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ORIGINAL ARTICLE

Potential cost-effectiveness for using patient decision aids to guide osteoporosis treatment

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Abstract
Summary We use a model to predict whether using a patient decision aid in patients considering bisphosphonate therapy would be a good use of health resources. We found that if the decision aid improved adherence, and only marginally increased time physicians needed with their patients, then the decision-aid would be cost-effective.
Introduction Oral bisphosphonates have been shown to reduce the risk of osteoporotic fracture. Adherence is crucial but suboptimal. A recent study suggests that a patient decision aid, which facilitates shared decision-making, could be effective in increasing adherence to bisphosphonates. But decision aids come at a cost in terms of additional time spent with physicians. This study considers the emerging evidence on the role of patient decision aids in improving adherence to bisphosphonates and their potential costs to inform future decision-making and research priorities.
Methods We estimate the hypothetical cost-effectiveness of a patient decision aid detailing the benefits and risks of bisphosphonates for osteoporotic patients, from a Canadian healthcare perspective. A previously developed and validated Markov microsimulation model was adapted to include use of a patient decision aid to support the decision of whether to initiate bisphosphonate therapy, and subsequent influence on adherence and future fractures. We considered 2014 costs and benefits in terms of quality-adjusted life-years (QALYs).
Results A patient decision aid that could improve treatment initiation rates or persistence (adherence) by 20 %, or a linear combination of the two, in osteoporotic women aged 70+ over a 3-year treatment period was found to have an incremental cost-effectiveness ratio below $50,000/QALY.
Conclusions Patient decision aids have the potential to be cost-effective in osteoporosis so long as they increase adherence under certain conditions. Funding further research on the long-term effectiveness and costs of a patient decision aid which outlines all treatment options for osteoporosis patients is justified.

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Keywords Adherence · Bisphosphonates · Cost-effectiveness · Osteoporosis · Patient decision aid · Shared decision-making

Introduction

Osteoporosis is an important health problem affecting approximately one in three women and one in five men over the age of 50 [1]. Bone fractures are the major cause of morbidity and mortality associated with osteoporosis. Osteoporosis consequently has a large impact on healthcare budgets [2]. An aging population means this burden is likely to increase, making fracture prevention a priority for most healthcare systems.

Fortunately, effective therapies exist to decrease the risk of fracture. Oral bisphosphonates are the most widely prescribed medication for osteoporosis [3] and have been found to be effective and, in osteoporotic patients over 70, cost-effective [4]. However, adherence to oral bisphosphonates is poor and suboptimal adherence has been shown to lower the efficacy of treatment, resulting in an increased risk of fracture compared to highly adherent patients and higher incremental cost-effectiveness ratios (ICERs) in Ireland [5], with more international evidence cited.

Several potential reasons for suboptimal adherence to oral bisphosphonates have been suggested [6]. These include the cost of prescriptions, drug side effects, complicated dosing regimens, and the fact that the asymptomatic nature of osteoporosis obscures the benefits for patients. Strategies to improve adherence have focused on less frequent dosing regimens, patient education and monitoring, and electronic prescriptions, often with limited impact [7]. An alternative strategy to improve adherence is through the use of patient decision aids [7].

Patient decision aids are an important tool to encourage shared decision-making. It is argued that by informing and engaging patients more fully about the benefits and risks of potential options, and the treatment decision, they will be more likely to adhere to treatment [8, 9] and successfully manage their condition. If patient decision aids could improve adherence and therefore the real-world effectiveness of bisphosphonate therapy, this could lead to downstream cost savings due to fewer fractures. A patient decision aid for bisphosphonate treatment in osteoporosis has been found to be effective in increasing the proportion of patients who remain highly adherent over 6 months in a US trial [10]. However, although decision aids are available [10], the evidence on the cost-effectiveness of patient decision aids, which would support policy-level decisions to introduce them into routine clinical practice, is limited [9].

The aim of this study was to establish the potential cost-effectiveness of a hypothetical patient decision aid outlining the benefits and risks associated with oral bisphosphonate therapy for the treatment of osteoporosis. We consider the Canadian healthcare system where osteoporosis was estimated to cost between $2.3 and $3.9 billion per year in 2010 [2].

Methods

Model overview

To evaluate the cost-effectiveness of a patient decision aid aiming to improve adherence to oral bisphosphonates, we adapted an existing, previously published and validated Markov microsimulation model, developed to assess the cost-effectiveness of a range of pharmacological interventions in osteoporosis [5, 11–13]. The model has a cycle length of 6 months. Costs are expressed in 2014 Canadian dollars (CAD) and, where necessary, were inflated using the Statistics Canada Consumer Price Index annual averages [14]. Effectiveness was measured using quality-adjusted life-years (QALYs). A discount rate of 5 % was applied to both costs and QALYs, and the analysis takes the perspective of the Canadian healthcare payer, including only direct medical costs, in line with recommendations in Canadian health technology assessment [15]. The model takes a lifetime perspective, simulating the impact of fractures on costs and health-related quality of life (HRQoL) until a patient dies or reaches the age of 100. All analyses were conducted using TreeAge Pro 2014 (TreeAge Pro Inc., Williamston, MA).

The model structure and health state transitions are shown in Fig. 1. Patients enter the model fracture free at the age of 70. All patients are assumed to have a BMD t-score ≤−2.5, equivalent to a diagnosis for osteoporosis. Upon entry into the model, individuals receive a densitometry BMD measurement and a physician consultation to discuss results. During this consultation, patients are assumed to receive either a decision aid outlining the benefits and risks associated with oral bisphosphonate treatment or usual care (review of BMD results without estimation of fracture risk). Following this, the patient either receives treatment with oral bisphosphonates or continues with no treatment.

The model contains 10 health states: hip, wrist, clinical vertebral (CV) and other fracture, the four corresponding post-fracture states, no fracture, and dead. Every 6-month cycle, individuals have a probability of transitioning from fracture free to any fracture state or death. From any fracture state, individuals can transition to the relevant post-fracture state, to death or to any fracture state, including the current fracture state if they re-fracture. From post-fracture, individuals can experience any type of fracture, die, or transition to fracture free. Transition probabilities depend on age, prior fractures, and whether the individual resides in the community or long-term care (LTC). Tracker variables record prior fractures, including type and number experienced, and residential status for each individual. These are used to calculate transition probabilities, costs, and utilities.

Fracture incidence

The national incidence of hip fracture in Canada was estimated using the Hospital Morbidity Database (HMDB) in a study by Leslie et al. [16]. Hospitalizations for proximal femoral fracture between 2000 and 2005 were identified and used to derive age-specific hip fracture rates for women and men [16]. National Canadian data on non-hip fracture rates could not be identified, so the incidence of vertebral, wrist, and other fractures was estimated relative to that of hip fractures using relative incidences found in Sweden [17]. Age-specific probabilities of each type of fracture were adjusted to reflect the

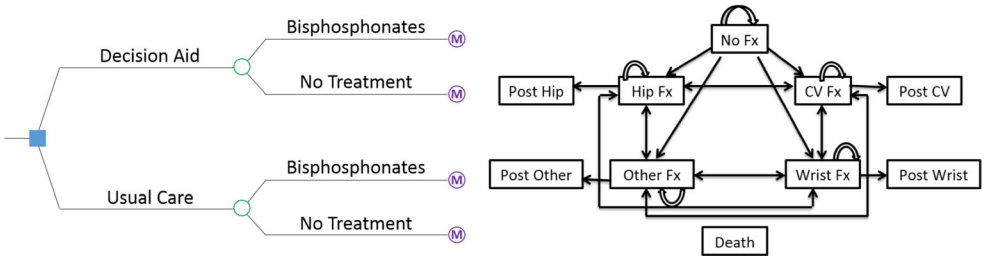

Fig. 1 Model structure and health state transitions. Decision Tree component; Markov Model component. Patients enter the model fracture (Fx) free. Patients can transition to death from any state. From post-fracture, patients can transition to any facture state including no fracture. The Markov model component was redrawn from Value in Health, 2012, 15(5), M Hiligsmann,B McGowan,K Bennett,M Barry,JY Reginster, The Clinical and Economic Burden of Poor Adherence and Persistence with Osteoporosis Medications in Ireland, 604-612. Copyright (2016), with permission from Elsevier

increased relative risk of fracture associated with low BMD [18], both shown in Table 1. Prior hip, CV, wrist, and other fractures within the model were assumed to lead to an increased relative risk of fracture at the same site of 2.3, 4.4, 3.3, and 1.9, respectively [12, 19]. Prior vertebral fractures also result in a relative risk of hip fracture of 2.3 [12]. Increased risks of fracture due to prior fractures were increased by a factor of 1.7 in the first year following fracture [12, 20] and reduced by 10 % for every decade over the age of 70 [12, 21].

Bisphosphonate efficacy

The efficacy of oral bisphosphonates in reducing the risk of fracture was obtained from a meta-analysis of the efficacy of alendronate and risedronate [4]. Patients taking oral bisphosphonates had a relative risk of 0.71 of hip fracture, 0.58 of vertebral fracture, and 0.78 of other fractures. In all but one of the studies, the rate of adverse events was insignificantly different between treatment and placebo arms, justifying the tendency in cost-effectiveness studies of bisphosphonates to ignore adverse events [5]. A period of residual efficacy has been shown following discontinuation from treatment [22]. Therefore, an offset period was included, assuming a linear decline in treatment efficacy for a period equal to that of persistence [5].

Bisphosphonate adherence

In the absence of detailed Canadian data on adherence and persistence, data from the Irish Health Services Executive-Primary Care Reimbursement Services (HSE-PCRS) pharmacy claims database was used [5] (Table 2). All prescription items for the management of osteoporosis in new users aged 55 and over between 2006 and 2009 were identified. This resulted in 70,669 women and 12,613 men, the majority of whom were over the age of 75 [5]. Persistence is defined as the length of time between treatment initiation and discontinuation [5]. The proportion of patients persistent (according to a permissible gap (PG) of 9 weeks to account for monthly dosing regimens) at 6-month intervals up to 3 years was recorded. The proportion of patients considered highly and poorly adherent, within the subgroup of persistent patients, was measured using the medication possession ratio (MPR), defined as the number of days supply of medication received divided by the number of days in the time interval [3]. At each 6-month interval, the proportion of patients who were highly and poorly adherent and the mean MPR of both these groups were also recorded. Patients were considered highly (poorly) adherent if they had a MPR $\geq$ 80 % (<80 %). Similar proportions of women have been estimated persistent to oral bisphosphonates at 6-month intervals in a Canadian economic evaluation [23], using PGs of 30 days or 1.5 times the duration of the prescription, when compared to the proportions of women found persistent in Ireland using a PG of 5 weeks.

The efficacy of bisphosphonates has been shown to decline with suboptimal adherence. Two studies have reported similar estimates. In one, an increased risk of fracture of 1.167 was estimated due to poor adherence (MPR < 80 %) [24]. This figure was similar to a Canadian study which found that the fracture rate in highly adherent patients was 16 % lower using the same MPR cutoff [25]. Cycle-specific treatment efficacy was estimated according to the proportion of individuals persistent and highly and poorly adherent in that cycle, accounting for the offset period. Those who discontinued in the first 6 months of treatment were assumed to receive no efficacy, in line with a lack of findings in this period [26].

Decision aid efficacy

Data on the impact of decision aids on adherence to oral bisphosphonates was limited. Where possible, base-case values were taken from the literature. However, these values were varied to give an idea of the potential cost-effectiveness of a decision aid across a range of adherence improvements.

Table 1 Fracture incidence, costs and disutility, RR of fracture due to low BMD, and general population utility for men and women

Fracture incidence (rate/1000 person years)									Ref
	Women				Men				
Age	Hip	CV	Wrist	Other	Hip	CV	Wrist	Other	[16, 17]
60–64	0.67	0.82	1.88	1.46	0.51	0.63	1.45	1.13	
65–69	1.38	1.54	2.96	3.33	0.90	1.00	1.92	2.17	
70–74	2.65	3.04	3.92	3.23	1.57	1.80	2.33	1.92	
75–79	5.60	3.88	4.00	6.76	2.96	2.05	2.11	3.57	
80–84	10.45	4.91	5.54	8.72	5.47	2.57	2.90	4.56	
85–89	18.48	7.14	6.55	18.61	10.61	4.10	3.76	10.68	
90+	27.14	10.49	9.63	27.33	16.50	6.38	5.85	16.61	
Relative risk of fracture due to low BMD									
	Women				Men				
Age	Hip	CV	Wrist	Other	Hip	CV	Wrist	Other	[18]
60–69	3.39	2.18	1.61	1.90	4.76	2.65	1.81	2.23	
70–79	2.25	1.77	1.43	1.61	3.58	2.39	1.70	2.05	
80+	1.57	1.51	1.30	1.42	2.05	1.93	1.50	1.73	
Direct fracture cost first year (CAD 2014)									
	Women				Men				
	First 6 months (age-dependent)		Extra care first year		First 6 months (age-dependent)		Extra care first year		
Hip	21,301.90–18,313.74		19,446.53		24,593.06–19714.84		19,516.52		[32]
CV	16,779.56–14,425.77				15,618.62–12,374.54				[32, 35]
Wrist	3775.29–3245.70				8025.55–6358.60				[32, 35]
Other	13,102.95–11,264.91				10,887.94–8626.45				[32, 35]
Annual long-term cost of hip fracture (CAD 2014)									[13, 33]
	Women				Men				
>70 years old	29,336.88				29,336.88				
<70 years old	38,137.94				38,137.94				
General population health state utility values									[30]
Age	Mean		SD						
55–64	0.828		0.206						
65–74	0.79		0.237						
75+	0.705		0.245						
Fracture disutility multipliers									[31]
			Hip	CV	Wrist	Other			
First year			0.8	0.72	0.94	0.91			
Subsequent years			0.9	0.93	1	1			

Treatment initiation

Data on the effect of a decision aid for oral bisphosphonates on treatment initiation was obtained from a randomized trial investigating the efficacy of the Osteoporosis Choice Decision aid in the USA [10]. This study included 100 women over the age of 50 with BMD t-scores≤–1. Patients either received the Osteoporosis Choice Decision aid [10] or usual care. The decision aid outlined the individual's 10-year risk of major osteoporotic fracture, the absolute risk reduction expected with alendronate, and the dosing requirements, risks, and costs of weekly oral bisphosphonate therapy. Patients were given the decision aid during consultation with a physician for discussion and then took it home. Usual care involved a review of densitometry results without fracture risk calculation during their consultation with the physician and receipt of an osteoporosis information booklet. Forty-four percent (23/52) of patients randomized to receive the decision aid initiated bisphosphonate therapy compared with 40 % (19/48) in the usual care group, an improvement in initiation of 11.74 % with the decision aid [10] which we used in the base-case (relative risk of treatment initiation of 1.1174). This was varied between no improvement and 20 % improvement in sensitivity analysis.

Table 2 Adherence data used in the model [5]

	Follow-up					
	6 months	1 year	1.5 years	2 years	2.5 years	3 years
Women (%)						
Non-persistence	26.2	35.7	41.9	47.3	51.9	55.0
Poor adherence	13.1	7.7	5.9	4.7	4.1	3.5
High adherence	60.8	56.6	52.2	48.0	43.9	41.5
Men (%)						
Non-persistence	40.0	51.8	58.9	64.0	68.1	70.6
Poorly adherence	10.0	5.1	3.4	2.6	2.3	2.1
Highly adherence	50.0	43.2	37.7	33.5	29.6	27.3

Persistence

Data was only collected to 6 months in this trial, and neither the permissible gap assumed, nor were the proportion of patients persistent in each group at 6 months reported [10]. However, in the wider literature, evidence suggests that patients who receive a treatment they prefer are more motivated to adhere and more willing to tolerate side-effects since they know keeping with treatment could improve health outcomes [27]. It seems reasonable that persistence would therefore be improved using a decision aid for bisphosphonates, but since we do not know by what level, we considered expert opinion and used the model to examine the influence of this assumption in sensitivity analysis. In the base-case, it was assumed that those in the decision aid arm would be 10 % less likely to discontinue therapy in any treatment cycle. This effect was varied between no impact and 20 % in sensitivity analysis.

Adherence

The percentage of patients who remained highly adherent at 6 months (MPR ≥ 80 %) was found to be significantly higher in the decision aid group (100 versus 74 %, $p = 0.009$) [10], suggesting a 35 % improvement. Due to high levels of highly adherent patients in the Irish data, this improvement could not be achieved. Therefore, the improvement in the percentage of patients in the decision aid arm found highly adherent was varied between 0 and 25 %. The mean MPR of each group was assumed to be unchanged.

Since the Osteoporosis Choice trial only followed up to 6 months, there was no evidence available on the longer-term impact of the decision aid on adherence. Informing patients more fully about the benefits and risks of treatment options and involving them more in the decision could increase the likelihood that they will remain adherent. In the base-case, it was assumed that the effect of an informed decision on adherence would remain constant over time. However, due to a lack of evidence about the long-term impact, we considered that the impact of a one-off behavioral intervention might reduce over long time periods. Therefore, in sensitivity analysis, we assumed that the improvements in the proportion of individuals remaining persistent and highly adherent would decline linearly until there was no difference between the treatment groups at 3 years.

Quality-adjusted life-years

QALYs are derived by adjusting duration of life by the HRQoL associated with that health state. To estimate duration of life, we used age-specific mortality rates obtained from Statistics Canada life tables 2009–2011 [28]. Excess mortality following hip and CV fractures was obtained from a meta-analysis [29], which estimated a relative risk of death for women (men) of 4.53 (5.75) in the first 6 months, 1.75 (2.31) 6–12 months after fracture, and 1.78 (1.69) in subsequent years. However, some of this excess mortality may have been due to other comorbidities. Therefore, it was assumed that 25 % of excess mortality was attributable to fracture [13].

HRQoL for QALY calculations is typically expressed using utility values, ranging between 1 (full health) and 0 (death). We used age-specific Canadian general population utility values, measured using the EQ-5D [30], and modified these to consider the impact of fractures from published values in a systematic review [31]. Separate multipliers were provided for the impact on HRQoL in the first year vs subsequent years after fracture (Table 1). A repeat fracture at the same site is assumed to halve the impact on HRQoL of the original fracture [12].

Costs

Fracture

Costs of hip fracture in Canada were based on hip fracture cases in Ontario between 2004 and 2008 identified through medical claims data and the Ontario Drug Benefit Program

[32]. This study reported age-specific costs attributable to hip fracture (the difference in costs between cases and age and sex-matched controls) and the proportion of total mean attributable costs resulting from acute hospitalization and elements of extra care (e.g., same day surgeries, emergency visits, complex continuing care, rehabilitation, LTC, home care, physician services, and prescription medications) in the year following hip fracture. This enabled the estimation of age-specific hospitalization costs in the first 6 months and the attributable cost of extra care in the year following hip fracture.

Long-term costs of hip fracture included the cost of excess admission to LTC. The daily cost of LTC in Canada, obtained from the Ontario Ministry of Health and Long-Term Care, was $160.75 [33]. The rate of institutionalization post-hip fracture was obtained from a Canadian study, which found that 3 months after hip fracture, 6 % of patients under 75, 17 % patients aged 75–84, and 30 % of patients aged 85+ were living in LTC [34]. The model assumed that once residing in LTC, patients remained there for the duration of the model. We assumed that the proportion of admissions attributable to hip fracture declined with age. Therefore, 65 % of the cost of LTC for those below the age of 70 and 50 % of the cost for those 70 and above were assumed attributable to hip fracture [13].

Costs of vertebral, wrist, and other types of fracture were estimated relative to the cost of hip fracture using cost ratios derived from a Canadian study [35]. CV fractures were assumed to incur 40.17 % (33.89 %) of the total attributable first year costs of hip fracture in women (men). The relative costs of wrist and other fractures were 9.04 % (17.42 %) and 31.37 % (23.63 %), respectively. Non-hip fractures were assumed not to incur long-term costs.

Treatment

Treatment with oral bisphosphonates was assumed to last a maximum of 3 years. Unit drug costs were obtained from the Alberta Drug Benefit List [36]. The cheapest unit costs, including generics, for daily and weekly alendronate and risedronate and cyclical etidronate with calcium, were converted into annual costs. The unit costs of other generics of these drugs available in Alberta all fell within the 20 % sensitivity analysis on drug cost, except one risedronate alternative that exceeded this boundary by $0.01. Unit costs in Alberta were also compared to those in Ontario, where unit costs of all generics also fell within the 20 % sensitivity analysis. Unit costs in Alberta were found slightly higher so they were used as a conservative estimate. The proportion of Canadian oral bisphosphonate prescribing allocated to each drug was obtained from 2005 data [37] and used to estimate an average annual drug cost of $221.11, assuming full adherence. This annual drug cost was multiplied by the mean MPR of highly and poorly adherent patients to estimate a cycle- and treatment group-specific drug cost.

During treatment, we assumed that patients were monitored with annual physician visits [13] and DXA scans in years 1 and 3 [13, 38]. The costs of densitometry and physician services were obtained from the British Columbia Medical Services Commission (BC MSC) payment schedule [39]. The costs of a DXA scan for one area and an in-office GP consultation for a patient aged 70–79 were $66.43 and $95.81, respectively.

Decision aid

Use of the decision aid was assumed to result in a one-off cost in the first year. The per patient cost of the decision aid was split into the cost of creating and distributing the aid and the cost of additional physician time required to discuss the aid with patients. Data on the cost of developing and distributing the Osteoporosis Choice decision aid was not provided [10]. Elsewhere, the cost per patient of developing a decision aid has been estimated to be $0.20 USD2000 [40] ($0.27 CAD2014) and the cost of delivering and administering a decision aid (excluding extra physician time) was estimated to be $13.11 ($13.37 CAD2014) per patient [41]. Combining these estimates gives a base-case cost of CAD$13.64 for developing and distributing the decision aid (excluding the cost of extra physician time required for discussion). This cost was varied in sensitivity analysis.

In the Osteoporosis Choice decision aid trial, the decision aid group had a median additional consult time of 3 min compared with usual care [10]. This figure was used in the base-case as it was similar to findings in other evaluations, where median increases in physician time of 2.5 and 2.55 min were recorded [41, 42]. The cost of prolonged counseling was taken from the BC MSC payment schedule for GP services [39]. Prolonged counseling reimbursement, assumed to be a minimum of 20 min, is set at $68.21. Therefore, a cost of $10.23 was assumed to cover the extra 3 min. To reflect the variation in additional physician time (Osteoporosis Choice trial additional time ranged from 2.3 to 27.4 min [10]), sensitivity analysis included 10- and 20-min prolonged counseling sessions.

Analyses

Total discounted costs and QALYs accumulated by the decision aid and usual care arms over the patients' lifetime were estimated and ICERs were calculated. The ICER is defined as the difference in the total costs of the decision aid and usual care strategies, divided by the difference in QALYs. Since we are uncertain of the potential for decision aids to improve

persistence, treatment initiation, and adherence, we ran a series of scenarios using plausible ranges for these parameters. Probabilistic sensitivity analysis (PSA) was used to account for other parameter uncertainty. A cost-effectiveness acceptability curve (CEAC) was constructed to show the probability that the decision aid is cost-effective for the base-case adherence improvement in women, over a range of willingness to pay (WTP) thresholds.

We performed a series of one-way scenario and sensitivity analyses to explore the influence of individual parameters. For this, we chose a base-case scenario: a cohort of 70-year-old women where a decision aid improved the proportion of individuals initiating treatment and remaining persistent and highly adherent by 11.74, 10, and 15 %, respectively. It was assumed that these improvements would remain constant over the 3-year treatment duration.

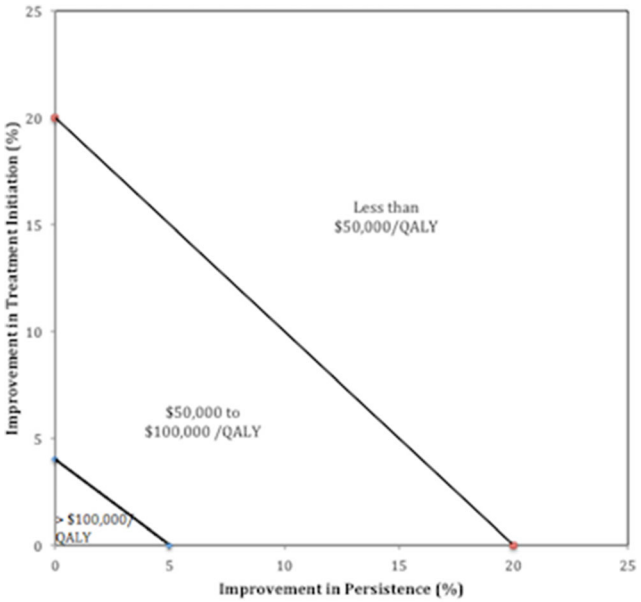

Fig. 2 Improvements in treatment initiation and persistence required for the decision aid to be cost-effective in women at various willingness to pay thresholds in Canada

Results

Main results

The cost-effectiveness of the decision aid was estimated over a range of improvements in treatment initiation and the proportion of patients persistent and highly adherent. Improvements in the rate of treatment initiation and persistence were found to have the largest impacts on cost-effectiveness. Figure 2 shows the improvements in persistence and treatment initiation required by the decision aid in order for it to be cost-effective in women at thresholds of $100,000 and $50,000, assuming the base-case improvement in the proportion of patients highly adherent of 15 %. For the decision aid to be cost-effective at a WTP threshold of $50,000 per QALY, it needs to increase either persistence or treatment initiation by 20 %, or a linear combination of the two.

The base-case resulted in mean (95 % CI) incremental costs and QALYs of $41.51 (26.37, 54.87) and 0.0009 (0.0002, 0.0019) and an ICER of $44,837/QALY in 70-year-old women. The CEAC in Fig. 3 shows the probability that the decision aid and usual care are cost-effective in women over a range of WTP thresholds. At thresholds of $50,000 and $100,000 the chance that the decision aid is the cost-effective option is 57 and 90 %, respectively, suggesting there is still a small chance of usual care being the most cost-effective option even at this high threshold.

Scenario analysis

At a starting age of 60, the ICER increased to $198,926, suggesting that the decision aid would not be cost-effective in younger adults. However, at a starting age of 80, the decision aid was found to dominate usual care, costing less and increasing HRQoL. The decision aid was less cost-effective in men than women with an ICER of $63,814 /QALY.

Sensitivity analysis

One-way sensitivity analyses were performed around the base-case adherence improvements in women aged 70 in order to test the impact of assumptions on the ICER. The results of these sensitivity analyses are shown in the tornado plot in Fig. 4. The parameters that have the biggest impact on results are fracture incidence and fracture costs. Increasing either of these increases the cost-effectiveness of the intervention as more fractures occur in the usual care group. Increases in treatment costs and the cost of the decision aid lower the cost-effectiveness of the intervention as treatment is initiated and adhered to more in the decision aid group, increasing incremental cost. The size of the impact of treatment costs correspond, as expected, with the size of the cost, with drug costs having the largest impact and the cost of developing and distributing the decision aid having the smallest impact. Increases in the cost of LTC or the probability of admission lower the ICER as more LTC admissions occur in the usual care group. When prolonged counseling periods of 10 and 20 min were considered, the ICERs increased substantially to $65,327/QALY and $72,644/QALY, respectively. When assuming that the improvements in adherence associated with the decision aid would decline linearly to no improvement over the usual care group at 3 years, the ICER rose to $54,964/QALY.

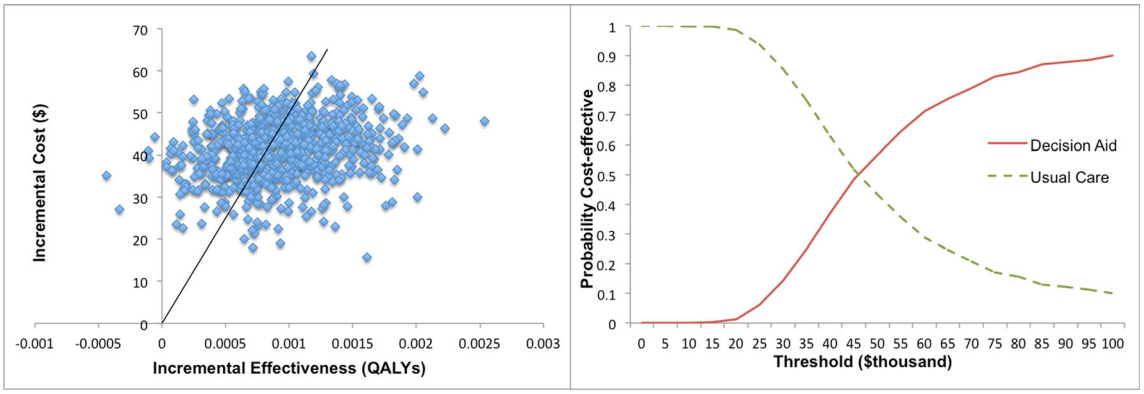

Fig. 3 Base-case cost-effectiveness plane (CEP) and cost-effectiveness acceptability curve (CEAC) in women CEP; CEAC. The cost-effectiveness plane shows the incremental cost and incremental effectiveness of each base-case PSA sample. The trendline shows the points with an ICER of $50,000/QALY. Points to the *right* (*left*) of this would (would not) be cost-effective at this threshold. The CEAC shows the probability that the decision aid and usual care are cost-effective over a range of thresholds

Discussion

Our analysis suggests that a decision aid that provides information about bisphosphonate treatment for osteoporotic women aged 70 could be cost-effective. However, for this to be the case, the decision aid would have to improve treatment initiation or the proportion of patients persistent by 20 %, or a linear combination of the two in this population, over a treatment period of 3 years. Results are sensitive to some key assumptions, including adherence improvements achieved, patient age, and the amount of prolonged counseling required.

To our knowledge, this analysis is the first to estimate the cost-effectiveness of a decision aid for bisphosphonate therapy in osteoporosis. With many patient decision aids currently being developed, the objective of this analysis was to determine how effective a decision aid for bisphosphonate therapy would have to be in order to be a prudent use of healthcare resources. The resources required to implement decision aids is often ignored and perceived to be an important barrier to their use [9].

A study using a previous version of this model with the same adherence data in an Irish setting found a hypothetical adherence improving intervention costing approximately $150 and which improved adherence by 10 % to result in an ICER of €32,906, approximately $50,000 [5]. In our base-case analysis, we assumed that the decision aid would be less effective and less expensive, but found it would result in a similar ICER of $44,837. This and another hypothetical analysis have suggested adherence-improving interventions to be less cost-effective in men and more cost-effective with increasing age [5, 43], in line with our findings. The one-way sensitivity analyses reported in the recent study of a hypothetical adherence-improving intervention in the USA [43] also reported similar effects on the ICER of changes in discount rates, fracture cost, and drug cost, increasing confidence in our results.

A limitation of this study was the availability of Canadian data for some parameters. Incidence of non-hip fractures had to be estimated relative to the Canadian incidence of hip fracture using Swedish data [17]. Although it is fairly common

Fig. 4 One-way sensitivity analysis tornado plot. A tornado plot showing the one-way sensitivity analysis around the base-case of $44,387 in 70-year-old women. *Fx* fracture. *Eff* efficacy. *DA* decision aid

practice to make such assumptions [5], fracture rates can differ substantially between countries [16], and these assumed relationships may not hold. The hip fracture rates used in this study were found to be comparable, if slightly lower, to a recent Canadian economic evaluation [23]. It was shown in sensitivity analysis that lower fracture rates increase the ICER, suggesting that our estimate may be conservative. The fracture disutilities used in the analysis [31] were also not from a Canadian setting. Utility values can vary substantially between countries, samples, and instruments used [31]. While fracture disutility values specific to Canada would have been preferable, the multipliers found were combined with Canadian general population EQ-5D data [30] which should limit the effect of this assumption. Adherence data from Ireland, known to oversample the low income and elderly, was also used [5]. However, the sample size was large and the resulting adherence data was more detailed than provided by Canadian sources found. Finally, despite a substantial proportion of osteoporotic fracture occurring in men, there are still gaps in the evidence for this group. This was the case for the efficacy of bisphosphonates for poorly adherent men and the effectiveness of the decision aid in improving adherence. Therefore, our cost-effectiveness estimate for men is tentative and requires further research. The reduced cost-effectiveness of the decision aid in men is potentially due to the lower incidence of fracture in men, shown to substantially increase the ICER in sensitivity analysis. Future research should work towards filling gaps in available data.

Another limitation was the lack of data surrounding the effectiveness of decision aids in improving adherence to bisphosphonates as well as the costs of developing and using such decision aids. Existing studies of the effectiveness of decision aids for oral bisphosphonates were small, especially once considering adherence, as many chose not to initiate treatment, with short-term follow-up [10, 44]. Neither study detailed the costs of the intervention. Therefore, we considered the cost-effectiveness of a hypothetical decision aid for oral bisphosphonate treatment; at varying levels of treatment initiation, persistence and adherence improvements was analyzed in the hope that this would encourage future work in this area.

An interesting finding is the impact of prolonged counseling on the cost-effectiveness of decision aids. This parameter is often not measured in decision aid trials, but our results suggest it should be considered a key outcome. Time is a key barrier for physicians not employing shared decision-making, particularly in a fee-for-service setting [45]. If physicians are not provided sufficient time and reimbursement for the discussion of a decision aid with their patients, then they may be unwilling to fully involve themselves in shared decision-making. However, if reimbursement is set too high, the intervention will not be cost-effective. More evidence is required on the length of prolonged counseling required for the decision aid to be effective and cost-effective.

Future research should also examine the cost-effectiveness of a decision aid providing patients with all available options for treating osteoporosis. Denosumab, an injectable human monoclonal antibody for treating osteoporosis, has now been approved in Canada, representing another choice in the treatment decision for patients. Adherence to 6-monthly injections of denosumab has been suggested to be superior to oral bisphosphonates [11]. Increasing initiation of denosumab may further reduce fracture rates, but will further increase the already more expensive cost of treatment compared to bisphosphonates. Further research into the cost-effectiveness of a decision aid including denosumab using a model such as this would be of interest.

In conclusion, our study suggests that further development of decision aids for treatments in osteoporosis is warranted. We provide parameters that Canadian decision aid trials should meet in order for them to be cost-effective. These future studies should be of sufficient length and size such that they are powered to detect the impact on comprehensive measures of adherence, including treatment initiation, persistence, and the proportion of patients highly and poorly adherent.

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Compliance with ethical standards

Conflicts of interest Hannah Penton, Mickael Hiligsmann, Mark Harrison, Jean-Yves Reginster, Annelies Boonen, and Nick Bansback declare that they have no conflict of interest.

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