

ORIGINAL ARTICLE

# An evaluation of patient preference for an alternative insulin delivery system compared to standard vial and syringe\*

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## ABSTRACT

**Background:** Diabetes mellitus (DM) affects over 18.2 million Americans and diabetes-related medical costs exceed 132 billion dollars per year, totaling more than 12% of the United States healthcare budget. The Diabetes Control and Complications Clinical Trial demonstrated that intensive insulin therapy and the control of plasma glucose can significantly reduce the incidence of late diabetic complications and delay the progression of existing conditions in type 1 diabetes. Optimal glycemic control often requires intensive insulin therapy to maintain a hemoglobin A<sub>1c</sub> (A1C) of less than 7% as recommended by the American Diabetes Association. It is estimated that more than half of the approximately 7 million Americans using insulin do so with suboptimal treatment and while administering one or two insulin injections per day. Non-adherence may be a contributing factor in suboptimal treatment. For a variety of reasons, many patients diagnosed with diabetes and treated with insulin are non-adherent.

**Scope:** The primary objective of this study was to evaluate preference for an insulin delivery system

comparing a disposable doser (InnoLet) to the standard vial/syringe. In a prospective, randomized, open-label, two-period, crossover study, 260 patients were enrolled (age ≥ 18 years, with type 1 or 2 diabetes, and receiving NPH or regular or 70/30 insulin for at least 6-months). A total of 162 patients completed both treatment arms. Excluded were those unable to read/write English or administer their own injections, pregnant/lactating women, those using antipsychotics, and those with a history of alcohol abuse or cognitive impairment. Patients completed the eight-item Diabetes Fear of Self-Injection Questionnaire at baseline, week 12 and week 24. Items were rated on a 4-point Likert scale (1 = almost never; 4 = almost always) with a maximum fear score of 32. At week 24, patients completed a preference survey.

**Findings:** Of the 162 patients completing both treatment arms, 89 (55.0%) were in the vial/syringe to disposable doser treatment arm, 50% were female and mean age was 60 ± 11 years. Patients in both treatment arms displayed little significant differences in baseline characteristics. Patients reported significantly lower fear of

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self-injection after using the disposable doser compared to vial/syringe (mean  $\pm$  SEM:  $9.5 \pm 0.2$  vs.  $11.2 \pm 0.4$ ;  $p < 0.0001$ ). Most patients (71.5%) indicated a preference for the disposable doser compared to the vial/syringe method ( $p < 0.0001$ ). *Conclusion:* The majority of patients preferred the disposable doser, and reported significantly less fear of self-injection using this delivery system. There are some potential limitations to consider. A randomization bias may have been present, patients

who enrolled in this study were those who were actively seeking medical treatment for diabetes, insulin pens and cartridges are not available for all types of insulin regimens, pre-filled pens and cartridges may not be altered and, in general, alternative insulin delivery systems tend to be more costly than insulin sold in traditional vials. However, insulin may have greater patient acceptance and less psychological distress when administered via an alternative delivery system.

## Introduction

Diabetes mellitus (DM) affects over 18.2 million Americans and diabetes-related medical costs exceed 132 billion dollars per year, totaling more than 12% of the United States healthcare budget<sup>1,2</sup>. A portion of this budget is used to treat complications associated with diabetes, primarily among those whose diabetes is poorly controlled. The Diabetes Control and Complications Clinical Trial<sup>3</sup> demonstrated that intensive insulin therapy and the control of plasma glucose can significantly reduce the incidence of late diabetic complications and delay the progression of existing conditions in type 1 diabetes. Optimal glycemic control often requires intensive insulin therapy to maintain a hemoglobin A<sub>1c</sub> (A1C) less than 7% as recommended by the American Diabetes Association<sup>4</sup>. It is estimated that more than half of the approximately 7 million Americans using insulin do so with suboptimal treatment and while administering one or two insulin injections per day<sup>5,6</sup>.

Non-adherence may be a contributing factor in suboptimal treatment. For a variety of reasons, many patients diagnosed with diabetes and treated with insulin are non-adherent. Lack of diabetes education, poverty, stigma and fear associated with needles, denial, and lifestyle all contribute to non-adherence with insulin injections and poor glycemic control. In 1987 insulin pens were introduced in the United States and, through the years, additional alternative insulin delivery systems have become available. The development of alternative insulin delivery systems have offered patients improved flexibility, more accurate dosing, convenience and improved social acceptability with administration of their insulin regimen. Moreover, these benefits may have improved patients' adherence to their insulin regimen. Two multicenter surveys of 1310 insulin users showed that 77% of patients found insulin adherence to be easier with the use of an insulin pen, and 85% of insulin pen users never missed a scheduled injection, as compared to 73% of the vial and syringe users<sup>7</sup>. In 1993, Plevin and Sadur<sup>8</sup> assessed patient acceptance of insulin pens and found that 98% of the patients reported that the insulin pen was easier to use and 91% preferred to

continue using the pen. Recognizing the increasing importance of patient preference, we investigated through a multicenter, randomized, cross-over trial whether patients diagnosed with diabetes and treated with insulin therapy would prefer the disposable doser (InnoLet, Novo Nordisk Inc., Princeton, NJ) over the standard vial and syringe, as has been found among patients using insulin pens.

The disposable doser is similar to an insulin pen in that it is a pre-filled disposable insulin delivery system. It has a large dial that is easy to read, with audible clicks to help patients select the correct dose of insulin. To use the system, patients set their dose, insert the needle and press a button.

## Methods

### Study design

This was a randomized, open-label, two-period cross-over study conducted at 50 physician offices within Arizona, California, Colorado, Oregon, Texas, Washington and Wyoming with patient enrollment occurring from August 1, 2003 through May 5, 2004. The majority of physician investigators who participated specialized in internal medicine (54.0%) followed by family medicine (36.0%), endocrinology (8.0%) and general medicine (2.0%). Conduct of this trial conformed to the human experimentation guidelines of the Declaration of Helsinki and title 21 parts 50 and 56 of the United States Code of Federal Regulations<sup>9,10</sup>. An institutional review board for each clinical center approved the protocol, and all study participants gave written informed consent.

## Patients

Patients were eligible for inclusion if they were at least 18 years of age at the time of enrollment, diagnosed with type 1 or 2 DM and had an A1C value of  $\leq 10\%$ . Patients were required to use at least one daily injection of neutral protamine hagedorn (NPH), regular or 70/30 insulin, and to have been using insulin for at least 6 months. Patients were excluded if they were unable

to read or write English, were unable to administer their own injections, had used an alternative insulin delivery system during the 6 months prior to enrollment, were pregnant or lactating (or had the intention of becoming pregnant), or were using antipsychotics. Patients were also excluded if they had any form of cognitive impairment or a history of alcohol abuse.

## Organization of the study

All patients were identified during routine physician office visits. Three study visits were performed: visit 1 at baseline (week 0), visit 2 for treatment crossover (week 12), and visit 3 for the final visit (week 24). Patients were randomized to either the disposable doser or vial/syringe for approximately 12 weeks and then ‘crossed over’ to the alternate treatment for an additional 12 weeks (Figure 1).

At visit 1 (week 0), patients who enrolled were randomly assigned to receive the disposable doser or vial/syringe on the basis of a computer-generated randomization scheme. If randomized to the disposable doser, the investigator, or trained staff, taught the patients how to use it. Patients were required to demonstrate proficiency in the use of the delivery system. In addition, the patients were given written instructions on the use of the device.

At each visit, A1C testing was performed at the site using a disposable monitor, which had been waived by the Clinical Laboratory Improvement Amendments (CLIA) and certified by the National Glycohemoglobin Standardization Program (NGSP). Patients also completed the following questionnaires: Diabetes Fear of Self-Injection<sup>11</sup>, Thoughts about Taking Insulin, Insulin Treatment Satisfaction Questionnaire (ITSQ)<sup>12</sup>, and Problem Areas in Diabetes (PAID)<sup>13,14</sup> (Appendix

A). During visit 3, patients also completed the Insulin Device Preference Questionnaire (Appendix A). Patients were required to complete the questionnaires in the exam room prior to leaving the site.

To obtain study medication, patients were given a pharmacy purchase card to present to their community pharmacy. Therefore, all patients received study medication, delivery systems and supplies at no charge. In addition, after each visit, patients were compensated for their time with a gift card of a nominal amount to redeem at a national chain retail store.

## Efficacy assessments

The primary efficacy endpoint was patient preference of an insulin delivery system: disposable doser or vial/syringe as measured by the Insulin Device Preference Questionnaire. Secondary measures included patient responses to the following questionnaires: Diabetes Fear of Self Injection<sup>11</sup>, Thoughts about Taking Insulin, ITSQ<sup>12</sup>, and PAID<sup>13,14</sup> (Appendix A). To assess delivery system preference and patients’ thoughts about taking insulin, the Device Preference and Thoughts About Taking Insulin Questionnaires were developed.

In addition, baseline demographics and clinical characteristics of patients were evaluated to describe the population, and to determine if there were any differences in study outcomes based on patients’ characteristics. The demographics evaluated included age, gender, body mass index, and race. The clinical characteristics evaluated included type of diabetes, duration of diabetes, and duration of insulin use, Charlson Co-morbidity Index (CCI), and A1C values.

The CCI for each patient was calculated from the patient’s concomitant illnesses and was used as a measure

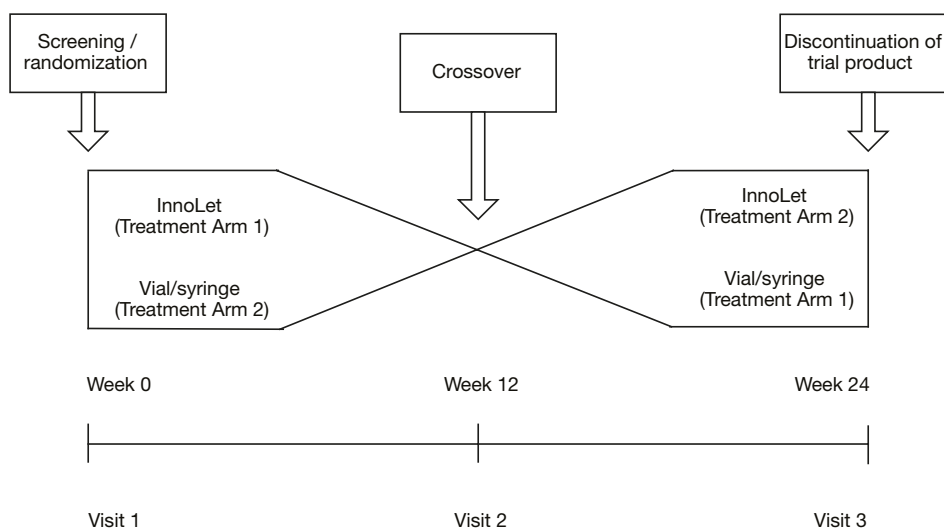


Figure 1. Treatment schedule

of co-morbidity<sup>15</sup>. The CCI contains 17 categories of diseases, each assigned an associated weight based on the adjusted risk of one-year mortality<sup>16</sup>. The overall score reflects the cumulative increased likelihood of one-year mortality. The higher the score, the more severe the burden of comorbidity<sup>15,16</sup>.

## Statistical analysis

Due to the non-systematic distribution of missing data across study variables, the number of patients with missing data for each study variable is reported. All data are presented as mean  $\pm$  standard error of the mean (SEM) or *N* (%; percent) and stratified by either treatment arm or treatment response (completion of disposable doser or vial/syringe use) as appropriate for the data. To compare baseline demographic and clinical characteristics between treatment arms, *t*-test and chi-square analyses were performed on non-missing data.

Patient preference rates for each of the survey questionnaires were reported from the questionnaires completed during visit 2 and visit 3. To test the preference rates, a one-sample test of proportions was used. Proportions were compared to a baseline value of 0.50 (i.e. no preference). To compare treatment effect, only non-missing pairs (i.e. for patients with non-missing data upon completion of each treatment arm) were included in the analysis. The mean treatment effect was first determined within each treatment arm among non-missing pairs, then the unweighted average of the two treatment arms was calculated as the overall treatment effect. The *t*-test or Wilcoxon signed rank was used to compare the treatment effect for continuous or ordinal variables.

Logistic regression was performed to identify potential factors that influence a patient's preference for the disposable doser versus no preference for the disposable doser. The no-preference category included patients who reported no preference plus those who reported preference for vial/syringe. Variables entered into the model included: age at enrollment, gender, diabetes type and treatment arm. Two-way interaction terms were checked for significance and included in the final model if significant.

Reported *p*-values for the preference survey questionnaire are one-sided, all other reported *p*-values are two-sided. An alpha level of 0.05 was used for all statistical analyses.

## Results

A total of 260 patients were enrolled in the study. To be included in the primary analysis, a patient had to have met all inclusion and exclusion criteria, completed

all study visits within the designated timeframe and completed the preference outcome (*n* = 162). Patient demographics are displayed in Table 1. Ninety-eight patients failed to meet these requirements and were excluded for the following reasons: one patient (0.4%) used insulin for less than 6 months prior to enrollment, 53 (20.4%) were lost to follow-up, 32 (12.3%) were exposed to either delivery system for less than 9 weeks or had greater than a 15-week gap between visit dates, seven (2.7%) had a serious adverse event (all were deemed unrelated to study treatment), two (0.7%) did not complete the preference outcome, and three (0.7%) had a history of alcohol abuse or dementia.

## Delivery system preference

Of the entire cohort, 71.5% of the patients reported an overall preference for the disposable doser (*p* < 0.0001; Table 2). Patients reported that the disposable doser was a more convenient method for the administration of insulin (74.1%, *p* < 0.0001), an easier method for insulin administration (75.2%, *p* < 0.0001), was more comfortable to use in public (72.3%, *p* < 0.0001), was the least unpleasant method to use (67.9%, *p* < 0.0001), made it easier to take all of their daily insulin doses (62.3%, *p* = 0.0006), and made life with diabetes easier (62.2%, *p* = 0.0007; Table 3). Although not statistically significant, a slightly higher percentage of patients reported that the disposable doser allowed a more enjoyable social life (52.5%, *p* = 0.2658), was the method of insulin administration that least interfered with daily activities (51.5%, *p* = 0.3569), and provided an overall better quality of life (55.6%, *p* = 0.0763). No statistical test was performed on the questions for preference of the disposable doser providing a more flexible method to deliver insulin, a method of insulin administration that provides better control over blood sugar, and a method of insulin administration that makes them less dependent on others, because the proportion of patients who selected the disposable doser as the preferred method was less than the baseline comparison value of 0.50 (i.e. no preference).

The degree of patient preference (slight, some, strong, very strong) was examined for each subset: those who preferred the disposable doser and those who preferred the vial/syringe. Of the subset of patients who preferred the disposable doser (*n* = 117), 78.6% (*n* = 92) had a strong or very strong preference for this delivery system. Of the subset of patients who preferred vial/syringe (*n* = 36), 66.7% (*n* = 24) had a strong or very strong preference for this delivery system.

Factors that influenced preference for the disposable doser included age and treatment arm. For each additional year age increased, patients reported a decrease

**Table 1.** Baseline demographic and clinical characteristics

	Randomized group		Overall ( <i>n</i> = 162)
	Arm 1 Disposable doser to vial/syringe ( <i>n</i> = 73)	Arm 2 Vial/syringe to disposable doser ( <i>n</i> = 89)	
Age in years (mean ± SD)	59.6 ± 10.2	59.9 ± 11.2	59.8 ± 10.7
Men (%)	53.4	47.2	50.0
Race (%)			
American Indian	1.4	0	0.6
Asian/Pacific Islander	1.4	2.3	1.9
Black/African American	5.5	15.7	11.1
White/Caucasian	69.9	58.4	63.6
White/Hispanic	19.2	22.5	21.0
Other	2.7	1.1	1.9
Type of DM (%)			
Type 1	12.3	10.1	11.1
Type 2	87.7	89.9	88.9
Duration of diabetes (%)			
< 5 years	11.0	12.4	11.7
5–10 years	26.0	19.1	22.2
11–15 years	24.7	28.1	26.5
15+ years	38.4	39.3	38.9
Duration of insulin use (%)			
6 months – 1 year	11.0	4.5	7.4
1 – < 2 years	8.2	13.5	11.1
2 – < 3 years	4.1	5.6	4.9
3 – < 4 years	5.5	9.0	7.4
4 – < 5 years	4.1	12.4	8.6
5+ years	67.1	55.1	60.5
BMI (%)			
Normal: 18.5–24.9	9.6	11.2	10.5
Overweight: 25–29.9	28.8	19.1	23.5
Obesity: ≥ 30	61.6	69.7	66.1
A1C* (mean ± SD)	7.2 ± 1.3	7.8 ± 1.3	7.5 ± 0.1
Charlson Co-morbidity Index (mean ± SD)	3.0 ± 2.0	2.8 ± 2.1	2.9 ± 2.0

\* *p* < 0.05 for the comparison between treatment arms  
SD = Standard deviation

in their preference for the disposable doser (odds ratio [OR], 0.948; 95% CI 0.911–0.986). Those who were randomized to arm 2 (vial/syringe to disposable doser) preferred the disposable doser more than those who were randomized to arm 1 (disposable doser to vial/syringe) (OR, 2.170; 95% CI 1.051–4.478).

### Fear of Self-Injection Questionnaire

Results for all of the eight items, as well as the summary score, on the Fear of Self-Injection Questionnaire showed a statistically significant difference, where after using the disposable doser, patients reported a lower fear of self-injection (*p* < 0.05; Table 4). The summary score for overall fear of self-injection was lower after

using the disposable doser than after using vial/syringe (mean ± SEM: 9.5 ± 0.2 vs. 11.2 ± 0.4).

### Thoughts About Taking Insulin Questionnaire

Results for six of the seven items, as well as the summary score, on the Thoughts About Taking Insulin Questionnaire showed a statistically significant difference, where after using the disposable doser, patients reported a lower degree of non-compliance (*p* < 0.05; Table 5). The summary score for overall degree of non-compliance was lower after using the disposable doser than after using vial/syringe (mean ± SEM: 10.3 ± 0.3 vs. 12.0 ± 0.5).

**Table 2.** Patient preference for insulin administration delivery system stratified by randomization

	Randomized group		Overall n (%)
	Arm 1 Disposable doser to vial/syringe n (%)	Arm 2 Vial/syringe to disposable doser n (%)	
Total in each arm	73 (45.06)	89 (54.94)	162 (100.00)
Choice of disposable doser versus vial/syringe as preferred method of insulin use?			
Disposable doser	47 (64.38)	70 (78.65)	117 (72.22)
Vial/syringe	20 (27.40)	16 (17.98)	36 (22.22)
No difference	6 (8.22)	3 (3.37)	9 (5.56)
Which method is more convenient to use?			
Disposable doser	50 (68.49)	71 (79.78)	121 (74.69)
Vial/syringe	14 (19.18)	12 (13.48)	26 (16.05)
No difference	9 (12.33)	6 (6.74)	15 (9.26)
Which method is easier to use?			
Unknown/missing	0 (0)	1 (1.12)	1 (0.62)
Disposable doser	50 (68.49)	72 (80.90)	122 (75.31)
Vial/syringe	15 (20.55)	11 (12.36)	26 (16.05)
No difference	8 (10.96)	5 (5.62)	13 (8.02)
Which method is offers greater flexibility?			
Unknown/missing	2 (2.74)	1 (1.12)	3 (1.85)
Disposable doser	33 (45.21)	45 (50.56)	78 (48.15)
Vial/syringe	8 (10.96)	6 (6.74)	14 (8.64)
No difference	30 (41.10)	37 (41.57)	67 (41.36)
Which method is more comfortable to use in public?			
Unknown/missing	1 (1.37)	2 (2.25)	3 (1.85)
Disposable doser	47 (64.38)	69 (77.53)	116 (71.60)
Vial/syringe	8 (10.96)	6 (6.74)	14 (8.64)
No difference	17 (23.29)	12 (13.48)	29 (17.90)
Which method allows a more enjoyable social life?			
Unknown/missing	1 (1.37)	1 (1.12)	2 (1.23)
Disposable doser	33 (45.21)	52 (58.43)	85 (52.47)
Vial/syringe	9 (12.33)	6 (6.74)	15 (9.26)
No difference	30 (41.10)	30 (33.71)	60 (37.04)
Which method least interferes with daily activities?			
Unknown/missing	1 (1.37)	1 (1.12)	2 (1.23)
Disposable doser	34 (46.58)	49 (55.06)	83 (51.23)
Vial/syringe	7 (9.59)	4 (4.49)	11 (6.79)
No difference	31 (42.47)	35 (39.33)	66 (40.74)
Which method provides better control over blood sugar?			
Unknown/missing	1 (1.37)	4 (4.49)	5 (3.09)
Disposable doser	27 (36.99)	40 (44.94)	67 (41.36)
Vial/syringe	12 (16.44)	9 (10.11)	21 (12.96)
No difference	33 (45.21)	36 (40.45)	69 (42.59)
Which method is least unpleasant to use?			
Unknown/missing	1 (1.37)	1 (1.12)	2 (1.23)
Disposable doser	43 (58.90)	67 (75.28)	110 (67.90)
Vial/syringe	9 (12.33)	12 (13.48)	21 (12.96)
No difference	20 (27.40)	9 (10.11)	29 (17.90)

**Table 2.** (Continued)

	Randomized group		Overall n (%)
	Arm 1 Disposable doser to vial/syringe n (%)	Arm 2 Vial/syringe to disposable doser n (%)	
Which method makes it easier to take all of your daily insulin doses?			
Unknown/missing	1 (1.37)	1 (1.12)	2 (1.23)
Disposable doser	39 (53.42)	62 (69.66)	101 (62.35)
Vial/syringe	13 (17.81)	10 (11.24)	23 (14.20)
No difference	20 (27.40)	16 (17.98)	36 (22.22)
Which method makes you less dependent on others?			
Unknown/missing	1 (1.37)	3 (3.37)	4 (2.47)
Disposable doser	30 (41.10)	48 (53.93)	78 (48.15)
Vial/syringe	6 (8.22)	5 (5.62)	11 (6.79)
No difference	36 (49.32)	33 (37.08)	69 (42.59)
Which method makes life with diabetes easier?			
Unknown/missing	0 (0)	1 (1.12)	1 (0.62)
Disposable doser	41 (56.16)	60 (67.42)	101 (62.35)
Vial/syringe	10 (13.70)	6 (6.74)	16 (9.88)
No difference	22 (30.14)	22 (24.72)	44 (27.16)
Which method provides an overall better quality of life?			
Unknown/missing	0 (0)	2 (2.25)	2 (1.23)
Disposable doser	35 (47.95)	55 (61.80)	90 (55.56)
Vial/syringe	10 (13.70)	5 (5.62)	15 (9.26)
No difference	28 (38.36)	27 (30.34)	55 (33.95)

**Table 3.** Comparison\* of overall preference for the disposable doser upon study completion

Patient preference for insulin device	n	Percent of cohort that preferred disposable doser	p-value
Disposable doser for administration of insulin	162	71.51	<0.0001
Disposable doser as the more convenient method for administration of insulin	162	74.13	<0.0001
Disposable doser as the easier method for administration of insulin	161	75.15	<0.0001
Disposable doser as the more flexible method for administration of insulin	159	48.80	N/A
Disposable doser as the method of administration for insulin that is more comfortable to use in public	159	72.29	<0.0001
Disposable doser as the method of administration for insulin that allows a more enjoyable social life	160	52.46	0.2658
Disposable doser as the method of administration for insulin that least interferes with daily activities	160	51.45	0.3569
Disposable doser as the method of administration for insulin that provides better control over blood sugar	157	42.27	N/A
Disposable doser as the method of administration for insulin that is least unpleasant to use	160	67.92	<0.0001
Disposable doser as the method of administration for insulin that makes it easier to take all of their daily insulin doses	160	62.31	0.0006
Disposable doser as the method of administration for insulin that makes them less dependent on others	158	48.74	N/A
Disposable doser as the method of administration for insulin that makes life with diabetes easier	161	62.17	0.0007
Disposable doser as the method of administration for insulin that provides an overall better quality of life	160	55.58	0.0763

\*Comparisons performed on non-missing data only

**Table 4.** Responses to Diabetes Fear of Self-Injection Questionnaire upon completion of disposable doser versus vial/syringe

Question: <i>When I have to inject an insulin dose...</i>	Scoring scale	Completed disposable doser		Completed vial/syringe	
		No. of patients	Mean (SEM)	No. of patients	Mean (SEM)
I become restless	1 (almost never) to 4 (almost always)	160	1.23 (0.04)	162	1.41 (0.06)
I feel tense	1 (almost never) to 4 (almost always)	160	1.28 (0.04)	162	1.57 (0.06)
I feel afraid	1 (almost never) to 4 (almost always)	160	1.08 (0.02)	162	1.29 (0.05)
I worry about it	1 (almost never) to 4 (almost always)	160	1.19 (0.04)	161	1.42 (0.06)
I feel nervous	1 (almost never) to 4 (almost always)	159	1.18 (0.03)	162	1.43 (0.06)
I brood about it	1 (almost never) to 4 (almost always)	160	1.18 (0.04)	162	1.36 (0.06)
I try to postpone it	1 (almost never) to 4 (almost always)	160	1.21 (0.04)	161	1.39 (0.06)
I get angry	1 (almost never) to 4 (almost always)	160	1.14 (0.03)	162	1.36 (0.06)
Overall Fear of Insulin Injection score	Max score = 32	159	9.47 (0.21)	161	11.23 (0.39)

**Table 5.** Responses to Thoughts About Taking Insulin Questionnaire upon completion of disposable doser versus vial/syringe

Question: <i>During the past 4 weeks, how often did you...</i>	Scoring scale	Completed disposable doser		Completed vial/syringe	
		No. of patients	Mean (SEM)	No. of patients	Mean (SEM)
Think about postponing your insulin dose to a more convenient time?	1 (never) to 6 (always)	160	1.65 (0.07)	162	1.98 (0.10)
Think about skipping or not taking your insulin dose?	1 (never) to 6 (always)	160	1.43 (0.06)	162	1.65 (0.09)
Postpone taking your insulin until a more convenient time?	1 (never) to 6 (always)	160	1.68 (0.07)	162	1.98 (0.10)
Miss an insulin dose on purpose?	1 (never) to 6 (always)	160	1.29 (0.05)	161	1.46 (0.07)
Miss an insulin dose because you forgot to take it?	1 (never) to 6 (always)	159	1.71 (0.07)	162	1.90 (0.08)
Miss an insulin dose because you forgot your insulin supplies?	1 (never) to 6 (always)	160	1.36 (0.05)	162	1.61 (0.08)
Miss an insulin dose because you wanted to avoid the hassle of injecting?	1 (never) to 6 (always)	160	1.20 (0.05)	162	1.43 (0.07)
Overall score for Thoughts About Taking Insulin Questionnaire	Max score = 42	159	10.33 (0.31)	161	12.03 (0.49)

### Insulin Treatment Satisfaction Questionnaire (ITSQ)

There was a statistically significant difference in all transformed score categories of the ITSQ, as well as the overall summary score ( $p < 0.05$ ; Table 6). After using the disposable doser, patients had higher insulin treatment satisfaction in the areas of convenience of regimen ( $p < 0.0001$ ),

lifestyle flexibility ( $p = 0.0006$ ), glycemic control ( $p < 0.0001$ ), hypoglycemic control ( $p < 0.0001$ ), insulin delivery system satisfaction ( $p < 0.0001$ ) and overall satisfaction ( $p < 0.0001$ ) compared to after using vial/syringe. The transformed summary score for overall insulin treatment satisfaction was higher after using the disposable doser than after using the vial/syringe (mean  $\pm$  SEM: 79.0  $\pm$  1.3 vs. 70.4  $\pm$  1.7; Table 7).



**Table 6.** Responses to Insulin Treatment Satisfaction Questionnaire upon completion of disposable doser versus vial/syringe

Question:	Scoring scale	Completed disposable doser		Completed vial/syringe	
		No. of patients	Mean (SEM)	No. of patients	Mean (SEM)
How convenient is it for you to take all your daily insulin doses as prescribed?	1 (extremely convenient) to 7 (not convenient at all)	161	2.24 (0.12)	161	2.86 (0.14)
How much of a bother is it for you to take all your daily insulin doses as prescribed?	1 (no bother at all) to 7 (a tremendous bother)	161	2.12 (0.11)	161	2.77 (0.14)
How much does your current insulin treatment interfere with your ability to enjoy social or leisure activities?	1 (does not interfere at all) to 7 (interferes tremendously)	161	2.00 (0.09)	161	2.65 (0.14)
How much does your current insulin treatment interfere with your work or school activities?	1 (does not interfere at all) to 7 (interferes tremendously)	161	1.85 (0.10)	162	2.35 (0.13)
How much do you have to plan the timing of your meals or snacks around the insulin you currently use?	1 (no planning at all) to 7 (a tremendous amount of planning)	160	2.59 (0.13)	162	3.10 (0.13)
How much do you have to plan what you eat with your current insulin treatment?	1 (no planning at all) to 7 (a tremendous amount of planning)	159	2.99 (0.14)	162	3.21 (0.13)
How much do you have to plan your physical activities (such as exercise or strenuous household chores) around your current insulin treatment?	1 (no planning at all) to 7 (a tremendous amount of planning)	161	2.45 (0.13)	162	2.75 (0.13)
How confident are you that you can avoid symptoms of low blood sugar (such as sweating, trembling, dizziness, blurred vision) with your current insulin treatment?	1 (extremely confident) to 7 (not at all confident)	160	2.45 (0.11)	162	3.00 (0.13)
How confident are you that you can avoid severe episodes of low blood sugar that result in loss of consciousness (fainting or passing out) with the insulin you currently use?	1 (extremely confident) to 7 (not at all confident)	160	1.93 (0.10)	161	2.42 (0.12)
In general, how bothered are you by symptoms of low blood sugar (such as sweating, trembling, dizziness, blurred vision) due to the insulin you currently use?	1 (no bother at all) to 7 (a tremendous bother)	161	2.32 (0.10)	162	2.85 (0.12)
How much do you feel that the insulin you are currently using increases the chances that you will experience low blood sugar?	1 (not at all) to 7 (extremely)	161	1.99 (0.09)	162	2.43 (0.11)
How worried are you about experiencing low blood sugars during the night with the insulin you currently use?	1 (not worried at all) to 7 (extremely worried)	161	2.11 (0.10)	162	2.66 (0.13)
How confident are you that you can avoid symptoms of <i>high</i> blood sugar (such as dry mouth, thirst, frequent urination, fatigue, increased appetite) with your current insulin treatment?	1 (extremely confident) to 7 (not at all confident)	161	2.54 (0.10)	162	2.88 (0.13)
How satisfied are you with the stability of your blood sugar levels with your current insulin treatment?	1 (extremely satisfied) to 7 (not at all satisfied)	159	2.50 (0.12)	161	2.85 (0.13)

**Table 6.** (Continued)

Question:	Scoring scale	Completed disposable doser		Completed vial/syringe	
		No. of patients	Mean (SEM)	No. of patients	Mean (SEM)
How time consuming is it for you to manage your current insulin treatment?	1 (not at all time consuming) to 7 (extremely time consuming)	160	2.24 (0.11)	161	2.73 (0.13)
Overall, how pleased are you with the blood sugar control you achieve with your current insulin treatment?	1 (extremely pleased) to 7 (not at all pleased)	160	2.53 (0.12)	161	2.77 (0.12)
In general, how stressful is it for you to manage taking your current insulin treatment?	1 (not at all stressful) to 7 (extremely stressful)	159	2.06 (0.10)	161	2.63 (0.13)
How burdensome is it for you to manage your current insulin treatment?	1 (not at all burdensome) to 7 (extremely burdensome)	159	2.10 (0.10)	161	2.75 (0.14)
To what extent do you sometimes feel down or depressed because of your current insulin treatment?	1 (not at all down or depressed) to 7 (extremely down or depressed)	160	2.13 (0.10)	161	2.69 (0.13)
How easy is it for you to take the correct amount of insulin each time with your current method of taking insulin?	1 (extremely easy) to 7 (not easy at all)	159	1.64 (0.10)	162	2.40 (0.13)
How convenient is your current method of taking insulin when you are away from home?	1 (extremely convenient) to 7 (not convenient at all)	160	2.11 (0.12)	162	3.46 (0.16)
How much pain or other physical discomfort do you experience with your current method of taking insulin?	1 (no pain or discomfort) to 7 (a tremendous amount of pain or discomfort)	159	1.81 (0.09)	162	2.60 (0.12)

**Table 7.** Mean difference comparisons\* of transformed scored responses to Insulin Treatment Satisfaction Questionnaire upon completion of disposable doser versus vial/syringe

Question topic	n	Disposable doser to vial/syringe		p-value
		Mean difference	SEM	
Inconvenience of regimen (transformed score)	161	8.595	1.811	<0.0001
Lifestyle flexibility (transformed score)	161	6.556	1.884	0.0006
Glycemic control (transformed score)	161	6.832	1.633	<0.0001
Hypoglycemic control (transformed score)	161	7.323	1.557	<0.0001
Insulin delivery device satisfaction (transformed score)	161	12.62	2.030	<0.0001
Overall summary score (transformed score)	161	8.385	1.489	<0.0001

\*Comparisons performed on non-missing pairs only

### Problem Areas in Diabetes (PAID)

Results for 17 of the 20 items, as well as the summary score, on the PAID questionnaire showed a statistically significant difference, where after using the disposable doser, patients reported a lower amount of problem areas in diabetes ( $p < 0.05$ ; Table 8). The summary score for the overall problem areas in diabetes was lower after using the disposable doser

than after using the vial/syringe (mean  $\pm$  SEM: 20.8  $\pm$  1.5 vs. 26.1  $\pm$  1.9).

### Discussion

The primary objective of this study was to evaluate patients' preference for an insulin delivery system by comparing a disposable insulin doser to standard vial

**Table 8.** Responses to Problem Areas in Diabetes questionnaire upon completion of disposable doser versus vial/syringe

Question:	Scoring scale	Completed disposable doser		Completed vial/syringe	
		No. of patients	Mean (SEM)	No. of patients	Mean (SEM)
<i>Which of the following diabetes issues are currently problems for you?</i>					
Not having clear and concrete goals for your diabetes care?	0 (not a problem) to 4 (serious problem)	159	0.67 (0.07)	162	0.94 (0.08)
Feeling discouraged with your diabetes treatment plan?	0 (not a problem) to 4 (serious problem)	159	0.65 (0.07)	161	0.91 (0.08)
Feeling scared when you think about living with diabetes?	0 (not a problem) to 4 (serious problem)	159	0.98 (0.09)	161	1.24 (0.10)
Uncomfortable social situations related to your diabetes care (e.g., people telling you what to eat)?	0 (not a problem) to 4 (serious problem)	159	0.78 (0.08)	162	1.11 (0.09)
Feelings of deprivation regarding food and meals?	0 (not a problem) to 4 (serious problem)	159	0.92 (0.08)	161	1.21 (0.09)
Feeling depressed when you think about living with diabetes?	0 (not a problem) to 4 (serious problem)	159	0.96 (0.08)	162	1.23 (0.10)
Not knowing if your mood or feelings are related to your diabetes?	0 (not a problem) to 4 (serious problem)	157	1.03 (0.08)	161	1.24 (0.10)
Feeling overwhelmed by your diabetes?	0 (not a problem) to 4 (serious problem)	158	0.84 (0.08)	161	1.11 (0.10)
Worrying about low blood sugar reactions?	0 (not a problem) to 4 (serious problem)	159	1.01 (0.08)	160	1.19 (0.09)
Feeling angry when you think about living with diabetes?	0 (not a problem) to 4 (serious problem)	158	0.72 (0.08)	160	0.94 (0.10)
Feeling constantly concerned about food and eating?	0 (not a problem) to 4 (serious problem)	159	1.05 (0.08)	162	1.30 (0.10)
Worrying about the future and the possibility of serious complications?	0 (not a problem) to 4 (serious problem)	159	1.65 (0.10)	161	1.80 (0.11)
Feelings of guilt or anxiety when you get off track with your diabetes management?	0 (not a problem) to 4 (serious problem)	158	1.33 (0.09)	162	1.41 (0.10)
Not 'accepting' your diabetes?	0 (not a problem) to 4 (serious problem)	161	0.56 (0.07)	162	0.73 (0.08)
Feeling unsatisfied with your diabetes physician?	0 (not a problem) to 4 (serious problem)	160	0.11 (0.03)	162	0.21 (0.05)
Feeling that diabetes is taking up too much of your mental and physical energy every day?	0 (not a problem) to 4 (serious problem)	161	0.69 (0.07)	160	0.93 (0.09)
Feeling alone with your diabetes?	0 (not a problem) to 4 (serious problem)	157	0.60 (0.07)	161	0.72 (0.08)
Feeling that your friends and family are not supportive of your diabetes management efforts?	0 (not a problem) to 4 (serious problem)	161	0.38 (0.06)	161	0.52 (0.07)
Coping with complications of diabetes?	0 (not a problem) to 4 (serious problem)	160	1.03 (0.08)	162	1.21 (0.10)
Feeling 'burned out' by the constant effort needed to manage diabetes?	0 (not a problem) to 4 (serious problem)	160	0.85 (0.08)	162	1.21 (0.10)
Overall Score for Problem Areas in Diabetes Questionnaire	Max. Score = 100	150	20.76 (1.46)	151	26.10 (1.86)

and syringe. We have shown that in the real world setting, after using both delivery systems, patients reported a greater preference for the disposable insulin doser.

The goal of insulin therapy is to return blood glucose levels to normal or near-normal levels. It has been extensively documented that glycemic control may prevent both short-term and long-term effects of poorly controlled blood glucose<sup>1-3</sup>. However, for long-term regimens, such as insulin therapy, to be effective, patients must be willing to adhere to their treatment plan. While there are many factors that affect adherence, factors that may enhance patients' willingness to adhere include ease and convenience of administration, minimization of lifestyle disruptions, and the ability to be confident in the skills necessary to manage the regimen. We found factors that contributed to patients' preference for the disposable doser included its convenience, ease of use, comfort of use in public and social settings, lessening fear of self-injection, lessening feeling of being overwhelmed by diabetes and making life with diabetes easier. Our findings of 71.5% overall preference for the disposable doser are consistent with the results of a previous clinical trial that showed patients' preference for use of an alternative insulin delivery system over vial and syringe<sup>7,8</sup>. Furthermore, a two-sided test was conducted and there was no significant difference in the study findings.

While we found many factors that may contribute to patients being more adherent to their insulin treatment regimen, we did not find a significant difference in A1C concentrations between the two treatment groups during the study observation period. While a few of the patients had a change in their insulin regimen between study visits, the majority did not and generally, patients switched their insulin delivery system rather than the type, frequency and/or dose of insulin.

The design of this study required that patients used insulin therapy for at least 6 months; however, the majority of patients had been using insulin therapy for 5 or more years. Therefore, it is reasonable to assume that these patients had mastered the manual dexterity and hand-eye coordination necessary to administer insulin via vial and syringe. However, patients reported that using the disposable doser to administer insulin consumed even less time, made it easier to give the correct amount of insulin, caused less pain, and postponed or missed insulin doses occurred less often. These enhanced efficiencies may result in greater patient acceptance of insulin therapy, more accurate insulin administration, fewer insulin administration errors and missed doses, and thereby may delay or prevent the onset of long-term complications of diabetes.

## Limitations

There are some study limitations to consider. Although patients were randomized, there were some differences in baseline characteristics between the patients within the two treatment arms. Therefore, logistic regression was performed to adjust for age, gender, type of diabetes, and treatment arm. For the majority of patients, only the delivery system changed so any potential drug or efficacy bias that would affect preference was removed. However, a randomization bias may have been present. To correct this potential bias, Koch's method was used when performing tests of treatment effect; however, one cannot be certain if it was completely eliminated. While our findings were statistically significant, we cannot be certain that patients' preference for an insulin delivery system would result in an improvement in their clinical status. Additional research exploring the clinical significance of each of the delivery systems would be helpful. In addition, patients who enrolled in this study were those who were actively seeking medical treatment for diabetes. It is not known if these findings would be similar for the general population of patients treated for diabetes. This study had a large proportion of patients with type 2 diabetes. Therefore, our study finding may not be generalizable to the entire insulin-dependent population. Finally, some disadvantages exist with the use of alternative insulin delivery systems. Insulin pens and cartridges are not available for all types of insulin regimens, pre-filled pens and cartridges may not be altered and, in general, alternative insulin delivery systems tend to be more costly than insulin sold in traditional vials.

## Conclusion

In real-world clinical practice settings, after using both the disposable doser and vial and syringe, patients in this study preferred the disposable doser to administer their insulin therapy. The importance of patient preference should not be underestimated. When prescribing insulin therapy, physicians may consider asking patients which delivery system they would prefer. An alternative insulin delivery system may offer greater patient acceptance of insulin therapy and, as was found in our study, improved treatment satisfaction. These findings may be clinically significant, given the potential health gains that can be obtained through improved diabetes self-management. Further research is needed to examine long-term use of the alternative insulin delivery systems.

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## References

1. American Diabetes Association. Economic costs of diabetes in the US in 2002. *Diabetes Care* 2003;26:917-32
2. Centers for Disease Control and Prevention. National Diabetes Fact Sheet [online]. Atlanta, GA.; Available at: <http://www.cdc.gov/diabetes/pubs/estimates.htm#incidence>. [last accessed 4 Oct 2005]
3. Diabetes Control and Complication Trial Research Group. The effects of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;329:977-86
4. American Diabetes Association. Clinical practice recommendations 2005. *Diabetes Care* 2005;28 (Suppl 1): S1-79
5. DeWitt DE, Hirsch IB. Outpatient insulin therapy in type 1 and type 2 diabetes mellitus. *JAMA* 2003; 289:2254-64
6. Tabak AG, Tamas G, Zgibor J, et al. Targets and reality. *Diabetes Care* 2000;23:1284-9
7. Summers KH, Szeinbach SL, Lenox SM. Preference for insulin delivery systems among current insulin users and nonusers. *Clin Ther* 2004;26:1498-505
8. Costa S, Brackenridge B, Hicks D. A comparison of insulin pen use in the United States and the United Kingdom. *Diabetes Educator* 2002;28:52-6
9. World Medical Association Declaration of Helsinki. Recommendations guiding physicians in biomedical research involving human subjects. Amended by 48th General Assembly, Somerset West, Republic of South Africa, October 1996. *JAMA* 1997;277(11)
10. International Conference on Harmonisation (ICH) Topic E6. Harmonised Tripartite Guideline for Good Clinical Practice. Step 5, Consolidated Guideline 1 May 1996
11. Mollema E, Snoek FJ, Pouwer F, et al. Diabetes fear of injecting and self testing questionnaire: a psychometric evaluation. *Diabetes Care* 2000;23:765-9
12. Anderson RT, Skovlund SE, Marrero D, et al. Development and validation of the Insulin Treatment Satisfaction Questionnaire. *Clin Ther* 2004; 26:565-78
13. Welch G, Weinger K, Anderson B, Polnsky WH. Responsiveness of the Problem Areas in Diabetes (PAID) questionnaire. *Diabetes Medicine* 2003;20:69-72
14. Snoek FJ, Pouwer F, Welch G, Polonsky WH. Diabetes-related emotional distress in Dutch and US diabetic patients. *Diabetes Care* 2000;23:1305-9
15. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chron Dis* 1987;40: 373-83
16. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol* 1992; 45:613-19

## Appendix A – Study Questionnaires

### Insulin Treatment Satisfaction Questionnaire

This questionnaire consists of two parts with a total of 22 items. Each item has a range of 1 (highest satisfaction) to 7 (lowest satisfaction). A summary score for the ITSQ was calculated by grouping the original 22 items into six scales. The scale categories were: inconvenience of regimen, lifestyle flexibility, glycemic control, hypoglycemic control, insulin device satisfaction and an overall summary score. Raw scores for each individual item were first transformed to a 0–100 scale where higher scores indicated better satisfaction. The transformed score was calculated as (7 minus the raw score) divided by 6 (i.e. 7 minus 1), multiplied by 100. The final transformed score for each of the scale categories was calculated as the mean of the non-missing transformed items used to define each scale.

### Diabetes Fear of Self-Injection Questionnaire

This questionnaire consists of eight items. The range of each item is 1 (Never) to 4 (Always). A summary score was calculated for each patient by taking the sum of all eight items, 8 representing the lowest amount of fear and 32 representing the highest amount of fear. If a response to any of the eight items was missing, then no summary score could be calculated and was reported as a missing value.

### Thoughts about Taking Insulin Questionnaire

This questionnaire consists of seven items. Each item has a range of 1 (Never) to 6 (Always). A summary score was calculated for each patient by taking the sum of all seven items, 7 representing the lowest amount of noncompliance and 42 representing the highest amount of noncompliance. If a response to any of the seven items was missing, then no summary score could be calculated and was reported as a missing value.

### Problem Areas in Diabetes

This questionnaire consists of 20 items. The range of each item is 1 (not a problem) to 4 (serious problem). A summary score was calculated for each patient by taking the sum of all 20 items and multiplying this total by 1.25 to achieve a scale of 0 (lowest amount of problems) to 100 (highest amount of problems). If a response to any of the 20 items was missing, then no summary score could be calculated and was reported as a missing value.

### Insulin Device Preference Questionnaire

This questionnaire consists of two parts with a total of 14 items. The first part determined which device the patient preferred overall (or if there was no preference for either device) and how strong their preference was for the device if the disposable doser or vial/syringe was chosen. The second part asked which device was preferred (or if there was no preference) on a series of questions ranging from convenience of use to providing an overall better quality of life.

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