Cost-Utility Analysis of the Ontario Fracture Screening and Prevention Program

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Background: The Fracture Screening and Prevention Program (FSPP), a fracture liaison service (FLS), was implemented in the province of Ontario, Canada, in 2007 to prevent recurrent fragility fractures and to improve post-fracture care. The objective of this analysis was to determine the cost-effectiveness of the current model of the FSPP compared with usual care (no program) from the perspective of the universal public health-care payer (Ontario Ministry of Health and Long-Term Care [MOHLTC]), over the lifetime of older adults who presented with a fragility fracture of the proximal part of the femur, the proximal part of the humerus, or the distal part of the radius and were not taking medications to prevent or slow bone loss and reduce the risk of fracture (bone active medications).

Methods: We developed a state-transition (Markov) model to conduct a cost-effectiveness analysis of the FSPP in comparison with usual care. The model simulated a cohort of patients with a fragility fracture starting at 71 years of age. Model parameters were obtained from published literature and from the FSPP. Quality-adjusted life-years (QALYs) and costs in 2018 Canadian dollars were predicted over a lifetime horizon using a 1.5% annual discount rate. Health outcomes included subsequent proximal femoral, vertebral, proximal humeral, and distal radial fractures. Scenario and subgroup analyses were reported.

Results: The FSPP had lower expected costs ($274 less) and higher expected effectiveness (by 0.018 QALY) than usual care over the lifetime horizon. Ninety-four percent of the 10,000 Monte Carlo simulated incremental cost-effectiveness ratios (ICERs) demonstrated lower costs and higher effectiveness of the FSPP.

Conclusions: The FSPP appears to be cost-effective compared with usual care over a lifetime for patients with fragility fracture. This information may help to quantify the value of the FSPP and to assist policy-makers in deciding whether to expand the FSPP to additional hospitals or to initiate similar programs where none exist.

Level of Evidence: Economic and Decision Analysis Level II. See Instructions for Authors for a complete description of levels of evidence.

The estimated cost of fragility fractures in Canada was $4.6 billion in 2011[1]. Fractures are associated with lower health-related quality of life[2,3] and increased mortality[4,5]. Individuals with fragility fractures are more likely to experience a recurrent fracture[6]. The fracture liaison service (FLS) model of care has been shown to be effective for identifying individuals with fragility fractures and initiating preventive interventions to reduce recurrent fracture(s)[7-10].

One such program is the Fracture Screening and Prevention Program (FSPP), established in 2007 and gradually rolled out in 37 outpatient fracture clinics in the province of Ontario, Canada (population, 14.5 million). As part of the FSPP, fracture prevention coordinators identify, screen, assess, refer, and educate patients with a fragility fracture and provide guideline-based information to their primary care providers. This educational-communication model was implemented in the first phase of the program starting in 2007 and was replaced in 2011 by a more intensive model that added fracture risk assessment and referrals to specialists[11]. The cost-effectiveness of FLS programs was summarized in a 2018 systematic review[12]. Among 23 studies examined, 5 were Canadian and all concluded that the FLS could be a cost-effective option compared

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with no intervention[13-17]. One study examined the educational-communication version of the Ontario FSPP (2008 to 2013) and estimated an incremental cost of $19,132 per quality-adjusted life-year (QALY)[17]. The present cost-utility analysis focused on the more intensive model that began in 2011 and is ongoing. The purpose of this analysis was to estimate the cost-effectiveness of the current FSPP compared with usual care (no program) from the perspective of the public health-care payer in Ontario, Canada.

Materials and Methods

A model-based economic evaluation was conducted following Canadian Agency for Drugs and Technologies in Health (CADTH) guidelines[18] and was reported following the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement[19]. A lifetime horizon was utilized and costs and outcomes after 1 year were discounted at 1.5% annually[18,19].

Target Population and Setting

The target population was patients who were ≥50 years of age, presented to fracture clinics with fragility fractures, and were not currently taking medications to prevent or slow bone loss and reduce the risk of fracture (bone active medication).

Model Structure

A state-transition model was constructed for this analysis using TreeAge Pro 2018 R2 (TreeAge Software), in collaboration with the FSPP operations team, the evaluation team, and clinical experts to ensure that it accurately reflected the clinical pathways of the target population.

A decision tree (Fig. 1) was used to allocate a theoretical cohort of 71-year-old patients with an index proximal femoral, distal radial, or proximal humeral fracture to the FSPP or usual care and model their pathway to pharmacotherapy initiation, specifically risedronate, denosumab, or none at all.

Following pharmacotherapy assignment, patients entered the Markov model (Fig. 2), which used annual cycles and consisted of 5 post-fracture health states and a death state. For each post-fracture health state (first proximal femoral fracture, second proximal femoral fracture, distal radial fracture, proximal humeral fracture, and vertebral fracture), there was a state for those receiving and not receiving pharmacotherapy. Upon entering the model, patients in both the FSPP and usual care arms began in the post-fracture health state of the index fracture. Patients who had a previous fragility fracture (i.e., before the index fracture) were entered into the post-fracture health state of the index fracture.

Patients who had a non-proximal femoral index fracture could transition to any other health state. We assumed that patients with a proximal femoral fracture could only have a subsequent

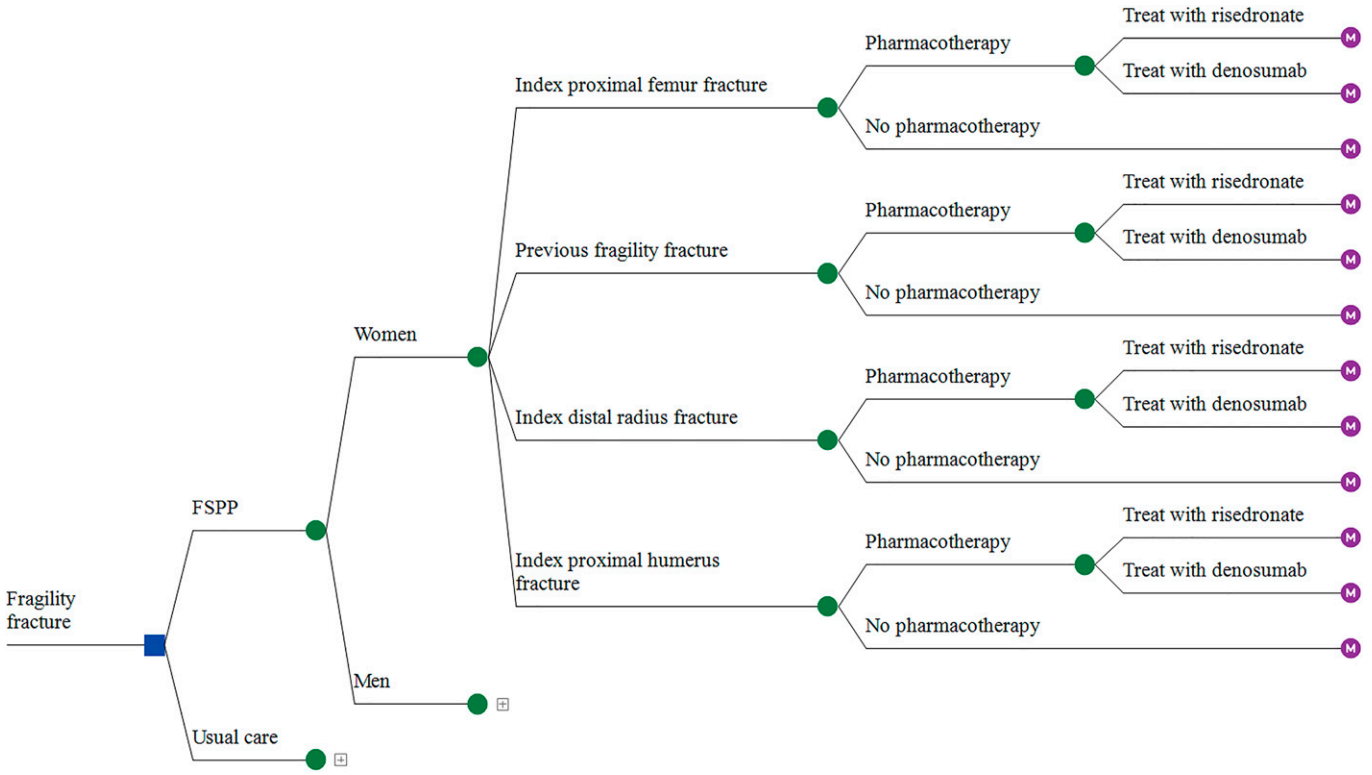

Fig. 1

Decision tree depicting the pathway to pharmacotherapy initiation for the FSPP and usual care. Details are shown for women with fragility fractures receiving the FSPP. Branches emanate identically for men in the FSPP and for usual care as indicated by the plus sign in the box. At the end of the decision tree, patients are either on pharmacotherapy or not and enter the Markov model, indicated by a circle with an M.

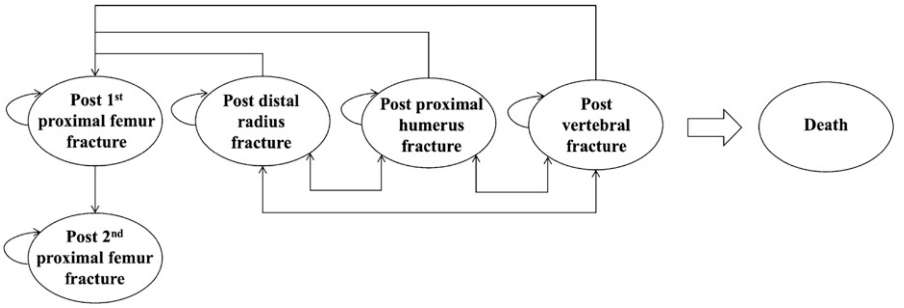

Fig. 2

Markov model structure. Patients may remain in their current health state or transition among the health states after each 1-year cycle. The model ran for 50 years in our reference case to ensure that the entire cohort reached the death state. Arrows represent allowable transitions between health states. The straight arrows indicate a fracture event and the patient moving to a new post-fracture health state, and the curved arrows show a patient remaining in the same health state. Transitions to death, represented by the block arrow, are possible from any health state.

proximal femoral fracture and no subsequent non-proximal femoral fractures. This assumption was made to capture the reduced quality of life and increased mortality associated with proximal femoral fractures. We assumed that patients could have at most 2 proximal femoral fractures in their lifetime.

Outcomes

The primary outcome was the incremental cost-effectiveness ratio (ICER) with effectiveness measured in QALYs. Each health state was associated with a health-related quality of life estimated by a utility weight. Using the utility weight and the length of time spent in each health state, we estimated the total expected QALYs. The secondary outcomes included the estimated life-years and the number of fractures prevented.

Model Parameters

The parameters used in the decision tree are presented in Tables I and II and Appendix A. The Markov model parameters are presented in Table III and Appendix B. All parameters are defined by probability distributions unless otherwise indicated. Some of the parameters were based on the data that the FSPP collects routinely. Data on all 5,264 patients who met inclusion criteria from July 1, 2017, to May 15, 2018, were used and were denoted as the FSPP data.

Distribution of Patients

The cohort entered into the model reflected the distribution of sex, type of index fracture, type of pharmacotherapy received, and mean age of the FSPP data (Tables I and II and Appendix A).

Treatment Uptake and Persistence

The proportion of patients who received pharmacotherapy came from the FSPP data for the intervention arm and the values from the literature were used for the usual care arm[20,21] (Table II). Risedronate and denosumab accounted for 80% of all pharmacotherapies prescribed in the FSPP. We assumed that everyone would be treated with only 1 of these 2 pharmacotherapies in both the FSPP and usual care in the proportions seen in the FSPP.

Patients initiated treatment at the beginning of the model. The proportion of people who persisted with pharmacotherapy was estimated using literature values Appendix B. We assumed that those who persisted with treatment for 1 year remained on treatment for a total of 5 years, if they survived. For the proportions who persisted with risedronate and denosumab at 1 year, we relied on North American data at 63.1% for risedronate and 81.9% for denosumab[22,23]. Following the discontinuation of risedronate for 5 years, a residual treatment effect was applied; no residual treatment effect was applied for denosumab[24,25]. Those who discontinued treatment early received no treatment effect.

TABLE I Distribution of Index Fracture Types

	Women			Men		
		Beta Distribution*			Beta Distribution*	
Parameters for Both Arms	Base Value	Alpha	Beta	Base Value	Alpha	Beta
Index proximal femoral fractures	15.1%†	546	3,073	31.8%†	262	562
Previous fragility fractures	18.0%†	651	2,968	13.6%†	112	712
Index proximal humeral fractures	19.9%†	722	2,897	19.3%†	159	665
Index distal radial fractures	47.0%†	1,700	1,919	35.3%†	291	533

*Beta distributions were specified by the parameters alpha and beta. †FSPP data represent all 5,264 patients who met inclusion criteria for the program between July 1, 2017, and May 15, 2018.

TABLE II Proportion of Patients Who Received Pharmacotherapy

Parameter	Women			Men		
		Beta Distribution*			Beta Distribution*	
	Base Value	Alpha	Beta	Base Value	Alpha	Beta
FSPP						
Index proximal femoral fractures	51.8%†	127	118	48.5%†	49	52
Previous fragility fractures	49.7%†	154	156	53.6%†	30	26
Index proximal humeral fractures	33.3%†	47	94	20.0%†	7	28
Index distal radial fractures	32.7%†	102	210	22.9%†	16	54
Usual care						
Index proximal femoral fractures	16.3%[22]	48	245	16.3%[22]	48	245
Previous fragility fractures	16.3%[22]	48	245	16.3%[22]	48	245
Index proximal humeral fractures	9.4%[21]	42	403	9.4%[21]	42	403
Index distal radial fractures	9.4%[21]	42	403	9.4%[21]	42	403

*Beta distributions were specified by the parameters alpha and beta. †FSPP data represent all 5,264 patients who met inclusion criteria for the program between July 1, 2017, and May 15, 2018.

Pharmacological Treatment Efficacy

Efficacy parameters are presented in Table III. The efficacy of treatment for risedronate was taken from a meta-analysis[26] and that for denosumab was taken from a randomized controlled trial[27].

Recurrent Fracture Risk

Recurrent fracture risk was estimated by age and sex using the incidence of fracture from a study of administrative data of the Minnesota general population[28]. A multiplier was applied to reduce the incidence to only fragility fractures[29]. A relative risk was applied to obtain the incidence of recurrent fragility fractures in patients with an index fragility fracture compared with those with no index fragility fracture[6].

Mortality

All-cause mortality parameters were taken from Statistics Canada life tables[30]. We incorporated excess mortality due to proximal femoral, vertebral, and proximal humeral fractures using age-adjusted relative risks[4]. A second proximal femoral fracture further increased mortality and was estimated using values from the published literature[5].

Costs

We included health-care costs incurred to the Ontario Ministry of Health and Long-Term Care (MOHLTC) Appendix C. All costs were inflated to 2018 Canadian dollars using the Consumer Price Index for health-care services[31]. The excess cost of fractures was obtained from a Canadian study that used provincial administrative data[32]. We used incident fracture costs for year 1 after the fracture and prevalent fracture costs for years 2 to 8 after the fracture and assumed zero cost thereafter.

We applied an initial cost for bone mineral density (BMD) testing by calculating the cost of the diagnostic test plus the cost of a physician visit, assuming that 80% of people will visit their physician after a BMD test[33]. The proportion of people who received a BMD test in the FSPP arm was based on the FSPP data by sex and index fracture. The proportion of people who received a BMD test in the usual care arm by sex and index fracture was obtained from 2005 data included in the

TABLE III Treatment Efficacy

Parameter	Risedronate Group*		Denosumab Group*	
	Base Value	Lognormal Distribution†	Base Value	Lognormal Distribution†
Proximal femoral fracture	0.74[27]	0.59 to 0.93	0.60[28]	0.37 to 0.97
Proximal humeral fracture	0.46[27]	0.23 to 0.93	0.80[28]	0.67 to 0.95
Vertebral fracture	0.64[27]	0.52 to 0.79	0.32[28]	0.26 to 0.41
Distal radial fracture	0.68[27]	0.43 to 1.07	0.80[28]	0.67 to 0.95

*Both groups were compared with placebo. The values are given as the relative risk. †Lognormal distributions were defined using the 95% CI.

TABLE IV Lifetime Cost-Effectiveness Results Comparing FSPP with Usual Care

	FSPP	Usual Care	Incremental Value
Cost*	$117,820	$118,097	−$277
QALYs	9.203	9.185	0.018
Life-years	13.750	13.743	0.008
ICER (incremental cost per QALY)			Dominant†
ICER (incremental cost per life-year)			Dominant†

*Costs represent 2018 Canadian dollars. †Dominance occurs when an intervention has lower costs and higher effectiveness relative to a comparator (i.e., the intervention is the dominant option).

2017 Ontario Osteoporosis Strategy Technical Report[34,35], prior to the FSPP implementation in 2007.

The FSPP costs included salary and benefits of staff, training, and overhead costs. It was assumed that 8,000 patients would be screened per year and cost approximately $143 per patient.

The costs of pharmacotherapy were obtained from the Ontario Drug Benefit Formulary[36] and included an 8% markup fee and a $10 dispensing fee[37-39] The cost for denosumab injection by a health professional was included[33]. We assumed that risedronate was dispensed 4 times per year and denosumab was dispensed 2 times per year.

Utility and Clinical Outcomes

Age and sex-stratified utility weights of the Canadian population were obtained from a literature source that obtained values using the Health Utilities Index Mark 3 instrument[40]. Utility multipliers for each of the post-fracture health states were obtained from the published literature that used the EuroQol-5 Dimensions Questionnaire, mainly in European populations (Appendix C). Utility multipliers differed in the first year and subsequent years after the fracture. The utility multipliers for proximal femoral and distal radial fractures were taken from a systematic review on utility losses due to osteoporotic fractures[2]. Upon consultation with clinical experts, proximal femoral fractures were assigned the lowest health-related quality of life. To maintain this order of severity, the utility multiplier of a vertebral fracture was taken from a study of an Icelandic population[3]. The value for proximal humeral fractures from the Icelandic study was also used[3]. A utility value for a second proximal femoral fracture could not be found in the literature. A value for the first year after a second proximal femoral fracture was estimated by multiplying the utility value for subsequent years of a first proximal femoral fracture by the first year of a proximal femoral fracture. A value for subsequent years after a second proximal femoral fracture was estimated by squaring the utility value for subsequent years of a first proximal femoral fracture[41].

Face validity was confirmed by a clinical expert and all assumptions were approved and are summarized in Appendix D.

Statistical Analysis

The analysis was conducted probabilistically and expected costs and QALYs were reported for the FSPP and usual care[18]. Probabilistic results were generated by performing 10,000 Monte Carlo simulations, varying each parameter over its respective distribution. Cost-effectiveness was determined by the ratio of the incremental costs and QALYs comparing the FSPP with usual care. Results in which the FSPP cost less and had greater effectiveness (QALYs) were considered cost-saving (dominant). When the FSPP was more costly and more effective than usual care, the ICER was considered cost-effective if it was below a willingness-to-pay threshold. Commonly used willingness-to-pay thresholds range from $20,000/QALY to $100,000/QALY[42].

Deterministic 1-way sensitivity analyses were used to assess model validity and identify model-driving parameters by varying parameters over their respective 95% confidence intervals (CIs) or clinically plausible ranges Appendix E. We conducted scenario analyses for the discount rate, the proportion of patients who received denosumab, the length of time that a person was at increased risk of subsequent fracture[6,43], and the proportion of people who persisted with denosumab for 1 year[44]. In addition, subgroup analyses were conducted for women only and starting ages in 5-year increments from ages 50 to 85 years.

Results

The FSPP was less costly (by $274) and more effective (by 0.018 QALY and 0.008 life-year) than usual care from the universal public health-care payer perspective over the lifetime of the patient (Table IV). From the analysis, 18 fractures were modeled to be prevented per 1,000 patients over their lifetime, including 3 proximal femoral fractures, 12 vertebral fractures, 1 proximal humeral fracture, and 2 distal radial fractures.

The results demonstrated that the FSPP was consistently more effective than usual care (Fig. 3). From the cost-effectiveness acceptability curve, at a willingness-to-pay threshold of $0/QALY, the probability that the FSPP was cost-effective compared with usual care was approximately 94% (Fig. 4). At a willingness-to-pay threshold of $20,000/QALY, the probability that the FSPP was cost-effective was approximately 99%.

One-Way Sensitivity Analysis

Although the ICER remained cost-saving for all sensitivity analyses, the greatest impact on the ICER resulted from varying the cost of denosumab, the relative risk of a proximal femoral fracture while an individual is taking denosumab, and the relative risk of a recurrent vertebral fracture given a vertebral fracture.

Scenario Analyses

Scenario analyses were run to assess the assumption that the increased relative risk of a recurrent fracture based on the index fracture applied for 10 years. Results did not change when the relative risk was applied for 12 years (Appendix F). We also considered the uncertainty in the proportion of people who persisted with denosumab for 1 year, the proportion of

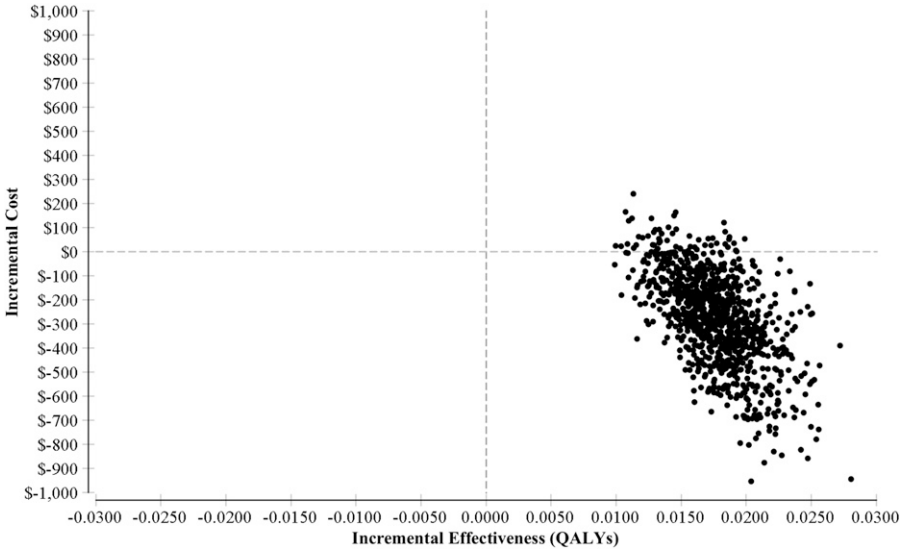

Fig. 3

Incremental cost-effectiveness comparing the FSPP with usual care over the lifetime of the patient from the perspective of the Ontario MOHLTC. The circles in the lower right quadrant represent trials in which the FSPP was less costly and more effective than usual care. The expected incremental cost was $274 less and the expected incremental effectiveness was 0.018 QALY more.

treated patients who received denosumab, and the discount rate. The ICER remained dominant in all scenario analyses Appendix F.

Subgroup Analyses

We ran subgroup analyses for women and different ages at the time of the index fracture. Among women only, the FSPP remained dominant over usual care. The subgroup analyses varying the starting cohort age revealed that, generally, cost-effectiveness improved with age (Appendix G).

Discussion

Based on the model results and the available literature, our analysis suggests that the current Ontario FSPP is cost-saving compared with usual care over the lifetime of the patient. These findings, largely driven by the increased uptake of pharmacotherapy, are consistent with the majority of the literature on FLS programs[12] and were more favorable than the results of the cost-utility analysis of the previous iteration of the FSPP[17]. This could be because our analysis accounted for recurrent proximal femoral, vertebral, proximal humeral, and

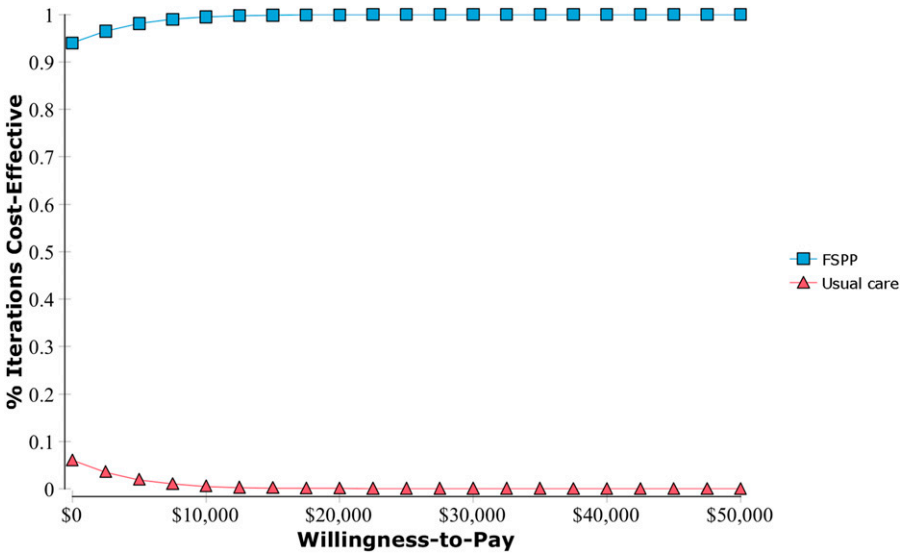

Fig. 4

Cost-effectiveness acceptability curve comparing the FSPP with usual care over the lifetime of the patient from the perspective of the Ontario MOHLTC. The y axis represents the proportion of the 10,000 simulations that fell below a range of willingness-to-pay thresholds indicated on the x axis.

distal radial fractures prevented. The current analysis did not include other aspects of the FSPP such as patient education, vitamin D supplementation, and fall prevention interventions. Future work could examine how these components of the FSPP impact cost-effectiveness. Another possible explanation is the increased intensity of the current program compared with the previous version of the FSPP.

Limitations

There are a number of limitations to consider when interpreting the findings of our study. We did not incorporate potential treatment-related side effects and their costs, which may have overestimated the cost-effectiveness of the FSPP. We included only 2 types of pharmacotherapy and assigned them independent of patient characteristics, unlike the FSPP, which seeks optimal pharmacotherapy for every enrolled patient. We assumed that those who persisted for 1 year with bone active medication would remain on treatment for a total of 5 years, which may have overestimated the cost-effectiveness. However, although persistence has been found to decline over time, a large proportion of patients reinitiate treatment within a short time frame[22,44]. Because the Ontario FSPP has existed since 2007, it was challenging to identify usual care (no program) data. We used a study from 2002 when osteoporosis clinical guidelines differed[21,45,46] and a study from another region where care may differ[20]. Although we assumed that patients with a proximal femoral fracture do not sustain subsequent non-proximal femoral fractures, we expect that this underestimated the number of fractures and therefore provided a more conservative cost-effectiveness estimate. In the absence of available studies, we used post-fracture utility multipliers from studies on European populations. Finally, the incidence of fracture in the general population was taken from an older study from 1999. To estimate the probability of subsequent fractures, we applied a relative risk of a recurrent fracture given a previous fracture. This may have overestimated the incidence of fractures because the general population could have included people with a previous fracture. The findings should be interpreted recognizing these limitations.

Strengths

The main strength of our analysis is that this study incorporated data from a real-world, provincewide, multisite FLS program. Our analysis built upon the previously conducted analysis by developing a new model that included separate health states and estimates the 3 most common index fractures (proximal femoral, proximal humeral, and distal radial) in the FSPP. Additionally, we captured 4 types of subsequent fractures (proximal femoral, vertebral, proximal humeral, and distal radial). We conservatively assumed that the proportion of people persisting with pharmacotherapy at 1 year would be the same in both the FSPP and usual care. The value for persistence with risedronate was based on all Ontarians who received prescriptions for risedronate, of whom only 6% had a prior fragility fracture[22]. This may be a conservative estimate as the proportion of people persisting with treatment in our cohort could be higher, given that all had a prior fracture and received an educational intervention[47]. To account for heterogeneity, we conducted subgroup analyses for women and by starting age. Additionally, we conducted scenario analyses to assess uncertainty in some of our structural assumptions. The results of the study could be applied to other acute care settings considering implementing a similar FLS program.

Conclusions

We conducted a model-based economic evaluation of the Ontario FSPP and found that, within the limitations of the model described above, the program prevents subsequent fractures and is cost-saving compared with usual care over the lifetime of the patient.

Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJS/G428). ■

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