

Cost-Effectiveness of Osteoporosis Interventions for 'Incidental' Vertebral Fractures

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ABSTRACT

BACKGROUND: Vertebral fractures detected “incidentally” by chest radiograph usually do not trigger osteoporosis treatment in older patients. In a 3-arm controlled trial we reported that both physician-directed and enhanced (physician plus patient activation) interventions increased treatment rates more than 10-fold (15%-20% absolute increases) compared with usual care; the cost-effectiveness of these interventions is unknown.

METHODS: Incremental cost-effectiveness of these 2 interventions compared with usual care was assessed using a Markov decision-analytic model, populated with 1-year outcomes data and direct intervention costs from the trial. Costs were expressed in 2009 Canadian dollars and effectiveness based on quality-adjusted life years (QALYs) gained. The perspective was health care payer; horizon was projected lifetime; costs and benefits were discounted at 3%; and deterministic and probabilistic sensitivity analyses were conducted.

RESULTS: Per patient, the physician and enhanced interventions cost \$34 and \$42, respectively. Compared with usual care, for every 1000 patients exposed to the physician intervention there were 4 fewer fractures, 8 more QALYs gained, and \$282,000 saved. Compared with physician interventions, for every 1000 patients exposed to enhanced interventions there were 6 fewer fractures, 6 more QALYs gained, and \$339,000 saved. Both interventions dominated usual care and were cost-effective in ~80% of 10,000 probabilistic simulations. Although the enhanced intervention cost \$8 more per patient, it still dominated the physician intervention and usual care, and was the most economically attractive option.

CONCLUSIONS: Pragmatic and inexpensive interventions directed at patients with incidentally detected vertebral fractures and their physicians are highly cost-effective at improving osteoporosis treatment, and in most circumstances also are cost-saving.

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data and were involved in conception and design and interpretation, and provided critical revision to manuscript drafts. DL undertook all economic analyses. SRM also wrote the first draft, obtained funding, and will act as guarantor for the results.

Trial Registry: clinicaltrials.gov: NCT00388908.

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Osteoporosis is a common and chronic condition that is underdiagnosed and undertreated.¹ In another example of the risk-treatment paradox wherein those at highest risk of events are least likely to be treated, patients with major fractures of the spine, hip, proximal humerus, and distal forearm have rates of osteoporosis treatment <10%-20% in the year following fracture.¹ Several interventions have been tested in controlled trials to improve quality of osteoporosis care in patients with recent symptomatic fractures of the hip and upper extremity.²

There exists, however, a large population of patients with prevalent but *asymptomatic* osteoporosis-related vertebral compression fractures.^{3,4} Although routine spinal radiographic screening is not recommended, many older patients already undergo chest radiographs for other reasons. These chest radiographs commonly document incidental vertebral fractures and reporting is very specific—although 40% of vertebral fractures still go unreported.^{3,4} We recently reported a controlled trial of 2 different interventions (one targeting primary care physicians, the other targeting both patients and their physicians) directed at improving bone mineral density testing and osteoporosis treatment in patients with chest radiograph-detected vertebral fractures.⁵ Compared with usual care, these 2 interventions increased absolute rates of osteoporosis treatment by 15%-20% (10- to 11-fold relative improvements).⁵ Although both interventions tested were effective at increasing osteoporosis treatment compared with usual care, it remains to be determined whether or not these interventions are worthwhile or represent good value for the money.

Therefore, we conducted a formal health economic analysis. We took a third-party health care payer perspective and a patient lifetime horizon. The trial provided direct estimates of intervention costs and utilization and outcomes for 1 year after study entry; literature reviews and expert opinions were then required to fully populate models.

METHODS

Description of the AVOID Trial

The methods, patient characteristics, and trial results have been previously reported.⁵ In summary, we conducted a nonrandomized controlled trial with blinded end point ascertainment and compared usual care with 2 different osteoporosis-related quality interventions. We enrolled 240 patients aged 60 years and older who had incidentally detected vertebral fractures reported on routine chest radio-

graphs taken in 2 Emergency Departments in Edmonton, Alberta, Canada. Usual care (control) consisted of sending to each patient's primary care physician, copies of all Emergency Department-related paperwork, the official chest radiograph reporting vertebral fractures, and proposed plans

for follow-up visits. The first intervention was directed at primary care physicians and consisted of opinion-leader-endorsed evidence summaries and treatment guidelines and patient-specific reminders that were faxed, e-mailed, or mailed along with the official chest radiograph report. The second "enhanced" intervention included a patient activation strategy (consisting of written educational materials and telephone-based osteoporosis counseling by a nurse practitioner) as well as the physician intervention, and it was administered to usual care controls that remained untreated for osteoporosis 3 months after their initial Emergency Department visit. The primary study outcome was starting a proven effective osteoporosis treatment

within 3 months of study entry. All patients provided written informed consent, and the study was approved by the Health Research Ethics Board of the University of Alberta.

Cost-effectiveness Analysis

Overview. We hypothesized that the enhanced intervention would be cost-effective compared with the physician intervention, and that both quality improvement interventions would be superior to usual care. Our trial provided data about the population at risk, achieved rates of osteoporosis testing and treatment across experimental arms within 3 months, and 1-year rates of treatment persistence and other clinical events. Beyond 1 year, all utilization and event data were based on literature review. Cost-effectiveness was assessed through a lifetime decision analytic model incorporating Markov processes to estimate incremental costs and effectiveness based on quality-adjusted life years (QALYs) gained.⁶⁻¹⁰ A third-party (public) health care payer perspective was used to maximize external validity.

Decision Analytic Model. **Figure 1** illustrates the model structure, relating the 3 study arms and 6 osteoporosis-related diagnosis and treatment pathways possible following vertebral fracture identification. The proportion of patients within each group was calculated by multiplying probabilities along each of the 6 pathways (**Table 1**). Then we applied 3 unique Markov processes differentiated only by their transition probabilities:⁶⁻¹⁰ low bone mass documented and receiving osteoporosis treatment (M1), low bone mass

CLINICAL SIGNIFICANCE

- Osteoporotic fractures are underdiagnosed and undertreated, but radiographic screening is not recommended.
- Older patients get chest radiographs that often incidentally report vertebral fractures.
- In a previously reported controlled trial, physician- or patient-directed interventions led to 10-fold improvements in osteoporosis treatment.
- Economic analyses now show these interventions were highly cost-effective, dominated usual care, and in most settings would lead to health system savings.

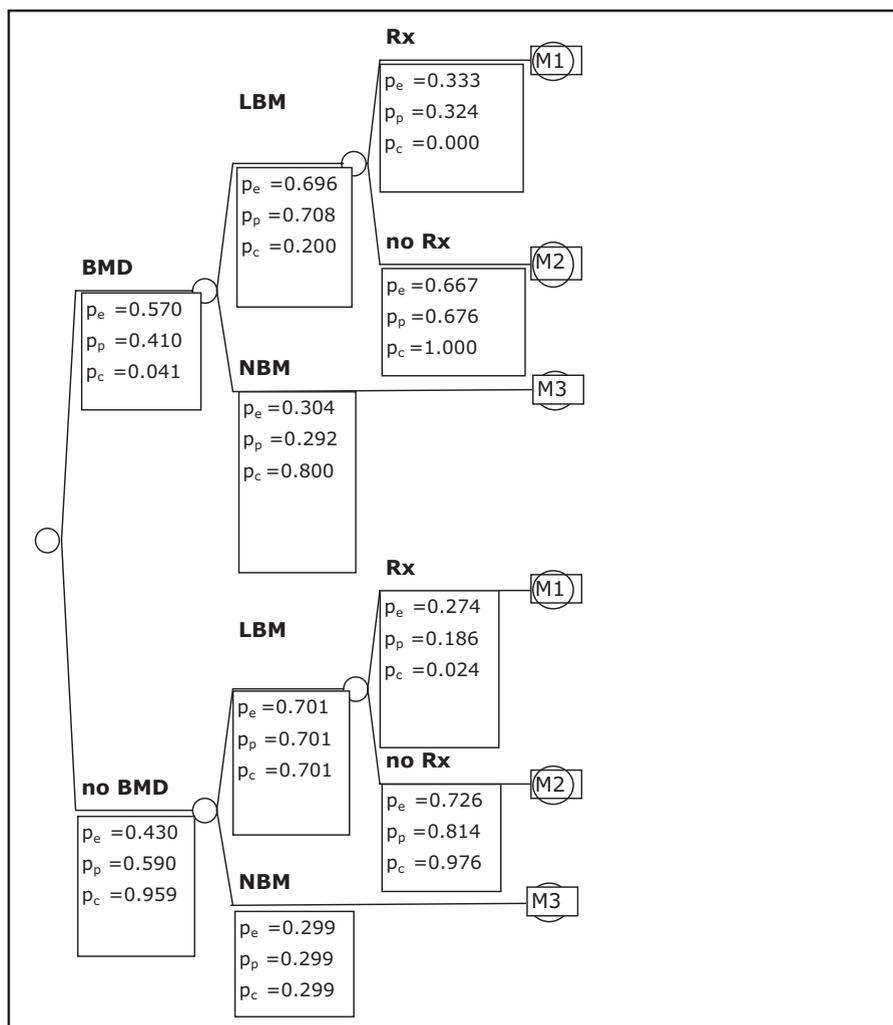


Figure 1 Decision tree of the model with Markov processes.*

*Probabilities associated with the enhanced intervention, physician intervention, and control arms of the study are denoted by p_e , p_p , and p_c , respectively. BMD = bone mineral density; LBM = low bone mass; NBM = normal bone mass; Rx = treatment with alendronate. M1, M2, and M3 refer to the individual Markov processes; also see the Methods section and [Figure 2](#).

detected but not receiving osteoporosis treatment (M2), and normal bone mass documented and appropriately not treated (M3; [Figure 1](#)). The M1 and M3 processes represent high-quality guideline-concordant care.

The structure of the Markov process ([Figure 2](#)) was adapted from the International Osteoporosis Foundation cost-effectiveness reference model,^{9,10} our prior work,^{11,12} and suggestions made by Johnell et al.⁸ The model incorporates 6 health states that simulate the movement of patients from the time of vertebral fracture identification at age 65 years until the age of 100 years or death. By study design, all patients enter the model in the “remote” post-vertebral fracture state at home. Then a proportion of the cohort moves to one of the other 5 states once per annual cycle, in accordance with transition probabilities derived from fracture rates specific to the type of fracture incurred, presence or absence of low bone mass, population-based

age-specific death rates, and fracture type-specific reductions in fractures. Half-cycle corrections were applied to both costs and QALYs.

Model Assumptions. The model is based on 4 broad simplifying assumptions. First, much of the input data in our model are derived from women because of the paucity of data related to fracture rates, osteoporosis treatments, and outcomes for men (56% of our trial population). Second, patients were considered to have normal (T-scores better than -1.0 at all skeletal sites measured) or treatably low levels of bone mass (T-scores of -1.0 or worse, encompassing densitometric osteopenia and osteoporosis) based on bone mineral density measurements collected during the trial. Third, we assumed all patients were treated with alendronate, because it is an oral bisphosphonate with strong evidence for vertebral and nonvertebral fracture reduction

Table 1 Distribution of Patients by Sub-Group and Study Arm

Sub-group	Enhanced Intervention (%)	Physician Intervention (%)	Control (%)
BMD, LBM, Rx	13.2	9.4	0.0
BMD, LBM, no Rx	26.4	19.7	0.8
BMD, NBM	17.4	12.0	3.3
No BMD, LBM, Rx	8.3	7.7	1.6
No BMD, LBM, no Rx	21.9	33.6	65.6
No BMD, NBM	12.8	17.6	28.7
Total	100.0	100.0	100.0

Abbreviations: BMD = bone mineral density; LBM = low bone mass; NBM = normal bone mass; Rx = treated with alendronate.

Patients that did not undergo a BMD test in the trial were assumed to have the same distributions of bone mass as the patients who were tested.

and because comparative effectiveness studies suggest little clinically important difference in benefits across the available oral bisphosphonates such as risedronate.¹³ Furthermore, alendronate has a generic formulation and it is the bisphosphonate prescribed most frequently in our jurisdiction.^{11,12} Last, it was assumed that once a patient had a hip fracture, no additional nonhip fractures would occur, although a repeat hip fracture was permitted.

Model Inputs.

- Repeat Fracture Rates.** Fracture rates were constant with age and type specific, and based on recent US Medicare data.^{14,15} Fracture rates for low-bone-mass patients not treated for osteoporosis are presented in **Table 2**. Fracture rates for patients with documented normal bone mass were considered to be the same as low-bone-mass patients treated with oral bisphosphonates.
- Fracture Reduction with Bisphosphonate Treatment.** Estimates of fracture reduction with alendronate were

Table 2 Annual Fracture Rates for Patients with Low Bone Mass*

Prior Fracture Type	Rates (%) by Subsequent Fracture Type		
	Hip	Clinical Vertebral	Forearm/Upper Extremity
Hip	2.3	—	—
Post remote vertebral fracture	2.8	1.5	2.3
Forearm/upper extremity	1.8	0.8	1.5

*Adapted from references.^{14,15}

obtained from systematic reviews and included a pooled 49% reduction in risk of hip and vertebral fractures and a pooled 48% reduction for humeral and distal radial fractures.^{16,17} In the base case analysis, alendronate treatment was for 5 years duration. In the first year of treatment, fracture reduction was assumed to be 50% of the full achievable benefit achieved over 5-10 years of treatment. As well, a residual positive effect of alendronate was assumed for an additional 5 years following discontinuation.^{18,19} This residual effect was modeled as linear but with diminishing benefits over a 5-year “set time” following discontinuation.^{18,19} In our trial, 1-year persistence with bisphosphonate treatment was 60%; we assumed this same rate of persistence would continue for the next 4 years.

- Costs.** All costs were expressed in constant 2009 Canadian (CDN) dollars. In the base case, all costs and outcomes were discounted at 3% per annum.²⁰
 - Costs of the Interventions.** For personnel costs, we used the hourly wage rate from the mid-point on our local salary payment grid for an experienced registered nurse, plus benefits and an additional 30% for overhead. The physician intervention cost \$34 per patient

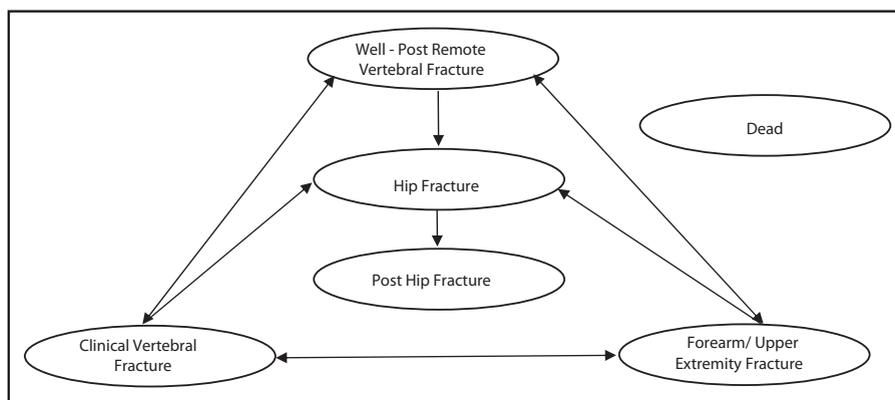


Figure 2 Structure of the Markov process.*

*Adapted from references 8-12. There are potential transitions from each health state to the Dead state that are not shown in the **Figure 1**, for purposes of clarity.

for this nurse to screen an average of 83 chest radiograph reports per enrolled patient, and then to generate and send out the entire intervention package. The enhanced intervention added an average of \$8 (for the nurse to counsel each patient by telephone) to physician intervention costs. The one-time cost induced by the interventions of providing a bone mineral density test with interpretation and associated physician visit was \$190.²¹

- **Costs of Osteoporosis Treatment.** We assumed all treated patients received generic alendronate, at a dosage of 70 mg per week. The Alberta drug plan covers generic alendronate for older patients with low-trauma fragility fractures.²² Total annual cost of medication and one annual osteoporosis-related primary care physician visit for re-evaluation and prescription refills was estimated at \$297 per patient.^{21,22} As have others,²⁰ we assumed alendronate would generate trivial direct medical costs related to side effects, and we did not account for the possibility of extremely rare but potentially fatal and certainly costly complications such as anaphylactic reactions or osteonecrosis of the jaw.
 - **Costs of Subsequent Fractures.** **Table 3** summarizes estimated annual costs for the health states related to the management of subsequent clinically symptomatic spine, hip, and proximal humerus and distal radius fractures. Costs were estimated based on standardized physician fees, while other health services such as physiotherapy and occupational therapy and their unit values were obtained from regional and national databases.²¹⁻²⁴ We assumed hip fractures would require surgical fixation and a 16-day hospital stay.²⁴ A case-mix method was used for inpatient costs.²³ Orthopedic surgeon and internist costs were based on daily visits. It was assumed that 80% of patients would be discharged home after hip fracture and 20% to long-term care facilities; costs of long-term care were based on provincial per diems minus patient copayments.²³ Only 10% of patients with clinically symptomatic vertebral fractures were assumed to require inpatient care.²⁵ Hospital costs were estimated in a similar manner as hip fractures, with daily internist visits for 16 days.²⁴ The 90% of clinically symptomatic vertebral fracture patients not hospitalized required 4 physician visits, 1 spinal radiograph, and 7 visits of outpatient rehabilitation. Patients with subsequent proximal humerus and distal radius fractures were assumed to present to an Emergency Department or fracture clinic for treatment, and had 1 closed fracture reduction, 2 physician follow-up visits, 1 post-reduction radiograph, 7 outpatient rehabilitation visits, and no subsequent surgical repair.
4. **Mortality Rates.** Patients were assumed to have the same risk of death as the general population, except in the year following a hip fracture.^{8,9} Published life tables were used for age-specific death rates.²⁶ For the age-

Table 3 Cost Assumptions

Cost Elements for Each of the 6 Health States	Cost*
Prior costs	
Enhanced intervention cost†	42
Physician intervention cost‡	34
Bone mineral density test§	190
I. Well—post remote vertebral fracture state	0
II. Hip fracture state	
Acute hospital, including physician fees (16 days) — all patients	23,601
Sub-acute rehabilitation (30 days) — 48% of patients	22,680
Home care (20 hours) — 48% of patients	1200
Long-term care with physician fees (349 days) — 20% of patients	57,211
III. Clinical vertebral fracture state	
Acute hospital with physician fees (16 days), follow-up — 10% of patients	18,380
Physician care (4 visits + X-ray) — 90% of patients	332
Outpatient rehabilitation (7 visits) — all patients	278
IV. Forearm/upper extremity fracture state	
Emergency visit including X-ray + physician fees — all patients	1274
Physician care (2 visits + X-ray) — all patients	185
Outpatient rehabilitation (7 visits) — all patients	278
V. Post hip fracture state	
Long-term care, including physician fees (365 days) — 20% of patients	59,827
VI. Dead state	0
Alendronate treatment	297

*Average cost of patients receiving each service, per model cycle (1 year). These costs are expressed in constant 2009 Canadian dollars (multiply by 0.92 to convert to US dollars).

†One-time cost for all patients in the enhanced intervention group.

‡One-time cost for all patients in the physician intervention group.

§One-time cost for patients, in any study group, who receive an initial bone mineral density test.

specific rates of death in the year following hip fracture, estimates were derived from the International Osteoporosis Foundation reference model.^{9,10}

5. **Health-related Quality of Life.** We used age-specific utility weights for each health state based on published utilities and proposed multipliers (**Table 4**).^{10,27}

Deterministic Sensitivity Analyses. Conventional one-way deterministic sensitivity analyses were conducted to evaluate the robustness of the model. In addition, because recent studies suggest that patients may derive an all-cause mortality reduction with bisphosphonate treatment,²⁸ we included a sensitivity analysis to assess the impact of an 11% bisphosphonate-related mortality reduction in the year following a new fracture.²⁸

Probabilistic Sensitivity Analysis. In order to better assess the impact of parameter uncertainty, we also conducted a probabilistic sensitivity analysis. Probability distributions

Table 4 Utility Weights* by Health State and Age

Health State	60-79 Years	≥80 Years
Well—post remote vertebral fracture	0.79	0.74
Hip fracture	0.55	0.52
Symptomatic vertebral fracture	0.47	0.44
Forearm or upper extremity fracture	0.76	0.71
1-year post hip fracture	0.63	0.59
Dead	0.00	0.00

*Utilities anchored at 0 (dead) and 1 (perfect health), and adapted from references.^{10,27}

were assigned to all variables for which there was uncertainty associated with the value used in the base case models (distribution parameters available upon request). We chose a gamma distribution to generate random values for unit costs but otherwise used a beta distribution, and then undertook 10,000 simulations relative to the base case.²⁹ Results were summarized using cost-effectiveness acceptability curves, which represent the percent of simulations that were cost-effective for each study arm at various potential levels of willingness to pay. Willingness to pay represents the theoretical maximum amount that society is willing to pay for one additional QALY; we did not survey payers to determine what their actual willingness to pay might be. All analyses were conducted using the TreeAge Pro Healthcare Module 2011 (TreeAge Software Inc., Williamstown, Mass).

RESULTS

Patient Characteristics

The full results of the study are published elsewhere.⁵ Briefly, 75% of study patients were 65 years or older, 56%

were men, 50% reported a prior nonvertebral fracture, 17% reported a prior vertebral fracture, and (by study design) none were treated for osteoporosis. Two thirds of patients had low bone mass at one or more skeletal sites.

Intervention Effects

Compared with usual care, the physician intervention increased rates of bone mineral density testing (44% vs 4%, 40% absolute difference, $P < .001$) and bisphosphonate treatment (17% vs 2%, 15% absolute difference, $P < .001$). The enhanced intervention also attained significantly higher rates of bone mineral density testing (57%) and bisphosphonate treatment (22%) compared with the usual care rates. Of the 48 patients that started bisphosphonate treatment, 29 (60%; 95% confidence interval [CI], 46%-75%) were still filling their prescriptions at 1 year.

Cost-effectiveness of the Interventions (Base Case Analysis)

The base case analysis is presented in **Table 5**. The model suggests that, over their lifetime, patients with a chest radiograph-detected incidental vertebral fracture exposed to the physician intervention would be less likely to incur another fracture compared with usual care. For every 1000 patients participating in the physician intervention, an additional 400 bone mineral density tests would be performed and an additional 150 patients would be treated with bisphosphonate, resulting in avoidance of about 2 hip fractures and 4 total fractures. There also was an associated but modest increase of 8 QALYs gained per 1000 patients. Lifetime costs were less for physician intervention compared with usual care, with an incremental cost saving of \$282 (\$US 259) per patient. Thus, the physician intervention strategy dominated usual care.

Table 5 Costs and Health Outcomes per Patient by Intervention Status—Base Case

Study Group	Average Cost (\$)*	Average Hip Fractures†	Average Total Re-fractures‡	Average QALYs§
Enhanced intervention	39,965	0.418	0.874	10.049
Physician intervention	40,304	0.421	0.880	10.043
Control	40,586	0.423	0.884	10.035
Incremental analysis				
Physician vs control	-282	-0.002	-0.004	0.008
Enhanced vs physician	-339	-0.003	-0.006	0.006
ICER				
Physician vs control	Not applicable, physician intervention is dominant			
Enhanced vs physician	Not applicable, enhanced intervention is dominant			

ICER = incremental cost-effectiveness ratio.

*Lifetime average costs per patient, discounted at 3%. These costs are expressed in constant 2009 Canadian dollars (multiply by 0.92 to convert to US dollars).

†Refers to incident hip fractures per patient, subsequent to the initial remote vertebral fracture.

‡Includes hip, clinical vertebral and forearm/upper extremity re-fractures per patient.

§Average quality adjusted life years per patient, discounted at 3%.

Table 6 Deterministic Sensitivity Analyses

Scenario	Incremental Costs*		QALYs Gained	
	Physician vs Control	Enhanced vs Physician	Physician vs Control	Enhanced vs Physician
Base case	−282	−339	0.008	0.006
Intervention costs				
100% increase	−248	−331	0.008	0.006
200% increase	−214	−323	0.008	0.006
Persistence with treatment				
30%, rather than 60%	172†	−209	0.000	0.004
Alendronate price				
100% increase	−173	−308	0.008	0.006
200% increase	−66	−277	0.008	0.006
500% increase	258‡	−185	0.008†	0.006
Effect of alendronate—35% fracture reduction	27§	−251	0.003‡	0.006
Proportion of intervention patients obtaining BMD (50% reduction)	−238	−341	0.006	0.007
Treatment duration—(10 years, rather than 5 years)	−799	−485	0.017	0.010
Discount rate (rather than 3%)				
0% discount rate	−370	−492	0.010	0.009
5% discount rate	−232	−269	0.007	0.006
Mortality effect (11% reduction rather than no effect)	−230	−324	0.017	0.010

Abbreviations: BMD = bone mineral density; QALYs = quality-adjusted life years.

*Costs are expressed in constant 2009 Canadian dollars (multiply by 0.92 to convert to US dollars).

†The physician intervention is weakly dominated by the control, as incremental cost is positive but there is no difference between arms with respect to QALYs.

‡Non-dominant case; the incremental cost-effectiveness ratio = \$32,250.

§Non-dominant case; the incremental cost-effectiveness ratio = \$9000.

The enhanced intervention led to better outcomes than the physician intervention (Table 5). Enhanced intervention dominated the physician intervention as costs were less and life-years gained were greater (Table 5). The incremental cost savings were \$339 (\$US 312) per patient compared with physician intervention.

Deterministic Sensitivity Analyses

One-way sensitivity analyses indicate that the results of the base case are robust to both plausible and fairly implausible assumptions (Table 6). In all scenarios, the enhanced intervention dominated both the physician intervention and usual care. The physician intervention also dominated usual care in most scenarios (Table 6). Overall, the parameter that had the greatest impact on cost was the price of alendronate. The parameter that had the largest impact on effectiveness was the introduction of a treatment-related mortality reduction with the bisphosphonates.

Probabilistic Sensitivity Analysis

Figure 3 also illustrates the robustness of the base case analysis and confirms the economic attractiveness of both interventions — but particularly the enhanced intervention. The ranking of the 3 study arms was consistent across all potential levels of willingness to pay, with the enhanced intervention being cost-effective in at least half of the simulations (Figure 3). Considered together as an “osteoporosis

quality improvement strategy” combining the results of the 2 interventions we studied demonstrated cost-effectiveness in over 80% of simulations (Figure 3).

DISCUSSION

Vertebral fractures incidentally detected and reported on chest radiographs of older patients are common but rarely lead to the diagnosis or treatment of osteoporosis.³⁻⁵ In the only controlled intervention trial that has addressed this problem, we reported that pragmatic osteoporosis interventions directed at physicians or physicians and patients were inexpensive (\$34-\$42 per patient) and very effective (10- to 11-fold improvements in bone mineral density testing or osteoporosis treatment) compared with usual care.⁵ In a formal health economic analysis, we now demonstrate that both interventions dominate usual care, and over a patients' lifetime horizon either intervention would reduce fractures, increase quality-adjusted life expectancy, and save the health care system money. Of the options studied, the base case analysis indicates that the enhanced (physician plus patient) intervention is most effective and most economically attractive.

Perhaps not surprisingly, osteoporosis drug prices had the greatest impact on cost estimates in our sensitivity analysis. More noteworthy, inclusion of a post-fracture all-cause mortality reduction (as recently suggested by meta-analysis of randomized trials²⁸) with bisphospho-

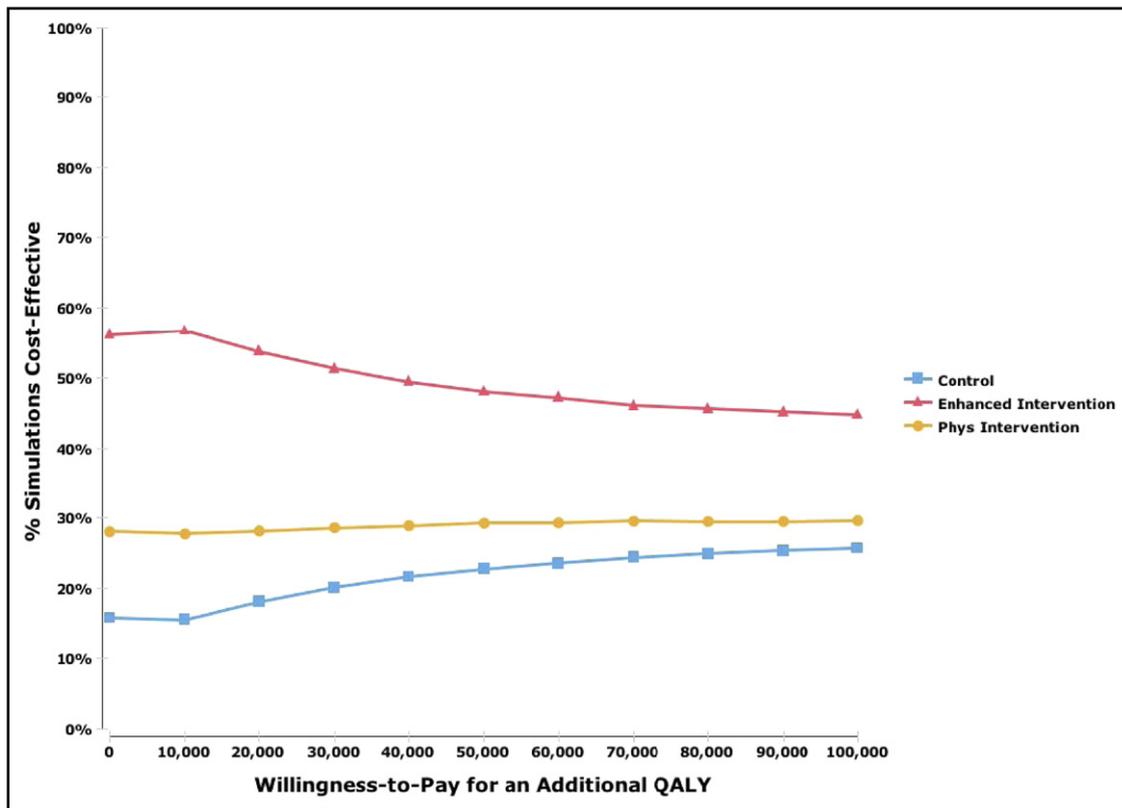


Figure 3 Cost-effectiveness acceptability curve based on simulation results.*

*Monte Carlo simulations (n = 10,000) of incremental cost and QALYs (quality-adjusted life years).

nate treatment had the greatest impact on effectiveness estimates. To our knowledge, modeling mortality reduction has not been considered in previous economic analyses of osteoporosis-related quality improvement interventions, and we conservatively did not consider this in our base case. This finding does suggest to us that, in general, if there is a treatment-related mortality reduction, then most previous analyses (including our base case) have underestimated the cost-effectiveness.

Mortality reductions with treatment notwithstanding, it should be noted that all of the assumptions underpinning our analyses were conservative. We did not incorporate the fact that untreated patients continue to lose bone mass over time and thus have increasing risk of fracture rather than a constant risk; we accorded no benefits to prevention of “asymptomatic” vertebral fractures; we did not include surgical fixation or other procedures for nonhip fractures; and we did not include indirect costs such as productivity losses or informal care-giving that some have suggested are triple the estimates for direct costs attributable to fracture.³⁰

LIMITATIONS

Our work has several major limitations. First, the trial population studied consisted of only 240 patients with 1 year of follow-up; many assumptions, based on expert opinion and literature review, were needed to model lifetime projections.

Second, although it was a controlled trial with blinded ascertainment of endpoints, we acknowledge that it was a nonrandomized study. Reassuringly, the intervention effect sizes that we reported are virtually identical to those derived from a recent meta-analysis of 13 prior randomized controlled trials of osteoporosis quality improvement: pooled 20% (95% CI, 7%-33%) absolute increases in treatment and pooled 40% (95% CI, 32%-48%) increases in bone mineral density testing.² Third, the trial population consisted of osteoporosis treatment-naïve patients with a remote (ie, age indeterminate) vertebral fracture. Thus, our results cannot be easily generalized to those with acute vertebral fractures or the 45% of patients on treatment at the time of chest radiograph who were excluded from the parent trial. Fourth, our entire analytic approach is conditioned upon intervening when vertebral fractures are reported on chest radiograph. Although we did not model it, clearly the most important (and inexpensive) next step should be finding ways to improve reporting rates by radiologists given that fully 40% of moderate-to-severe vertebral fractures remain un-reported.⁴ Fifth, we could not calculate individual patients’ long-term absolute fracture risk using FRAX (University of Sheffield, UK) or other tools, and we used dichotomous “treat versus don’t treat” cut points for bone mineral density test results. That said, the approach we took in our model was evidence based, and more importantly, the approach that was sug-

gested to treating physicians in the trial proper. Last, there may be concerns about external validity given that our study was conducted in one large region of Canada and that all patients had universal health coverage.

CONCLUSIONS

In the absence of any intervention strategies, chest radiograph-detected vertebral fractures are unlikely to trigger the diagnosis or treatment of osteoporosis. Based on a controlled trial and a health economic analysis, our work suggests that pragmatic, scalable, and inexpensive interventions directed at patients with incidental vertebral fractures and their physicians are highly effective at improving quality of osteoporosis care—and in most circumstances, the interventions we studied are likely to be very cost-effective if not cost-saving.

References

- Majumdar SR. A T-2 translational research perspective on interventions to improve post-fracture osteoporosis care. *Osteoporos Int*. 2011; 22(Suppl 3):S471-S476.
- Little EA, Eccles MP. A systematic review of the effectiveness of interventions to improve post-fracture investigation and management of patients at risk of osteoporosis. *Implement Sci*. 2010;5:80-88.
- Delmas PD, Langerjit LV, Watts NB, Eastell R, Genant H; IMPACT Investigators. Underdiagnosis of vertebral fractures is a worldwide problem. *J Bone Miner Res*. 2005;20:557-563.
- Kim N, Rowe B, Raymond G, et al. Underreporting of vertebral fractures on routine chest radiography. *AJR Am J Roentgenol*. 2004; 182:297-301.
- Majumdar SR, McAlister FA, Johnson JA, et al. Interventions to increase osteoporosis treatment in patients with “incidentally” detected vertebral fractures. *Am J Med*. 2012;125:929-936.
- Sonnenberg F, Beck R. Markov models in medical decision-making: a practical guide. *Med Decis Making*. 1993;13:322-338.
- Tosteson AN, Jönsson B, Grima DT, O'Brien BJ, Black DM, Adachi JD. Challenges for model-based economic evaluations of postmenopausal osteoporosis interventions. *Osteoporos Int*. 2001;12:849-857.
- Johnell O, Jönsson B, Jönsson L, Black D. Cost effectiveness of alendronate for the treatment of osteoporosis and prevention of fractures. *Pharmacoeconomics*. 2003;21:305-314.
- Zethraeus N, Borgström F, Ström O, Kanis J, Jönsson B. Cost-effectiveness of the treatment and prevention of osteoporosis—a review of the literature and a reference model. *Osteoporos Int*. 2007;18:9-23.
- Strom O, Zethraeus N, Borgström F, Johnell O, Jönsson B, Kanis J. IOF cost-effectiveness reference model: background document. International Osteoporosis Foundation. Available at: <http://www.iofbonehealth.org>. Accessed September 10, 2012.
- Majumdar SR, Lier DA, Beaupre LA, et al. Osteoporosis case-manager for hip fracture patients: results of a cost-effectiveness analysis conducted alongside a randomized trial. *Arch Intern Med*. 2009;169: 25-31.
- Majumdar SR, Lier DA, Rowe BH, et al. Cost-effectiveness of a multi-faceted intervention to improve quality of osteoporosis care after wrist fracture. *Osteoporos Int*. 2011;22:1799-1808.
- Cadarette SM, Katz JN, Brookhart A, Sturmer T, Stedman MR, Solomon DH. Relative effectiveness of osteoporosis drugs for preventing non-vertebral fracture. *Ann Intern Med*. 2008;148:637-646.
- Song X, Shi N, Badamgarav E, et al. Cost burden of second fracture in the US health system. *Bone*. 2011;48(4):828-836.
- Taylor AJ, Gary LC, Arora T, et al. Clinical and demographic factors associated with fractures among older Americans. *Osteoporos Int*. 2011;22:1263-1274.
- Cranney A, Guyatt GH, Griffith L, Wells G, Tugwell P. Summary of meta-analyses of therapies for postmenopausal osteoporosis. *Endocrinol Rev*. 2002;23:570-578.
- Maclean C, Newberry S, Maglione M, et al. Systematic review: comparative effectiveness of treatments to prevent fractures in men and women with low bone density or osteoporosis. *Ann Intern Med*. 2008; 148:197-213.
- Tonino RP, Meunier PJ, Emkey RD, et al. Skeletal benefits of alendronate: 7-year treatment of postmenopausal osteoporotic women. *J Clin Endocrinol Metab*. 2000;85:3109-3115.
- Bone HG, Hosking D, Devogelaer JP, et al. Ten years' experience with alendronate for osteoporosis in postmenopausal women. *N Engl J Med*. 2004;350:1189-1199.
- Schousboe JT, Nyman JA, Kane RL, Ensrud KE. Cost-effectiveness of alendronate therapy for osteopenic postmenopausal women. *Ann Intern Med*. 2005;142:734-741.
- Alberta Health Care Insurance Plan. Schedule of medical benefits (procedures and price list). Edmonton, AB, Canada; 2009. Available at: <http://www.health.alberta.ca/professionals/SOMB.html>. Accessed September 10, 2012.
- Alberta Health and Wellness. Drug benefits list. Edmonton, AB, Canada; 2009. Available at: <http://www.health.alberta.ca/AHCIP/drug-benefit-list.html>. Accessed September 10, 2012.
- Alberta Health and Wellness. Alberta case costing report. Edmonton, AB, Canada; 2009. Available at: <http://www.health.alberta.ca/newsroom/pub-annual-reports.html>. Accessed September 10, 2012.
- Canadian Institute for Health Information. DAD resource intensity weights and expected length of stay. Ottawa, ON, Canada; 2010. Available at: http://www.cihi.ca/cihi-ext-portal/internet/en/document/standards+and+data+submission/standards/case+mix/bul_31may11_d. Accessed September 10, 2012.
- Cooper C, Atkinson EJ, O'Fallon WM, Melton LJ. Incidence of clinically diagnosed vertebral fractures: a population based study in Rochester, Minnesota, 1985-1989. *J Bone Miner Res*. 1992;7:221-227.
- Statistics Canada. *Life Tables – Canada, Provinces and Territories, 2000-2002* (84-537-XIE). Ottawa, ON, Canada: Statistics Canada; 2006.
- Peasgood T, Herrmann K, Kanis JA, Brazier JE. An updated systematic review of health state utility values for osteoporosis related conditions. *Osteoporos Int*. 2009;20:853-868.
- Bolland MJ, Grey AB, Gamble GD, Reid IR. Effect of osteoporosis treatment on mortality: a meta-analysis. *J Clin Endocrinol Metab*. 2010;95:1174-1181.
- Dong H, Buxton M. Early assessment of the likely cost-effectiveness of a new technology: a Markov model with probabilistic sensitivity analysis of computer-assisted knee replacement. *Int J Technol Assess Health Care*. 2006;22:191-202.
- Cooper MS, Palmer AJ, Seibel MJ. Cost effectiveness of the Concord Minimal Trauma Fracture Liaison service, a prospective controlled fracture prevention study. *Osteoporos Int*. 2012;23:97-107.