

Cost-effectiveness of Bone Densitometry Followed by Treatment of Osteoporosis in Older Men

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AS THE POPULATION AGES, osteoporotic fractures are increasingly recognized as a common and serious health problem among elderly men.^{1,2} White men at age 60 years have a 29% chance of experiencing such a fracture during their remaining lifetimes.³ One-third of all hip fractures occur in men⁴⁻⁶ and are associated with as much morbidity as and higher mortality than those that occur in women.⁷⁻⁹ Vertebral fractures are also quite prevalent among older men^{10,11} and are strongly associated with subsequent hip¹² and other clinical fractures¹³ and probably as much morbidity in men as in women.¹⁴

For these reasons, the International Society for Clinical Densitometry¹⁵ and the Canadian Osteoporosis Society,¹⁶ respectively, have advocated (based on expert opinion) bone densitometry for all men older than 70 and 65 years. However, the US Preventive Services Task Force and the Canadian Task Force on Preventive Health Care have made no

Context Osteoporotic fractures are common among elderly men.

Objective To evaluate among older men the cost-effectiveness of bone densitometry followed by 5 years of oral bisphosphonate therapy to prevent fractures for those found to have osteoporosis (femoral neck T score ≤ -2.5), compared with no intervention.

Design, Setting, and Population Computer Markov microsimulation model using a societal perspective and a lifetime horizon. Simulations were performed for hypothetical cohorts of white men aged 65, 70, 75, 80, or 85 years, with or without prior clinical fracture. Data sources for model parameters included the Rochester Epidemiology Project for fracture costs and population-based age-specific fracture rates; the Osteoporotic Fractures in Men (MrOS) study and published meta-analyses for the associations among prior fractures, bone density, and incident fractures; and published studies of fracture disutility.

Main Outcome Measures Costs per quality-adjusted life-year (QALY) gained for the densitometry and follow-up treatment strategy compared with no intervention, calculated from lifetime costs and accumulated QALYs for each strategy.

Results Lifetime costs per QALY gained for the densitometry and follow-up treatment strategy were less than \$50 000 for men aged 65 years or older with a prior clinical fracture and for men aged 80 years or older without a prior fracture. These results were most sensitive to oral bisphosphonate cost and fracture reduction efficacy, the strength of association between bone mineral density and fractures, fracture rates and disutility, and medication adherence.

Conclusions Bone densitometry followed by bisphosphonate therapy for those with osteoporosis may be cost-effective for men aged 65 years or older with a self-reported prior clinical fracture and for men aged 80 to 85 years with no prior fracture. This strategy may also be cost-effective for men as young as 70 years without a prior clinical fracture if oral bisphosphonate costs are less than \$500 per year or if the societal willingness to pay per QALY gained is \$100 000.

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recommendations on use of bone densitometry among elderly men. Universal bone densitometry for women older than 65 years has been demonstrated to be cost-effective,¹⁷ but the age-specific prevalence of osteoporosis and incident fracture rates are much lower among men than women. Among men, increased age is associated not only with increased prevalence of osteoporosis and fracture rates but also with increased mortality, so it is unclear a priori if bone densitometry followed by treatment of men with osteoporosis is cost-effective at any age. Only 1 modeling study has assessed the cost-effectiveness of pharmacologic therapy to prevent fracture in osteoporotic men, and it included neither the costs of bone densitometry to identify the treatment cohort nor the disutility associated with incident radiographic but clinically unrecognized vertebral fractures.¹⁸ Thus, despite the importance of the problem of osteoporosis in men, clinical decision making is hampered by a lack of evidence-based cost-effectiveness analyses of common diagnostic and therapeutic interventions. The lack of consensus concerning this issue is reflected in very low rates of clinical intervention for osteoporosis in men.¹⁹

The purpose of this modeling study was to estimate the lifetime costs and health benefits of bone densitometry followed by 5 years of oral bisphosphonate therapy for men found to have osteoporosis (femoral neck T score ≤ -2.5 , using healthy young white men as the reference) among hypothetical subsets of elderly men with or without prior clinical fracture since age 50 years, compared with no intervention. We chose to stratify the analyses according to self-reported fracture history because self-reports of prior fractures are reasonably accurate^{20,21} and are an important predictor of subsequent fractures.^{22,23}

METHODS

We constructed a Markov cost-utility model using Data Pro Healthcare 2005 software, release 0.4 (TreeAge, Williamstown, Massachusetts) to compare bone densitometry followed by oral bis-

phosphonate therapy for those with osteoporosis vs no intervention.

Model Structure

The model health states were no fracture, post-distal forearm fracture, post-clinical vertebral fracture (ie, clinically evident at onset), post-radiographic vertebral fracture (ie, not recognized clinically at onset), post-hip fracture, post-other fractures (ie, of the proximal forearm, humerus, scapula, clavicle, sternum, ribs, pelvis, distal femur, patella, tibia, or proximal fibula), post-hip and vertebral fracture, and death (FIGURE 1). Beginning in the no-fracture state, a fracture may occur, at which time transition to that postfracture state occurs. The costs of that fracture are assigned as a transition cost. Fracture disutility is modeled as a lower value of a quality-adjusted life-year (QALY) compared with the no-fracture state. Long-term care costs after hip fracture are assigned in the post-hip fracture and post-vertebral/hip fracture states. Individuals are eligible for (at risk of) transition to a different state once every 3 months and are followed up through the model until death or age 105 years to capture the permanent disutility that may follow hip and clinical vertebral fractures. We assumed discount rates of 3% for both costs and health benefits.

Probability of Mortality

Background mortality was estimated from 2003 US vital statistics.²⁴ The mortality for the first year after hip fracture was estimated to be 1.375 times the background rate.²⁵ Because the excess mortality associated with vertebral fracture may be attributable to preexisting comorbidity and not to the fracture itself,^{26,27} we assumed no excess mortality directly attributable to vertebral or other nonhip fractures.

Fracture Probabilities

The probabilities of each type of fracture due to mild or moderate trauma were established as functions of age, presence of osteoporosis (femoral neck T score ≤ -2.5), presence or absence of prior clinical fracture, and presence or

absence of bisphosphonate therapy. The risks of each type of fracture as a function of age were developed from comprehensive population-based, age-specific data for men from the Rochester Epidemiology Project,²⁸ which captures virtually all health care utilization within Olmsted County, Minnesota.²⁹ Since the odds ratio of a radiographic vertebral fracture in Olmsted County being clinically unrecognized vs clinically recognized is 1.86,³⁰ the incidence rate of radiographic (but clinically unrecognized) vertebral fracture was set at 1.86 times that of clinical vertebral fracture. Fracture rates were plotted against age, and a best-fitting power curve was determined for each fracture type. These power curves represent fracture rates as continuous functions of age for the entire male population of Olmsted County (90% of which is white), including those with or without osteoporosis and/or prior fracture. Because fracture reduction from bisphosphonates was modeled from direct data rather than indirectly through changes in bone mineral density (BMD), changes in BMD from bisphosphonate therapy were not included in the model.

Fracture Risks Attributable to Osteoporosis and Self-reported Clinical Fracture

The relative risks of hip fracture for each 1-SD decrease in femoral neck BMD, derived from the largest meta-analysis of hip fracture predictors performed to date,³¹ were assumed to decrease with age from 3.38 for men aged 65 years to 2.26 for men aged 85 years. Based on this same meta-analysis, the relative risks of hip fracture in those with (vs without) prior clinical fracture were assumed to decrease with age from 2.77 for men aged 65 years to 1.61 for men aged 85 years.³² Based on the observational Rotterdam study, we assumed a relative risk of incident vertebral fractures of 1.8 per SD decrease of femoral neck BMD and a relative risk of 2.4 in those with (vs without) prior clinical fracture.³³

The relative risk of nonvertebral non-hip fractures was assumed to be 1.34 per 1-SD decrease in femoral neck BMD

based on data from the Osteoporotic Fractures in Men (MrOS) study,³⁴ an observational study including 5362 white US men aged 65 years or older.^{35,36} We used unpublished MrOS data to estimate the relative risk of nonvertebral nonhip fractures in those with vs without prior clinical fracture. At the baseline MrOS examination, 17% of the white participants (913 men) reported a prior clinical fracture since age 50 years. Incident clinical fractures were assessed by self-report on questionnaires mailed every 4 months, and reported fractures were confirmed by review of radiographic reports, with 99% complete ascertainment. Through 4.9 years of follow-up, 329 nonvertebral nonhip fractures occurred. For those with vs without prior clinical fracture, the relative risk of incident nonvertebral nonhip fractures was 2.01, adjusted for age, enrollment site, and BMD.

For each starting age, the relative risks of fractures in those with vs without prior clinical fracture were further adjusted for the prevalence of prior clinical fracture to derive the risks of fractures attributable to prior clinical fracture relative to the entire male population of that same age (technical supplement available on request from corresponding author).

Relative Risk of Fracture With Drug Therapy

We assumed relative risks of 0.36 and 0.73, respectively, for incident verte-

bral and nonvertebral fractures during use of oral bisphosphonates vs no drug therapy, based on a meta-analysis of the 2 published prospective, randomized clinical trials of alendronate in men.³⁷ The fracture reduction benefit was assumed to start 6 weeks after the start of therapy. After a 5-year treatment course, a gradual linear loss of fracture reduction benefit was assumed to occur over the subsequent 5 years.

Prevalence of Osteoporosis in Men With and Without Prior Fracture by Age

The prevalence of osteoporosis at the femoral neck for each screening initiation in the white male US population was estimated from the Third National Health and Nutrition Examination Survey.³⁸ Then, the proportions of those with and without prior clinical fracture who have osteoporosis at each age were estimated, assuming an age-adjusted relative risk of 1.91 (derived from MrOS baseline data using a logistic regression model) for presence of femoral neck osteoporosis in those with (vs without) prior clinical fracture.

Direct Costs

We assumed the cost of oral bisphosphonates to be the average US wholesale price for alendronate in 2004 (\$1000/y)³⁹ and that adverse effects of bisphosphonate would generate only trivial direct medical costs. We assigned the cost of 1 physician visit (\$52

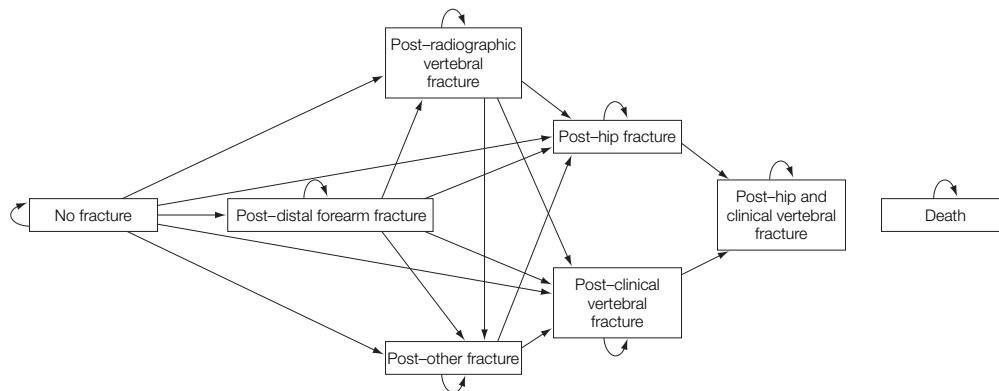
for each year of bisphosphonate therapy and the cost of 1 additional bone density test after 2 years of drug therapy. The direct medical costs of acute hip, clinical vertebral, distal forearm, and other fractures (TABLE 1) were based on societal opportunity cost estimates, expressed in 2004 US dollars.⁴⁴ The direct cost of radiographic (clinically unrecognized) vertebral fractures was assumed to be zero. We assumed the cost of a bone density test to be the mean 2007 Medicare reimbursement (\$82),⁴⁹ reflecting recent concerns that previous reimbursement rates were in excess of the true cost of performing and interpreting bone density tests.⁵⁰

The long-term care cost for the first year after hip fracture, averaged across all hip fracture patients, was estimated from nursing home use following hip fracture compared with an age- and sex-matched control group,⁴⁵ the US cost per day of long-term care,⁵¹ and the mean length of nursing home stay following hip fracture for those who were community dwelling before fracture (Table 1). Permanent long-term care in men who were community dwelling before fracture was estimated to be required for 12.2% following hip fracture, costing \$7302 per year averaged across all hip fracture patients.

Indirect Costs

Lost productivity from hip, clinical vertebral, other, and distal forearm fractures, respectively, was estimated to be

Figure 1. Markov Diagram of Health States and Possible Transitions Among Them During Each 3-Month Cycle



Transition to death may also occur from any state (not shown by arrows).

0.348, 0.149, 0.127, and 0.095 years.⁴⁶ Indirect costs were calculated as this proportion multiplied by the mean yearly earnings for employed white men in the United States for 2004 (stratified according to age)⁵² and adjusted by age-specific workforce participation rates (Table 1).⁵³

QALYs Associated With Each Health State

Based on population-based surveys, we assumed a QALY value of 0.7 associated with the no-fracture state for elderly men.⁴⁰ The disutilities for the first year following incident hip, distal forearm, and clinical vertebral fractures were derived from a Swedish prospective study of elderly men and women (Table 1).¹⁴ The assumed disutilities for the first year following "other" fractures,²³ for all fractures more than 1 year after their occurrence,²³ and for the post-hip and post-vertebral fracture states⁴³ are shown in Table 1. Radio-

graphic vertebral fractures were assumed to cause a loss of quality of life only 6 years after their occurrence because such fractures that are more than 4 to 8 years old do not appear to be associated with increased pain or limited activity.^{54,55} Secondary analyses were performed assuming a QALY value of 1.0 to compare estimated life-years saved with the densitometry and treatment strategy vs with no intervention.

Medication Adherence

For the base-case analysis, we assumed that only 85% of prescribed medication would be purchased and taken in the first 3 months and that this percentage would drop to 65% by the end of the first year, to 60% by the end of the second year, and to 55% by the end of the fifth (and final) year of oral bisphosphonate therapy.⁵⁶ Medication costs and fracture reduction efficacy were assumed to be proportional to adherence.

Sensitivity Analyses

Univariate sensitivity analyses were performed varying discount rates, fracture rates, fracture costs, fracture disability, the costs of bone densitometry, the offset of fracture reduction benefit following cessation of drug therapy, preventable mortality due to vertebral fracture, medication adherence, the relative risks of fractures attributable to osteoporosis or prior clinical fracture, yearly oral bisphosphonate cost, and delaying the onset of fracture reduction benefit for 7.5 months after the start of therapy. Because of uncertainty regarding the nonvertebral fracture reduction efficacy of oral bisphosphonates for men, 2-way sensitivity analyses were performed assuming reduced nonvertebral fracture efficacy, using different yearly oral bisphosphonate costs.

Probabilistic sensitivity analyses were performed using log-normal distributions of fracture direct costs⁴⁴ and normal distributions of fracture rates and permanent long-term care costs following hip fracture. The distributions of the relative risks of incident fractures associated with osteoporosis, prior fracture, and oral bisphosphonate therapy were assumed to be log-normal. Uniform distributions were used to model variability in fracture disability and indirect fracture costs. Full details of the derivation of the parameter distributions used for the probabilistic sensitivity analyses are available in an online technical supplement (on request from corresponding author). Cost-effectiveness acceptability curves were generated from these analyses.

Secondary analyses of the densitometry and follow-up treatment strategy compared with no intervention were also performed assuming treatment femoral neck T-score thresholds of -2.0 or lower and -3.0 or lower.

Model Validation

The model estimated the percentage of 50-year-old men who would have a hip fracture during their remaining lifetimes to be 6.2%, nearly identical to that estimated by Melton et al.⁵⁷ The model

Table 1. Model Parameters

Parameters	Value
Disutility per year ^a	
No fracture state ^{40,41}	0
Post-distal forearm fracture ¹⁴	0.06 in year 1, then 0.001
Post-hip fracture ¹⁴	0.17 in year 1, then 0.131
Post-clinical vertebral fracture ¹⁴	0.23 in year 1, then 0.064
Post-radiographic vertebral fracture ⁴²	0.126 in year 1, then 0.06 in years 2-6, then 0
Post-hip and clinical vertebral fracture ⁴³	0.36 in year 1, then 0.20
Post-other fracture ²³	0.073 in year 1, then 0.023
Direct medical costs	
Acute hip fracture	\$28 297
Direct medical costs ⁴⁴	\$17 961
Year 1 long-term care ⁴⁵	\$10 336
Acute clinical vertebral fracture ⁴⁴	\$7 488
Acute distal forearm fracture ⁴⁴	\$4 065
Acute other fracture ⁴⁴	\$5 586
Alendronate per year ³⁹	\$1 000
Annual long-term care >1 year after hip fracture ⁴⁵	\$7 302
Indirect fracture costs ⁴⁶	
Hip fracture	\$4 218 (age 65-69 y) to \$11 156 (age >75 y)
Spine fracture	\$1 806 (age 65-69 y) to \$495 (age >75 y)
Distal forearm fracture	\$1 152 (age 65-69 y) to \$316 (age >75 y)
Other fracture	\$1 540 (age 65-69 y) to \$422 (age >75 y)
Relative risk of fracture during bisphosphonate therapy ^{37,47,48}	
Nonspine fracture	0.73
Spine fracture	0.36

^aDisutility is the difference in quality-adjusted life-years between the specified postfracture state and the no-fracture state and represents the loss of quality-adjusted life-years due to the fracture.

estimated that 6.9% and 1.2%, respectively, would have 1 or more lifetime clinical vertebral and distal forearm fractures, compared with the estimates of Melton et al of 5.0% for vertebral and 2.5% for distal forearm fractures.⁵⁷ However, for men aged 65 to 84 years (the age range over which treatment vs no treatment was modeled), model-predicted and actual rates, respectively, of distal forearm fractures reported from the Rochester Epidemiology Project were close to each other (46 vs 49 per 100 000 person-years). Similarly, age-adjusted actual and model-predicted clinical vertebral fractures, respectively, were 495 and 506 per 100 000 person-years.

Model Simulation Runs and Calculation of Cost-effectiveness

For the base-case analyses, we ran the model for subsets of elderly men with or without a prior clinical fracture at 5 different starting ages (65, 70, 75, 80, and 85 years) using Monte Carlo simulations. For each simulation, 50 000 men were put through each of the 2 strategies of the microsimulation model, one at a time. The incremental cost-effectiveness ratio was computed as the difference in lifetime mean costs per man divided by the difference in lifetime mean accumulated QALYs per man between the strategies. An incremental cost-effectiveness ratio represents the cost of gaining 1 QALY.

Univariate and bivariate sensitivity analyses were also run with 50 000 trials each. Probabilistic sensitivity analyses were performed with 500 simulations and 5000 trials per simulation, with a new set of values for all of the above variables randomly selected from their respective distributions for each simulation.

To estimate the proportion of men for whom clinical vertebral, hip, distal forearm, and other fractures would be prevented by the densitometry and treatment strategy, models were run with a 10-year horizon corresponding to the 5-year treatment period and gradual loss of fracture reduction benefit over the subsequent 5 years.

RESULTS

The estimated prevalence of femoral neck osteoporosis among men with a prior fracture ranged from 14.5% at age 65 years to 33.6% at age 85 years. Osteoporosis prevalence in the absence of a prior clinical fracture was lower, ranging from 7.6% at age 65 years to 17.6% at age 85 years. The densitometry and treatment strategy modestly reduced the absolute 10-year incidence of clinical fractures by a range of 2.1% for 65-

year-old men without a prior fracture to 4.5% among 85-year-old men with a prior fracture (FIGURE 2).

The costs per QALY gained for the densitometry and treatment strategy compared with no intervention decreased with age and were substantially lower for men with a self-reported history of clinical fracture since age 50 years. In the base-case model (TABLE 2), the costs per QALY gained were less than \$50 000 for those with

Figure 2. Ten-Year Clinical Fracture Incidence According to Age, Prior Clinical Fracture Status, and Intervention Assignment

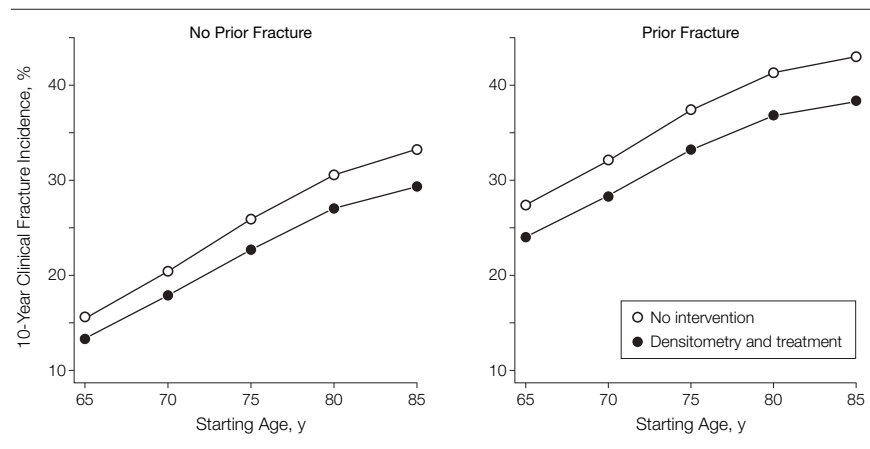


Table 2. Cost per QALY Gained for the Densitometry and Treatment Strategy According to Age and Prior Fracture Status

Lifetime Outcomes	No Prior Clinical Fracture		Prior Clinical Fracture	
	Densitometry and Treatment	No Intervention	Densitometry and Treatment	No Intervention
Age 65 y				
Costs, \$	24 093	20 713	36 354	34 102
QALYs	8.317	8.291	8.083	8.036
Costs per QALY gained, \$	129 665		47 537	
Age 70 y				
Costs, \$	22 278	19 409	31 330	29 524
QALYs	6.884	6.853	6.747	6.696
Costs per QALY gained, \$	92 769		35 037	
Age 75 y				
Costs, \$	20 654	18 371	26 599	23 231
QALYs	5.592	5.558	5.461	5.402
Costs per QALY gained, \$	66 071		23 260	
Age 80 y				
Costs, \$	18 353	16 621	22 734	21 821
QALYs	4.428	4.390	4.368	4.309
Costs per QALY gained, \$	45 587		15 477	
Age 85 y				
Costs, \$	15 438	14 150	19 197	18 934
QALYs	3.437	3.399	3.377	3.321
Costs per QALY gained, \$	33 666		4700	

Abbreviation: QALY, quality-adjusted life-year.

a prior clinical fracture at all ages, as well as among men aged 80 or 85 years without a prior clinical fracture. The costs per QALY gained were below \$100 000 for men aged 70 years or older without a prior fracture. Among all the base-case scenarios, the maximum gain in life-years was 0.007 (2.5 days).

Impact of Bisphosphonate Cost and Assumed Reduction in Nonvertebral Fracture Risk

These results were sensitive to the assumed yearly cost of oral bisphosphonate therapy (FIGURE 3). For example, if the yearly cost of oral bisphosphonate therapy was only \$500 per year, then the cost per QALY gained for 70-year-old men without a history of clinical fracture was less than \$50 000, compared

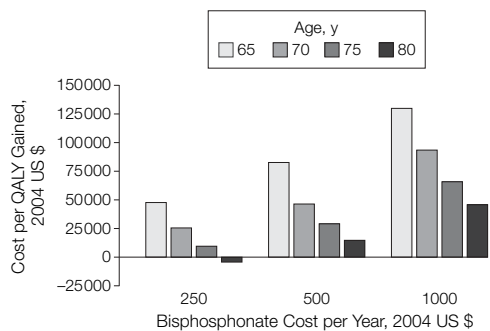
with \$70 000 if the yearly cost of therapy was \$1000. These results were also quite sensitive to the assumed nonvertebral fracture reduction benefit from bisphosphonate therapy, such that the costs per QALY gained for 80-year-old men without a history of clinical fracture would be \$97 000 if nonvertebral fractures were reduced only 10% by oral bisphosphonates, compared with \$46 000 in this same group if nonvertebral fractures were reduced by 27% by therapy (base model) (FIGURE 4). If bisphosphonate cost was only \$500 per year, however, then the cost per QALY gained for 80-year-old men without prior clinical fracture would be close to \$50 000 or less per year even if nonvertebral fractures were reduced only 10% by treatment.

Other Sensitivity Analyses

Univariate sensitivity analyses showed these estimated costs per QALY gained to be quite sensitive to reasonable changes in fracture rates, fracture disutility, and the relative risks of fractures attributable to osteoporosis (TABLE 3) and modestly sensitive to the cost of bone densitometry. Assuming a yearly bisphosphonate cost of \$1000 and a societal willingness to pay of \$50 000 per QALY gained, acceptability curves generated by probabilistic sensitivity analyses showed that the densitometry and treatment strategy has only a 10% probability of being cost-effective for 70-year-old men without a prior clinical fracture but a 78% probability of being cost-effective for 75-year-old men with a prior fracture (FIGURE 5). These analyses show that the cost-effectiveness of the densitometry and treatment strategy is less certain for men aged 80 years without a prior fracture and 65-year-old men with a prior fracture. However, if yearly bisphosphonate costs are reduced to \$500, the probabilities for the cost per QALY gained for the densitometry and treatment strategy being below \$50 000 are increased to 85% and 84%, respectively, for 80-year-old men without a prior fracture and 65-year-old men with a prior fracture.

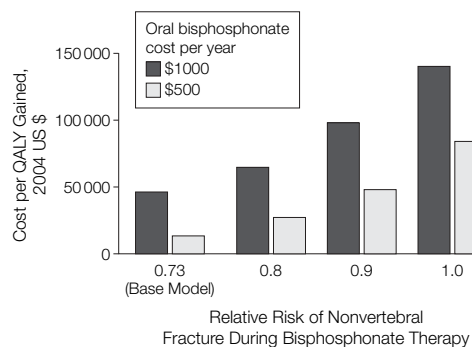
If the densitometry and treatment strategy used a T-score treatment threshold of -2.0 instead of -2.5, then the costs per QALY gained compared with no drug therapy would be higher for 80-year-old men without a prior fracture (\$60 938) compared with the base case (\$45 587) as well as for 65-year-old men with a prior fracture (\$66 781) compared with the base case (\$47 537). However, if the densitometry and treatment strategy used a T-score treatment threshold of -3.0, then the costs per QALY gained would be slightly lower for 65-year-old men with a prior fracture (\$37 837) and the same for 80-year-old men without a prior fracture (\$45 714) compared with the base-case scenarios.

Figure 3. Cost per QALY Gained for the Densitometry and Treatment Strategy According to Yearly Cost of Oral Bisphosphonates and Age in Men Without Prior Clinical Fracture



QALY indicates quality-adjusted life-year.

Figure 4. Cost per QALY Gained for the Densitometry and Treatment Strategy According to Nonvertebral Fracture Reduction Efficacy and Cost of Oral Bisphosphonates in an 80-Year-Old Man With No Prior Fracture



QALY indicates quality-adjusted life-year.

COMMENT

Osteoporotic fractures are an important cause of morbidity among elderly men, and widespread bone densitometry screening programs for men older than 70 years have been recommended^{1,2,15} but are based on expert opinion and have not been widely adopted.¹⁹ This study provides a firm basis for developing rational clinical paradigms for the detection and treatment of men with osteoporosis.

Assuming a societal willingness to pay per QALY gained of \$50 000 and current drug costs, bone densitometry followed by oral bisphosphonate therapy for those with a femoral neck T score of -2.5 or lower may be cost-effective for men aged 65 years or older with a history of clinical fracture. However, in the absence of a prior fracture or other substantial additional fracture risk factors, the densitometry and follow-up treatment strategy may be cost-effective only for men aged 80 years or older. The cost-effectiveness of the densitometry and screening strategy increases with age, even up to age 85 years, because the risk of hip and other fractures increases with age as fast or faster than mortality and because the prevalence of osteoporosis (and therefore the proportion selected for drug therapy) increases substantially with age. Universal bone densitometry for all men aged 70 years or older does not appear to be justifiable with current bisphosphonate costs, at least on grounds of cost-effectiveness. Moreover, the overall fracture burden among elderly men with osteoporosis would be affected only to a modest degree by this strategy, largely because of suboptimal medication adherence and only modest reduction of nonvertebral fractures by oral bisphosphonates.

If the societal willingness to pay per QALY is \$100 000 or bisphosphonate therapy costs less than \$500 per year, however, bone densitometry followed by drug therapy may be cost-effective for men aged 70 years or older, even without a prior fracture. Since alendronate will lose patent protection in the United States in 2008, the cost of oral

bisphosphonate therapy in the near future may be much less than the current average US wholesale price.

Our results suggest that the cost-effectiveness of the densitometry and treatment strategy may be slightly improved by use of stricter bone density treatment thresholds. More liberal treatment thresholds expand the proportion of those eligible for drug therapy,

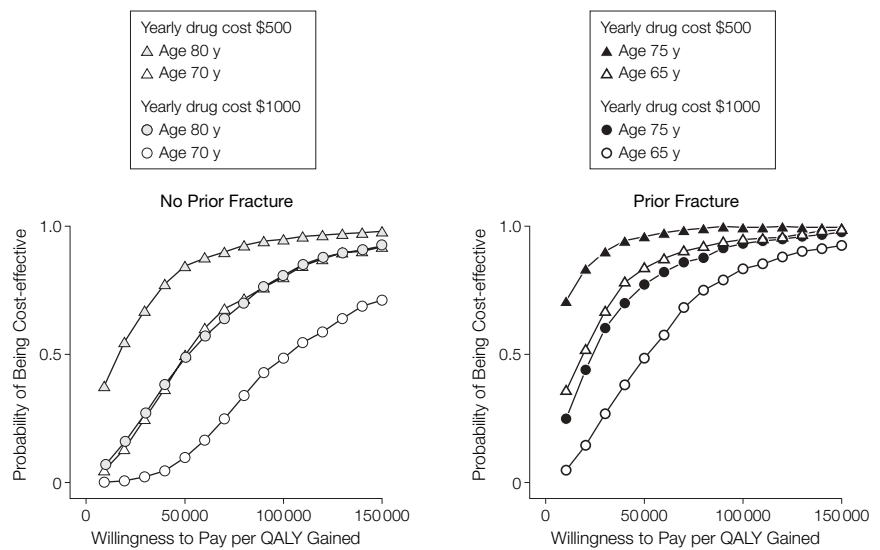
thereby lowering the screening densitometry cost per treated person, but this is offset by the treated cohort having a lower risk of fracture. Moreover, among postmenopausal women, oral bisphosphonates may effectively reduce nonvertebral fractures only among those with a sex-specific femoral neck BMD T score of -2.5 or lower.^{58,59} If the fracture reduction efficacy of oral bisphos-

Table 3. Univariate Sensitivity Analyses for an 80-Year-Old Man With No Prior Fracture

Parameters	Range, Low to High	Cost per QALY Gained by Parameter, \$	
		Low	High
Discount rates	0 to 0.06	34 667	57 215
Fracture costs	0.7 to 1.3 × base-case costs	58 292	38 759
Fracture rates	0.6 to 1.4 × base-case rates	98 885	26 040
Fracture disutility	0.5 to 1.5 × base-case values	84 550	30 480
Preventable vertebral and hip fracture mortality	No vs yes	50 713	42 192
Treatment benefit offset	0 to 10 y	65 020	30 583
Relative risk of fracture due to osteoporosis	Vertebral, 1.28 to 2.54	84 896	16 947
	Hip, 2.09 to 3.40		
	Distal forearm/other, 1.17 to 1.53		
Relative risk of fracture due to prior fracture	Vertebral, 1.19 to 4.80	37 547	60 389
	Hip, 1.37 to 2.14		
	Distal forearm/other, 1.59 to 2.55		
Adherence	100% to 40%	33 129	55 242
Densitometry cost	\$41 to \$139	40 051	56 327
Delay of onset of fracture reduction benefit	1.5 to 7.5 mo	45 587	54 935

Abbreviation: QALY, quality-adjusted life-year.

Figure 5. Cost-effectiveness Acceptability Curves: Cost per QALY Gained for the Densitometry and Treatment Strategy According to Oral Bisphosphonate Cost



QALY indicates quality-adjusted life-year.

phonates is also inversely correlated with BMD in men, then the cost-effectiveness of strategies that use a more restrictive treatment BMD threshold may be even more favorable relative to strategies with more liberal treatment thresholds.

Our study is the first to assess the cost-effectiveness of widespread bone densitometry screening and subsequent drug therapy to prevent osteoporotic fracture among elderly men. We used population-based estimates of white male fracture rates, age-specific proportions of men who have osteoporosis, and direct medical costs of fractures. We used probabilistic sensitivity analyses that allowed nearly all major model parameters to vary over reasonable ranges to test the robustness of our conclusions to changes in these parameters. In contrast with virtually all previously published cost-effectiveness studies of drug therapy for osteoporosis,⁶⁰ we have incorporated empirical estimates of medication nonadherence in our base-case analyses.

There are also important limitations to our study. First, these results are applicable to a treatment duration of only 5 years. Since treatment for 10 years may not reduce the risk of nonvertebral fractures more than treatment for 5 years,⁶¹ treatment for longer than 5 years may be less cost-effective. Second, these results are not applicable to treatment decisions based on BMD measured at skeletal sites other than the femoral neck, such as the lumbar spine. Third, this study is applicable only to white men residing in the United States. In particular, age-adjusted fracture rates are significantly lower among Hispanic and especially African American men compared with white US men, and hip fracture rates among Asians are lower. Fourth, our estimates of fracture disutility and fracture costs are based on studies in which a minority of the participants were men, although these studies do not indicate a significant difference in these parameters between the sexes. Fifth, there are no precise estimates of the nonvertebral fracture re-

duction efficacy of oral bisphosphonates among elderly men. Additional clinical trials yielding accurate estimates of nonvertebral fracture reduction with bisphosphonate therapy will allow completion of more precise modeling studies of the cost-effectiveness of oral bisphosphonate therapy. Finally, these analyses are applicable only to those with average risks based on age and prior fracture status and do not incorporate additional fracture risk factors, such as long-term systemic glucocorticoid use.

In conclusion, universal bone densitometry followed by oral bisphosphonate therapy among those found to have osteoporosis for all men aged 70 years or older regardless of fracture history or other fracture risk factors is not cost-effective using current drug costs. However, this strategy may be cost-effective for men aged 65 years or older with a prior clinical fracture and for men aged 80 years or older without a prior fracture, assuming a societal willingness to pay per QALY gained of \$50 000. This densitometry and treatment strategy may also be cost-effective for white men aged 70 years or older without a prior clinical fracture if the cost of oral bisphosphonate therapy is less than \$500 per year or if the societal willingness to pay per QALY gained is \$100 000.

Author Contributions: Drs Schousboe and Taylor had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Schousboe, Kane.

Acquisition of data: Schousboe, Cummings, Orwoll, Melton, Ensrud.

Analysis and interpretation of data: Schousboe, Taylor, Fink, Cummings, Orwoll, Melton, Bauer, Ensrud.

Drafting of the manuscript: Schousboe.

Critical revision of the manuscript for important intellectual content: Schousboe, Taylor, Fink, Kane, Cummings, Orwoll, Melton, Bauer, Ensrud.

Statistical analysis: Schousboe, Taylor, Fink.

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