

# Risk Factors for Osteoporosis and Fractures in Postmenopausal Women Between 50 and 65 Years of Age in a Primary Care Setting in Spain: A Questionnaire

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**Abstract:** *Introduction:* Osteoporosis (OP) is a major, highly prevalent health problem and osteoporosis-related fractures account for high morbidity and mortality. Therefore, prevention and early detection of osteoporosis should strive to substantially reduce this risk of fracture.

*Objective:* The present observational, descriptive, cross-sectional study sought to assess the prevalence of risk factors for osteoporosis and fractures in a large sample of postmenopausal women aged 50 to 65 years attending Primary Care facilities in Spain.

*Methods:* We recruited 4,960 women, at 96 Primary Care centers. Demographic and anthropometrical data, as well as information regarding risk factors for OP were collected using a questionnaire.

*Results:* The prevalence rates for the major osteoporosis risk factors in our population were: low calcium intake, 43%; benzodiazepine use, 35.1%, and height loss, 30.1%. Other relatively prevalent factors include: having suffered at least one fall during the preceding year; positive family history of falls (particularly on the mother's side), smoking, kyphosis, presence of any disease affecting bone metabolism, personal history of falls, and inability to rise from a chair without using one's arms. The least frequent factors were weight loss of greater than 10% over the preceding 10 years and problems in sensory perception that affect patient's ability to walk.

*Conclusions:* The main risk factors for osteoporosis in women 50-65 years of age are low calcium intake, use of benzodiazepines, and observed loss of height. Our results may help physicians to identify groups at risk for OP and fractures at early stages and consequently, optimize prevention and early diagnosis of osteoporosis in postmenopausal women.

**Keywords:** Postmenopausal women, risk factors, osteoporosis, primary health care.

## INTRODUCTION

Osteoporosis (OP) is a highly prevalent disease particularly in postmenopausal women, characterized by decreased bone density resulting in increased susceptibility to fracture [1, 2]. The clinical relevance of OP is derived not only from the increase in morbidity and mortality, but also the pain, physical impairment, and loss of functional ability that have an important impact on patients' quality of life. It also entails significant cost to society: hospitalization costs are increased as are medical tests, length of stay in nursing homes and consulting rooms, as well as the costs associated with patients' diminished activity [3-5]. According to the World Health Organization (WHO), 30% of Caucasian

women over the age of 50 suffer from OP versus 8% in males [6]. In Spain, 17.2% of females aged 50-60 years may suffer from OP. The percentage of affected women rises to 40% between 60-70 years of age [7].

OP is a chronic disease requiring chronic treatment. However, as this condition produces little or no symptoms, patients go undiagnosed until a fracture occurs and the osteoporosis is more severe. Hence, disease prevention and early diagnosis are particularly important. Nevertheless, effective diagnostic tools are currently not available to assist Primary Care physicians in detecting individuals at risk for developing OP and associated fractures in the future. Identifying OP risk factors will aid Primary Care physicians in selecting patients for evaluation and intervention.

That is why it is important to assess not only the risk factors associated with osteoporosis *per se*, which are fairly well-known, but also their prevalence in the general population. Several studies have shown that there are many

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risk factors that need to be taken into account: age, early menopause, history of previous fractures, family history, being underweight or treatment. The prevalence of these factors has been analyzed [8-10] however, most of these studies have been conducted in women over the age of 65 years.

Consequently, little information is available on the most prevalent risk factors for OP in postmenopausal women aged 50-65 [11, 12] which is where OP prevention schemes should be focused on substantially decreasing the incidence of OP and fractures.

This study sought to assess the prevalence of risk factors for osteoporosis and fractures in a large sample of postmenopausal women aged 50 to 65 years cared for at Primary Care facilities in Spain.

## MATERIALS AND METHODS

### Study Design

An observational, cross-sectional, descriptive study was designed to analyze the prevalence of different OP risk factors. The study was conducted at Primary Care centers belonging to the public healthcare system in Spain. The distribution of sites (100 sites planned) across the Spanish geography and sample size (50 patients per site) was calculated on the basis the number of patients with this specific age according the 1998 Census by quotes and geographic distribution to achieve a truly representative sample.

Dedication to the study was reimbursed according to European Medicines Evaluation Agency (EMA) guidelines for studies of this kind [13]. The protocol was approved by an independent review board.

### Patients and Procedures

Postmenopausal women with ages between 50 and 65 years attending a routine visit with any of the participating physicians were invited to participate in the study, regardless of the reason for consultation. A signed authorization for the collection and use of clinical data in accordance with standing regulations regarding personal data protection was obtained from all subjects prior to enrollment. Patients participating in any other clinical study of OP drug treatment were excluded.

Demographic, anthropometric, and risk factors for OP and fracture data were recorded for patients included in the study using a 14-item questionnaire administered by physician. The questionnaire included the following information: personal data (date of birth, age at menarche, age at onset of menopause, type of menopause, number of children), physical examination (weight, height, pulse), osteoporosis and fracture risk factors (weight loss greater than 10% in the last 10 years or if the loss it has compared with in weight that it had to the 35 years, loss of height, kyphosis, disturbances of sensory perception, number of falls in the previous year, ability to stand up from a chair unaided), patient life style factors (dietary consumption of dairy products in mg, physical activity, cigarette smoking), personal history of previous fragility fractures (excluding trauma fractures), family history of osteoporotic fracture (father, mother, or sisters), prior and present use of drugs

affecting bone metabolism (bisphosphonates, HRT, calcitonins, calcium and vitamin D, raloxifene, tibolone), drugs that increase the risk of osteoporosis or fractures (anticonvulsants, thyroid hormones, oral and inhaled glucocorticoids, oral anticoagulants, benzodiazepines, antiarrhythmics, oral insulins, hypoglycemics, lithium), and disorders that affect bone metabolism and increase the risk of falls (chronic liver disease, Cushing's syndrome, hyperparathyroidism, stroke, malabsorption syndromes, secondary amenorrhea lasting at least one year, obstructive pulmonary disease, rheumatoid arthritis, urolithiasis, Parkinson's disease, hyperthyroidism, gastrectomy, and type I diabetes).

### Statistics

Quantitative variables were described in terms of mean and median values, as well as typical deviation, first and third quartile, and range (maximum and minimum values). They are analyzed using an ANOVA model. Qualitative variables were described by frequency and percentage and analyzed using the Chi square test or, if not applicable, by means of Fisher's exact test. The 95% confidence intervals are used for all variables.

Patients were included on an intention-to-treat (ITT) basis.

## RESULTS

A total of 4960 women were screened for the study over a 10-month period (July 2002-April 2003) at 96 primary care centers. All patients signed the inform consent. Sixty-two patients were excluded because they did not meet inclusion/exclusion criteria (mainly age). As a result, 4898 patients were finally included in the analysis and distributed into three age subgroups: 39% of the patients were 50-55 years of age (n=1905), 28% were 56-59 (n= 1378), and 33% were 60-65 (n=1615).

General characteristics (N=4898) are summarized in Table 1. No significant differences were observed between age groups for physical characteristics on the whole; we therefore examined more detailed data for the entire group. Mean age at menarche was 12.87 (SD: 1.6), slightly higher in the 60-65 year age group (13.6). Mean age at onset of menopause was 48.5 (SD: 4.5). Menopause was natural in 84.9% of the subjects. The data collected from the physical examination yielded a mean weight of 69.7 kg and mean height of 157 cm. Mean body mass index was 28.3 kg/m<sup>2</sup> indicating that our population is somewhat overweight.

The prevalence of risk factors is detailed in Table 2. According to the data obtained, factors with a prevalence rate greater than 30% are: low calcium intake ( $\leq 600$ mg/day, measured by dairy product intake), 43%; use of drugs that can influence bone metabolism and/ or increase the risk of fracture, 35.1%; lack of physical activity (defined as no intentional physical activity declared by the patient), 31.8%, and observed height loss throughout the patient's life, 30.4%.

Other OP and fracture risk factors detected in our population included: having suffered at least one fall over the preceding year (22.8%). This percentage increased with age: 17.7% in the 50-55 year group; 23.2% in the 56-59 year old group, and 28.7% in the women aged 60-65 years.

**Table 1. General Characteristics (N=4898)**

	Mean	SD	95% CI	Median
Age at menarche (years)	12.87	1.6	12.8-12.9	13
Age at onset of menopause (years)	48.49	4.5	48.4-48.6	49
Number of children	2.46	1.5	2.4-2.5	2
Weight (kg)	69.7	11.8	69.4-70.0	68.5
Height (cm)	157.08	6.6	156.9-157.2	157
Body Mass Index	28.31	4.9	28.2-28.5	27.7
Number of falls in the preceding year	1.96	2.86	1.79-2.13	1
Number of hours of physical activity/ week	3.9	4.9	3.7-4.1	3

**Table 2. Prevalence of OP and Fracture Risk Factors (N=4898)**

	50-55 Years N=1905 (%)	56-59 Years N=1378 (%)	60-65 Years N=1615 (%)	Total N=4898 (%)	Chi-Square p-Value
Dairy product intake ( $\leq 600$ mg/ day)	773 (40.6)	600 (43.5)	738 (45.7)	2111 (43.1)	0.0087
Observed height loss	448 (23.5)	410 (29.8)	632 (39.1)	1490 (30.4)	<0.0001
Observed weight loss $\geq 10\%$ in 10 years	141 (7.5)	111 (8.1)	145 (9.0)	398 (8.1)	0.2971
Patients with at least one fall in the preceding year	337 (17.7)	319 (23.2)	463 (28.7)	1119 (22.8)	<0.0001
Presence of kyphosis	266 (14.0)	255 (18.5)	395 (24.5)	916 (18.7)	<0.0001
Inability to rise from a chair without using one's arms	166 (8.7)	128 (9.3)	196 (12.1)	490 (10.0)	0.0009*
Problems in sensory perception affecting patient's ability to walk	104 (5.5)	91 (6.6)	146 (9.0)	341 (7.0)	<0.0001*
Current and past smoking status	610 (32.0)	251 (18.2)	212 (13.1)	1163 (21.9)	<0.0001*
Lack of physical activity	601 (31.5)	421 (30.6)	534 (33.1)	1556 (31.8)	0.334
Personal history of osteoporotic fracture	136 (7.1)	123 (8.9)	246 (15.2)	505 (10.3)	<0.0001*
Family history of osteoporotic fracture	415 (21.8)	300 (21.8)	379 (23.5)	1094 (22.3)	0.1749
Mother	(18.2)	(17)	(17.2)	(17.5)	0.5869
Use of drugs that can influence bone metabolism and/ or increase risk of fracture: current or past	570 (29.9)	506 (36.7)	642 (39.8)	1718 (35.1)	<0.05
Presence of bone metabolism disorder or disease that increases risk of falls	194 (10.2)	145 (10.5)	246 (15.2)	585 (11.9)	<0.05

\*CMH (Cochran-Mantel-Haenszel).

Insofar as the prevalence of previous osteoporotic fractures is concerned (see Table 3), 10% of all patients had had at least one fracture in the past with the forearm the most common fracture site (35%). Twenty-two percent of the patients had a positive family history of osteoporotic fracture(s) (22.3%), predominantly on their mother's side (17.5%).

Other factors were presence of kyphosis (18.7%), observed weight loss greater than 10% over the previous 10 years (8%), inability to rise from a chair without using one's arms (10%), problems in sensory perception affecting the patient's ability to walk (from 5.5% to 9% depending on age group), and lifestyle-related factors such as, current or past smoking (21%).

Strikingly, 30.2% of the study subjects were taking any medication for OP (Table 4) and of them, 8.1% were only taking calcium and/or vitamin D.

**Table 3. Site of Prior Osteoporotic Fracture (n= 505)**

	Number of Fractures	%*
Forearm	179	3.65
Foot	103	2.10
Leg	89	1.81
Vertebra	48	1.0
Humerus	30	0.6
Sternum/ Ribs	17	0.34
Hip	16	0.32
Clavicle/ Scapula	10	0.2
Sacrum/ Coccyx	9	0.18

\*Calculated from the total study population N=4898.

As mentioned previously, 35% of the patients were taking drugs that could influence bone metabolism and/ or increase the risk of fracture (Table 4), the most frequent of which were: benzodiazepines (36%), thyroid hormones (5.5%), and oral antidiabetic agents (4.2%).

**Table 4. Drugs to Treat Bone Metabolism Disorder and those that can Affect Bone Metabolism**

	%*
<b>Drugs to treat bone metabolism disorder: current use</b>	
Calcium	16.9
Hormone replacement therapy	7.4
Vitamin D	7.2
Raloxifene	7.3
Biphosphonates	4.6
Calcitonin	1.3
Tibolone	2.2
<b>Drugs that can affect bone metabolism: past or current use</b>	
Benzodiazepines	22.6
Thyroid hormones	5.5
Hypoglycemics	4.2
Inhaled glucocorticoids	2.8
Oral glucocorticoids	2.6
Anticoagulants	1.9
Antiarrhythmics	1.8
Insulins	1.2
Anticonvulsants	1.1
Lithium	0.3

\*Calculated from the total study population N=4898.

Additionally, 11% of the participants were suffering from a bone metabolism disorder or a disease that increases the risk of falls; the most common of them were: urolithiasis in 3.7% and hypothyroidism and chronic pulmonary obstructive disease, both in 1.7% of the patients and rheumatoid arthritis in 1.5% of patients.

## DISCUSSION

The present naturalistic study reveals the prevalence of various risk factors in postmenopausal women aged 50 to 65 years visiting their physician for routine consultation.

From our results, the most prevalent OP and fracture risk factors (over 30%) are low calcium intake (less than 600 mg/day), use of drugs that affect bone metabolism (mainly benzodiazepines), and observed height loss, followed by lack of any physical activity. There is another important group of moderately prevalent factors (10-23%) including: having had at least one fall in the last year; family history of falls (especially on the mother's side), cigarette smoking, kyphosis, presence of a disorder affecting bone metabolism, personal history of falls, and inability to stand up from a chair without using one's arms. The least frequent risk

factors observed were weight loss greater than 10% in the last 10 years and problems in sensory perception that affect patient's ability to walk.

When relating the prevalence of the different risk factors found in our study with the relative importance of those factors with respect to osteoporosis as assessed in a published review [14], we have detected differences between both concepts. Some of the factors considered as high risk had a low prevalence; hence, their final importance may in fact be relative.

According to our study, with the exception of age, considered to be a high risk factor when over 70 years and therefore excluded from our study population, there is only one high risk factor that also displayed a high prevalence rate – physical inactivity. This is consistent with the findings of a retrospective review of the prevalence of risk factors in a general female population aged 50 years and older [15] and also with the improvements in dynamic balance and strength, both important determinants of risk for falls in a community-based exercise program conducted in a randomized control trial [16]. Van der Voort *et al.* also reports that practicing sports, even in the past, exhibited a slightly positive relationship with the patients' fractures [17].

Other important high risk factors that were identified are personal history of osteoporotic fracture [18, 19] and weight loss [14]. Nevertheless, both of them had a prevalence rate of approximately 10% in our study, which seems reasonable compared with the older population, due to the shorter time of deterioration given the fact that our population was younger.

The personal history of fracture reported in older women ranged from 39.2% to 24.3% [8, 20, 21]. The figure from a Spanish population was a lower (20.1%) [10], perhaps due to the lower incidence of osteoporotic fracture in the Spanish population versus the USA [22]. Nevertheless, data from our study yield a much lower figure of 10.3%; this is in line with studies in younger populations (patients over the age of 45 years) that present rates that range from 8 to 10% [23-25]. Weight loss had been considered to be the best predictor of low bone mineral density in elderly women [26], however it seems that it is less important in women under 65 years of age.

On the other hand, some of the moderate risk factors [14] were highly prevalent in our study population. We have established that low calcium intake was the most prevalent factor found in the study (43%). This deficiency was not compensated with calcium supplements as only 16.9% of study population was taken this type of supplements. Remarkably, only 22.1% of patients were taking specific medication for OP.

A positive family history of osteoporotic fracture, particularly on the mother's side, was also highly prevalent in our study population, 22.3%, albeit lower than data published in the literature that has been cited at around 30% [23, 27]. This seems reasonable since our population was younger, so that their families (mainly mother and sisters) were also younger and had less osteoporosis fractures. Once again, this difference can be attributed the lower incidence of osteoporotic fracture in the Spanish population versus the USA [22].

Another well-known risk factor [28], smoking, was present in 22% of our study population. Current and past cigarette smoking is the only factor that differed significantly in terms of prevalence between the different age groups in our study. The highest prevalence for this factor, 32.1%, was found in the youngest group (50-55 years) compared to the other two groups: 18.2% in the 55-60 year-old group and 13.1% in the oldest age group (60-65 years). This difference is easily accounted for if we consider lifestyle changes and increased rates of smoking among the female population in Spain. It is also consistent with the results obtained in the ESPO study in premenopausal women [29], which concluded that bone stiffness was negatively correlated to age and number of cigarettes and positively related to body weight, body weight at age 25, height, and estimated daily calcium intake in this special population. Nevertheless, data regarding smoking is highly variable in the literature because of the idiosyncratic, sociological influence on this range [10].

Similarly, the use of drugs that can influence bone metabolism and/ or increase risk of fracture is also conditioned by sociological idiosyncrasies. Different clinical and prescription habits can explain the high prevalence of benzodiazepine-based treatment that was consistent with another Spanish study carried out in an older patient population [10] but significantly higher than other published studies reporting data of approximately 9% [20, 21]. This is also the case with thyroid hormone use – our study detected a 5.5% rate of thyroid hormone use; a 3.5% rate is reported in the older Spanish population and between 11-18% in other literature reports [20, 24, 30].

This study has the inherent limitations owing to its naturalistic design. For instance, we cannot exclude the possibility of recall bias due to self-report of information regarding risk factors and history of previous fractures, despite the evidence indicating that self-report is highly accurate [31, 32]. Another limitation is that patients included into the study were those attending a routine visit to a Primary Care centers and are not general population. This inconvenience was minimized by selecting patients by quotes per age and geographic distribution according the 1998 Census to achieve a truly representative sample and offers them the study regardless of the reason for consultation. It is also noticeable that the prevalence of the risk factors identified may not reflect the actual importance of their contribution to osteoporosis, being for example of low frequent but high impact on the osteoporosis disease.

As we have already seen in the discussion, it is highly subject to idiosyncratic influences (for example: drug prescription, smoking habits...), but there are other general factors whose prevalence are of great overall relevance.

This is the first study to show the prevalence of risk factors for OP and fractures in a large sample of postmenopausal patients aged 50-65 years in a Primary Care setting. In contrast with the  $\geq 65$  years series [8-10] there are some factors that are found to be more prevalent in our population: low calcium intake (including low percentage of patients taking calcium or vitamin D), smoking habits, and family history of osteoporosis. With age, other factors take on greater relevance, such as personal history of osteoporotic fracture, other concomitant diseases, and the use of drugs

that can influence bone metabolism, weight loss, etc... [33, 34].

Taking into account that age itself is a clearly defined risk factor, it seems evident that other factors are of different relevance depending on patients' age; it will therefore be extremely valuable to have data about different factors at different ages.

Identifying prevalence factors in this younger population is especially important because, while certain risk factors such as age and gender can obviously not be modified, there are other risk factors such as calcium or vitamin D deficiency that can, at least theoretically, be changed [35].

## CONCLUSIONS

As we have pointed out, the relevance of the different risk factors for osteoporosis and fractures in postmenopausal women factors are clearly dependence on patients' age. According our results, the main factors for osteoporosis in postmenopausal women 50-65 years of age in the Primary Care setting are low calcium intake, benzodiazepine use, and observed height loss. Our results may help physicians to identify groups of patients who are at risk for OP and fracture at early stages and subsequently optimize prevention and/ or early diagnose of osteoporosis in postmenopausal women.

## ACKNOWLEDGEMENTS

The authors would like to thank all the Primary Care centers that participated in this study, as well as the patients who agreed to participate, provided consent for the use of part of their clinical data, and went to an additional visit to fulfill study procedures.

## CONFLICT OF INTEREST

Authors Maria Luz Rentero, and Marta Casillas are full-time employees of Lilly S.A., Avda. de la Industria, 30. 28108 Alcobendas – Spain.

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Received: September 16, 2008

Revised: October 7, 2008

Accepted: October 22, 2008

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