



Original Article

Cost-utility and Budget Impact Analysis of Primary Prevention With Alendronate of Osteoporotic Hip Fractures in Catalonia[☆]

María J. Pueyo,^{a,*} Marta Larrosa,^a Xavier Surís,^a Antonio J. Garcia-Ruiz^b

^a Plan director de enfermedades reumáticas y del aparato locomotor, Departament de Salut, Generalitat de Catalunya, Barcelona, Spain

^b Cátedra de Economía de la salud y uso racional del medicamento, Universidad de Málaga, Málaga, Spain

ARTICLE INFO

Article history:

Received 24 November 2011

Accepted 18 January 2012

Keywords:

Alendronate
Budgetary impact
Cost-utility
Drug prevention
Health economics
Hip fracture
Osteoporosis

ABSTRACT

Objectives: To determine whether primary drug prevention of osteoporotic hip fracture is a useful measure in Catalonia and what would be their budgetary impact.

Materials and methods: We performed a cost-utility social perspective study with a time horizon of 10–20 years. Univariate sensitivity analysis was performed. Doing nothing is compared with an intervention that includes screening for osteoporosis in women >64 years and in those diagnosed and who received treatment with generic alendronate for 10 years. Decision trees are developed for groups of 65–69, 70–74 and 75–79. HF data are from 2009 hospital discharges. Costs are derived from fees paid by public insurance.

Results: In 2009 there were 9262 HF. The direct cost was €55 million (€5943.4/patient). The total cost was €227 million for 10 years. The intervention dominates in all age groups in a 20-year perspective. In any horizon and age group, the different scenario puts the value per QALY below or within the proposed values for Spain. The budgetary impact is estimated at €8.9 million which increased by 31% the actual direct cost, and 0.5% of the public pharmacy budget. Considering the total costs and the prospect of 20 years, annual savings of 7.4 million € were seen.

Conclusions: The prevention of HF with alendronate in osteoporotic women >64 years is cost-useful in the long term (20 years) with a low budgetary impact in the 75–79 year group.

© 2011 Elsevier España, S.L. All rights reserved.

Análisis de coste-utilidad e impacto presupuestario de la prevención primaria con alendronato de la fractura osteoporótica de cadera en Cataluña

RESUMEN

Objetivos: Determinar si la prevención farmacológica primaria de la fractura osteoporótica de cadera es una medida coste-útil en Cataluña y conocer cuál sería su impacto presupuestario.

Material y métodos: Se realiza un análisis de coste-utilidad con perspectiva social y horizonte temporal de 10 y 20 años. Análisis de sensibilidad univariante. Se compara no hacer nada con una intervención que incluye el cribado de osteoporosis en mujeres > 64 años y, en las diagnosticadas, el tratamiento con alendronato genérico durante 10 años. Se elaboran árboles de decisión para los grupos de 65–69, 70–74 y 75–79 años. Los datos de FC provienen de las altas de 2009. Para los costes se utilizan las tasas pagadas por la aseguradora pública.

Resultados: En 2009 hubo 9.262 FC. El coste directo fue de 55 millones de euros (5.943,4 €/paciente). El coste total es de 227 millones de euros en 10 años. La intervención domina en todos los grupos de edad en una perspectiva de 20 años. En cualquier horizonte y grupo de edad, los diferentes escenarios sitúan el valor por AVAC inferior o dentro de los valores propuestos para España. El impacto presupuestario se calcula en 8,9 millones de euros que incrementa en un 31% el coste directo actual, y en un 0,5% el presupuesto público de farmacia. Considerando los costes totales y la perspectiva de 20 años, el ahorro anual es de 7,4 millones de euros.

Conclusiones: La prevención de FC con alendronato en mujeres osteoporóticas > 64 años es coste-útil a largo plazo (20 años) con bajo impacto presupuestario en el grupo de 75–79 años.

© 2011 Elsevier España, S.L. Todos los derechos reservados.

Palabras clave:

Alendronato
Coste-utilidad
Economía de la salud
Fractura de fémur
Impacto presupuestario
Osteoporosis
Prevención farmacológica

[☆] Please cite this article as: Pueyo MJ, et al. Análisis de coste-utilidad e impacto presupuestario de la prevención primaria con alendronato de la fractura osteoporótica de cadera en Cataluña. Reumatol Clin. 2012;8:128–34.

* Corresponding author.

E-mail address: mjpuoyo@catsalut.cat (M.J. Pueyo).

Introduction

Osteoporosis is a metabolic bone disease characterized by low bone mass and microarchitectural deterioration of bone tissue leading to increased risk of fractures. The most common fractures are distal forearm, spine and hip fractures (HF). Catalonia is the region with the highest incidence of HF in Spain.¹ According to the recorded minimum set of hospitalization database (MDS) of 2008,² the fracture rate was 74.2 cases per 10,000 in persons over 64 years of age. HF usually occurs in older people and causes major economic costs and an even greater loss of quality of life.³ The diagnosis of osteoporosis can be performed by densitometry which should be performed only in those who have risk factors for osteoporosis. Among the different existing criteria, we selected the criteria proposed by the Agency of Information, Evaluation and Quality in Health in Catalonia (AIEHQC) collected in Table 1.⁴ These criteria were developed as a proposal of the Department of Health and are directed at health care professionals in our community. Alendronate is the drug of choice for osteoporosis and is effective in preventing vertebral and nonvertebral fractures, especially in women aged 70 years or older at high risk of fracture. The relative risk (RR) of HF in postmenopausal women after treatment with this bisphosphonate, with calcium and vitamin D (Ca+ DV), is 0.61 (level of evidence 1++ as indicated in a recent systematic review⁵). Treatment with bisphosphonates should be maintained for a minimum of about 5 years, stretching up to 7–10 years. Systematic review of economic studies conducted by García-Ruiz et al.⁵ shows that drug treatment of osteoporosis, especially with alendronate, is cost-effective for people with major risk factors: higher age, low bone density and a history of previous fractures. It is currently difficult to clearly define what is the cutoff age at which treatment should be started. Because drugs for treating osteoporosis can reduce the incidence of HF, the objective of this study was to determine the rate of HF in Catalonia and to determine whether primary drug prevention with alendronate for HF can be a measure implemented in our public health system based on cost-utility criteria, and which would counteract the diseases' budgetary impact.

Table 1
Densitometry Indication Criteria. AIEHQC.

Densitometry Indicate Whether	
2 or more RF	4 or more RF
Elevated risk	Moderate risk
Age over 70	Female
BMI <20 or weight <40 kg	Smoker
Loss of over 10% of weight	Low sunlight exposure
Physical inactivity	Family history of osteoporotic fracture
Oral steroids	Iatrogenic menopause
Antiepileptics	Late menarche
Primary hyperparathyroidism	No breastfeeding
Diabetes mellitus 1	Poor calcium intake
Anorexia nervosa	Non specified hyperparathyroidism
Pernicious anemia	Hyperthyroidism
Prior osteoporotic fracture	Type 2 Diabetes mellitus
	Rheumatoid arthritis

Source: Estrada et al.⁴

Materials and Methods

In the cost-utility analysis we compared 2 alternatives: the current strategy of “no prevention” versus the alternative “intervention” based on drug prevention in women aged 64 years or older diagnosed with osteoporosis by densitometry. A societal perspective was adopted and the time horizons considered were 20 and 10 years. We used a reduction rate of 5%. In the description of the budgetary impact we adopted the payer's perspective.

Description of Alternatives

Description of Current Situation

In 2009 there were 9262 hospital admissions of people over 64 due to HF in Catalonia, and 72.5% were female with a mean age of 80.8 years. The average stay was 12.5 days and 29.4% of cases were discharged to a geriatric hospital. Hospital mortality was 4.7%. Studies in our country estimate that about 30% of patients lose their autonomy and become dependent after FC.³

Description of the Intervention

The intervention proposed in this study consisted of an osteoporosis screening by densitometry in women 65 years or older who presented risk factors defined by the AIEHQC (Table 1). Women in whom osteoporosis was diagnosed were given generic alendronate (70 mg per week) plus Ca+ vitamin D daily for 10 years.

Base Case and Uncertainty Analysis

The analysis was conducted in the following age groups: 65–69 years, 70–74 years and 75–79 years of age. For the base case we calculated a 100% compliance and a fracture risk reduction of 40% for the first year, with persistence of the effect during the 10 years of treatment. An example of a decision tree is presented in Fig. 1. In the uncertainty analysis we have considered the following scenarios:

- A decrease in compliance to 60%.
- A 15% reduction of the protective effect of alendronate at 10 years.
- Both effects.
- The administration of alendronate for 7 years with a fracture risk reduction of 15% in 10 and 20 years.
- A reduction rate of 3%.

Clinical Variables and Quality of Life

Prevalence of Osteoporosis and Hip Fracture Incidence

The prevalence of osteoporosis in the Spanish female population, measured by axial densitometry,⁶ and the incidence of HF are shown in Table 2. Among women over 64 years of age with osteoporosis, the fracture RR is 1.7 (95% CI, 1.4–2.2).⁷ The distribution of HF between osteoporotic and non-osteoporotic women (Table 2) was calculated using the following formulas:

$$I_{total} = I_{OP} + I_{no OP}$$

$$RR = I_{OP} / I_{no OP}$$

$$I_{no OP} = I_{total} / (RR + 1)$$

As I_{OP} the incidence in women with osteoporosis and $I_{no OP}$ incidence of OP in osteoporotic women.

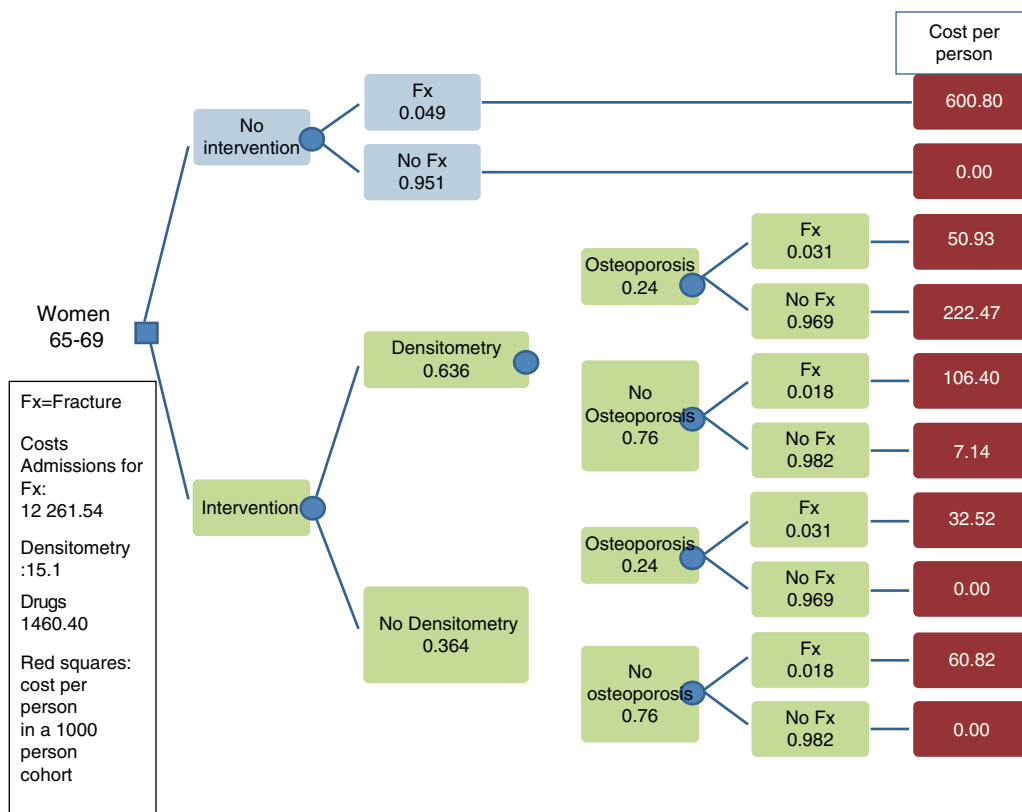


Fig. 1. Decision tree in women aged 65–69. Social perspective. 20-year time horizon.

Table 2 Prevalence of Osteoporosis by Axial Densitometry as Determined in Spanish Women; Incidence of HF in Women (2009) Based on Hospital Admission Records; Risk of HF in Women ≥65 Years at 10 and 20 Years and Estimated HF Distribution in Osteoporotic and Nonosteoporotic Women (Adopting an RR of 1.7).

Age	Prevalence of Osteoporosis in Women (%) ^a	Incidence of HF in Women (per 100) ^b	Risk of HF at 10 Years (%) ^c	Risk of HF at 20 Years (%) ^c	Estimated Incidence of HF in Osteoporotic Women at 20 Years (per 100) ^d	Estimated Incidence of HF in Nonosteoporotic Women at 20 Years (per 100) ^d
65–69	24.3	0.14	1.08	4.91	3.0	1.9
70–74	40.0	0.24	2.26	7.87	5.0	2.9
75–79	40.0	0.70	4.53	10.20	6.4	3.8
80–84	–	1.33	6.99	9.57	6.1	3.5
85–89	–	2.56	8.35	8.35	–	–
>90	–	3.26	5.94	5.94	–	–

^a Source: Diaz Curiel et al.⁶

^b Data obtained from hospital admission records.²

^c Data calculated with the Cutler–Ederer formula.⁸

^d Own calculations.

Risk of Hip Fracture

The likelihood of having a HF in the next 10–20 years (Table 2) was calculated with the Cutler–Ederer⁸ formula:

$$Risk\ events = 1 - (1 - I_a) * (1 - I_b) * \dots * (1 - I_n)$$

As the incidence *I_a* and *I_n* are the period of the incidence in the period *n*.

Indication of Densitometry

According to Roig-Vilaseca et al.,⁹ densitometry was indicated in 63.6% of women aged 65 years or older who attended primary health care centers if the criteria proposed by the AIEHQC were adopted.

Mortality

In addition to in-hospital mortality, in the first year after the fracture the mortality rate increased to 30%.¹⁰ However, in our

model it is assumed that after the first year, the mortality rate is the same as the corresponding age group according to the Register of Deaths in Cataluña.¹¹

Loss of Personal Autonomy (State Dependence)

About 50% of patients with HF have important disability.¹² We adopted the figure of 45% found in one Barcelona¹³ study and 30% for a long-term³ situation.

Utility

To calculate the adjusted quality of life years (QALYs), the values used were taken from a recent review,¹⁴ i.e. 0.797 for the first year after the fracture and 0.899 for the following years. The usefulness in those that have failed to present a fracture is considered to be 1, regardless of age group, to compare changes in QALYs due only to the intervention. We used a reduction rate of 5%.

Table 3
Direct and Indirect Current Costs of HF in Cataluña (2009) and Direct Costs of the Proposed Intervention.

Current Cost Situation				
Concept	Unit Cost, €	No. of Patients	Visits or Estimated Stay	Total Cost, €
Direct cost				
Emergency room visit cost	94.93	9262	1 visit	879 241.70
Acute hospital care cost	3149.68	9262	n.a.	29 172 301.80
<i>Hospital stay cost</i>				
Long term center stay	71.29	377	177.2 days	4 762 485.70
Convalescence unit	96.42	2346	50.8 days	11 491 027.10
Functional unit interdisciplinary care	37.1	2984	11 days	1 217 770.40
Cost of day visit	56.8	8827	4 visits	2 005 494.4
Cost of rehabilitation	625.34	8827	n.a.	5 519 876.20
Total direct costs				55 048 197.30
Indirect costs				
Dependency (30% of invoices)	8429.1	2648	7.7 years	171 866 768.32
Total Indirect costs				171 866 768.32
Direct Costs of Intervention				
Concept	Unit Cost, €	No.	Total, €	Value per Patient Treated*, €
Densitometry cost	40	1	40	15.4
Monthly generic alendronate (70 mg/week) for 10 years	15.42	120 months	1850.40	697.40
Monthly cost Ca+ vitamin D (daily administration)	10.55	120 months	1266.00	477.10
Cost of annual visits to primary care	37.9	20 visits	758.40	285.80

* Updated: reduction rate of 5% and 20 year perspective.

Cost Variables

Direct Costs of the Current Situation

Direct costs include visit to the emergency room, admissions to hospital, the stay of some patients in a geriatric hospital, outpatient visits and 4 control visits without added tests (or densitometry).¹⁵ The costs are calculated on the basis of the rates (hospital discharge or stay), paid by the public insurer.¹⁶ In cases where rates vary by type of hospital, we used the average of the rates. The estimated cost per stay has been multiplied by the average stay and the number of patients in order to obtain the total cost.

Indirect Costs of the Current Situation

We did not consider the costs associated with lost work productivity because we dealt with a retirement age population. In the study of the costs associated with a situation of dependency we considered severe dependency status in 30% of patients.¹⁷ Montserrat¹⁸ calculated the costs of the status of severe dependency, including the cost of health and social assistance, at € 9805.94 (value 2003). Without the direct health costs, such costs to date (3% per year) are € 8429.1. It was considered that the life expectancy of people in a situation of dependency is 7.7 years,¹⁹ regardless of age group.

Direct Costs of the Proposed Intervention

Direct costs include densitometry for women with risk factors, an annual visit to primary care and drug treatment. The cost (list price of generic alendronate in 2010), updated drug treatment and annual monitoring is € 1460.4 per person treated (in 20 years and with a reduction rate of 5%).

Cost per Year of Quality-adjusted Life

Since there is no consensus on the cost per QALY in our country, we adopted the range of values per QALY proposed by Abellán et al.,²⁰ which for 2010 is between € 9200 and € 44 000. Differences in costs and QALYs were calculated for 1000 women, with 1000 women interventions versus no intervention.

Results

Total Direct Costs

The total direct costs of hospitalized patients in 2009 was € 55 048 197.3 (Table 3), representing € 5943.4 per patient. With a time horizon of 20 years and a reduction rate of 5%, the current value per patient was approximately € 2240.0. Total costs (direct and indirect) over a period of 10 years was € 226 914 965.53, which account for € 9233.63 per person over 20 years with a 5% reduction (Table 3).

Comparison of the number of fractures, costs and years of quality-adjusted life with and without intervention by age group

Table 4 shows the differences in the number of fractures and in costs, QALYs and costs per QALY in the different age groups considering a 40% reduction in fracture risk. In a time horizon of 20 years, the intervention is dominant in all age groups and cheaper than non-intervention.

Uncertainty Analysis and Acceptance of the Intervention

The results of this analysis are shown in Fig. 2. In the 10-year time horizon, all scenarios would be acceptable, since the values are below the 44 000 €/QALY proposed for Spain. In the 75–79 year group, values fall below € 9200, which is the lowest limit suggested. With a 20-year perspective, the intervention is dominant in the 75–79 years of age group if the reduced risk of fracture is at least 15%. All other scenarios are acceptable in all age groups, as the QALY values do not exceed € 3000.

Budget Impact Analysis

We estimated the cost of implementing preventive intervention in 2 age groups: ≥65 and 75–79 years (Table 5). In the next 10 years the population of women over 64 years will be approximately about 750,000 with an average annual income, if no intervention is performed, of 6911 a year, which will provide direct costs of about 41.1 and total costs of 165.5 million euros. The average annual

Table 4
Number of Fractures, AVAC, Cost Per Person and Per AVAC in a Cohort of 1000 Women With and Without Intervention and a 10 and 2 Year Time Horizon.

10 Years	Fractures (1000 Person Cohort)			AVAC (1000 Person Cohort)			Cost per Person, € (Reduction Rate of 5%)			€/AVAC
	No Intervention	Intervention	Dif.	No Intervention	Intervention	Dif.	No Intervention	Intervention	Dif.	
65–69	11	4	-7	5765.9	5782.7	16.8	165.4	398.6	233.2	13 881.0
70–74	23	9	-14	5437.1	5468.7	31.6	345.9	665.9	320	10 126.6
75–79	45	19	-26	4772.2	4823.5	51.3	676.8	779.3	102.5	1998.1
20 Years	No Intervention	Intervention	Dif.	No Intervention	Intervention	Dif.	No Intervention	Intervention	Dif.	€/AVAC
65–69	49	20	-29	6118.1	6192.6	74.5	452.4	395.3	-57.1	-766.4
70–74	79	35	-44	5020.1	5113.5	93.4	726.7	635.7	-91	-974.3
75–79	102	45	-57	3526.5	3611.3	84.8	941.8	711.9	-229.9	-2711.1

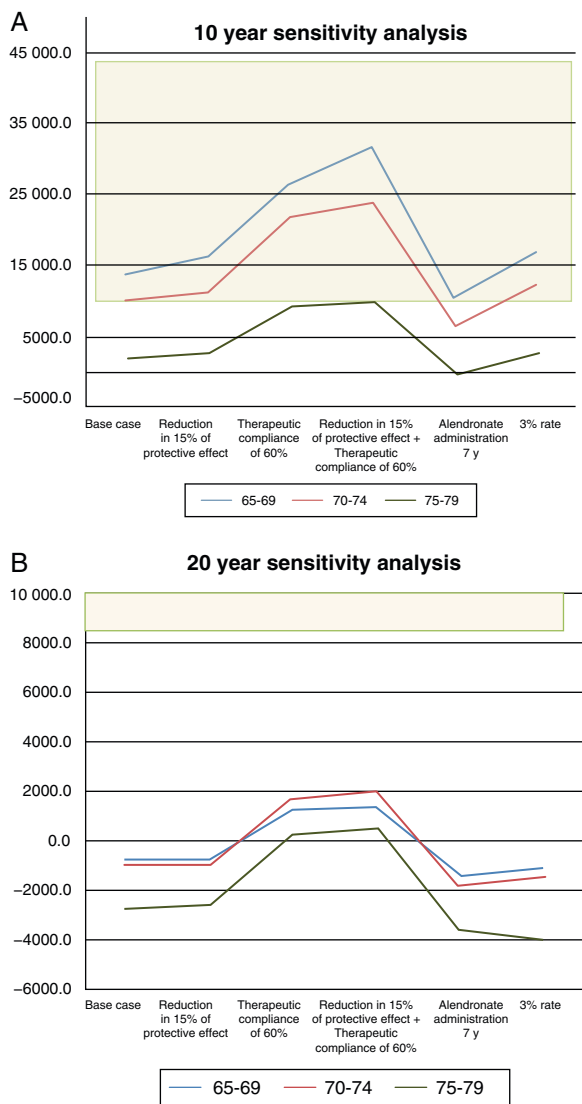


Fig. 2. Sensitivity analysis at 10 (A) and 20 (B) years.

direct cost of intervention in the ≥ 65 year age group and in the 75–79 year group would be about 63.4 and 38.2 million euros, respectively, for the next 10 years. The balance between the direct costs of the intervention and the costs of non-intervention, if prevention is performed in women over 65 for 10 years, would increase 34.2 million a year on average. Considering the total costs, the increase is 10.9 million. The balance of direct costs, for prevention in women 75–79 years for 10 years, showed an increase of 8.9 million per year on average. When considering the total costs,

Table 5
Budget Impact of the Intervention in a Cohort of Women ≥ 65 and 75–79 Years of Age Comparing It With No Intervention.

	≥ 65 Years	75–79 Years
<i>No intervention</i>		
Number of women ≥ 65		751 243
HF hospitalizations expected in women ≥ 65		6757
Direct hospitalization costs (millions of €)		29.2
Total costs (direct + indirect) (millions of €)		165.5
<i>Intervention</i>		
Persons under treatment	140 000	53 000
Costs of care and densitometry (millions of €)	41.6	14.2
Expected avoided hospitalizations	1839	1268
Direct costs (hospitalizations + treatment) (millions of €)	63.4	38.2
Total costs (millions of €)	160.9	113.1
<i>Balance (intervention-no intervention)</i>		
Balance of direct costs (millions of €)*	34.2	8.9
Balance of total costs (millions of €)*	10.9	-7.4

* Estimate of mean annual cost taking into account a 10-year period.

the balance is more favorable, since the intervention represents an annual saving of about 7.4 million. Considering only the perspective of the insurer, the above figure of 8.9 million represents an increase of 31% per annum of the actual cost of the HF, although the overall public drug budget²¹ does not reach a 0.5% increase.

Discussion

Drug prevention of HF is more efficient and cheaper than the option of doing nothing in the female population over 64 years, from a social and long-term perspective (20 years). Adopting the social^{22,23} perspective is based on the need to ensure that the use and distribution of public resources is done efficiently and with reasoned and transparent criteria. This justifies the use of QALYs as the unit of measure. The incorporation of the costs associated with a state of dependence due to FC can multiply the cost of HF 4, while a preventive policy proposal allows a saving of between 766.7 and €2711.1 per QALY gained, depending on the age group. The incorporation of these costs has previously justified the application of some health policies in Catalonia for the acute care of stroke.^{24,25} In the 10-year time horizon, the intervention is effective but more expensive in the three age groups, although the costs obtained per QALY (13,881 for the 65–69 year group, 10,126 for the 70–74 group and 1988 for the 75–79 year group) are within the recommended range of values. Moreover, the cost per QALY, especially in those aged 75–79, is not far from the values of other procedures prioritized in Catalonia, such as knee replacement surgery (€ 1353.5/QALY) or

the hip replacement surgery (€8419.4/QALY values of 2010).²⁶ The results are similar to those of other studies of cost-effectiveness. The cost per QALY gained in Germany from the strategy of screening and treatment of osteoporosis with alendronate²⁷ was highest in women 60–70 years of age (€ 16 589/QALY), reaching up to € 2337/QALY in the group of 80–89 years. The study by Kanis et al.²⁸ demonstrated that primary prevention is cost-effective in women aged 50 years, lowering the cost of QALY progressively from age 60 and remaining dominant in the ≥80 years of age group. The proposed intervention involves nearly a 31% increase in current spending, but would not involve more than 0.5% of the total drug budget of the public insurer. Both the low cost per QALY as well as its small budgetary impact could justify the introduction of this preventive intervention in the 75–79 years of age group of women. The introduction of this measure, to be feasible, should be managed from primary care, as would be the appropriateness of prescribing bisphosphonates to the target population, avoiding unwarranted treatments. One limitation of the study is the criterion for the selection of persons at risk of osteoporosis. Shortly after the completion of our study, a publication appeared, which predicted that the positive predictive value of AIEHCQ criteria for low bone density is 58.97% for women over 65 years of age, while the negative predictive value is high.²⁹ The likelihood of osteoporosis that we have adopted is the same in the group with densitometry than in the group without; therefore overestimating fractures in the group without making densitometry analysis results are more robust. The upcoming availability of screening tools based on the absolute risk of osteoporotic fracture, and validated in our population, will improve the efficiency of the preventive strategy. In this sense, the FRAX[®] index (available in <http://www.shef.ac.uk/FRAX/>) which helps calculate the risk of fracture, may be an easily performed and useful tool.³⁰ Another methodological limitation is the simplicity of the analysis employed, mainly based on point estimates of five-year age groups, the assumption of a linear increase (not exponential) of HF risk and uncertainty management through univariate sensitivity. However, it is assumed that the introduction of an exponential risk, the risk of a HF and transitional probabilities associated with age, would result in a greater number of fractures and greater cost-utility of preventive policy than has been analyzed. In summary, primary prevention of HF with alendronate plus Ca+ and vitamin D in women ≥65 years of age with osteoporosis is an intervention that has a long-term cost-utility (time horizon of 20 years). Within 10 years, the intervention in the group of women 75–79 years shows annual savings that reach 7.4 million euros on average, taking into account the total costs. The measure in that age group would have a budgetary impact on the public insurer.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this investigation.

Confidentiality of Data. The authors declare that no patient data appears in this article.

Right to privacy and informed consent. The authors declare that no patient data appears in this article.

Authorship

Mary J. Antonio Pueyo and J. Garcia-Ruiz developed the study design, analyzed the data and drafted the manuscript. Marta Larrosa Xavier Surís contributed to the idea of the project and the manuscript.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgements

We thank Dr. M. de la and Elena for their support for the realization of the International Master's Degree in Health Economics and Pharmacoeconomics (on line), 11th edition, from which the thesis that underlies this manuscript emerged.

References

- Alvarez-Nebreda ML, Jiménez AB, Rodríguez P, Serra JA. Epidemiology of hip fracture in the elderly in Spain. *Bone*. 2008;42:278–85.
- Activitat assistencial de la xarxa sanitària de Catalunya 2009 (CMBD). Editado por el Servicio Catalán de la Salud [accessed 24.03.11]. Available from: http://www10.gencat.net/catsalut/archivos/cmbd/cmbd_2009.pdf.
- Sosa M, Segarra MC, Limiñana JM, Hernández D, González A, Betancor P. Morbilidad y mortalidad de la fractura osteoporótica femoral tras un año de seguimiento. *Med Clin (Barc)*. 1993;101:481–3.
- Estrada MD, Ferrer A, Borràs A, Benítez D, Espallargues M. Guía per a la indicació de la densitometria òssia en la valoració del risc de fractura i en el control evolutiu de l'osteoporosi [accessed 24.03.11]. Actualització febrer 2006. Barcelona: Agència d'Avaluació de Tecnologia i Recerca Mèdiques. CatSalut. Departament de Salut. Generalitat de Catalunya. Available from: <http://www.gencat.cat/salut/depsan/units/aatrm/pdf/gp0601caex.pdf>.
- García-Ruiz AJ, Martos F, García-Agua N, Parrado C, Fernández Nebro A, Morata F. Revisión sistemática de evaluaciones económicas de los medicamentos para el tratamiento de la osteoporosis postmenopáusia comercializados en España 2008 [accessed 24.03.11]. Available from: <http://www10.gencat.net/catsalut/archivos/farmacia/CAEIP/osteoporosis.informe.es.2008.pdf>.
- Díaz Curiel M, García JJ, Carrasco JL, Honorato J, Pérez Cano R, Rapado A, et al. Prevalencia de osteoporosis determinada por densitometría en la población femenina española. *Med Clin (Barc)*. 2001;116:86–8.
- Tebé C, Espallargues M, Estrada MD, Casas L, Del Río LM, Di Gregorio S. Análisis de los factores de riesgo y la probabilidad de fractura por fragilidad en una cohorte de mujeres con indicación de densitometría ósea. Plan de Calidad para el sistema Nacional de Salud del Ministerio de Sanidad y Política Social. Ministerio de Ciencia e Innovación. Agència d'Informació, Avaluació i Qualitat en Salut de Catalunya; 2010 [accessed 31.03.11]. Informes de Evaluación de Tecnologías Sanitarias, AATRM núm.2009/04. Available from: http://www.gencat.cat/salut/depsan/units/aatrm/pdf/fractura_fragilidad_densito_pcsns_aiaqs2010.pdf.
- Cutler SJ, Ederer F. Maximum utilization of the life table method in analyzing survival. *J Chronic Dis*. 1958;8:699–712.
- Roig-Vilaseca D, Valero C. Proporción de individuos con criterios de indicación de densitometría ósea y frecuencia de los factores de riesgo de baja masa ósea en consultas de atención primaria. *Aten Primaria*. 2006;38:435–42.
- Cabasés JM, Carmona G, Hernández R. Incidencia, riesgo y evolución de las fracturas osteoporóticas de cuello de fémur en las mujeres en España, a partir de un modelo de Markov. *Med Clin (Barc)*. 2000;114:63–7.
- Servei d'Informació i Estudis. Anàlisi de la mortalitat a Catalunya, 2008 [accessed 24.03.11]. Barcelona. Department of Health. Government of Catalonia 2010. Available from: <http://www.gencat.cat/salut/depsalut/html/ca/dir1932/mortaliti2008.pdf>.
- Leibson CL, Tosteson AN, Gabriel SE, Ransom JE, Melton LJ. Mortality, disability, and nursing home use for persons with and without hip fracture: a population-based study. *J Am Geriatr Soc*. 2002;50:1644–50.
- Knobel H, Díez A, Arnau D, Alier A, Ibáñez J, Campodarve I, et al. Secuelas de la fractura osteoporótica de fémur en Barcelona. *Med Clin (Barc)*. 1992;98:441–4.
- Imaz Iglesia I, Rubio González B, López Delgado MA, Amate Blanco JM, Gómez Pajuelo P, González Enríquez J. Análisis coste-utilidad de los tratamientos farmacológicos para la prevención de fracturas en mujeres con osteoporosis en España [accessed 24.03.11]. IPE 63/2010. Madrid: AETS-Instituto de Salud Carlos III; 2010. Available from: http://www.isciii.es/ISCIII/es/contenidos/fd-publicaciones-isciii/fd-documentos/63_Osteoporosis_Coste_utilidad_farmacos.pdf.
- Compston J. Monitoring osteoporosis treatment. *Best Pract Res Clin Rheumatol*. 2009;23:781–8.
- Orden SLT/183/2010 y Orden SLT/182/2010 del Servei Català de la Salut DOGC 31/03/2010 [accessed 24.04.11]. Available from: <http://www.gencat.cat/eadop/imatges/5599/10083164.pdf> and <http://www.gencat.cat/eadop/imatges/5599/10083162.pdf>.
- Rodríguez-Cabrero G, Montserrat J. Modelos de atención sociosanitaria. Una aproximación a los costes de la dependencia. Madrid: Ministerio de Trabajo y Asuntos Sociales; 2002.
- Montserrat J. El coste de la dependencia. *Rev Mult Gerontol*. 2003;13:194–200.
- Braña FJ. Una estimación de los costes de un seguro público de dependencia de los mayores en España. *Estudios de Economía Aplicada*. 2004;22:723–57.
- Abellán JM, Sánchez FI, Martínez JE. La medición de la calidad de los estudios de evaluación económica. Una propuesta de check-list para la toma de decisiones. *Rev Esp Salud Pública*. 2009;83:71–84.

21. Departament de Salut. El sistema de salut i la xarxa sanitària pública de Catalunya. Línies estratègiques i evolució 2004-2009. Barcelona: CatSalut; 2010 [accessed 15.06.11]. Available from: http://www10.gencat.net/catsalut/archivos/publicacions/memories/2009/04_09_catsalut_resum.pdf
22. Jönsson B. Ten arguments for a societal perspective in the economic evaluation of medical innovations. *Eur J Health Econ.* 2009;10: 357–9.
23. Byford S, Raftery J. Perspectives in economic evaluation. *BMJ.* 1998;316:1529–30.
24. Generalitat de Catalunya. Departament de Salut Pla director de malalties de l'aparell circulatori [accessed 13.05.11] Barcelona: Direcció General de Planificació i Avaluació; 2006. Available from: http://www.gencat.cat/salut/depsalut/pdf/pd_circulatori_2510.pdf.
25. Jung KT, Shin DW, Lee KJ, Myungju O. Cost-effectiveness of recombinant tissue plasminogen activator in the management of acute ischemic stroke: a systematic review. *J Clin Neurol.* 2010;6:117–26.
26. Navarro JL, Hernández E. Cost-outcome analysis of joint replacement: evidence from a Spanish public hospital. *Gac Sanit.* 2008;22:337–43.
27. Mueller D, Weyler E, Gandjour A. Cost effectiveness of the German screen-and-treat strategy for postmenopausal osteoporosis. *Pharmacoeconomics.* 2008;26:513–36.
28. Kanis JA, Adams J, Borgström F, Cooper C, Jönsson B, Preedy D, et al. The cost-effectiveness of alendronate in the management of osteoporosis. *Bone.* 2008;42:4–15 [editorial].
29. Roig-Vilaseca D, Valero C, Boncompte MP, Muñoz López J, Contreras García C, Romera Baurés M, et al. Sensibilidad, especificidad y valor predictivo positivo y negativo de los criterios de indicación de densitometría ósea de la agencia de evaluación de tecnologías e investigación médicas de Cataluña. *Reumatol Clin.* 2011;7:161–6.
30. Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E. FRAX® and the assessment of fracture probability in men and women from the UK. *Osteoporos Int.* 2008;19:385–97.