



70 ANNI DI REUMATOLOGIA ALLE MOLINETTE



Osteoporosi, (cancro) e salute scheletrica

P. D'Amelio MD, PhD
Geriatrics e Malattie Metaboliche
dell'Osso

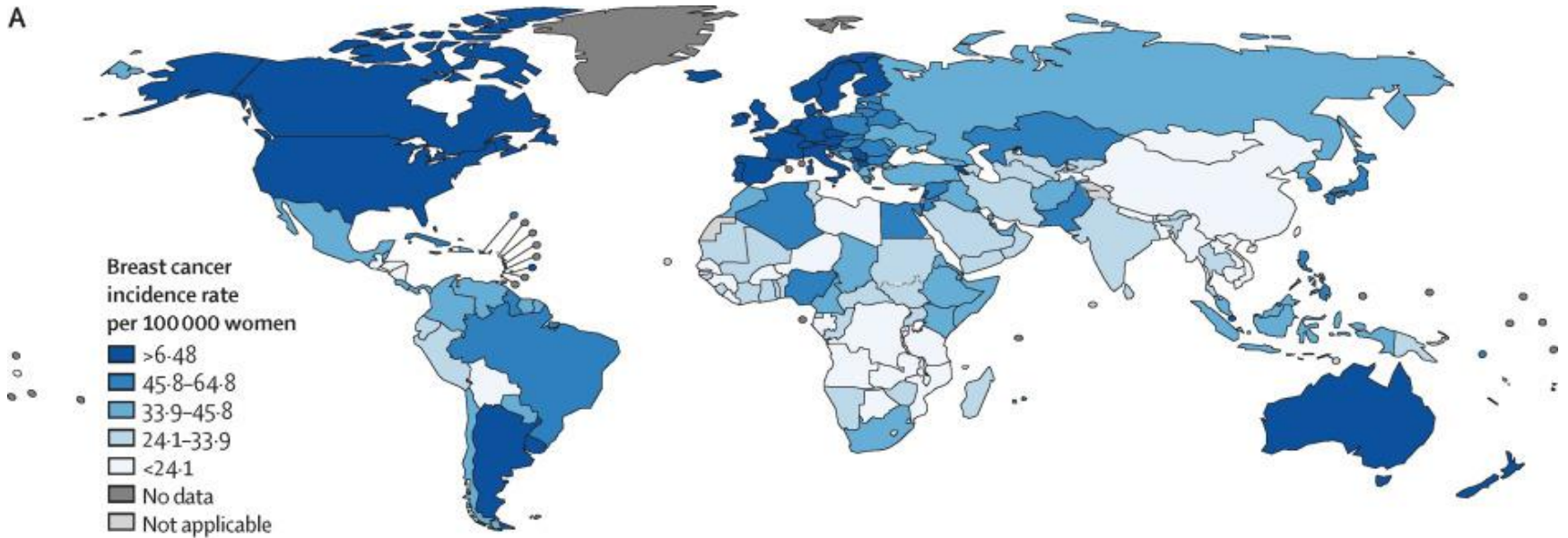
Torino, 12 Ottobre 2019

Qual è la
dimensione del
problema?

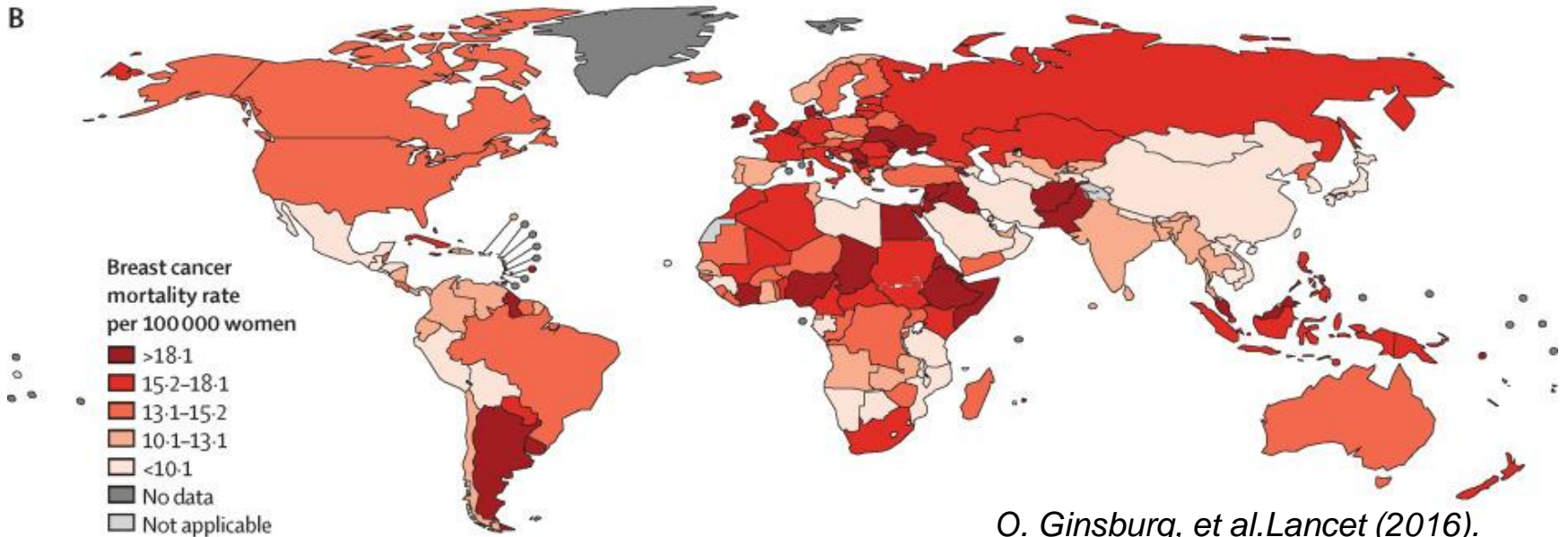


Incidence of breast cancer

A



B



O. Ginsburg, et al. Lancet (2016).

Incidence of prostate cancer



NATIONAL CANCER INSTITUTE

Surveillance, Epidemiology, and End Results Program

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Reports on Cancer

Home

Cancer Statistics ▾

SEER Data & Software ▾

Registry Operations ▾

News

About

Cancer Stat Facts

At a Glance

Common Cancer Sites

Cancer Disparities

Bladder

Breast (Female)

Colon and Rectum

Kidney and Renal Pelvis

Leukemia

Lung and Bronchus

Melanoma of the Skin

Non-Hodgkin Lymphoma

Pancreas

Prostate

Thyroid

Uterus

More Cancer Types

Estimated New Cases in 2018

164,690

% of All New Cancer Cases

9.5%

Estimated Deaths in 2018

29,430

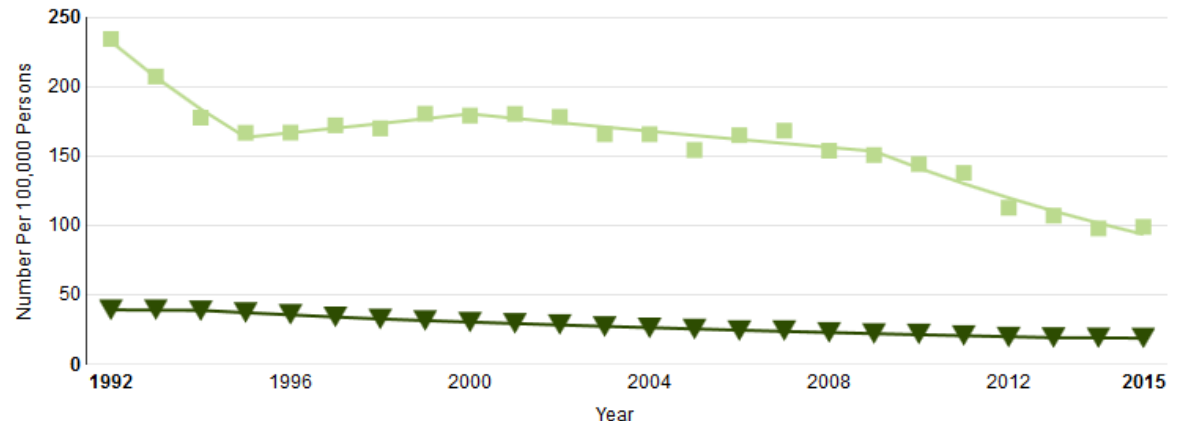
% of All Cancer Deaths

4.8%

Percent Surviving
5 Years

98.2%

2008-2014

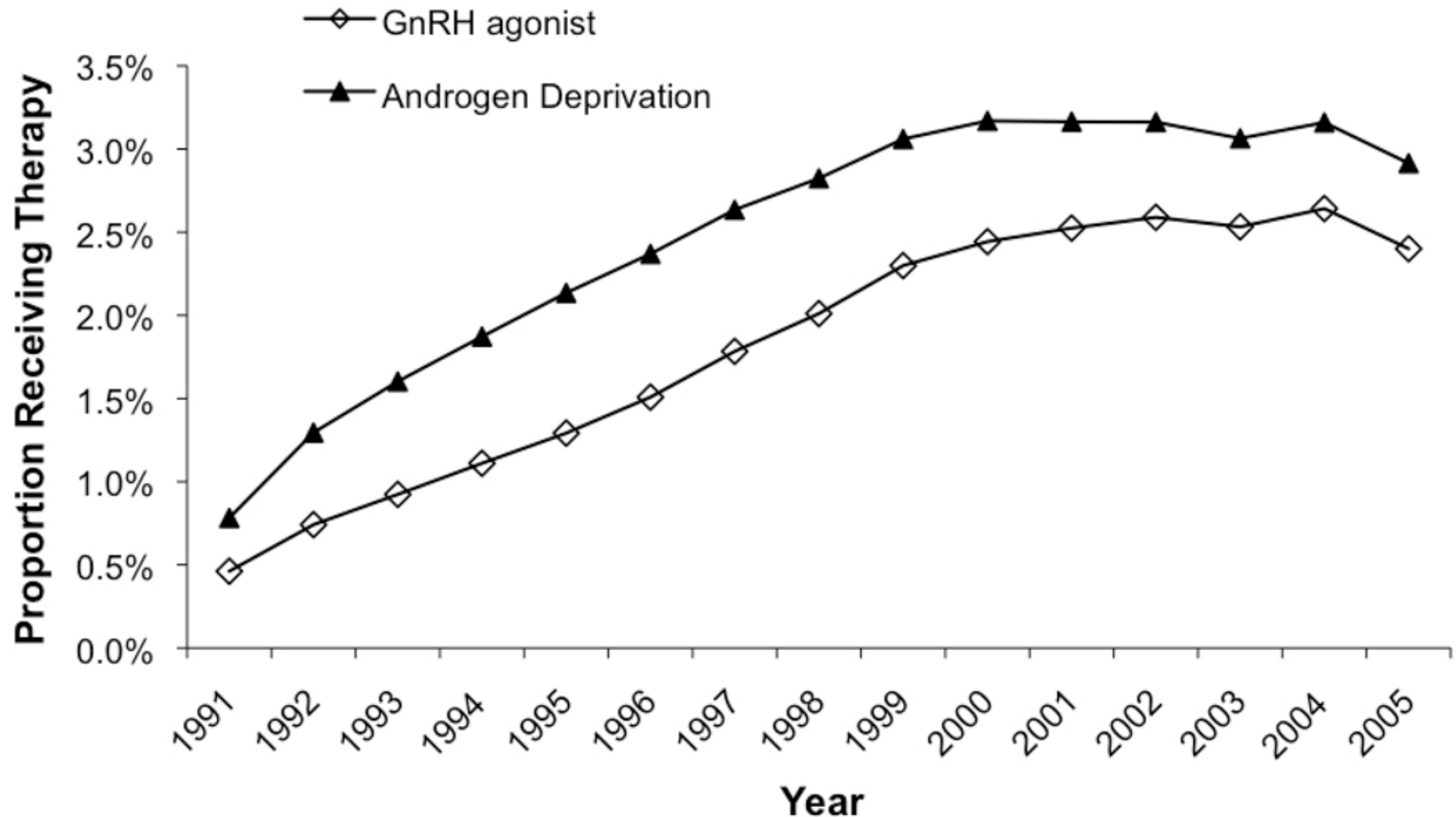


■ New Cases - SEER 13

▼ Deaths - U.S.

<https://seer.cancer.gov/statfacts/html/prost.html>

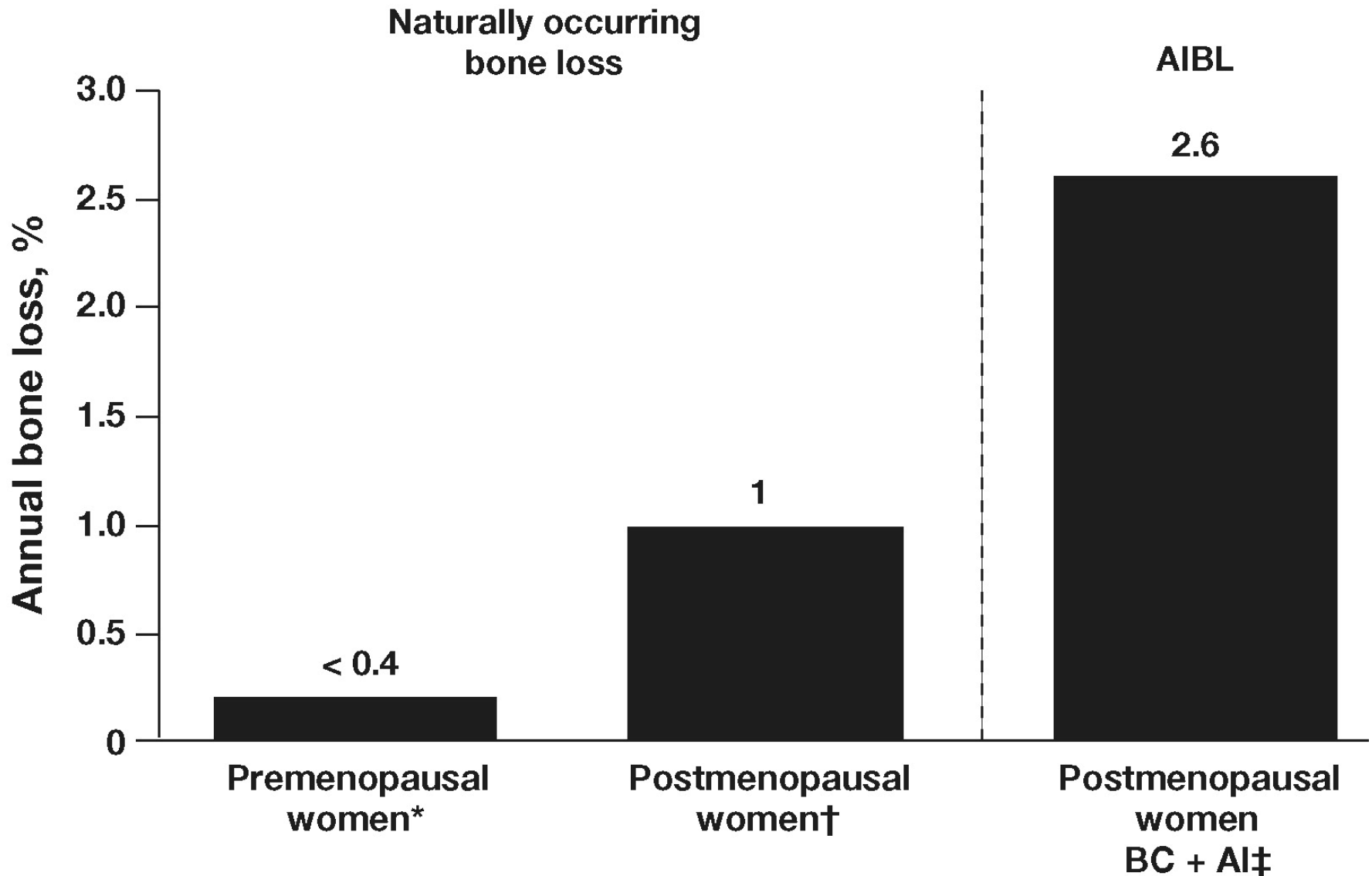
Use of endocrine therapy in prostate cancer



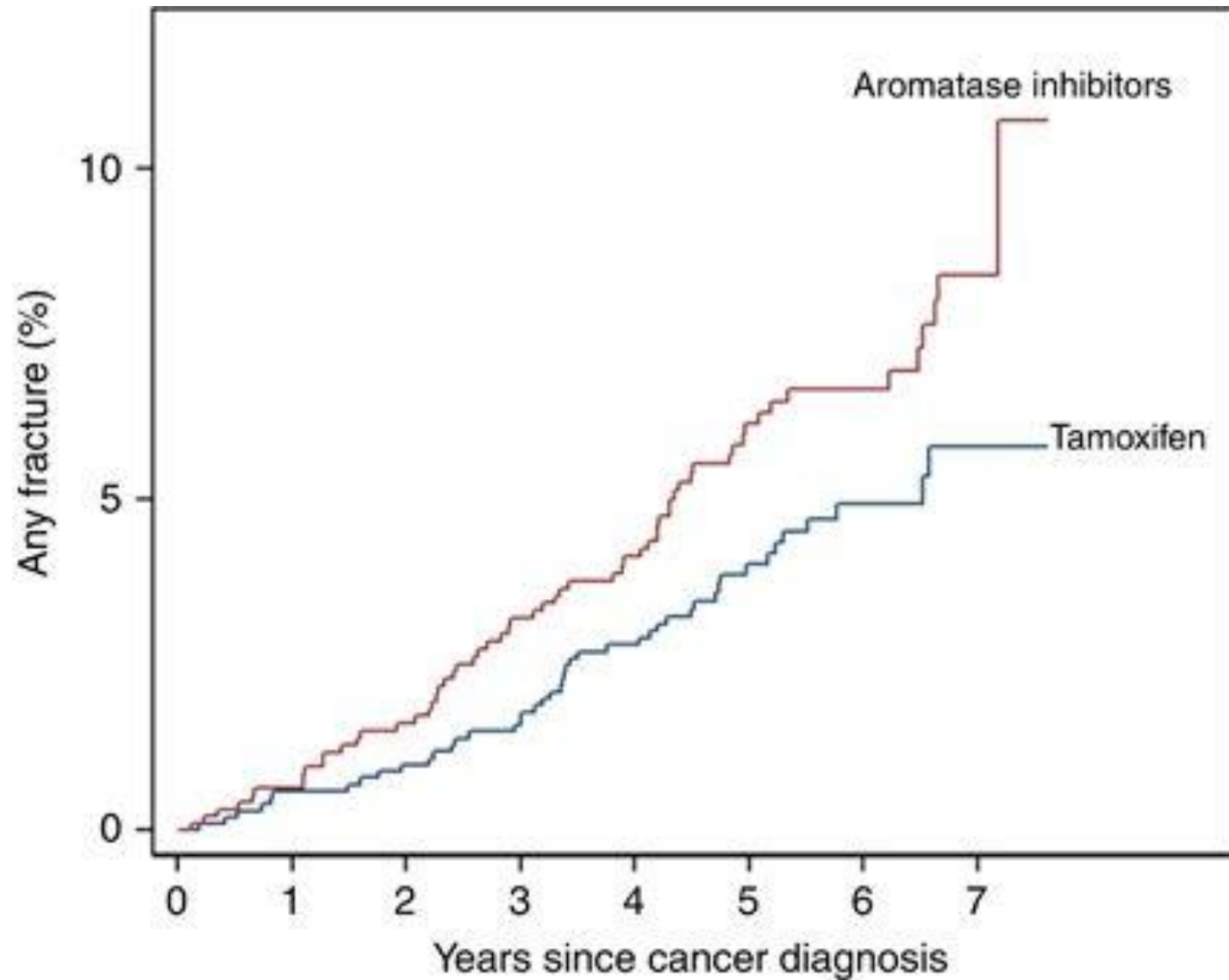
Siamo pratici!
Perché mi dovrei
interessare
dell'osso?



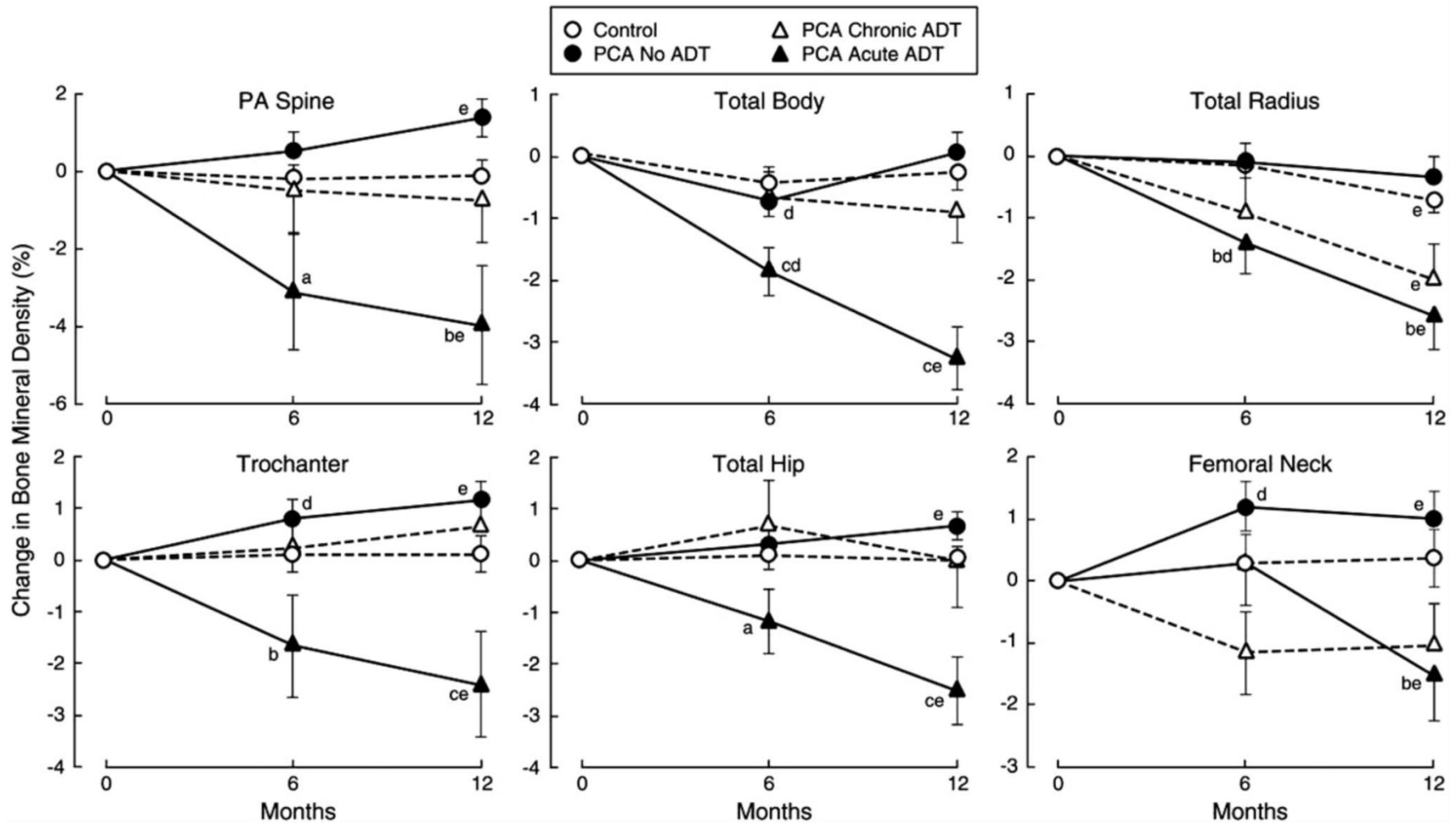
Aromatase inhibitors and bone loss



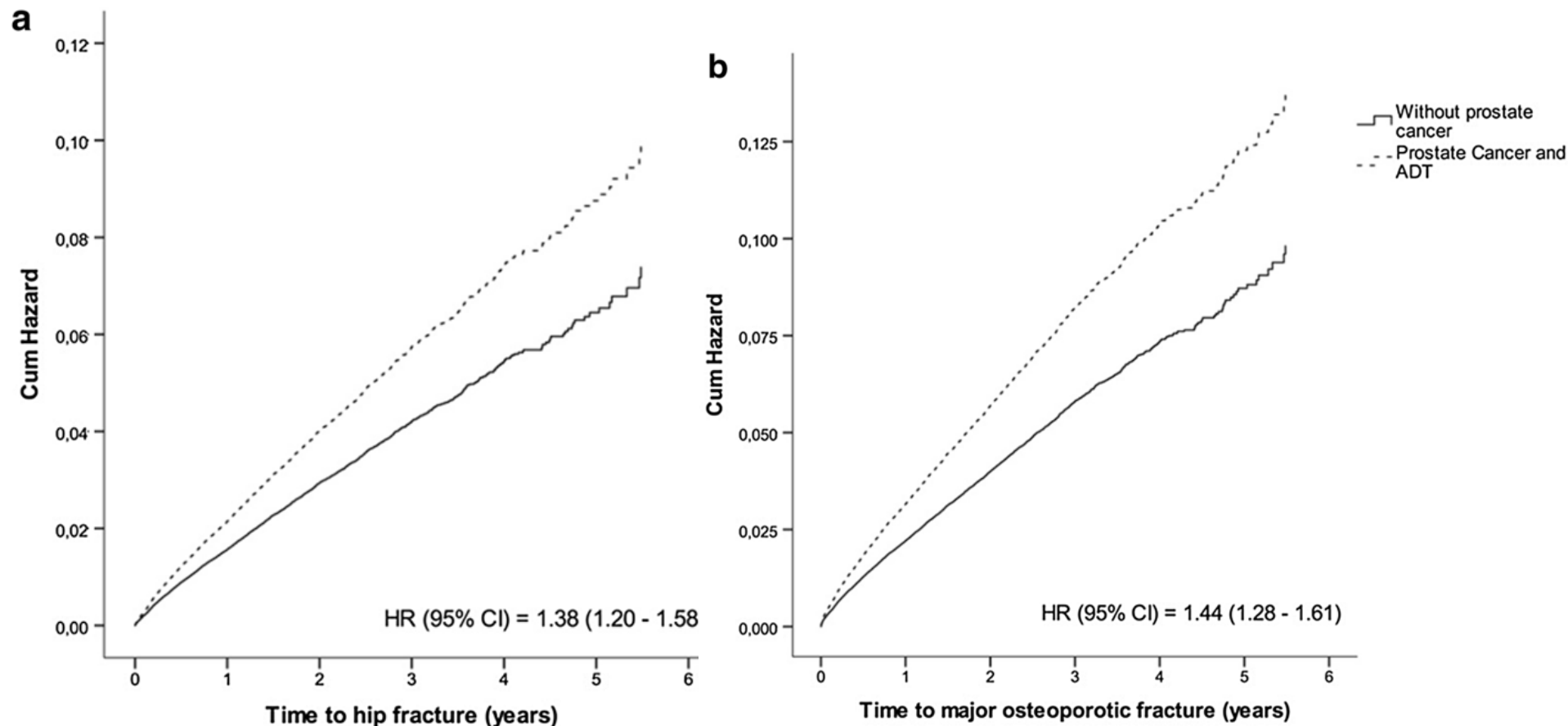
Aromatase inhibitors and fractures



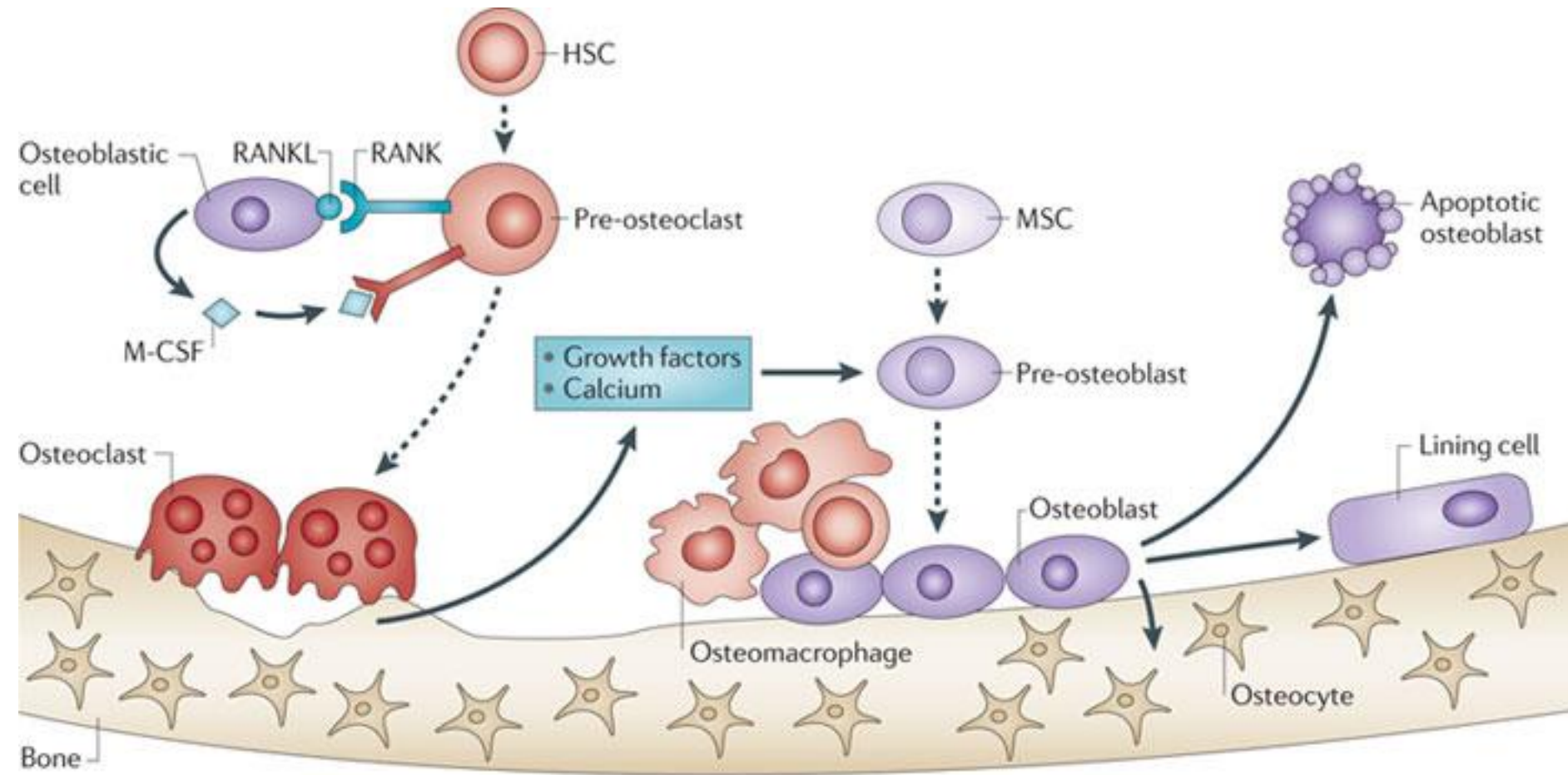
Androgen deprivation therapy and bone loss



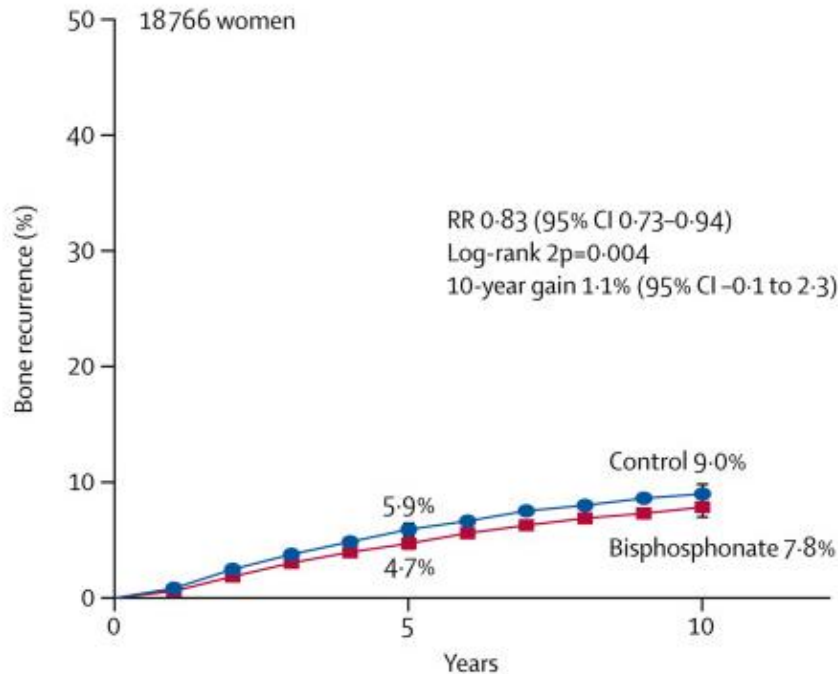
Androgen deprivation therapy and fractures



Cancer to bone: a fatal attraction.

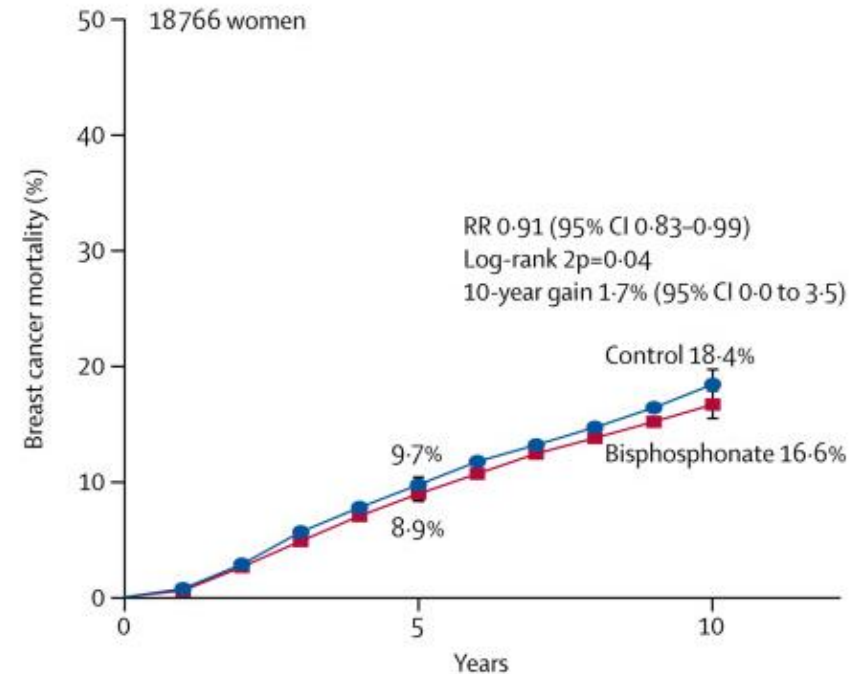


BSP and disease progression in breast cancer



Bone recurrence rate/year (%), events/woman-years and log-rank statistics

Allocation	Years 0–4	Years 5–9	Years ≥10
Bisphosphonate	0.99 (391/39 559)	0.76 (104/13 746)	0.10 (2/1932)
Control	1.21 (441/36 571)	0.71 (99/13 031)	0.10 (2/1941)
Rate ratio (95% CI)	0.79 (0.66–0.92)	1.02 (0.73–1.31)	0.61 (0.08–2.25)
from (O-E)/V	-45.0/189.5	0.8/46.8	-0.4/0.9

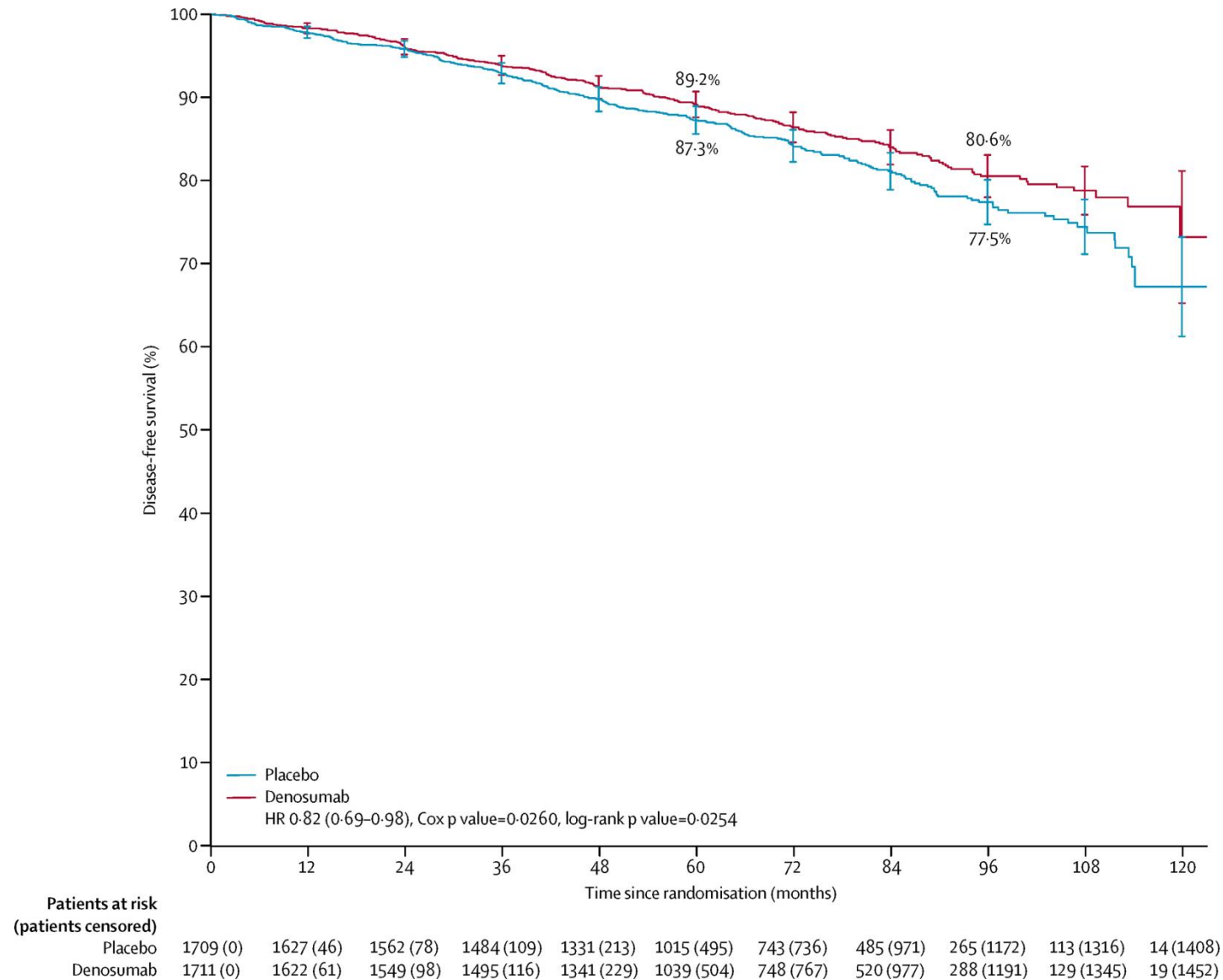


Death rates (%/year: total rate minus rate in women without recurrences) and log-rank statistics

Allocation	Years 0–4	Years 5–9	Years ≥10
Bisphosphonate	1.83 (1.70–1.97)	1.81 (1.59–2.03)	1.21 (0.72–1.69)
Control	1.98 (1.84–2.12)	1.97 (1.75–2.20)	1.69 (1.12–2.25)
Rate ratio (95% CI)	0.91 (0.81–1.01)	0.92 (0.75–1.10)	0.66 (0.18–1.15)
from (O-E)/V	-30.5/321.7	-9.5/121.0	-4.5/10.9

7 CLOD
BSP 31
Total patients
22027

DMAb and disease progression in breast cancer



Siamo pratici!
Chi devo
trattare?



Source	Whom to treat
ESMO SIOG	All women receiving AI therapy with ≥ 1 of the following T-score ≤ -2.0 . Any 2 of the following risk factors T-score < -1.5 , age > 65 yr, low BMI (< 20 kg/m ²), family history of hip fracture, personal history of fragility fracture after age 50, oral corticosteroid use > 6 mo, and smoking
ASCO	Women with T-score ≤ -2.5 Women with T-score between -1.0 and -2.5 should receive individualized therapy
St. Gallen	No treatment for women with normal BMD Premenopausal women with ovarian suppression/failure or
UK Expert Group	Postmenopausal women receiving AI therapy with ≥ 1 of the following: T-score < -2.0 Vertebral fracture Annual bone loss $> 4\%$ at LS or TH
Belgian Bone Club	Women with T-score < -2.5 or history of fragility fracture

Source	Whom to treat
International Expert Group (Hadji et al.)	All women receiving AI therapy with ≥ 1 of the following T-score ≤ -2.0 . Any 2 of the following risk factors T-score < -1.5 , age > 65 yr, low BMI (< 20 kg/m ²), family history of hip fracture, personal history of fragility fracture after age 50, oral corticosteroid use > 6 mo, and smoking
International Expert Panel (Aapro et al.)	Women with ≥ 2 of the following risk factors: AI use, T-score < -1.5 , age > 65 yr, corticosteroid use > 6 mo, family history of hip fracture, personal history of fragility fracture after age 50; T-score < -2.0
ESCEO position paper	All women receiving AI therapy with (T-score hip/spine < -2.5 or ≥ 1 prevalent fragility fracture), to women aged ≥ 75 irrespective of BMD, and to patients with T-score $< -1.5 + \geq 1$ clinical risk factor or T-score $< -1.0 + \geq 2$ clinical risk factors or FRAX-determined 10-year hip fracture probability $\geq 3\%$

Patients with cancer and endocrine treatment known to accelerate bone loss (aromatase inhibitors, ADT)

T score >-2.0 and no additional risk factors

Exercise,
Calcium and vitamin
D if needed

Monitor risk and
BMD every 1-2 yrs

Any of the following risk factors:

- age >65 yrs
- T score < 1.5
- Smoking
- BMI <20
- Family history of hip fractures
- fractures > 50 yrs
- Oral GC > 6 months

T score <-2.0

Exercise,
Calcium and vitamin
D and anti-
resorptives

Monitor risk and
BMD every 2 yrs

NOTA 79

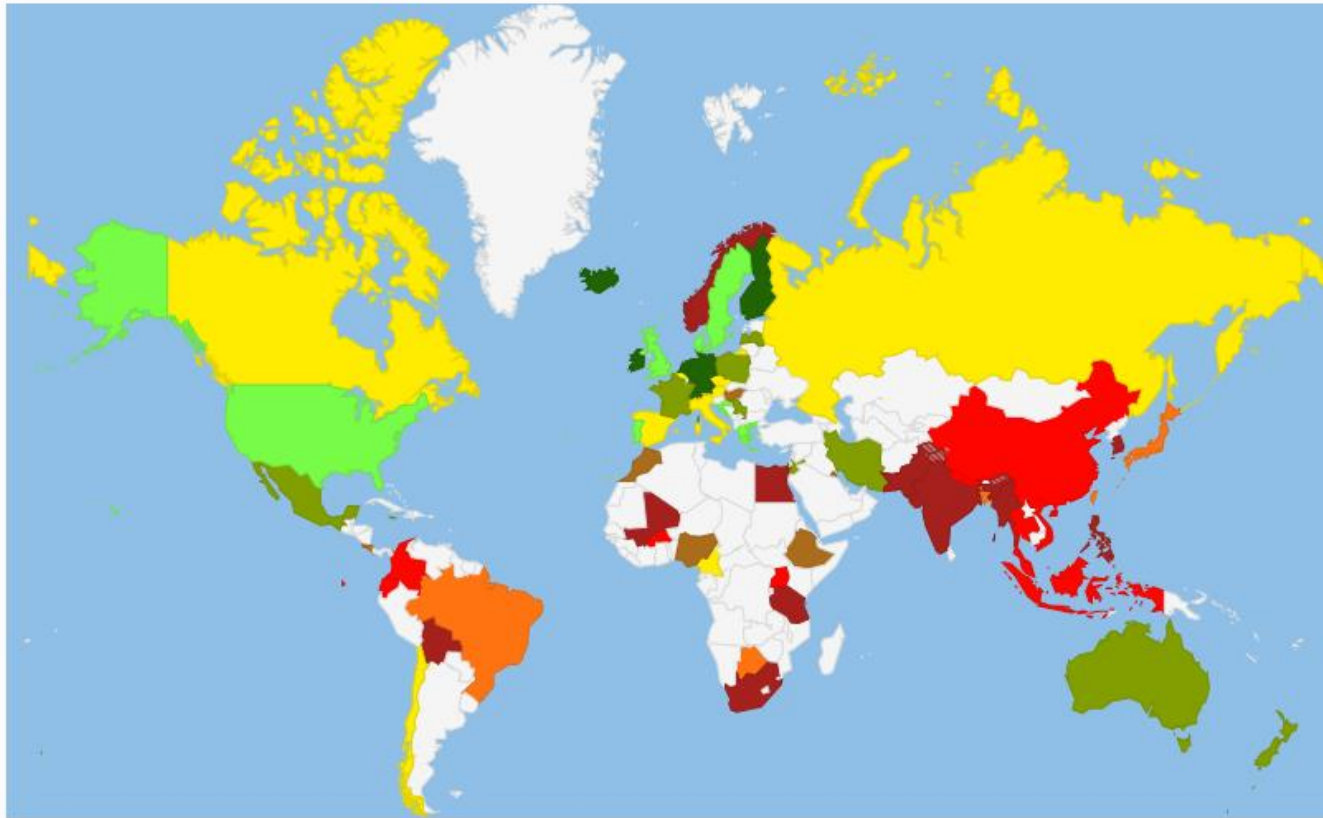
Prevenzione primaria in donne o uomini ≥ 50 anni a rischio elevato di frattura a causa di almeno 1 delle condizioni sotto elencate:

Condizione	Trattamento I scelta	II scelta	III scelta
Trattamento in atto o previsto per > 3 mesi con prednisone o equivalente ≥ 5 mg/die	Alendronato Risedronato Zoledronato	Denosumab	-----
Trattamento in corso di blocco ormonale adiuvante	Alendronato Risedronato Zoledronato Denosumab	-----	-----
T score colonna o femore ≤ -3 +: 1. Familiarità 2. AR o altre connettiviti, Diabete, BPCO	Alendronato Risedronato	Denosumab Zoledronato Ibandronato Raloxifene Basedoxifene	Stronzio Ranelato
Nuova frattura vertebrale o femorale nonostante il trattamento in nota 79 da almeno 1 anno			

Siamo pratici!
Devo dare il calcio
e la vitamina D?
Quanto?



Calcium intake map



Average dietary calcium intake (mg/d)

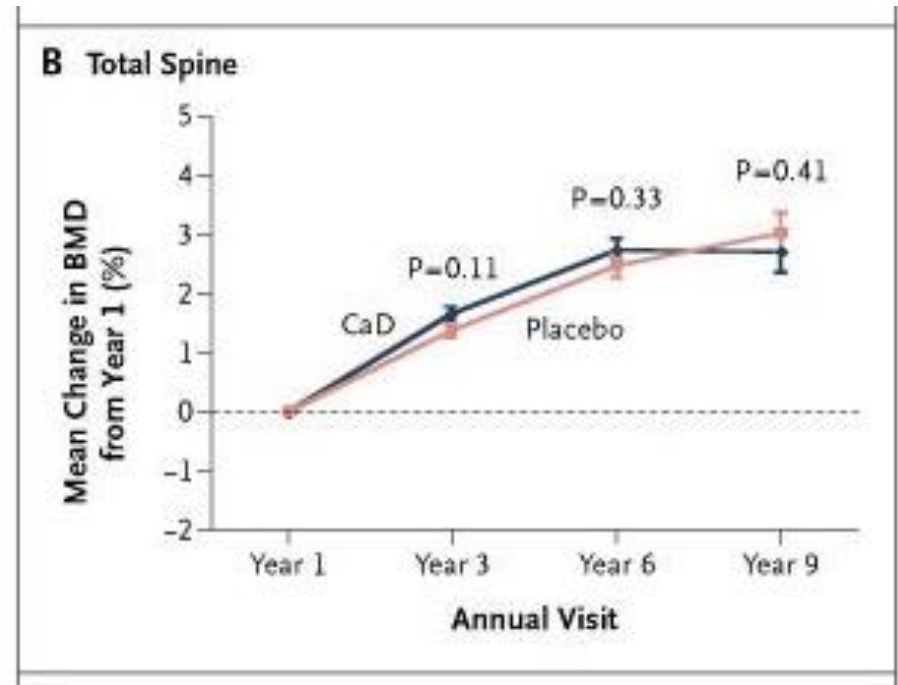
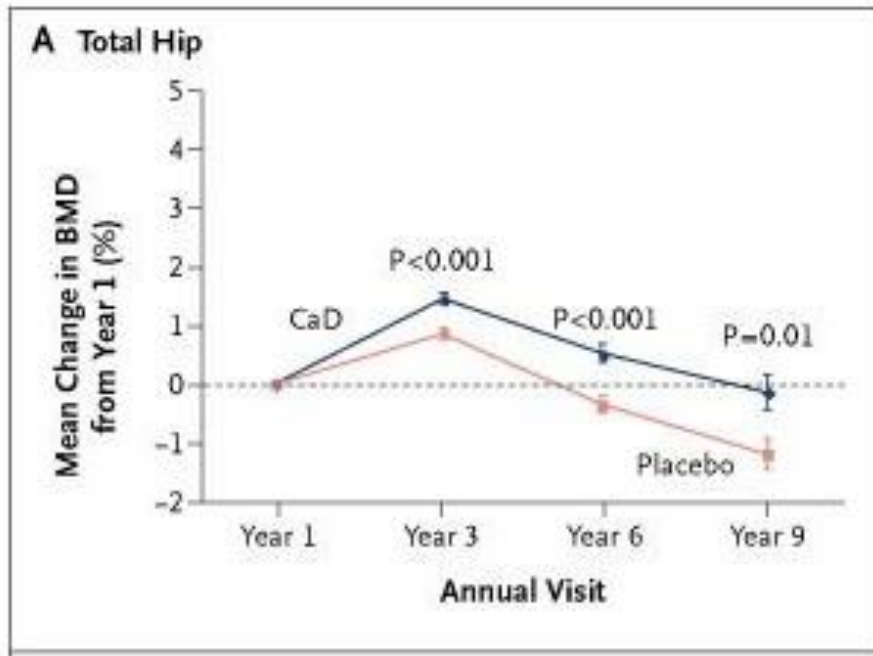
< 400 **400-500** **500-600** **600-700** **700-800** **800-900** **900-1000** **> 1000**

Adapted from Osteoporos Int. 2017; 28:3315-3324

<https://www.iofbonehealth.org/facts-and-statistics/calcium-map>

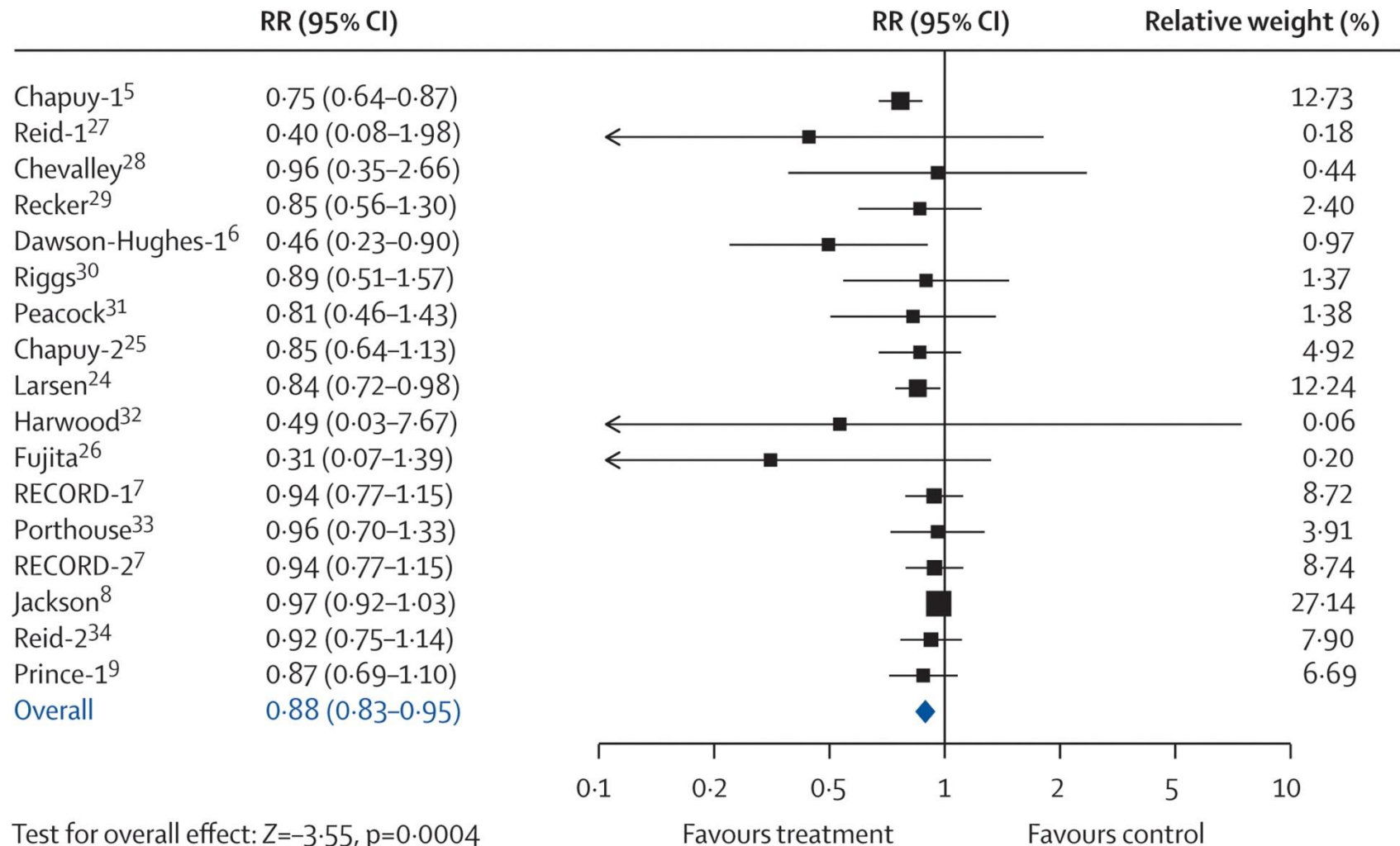
Calcium intake and BMD

> 36000 healthy post-menopausal women



Calcium supplements and risk of fracture

52 000 patients



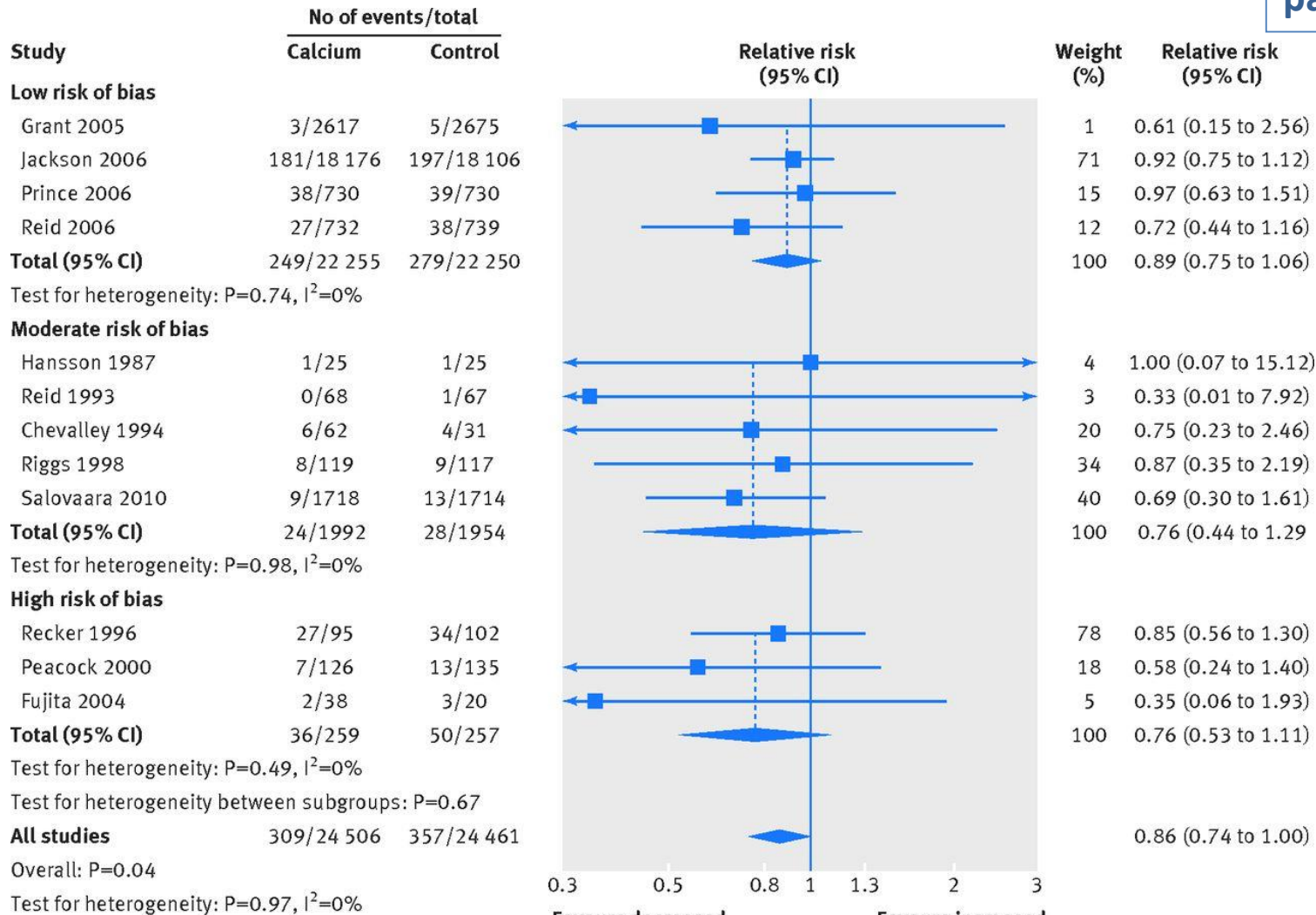
Test for overall effect: $Z=-3.55$, $p=0.0004$

Test for heterogeneity: $p=0.20$, $I^2=20\%$

Tang BM, et al. Lancet 2007

Calcium supplements and risk of fracture

69 107
participants



Calcium supplements and risk of non-vertebral fracture

51 145 participants

Study or Subgroup	Calcium		Placebo or No Treatment		Risk Ratio (95% CI)
	No. With Fracture	Total No.	No. With Fracture	Total No.	
Hip fracture					
Reid et al, ⁴² 1993	0	68	2	67	0.20 (0.01-4.03)
Baron et al, ⁴⁷ 1999	1	464	0	466	3.01 (0.12-73.77)
Avenell et al, ⁵¹ 2004	1	29	1	35	1.21 (0.08-18.46)
RECORD, ⁵⁴ 2005	49	1311	41	1332	1.21 (0.81-1.83)
Prince et al, ⁵⁶ 2006	11	730	6	730	1.83 (0.68-4.93)
Reid et al, ⁵⁷ 2006	17	732	5	739	3.43 (1.27-9.26)
Total	79	3334	55	3369	1.53 (0.97-2.42)

Heterogeneity: $\tau^2 = 0.05$; $\chi^2_5 = 5.74$ ($P = .33$); $I^2 = 13\%$

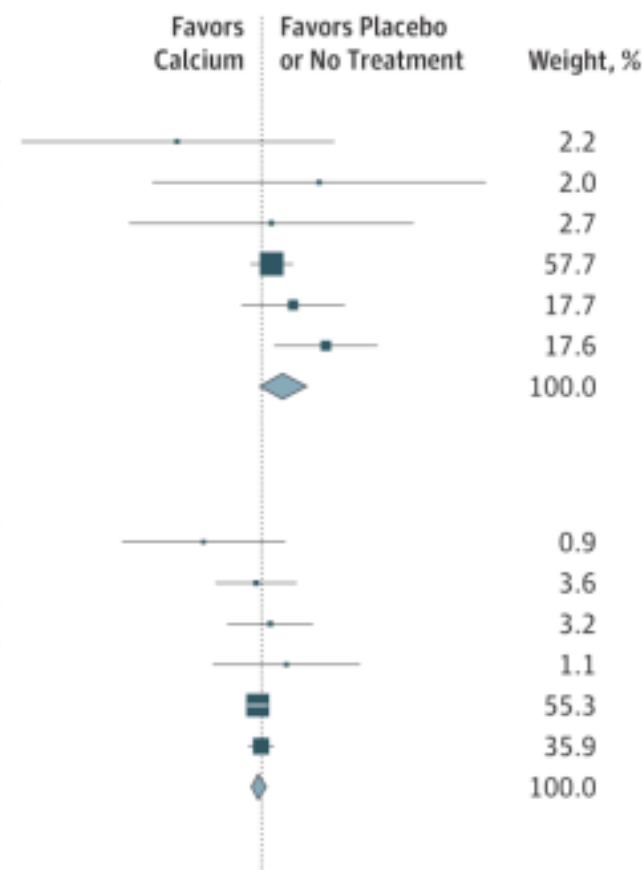
Test for overall effect: $z = 1.84$ ($P = .07$)

Nonvertebral fracture

Reid et al, ⁴² 1993	2	68	6	67	0.33 (0.07-1.57)
Riggs et al, ⁴⁶ 1998	11	119	12	117	0.90 (0.41-1.96)
Peacock et al, ⁴⁹ 2000	11	126	10	135	1.18 (0.52-2.68)
Avenell et al, ⁵¹ 2004	4	29	3	35	1.61 (0.39-6.62)
RECORD, ⁵⁴ 2005	163	1311	178	1332	0.93 (0.76-1.13)
Reid et al, ⁵⁷ 2006	107	732	109	739	0.99 (0.77-1.27)
Total	298	2385	318	2425	0.95 (0.82-1.11)

Heterogeneity: $\tau^2 = 0.00$; $\chi^2_5 = 2.74$ ($P = .74$); $I^2 = 0\%$

Test for overall effect: $z = 0.62$ ($P = .54$)



Calcium supplements and risk of vertebral-fracture

51 145 participants

Vertebral fracture

Hansson and Roos, ⁴¹ 1987	1	25	1	25	1.00 (0.07-15.12)
Reid et al, ⁴² 1993	0	68	1	67	0.33 (0.01-7.92)
Recker et al, ⁴⁴ 1996	27	95	34	102	0.85 (0.56-1.30)
Riggs et al, ⁴⁶ 1998	8	119	9	117	0.87 (0.35-2.19)
Peacock et al, ⁴⁹ 2000	7	126	13	135	0.58 (0.24-1.40)
Avenell et al, ⁵¹ 2004	0	29	1	35	0.40 (0.02-9.46)
RECORD, ⁵⁴ 2005	3	1311	1	1332	3.05 (0.32-29.26)
Prince et al, ⁵⁶ 2006	38	730	39	730	0.97 (0.63-1.51)
Reid et al, ⁵⁷ 2006	27	732	38	739	0.72 (0.44-1.16)
Total	111	3235	137	3282	0.83 (0.66-1.05)

Heterogeneity: $\tau^2=0.00$; $\chi^2_8=3.37$ ($P=.91$); $I^2=0\%$

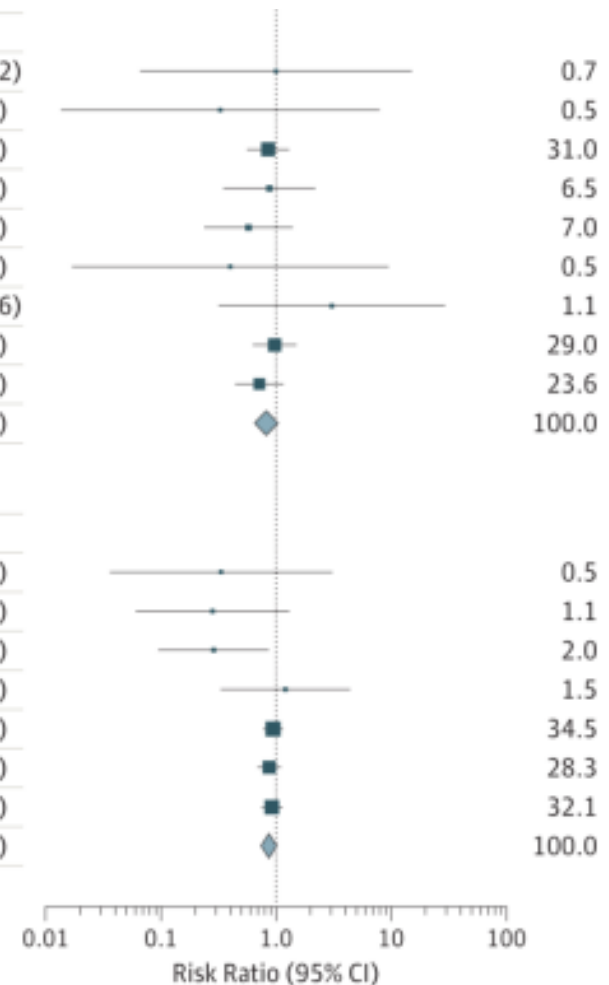
Test for overall effect: $z=1.52$ ($P=.13$)

Total fracture

Inkovaara et al, ⁴⁰ 1983	1	42	3	42	0.33 (0.04-3.08)
Reid et al, ⁴² 1993	2	68	7	67	0.28 (0.06-1.31)
Baron et al, ⁴⁷ 1999	4	464	14	466	0.29 (0.10-0.87)
Avenell et al, ⁵¹ 2004	4	29	4	35	1.21 (0.33-4.41)
RECORD, ⁵⁴ 2005	166	1311	179	1332	0.94 (0.77-1.15)
Prince et al, ⁵⁶ 2006	110	730	126	730	0.87 (0.69-1.10)
Reid et al, ⁵⁷ 2006	134	732	147	739	0.92 (0.75-1.14)
Total	421	3376	480	3411	0.88 (0.75-1.03)

Heterogeneity: $\tau^2=0.01$; $\chi^2_8=7.63$ ($P=.27$); $I^2=21\%$

Test for overall effect: $z=1.56$ ($P=.12$)



Effects of vitamin D supplementation on musculoskeletal health: a systematic review, meta-analysis, and trial sequential analysis

Mark J Bolland, Andrew Grey, Alison Avenell



Lancet Diabetes Endocrinol
2018; 6: 847–58

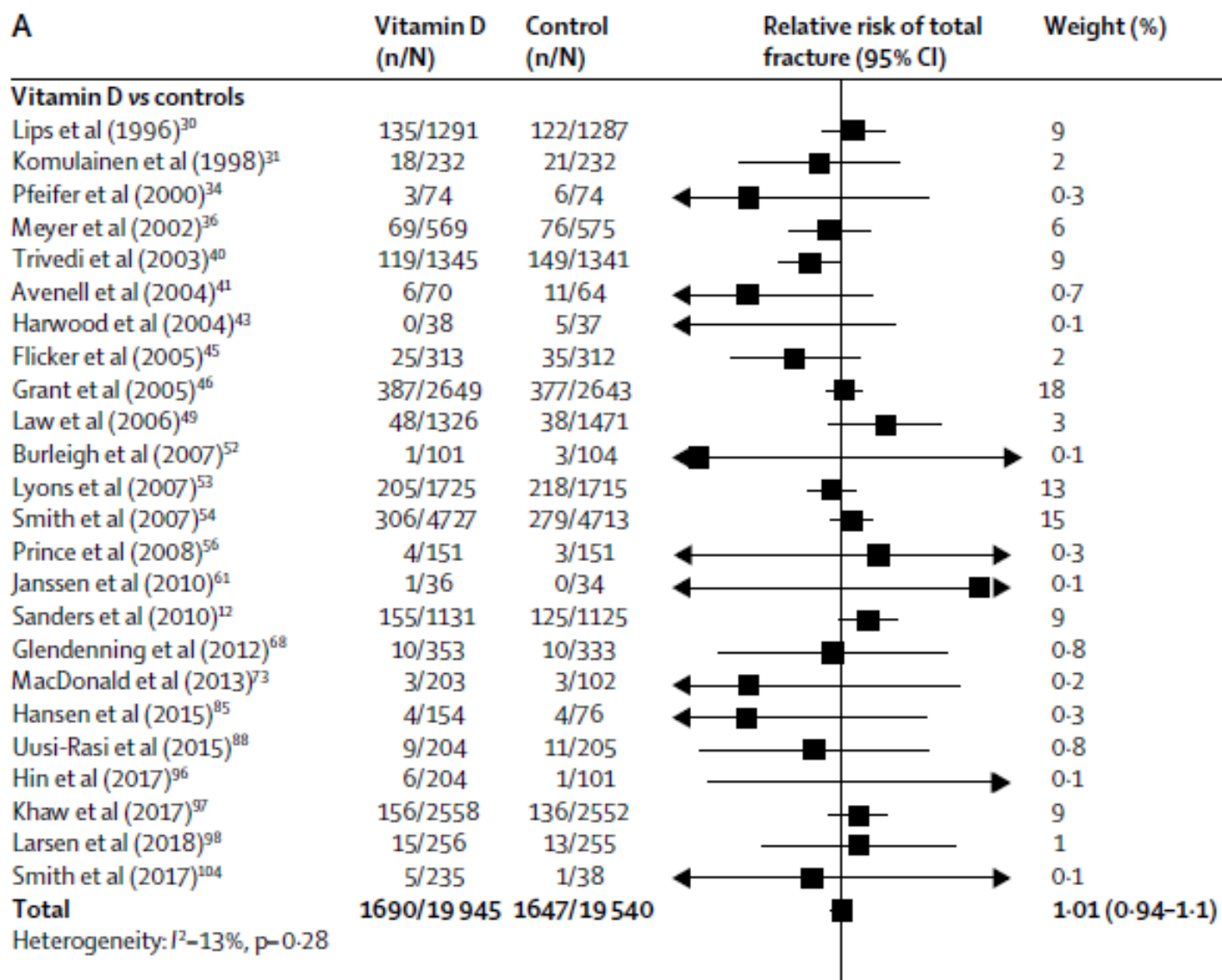
81 RCT (n=53 537 subjects)

Fractures n=42

falls n=37

BMD n=41

No effects on fractures prevention



No effects on fractures prevention

51 145 participants

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	No. With Fracture	Total No.	No. With Fracture	Total No.	
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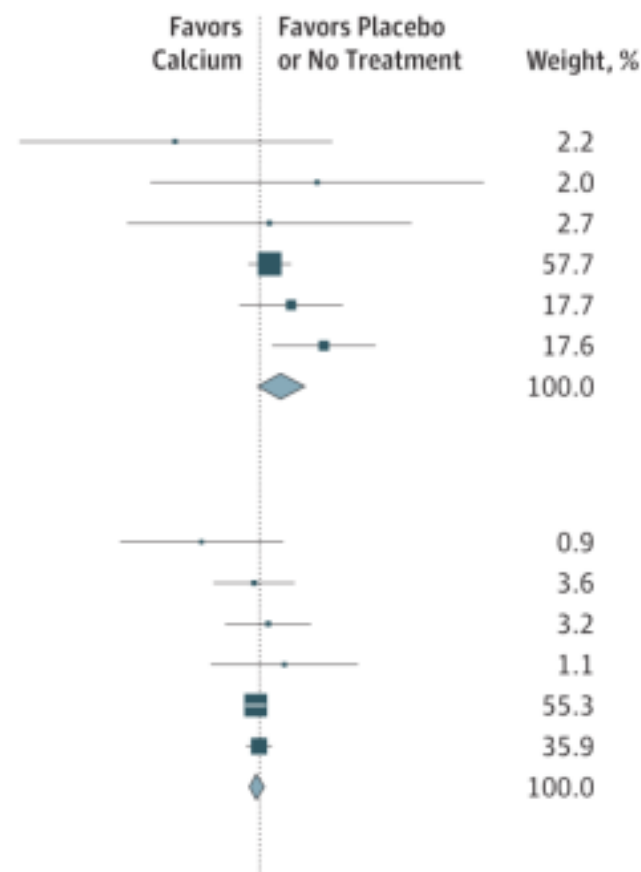
Test for overall effect: $z = 1.84$ ($P = .07$)

Nonvertebral fracture

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Test for overall effect: $z = 0.62$ ($P = .54$)



Health

Vitamin D supplements don't help bone health, major study concludes

Biggest ever review of evidence recommends the government ditch its advice to take them throughout winter

Sarah Boseley
Health editor

Thu 4 Oct 2018
23.30 BST



5911

This article is over 1 month old



▲ Woman holding glass ampoule of vitamin D. Photograph: Alamy Stock Photo

Vitamin D supplements do nothing for bone health and the government should ditch its advice that everyone should take them throughout the winter months, according to the authors of the biggest review of the

most viewed



Lion Air crash: pilot fought to keep plane in air, says report



Dominic Raab: Theresa May's deal worse than staying in EU



I made a tremendous difference: Trump heaps Thanksgiving praise on
Ha Web Slice osteology



The New York Times

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Vitamin D Supplements Don't Lead to Stronger Bones

Taking vitamin D did not help prevent fractures, increase bone mineral density or prevent falls in adults, a large review of studies found.



By Nicholas Bakalar

Oct. 11, 2018



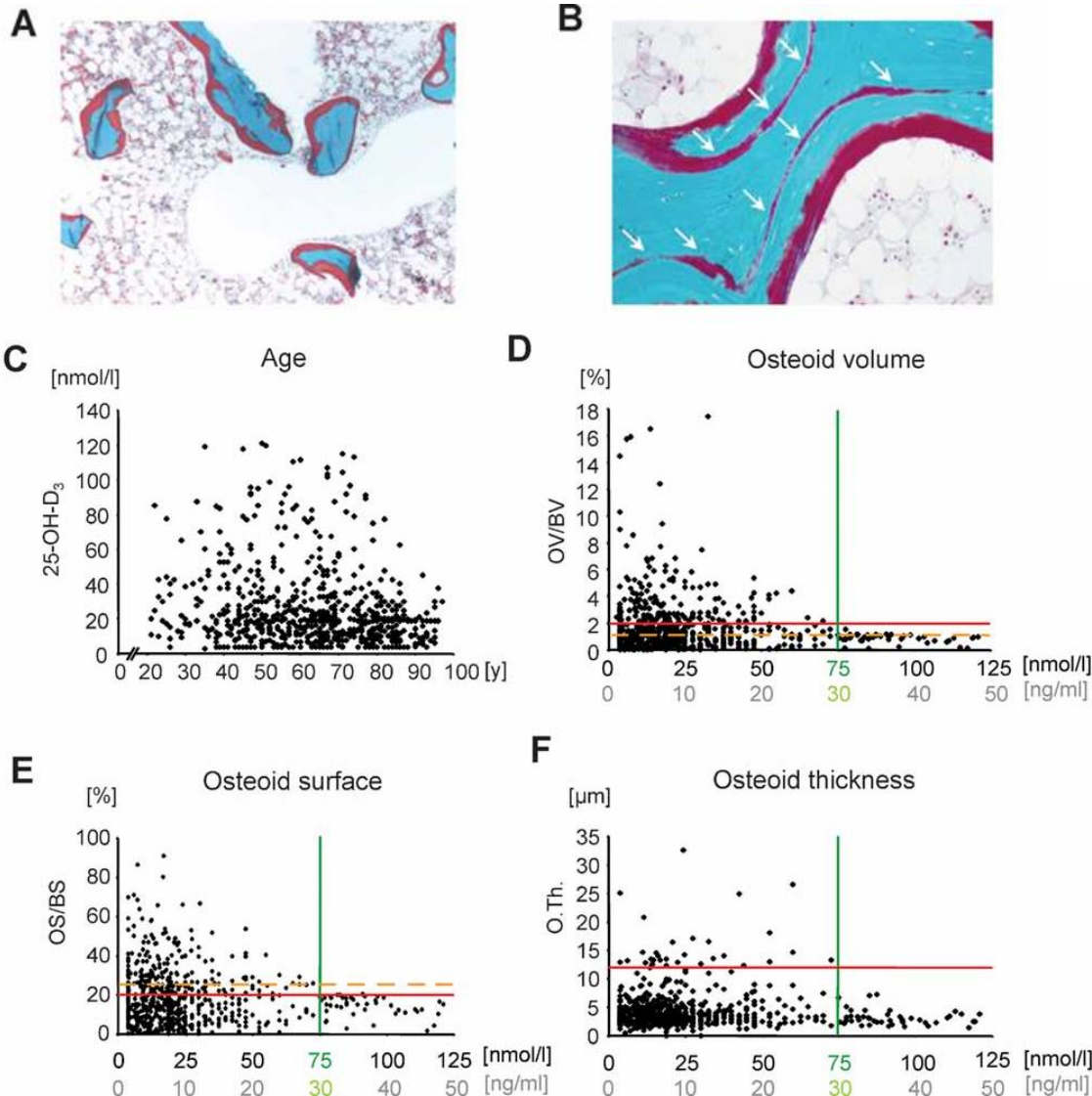
Vitamin D supplements do not help prevent fractures, increase bone mineral density or prevent falls in adults, a large review of studies has

Livelli raccomandati

Source	Deficiency	Insufficiency	sufficiency
IOM (2010)	30 nMol/L	30-50 nMol/L	75-250 nMol/L
USA Endocrine Society (2011)	50 nMol/L	50-75 nMol/L	75-250 nMol/L
SIOMMS 2016	<25 nmol/l	25-50 nmol/l	50-80 nmol/l
AME (2018)			>75 nmol/L in patients at risk of bone disease

25(OH)D and osteomalacia

675 patients





25OHvitaminD at baseline	
<25 nmol/l	4/72 (6%)
<50 nmol/l	41/72 (57%)
<75 nmol/l	71/72 (99%)
Achieved 25OHvitaminD at baseline	
≥50 nmol/l	69/76 (91%)
≥75 nmol/l	44/76 (58%)

Bolland M et al Lancet Diab Endocr 2018



RECENT JAMA STUDY QUESTIONING BENEFITS OF VITAMIN D AND CALCIUM SUPPLEMENTS IN PREVENTING BONE BREAKS AND FRACTURES MAY CREATE CONFUSION FOR THOSE WHO COULD BENEFIT

December 29, 2017

The [American Society for Bone and Mineral Research](#) (ASBMR), the world's leading scientific organization for bone health experts, urges caution to patients, their caregivers and physicians regarding the new findings published in the [Journal of the American Medical Association](#) (December 26, 2017) that found no clear benefit in the use of vitamin D and calcium supplements in older adults who live in the general community.

Although the study reports that there is no evidence that these supplements prevent bone breaks or hip fractures for adults over 50 who are not living in hospitals, nursing homes or other facilities, it is critical for all to understand that this analysis focuses only on healthy adults. The results of this study do not apply to people with osteoporosis or other metabolic bone diseases or to people taking bone protective medications. For them, adequate calcium intake and vitamin D status needs to be ensured for their medications to be effective in preventing fractures.

"These findings may cause continued confusion for patients, their caregivers and their physicians about who should and who should not be taking supplemental vitamin D and calcium," said Michael Econs, MD, ASBMR President and Professor of Medicine at Indiana University School of Medicine. "It's important that everyone understand the guidelines that pertain to their health conditions and risks."

For generally healthy adults over 50 living in the community, people should aim to get calcium in the diet from foods such as milk, vegetables, fruits and bean products. Vitamin D is in some foods and is synthesized in the skin and can be obtained by daily exposure to sunlight. This is in line with draft updated recommendations from US Preventive Services Task Force as of October 2017, although the final recommendations have not been published.

For interviews with ASBMR President Dr. Michael Econs, please contact: Ann L. Elderkin at 207-712-3957 or aelderkin@asbmr.org.



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Raccomandazioni AME: quali sono i pazienti a rischio

- Osteomalacia
- Osteoporosis
- Older adults with history of falls
- Older adults with history of non-traumatic fractures
- Pregnant and lactating women
- Obese children and adults
- People not exposed to sufficient sun exposure
- Malabsorption syndromes Chronic kidney disease
- Hepatic failure
- Cystic fibrosis
- Hyperparathyroidism
- Drug interfering with vitamin D metabolism

Take home messages

Remember the bone health is important for your patient!

We have effective drugs, why not to use it!

GRAZIE!!!!

