



# Calcio: niveles y dosis deseadas en pacientes con/sin tratamiento antiosteoporótico. Cómo pautarlo.



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# Depósitos de Calcio

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El esqueleto contiene el 99% del calcio corporal total en una forma cristalina que se parece a la hidroxiapatita; otros iones, incluidos  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Mg}^+$  y Fosfatos $^-$ , también están presentes en la red cristalina.

Goodman y Gilma Bases Farmacológicas de la Terapéutica 2014  
14 ed, Ed Mcgraw Hill

# Calcio

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El calcio elemental es esencial para muchas funciones biológicas:

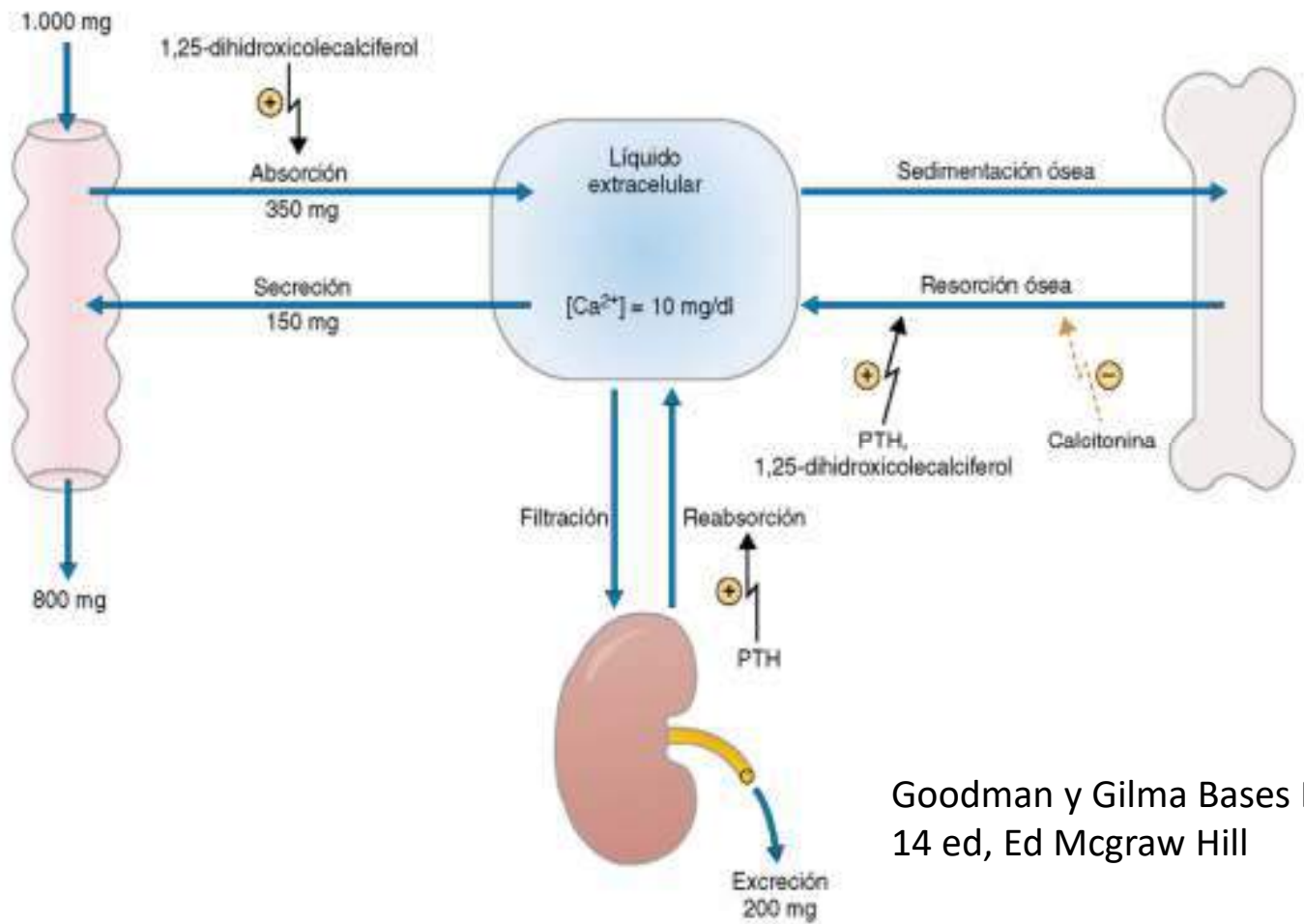
- Contracción muscular,
- Señalización intracelular
- Coagulación sanguínea
- Formación y remodelación continua del esqueleto.

Concentración sérica normal de  $\text{Ca}^{2+}$  varía de 8.5 a 10.4 mg/dL (4.25-5.2 mEq/L, 2.1-2.6 mM)

Formas químicas distintas:

- *ionizado* (50%),
- *unido a proteínas* (40%) y
- *como parte de complejos* (10%)
- El **Ca<sup>2+</sup> ionizado** libre llega a representar el 50% del total (es decir, 5 mg/dl) y *es la única forma de Ca<sup>2+</sup> que es biológicamente activa.*

### HOMEOSTASIS DEL $\text{Ca}^{2+}$




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“La homeostasis del  $\text{Ca}^{2+}$  comporta la interacción coordinada de tres órganos o sistemas (hueso, riñón e intestino) y tres hormonas (hormona paratiroidea, calcitonina y vitamina D)”

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# Osteoporosis

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La osteoporosis es una condición de baja masa ósea y alteración microarquitectural que origina fracturas con un trauma mínimo.

Muchas mujeres (30 al 50%) y hombres (15 al 30%) tienen fracturas relacionadas con la osteoporosis.


*La osteoporosis primaria* representa dos condiciones diferentes: *osteoporosis tipo I*, caracterizada por la pérdida de hueso trabecular debido a la falta de estrógenos en la menopausia y la *osteoporosis tipo II*, caracterizada por la pérdida de hueso cortical y trabecular en los hombres y las mujeres debido a la ineficiencia en el remodelado durante largo tiempo, la dieta inadecuada y activación del eje paratiroideo con la edad.

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*La osteoporosis secundaria* es debido a enfermedades sistémicas y al uso crónico de medicamentos como los glucocorticoides o fenitoína.

Ya sea primaria o secundaria, la osteoporosis se asocia con la remodelación ósea desordenada, por lo que las mismas terapias se pueden utilizar en ambas condiciones.

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This article was published at [www.annals.org](http://www.annals.org) on 26 February 2013.

Annals of Internal Medicine

CLINICAL GUIDELINE

## Vitamin D and Calcium Supplementation to Prevent Fractures in Adults: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, MPH, on behalf of the U.S. Preventive Services Task Force\*

**Description:** New U.S. Preventive Services Task Force (USPSTF) recommendation statement on vitamin D and calcium supplementation to prevent fractures in adults.

**Methods:** The USPSTF commissioned 2 systematic evidence reviews and a meta-analysis on vitamin D supplementation with or without calcium to assess the effects of supplementation on bone health outcomes in community-dwelling adults, the association of vitamin D and calcium levels with bone health outcomes, and the adverse effects of supplementation.

**Population:** These recommendations apply to noninstitutionalized or community-dwelling asymptomatic adults without a history of fractures. This recommendation does not apply to the treatment of persons with osteoporosis or vitamin D deficiency.

**Recommendation:** The USPSTF concludes that the current evidence is insufficient to assess the balance of the benefits and harms

of combined vitamin D and calcium supplementation for the primary prevention of fractures in premenopausal women or in men. (I statement)

The USPSTF concludes that the current evidence is insufficient to assess the balance of the benefits and harms of daily supplementation with greater than 400 IU of vitamin D<sub>3</sub> and greater than 1000 mg of calcium for the primary prevention of fractures in noninstitutionalized postmenopausal women. (I statement)

The USPSTF recommends against daily supplementation with 400 IU or less of vitamin D<sub>3</sub> and 1000 mg or less of calcium for the primary prevention of fractures in noninstitutionalized postmenopausal women. (D recommendation)

*Ann Intern Med.* 2013;158:691-696.

[www.annals.org](http://www.annals.org)

For author affiliation, see end of text.

\* For a list of the members of the USPSTF, see the **Appendix** (available at [www.annals.org](http://www.annals.org)).

This article was published at [www.annals.org](http://www.annals.org) on 26 February 2013.

**T**he U.S. Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific clinical preventive services for patients without related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in

primary prevention of fractures in noninstitutionalized postmenopausal women. (I statement)

The USPSTF recommends against daily supplementation with 400 IU or less of vitamin D<sub>3</sub> and 1000 mg or less of calcium for the primary prevention of fractures in noninstitutionalized postmenopausal women. (D recommendation)

The USPSTF has previously concluded in a separate recommendation that vitamin D supplementation is effective in preventing falls in community-dwelling adults aged 65 years or older who are at increased risk for falls. (B recommendation)

See the Clinical Considerations section for suggestions



*Figure.* Vitamin D and calcium supplementation to prevent fractures in adults; clinical summary of U.S. Preventive Services Task Force recommendation.

## Annals of Internal Medicine



### VITAMIN D AND CALCIUM SUPPLEMENTATION TO PREVENT FRACTURES IN ADULTS CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

<b>Population</b>	Men or premenopausal women	Community-dwelling postmenopausal women at doses of >400 IU of vitamin D <sub>3</sub> and >1000 mg of calcium	Community-dwelling postmenopausal women at doses of ≤400 IU of vitamin D <sub>3</sub> and ≤1000 mg of calcium
<b>Recommendation</b>	No recommendation. Grade: I statement	No recommendation. Grade: I statement	Do not supplement. Grade: D
<b>Preventive Medications</b>	<p>Appropriate intake of vitamin D and calcium are essential to overall health. However, there is inadequate evidence to determine the effect of combined vitamin D and calcium supplementation on the incidence of fractures in men or premenopausal women.</p> <p>There is adequate evidence that daily supplementation with 400 IU of vitamin D<sub>3</sub> and 1000 mg of calcium has no effect on the incidence of fractures in postmenopausal women.</p> <p>There is inadequate evidence regarding the effect of higher doses of combined vitamin D and calcium supplementation on fracture incidence in community-dwelling postmenopausal women.</p>		
<b>Balance of Benefits and Harms</b>	Evidence is lacking regarding the benefit of daily vitamin D and calcium supplementation for the primary prevention of fractures, and the balance of benefits and harms cannot be determined.	Evidence is lacking regarding the benefit of daily supplementation with >400 IU of vitamin D <sub>3</sub> and >1000 mg of calcium for the primary prevention of fractures in postmenopausal women, and the balance of benefits and harms cannot be determined.	Daily supplementation with ≤400 IU of vitamin D <sub>3</sub> and ≤1000 mg of calcium has no net benefit for the primary prevention of fractures.
<b>Other Relevant USPSTF Recommendations</b>	The USPSTF has made recommendations on screening for osteoporosis and vitamin D supplementation to prevent falls in community-dwelling older adults. These recommendations are available at <a href="http://www.uspreventiveservicestaskforce.org">www.uspreventiveservicestaskforce.org</a> .		


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La ingesta adecuada de vitamina D y calcio es esencial para la salud en general. Sin embargo no hay pruebas suficientes para determinar el efecto de los suplementos combinados de vitamina D y calcio sobre la incidencia de fracturas en hombre y mujeres post menopausicas


No Existe evidencia sobre el efecto de dosis más altas de suplementos combinados de vitamina D y calcio en la incidencia de fracturas en mujeres posmenopáusicas que viven en la comunidad.

Existe evidencia, que la suplementación diaria con 400 UI de vitamina D3 y 1000 mg de calcio, no tiene ningún efecto sobre la incidencia de fracturas en mujeres post menopáusicas.



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Existe evidencia que el uso de vitamina D y calcio podría ser causal de cálculos renales, Women's Health Initiative (WHI) sin embargo la USPSTF considera que este riesgo en realidad es muy bajo.




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El Instituto Nacional de Medicina de los EEUU y la OMS recomiendan estándares para la ingesta de suplementos de Calcio y Vitamina D como parte de la salud general.

Pero ninguno lo recomienda como suplemento para la prevención de fractura de cadera

Queda pendiente el desafío de determinar la ingesta adecuada de Calcio y vitamina D incluso para evitar la exposición al sol y adquirir cáncer de piel



Research

JAMA | Original Investigation

## Association Between Calcium or Vitamin D Supplementation and Fracture Incidence in Community-Dwelling Older Adults A Systematic Review and Meta-analysis

Jia-Guo Zhao, MD; Xian-Tie Zeng, MD; Jia Wang, MD; Lin Liu, MD

 Supplemental content

**IMPORTANCE** The increased social and economic burdens for osteoporosis-related fractures worldwide make the prevention of such injuries a major public health goal. Previous studies have reached mixed conclusions regarding the association between calcium, vitamin D, or combined calcium and vitamin D supplements and fracture incidence in older adults.

**OBJECTIVE** To investigate whether calcium, vitamin D, or combined calcium and vitamin D supplements are associated with a lower fracture incidence in community-dwelling older adults.

**DATA SOURCES** The PubMed, Cochrane library, and EMBASE databases were systematically searched from the inception dates to December 24, 2016, using the keywords *calcium*, *vitamin D*, and *fracture* to identify systematic reviews or meta-analyses. The primary randomized clinical trials included in systematic reviews or meta-analyses were identified, and an additional search for recently published randomized trials was performed from July 16, 2012, to July 16, 2017.

**STUDY SELECTION** Randomized clinical trials comparing calcium, vitamin D, or combined calcium and vitamin D supplements with a placebo or no treatment for fracture incidence in community-dwelling adults older than 50 years.

**DATA EXTRACTION AND SYNTHESIS** Two independent reviewers performed the data extraction and assessed study quality. A meta-analysis was performed to calculate risk ratios (RRs), absolute risk differences (ARDs), and 95% CIs using random-effects models.

**MAIN OUTCOMES AND MEASURES** Hip fracture was defined as the primary outcome. Secondary outcomes were nonvertebral fracture, vertebral fracture, and total fracture.

**RESULTS** A total of 33 randomized trials involving 51 145 participants fulfilled the inclusion criteria. There was no significant association of calcium or vitamin D with risk of hip fracture compared with placebo or no treatment (calcium: RR, 1.53 [95% CI, 0.97 to 2.42]; ARD, 0.01 [95% CI, 0.00 to 0.01]; vitamin D: RR, 1.21 [95% CI, 0.99 to 1.47]; ARD, 0.00 [95% CI, -0.00

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Se revisaron revisiones sistemáticas de los últimos 10 años, del 2006 al 2016.

Se evaluó un total de 33 estudios randomizados, con un total de 51145 participantes que cumplían los criterios de inclusión.

palabras clave:

- calcio, vitamina D y fracturas revisiones sistemáticas y metaanálisis que evalúan la asociación entre calcio, vitamina D o suplementos combinados de calcio y vitamina D y la incidencia de fracturas

Outcome:


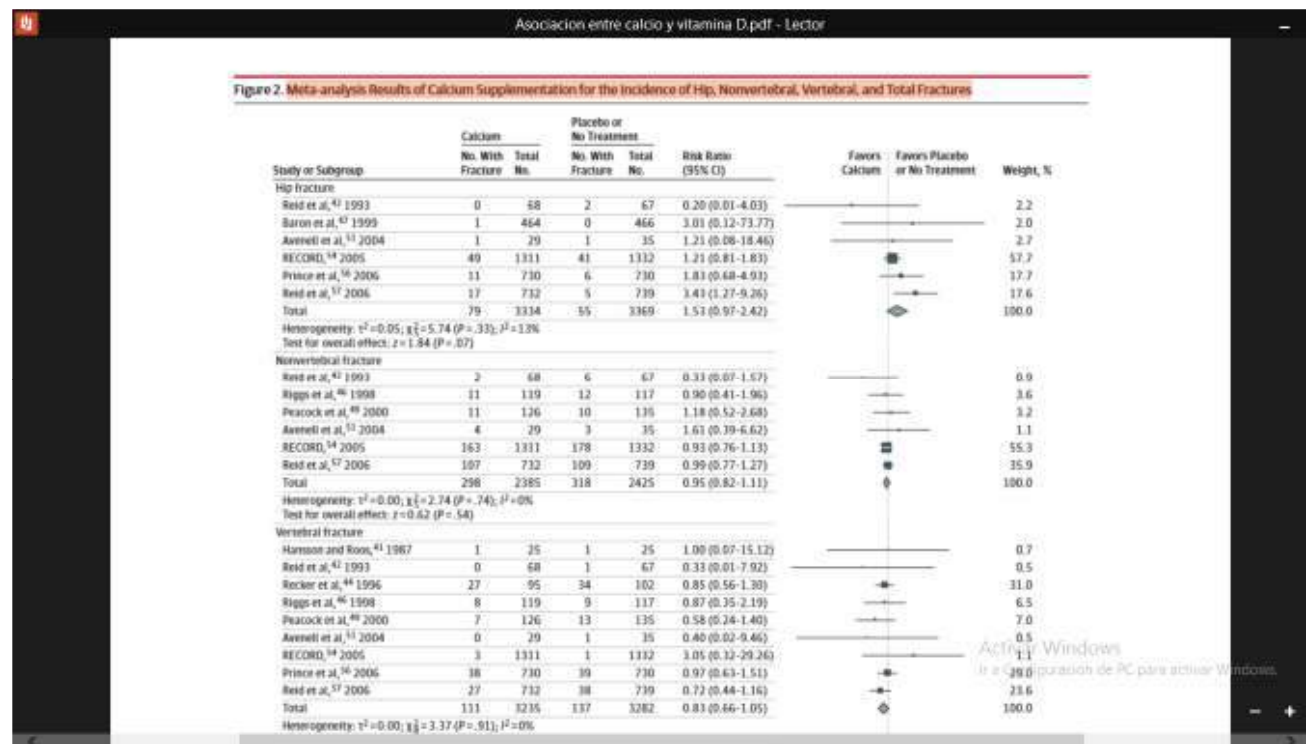
- Fractura de cadera,
  - Fractura no vertebral, vertebral y fracturas totales.
- 

Table 1. Characteristics of the Included Trials and Participants

Included Trials	Treatment	Women, No. (%)	Mean Age, y	Previous Fracture	Calcium Intake, mg/d	Baseline 25OHD, ng/mL	Treatment Duration
<b>Calcium vs Placebo or No Treatment</b>							
Inkovaara et al, <sup>40</sup> 1983 (Finland)	1.2 g/d (n = 42) Placebo (n = 42)	69 (82)	80.1	NA	NA	NA	9 mo
Hansson and Roos, <sup>41</sup> 1987 (Sweden)	1 g/d (n = 25) Placebo (n = 25)	50 (100)	65.9	Yes	NA	NA	3 y
Reid et al, <sup>42</sup> 1993 (New Zealand)	1 g/d (n = 68) Placebo (n = 67)	135 (100)	58	No vertebral fracture	750	37.5	4 y
Recker et al, <sup>44</sup> 1996 (United States)	1.2 g/d (n = 95) Placebo (n = 102)	197 (100)	73.5	Partial <sup>c</sup>	434	25.5 <sup>e</sup>	4 y
Riggs et al, <sup>46</sup> 1998 (United States)	1.6 g/d (n = 119) Placebo (n = 117)	236 (100)	66.2	No	714	30.1	4 y
Baron et al, <sup>47</sup> 1999 (United States)	1.2 g/d (n = 464) Placebo (n = 466)	258 (28)	61.0	NA	877	NA	4 y
Ruml et al, <sup>48</sup> 1999 (United States)	0.8 g/d (n = 29) Placebo (n = 34)	63 (100)	52	No	613	NA	2 y
Peacock et al, <sup>49</sup> 2000 (United States)	0.75 g/d (n = 126) Placebo (n = 135)	187 (72)	73.8	Partial <sup>c</sup>	597	25.0	4 y
Avenell et al, <sup>51</sup> 2004 (United Kingdom)	1 g/d (n = 29) No treatment (n = 35)	NA <sup>a</sup> (83)	78 <sup>b</sup>	Yes	NA	NA	3.8 y
RECORD Grant et al, <sup>54</sup> 2005 (United Kingdom)	1 g/d (n = 1311) Placebo (n = 1332)	2241 (85)	77	Yes	NA	15.2 <sup>e,f</sup>	2-5 y
Prince et al, <sup>56</sup> 2006 (Australia)	0.48 g/d (n = 730) Placebo (n = 730)	1460 (100)	75.2	Partial <sup>c</sup>	915	31.0 <sup>e</sup>	5 y
Reid et al, <sup>57</sup> 2006 (New Zealand)	1 g/d (n = 732) Placebo (n = 739)	1471 (100)	74.3	Partial <sup>c</sup>	857	20.7	5 y
Mitri et al, <sup>62</sup> 2011 (United States)	0.8 g/d (n = 22) Placebo (n = 24)	23 (50)	58.0	NA	923	24.5	4 mo

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# Metaanalysis Results of Calcium Supplementation for the Incidence of Hip, Non vertebral ,Vertebral, and Total Fractures





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## Discusión

- A pesar que otros autores, como Tang et al, Bolland, sugieren que habría cierta disminución de fracturas, con el suplemento de Calcio, estos autores lo desestiman
- Avenell et al en un revisión Cochrane, estimo que habría disminución de fracturas de cadera y todas las fracturas tomando un suplemento de Calcio y Vitamina D
- El Estudio de Mujeres demostró cierta protección en el uso de hormono terapia y la asociación de suplementos de Calcio y vitamina D

The Women's Health Initiative Dietary Modification Trial:  
Overview and Baseline Characteristics of Participants CHERYL  
RITENBAUGH, et aal  
Ann Epidemiol 2003;13:S87–S9



# The Women's Health Initiative Dietary Modification Trial: Overview and Baseline Characteristics of Participants

CHERYL RITENBAUGH, PhD, MPH, RUTH E. PATTERSON, PhD, RD,  
ROWAN T. CHLEBOWSKI, MD, PhD, BETTE CAAN, DRPH,  
LESLEY FELS-TINKER, PhD, RD, BARBARA HOWARD, PhD, AND JUDY OCKENE, PhD

*Ann Epidemiol* 2003;13:S87–S97. © 2003 Elsevier Inc. All rights reserved.

**KEY WORDS:** Low-fat Diet, Disease Prevention, Clinical Trial, Behavioral Modification, Breast Cancer, Colorectal Cancer, Women's Health, Postmenopausal Women.

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## INTRODUCTION

The Dietary Modification (DM) component of the Women's Health Initiative (WHI) is a randomized controlled evaluation of a low-fat diet that is high in fruits.

studies of fat and breast and colorectal cancers have yielded inconsistent or null results (9–11). However, there are substantial obstacles to finding clear and interpretable relationships in these studies (12):

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## Resultados

En este metaanálisis de ensayos clínicos controlados, el uso de suplementos que incluían calcio, vitamina D, o ambos comparados con el tratamiento con placebo o sin tratamiento, no se asoció Disminucion del riesgo de fracturas entre los adultos mayores que viven en la comunidad.

2019



Journal of the American College of Nutrition



ISSN: 0731-5724 (Print) 1541-1087 (Online) Journal homepage: <https://www.tandfonline.com/loi/uacn20>

## The Evidence and Controversy Between Dietary Calcium Intake and Calcium Supplementation and the Risk of Cardiovascular Disease: A Systematic Review and Meta-Analysis of Cohort Studies and Randomized Controlled Trials

Chao Yang, Xiangling Shi, Hui Xia, Xian Yang, Hechun Liu, Da Pan & Guiju Sun

To cite this article: Chao Yang, Xiangling Shi, Hui Xia, Xian Yang, Hechun Liu, Da Pan & Guiju Sun (2019): The Evidence and Controversy Between Dietary Calcium Intake and Calcium Supplementation and the Risk of Cardiovascular Disease: A Systematic Review and Meta-Analysis of Cohort Studies and Randomized Controlled Trials, Journal of the American College of Nutrition, DOI: [10.1080/07315724.2019.1649219](https://doi.org/10.1080/07315724.2019.1649219)

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Published online: 18 Oct 2019.



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El Instituto de Medicina y el Instituto Nacional de Salud recomiendan un consume diario de calcio de 1200 mg a 1500 mg para los mayores de 65 años.


Existen algunos estudios prospectivos que concluyen un efecto beneficioso del calcio para la prevencion de la incidencia y mortalidad de algunas enfermedades cardiovasculares.

Ross AC, Manson JE, Abrams SA, Aloia JF, Brannon PM, Clinton SK, Durazo-Arvizu RA, Gallagher JC, Gallo RL, Jones G, et al. The 2011 report on dietary reference intakes for calcium and vitamin d from the institute of medicine: what clinicians need to know. *J Clin Endocrinol Metab.* 2011;96(1):53–58. doi: 10.1210/jc.2010-2704.

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El presente estudio desea demostrar que la ingesta de calcio esta asociada a un aumento de la mortalidad o el riesgo de infarto al miocardio o de accidente cerebro vascular, especialmente aquellos que toman suplementos de calcio.

42 artículos cumplieron con los criterios de inclusión, incluidos 26 estudios de prospectivos de cohorte y 16 ensayos clínicos controlados.



# No existe Asociación entre ingesta de calcio dietético y enfermedad cardiovascular.

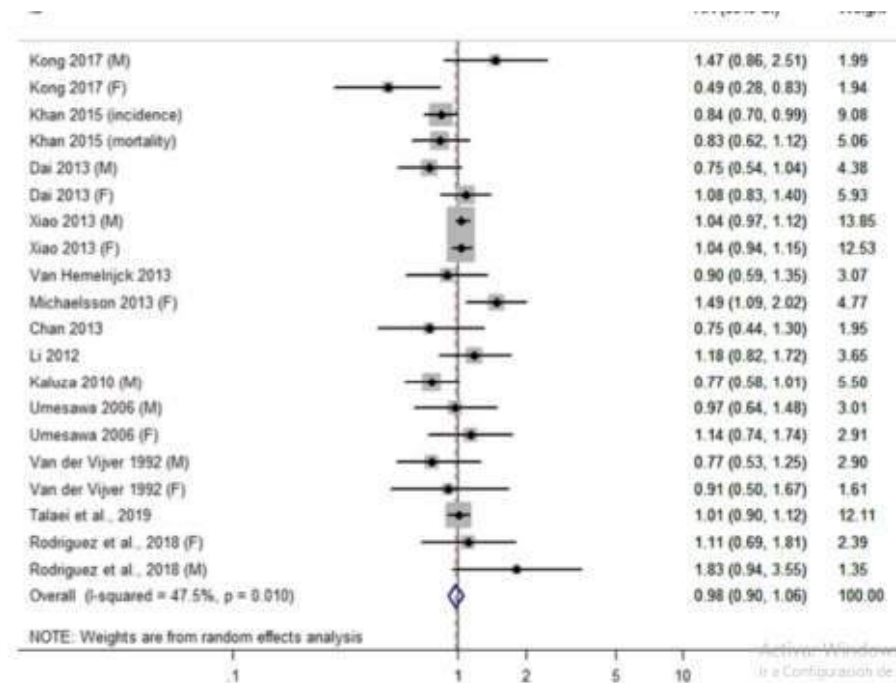


Figure 2. The association between dietary calcium intake and the risk of cardiovascular disease (CVD). For Kong 2017, the RR of the CVD risk was reported separately by sex, respectively showed by Kong (M) and Kong (F). Other studies that differentiate gender used the same annotation mentioned above, such as Dai 2013, Xiao 2013, Umesawa 2006, Van der Vijver 1992. For studies involving incidence and mortality, (incidence) and (mortality) annotation were used, respectively, like

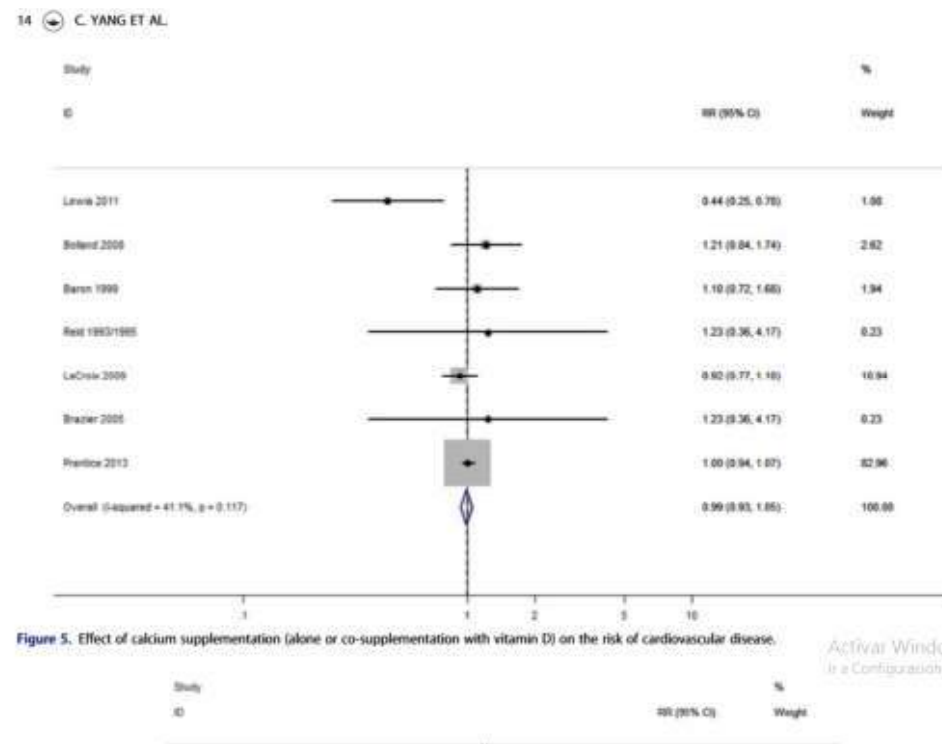
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No se encontró asociación entre el consumo de calcio dietético y enfermedad cardiovascular, ni cerebro vascular.

Incluso se puede plantear un efecto protector del calcio dietético en en las enfermedades cardiovasculares.



# Calcio suplementario y enfermedad cerebrovascular



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# Calcio suplementario y enfermedad coronaria

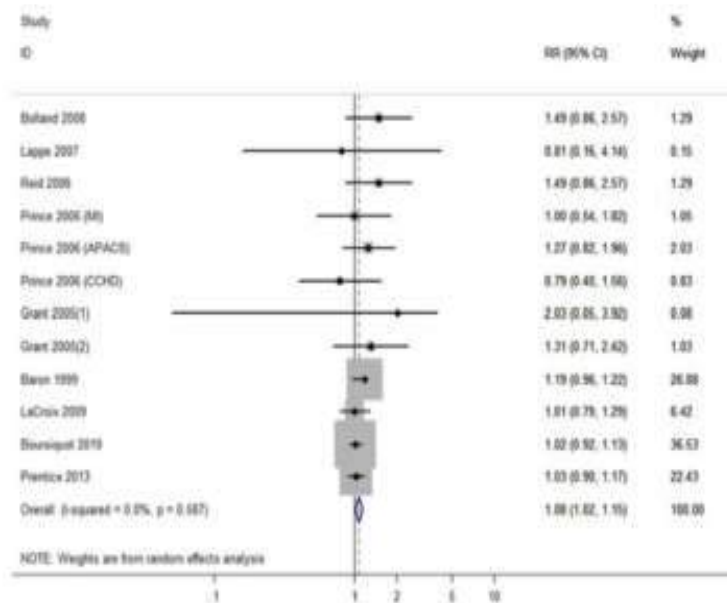


Figure 6. Effect of calcium supplementation (alone or co-supplementation with vitamin D) on the risk of coronary heart disease.

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El riesgo de adquirir un IM con calcio suplementario aumenta un 21%

Una dieta adecuada de calcio no aumenta el riesgo de enfermedad cardiovascular incluido enfermedad coronaria y stroke.

Recomiendan como acción de salud publica tomar calcio de la dieta.

Calcio suplementario mas de 1400 mg es potencialmente riesgoso para enfermedad coronaria en particular el IM

El consumo de calcio suplementario menor de 1000 mg y combinado con vit D puede ser menos nocivo que administrar calcio solo

Individualizar siempre cada caso



Jan 2020.

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## Calcium and vitamin D supplementation in osteoporosis

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**Literature review current through:** Jan 2020. | **This topic last updated:** Oct 07, 2019.

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### INTRODUCTION

Osteoporosis is characterized by low bone mass, microarchitectural disruption, and increased skeletal fragility. Multiple therapeutic regimens have been designed to prevent or treat bone loss in postmenopausal women and older adults. The first step in the prevention or treatment of osteoporosis is ensuring adequate nutrition, particularly maintaining an adequate intake of calcium and vitamin D. Vitamin D enhances intestinal absorption of calcium and phosphate. Low concentrations of vitamin D are associated with impaired calcium absorption, a negative calcium balance, and a compensatory rise in parathyroid hormone (PTH), which results in excessive bone resorption.

Calcium and vitamin D supplementation in the treatment of osteoporosis will be reviewed here. Detailed information regarding pharmacologic therapy for osteoporosis and the role of calcium in the

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No hay consenso en la cantidad de calcio, tanto del calcio de la dieta como el calcio suplementario. Recomienda 1200 mg de calcio y 800 de vitamina D.

Refiere que es mejor consumir el calcio de manera natural de los productos lácteos que los suplementos. Pues los suplementos tienen varios efectos en particular los cálculos renales

El consumo de suplemento de calcio solo no previene la fractura de cadera.



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## Consumo de calcio

Productos lácteos, nueces, vegetales verdes (brócoli), soya y algunas bebidas fortificadas.

Calcio suplementario 2 formas, carbonato (mas barato) y citrato.

El citrato tiene mejor absorcion. El carbonato debe de administrarse con alimentos y no se absorbe bien si se administra con inhibidores de H<sup>2</sup> o bomba de protones.

Algunos preparados de calcio a base de las conchas marinas tienen plomo, algunos autores consideran que no es perjudicial



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Se debe de tomar en cuenta el calcio elemental, el carbonato de calcio tiene 40% de calcio elemental, por ejemplo si se consume 1250, se ingiere 500 mg de calcio elemental.

Dosis por encima de 500 mg deben de administrarse de manera fraccionada

No se debe de pasar los 2000 mg de calcio por día por el riesgo de efectos colaterales

En teoría la formación de cálculos renales por consumo de calcio es infundada



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El estudio de Women's Health Initiative (WHI), reportó un aumento del riesgo de calculos renales en mujeres post menopausicas que consumieron calcio suplementario con vitamina D comparado con placebo.


El consumo de suplementos de calcio y el riesgo de infarto miocardio es controversial. Otros autores le dan un efecto protector

The National Osteoporosis Foundation considera que a dosis adecuadas el riesgo cardiovascular no es considerado



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Otros efectos del calcio es dyspepsia, constipacion, interferencia con la absoción de hierro y hormona tiroidea. De ahi que no deben de administrarse juntos.



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La administración de suplementos de calcio ya sea solo o con vitamina D, parece ser superior en institucionalizados que en la comunidad.

Chung M, Lee J, Terasawa T, et al. Vitamin D with or without calcium supplementation for prevention of cancer and fractures: an updated meta-analysis for the U.S. Preventive Services task force *Ann Inter Medic* 2011 155 827



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Un metaanálisis que compare calcio, vitamina D solos y juntos con placebo y sin tratamiento en mujeres post menopausicas y hombres ancianos en la comunidad, nursing home y en el hospital, report una reduccion en las fracturas en los que consumieron calcio o calcio con vitamina D pero no con los que consumieron vitamina D sola.

**Bolland MJ, Leung W, Tai V, et al. Calcium intake and risk of fracture: systematic review. BMJ 2015; 351:h4580**

# Conclusiones y recomendaciones

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La dosis optima de calcio y vitamina D es incierta

En mujeres post menopausicas con osteoporosis, 1200 mg de calcio diario (dieta y suplemento) y 800 UI de Vit D

Se prefiere que la fuente de calcio sea de Fuentes naturales.

Si no se logra de Fuentes naturales, se recomienda suplementos de calcio y vitamina D en pacientes con osteoporosis (evidencia 2B)

No pasar de 2000 mg de calcio por dia

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Sobre el riesgo de infarto al miocardio asociado al consumo de suplementos de calcio esperar mayor evidencia y no tomar mas de 500 mg dia.

Siempre individualizar

A pesar que el consumo de calcio no previene las fracturas el consumo de calcio es importante para otras funciones del organismo

Se sigue recomendando el consumo de calcio para la osteoporosis



Muchas Gracias !!!

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