Economic Evaluation of Oral Alendronate Therapy for Osteoporosis in Chinese Postmenopausal Women: The Impact of Medication Compliance and Persistence

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June 3, 2020

Abstract

Aims: The purpose of the present research was to evaluate the cost-effectiveness of oral alendronate for individuals with osteoporosis. We also assessed the impact of medication compliance and persistence on economic outcomes of alendronate, and potential economic evaluations of persistence-enhancing interventions. Methods: We constructed an individual-level state-transition model to project health outcomes and costs of oral alendronate for Chinese postmenopausal osteoporotic women. The impact of medication compliance and persistence on economic evaluation was addressed in various scenario analyses. Model inputs were derived from clinical trials and published sources where available. Deterministic and probabilistic sensitivity analyses were conducted to explore the impact of uncertainties and assumptions on the cost-effectiveness results. Results: Compared to no treatment, alendronate treatment was associated with an additional 0.052 QALYs at an additional cost of USD 738, which yielded an ICER of USD 14,192.308/QALY. The ICER for the different scenarios (full compliance, full persistence, both full persistence and full compliance) were USD 4933.333/QALY, USD 3006.84/QALY and USD 2019.822/QALY, respectively. One-way sensitivity analysis showed the ICER was most sensitive to variations in time horizon and residual effect. Probabilistic sensitivity analysis demonstrated that, at a willingness-to-pay of USD 29,340/QALY, the probability that oral alendronate therapy will be cost-effective is approximate 80%. Conclusions: The findings support the view that oral alendronate is cost-effective for the treatment of osteoporotic fractures in Chinese postmenopausal women. Medication persistence is found to have a greater impact on cost-effectiveness than compliance, and interventions to improve persistence to be an efficient use of resources.

What is already known about this subject

Poor medication compliance and persistence are common problems of osteoporosis management and they affect both the clinical and cost-effectiveness of osteoporosis interventions. The potential loss of benefits resulting from poor compliance and persistence with oral alendronate in the China setting has not been well described.

What this study adds

- This study explored the cost-effectiveness of oral alendronate therapy for postmenopausal osteoporotic women from the perspective of Chinese health care payer.
- We incorporated medication persistence and compliance into our hybrid modeling and extensively examined how these changes in parameters have an impact on the pharmacoeconomic evaluation of oral alendronate treatment.

- Medication persistence is found to have a greater impact on cost-effectiveness than compliance, and we further assessed the potential economic value of persistence-enhancing interventions according to a given range of their costs and effectiveness values.

1 Introduction

Osteoporosis, or porous bone, is a disease characterized by low bone mass and structural deterioration of bone tissues, leading to bone fragility and an increased risk of fractures [1]. The International Osteoporosis Foundation (IOF) estimates that by 2050, more than 50% of all osteoporotic fractures will occur in Asia-and China will be most severely affected due to its large population of seniors[2]. Fractures significantly affect patients by impairing their ability to perform daily activities. Moreover, a health economics model was developed and forecasted that the costs of osteoporotic fractures in China will double by 2035, and rising to approximately USD 25.58 billion by 2050, indicating that in addition to morbidity and mortality, osteoporotic fractures are also associated with a significant health care expenditure to the society [3, 4].

Fortunately, medical advancements have increased the range of therapeutic options available for the prevention and treatment of fractures [5]. Currently, oral bisphosphonates are the most potent antiresorptive drugs for treatment of osteoporosis in postmenopausal women [6]. Multiple meta-analyses and systematic reviews have shown that bisphosphonates are effective in decreasing the risk of various types of bone fractures[7, 8]. However, it is widely acknowledged that compliance and persistence with oral osteoporosis medications is poor[9-11]. A recent observational study estimated that 53% of the study population achieved a medication possession ratio (MPR) of 80% or higher 6 months after initiating therapy, and the equivalent value for 7–12 months was only 43% [12]. Persistence, or the length of time a patient continues therapy, is similarly poor. It has been reported that the rate of persistence among new users was 46% after 7–12 months treatment period [12].

Although poor compliance and persistence decrease the cost of the intervention, the effectiveness of treatment is also reduced, which reduces bone mineral density, and in turn leads to higher risk of fractures [13, 14]. Hence, in order to estimate the cost-effectiveness of the intervention in real-world settings, it is important that economic evaluations take compliance and persistence into account.

The purpose of the present research was to evaluate the potential loss of benefits resulting from poor compliance and persistence with oral alendronate in osteoporotic individuals. More specifically, we first compared the clinical and economic outcomes derived from real-life setting with those expected with full compliance and persistence. In additional, we further evaluated the potential economic value of persistence-enhancing interventions.

2 Methods

2.1 Overview

The development of this model adhered to the recommendations for the conduct of economic evaluations in osteoporosis [15]. We used an updated version of previously validated individual-level state-transition model [16] to estimate the impact of the compliance and persistence on the cost effectiveness of alendronate treatment for Chinese postmenopausal osteoporotic women aged 65 and older. The model estimated the outcomes including number of fractures quality adjusted life-years (QALYs); direct societal costs in 2018 US dollars (USD); and incremental cost-effectiveness ratios (ICERs) per QALY gained. Costs and health outcomes beyond the first year were discounted at an annual of 3%, which is consistent with Chinese guidelines for pharmacoeconomic evaluations [17]. We assessed cost-effectiveness from the health care payer perspectives and considered three times of per capita gross domestic product of China in 2018 (USD 29,340) as the willingness-to-pay (WTP) threshold. We used TreeAge Pro 2018 (TreeAge Software Inc., Williamston, MA, USA) to perform our analyses.

2.2 Model structure

We modeled the disease progression of osteoporosis through six states: no fracture, hip fracture, clinical

vertebral fracture, wrist fracture, other osteoporotic fracture, and death. The other osteoporotic fracture state as defined by the IOF-EFPIA report [18]. The cycle length of the model was 1 year which chosen to represent a clinically meaningful time interval. Each individual can sustain only one fracture per cycle, and can experience up to two hip fractures but unlimited clinical vertebral, wrist and other osteoporotic fractures during the entire study period. We used tracker variables to record individual characteristics and disease histories, which adjusted transition probabilities, costs and utilities. **Table 1** shows the key parameters used in the health economics model. A more detailed description of the model can be found in our previously published work[16].

2.3 Fracture incidence and mortality rates

Hip and vertebral fracture incidences were derived from reported epidemiological data in China [19, 20]. Estimation of the incidence rates of the wrist and other osteoporotic fractures in the Chinese context was not available, hence we utilized data collected from an Asian population[21, 22]. The incidence of fracture in the general population was further adjusted to accurately reflect the fracture risks of women with osteoporosis. The method calculated the relative risks for bone mineral density using a method previously described [23-25].

Baseline mortality rates for age-stratified Chinese women were retrieved from the China Public Health Statistical Yearbook [26]and an increased mortality was assumed for individuals who experienced the hip fracture [27]. Because excess mortality may be attributable to comorbidities in this older population, only 25% of the excess mortality was considered to be attributable to the fractures themselves [28]. There was no increase in mortality following clinical vertebral, wrist and other fractures[29, 30].

2.4 Treatment

We assumed that treated women received alendronate 70 mg once weekly for five years. Relative risks for fractures in women taking alendronate were based on the recent systematic reviews [31, 32]. It was assumed that reductions in fracture risk during therapy were consistent regardless of patients' age and there was no significant change in bioequivalence between brand name and generic drugs. We also assigned the cost of one general consultation visit, bone mineral density and biochemical test per year, as suggested by the Chinese guidelines for the diagnosis and treatment of primary osteoporosis[33].

Inadequate medication compliance and persistence are known to be major problems in all patients with osteoporotic disease [34]. We considered compliance and persistence rates of alendronate obtained on the observational studies in the Chinese or Asian population[35, 36]. Compliance rates with oral alendronate were higher in clinical than observational studies. The influence of their difference was incorporated into the microsimulation model by assuming a linear relationship between the relative risk reduction and medication compliance [29, 30]. In addition, we modeled the residual effects of alendronate for those who discontinue therapy (called offset-time effect). We assumed that if individuals stopped treatment, they received no further therapy and offset-time was assumed to be equal to their treatment period [11].

2.5 Costs

The cost of alendronate was based on different brand prices and corresponding market share in China. Total medication costs were multiplied by their compliance and persistence level. We charged the cost of 6-month alendronate supply for individuals who discontinued alendronate within the first year. The estimated annual costs related to hip fracture of the first year and long-term care costs were obtained from previously published studies in Chinese setting[37, 38]. Costs of physician visits, DXA scan, laboratory tests and nursing home residence were collected from the health system or the National Development and Reform Commission of China[39]. All original costs were converted to a common currency and price year, 2018 United States dollars (USD), given the latest version of a web-based cost converter [40].

2.6 Utilities

The Chinese National Health Services Survey in China has established the utility values in osteoporosis [41].

No disutilities was assumed for simulated individuals without fractures. Fracture events were associated with decrements in utility values which differed between the fracture sites and time. The quality of life multipliers were based on a recent meta-analysis [42, 43].

2.7 Model simulation and sensitivity analysis

We performed base-case, deterministic (one-way) sensitivity, probabilistic sensitivity and scenario analyses. For baseline analysis, we ran the model with 100,000 iterations (100,000 individuals through the model one at a time). One-way sensitivity analysis was undertaken to examine the effect of each key model parameter, including fracture costs and disutilities, medication costs, initial age of treatment, time horizon, residual effect and discount rates. Probabilistic sensitivity analysis was conducted to evaluate the impact of the joint uncertainty surrounding the model variables using Monte-Carlo simulations (1000 simulations and 10,000 trials per simulation). We also examined different scenarios in which: (A) the individuals with full compliance, (B) the individuals with full persistence, (C) the individuals with both full persistence and full compliance, and (D) potential persistence-enhancing interventions.

3 Results

3.1 Model validation

The probability of dying by 105 years for untreated individuals at the ages of 65, 70, 75, 80 predicted by our model were 99.0%, 98.8%, 98.5% and 98.5%, respectively. Model-predicted mortality risks were comparable to the Chinese life table [26]. We also projected that without an intervention, the cumulative probability of having at least one hip fracture or clinical vertebral fracture equal to 11.099% and 39.693%, respectively, which is comparable to the epidemiological data in China [33].

3.2 Base-case findings

Table 2 presented the total health care costs, number of fractures, QALYs and ICER estimated by the model. Compared with no treatment (mean cost USD 9411; mean effect 12.623 QALYs), alendronate treatment in the real-world setting (mean cost USD 10,149; mean effect 12.675 QALYs) was associated with overall increase in total health care cost of USD 738 and in QALYs of 0.052, yielded in an ICER of USD 14,192.308/QALY gained. Besides, both NMB and NHB were positive, further indicated oral alendronate is more cost-effective than no intervention.

3.3 Sensitivity analyses findings

Deterministic sensitivity analysis showed that the most impactful parameters in the model were the time horizon and the residual effect. The ICER was markedly increased to USD 994,000/QALY when reducing the time horizon from lifetime to 5 years. Assuming no residual effect following treatment resulted in the ICER increased to USD 49,294.118/QALY (**Table 3**).

Probabilistic sensitivity analysis confirmed the aforementioned results (**Figure 1**). At a willingness-to-pay threshold of USD 29,340/QALY, the probability that alendronate would be cost-effective was approximate 80% for individuals age 65.

3.4 Scenario analyses findings

The results of the scenario analysis considering alendronate therapy compliance and persistence were shown in **Table 2** and**Figure 2** . The lifetime cost per person was USD 9707 for the full compliance scenario, USD 9850 for the full persistence scenario, and USD 9987 for both full persistence and full compliance scenario. Total cost was lower in the scenario analysis than in the real-world setting, as the prevented costs of treating additional osteoporotic fractures resulting from non-compliance and persistence exceed the cost of the additional therapy induced by the improved compliance and persistence.

Effectiveness was measured as the number of all osteoporotic fractures and quality-adjusted life-years. The lifetime number of all fractures per person was 1.438 for the full compliance scenario, 1.418 for the full persistence, and 1.350 for both full compliance and full persistence. Hence, the number of osteoporotic

fractures prevented in real-world setting represent 81.2%, 43.8%, and 17.1% to that estimated with full compliance, full persistence, and both full compliance and full persistence scenario, respectively. Mean lifetime QALYs were estimated at 12.683, 12.769, and 12.904 in all scenarios tested, respectively. The QALYs gained in the real-world scenario represents 86.7%, 35.6%, and 18.5% to that obtained under the above three scenarios, respectively.

Compared to no treatment, the ICER for the three scenarios ranged from USD 2019.822/QALY to USD 4933.333/QALY. These results were all lower than that derived from real-world analysis. It should be noted that three different scenarios were associated with lower costs and great QALYs than the real-world setting, indicated that the improvement of compliance and persistence was found to be cost-saving.

Figure 3 displayed the economic assessment of persistence-enhancing interventions based on differential reduction in treatment discontinuation and their corresponding cost. When the reductions in treatment discontinuation were high ($>$ 30%) and the invention costs were low ($<$ USD 100), the ICER was less than USD 9780/QALY (1$\times$ GDP per capita) and could be considered highly cost-effective. Conversely, when the invention costs were high ($>$ USD 400) and the reductions in treatment discontinuation were low ($<$ 10%), the ICER was more than USD 29340/QALY (3 $\times$ GDP per capita) and could be considered not cost-effective. For other potential combination of values within the given range, the ICER between USD 9780/QALY and USD 29,340/QALY, which regarded as acceptable cost-effectiveness limits.

4 Discussions

In this study, we used a modeling approach incorporating the medication compliance and persistence to examine the cost-effectiveness of oral alendronate treatment versus no intervention in the treatment of osteoporosis in Chinese postmenopausal women. Our base case analysis revealed that compared with no treatment, oral alendronate therapy 70 mg once weekly for five years was a high-value treatment at a willingness-to-pay threshold of USD 29,340/QALY.

The key variable in the current research was the medication persistence and compliance. Although oral alendronates have been demonstrated to be high value with current medication discipline, they are more cost-effective with full compliance and persistence. In addition, persistence was found to have a greater impact on cost-effectiveness than compliance. Full persistence in our model would yield an ICER of USD 3006.849/QALY, lower than the equivalent value for the full compliance (USD 4933.333/QALY). It should be noted that this heightened persistence rate of oral alendronate was emphasized by our assumption of a residual effect from treatment; the risk for fracture returned to rates in the absence of therapy over the same years as the treatment duration in a gradual linear fashion after completing the therapy. This is also examined by deterministic sensitivity analyses, in which we assumed no residual effect after the treatment, the ICER of oral alendronate was sharply increased to USD 9294.118/QALY. Hence, interventions to enhance persistence are necessary to decrease the considerable economic burden caused by the non-persistence with oral alendronate.

Our results confirmed prior work that it is important to include medication persistence and compliance in pharmacoeconomic analysis of osteoporosis treatment. The two studies of Hiligsmann and colleagues'[13, 14] which were focused on oral bisphosphonates suggested that poor adherence with osteoporosis medications results in approximately a 50% reduction in the potential benefits observed in clinical trials and a doubling of the cost per QALY gained from these medications. Programs to improve compliance were considered to be an efficient use of resources. In contrast, the study of Chen and colleagues' [37] in the China setting compared raloxifene treatment with conventional treatment (Alendronate, Calcitonin, Calcium combined with vitamin D) found opposite results. In this study, although high persistence and compliance increased both clinical effectiveness and average costs, the improvement on effectiveness was marginal in their research, thus resulting in higher ICER compared with the real-world scenario. The main reasons for such a difference could be attributed to the costs for fracture inpatients and the comparator.

In our previous study [16], in which we examined cost-effective of once-yearly injection of zoledronic acid compared with oral alendronate once weekly for postmenopausal osteoporotic women without prior history

of fracture in China, we concluded that zoledronic acid was cost-effective at all starting ages and even cost-saving in scenario analysis mainly based on zoledronic acid's higher persistence leading to higher efficacy. In this study, we came to a similar conclusion that the medication persistence plays a key role in shaping perceptions of fracture risk and osteoporosis drug effectiveness. In addition, we extend the prior work by design a meaningful framework for assessing the economic value of persistence-enhancing interventions. We assessed the potential combination of the intervention costs from USD 100–500 and the relative reduction in discontinuation from 10%–50%.

There are limitations associated with the current study. First, like all models, generalizability of the results to the target population of other races/ethnicities or in other countries may be uncertain due to the heterogeneity of payer perspectives and the country-specific epidemiologic data used. Moreover, although much of the data constructed the model were obtained from Chinese context, some data were also extrapolated from other countries. An updated pharmacoeconomic analysis should be explored when these data are available in Chinese setting. Second, compliance and persistence rates were derived from a retrospective study [35] in which whether patients actually took the dispensed drug is unknown. The study assumed that patients who obtain prescription refills do take their medications based on chart review. As a result, compliance may be overestimated. Third, our analysis did not examine the impact of restart therapy after discontinuation. We assumed those who did not take alendronate continued not to take medication in this model, which may not always mimic treatment in the real world because some patients might return to treatment after this period. Finally, we did not perform a budget impact analysis to assess the potential cost savings of this strategy. Due to the enormous amount of osteoporosis cases in China, the financial burdens for the health care system might be heavy.

Despite these limitations, our research has several key strengths. First, to the best of our knowledge, this is the first pharmacoeconomic analysis that compared oral alendronate to no treatment in a Chinese population. Second, we incorporated medication persistence and compliance, which are considered to be critical impede to osteoporosis management, into our hybrid modeling and extensively examined how these changes in parameters have an impact on model results. We further assessed the potential cost-effectiveness of persistence-enhancing interventions according to a given range of their costs and effectiveness values.

5 Conclusion

In conclusion, oral alendronate is considered to be a high-value therapy option for postmenopausal osteoporotic women from the perspective of Chinese health care payer, and further interventions to improve osteoporosis medication persistence will likely have favorable ICERs.

Acknowledgment

The authors acknowledge Takahiro Mori for the contribution to build the Markov model, which we updated and used in our analysis.

Conflict of interest statement

There are no competing interests to declare.

Funding information

This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

Contributors

ZJ Liu conceived and designed the research, RX You collected and analyzed the data. All authors wrote the manuscript.

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Table 1 Summary of key parameters in the model

Parameter	**Value**	**Range**
Alendronate therapy		
Relative risk of hip fracture	0.45	0.27–0.68
Relative risk of clinical vertebral fracture	0.50	0.33–0.79
Relative risk of wrist fracture	0.50	0.34–0.73
Relative risk of other fracture	0.78	0.66–0.92
Persistence rate	0.57 (year 1)	N/A
Compliance rate	0.71 (year 1)	N/A
Costs (2018 US dollars)		
Annual cost for Alendronate	761.64	533.15–990.13
Hip fracture, direct costs	7103.25	4972.28–9234.23
Clinical vertebral fracture, direct costs	1310.11	917.08–1703.14
Wrist fracture, direct costs	967.34	677.14–1257.54
Other fracture, direct costs	1692.41	1184.69–2200.13
Annual cost for the post-hip fracture	4438.08	3106.66–5769.50
DXA scan	85	59.5–110.5
Blood tests	72	50.4–93.6
Physician visit	10	7–13
Utilities		
Age 65-69	0.806	0.765–0.846
Age 70-74	0.747	0.709–0.784
Age 75-79	0.731	0.694–0.767
Age 80-84	0.699	0.664–0.733
Age 85+	0.676	0.642–0.709
Hip fracture, first year(multiplier)	0.776	0.720–0.844
Hip fracture, subsequent year(multiplier)	0.855	0.800–0.909
Clinical vertebral fracture, first year(multiplier)	0.724	0.667–0.779
Clinical vertebral fracture, subsequent year(multiplier)	0.868	0.827–0.922
Wrist fracture(multiplier)	0.940	0.910–0.960
Other fracture(multiplier)	0.910	0.880–0.940
Annual fracture incidence per 1000 persons (without intervention)		
Hip fracture, age 65-69	0.96	N/A
Hip fracture, age 70-74	2.33	N/A
Hip fracture, age 75-79	4.08	N/A
Hip fracture, age 80-84	6.44	N/A
Hip fracture, age 85+	6.59	N/A
Clinical vertebral fracture, age 65-69	5.64	N/A
Clinical vertebral fracture, age 70-74	8.74	N/A
Clinical vertebral fracture, age 75-79	12.05	N/A

Parameter	Value	Range
Clinical vertebral fracture, age 80-84	21.19	N/A
Clinical vertebral fracture, age 85+	26.89	N/A
Wrist fracture, age 65-69	12.95	N/A
Wrist fracture, age 70-74	13.17	N/A
Wrist fracture, age 75-79	13.87	N/A
Wrist fracture, age 80-84	15.01	N/A
Wrist fracture, age 85+	15.10	N/A
Other osteoporotic fracture, age 65-69	6.60	N/A
Other osteoporotic fracture, age 70-74	9.84	N/A
Other osteoporotic fracture, age 75-79	14.44	N/A
Other osteoporotic fracture, age 80-84	18.06	N/A
Other osteoporotic fracture, age 85+	26.06	N/A
Relative risks of fractures for individuals with osteoporosis		
Hip fracture, age 65-69	3.91	3.28–4.56
Hip fracture, age 70-74	3.13	2.80–3.47
Hip fracture, age 75-79	2.60	2.39–2.82
Hip fracture, age 80-84	2.04	1.91–2.17
Hip fracture, age 85+	1.92	1.78–2.05
Clinical vertebral fracture, age 65-69	2.59	1.19–4.27
Clinical vertebral fracture, age 70-79	2.15	1.15–3.15
Clinical vertebral fracture, age 80+	1.82	1.12–2.41
Wrist fracture, age 65-69	1.78	1.78–2.19
Wrist fracture, age 70-79	1.6	1.60–1.88
Wrist fracture, age 80+	1.45	1.45–1.64
Other osteoporotic fracture, age 65-69	2.19	1.78–2.59
Other osteoporotic fracture, age 70-79	1.88	1.60–2.15
Other osteoporotic fracture, age 80+	1.64	1.45–1.82
Annual mortality rate		
65-69	0.01031	N/A
70-74	0.02036	N/A
75-79	0.03784	N/A
80-84	0.06998	N/A
85+	0.13603	N/A
Excess mortality after a hip fracture		
Relative hazard for mortality within a year after a hip fracture	2.87	2.52–3.27
Relative hazard for mortality for second and beyond after a hip fracture	1.73	1.56–1.90
Proportion of excess mortality after a hip fracture directly attributable to a hip fracture	0.25	N/A
Discounts		
Costs	0.03	0–0.05
Effectiveness	0.03	0–0.05

Table 2 Results of base case and scenario analyses

	Different scenarios	Different scenarios	Different scenarios	Different
	NT	RW	FC	FP
Patient cost over lifetime (2018 USD)				
Treatment cost	0	890	1021	1943
Total disease cost	9411	9254	8670	7907
Acute fracture cost	3768	3712	3610	3427

	Different scenarios	**Different scenarios**	**Different scenarios**	**Different**
Long-term fracture cost	5643	5542	5060	4480
Total health care cost	9411	10149	9707	9850
Outcome over lifetime				
All fractures per patient	1.461	1.442	1.438	1.418
QALYs per patient	12.623	12.675	12.683	12.769
ICER				
NHB				
NMB				

Abbreviations: USD, United states Dollars; QALYs, quality-adjusted life years; ICER, incremental cost-effectiveness ratio; NHB, net health benefit; NMB, net monetary benefit; NT, no treatment; RW, real-world setting; FC, full compliance; FP, full persistence

Table 3 Results of one-way analyses

Parameter	**Cost (2018 USD)**	**Cost (2018 USD)**	C	**Effectiveness(QALYs)**	**Effectiveness(QALYs)**	E	**ICER(USD/ QALY gained)**
	No treatment	Alendronate		No treat	Alendronate		
Starting age of treatment : 80	4816	5283	467	5.351	5.400	0.049	9530.612
Starting age of treatment : 75	6483	7003	520	7.321	7.368	0.047	11063.830
Starting age of treatment : 70	8076	8651	575	9.631	9.675	0.044	13068.182
5-year time horizon	604	1598	994	3.860	3.870	0.010	99400.000
No residual effect	9422	10260	838	12.649	12.666	0.017	49294.118
Discount rate: 0	10557	11421	864	13.867	13.941	0.074	11675.676
Discount rate: 0.05	8407	9032	625	11.661	11.692	0.031	20161.290
Fracture costs 30% higher	12319	12808	489	12.654	12.681	0.027	18111.111
Fracture costs 30% lower	6605	7329	724	12.647	12.686	0.039	18564.103

Parameter	Cost (2018 USD)	Cost (2018 USD)	C	Effectiveness(QALYs)	Effectiveness(QALYs)	E	ICER(USD/ QALY gained)
Fracture disutilities 30% higher	9461	10098	637	12.888	12.925	0.037	17216.216
Fracture disutilities 30% lower	9542	10176	634	12.438	12.474	0.036	17611.111
Alen costs 30% higher	9418	10204	786	12.634	12.678	0.044	17863.636
Alen costs 30% lower	9457	9925	468	12.641	12.679	0.038	12315.789
Excess mortality 50% higher	11647	12273	626	12.917	12.945	0.028	22357.143
Excess mortality 0%	8819	9483	664	12.571	12.604	0.033	20121.212

Figure legends

Fig.1. Results of probabilistic sensitivity analyses. The cost-effectiveness acceptability curves represent probabilities of being cost-effective achieved by the alendronate strategy compared to no treatment at willingness-to-pay thresholds for postmenopausal osteoporotic women.

Fig.2. Impact of medication compliance and persistence on therapy, disease, and total costs and on health outcomes (expressed as number of fractures prevented and QALY gained). QALY, quality-adjusted life-year.

Fig.3. Economic value of persistence-enhancing interventions according to a given range of their costs and effectiveness values. Each block represents a possible intervention characterized by its cost and effectiveness. The color coding denotes the cost-effectiveness of the intervention.