EXPERT OPINION

Evaluation of a new durable insulin pen with memory function among people with diabetes and healthcare professionals

Xiaohui Guo[†], Bärbel Sommavilla, Grace Vanterpool, Marianne Qvist, Matthias Bethien & Søren Kruse Lilleøre

[†]Peking University First Hospital, Department of Endocrinology, Xicheng District, Beijing, China

Objectives: The aim of the study was to evaluate durable insulin pens among people with diabetes (PwD) and healthcare professionals (HCPs), by comparing two durable insulin pens with memory function: NovoPen® 5 (NP5) and HumaPen® Memoir™ (HPM), and two durable insulin pens without memory function: HumaPen Luxura® (HPL) and ClikSTAR® (CS).

Research design and methods: This cross-over, multicentre usability test was conducted in China, Germany and the UK. Participants evaluated all four pens in randomised order by performing handling and usability tasks related to everyday use during a face-to-face interview. Tasks, pens and preferences were rated by completing a questionnaire comprising of rating and open-ended questions.

Results: NP5 was preferred by 51% of participants compared with HPM (22%, p < 0.01), HPL (12%, p < 0.01) and CS (15%, p < 0.01). Participants preferred the design of NP5 (in particular, appearance, length and robustness). Memory function for the two pens was rated equally by participants, but 54% of PwD rated NP5 as 'very easy' to learn to use versus 22% for HPM and significantly more HCPs found it 'very easy' to teach patients to use NP5 versus HPM (6-point rating scale; difference in mean score, p < 0.01). Substantially, more PwD would be confident in using NP5 (64%) compared with HPM (43%), HPL (49%) and CS (45%) (6-point rating scale; difference in mean score, p < 0.01).

Conclusions: NP5 was preferred by > 50% of PwD and HCPs. NP5 was more highly rated for design, memory function and ease of learning/teaching compared with HPM. Most PwD would be confident in using NP5 for administering daily insulin injections.

Keywords: diabetes, ease of use, insulin pen, memory function

1. Introduction

Diabetes is a rapidly growing health problem and projections indicate that there will be 439 million people with diabetes (PwD) worldwide by 2030 [1]. It was estimated that worldwide, 12% of healthcare expenditure was spent on diabetes care in 2010 [2]. Diabetes self-management and maintaining independence are important life goals for PwD [3]. Consequently, part of the healthcare burden is associated with providing support for PwD so they can maintain their independence.

All people with type 1 diabetes require lifelong insulin administration [4] and most patients with type 2 diabetes eventually will require treatment with exogenous insulin for effective glycaemic control [5,6]. Adherence is a major factor in insulin

informa
healthcare

RIGHTSLINK

treatment success, with diabetes posing a challenge because it is a lifelong chronic illness and patients may not feel the immediate consequences of missing doses [7]. Poor adherence to insulin treatment including forgotten/omitted insulin injections leads to poor glycaemic control and occurs among all populations of insulin users [8-11], which may contribute to the serious complications associated with diabetes [12-14].

Due to the greater accuracy particularly at low doses and precise delivery that insulin injection pens provide, they are increasingly used to administer insulin injections [15,16] compared with vials and syringes [17-19]. Several studies have shown that PwD prefer the ease of use, discretion flexibility and convenience of insulin pen use [20-24]. The accuracy and handling of insulin pens also contribute to patient satisfaction, confidence and trust in the use of insulin pens [22,23,25]. Importantly, adherence to treatment improved when patients switched from vial and syringe to insulin pens to administer insulin [26].

The addition of a memory function is another feature of an insulin pen that may aid adherence and help to monitor insulin injections. NovoPen® 5 (NP5; Novo Nordisk A/S, Bagsværd, Denmark) is a new durable insulin pen, based on the design and technology of NovoPen® 4 (NP4; Novo Nordisk A/S, Bagsværd, Denmark). However, NP5 also includes a simple memory function that records the dose and hours passed since the last injection. The memory function of an insulin pen may be an important feature for PwD with a busy career or lifestyle and for those most vulnerable in society who may be cared for by others, for example, patients in nursing and residential homes, patients who do not have the necessary mental capacity or those with learning difficulties. In addition, the pen has a range of features similar to NP4, which include a large, clear dose display, an end-of-dose click to confirm insulin delivery, smooth and easy dose dialling, an easy-to-press dose button, a low injection force and dose increments from 1 international unit (IU) to 60 IU [27-29]. In previous studies, PwD reported a significant preference for NP4 compared with other commercially available insulin pen devices, particularly in relation to ease of use and ease of learning to use [30,31].

The purpose of this study was to evaluate preference for NP5 compared with the commercially available durable insulin pens HumaPen® Memoir™ (HPM; Eli Lilly & Co., Indianapolis, IN, USA), HumaPen Luxura® (HPL; Eli Lilly & Co., Indianapolis, IN, USA) and ClikSTAR® (CS; Sanofi, Paris, France), among PwD and healthcare professionals (HCPs).

2. Methods

2.1 Study design

This was a multicentre usability study in people with type 1 or type 2 diabetes and in physicians and nurses who had a minimum of 2 years' experience in the management of diabetes. The test evaluated NP5, HPM, HPL and CS in a cross-over design where participants tested all four pens in random order. The test was managed, conducted and analysed by an independent clinical research organisation (SirValUse, Hamburg, Germany). The study was carried out at multiple sites: two in Shanghai, China; one in Hamburg, Germany and one in London, UK. Participants were recruited from each country in equal numbers by local market research institutes familiar with healthcare industry research procedures. The study was sponsored by Novo Nordisk, A/S, Denmark, but participants were not informed of the identity of the study sponsor at any point in the recruitment or interview process. The study was carried out in accordance with the Declaration of Helsinki Ethical Principles for Medical Research in Human Subjects [32].

In line with good medical practice procedures, informed consent and confidentiality agreements regarding test products were obtained before any test-related activities were initiated.

2.2 Inclusion criteria

Inclusion criteria for patients: males or females with type 1 or type 2 diabetes who were ≥ 18 years of age and had been using an insulin pen for ≥ 3 months were eligible for inclusion. A minimum of 10% of PwD were left-handed to ensure that the study group was representative of the general population, a minimum of 15% injected basal insulin alone, a minimum of 15% injected pre-mixed insulin and a minimum of 15% injected basal plus bolus insulin. The number of PwD who had experience with one of the test pens was limited to 20%.

Inclusion criteria for HCPs included: a minimum of 2 year's of experience and managing at least 10 PwD each week. A third of HCPs were planned to be diabetes specialists, 33% general practitioners and 33% diabetes nurses.

2.3 Exclusion criteria

Exclusion criteria included: mental or physical incapacity, unwillingness or language barriers that precluded an adequate understanding or co-operation within the study, any personal or family tie to a pharmaceutical company, a market research company or the clinical research organisation conducting the usability test on behalf of Novo Nordisk, any disease or condition that may have interfered with the test and participation in other usability tests or market research with pen devices within the past 3 months.

2.4 Materials and procedures

Pens tested were NP5 with 3 ml PenFill® cartridges containing inert test medium (Novo Nordisk A/S) (Lot number: YS64107), HPM (Lot number: A810671) with 3 ml Humalog® cartridges (Eli Lilly & Co.) (Lot number: 0F130A), HML (Lot number: A822892) with 3 ml Humalog® cartridges (Eli Lilly & Co.) (Lot number: 0F130A) and CS (43H041/40H043) with 3 ml Apidra® cartridges (Sanofi) (Lot number: A810671). All pens were fitted with NovoFine® 6 mm 32 G tip extra thin wall needles (Novo Nordisk A/S), which were compatible with the pens tested [33]. Comparator

Table 1. Study questions and available responses.

Questions	Available responses
How do you like the length of this pen?	1 = far too short; 2 = a little too short; 3 = ideal size; 4 = a little too long; 5 = far too long
How do you like the weight of this pen?	1 = far too light; 2 = a little too light; 3 = ideal weight; 4 = a little too heavy; 5 = far too heavy
How robust does this pen feel?	1 = very robust; 6 = not robust at all
How do you like the grip of the pen?	1 = like it very much; 6 = do not like it at all
Now can you rate this pen in terms of design: I like the colours of the pen I like the shape of the pen I like the diameter/width of the pen I like the overall appearance of the pen	1 = completely agree; 6 = completely disagree
Please start with inserting a new cartridge Removes the pen cap Screws the pen apart Inserts the new cartridge Screws the cartridge holder onto the pen Attaching the needle Priming the pen Pulls out the dose button Dials exact dose of 30 units Please adjust the dose to 15 units before injecting it Please inject the dose into the cushion Activates memory function correctly	Easily completed; completed with some problems; not completed without help
Task completion Inserting the cartridge Attaching the needle Dialling a dose Dials the exact dose of 30 units Please adjust the dose to 15 units before injecting it Please inject the dose into the cushion Activates memory function correctly Is able to read correct amount of last dose Is able to read correct time of last dose	Succeeded; failed
How do you rate the amount of force needed to dial a dose?	1 = far too low; 2 = a little too low; 3 = ideal force; 4 = a little too high; 5 = far too high
How easy or difficult was it to read the dose scale? Please tell me how easy or difficult you found it to adjust a dose? Please tell me about the force needed to inject the dose	1 = very easy; 6 = very difficult
How confident you are that you inject the full dose?	1 = very confident; 6 = not confident at all
Why do you feel confident the full dose was delivered?	Audible click sound; touch and feel of the dose button; visual confirmation; other (specify)
How easy or difficult was it to use the memory function?	1 = very easy; 6 = very difficult
To what extent does the memory function meet your needs?	1 = meets my needs very much; 6 = does not meet my needs at all
To what extent does the memory function meet your patients' needs?	1 = meets my patients' needs very much; 6 = does not meet my patients' needs at all
After having used the pen: In how far do the following statements apply to the pen? I am very satisfied with this insulin pen I got used to this pen quickly	1 = fully applies; 6 = doesn't apply at all

Table 1. Study questions and available responses (continued).

Questions	Available responses
This insulin pen is easy to use	1 = fully applies; 6 = doesn't apply at all
This insulin pen is convenient for everyday use	
This insulin pen is of high quality	
This insulin pen meets my patients' requirements	
Overall how confident would you feel using this insulin pen for your daily requirements?	1 = very confident; 6 = not confident at all
Overall how confident would you feel in your patient's ability to manage their daily insulin injections using this pen?	1 = very confident; 6 = not confident at all
Please tell me how easy or difficult you found it to learn how to use this pen?	1 = very easy; 6 = very difficult
Please tell me how easy you think it will be to teach your patients in using this pen?	1 = very easy; 6 = very difficult
How many of your patients do you think will learn to use this pen the first time?	All of them; nearly all of them; three-fourths; half; one-fourth; nearly none of them; none of them

pens were chosen because they were among the newest and most frequently used durable pens from the main device manufacturers and insulin makers in the countries involved in this study. HPM was chosen because it was one of the few commercially available insulin pens with a memory function. For balance, we chose a mainstream pen from the same manufacturer (HPL). CS was chosen because it was the newest pen among the comparator pens.

Participants were screened for suitability by telephone before enrolment into the study. A standardised recruitment questionnaire was used to eliminate selection bias in the study population. The test was carried out during one face-to-face interview which lasted 90 min. Each participant was randomly assigned to start with NP5, HPM, HPL or CS. The order in which participants assessed the pens was also randomised.

Participants were introduced to one pen at a time and during the process the interviewer gave a brief instruction for the pen to be tested according to the quick guide for the appropriate pen. After the instruction, the participants evaluated the design of the pen (Table 1). Participants were then asked to carry out the following tasks: insert the cartridge; attach the needle; dial a dose of 30 units; correct a dose from 30 to 15 units; inject a dose of 15 units into a cushion and use the memory function for NP5 and HPM. Assessment of success for the operating tasks was assessed by the interviewer. Participants answered different questions related to the tasks and gave an overall evaluation of the pen. The test was then repeated for each of the three other pens.

Participants then answered further written questions in relation to device handling, operation, importance of general pen features and their relevance for certain user groups (Table 1). Within the questionnaire there were two different types of rating questions, which were interspersed within the questionnaire.

First, there were rating questions on a 5-point scale with the middle score equating to an ideal rating (Table 1). For example, 'How do you rate the amount of force needed

to dial a dose?' – possible answers were 1 = 'Far too low', 2 = 'A little too low', 3 = 'Ideal force', 4 = 'A little too high' and 5 = 'Far too high'. For the comparison of these rating questions, the percentage of participants giving an ideal rating for each pen was compared statistically.

Second, there were rating questions on a 6-point scale (Table 1), in which the lowest score indicated the best rating (e.g., 1 = 'very easy' and 6 = 'very difficult'). However, only the lowest and highest scores were labelled, and the four points between these poles allowed the participants to grade the pens between the lowest and highest values. For comparison of these rating questions between pens, the mean rating for each pen was compared statistically.

Rating questions included: opinions about the design of the pen (size, weight, design); ease of using the pen (inserting cartridge, dose setting, dose correction, reading the dose scale, dose force); confidence in correct dose delivery; opinions about memory function (NP5 and HPM only); overall satisfaction with pen; ease of learning how to use and train others to use the pen and preference compared with current pen.

Participants were also assessed on their ability to successfully complete handling tasks for the pens and the percentage of participants successfully completing each handling task was compared statistically. In addition, participants were assessed by the facilitator on their ability to complete the handling tasks 'easily' and this subjective assessment was not compared statistically.

After participants had used and evaluated all the pens, they were asked to rate each pen according to preference and importance of the memory function. Participants were also asked open questions relating to their reasons for their preference these questions were not compared statistically.

2.5 Statistical analysis

The statistical significance level employed throughout the statistical analyses was 5%, and correspondingly, all confidence

Table 2. Baseline characteristics.

Variable	%*
PwD, n	**278**
China, n	90
Germany, n	99
UK, n	89
Age, years (mean (range))	49.8 (18 – 69)
Gender	
Male	46
Female	54
Left-handed	11
Type 1 diabetes	26
Type 2 diabetes	74
Current pen use[‡]	
NovoPen® 3	30
NovoPen® 4	21
FlexPen®	16
HumaPen Luxura®	12
SoloSTAR®	10
BerliPen®	4
HumaPen® Memoir™	3
KwikPen®	3
OptiPen® Pro	3
NovoPen® Junior	1
ClikSTAR®	1
HumaPen Luxura® HD	1
Other	28
Number of years injecting insulin	
< 1 year	9
1 – < 2 years	14
2 – < 4 years	17
4 – < 6 years	14
6 – < 10 years	18
≥ 10 years	28
HCPs, n	**102**
China, n	35
Germany, n	34
UK, n	33
Diabetes physicians, n	32
Diabetes nurses, n	34
General practitioners, n	36
Age, years (mean (range))	42.8 (21 – 62)
Gender	
Male	37
Female	63
Which pens for insulin injections are you familiar with[‡]	
NovoPen® 3	79
NovoPen® 4	83
FlexPen®	66
HumaPen Luxura®	64
Solostar®	62
BerliPen®	24
HumaPen® Memoir™	36
KwikPen®	51
OptiPen® Pro	51
NovoPen® Junior	38
ClikSTAR®	38
HumaPen Luxura®	12
NovoPen Echo®	7
Other	34

*Percentage unless otherwise indicated.
[‡]Multiple answers possible.
HCPs: Healthcare professionals; PwD: People with diabetes.

intervals were 95%. All tests were conducted as two-sided tests. The primary objective of the usability study was to evaluate preference for NP5 compared with HPM, HPL and CS, among the total participants, PwD and HCPs. Preference of NP5 versus HPM, HPL and CS, was assessed by means of a questionnaire where participants ranked all four devices. The proportion preferring NP5 was tested against the proportion preferring the three other devices by performing three individual χ^2 tests each at a 5% significance level.

The secondary end points were the rating questions (answers given on an ordinal 5- or 6-point scale) and these were tested by Wilcoxon signed rank test.

3. Results

The characteristics of the participants in the study are shown in **Table 2**. All the PwD participating in the study had at least 6 months' experience of using insulin pens and 28% had over 10 years' experience. Seventy-four percent (205/278) of PwD had type 2 diabetes. The number of PwD with NP4 experience enrolled in the study went slightly over target, due to recruitment difficulties within the study timelines. As a consequence, a total of 21% of the PwD enrolled in the study had experience with NP4.

3.1 Preference

Significantly more participants (both HCPs and PwD) rated NP5 as the pen they liked the most compared with HPM, HPL and CS (**Figure 1**, $p < 0.01$ for all comparisons). In open questions exploring the main reasons for pen preference, 59% of participants preferred the design of NP5 compared with 33% who preferred the design of HPM ($p < 0.01$), 30% who preferred the design of HPL ($p < 0.01$) and 44% who preferred the design of CS ($p < 0.05$); 47% liked NP5 because it had a memory function compared with 59% for HPM. Twenty-seven percent of participants liked the shape and diameter of NP5 compared with 13% for HPM, 7% for HPL and 11% for CS ($p < 0.05$ for all comparisons of shape and diameter). Significantly more participants (HCPs and PwD) were very satisfied with NP5 compared with HPM, HPL and CS (**Figure 2**; where 1 = fully agree and 6 = does not apply at all; mean values $p < 0.01$ for NP5 versus comparators).

3.2 Design

Significantly more HCPs and PwD liked the overall appearance of NP5 compared with the other pens (**Figure 3**; where 1 = fully agree and 6 = completely disagree; mean values $p < 0.01$ for NP5 versus comparators). Considerably more participants gave the best rating of 'fully agree' for liking the overall appearance of NP5 (48%, 182/380) than gave this rating for HPM (16%, 62/380), HPL (22%, 84/380) and CS (30%, 113/380). When asked about the diameter/width of the pens, substantially more participants (53%, 200/380) fully agreed that they liked the diameter/width of
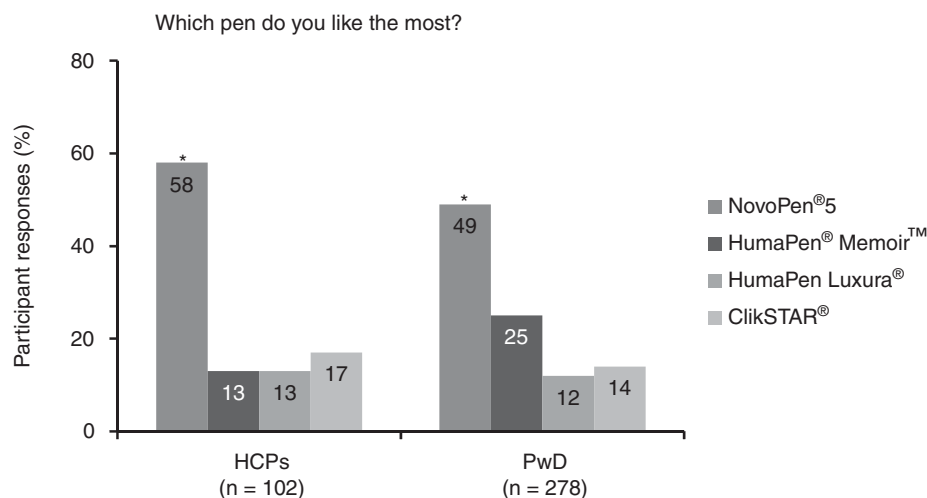
Which pen do you like the most?

Figure 1. Overall preference for durable insulin pens for HCPs and PwD.

*p<0.01 NovoPen®5 versus other pens.

NP5 than for the other test pens (HPM: 11%, 41/380; HPL: 23%, 89/380 and CS: 24%, 90/380; mean values were significant, **Figure** 3).

Significantly more HCPs and PwD found the length of NP5 (HCPs 75/102, 74%; PwD 204/278, 73%) to be ideal than gave this rating for HPM (HCPs 26/102, 25%; PwD 98/278, 35%), HPL (HCPs 47/102, 46%; PwD 153/278, 55%) and CS (HCPs 33/102, 32%; PwD 124/278, 45%) (p < 0.01 for all comparisons). Overall substantially more HCPs and PwD rated NP5 (mean values HCPs 1.57; PwD 1.54) to be 'very robust' (where 1 = very robust and 6 = not robust at all) than gave this rating for HPM (mean values HCPs 1.83, p < 0.02; PwD 1.58, p = 0.3), HPL (mean values HCP 1.88, p < 0.01; PwD 1.87, p < 0.01) and CS (HCPs 2.75, p < 0.01; PwD 2.59, p < 0.01). Similarly, significantly more HCPs and PwD 'very much' liked the grip (1 = like it very much and 6 = do not like it at all) of NP5 (mean values HCP 1.89; PwD 1.90) than of HPM (HCP 2.58; PwD 2.68), HPL (HCP 2.21; PwD 2.31) and CS (HCP 2.41; PwD 2.37) (p < 0.01 for NP5 versus comparators).

3.3 Pen handling

In general, all pens received similar ratings for handling tasks and usability tasks (**Tables** 3 and 4) with minor differences between pens for tasks including: attaching a needle, checking insulin flow, dialling a dose and injecting a dose. However, significantly fewer HCPs and PwD successfully inserted the cartridge into NP5 compared with HPM and HPL (**Table** 3). Significantly more PwD correctly dialled a dose with NP5 compared with CS, but significantly more PwD successfully adjusted the dose using HPM compared with NP5.

The last dose memory of NP5 and the memory of HPM, which records the last 16 doses, received similar ratings regarding ease of use (1 = very easy to use and 6 = very difficult

to use; p = 0.93 for HCPs and PwD combined; **Figure** 4). There was no significant difference in the overall preference of the memory function. When asked to give their reasons, among the participants who preferred the NP5 memory function, 118/182 (65%) found it simpler and easier to use, and 86/182 (47%) preferred to have information only about the last injection, whereas of those who preferred the HPM memory, 107/198 (54%) preferred to have information about several doses, and 72/198 (36%) preferred to have information about the exact time of day of the last dose.

3.4 Ease of learning and teaching

Overall, 151/278 (54%) PwD found NP5 'very easy' to learn how to use compared with 62/278 (22%) for HPM (1 = very easy and 6 = very difficult; mean values NP5 1.73 versus HPM 2.70, p < 0.01), 212/278 (76%) for HPL (mean value 1.37, p < 0.01 versus NP5) and 209/278 (75%) for CS (mean value 1.31, p < 0.01 versus NP5).

More HCPs (16/102; 16%) found it 'very easy' to teach NP5 to other people compared with 1/102 (1%) for HPM (1 = very easy and 6 = very difficult; mean values NP5 2.44 versus HPM 3.71, p < 0.01). HPL was rated 'very easy' to teach others to use by 37/102 (36%) HCPs (mean value 1.90, p < 0.01 versus NP5), while CS received this rating from 35/102 (34%) HCPs (mean value 1.99, p < 0.01 versus NP5).

3.5 Confidence in managing daily insulin injections

Considerably more PwD would be 'very confident' in managing their daily insulin injections with NP5 (64%, 179/278) compared with HPM (43%, 119/278), HPL (49%, 136/278) and CS (45%, 126/278) (1 = very confident and 6 = not confident at all; mean values for NP5 1.59; HPM 2.29; HPL 2.14 and CS 2.02, p < 0.01 for NP5 versus comparators) (**Table** 5). The main reasons for confidence
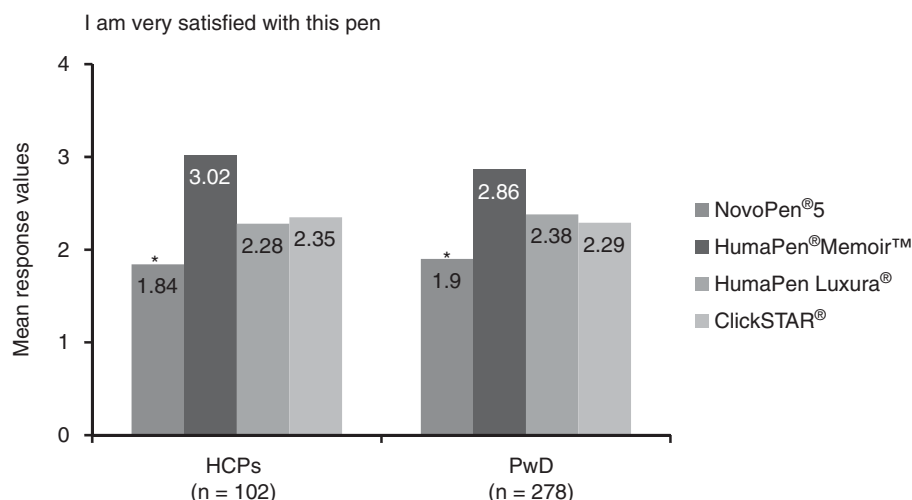
I am very satisfied with this pen

Figure 2. Participants' satisfaction with durable insulin pens. Mean values shown for HCPs and PwD.
p<0.01 NovoPen® 5 versus other pens 1 = fully agree ana 6 = does not apply at all.

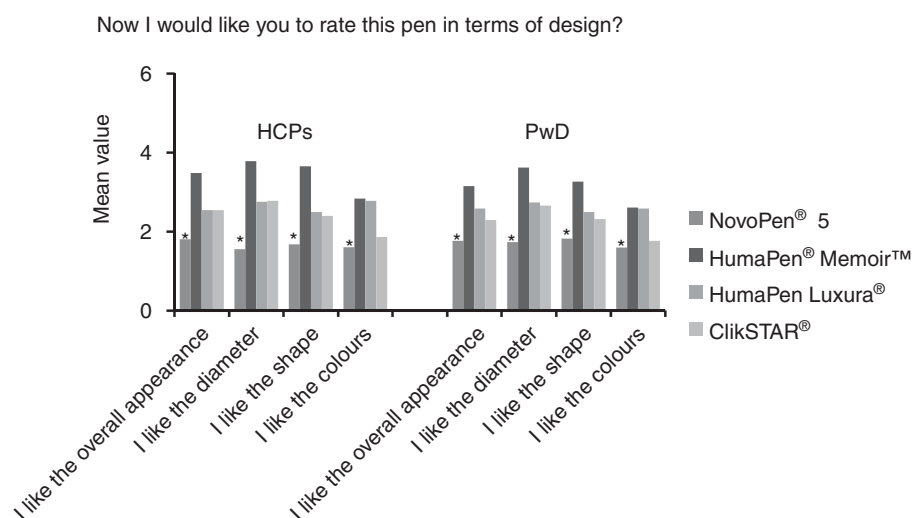Now I would like you to rate this pen in terms of design?

Figure 3. Mean values for how participants rated the design of NP5 compared with HPM, HPL and CS.
*p<0.01 NovoPen®5 versus other pens.

that the full amount of insulin had been delivered with NP5 were visual confirmation of the dose scale returning to zero (68/258, 26%) and audible end-of-dose click (44/258, 17%).

When PwD were asked how confident they would be in using an insulin pen with memory function compared with the conventional pen they were currently using (1 = very confident and 6 = not confident at all), they responded: 1 (46%, 129/278), 2 (21%, 57/278), 3 (11%, 30/278), 4 (5%, 13/278), 5 (5%, 14/278) and 6 (4%, 10/278), while 3% (7/278) stated they were currently using a pen with memory and 6% (18/278) didn't find memory function relevant.

When HCPs were asked how confident their patients would be in using an insulin pen with memory function compared with a conventional pen (1 = very confident and 6 = not confident at all), they responded: 1 (23%, 23/102), 2 (36%, 37/102), 3 (26%, 27/102), 4 (10%, 10/102), 5 (4%, 4/102) and 6 (1%, 1/102).

3.6 Important pen features
When asked how important pen functions and features were for the daily use of a pen (1 = very important and 6 = not important at all), 294/380 (77%) participants indicated that the high quality of a device was 'very important';

Table 3. Summary data for those who successfully handled tasks.

	HCPs Users who successfully completed the task n = 102 (%)				PwD Users who successfully completed the task n = 278 (%)			
	NP5	HPM	HPL	CS	NP5	HPM	HPL	CS
Inserting the cartridge	102 (100)*	98 (96)*	101 (99)*	98 (96)	252 (91)‡	272 (98)‡	273 (98)‡	257 (92)
Attaching the needle	102 (100)	102 (100)	101 (99)	100 (98)	271 (97)	269 (97)	272 (98)	275 (99)
Priming the pen	84 (82)	86 (84)	86 (84)	89 (87)	193 (69)	190 (68)	204 (73)	194 (70)
Dialling a dose	101 (99)	101 (99)	101 (99)	98 (96)	273 (98)§¶	274 (98)	263 (95)§	258 (93)¶
Adjusting the dose	101 (99)	102 (100)	101 (99)	100 (98)	265 (95)#	273 (98)#	257 (92)	258 (93)
Injecting the dose	100 (98)	101 (99)	102 (100)	101 (99)	266 (96)	272 (98)	273 (98)	272 (98)
Activated memory function correctly	85 (83)	83 (81)	NA	NA	180 (65)	173 (62)	NA	NA

*p = 0.04 NP5 versus HPM and CS.
‡p < 0.01 HPM and HPL versus NP5.
§p = 0.02 NP5 versus HPL.
¶p < 0.01 NP5 versus CS.
#p = 0.04 HPM versus NP5.
CS: ClikSTAR®; HCPs: Healthcare professionals; HPL: HumaPen Luxura®; HPM: HumaPen® Memoir™; NA: Not applicable; NP5: NovoPen® 5; PwD: People with diabetes.

294/380 (77%) indicated that 'easy to dial a dose' was 'very important', 294/380 (77%) indicated 'easy to inject' was 'very important' and 276/380 (73%) indicated that an end-of-dose click was 'very important'.

3.7 Importance of memory function

When asked 'how confident you are/think your patients will be' when using an insulin pen with memory function compared with a conventional pen (1 = very confident and 6 = not confident at all), 246/380 (65%) of the total group indicated that they were 'very confident' (answer 1) or confident (answer 2) in using an insulin pen with memory function. In relation to 'how important it was for you/your patient to see the amount of the last dose of insulin delivered' (1 = very important and 6 = not important at all), 159/380 (42%) indicated it was 'very important' to see the last dose. Being able to see how long ago the last injection was made was rated as being 'very important' by 139/380 (37%) participants. In general, the HCPs agreed that a pen with memory function was important for most patients irrespective of diabetes type and insulin treatment regimen. The majority of HCPs (76/102; 75%) agreed that a pen with memory function was 'very important' for patients who forget to perform their injections. Memory function was also rated as 'very important' by 42/102 (41%) of the HCPs for patients on a basal/bolus regimen (two types of insulin) with four or more daily injections.

4. Discussion

In this study, 51% of PwD and HCPs preferred NP5 to the other durable insulin pens. PwD found NP5 significantly easier to learn how to use and HCPs found NP5 significantly easier to teach others how to use compared with HPM, the other durable insulin pen with a memory function. Substantially more participants preferred the overall appearance (the length, diameter/width and robustness) of NP5 compared with the other pens. However, in general, all pens in the study received similar ratings for handling and usability tasks.

NP5 builds on the technology and features of NP4, such as an audible end-of-dose click that confirms that the full dose has been administered and an easy-to-read dose scale [28,30,34,35], but its range of features has been expanded with a simple last-dose memory function (size of last dose and time in hours since the injection was performed). These features of NP5 have been designed to assist PwD with self-management of their diabetes by building confidence and providing reassurance. Indeed, the visual confirmation of the dose scale (returning to zero) and the end-of-dose audible click were the main reasons given by the participants for the confidence that they had injected the full dose of insulin with NP5. Surprisingly, only a small proportion of the participants used the memory function to assess or confirm the full dose had been delivered. However, this may partly be explained by the fact that only a few of the PwD among the participants were currently using pens with memory function (3% HPM and 0% NovoPen Echo® (NPE; Novo Nordisk A/S, Bagsvaerd, Denmark)). It is anticipated that some experience of using an insulin pen with memory function will be required before memory function and its features are fully integrated into everyday injection routines, in particular among experienced pen users. In this respect, HCPs may play a pivotal role in educating PwD and in empowering them in the self-management of their disease [36-39].

Table 4. Summary data for those who 'easily' completed handling tasks.

	HCPs Users who easily completed the task n = 102 (%)				PwD Users who easily completed the task n = 278 (%)			
	NP5	HPM	HPL	CS	NP5	HPM	HPL	CS
Removing the pen cap	101 (99)	99 (97)	101 (99)	99 (97)	269 (97)	264 (95)	272 (98)	263 (95)
Unscrewing the pen	91 (89)	100 (98)	100 (98)	99 (97)	209 (75)	263 (95)	268 (96)	256 (92)
Inserting a new cartridge	88 (86)	98 (96)	95 (93)	99 (97)	226 (81)	257 (92)	260 (94)	256 (92)
Screwing the cartridge holder onto the pen	93 (91)	99 (97)	100 (98)	92 (90)	232 (83)	261 (94)	262 (94)	239 (86)
Attaching the needle	101 (99)	101 (99)	100 (98)	99 (97)	270 (97)	264 (95)	266 (96)	269 (97)
Priming the pen	82 (80)	82 (80)	85 (83)	84 (82)	171 (62)	171 (62)	195 (70)	186 (67)
Extending the dose button	97 (95)	NA	NA	NA	256 (92)	NA	NA	NA
Dialling the exact dose of 30 units	102 (100)	99 (97)	100 (98)	95 (93)	273 (98)	264 (95)	260 (94)	259 (93)
Adjusting the dose to 15 units	100 (98)	102 (100)	99 (97)	99 (97)	264 (95)	268 (96)	253 (91)	250 (90)
Injecting the dose	100 (98)	101 (99)	102 (100)	101 (99)	266 (96)	272 (98)	273 (98)	272 (98)
Activating the memory function correctly	93 (91)	88 (86)	NA	NA	206 (74)	177 (64)	NA	NA
Able to read the correct amount of the last dose	100 (98)	78 (76)	NA	NA	218 (78)	169 (61)	NA	NA
Able to read the correct time of last dose	83 (81)	81 (79)	NA	NA	152 (55)	164 (59)	NA	NA
Able to read the correct amount of second last dose	NA	79 (71)	NA	NA	NA	156 (56)	NA	NA
Able to read the correct time of second last dose	NA	80 (78)	NA	NA	NA	165 (59)	NA	NA

CS: ClikSTAR®; HCPs: Healthcare professionals; HPL: HumaPen Luxura®; HPM: HumaPen® Memoir™; NA: Not applicable; NP5: NovoPen® 5; PwD: people with diabetes.

When PwD were asked about confidence in using an insulin pen with memory function versus their conventional pen, 46% responded that they were 'very confident' in using a pen with memory function. This finding is encouraging, as memory function is a completely new feature for most pen users. However, when HCPs were asked a similar question about their patients' confidence in using a pen with memory, the results were less encouraging as only 23% of HCPs responded that they were 'very confident'. However, if the top two scores on a 6-point scale were taken into consideration, the figure would rise to 59% of HCPs being confident in their patients being able to use a memory pen compared with a conventional pen. Despite this, when looking specifically at confidence ratings for each of the individual pens, NP5 received higher ratings from both HCPs and PwD than the comparator pens with or without memory function. This may partly be explained by the familiarity among participants with the design of the predecessor pen, NP4.

The pens without a memory function were rated the easiest to learn and teach how to use. However, this study highlighted that it was easier for PwD to learn how to use NP5 and easier for HCPs to teach others how to use NP5, compared with HPM, both of which have a memory function. If the memory function adds value for the patients and promotes confidence in their ability to self-manage insulin injections, the extra time for training and learning compared with pens without memory function may be

worthwhile. Therefore, the extra training time may subsequently be considered as a positive investment, and this study confirms that the memory function of NP5 was one of the dominant reasons for the higher preference for this pen. Concurrently, the use of an insulin pen with a memory function may reduce the healthcare burden associated with ongoing diabetes management.

Other studies have shown that despite the higher acquisition costs of insulin pens compared with vials and syringes, there is very little increase in total healthcare costs with insulin pens [26,40]. Although more training time can be expected for some PwD, the amount of support required after learning to use the pen may be lower since patient confidence and presumably concordance to prescribed insulin regimens is higher with an insulin pen with memory function. In a recent observational study of NPE among children and adolescents with type 1 diabetes, participants reported improved confidence in managing daily insulin treatment, as well as having an increased assurance that they had taken all their insulin injections, when using NPE for 3 months compared with their previous injection method of pen/syringe [41]. An easy-to-teach pen with a memory function should assist in further reducing the healthcare costs associated with the management of diabetes by potentially improving concordance with dosing regimens and lowering the risk of double-dosing.

Participants in this study indicated that the most important features of the memory function were the ability to visualise the amount of insulin that was injected at the last dose and
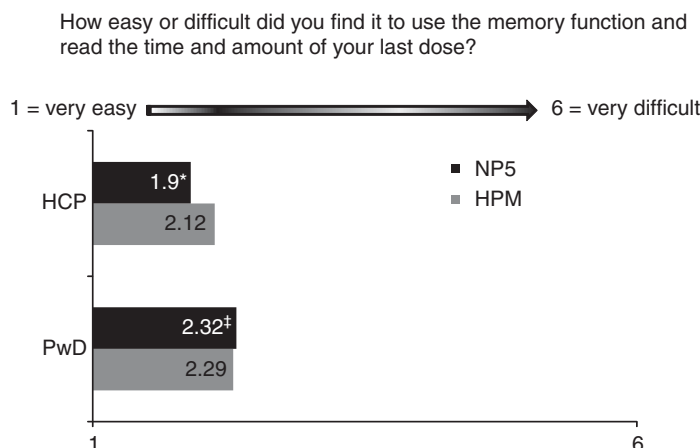
How easy or difficult did you find it to use the memory function and
read the time and amount of your last dose?

Figure 4. Percentage of HCPs and PwD who rated the memory function 1 = 'very easy' or 6 = 'very difficult' to use, NP5 compared with HPM.
*p = 0.75 NP5 versus HPM
†p = 0.96 NP5 versus HPM

Table 5. Summary data for confidence ratings.

Rating	% of PwD (n = 278)			
	NP5	HPM	HPL	CS
1 = Very confident	64	43	49	45
2	22	23	20	32
3	9	13	15	10
4	1	10	6	5
5	1	5	5	4
6 = Not confident at all	2	6	5	4
Mean value	1.59*	2.29	2.14	2.02

Overall how confident would you feel managing your daily insulin injections using this pen?
*p < 0.01 NP5 versus other pens.
CS: ClikSTAR®; HCPs: Healthcare professionals; HPL: HumaPen Luxura®;
HPM: HumaPen® Memoir™; NP5: NovoPen® 5; PwD: People with diabetes.

the amount of time that had elapsed since the last dose was injected. Indeed, PwD fear hypoglycaemia more than they fear the long-term complications of diabetes [42]. This fear may result in patients administering suboptimal medication in order to avoid further hypoglycaemic events [43]. Previous experience of hypoglycaemia is also associated with significantly lower treatment satisfaction and with reduced treatment adherence [44]. The ability to read the amount and time of the last dose with NP5 may be beneficial to this group of patients because it could prevent double-dosing and aid those who are unsure when they last took their insulin. Indeed, the memory capability of NP5 may be one reason for 86% (answer 1 or 2) of PwD having a high confidence in using this pen for their daily insulin management.

One limitation of the study was that 51% of patients were currently using a durable pen manufactured by the study sponsor (NovoPen® 3 or NP4), while only 16% were using one of the other three pens used in the study. However, the aim was that the inclusion of PwD with NP4 experience was limited to 20% of total participants, although a modest over recruitment of PwD with NP4 experience did occur. No restriction was placed on those with experience with any other pen manufactured by the study sponsor. As a consequence, a considerable number of the PwD enrolled had experience with the older versions of NP. It is possible that the results were influenced by this considerable proportion of NP users. Another aspect of the study to consider was the selection of comparator pens, as not all commercially available durable insulin pens obtainable in the participating countries were included. The comparator pens were selected because they were widely used in the participating countries and among the newest pens on the market. The inclusion of a larger selection of comparator pens in the study was not feasible due to cost and practical considerations of patient recruitment and study execution. Also the time required for performing multiple pen handling tests and interviews were taken into consideration when deciding on the number of study pens, as the total duration of the interview session could impact on the validity of the participant responses.

Easy-to-learn, easy-to-teach devices with a simple memory function should be useful for all age groups of PwD. HCPs agreed that memory function was important for all patients irrespective of diabetes type and insulin treatment regimen, but placed the highest importance for those on intensified regimens and taking multiple daily injections. The memory function was rated as 'very important' by the majority of HCPs for people who were prone to forgetting to take injections or had difficulty in tracking their injection history. Caregivers of elderly PwD may also benefit from using a pen with

memory function, since this will allow them to track an injection made by another caregiver and potentially prevent dose omissions or double-dosing.

improved self-management skills in PwD and thereby greater independence and confidence in their ability to manage their diabetes.

5. Conclusions

NP5 was preferred to other durable insulin pens by most PwD and HCPs. Most PwD would be very confident in using NP5 for everyday management of their diabetes. The simple memory function and design features may contribute to overall preference and significantly higher patient satisfaction with NP5 compared with other commercially available durable pens. These features may collectively contribute to

Declaration of interest

Bibliography

1. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010;87:4-14

2. Zhang P, Zhang X, Brown J, et al. Global healthcare expenditure on diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010;87:293-301

3. Morrow AS, Haidet P, Skinner J, et al. Integrating diabetes self-management with the health goals of older adults: a qualitative exploration. Patient Educ Couns 2008;72:418-23

4. Lernmark A. Type 1 diabetes. Clin Chem 1999;45:1331-8

5. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998;352:837-53

6. Wright A, Burden AC, Paisey RB, et al. Sulfonylurea inadequacy: efficacy of addition of insulin over 6 years in patients with type 2 diabetes in the UK Prospective Diabetes Study (UKPDS 57). Diabetes Care 2002;25:330-6

7. Brunton S. Insulin delivery systems: reducing barriers to insulin therapy and advancing diabetes mellitus treatment. Am J Med 2008;121:S35-41

8. Donnelly LA, Morris AD, Evans JM. Adherence to insulin and its association with glycaemic control in patients with type 2 diabetes. QJM 2007;100:345-50

9. Morris AD, Boyle DI, McMahon AD, et al. Adherence to insulin treatment, glycaemic control, and ketoacidosis in insulin-dependent diabetes mellitus. The DARTS/MEMO Collaboration. Diabetes audit and research in tayside Scotland. medicines monitoring Unit. Lancet 1997;350:1505-10

10. Peyrot M, Rubin RR, Kruger DF, et al. Correlates of insulin injection omission. Diabetes Care 2010;33:240-5

11. Randlov J, Poulsen JU. How much do forgotten insulin injections matter to hemoglobin a1c in people with diabetes? A simulation study. J Diabetes Sci Technol 2008;2:229-35

12. Hokkam EN. Assessment of risk factors in diabetic foot ulceration and their impact on the outcome of the disease. Prim Care Diabetes 2009;3:219-24

13. Landman GW, van Hateren KJ, Kleefstra N, et al. The relationship between glycaemic control and mortality in patients with type 2 diabetes in general practice (ZODIAC-11). Br J Gen Pract 2010;60:172-5

14. Lind M, Bounias I, Olsson M, et al. Glycaemic control and incidence of heart failure in 20,985 patients with type 1 diabetes: an observational study. Lancet 2011;378:140-6

15. Bohannon NJ. Insulin delivery using pen devices. Simple-to-use tools may help young and old alike. Postgrad Med 1999;106:57-8; 61-4, 8

16. IMS Health. Estimated number of patients using FlexPen®, based on worldwide sales in number of packs sold, IMS world wide data Q3'08 and Daily Defined Dosage (DDD) for insulin as issued by WHO; 2008

17. Gnanalingham MG, Newland P, Smith CP. Accuracy and reproducibility of low dose insulin administration using pen-injectors and syringes. Arch Dis Child 1998;79:59-62

18. Keith K, Nicholson D, Rogers D. Accuracy and precision of low-dose insulin administration using syringes, pen injectors, and a pump. Clin Pediatr (Phila) 2004;43:69-74

19. Lteif AN, Schwenk WF. Accuracy of pen injectors versus insulin syringes in children with type 1 diabetes. Diabetes Care 1999;22:137-40

20. Korytkowski M, Bell D, Jacobsen C, et al. A multicenter, randomized, open-label, comparative, two-period crossover trial of preference, efficacy, and safety profiles of a prefilled, disposable pen and conventional vial/syringe for insulin injection in patients with type 1 or 2 diabetes mellitus. Clin Ther 2003;25:2836-48

21. Lombardo F, Salzano G, Messina MF, et al. Compliance and administration methods in management of type 1 diabetes. Acta Biomed 2005;76(Suppl 3):66-9

22. Olsen BS, Lilleore SK, Korsholm CN, et al. Novopen Echo for the delivery of insulin: a comparison of usability, functionality and preference among pediatric subjects, their parents and health care professionals. J Diabetes Sci Tech 2010;4:1468-75

23. Sommavilla B, Jorgensen C, Jensen KH. Safety, simplicity and convenience of a modified prefilled insulin pen. Expert Opin Pharmacother 2008;9:2223-32

24. Summers KH, Szeinbach SL, Lenox SM. Preference for insulin delivery systems among current insulin users and nonusers. Clin Ther 2004;26:1498-505

25. Pfutzner A. FlexPen for the delivery of insulin: accuracy, injection force and patient preference. Expert Rev Med Devices 2009;6:115-23

26. Baser O, Bouchard J, DeLuzio T, et al. Assessment of adherence and healthcare costs of insulin device (FlexPen) versus conventional vial/syringe. Adv Ther 2010;27:94-104

27. Asakura T, Seino H, Jensen KH. NovoPen® 4 is easier to teach, more intuitive to use and preferred by patients compared to OptiClik®.. Diabetes 2006;55:A456

28. Donsmark M, Herold L, Kristensen CM. A comparison of injection force and dosage scale size between NovoPen 3 and NovoPen 4. Diabetes Technol Ther 2009;11:581-5

29. Kristensen CM, Donsmark M. Dose accuracy and durability of the NovoPen 4 insulin delivery device before and after simulation of 5 years of use and under various stress conditions. Clin Ther 2009;31:2819-23

30. Asakura T, Seino H, Jensen KH. Patient acceptance and issues of education of two durable insulin pen devices. Diabetes Technol Ther 2008;10:299-304

31. Israel-Bultman H, Hyllested-Winge J, Kolaczynski M, et al. Comparison of preference for NovoPen((R)) 4 with previous insulin pen treatments after 12 weeks in adult patients with type 1 and type 2 diabetes: a multicenter observational study. Clin Ther 2011;33:346-57

32. World Medical Association. Declaration of Helsinki - ethical principles for medical research involving human subjects. 2008. Available from: http://wwwriip-influenzaorg/wp-content/ uploads/2011/08/Helsinki-2008-ENpdf [Accessed 8 November 2011]

33. Buus P, Lilleore SK, Larsen K. Compatibility testing of two types of pen needles with a range of injection pens for diabetes medication. Curr Med Res Opin 2011;27:589-92

34. Asakura T. Comparison of clinically relevant technical attributes of five insulin injection pens. J Diabetes Sci Technol 2011;5:1203-9

35. Asakura T, Seino H. Assessment of dose selection attributes with audible notification in insulin pen devices. Diabetes Technol Ther 2005;7:620-6

36. Chatzimarkakis J. Why patients should be more empowered: a European perspective on lessons learned in the management of diabetes. J Diabetes Sci Technol 2010;4:1570-3

37. LaSalle JR. Empowering patients during insulin initiation: a real-world approach. J Am Osteopath Assoc 2010;110:69-78

38. Rakel RE. Improving patient acceptance and adherence in diabetes management: a focus on insulin therapy. Adv Ther 2009;26:838-46

39. Serrano-Gil M, Jacob S. Engaging and empowering patients to manage their type 2 diabetes, Part I: a knowledge, attitude, and practice gap? Adv Ther 2010;27:321-33

40. Bastian MD, Wolters NE, Bright DR. Insulin pens vs. vials and syringes: differences in clinical and economic outcomes. Consult Pharm 2011;26:426-9

41. Adolfsson P, Huot C, Veijola R, et al. Safety and patient perception of an insulin pen with simple memory function for children and adolescents with type 1 diabetes - the REMIND study. Pediatr Diabetes 2011;12(Suppl 15):49

42. Defining and reporting hypoglycemia in diabetes: a report from the American Diabetes Association Workgroup on Hypoglycaemia. Diabetes Care 2005;28:1245-9

43. Fidler C, Elmelund Christensen T, Gillard S. Hypoglycemia: An overview of fear of hypoglycemia, quality-of-life, and impact on costs. J Med Econ 2011;14:646-55

44. Alvarez Guisasola F, Tofe Povedano S, Krishnarajah G, et al. Hypoglycaemic symptoms, treatment satisfaction, adherence and their associations with glycaemic goal in patients with type 2 diabetes mellitus: findings from the Real-Life Effectiveness and Care Patterns of Diabetes Management (RECAP-DM) Study. Diabetes Obes Metab 2008;10(Suppl 1):25-32

Affiliation

Xiaohui Guo[†1], Bärbel Sommavilla[2], Grace Vanterpool[3], Marianne Qvist[4], Matthias Bethien[5] & Søren Kruse Lilleøre[4]
[†]Author for correspondence
[1]Peking University First Hospital, Department of Endocrinology, #8 Xishiku Street, Xicheng District, Beijing 100034, China
Tel: +86 10 8357 5662;
E-mail: Guoxh@medmail.com.cn
[2]Paracelsus Medical University, General Hospital, Center for Prevention and Care, Muellner-Hauptstrasse 48, 5020 Salzburg, Austria
[3]CLCH Diabetes, Intermediate Service, 1 – 13 Milson Road H C, London W14 0LJ, UK
[4]Novo Nordisk A/S, Vandtårnsvej 114, DK-2860 Søborg, Denmark
[5]GfK SirValUse Consulting GmbH, Burchardstraße 19, Hamburg, Germany