



## Primary and secondary prevention actions related to risk factors for osteoporosis

### *Ações de prevenção primária e secundária relacionadas aos fatores de risco para osteoporose*

### *Acciones de prevención primaria y secundaria relacionadas con los factores de riesgo para osteoporosis*

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#### ABSTRACT

**Objective:** To analyze the effectiveness of the International Osteoporosis Foundation (IOF) test for primary and secondary prevention related to risk factors for osteoporosis. **Methods:** This is a cross-sectional study conducted in the interior of São Paulo, Brazil, during the Osteoporosis Prevention Campaign carried out in October 2016. 400 people, selected at random, interviewed according to the IOF one-minute osteoporosis risk test, participated. Statistical analysis used the Kolmogorov-Smirnov test, Pearson's chi-square test, Mann-Whitney, and multivariate analysis for risk factors associated with osteoporosis using the binary logistic regression model. The results were presented in odds ratios, with a 95% confidence interval. **Results:** The sample consisted of 260 women and 140 men, with a median of 57 years, and 95% indicated having some risk factor. The questions with the highest positivity index indicated that both sexes are exposed to low exposure to the sun, low intake of foods rich in vitamin D ( $p=0.140$ ), and the habit of physical activities for less than 30 min ( $p=0.657$ ). The body mass index (BMI) less than 19 kg/m<sup>2</sup> ( $p=0.336$ ) indicated less positivity. Logistic regression showed an association between four risk factors (bone densitometry, fall due to weakness, change in height after 40 years and sex) and the study population over 60 years. **Conclusion:** The IOF test proved to be a functional tool in promoting health and primary care, and can bring socioeconomic benefits.

**Descriptors:** Primary Prevention; Secondary Prevention; Risk Factors; Osteoporosis; Public Health.

#### RESUMO

**Objetivo:** Analisar a efetividade do teste da International Osteoporosis Foundation (IOF) para as prevenções primária e secundária relacionadas aos fatores de risco para a osteoporose. **Métodos:** Estudo transversal realizado no interior de São Paulo, Brasil, durante a Campanha de Prevenção à Osteoporose realizada em outubro de 2016. Participaram 400 pessoas, selecionadas aleatoriamente, entrevistadas de acordo com o teste de um minuto para risco de osteoporose da IOF. A análise estatística utilizou



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Received on: 06/27/2019

Accepted on: 04/22/2020

o teste de Kolmogorov-Smirnov, o teste qui-quadrado de Pearson, o Mann-Whitney e a análise multivariada para fatores de risco associados à osteoporose pelo modelo de regressão logística binária. Os resultados foram apresentados em odds ratio, com intervalo de confiança de 95%. **Resultados:** A amostra foi composta por 260 mulheres e 140 homens, com mediana de 57 anos, e 95% indicaram possuir algum fator de risco. As questões com maior índice de positividade indicaram que ambos os sexos estão expostos à baixa exposição ao sol, à baixa ingestão de alimentos ricos em vitamina D ( $p=0,140$ ) e ao hábito de atividades físicas por tempo inferior a 30 min ( $p=0,657$ ). O índice de massa corporal (IMC) menor que  $19\text{kg}/\text{m}^2$  ( $p=0,336$ ) indicou menor positividade. A regressão logística mostrou associação entre quatro fatores de risco (densitometria óssea, queda por fraqueza, mudança de altura após os 40 anos e sexo) e a população em estudo acima de 60 anos. **Conclusão:** O teste da IOF se mostrou uma ferramenta funcional na promoção da saúde e atenção primária, podendo trazer benefícios socioeconômicos.

**Descritores:** Prevenção Primária; Prevenção Secundária; Fatores de Risco; Osteoporose; Saúde Pública.

## RESUMEN

**Objetivo:** Analizar la efectividad de la prueba de la International Osteoporosis Foundation (IOF) para las prevenciones primaria y secundaria relacionadas con los factores de riesgo para osteoporosis. **Métodos:** Estudio transversal realizado en una ciudad de São Paulo, Brasil, durante la Campaña de Prevención de Osteoporosis realizada en octubre de 2016. Participaron 400 personas que han sido elegidas de modo aleatorio y entrevistadas según la prueba de un minuto para riesgo de osteoporosis de la IOF. El análisis estadístico utilizó la prueba de Kolmogorov-Smirnov, la prueba de Chi-cuadrado de Pearson, la de Mann-Whitney y el análisis multivariado para los factores de riesgo asociados con la osteoporosis por el modelo de regresión logística binaria. Se ha presentado los resultados en odds ratio con intervalo de confianza del 95%. **Resultados:** La muestra fue de 260 mujeres y 140 hombres con mediana de la edad de 57 años y el 95% indicaron tener algún factor de riesgo. Las preguntas con mayor índice de positividad han indicado que ambos sexos tienen baja exposición solar, baja ingestión de alimentos con vitamina D ( $p=0,140$ ) y la costumbre de actividades físicas de tiempo menor que 30 min ( $p=0,657$ ). El índice de masa corporal (IMC) de menos de  $19\text{kg}/\text{m}^2$  ( $p=0,336$ ) ha indicado menor positividad. La regresión logística ha mostrado asociación entre cuatro factores de riesgo (densitometría ósea, caída causada por debilidad muscular, cambio de altura después de los 40 años y sexo) y la población del estudio con más de 60 años. **Conclusión:** La prueba de la IOF se presentó como una herramienta funcional para la promoción de la salud y atención primaria lo que puede llevar a beneficios socioeconómicos.

**Descriptorios:** Prevención Primaria; Prevención Secundaria; Factores de Riesgo; Osteoporosis; Salud Pública.

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## INTRODUCTION

One of the major challenges to be considered in Brazil and public health is the aging of the population, making primary and secondary prevention of chronic diseases indispensable, especially when considering the causes of morbidity and mortality among adults and the elderly<sup>(1)</sup>.

It is important to highlight that the country has a heterogeneous population concerning demographic, cultural, racial, social issues, and access to health services, a factor that hinders epidemiological studies on the prevalence of osteoporosis and its interference in public health spending<sup>(2)</sup>.

Regarding osteoporosis, it is emphasized that it is a silent disease whose prevalence, according to national studies, affects 15% to 33% of postmenopausal women<sup>(3-5)</sup>. Other data indicate that it affects 10 million Brazilians, most of them over 65 years old. When compared to other diseases, in women over 45 years of age, osteoporosis has a greater number of days of hospitalization for treatment, generating greater financial expenditure in the scope of public health<sup>(2)</sup>.

Most of the scientific articles on osteoporosis deal with studies on bone fractures resulting from the evolution and complications of the disease, which represent high public health costs and are directly related to the negative impact on the quality of life of the elderly population, in addition to representing a high mortality rate<sup>(2,4)</sup>. Thus, the indication of treatment for the prevention of bone fractures related to osteoporosis means an impact on the public health system<sup>(5,6)</sup>, thus justifying the need for both primary and secondary prevention<sup>(6)</sup>.

The greatest clinical interest should be the decrease in the incidence of osteoporosis and its complications, with a focus on modifiable risk factors, such as inadequate sun exposure, non-vitamin D supplementation, and smoking<sup>(5,7)</sup>.

More recently, public health recommendations, such as the habit of avoiding sun exposure, are aimed at preventing skin cancer, which can contribute to both sexes acquiring another risk factor for osteoporosis<sup>(2,8)</sup>. It is understood that, in the context of primary prevention, measures are included to encourage physical exercise, healthy eating habits, adequate intake of calcium and vitamin D in the diet, as well as exposure to the sun. In the comparison between

the sexes, it is noted that, in postmenopausal women, primary prevention actions also help to decrease the rate of bone loss<sup>(7)</sup>.

Secondary prevention, on the other hand, would encompass population strategies for its early detection, including tracking target populations. Screening methods target more specifically women's health, especially during post-menopause, while male coverage does not have the same approach<sup>(7)</sup>.

European, North American, and Asian studies, aiming to prevent complications from osteoporosis, have shown the clinical relevance of tools and strategies that can contribute to the identification of individuals at greater risk of developing osteoporosis and, consequently, collaborate for health promotion<sup>(9)</sup>.

In this scenario, to meet the needs of public health, to identify modifiable actions, and to have an early diagnosis, studies have shown the clinical importance of tools capable of indicating early risk factors as the main goal in the introduction of effective osteoporosis prevention strategies, which can be used to differentiate individuals at higher risk of developing it<sup>(2,7,8)</sup>.

However, even if there are treatments capable of collaborating for the prevention of this disease offered by Brazil's Unified Health System (*Sistema Único de Saúde - SUS*), the lack of adequate epidemiological knowledge causes the little access of the Brazilian population to early diagnosis and damage to health programs. Furthermore, osteoporosis prevention strategies have as their main goal the early identification of risk factors<sup>(3)</sup>. Therefore, we proposed to develop the present study, which aims to analyze the effectiveness of the International Osteoporosis Foundation (IOF) test for primary and secondary preventions related to risk factors for osteoporosis.

## METHODS

This is a cross-sectional study carried out in São José do Rio Preto, São Paulo, Brazil, where an osteoporosis prevention campaign was promoted by a college. During October 23 and 24, 2016, in a shopping mall located in the central region of the city during business hours, with the support of 44 students, nutritionists, physiotherapists, and rheumatologists, guidelines for preventing osteoporosis were carried out. This event was widely publicized on social networks and visual media in the region and was supported by IOF.

For the delineation of risk factors related to osteoporosis and the characterization of the population, the one-minute IOF osteoporosis risk test was applied with 400 participants randomly selected during the event. The study included people over 18 years of age willing to receive guidance on the disease and attended by primary care in the municipality of origin, excluding participants who answered the questionnaires incompletely.

Data collection was restricted to the IOF test, consisting of 19 questions, whose answers (affirmative or negative) took about one minute, representing a random screening method for risk factors, without age and sex restriction. Their statements do not mean a diagnosis of osteoporosis but point to clinically proven risk factors for developing osteoporosis and fracture<sup>(10-12)</sup>.

Based on the results obtained in the test, the IOF's suggestion is to carry out actions to clarify and inform the population about the risks to which they are subject, through prevention plans, even if there are only negative responses to the questionnaire. There are international studies that have also used this test as an awareness tool, warning about possible risk factors for osteoporosis and, consequently, the importance of its early detection<sup>(10-12)</sup>.

Based on the test, the study variables were: diagnosis of osteoporosis, bone densitometry, previous and current treatment, family history, presence of kyphosis, age, alcoholism, smoking, history of fracture by fall, fall by weakness, change in height after age 40, body mass index, use of corticosteroid therapy for three months, comorbidities (such as rheumatoid arthritis and thyroid disease), exercises <30min daily, sun exposure, and vitamin D intake. Exploratory data analysis included mean, median, standard deviation, and variation for continuous variables, as well as number and proportion for categorical variables. The normal distribution of continuous variables was analyzed by asymmetry, kurtosis, and the Kolmogorov-Smirnov test. Associations of categorical variables between two groups were performed using Pearson's chi-square test and continuous variables using the Mann-Whitney test. Multivariate analysis for risk factors associated with osteoporosis was performed using the binary logistic regression model (stepwise with backward elimination method), presenting the results in odds ratios with a 95% confidence interval. Besides, using the IBM-SPSS Statistics software, version 24 (IBM Corporation, NY, USA), a statistical analysis was performed, bearing in mind that all tests were two-tailed, considering p values <0.05 significant.

This study was approved by the Research Ethics Committee (CEP), with Opinion No. 1,445,235, by CNS Resolution No. 466/12.

## RESULTS

260 women and 140 men (220 adults and 180 elderly people) participated in the present study, with a mean age of 57 years, ranging from 82 years and 32 years. Approximately 95%, of both sexes, answered affirmatively to at least one test question, indicating the presence of clinically proven risk factors for osteoporosis.

The incidence of risk factors by sex showed that both followed the same proportion. Only 12 women (5%) and 5 men (4%) did not indicate having a risk factor for osteoporosis, according to the IOF test. Analysis of the questionnaires confirmed that the diagnosis of osteoporosis remains more prevalent in women when compared to men ( $p < 0.001$ ). Women are also more frequently submitted to bone densitometry ( $n = 116$ ; 44.6%) when compared to men ( $n = 23$ ; 16.4%) ( $p < 0.001$ ).

Regarding the incidence of positive responses per question, it was observed that questions 3, 17, 16 and 19 obtained a higher positivity index, referring, respectively, to the following statements: "Are you 40 or older?" ( $n = 318$ ; 79.5%), "Is your daily exercise quota less than 30 minutes?" ( $n = 174$ ; 43.5%), "Do you smoke or have you ever been a smoker?" ( $n = 147$ ; 36.75%) and "You spend less than 10 minutes a day outdoors with part of your body exposed to the sun ( $n = 134$ ; 33.5%) without eating foods or supplements rich in vitamin D?" ( $n = 81$ ; 20.25%) (Table I).

Most participants over 40 years old were women (76.5%;  $n = 119$ ;  $p = 0.046$ ). In contrast, both sexes were exposed to the following risk factors: lack of habit of practicing physical activities, low / no intake of milk and dairy products, and poor sun exposure. The risk factor "smoking" was statistically equivalent for both sexes and alcoholism remained more prevalent in men (Table I).

The least positive alternative during the survey was number 7, which addresses the verification of weight from a body mass index (BMI) less than 19kg / m<sup>2</sup>.

Regarding the comparison between sex and "presence of osteoporosis in parents", there was a significant difference ( $p = 0.005$ ), as well as a fall due to weakness ( $p = 0.04$ ), a change in height after 40 years ( $p = 0.005$ ), presence of rheumatoid arthritis ( $p = 0.007$ ) and thyroid disease ( $p = 0.011$ ). Regarding the age group, in the participants under the age of 40 years (20.5%), the use of corticosteroids ( $p = 0.129$ ) was not prevalent.

When controlling the effect of the variables together by the binary logistic regression model, an association was observed between the risk factors bone densitometry, fall due to weakness, change in height after 40 years, and sex concerning the study population over 60 years, as described in Table II.

Table I - Represents the number of answers categorized as yes or no and for the IOF test question (International Osteoporosis Foundation) classified by sex ( $n = 400$ ). São José do Rio Preto, São Paulo, 2016.

Variables	Male (n = 140)		Female (n = 260)		Value p
	Yes	No	Yes	No	
Diagnosis of osteoporosis	6 (4.3%)	134 (95.7%)	45 (17.3%)	215 (82.7%)	0.000*
Bone densitometry	23 (16.4%)	117 (83.6%)	116 (44.6%)	144 (55.4%)	<0.001*
Previous osteoporosis treatment	6 (4.3%)	134 (95.7%)	36 (13.8%)	224 (86.2%)	0.003*
Current osteoporosis treatment	4 (2.9%)	136 (97.1%)	27 (10.4%)	233 (89.6%)	0.007*
Osteoporosis in parents	19 (13.6%)	121 (86.4%)	67 (25.8%)	193 (74.2%)	0.005*
Kyphosis parents	16 (11.4%)	124 (88.6%)	42 (16.2%)	218 (83.8%)	0.2
Age > 40 years	119 (85%)	21 (15%)	199 (76.5%)	61 (23.5%)	0.046*
Post-fall fracture	35 (25%)	105 (75%)	48 (18.5%)	212 (81.5%)	0.129
Fall by weakness	11 (7.9%)	129 (92.1%)	48 (18.5%)	212 (81.5%)	0.004*
Height change after 40 years	24 (17.1%)	116 (82.9%)	67 (25.8%)	193 (74.2%)	0.050*
Low BMI	9 (6.4%)	131 (93.6%)	11 (4.2%)	249 (95.8%)	0.336
Corticotherapy for 3 months	17 (12.2%)	123 (87.2%)	47 (18.1%)	213 (81.9%)	0.129
Rheumatoid arthritis	11 (7.9%)	129 (92.1%)	46 (17.7%)	214 (82.3%)	0.007*
Thyroid disease	7 (5%)	133 (95%)	34 (13.1%)	226 (86.9%)	0.011*
Alcoholism	18 (12.9%)	122 (87.1%)	10 (3.8%)	250 (96.2%)	0.001*
Smoking	57 (40.7%)	83 (59.3%)	90 (34.6%)	170 (65.4%)	0.228
Exercises <30min	63 (45%)	77 (55%)	111 (42.7%)	149 (57.3%)	0.657
Absence of milk and dairy products	34 (24.3%)	106 (75.7%)	47 (18.1%)	213 (81.9%)	0.141
Sun exposure <10min	48 (34.3%)	92 (65.7%)	86 (33.1%)	174 (66.9%)	0.807

\* values  $p < 0.05$ . statistically significant; BMI: body mass index; min: minutes

Table II - Representation of binary logistic regression of risk factors for osteoporosis associated with the elderly. São José do Rio Preto. São Paulo. 2016.

Variables	<i>p</i> - valor	OR *	IC 95%**
Bone densitometry	< 0.001	5.013	2.823 – 8.902
Fall by weakness	0.027	2.104	1.087 – 4.074
Height change after 40 years	< 0.001	3.787	2.104 – 6.816
Sex	< 0.001	6.086	3.521 – 10.518

\*OR: Odds ratio; odds ratio for osteoporosis; \*\* 95% CI: 95% confidence interval for OR

## DISCUSSION

The IOF one-minute test for osteoporosis risk is a questionnaire that presents itself as a strategy for defining the actions to be developed during primary and secondary osteoporosis prevention, as it allows to identify which risk factors affect the analyzed region and its relationship with age group and sex. In the literature, most articles discuss bone fractures as complications of osteoporosis, the impacts of bisphosphonate treatment on the public health system, and treatment guidelines<sup>(5,6,13)</sup>.

The results of the present study demonstrate that the IOF test can stimulate its use by professionals in health promotion, as it is easy to access, fast, has low cost, and can be used as a tool for primary care guidance groups, besides contributing to the characterization of the population of primary networks. In the same sense, it allows identifying that, in addition to presenting a higher incidence in the female population, as described by other studies<sup>(14,15)</sup>, other risk factors of greater significance should be considered, such as the lack of habit of practicing physical activities, low/no intake of milk and dairy products, and poor sun exposure.

Family history was seen as a risk factor for osteoporosis, which is more present in women. To understand this finding, two hypotheses already highlighted in the scientific literature can be considered: genetics determines the peak of bone mass and, in the case of post-menopausal women, the rate of bone loss in the first years after menopause (also genetically determined)<sup>(14,15)</sup>. And the second hypothesis: women continue to be a family reference as caregivers and knowledgeable about their health and their close relatives, such as children and spouses<sup>(16)</sup>, corroborating with the data of the present study, in which women, in addition to having more memories about their family histories, have greater access to the health system and participate in disease prevention campaigns.

The present study shows that bone densitometry is more performed by women, which favors the identification of low bone mineral density (BMD) as a risk factor for osteoporosis in this group. The indication for the examination must consider the corresponding age range of risk: women in menopause and post-menopause, history of bone fracture after 50 years, radiological vertebral abnormalities and adults with conditions associated with low bone mass<sup>(5,7,13)</sup>.

Regarding hypothyroidism, the data highlight the importance of tracking this disease in the population and its strong relationship as a risk factor for osteoporosis, especially in the female population. The hormonal changes resulting from this pathology can interfere with the menstrual cycle and estrogen levels, related to the development of osteoporosis due to loss of bone mineral density (BMD) caused by increased reabsorption by osteoclasts<sup>(5,15,16-19)</sup>.

The present study demonstrates that most men and women do not make the adequate intake of milk and dairy products. These data contradict other Brazilian studies, in which only 15.8% of participants avoided milk and dairy products<sup>(5,18)</sup>. There are also studies indicating a higher incidence of the absence of milk and dairy products in the male population, which has a preference for eggs and meat<sup>(20,21)</sup>.

Thus, the low intake of milk and dairy products as a risk factor for osteoporosis may become even more present, as it is already reported that the intake is lower among younger individuals, who should be encouraged to consume milk and dairy products<sup>(21)</sup>. A probable explanation for this difference may be economic and socio-cultural reasons related to diet with no lactose, which is increasingly common in populations in tropical regions, in which other foods rich in calcium are not considered<sup>(20,21)</sup>.

As with other Brazilian and Italian studies, which describe inadequate physical activity time as a risk factor in the studied population, the practice of regular physical exercises is not a routine for both sexes<sup>(10-12,15,22,23)</sup>.

Although the study participants live in a tropical region, daily exposure to the sun is not a reality, which may be related to the low knowledge of the benefits of sun exposure at appropriate times by the lay population. In addition, considering the modern standard of living and violence, motor vehicles are increasingly used for locomotion than walking, with a preference for physical exercise in closed gyms (not outdoors) and the use of vehicles motorized for locomotion, which causes the lack of daily sun exposure<sup>(11,23)</sup>.

Other issues that could explain this decrease in sun exposure would be the campaigns that propose actions to mitigate the risk factors for skin cancer and the increase in temperature in cities with a tropical climate. Thus, the replacement of vitamin D and calcium for the population with risk factors could be an option in public health<sup>(7,18)</sup>.

The relationship between sun exposure and prevention of osteoporosis can be explained by vitamin D, a popular name for the steroid hormone calcitriol, which helps with calcium absorption and bone metabolism. This vitamin is formed by two bioequivalent forms, vitamin D2 (ergocalciferol) obtained by the body through vegetables and supplementation, and vitamin D3 (cholecalciferol) obtained mainly by exposing the skin to sunlight and eating certain foods, such as milk and dairy products<sup>(24,25)</sup>.

Another risk factor identified in the study population is the prevalence of rheumatoid arthritis in women when compared to men. In fact, it is described that osteoporosis can be a complication of rheumatoid arthritis and other autoimmune diseases; however the literature is still controversial when considering the relationship with these diseases. One of the possible explanations for such relationship would be flaws in the bone regulation systems. It is known that patients with rheumatoid arthritis have a higher risk of fractures, have a lower BMD in the hip and spine, and are at higher risk of osteoporosis in the case of elderly patients. In addition, another factor that contributes to the relationship between rheumatic diseases and osteoporosis is the prolonged use of corticosteroids as treatment<sup>(7,19,25)</sup>. Glucocorticoids reduce the quantity and function of osteoblasts. RANK-L expression is increased and OPG is reduced, favoring osteoclast activation and consequently, contributing to low BMD<sup>(25)</sup>.

According to one study, tobacco could have an osteoblast-inhibiting action, but on the other hand, the relationship between smoking and low BMD could also be clarified by interferences in calcium absorption and a lower level of estradiol<sup>(15)</sup>. In the current study, it was not possible to understand this relationship, however, its data are in agreement with European studies that describe that women are acquiring two more aggravating factors in favor of osteoporosis - smoking and alcoholism - since these habits are more and more frequent in the female population<sup>(5,10-12)</sup>.

The association of advanced age with osteoporosis is known, as well as the greater chance of developing this disease in postmenopausal women by reducing BMD<sup>(15,24)</sup>. In the present study, through logistic regression, aging was related to an increase in the chances of developing osteoporosis due to weakness, height change after 40 years and bone densitometry.

The IOF test was also able to identify the prevalence, in both sexes, of BMI greater than 19, which may portray the predominance of the obese population. Therefore, they are data similar to the literature and clarify that the studied population would have a protective factor on bone mass related to the increased production of estrogens resulting from the action of aromatase in adipocytes<sup>(15,23)</sup>.

As a limitation of the study, there is a lack of sociodemographic data to relate the risk factors associated with the disease, a point to be observed. However, the implementation of the IOF test in public health can bring improvements to the prevention of this disease in the country, allowing the reduction of the socioeconomic impact on health services.

It should be noted that, among the risk factors identified by the test, those related to calcium and vitamin D supplementation, as well as sun exposure, represent immediate actions that promote the health of the population in both sexes.

Finally, factors such as bone densitometry, changes in height, and fracture represent warning signs for health professionals, as they increase the chance of elderly women to develop osteoporosis.

## CONCLUSION

The analysis of the IOF test, developed concerning its effectiveness in identifying risk factors, demonstrated that it is a functional and reliable test, indicating it as a tool in health promotion and primary care. Based on the results, it is up to the public health professional to guide the users of the health system on the preventive measures to be followed, aiming to reduce the complications of this disease, such as bone fractures, reducing costs, disabilities and deaths.

## CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest, both in the execution of the research project's actions and in the writing of this manuscript.

## COLABORATIONS

*International Osteoporosis Foundation (IOF).*

## CONTRIBUTIONS

**Giulia Franco** contributed to the research design and elaboration and data analysis. **Giulia Sestini, Gabriel Antonio Cabriott Dumbra** and **Mariana Storino Conte** contributed to the research design and elaboration, and the data collection and analysis. **Felipe Colombelli Pacca** contributed to the design and elaboration of the research. **Daniela Vichiato Polizelli Roma** contributed to data collection and research. **Patrícia da Silva Fucuta** contributed to data analysis and article review. **Tamara Veiga Faria** contributed to the design and elaboration of the research and the review of the article.

## FUNDING SOURCES

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**How to cite:** Franco GO, Sestini G, Dumbra GAC, Conte MS, Pacca FC, Roma DVP, et al. Primary and secondary prevention actions related to risk factors for osteoporosis. *Rev Bras Promoç Saúde*. 2020;33:9644.

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