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Research paper

Development and validation of an osteoporosis treatment questionnaire (OSTREQ) evaluating physicians' criteria in the choice of treatment

Polyzois Makras,[1] Antonios Galanos,[2] Stavroula Rizou,[3] Athanasios D. Anastasilakis,[4] George P. Lyritis[3]

[1]Department of Endocrinology and Diabetes, 251 Hellenic Air Force & VA General Hospital, Athens; [2]Laboratory for the Research of the Musculoskeletal System, University of Athens, Athens; [3]Hellenic Osteoporosis Foundation, Athens; [4]Department of Endocrinology, 424 Military Hospital, Thessaloniki; Greece

ABSTRACT

OBJECTIVE: This article describes the development and validation of the osteoporosis treatment questionnaire (OSTREQ), which is a physician-reported outcome tool aiming to evaluate physicians' criteria in the choice of osteoporosis treatment. DESIGN: The questionnaire –named OSTREQ– consisting of 17 questions that were divided into eight sections "Health Care System", "Patients' Preference in administration routes", "Usage, Cost", "Severity of Disease", "Treatment Efficacy", "Safety Profile", "Pharmaceutical Industry", affecting the decision and overall execution of a therapeutic approach, was developed by an expert panel and was later officially translated into English. In the second phase, orthopedic surgeons were asked to complete OSTREQ. Six indirect methods to evaluate validity were adopted: exploratory factor analysis, confirmatory factor analysis, subscale validity, known group validity, floor or ceiling effects, interpretability. To assess the reliability of the questionnaire, internal consistency validity as well as test-retest and parallel forms were calculated. RESULTS: One hundred seventy-two orthopedic surgeons were interviewed with an average period of experience in clinical practice of 10.5 years (SD ±8.9 years). The factors "Severity of Disease" and "Treatment Efficacy" were the most important in the choice of osteoporosis treatment, while the factor "Pharmaceutical Industry" had the least impact. The methodology of validation proved that the questionnaire possesses construct validity, discriminate ability, reliability, and sensitivity to change. CONCLUSIONS: OSTREQ represents a comprehensive and focused tool that, for the first time, assesses physicians' criteria in the choice of osteoporosis treatment. This tool could assist health care systems and pharmaceutical companies to be aware which parameters drive physicians' preferences regarding osteoporosis treatment.

Key words: Osteoporosis, Physicians, Questionnaire, Treatment, Validation

Address for correspondence:
Dr. Polyzois Makras, MD, Phd, Dept. of Endocrinology & Diabetes, 251 Hellenic Air Force & VA General Hospital, 3 Kanellopoulou street, 115 25 Goudi, Athens, Greece; Tel.: +30 210 7463606, Fax: +30 210 9638501, E-mail address: makras@internet.gr

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INTRODUCTION

Osteoporosis is a generalized skeletal disorder and represents a major health issue worldwide with serious complications that may even be life-threatening, especially for the elderly. Furthermore, osteoporosis creates a significant economic burden. The International Osteoporosis Foundation (IOF) estimated the total costs resulting from osteoporotic fractures at €37 billion in 2010 for countries within the European Union.[1] For Greece, the cost was €680 million and, based on anticipated demographic changes, is expected to increase to €814 million by 2025.[2]

The proper management of osteoporosis and its associated fractures is essential for maintaining high health care standards and quality of life for patients. Although the disease is traditionally defined as a T-score of 2.5 standard deviations or more compared to young normal populations, the majority of fragility fractures occur in patients within the osteopenic and not the osteoporotic range.[3,4] Therefore, the decision treatment should consider, in addition to the well-known bone mineral density (BMD) index, the individual fracture risk profile. Several clinical factors associated with increased fracture risk have been identified and assessment tools for the prediction of osteoporotic fractures have been developed. The most widely used is the FRAX model (https://www.shef.ac.uk/FRAX).[5]

Different criteria for the initiation of anti-osteoporotic treatment have been set in each country. The FRAX model has been calibrated for the Greek population and has been incorporated in the national diagnostic and therapeutic guidelines.[6] Bearing in mind that cost-effective intervention thresholds should ideally be country-specific, we recently established the thresholds considered cost-effective within the Greek setting.[7]

Individualized treatment is considered the ideal way of dealing with the disease. After establishing the need to initiate osteoporosis treatment, physicians are expected to choose the most suitable regimen for the patient based on medical history information, fracture risk assessment and previous anti-osteoporotic treatment. Moreover, the risk to benefit ratio should be constantly considered in the design and implementation of a chosen therapeutic approach.[8] Apart from patients' characteristics, the choice to initiate, change or continue a specific therapeutic intervention could be influenced by a wide range of factors including physician-related issues, health care system rules and, probably, pharmaceutical industry support and promotion. Therefore, and given the multiple available choices for osteoporosis treatment, it is still unclear how physicians reach their decision on a specific regimen and which factors influence their choices.

In this study, we aimed to develop and validate a simple questionnaire in order to evaluate the factors that influence clinicians' decision to initiate, continue or change a regimen for osteoporosis treatment.

METHODS

In order to develop the questionnaire, 10 experts (4 orthopedic surgeons, 4 endocrinologists, and 2 rheumatologists), recognized for their significant contribution to the field of osteoporosis, were invited to assist in this project. Each expert was asked to list the 10 most important factors that drive his/her decision when choosing a specific regimen for osteoporosis treatment (including initiation, continuation or change of a regimen), and a list of 100 questions was subsequently developed. After excluding his/her own 10 questions, each member of the panel was given the remaining 90 questions in order to evaluate each one as "necessary", "useful but not necessary" or "not necessary". Similar questions were merged and the content validity ratio for each question was estimated; all questions with a score between 0.7 and 1 were included in the final questionnaire.[9] The final questionnaire consisted of 17 questions divided into eight sections detailing the issues affecting the decision on and overall execution of a therapeutic approach, namely "Health Care System", "Patients' Preferences regarding regimen's administration", "Usage", "Cost", "Severity of Disease", "Treatment Efficacy", "Safety Profile", and "Pharmaceutical Industry". Given that the study is aimed at developing and validating an "OSteoporosis TREatment Questionnaire", the acronym OSTREQ was created.

As the questionnaire was originally developed in Greek, a translation into English also took place in accordance with the existing guidelines.[10] Specifically, two bilingual translators, one with a medical

background, produced the English translation and reached a consensus on the result. Two other translators, totally blind to the original translation, translated back the English version of the questionnaire into Greek in order to ensure that the translated version reflected the same item content as the original. Next, the study committee reviewed all translations and reached a consensus on the pre-final version, which was tested on 30 orthopedic surgeons who completed the questionnaire and were also interviewed about the meaning of each question. Finally, the study committee, in coordination with the developers of the questionnaire, adapted the final version, which is presented herein (Figure 1).

In the second phase of the study, orthopedic surgeons were asked to complete OSTREQ. The only inclusion criterion was their exclusive occupation in private practice; their demographic and professional characteristics are shown in Table 1. Participants were recruited from all over Greece in a representative manner according to the distribution of the specialty of orthopedics within the Greek territory. The questionnaire was scored so that the higher the score in each question the more the doctor was positively influenced

Evaluation of factors affecting treatment choices for osteoporosis	Absolutely preventative	Partially preventative	Neither preventative nor encouraging	Partially encouraging	Absolutely encouraging
Health Care System					
1. Approval procedures and/or reimbursement policy of Health Care System	1	2	3	4	5
Patients' preferences regarding regimen's administration					
2. Patient preferring oral administration	1	2	3	4	5
3. Patient preferring injectable administration	1	2	3	4	5
4. Patients' preferences regarding frequency of administration	1	2	3	4	5
Usage					
5. Patients' capability in following required administration procedures	1	2	3	4	5
6. Procedures and requirements for the preservation of regimen	1	2	3	4	5
Cost					
7. Cost for the Health Care System	1	2	3	4	5
8. Cost for the patient	1	2	3	4	5
Severity of disease					
9. Decreased bone mineral density	1	2	3	4	5
10. Risk of future osteoporotic fractures	1	2	3	4	5
11. Prevalent osteoporotic fractures	1	2	3	4	5
Treatment efficacy					
12. Effect on reducing fracture risk	1	2	3	4	5
13. Effect on bone mineral density	1	2	3	4	5
14. Effect on patients' quality of life	1	2	3	4	5
Safety profile					
15. Possible adverse events	1	2	3	4	5
Pharmaceutical industry					
16. Patients' program support	1	2	3	4	5
17. Physicians' program support	1	2	3	4	5

Figure 1. OSTREQ questionnaire.

Table 1. Demographic and professional characteristics of participating physicians

Gender (male/female) n (%)	163 (94.8%) / 9 (5.2%)
Age (yrs)	47.21±7.68
Yrs of specialty	8 (14) [1-43]
Patients per month	200 (207.5) [15-1000]
Osteoporotic patients per month	40 (56.5) [2-350]
% osteoporotic patients per month	22.2% (18) [3.3-75]

Footnote: With the exception of age (mean±SD), all other parameters are presented as median (IQR) [min-max] due to the sample's distribution.

towards selection of a treatment. No specific treatment was evaluated as the participants were instructed to fill in the questionnaire bearing in mind all available anti-osteoporotic medications.

All questions were coded and scored and the completed questionnaires were included in the data set. Individual unanswered items were excluded from the analysis. All the data were entered, checked for missing values, and analyzed using the statistical programs SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) and SAS version 7.0 (SAS Institute, Cary, NC, USA). Data are presented as means (±SD). The normal distribution of the data was examined using the Kolmogorov-Smirnov test and P-P plots. Next, six indirect methods to evaluate validity were adopted: exploratory factor analysis; confirmatory factor analysis; subscale validity; known groups validity; floor or ceiling effects; interpretability. To assess the reliability of the questionnaire, the internal consistency validity as well as test-retest and parallel forms were calculated.

We chose not to describe the validity and reliability methods in the "Methods" section but to elaborate upon them in the "Results" section together with the outcome of analysis in order to facilitate and improve the readability of the paper and help the reader follow the methodology.

The study was approved by the local Institutional Review Board of 251 Hellenic Air Force & VA General Hospital, Athens. All participants provided their written informed consent.

RESULTS

A total of 226 orthopedic surgeons were invited to participate: 172 responded positively and completed the questionnaire (response rate: 76.1%). Their average period of experience in clinical practice was 10.5 years (± 8.9 years).

The descriptive statistics of the completed questionnaires are presented in Table 2 and in supplementary Table 1. The responses to most of the questions were normally distributed. Skewness is a measure of asymmetry and a value of more than 1 or less than -1 indicates skewness in the data. Skewness values ranged between -2.09 and 0.6; only 2 questions had skewness lower than -1, indicating skewed or non-

Table 2. Descriptive statistics initial assessment and reassessment

		Mean	SD	Min	Max
Initial assessment (n=172)	Administration - Usage	17.44	2.96	6.00	23.00
	Disease-Treatmenttt efficacy	25.77	5.25	7.00	30.00
	Health care system-cost	9.19	2.41	4.00	15.00
	Pharmaceutical industry	7.19	1.67	3.00	10.00
	Total score	62.32	7.83	35.00	79.00
Reassessment (n=40)	Administration-Usage	18.43	2.04	14.00	22.00
	Disease-Treatmenttt efficacy	27.18	1.96	24.00	30.00
	Health care system-cost	8.23	1.76	6.00	13.00
	Pharmaceutical industry	6.98	1.10	4.00	10.00
	Total score	63.28	5.24	53.00	76.00

SD: standard deviation.

normal distribution of the responses to these questions.

In this particular group of physicians, the factors "Severity of Disease" and "Treatment Efficacy" were the most important in the choice of osteoporosis treatment, while the factor "Pharmaceutical Industry" had the least importance (Table 2). More specifically, in terms of each particular query, question 12 regarding the effect of an agent on reducing fracture risk had the higher score (4.51), followed by question 14 (4.42) regarding the effect on patients' quality of life, which included the parameters mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (supplementary Table 1). By contrast, question 15 concerning the possible adverse events had the lowest impact on treatment choice (2.73), followed by question 7 (3.03) regarding the cost borne by the National Health System (supplementary Table 1).

Exploratory factor analysis *(EFA)* was conducted using the principal component extraction method with Varimax rotation to determine the factor structure of the 17 questions of the OSTREQ questionnaire. Questions with factor loadings ≥40 (including values that rounded to 0.40) and those that did not load on more than one factor were retained. Questions not meeting these criteria were removed one at a time. Factor analyses were repeated until a solution was attained in which all questions included in the analysis met all criteria.[11,12]

The Bartlett Test of Sphericity was 1590 and was highly significant ($p < 0.001$). The Kaiser-Meyer-Olkin Measure of Sampling Adequacy was equal to 0.801, showing that the data were suitable for factor analysis. The 17 questions were analyzed via the maximum likelihood extraction method using a Varimax rotation. Four factors, with an eigenvalue of over 1 and questions factor loadings greater than or equal to 0 ≥40, were identified. We used the scree test to determine the number of factors to retain and rotate, which again suggested a 4-factor solution. Only question 15 was excluded from the analysis because it was loaded on more than one factor and its loadings were not greater or equal to 0.40. Finally, the EFA yielded 16 questions with a 4-factor solution, the eigenvalue for the first factor being 5.2, accounting for 30.4% of the variance, for the second factor it 2.9, accounting for 17.1%, for the third factor 2.1, accounting for 12.1% of the variance, and for the fourth factor 1.3, accounting for 7.8%. Factor loadings, which are the correlation coefficients between the questions and the factor, ranged from 0.65 to 0.90 (Tables 3 and 4).

Confirmatory factor analysis *(CFA)* was used to examine and confirm the factor structure of the questionnaire as suggested by the EFA of the questionnaire. The *CFA* was carried out using the Analysis of Moment Structure (AMOS) Version 7.0.[13] The sample size required for the CFA based on researchers' conventions ranged for the participants' ratio from 3:1 to as high as 12:1. Stable factor models can be found with samples as small as 100[14] and with samples as small as 150 if 10 or more items load at 0.4 or higher.[15] The OSTREQ consisted of 17 questions, thus our sample size of 172 is within the above guidelines. Rejecting or accepting a model was based on a number of global fit indices: chi-square tested the fit of the observed covariance matrix obtained under the constraints of the model; the root mean square error of approximation (RMSEA); the comparative fit index (CFI); the normed fit index (NFI); the goodness fit index (GFI); and the adjusted GFI (AGFI). Chi-square-degrees of freedom (d.f.) ratio <2.0**,** RMSEA <0.06**,** CFI >0.90,

Table 3. Eigenvalues and explained variance

Component	Eigenvalues	% of Variance
1	5.17	30.41
2	2.91	17.10
3	2.06	12.14
4	1.34	7.85
5	0.84	5.51
6	0.79	4.65
7	0.64	3.75
8	0.57	3.33
9	0.50	2.94
10	0.42	2.44
11	0.37	2.19
12	0.31	1.83
13	0.30	1.76
14	0.23	1.36
15	0.19	1.13
16	0.16	0.93
17	0.12	0.68

Table 4. Factor loadings

Items	Disease - Treatment Efficacy	Administration - Usage	Health Care System - Cost	Pharmaceutical Industry
Q12	0.878			
Q13	0.873			
Q11	0.868			
Q10	0.863			
Q14	0.846			
Q9	0.771			
Q5		0.764		
Q6		0.737		
Q4		0.730		
Q3		0.712		
Q2		0.654		
Q8			0.853	
Q7			0.844	
Q1			0.723	
Q17				0.898
Q16				0.878

Question 15 excluded from the analysis; all loadings below 0.4 are not presented.
Extraction Method: Principal Component Analysis. Rotation Method: Varimax with Kaiser Normalization

GFI >0.85, AGFI >0.80, NFI >0.90 indicate an acceptable fit.[16-19]

A 4-factor model was conducted by confirmatory factor analysis (Figure 2) yielding acceptable global fit indices. The resulting global fit indices $X^2 = 113.23$, $p < 0.001$, chi-square-degrees of freedom (d. f.) ratio = 2.01, RMSEA = 0.062, CFI = 0.91, NFI = 0.85, GFI = 0.85, AGFI = 0.81 showed that the 4-factor solution proposed herein should be retained.

Convergent or criterion validity was not performed because the OSTREQ is the first questionnaire which examines the factors that clinicians take into consideration when choosing a particular regimen either to initiate or to continue or to change a treatment for osteoporosis.

Subscale validity was evaluated by examining the subscale correlations. There was a low correlation between the 4 factors of the OSTREQ questionnaire ($r<0.25$), indicating uncorrelated factors as expected. Only the factor "Disease - Treatment Efficacy" had a low statistically significant correlation with the factors "Pharmaceutical Industry" ($r = 0.201$ $p = 0.008$) and "Administration - Usage" ($r = 0.285$ $p < 0.001$) (supplementary Table 2).

Known groups validity of the OSTREQ questionnaire was examined in terms of the ability of the questionnaire to distinguish between subgroups of doctors on the basis of their time of clinical experience (less than 5 years vs 5-15 years vs more than 15 years). The ANOVA model was used for the statistical analysis.

The OSTREQ questionnaire discriminated well between subgroups of physicians on the basis of their clinical experience. Only the "Administration - Usage" and "Disease - Treatment Efficacy" subscales tended to be lower in physicians with 15+ years working experience compared with those with less than 5 years, and 5-10 years, respectively (Table 5).

Floor or ceiling effects are considered to be present if more than 15% of responders achieve the lowest or highest possible score, respectively.[20] If floor or ceiling effects are present, it is likely that extreme items are missing at the lower or upper end of the scale, indicating limited content validity. As a consequence, physicians with the lowest or highest possible score

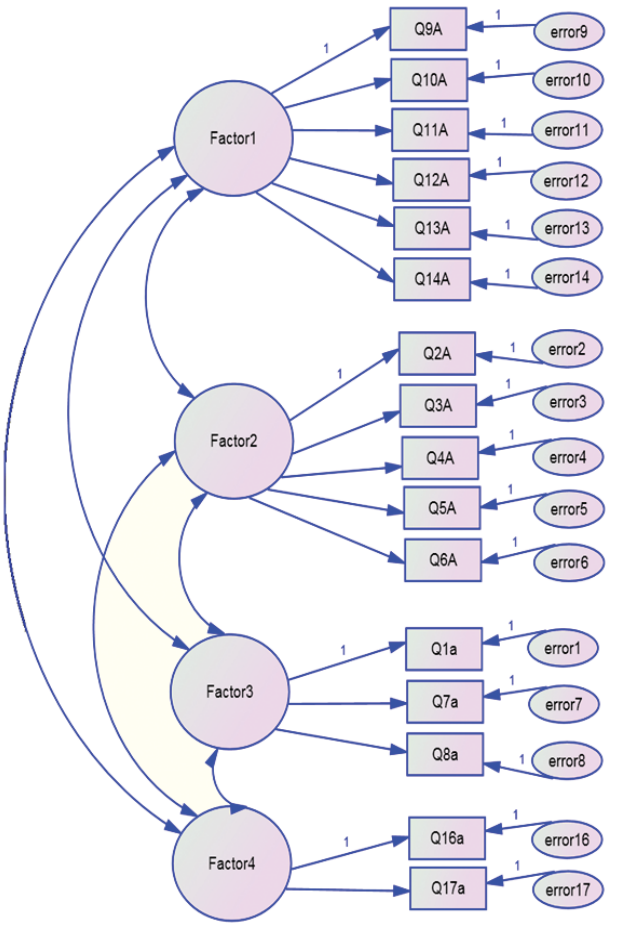

Figure 2. Confirmatory factor analysis, 4-factor structure.

cannot be distinguished from each other, thus reliability is reduced. Furthermore, the responsiveness is limited because changes cannot be measured in these physicians.

The percentage of physicians scoring at the lowest possible level of the scale and at the highest possible level for the "Administration - Usage", "Disease - Treatment Efficacy", "Health Care System - Cost" and "Pharmaceutical Industry" factors were 0.6%, 3.5% - 0.6%, 26.2% - 1.2%, 4.1% and 0.6%, 10.2%, respectively. The critical value of 15% was surpassed only for the "Disease - Treatment Efficacy" factor which had a ceiling effect, thus it can conclusively be stated that there were no floor and ceiling effects for all factors.

Interpretability: The error associated with a single application of the OSTREQ was analyzed using the standard error of measurement (SEM). The SEM provides an estimate of how reliably a scale estimates an individual's "true score", which is the score that would be obtained for the person if the scale were measured perfectly, without any error. Because clinicians are more interested in the error associated with an instant in time rather than over a short time interval, the SEM was calculated based on the alpha coefficient with the formula: SEM = standard deviation x [square root (1- Cronbach alpha)]. The SEM carries with it 68% CI. To achieve 90% CI, the SEM was multiplied by the z value associated with the 95% CI (z = 1.96).

Table 5. Known-groups validity

	Clinical status	N	Mean±SD	P value
Administration - Usage	Below 5 years	71	18.62±2.53	**0.050**
	5-15 years	46	19.04±2.52	
	15+ years	54	17.17±2.92	
Disease - Treatment Efficacy	Below 5 years	71	27.98±2.49	**0.055**
	5-15 years	46	27.23±4.56	
	15+ years	54	26.28±2.10	
Health Care System - Cost	below 5 years	71	8.81±2.14	0.515
	5-15 years	46	8.65±1.96	
	15+ years	54	8.11±2.42	
Pharmaceutical Industry	Below 5 years	71	7.12±1.29	0.468
	5-15 years	46	7.42±1.36	
	15+ years	54	6.94±1.35	
Total	Below 5 years	71	65.19±4.92	0.346
	5-15 years	46	64.12±6.64	
	15+ years	54	62.94±5.26	

The error associated with the "Administration - Usage", "Disease - Treatment Efficacy", "Health Care System - Cost" and "Pharmaceutical Industry" factors at a given point in time (SEM) were 0.21, 1.15, 0.48, and 0.26 scale points, respectively (supplementary Table 3).

Internal consistency validity of the OSTREQ was determined by calculating the Cronbach alpha coefficient.[21] A Cronbach alpha coefficient value of 0.7 indicates sufficient reliability for research purposes and suggests that items are interdependent and homogeneous in terms of the construct they measure. For clinical applications a >0.8 is desirable.[22] The

internal consistency of the 17 items of the OSTREQ questionnaire was measured with Cronbach's alpha and yielded a value from 0.780 for the factor "Disease - Treatment Efficacy" to 0.93 for the factor "Administration - Usage", which indicate excellent internal consistency; the items are interdependent and homogeneous in terms of the construct they measure (supplementary Table 4).

Test-retest reliability (stability) indicates the stability of patients' response in time and it was determined by calculating ICC (intraclass correlation coefficient: the error in measurements as a proportion of the total variance) between the total scores of the initial assessment of the OSTREQ and the total scores of the reassessment after 3 days. Because this coefficient does not correct for systematic differences and agreement by chance, the scores of the 2 assessments were tested for systematic differences by using the paired *t*-test.[23-25]

The paired samples t-test between initial assessment and reassessment of all factors indicated no statistically significant differences. ICC between initial assessment and reassessment of the test ranged between 0.890 and 0.925 ($p < 0.001$). The above results of stability indicated that OSTREQ's factors were remarkably consistent between the two occasions (supplementary Table 5).

Parallel forms reliability is a measure of reliability obtained by administering different versions of the OSTREQ questionnaire (both versions must contain questions that probe the same construct, skill, knowledge base, etc.) to the same group of individuals. The scores from the two versions can then be correlated in order to evaluate the consistency of results across alternate versions.[23-25] The reliability of the parallel forms was examined using a sample of 40 random physicians. An example of the form of questions is presented in supplementary Figure 1. The scores from the two different versions of the OSTREQ questionnaire were very highly correlated for all factors ($r > 0.9890$), which proved the consistency of results across alternate versions.

DISCUSSION

Several questionnaires have been developed to assess the risk of fracture and the necessity of treatment in patients with decreased bone mass.[26-28] Furthermore, there are studies evaluating questionnaires based on patients' preferences regarding osteoporosis treatment.[29-32] However, all these tools are exclusively addressed to patients. In the present study, we aimed to develop what is, to the best of our knowledge, the first questionnaire evaluating the factors that influence the physician's decision to initiate, continue or change a regimen for osteoporosis treatment.

Our questionnaire was completed by physicians of the same specialty. In contrast to other countries, orthopedic surgeons represent the specialty with the highest percentage of prescriptions for osteoporosis treatment in Greece. The participants were representatively selected from all regions of Greece in order to avoid local or regional biases in their responses. From their ranking, it is evident that questions associated with the severity of the disease and the efficacy of each treatment weigh the most in a physician's decision to administer a specific treatment, while cost, system approval procedures and pharmaceutical industry support are considered of less importance. In addition, it seems that the possibility of adverse events is not a major issue of concern among this group of physicians, indicating that osteoporosis treatment is still regarded as a reasonably safe therapeutic intervention with minimum and rare unfavorable events. More experienced physicians tended to value patients' preferences and difficulties in the procedures of treatment less than physicians with fewer years of experience. In addition OSTREQ failed to discriminate between subgroups of physicians on the basis of their clinical experience as concerns the subscales of "Health Care System - Cost" and "Pharmaceutical Industry". However, this phenomenon is clinically relevant as clinical experience is obviously important in terms of administration and usage of medication as well as regarding factors such as the disease per se and the treatment used. Factors such as health care system, cost, and pharmaceutical industry are expected to have a universal impact on physicians and this was proved with the analysis of "known group's validity" in this group of doctors.

The same questionnaire could be completed by other specialties involved in the management of osteoporosis, e.g. endocrinologists, rheumatologists, etc.;

in that case, the recorded responses could be considerably different from those recorded by the orthopedic surgeons in the present study. Furthermore, physicians from different countries could respond quite differently based on their culture and professional habits as well as their national guidelines. However, this fact does not negate the validation of the instrument, which was adequately designed and performed very satisfactorily. To our knowledge, there are no data regarding the physicians' attitudes in other countries, as information is only given after the implementation of national guidelines and health care system rules and not as a consequence of personal preferences and decisions; OSTREQ might be helpful to clarify the parameters affecting the physicians' decision in every country and specialty and thereby guide both medical education and health care policies.

The present tool was developed as a general osteoporosis treatment questionnaire; however, it could be used easily and with minimal modifications to evaluate physicians' opinion on a specific antiosteoporotic agent. Finally, our questionnaire could serve as the basis for the development of physician-addressed questionnaires evaluating other diseases and conditions, e.g. diabetes mellitus, arterial hypertension, etc.

In conclusion, we developed and validated a general osteoporosis treatment questionnaire that could provide assessment of the criteria that physicians take into consideration when they decide to implement a regimen for osteoporosis. This tool could assist health care systems and pharmaceutical companies understand which parameters drive physicians' choices regarding the treatment of osteoporosis.

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