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Original article

Patients' preferences for anti-osteoporosis drug treatment: a cross-European discrete choice experiment

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Abstract

Objectives. To estimate the preferences of osteoporotic patients for medication attributes, and analyse data from seven European countries.

Methods. A discrete choice experiment was conducted in Belgium, France, Ireland, the Netherlands, Spain, Switzerland and the UK. Patients were asked to choose repeatedly between two hypothetical unlabelled drug treatments (and an opt-out option) that varied with respect to four attributes: efficacy in reducing the risk of fracture, type of potential common side effects, and mode and frequency of administration. In those countries in which patients contribute to the cost of their treatment directly, a fifth attribute was added: out-of-pocket cost. A mixed logit panel model was used to estimate patients' preferences.

Results. In total, 1124 patients completed the experiment, with a sample of between 98 and 257 patients per country. In all countries, patients preferred treatment with higher effectiveness, and 6-monthly subcutaneous injection was always preferred over weekly oral tablets. In five countries, patients also preferred a monthly oral tablet and yearly i.v. injections over weekly oral tablets. In the three countries where the out-of-pocket cost was included as an attribute, lower costs significantly contributed to the treatment preference. Between countries, there were statistically significant differences for 13 out of 42 attribute/level interactions.

Conclusion. We found statistically significant differences in patients' preferences for anti-osteoporosis medications between countries, especially for the mode of administration. Our findings emphasized that international treatment recommendations should allow for local adaptation, and that understanding individual preferences is important if we want to improve the quality of clinical care for patients with osteoporosis.

Key words: cross-country comparison, discrete choice experiment, drug treatment, osteoporosis, patients, preferences

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Rheumatology key messages

- Osteoporotic patients are willing to pay or to trade treatment efficacy for their preferred mode of administration.
- Significant heterogeneity in patients' preferences for osteoporotic drug treatment and country differences were observed.

Introduction

It is recognized that clinical and policy decision should include the patient's perspective. Product development and acceptance could also benefit from knowledge about what patients value and prefer regarding their treatment [1]. Patients' preferences can also be useful for the appraisal of health-care programmes, alongside the clinical, economic, social and ethical considerations. Recent examples include the attention to and inclusion of the patient's perspective in health technology assessment, coverage decisions and clinical practice guideline development [2–4]. Health professionals may find that knowledge of patients' preferences and how patients value different aspects of care helps them to improve disease management. Patients who are more involved in decision-making could have better therapy adherence [5]. In response, an increasing number of studies elicit patients' preferences in the health-care setting. In particular, the application of discrete choice experiments (DCEs) as a method of eliciting patients' preferences has increased in recent years [6, 7]. A DCE is a stated-preference method in which respondents are asked to repeatedly choose between hypothetical treatment options that systematically differ in several attributes of interest, such as effectiveness, cost, side effects and mode of administration. DCEs are a useful method for quantifying the relative importance of attributes and the trade-offs that respondents make between them [5].

Results from a recent DCE study [8] to assess the preferences of osteoporotic patients for drug treatment in Belgium suggest that osteoporotic patients preferred treatment modes of 6-month s.c. injection and an oral monthly tablet, and disliked gastrointestinal disorders as side effects. In addition, patients were willing to trade treatment effectiveness or a personal monetary contribution for their preferred mode of administration.

Little is known about how comparable patients' preferences are between countries. The previous study [8] was carried out in two osteoporosis centres in Belgium. An editorial accompanying the previous study [9] suggested that the generalizability of the results should be further investigated. We therefore extended the previous study to six additional Western European countries. The aim of this paper was to evaluate and compare the preferences of osteoporotic patients from several European countries for medication attributes. This study will therefore not only reveal whether patients' preferences differ between a number of countries, but will also provide further insights for policy-makers and health professionals into the generalizability of patients' preferences for osteoporotic drug treatment.

Methods

We used a DCE to examine preferences for drug treatment among patients with, or at risk of, osteoporosis. In the DCE, patients were asked to make a series of hypothetical choices between two unlabeled drug alternatives that varied along several attributes of interest (and a no treatment option). State of the art methods recommended in DCE guidelines were used to select the attributes and levels, to design the DCE and to conduct the statistical analysis [5, 10]. Details of the DCE development can be found in a previous publication [8], and access to the English language questionnaire is available online as an additional file [8]. A brief description of the various components of the DCE is provided below.

Attributes and levels

The attributes included in the DCE were selected from the results of qualitative research [11, 12]. Patient group discussions in Belgium and the Netherlands were used to prioritize a list of 12 potentially important osteoporosis drug therapy attributes. The list was based on existing literature and expert opinion. Patients identified five important attributes, and all were included in the DCE: effectiveness, side effects, mode of administration, frequency of administration and, in Belgium, out-of-pocket cost (see Table 1). The out-of-pocket cost attribute was only included in countries where patients pay out-of-pocket for osteoporotic treatment (i.e. Belgium, Ireland and Switzerland). Levels for each attribute were assigned based on current treatment, using a literature review and expert opinion ($n = 5$). For the side effects attribute, the three levels were related to the nature of common side effects.

Experimental design

The set of treatment options to be presented to the respondents was based on an experimental design. Specifically, we used a Bayesian efficient design to maximize the D-efficiency of the chosen choice sets using Ngene software (Version 1.1.1, http://www.choice-metrics.com). A Bayesian efficient design aims to maximize the precision of the estimated parameters of the attributes for a given number of choice tasks by incorporating *a priori* information about the sign and value of parameters. Parameter estimates derived from a pilot study ($n = 10$) were used as *a priori* information to construct the choice sets. Fifteen choice tasks were created in which respondents were asked, in each case, to choose between two unlabelled drug alternatives (A and B) and a no treatment option. The experimental design was restricted to include only realistic combinations of mode and frequency of administration. There was a small correlation between

attributes in the experimental design because it was optimized on efficiency. One of the choice tasks was repeated at the end of the choice tasks to assess test–retest reliability of respondents' choices. Each respondent therefore received 16 choice tasks. An example of a choice task is shown in Fig. 1.

Questionnaire, data collection and patients' recruitment

The questionnaire was paper-based. The attributes and levels were first described and an example of a completed choice task was included. After respondents had completed the 16 choice tasks, they were asked how difficult they found the tasks on a seven-point Likert scale. Data on patients' demographics and socio-economic characteristics and experiences with osteoporosis and treatments were also collected. Three versions of the questionnaire were designed that differed in attribute presentation to control for an attribute ordering effect.

The questionnaire was developed in English by a working group that included a patient, DCE experts and clinical experts. This version was approved by two native English speakers who are osteoporosis experts. The questionnaire was translated into three languages (French, Spanish and Dutch) by a medical translation company specializing in patient-reported outcome measures translation (Pharma Quest Ltd, Oxford, UK). The four languages covered the languages spoken across the countries in our sample. Each language version was checked and approved by at least two native speakers. The English survey was pilot-tested (n=10) to check for any problems with interpretation and face validity; only minor changes to layout were made.

The study was conducted in seven European countries—Belgium, France, Ireland, the Netherlands, Spain, Switzerland and the UK—between March and October 2012. The analysis for Belgian patients has been published previously [8]. Patients with, or at risk for, osteoporosis to whom medication (or lifestyle changes) was at least proposed were consecutively recruited during outpatient clinics. The questionnaire was completed by the patient at the clinic, or at home and returned in a postage-paid envelope. Calculation of optimal sample sizes was not possible, as they depend on the true values of the unknown parameters estimated in the DCE [13]. Hence, a minimum of 100 patients per country was targeted, which was sufficient based on common rules-of-thumb for minimum sample size [14].

Approval for this study was obtained from the Medical Ethics Committee of the Academic Hospital Maastricht

Table 1 List of attributes and levels

Efficacy in reducing the risk of future fractures (%)
20
30
40
50
Possible side effects (affecting 1 in 50 patients)
Gastrointestinal disorders
Flu-like symptoms
Skin reactions
Mode of administration
Oral tablet
s.c. injection
i.v. injection
Frequency of administration
Weekly
Monthly
Every 3 months
Every 6 months
Yearly
Cost to you (per month)
€5
€15
€25
€40

Fig. 1 Example choice set of DCE experiment

Question 14

	Treatment A	Treatment B
Efficacy (their effect) in reducing the risk of future fractures	20%	50%
Possible side effects (affecting 1 in 50 patients)	Gastro-intestinal disorders	Flu-like symptoms
Mode of administration	Intravenous	Subcutaneous
Frequency of administration	3-month	6-month
Cost to you	€25 (per month)	€40 (per month)

Which treatment would you choose? Treatment A ☐ Treatment B ☐ No treatment ☐

(Tick one box only)

and Maastricht University. A team from this university coordinated the project. Participants gave informed written consent according to the 1964 Declaration of Helsinki. Additional local ethics approval was obtained from those participating centres that required ethics approval for a DCE study, that is, the Research Ethics Committee of the Sligo University Hospital, the Southampton Joint Ethics Committee, the CEIC-Parc de Salut Mar (Committee of Ethics and Clinical Investigation) and the Commission cantonale d'éthique de la recherche of Geneva.

Statistical analyses

Data analysis was carried out using Nlogit software, version 5.0. Data of patients who completed less than five choice sets were excluded. To allow for preference heterogeneity within each country, a mixed logit model was estimated [15]. This model is based on the assumption that parameters are randomly distributed in the population, and captures heterogeneity by estimating the standard deviation of the parameter's distribution. We used a panel mixed logit model to account for the panel nature of the data as each patient completed 15 choice sets.

The following utility model was estimated for each country *c*:

$$\begin{aligned} V_{ij} = {} & \beta_0 + (\beta_1 + \eta_{1i})\text{efficacy}_j + (\beta_2 + \eta_{2i})\text{cost}_j \\ & + (\beta_3 + \eta_{3i})\text{oral}_{1M_j} + (\beta_4 + \eta_{4i})\text{sub}_{3M_j} \\ & + (\beta_5 + \eta_{5i})\text{sub}_{6Mj} + (\beta_6 + \eta_{6i})\text{int}_{3Mj} \\ & + (\beta_7 + \eta_{7i})\text{int}_{1Yj} + (\beta_8 + \eta_{8i})\text{flusympt}_j \\ & + (\beta_9 + \eta_{9i})\text{skinreact}_j + \varepsilon_{ijt}, \end{aligned}$$

where *V* represents the systematic relative utility, β_0 is the constant reflecting the average preference for selecting treatment relative to no treatment across the different choice sets, β_1–β_9 are coefficients of the attributes levels indicating the relative preference for each attribute level, and η_{1i}–η_{9i} are error terms capturing individual-specific unexplained variation around the mean. Effects coding was used to describe the categorical variables (mode and frequency of administration, and side effects). Using effect coding, mean attributes are normalized to zero and preference weights are relative to the mean effect of the different levels of the attribute. A positive sign for a given level therefore indicates a level has a positive effect on utility compared with the mean effect of the attribute. If the 95% CI around two levels did not overlap, the differences between the preference weights were considered to be statistically different. Although the attributes efficacy in reducing the risk of future fractures and out-of-pocket contribution are presented as discrete levels in the experiment, they were coded as continuous variables in the model with a linear specification, allowing willingness to pay estimates and providing a better model fit.

We took preference heterogeneity into account by specifying all parameters as random parameters. The random parameters for the cost and efficacy were drawn from a log-normal distribution in order to constrain the parameter on the negative and positive scale, respectively [15]. All other random parameters were drawn from a normal distribution. If the standard deviation of the random parameters was significantly different from zero, this was interpreted as evidence of significant preference heterogeneity for the attribute within the population. The estimation was conducted by using 2000 Halton draws. Model fit was assessed using log-likelihood, McFadden's pseudo-R^2 and the Akaike Information Criterion.

Two subgroups analyses were conducted to investigate potential differences between countries. We wish to allow preferences to be systematically different in countries with the cost attribute (Belgium, Ireland and Switzerland) and in countries without (France, the Netherlands, Spain, the UK). To assess whether preferences were significantly different between countries within each subgroup (with and without a cost attribute), a joint model was estimated using interaction terms to capture potentially systematic differences in preference between countries. Preferences were considered to vary across countries within a subgroup if the parameters estimated for the interaction terms were statistically different from zero (5% level). To take scale heterogeneity into account and thus to control for the fact that differences between countries can also be due to difference in the unobserved error scale, a normally distributed random component was added for each country dummy [16]. This allowed us to test whether a significant difference in the interaction terms reflected a systematic difference in preference, and not merely a difference in the scale of the random error between countries.

In addition, at the country level we analysed the impact of previous fractures on patients' preferences that was shown to be a relevant covariate in previous research [8, 17, 18]. To assess the significance of the differences between patients with and without previous fractures, a joint model per country was estimated using interaction terms. A normally distributed random component was added for the dummy variable designed for previous fractures.

Results

Patients' characteristics

A total of 1201 questionnaires were returned. Of these, 1124 questionnaires were sufficiently completed (i.e. at least 10 choice tasks completed) and included in the analysis, with a sample of between 98 and 257 patients per country. The respondents had a mean age of 65.0 years, and 85.3% were female. Of all respondents, 73.9% were diagnosed with osteoporosis, 52.1% had a prior fracture and 55.4% received osteoporosis drug treatment. Sociodemographics and health characteristics are shown in Table 2 by country. A total of 85.2% of the respondents (country range: 80.9–89.4%) selected the same alternative in the test–retest exercise. On average, the task was seen as relatively easy, with an average score of 3.04 (country range: 2.62–3.41), based on responses to a seven-point scale (one for extremely easy and seven for extremely difficult). Both test–retest reliability and the perceived level of task difficulty are in line with previous studies [19].

TABLE 2 Patients' characteristics

Socio-demographics and health characteristics	Countries with cost attribute			Countries without cost attribute			
	Belgium (*n* = 257)	Ireland (*n* = 200)	Switzerland (*n* = 98)	France (*n* = 100)	Netherlands (*n* = 188)	Spain (*n* = 183)	UK (*n* = 100)
Age, mean (S.D.), years	67.1 (10.4)	63.9 (11.9)	62.6 (9.3)	67.8 (11.0)	65.3 (11.9)	59.2 (9.8	71.1 (8.4)
Female gender	83.3	86.8	81.1	88.4	78.1	91.1	91.9
Educational level, %							
Primary	8.4	19.4	10.2	5.3	12.7	23.4	3.0
Some high school	35.9	25.0	15.3	31.6	36.4	10.8	55.0
High-school graduate	30.3	29.6	36.7	14.7	28.8	32.9	20.0
College or University	25.5	26.0	37.8	48.4	22.0	32.9	22.0
Diagnosis of osteoporosis, %	89.8	45.9	93.3	94.7	70.0	54	93
Years since osteoporosis, mean (S.D.)	8.9 (6.1)	5.4 (5.1)	7.4 (5.7)	9.0 (8.8)	4.7 (5.6)	8.9 (10.5)	8.8 (6.5)
With prior fracture(s), %	52.5	45.3	53.7	71.2	61.6	33.8	60.2
Patients on osteoporotic treatment, %	69.8	37.8	74.4	65.6	50.7	38.2	65.3
Administration mode of current treatment, %							
Oral	72.2	41.3	65.7	75.4	73.5	86.0	81.5
s.c.	15.4	42.7	11.4	1.9	15.7	4.0	6.1
i.v.	12.4	16.0	22.9	22.6	10.8	10.0	12.3
Test–retest, %	85.2	89.4	81.6	88.9	93.6	80.9	84.0
Task difficulty, range 1–7	3.35	2.66	2.94	2.77	3.41	3.05	2.62

Patients' preferences

The panel mixed logit model results are presented in Table 3. The estimated coefficients for efficacy and costs (when included) were statistically significant in all countries. The positive sign of the efficacy parameter indicates that treatment utility increases with higher treatment efficacy and the negative sign of the cost parameter indicates that respondents prefer to pay less for treatment.

In all countries, patients preferred a 6-monthly subcutaneous injection over weekly oral tablets (see Fig. 2). In most countries, patients also preferred a monthly oral tablet and/or yearly i.v. injections over weekly oral tablets. In all countries, except Switzerland where no statistical differences were observed, patients disliked being at risk of gastrointestinal disorders more than being at risk of skin reactions and flu-like symptoms. The two parameters for the side effects attribute had a positive sign, indicating that patients disliked being at risk of gastrointestinal disorders more than being at risk of skin reactions and flu-like symptoms. Standard deviations parameters were significant for most of the attributes in all countries, indicating the presence of preference heterogeneity between patients, and hence variations in the importance of the attributes/levels.

There were statistical significant differences for 13 out of 42 attribute/levels interactions between countries (Table 4). Countries with the largest sample were used as a reference, that is, Belgium for countries with the cost attribute and the Netherlands for those without, respectively. In comparison with Belgium, patients in Ireland had a significantly stronger preference for i.v. every 3 months or yearly, and preferred being at risk for flu-like symptoms and skin reactions compared with gastrointestinal disorders. In Switzerland, a significantly higher value was attached to s.c. administration every 6 months and yearly i.v. administration compared with Belgium, while a monthly oral tablet was significantly less preferred.

In comparison with the Netherlands, patients in France, UK and Spain are found to have only a few significant interaction differences. For example, in the UK, a monthly oral tablet was significantly less preferred while i.v. administration every 3 months was significantly more preferred. Efficacy was less preferred in France and Spain than in the Netherlands.

The presence of previous fractures significantly reduced the importance of the cost attribute in two of the three countries with a cost attribute (see supplementary Table S1, available at *Rheumatology* Online). In Belgium and Switzerland, patients with previous fractures are willing to pay more for osteoporosis medication than patients without fractures. In countries without the cost attribute, the presence of a previous fracture was shown to positively and significantly affect the importance of drug effectiveness, with the exception of France.

Discussion

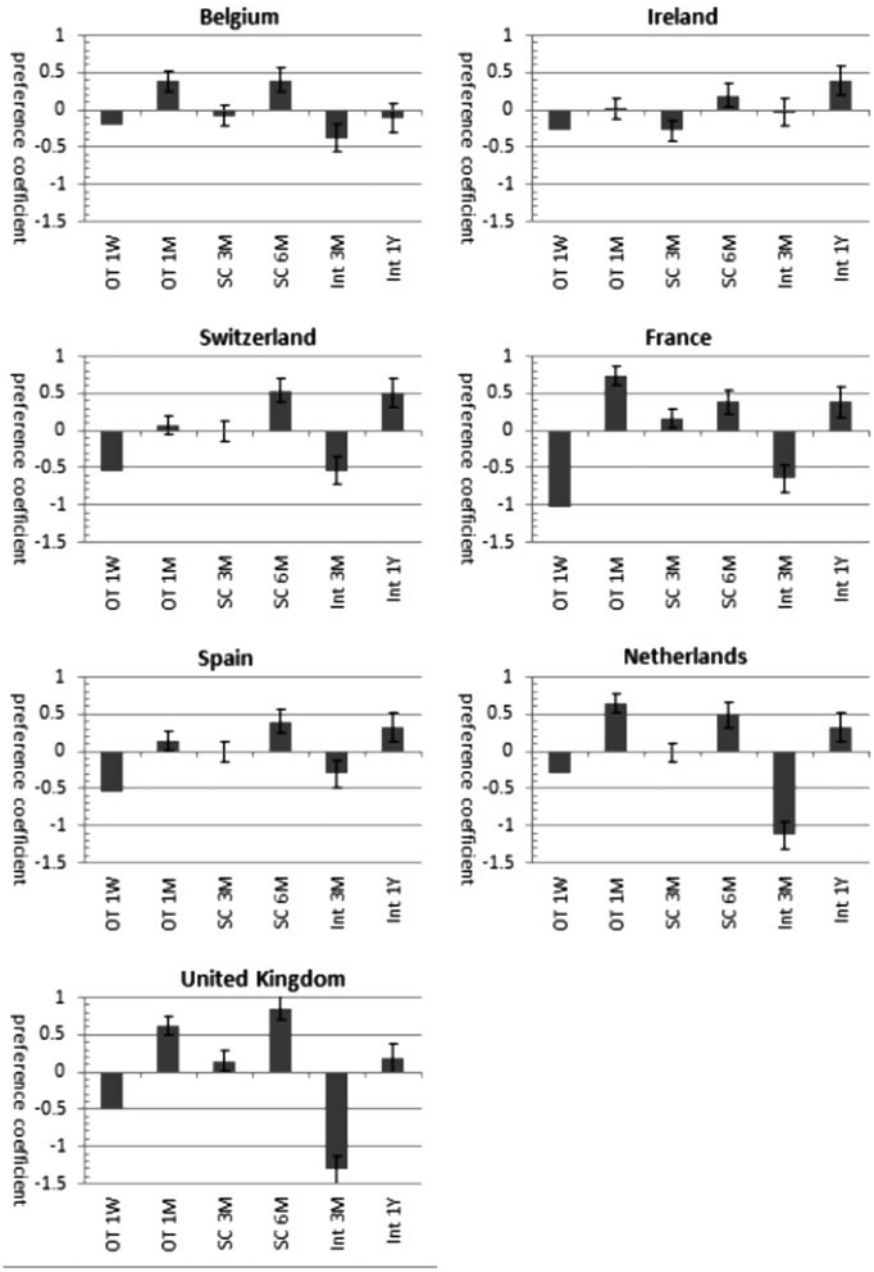
This study used a DCE to evaluate the preferences of patients with, or at risk of, osteoporosis for medication attributes in seven European countries. In line with a previous study conducted in Belgium only [8], osteoporotic patients across Europe trade between attributes when making treatment choices, and all attributes were

Table 3 Results from the panel mixed logit model

Attributes and levels	Countries with the cost attribute						Countries without the cost attribute							
	Belgium		Ireland		Switzerland		France		Netherlands		Spain		UK	
	Coef (S.D.)	S.D.[a]	Coef	S.D.	Coef	S.D.	Coef	S.D.	Coef	S.D.	Coef	S.D.	Coef	S.D.
Constant	1.97*** (0.06)		2.25*** (0.08)		0.11 (0.13)		−1.45*** (0.20)		−1.62***		0.77*** (0.05)	–	−1.57*** (0.03)	–
Efficacy (1% risk reduction)	0.04*** (0.01)	1.38***	0.05*** (0.01)	1.37***	0.10*** (0.02)	1.24***	0.08*** (0.02)	1.07***	0.07***(0.01)	0.83***	0.05*** (0.01)	1.33***	0.11*** (0.01)	1.58***
Cost per month (€1 or CHF1)	−0.04*** (0.01)	1.38***	−0.01*** (0.00)	1.51***	−0.03*** (0.01)	1.16***	—	—	—	—	—	—	—	—
Mode of administration														
Weekly oral tablet (Reference level)	−0.20	-	−0.27	-	−0.55	-	−1.02	-	−0.29	-	−0.54	-	−0.50	-
Monthly oral tablet	0.38*** (0.06)	0.16	0.01 (0.08)	0.09	0.07 (0.14)	0.65***	0.74*** (0.12)	0.21	0.64*** (0.12)	0.88***	0.14** (0.07)	0.04	0.62*** (0.13)	1.00***
Subcutaneous 3-monthly	−0.08 (0.07)	0.33**	−0.28*** (0.09)	0.47***	−0.02 (0.14)	0.31	0.16 (0.12)	0.24	−0.02 (0.12)	0.76***	−0.01 (0.07)	0.18	0.15 (0.17)	0.44**
Subcutaneous 6-monthly	0.40*** (0.08)	0.12	0.19* (0.11)	0.46***	0.53** (0.22)	1.05***	0.39* (0.23)	1.14***	0.48*** (0.18)	1.41***	0.40*** (0.11)	0.64***	0.86*** (0.21)	1.36***
Intravenous 3-monthly	−0.38*** (0.09)	0.56***	−0.04 (−0.10)	0.20	−0.54** (0.24)	0.86**	−0.65*** (0.27)	1.09***	−1.13*** (0.18)	1.25***	−0.31** (0.13)	0.46**	−1.32*** (0.26)	0.92***
Intravenous yearly	−0.12 (0.10)	0.57***	0.39*** (0.11)	0.23	0.50* (0.27)	1.29***	0.38 (0.24)	0.97***	0.32*** (0.16)	1.03***	0.32*** (0.10)	0.39***	0.18 (0.24)	1.83***
Side effects														
GI disorders (reference level)	−0.41	-	−1.18	-	−0.33	-	−0.71	-	−1.02	-	−0.18	-	−1.50	-
Flu-like symptoms	0.26*** (0.05)	0.42***	0.67*** (0.10)	0.77	0.17 (0.12)	0.66***	0.43*** (0.12)	0.87***	0.63*** (0.11)	0.98***	0.05 (0.05)	0.39***	1.08*** (0.11)	1.40***
Skin reactions	0.15*** (0.06)	0.45***	0.51*** (0.09)	0.74	0.16* (0.09)	0.46***	0.28*** (0.12)	0.80***	0.39*** (0.09)	0.89***	0.12*** (0.04)	0.22***	0.42*** (0.10)	0.58***
Pseudo R^2	0.39		0.49		0.39		0.44		0.38		0.30		0.49	
Log likelihood	−2540.61		−1674.04		−968.98		−907.54		−1891.87		−2063.56		−838.14	

[a]S.D. values correspond to the random component of the model coefficients (as opposed to the standard deviations of the coefficients themselves reported as S.D.s).
$^{*}P < 0.10$, $^{**}P < 0.05$, $^{***}P < 0.01$. GI: Gastrointestinal.

FIG. 2 Preferences of osteoporotic patients for mode of administration per country



OT: oral tablet; W: weekly; M: monthly; Y: yearly; SC: subcutaneous; Int: intravenous.

significant and thus important for patients' decisions. As expected, patients preferred higher efficacy and lower costs; and mode of administration was an important attribute for patients [17, 20]. In all countries, patients preferred on average a 6-monthly s.c. injection compared with a weekly oral tablet, and in some countries, patients also preferred a monthly oral tablet or yearly intravenous administration compared with weekly oral tablets.

To the best of our knowledge, this study is one of the first DCE studies that have elicited preferences across several countries [21] and therefore provides information on the comparability of patients' preferences across countries, and it is the first to do so for osteoporosis. Our study suggests that patients' preferences for osteoporosis drug therapy are the same on many key attributes for several European countries, although some statistical differences between countries were observed for a small number of attributes, especially modes of administration. Depending on policy objectives, this may imply that a pan-European policy could be promoted or that local

Table 4 Interaction models to assess differences between countries with and without cost attributes

Attributes and levels	Countries with cost (reference = Belgium)		Countries without cost (reference = Netherlands)		
	Ireland	Switzerland	France	Spain	UK
Constant				+	
Efficacy (1% risk reduction)		−	−	−	
Cost per month (€1 or CHF1)			×	×	×
Mode of administration					
Monthly oral tablet		−			−
s.c. 3-monthly					
s.c. 6-monthly		+			
i.v. 3-monthly	+				+
i.v. yearly	+	+			
Side effects					
Flu-like symptoms	+				−
Skin reactions	+				

+: above average reference country ($P < 0.05$); −: below average reference country ($P < 0.05$); ×: no cost attribute in these countries ($P < 0.05$).

differences in policy may be facilitated. Further work on the transferability of patients' preferences between countries would be needed to assess whether individual patients' characteristics or system level factors, such as jurisdiction, affect preferences. Of note, in this study we did not investigate the underlying drivers of preference differences between countries. Nevertheless, this study's finding emphasized that international treatment recommendations should allow for local adaptation and highlighted the importance of accounting for individual preferences in policies that aim to improve the quality of clinical care for patients with osteoporosis. Our study revealed that the effect of one covariate (previous fractures) on preferences was not the same across countries. Previous fractures only affected the cost attribute in countries where patients pay an out-of-pocket payment, but they affected preferences for treatment effectiveness in countries with no out-of-pocket payment. This trend was not found in all the countries. The impact of covariates on preferences could not be transferable between countries.

The substantive results from this international study could be very useful for health professionals and decision-makers, especially given the poor adherence to weekly oral regimens, which substantially affects the clinical and economic burden of these medications [22, 23]. Our study suggests that in all countries patients preferred on average 6-month s.c. injection compared with a weekly oral tablet, and in some countries, they also preferred a monthly oral tablet or yearly intravenous administration compared with a weekly oral tablet. Treatment that is in line with what patients prefer would increase patient satisfaction with, as well as trust in, their health care and potentially lead to improved adherence [5]. We also found that preferences elicited at the group level show large variance around the estimated coefficients, indicating heterogeneity in preferences between patients. For clinical practice, this indicates that tools are needed to reveal individual patients' preferences and to support shared decision-making. These tools should balance drug effectiveness against patients' beliefs and preferences [17]. Several decision aids are already available in osteoporosis to support the decision of whether to start an oral bisphosphonate or not, or how to select an appropriate medication [24–26]. The use of decision aids has the potential to be cost-effective [27], and our results suggest that tailoring treatments to individual patients can increase their satisfaction with the treatment. As such, our findings might assist decision-makers to identify treatments that are more likely to be cost-effective in practice [9].

Our study has some limitations. First, although we used a rigorous method to define attributes and levels, some decisions were made to focus on specific aspects of the research question. We focused on the nature of common side effects and not on their frequency or on more severe but rare side effects. Rare adverse events such as osteonecrosis of the jaw and atypical femoral fracture [28] could occur with osteoporosis medications. They are infrequent in all categories of osteoporosis medications and therefore patients' preferences would probably not differentiate between drugs for this reason. Alarming information in the media on these side effects could perhaps, however, influence patients' choices and lead to subjective perception. A second potential limitation is that data collection was performed in 2012, and treatment patterns could have changed since then. Temporal variations in preferences need to be better understood, particularly as patients' preferences could change over the course of treatment [9]. Third, we did not incorporate all types of osteoporosis medications in our study and focused on common osteoporosis medications. For example, the daily subcutaneous injection of teriparatide (only prescribed under specific conditions for patients with severe osteoporosis), or the oral administration of a dissolved powder (strontium ranelate) were not included. Fourth, in most countries in our research, the

study was only conducted in one centre; we therefore acknowledge that the data may not be generalizable to all individuals from the country. Fifth, despite the care taken in translation and adaptation of the survey instrument, including the use of a medical translation company specializing in the translation of patient-reported outcome measures, and a further check and approbation by two native speakers per version, the questionnaire was not back-translated. It is therefore possible that patients' understanding of the descriptions slightly differed between language versions. Sixth, while DCEs are widely used, an inherent limitation is that respondents are evaluating hypothetical medications. Therefore, what respondents declare they will do may potentially be different from what they would actually do if faced with the choice in real life. Some studies about the external validity of DCEs have already been conducted in health care [28, 29] but this has not yet occurred in the field of osteoporosis. Previous studies have suggested that predicted and actual treatment choices could differ at the individual level and that further work needs to be done to understand the reasons for these differences [29, 30]. Combining stated preference with actual choice data in osteoporosis would therefore be interesting in the future [9]. Seventh, the *a priori* information used to construct the choice sets was derived from a pilot study using 10 patients from one country. Although this is a relatively small number, the results of this pilot were consistent with expectations and guided the subsequent design of the main experiment. To maintain consistency across countries, the same design was used in all countries. Potentially more efficient designs could have been obtained at the individual country level, but this would have restricted the comparability of the task between countries. Finally, although we assessed the impact of previous fractures on patients' preferences on a country basis, our aim was not to assess the impact of additional characteristics of the individual patient as covariates on the preferences. Previous studies [12, 18] reported that preferences could differ between populations, and that factors such as age, gender, income, education and prior fractures could affect preferences for osteoporosis medications. Further work at a country level is needed to assess whether preferences for attributes and levels may not differ according to a number of factors, such as age and gender.

In conclusion, this study provides evidence that across seven western European countries osteoporotic patients are willing to trade efficacy or to pay money for preferred mode of administration, and that on average patients preferred 6-monthly s.c. injection over weekly oral tablets. In addition, our study suggests that the preferences of patients for many attributes of osteoporotic drug therapy are similar across seven European countries, but that for levels of some attributes, significant differences were observed. The heterogeneity of preferences within each country highlights the importance of incorporating the preferences of individual patients in clinical decision-making, to improve osteoporosis care.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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