

## Cost-effectiveness of strontium ranelate versus risedronate in the treatment of postmenopausal osteoporotic women aged over 75 years

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### ABSTRACT

**Objective:** To estimate the cost-effectiveness of strontium ranelate in the treatment of postmenopausal osteoporotic women aged over 75 years.

**Materials and methods:** A validated Markov microsimulation model with a Belgian payer's perspective estimated the cost per quality-adjusted life-year (QALY) of a 3-year strontium ranelate treatment compared with no treatment and with the bisphosphonate risedronate. Data on the effect of both treatments on fracture risk were taken from the Cochrane Database of Systematic Reviews. Analyses were performed for postmenopausal women aged 75 and 80 years, either with a diagnosis of osteoporosis (i.e. bone mineral density  $T$ -score  $\leq -2.5$  SD) or with prevalent vertebral fractures (PVF). Parameter uncertainty was evaluated using both one-way and probabilistic sensitivity analyses.

**Results:** Strontium ranelate was dominant (i.e. more effective and less costly) versus risedronate for women with osteoporosis aged over 75 years and for women with PVF aged 80 years. The cost per QALY gained of strontium ranelate compared with risedronate at 75 years of age was €11,435 for women with PVF. When compared with no treatment, the costs per QALY gained of strontium ranelate were €15,588 and €7,708 at 75 and 80 years of age for women with osteoporosis; the equivalent values were €16,518 and €6,015 for women with PVF. Probabilistic sensitivity analyses showed that strontium ranelate was generally more cost-effective than risedronate, in the range of 60% in all cases.

**Conclusion:** The results of this study suggest that strontium ranelate is a cost-effective strategy, in a Belgian setting, for the treatment of postmenopausal osteoporotic women aged over 75 years.

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### Introduction

Osteoporosis is a common disease characterized by low bone mass and deterioration of bone tissues, resulting in increased bone fragility and fracture risk. Osteoporotic fractures are a significant cause of morbidity and mortality, particularly in the developed countries and impose a huge financial burden on health-care systems [1].

Many agents have been developed for the management of postmenopausal osteoporosis. Oral bisphosphonates are well established for osteoporosis management, and have been shown to reduce the risk of vertebral and non-vertebral fractures [2]. However, for daily and weekly formulations, adherence remains poor and limits their benefits in routine clinical practice [3]. Strontium ranelate has recently been introduced for the treatment of osteoporosis. Strontium ranelate was found to simultaneously decrease bone resorption and stimulate bone formation in vitro [4], and to significantly reduce the risk of vertebral and non-vertebral fractures in a wide range of patient

profiles and over a long-period of time [5–8]. In addition to the therapeutic value of a drug, it is becoming increasingly important to evaluate the cost-effectiveness compared with the most relevant alternative treatment. Cost-effectiveness analysis is commonly used to help allocate economic resources in a more efficient manner [9], and the results often guide healthcare decisions and assist physicians in comparing alternative strategies.

Previous studies have shown strontium ranelate to be cost-effective in the treatment of postmenopausal osteoporosis [10–12]. In a Swedish-based study, strontium ranelate was cost-effective compared with no treatment for postmenopausal women with low bone mineral density and who are similar to patients included in the clinical trials or even cost-saving in patients over 80 years old [10]. Recently, long-term treatment with strontium ranelate over 5 years was shown, in a Belgian setting, to be cost-effective compared with no treatment in the target populations for routine use of the product [11], and strontium ranelate was cost-effective in the treatment of established osteoporosis in UK women over the age of 65 years [12]. These studies were however restricted to the comparison of strontium ranelate versus no treatment. For decision-makers, it would be useful to compare strontium ranelate with other treatments, such as oral bisphosphonates. The cost-effectiveness of a treatment should ideally

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be compared with the most relevant alternative [13]. No one comparator has however been universally used in economic evaluations of osteoporosis medications [14]. The main reason is that no direct comparison between treatments is available, making it difficult to assess the relative efficacy. Cost-effectiveness between treatments can only be estimated by making indirect comparisons.

The objective of this study was to assess the cost-effectiveness of strontium ranelate compared with no treatment and with the bisphosphonate risedronate in the treatment of postmenopausal Belgian osteoporotic women over 75 years old. Risedronate is currently registered in Europe for the treatment of osteoporosis and has been shown to significantly reduce the risk of fractures in postmenopausal women with osteoporosis [15–17]. It is currently the only bisphosphonate investigated in a population of elderly women, with hip fracture reduction used as the primary endpoint [15]. Subsequently, risedronate is the comparator of choice for the current study, based on its age-perspective as well as based on the results obtained on hip fracture reduction, in a subset of the TROPOS trial population, including women with osteoporosis and aged over 74 years [7]. The cost-effectiveness of risedronate compared with no treatment in women with osteoporosis has been demonstrated in several countries [18–20], but the cost-effectiveness of risedronate has never been tested against any other active medication, in women aged 75 years and older.

## Materials and methods

### Simulation model

Cost-effectiveness analysis was performed using a Markov micro-simulation model, which has been validated elsewhere [21]. The model has also been used to estimate the effects of changes in baseline population risk and changes in life expectancy on absolute lifetime fracture risks [22], as well as to assess the cost-effectiveness of osteoporosis screening [23,24].

This study was performed from a payer's perspective, including direct healthcare costs paid by the national health insurance and the individual patient's out-of-pocket contribution, in accordance with Belgian methodological guidelines for pharmacoeconomic evaluations [25].

The cycle length of the model was set to 1 year and a patient lifetime horizon was used, as recommended [26,27]. Beginning in the no fracture state, each patient had, every year, a certain probability of the following events: hip, clinical vertebral, wrist, or other fracture; no fracture; or death. The incidence of hip fracture was derived from a Belgian study, and the incidence of other fractures was imputed using fracture rates from other countries, assuming that the ratio between hip and other fractures would be similar between countries [22]. Each state had an associated cost and effectiveness, depending on patient characteristics. Transition costs included direct fracture costs in the year following the fracture and long-term costs beyond the first year for women institutionalized after a hip fracture. The direct cost of hip fracture was derived from Belgian studies [28,29] and the costs of clinical vertebral and other fracture were quantified relative to hip fracture on the basis of their costs [30,31]. Effectiveness was expressed in quality-adjusted life years (QALYs). The QALY estimator is an attractive outcome measurement in the field of osteoporosis because it offers the advantage of capturing the benefits from reductions in both morbidity and mortality [32]. Fracture disutility was modelled as a lower value for QALY and was derived from a systematic review of the literature [33]. Excess mortality was also assumed after hip and clinical vertebral fractures. Discount rates of 3% and 1.5% were assumed for cost (expressed in €2006) and effectiveness, respectively [25]. A detailed description and explanation of the model and data has been published elsewhere [21].

### Target populations

Cost-effectiveness analyses were performed in two populations for whom osteoporosis medications are currently reimbursed in Belgium, i.e. women with a diagnosis of osteoporosis (BMD  $T$ -score  $\leq -2.5$  SD) and women with prevalent vertebral fractures (PVF). In order to accurately reflect the fracture risk in these populations, the risk of first fracture in the general population [22] was adjusted by a relative risk (RR).

The RR for all osteoporotic women was estimated using a previously validated method [34], which estimates the risk of individuals below the threshold value compared with the fracture risk in the general population of that age. This is therefore appropriate for considering a group of individuals such as all women with osteoporosis [34]. BMD values were derived from the recommended NHANES III [35] database at the femoral neck, and one SD decrease in BMD was associated with an RR of 1.8, 1.4 and 1.6 for clinical vertebral, forearm, and other osteoporotic fracture, respectively [36]. For hip fracture, the RR ranged from 3.68 at 50 years to 1.93 at 85 years [37].

The RRs for patients with PVF were 2.3, 4.4, 1.4, and 1.8 for hip, clinical vertebral, wrist, and other fracture, respectively [38]. These RRs were reduced by 10% per decade above the age of 70 years [39]. For women with PVF, no additional increase in fracture risk was assumed for further fractures during the simulation process.

### Interventions

Data on the effect of both treatments on fracture risk were taken from the Cochrane Database of Systematic Reviews [40,41]. (Table 1) Strontium ranelate was assumed to reduce the risk of clinical vertebral fracture by 38% (RR 0.62, 95% confidence interval (CI) 0.47–0.83) and the risk of wrist and other fracture by 19% (RR 0.81, 95% CI 0.66–0.98) versus placebo, using the fracture risk reduction estimated for major nonvertebral fracture [40]. The effect of strontium ranelate on hip fracture was derived from a subgroup of women at high risk of hip fracture (i.e. women aged 74 years and older with a femoral BMD  $T$ -score  $\leq -2.4$  SD according to NHANES III). The RR for hip fracture was therefore 0.64 (95% CI 0.41–0.99). For risedronate, the RRs versus placebo were 0.60 (95% CI 0.50–0.76) for vertebral fracture, 0.74 (95% CI 0.59–0.94) for hip fracture, 0.67 (95% CI 0.42–1.07) for wrist fracture, and 0.80 (95% CI 0.72–0.90) for other fracture [41].

Patients were treated for 3 years as in the clinical trials and the treatment effect was instantaneous. After stopping therapy, the risk reduction was assumed to decline in a linear manner over a 3-year period, denoted the offset time, in line with clinical studies [42,43].

The annual costs of drug therapy were estimated at €512.48 for strontium ranelate (Protelos<sup>®</sup>, €117.94 for a pack of 84 sachets [44]) and at €422.31 for risedronate (Actonel<sup>®</sup>, €97.19 for a pack of 84 tablets [45]). The costs of one yearly physician visit (estimated at €20) and of a BMD measurement at years 1 and 3 (estimated at €47) were also assigned. We also assumed that patients were fully adherent and had no adverse events in the base-case analysis.

**Table 1**

Treatment effect expressed as relative risk at the sites shown and annual cost of therapy.

Parameters	Strontium ranelate	Risedronate
Relative risk of fracture during therapy	[40]	[41]
Hip fracture	0.64 (95% CI 0.41–0.997)	0.74 (95% CI 0.59–0.94)
Vertebral fracture	0.62 (95% CI 0.47–0.83)	0.60 (95% CI 0.50–0.76)
Wrist fracture	0.81 (95% CI 0.66–0.98)	0.67 (95% CI 0.41–1.07)
Other fracture	0.81 (95% CI 0.66–0.98)	0.80 (95% CI 0.72–0.90)
Annual therapy cost	€ 512.48 [44]	€ 422.31 [45]

CI = confidence interval.

### Incremental cost-effectiveness ratio

Results are presented in terms of incremental cost-effectiveness ratio (ICER), which is defined as the difference between strontium ranelate and comparator in terms of costs divided by the difference between them in terms of effectiveness, expressed in QALYs. An ICER represents the additional cost of strontium ranelate per one QALY gained. Although the ICER is increasingly used in the decision-making progress, there is no consensus on the cost per QALY that represents acceptable value for money [46]. The decision-making process is multifactorial and depends on many elements other than efficiency, such as budget impact or preferences. Belgian decision makers have therefore not defined threshold values below which an intervention can be considered cost-effective [47]. Some countries have however defined explicit ICER thresholds. For example, the UK currently uses an explicit threshold value of £20 000 (approximately €23 500) or £30 000 (approximately €35 000) per QALY gained [48].

### Handling uncertainty

Health economic evaluations are inevitably associated with some degree of uncertainty. Uncertainty in the model parameters was explored through one-way and probabilistic sensitivity analyses. One-way sensitivity analyses were used to assess the impact of single parameters on the results and were conducted varying discount rates, fracture costs, fracture risk and fracture disutility. Robustness to changes in therapy cost, treatment efficacy, offset time, and adherence was also examined. Adherence to osteoporosis medications in real-life settings remains poor and may result in a significant change in the cost-effectiveness [21]. Adherence was investigated via persistence (treatment period) and compliance (how appropriately the treatment was correctly taken). We assumed in a sensitivity analysis that adherence to both therapies was similar to that observed for oral bisphosphonates in Belgium [3]. Therefore, 30%, 12%, 18% and 15% of patients discontinued therapy at 3 months, 6 months, 1 year and 2 years, respectively [3]. No treatment effect was assumed for those who discontinued therapy at 3 months and offset time was the same as the period of treatment. Compliance was estimated at 70.5% for persistent women and drug cost and treatment effect were assumed to be proportional to compliance.

Probabilistic sensitivity analyses were undertaken to examine the effect of the joint uncertainty surrounding the model variables. Nearly all parameters were varying simultaneously over plausible range of values. A description of the distributions has been published elsewhere [21]. Log-normal distributions were also assumed for the effect of treatment on fracture risk and the standard deviations were derived from the 95% CIs. Values from each distribution were randomly selected during each of 150 simulations. An ICER was therefore be calculated for each simulation. Cost-effectiveness acceptability curves (CEAC) were then constructed by calculating the proportion of simulations that fall below the different levels of willingness to pay for a QALY. In other terms, CEAC shows the probability that the intervention is cost-effective compared with the alternative, for a range of decision maker's willingness to pay. CEAC has been widely adopted as a method to quantify and represent uncertainty in cost-effectiveness analyses [49].

## Results

### Base-case scenario

The base-case analyses were conducted for women aged 75 and 80 years either with a diagnosis of osteoporosis (BMD *T*-score  $\leq -2.5$  SD) or with PVF. The incremental cost, QALYs, and the cost-effectiveness of strontium ranelate compared with no treatment and with risedronate are shown in Table 2. If strontium ranelate is less

**Table 2**

Incremental cost, QALY, and incremental cost-effectiveness ratio of strontium ranelate versus no treatment and risedronate.

	Strontium vs. no treatment		Strontium vs. risedronate	
	Osteoporosis <sup>a</sup>	PVF <sup>b</sup>	Osteoporosis <sup>a</sup>	PVF <sup>b</sup>
<i>Aged 75 years</i>				
Incremental cost, €	444.3	553.4	-35.7	49.2
Incremental QALY	0.0285	0.0335	0.0056	0.0043
ICER, €/QALY	15,588	16,518	Strontium dominant	11,435
<i>Aged 80 years</i>				
Incremental cost, €	139.05	172.0	-61.6	-90.5
Incremental QALY	0.0181	0.0286	0.0033	0.0031
ICER, €/QALY	7,708	6,015	Strontium dominant	Strontium dominant

ICER = Incremental Cost-Effectiveness Ratio, QALY = Quality-Adjusted Life-Year.

ICER was defined as the incremental cost between strontium ranelate and comparator divided by the incremental QALY between them. ICER was expressed as cost (in €) per QALY gained.

<sup>a</sup> Osteoporosis = BMD *T*-score  $\leq -2.5$  SD.

<sup>b</sup> PVF = prevalent vertebral fracture.

costly and more effective than its comparator, then it is said to be cost-saving, or dominant.

The cost per QALY gained of strontium ranelate decreased progressively with increasing age in both populations and versus both comparators, meaning that strontium ranelate became more cost-effective with increasing age. Strontium ranelate was always cost-effective at a willingness to pay of €20,000 per QALY gained in the target populations and was found to be dominant (i.e. more effective and less costly) compared with risedronate for women with osteoporosis aged over 75 years and for women with PVF aged 80 years. Relative to no treatment, the cost-effectiveness of strontium ranelate did not differ substantially between the two populations, while the cost-effectiveness relative to risedronate was higher for women with PVF than for those with osteoporosis at the age of 75 years.

### One-way sensitivity analyses

One-way sensitivity analyses are presented on Tables 3 and 4, allowing to identify parameters that have substantial impact on the cost-effectiveness. Strontium ranelate becomes more cost-effective

**Table 3**

Incremental cost-effectiveness ratio of strontium ranelate versus no treatment: one-way sensitivity analyses.

	Osteoporosis <sup>a</sup>		PVF <sup>b</sup>	
	75 years	80 years	75 years	80 years
Base case	15,588	7708	16,518	6015
Model parameters				
Discount rates 5% (costs and effects)	18,073	14,377	24,160	9686
0.7 time base case fracture disutility	15,063	14,954	21,522	12,438
0.7 time base case fracture costs	23,003	22,531	25,438	11,730
0.7 time base case fracture risk	30,282	41,523	32,855	22,843
Intervention				
Strontium cost 10% higher	20,441	15,009	20,646	10,635
Strontium cost 10% lower	10,736	406	12,390	1394
Strontium efficacy 10% higher	5154	4777	13,875	571
Strontium efficacy 10% lower	16,984	20,997	19,575	11,150
Adherence similar to bisphosphonates	20,662	14,372	19,243	12,296
Offset time 2 years	15,919	14,952	20,833	11,236
Offset time 4 years	14,395	5282	14,123	CS

CS: cost-saving (i.e. lower cost and greater effectiveness compared with no treatment). Strontium ranelate becomes more cost-effective with a lower ICER, because we are then paying less for a unit of effectiveness.

<sup>a</sup> Osteoporosis = BMD *T*-score  $\leq -2.5$  SD.

<sup>b</sup> PVF = prevalent vertebral fracture.

**Table 4**  
Incremental cost-effectiveness ratio of strontium ranelate versus risedronate: one-way sensitivity analyses.

	Osteoporosis <sup>a</sup>		PVF <sup>b</sup>	
	75 years	80 years	75 years	80 years
Base case	Dominant	Dominant	11,435	Dominant
Model parameters				
Discount rates 5% (costs and effects)	Dominant	Dominant	12,567	Dominant
0.7 time base case fracture disutility	Dominant	Dominant	6008	Dominant
0.7 time base case fracture costs	11,927	6879	22,097	1095
0.7 time base case fracture risk	15,753	15,827	36,159	3736
Intervention				
Strontium cost 10% higher	18,320	21,376	43,595	13,423
Strontium cost 10% lower	Dominant	Dominant	Dominant	Dominant
Strontium efficacy 10% higher	Dominant	Dominant	Dominant	Dominant
Strontium efficacy 10% lower	32,413	29,088	46,500	47,350
Adherence similar to bisphosphonates	1031	Dominant	15,574	Dominant
Offset time 2 years	Dominant	Dominant	13,326	Dominant
Offset time 4 years	Dominant	Dominant	1194	Dominant

Strontium ranelate becomes more cost-effective with a lower ICER. Strontium ranelate is said to be dominant when it is less costly and more effective than risedronate.

<sup>a</sup> Osteoporosis = BMD T-score ≤ -2.5 SD.

<sup>b</sup> PVF = prevalent vertebral fracture.

with a lower ICER, because we are then paying less for a unit of effectiveness.

The ICERs of strontium ranelate compared with no treatment (Table 3) were slightly sensitive to fracture cost and fracture disutility, and quite sensitive to discount rates and baseline fracture risk. Small changes in therapy cost, fracture efficacy and offset time resulted in a moderate increase in the cost per QALY gained. The cost-effectiveness increased substantially when assuming adherence similar to that observed for bisphosphonate therapies.

The cost-effectiveness of strontium ranelate versus risedronate was shown to be highly sensitive to baseline fracture risk, cost differential between therapies and the effect of strontium ranelate on fracture risk (Table 4). When assuming that the cost of strontium ranelate was 10% lower or that the fracture risk reduction with strontium ranelate was 10% higher, strontium ranelate was dominant in all cases while the cost per QALY greatly increased when assuming a 10% increase in strontium ranelate cost or a 10% decrease in fracture risk reduction. Adherence to treatment had a modest effect on the cost-effectiveness between therapies.

*Probabilistic sensitivity analyses*

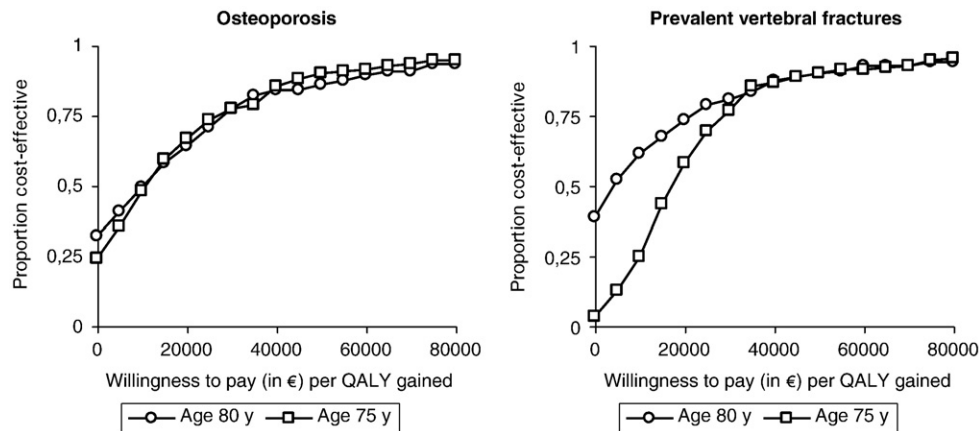
CEACs show the probability that strontium ranelate is cost-effective as a function of the decision maker's willingness to pay per

one QALY. At an assumed willingness to pay of €40,000 per QALY, there were at least 84.0% of chance that strontium ranelate would be cost-effective compared with no treatment, for both populations and ages (Fig. 1), i.e. the ICER of strontium ranelate fall below the threshold value at least 126 times out of the 150 simulations. For women aged 80 years, strontium ranelate was cost-saving (i.e. ICER being below €0) in 32.0% and 38.7% of the cases, for women with osteoporosis and women with PVF, respectively.

Relative to risedronate, the probability that strontium ranelate was cost-effective remained stable with decision-maker's willingness to pay per QALY gained (Fig. 2). At the age of 75 years and with a willingness to pay of €40,000 per QALY gained, strontium ranelate was cost-effective in 59.3% and 62.0% of the cases for women with osteoporosis and women with PVF, respectively. These probabilities increased to 65.3% and 64.0% for women aged 80 years. The probabilities of being cost-saving (i.e. ICER below €0) were 52.0% and 61.3% of at the ages of 75 and 80 years for women with osteoporosis respectively, while these values were 45.3% and 61.3% for women with PVF.

**Discussion**

Health economic evaluation has an increasingly important role to inform policy makers about the relative efficiency of competing



**Fig. 1.** Cost-effectiveness acceptability curves for strontium ranelate compared with no treatment. QALY = Quality-Adjusted Life-Year. Curves show the probability that strontium ranelate is cost-effective compared with no treatment as a function of the thresholds willingness to pay per QALY. Cost-effectiveness was expressed as incremental cost per QALY gained.

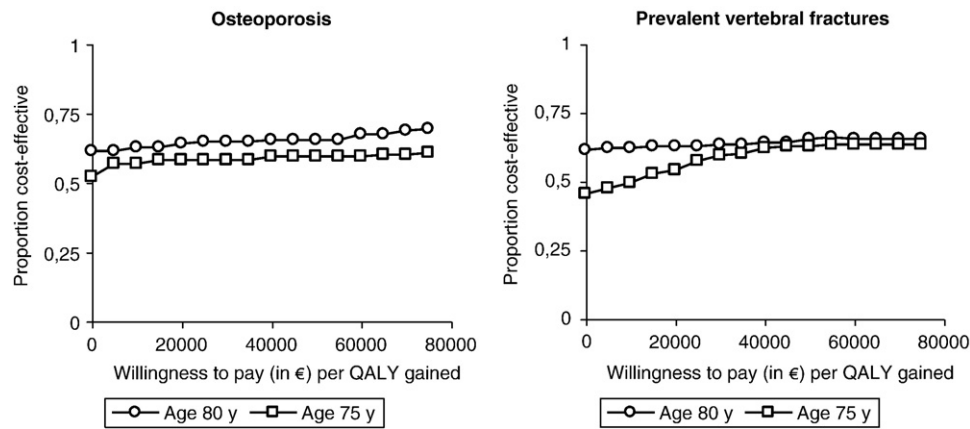


Fig. 2. Cost-effectiveness acceptability curves for strontium ranelate compared with risedronate. QALY = Quality-Adjusted Life-Year. Curves show the probability that strontium ranelate is cost-effective compared with risedronate as a function of the thresholds willingness to pay per QALY. Cost-effectiveness was expressed as incremental cost per QALY gained.

interventions and to assist physicians in determining the most appropriate treatment for their patients. In this study, we estimated the cost-effectiveness of strontium ranelate, compared with no treatment and with the bisphosphonate risedronate. Strontium ranelate is a recent antiosteoporotic agent that has been shown in clinical studies to be a safe and effective means of reducing the risk of fractures in clinical studies [5–8].

Previous studies have investigated the cost-effectiveness of strontium ranelate [10–12]. These analyses have shown strontium ranelate to be cost-effective in the treatment of postmenopausal osteoporotic women, but were restricted to the comparison of strontium ranelate versus no treatment. Another study found scenarios where strontium ranelate can be used cost-effectively compared with the bisphosphonate alendronate [50]. However given the probabilistic sensitivity analyses conducted, this study concluded that strontium ranelate appears to be less cost-effective than the bisphosphonate alendronate [50]. The current study estimated, for the first-time ever, the cost-effectiveness of strontium ranelate compared with the bisphosphonate risedronate.

The principal finding of our study is that strontium ranelate appears to be cost-effective compared with no treatment and with the bisphosphonate risedronate in women aged over 75 years in which postmenopausal osteoporotic treatment is reimbursed. The cost-effectiveness improves with increasing age, and sensitivity analyses showed that the results were sensitive to the effect of strontium ranelate on fracture risk.

Several treatments are currently available for the management of postmenopausal osteoporosis. However, oral bisphosphonates are the most widely prescribed drugs, worldwide. Therefore, we selected oral risedronate (i.e. an oral bisphosphonate available with a weekly formulation) as the comparator to strontium ranelate, in this particular study because strontium ranelate and risedronate are, currently, the only two anti-osteoporosis drugs that were specifically investigated, for their effect on hip fracture, in women aged 75 years and over [7,15]. Therefore, the results obtained, in this elderly population, by the comparison between strontium ranelate and risedronate provides additional information compared to previous comparisons of strontium ranelate versus no treatment or strontium ranelate versus alendronate. Actually, the clinical trials assessing the efficacy of alendronate in osteoporosis were conducted in younger population, with hip fracture being only regarded as a secondary endpoint [51].

The lack of direct head-to-head trials between strontium ranelate and risedronate makes it difficult to determine the relative efficacy between these treatments. Indirect comparison between drugs of efficacy may therefore be unreliable because of different baseline

characteristics of population studied and overlapping confidence intervals for the effect of treatment [52]. Moreover, sensitivity analyses showed a relative uncertainty in the results. One-way sensitivity analyses suggested that the results were very sensitive to the effect of strontium ranelate on fracture risk and to the cost differential between therapies. And probabilistic sensitivity analyses showed that, although strontium ranelate was generally more cost-effective than risedronate, these probabilities did not exceed 65%. Strontium ranelate is therefore not highly cost-effective compared with risedronate. It would be more reasonable to conclude that strontium ranelate seems at least as cost-effective as risedronate in the target populations. A more precise conclusion would require the completion of head-to-head trials between treatments with clinically relevant outcomes [53].

The current study was restricted to women aged over 75 years with high risk of fractures, in order to closely match the population included in the post-hoc analysis. The primary endpoint of the TROPOS trial was the reduction in nonvertebral fractures. At the request of the European Regulatory Agency, a *post hoc* analysis was conducted to see whether hip fractures were also significantly reduced in a subset of the population, aged 74 years and over and presenting with a low bone mineral density at the level of the femoral neck. Whereas one cannot exclude that the results from this *post hoc* analysis could be extrapolated, integrally, in the simulated populations, and that, subsequently, our results present a “best-case scenario”, we used these figures in our cost-effectiveness analysis, since no other data are currently available and that the simulated populations are closed to that included in the *post hoc* analysis.

Our results were therefore limited to the target populations and may not be generalized to other patient populations. Further research is needed to investigate the cost-effectiveness of strontium ranelate in other populations (e.g. younger women, women with osteopenia or at the threshold for osteoporosis) and also in other jurisdictions. There are many reasons to suppose why the results may not be easily transferable [9]. These include differences in fracture incidence, in fracture cost, in pharmacoeconomic guidelines or in therapy cost. However, jurisdictions with similar characteristics than those retained in this analysis would obtain similar results.

There are other potential limitations related to model assumptions and inputs. So, fracture costs were limited to direct fracture costs in the year following the fracture and long-term costs for women institutionalized after a hip fracture. Other fractures were conservatively assumed to be associated with no long-term costs. Moreover, adherence to strontium ranelate in real-life settings has not yet been documented. We therefore assumed in a sensitivity analysis that

adherence would be similar to that observed for oral bisphosphonates in Belgium, and that drug cost and treatment effect was proportional to compliance. Further researches are needed to assess adherence to strontium ranelate in real-life settings and on the relationship between compliance and fracture risk.

In conclusion, this study suggests that strontium ranelate is a cost-effective strategy, in a Belgian setting, for the treatment of postmenopausal osteoporosis women aged over 75 years.

#### Conflict of interest statement

Mickaël Hiligsmann has received research grant from Amgen, Novartis and Servier and lecture fees from Servier.

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