ORIGINAL INVESTIGATION

Osteoporosis Case Manager for Patients With Hip Fractures

Results of a Cost-effectiveness Analysis Conducted Alongside a Randomized Trial

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**Background:** In a randomized trial of patients with hip fractures, we previously demonstrated that a hospital-based case manager could increase rates of appropriate osteoporosis treatment to 51% compared with 22% for usual care (P < .001). Alongside that trial, we conducted an economic analysis.

**Methods:** Patients with hip fractures were randomized to usual care (n=110) or a case manager (n=110) and followed up for 1 year. Time-motion studies were used to determine intervention costs. From a third-party health care payer perspective and over the patient’s remaining lifetime, a Markov decision-analytic model was constructed to determine cost-effectiveness of the intervention compared with usual care. Costs and benefits were discounted at 3% and expressed in 2006 Canadian dollars.

**Results:** The intervention cost CAD $56 per patient. Compared with usual care, the intervention strategy was dominant: for every 100 patients case managed, 6 fractures (4 hip fractures) were prevented, 4 quality-adjusted life-years were gained, and CAD $260,000 was saved by the health care system. Irrespective of the number of patients case managed, the intervention reached a break-even threshold within 2 years. The intervention dominated usual care over the entire spectrum of 1-way sensitivity analyses and was cost-saving in 82% of probabilistic model simulations.

**Conclusions:** Compared with usual care, we found that using a case manager for patients with hip fractures increased rates of appropriate osteoporosis treatment. The intervention dominated usual care, and the analysis suggests that systems implementing an intervention similar to ours should expect to see a reduction in fractures, gains in life expectancy, and substantial cost savings.

**Trial Registration:** clinicaltrials.gov Identifier: NCT00175175


OSTEOPOROSIS IS A COMMON AND COSTLY CONDITION, AND IN 2005 IN THE UNITED STATES ALONE THERE WERE MORE THAN 2 MILLION FRACTURES COSTING NEARLY $17 BILLION.1 THE MOST DEVASTATING COMPLICATION OF OSTEOPOROSIS IS HIP FRACTURE. THOSE WHO SURVIVE THEIR HIP FRACTURE STILL HAVE A 20% TO 30% MORTALITY RATE DURING THE NEXT 12 MONTHS, A 2-TO 3-FOLD INCREASED RISK OF FUTURE FRACTURE DURING THE NEXT 5 TO 10 YEARS, AND A 5% TO 10% INCIDENCE OF ANOTHER HIP FRACTURE WITHIN THE YEAR.2,3 TREATMENT WITH THE BISPHOSPHONATES ALENDRONATE SODIUM AND RISREDONATE SODIUM IS ASSOCIATED WITH A 40% TO 60% RELATIVE REDUCTION IN RISK OF FUTURE OSTEOPOROSIS-RELATED FRACTURES,4 AND THE INTRAVENOUS BISPHOSPHONATE ZOLEDRONATE HAS EVEN BEEN ASSOCIATED WITH AN ALL-CAUSE MORTALITY REDUCTION AFTER HIP FRACTURE.5 UNFORTUNATELY, IN THE UNITED STATES, CANADA, AND ELSEWHERE, RATES OF APPROPRIATE OSTEOPOROSIS TREATMENT ARE LESS THAN 10% TO 20% IN THE YEAR AFTER HIP FRACTURE.2,5

In a randomized controlled trial conducted in hip fracture survivors, we demonstrated that use of a hospital-based osteoporosis case manager could lead to a 51% rate of bisphosphonate treatment within 6 months of fracture (vs 22% for controls; P < .001) and result in 67% of patients receiving guideline-concordant appropriate care (vs 26% for controls; P < .001).2 Although the osteoporosis case manager was effective and led to clinically meaningful improvements in quality of care, physicians, policy makers, and payers may remain unconvinced that the intervention would be worth the effort or cost of implementation. Therefore, alongside our randomized trial, we conducted a formal health economic analysis from the perspective of a third-party health care payer.
DESCRIPTION OF THE RANDOMIZED TRIAL

The main study has been published. Briefly, we conducted a population-based study including all 3 hospitals that manage hip fracture in Capital Health (Edmonton, Alberta, Canada). In terms of quality of usual surgical care and outcomes achieved, these study sites are comparable to and representative of other hospitals in Canada. Furthermore, in terms of osteoporosis care before the trial, our rates of undertreatment were identical to those achieved elsewhere in Canada and the United States. Consecutive patients 50 years or older were included. The main reasons for exclusion were residence in a nursing home (35% of all exclusions), refusal (19%), and bisphosphonate treatment (18%). Eligible patients were randomized to the case manager intervention (n = 110) or usual care (n = 110). The primary study outcome was starting bisphosphonate treatment within 6 months. Secondary outcomes included bone mass; NBM, normal bone mass; Rx, treated with alendronate and bisphosphonate treatment (18%). Eligible patients were randomized to the case manager intervention (n = 110) or usual care (n = 110). The primary study outcome was starting bisphosphonate treatment within 6 months. Secondary outcomes included bone mass; NBM, normal bone mass; Rx, treated with alendronate and bisphosphonate treatment (18%).

METHODS

COST-EFFECTIVENESS ANALYSIS

Overview

We hypothesized that the intervention would be cost-effective compared with usual care. Our trial provided data about the population at risk, effectiveness of the intervention, achieved rates of osteoporosis testing and treatment across experimental arms, 1-year treatment persistence, and direct health resource use related to hip fracture. We then used a decision analysis model incorporating Markov processes to simulate the osteoporosis experience of a cohort of patients with hip fracture similar to those in our trial but followed up over the rest of their projected remaining lifetime horizon. Cost-effectiveness was analyzed by estimating incremental cost and effectiveness, based on quality-adjusted life-years gained. Costs were reported from the third-party health care payer perspective, acknowledging that Canadians have universal health care coverage that includes prescription medications for this age group.

Decision Analytic Model

Figure 1 illustrates the 6 osteoporosis-related diagnosis and treatment pathways into which patients were grouped after randomization. The proportion of patients within each group (Table 1) was calculated by multiplying the probabilities along each pathway, with probabilities for the initial distribution ascertained from our trial. Then a Markov process, through which costs and outcomes were modeled, was applied to each of these groups. There were 3 unique Markov processes differentiated by their transition probabilities (Figure 1): patients with low bone mass receiving osteoporosis treatment (M1), patients with low bone mass not receiving treatment (M2), and patients with normal bone mass, ie, not eligible for treatment (M3). The M1 and M3 processes represent guideline-concordant appropriate care for this population.

The structure of the Markov process, shown in Figure 2, was adapted from previous work by Johnell and colleagues and the International Osteoporosis Foundation cost-effectiveness reference model. Our model incorporates 6 health states, simulating the movement of patients from age 74 years until 100 years or death. All patients begin in the post-hip fracture state at home, following discharge from the hospital. Once per annual cycle, a proportion of the cohort moves to one of the other 5 states, in accordance with prespecified transition probabilities. These transition probabilities were derived from fracture rates specific to the type of fracture incurred, presence of low bone mass, age-specific death rates, and (for patients receiving bisphosphonate treatment) fracture type-specific reductions in future fractures. A half-cycle correction was applied to transitions between health states.

Model Assumptions

We made a number of assumptions. Because of the scarcity of data related to osteoporosis treatments and outcomes for men (35% of our cohort), most of the input data in our model relate to women. Patients with hip fractures were considered to...
Fracture Rates. Fracture rates were type-specific and assumed to be constant with respect to age. We used the actual hip fracture rates (5.6%) and derived the rates for spine and wrist fractures (2.6% for each) from a large Canadian cohort study conducted in a similar population. We assumed that these rates represented the annual probability of type-specific fracture following a previous hip fracture for patients with untreated low bone mass. We could not find published refraction rates for patients with normal bone mass, and so we considered them to have the same rates of fracture as patients with low bone mass who were taking alendronate.

Reductions in Fracture Risk With Treatment. Estimates of reduction in fracture risk with alendronate were obtained from systematic reviews. Alendronate was associated with a 49% relative reduction in risk of hip and spine fractures and a 48% reduction for wrist fractures. In the base-case analysis, alendronate treatment was for 5 years’ duration. In the first year of treatment, the beneficial effect of alendronate was assumed to be 50% of the full achievable benefit. However, a further residual positive effect of alendronate treatment was assumed to occur for an additional 3 years after discontinuation. This residual effect was incorporated as a linear but declining benefit that they received no benefit.

Costs. All costs were expressed in constant 2006 Canadian dollars. In the base-case analysis, after the first year, all costs and outcomes were discounted at 3% per annum. The 1-time cost of the intervention was based on time-motion studies conducted in a random sample of patients in the trial. The case manager spent a median of 70 minutes per patient divided among 4 activities, including patient education, arranging for and interpreting BMD tests, providing prescriptions and medication counseling, and communicating with the primary care physician. We used the hourly pay scale for middle experience on our local salary grid for a registered nurse (CaD $32 per hour plus 15% benefits) with an additional 30% overhead. Thus, the case manager intervention cost was CaD $181. Total annual cost of medication was assumed that 80% of patients were discharged to home after a second hip fracture, no additional wrist or spine fractures occurred, although repeat hip fractures were permitted. Last, only the Death state was defined as “absorbing.”

Model Inputs

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Communicating with the primary care physician. We used the hourly pay scale for middle experience on our local salary grid for a registered nurse (CaD $32 per hour plus 15% benefits) with an additional 30% overhead. Thus, the case manager intervention cost was CaD $181. Total annual cost of providing a BMD test with a physician visit was CaD $181.

Costs of Osteoporosis Treatment. We assumed that all treated patients received alendronate sodium, 70 mg per week, for the duration of treatment. The provincial drug plan covers generic alendronate for any elderly person who has had a hip fracture. Of note, as of 2008, generic lower-cost alendronate is available in the United States. Total annual cost of medication and 1 annual physician visit related to osteoporosis evaluation and refilling of prescriptions was estimated at CaD $291 per patient. Patients who discontinued treatment in the first year were assumed to incur the full treatment costs for that year. We assumed that alendronate would generate only trivial direct medical costs related to adverse effects.

Costs of Subsequent Fractures. Table 2 summarizes estimated annual costs for the health states related to treatment of subsequent hip, spine, or wrist fractures. Cost estimates were based on data relating to use of health services and unit values obtained from regional or national databases. Physician fees were obtained from the provincial schedule. We assumed that the additional hip fracture would require surgical fixation and a 16-day hospital stay. A case-mix method was used for inpatient hospital costs, based on relative resource weights and the provincial average cost per weighted case. Orthopedic surgeon and internist costs were based on 1 visit each per day. It was assumed that 80% of patients were discharged to home after hip fracture and 20% to long-term care facilities; costs of long-term care were based on provincial per diem less patient
Mortality Rates. Patients were assumed to have the same risk of death as the general population, except in the year after a hip fracture.\(^2\) We used published life tables for age-specific death rates.\(^3\) Age-specific rates of death for the first year after hip fracture were derived by multiplying age-specific death rates by the excess mortality ratio derived from the International Osteoporosis Foundation cost-effectiveness reference model,\(^1\) which is virtually identical to hip fracture–related mortality rates from our health region.\(^6\)

Health-Related Quality of Life. The age-specific quality of life weights for each health state that we used were based on published utility weights and their proposed multipliers\(^1\) (Table 3). The state with the lowest weight, other than Death, is Spine fracture after Hip fracture.

Deterministic Sensitivity Analyses

Conventional 1-way deterministic sensitivity analyses were conducted to evaluate the robustness of the model with respect to intervention costs (CaD $112 and CaD $168, rather than CaD $36 in the base case), treatment persistence (50%, rather than 85%), treatment costs (increased by 100%, 200%, and 500% over the base-case cost of alendronate), the fracture reduction effects of alendronate (35% vs 50%),\(^\text{10}\) the proportion of patients in the intervention group obtaining a BMD test (40% vs 80%), the duration of treatment (10 vs 5 years), and discount rates (0% and 5%, rather than 3%).

Probabilistic Sensitivity Analysis

To better assess the impact of covariate uncertainty, we conducted a probabilistic sensitivity analysis. Probability distributions were assigned to each of the input variables; the estimated mean values, standard errors, and type of distribution for each variable are available from one of us (D.A.L.). We used a gamma distribution, with a range of 0 to infinity, to generate random values for all unit costs; otherwise a beta distribution was used for all probabilities and utilities. Parameters were defined such that the hierarchical relationship between variables was preserved, but differences between the variables were randomly selected.\(^2\) All analyses were conducted with TreeAge Pro software (TreeAge Software Inc, Williamstown, Massachusetts).

### RESULTS

#### PATIENT CHARACTERISTICS

Study patients were elderly (median age, 74 years), 142 (65%) were women, 210 (96%) were white, and 77 (35%) reported 4 or more comorbidities. By design, none was taking osteoporosis treatment at study entry, although 82 (37%) reported a previous fracture and 58 (27%) reported a previous BMD test. Of note, of the 120 patients who had a BMD test performed, fully 27 (22%) did not have low bone mass at either the hip or the spine.

#### INTERVENTION EFFECT

The case-manager intervention led to a rate of osteoporosis treatment of 51% compared with 22% for controls at 6 months (adjusted odds ratio, 4.7; 95% confidence interval, 2.4-8.9). Of the 80 patients who newly started osteoporosis treatment, 68 (85%) [95% confidence interval, 77%-93%] were still having their prescriptions filled at 1 year. All patients who persisted with treatment reported greater than 80% adherence.

#### COST-EFFECTIVENESS OF THE INTERVENTION (BASE-CASE ANALYSIS)

The base-case analysis is presented in Table 4. The model suggests that, over their lifetime, patients with hip fractures exposed to our case manager intervention would be less likely to incur a fracture than controls: for every 100 patients, approximately 4 hip fractures and 6 fractures in total would be avoided. There was also an asso-

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**Table 3. Quality-of-Life Weights by Health State and Age\(^a\)**

<table>
<thead>
<tr>
<th>Health State</th>
<th>70-79</th>
<th>≥80</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post–hip fracture (initial state)</td>
<td>0.71</td>
<td>0.67</td>
</tr>
<tr>
<td>Additional hip fracture</td>
<td>0.56</td>
<td>0.53</td>
</tr>
<tr>
<td>Spine fracture</td>
<td>0.45</td>
<td>0.42</td>
</tr>
<tr>
<td>Wrist fracture</td>
<td>0.70</td>
<td>0.65</td>
</tr>
<tr>
<td>Post–additional hip fracture</td>
<td>0.64</td>
<td>0.60</td>
</tr>
<tr>
<td>Death</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

\(^a\)Quality-of-life weights vary between 0 (death) and 1 (perfect health) and are adapted from Zethraeus et al\(^1\) and Ström et al.\(^2\)

**Table 4. Costs and Health Outcomes by Intervention Status: Base Case**

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Average Cost(^3)</th>
<th>Average No. of Hip Refractures</th>
<th>Average Total No. of Refractures(^b)</th>
<th>Average QALYs(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>33 043</td>
<td>0.511</td>
<td>0.850</td>
<td>5.958</td>
</tr>
<tr>
<td>Control</td>
<td>35 619</td>
<td>0.554</td>
<td>0.914</td>
<td>5.918</td>
</tr>
<tr>
<td>Difference</td>
<td>−2576</td>
<td>−0.043</td>
<td>−0.064</td>
<td>0.040</td>
</tr>
</tbody>
</table>

Abbreviations: ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life-years.

\(^3\)Lifetime average costs per patient, discounted at 3%. These costs are expressed in constant 2006 Canadian dollars (multiply by 0.88 to convert to US dollars).

\(^b\)Includes hip, spine, and wrist refractures.

\(^c\)Average QALYs per patient, discounted at 3%.
ciated modest increase in quality-adjusted life expectancy (0.04 quality-adjusted life-years gained per patient). Lifetime costs were also less for the intervention group than for controls, with an incremental cost saving of CaD $2576 (US $2267) per patient. Thus, the case manager strategy was dominant; it cost less and added more quality-adjusted life-years than usual care. In addition, a direct financial impact analysis suggests that, irrespective of the number of patients covered by a formal case management program, after 2 years the intervention would reach a break-even threshold, where the average third-party health care payers’ costs per patient would be equal for the intervention and usual-care groups. Beyond 3 years, the average cumulative cost was always lower with the intervention strategy.

**DETERMINISTIC SENSITIVITY ANALYSES**

One-way sensitivity analyses suggest that the results of the base case are robust (Table 5). In all analyses, the intervention dominated usual care even though selected factors were varied substantially. Moreover, in all scenarios the intervention achieved fewer fractures of all types per patient, and specifically fewer hip fractures, compared with usual care. Even increasing the cost of alendronate by 500% yielded eventual savings from the payer perspective. The single factor that had greatest effect on cost and effectiveness was the ability of the intervention program to provide BMD tests. When the proportion of patients in the intervention group obtaining a BMD was reduced from 80% to 40%, incremental savings dropped to CaD $544 per patient.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>No. of Hip Fractures Avoided</th>
<th>Total No. of Fractures Avoided</th>
<th>Incremental Costsa</th>
<th>QALYs Gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base case</td>
<td>0.043</td>
<td>0.064</td>
<td>−2576</td>
<td>0.040</td>
</tr>
<tr>
<td>Intervention costs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100% Increase</td>
<td>0.043</td>
<td>0.064</td>
<td>−2520</td>
<td>0.040</td>
</tr>
<tr>
<td>200% Increase</td>
<td>0.043</td>
<td>0.064</td>
<td>−2464</td>
<td>0.040</td>
</tr>
<tr>
<td>Persistence with treatment (50% rather than 85%)</td>
<td>0.028</td>
<td>0.041</td>
<td>−1569</td>
<td>0.025</td>
</tr>
<tr>
<td>Alendronate sodium price</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100% Increase</td>
<td>0.043</td>
<td>0.064</td>
<td>−2343</td>
<td>0.040</td>
</tr>
<tr>
<td>200% Increase</td>
<td>0.043</td>
<td>0.064</td>
<td>−2111</td>
<td>0.040</td>
</tr>
<tr>
<td>500% Increase</td>
<td>0.043</td>
<td>0.064</td>
<td>−1412</td>
<td>0.040</td>
</tr>
<tr>
<td>Effect of alendronate, 30% reduction</td>
<td>0.032</td>
<td>0.047</td>
<td>−1744</td>
<td>0.029</td>
</tr>
<tr>
<td>Proportion of intervention patients obtaining BMD, 50% reduction</td>
<td>0.011</td>
<td>0.017</td>
<td>−544</td>
<td>0.010</td>
</tr>
<tr>
<td>Treatment duration (10 y rather than 5 y)</td>
<td>0.066</td>
<td>0.098</td>
<td>−3223</td>
<td>0.053</td>
</tr>
<tr>
<td>Discount rate (rather than 3%)</td>
<td>0%</td>
<td>0.043</td>
<td>−3268</td>
<td>0.053</td>
</tr>
<tr>
<td></td>
<td>5%</td>
<td>0.043</td>
<td>−2223</td>
<td>0.034</td>
</tr>
</tbody>
</table>

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

a Costs are expressed in constant 2006 Canadian dollars (multiply by 0.88 to convert to US dollars).

**PROBABILISTIC SENSITIVITY ANALYSIS**

This analysis confirmed the economic attractiveness of the case manager intervention because 82% of the 10 000 simulations we conducted resulted in dominance over usual care (Figure 3). Specifically, Figure 3 graphically illustrates that 8200 of the 10 000 simulations yielded estimates for our case manager intervention that were more effective than usual care, and nearly all of the estimates in this scatterplot are below the horizontal axis, confirming that the intervention strategy is cost-saving for almost every simulation.

**COMMENT**

In a randomized controlled trial, we previously demonstrated that a hospital-based osteoporosis case manager could substantially increase the use of evidence-based osteoporosis testing and treatment when compared with usual-care controls. We then conducted a formal health economic analysis alongside the trial to answer the seldom asked or answered question, “Is it worthwhile?” Our analysis suggests that the answer is yes. The case-manager intervention dominated usual care: for every 100 patients exposed to the intervention, a total of 6 fractures would be prevented, 4 quality-adjusted life-years would be gained, and almost CaD $260 000 (US $230 000)
would be saved by the health care system. The results were robust, and the case-manager intervention remained a dominant strategy compared with usual care over many sensitivity analyses.

Furthermore, a probabilistic sensitivity analysis suggests that more than 80% of different model simulations would still yield a result where our intervention would be both more effective and cost-saving compared with usual care. This is all the more impressive because we used a modeling strategy whereby our assumptions were conservative and biased toward favoring usual care. For example, we assumed no excess mortality in patients after the first year after hip fracture and no excess mortality after spine fracture; we assumed no non–fracture-related mortality benefit in patients with hip fractures treated with bisphosphonates; we assumed no further clinical fractures after a second hip fracture; and we did not acknowledge that untreated patients with osteoporosis will continue to lose bone mass over time and have an even greater risk of future fracture. The robustness of our findings suggests that any quality improvement intervention for patients who survive a hip fracture that can achieve a rate similar to that of bisphosphonate treatment in our randomized trial (51% or more) at a similar cost (CaD $56 or less) would likely be worthwhile.

Several limitations need to be taken into account when acceptance of our findings is considered. First, the trial was conducted in 220 patients and had only 12 months of follow-up. Thus, clinical event rates and utilities were derived from the literature. We did, however, adapt our model from previously published and well-validated reference models for osteoporosis. Second, one-third of our trial population was male, but many inputs related to quality of life and antifracture benefit of bisphosphonates were drawn from literature based almost entirely on postmenopausal women. This is less a limitation of our analyses and more a bias in the scientific literature. Furthermore, because men have greater morbidity and mortality than women after hip fracture, a gain in life expectancy, and substantial cost savings.

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Author Contributions: Study concept and design: Majumdar, Lier, Hanley, Maksymowych, and Juby. Acquisition of data: Majumdar, Lier, Beaupre, and Morrish. Analysis and interpretation of data: Majumdar, Lier, Maksymowych, and Bell. Drafting of the manuscript: Majumdar and Lier. Critical revision of the manuscript for important intellectual content: Majumdar, Lier, Beaupre, Hanley, Maksymowych, Juby, Bell, and Morrish. Statistical analysis: Majumdar and Lier. Obtained funding: Majumdar and Morrish. Administrative, technical, and material support: Beaupre, Bell, and Morrish. Study supervision: Majumdar and Morrish.

Financial Disclosure: Dr Hanley is on the advisory boards of Merck Frosst Canada, Proctor and Gamble Canada, Eli Lilly Canada, Novartis, and NPS Pharmaceuticals. He has participated in conducting clinical trials for Merck Frosst Canada, Proctor and Gamble Canada, Aventis, Eli Lilly Canada, Novartis, NPS Pharmaceuticals, Pfizer, Agen, Wyeth-Ayerst, and Roche. He has received honoraria for speaking from most of these companies.

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