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Actions to Improve the Secondary Prevention of Fragility Fractures in Women with Postmenopausal Osteoporosis: A Social Return on Investment (SROI) Study

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Purpose: This study evaluates the Social Return on Investment (SROI) of implementing measures to prevent fragility fractures in postmenopausal women with osteoporosis (OP) in Spain.

Methods: A group of 13 stakeholders identified necessary actions for improving refracture prevention and assessed the investment required from the Spanish National Health System (SNHS), considering direct, indirect, and intangible costs over a one-year period. Unitary costs were sourced from scientific literature and official data, and intangible costs were estimated through surveys on women's willingness to pay for better health-related quality of life. The SROI ratio was calculated from both a social perspective (including all returns) and the SNHS perspective (including only direct and intangible costs). A sensitivity analysis evaluated the returns in worst- and best-case scenarios over three years.

Results: Stakeholders agreed on four main actions: 1) establishing fracture liaison services; 2) harmonizing clinical practice guidelines and provide training for healthcare professionals (HCPs); 3) promoting HCPs' adherence to fracture registries and 4) raising awareness of OP and fragility fractures. From the social perspective, implementing these actions would cost the SNHS €4,375,663 but yield a social return of €96,939,931 in the first year, resulting in a SROI ratio of €22.15 per euro invested (€28.69, 23.14, 24.29, and 10.70 for the four actions, respectively). From the SNHS perspective, the return would be €36,453,509 (€21,523,444 tangible), with a SROI of €8.33 (€4.92 tangible) and for the four actions: €9.99, 9.39, 8.45, and 3.79, respectively (€5.89, 5.54, 4.96 and 2.27 tangible). The investment would be lower than the return for all actions (3.49%, 4.32%, 4.12% and 9.34% of social perspective return, respectively) and scenarios.

Conclusion: According to our SROI method, implementing different actions to improve secondary fracture prevention would achieve a considerable social benefit, which, in terms of direct, indirect, and intangible costs, would far outweigh the investment.

Keywords: economic evaluation, healthcare investment, prevention measures, healthcare outcomes, fracture liaison services, health-related quality of life

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Introduction

Osteoporosis (OP) causes gradual loss of bone mineral density and bone structure deterioration, predisposing to bone fragility and, ultimately, fragility fractures,[1,2] mainly in the spine and hip.[3] It is a highly prevalent disease, diagnosed in around 200 million people worldwide[4] and it primarily affects postmenopausal women.[5] Fragility fractures are the most serious complication of OP and entail severe consequences for patients and society. The number of fragility fractures registered annually is estimated at around 9 million,[6] 300,000 of which occur in Spain (260,000 for women).[7]

Fragility fractures lead to a rapid decline in the patient's physical function as well as increased morbidity and risk of premature death.[8] Furthermore, the occurrence of a first fracture is a strong predictor of subsequent fractures,[9] which further add to patients' morbidity and disability.[10] The risk is particularly high the year after the initial fracture when the likelihood of another is five times higher than for those who have never had a fracture.[9]

At a societal level, fragility fractures account for more disability-adjusted life years (DALYs) lost than other predominant chronic diseases, such as chronic obstructive pulmonary disease (COPD) or stroke. This means fractures have more important associated mortality and morbidity rates than the aforementioned diseases. Thus, in several European countries, including Spain, incidence of fractures and their consequences are associated with substantial annual costs amounting to €37.5 billion, which are estimated to rise to €47.4 billion by 2030.[11]

Despite clinical, economic, and social consequences, both OP and fragility fractures are still overlooked and inadequately treated in clinical practice in European settings.[12] For instance, the scorecard for osteoporosis in Europe (SCOPE 2021) panel reported that around 71% of patients remained untreated within one year after fracture,[13] when there is an imminent risk of refracture. This inadequate management might be due to insufficient awareness of OP among healthcare providers and society or the lack of standardised clinical pathways for individuals with fragility fractures.[12]

Given the present situation, European scientific societies stress the need to take actions in order to improve and ensure both the proper management and prevention of fractures.[14–16] In this regard, the International Osteoporosis Foundation (IOF) has proposed a roadmap to address the fragility fracture issue in the European context.[17] This roadmap involves implementing specific actions that aim to reduce vertebral and hip fractures by 25% by the year 2025.[18]

In Spain, the main measures proposed for fracture prevention and post-fracture care call for the development of harmonised protocols; promotion of the registry of patients who have suffered a fracture and creation of a fracture code; promotion of patient awareness and engagement campaigns and the development and implementation of post-fracture care models, such as multidisciplinary fracture liaison services (FLSs).[7] However, to our knowledge, no comprehensive analysis has been carried out to assess the social value of these or other interventions in terms of improving the secondary prevention of fragility fractures.

The Social Return on Investment (SROI) is a well-established methodology that provides a well-based framework to assess the societal value of specific interventions relative to the investment required to implement them. SROI uses the monetary value to represent both costs and benefits obtained from these interventions and provides an estimation of a benefit-to-cost ratio.[19] Compared to traditional analyses, this methodology can measure broader socio-economic outcomes, analysing and computing views of multiple stakeholders in a singular monetary ratio.[20] This simple approach of representing a complex evaluation has been instrumental in guiding decision-making for interventions in different health issues, such as rheumatoid arthritis,[21] multiple sclerosis[22] or COPD.[23] Therefore, the possibility of applying this comprehensive approach to our field prompted this study, which aims to estimate the SROI of optimising the secondary prevention of fragility fractures in postmenopausal women with OP.

Materials and Methods

SROI Framework

For the social return analysis, various steps were carried out following the SROI framework:[19] 1) to define the actions required to improve the current secondary prevention of fragility fractures in Spain; 2) to estimate the costs of implementing these actions (initial investment); and 3) to estimate the monetary consequences of implementing them (social return). For the analysis, the investment was determined from the Spanish National Health System (SNHS)

perspective. In contrast, the social return was evaluated from a social perspective in the base-case scenario and also from the SNHS perspective as an alternative scenario.

Step 1 - Defining the Actions Required to Improve the Current Secondary Prevention of Fractures in Spain

This stage was mainly based on the consultation of experts comprising a multidisciplinary group of stakeholders. The group was composed of 13 experts in OP: 10 healthcare professionals (HCPs) with expertise in managing OP and fragility fractures (three orthopaedic surgeons, two geriatricians, two rheumatologists, two internists, and one endocrinologist), a specialist in health economics, a representative of a patient association, and an expert patient with postmenopausal OP.

The consultation consisted of two group meetings, including individual assessments. The first meeting was conducted to predefine the actions needed to improve secondary prevention of fragility fractures. A literature review was conducted on the likely critical points in managing fragility fractures, discussed in the first meeting mentioned above. In addition, the experts were asked about the actions required to address the unmet needs, as well as rating them according to their relevance (from 1 = minimal; to 10 = maximum relevance). Finally, a report containing the identified proposals was drawn up and distributed to all the experts to review the preliminary actions and propose alternatives if they considered them appropriate.

A second meeting was held to complete the definition of the individual actions and group them into relevant actions to improve secondary prevention of fractures. Additionally, experts were asked about the impact this set of actions might have on primary clinical outcomes. To do so, they had to estimate how the current values (without the actions) would be improved: the imminent risk of fragility fractures or refracture in the first year following the event (10%),[24] the percentage of patients on preventive treatment (28%),[11] and the adherence rates to this treatment (34%).[25]

A second report was drawn up, containing the final actions to optimize the secondary prevention of fragility fractures and the potential impact. The report was distributed to all the experts who were asked to rate the impact of each action on clinical outcomes (from 1 = minimum; to 100 = maximum impact). The mean score for each measure was estimated from the individual weights of each measure on the total impact. Those values were used to calculate the number of avoidable fragility fractures in the Spanish population suffering from postmenopausal OP.

Step 2 - Estimating the Costs of Implementing These Actions (Initial Investment)

First, the resources necessary to implement each action (medical and non-medical, human, and material) and their unitary costs were identified to define investment costs. Subsequently, the prices of resources were added up to obtain the total costs for each action. Finally, the sum of the costs of the different actions was computed, resulting in the total investment costs. The number of resources and unitary costs were collected from the scientific literature, official data, and the SNHS[26] costs.

Step 3 - Estimating the Monetary Consequences of Implementing These Actions (Social Return)

The costs of social return and the impact of the actions at clinical, welfare, and social levels were established as follows: 1) literature review; 2) expert consultation; and 3) a survey targeting women with previous fragility fracture (see details in [27]). Subsequently, the different fracture-associated costs (direct, intangible, professional, and informal care, and productivity loss) were estimated for each action. Finally, the sum of the total costs of individual activities was computed, resulting in the total costs for the social return of the set of actions. The total return costs were calculated for a one-year time frame. Table 1 lists the type of costs included in the estimation of social return. Only direct costs (including those of the acute event, follow-up, and professional care) and intangible costs for patients were considered to estimate the return to the SNHS (alternative scenario 1).

The unitary costs were collected from the scientific literature, official data, and public prices listed by the SNHS.[26,28] In addition, for intangible costs, patients' willingness to pay (WTP) to recover the state prior to the fragility fracture in different areas of their health-related quality of life (HRQoL) was estimated from the ad-hoc Spanish survey.[27] To estimate the cost, the proportion of patients affected in each domain was multiplied by the WTP cost assigned to each domain. The total cost was obtained by adding the result of each multiplication of each domain. To avoid cost overestimation, a 50% correction was applied to the WTP value of each domain assigned by patients to discount the possible influence of the improvement of other domains on that specific domain.

Table 1 Classification of the Costs Considered in the Return Estimation

Type of Costs	Costs Included
Direct costs[a]	- Costs of the fracture (acute event) and of the follow-up during the first year and in the following 2 years. - Professional care costs (medical care and personal care). - Pharmacological costs associated with the increase in the number of women receiving treatment.
Intangible costs[a]	- Estimate of patients' WTP to recover the pre-fracture state in each area of HRQoL. - The data on WTP were extracted from the ad-hoc Spanish survey results.[27]
Costs of health and social care	- Functional recovery/residential centres paid for by the patient or family members. - The data on patients' professional care needs were extracted from the ad-hoc survey results.
Informal care costs	- Informal caregivers (people who provide care to the patient without receiving any remuneration in return, including family members). - The data on patients' informal care needs were extracted from the ad-hoc survey results.
Indirect costs due to productivity loss	- Costs of productivity loss (absenteeism, work incapacity, sick leave, etc). - The data on productivity loss were extracted from the ad-hoc survey results.

Notes: [a]Costs considered for the return estimation to the Spanish National Health System.
Abbreviations: HRQoL, health-related quality of life; WTP, willingness to pay.

SROI Analysis

Finally, a SROI ratio was estimated, representing how much social return (in euros, €) could be generated for each euro invested in implementing agreed-upon actions. A SROI ratio greater than 1 was considered a positive result, meaning that the social impact was greater than the investment required to implement the improvement actions. A conservative strategy was undertaken to avoid overestimating the return on the investment (ie, the highest investment costs and the lowest impact on return were selected when possible). All prices were considered in euros (year 2020). A prospective approach was applied to the social return analysis, and a time frame of one year was considered for the base-case scenario and for the principal alternative scenario (SNHS perspective).

Sensitivity Analysis

A sensitivity analysis was conducted to assess the worst- and the best-case scenarios. These scenarios were obtained from varying the values of the assumptions considered to entail more uncertainty for the SROI analysis: reducing the imminent risk of new fractures and patients' WTP results. The minimum and maximum impact that the set of actions may have on imminent risk of new fractures according to the experts' opinion were considered for the worst- and best-case scenario, respectively. Regarding the WTP best-case scenario, the answers of all participants in the survey (not only the ones with the affectation on each domain) without applying any correction were considered. For the WTP worst-case scenario the additional WTP of the ones suffering the domain, compared to the ones not suffering it, was considered (patients suffering the domain reported higher WTP than the ones not suffering it).

Also, two alternative scenarios were included to represent a three-year time frame from social (alternative scenario 2) and SNHS (alternative scenario 3) perspectives. These scenarios focused on the returns derived from the costs associated with the fractures at three years, considering only the initial investment.

Results

Actions Required to Improve the Current Secondary Prevention of Fragility Fractures in Spain

After considering the unmet needs in the current prevention of fragility fractures and the possible actions to cover them (see Supplementary Table 1), the experts agreed on the need to undertake four main actions to improve secondary prevention of fragility fractures in Spain: 1) create FLSs; 2) harmonise clinical practice guidelines and provide training to HCPs; 3) promote the adherence of HCPs to fracture registries; 4) raise awareness of OP and fragility fractures among the population. The details of these proposals (objectives, sub-actions, and stakeholders) are presented in Supplementary Table 2.

The experts considered that this set of proposals would have a positive impact on relevant clinical outcomes related with secondary prevention of fragility fractures. They agreed that they would reduce the imminent risk of fractures (−4%), increase the percentage of patients on treatment to prevent new fragility fractures (+41%), and improve the adherence rates to OP treatment (+31%) (Table 2).

Such impacts might result, likewise, in a reduction in the occurrence of new fragility fractures and, consequently, the number of related deaths.[29] Specifically, it was estimated that implementing these four actions would prevent 8,640 fractures and 1,123 deaths during the first-year post-implementation. The weight of each action on each beneficial impact and the number of fractures and deaths that each action would prevent according to the experts' opinion are shown in Table 3.

Cost of Initial Investment in Implementing the Actions

To implement the set of actions, several resources and costs would necessary (Supplementary Table 3). Implementing them would involve an initial investment of €4,375,663 by the SNHS.

Social Return in a One-Year Time Frame

In order to estimate the return, it was assumed that the implementation of the actions would prevent new fragility fractures, which would likewise yield crucial medical cost savings in terms of the fractures themselves and their follow-

Table 2 Impact of the Actions on Relevant Clinical Outcomes According to the Experts' Opinion

Outcomes	Data from the Literature	Estimated Data After Applying the Set of Actions. (Mean [min.; max.])	Difference (Mean [mín.; max.])
Imminent risk of new fracture after a previous fracture (within the first year)	10%[24]	6% (3%; 9%)	−4% (−7%; −1%)
Women with pharmacological treatment after fracture (within the first year)	28%[11]	69% (35%; 99%)	+41% (7%; 71%)
Adherence to osteoporosis treatment	34%[25]	65% (40%; 100%)	+31% (6%; 66%)

Table 3 Weights Awarded by the Experts to Each Action and the Resulting Potential Clinical Impact of Each

	Weight of Each Action on Reducing Imminent Fracture Risk (%)	Weight of Each Action on Increasing the Frequency of Women on Treatment After Fracture (%)	Weight of Each Action on Increasing Medication Adherence (%)	Number of Fractures Prevented (N)	Number of Deaths Prevented in Year 1 (N)
Action 1. Create FLSs	31%	32%	29%	2,671	347
Action 2. Harmonise clinical guidelines and provide training to HCPs	51%	51%	53%	4,427	576
Action 3. Promote the adherence of HCPs to fracture registries	9%	9%	9%	765	99
Action 4. Raise social awareness of osteoporosis and fractures	9%	8%	9%	777	101
TOTAL	**100%**	**100%**	**100%**	**8,640**	**1,123**

Abbreviations: FLSs, fracture liaison services; HCPs, Healthcare professionals.

up. Similarly, preventing fractures would involve professional and informal care savings. By contrast, the actions would increase the number of patients undergoing preventive treatment, increasing pharmacological costs.

It was also assumed that prevention of refractures would have an impact on patients' HRQoL and would improve different aspects of patients' lives, such as their physical function, social relations, and emotional state. These improvements would be translated into cost savings quantified by the patients' WTP (see WTP results in Supplementary Table 4), that reflected how much patients would be willing to pay to recover their state prior to the fragility fracture in certain aspects of their HRQoL. Additionally, preventing new fractures would positively impact the working life of active patients, resulting in cost-saving due to increased productivity.

Improvement of all actions would yield a social return of € 96,939,931 in the first year. The 22.2% of the recovery would be associated with direct costs (avoidable cost of refractures and follow-up, associated professional care, pharmacological treatment, etc); 15.4% would be intangible (avoidable cost due to the improvement of patients' HRQoL and associated WTP based on fragility fracture impact); The remaining 62.4% would comprise professional socio-healthcare, non-professional care, and indirect avoidable costs due to the reduction of productivity losses (included in the base-case).

Table 4 details the social return within the one-year time frame per action, overall and the sum from the social perspective (base-case, all costs considered) and the SNHS perspective (alternative scenario 1, direct and intangible costs considered).

SROI Ratio Estimation

To implement these four actions to improve secondary prevention of fractures, €4,375,663 would be necessary for the initial investment, but they would yield a social return of €96,939,931 in the first year. Therefore, the SROI result after the implementation would result in the base-case scenario with a one-year time frame with 22.15 euros for each euro invested. The SROI ratio for each of the four improvement actions would be €28.69, €23.14, €24.29, and €10.70, respectively. The initial investment for action 1, 2, 3 and 4 would represent a 3.49%, 4.32%, 4.12% and 9.34% of their return, respectively. The estimated investment and return for the calculation and SROI are shown in Figure 1.

From the perspective of SNHS (alternative scenario 1, considering direct and intangible costs), the SROI ratio would be of €8.33 (€9.99, €9.39, €8.45, and €3.79 for actions 1, 2, 3, and 4, respectively) (Figure 2A). Considering only the direct costs (tangible return) the SROI would be €4.92 (€5.89, €5.54, €4.96, and €2.27 for actions 1, 2, 3, and 4, respectively) (Figure 2B).

Table 4 Social Return by Action (in Euros) and Type of Cost Considered (One-Year Time Frame)

	Direct Costs[a], €	Intangible Costs[a], €	Health and Social Care Costs, €	Informal Care Costs, €	Indirect Costs Due to Productivity Loss, €	TOTAL (Per Action), €	
						Social Perspective	SNHS Perspective
Action 1. Create FLSs	6,614,504	4,615,968	1,601,421	4,239,178	15,162,033	**32,233,104**	**11,230,472**
Action 2. Harmonise clinical guidelines and provide training to HCPs	11,025,145	7,650,636	2,654,241	7,026,135	25,129,985	**46,040,832**	**18,675,781**
Action 3. Promote the adherence of HCPs to fracture registries.	1,883,388	1,321,245	458,380	1,213,395	4,339,882	**9,216,290**	**3,204,632**
Action 4. Raise social awareness of osteoporosis and fractures	2,000,407	1,342,217	465,656	1,232,655	4,408,769	**9,449,705**	**3,342,624**
TOTAL	21,523,444	14,930,066	5,179,698	13,711,363	49,040,669	**96,939,931**	**36,453,509**

Notes: €: euros (year 2020). [a]Costs used to calculate the tangible return to the SNHS. The total costs (in euros) from the social and the SNHS perspective are in bold.
Abbreviations: FLSs, fracture liaison services; HCPs, Healthcare professionals; SNHS, Spanish National Health System.

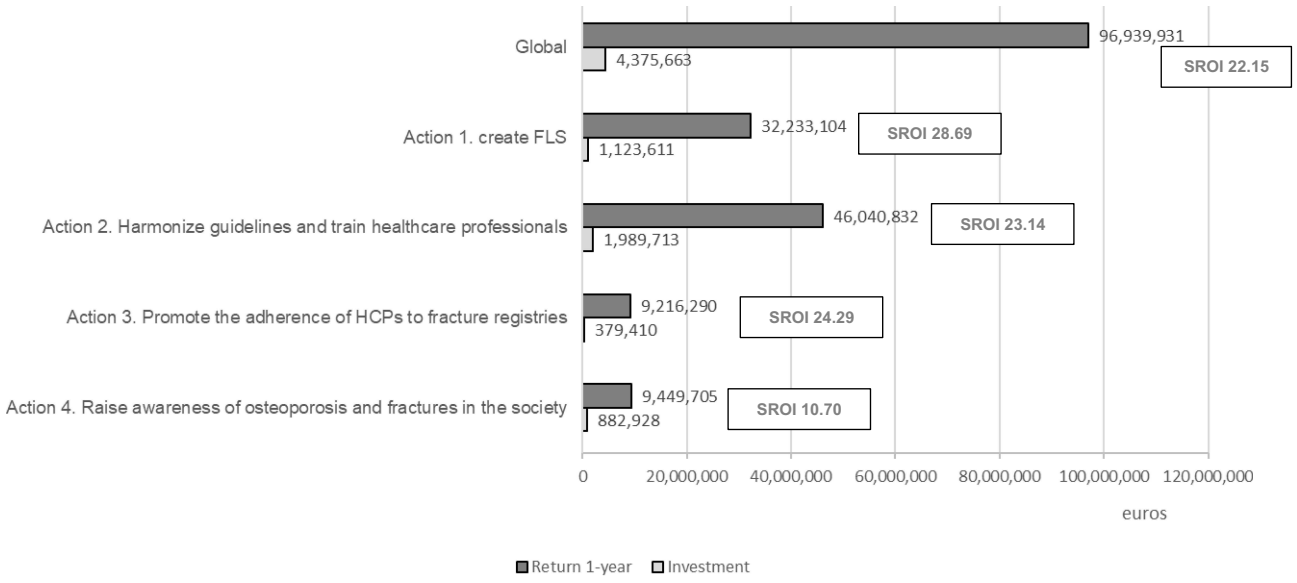

Figure 1 Investment, return and SROI ratio from the social perspective within a one-year time frame (€).
Abbreviations: FLS, fracture liaison services; HCPs, Healthcare professionals; SROI, Social Return on Investment.

Sensitivity Analysis

Regarding the worst- and the best-case scenarios, the SROI ratios were greater than 1 in all cases, including the worst-case scenario: €4.44 when modifying the reduction of the imminent risk of new fractures and €21.80 when changing the patients' WTP results (Figure 3) (Supplementary Table 4).

In the alternative scenarios with a time frame of three years from the social (alternative scenario 2) and SNHS perspectives (alternative scenario 3), the SROI ratio was €32.23 and €6.61, respectively. In the first case, the SROI ratio would be higher than in the base-case scenario (one-year time frame) because the avoidable costs for productivity losses and professional and non-professional care would remain similar in years 2 and 3, therefore, the social return would increase. From the SNHS perspective, the SROI would be lower in a three-year time frame because the cost derived from pharmacological treatment at two and three years is added (subtracted from the return), and the avoidable costs associated with the fracture are thus lower in years 2 and 3 (the first year after the fracture the cost for the SNHS is greater than in the following years). A summary of the results of all scenarios is presented in Supplementary Table 5.

Discussion

To the best of our knowledge, this is the first study to evaluate the SROI of different actions to comprehensively improve the secondary prevention of fragility fractures. Our SROI estimation shows that implementing specific actions would provide benefits not only in clinical terms and at the healthcare system level but also in terms of the patient's welfare and society. These benefits would amount to €22.15 for each euro invested in our base-case scenario within a one-year time frame (for the SNHS, €8.33; €4.92 tangible return).

The four improvement actions proposed are consistent with the IOF recommendations[7] and present a favourable individual SROI outcome ranging from €10.70 for each euro invested for raising social awareness to €28.69 for the creation of FLSs. FLSs making treatment recommendations have already been estimated to yield a mean SROI of 18.39.[30] The creation of FLSs is also aligned with the Fracture Working Group statement as a Best Practice Framework to improve the continuity of care for patients with fragility fractures.[31] In addition, previous economic evaluations have shown that these multidisciplinary specialised units represent a cost-effective strategy for reducing refractures and fracture-related mortality in different settings,[25,32,33] including Spain.[34] The success of the FLSs model is based on a multidisciplinary team and its integration and coordination with orthogeriatric units. This approach systematically optimizes the care of all fracture patients, encompassing identification, study, initiation of treatment and follow-up.[35] The

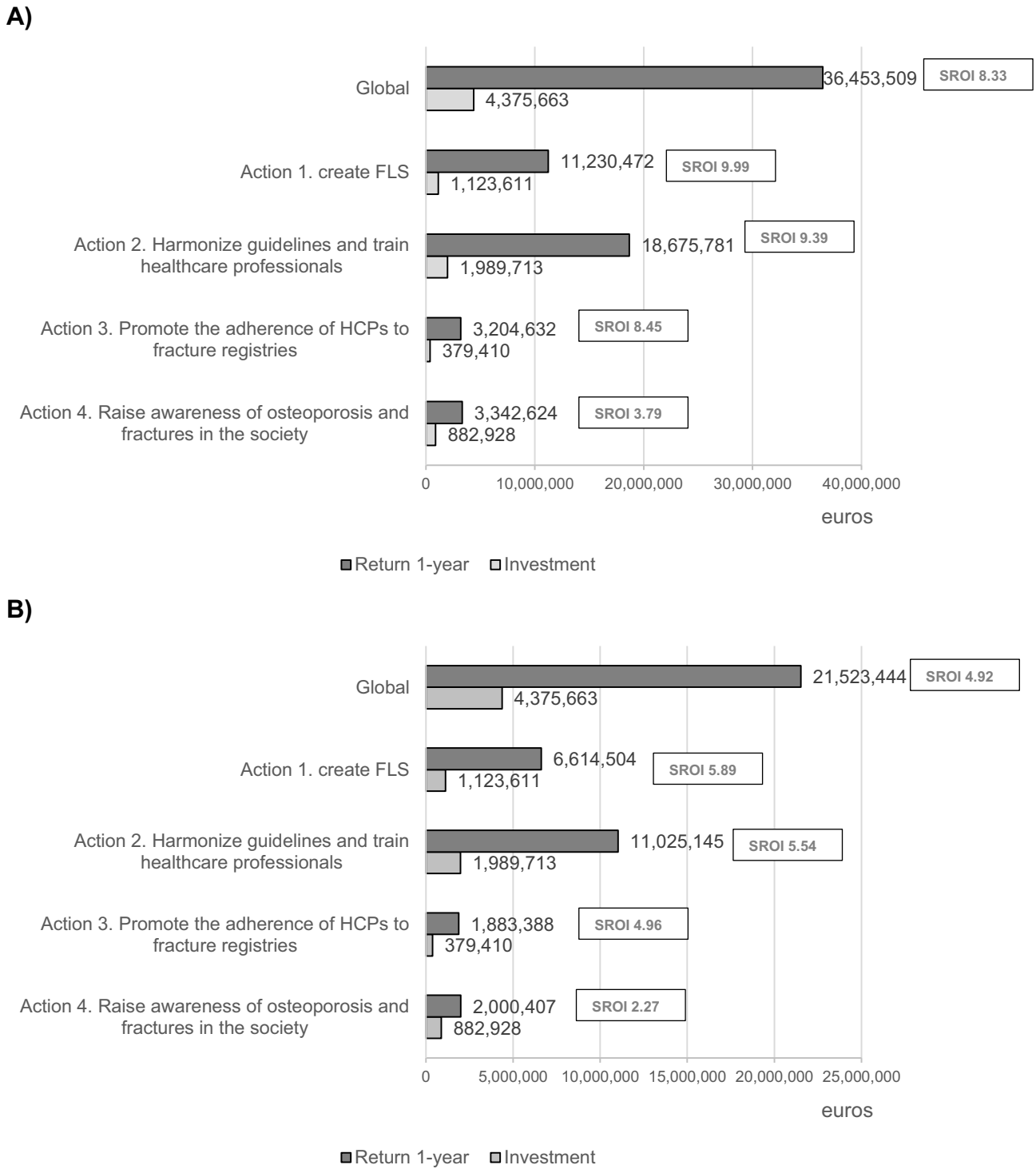

Figure 2 Investment, return and SROI ratio (€) from the SNHS perspective within a one-year time frame (**A**) and breakdown of tangible return (**B**).
Abbreviations: FLS, fracture liaison services; HCPs, Healthcare professionals; SNHS, Spanish National Health System; SROI, Social Return on Investment.

role of a case manager or liaison nurse has advantages regarding quality, safety, and cost-effectiveness, as it contributes to more efficient use of resources.[35,36] The demonstrated improvement of outcomes following the implementation of FLSs, which are considered the most effective interventions for secondary prevention,[25,37,38] may explain why the highest SROI was estimated for the action of FLSs creation.

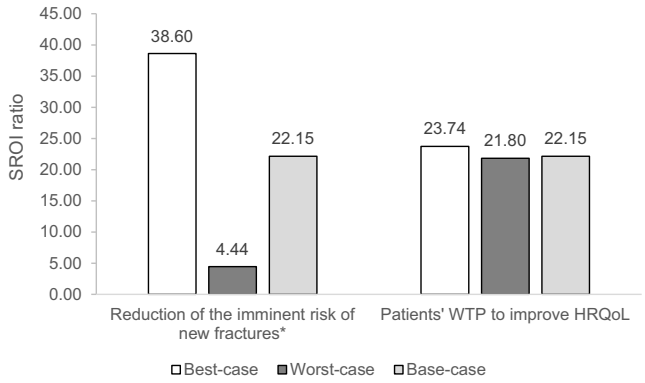

Figure 3 Sensitivity analysis for the SROI ratio: best- and worst-case scenarios. *Percentage of risk reduction: −7% best-case, −1% worst-case, −4% base-case.
Abbreviations: HRQoL, health-related quality of life; WTP, willingness to pay; SROI, Social Return on Investment.

The second proposal focused on harmonising clinical practice guidelines and promoting HCPs awareness of the best practice recommendations and the importance of fracture prevention, similar to initiatives in other countries.[39,40]

Another proposed action was to encourage the adherence to national fracture registries. There are two national registries in Spain: the national hip fracture registry (RNFC)[41] and the Spanish registry of fractures within the context of FLS (REFRA).[42] Both registries are well accepted by some specialties and hospitals; however, many Spanish hospitals do not participate in these registries.

Our findings also confirm that not only are actions involving healthcare institutions and HCPs efficient, but also those at the population level provide a notable social return. In this respect, the experts proposed carrying out a social awareness-raising campaign on OP and fragility fractures targeting the general population as the fourth improvement measure. Improving health literacy is essential to identify at-risk patients so they can be adequately treated, and the costs associated with preventable fractures can be avoided. In particular, information campaigns on bone health and healthy lifestyle habits (including fall prevention advice) can help raise awareness about the risk of fractures and secondary prevention, the benefits versus risks of treatment and the importance of adherence to treatment.[43] In line with experts' weights on the predicted impact on clinical outcomes, Action 4 was the action with the lowest SROI. However, its SROI was positive in all settings, and it resulted in a social return of more than €10 or €15 per euro invested in the 1-year and 3-years horizon, respectively. This suggests that higher benefits may be derived from social awareness campaigns in the long term.

The substantial social return of optimising secondary prevention of fragility fractures in women with postmenopausal OP, highlights the enormous disease burden. Calculation of the return considered the costs avoided by fractures prevented by the SNHS and, interestingly, those prevented by society.

The present study evaluates the costs of the formal and informal care of the disease based on a patient survey.[27] Notably, 53.3% of participants needed care, and the vast majority (76.5%) received non-professional care. The need for care is one of the silent OP-associated burdens having social impacts[17] and has also been highlighted in our study. Loss of labour activity is another social burden of fragility fractures, which has also been addressed. It is estimated that 20% of fractures occur at the pre-retirement age.[44] However, our survey revealed that 56% of postmenopausal women with OP suffer fractures at working age, and this has a considerable impact on work productivity (69.3% temporary disability, 17.3% permanent disability, 10.7% reduction in working hours, 10.7% loss of employment, 5.3% leave of absence, or 3.6% pre-retirement).[27]

Undoubtedly, one of the most significant silent burdens of fragility fractures is their impact on HRQoL, which has been considered in the SROI as an intangible disease cost. The effect of fragility fractures on HRQoL has been extensively evaluated previously.[45–47] Physical function is one of the most affected domains, resulting in difficulty performing everyday tasks. That, in turn, leads to decreased recreational and leisure activities and, therefore, impaired social function. This situation often affects emotional health, leading to anxiety and depression. Specifically, vertebral and hip fractures significantly impact patients' lives[48] due to the loss of mobility and independence.[49,50] Therefore, to

calculate the intangible cost of the disease, our study asked the patients considered herein to place a monetary value on regaining their pre-fracture status in different areas of HRQoL. As a result, the WTP was one of the values considered in the SROI, a calculation commonly used in economic evaluations of health interventions to measure changes in welfare.[51] The WTP values assigned by patients, reinforce that these measures would not only result in a positive social return for investment but also may improve patients' health status and HRQoL and help them cope with a disease as burdensome as OP and fragility fractures.

The usefulness of the SROI methodology in the Spanish healthcare setting is reflected in previous studies with estimations of positive balance (SROI > 1) in the application of improvements for the ideal approach to different pathologies such as multiple sclerosis,[22] rheumatoid arthritis[21] and COPD,[23] all of which have a lower associated burden (disability-adjusted life years) than fragility fractures.[52] The results are not comparable as they depend directly on the working group involved in each study and their opinions. Nevertheless, the high morbidity and mortality associated with fragility fractures could explain the higher balance (return, in euros, for each euro invested) obtained in the present SROI study compared to those previously mentioned. In any case, what is important is that in our analysis the benefit outweighs the investment required for fragility fracture prevention. These results may be helpful for decision-makers taking into account that these actions would be profitable and, even more importantly, they may promote patient care improvements and their HRQoL. Furthermore, the analysis carried out in the Spanish context could be replicated in other healthcare systems, where it could be appropriate to apply the same or other additional actions for fragility fracture prevention.

This SROI analysis is not without limitations. First, we acknowledge that there is no standardised method to measure the social return on the investment, while at the same time, providing greater flexibility. For this reason, in our analysis, we considered all types of costs that might affect patients and society as a whole (ie, we quantified intangible costs such as improvements in patients' HRQoL). We also applied a conservative approach so that the analysis would not overestimate the return on the investment (ie, we selected the highest investment costs and the lowest impact on return when possible). Second, due to the absence of published evidence for some data, we used experts' opinions, such as the impact of actions on reducing the imminent risk of new fractures. Since these opinions might add more uncertainty to the analysis, we conducted a sensitivity analysis evaluating the best- and worst-case scenarios that resulted in a positive SROI in all cases. Future research with real-world data collection may confirm the results obtained here. In addition, patients' willingness to pay is based on survey data, which may vary depending on the survey population. Nevertheless, although the population included in the survey was younger than average women with OP,[53,54] they already had a mean of 1.6 fragility fractures. Therefore, they were already facing the challenges of OP and fragility fractures. Moreover, their average age also agrees with the age of women with the same characteristics involved on previous surveys to evaluate HRQoL.[45,46] In addition, sensitivity analyses confirm the consistency of data. Similar SROI ratios were obtained when varying WTP, an intangible variable that is one of the most difficult to estimate. Furthermore, the imminent risk of fracture sensitivity analysis shows how crucial this outcome is as it has an important impact on the SROI. These results show that the calculations are aligned with the expected results (same investment, much lower return). Third, we adopted a prospective approach limited to a time frame of one year in the base case to up to three years in an alternative scenario, which might be insufficient to capture the consequences of the actions in the long term. In this respect, we considered that since the risk of refracture is particularly high in the first years after the event, a three-year time frame for the alternative scenario can enable us to capture the most significant benefits in reducing this risk.

Conclusion

In conclusion, according to our SROI results, implementing specific actions to improve secondary fracture prevention would provide a considerable benefit for society, which would far outweigh the investment in monetary terms. Furthermore, the proposals for improvement are aligned with IOF and other scientific organizations and focus on promoting FLSs, homogenisation of guidelines, adherence to fracture registries, and social awareness. Therefore, the results of the present study are of great interest to healthcare decision-makers to help them predict the benefits obtained after optimising the approach to postmenopausal OP and fragility fractures. Since decision-makers constantly face healthcare budget constraints, our findings provide valuable information for health policy decisions that are in line with the recommendations of scientific societies and healthcare professionals. More importantly, the implementation of

these actions would not only be positive in terms of social return of investment, but also may improve patients' health state and HRQoL.

Abbreviations

COPD, Chronic obstructive pulmonary disease; DALYs, Disability-adjusted life years; FLSs, Fracture liaison services; HCPs, Healthcare professionals; HRQoL, Health-related quality of life; IOF, International Osteoporosis Foundation; OP, Osteoporosis; SNHS, Spanish National Health System; SROI, Social Return on Investment; WTP, Willingness to pay.

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