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VIRTUAL CONGRESS HIGHLIGHTS

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AMGEN®

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AMGEN SYMPOSIUM

BONE HEALTH MATTERS: ADVANCING LONG-TERM CARE IN OSTEOPOROSIS

Friday 27 August 2021

The Amgen-sponsored symposium at ESCEO 2021 addressed key topics in the management and treatment of OP, including an overview of the WHO Decade of Healthy Ageing, fracture risk assessment and treatment thresholds, with analysis of society guideline recommendations.

Adolfo Diez-Pérez (Chair)	Chair and Head of the Department of Internal Medicine, Hospital del Mar Institute of Medical Investigation, Autonomous University of Barcelona, CIBER on Frailty and Aging, Spain
Cyrus Cooper	Professor of Rheumatology and Director, MRC Lifecourse Epidemiology Unit, University of Southampton, UK; Professor of Epidemiology, University of Oxford, UK; President, International Osteoporosis Foundation

BONE HEALTH AND FRACTURE PREVENTION IN THE DECADE OF HEALTHY AGEING

Cyrus Cooper

Professor Cooper began by introducing the WHO 'Decade of Healthy Ageing' initiative that aims to accelerate the impact of care on older people across several domains, including locomotion, cognition and sensory capacity.[1,2] He highlighted that **musculoskeletal disease is the 2nd greatest cause of disability globally and has the 4th greatest impact on overall health.**[3]

Professor Cooper presented results of the SCOPE study that showed that osteoporotic fractures account for a healthcare expenditure of ~55.3 billion €/year in the EU, which is 3.5% of overall healthcare spending.[4] The report also anticipates **significant increases in fragility fractures between 2019 and 2034 (+42.6% men; +29.6% women)**, which suggests a substantial treatment gap is likely to persist for patients with OP in the absence of adequate preventive measures.

Professor Cooper next showed that therapy for OP has achieved success in recent years with the introduction of effective antiresorptive and, more recently, bone-stimulating therapies. European guidance[5] (updated in 2019) has focused on the positioning of anabolic agents for the management of OP. Professor Cooper highlighted that **risk assessment is well validated and widely incorporated in international treatment guidelines** and the ESCEO/IOF management algorithm for assessment of risk now includes a very high-risk category where early introduction of anabolic agents is considered appropriate (Figure 1).[6]

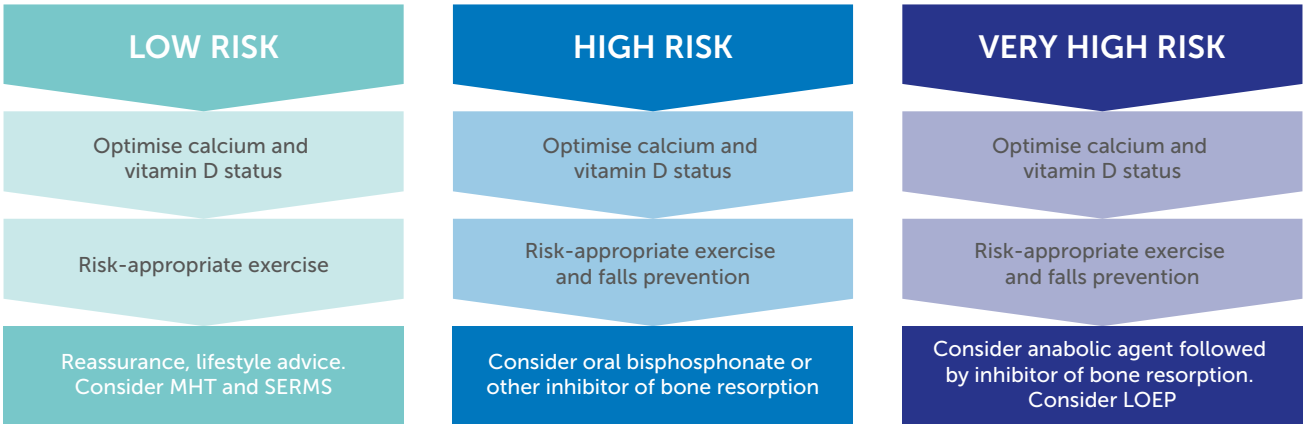


Figure 1: Management algorithm for patients with OP and low, high, and very high risk of fracture.[6]

Professor Cooper also presented results of the SCOOP study,[7,8] which evaluated the effect of screening tools on primary osteoporotic fracture prevention in the UK. The results showed a **cumulative 28% reduction in hip fracture incidence over 5 years of observation in women who underwent FRAX® screening compared with the usual care arm.** He then presented results of a meta-analysis published in 2020[9] including over 42,000 elderly participants from Denmark (ROSE study), the Netherlands (SOS) and the UK SCOOP study, which each showed the effectiveness of screening to reduce osteoporotic fractures and hip fractures. Accordingly, **the use of FRAX®-based screening in primary fracture prevention is currently on the policy agenda for discussion with healthcare authorities.**

Professor Cooper concluded by presenting the IOF's '**Capture the Fracture'[10] initiative for the prevention of secondary fractures.** As of April 2021, 'Capture the Fracture' included 623 FLSs in 48 countries with more than 500,000 recorded fragility fractures. In recent months 'Capture the Fracture' has included multi-stakeholder partnerships involving higher education institutions, the charitable sector, and corporate partners (Amgen and UCB) with the aim of **fostering the establishment of new post-fracture care and FLS services.**

LONG-TERM TREATMENT STRATEGIES FOR OSTEOPOROSIS

Adolfo Diez-Pérez

Professor Diez-Pérez began by summarising the goals of OP treatment. As defined by the ASBMR-NOF, treatment should aim to keep the patient free from fracture with a T-score greater than -2.5 or risk level below the threshold of treatment.[11] Another position paper from ESCEO/IOF suggested that the absence of incident fractures, reaching a fixed level of BMD, reaching a desired FRAX® score, and a specified level of bone turnover markers are the most important treatment targets.[12] However, both sets of recommendations acknowledge that these goals may not be possible with current treatments, especially for patients with very high risk of fracture or very low BMD.

ESCEO/IOF proposed to move from a treat-to-target to a target-to-treat strategy and to focus on targeting those at higher risk.[12] The need for improvement has been demonstrated in various studies including the GLOW study[13] in which fewer than 50% of women with high and very high-risk of fracture received effective treatment for OP. In the SPARE-HIP study[14] in Spain, reducing the risk of a future fracture was not considered a priority – fewer than 13% of patients with a hip fracture were given anti-OP treatment at discharge. To address the need for more effective treatment in very high-risk patients, the VERO study[15] found that an anabolic (teriparatide) was significantly more effective than an antiresorptive (risedronate) at preventing new vertebral fractures. Similarly, the ARCH study[16] compared romosozumab (anabolic) with alendronate (antiresorptive) for 12 months and found that romosozumab was significantly better at preventing new vertebral fractures. All patients were continued on alendronate for a further 12 months with the conclusion that anabolics are the more potent anti-OP drugs; however, as their effects are reversible, continuation therapy is needed.

The benefits of sequential therapy have been clearly demonstrated in other studies. In the DATA study,[17] teriparatide followed by denosumab (antiresorptive) was superior to denosumab followed by teriparatide. In the FRAME study,[18] romosozumab followed by denosumab offered a significantly better anti-OP effect than denosumab following Placebo. Further, in the FRAME extension study, 1 year of romosozumab followed by a year of denosumab had an effect on bone strength comparable to 7 years of denosumab treatment alone.[19] Professor Diez-Pérez summarised that **for very high-risk patients, sequential therapy with an anabolic followed by an antiresorptive is the preferred option.** An anabolic can be given during the 'rescue' period in which patients are rapidly recovered from the high-risk category, and consolidation with an antiresorptive is important to avoid the rebound effect observed with the long-term use of an anabolic (Figure 2).

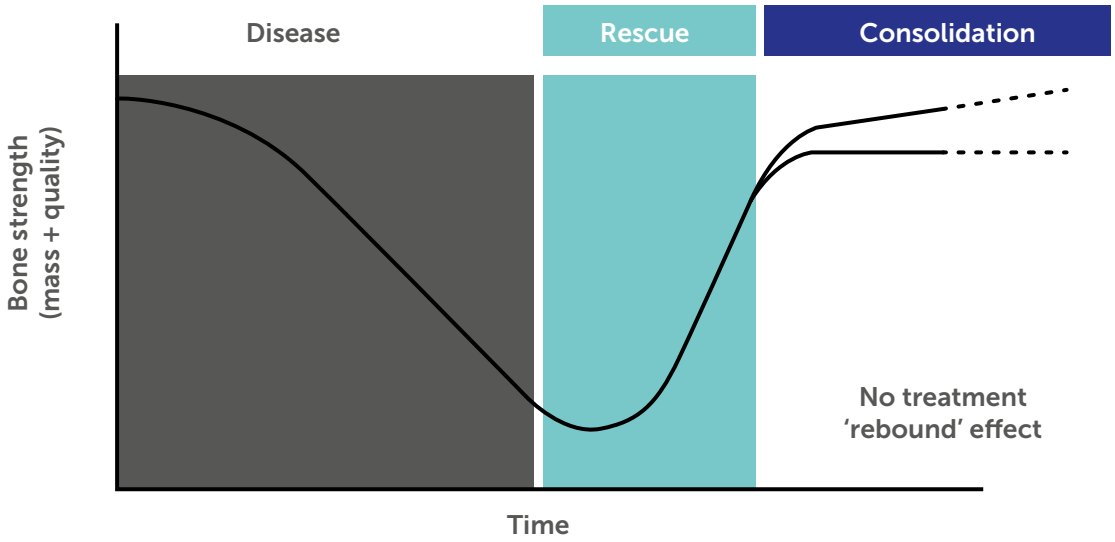


Figure 2: Optimal sequential therapy for patients with very high risk of fracture: an anabolic followed by an antiresorptive (courtesy of Adolfo Diez-Pérez).

In conclusion, Professor Diez-Pérez reiterated that **the goal of successful treatment is the absence of fractures,** and that sequential therapy with an anabolic followed by an antiresorptive should be the preferred option for patients at very high risk of fracture.

ABSTRACT SPOTLIGHT

SELF-INJECTION OF DENOSUMAB IN CLINICAL PRACTICE IN THE FRENCH PILOTE STUDY

Briot K, et al. Abstract P389.

PILOTE was a prospective, observational study that evaluated adherence to denosumab therapy over 24 months in postmenopausal women in France. In total, 478 patients were enrolled, and 27 of these patients self-injected denosumab at least once. Twelve patients self-injected from the beginning of the study, 15 self-injected after receiving injection from a healthcare provider. Those who self injected were slightly younger overall with a longer duration of OP, and a higher proportion had a prior fracture compared with the overall population (Table 1).

Although numbers were small, **self-administration of denosumab appears to be a valuable and feasible option for women with postmenopausal OP,** especially in the context of the COVID-19 pandemic when office visits are restricted.

	Patients who self-injected at least once (n=27)	All patients (N=478)
Age (mean ± SD)	69.81 ± 10.29	72.48 ± 9.73
Number of comorbidities – n (%)		
< 3	19 (70.4)	349 (73.0)
≥ 3	8 (29.6)	129 (27.0)
Prior treatment with OP therapies – n (%)	25 (92.6)	434 (90.8)
Bisphosphonate	22 (81.5)	416 (87.0)
Teriparatide	7 (25.9)	44 (9.2)
History of OP-related fracture – n (%)	20 (74.1)	291 (60.9)
Years since PMO diagnosis (mean ± SD)	8.74 ± 6.36	7.82 ± 6.00

Table 1: BL characteristics of patients enrolled in the PILOTE study.

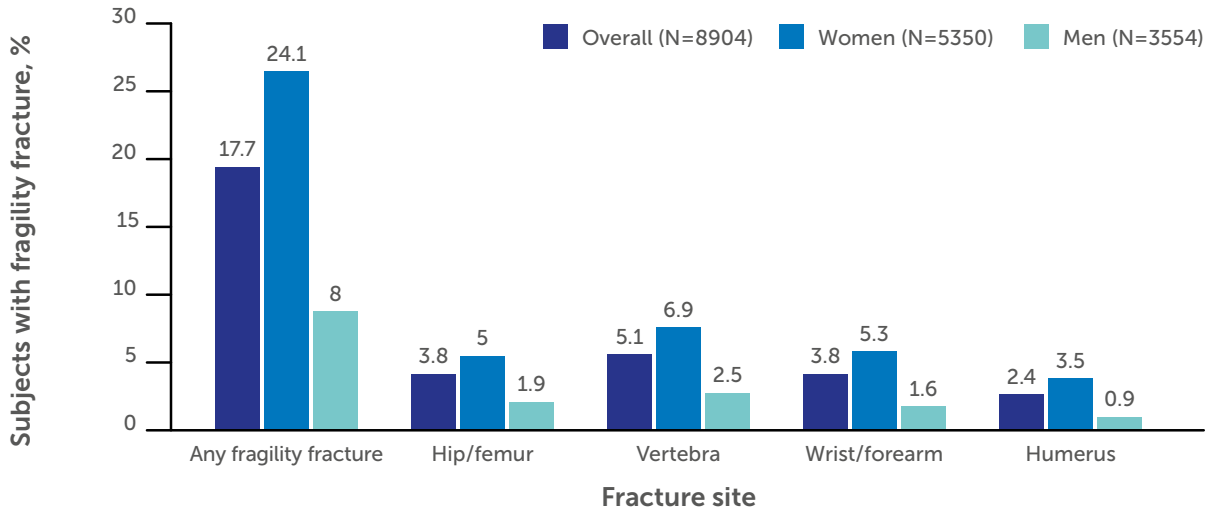
PREVALENCE OF FRAGILITY FRACTURES IN PRIMARY CARE IN SPAIN: FINAL RESULTS OF THE PREFRAOS STUDY

Carbonell C, et al. Abstract P418.

The objectives of the PREFRAOS study were to estimate the prevalence of fragility fractures among patients ≥ 70 years old and to describe the main characteristics and management of these patients in Spanish primary care. Overall, 44,062 medical records were reviewed, and 8904 patients ≥ 70 years old were identified, most of whom were women (5350/8904; 60.1%).

The prevalence of fragility fractures in the overall population was 17.7%, and prevalence was 3-fold higher in women compared with men. Vfx was identified as the most common fragility fracture (Figure 3).

These results highlight a high prevalence of fragility fractures among patients ≥ 70 years old in Spanish primary care and suggest a need to improve fracture risk assessment in elderly patients.



N=number of subjects eligible for Phase A

Figure 3: Prevalence of fragility fractures overall and by site in patients ≥ 70 years old

A RETROSPECTIVE OBSERVATIONAL STUDY OF OSTEOPOROSIS MANAGEMENT AFTER A FRAGILITY FRACTURE IN PRIMARY CARE

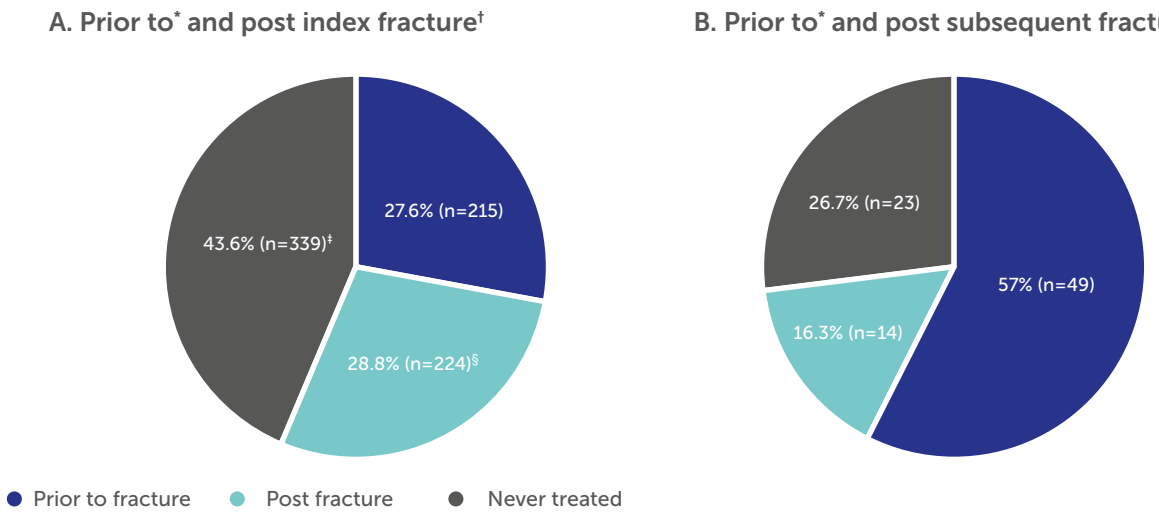
Bell A, et al. Abstract P324.

This study aimed to characterise post-fracture management in the Canadian primary care setting. A total of 778 patients with an index fracture were included in the analysis.

Overall, 215/778 patients (27.6%) were on OP treatment at the time of their index fracture (Figure 4A). Of the 563 patients who were not, 39.8% (n=224) were started on OP therapy post index fracture, leaving the remaining 60.2% (n=339) untreated until the end of the follow-up period (Figure 4A). Forty-three percent (37/86) of patients who had ≥ 1 subsequent fracture during follow-up were untreated at the time of their subsequent fracture. Of these patients, 62.2% (n=23) remained untreated thereafter (Figure 4B).

In total, 11.6% (90/778) of patients had a FRAX® and/or CAROC assessment completed ≤ 5 years prior to their index fracture, and 16.8% (n=131) were assessed after their index fracture, during the follow-up period.

These data suggest that **fragility fracture is not well-recognised as a sentinel clinical event in the primary care setting** and highlight the need to **support primary care physicians in integrating evidence-based secondary fracture prevention practices.**



*Included patients who had OP treatment recorded within 1 year prior to index fracture and continued same treatment at time of index fracture, as well as post index fracture. †Of 778 patients in the full index fracture cohort. ‡In 339 patients who remained untreated after their index fracture, 7 discontinued treatment within 1 year prior to index fracture and never restarted treatment (same or different) after index fracture. §In 224 patients who started OP treatment post index fracture, 12 discontinued treatment within 1 year prior to index fracture and restarted with a different treatment after index fracture. ¥Of 86 patients with at least one subsequent fracture reported during study follow-up.

Figure 4: OP treatment initiation patterns in Canadian primary care.

LONGITUDINAL CHANGE IN BONE MINERAL DENSITY AMONG ADULTS AGED 55 YEARS AND OLDER USING THE HEALTHY AGING LONGITUDINAL STUDY IN TAIWAN (HALST)

Hsieh T-JH, et al. Abstract P222.

Limited data are available to understand longitudinal change in BMD in the elderly population of Taiwan. This study was conducted to assess BMD change over 6 years according to sex and OP status among adults ≥ 55 years old in Taiwan.

Among the 1508 participants with BMD measurements at BL and follow-up, 52% (n=782) were women and 62% (n=932) were aged ≥ 65 years. Overall, 14% (n=215) had OP, 33% (n=500) had osteopenia, and 3% (n=47) had a recent history of treatment with an anti-OP medication. At 6 years of follow-up, the largest BMD reduction had occurred among women aged 55–65 years (-3.1%, 95% CI: -3.8%, -2.4%) (Figure 5).

Among healthy adults in Taiwan aged ≥ 55 years, **women aged 55–65 experienced the most significant BMD loss in the LS over a 6-year observation period.** These women may benefit most **from interventions to reduce bone loss and decrease the risk of developing OP.**

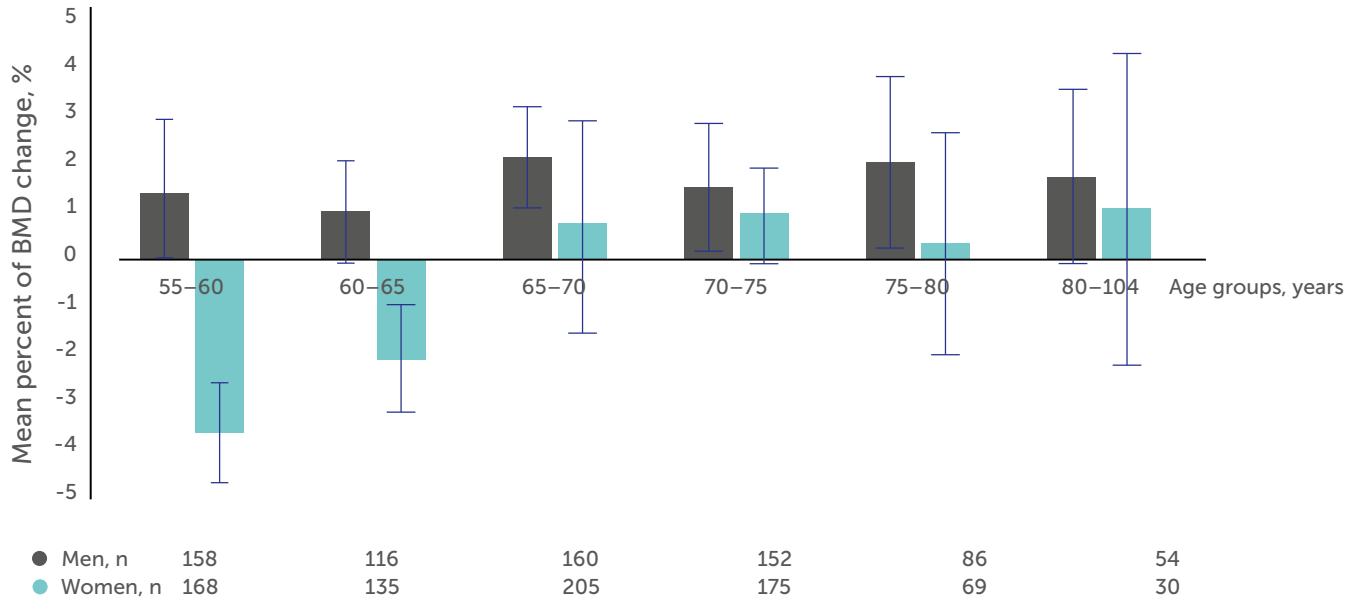


Figure 5: Percentage change in LS BMD for males and females by age group in Taiwan.

COST-EFFECTIVENESS ANALYSIS OF FRACTURE LIAISON SERVICE IN SECONDARY PREVENTION OF FRAGILITY FRACTURES IN SPAIN

Naranjo A, et al. Abstract P284.

This study considered the cost-effectiveness of an FLS model compared to standard care for secondary prevention of fragility fractures in Spain. Within a cohort of OP patients after initial fragility fracture who were candidates to initiate anti-OP treatment, disease progression was simulated with a Markov model through seven health states: with and without anti-OP treatment, subsequent hip, vertebral, forearm and humerus fracture, and death. Mean patient age was 65 years old and 90.7% were women.

The analysis found that implementing an FLS for the secondary prevention of fragility fractures in Spain would provide greater anti-OP treatment initiation and persistence. This would reduce subsequent fragility fractures, with a reduction in disability and deaths. The results showed a greater clinical benefit (0.01 and 0.08 life-years and QALYs gained per patient, respectively) compared to standard of care. This would imply a higher cost (€563.69 per patient) leading to an incremental cost-utility ratio of €6855.23 per QALY gained.

From the Spanish NHS perspective and considering the locally established willingness-to-pay thresholds, the study concluded that the implementation of an FLS would be cost-effective in the Spanish setting in comparison with standard care for secondary prevention of fragility fractures.

ABBREVIATIONS

ARCH, Active-Controlled Fracture Study in Postmenopausal Women with Osteoporosis at High Risk; ASBMR-NOF, American Society for Bone and Mineral Research and the United States National Osteoporosis Foundation; BL, baseline; BMD, bone mineral density; CAROC, Canadian Association of Radiologists and Osteoporosis Canada; CI, confidence interval; CV, cardiovascular; DATA, Denosumab and Teriparatide Administration; ESCEO, European Society for Clinical and Economic Aspects of Osteoporosis; FLS, fracture liaison service; FRAME, FRActure study in postmenopausal woMen with osteoporosis; FRAX®, Fracture Risk Assessment Tool; GLOW, Global Longitudinal study of Osteoporosis in Women; IOF, International Osteoporosis Foundation; LOEP, local osteo-enhancement procedure; LS, lumbar spine; MHT, menopausal hormone therapy; NHS, National Health Service; OP, osteoporosis; PILOTE, Characteristics and Management of Postmenopausal Women With Osteoporosis Treated With Prolia® in France; PMO, postmenopausal osteoporosis; PREFRAOS, Prevalencia de fracturas por fragilidad, diagnóstico y tratamiento de la osteoporosis tras una fractura por fragilidad en sujetos con edad igual o superior a 70 años en Atención Primaria en España; QALY, quality-adjusted life year; ROSE, Risk-stratified Osteoporosis Strategy Evaluation; SCOOP, screening in the community to reduce fractures in older women; SCOPE, Scorecard for Osteoporosis in Europe; SD, standard deviation; SERM, selective oestrogen receptor modulator; SOS, SALT Osteoporosis Study; SPARE-HIP, SPAnish REgistry of osteoporostic HIP fractures; VERO, VERtebral fracture treatment comparisons in Osteoporotic women; Vfx, vertebral fracture; WHO, World Health Organization.

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