APPROCCI INTERDISCIPLINARI IN REUMATOLOGIA
GERIATRIA E MALATTIE REUMATICHE

AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

L'IPOVITAMINOSI D

Marco Di Stefano
S.C. Geriatria e Malattie Metaboliche dell'Osso-
AOU Città della Salute e della Scienza di Torino

Torino, 12 ottobre 2018

CONFLITTO DI INTERESSI

SPA

Abiogen

Eli Lilly

Quale parametro per definire carenza?

Colecalciferolo (vit. D3)

Ergocalciferolo (vit. D2)

Non sono dosate nella pratica clinica

Idrossilazione in 25

Emivita 2 settimane, **marcatore universalmente accettato** dello stato vitaminico D

25-OH vitamina D
(Calcifediolo o Calcidiolo)

Calcitriolo

Emivita breve (ore), risultati condizionati da regolazione dell'1α–idrossilasi
Utile solo in casi particolari (rachitismi, mal. granulomatose, osteomalacia oncogenica)

Qual è il range ottimale di 25(OH)D?

Vitamin D status	Institute of Medicine	Endocrine Society
deficiency	<12ng/ml (30nmol/l)	< 20ng/ml (50nmol/l)
Risk of inadequacy[1] Insufficiency[2]	12-20ng/ml (30-50nmol/l)	21-29ng/ml (52.5-72.5nmol/l)
Sufficiency	>20ng/ml (50nmol/l)	≥30ng/ml (75nmol/l)

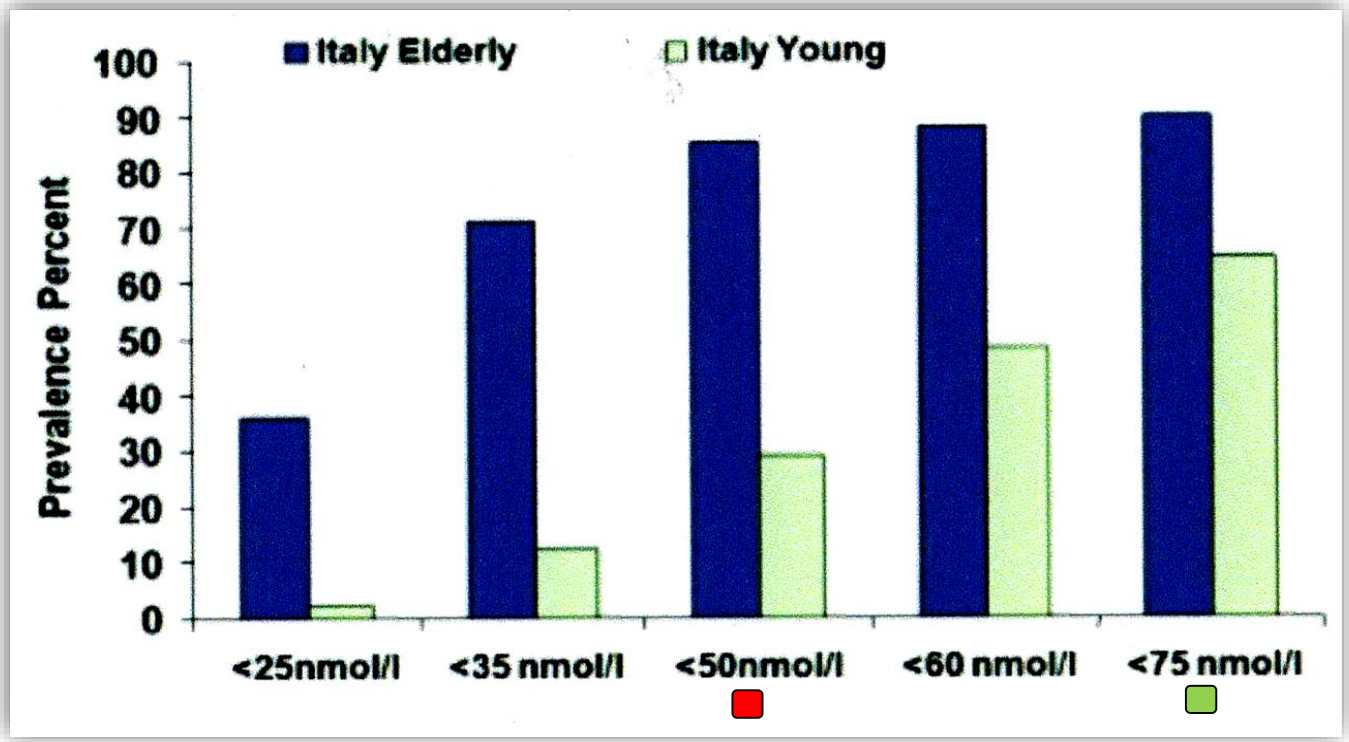
Tutti d'accordo per 25(OH)D >20ng/ml

Prudenza: non andare oltre 40-50ng/ml
(possibili effetti tossici non classici)

OTTIMALE Circa 30ng/ml
(20-25→ 40-50)

NON 30-100 ng/ml

PREVALENZA DI IPOVITAMINOSI D IN ITALIA

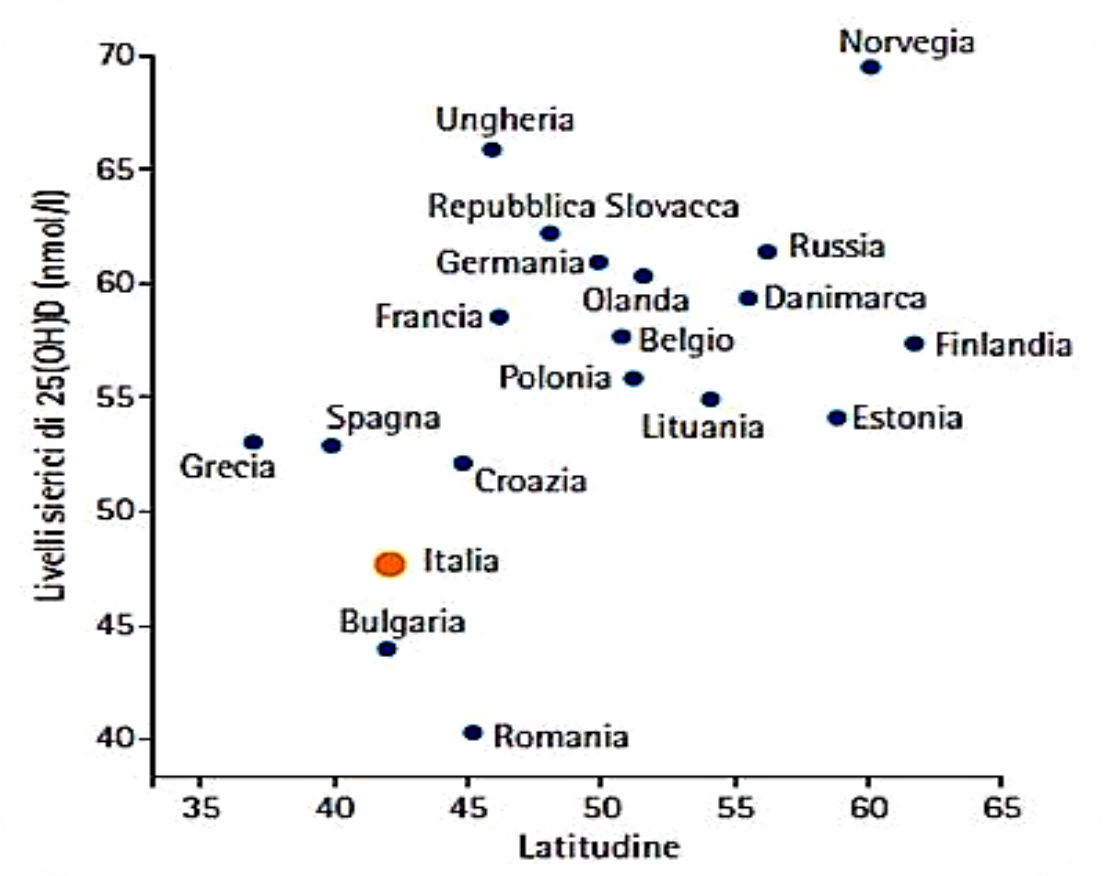


Negli anziani uno stato di* carenza *di 25(OH)D è presente in 2 pazienti su 3;
livelli* insufficienti *di 25(OH)D in oltre il 95%.

Nei giovani sani livelli insufficienti di 25(OH)D è stato riscontrato in oltre il 60%

Adami et al…Bone 2009
Adami et al…Bone 2008
Isaia et al.. Ost Int 2003

PREVALENZA DI IPOVITAMINOSI D IN EUROPA



Molteplici studi hanno dimostrato che la maggiore incidenza di ipovitaminosi D si verifica nei paesi Mediterranei quali Italia, Grecia e Spagna

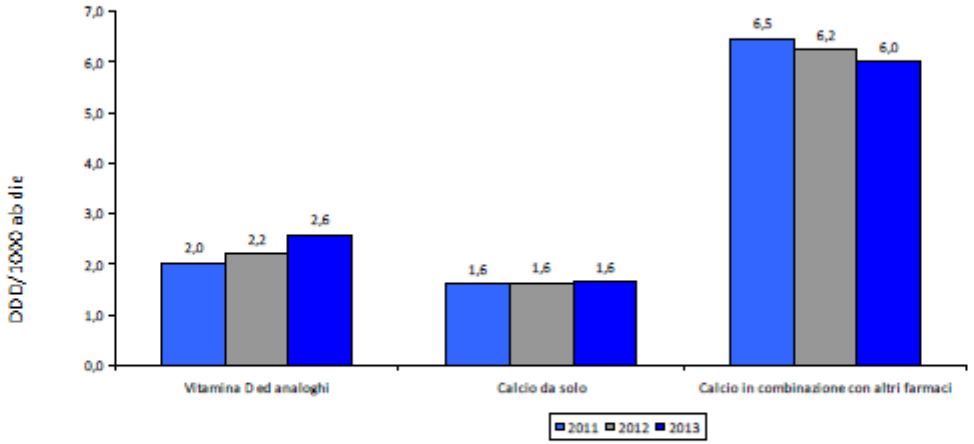
L'uso dei Farmaci in Italia: Rapporto Nazionale

Gennaio-Settembre 2013

Luca Pani
DG@aifa.gov.it

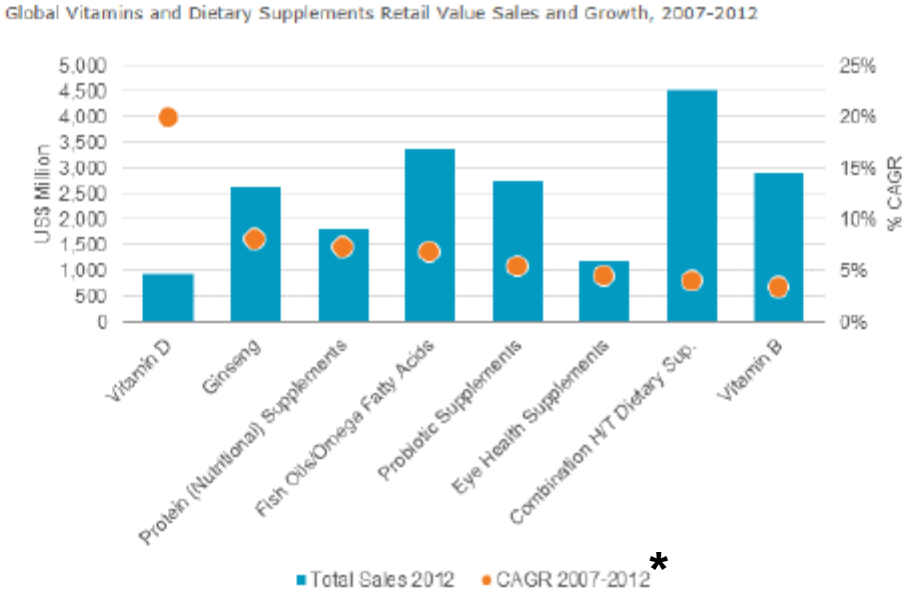
Roma, 6 febbraio 2014

Confronto consumo Vitamina D ed analoghi (Classe A-SSN) (primi nove mesi 2011-2013)



Il mercato totale della vitamina D ammonta a **187** milioni di euro su base annua. Il consumo di farmaci a base di calcio in combinazione con Vitamina D è in riduzione negli ultimi anni (-3,6% rispetto al 2012), quello del calcio da solo è costante mentre l'utilizzo della vitamina D è in continuo aumento (**+17,6%** rispetto al 2012).

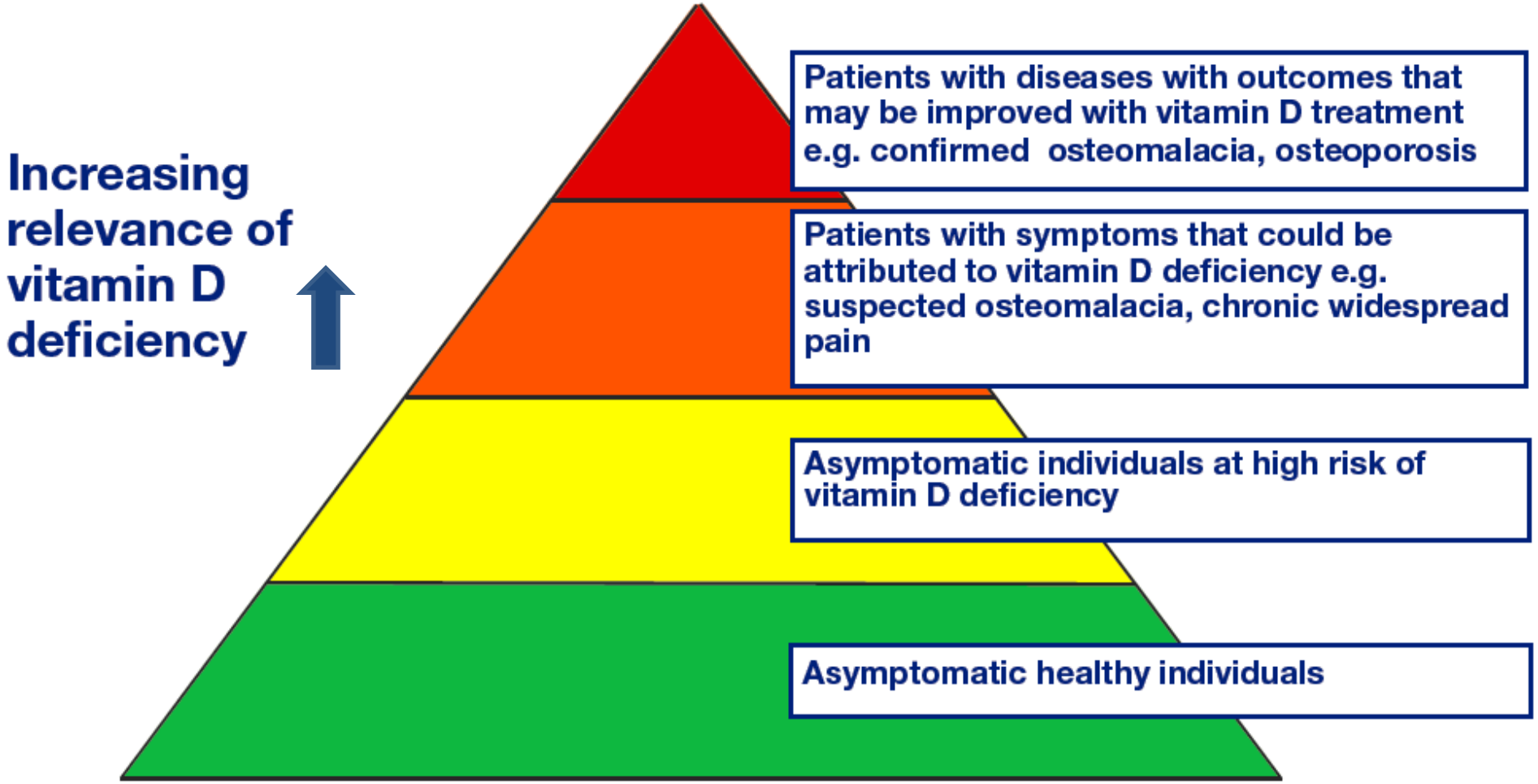
Vitamina D:un mercato da 1,3 miliardi di dollari nel 2017



La vitamina D ha fatto registrare il più alto tasso annuo di crescita composto (20%) dell'intero comparto tra il 2007 e il 2012. Secondo le previsioni più recenti potrebbe raggiungere quota 1,3 miliardi di dollari entro il 2017.

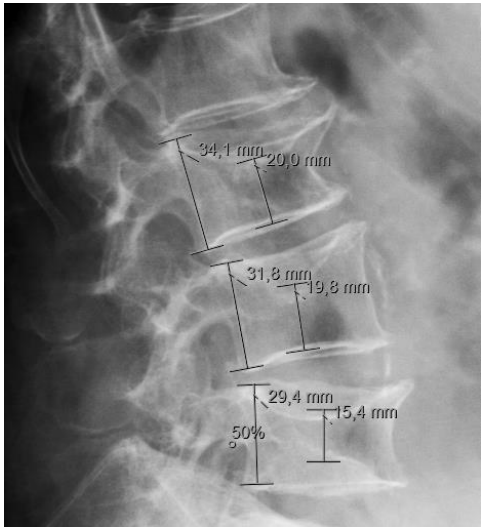
*** CAGR= Compound Annual Growth Rate**

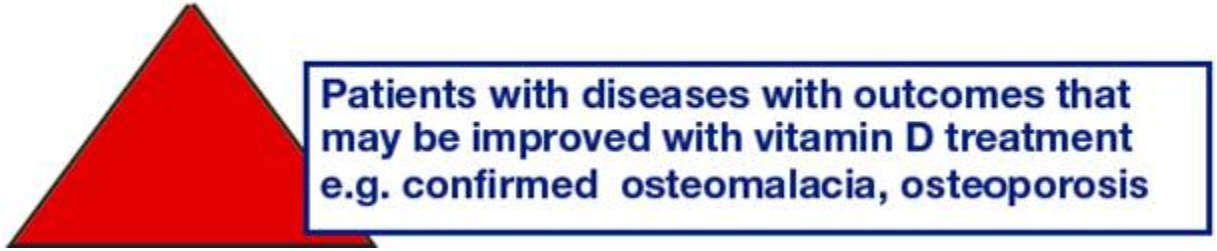
Si somministra vit. D nei soggetti che traggono sicuro beneficio da correzione di carenza



National Osteoporosis Society 2013

Si somministra vit. D nei soggetti che traggono sicuro beneficio da correzione di carenza





Fragilità ossea
!! Farmaci per osteoporosi

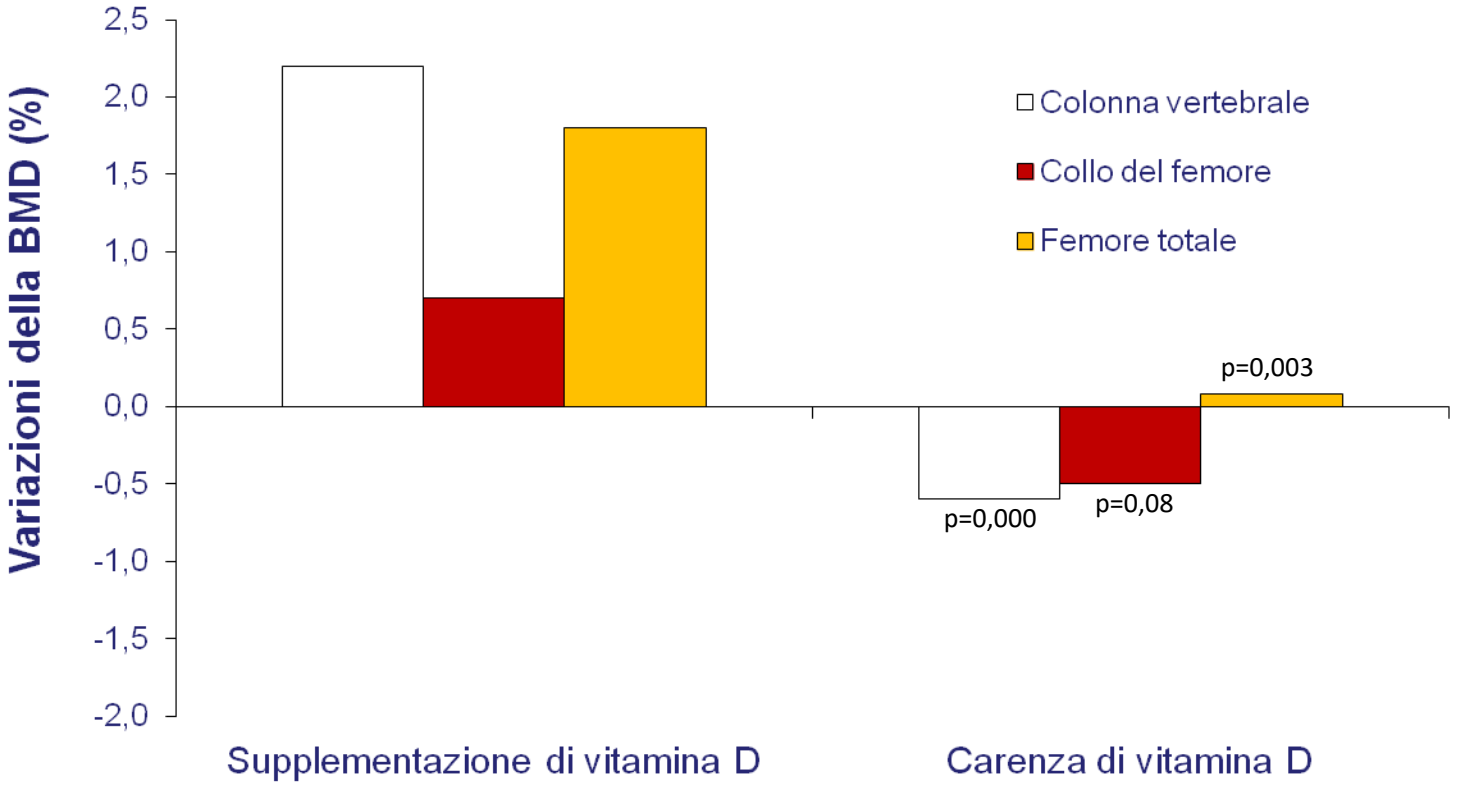
Prevenzione cadute

NOTA 79

Prima di avviare la terapia con i farmaci sopraindicati, in tutte le indicazioni è raccomandato un adeguato **apporto di calcio e di vitamina D**, **ricorrendo**, ove dieta ed esposizione solare siano inadeguati, **a supplementi con sali di calcio e vitamina D3 (e non ai suoi metaboliti idrossilati)**.

E' stato documentato inoltre che **la carenza di vitamina D può vanificare in gran parte l'effetto dei farmaci per il trattamento dell'osteoporosi**.

Supplementazione di vitamina D e risposta al trattamento con farmaci antiriassorbitivi



Effect of Vitamin D on Falls

A Meta-analysis

Heike A. Bischoff-Ferrari, MD, MPH
Bess Dawson-Hughes, MD
Walter C. Willett, MD, DrPH
Hannes B. Staehelin, MD
Marlet G. Bazemore, MD
Robert Y. Zee, MD
John B. Wong, MD

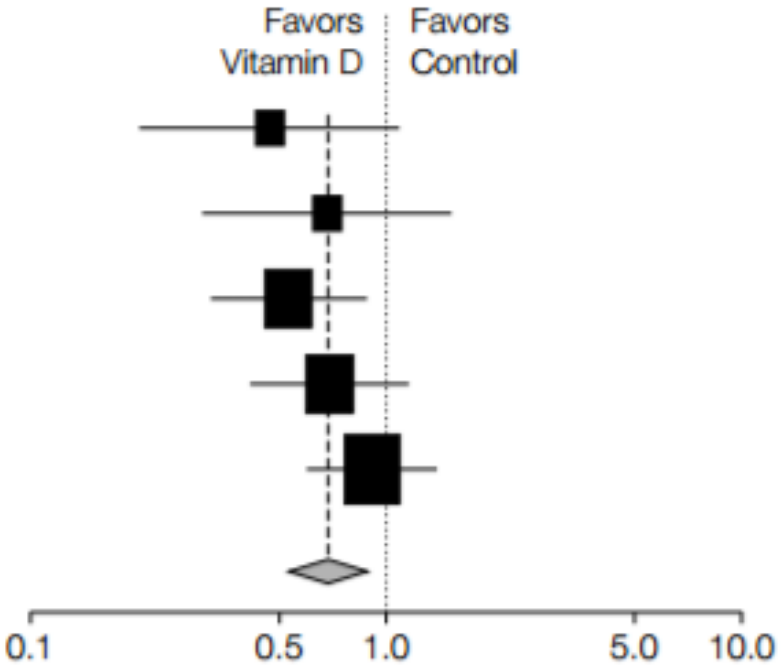
Context Falls among elderly individuals occur frequently, increase with age, and lead to substantial morbidity and mortality. The role of vitamin D in preventing falls among elderly people has not been well established.

Objective To assess the effectiveness of vitamin D in preventing an older person from falling.

Data Sources MEDLINE and the Cochrane Controlled Trials Register from January 1960 to February 2004, EMBASE from January 1991 to February 2004, clinical experts, bibliographies, and abstracts. Search terms included trial terms: *randomized-controlled trial* or *controlled-clinical trial* or *random-allocation* or *double-blind method*,

Fall risk
5 RCT
N=1237

Source	Odds Ratio
Pfeifer et al,[11] 2000	0.47 (0.20-1.10)
Bischoff et al,[12] 2003	0.68 (0.30-1.54)
Gallagher et al,[17] 2001	0.53 (0.32-0.88)
Dukas et al,[18] 2004	0.69 (0.41-1.16)
Graafmans et al,[19] 1996	0.91 (0.59-1.40)
Pooled (Uncorrected)	**0.69 (0.53-0.88)**



JAMA 2004

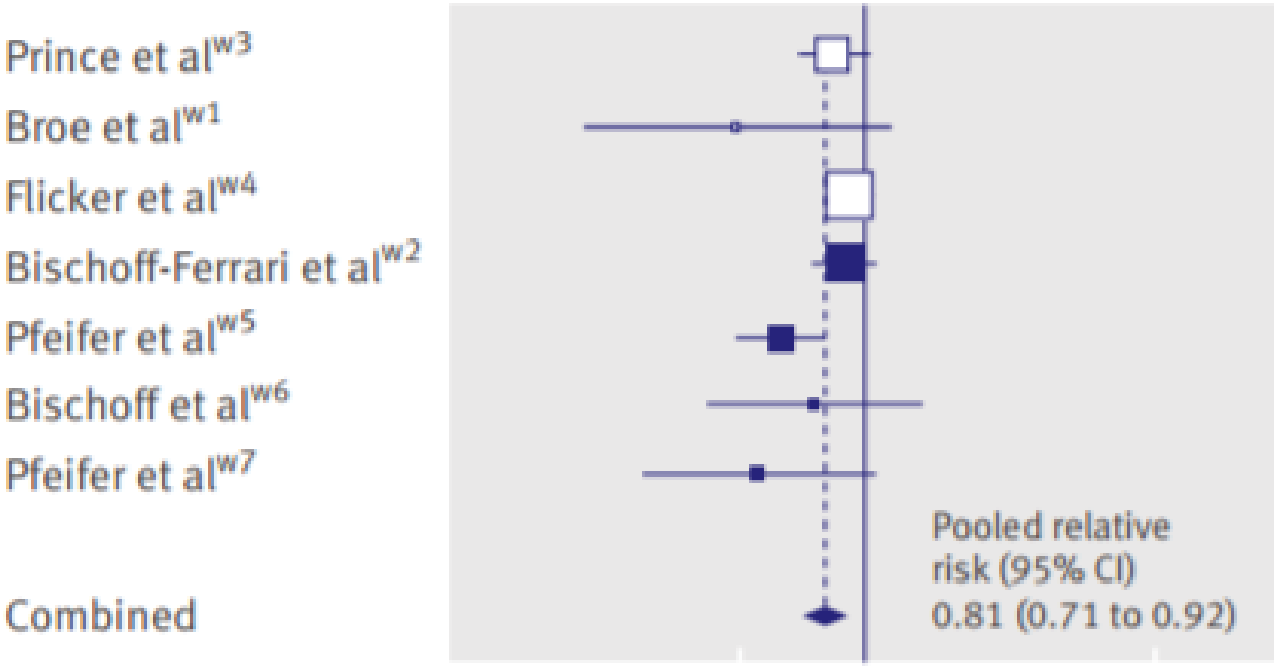
Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials

H A Bischoff-Ferrari, director of centre on aging and mobility,[1,2] B Dawson-Hughes, director of bone metabolism laboratory,[3] H B Staehelin, professor emeritus ,[4] J E Orav, associate professor of biostatistics,[5] A E Stuck, professor of geriatrics,[6] R Theiler, head of rheumatology,[7] J B Wong, professor of medicine ,[8] A Egli, fellow,[1] D P Kiel, associate professor of medicine,[9] J Henschkowski, fellow[1,6]

Fall risk
7 RCT
N=1921

«Alta dose» (700-1000 UI die di colecalciferolo)

Risk ratio



0.81 (0.71-0.92)

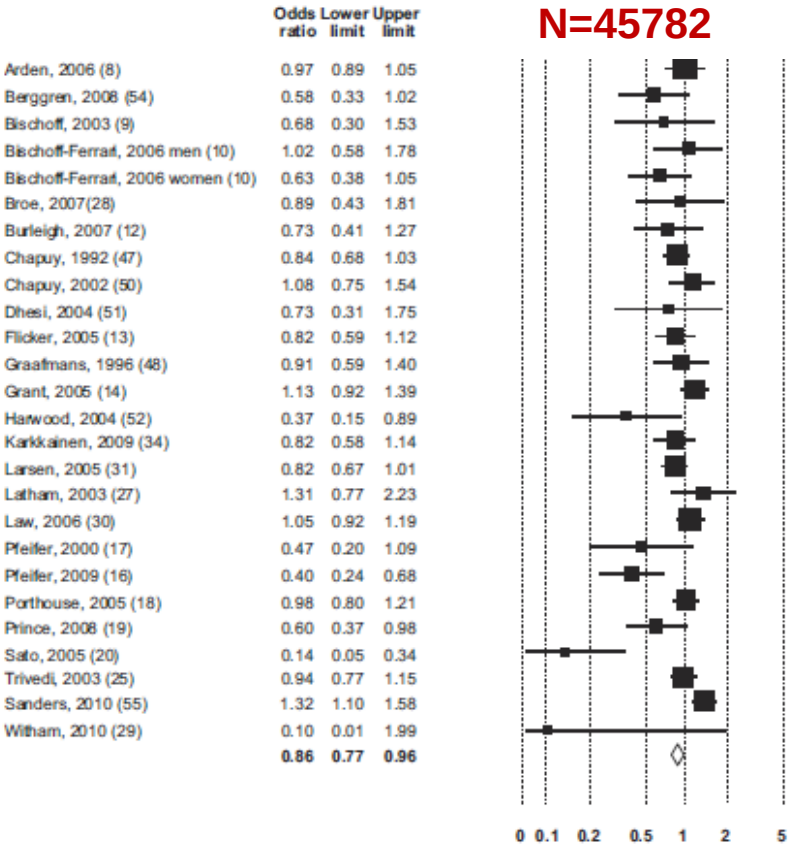
BMJ 2009

The Effect of Vitamin D on Falls: A Systematic Review and Meta-Analysis

Mohammad Hassan Murad, Khalid B. Elamin, Nisrin O. Abu Elnour, Mohamed B. Elamin, Aziz A. Alkatib, Mitra M. Fatourechi, Jaime P. Almandoz, Rebecca J. Mullan, Melanie A. Lane, Hau Liu, Patricia J. Erwin, Donald D. Hensrud, and Victor M. Montori

Fall risk
26RCT
N=45782

Number of fallers
Odds Ratio 0.86
(95% CI 0.77-0.96)



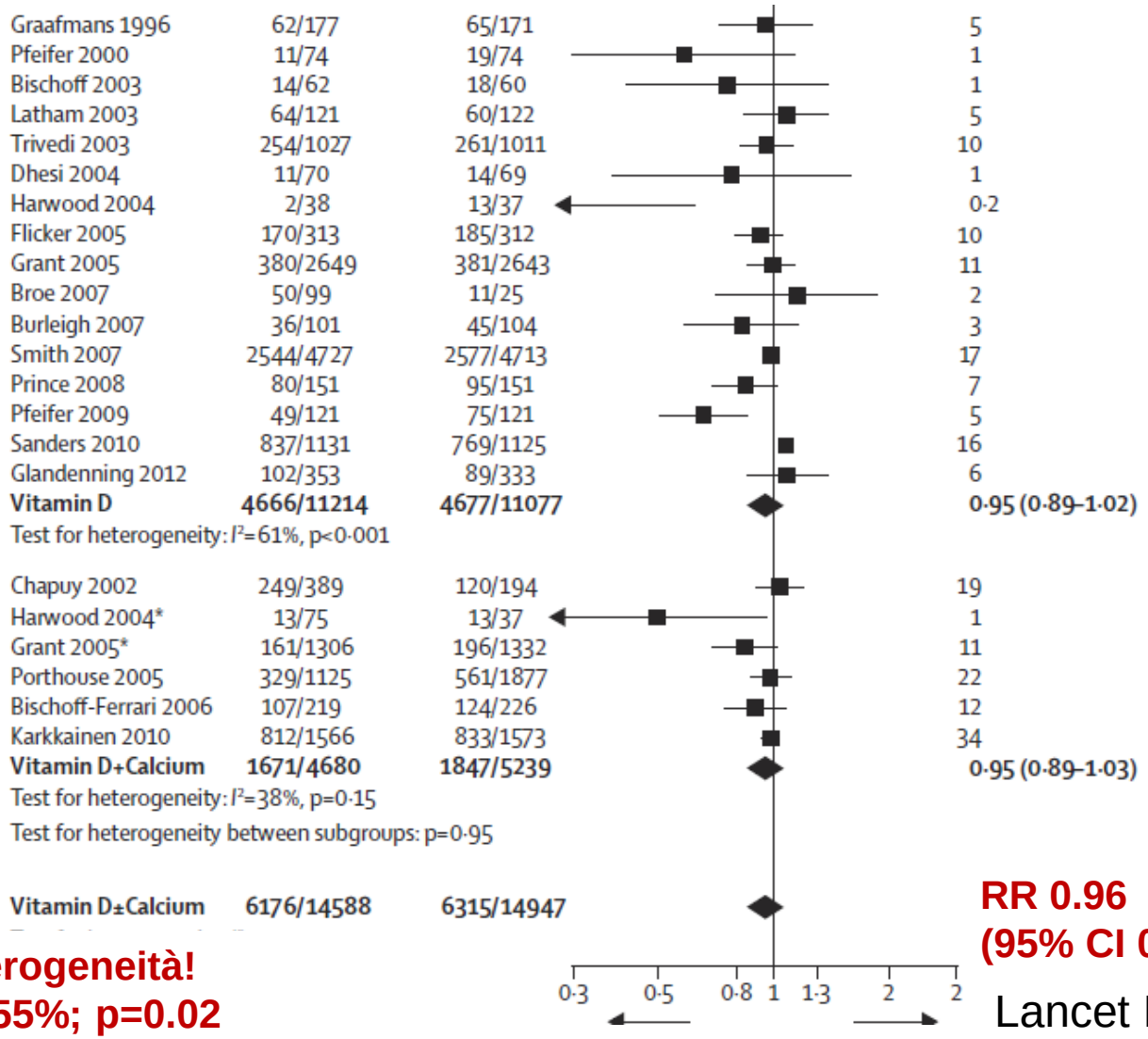
Number of falls
Odds Ratio 0.79
(95% CI 0.70-0.88)

JCEM, 2011

Vitamin D supplementation and falls: a trial sequential meta-analysis

Mark J Bolland, Andrew Grey, Greg D Gamble, Ian R Reid

RR of falls
20RCT
N=29535



RR 0.96
(95% CI 0.91-1.01;p=0.12)

Eterogeneità!
I^2=55%; p=0.02

Lancet Diabet Endocrinol, 2014

Vitamin D supplementation and falls: a trial sequential meta-analysis

Mark J Bolland, Andrew Grey, Greg D Gamble, Ian R Reid

Eterogeneità?

solo chi è carente risponde

Eterogeneità!
I^2=55%; p=0.02

Interventions for preventing falls in older people living in the community

Lesley D Gillespie[1], M Clare Robertson[1], William J Gillespie[2], Catherine Sherrington[3], Simon Gates[4], Lindy M Clemson[5], Sarah E Lamb[4]

Patients selected for low basal levels of 25(OH)D

In the community, vitamin D supplementation reduced the rate of falls (RaR 0.57, 95% CI 0.37 to 0.89; 5 trials, 263 participants),

and the risk of falling (RR 0.70, 95% CI 0.56 to 0.87; 4 trials, 804 participants).

THE COCHRANE COLLABORATION®

2013

Interventions for preventing falls in older people in care facilities and hospitals

Ian D Cameron[1], Lesley D Gillespie[2], M Clare Robertson[2], Geoff R Murray[3], Keith D Hill[4], Robert G Cumming[5], Ngaire Kerse[6]

Patients in care facilities: usually low basal levels of 25(OH)D

In care facilities, vitamin D supplementation reduced the rate of falls (RaR 0.63, 95% CI 0.46 to 0.86; 5 trials, 4603 participants),

but not risk of falling (RR 0.99, 95% CI 0.90 to 1.08; 6 trials, 5186 participants).

THE COCHRANE COLLABORATION®

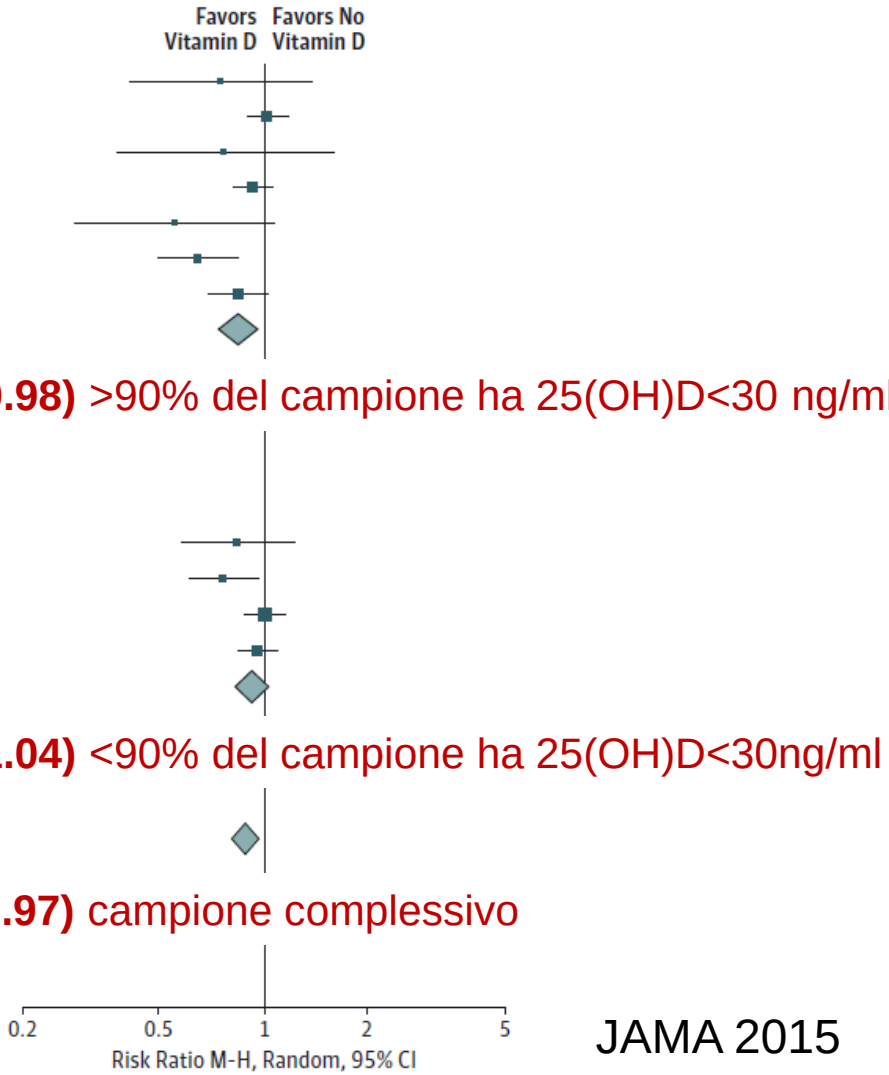
2013

Vitamin D and Falls—Fitting New Data With Current Guidelines

Erin S. LeBlanc, MD, MPH; Roger Chou, MD

Risk ratio

Study or Subgroup	Vitamin D Events	Vitamin D Total	Placebo Events	Placebo Total	Weight, %	Risk Ratio M-H, Random, 95% CI
Low Vitamin D Levels (90% of Population <30 ng/mL)						
Bischoff et al, 2003	14	62	18	60	2.0	0.75 (0.41-1.37)
Chapuy et al, 2002	251	393	118	190	15.0	1.03 (0.90-1.18)
Dhesi et al, 2004	11	70	14	69	1.4	0.77 (0.38-1.59)
Karkkainen et al, 2010	179	287	205	306	16.2	0.93 (0.83-1.05)
Pfeifer et al, 2000	11	70	19	67	1.6	0.55 (0.29-1.08)
Pfeifer et al, 2009	49	122	75	120	7.8	0.64 (0.50-0.83)
Prince et al, 2008	80	151	95	151	10.9	0.84 (0.69-1.02)
Subtotal (95% CI)		1155		963	54.9	0.85 (0.73-0.98)
Total events	595		544			
Heterogeneity: $\tau^2 = 0.02$; $\chi^2_6 = 14.12$ ($P = .03$); $I^2 = 58\%$						
Test for overall effect $z = 2.23$ ($P = .03$)						
Not Low Vitamin D Level (<90% of Population <30 ng/mL or Not Reported)						
Dukas et al, 2004	40	193	46	187	4.5	0.84 (0.58-1.22)
Gallagher et al, 2001	59	123	77	123	9.0	0.77 (0.61-0.96)
Porthouse et al, 2005	283	914	498	1627	16.0	1.01 (0.90-1.14)
Uusi-Rasi et al, 2015	136	196	145	201	15.6	0.96 (0.85-1.09)
Subtotal (95% CI)		1426		2138	45.1	0.93 (0.83-1.04)
Total events	518		766			
Heterogeneity: $\tau^2 = 0.00$; $\chi^2_3 = 4.87$ ($P = .18$); $I^2 = 38\%$						
Test for overall effect $z = 1.23$ ($P = .22$)						
Total (95% CI)		2581		3101	100	0.89 (0.82-0.97)
Total events	1113		1310			
Heterogeneity: $\tau^2 = 0.01$; $\chi^2_{10} = 19.34$ ($P = .04$); $I^2 = 48\%$						
Test for overall effect $z = 2.56$ ($P = .01$)						
Test for subgroup differences $\chi^2_1 = 1.00$, ($P = .32$); $I^2 = 0\%$						



0.85 (0.73-0.98) >90% del campione ha 25(OH)D<30 ng/ml

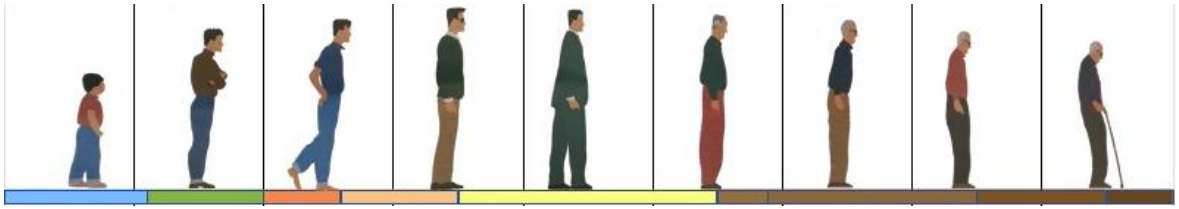
0.93 (0.83-1.04) <90% del campione ha 25(OH)D<30ng/ml

0.89 (0.82-0.97) campione complessivo

JAMA 2015

Vitamin D and muscle function

Bess Dawson-Hughes



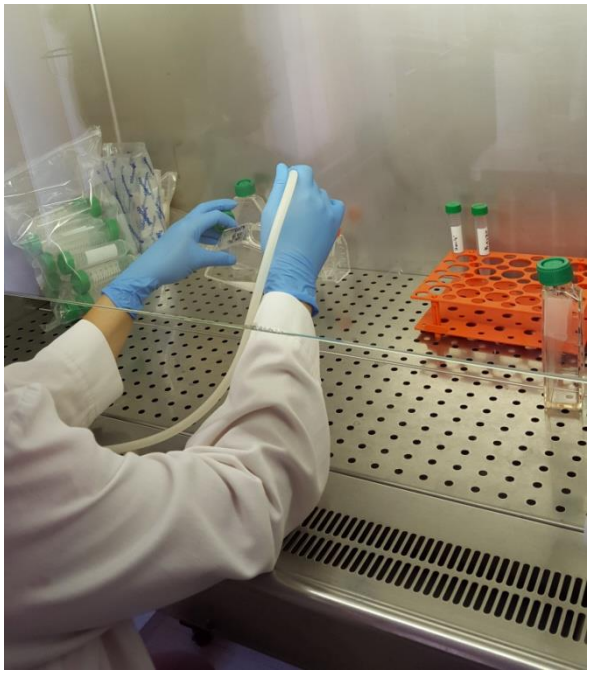
Invecchiamento e deficit di vitamina D:
sovrapposizione di effetti sul muscolo

Atrofia preferenziale di fibre tipo II
(prime ad attivarsi per prevenire caduta)
Fibrosi
Infiltrazione di grasso
Eccesso di glicogeno (granuli)
↓ VDR
↑ proteolisi

J Steroid Biochem Mol Biol 2017

Vitamin D, muscle and bone: Integrating effects in development, aging and injury

Christian M. Girgis [a,b,c,*], Paul A. Baldock [c], Michael Downes [d]



Numerosi dati sperimentali

Modello del topo knock-out per VDR

- ↓ crescita / osteomalacia
- ≠ differenziazione muscolare
- goffo (swimming impairment)

Mol Cell Endocrinol 2015

Vitamin D, muscle and bone: Integrating effects in development, aging and injury

Christian M. Girgis [a,b,c,*], Paul A. Baldock [c], Michael Downes [d]

Numerosi dati sperimentali

Effetti indiretti

↓ fosforo e calcio

↑ PTH (proteolisi; ↓ fosfato)

Effetti diretti di vit. D (genomici e non)

differenziazione / proliferazione

trasporto del calcio intracellulare

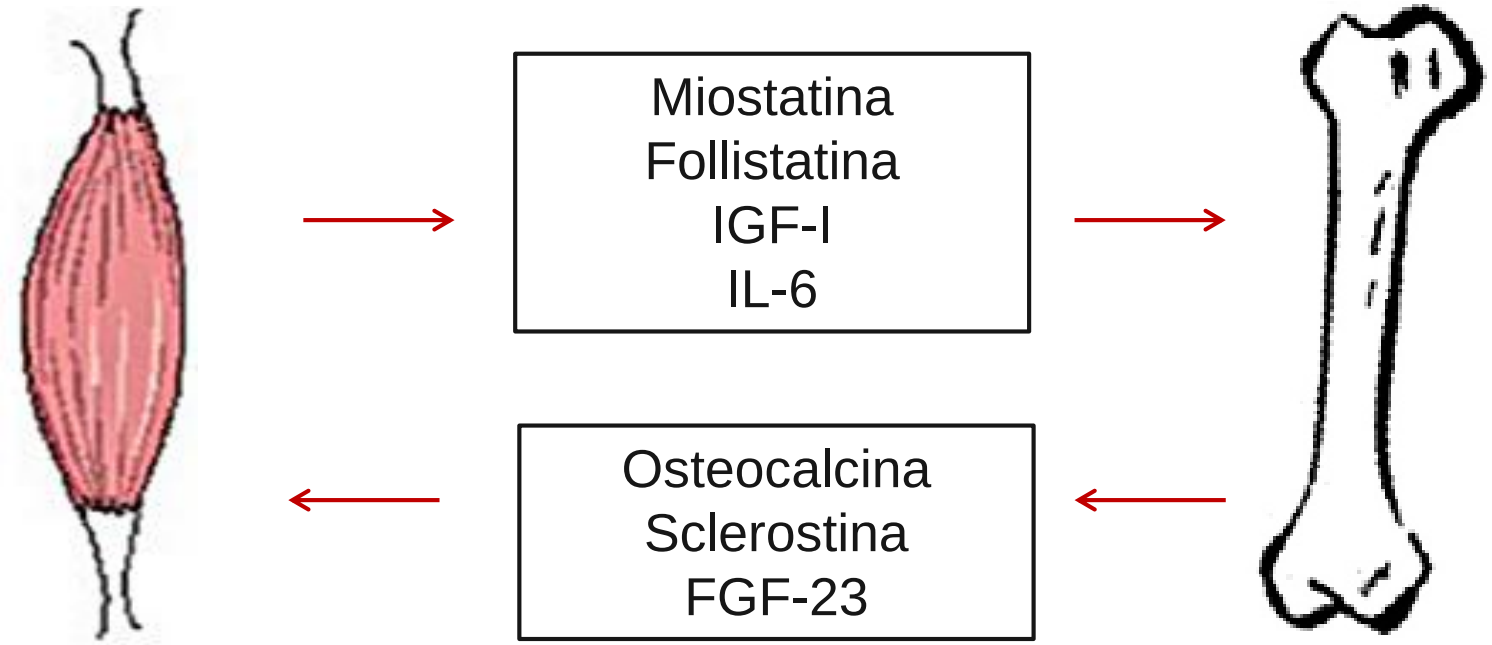
sintesi proteica

Mol Cell Endocrinol 2015

Vitamin D, muscle and bone: Integrating effects in development, aging and injury

Christian M. Girgis [a,b,c,*], Paul A. Baldock [c], Michael Downes [d]

Cross-talk osso-muscolo: Modulazioni proposte per vit. D



Deposito di colecalciferolo
Presenza di 1-idrossilasi

Presenza di 1-idrossilasi

Mol Cell Endocrinol 2015

Effect of Vitamin D Supplementation on Muscle Strength, Gait and Balance in Older Adults: A Systematic Review and Meta-Analysis

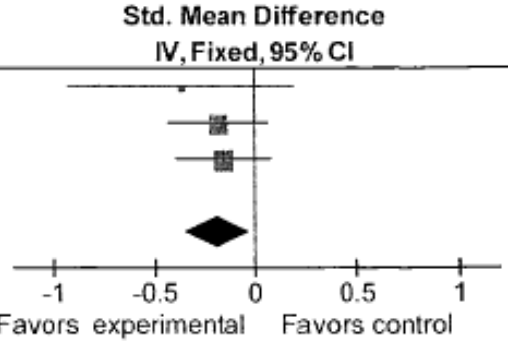
Susan W. Muir, PhD,[*] and Manuel Montero-Odasso, MD, PhD, AGSF[†‡]*

Timed up & go test
3 RCT
N=551

Std Mean Difference

Study or Subgroup	Vitamin D supplementation Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Bunout 2006	13.8	2.5	24	15.2	4.7	24	8.6%	-0.37 [-0.94, 0.21]
Pfeifer 2009	7.5	3.4	121	8.3	5.1	121	44.0%	-0.18 [-0.44, 0.07]
Zhu 2010	8.1	3.9	129	9	7	132	47.4%	-0.16 [-0.40, 0.09]
Total (95% CI)			**274**			**277**	**100.0%**	**-0.19 [-0.35, -0.02]**

Heterogeneity: Chi² = 0.43, df = 2 (P = 0.81); I² = 0%
Test for overall effect: Z = 2.19 (P = 0.03)



-0.19 (-0.35, -0.02)
P=0.03

JAGS, 2011

Effect of Vitamin D Supplementation on Muscle Strength, Gait and Balance in Older Adults: A Systematic Review and Meta-Analysis

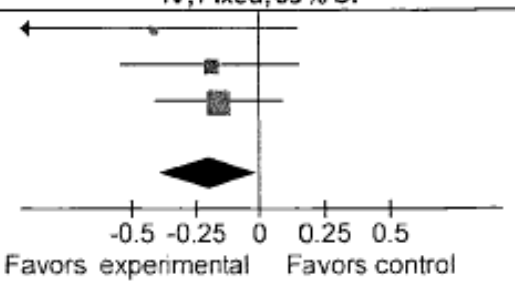
Susan W. Muir, PhD, and Manuel Montero-Odasso, MD, PhD, AGSF*†‡*

Balance sway
3RCT
N=413

Std Mean Difference

	Vitamin D supplementation			Control				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Fixed, 95% CI**	**IV, Fixed, 95% CI**
Bunout 2006	119.8	38.3	24	134.7	31.9	24	11.4%	-0.42 [-0.99, 0.16]	
Dhesi 2004	0.0899	0.046	62	0.0999	0.057	61	29.8%	-0.19 [-0.55, 0.16]	
Pfeifer 2009	81	32	121	86	30	121	58.8%	-0.16 [-0.41, 0.09]	
Total (95% CI)			**207**			**206**	**100.0%**	**-0.20 [-0.39, -0.01]**	

Heterogeneity: Chi² = 0.64, df = 2 (P = 0.73); I² = 0%
Test for overall effect: Z = 2.02 (P = 0.04)



-0.20 (-0.39, -0.01)
P=0.04

JAGS, 2011

Effect of Vitamin D Supplementation on Muscle Strength, Gait and Balance in Older Adults: A Systematic Review and Meta-Analysis

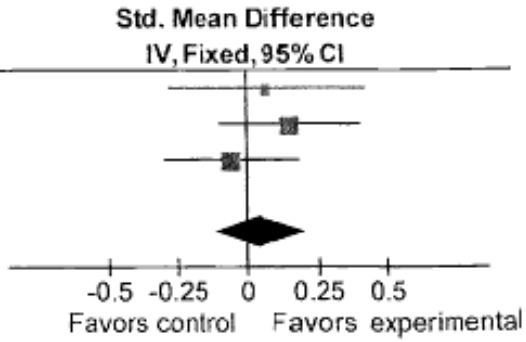
Susan W. Muir, PhD, and Manuel Montero-Odasso, MD, PhD, AGSF*†‡*

Lower extremity strength
3RCT
N=626

Std Mean Difference

	Vitamin D supplementation			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Dhesi 2004	204	92.4	62	198	79.7	61	19.7%	0.07 [-0.28, 0.42]
Pfeifer 2009	236	75	121	224	83	121	38.6%	0.15 [-0.10, 0.40]
Zhu 2010	176.5	49	129	179.5	54	132	41.7%	-0.06 [-0.30, 0.18]
Total (95% CI)			**312**			**314**	**100.0%**	**0.05 [-0.11, 0.20]**

Heterogeneity: Chi² = 1.39, df = 2 (P = 0.50); I² = 0%
Test for overall effect: Z = 0.60 (P = 0.55)



0.05 (-0.11, 0.20)
P=0.55

JAGS, 2011

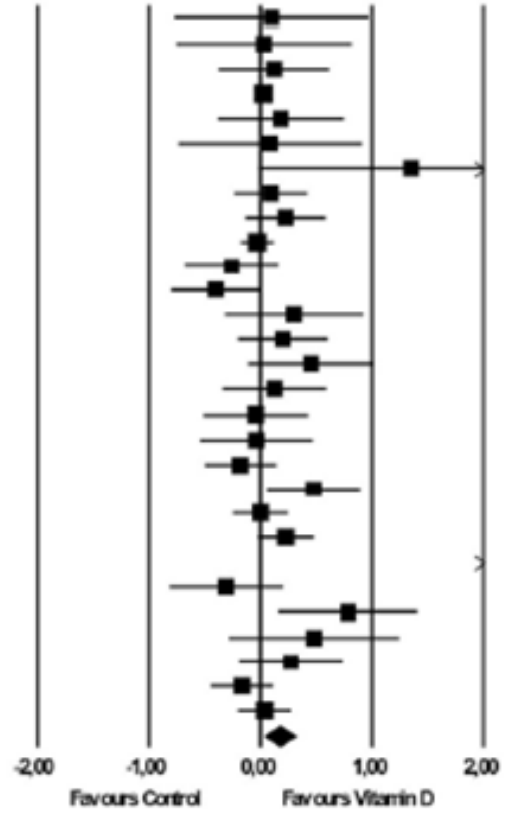
The Effects of Vitamin D on Skeletal Muscle Strength, Muscle Mass, and Muscle Power: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Charlotte Beaudart, Fanny Buckinx, Véronique Rabenda, Sophie Gillain, Etienne Cavalier, Justine Slomian, Jean Petermans, Jean-Yves Reginster, and Olivier Bruyère

Muscle strength
29RCT
N=5533

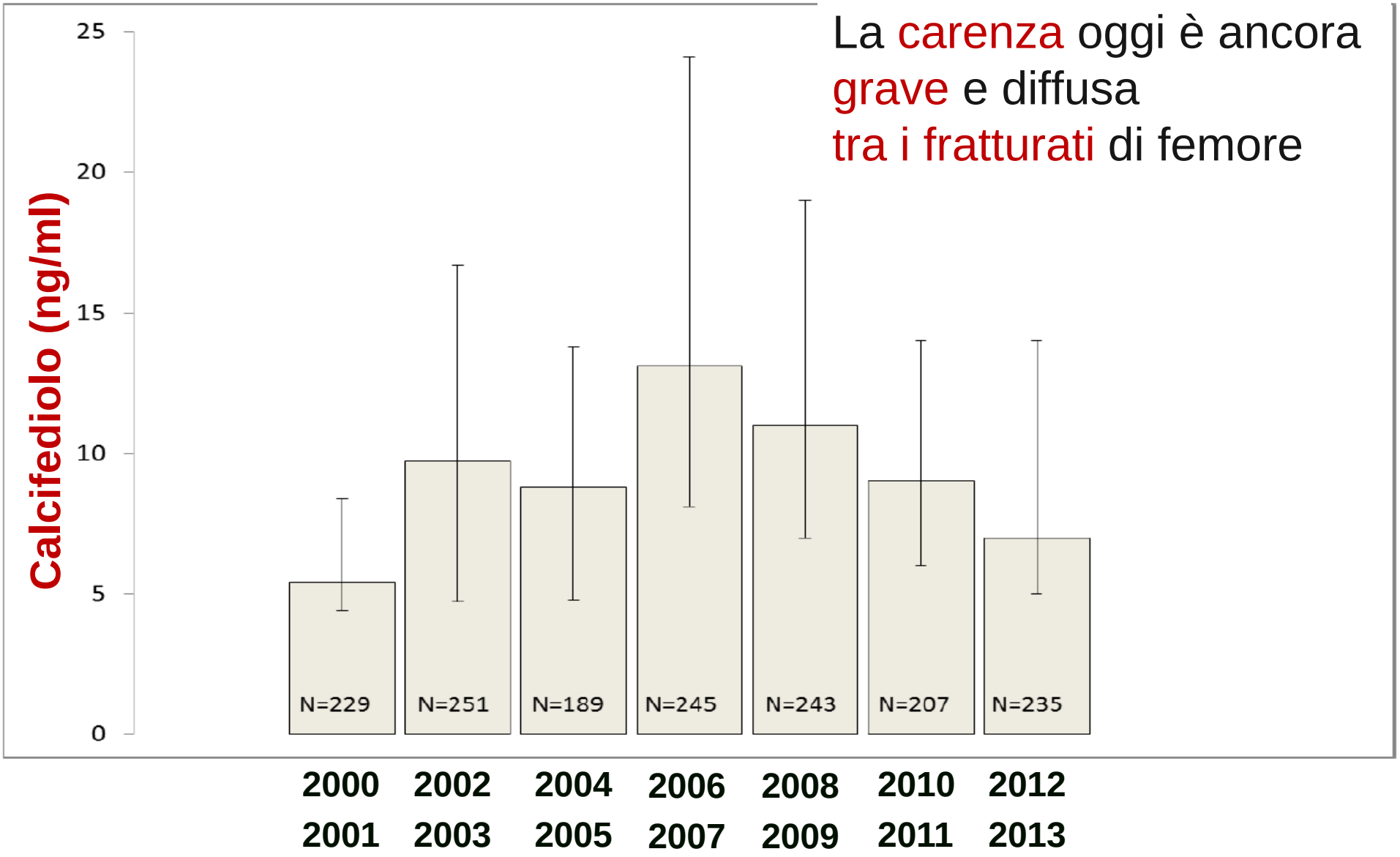
Std Mean Difference 0.17
(95% CI 0.03-0.31;p=0.02)

Study name	Statistics for each study			
	Std diff in means	Lower limit	Upper limit	p-Value
Barker et al. 2012	0,099	-0,778	0,976	0,824
Binder E. 1995	0,030	-0,759	0,820	0,940
Bischoff et al. 2003	0,123	-0,376	0,622	0,629
Brunner et al. 2008	0,026	-0,055	0,107	0,526
Buncut et al. 2006	0,183	-0,384	0,750	0,527
Carrillo et al. 2012	0,087	-0,738	0,911	0,837
Close et al. 2012	1,353	-0,021	2,727	0,054
Dhesi et al. 2004	0,093	-0,240	0,425	0,585
El-Hajj Fuleihan et al. 2006	0,226	-0,138	0,589	0,224
Glendenning et al. 2012	-0,028	-0,178	0,122	0,715
Goswami et al. 2012	-0,257	-0,852	0,167	0,236
Grady et al.	-0,403	-0,803	-0,003	0,048
Gupta et al. 2010	0,300	-0,324	0,923	0,346
Hara et al. 2013	0,203	-0,203	0,609	0,328
Hornick et al. 2012	0,455	-0,113	1,022	0,116
Janssen et al. 2010	0,126	-0,343	0,595	0,599
Kampman et al. 2012	-0,042	-0,518	0,434	0,863
Kenny et al. 2003	-0,038	-0,544	0,469	0,884
Knutsen et al. 2014	-0,179	-0,504	0,146	0,280
Kukuljan et al. 2009	0,476	0,066	0,897	0,027
Latham et al. 2003	0,000	-0,251	0,251	1,000
Pfeifer et al. 2009	0,228	-0,025	0,480	0,078
Sato et al. 2005	2,741	2,183	3,298	0,000
Smedshaug et al. 2007	-0,308	-0,818	0,202	0,237
Songpatanasilp et al. 2009	0,786	0,158	1,414	0,014
Verhaar et al. 2000	0,481	-0,285	1,246	0,218
Ward et al. 2010	0,273	-0,191	0,737	0,249
Wood et al. 2014	-0,166	-0,446	0,115	0,248
Zhu et al. 2010	0,038	-0,205	0,281	0,759
	0,170	0,031	0,310	0,017



JCEM, 2014

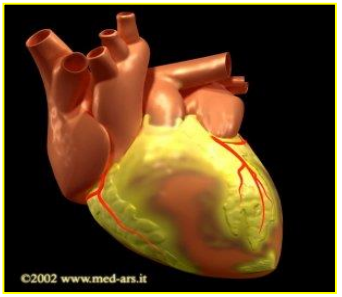
Livelli mediani di calcifediolo tra il 2000 e il 2013 in 1599 pazienti con fr. femore Di Monaco M et al, Eur J Phys Rehabil Med 2016



Effetti extrascheletrici di vitamina D: non sicuro beneficio

VIT D

- Tumori
- Malattie Cardiovascolari
- Diabete
- Malattie Autoimmuni
- Malattie Degenerative
- Infezioni



Effetti extrascheletrici di vit. D: non sicuro beneficio

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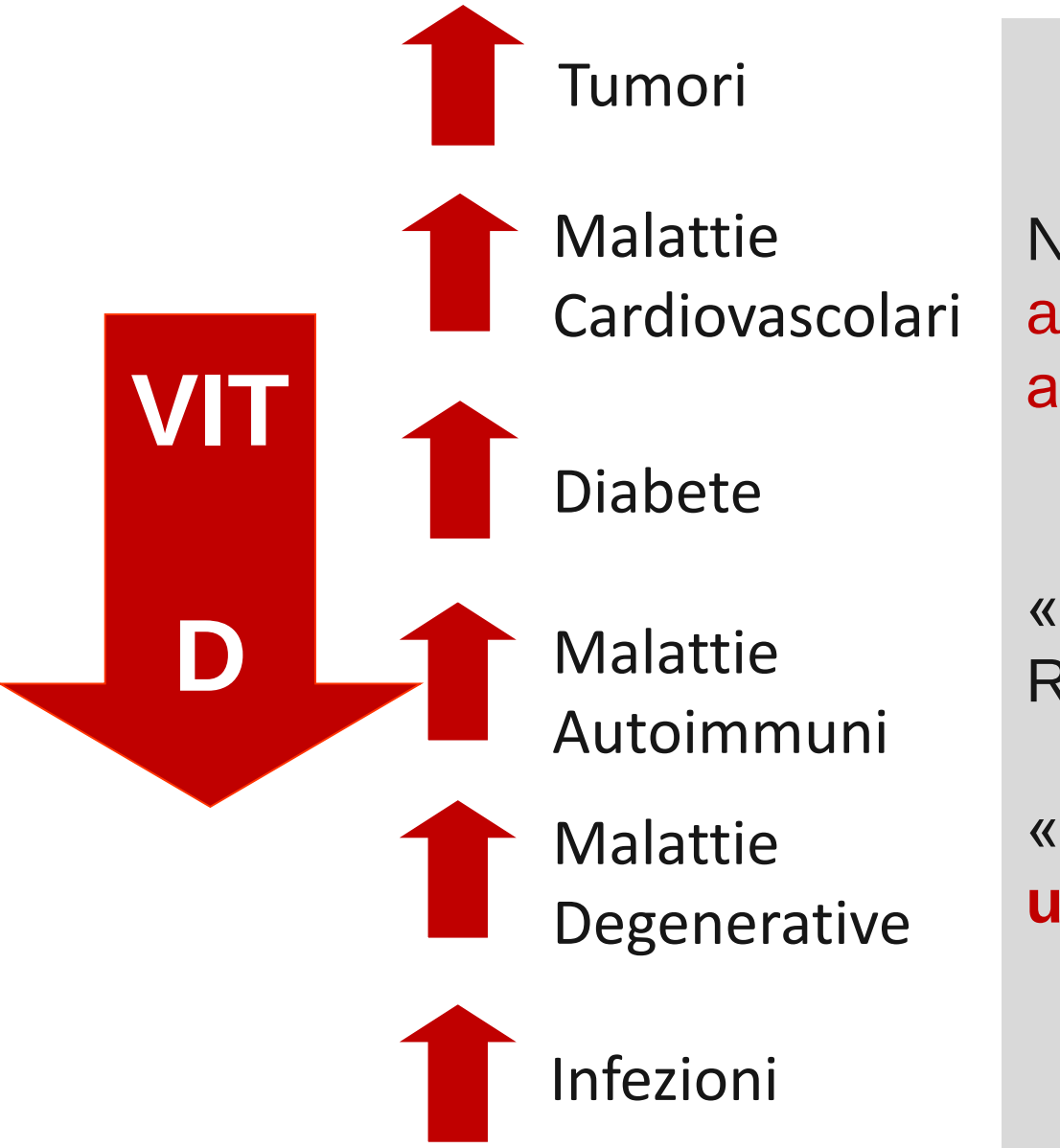
PubMed.gov
US National Library of Medicine
National Institutes of Health

Nei soli ultimi 3 mesi, almeno una review dedicata a vitamina D e…:

LES, Fibromialgia, IBD,
Mal. Cardiovascolari
Sclerosi multipla, Dolore,
Preeclampsia,Tumori
Ipertensione arteriosa
Scompenso cardiaco, Asma
Disautonomia,
Mal tiroidee, Gonartrosi
Mal. Epatiche croniche

Effetti extrascheletrici di vit. D: non sicuro beneficio



PubMed.gov
US National Library of Medicine
National Institutes of Health

Nei soli ultimi 3 mesi, almeno una review dedicata a vitamina D e…:

«… manca prova da RCTs…»

«…**sono necessari ulteriori studi**…»

Non possiamo raccomandare l'esposizione al sole

(o a dispositivi abbronzanti):

There is no safe threshold level of UV exposure that allows for maximal vitamin D synthesis without increasing skin cancer risk

"Because of the known side effects of UV exposure, vitamin D should not be obtained from unprotected exposure to ultraviolet (UV) radiation"

Non possiamo prescrivere dieta ricca di vitamina D

Source	Vitamin D content
Cod liver oil, one teaspoon	400 – 1000 IU vit. D3
Salmon, fresh wild caught, 100g	600 – 1000 IU vit D3
Salmon, fresh farmed, 100g	100 – 250 IU vit D3 – D2
Salmon, canned, 100g	300 – 600 IU vit D3
Sardines canned, 100g	300 IU vit D3
Mackerel, canned, 100g	250 IU vit D3
Tuna, canned, 100g	230 IU vit D3
Shiitake mushrooms, fresh, 100g	100 IU vit D2
Shiitake mushrooms, sun dried, 100g	1600 IU vit D2
Egg yolk, one	20 IU vit D3 – D2

(adapted from Holick et al, JCEM, 2011)

Quale molecola per ottenere correzione?

Colecalciferolo (vit. D3)

Ergocalciferolo (vit. D2)

Idrossilazione in 25

25-OH vitamina D
(Calcifediolo o Calcidiolo)

Idrossilazione in 1α

Calcitriolo

SUPPLEMENTAZIONE DI VITAMINA D

Safety profile of drugs used in the treatment of osteoporosis: a systematical review of the literature*

**On behalf of The Italian Society of Osteoporosis, Mineral Metabolism, and Skeletal Diseases (SIOMMMS);*
**Endorsed by the Italian Society of Rheumatology (SIR);*

M. Varenna[1], F. Bertoldo[2], M. Di Monaco[3], A. Giusti[4], G. Martini[5], M. Rossini[6]

Vitamin D metabolites hydroxylated in position 1 (calcitriol and alfacalcidol) can cause hypercalcemia and hypercalciuria and their administration is not recommended in osteoporosis treatment.

D2, D3, 25-OH D3: tutte aumentano efficacemente 25(OH)D, ma:

- dati su fratture, cadute, trial con farmaci per osteoporosi forme non idrossilate
- per avere lo stesso effetto su 25(OH)D circolante occorrono dosi diverse di D3 e 25(OH)D3

Am J Clin Nutr 2012

Relative effectiveness of oral 25-hydroxyvitamin D_3 and vitamin D_3 in raising wintertime serum 25-hydroxyvitamin D in older adults[1–4]

Kevin D Cashman, Kelly M Seamans, Alice J Lucey, Elisabeth Stöcklin, Peter Weber, Mairead Kiely, and Tom R Hill

autore	rivista e anno	«Potenza» 25-OH D3 vs D3
Cashman KD et al	Am J Clin Nutr 2012	4-5 x
Bischoff-Ferrari HA et al	J Bone Miner Res 2012	3.5 x
Barger-Lux MJ et al	Osteoporos Int 1998	4.2 x

L'INCREMENTO DEI LIVELLI DI 25(OH)D E' INVERSAMENTE PROPORZIONALE AI LIVELLI BASALI

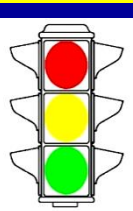


TABLE 2

Increase in serum 25-hydroxyvitamin D in vitamin D_3–treated group stratified into tertiles by baseline 25-hydroxyvitamin D concentration[1]

Tertile	Baseline	Increase[2]
	nmol/L	
1, 10–34 nmol/L (n = 19)	22.3 ± 7.9	30.6 ± 16.2
2, 35–49 nmol/L (n = 18)	41.1 ± 4.1	25.5 ± 11.7
3, 50–86 nmol/L (n = 18)	61.5 ± 8.5	13.3 ± 13.9[3]

[1] $\bar{x}$ ± SD.

[2] Significant differences according to tertile of baseline 25-hydroxyvitamin D concentration, $P = 0.002$ (one-way ANOVA).

[3] Significantly less than for tertile 1, $P = 0.001$, and tertile 2, $P = 0.03$ (Tukey's honestly significant-difference test).

Heung M Trang, David EC Cole, Lawrence A Rubin, Andreas Pierratos, Shirley Siu, and Reinhold Vieth

Am J Clin Nutr 1998;68:854–8.

Valore basale di 25(OH)D	Dose terapeutica cumulativa di vitamina D	Dose giornaliera di mantenimento
<10 ng/ml o 25 nmol/l	1.000.000	2.000
10-20 ng/ml o 25- 50 nmol/l	600.000	1.000
20-30 ng/ml o 50-75 nmol/l	300.000	800

Short-Term Effects on Bone Turnover Markers of a Single High Dose of Oral Vitamin D_3

Maurizio Rossini, Davide Gatti, Ombretta Viapiana, Elena Fracassi, Luca Idolazzi, Silvia Zanoni, and Silvano Adami

(*J Clin Endocrinol Metab* 97: E622–E626, 2012)

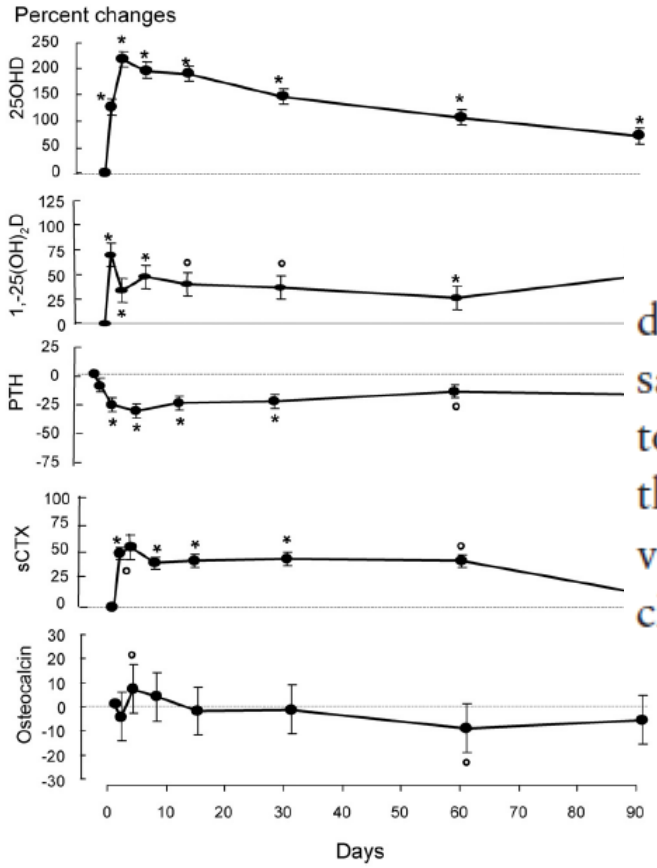
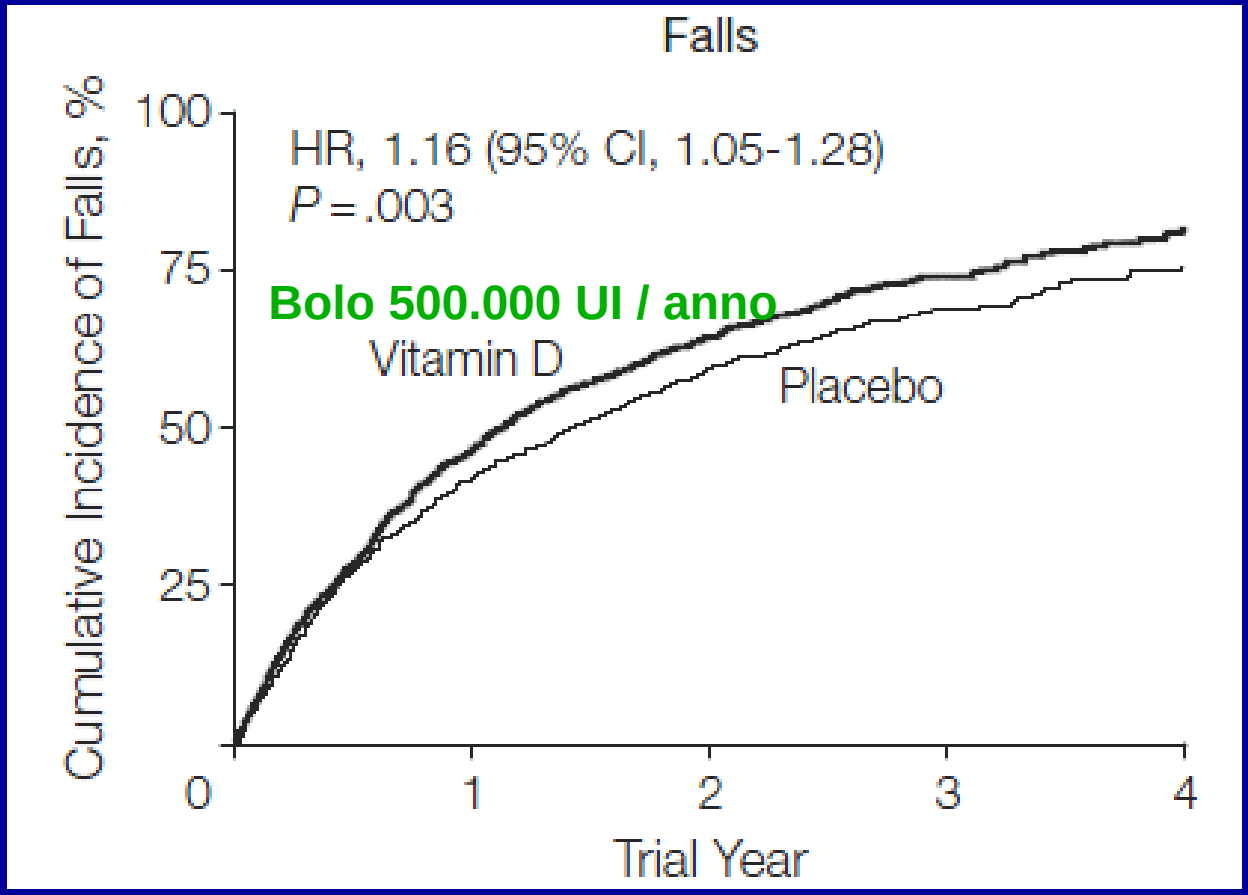


FIG. 1. Effects (percent changes ± SEM *vs.* baseline) of a single oral bolus of 600,000 IU vitamin D_3 on 25OHD, 1,25$(OH)_2$D, PTH, sCTX, and osteocalcin serum levels. *, $P < 0.01$; °, $P < 0.05$.

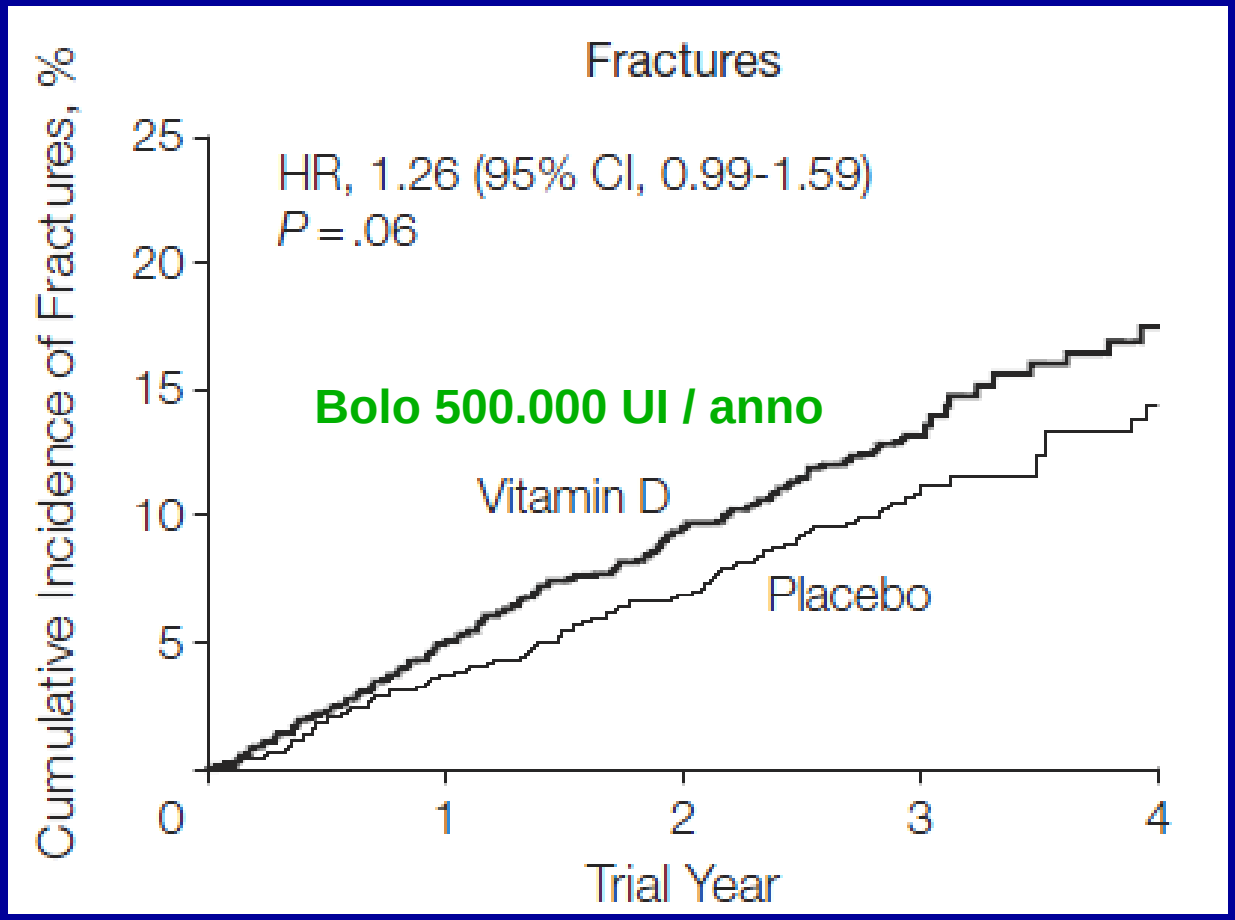
Our results clearly indicate that the use of oral mega-doses of vitamin D may be counterproductive and that the safety issues about vitamin D dosing should not be limited to hypercalcemia and hypercalciuria. The acute increase in the sCTX and sNTX levels we observed in subjects with vitamin D insufficiency is also challenging the common clinical practice of treating vitamin D-deficient patients

SUPPLEMENTAZIONE DI VITAMINA D



JAMA. 2010;303(18):1815-1822

SUPPLEMENTAZIONE DI VITAMINA D



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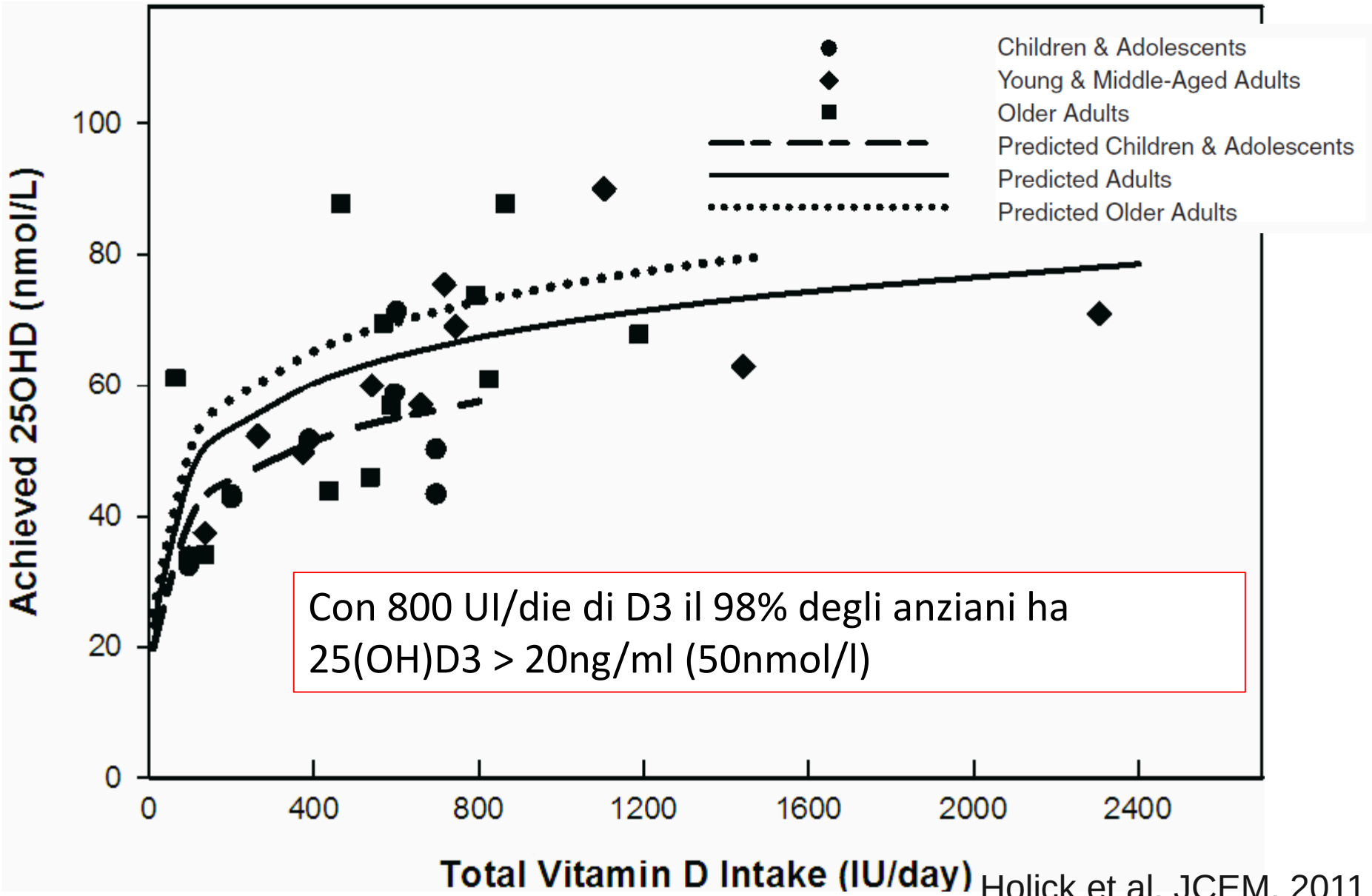
the use of fractionated doses such as daily, weekly or monthly doses is to be preferred.

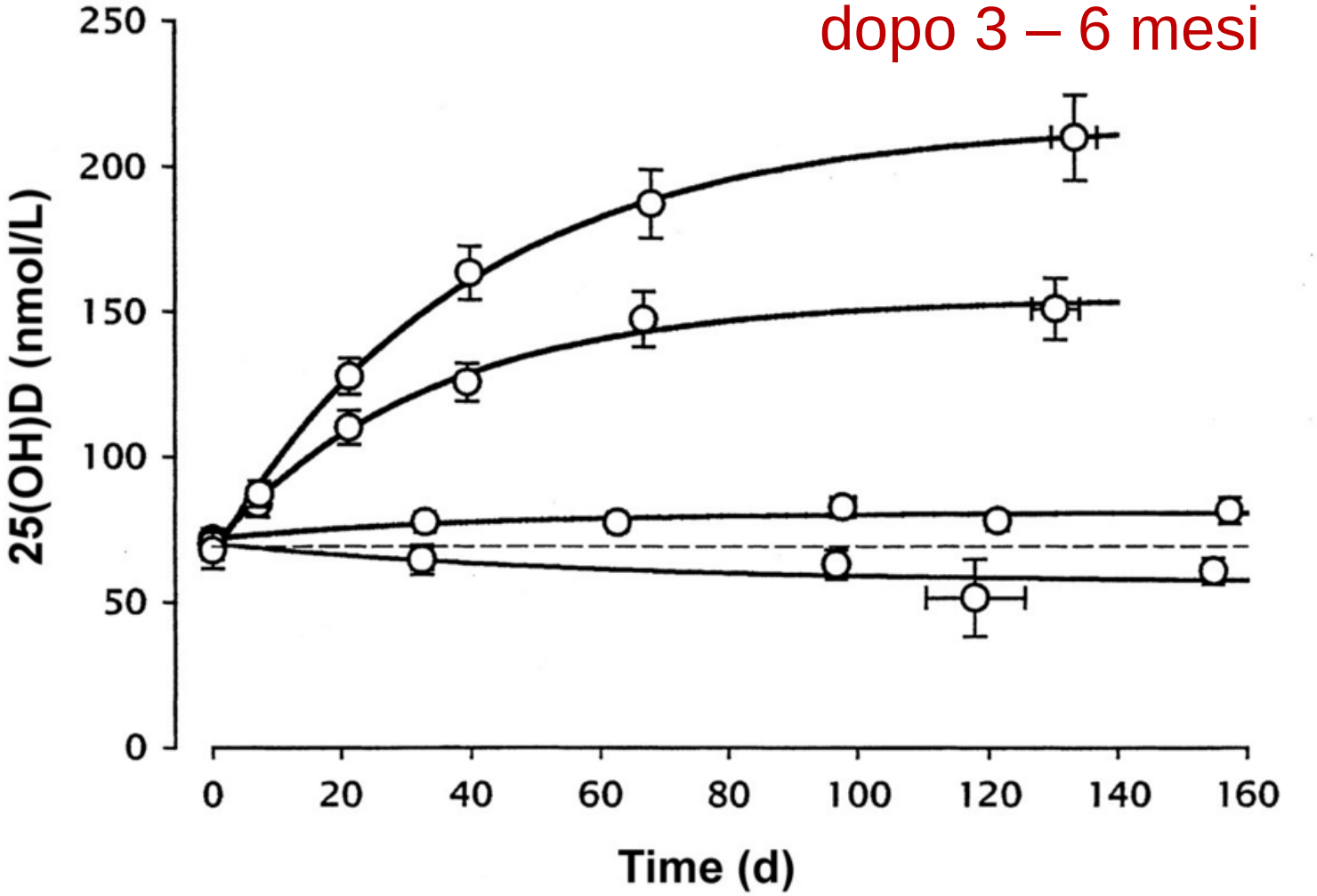
La dose di supplemento dipende soprattutto dal livello che si vuole raggiungere, non tanto dal livello di partenza



Holick et al, JCEM, 2011

Dosaggio sierico di 25(OH)D?
Iniziare con dose modesta, poi controllare di essere a bersaglio

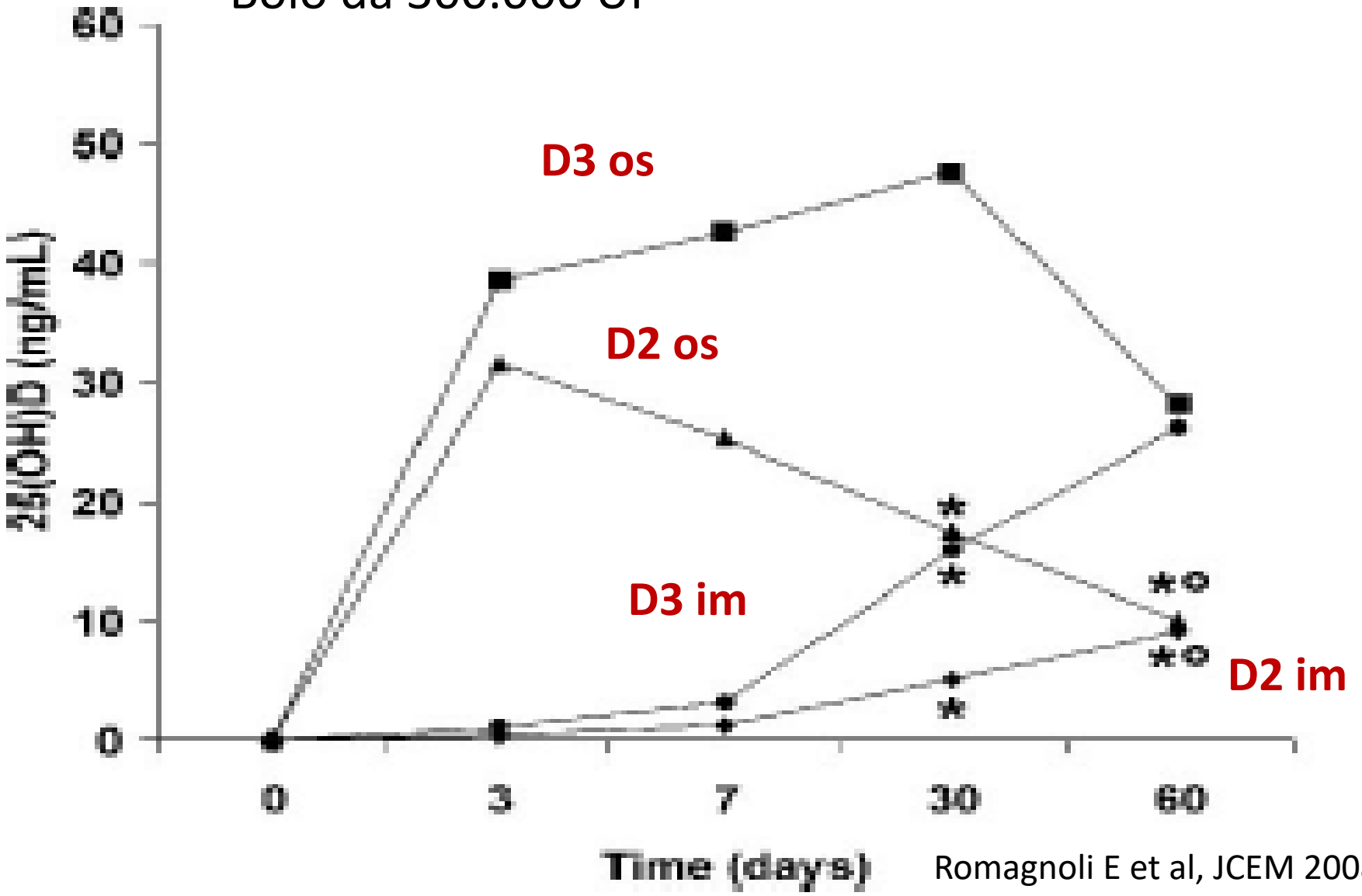
dopo 3 – 6 mesi



Heaney et al, Am J Clin Nutr, 2003

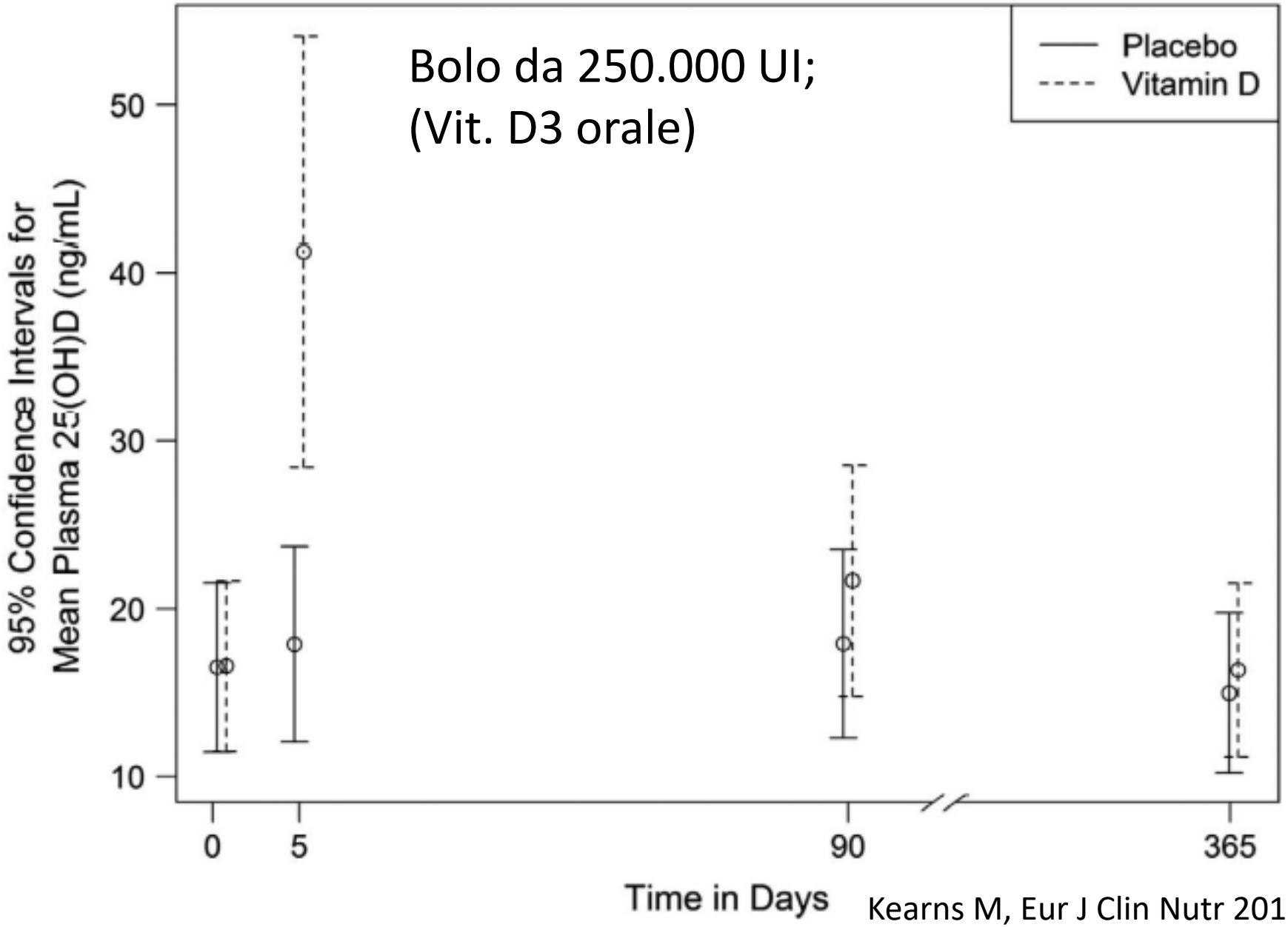
Il carico iniziale serve solo a correggere in modo rapido il deficit (non ha effetti duraturi certi)

Bolo da 300.000 UI



Romagnoli E et al, JCEM 2008

Il carico iniziale serve solo a correggere in modo rapido il deficit (non ha effetti duraturi certi)



Kearns M, Eur J Clin Nutr 2015

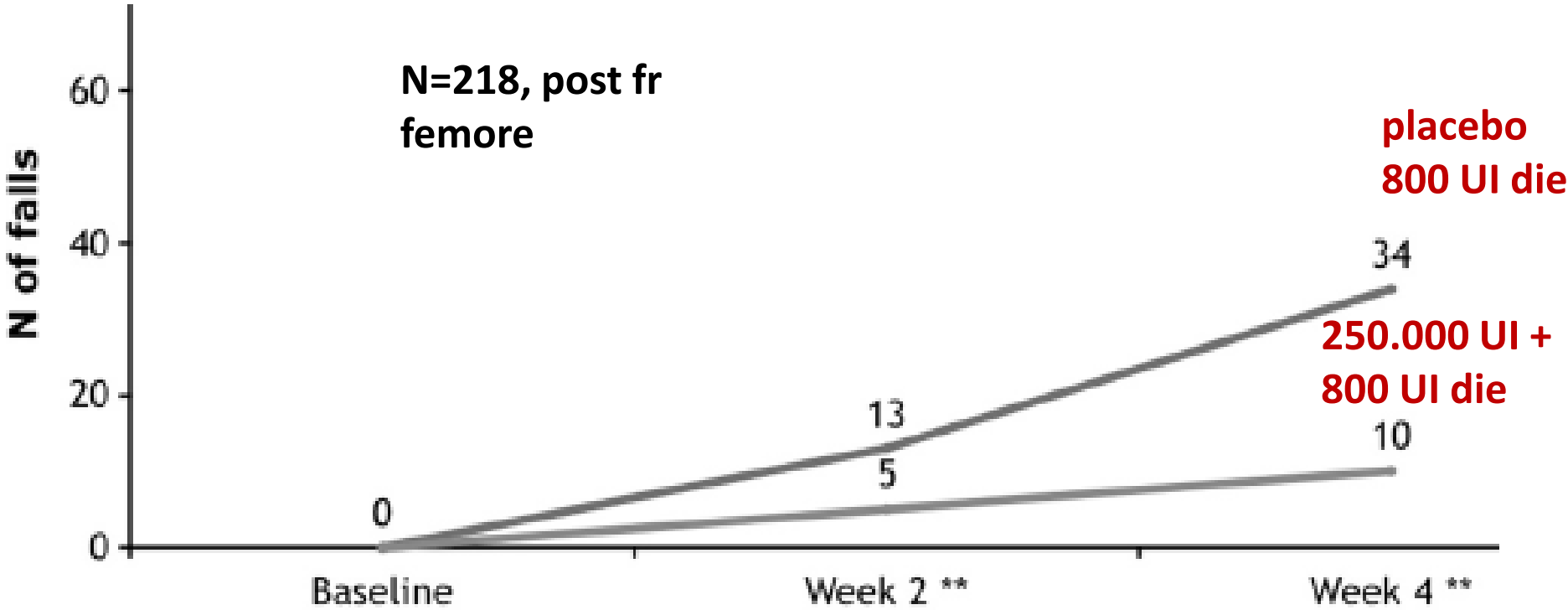
Il carico iniziale serve solo a correggere in modo rapido il deficit (non ha effetti duraturi certi)

Indicazione alla dose di carico iniziale (NOS 2013):

Inizio di terapia con denosumab o zoledronato

Osteomalacia sintomatica

Fr. Femore e alto rischio di caduta (?)



Mak JC et al, BMC Musculosk Dis, 2016