

abstract

**Objectives:** to describe cardiovascular risk data associated with the use of calcium supplements in contrast with their effects on the prevention of fractures. **Methods:** recent studies and systematic reviews evaluating cardiovascular risk of calcium supplements are presented. To counterweight the benefit, systematic reviews on the effects of calcium supplements on fracture prevention are also presented. The search was carried through the TRIP database and PubMed, and updated on the 4 April 2012. **Results and conclusions:** there are data supporting that calcium supplements can increase cardiovascular risk, but these are hardly consistent when compared to calcium associated with vitamin D. In persons under 70 years and with an adequate diet, calcium supplements have not shown to be effective in preventing fractures. Menopause is not an indication for calcium supplements. Elderly patients can benefit from this treatment. Data on hip fractures and cardiovascular risk support the use of calcium combined with vitamin D. **Key words:** calcium supplements, cardiovascular risk, fractures, vitamin D.

## Calcium supplements: Are we doing it right?



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## Introduction

Calcium (Ca) is a constitutive element of the human body. Its deficiency provokes mineralization-related problems affecting the skeleton, and therefore its inclusion in the diet as a supplement is recommended as a safe measure to prevent osteoporosis and consequently osteoporosis-related fractures. Since the 1960's, it has been asserted that calcium could have a positive effect on cardiovascular risk specifically on cholesterol, blood pressure and weight<sup>1</sup>. In some epidemiological studies, although not all, the inadequate consumption of calcium and vitamin D was associated with a greater risk of cardiovascular events<sup>2</sup>. However, some recent studies have raised doubts on the safety of calcium supplements with regard to this issue.

This report presents the data on updated studies and systematic reviews that have caused alarm due to the finding of an increase in cardiovascular risk associated with the use of calcium supplements. To counterweight the benefits, systematic reviews on the efficacy of the supplements in the prevention of fractures have been evaluated. Our search was carried out through the TRIP data base and Pubmed, updated on the 4 July 2012.

### What evidence is there on the cardiovascular risk related to calcium supplements?

Alarming news surged from a clinical trial carried out in New Zealand by Bolland and cols. In this study, 1,471 postmenopausal women of an average age of 74 years participated and received calcium (1000 mg daily), with no vitamin D and they were followed up for 5 years. The main objective of the study was to measure the efficacy in the prevention

of fractures. A protocol was established to recollect data on cardiovascular events with the hypothesis that calcium supplements had a protective effect. However, the results showed an increase in the composite endpoint of myocardial infarction, stroke and sudden death, with rates of up to 23.3 events/1000 patient-years and 16.3 in the case placebo group, Rate Ratio = 1.43 (95%CI, 1.01-2.04)<sup>3</sup>.

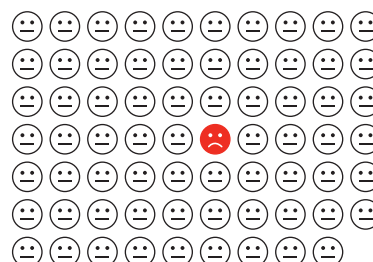
There are some characteristics of this study that are worth considering such as the surprising finding that the incidence of angina followed a contrary pattern to that of myocardial infarction while the sum of both events was similar in both groups. An adjusted analysis for various cardiovascular risk factors (excluding smoking) did not show statistical significance.

These data encouraged the researchers to carry out a systematic review of the relationship between calcium supplements and the risk of suffering from a cardiovascular event. The analysis included trials on vitamin D alone when administered to both the calcium and the placebo groups. Two meta-analyses were carried out, one from the results of clinical trials and another from individual patient data. A total of 11 trials (11,921 patients) of which 5 provided individual patient data (8,151 patients) were included. The main analysis was carried out on those studies where individual data were available (table 1).

In the meta-analysis of all the trials, the results were similar. The authors concluded that calcium supplements without vitamin D were associated with increased risk of myocardial infarction. Although discrete, this could be relevant given their widespread use and the modest efficacy in the prevention of fractures. Their role therefore in the prevention of osteoporosis should be reconsidered<sup>4</sup>.

**Table 1.** Results of the systematic review by Bolland. Cardiovascular risk of calcium supplements alone<sup>4</sup>.

Outcome	HR (95% CI)	NNH for 5 years (95% CI)
Myocardial infarction	1.31 (1.02 - 1.67)	69 (32 - 1070)*
Stroke	1.20 (0.96 - 1.50)	n.s.
Death	1.09 (0.96 - 1.23)	n.s.
Myocardial infarction, stroke or sudden death	1.18 (1.00 - 1.39)	n.s.



NNH: Number of patients needed to treat to produce an event (harm).

\* Confidence interval not provided in the original publication, calculated for this article.

The main limitations of this trial are that the aim of the study was not precisely the evaluation of cardiovascular risk, and neither was the recollection of data carried out in a systematic fashion. Moreover, the exclusion of studies on calcium supplements associated with vitamin D may limit its general application.

A post hoc analysis of this study showed an increased risk in those patients with an intake of calcium supplements in diet above the median (805 mg daily)<sup>1</sup>.

Wang and cols carried out a systematic review to evaluate whether calcium supplements, vitamin D or their combination reduce cardiovascular risk. To do so they searched for prospective studies (cohort or clinical trials) published in English and that offered data on cardiovascular events. This review included less clinical trials with calcium alone than the Bolland study, as unpublished data were not solicited. Neither the meta-analysis of the clinical trials nor the results of cohort study showed an increase in cardiovascular risk associated with calcium supplements<sup>2</sup> (tables 2 and 3). In contrast, the cohort EPIC-Heidelberg found a greater risk of myocardial infarction associated with the use of calcium supplements, but no increase in risk for stroke or cardiovascular death<sup>5</sup>.

*Calcium alone can increase cardiovascular risk. In combination with vitamin D, it is not clear*

Los datos de los ensayos clínicos de calcio asociado a vitamina D provenían en su práctica totalidad del estudio WHI CaD. En éste se había aleatorizado a 36.282 mujeres postmenopáusicas de 50 a 79 años a recibir calcio más vitamina D (1.000 mg/400 UI/d) o placebo con un seguimiento de 7 años. El uso de suplementos de calcio no aumentó de forma significativa el riesgo de infarto o muerte por enfermedad coronaria (HR=1,04; 0,92 a 1,18) ni el de ictus (HR=0,95; 0,82 a 1,10)<sup>6</sup>.

Given the findings from the WHI CaD, Bolland and cols questioned whether the personal use of calcium supplements could have affected the results given that, at the moment of randomization, 54% of the participants took calcium supplements on their

**Table 2.** Meta-analysis of clinical trials on calcium supplements and cardiovascular events (Wang)<sup>2</sup>.

	No trials	Calcium; events/total	Placebo; events/total	RR (95% CI)
Calcium alone (1000-1200 mg/d)	3	178/1926	158/1935	1.14 (0.92-1.41)
Calcium+ vitamin D (1000 mg/400 IU/d)	2	505/18271	480/18202	1.04 (0.92-1.18)

**Table 3.** Cohort studies on calcium supplements and cardiovascular risk<sup>2,5</sup>.

STUDY, YEAR, DURATION	POPULATION	DOSES SUBGROUPS	OUTCOMES	RR (95% CI)
HPFS 1998 8 years	43738 men, 40–75 years, with no history of cardiovascular events or diabetes	0 mg/d; ≥400 mg/d	Stroke (n=328)	0.88 (0.60-1.27)
IWHS 1999 8 years	34486 women, 55–69 years; with no history of cardiopathy	0 mg/d; 1-500 mg/d; >500 mg/d	Death due to ischemic cardiopathy (n=387)	Against not using: [1-500 mg/d]: 0.76 (0.58-1.00) [>500 mg d]: 0.88 (0.64-1.23)
NHS 1999 14 years	85764 women, 34–59 years; with no cardiovascular disease or cancer	0 mg/d, <400 mg/d, ≥400 mg/d	Stroke (n=690)	≥400 mg/d versus no use: 0.88 (0.66-1.18)
HPFS 2003 12 years	39800 men, 40–75 years; with no cardiovascular disease	Median quintiles: 0; 57; 200; 325; 500; 1000 mg/d	Fatal coronary disease + non fatal infarction (n=1458)	Maximum quintile versus minimum: 0.87 (0.64-1.19)
EPIC-Heidelberg 2012 <sup>5</sup> 11 years	23908 men and women, 35-54 years with no history of cardiovascular events	Use of supplements versus no use (doses not recorded)	Myocardial infarction (n=354) Stroke (n=260) Cardiovascular death (n=267)	HR=1.86 (1.17-2.96) 1.05 (0.55-1.99) 1.02 (0.51-2.00)

*No supplements are necessary if there is no deficiency*

own, while 47% took vitamin D supplements. The database of the WHI CaD study was analysed in search of statistical interaction between the use of calcium out of protocol and the allocation to calcium and vitamin D in the results of cardiovascular events. The data were analyzed separately for patients who took out-of-protocol calcium and those who did not. A statistically significant interaction was found for myocardial infarction and stroke with a greater risk in the group that did not take calcium supplements on their own.

With the data on patients who did not take out-of-protocol calcium supplements and the unpublished data from the two clinical trials compared to placebo, a meta-analysis on cardiovascular risk associated with calcium supplements and vitamin D was carried out. A total of 20,090 patients were included and the follow-up period lasted for 6.2 years on average. An increase in risk of myocardial infarction associated with the use of calcium and vitamin D (RR = 1.21, 1.01-1.44), but not significant for stroke (RR = 1.20, 1.00-1.43) and significant in the case of the composite endpoint including myocardial infarction and stroke (RR = 1.16, 1.02-1.32) was observed.

Given this data, the authors updated the previous meta-analysis to include the calcium supplements alone and in combination with vitamin D. They included data from 8 trials, to which the patients from the WHI trial who did not take supplements were included. The total reached 28,072 patients, of which 1384 suffered from a myocardial infarction or stroke. A greater risk of infarction was observed

in those patients taking calcium supplements alone or combined with vitamin D (RR = 1.24, 1.07-1.45), while no significant differences were found regarding either stroke (RR = 1.15, 1.00-1.32) or in the composite endpoint of infarction and stroke (RR = 1.15, 1.03-1.27). Nor was there an increase in mortality (RR = 1.04, 0.95-1.13). The authors concluded that calcium supplements, in combination or not with vitamin D, mildly increase the risk of cardiovascular events, especially myocardial infarction and that their use in the management of osteoporosis should be placed under reconsideration<sup>7</sup>.

These results should be taken with great precaution. The women with no personal use of calcium is a post hoc subgroup. Therefore, it cannot be assured that randomization distributed homogeneously the possible confounding variables between the subgroups.

The subgroup from the WHI CaD trial provides the majority of the data from the meta-analyses which were later carried out. In this analysis there was no evidence of a dose-response relationship between the consumption of calcium (adding diet and calcium supplements in and out of protocol) and cardiovascular risk<sup>6</sup>.

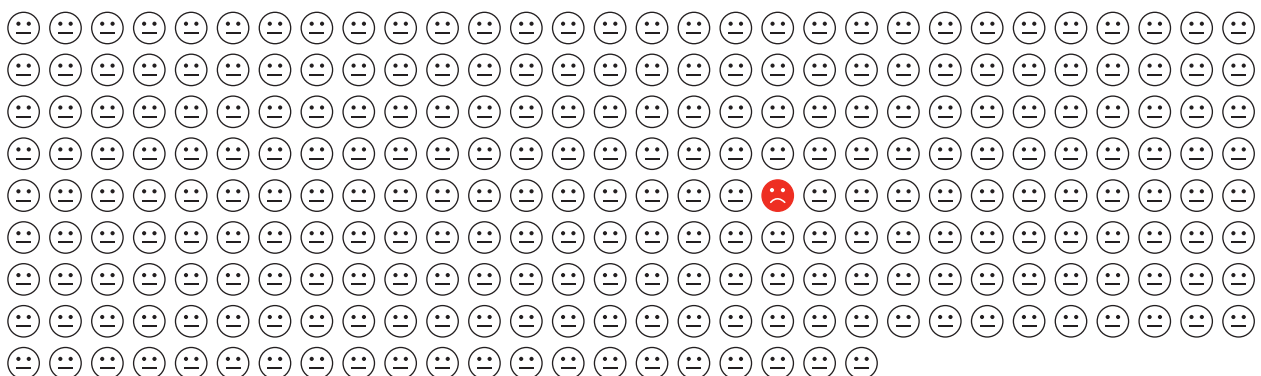
There seems to be a contradiction between the different post hoc meta-analyses carried out by Bolland. In the first, the increase in the risk was limited to patients with high dietary calcium consumption; while in the second, the risk was limited to those who did not take supplements<sup>8</sup>.

The British MHRA (Medicines and Healthcare products Regulatory Agency) published a report indicating that, given the limitations of the study, no change in prescription was recommended<sup>9</sup>.

**And what of the kidney stones?**

In the WHI CaD trial the use of calcium plus vitamin D was associated with a higher risk of kidney stones (HR = 1.17, 1.02-1.34) (0.35% vs 0.30% per year)<sup>10</sup> (NNH = 261, 143-1000 after 7 years of treatment).

**WHI CaD trial. NNH for kidney stones.**





**Do calcium supplements prevent fractures?**

The use of calcium supplements is justified for individuals with deficiencies. The problem lies with the definition of deficiency. Dietary recommendations for elderly people vary among different countries, ranging between 700 to 1300 mg daily<sup>11</sup>.

Here we will regard the use of calcium supplements for the prevention and treatment of osteoporosis and therefore its efficacy in the prevention of fractures. When comparing epidemiological studies from different countries, paradoxically there is a direct relationship between the consumption of calcium and the rate of fractures. In those countries in which the consumption of calcium is close to the recommended dose, there is no relationship between calcium intake and hip fractures. In different studies in southern Europe, higher risk is associated with low consumption of calcium, but no additional reductions are achieved with an above average intake<sup>12</sup>.

A systematic review of prospective cohort studies evaluated the relationship between calcium consumption and the risk of fracture. Clinical trials including vitamin D were excluded. Eight prospective cohort studies (n = 239,597) were included. Four of them included total intake of calcium from dietary sources and supplements. Another four studies evaluated only the total intake of calcium from diet. The

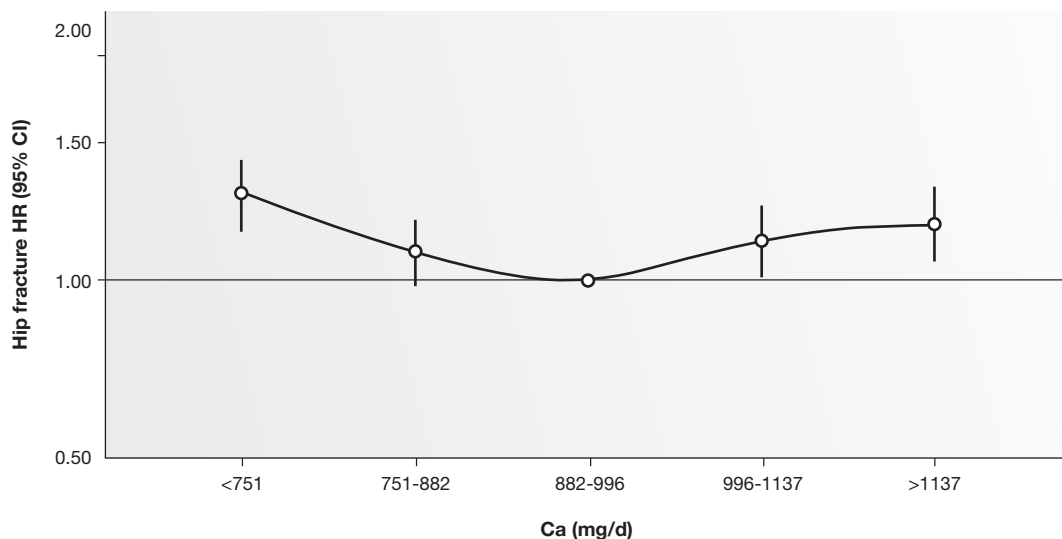
relative risk of increments of 300 mg daily of calcium consumption was studied. There was no significant association between calcium consumption and the risk of hip fracture, for either men (5 studies, n = 68,606; 214 fractures, RR = 0.92, 0.82-1.03) or women (7 studies, n = 170,991, 2954 fractures, RR = 1.01, 0.97-1.05). On grouping quintiles no significant differences were found either<sup>13</sup>.

After this review, there have been new publications on observational studies that offer new data or update the previous information. The Swedish Mammography Cohort was included in the above-mentioned review, but later new data has been published. This is a Swedish cohort of 61,433 women of an average of 53 years at the onset. The follow up period was 19 years. Questionnaires on frequency of dietary habits in consumption of food and calcium supplements were carried out. The primary endpoints were the incidence of overall fractures and hip fractures. Some sort of fracture was observed in 24% of the participants while 6% suffered from hip fracture. The relationship between calcium consumption and the outcomes were not linear. Taking as reference the third quintile of consumption of calcium, the risk of any fracture and hip fracture were greater in the first quintile (lowest consumption). However, there was no decrease in risk in those above the third quintile. In fact there was an increase in risk of hip fracture related to higher intake of calcium (table 3, figure 1).

**Table 3.** Swedish Mammography Cohort.

QUINTILE	1	2	3	4	5
Ca (mg/d)	<751	751-882	882-996	996-1137	>1137
Adjusted HR for fracture (95%CI)	1.18 (1.12-1.25)	1.04 (0.98-1.10)	1.0 (Reference)	1.02 (0.96-1.07)	1.00 (0.95-1.06)
Adjusted HR for hip fracture (95% CI)	1.29 (1.17-1.43)	1.09 (0.98-1.21)	1.0 (Reference)	1.13 (1.01-1.26)	1.19 (1.06-1.32)

**Figure 1.** Relationship between the calcium intake and first hip fracture in the Swedish Mammography Cohort.



*It is reasonable  
to combine calcium  
with vitamin D*

The authors concluded that the increase in the daily consumption of calcium of over 750 mg was not associated with further reductions in fracture risk or osteoporosis<sup>11</sup>.

The NORA study evaluated the association between calcium intake and vitamin D over a life time period and the risk of fracture in 52,144 white menopausal women in the USA after a three-year prospective follow-up. After adjusting for confounding factors, no statistically significant relationship was found (table 4)<sup>14</sup>.

#### Systematic reviews of clinical trials

There is a systematic review on the efficacy of calcium supplements (alone and in combination with vitamin D) in the prevention of fractures in adults<sup>15</sup>. Another review evaluates calcium supplements alone<sup>13</sup> and two more evaluate the effects of vitamin D while reporting also on the efficacy of the association with calcium<sup>16,17</sup>. A meta-analysis of individual patient data from the most important studies confirms the results of the latter studies mentioned<sup>18</sup> (table 5).

We will now present the results of the subgroup analysis in an attempt to determine the types of patients that could benefit from the use of calcium supplements. Unless specified, we will present the relative risk of fractures at any location, compared

to the use of calcium supplements against placebo. When various meta-analyses reach the same conclusion, the RR data shown are those of the first reference cited.

#### Limitations of these data

Precaution should be taken on interpreting these data, as in general they proceed from some of the numerous subgroup analyses carried out. The interpretation of the evidence is complicated by the use or not of vitamin D, different doses employed, and the inclusion of studies carried out in populations in which probably there was no need for supplements given an adequate calcium intake.

Evidence of publication bias was found which, according to the authors, did not affect the conclusions<sup>15</sup>. It is also worth mentioning that in the systematic reviews there was very little data on men.

#### Global efficacy<sup>15</sup>

The most ample review includes 17 trials (table 6). The majority of the data were studies combining calcium with vitamin D. A protective effect was found for calcium supplements (RR = 0.88, 0.83-0.95). The relative risks were similar on analyzing separately hip and vertebral fractures.

#### Patients living in nursing homes<sup>15-17</sup>

There was a greater effect found in trials in elderly patients and in those living in nursing homes (RR = 0.76, 0.66-0.88) versus those living in the community (RR = 0.94, 0.90-0.99). In those trials at nursing homes, patients were given a combination of calcium supplements and vitamin D.

**Table 4.** NORA study. RR of fracture in relation to calcium intake.

	<500 mg/d	500-800 mg/d	≥800 mg/d
Osteoporosis-related fractures (2205)	1.0 (ref.)	0.94 (0.80-1.10)	0.92 (0.81-1.06)
Hip fractures (337)	1.0 (ref.)	0.89 (0.61-1.31)	0.87 (0.63-1.21)

**Table 5.** Systematic reviews on calcium supplements in the prevention of fractures.

REVIEW	PRIMARY ENDPOINT	TREATMENT	No TRIALS	No PATIENTS	RR (95% CI) VS PLACEBO
Tang 2007 <sup>15</sup>	Fractures at any site	Ca Ca + Vit D	9 8	6,565 55,751	0.90 (0.80 to 1.00) 0.87 (0.77 to 0.97)
Bischoff-Ferrari 2007 <sup>13</sup>	Hip fractures	Ca	4	6,504	1.64 (1.02 to 2.64)
Avenell 2009 <sup>16</sup>	Hip fractures	Ca + Vit D	8	46,658	0.84 (0.73 to 0.96)
Chung 2011 <sup>17</sup>	Fractures at any site	Ca + Vit D	11	52,915	0.88 (0.79 to 0.99)
DIPART 2010 <sup>18</sup>	Fractures at any site	Ca + Vit D	4	51,839	HR=0.92 (0.86 to 0.99)

**Table 6.** Systematic review by Tang. Clinical trials with calcium supplements in the prevention of fractures<sup>15</sup>.

STUDY YEAR	POPULATION	AVERAGE AGE (SD OR RANGE)	TREATMENT	N	RR	95%CI LOW. LIM.	95%CI UPP. LIM.
Chapuy, 1992	Elderly women with mobility in nursing homes	84 (6)	Ca+vit D (1200 mg/800 IU)	2,790	0.75	0.64	0.87
Reid, 1993	Healthy postmenopausal women	58 (5)	Ca (1000 mg)	122	0.40	0.08	1.98
Chevalley, 1994	Healthy elderly men and women	72 (7)	Ca (800 mg)	156	0.96	0.35	2.66
Recker, 1996	Independent postmenopausal women	74 (7)	Ca (1200 mg)	197	0.85	0.56	1.30
Dawson-Hughes, 1997	Healthy men and women	71	Ca+vit D (500 mg/700 IU)	389	0.46	0.23	0.90
Riggs, 1998	Healthy postmenopausal women	66 (3)	Ca (1600 mg)	236	0.89	0.51	1.57
Peacock, 2000	Independent elderly men and women	75 (8)	Ca (750 mg)	261	0.81	0.46	1.43
Chapuy, 2002	Elderly walking women in nursing homes	85	Ca+vit D (1200 mg/800 IU)	583	0.85	0.64	1.13
Larsen, 2004	Elderly men and women	74 (66-103)	Ca+vit D (1000 mg/400 IU)	9,605	0.84	0.72	0.98
Harwood, 2004	Elderly women with previous fractures	81 (67-92)	Ca+vit D (1000 mg/800 IU)	150	0.49	0.03	7.67
Fujita, 2004	Elderly women in nursing homes	81	Ca (900 mg)	19	0.31	0.07	1.39
RECORD-1, 2005	Elderly men and women with previous fractures	78 (6)	Ca (1000 mg)	2,638	0.94	0.77	1.15
RECORD-2, 2005	Elderly men and women with previous fractures	77 (6)	Ca+vit D (1000 mg/800 IU)	2,643	0.94	0.77	1.15
Porthouse, 2005	Women with risk factors for hip fracture	77 (5)	Ca+vit D (1000 mg/800 IU)	3,314	0.96	0.70	1.33
Jackson, 2006 (WHI Ca D)	Healthy postmenopausal women	62 (7)	Ca+vit D (1000 mg/400 IU)	36,282	0.97	0.92	1.03
Reid, 2006	Healthy postmenopausal women	74 (4)	Ca (1000 mg)	1471	0.92	0.75	1.14
Prince, 2006	Healthy elderly women	75 (3)	Ca (1200 mg)	1,460	0.87	0.69	1.10
			<b>Overall</b>	<b>62,316</b>	<b>0.88</b>	<b>0.83</b>	<b>0.95</b>

Given the data from the Avenell review<sup>16</sup>, the number of patients needed to treat for 3 years to prevent a fracture was: NNT = 37 (22-112).

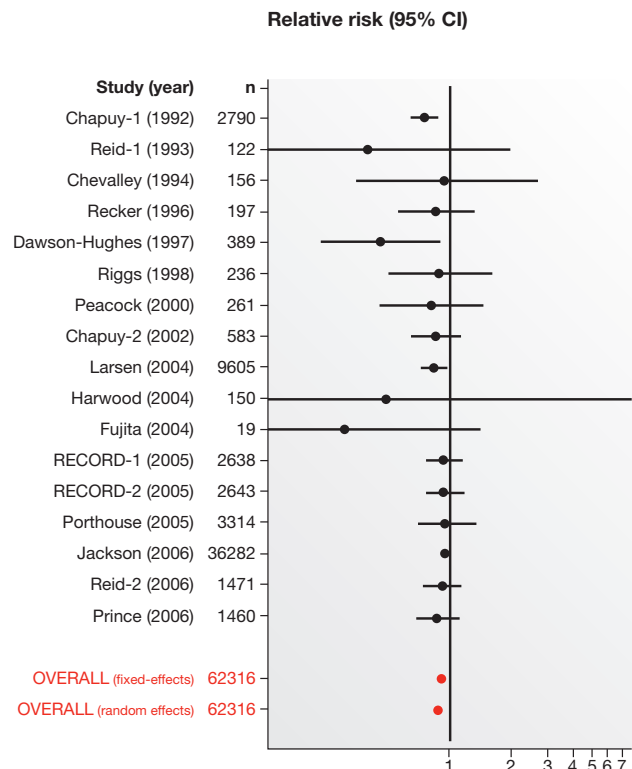


For non-vertebral fractures: NNT\* = 38 (20-334).

**Dietary intake of calcium<sup>15</sup>**

There was a greater effect when consumption of calcium was low (<700 mg daily) but no evidence of a significant effect if the diet intake was higher.

DIETARY INTAKE OF Ca	RR (95%CI)
<700 mg/d	0.80 (0.71-0.89)
≥700 mg/d	0.95 (0.91-1.00)



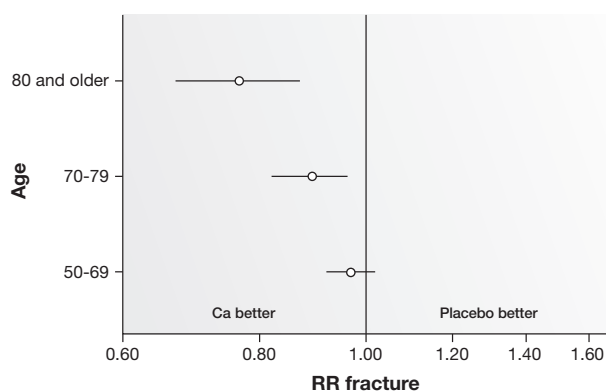
\* NNT not provided in the original publication, calculated by the author of this article.

*To ensure that the benefits are greater than the risks, supplements should be indicated to those who really need them*

### Age<sup>15</sup>

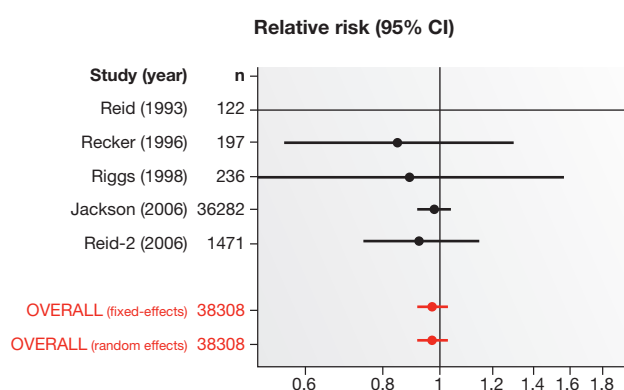
The efficacy was greater in the studies in older patients. There was no evidence of efficacy in younger patients.

AGE	RR (95%CI)
80 and more	0.76 (0.67-0.87)
70-79	0.89 (0.82-0.96)
50-69	0.97 (0.92-1.02)



### Menopause<sup>15</sup>

When evaluating studies in which the inclusion criteria was simply menopause, no evidence was found on any effect of calcium supplements. (RR = 0.96; 0.91 – 1.02)\*



### Patients with previous fracture<sup>15-17</sup>

In patients with previous fractures living in the community, calcium alone or combined with vitamin D did not show any beneficial effect (RR = 0.93; 0.82-1.06).

### Calcium alone or combined with vitamin D. Efficacy in the overall fractures

No evidence has been found among the studies with calcium supplements alone (RR = 0.90, 0.80-1.00) or in combination with vitamin D (RR = 0.87, 0.77-0.97). The direct comparisons neither have shown differences between calcium associated with vitamin D versus calcium alone<sup>16</sup>.

### Efficacy in hip fracture

Calcium in combination with vitamin D has shown efficacy in the reduction of hip fracture risk (RR = 0.84, 0.73-0.96)<sup>16,19</sup>. However this has not been so in the studies with calcium alone, in which a higher risk was found (RR = 1.64, 1.02-2.64)<sup>13,19</sup>. However, in direct comparisons no differences have been shown: calcium plus vitamin D versus calcium alone, RR = 0.83, 0.61-1.12)<sup>16</sup>.

### Efficacy of vitamin D alone<sup>16-18,20</sup>

In the absence of calcium supplements, vitamin D has not proved effective in the prevention of fractures (RR new fracture = 1.01, 0.93-1.09; RR hip fracture = 1.15; 0.99-1.33).

### Vitamin D dose

There is some controversy regarding the appropriate dose of vitamin D<sup>18,21</sup>. When prescribing, it seems reasonable to consider the amount received from other sources. In studies in institutionalized patients where supplements have shown greater efficacy, the doses employed were calcium 1200 mg and vitamin D 800 IU.

### Patients with other treatments for osteoporosis

In practically all the clinical trials with drugs for osteoporosis (bisphosphonates, selective estrogen receptor modulators, strontium ranelate, denosumab, calcitonin, teriparatide, parathyroid hormone) calcium supplements were included in all treatment arms. Therefore the efficacy of calcium in the absence of these drugs remains unknown. In the drug reports it is assumed that dietary intake is

\* Analysis not done in the original publication. Calculated by the author of this article with EPIDAT v 3.1 (Xunta de Galicia-OPS/OMS)



insufficient and that patients should receive calcium supplements and/or vitamin D.

**Calcium consumption in Navarre**

Patients that received at least one prescription of calcium supplements or vitamin D in Navarre in 2011.

	NO PATIENTS	AGE, MEAN (SD)	% WOMEN
Ca + Vitamin D	20046	70 (13)	88%
Ca alone	2472	71 (14)	87%
Vitamin D alone	1506	67 (16)	76%

*An adequate diet in the context of an active lifestyle is the best strategy to prevent osteoporosis-related fractures*

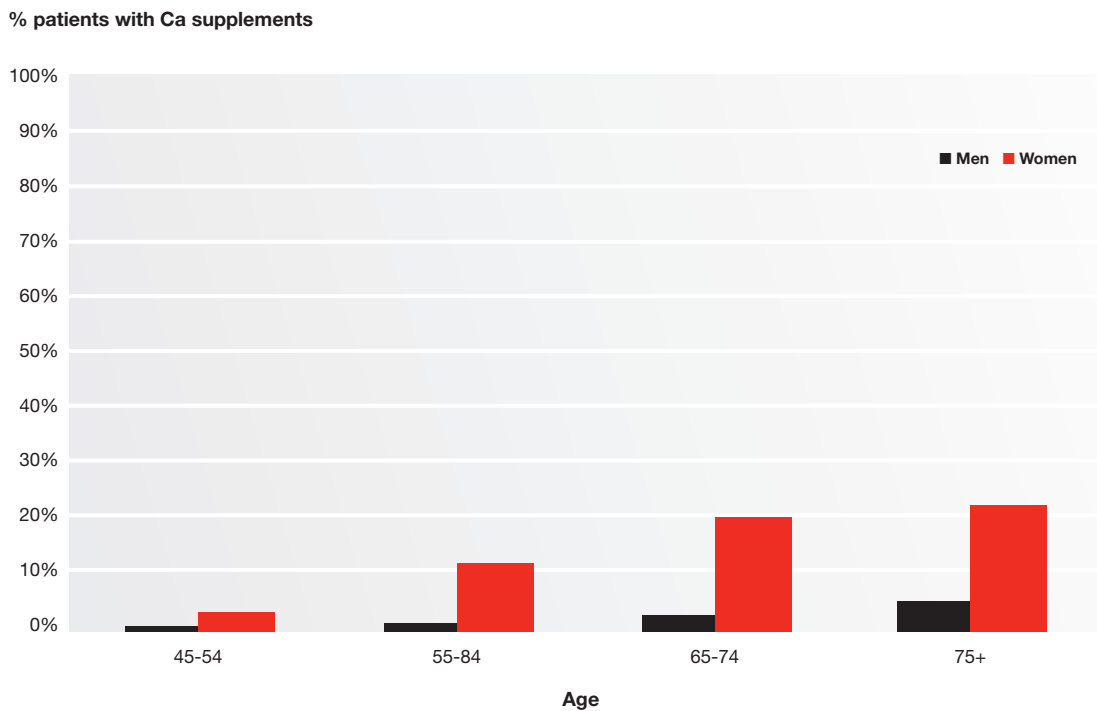
**Use of drugs for osteoporosis in patients receiving calcium supplements.**

DRUGS FOR OSTEOPOROSIS*	% PATIENTS	AGE, MEAN (SD)	% WOMEN
NO	49%	68 (15)	84%
YES	51%	72 (11)	91%

\*Bisphosphonates, strontium ranelate, denosumab, SERMs, calcitonin, teriparatide, parathyroid hormone.

In half of the patients who received calcium supplements, their prescription was made as a complement of other drugs employed for osteoporosis. The average age of the users of calcium supplements (mainly women) is considerably lower than the participants in clinical trials where efficacy was shown. In fact, the percentage of calcium consumers among women between 65 and 74 years is very similar to the use observed in women over 75 years. The efficacy of calcium supplements has only been shown in the latter.

Patients who received at least one prescription of calcium supplements (2011).



### Conclusions

Calcium supplements could increase cardiovascular risk, but when considering combined calcium and vitamin D the data available are not consistent.

Calcium supplements and vitamin D can slightly increase the incidence of kidney stones.

There is no evidence that calcium supplements provide any benefit to patients with an adequate dietary intake.

Menopause is not an indication for calcium supplements.

Calcium alone has not proved beneficial in preventing hip fractures. Neither has vitamin D alone shown efficacy in fractures. The best results obtained come from their combination.

Frail elderly people, especially women who do not leave their homes can benefit from this intervention.

When employing drugs for osteoporosis, an adequate dietary intake of calcium and vitamin D should be assured. If not, then supplements can be employed.

No supplements are necessary when there is no deficiency detected.

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