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Evidence to Inform Decision Makers in Thailand: A Cost-Effectiveness Analysis of Screening and Treatment Strategies for Postmenopausal Osteoporosis

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A B S T R A C T

Objectives: To assess value for money of providing systematic screening for osteoporosis among postmenopausal women and medical treatments for those diagnosed with osteoporosis as evidence-based decision making for the revision of the National List of Essential Medicines. **Methods:** Decision analytic models were constructed, using a societal perspective, to assess the cost per quality-adjusted life-years (QALYs) gained from systematic screening using the Osteoporosis Self-Assessment Tool and dual-energy X-ray absorptiometry or dual-energy X-ray absorptiometry alone compared with no screening. Alendronate, risedronate, raloxifene, and nasal calcitonin were economically evaluated to determine a treatment of choice for the prevention of osteoporosis-related fractures. Most input parameters were obtained from literature reviews, and systematic reviews and meta-analyses, if available. The service costs and related household expenses were based on the Thai setting. Probabilistic and one-way sensitivity analyses were used to incorporate the impact of parameter uncertainty. **Results:** The Osteoporosis Self-Assessment Tool and sequential dual-energy X-ray absorptiometry provided better value for money for osteoporosis screening among young age groups (<60 years old). Although there was no significant difference in cost per QALY for older age groups, alendronate provided the lowest incremental cost-effectiveness ratio while nasal calcitonin presented the highest incremental cost-effectiveness ratio. It was shown that providing medication for a secondary prevention yielded a much higher cost per QALY gained compared with providing medication for a primary prevention. **Conclusions:** Given the benchmark set at 100,000 Thai baht per QALY gained, providing systematic screening and treatment for osteoporosis was cost-ineffective in the Thai setting.

Keywords: cost-utility analysis, decision analysis model, postmenopausal osteoporosis, screening, treatment.

Background

Osteoporosis is one of the most significant factors contributing to fractures in postmenopausal women worldwide. It is caused by an imbalance between bone formation and bone resorption, often defined by a reduction in bone mineral density (BMD). BMD reaches its maximum at the age of 20 to 30 years, and then declines over time [1,2]. It has been estimated that one-fifth of women aged between 40 and 80 years in Thailand live with osteoporosis, resulting in approximately 126,000 hip fractures annually [3,4]. The mortality rate among those with major fractures is high. This, in turn, leads to a significant economic burden on society as well as a reduction in quality of life for those individuals who survive [1,5–7].

At present, dual-energy X-ray absorptiometry (DXA) is a gold standard for measuring BMD and is used for the diagnosis and monitoring of osteoporosis [8]. DXA, however, is relatively expensive, and there is also a lack of information concerning whom to examine, the potential risks and benefits of undertaking the test, and ultimately, whether it is worth offering this service under the public health insurance scheme. As a result, DXA has rarely been used by Thai women. The Osteoporosis Self-Assessment Tool (OST), a risk assessment instrument, was first developed and validated in Asian postmenopausal women [9]. It is a simple tool that requires only age and weight parameters; however, it is not appropriate to be used as a stand-alone method for the diagnosis of osteoporosis because it has a high sensitivity but low specificity. A previous study conducted in Thailand showed that screening with OST and sequential DXA for those identified at high risk for osteoporosis from OST is the most cost-effective option compared with other screening modalities [10]. Therefore, OST in conjunction with DXA is considered to have the potential to be used for osteoporosis screening at the national level.

Various medications are currently available in the market to reduce the risk of fractures among osteoporosis patients. In Thailand, alendronate has been reported to be the most prescribed drug (39%), followed by raloxifene (26%), nasal calci-

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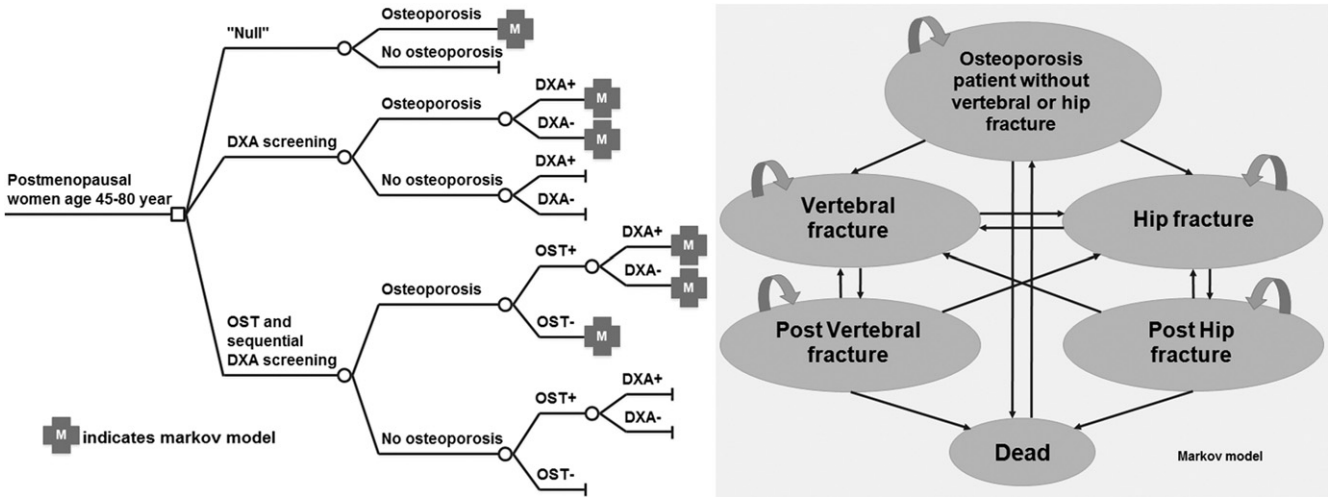

Fig. 1 – Decision tree illustrating two systematic screening compare to 'Null' scenario, followed by Markov model representing a disease partway once postmenopausal women are diagnosed with osteoporosis.

tonin (13%), and risedronate (2%) [11]. At present, there have been no economic evaluation studies conducted in developing settings. These drugs are not included in the National List of Essential Medicines (NLEM) in Thailand; thus, a majority of Thai patients need to pay for the cost of their prescription themselves. This has resulted in only a minority of osteoporosis patients currently receiving treatment.

This present study was conducted as a result of a request from the Subcommittee for Development of the NLEM to provide information on the long-term effectiveness and cost-effectiveness of the screening of osteoporosis and its medical management. This information was then used to inform the Subcommittee regarding the selection of osteoporosis drugs for public reimbursement nationwide [12]. It is expected that the findings from this study will be useful to decision makers in other developing countries, where health resources and infrastructure are constraints and the screening and treatment of osteoporosis are underutilized.

Methods

Analyses and model

The hybrid model consisting of a decision tree and a Markov model (Fig. 1) was constructed to compare the short- and long-term costs and outcomes of systematic screening for osteoporosis among postmenopausal women and offering medical management to those diagnosed with osteoporosis. Quality-adjusted life-years (QALYs) were used as an outcome measure in the analysis because they contain both longevity and quality of life, allowing comparisons across different diseases and treatment modalities. The study was conducted in regard to the Thai context by using the societal viewpoint, with a hypothetical cohort of postmenopausal women aged between 45 and 80 years. The lifetime time horizon was used as the base case, with both costs and outcomes discounted at 3%, as recommended by the guideline of economic evaluation in Thailand [13]. All analyses were performed in Microsoft Excel® 2003 (Microsoft).

To identify the number of people who are diagnosed with osteoporosis, a decision tree was then developed by comparing the costs and consequences of three screening strategies, namely, 1) "null" scenario, 2) a systematic screening using DXA, and 3) a systematic screening using OST and sequential DXA. For the null scenario, no screening and no treatment was offered besides calcium and vitamin D supplements. Only those who were confirmed with DXA to have low BMD received medical management. The Markov model was, then, used to compare the long-term cost and outcome of treating osteoporosis based on the nature of the disease's progression (presented as "M" signs at the end of the decision tree). All hypothetic cohorts of those who had been diagnosed with osteoporosis received either calcium and vitamin D supplements, null, or four choices of treatment: alendronate, risedronate, raloxifine, or nasal calcitonin for both the primary prevention—prevention of fragility fractures in women with osteoporosis—and the secondary prevention—prevention of new fractures in women with osteoporosis and a previous history of fragility fractures. All the four drugs are widely available and commonly used under the Thai health-care setting for averting osteoporosis-related fractures [11]. The comparators were also approved as appropriate alternatives for the treatment of osteoporosis in Thailand by Thai experts (a senior orthopedist, endocrinologists, and a gynecologist) (see details in the "Acknowledgment" section). Consequences only from hip and vertebral fractures were considered in the Markov model because a number of studies had indicated a nonsignificant difference in mortality and morbidity among patients with wrist fractures and among the general population [5–7]. This model was then validated by the same group of experts. The model worksheet is freely available online at www.hitap.net/projects_detail_en.php?p_id=90.

Model inputs

Key parameters used in the decision models are summarized in Table 1. Because the aim of this analysis was to inform decision makers in Thailand, we identified the parameters from sources that were most relevant to the Thai context [3,11,16,19], and if not applicable, international publications [7,14,15,17,18,20] were retrieved. The effectiveness, in terms of relative risk reduction of vertebral and hip fractures, of each drug was derived from literature searches and meta-analysis by using a Bayesian mixed treatment comparison. The justification of each parameter and details of systematic review and meta-analysis are available in the Supplemental Materials found at doi:10.1016/j.jval.2011.11.015. For intercountry comparisons, costs can be converted into US dollars by using the purchase power parity exchange rate of US$1 = 12.615 THB (Thai baht) [21]. All costs were adjusted to 2007 values by using the general consumer price index [22].

Table 1 – Model parameters, value, parameter distribution, and data sources used in the Markov model and the decision tree model.

Parameters	Mean (SE)	Parameter distribution	Data source
1. Epidemiological data			
Prevalence of osteoporosis			
In women aged between 40 and 44 y	0.0040 (0.0040)	Gamma	[3]
In women aged between 45 and 49 y	0.0160 (0.0160)	Gamma	[3]
In women aged between 50 and 54 y	0.0490 (0.0490)	Gamma	[3]
In women aged between 55 and 59 y	0.1030 (0.1030)	Gamma	[3]
In women aged between 60 and 64 y	0.2010 (0.2010)	Gamma	[3]
In women aged between 65 and 69	0.3260 (0.3260)	Gamma	[3]
In women aged between 70 and 74 y	0.4960 (0.4960)	Gamma	[3]
In women aged 75 years and above	0.5920 (0.5920)	Gamma	[3]
Transitional probability of the following vertebral and hip fractures			
Osteoporosis patient with previous vertebral fracture developing the second vertebral fracture in the following year	0.0290 (0.0057)	Beta	[14]
Osteoporosis patient with previous hip fracture developing the second hip fracture in the following year	0.0136 (0.0051)	Beta	[14]
Osteoporosis patient with current vertebral fracture developing hip fracture in the following year	0.0124 (0.0037)	Beta	[14]
Osteoporosis patient with current hip fracture developing vertebral fracture in the following year	0.0362 (0.0081)	Beta	[14]
Osteoporosis patient with previous vertebral fracture developing hip fracture in the following year	0.0068 (0.0028)	Beta	[14]
Osteoporosis patient with previous hip fracture developing vertebral fracture in the following year	0.0178 (0.0059)	Beta	[14]
Osteoporosis patient with current vertebral fracture developing second vertebral fracture in the following year	0.0293 (0.0057)	Beta	[14]
Osteoporosis patient with current hip fracture developing second hip fracture in the following year	0.0190 (0.0060)	Beta	[14]
2. Accuracy of screenings and effectiveness of treatments			
Accuracy of screenings			
Sensitivity of OST to detect osteoporosis	0.9100 (0.0740)	Gamma	[15]
Specificity of OST to detect osteoporosis	0.5700 (0.1122)	Gamma	[15]
Effectiveness of treatments			
Alendronate RR reduction in vertebral fracture	0.5660 (0.0906)	Gamma	Meta-analysis
Alendronate RR reduction in second vertebral fracture	0.5024 (0.0716)	Gamma	
Alendronate RR reduction in hip fracture	0.5824 (0.1286)	Gamma	
Risedronate RR reduction in vertebral fracture	0.6473 (0.2630)	Gamma	
Risedronate RR reduction in second vertebral fracture	0.5450 (0.0642)	Gamma	
Risedronate RR reduction in hip fracture	0.6533 (0.1097)	Gamma	
Raloxifene RR reduction in vertebral fracture	0.5009 (0.0799)	Gamma	
Raloxifene RR reduction in second vertebral fracture	0.5870 (0.0666)	Gamma	
Raloxifene RR reduction in hip fracture	1.0063 (0.2368)	Gamma	
Nasal calcitonin RR reduction in vertebral fracture	0.6079 (0.2169)	Gamma	
Nasal calcitonin RR reduction in second vertebral fracture	0.7358 (0.1230)	Gamma	
Nasal calcitonin RR reduction in hip fracture	0.4648 (0.2373)	Gamma	
3. Costs and the resource used			
Annual cost of alendronate 10 mg	16,255.56		*
Annual cost of risedronate 5 mg	14,707.68		*
Annual cost of raloxifene 60 mg	19,221.00		[16]
Annual cost of nasal calcitonin 200 IU	60,000.00		*
Cost per visit to outpatient department for osteoporosis patient (exclude drugs)	497.88 (26.76)	Gamma	[11]
Average number of outpatient visits per year for osteoporosis patient	4.26 (0.50)	Gamma	[11]
Cost per visit to outpatient department for osteoporosis patient with vertebral fracture (exclude drugs)	1921.34 (688.72)	Gamma	[11]
Average number of outpatient visits per year for osteoporosis patient with vertebral fracture	10.41 (1.47)	Gamma	[11]
Cost per visit to inpatient department for osteoporosis patient with vertebral fracture (excluding drugs)	56,588.56 (20,007.08)	Gamma	[11]
Average number of inpatient visits per year for osteoporosis patient with vertebral fracture	1.00 (0.50)	Gamma	[11]

(*continued on next page*)

Table 1 (*continued*)

Parameters	Mean (SE)	Parameter distribution	Data source
Cost per visit to outpatient department for osteoporosis patient with hip fracture (exclude drugs)	354.5 (47.99)	Gamma	[11]
Average number of outpatient visits per year for osteoporosis patient with hip fracture	7.14 (0.66)	Gamma	[11]
Cost per visit to inpatient department for osteoporosis patient with hip fracture (exclude drugs)	77,537.04 (11,191.51)	Gamma	[11]
Average number of inpatient visits per year for osteoporosis patient with hip fracture	1.00 (0.27)	Gamma	[11]
Cost per visit to outpatient department for osteoporosis patient following vertebral fracture (exclude drugs)	497.88 (26.76)	Gamma	[11]
Average number of outpatient visits per year for osteoporosis patient with previous vertebral fracture	4.89 (0.82)	Gamma	[11]
Cost per visit to outpatient department for osteoporosis patient following hip fracture (exclude drugs)	497.88 (26.76)	Gamma	[11]
Average number of outpatient visits per year for osteoporosis patient with previous hip fracture	4.89 (0.82)	Gamma	[11]
Nonmedical direct cost of osteoporosis patient	7,635.56 (3,453.85)	Gamma	Survey
Nonmedical direct cost of osteoporosis patient with fracture	38,250.33 (15,375.99)	Gamma	Survey
Cost of OST screening	497.88 (26.76)	Gamma	[11]
Cost of DXA screening	786.85 (182.22)	Gamma	[11]
Traveling cost per visit	525.56 (191.15)	Gamma	Survey
Food cost per visit	78.89 (19.40)	Gamma	Survey
4. Utility estimates			
Utility of osteoporosis patients	0.9100 (0.0153)	Beta	[17]
Utility of vertebral fracture patients	0.7200 (0.0293)	Beta	[18]
Utility of post–vertebral fracture patients	0.9310 (0.0077)	Beta	[18]
Utility of hip fracture patients	0.7970 (0.0140)	Beta	[18]
Utility of post–hip fracture patients	0.8990 (0.0064)	Beta	[18]

DXA, dual-energy X-ray absorptiometry; IU, international units; OST, Osteoporosis Self-Assessment Tool; RR, relative risk; SE, standard error.
* The quoted price submitted by pharmaceutical companies to the Subcommittee for Development of the National List of Essential Medicines (October 2007).

Sensitivity analyses

Two types of sensitivity analysis concerning both parameter uncertainty and assumptions used in the model were examined. For the first source of uncertainty, a probabilistic sensitivity analysis was carried out by using 1000 times the second-order Monte Carlo simulation that incorporates the statistical uncertainty, that is, probability distributions for the input variables, into the model (see Table 1 for the distribution used). The rationale for the selection of distributional assumption for each variable has been illustrated in detail elsewhere [23]. Cost-effectiveness acceptability curves were provided to show the relationship between the values of the ceiling ratio (willingness to pay for a QALY gained [WTP/QALY]) and the probability of favoring each treatment strategy. To quantify the ceiling ratio for the Thai population, we applied the threshold that was recommended by the Subcommittee for Development of the NLEM, in which results from this study were fed to the Subcommittee to decide whether or not to include these drugs in the NLEM. This threshold was set at 100,000 THB [24] where the current gross domestic product (GDP) per capita in the year 2005 was 120,036 THB [25].

For the second source of uncertainty, methodological uncertainty [26], the impact of different assumptions used in the model, which are drug compliance and treatment duration, was examined. It was recognized that the treatment of osteoporosis was associated with low drug compliance, especially among those with longer treatment times [27]. Because our reference case assumes 100% compliance with therapy, it is worthwhile to examine the effect of different drug compliance by using information from existing published literature [27]. The probabilities of patients continuing to use bisphosphonates, raloxifene, or calcitonin in the first 3 years following the initial treatment are given in Table 2. No further discontinuation of the drugs after the third year of treatment was assumed.

In addition, empirical evidence showed that after continuous bisphosphonate treatment for some periods of time, for example, 5 years, the protective effect in terms of the prevention of osteoporotic fractures is still sustained for up to 5 years after discontinuation of the drugs [28–30]. We assumed in our model that this assumption holds for both alendronate and risedronate but not for other groups of osteoporotic drugs. Currently, there are no published results of the effect of discontinuation beyond 10 years, and so our sensitivity analysis applied a 10-year time horizon from the time of initial treatment.

Table 2 – Probabilities of patients continue using bisphosphonates, raloxifene, or nasal calcitonin in the following years for the first 3 years.

Year in which drugs are taken	Probabilities of discontinuation		
	Bisphosphonates	Raloxifene	Nasal calcitonin
Year 1	0.3500 (0.0321)	0.5800 (0.0201)	0.5000 (0.0195)
Year 2	0.2200 (0.0598)	0.4100 (0.0353)	0.3200 (0.0411)
Year 3	0.1400 (0.1157)	0.3200 (0.0566)	0.1900 (0.0951)

Values indicate mean and standard error.

Table 3 – Lifetime costs of providing different medical managements to postmenopausal osteoporosis patients by age group.

Age (y)	Null scenario	Alendronate		Risedronate		Raloxifene		Nasal calcitonin	
		Primary prevention	Secondary prevention	Primary prevention	Secondary prevention	Primary prevention	Secondary prevention	Primary prevention	Secondary prevention
45	234,066	550,571	248,634	519,782	247,263	611,129	251,836	1,437,414	290,558
50	220,097	508,469	234,437	480,273	233,076	563,602	237,594	1,317,788	275,747
55	200,590	458,379	214,633	433,022	213,298	507,954	217,701	1,186,401	254,920
60	181,365	410,201	193,858	387,566	192,676	453,886	196,595	1,056,769	229,778
65	159,325	356,732	170,546	337,151	169,480	394,702	173,003	917,941	202,799
70	140,387	307,298	150,558	290,798	149,593	339,958	152,767	785,369	179,783
75	120,888	259,651	130,468	246,344	129,558	288,271	132,565	662,275	158,205
80	104,115	219,738	112,212	208,924	111,442	244,479	113,974	557,321	135,574

Note: Costs are given in 2007 Thai baht.

Table 4 – Quality-adjusted life-years of providing different medical managements to postmenopausal osteoporosis patients by age group.

Age (y)	Null scenario	Alendronate		Risedronate		Raloxifene		Nasal calcitonin	
		Primary prevention	Secondary prevention	Primary prevention	Secondary prevention	Primary prevention	Secondary prevention	Primary prevention	Secondary prevention
45	17.869	18.413	17.878	18.300	17.877	18.231	17.875	18.452	17.875
50	16.219	16.800	16.227	16.703	16.226	16.598	16.224	16.831	16.224
55	14.473	15.080	14.481	14.991	14.480	14.873	14.478	15.136	14.478
60	12.784	13.372	12.792	13.267	12.791	13.154	12.789	13.425	12.789
65	11.042	11.599	11.049	11.500	11.048	11.392	11.047	11.662	11.047
70	9.392	9.869	9.398	9.786	9.398	9.658	9.396	9.932	9.397
75	7.984	8.332	7.990	8.264	7.989	8.163	7.988	8.367	7.989
80	6.730	6.975	6.734	6.930	6.734	6.849	6.732	7.015	6.733

Results

Treatment options for the prevention of osteoporotic fractures

Tables 3 and 4 shows lifetime costs and QALYs, respectively, of providing each treatment to osteoporosis patients by age group compared with a null scenario using the societal perspective. The lifetime cost of treatments and QALYs for the prevention of osteoporotic fractures varies depending on the patient's age at the start of treatment and whether the patient had previous fractures and drug regimens. It is obvious that treating patients at younger ages, especially primary prevention, reflects a higher lifetime cost than treating patients at older ages because our base-case analysis applied lifetime treatment costs. The total lifetime costs of disease management increased with the addition of osteoporosis drugs. Comparing between different treatments of osteoporosis, risedronate had the lowest cost followed by alendronate, raloxifene, and nasal calcitonin. Nasal calcitonin, however, yielded the highest QALYs gained in the primary prevention of osteoporosis, followed by alendronate, risedronate, and raloxifene. It is noteworthy that providing secondary prevention added very little QALYs gained compared with the null scenario.

Compared with the null scenario, alendronate provided the lowest incremental cost-effectiveness ratio (ICER) for both primary and secondary prevention followed by risedronate, raloxifene, and nasal calcitonin. When providing treatment for patients

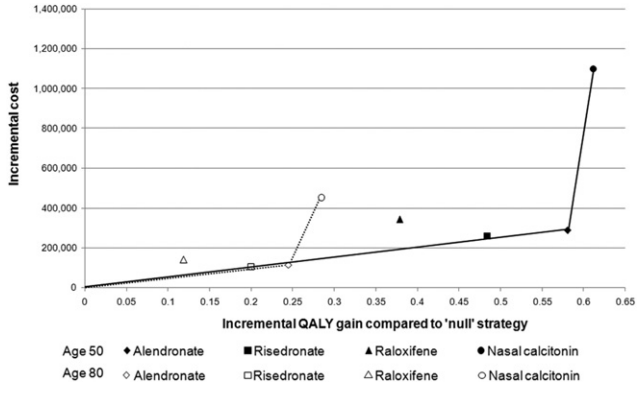

Fig. 2 – Incremental cost-effectiveness plane illustrating two selected age group, 50 years and 80 years.

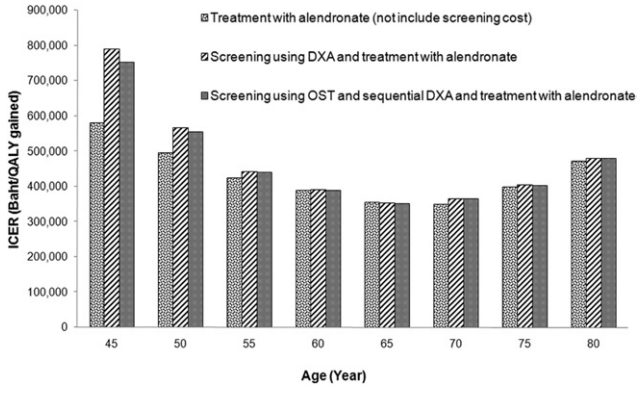

Fig. 3 – Incremental cost-effectiveness ratios of providing different universal screening strategies at various age groups.

without prior fractures, primary prevention was more cost-effective than secondary prevention. Primary and secondary prevention of osteoporotic fractures for older women (up to 75 years old) was found to be more cost-effective. Figure 2 demonstrates the results of the base-case ICERs for the primary prevention of osteoporotic fractures compared with the null scenario in patients aged 50 and 80 years. Providing primary prevention with alendronate yielded 496,286 THB per QALY for patients aged 50 years and 471,811 THB per QALY for patients aged 80 years. Alendronate offered 1,753,378 THB per QALY for a patient aged 50 years and 1,702,343 THB per QALY for a patient aged 80 years in the secondary prevention.

Adding screening to diagnose osteoporosis

Because offering alendronate for the primary prevention of osteoporotic fractures gave the best value for money, it was used to estimate the ICERs of adding systematic screening (Fig. 3). OST and sequential DXA was a favorable option for universal screening among the younger age groups (45–55 years). There was, however, only a slight difference in ICERs between OST and sequential DXA, and DXA alone among older age groups (60–80 years). The ICER of screening with OST and sequential DXA was lowest at 351,459 THB (for patients 65 years old) and highest at 753,229 THB (for patients 45 years old).

Sensitivity analysis

Figure 4 presents cost-effectiveness acceptability curves and summarizes the robustness of the model regarding uncertainty about the costs and effects of each treatment strategy in both primary (Fig. 4A) and secondary prevention (Fig. 4B). The findings present the different results of the model for patients aged 50 and 80 years. If decision makers are willing to pay less than 100,000 THB per QALY, the null scenario is the best policy option for both primary and secondary prevention of osteoporotic fractures in osteoporo-

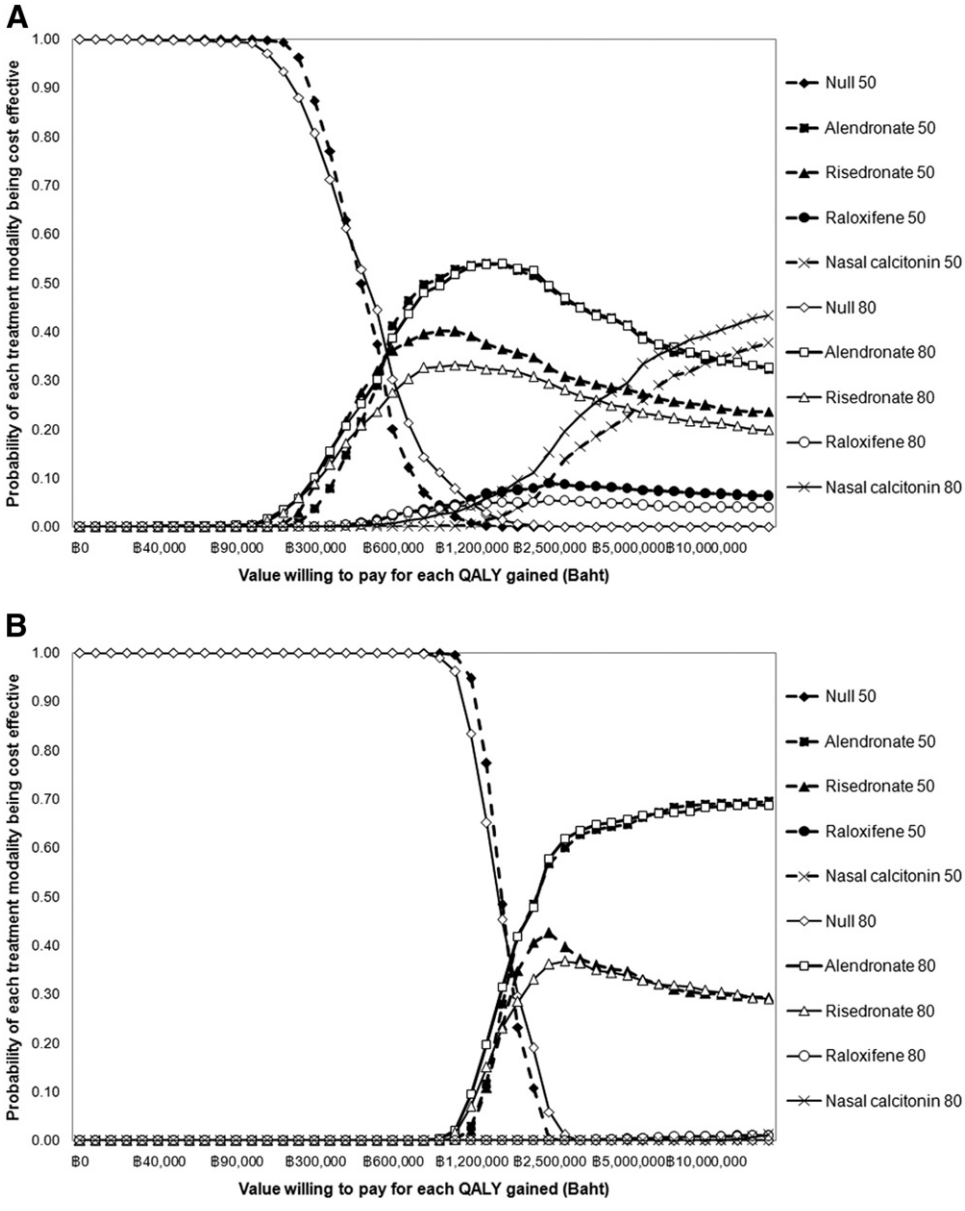

Fig. 4 – Cost-effectiveness acceptability curves of treatment options (A) in patients who start the treatments for primary prevention of osteoporotic fractures at the ages of 50 and 80 (B) in patients who start the treatments for secondary prevention of osteoporotic fractures at the ages of 50 and 80.

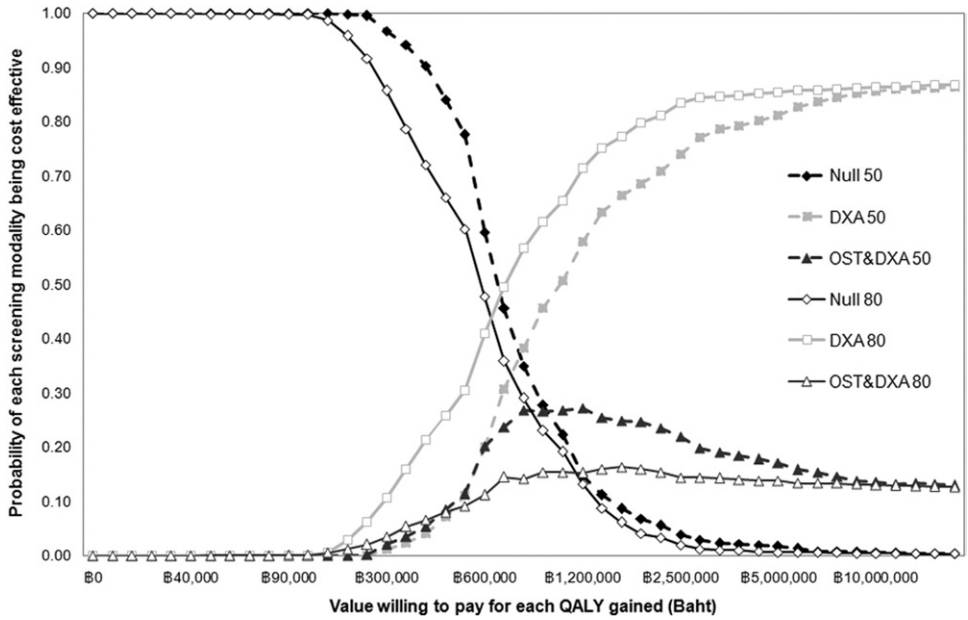

Fig. 5 – Cost-effectiveness acceptability curves of screening modalities for osteoporosis in postmenopausal women ages 50 and 80. If positive results confirm with DXA, alendronate will be given to osteoporosis patients for primary prevention of osteoporotic fractures.

sis patients aged 50 and 80 years; however, if decision makers are willing to pay beyond this threshold, that is, 600,000 THB per QALY for primary prevention and 1,700,000 THB per QALY for secondary prevention, treatment with alendronate and risedronate becomes the better option. In addition, the patient's age did not strongly affect the results shown in the cost-effectiveness acceptability curves.

In comparison to the null scenario, offering systematic screening by using DXA among postmenopausal women and treatment with alendronate, if appropriate, become a better choice when the WTP threshold reaches 650,000 THB per QALY and 750,000 THB per QALY at the age of 80 and 50 years, respectively (see Fig. 5).

Results of the sensitivity analysis concerning methodological uncertainties, that is, drug compliance and discontinuation of bisphosphonates, are depicted in Figures 6 and 7 for the primary and secondary prevention of osteoporotic fractures, respectively. Adjusting for only drug compliance provides little difference in terms of ICERs across the medications for the prevention of osteoporotic fractures compared with the base cases (approximately 0.6–0.9 times). This is because the cost of treatment will be deducted if the medication is stopped, which will limit the benefit of the drugs, thereby causing minimal impact on the ICER. In the primary prevention of osteoporotic fractures, the discontinuation of alendronate and risedronate after 5 years of continuous treatment generates 49% higher ICERs compared with the base case because this scenario is concerned with only 10-year treatment effect whereby the increased chance of fractures was observed in the older age groups. On the other hand, the discontinuation of bisphosphonates in the secondary prevention halves their ICERs compared with the base case because it significantly reduces the cost of treatment while the forgone benefit of preventing fracture is minimized.

Discussion

This article aims to assess the value for money of providing comprehensive care, that is, screening and medical management, for

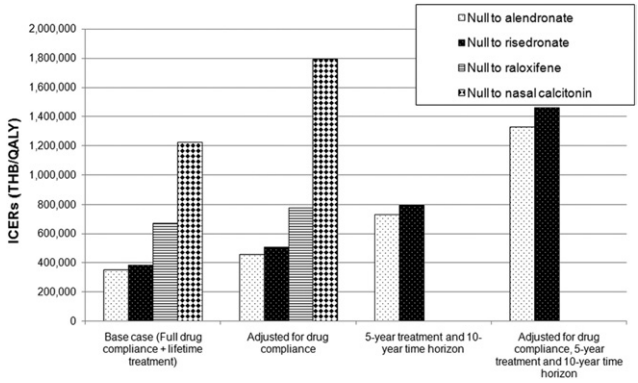

Fig. 6 – One-way sensitivity analysis of adjusting drug compliance of all drugs and discontinuation of bisphosphonate (Primary prevention of osteoporotic fractures).

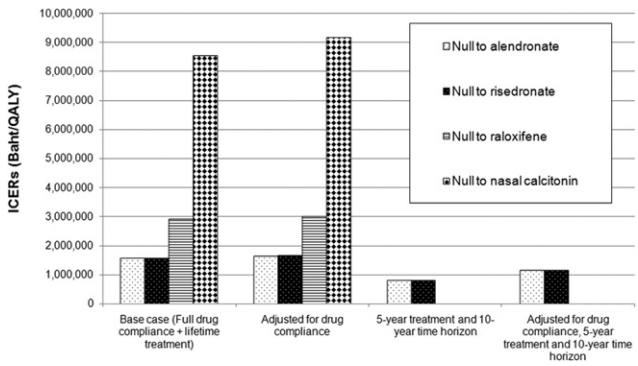

Fig. 7 – One-way sensitivity analysis of adjusting drug compliance of all drugs and discontinuation of bisphosphonate (Secondary prevention of osteoporotic fractures).

postmenopausal osteoporosis patients. It indicates that most of the drugs offered additional QALYs compared with the null scenario for both the primary and secondary prevention of osteoporotic fractures among postmenopausal women. When comparing the costs and outcomes of each drug, alendronate seemed to be superior to other alternatives, followed by risedronate, raloxifene, and nasal calcitonin. Providing treatment for the primary prevention of osteoporotic fractures was found to be favorable to the secondary prevention for all drugs because it offsets the cost of treatment of the first fracture and also averts QALYs that would have been lost from the worsening health states. In addition, the ICERs were highest among very young and very old age groups and lowest at the age of 70 years. This can be explained by the fact that osteoporosis treatment is lifelong, and so providing treatment for younger age groups than for older age groups is more expensive. The lower fracture incidence rate, however, was observed among patients with very old age groups (75 years or above). Results from one-way sensitivity analyses indicated that adjusting for the drug compliance of all drugs and discontinuation of bisphosphonates did not change the conclusions in which the treatment is cost-ineffective according to the Thai threshold.

Because the cost of the systematic screenings was minor (0.54% for DXA, 0.31% for DXA sequential OST) compared with the lifetime treatment cost for osteoporosis patients, adding either of the systematic screenings into the economic model did not affect the overall ICERs compared with the treatment alone. It seems that using OST in conjunction with sequential DXA is superior to the use of DXA alone, especially for the younger age groups. Because of the lower prevalence of osteoporosis in younger women, providing a more expensive and more accurate screening—DXA—yielded higher ICERs.

Results from this study clearly demonstrated that the screening and treatment of osteoporosis were not cost-effective and that the drugs should not be included in the NLEM. The threshold set was used in the NLEM 2008 revision. In the near future, this threshold might be changed according to the nation's economic situation and the availability of information from a research project that aims to identify the societal WTP per QALY under the Thai setting [31].

To our knowledge, this was the first study that comprehensively assessed the cost-effectiveness of screening and treatment options for osteoporosis in postmenopausal women in a developing country. All previous economic evaluation studies were conducted in Europe and North America where the cost of treatment of fractures and the WTP per QALY are significantly higher than in Thailand. However, this study is still comparable to those studies. For example, a study conducted in Sweden revealed that providing treatment with alendronate for osteoporosis in older women was more cost-effective than treating younger women [32]. Another study conducted in the United States concluded that alendronate was the most favorable choice compared with hormonal replacement therapy and raloxifene [33]. Our study, however, differs from the Swedish study result, which favored secondary prevention over primary prevention of osteoporotic fractures. This may be because the Swedish study did not take into account the cost of treating initial fractures in the model for secondary prevention. We, however, considered that the cost should be included because the government or society needs to pay for that treatment as well, and so omitting this cost would lead to bias toward secondary prevention.

There are some limitations regarding the design and data used in this simulation study. First, this study was model based in which input parameters were to be derived from various sources. This would lead to a compromise in internal validity; instead, most of the data were obtained from systematic reviews and meta-analyses, which would increase the external validity or generalizability of the data. Second, the model focused on effectiveness of drugs in terms of prevention of hip and vertebral fractures only and ignored the benefits of prevention of other fractures such as wrist fractures. It also ignored other potential benefits of some osteoporosis drugs, for example, a reduction in breast cancer incidence by raloxifene [34]. Third, a utility score of 1 for the general population was assumed. This would lead us to overestimate the benefit of primary prevention compared with secondary prevention. Fourth, it is true that assuming 100% accuracy of DXA may overestimate a DXA-based strategy, especially universal screening of DXA. Our findings, however, found in contrast that OST followed by DXA is more cost-effective than universal DXA screening. Furthermore, it must be stated that the present study was undertaken in the Thai setting and that the conclusions are not necessarily applicable elsewhere, because costs might be different in other countries. In other settings, it would be necessary to acquire country-specific data on the cost-effectiveness and intervention thresholds.

Conclusions

At the current prices, it was concluded that screening and medical management to prevent osteoporotic fractures are cost-ineffective given the agreeable threshold set by the Subcommittee for Development of the NLEM. The interventions have not yet been included in the public health benefit packages, causing a significant barrier for Thai women seeking access to appropriate screening and medical management of osteoporosis.

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Supplemental Materials

Supplemental material accompanying this article can be found in the online version as a hyperlink at doi: 10.1016/j.jval.2011.11.016 or, if a hard copy of article, at www.valueinhealthjournal.com/issues (select volume, issue, and article).

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