference.[22,24]

Other factors that can influence patient satisfaction are the level of individualized, verbal instruction that they receive and the provision of written material.[25,26] In this study, after the initial intuitive assessment of NovoPen 4, patients received detailed, personalized demonstrations and explanations for using this device until they could confidently handle it. In a normal clinical setting, patients do not always receive such patient-centered communication, although it has been shown to increase patient satisfaction.[27] Even if intensive patient-centered communication is delivered, however, patients should also receive both medical information about their treatment, which has been shown to increase patient knowledge and consequently treatment satisfaction,[26] and an operating manual for the specific pen device they will use that is easy to read and follow, which can be referred to, for instance, when patients need to change an insulin cartridge or a technical device problem arises.

As the number of people diagnosed with T1DM and T2DM continues to grow worldwide,[28] insulin delivery devices that are easy to learn and easy to teach can help overcome the psychological insulin resistance patients and physicians have to initiating insulin therapy and encourage patients to establish better metabolic control over their disease.[11] In our study, insulin-naïve participants learned more quickly how to complete the handling tasks with NovoPen 4 than with NovoPen 3. All NovoPen 3 users were able to grasp intuitively how the newer NovoPen worked. Ease of learning, along with the high ratings NovoPen 4 received from both groups for ease of use, convenience, and appearance suggest that this pen would be suitable for patients who are currently on insulin therapy, as well as for those in whom insulin should be initiated.

Conclusions

The durable insulin device NovoPen 4 is simpler to learn, easier to use, and more appropriate in appearance than NovoPen 3. In our study, 96.3% of NovoPen 3 users and 100% of insulin-naïve patients selected for inclusion declared that they preferred to use NovoPen 4 rather than the previous version of NovoPen ($p < .0001$). The mean times required to complete handling tasks and educate participants, along with the responses to questionnaires, suggest that, overall, both the current NovoPen 3 users and insulin-naïve patients had less difficulty and were more confident handling NovoPen 4 than NovoPen 3.

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