A discrete choice experiment to understand preferences of patients with type 2 diabetes treated with injectable non-insulinic agents

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ABSTRACT

Objective: To identify and evaluate the Spanish diabetes mellitus type 2 patients' preferences on injection and medication frequency and complexity of the treatment of diabetes. Additionally, patients' willingness to pay is evaluated.

Methods: A total of 180 patients recruited from 5 health care centres in Spain completed a discrete choice experiment survey designed to evaluate patients' preferences over three attributes discriminating by age, sex and patients experience with previous treatment. The resulting model was analysed using a conditional (fixed-effects) logistic regression.

Results: Naïve and non-naïve patients were willing to pay 83.25€ for a 'no preparation required' dose. In addition, both groups of patients were willing to pay 44.30€ for a 'simple preparation' dose. In terms of treatment frequency, no-naïve patients preferred a daily injection with freedom of timing before a daily scheduled injection, willing to pay 22.20€. In addition, no-naïve patients were willing to pay 34.61€ for a weekly injection. Finally, the most valued treatment change in naïve patients was to exchange a daily scheduled injection for a weekly injection, willing to pay 14.35€ for that change.

Conclusions:

This study shows that patients highly value the avoidance of injections, with weekly dosing clearly preferred over daily dosing. Of the other attributes, a 'no preparation required' dose is clearly preferred over a 'simple preparation' dose. These findings may provide a better understanding of what patients prefer and value in their treatment and provide guidance for clinicians making therapeutic decisions regarding T2DM treatments.

KEYWORDS

Discrete choice experiment; patient preference; type 2 diabetes; willingness to pay; health technology assessment; Spain

Word count: 3,702

1. INTRODUCTION

Diabetes Mellitus (DM) is a chronic condition characterised by persistent increased blood levels of glucose as a consequence of a deficiency in insulin production or the ineffectiveness of the insulin produced. In type 2 diabetes mellitus (DMT2) the organism becomes resistant to the insulin produced by the pancreas. DM is one of the most common chronic diseases in many countries, affecting around 425 million people all over the world [1]. The prevalence of diabetes mellitus in the population over 18 in Spain is 13.8%.[2].

Diabetes-derived complications are the main cause for disability and a diminished life quality, and diabetes-related healthcare costs are estimated to constitute up to 12% of the total healthcare budget [1]. The prevalence of the disease has made clear a need to educate the population on DMT2 prevention, as well as on taking a better care of DM patients.

The patient role in DM managing is crucial to avoid or decrease further complications. There is a wide variety of options to control patient blood glucose levels, and treatment options. Assessing patient's preferences could be key to ensure patients adherence to treatment and a correct control of the disease, considering that an insufficient understanding of the treatment plan has an influence on medication adherence [3].

The use of discrete-choice experiments (DCE) allows evaluating the preference for features involved in patients care, permitting the evaluation of individual attributes. DCEs are an attribute based measure of benefit [4] that is based on the assumptions that

healthcare interventions, services, or policies can be described by their attributes and an individual's valuation depends on the levels of these attributes. This method provides information on patient's preferences and willingness to accept trade-offs among features of multi-attribute products [5].

DMT2 patient concerns have been previously evaluated. A DCE study conducted in 2015 determined the preferences of 643 DMT2 patients in relation to the frequency of glucagon-like peptide-1 receptor agonist injections, showing patients clear preference of changing injection frequency from daily to weekly [6]. Another study developed in The Netherlands showed that the most important aspects of diabetes care for patients with T2DM are the frequency of consultations, the approach on emotional support, and the use lifestyle education methods [7]. Other important parameters as treatment complexity or the costs it has for patients have not been extensively analysed, and such studies purely assessing patient's preferences have never been conducted with Spanish patients.

The present study pretends to use DCE to obtain useful information on Spanish DMT2 patients' preferences regarding injection and medication frequency and complexity of the treatment of diabetes. Additionally, patients' willingness to pay is evaluated.

2. METHODS

2.1. Survey design

DCE methodology was used to quantify the preference weights of attributes and attribute levels with different attribute combinations. The first part of the survey included questions on demographics (age, sex, employment status), disease experience (time since diagnosis, experience of hypoglycaemia, general discomfort, previous drug prescription, blood sugar measurement, preventive measures), comorbidities (cardiac disease) and others, as the existence of a supportive family structure or a social worker.

A second part was based on DCE questions about treatment choice. Method characteristics were consistent with the requirements stated by Shackley and Ryan (1995) [8]. This DCE offers patients 9 elections among three hypothetical but realistic options, described using a limited number of attributes, what allows the analysis of choice probability. Attributes and levels were designed after literature review and experts' consultation (Table 1). The experts were endocrinologists and diabetes educators. The most commonly listed attributes in the literature review have been efficacy, adverse effects, and dosing frequency. After the expert's consultation, the three selected attributes were considered: treatment complexity, administration frequency and costs. The treatment attributes selected represent characteristics of different GLP-1 drugs. Total costs were hypothetical given that Spanish patients rarely assume medication costs. The cost attribute was included because the responses of a DCE are modelled within a benefit (or satisfaction) function which provides information on whether or not the given

attributes are important; the relative importance of attributes; the rate at which individuals are willing to trade between attributes; and overall benefit scores for alternatives. We choose cost as the attribute to measure the importance patients gave to each attribute.

The cost levels were determined based on the current costs of GLP-1 drugs in Spain [9]. The higher costs in Spain were 145€, so in consensus with the experts, we defined the maximum cost as 100€ per month and the minimum cost, the half. The third cost was a cost between the maximum and the minimum cost.

The last part of the survey contained a series of closed Likert scale questions included as an internal consistency check. The Likert questions consisted on 9 questions about the importance of preparation and the medication frequency. Some examples are: a) it is more important to me that the medicine is easy to prepare than if I have to administer it every day or once a week; b) I would feel less ill if I only had to take my medication once a week; and c) It would be harder for me to remember to need an injection once a week instead of every day.

A pilot study with 50 patients was conducted prior to launching the main field phase to determine whether any changes to the content or design of the DCE were required. Some minor changes were made to the first part of the survey because demographic data revealed inconsistencies.

The first change made was to the question on monthly income, where the values of monthly income were changed when it was found that more than 54% of the participants

did not answer the question and that, in addition, the answers were accumulated in the first two options. Therefore, it was decided that the values of monthly income should be lower and also the variation between each option, thus trying to make the options more in line with real life. The question about the knowledge of preventive measures was eliminated as it did not provide information since all patients answered the same. The wording of the answer options in the question about the administration method was also modified to make the options clearer and more understandable. Finally, the question about the number of blood glucose controls was changed from having two answer options to having four options in order to be able to determine more precisely the current control patterns.

The above changes were communicated to the ethics committee that had previously approved the study.

2.2. Survey population

A total of 180 patients were included in the study, recruited from 5 Spanish health care centres in Barcelona, Madrid, Alicante and Elda. All patients were diagnosed with DMT2 and remained treatment-naïve for Glucagon-like peptide-1 (GLP-1), although they could be treated with oral antidiabetic drugs (OAD) or insulin. To calculate the sample size, a literature review has been conducted to determine the final size needed. Hall et al [10] suggested that 20-30 respondents per set of choice can provide accurate parameter estimates, while Lancsar et al [11] suggested that it is unusual to require more than 20

observations per set of choice to estimate a reliable model. Therefore, the sample size needed to estimate a reliable model is 180 surveys.

To qualify for the survey, respondents had to meet the following inclusion criteria: a) patients over 18 years of age, b) male or female, c) diagnosis of DM2, d) patients with prescription of OAD and/or insulin, e) patients naïve in the use of GLP-1, f) patients treated in hospitals (or specialised centres) and primary care centres and g) patients who have signed the informed consent form.

Patients with an insufficient level of Spanish to be able to write and/or understand the methodology of the questionnaire and follow the instructions described were excluded from the study. Patients who did not respond more than 3 questions on the DCE were eliminated and their responses were not considered in the study.

The survey was completed by the patients at the visit to the endocrinologist. Endocrinologists and diabetes educators provided an explanation guided by the example proposed in the survey to show patients how a DCE survey works. After the explanations, the patients completed the questionnaire on their own. Surveys were collected from 26 June 2017 to 7 June 2018.

2.3. Statistical analysis

The data acquired through DCE was analysed using STATA. The statistical test employed for the analysis was a conditional (fixed-effects) logistic regression. In an initial model all observed attributes were considered variables, except for one attribute per level, which was considered the reference level. For the final model, the 'cost' feature was turned into

a continuous variable to enable the calculation of patients' willingness to pay in each level. This last model was the one chosen for further analysis. The model was then divided in distinct clusters according to patients' age, sex and patients experience.

To determine at what age to divide into two groups to carry out the data analysis by age a cumulative table has been elaborated and it has been determined to divide in 65 years, since it is in the age in which the cumulative table accumulates the 50% of the population.

2.4. Ethical considerations

The study followed the ethical recommendations of the Declaration of Helsinki, the norms for a Good Clinical and Pharmacoepidemiology practices, and local legislation that applies to observational studies. It had the approval of the Hospital de Bellvitge Ethics Committee and received ratification from all other participant centres.

3. RESULTS

3.1. Study population

A total of 180 participants were included in the study, the mean age of which was 63.35 years (SD=11.49). The youngest patient was 19 years old, while the oldest was 86 years old. 63.28% of the participants were men. The non-response rate was 0%, as all patients responded the questionnaire and those patients who did not respond all the questions missed less than 3 questions. The 46.82% of patients did not respond some question. With regard to employment status, more than half of the participants were pensioners. In relation to the salary level, many participants (44.62%) did not answer this question (Table 2). There are another 2.22% of patients that did not respond some question, but the

missing data for these variables were not included in the tables as it was below 1%, so considered negligible.

All the patients were ambulatory patients collected during their regular visits to the endocrinologist or to the diabetes educator.

Regarding questions related to the disease, more than half of the patients were diagnosed more than 10 years ago, and more than 80% have never suffered a severe hypoglycaemic event (Table 2). In terms of the symptomatic part of the disease, more than 70% of patients felt general malaise and more than 50% suffered from cardiovascular disease (Table 2). Regarding medication, 70% of patients used a combination of oral and injected medication, the latter being in the form of a pen in more than 88% of cases (Table 2). Finally, more than 50% of participants take more than one blood glucose measurement per day (Table 2).

3.2. Survey results

The distinct features' preferences were evaluated in relation to different patient clusters.

The first cluster was determined by patients with (no-naïve) or without experience (naïve) on the use of injected treatments, which revealed significant differences (Table 3). The demographic variables analysed showed that there were significant differences between naïve and non-naïve patients in terms of sex, employment situation, salary level, diagnosis, severe hypoglycemic event, general malaise, cardiovascular disease, glycemic control and social or family support.

Both, naïve and no-naïve patients consider treatment cost very important, and viewed positively weekly injections (Table 4). However, they rated negatively a complex preparation of the dose (p<10%). Naïve patients didn't consider administration timing of importance, neither have they discriminated between a treatment with no-preparation required, and one with simple preparation required. No-naïve patients on the other hand, consider of the utmost importance the complexity of preparation, and value as well freedom in administration timing.

The analysis of patients' sex uncovered as well minor distinctive preferences; both male and female positively valued freedom of timing of injection (non-scheduled), with p=0.0058 in females and p=0.003 in males (Table 5). They also give value to treatment with no preparation time prefer a simple preparation vs. a complex one. Costs received worse rates as they increased in both groups.

Data analysis in relation to patients' age was performed separating patients in two groups: younger than 65 and 65 or older. In this case, both age groups preferred a weekly injection instead of a daily non-scheduled injection, although older patients consider more important having freedom of injection timing vs. a scheduled injection (Table 6). Both cases view positively an injection that requires no preparation. Costs received worse rates as they increased in both groups.

Finally, two models have been taken into account to determine patients' willingness to pay to change attributes. The first was the model without subgroups (Table 7) and the second the model clustered by naïve and no naïve patients (Table 8).

The results of the first model reported that patients with type 2 diabetes were willing to pay 83.25€ to change a 'somewhat complex preparation' dose to a 'no preparation required' dose and 44.52€ to change a 'somewhat complex preparation' dose to a 'simple preparation' dose. In terms of treatment frequency, type 2 diabetes patients preferred a daily scheduled injection before a daily injection with freedom of timing, willing to pay 22.09€ to make that change. In addition, type 2 diabetes patients were willing to pay 37.65€ to change daily injection with freedom of timing for a weekly injection (Table 9).

Naïve and non-naïve patients were willing to pay 83.25€ to change a 'somewhat complex preparation' dose to a 'no preparation required' dose. In addition, both groups of patients were willing to pay 44.30€ to change a 'somewhat complex preparation' dose to a 'simple preparation' dose. In terms of treatment frequency, no-naïve patients preferred a daily injection with freedom of timing before a daily scheduled injection, willing to pay 22.20€ to make that change. In addition, no-naïve patients were willing to pay 34.61€ to change daily scheduled injection for a weekly injection. Finally, the most valued treatment change in naïve patients was to exchange a daily scheduled injection for a weekly injection, willing to pay 14.35€ for that change (Table 10).

The comparison of additional models with interactions between attributes showed no significant differences.

4. DISCUSSION

Previous studies demonstrated the importance of assessing patients' preferences in order to establish a more efficient healthcare system. This has been vital for DMT2 patients to

reduce complications derived from an improper treatment [6]. Overall, a large number of attributes have been identified in terms of diabetic patients' preferences, with consistency among independent studies. The most commonly listed attributes have been efficacy, adverse effects, and dosing frequency [9], although other variables might become of importance depending on the patient population that is analysed. To our knowledge, this is the first study assessing patients' preferences on injection frequency, patients' opinion on treatment complexity and willingness to pay in Spain.

Patients included in this study were treatment-naïve for GLP-1, because the side effects of the GLP1 like nausea /vomiting, fear of pancreatitis, potential for weight loss, impact on glycaemic control and out of pocket cost of medication can often influence patient choice [12,13].

Most patients demonstrated the greatest preference for weekly injections with emphasis on injections with no preparation time. Costs were, in all cases, more negatively rated as they increased.

These results are consistent with previous studies on patients' injection frequency preferences. A recent study in Australia listed injection frequency as the second attribute in importance after weigh change [14], while in another DCE in Italy, patients considered injection frequency less important than other attributes as risk of nausea or of urinary-tract infections [15]. Herein, patients show strong preferences regarding injection frequency. Some patient clusters prefer weekly injections, while most of them value more

positively having freedom of timing of administration, willing to pay 22.20€ for that feature.

Patients' preference in complexity of preparation has not been as extensively evaluated, although it has been pointed as one of the most significant factors for treatment adherence [3, 16]. When given the choice most patients prefer injections with a simple preparation or no preparation time. No-naïve patients were willing to pay 83.25€ to avoid preparation of insulin, similarly to the tendency observed in groups of patients in North America, South America, and Europe [17].

Despite the small differences among patient clusters, the global tendency is equal in all groups, being the attributes reported consistent with previous studies. Conversely, this study had a number of limitations. Although patient sample was considered representative, patients were recruited from 5 centres in Spain not illustrating all Spanish regions. Patient financial status was not taken into account; however, patient sample was socioeconomically heterogenic. The number of attributes was limited to increase statistical potency and maintain a manageable sample size; further studies including other features might be of interest.

5. CONCLUSIONS

This study shows that patients highly value the avoidance of injections, with weekly dosing clearly preferred over daily dosing. Of the other attributes, a 'no preparation required' dose is clearly preferred over a 'simple preparation' dose. These findings may provide a better understanding of what patients prefer and value in their treatment and provide

guidance for clinicians making therapeutic decisions regarding T2DM treatments. Consideration of patient preference is important when making therapeutic decisions and can improve health outcomes, but have also an important role in health technology assessment, as the importance weighting for each treatment attribute as well as the identification of the value may assist funding decisions.

TRANSPARENCY SECTION

Declaration of funding

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Declaration of financial and other interest

J Darbà is employed by the University of Barcelona. M Ascanio is an employee of BCN Health Economics & Outcomes Research S.L., Barcelona, Spain, an independent contract health economic organization. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed. BCN Health Economics and Outcomes Research S.L. provided statistical analysis and editorial support. BCN Health Economics & Outcomes Research services have been funded by AstraZaneca Farmacéutica Spain.

Data Availability Statement

The data generated during and/or analysed during the current study are not publicly available.

Author contributions

All authors contributed to the conception, design, and interpretation of the DCE. MA carried out the analysis. All authors contributed to the drafting of the paper or to revising it critically for intellectual content. All authors gave final approval of the version to be published and agree to be accountable for all aspects of the work.

Ethics approval

The study followed the ethical recommendations of the Declaration of Helsinki, the norms for a Good Clinical and Pharmacoepidemiology practices, and local legislation that applies to observational studies. It had the approval of the Hospital de Bellvitge Ethics Committee and received ratification from all other participant centres.

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Not applicable.

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas, 8th edn. Brussels, Belgium: International Diabetes Federation, 2017.
2. Soriguer F, Goday A, Bosch-Comas A, et al. Prevalence of diabetes mellitus and impaired glucose regulation in Spain: the Di@bet.es Study. Diabetologia (2012). https://doi.org/10.1007/s00125-011-2336-9
3. Larkin AT, Hoffman C, Stevens A, et al. Determinants of adherence to diabetes treatment. Journal of Diabetes (2015). https://doi.org/10.1111/1753-0407.12264
4. Ryan M, Gerard K. Using discrete choice experiments to value health care programmes: current practice and future research reflections. Appl Health Econ Health Policy 2003;2(1):55e64.
5. Reed Johnson F, Lancsar E, Marshall D, et al. Constructing experimental designs for discrete-choice experiments: report of the ISPOR Conjoint Analysis Experimental Design Good Research Practices Task Force. Value Health (2013). https://doi.org/10.1016/j.jval.2012.08.2223
6. Hauber AB, Nguyen H, Posner J, et al. A discrete-choice experiment to quantify patient preferences for frequency of glucagon-like peptide-1 receptor agonist injections in the treatment of type 2 diabetes. Current Medical Research and Opinion (2015). https://doi.org/10.1185/03007995.2015.1117433
7. Hertroijs D, Brouwers M, Elissen A, et al. Patients' preferences for diabetes care: a discrete choice experiment. International Journal of Integrated Care (2018). https://doi.org/10.5334/ijic.s2283

8. Shackley P, Ryan M. Involving consumers in health care decision making health care analysis. Health Care Analysis (1995). https://doi.org/10.1007/BF02197669
9. Rowen D, Stevens K, Labeit A, et al. Using a discrete choice experiment involving Cost to value a classification system measuring the quality-of-life impact of self-management for diabetes. Value in Health (2017). https://doi.org/10.1016/j.jval.2017.06.016
10. Hall J, Kenny P, King M, et al. Using stated preference discrete choice modelling to evaluate the introduction of varicella vaccination. Health Econ 2002;11:457–65.
11. Lancsar E, Louviere J. Conducting discrete choice experiments to inform healthcare decision making: a user's guide. Pharmacoeconomics 2008;26:661–77-
12. Sikirica MV, Martin AA, Wood R, et al. Reasons for discontinuation of GLP1 receptor agonists: data from a real-world cross-sectional survey of physicians and their patients with type 2 diabetes. Diabetes Metab Syndr Obes. 2017;10:403-412. https://doi.org/10.2147/dmso.s141235
13. Filippatos TD, Panagiotopoulou TV, Elisaf MS. Adverse Effects of GLP-1 Receptor Agonists. Rev Diabet Stud. 2014;11(3-4):202-30. https://doi.org/10.1900/rds.2014.11.202
14. Fifer S, Rose J, Hamrosi KK, et al. Valuing injection frequency and other attributes of type 2 diabetes treatments in Australia: a discrete choice experiment. BMC Health Services Research (2018). https://doi.org/10.1186/s12913-018-3484-0

15. Marchesini G, Pasqualetti P, Anichini R, et al. Patient preferences for treatment in type 2 diabetes: the Italian discrete-choice experiment analysis (2018). https://doi.org/10.1007/s00592-018-1236-6
16. García-Pérez LE, Álvarez M, Dilla T, et al. Adherence to Therapies in Patients with Type 2 Diabetes. Diabetes Therapy (2013). https://doi.org/10.1007/s13300-013-0034-y
17. Feher MD, Brazier J, Schaper N, et al. Patients' with type 2 diabetes willingness to pay for insulin therapy and clinical outcomes (2016). https://doi.org/10.1136/bmjdrc-2016-000192

Tables

Table 1 Treatment attributes and their levels.

Attributes	Levels
Treatment complexity	No preparation required Simple preparation required[a] Somewhat complex preparation required[b]
Administration frequency	Daily, non-scheduled (timing is not important) Daily, scheduled (the timing is important) Weekly, non-scheduled (timing is not important)
Costs (€)	Monthly cost 50€ Monthly cost 70€ Monthly cost 100€

a) Simple preparation required: injection requires simple preparation and takes little time to set up before being injected; b) somewhat complex preparation required: the injection requires somewhat more complex preparation before administration and takes longer because it has more steps to follow.

Table 2 Population characteristics

Variables		Total population N= 180
Age, mean (SD)		63.35 (11.49)
Sex	**Woman**	36.72%
	Man	63.28%
Employment situation	**Active worker**	25.78%
	Retired	57.81%
	Others	16.41%
Salary level	**< 1000 €**	30.00%
	1000 € -1500€	10.00%
	1501€ - 2000€	7.69%
	>2000€	7.69%
	No respondents	44.62%
Diagnosis	**< 5 years**	22.66%
	5-10 years	22.66%
	> 10 years	54.69%
Severe hypoglycemic event	**Yes**	18.11%
	No	81.89%
General malaise	**Yes**	29.69%
	No	70.31%
Cardiovascular disease	**Yes**	48.41%
	No	51.59%
Other comorbidities	**Yes**	50.00%
	No	50.38%

Medication	**Oral, 1/day**	3.94%
	Oral, >1/day	18.11%
	Injection, 1/day	3.94%
	Injection, >1/day	3.97%
	Oral + injection	70.08%
Medication status	**Naïve**	22.05%
	Syringe	0.91%
	Pen	88.18%
Glycemic control	**1/month**	0.00%
	1/week	8.00%
	1/day	38.40%
	>1/day	53.60%
Social/family support	**Yes**	45.67%
	No	54.33%

Table 3 Population characteristics clustered by experience

Variables		**No Naïve N= 140**	**Naïve N= 40**	**X_2**
Age, mean (SD)		63.63 (10.35)	61.75 (14.50)	
Sex	**Woman**	45.75%	63.49%	58.39 (p=0.000)
	Man	54.25%	36.51%	
Employment situation	**Active worker**	35.76%	25.53%	108.53 (p=0.000)
	Retired	27.82%	51.06%	
	Others	36.42%	23.41%	
Salary level	**< 1000 €**	20.33%	19.00%	102.64 (p=0.000)
	1000 € -1500€	22.53%	12.36%	
	1501€ - 2000€	22.53%	12.36%	
	>2000€	13.31%	40.19%	
	No respondents	21.30%	16.08%	
Diagnosis	**< 5 years**	25.83%	56.64%	128.06 (p=0.000)
	5-10 years	37.77%	19.56%	
	> 10 years	36.40%	23.80%	
Severe hypoglycemic event	**Yes**	46.79%	64.34%	25.35 (p=0.000)
	No	53.21%	35.66%	
General malaise	**Yes**	48.51%	55.50%	11.06 (p=0.015)
	No	51.49%	44.50%	
Cardiovascular disease	**Yes**	45.82%	65.22%	64.72 (p= 0.000)
	No	54.24%	34.78%	
Other comorbidities	**Yes**	49.86%	50.52%	1.32

	No	50.14%	49.48%	(p=0.802)
Glycemic control	**1/month**	0.00%	0.00%	134.46 (p=0.000)
	1/week	19.47%	63.44%	
	1/day	40.57%	17.63%	
	>1/day	39.96%	18.94%	
Social/family support	**Yes**	53.83%	36.04%	52.38 (p=0.000)
	No	46.17%	63.96%	

Table 4 Results clustered by experience.

	NAÏVE	**NO NAÏVE**
Treatment complexity: no preparation required vs. simple preparation required	Not valued	Very important aspect
Treatment complexity: somewhat complex preparation vs. daily, scheduled	Rated negatively (with p = 10%)	
Administration frequency: weekly, non-scheduled vs. daily, scheduled	Very positively valued	
Administration frequency: daily, non-scheduled vs. daily, scheduled	Not valued	
Cost	Very important	

Table 5 Results clustered by sex.

	WOMEN	**MEN**
Treatment complexity: no preparation required vs. simple preparation required	Highly valued and statistically significant	
Treatment complexity: somewhat complex preparation required vs. simple preparation required	Preference for a simple preparation and in a statistically significant way	
Administration frequency: daily, non-scheduled vs. daily, scheduled	Positively evaluated and preferred (with p = 0.0058)	Positively evaluated and preferred (with p = 0.003)
Administration frequency: weekly, non-scheduled vs. daily, scheduled	Highly valued and statistically significant	
Cost	It is not preferable as it increases, in a statistically significant way	

Table 6 Results clustered by age.

	<65 YEARS	≥65 YEARS
Administration frequency: weekly, non-scheduled vs. daily, scheduled	Preferred and statistically significant	
Administration frequency: daily, non-scheduled vs. daily, scheduled	It is preferable to administer the injection daily at any time, but not significantly	It is preferable to administer the injection daily at any time
Treatment complexity: no preparation required vs. simple preparation required	Positively assessed in a statistically significant way (with p <1%)	
Treatment complexity: somewhat complex preparation required vs. simple preparation required	Not preferred, statistically significant	
Cost	Rated negatively and not preferable as it increases, in a statistically significant way	

Table 7 Results of the discrete choice experiment (DCE).

Attribute	Level	Coefficient	P value
Cost	Continuous	-0.0376708	0.000
Treatment complexity	No preparation required	3.137087	0.000
	Simple preparation required	1.676946	0.000
	Somewhat complex preparation required	Reference	
Administration frequency	Daily, unscheduled	0.8322325	0.000
	Weekly, unscheduled	1.4184407	0.000
	Daily, scheduled	Reference	

Table 8 Results of the discrete choice experiment (DCE) by experience.

Attribute	Level	Coefficient	P value
Cost	Continuous	-0.0378668	0.000
Treatment complexity	No preparation required	3.152286	0.000
	Simple preparation required	1.677382	0.000
	Somewhat complex preparation required	Reference	
Administration frequency	Daily, unscheduled	0.8406848	0.000

	Weekly, unscheduled	1.310408	0.000
	Daily, scheduled	Reference	
Naïve administration frequency	Daily, unscheduled	-0.00814	0.974
	Weekly, unscheduled	0.5432567	0.066
	Daily, scheduled	Reference	

Table 9 Willingness to pay (WTP) to change level.

Attribute	Level	WTP
Treatment complexity	No preparation required	83.27 €
	Simple preparation required	44.52 €
Administration frequency	Daily, unscheduled	22.09 €
	Weekly, unscheduled	37.65 €

Table 10 Willingness to pay (WTP) to change level by experience.

Attribute	Level	WTP no naïve	WTP naïve
Treatment complexity	No preparation required	83.25 €	83.25 €
	Simple preparation required	44.30 €	44.30 €
Administration frequency	Daily, unscheduled	22.20 €	Not significant
	Weekly, unscheduled	34.61 €	14.35 €