Chinese patients' preference for pharmaceutical treatments of osteoporosis: a discrete choice experiment

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Abstract

Purpose: This study was performed to elicit Chinese patients' preferences for osteoporosis medication treatment and to investigate the heterogeneities of the preferences in subgroups.

Methods: A discrete choice experiment comprising 15 choice sets with 4 important attributes was conducted in a Chinese population at risk of osteoporotic fracture. The four attributes were treatment efficacy in reducing the risk of fracture, out-of-pocket cost per year, adverse

effects of treatment, and mode of administration. The patients were asked to choose between two hypothetical treatments; they could also choose no treatment. Mixed logit models were used, and any observed heterogeneity in the patients' preferences was further assessed in subgroup analyses.

Results: In total, 267 patients were analysed. On average, the patients preferred to receive treatment rather than no treatment. The patients preferred treatment with higher efficacy in preventing fracture and lower out-of-pocket cost. The least preferred adverse effect of medication was gastrointestinal disorders, followed by flu-like symptoms and finally skin reactions. The most preferred mode of administration was annual intravenous infusion, followed by 6-month subcutaneous injection, a weekly oral tablet, and daily nasal spray; daily oral tablets ranked as the least preferred mode of administration. The differences in the patients' preferences among all attributes were statistically significant ($p<0.05$). Patients' age was found to contribute to the observed preference heterogeneity in most of the included attributes.

Conclusions: This study revealed Chinese patients' preferences for osteoporosis treatments. Annual intravenous infusion and 6-month subcutaneous injection were significantly preferred over weekly oral tablets in this Chinese population.

Keywords: discrete choice experiment, pharmaceutical treatment, osteoporosis, patient preferences, Chinese

Mini Abstract:

While adherence to osteoporosis treatment is low, patients' preference for osteoporosis treatment is unknown in Chinese patients. Chinese patients are willing to receive treatments

with higher clinical efficacy and lower out-of-pocket cost. In addition, annual intravenous infusion and 6-month subcutaneous injection are preferred over weekly oral tablets.

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Conflict of Interest

Lei Si, Liudan Tu, Ya Xie, Andrew J Palmer, Yuanyuan Gu, Xuqi Zheng, Jiamin Li, Qing Lv, Jun Qi, Zhiming Lin, Mingsheng Chen, Jieruo Gu and Mickaël Hiligsmann declare that they have no conflict of interest.

Introduction

Osteoporosis is defined by a bone mineral density (BMD) 2.5 standard deviation (SD) or more below the adult mean value, and patients with osteoporosis have a higher risk of fractures throughout their remaining life [1]. Pharmaceutical treatments of osteoporosis mainly focus on maintaining a healthy bone mineral density to reduce the risk of fragility fracture. While many medications are available to patients with a high risk of osteoporotic fractures (e.g., calcium, bisphosphonates, parathyroid hormone analogues, calcitonin receptor activator of nuclear factor kappa-B ligand inhibitors, oestrogen agonists, cathepsin K inhibitors, and monoclonal antibody to sclerostin), persistence and adherence to treatment continue to be a major concern [2]. Poor persistence and adherence to osteoporosis treatment not only jeopardizes the medication efficacy of preventing fracture [3] but also substantially reduces the cost-effectiveness of drug therapies [4, 5].

Understanding the causes of poor adherence is therefore important. Although some intentional factors can contribute to poor medication adherence and persistence [6, 7], evidence has shown that interventions that using simplified dosing regimens, electronic prescription, patient decision aids, and patient education might improve osteoporosis medication persistence and adherence [8]. Understanding the patients' needs and preferences and involving them in treatment decision-making could improve medication adherence [2].

Discrete choice experiments (DCEs) are increasingly used to elicit patients' preference for a health intervention based on the trade-offs among important attributes that might affect the patients' behaviours in taking medications [9]. A few studies in Europe have investigated patients' preferences for osteoporosis treatment. Despite converging evidence showing that patients had a preference for and were willing to trade among medications' attributes, some differences in the most preferred level of each of the attributes were observed [10, 11]. For

example, in a cross-European DCE study, all patients in Belgium, France, Ireland, the Netherlands, Spain, Switzerland, and the United Kingdom expressed their preference for medications with lower out-of-pocket (OOP) costs and higher treatment efficacy [11]. With respect to the mode of administration, while 6-month subcutaneous injections was the most preferred mode in Belgium, Switzerland, Spain, and the United Kingdom, monthly oral tablets was the most preferred mode in France and the Netherlands [11]. Because of potential variations in patients' preferences, application of the study results to other populations is limited. To our knowledge, no study has evaluated patients' preferences for osteoporosis treatment in the Chinese population. Although osteoporotic fracture imposes dramatic disease and economic burdens onto Chinese society [12], persistence and adherence to osteoporosis treatment remains suboptimal [13]. Therefore, the present study was performed to gain insight into Chinese patients' preferences for osteoporosis medication treatment. We also investigated the heterogeneity of the preferences in several subgroups of patients and compared Chinese patients' preferences with European patients' preferences.

Methods

Design of DCE

The DCE questionnaire followed those used in previous European studies [10, 11]. The attributes included in the previous DCE were selected from patient interviews using the nominal group technique (NGT) [14, 15]. The NGT is a structured, multistep, facilitated group meeting technique used to elicit and prioritize responses to a specific question to prioritise health and healthcare problems [16]. The NGT has been shown feasible to select attributes in osteoporosis treatment DCEs [17]. Five focus groups from the Netherlands and Belgium participated in the interview. From an initial list of 12 potentially important attributes derived from the

literature, the focus groups revealed 4 important treatment attributes: effectiveness, adverse effects, mode of administration, and frequency of administration [15]. In addition, the OOP contribution was found to be important in Belgium, but it was not an important attribute in the Dutch population because there are no co-payments for medications in the Netherlands [15]. In line with the European DCE and after discussion/approval with Chinese clinicians (JG, AP, LT, YX, JL, QL, JQ, and ZL), we included the four most important attributes and combined the mode and frequency of administration as one attribute. In addition, because patients have co-payments and the amount of each co-payment depends on the type of service and health insurance [18], we also included OOP cost in this DCE. Finally, the four attributes evaluated in this study were the treatment efficacy in reducing the risk of fracture, OOP cost per year, adverse effects of treatment, and mode of administration (Table 1).

<Table 1 should be inserted here>

The experimental design was based on the characteristics of real osteoporosis medications that are currently used by Chinese patients including alendronate, zolendronic acid, raloxifene, calcitonin, denosumab and calcium/vitamin D_3 [19, 20]. Calcium/vitamin D was the most commonly used drug followed by pain relievers, calcitonin and bisphosphonates in Chinese patients who sustained a fracture [19]. In addition, we aimed to design our DCE as close as possible to the European study for the sake of international comparison. The treatment efficacy in reducing the risk of fracture was determined based on the results of previous meta-analyses or clinical trials of common osteoporosis treatments [21-24]. The OOP cost per year was set according to the retail price of common osteoporosis medications at the Third Affiliated Hospital of Sun Yat-Sen University. For this question, patients were required to imagine to pay this amount themselves even if they were covered by health insurance and the medications might be fully or partially covered. Adverse effects and modes of administration were also set based on current treatment using a literature review and expert opinion. To

construct the choice sets presented to the patients, a Bayesian efficient design was used to maximize the D-efficiency of the attributes using Ngene software (version 1.1.1, http://www.choice-metrics.com). The prior distributions for the Bayesian optimal design were taken from the European study [11].

Data collection

In total, 15 choice sets were used for the DCE. In each choice set, the patients were asked to choose between two hypothetical medications (A and B) and indicate their preferred treatment option; a "no treatment" option was also available. An example of an English-translated question is shown in Figure 1.

<Figure 1 should be inserted here>

The following patient demographic and socioeconomic data were collected: age, sex, education level, family income, weight, height, self-reported diagnosis of osteoporosis, bone mineral density, and previous clinical fracture. Living standard was measured by the per-adult household income, which was calculated by the annual household income per annum divided by the number of adult equivalents [25].

Patient recruitment

Convenience sampling was used to recruit study participants. Patients who attended the Department of Rheumatology of the Third Affiliated Hospital of Sun Yat-Sen University were assessed by the clinician on their risk of osteoporotic fracture. In this study, the inclusion criteria of study participants were as follows: 1) patients who were at risk of osteoporotic fracture; 2) patients who were willing to participate in our study. The paper-based survey was supervised by a senior rheumatologist (JG) and was conducted by the onsite clinicians (LT, YX, JL, QL, JQ, and ZL). The study participants were provided with a thorough description of the questions before the survey and were given further assistance to

promote an understanding of the questions during the survey if needed. We have targeted to recruit 300 patients in our DCE given the common rules-of-thumb for minimum sample size in DCE and our experience in the European study [11, 26]. Patient recruitment was conducted from July 2017 to June 2018. All participants provided written informed consent. The study was approved by the Sun Yat-Sen University Ethics Committee.

Statistical analysis

The data were analysed using a mixed logit model [27] based on the random utility theory, wherein the utility that respondent i derives from choosing alternative j in choice set t is given by

$$U_{ijt} = X_{ijt}\beta_i + \varepsilon_{ijt};\ \ i = 1, \dots, n; j = 1,2,3; t = 1, \dots, 15,$$

where X_{ijt} is a vector of variables representing the alternative specific constant (ASC) and attributes of alternative j, and β_i is a vector of random coefficients assumed to be uncorrelated and normally distributed except for the coefficients of the cost and effectiveness attributes, which were assumed to be distributed log-normally. The ASC represents preferences that are inherent and independent of specific attribute values. A positive coefficient of the level within the attribute indicates a stronger preference compared to the reference group and a negative coefficient denotes a stronger preference for the reference. The cost attribute was entered into the model in its negative form. The errors ε_{ijt} were independently and identically distributed as a type 1 extreme value.

The willingness to pay (WTP) distributions were simulated using the ratio of random coefficients (with the coefficient of the cost attribute as the denominator). The mean WTPs and percentiles were then estimated using the random draws from the simulated distributions. In the calculation, we accounted for parameter uncertainty by using all information in the

parameter distribution including the covariance matrix rather than just the mean and standard deviation. As noted by Hensher and Greene [28] in 2003, this is preferred because using just the mean and standard deviation ignores the sampling variance in the point estimates.

To determine whether the respondents' characteristics impacted their preferences, dummy variables representing individual characteristics were interacted with the preference coefficients at their means. This essentially split the sample into two groups with group-specific mean preferences to be estimated. The statistical significance of the coefficients of the interaction terms was used to test the preference homogeneity assumption between two groups.

Statistical analyses were conducted with STATA 14 (StataCorp, College Station, TX, USA). The mixed logit models were estimated by the simulated maximum likelihood using the STATA command developed by Hole [29]. In total, 2,000 Halton draws were used to simulate the likelihood.

Results

A total of 282 patients returned the questionnaire. The patients' characteristics are summarized in Table 2. More than four-fifths were women, around 40% of the population reported that they were diagnosed with osteoporosis, and one-fifth had a history of fracture. The mean age of the population was 63.4 years (SD, 10.2 years), most patients had a normal weight (average body mass index [BMI], 22.6 kg/m^2), and the mean T-score of the population was −2.1 (SD, 0.8). Approximately 11% of the population had no school education, and 14% had a university education or above. On average, 2.3 adults were living in each household, and an annual per-adult income of 50,000 Yuan roughly separated the

households in half. One patient rated easiest (0) and 6 patients rated hardest (10) for the difficulty of DCE. On average, the patients scored 5.7 (SD, 2.0, median, 6) indicating that the DCE tended to be moderately difficult for patients to complete.

<Table 2 should be inserted here>

Fifteen patients were unwilling to participate in the DCE and always opted out from the choices; hence, they were removed from the final analysis. Therefore, 267 (94.7%) patients were included in the final analysis of medication preferences. The patients' preferences for the attributes of osteoporosis pharmaceutical treatments are shown in Table 3. The mean ASC was 9.57, which indicated that on average, patients preferred to receive treatment than no treatment. In addition, the SD of the constant was statistically significant, indicating the presence of significant preference heterogeneity for treatment in this population. With respect to adverse effects of medication, the patients generally preferred being at risk for flu-like symptoms and skin reactions compared with gastrointestinal (GI) disorders. The preference was statistically significant. There was no statistically significant preference heterogeneity for adverse effects. Using a daily oral tablet as the reference for the mode of administration, the patients' preferences for the other four modes of administration were assessed. Notably, the patients' preference for yearly intravenous infusion was the strongest, followed by 6-month subcutaneous injections, weekly oral tablets, and daily nasal spray. In addition, patients significantly preferred yearly intravenous infusion and 6-month subcutaneous injection compared with weekly oral tablets. With the exception of weekly oral tablets, statistically significant preference heterogeneity was present for other three modes of administration, especially for yearly intravenous infusion. In addition, the patients significantly preferred medications with higher clinical efficacy and lower OOP cost.

<Table 3 should be inserted here>

Table 4 shows patients' WTP for attributes in the DCE. Using GI disorders as the reference, the patients were willing to pay 3,712 Yuan (the 5th and 95th percentiles: 875 and 7,121 Yuan, respectively) and 5,650 Yuan (5th and 95th percentiles: 2,714 and 9,445 Yuan, respectively) more per annum for treatment with flu-like symptoms and skin reactions, respectively. With respect to the mode of administration, patients were willing to pay 5,576 Yuan (5th and 95th percentiles: 2,190 and 10,133 Yuan, respectively), 26,395 Yuan (5th and 95th percentiles: 17,005 and 39,261 Yuan, respectively), 30,884 Yuan (5th and 95th percentiles: 19,435 and 46,808 Yuan, respectively), and 15,837 Yuan (5th and 95th percentiles: 10,067 and 23,730 Yuan, respectively) more per annum if they could choose daily nasal spray, 6-month subcutaneous injection, yearly intravenous infusion, and weekly oral tablets over daily oral tablets. In addition, patients were willing to pay 3,689 Yuan (5th and 95th percentiles: 2,037 and 6,532 Yuan, respectively) more per annum for a 1% improvement in medication efficacy of preventing fractures.

<Table 4 should be inserted here>

Patient age was found to be a main contributor to the heterogeneity of preferences (Table 5). Patients aged ≤60 years showed a statistically significant difference in their preference for adverse effects, while those aged >60 years did not. Moreover, the preference for skin reactions over GI disorders was significantly profound in young patients. While both age groups showed statistically significant differences in their preference for most of the modes of administration, the preference was stronger in patients aged ≤60 years, and the between-group difference was statistically significant for daily nasal spray, 6-month subcutaneous injection, and yearly intravenous infusion. Similarly, patients aged ≤60 years also showed a stronger preference for lower OOP cost and higher clinical efficacy than their older counterparts.

<Table 5 should be inserted here>

We further investigated whether sex, BMI, education, per-adult household income, a history of fracture, the visual analogue scale (VAS) score, and a self-reported diagnosis of osteoporosis contributed to between-group differences in preferences. The detailed results are provided in Appendix 1. Patients who were women, those with a non-healthy BMI, those with a school education of senior high school or above, and those with osteoporosis had a stronger preference ($p<0.05$) for receiving osteoporosis medication (Appendix Tables 1, 2, 3, and 7). Interestingly, despite the fact that 6-month subcutaneous injection was preferred over daily oral tablets, the preference was significantly stronger ($p<0.05$) in men (Appendix Table 1), those with a junior high school education or lower (Appendix Table 3), and those with a VAS score of ≤60 (Appendix Table 6). In addition, patients with a history of fracture had a significantly stronger preference ($p<0.05$) for weekly oral tablets, but the preference for other modes of administration was not statistically stronger than that in patients with no previous fracture (Appendix Table 5). Finally, household income did not contribute to the heterogeneity of medication preference (Appendix Table 4).

Discussion

This study was performed to estimate Chinese patients' preferences for osteoporosis medications using a DCE. Chinese patients preferred being at risk of skin reactions over flu-like symptoms and GI disorders. Yearly intravenous infusion and 6-month subcutaneous injection were significantly preferred over weekly oral tablets, daily nasal spray, and daily oral tablets. Moreover, Chinese patients preferred a medication with a lower OOP cost and higher clinical efficacy. Patient characteristics including age, sex, level of education, self-

reported VAS score, and previous fracture status contributed to the heterogeneity of preferences for osteoporosis medications.

Our study reports, for the first time, Chinese patients' preference for osteoporosis medications and we have investigated the preference orderings as well as patients' WTP to trade between attributes in the DCE; Second, we have attempted to investigate the impact of covariates (e.g. age, sex, education level etc.) on individual preferences; Finally, our study results are helpful to HTA bodies or health policy decision makers when they make reimbursement decision on osteoporosis medications. It is broadly accepted that there is value in using patient preferences to inform HTA assessment and medication reimbursement decision making [30-32]. At the moment, many osteoporosis medications that demonstrate good clinical efficacy are still not publicly funded in China, such as denosumab [33]. On the other hand, many medications that are shown to be less clinically effective or poorer safety profile are still being used as first line treatment for osteoporosis in China, such as calcitonin [19]. Due to the financial barrier to patients, doctors are more likely to choose osteoporosis medications that are publicly funded. As a consequence, Chinese access to medications with higher clinical efficacy in preventing fracture and strong patient preference is limited. Our study results will be helpful when seeking reimbursement for such medications from Chinese health policy decision making bodies.

In a previous review of patient preferences for osteoporosis drug treatment, medication effectiveness was listed as the most important attribute of osteoporosis medications in many populations [34]. In the present study, patients also preferred medications with higher clinical efficacy/effectiveness of reducing fracture risk: patients were willing to pay 3,689 Yuan for a 1% increase in medication efficacy. If a medication could further reduce the fracture risk by 10%, the WTP was higher than any of the trade-offs among levels in other attributes (Table 4). The medication dosing frequency has been found to be an important attribute that

influences patient behaviour. Chinese patients tended to prefer osteoporosis medications with a longer dosing frequency, which is consistent with other populations [35]. The preference for a longer dosing frequency is explained by medication convenience and ease of following a treatment regimen for a long time [36]. Not surprisingly, GI disorders were less preferred than flu-like symptoms and skin reactions and it was chosen as the reference. In addition, there was no heterogeneity in the preference for flu-like symptoms and skin reactions among the study population. GI disorders were related to the choice of treatment, and having a GI event was associated with reduced patient compliance to osteoporosis treatment [37].

A better understanding of patients' preferences might improve medication persistence and adherence, in turn improving the clinical and economic outcomes [4]. The current study followed the design of a study of patients' preference for osteoporosis treatments among seven European countries [11]. Regarding the mode of administration, 6-month subcutaneous injection was the most preferred mode in Belgium, Switzerland, Spain, and the United Kingdom. Monthly oral tablets was the most preferred mode in France and the Netherlands. Interestingly, yearly intravenous infusion was the most preferred mode only in Ireland in this European study [11], and it was the most preferred mode in our Chinese population. Yearly intravenous infusion and 6-month subcutaneous injection were consistently preferred over weekly oral tablets in both European and Chinese populations. In addition, GI disorders were the least preferred adverse effect in all European populations [15] and our Chinese population. The differences in patients' preferences for osteoporosis medications across these European and Chinese populations might be useful to pharmaceutical companies when they determine the formulation of their osteoporosis medications.

This study has some limitations. First, the attributes and levels used in our DCE were taken from a European study instead of from interviews with local patients [38]. Although the similarities in the design between the Chinese and European studies makes the results

comparable, we might have missed some attributes that were important to the Chinese population. However, we consulted several local clinicians in our research team to verify attributes for a remedy. Second, we have only included three side effects while others such as osteonecrosis of the jaw (ONJ) and atypical femoral fractures might also make patients afraid of taking osteoporosis medications. Nevertheless, incidence of ONJ is limited and highest in patients with malignancy receiving high doses of intravenous bisphosphonates and denosumab and it is not common in our study population [39]. Third, the *a priori* information used to develop the choice set was derived from a European study [11]. Although the same *a priori* distribution used in both studies made the results comparable, a more efficient design might be helpful to improve the precision of the estimated choice model parameters [40]. Fourth, this study involved a small sample of a population in China from one centre only and only one fifth of the study population were men. Consequently, the results might not be applicable to the entire Chinese population. Nevertheless, it is the first endeavour to elicit patient preferences for osteoporosis treatments in China. Future studies using a larger representative samples from China would be useful for comparison. Finally, one caveat must be raised for the interpretation of our study results. Although an understanding of patients' preferences for medications might be helpful, it might not automatically lead to the improvement of medication adherence.

Conclusion

This is the first study to elicit Chinese patients' preferences for osteoporosis medications and investigate patients' characteristics that contribute to the heterogeneity of these preferences. The study results are useful to clinicians with respect to informing their prescribing behaviours in osteoporosis medications, and the better understanding of patients' preferences

provided by this study is paramount for new drug development. The results could also be helpful to HTA bodies or health policy decision makers when they make reimbursement decision on osteoporosis medications.

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Table 1. Attributes and levels in the discrete choice experiment

Treatment efficacy in reducing the risk of fracture	20%
	30%
	40%
	50%
Out-of-pocket cost per year, RMB Yuan[a]	520
	2,600
	4,160
	5,200
	26,000
Adverse effects of treatment[b]	Flu-like symptoms
	Skin reactions
	Gastrointestinal disorders
Mode of administration	Daily oral tablet
	Daily nasal spray
	6-month subcutaneous injection
	Yearly intravenous infusion
	Weekly oral tablet

[a]1 RMB Yuan = 0.15 US dollars in 2018.

[b]Adverse effects of treatment were assumed to occur in 1 of every 50 patients undergoing treatment. Each of these adverse effects was relatively mild, disappeared after a few days, and had no long-term or severe consequences.

Table 2. Characteristics of participants

	N = 282
Number of women	228
Age, years	63.4 (10.2)
BMI, kg/m^2	22.6 (3.4)
Education	
No school education	31 (11.1%)
Primary school	65 (23.3%)
Junior high school	68 (24.4%)
Senior high school or equivalent	76 (27.2%)
University education or above	39 (14.0%)
Household income per annum, RMB Yuan	51,353 (52,874)
Per adult household income of <50,000 Yuan	151 (53.6%)
Per adult household income of ≥50,000 Yuan	131 (46.4%)
Number of patients with previous fracture	66
Number of patients with self-reported osteoporosis	119
Years since self-reported diagnosis	2.9 (3.0)
Bone mineral density, T-score	-2.1 (0.8)
Number of patients with osteoporosis defined by T-score	88
VAS score	68.5 (16.5)
Difficulty score[a]	5.7 (2.0)

Data are presented as mean (SD) or n (%).

BMI, body mass index; VAS, visual analogue scale.

[a]Difficulty was evaluated on a 0- to 10-point scale, where 0 indicated easiest and 10 indicated hardest.

Table 3. Patients' preferences for osteoporosis pharmaceutical treatments

	Mean of coefficient	95% CI	SD of coefficient	95% CI
ASC	9.57	7.51, 11.63	6.06	4.80, 7.33
Adverse effects				
Gastro-intestinal disorders	Reference group			
Flu like symptoms	0.24	0.06, 0.42	0.26	-0.01, 0.53
Skin reactions	0.38	0.19, 0.55	0.25	-0.11, 0.62
Mode of administration				
Daily oral tablet	Reference group			
Daily nasal spray	0.36	0.15, 0.57	0.51	0.18, 0.85
6-months subcutaneous injection	1.71	1.41, 1.99	1.16	0.87, 1.46
Yearly intravenous infusion	2.00	1.57, 2.42	1.99	1.54, 2.43
Weekly oral tablet	1.02	0.87, 1.23	0.02	-0.30, 0.33
Clinical efficacy [a]	0.23	0.17, 0.30	1.32	0.39, 2.25
OOP cost [b]	-1.03	-1.27, -0.79	3.96	2.33, 5.58

ASC, alternative specific constant; SD, standard deviation; CI, confidence interval; OOP, out-of-pocket

[a]Preference was measured based on a 1% increase in medication efficacy of fracture prevention.

[b]Preference was measured based on a 1,000-Yuan increase in OOP payment. 1 RMB Yuan = 0.15 US dollars in 2018.

Table 4. Patients' willingness to pay[a] for attributions in the discrete choice experiment

	Mean of coefficient	5th and 95th percentiles
Adverse effects		
Gastro-intestinal disorders	Reference group	
Flu like symptoms	3,712	875, 7,121
Skin reactions	5,650	2,714, 9,445
Mode of administration		
Daily oral tablet	Reference group	
Daily nasal spray	5,576	2,190, 10,133
6-months subcutaneous injection	26,395	17,005, 39,261
Yearly intravenous infusion	30,884	19,435, 46,808
Weekly oral tablet	15,837	10,067, 23,730
Clinical efficacy [b]	3,689	2,037, 6,532

[a]Willingness to pay is presented in 2018 RMB Yuan per annum. 1 RMB Yuan = 0.15 US dollars in 2018.

[b]Willingness to pay was measured based on a 1% increase in medication efficacy of fracture prevention.

Table 5. Differences in treatment preferences between patients aged ≤60 and >60 years

	Mean of coefficient (95% CI)	
	≤ 60 years	>60 years
ASC	14.33 (11.10, 17.56)	12.37 (9.41, 15.32)
Adverse effects		
Gastro-intestinal disorders	Reference group	
Flu like symptoms	0.32 (0.00, 0.64)	0.07 (-0.23, 0.37)
Skin reactions	0.55 (0.24, 0.86)	0.10 (-0.17, 0.38)
Mode of administration		
Daily oral tablet	Reference group	
Daily nasal spray	0.68 (0.32, 1.05)	0.11 (-0.17, 0.40)
6-month subcutaneous injection	2.30 (1.80, 2.81)	1.40 (0.98, 1.83)
Yearly intravenous infusion	2.78 (2.04, 3.51)	1.59 (1.06, 2.12)
Weekly oral tablet	1.08 (0.74, 1.42)	1.01 (0.75, 1.29)
Clinical efficacy [a]	0.15 (0.10, 0.19)	0.10 (0.06, 0.14)
OOP cost [b]	-1.12 (-1.33, -0.90)	-1.08 (-1.30, -0.86)

Level in bold indicates that the between-group difference is statistically significant.

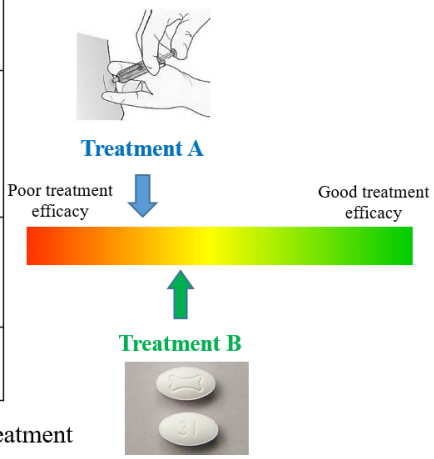
ASC, alternative specific constant; CI, confidence interval; OOP, out-of-pocket

[a]Preference was measured based on a 1% increase in medication efficacy of fracture prevention.

[b]Preference was measured based on a 1,000-Yuan increase in OOP payment. 1 RMB Yuan = 0.15 US dollars in 2018.

Figures

	Treatment A	Treatment B
Mode of administration	6-months subcutaneous injection	Weekly oral tablet
Side effects from treatment (1 in 50 patients would suffer the side effect)	Gastro-intestinal disorders	Flu like symptoms
Treatment efficacy in reducing the risk of fracture	30%	40%
Out-of-pocket cost per year	520 Yuan per annum	26,000 Yuan per annum



Which treatment would you choose? (Tick one box only) ☐ Treatment A ☐ Treatment B ☐ No treatment

Figure 1. A choice set in the discrete choice experiment. Patients were asked to choose between hypothetical Treatments A and B; they could also choose "No treatment" if they did not like any of the treatments. 1 RMB Yuan = 0.15 US dollars in 2018.