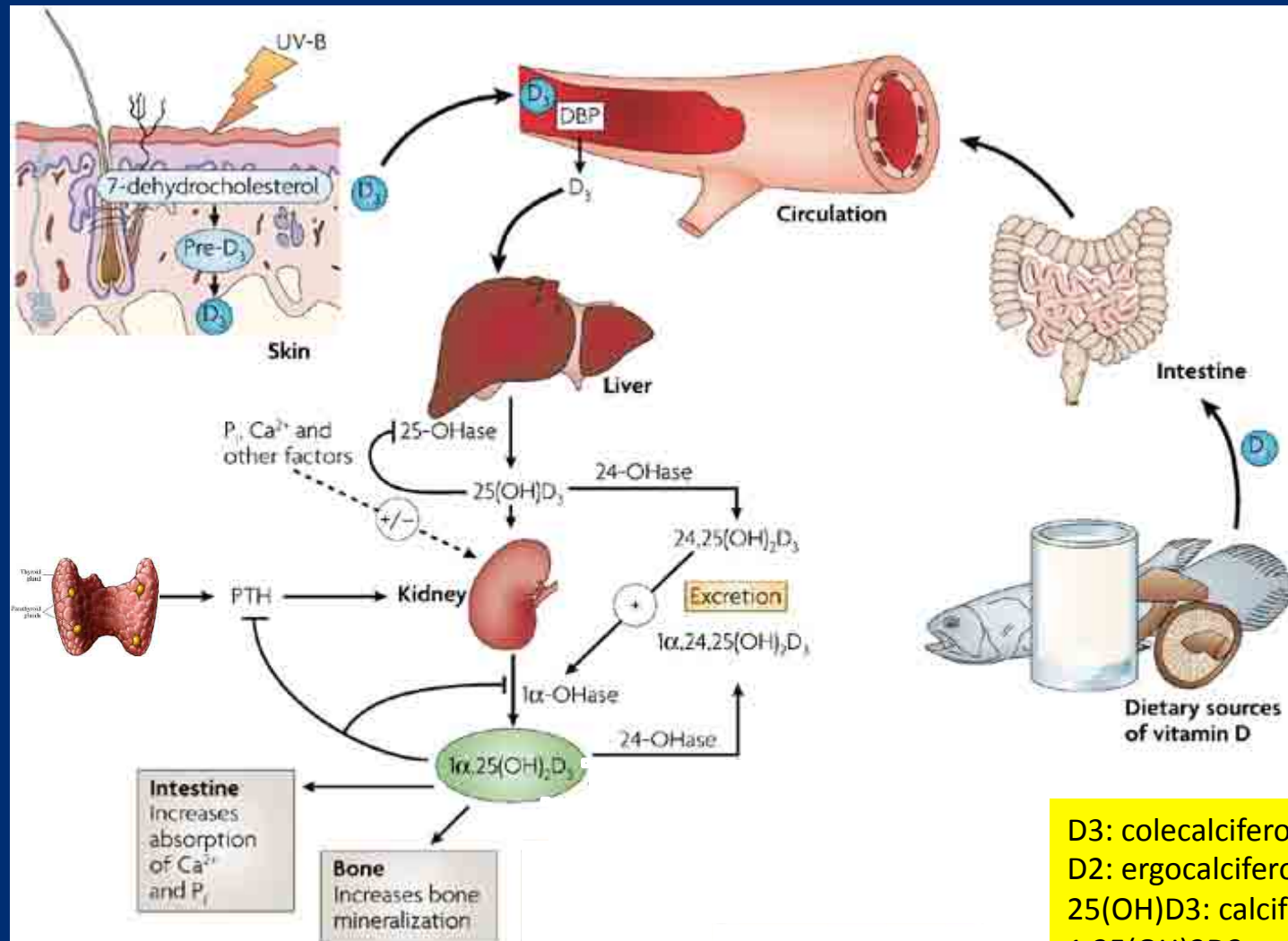




OSTEOPOROSI PER NON OSTEOPOROLOGI

IL RUOLO DELLA VITAMINA D

Graziano Ceresini
SS Endocrinologia Metabolica Geriatrica
Università di Parma
Az Ospedaliero-Universitaria di Parma



Livelli circolanti di vitamina D

- Livelli Sufficienti : $> 30 \text{ ng/mL}$ (75 nmol/L)
- Insufficienza: $20\text{-}30 \text{ ng/mL}$ ($50\text{-}75 \text{ nmol/L}$)
- Carenza: $< 20 \text{ ng/mL}$ ($<50 \text{ nmol/L}$)

Vitamina D ed osso: studi osservazionali

Vitamin D and BMI in YOUNGER ADULTS

25-Hydroxy Vitamin D Levels and Bone Mineral Density/Bischoff-Ferrari et al

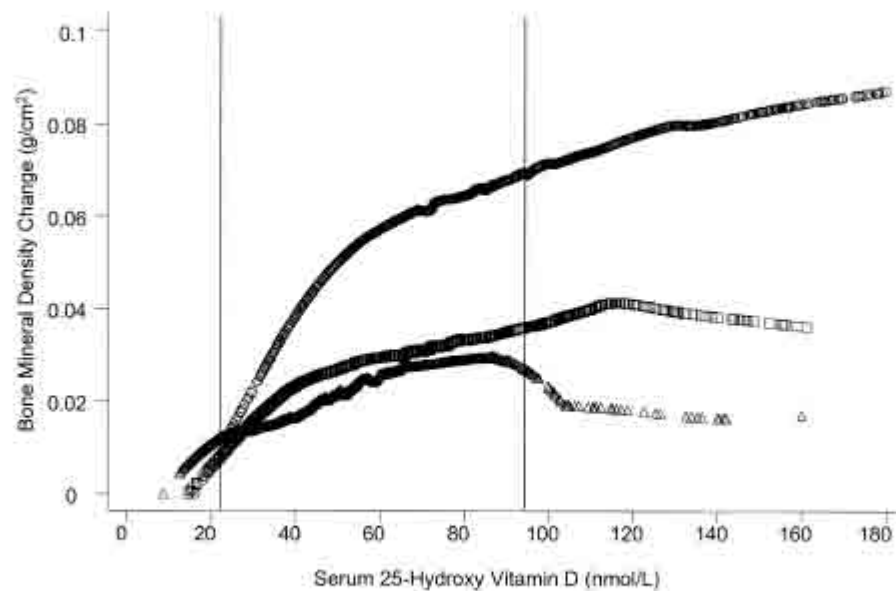


Figure 1. Regression plot of bone mineral density by 25-hydroxy vitamin D level in younger adults (20 to 49 years). Circles represent whites, squares represent Mexican Americans, and triangles represent blacks.

Vitamin D and BMI in OLDER ADULTS

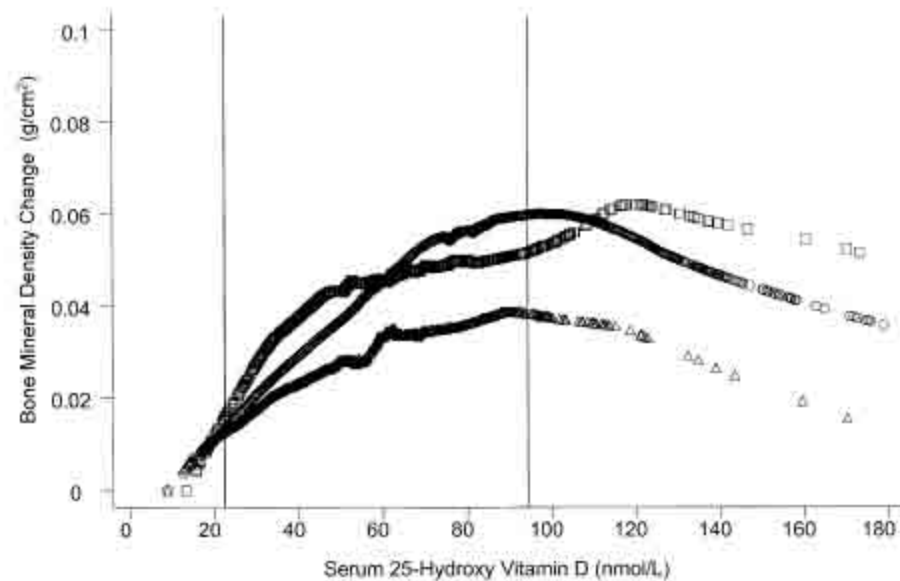


Figure 2. Regression plot of bone mineral density by 25-hydroxy vitamin D level in older adults (≥ 50 years). Circles represent whites, squares represent Mexican Americans, and triangles represent blacks.



Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone



25-hydroxy vitamin D levels in healthy premenopausal women: Association with bone turnover markers and bone mineral density

Silvano Adami^{a,*}, Francesco Bertoldo^b, Vania Braga^d, Elena Fracassi^d, Davide Gatti^d, Giorgio Gandolini^c, Salvatore Minisola^d, Giovanni Battista Rini^e

Regression coefficients between the logarithmic values of 25OHD concentrations and other study variables, unadjusted and adjusted for age and BMI.

Variable	Unadjusted		Age and BMI adjusted	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Age (years)	-0.063	0.054		
Body mass index (BMI)	-0.208	0.000		
S. Calcium	+0.034	n.s.	+0.023	n.s.
S. PTH	-0.154	0.000	-0.122	0.002
S. Phosphate	+0.144	0.000	0.130	0.001
S. Magnesium	-0.111	0.003	-0.115	0.004
S. CTX	+0.116	0.002	+0.096	0.024
S. PINP	+0.053	0.095	+0.026	n.s.
S. Osteocalcin	+0.054	0.093	+0.006	n.s.
S. Bone AP	-0.111	0.003	-0.095	0.017
Spine BMD	+0.025	n.s.	+0.084	0.043
Femoral neck BMD	-0.074	0.034	+0.013	n.s.
Total hip BMD	-0.047	n.s.	+0.021	n.s.

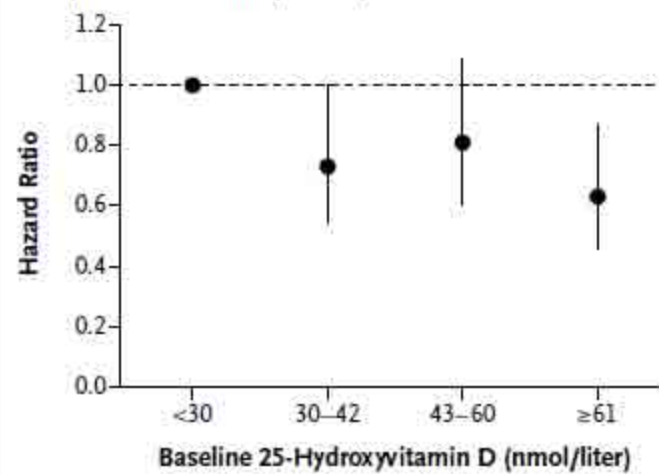
P values reported if <0.1, otherwise reported as non-significant (n.s.).

ORIGINAL ARTICLE

A Pooled Analysis of Vitamin D Dose Requirements for Fracture Prevention

Heike A. Bischoff-Ferrari, M.D., Dr.P.H., Walter C. Willett, M.D., Dr.P.H.,
Endel J. Orav, Ph.D., Paul Lips, M.D., Pierre J. Meunier, M.D.,
Ronan A. Lyons, M.D., M.P.H., Leon Flicker, M.D., John Wark, M.D., Ph.D.,
Rebecca D. Jackson, M.D., Jane A. Cauley, Dr.P.H.,
Haakon E. Meyer, M.D., Ph.D., Michael Pfeifer, M.D., Kerrie M. Sanders, Ph.D.,
Hannes B. Stähelin, M.D., Robert Theiler, M.D., and Bess Dawson-Hughes, M.D.

A Hip-Fracture Events (N=313)



B Nonvertebral-Fracture Events (N=914)

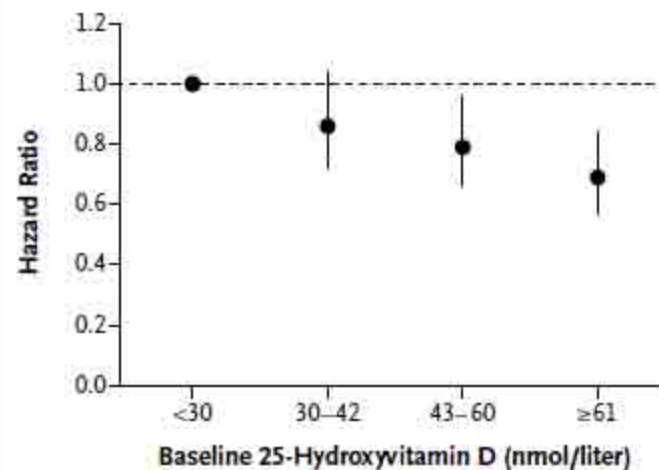


Figure 1. Threshold Assessment for the Risk of Fracture, According to Quartile of Baseline 25-Hydroxyvitamin D Level.

REVIEW

Management of osteoporosis of the oldest old

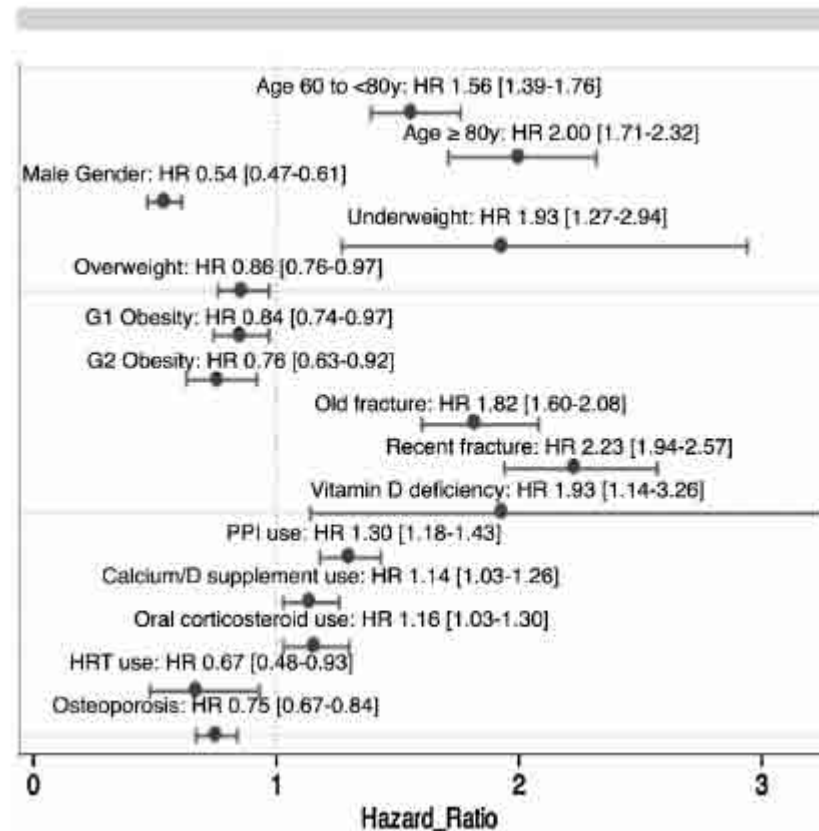
R. Rizzoli • J. Branco • M.-L. Brandi • S. Boonen • O. Bruyère • P. Cacoub • C. Cooper • A. Diez-Perez • J. Duder • R. A. Fielding • N. C. Harvey • M. Hiligsmann • J. A. Kanis • J. Petermans • J. D. Ringe • Y. Tsouderos • J. Weinman • J.-Y. Reginster

Table 2 Threshold levels of 25-hydroxy-vitamin D in the serum and their impact on bone health

Serum 25-OH-D level	Definition	Impact on bone health
< 25 nmol/L (<10 ng/L)	Vitamin D deficiency	Mineralization defects
< 50 nmol/L (<20 ng/L)	Vitamin D insufficiency	Increased bone turnover and/or PTH
50–75 nmol/L (20–30 ng/L)	Vitamin D sufficiency	Neutral effect (bone turnover and PTH normalised), desirable benefits on fracture, falls and mortality
> 75 nmol/L (>30 ng/L)		Desirable target in the fragile individuals or oldest old due to the optimal benefits on fracture, falls and mortality
125 nmol/L (50 ng/L)	Upper limit of adequacy	Possibility of adverse effects above this level

Adapted from Rizzoli et al, [47]

Predictors of Fracture While on Treatment With Oral Bisphosphonates: A Population-Based Cohort Study



Vitamina D ed osso: studi di intervento

Supplemental Material can be found at:
<http://jn.nutrition.org/content/suppl/2015/09/02/jn.115.21500.4.DCSupplemental.html>

The Journal of Nutrition
Nutrition and Disease



Oral Vitamin D Supplements Increase Serum 25-Hydroxyvitamin D in Postmenopausal Women and Reduce Bone Calcium Flux Measured by ^{41}Ca Skeletal Labeling¹⁻³

Andreas Schild,⁴ Isabelle Herter-Aeberli,⁵ Karin Fittinger,⁴ Sarah Anderegg,⁵ Tim Schulze-König,⁶ Christof Vockenhuber,⁶ Hans-Arno Synal,⁶ Heike Bischoff-Ferrari,^{7,9} Peter Weber,⁸ Arnold von Eckardstein,¹⁰ and Michael B Zimmermann^{5*}

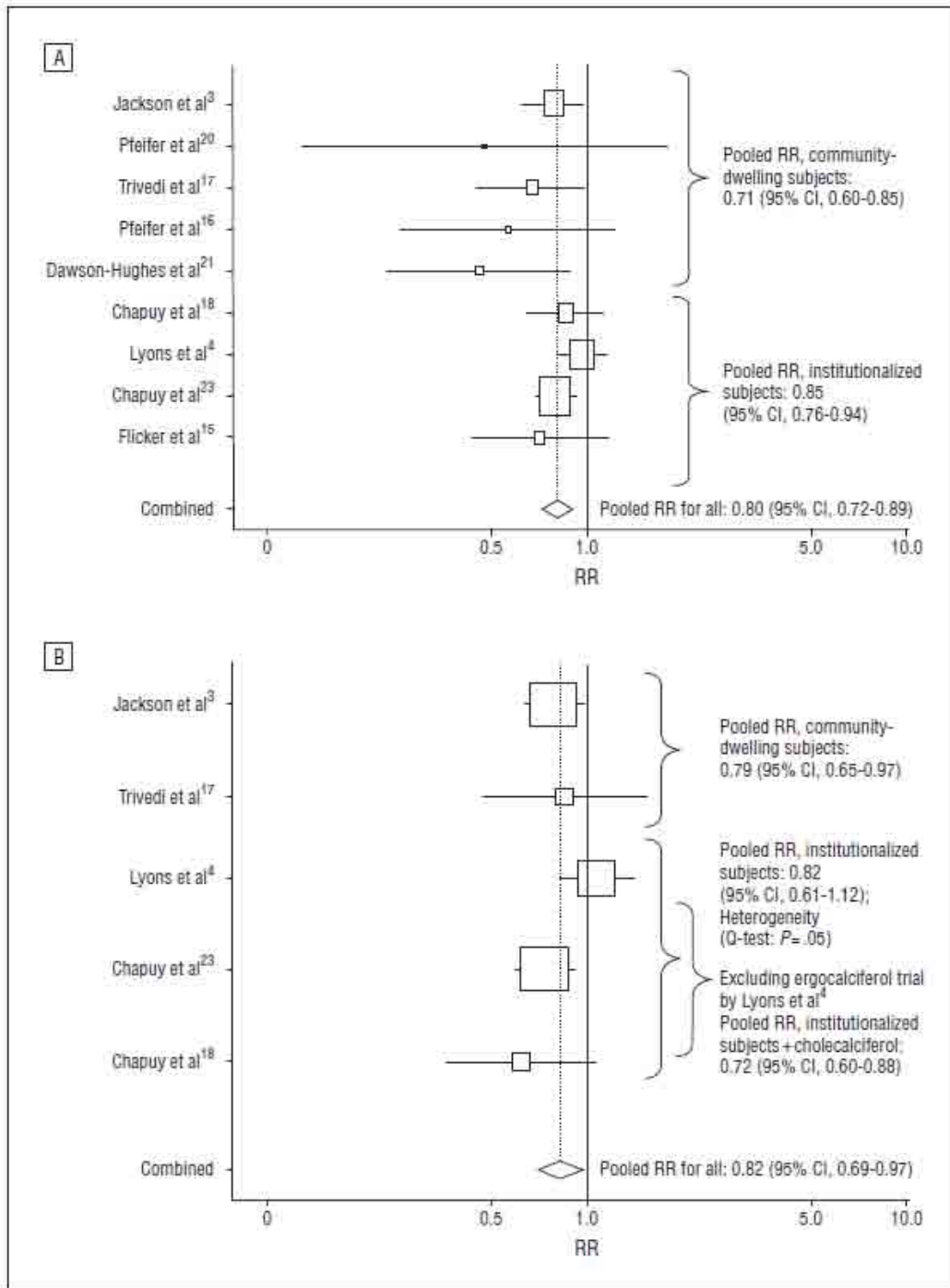
J Nutr 2015

REVIEW ARTICLE

Prevention of Nonvertebral Fractures With Oral Vitamin D and Dose Dependency

A Meta-analysis of Randomized Controlled Trials

Heike A. Bischoff-Ferrari, DrPH; Walter C. Willett, DrPH; John B. Wong, MD; Andreas E. Stuck, MD;
Hannes B. Staehelin, MD; E. John Orav, PhD; Anna Thoma, MD; Douglas P. Kiel, MD; Jana Henschkowski, MD



Bischoff-Ferrari et al
Arch Intern Med, 2009

Prevention of Nonvertebral Fractures With Oral Vitamin D and Dose Dependency

A Meta-analysis of Randomized Controlled Trials

Heike A. Bischoff-Ferrari, DrPH; Walter C. Willett, DrPH; John B. Wong, MD; Andreas E. Stuck, MD;
Hannes B. Staehelin, MD; E. John Orav, PhD; Anna Thoma, MD; Douglas P. Kiel, MD; Jana Henschkowski, MD

Conclusion: Nonvertebral fracture prevention with vitamin D is dose dependent, and a higher dose should reduce fractures by at least 20% for individuals aged 65 years or older.

Arch Intern Med. 2009;169(6):551-561

Vitamin D and vitamin D analogues for preventing fractures in post-menopausal women and older men (Review)

Avenell A, Mak JCS, O'Connell D

«Vitamin D alone is unlikely to prevent fractures in older people.

Supplements of vitamin D and calcium may prevent hip or any type of fracture»

Avenell A, Mak JCS, O'Connell D.
Vitamin D and vitamin D analogues for preventing fractures in post-menopausal women and older men.
Cochrane Database of Systematic Reviews 2014, Issue 4. Art. No.: CD000227.
DOI: 10.1002/14651858.CD000227.pub4.

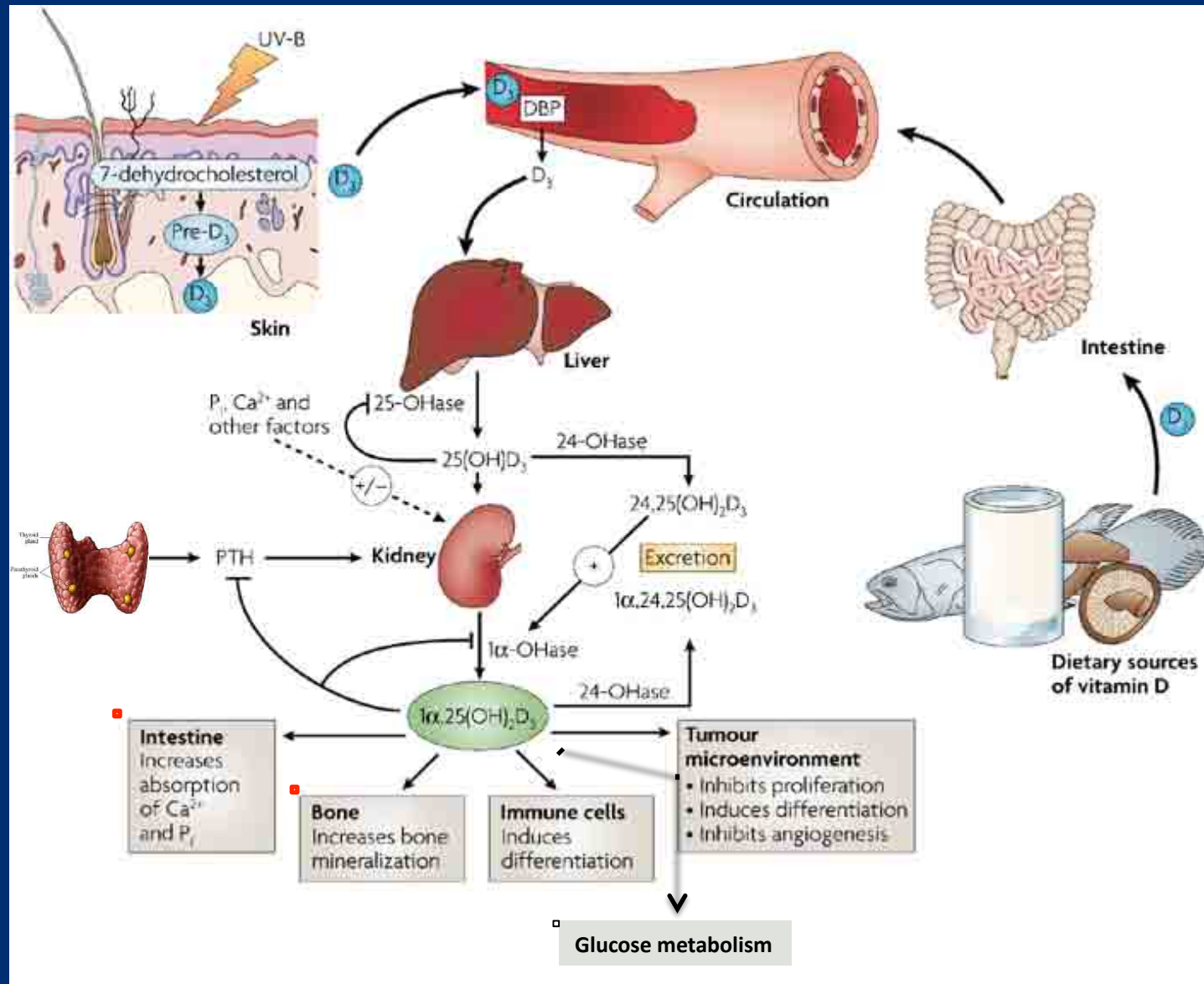
www.cochranelibrary.com

- Difficoltà nel confronto tra gli studi:

Genetica di popolazione

Bias di selezione

METODO DI DOSAGGIO DELLA VIT D





www.associazionemediciendocrinologi.it

ame news

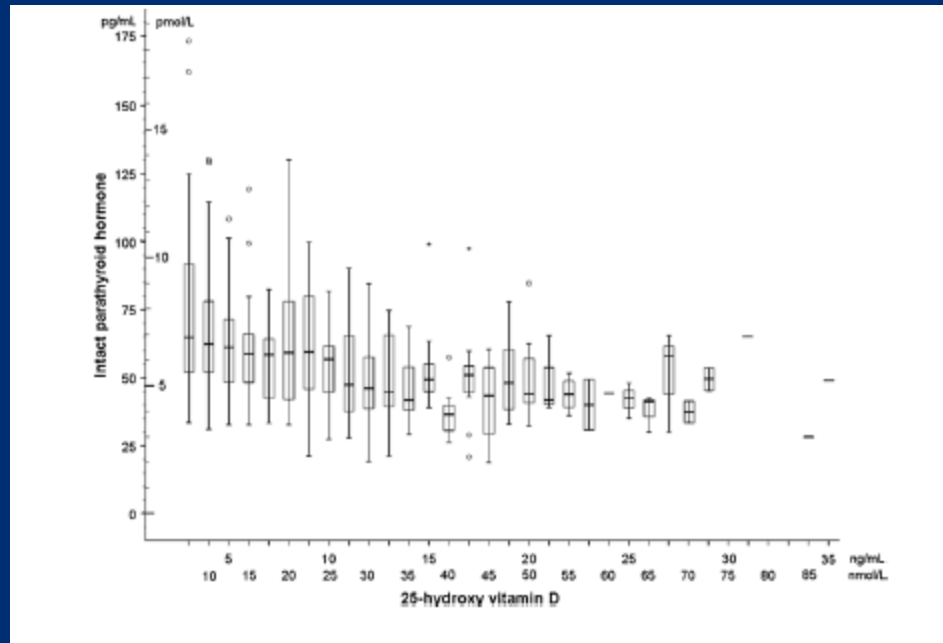
nr. 19 - marzo 2016

LA VITAMINA D NON È PANACEA

Responsabile Editoriale
Renato Cozzi

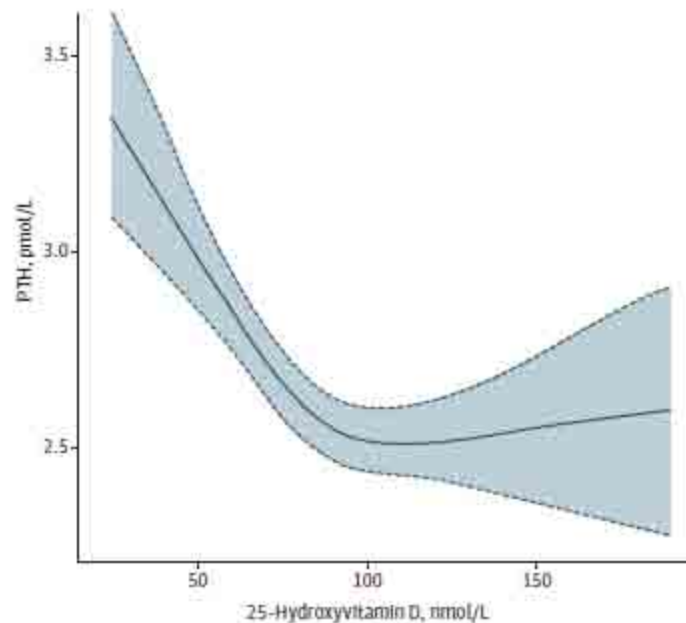
Nella mitologia greca, Panacea, figlia di Asclepio e Lampezia, era la personificazione della guarigione universale e onnipotente. Per qualche tempo, qualcuno ha pensato che questo ruolo potesse essere degnamente assunto dalla vitamina D, che negli ultimi anni ha visto la sua popolarità aumentare in tutto il mondo. Oggi cominciano a esserci evidenze che non è proprio così, almeno per l'ipotizzata capacità di migliorare il controllo glicemico nel diabete tipo 2 (DMT2).

Relationship between PTH and Vitamin D



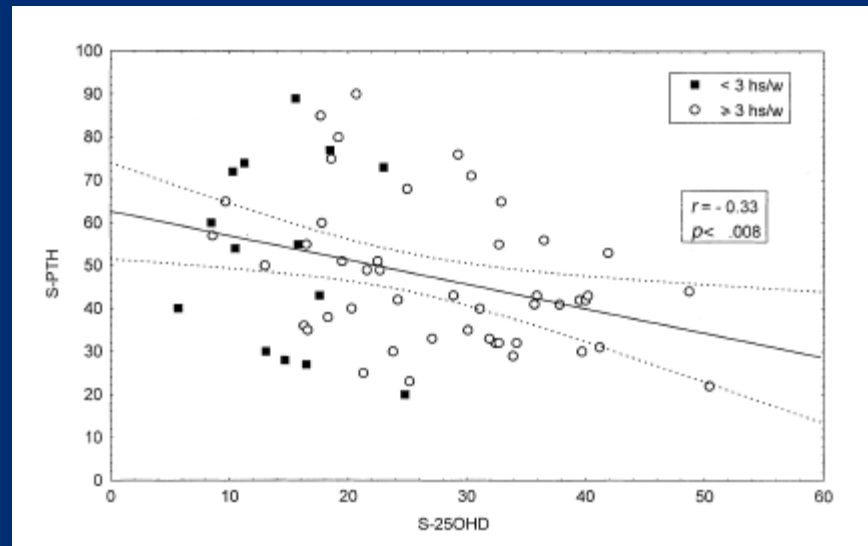
Parathyroid Hormone as a Functional Indicator of Vitamin D Sufficiency in Children

Figure. Plot of the Regression Model for 25-Hydroxyvitamin D and Parathyroid Hormone (PTH)



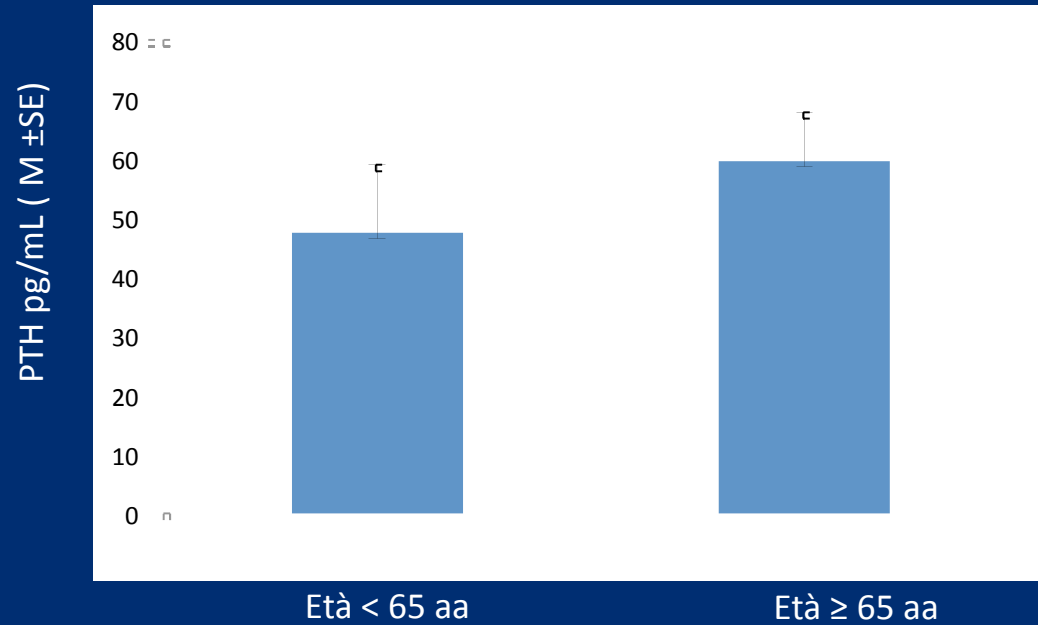
Shaded areas inside the dashed lines represent 95% confidence intervals.

Relationship between Vitamin D and PTH in elderly subjects



Melin A et al, 2014

Livelli circolanti di PTH in soggetti giovani ed anziani con carenza di Vit D



JOURNAL OF BONE AND MINERAL RESEARCH

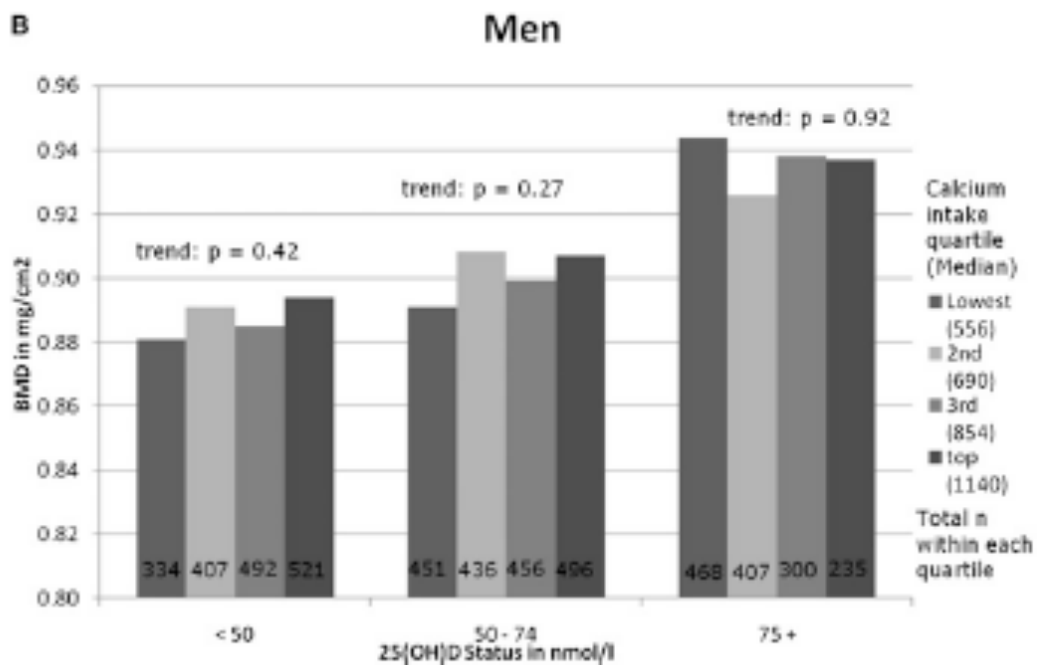
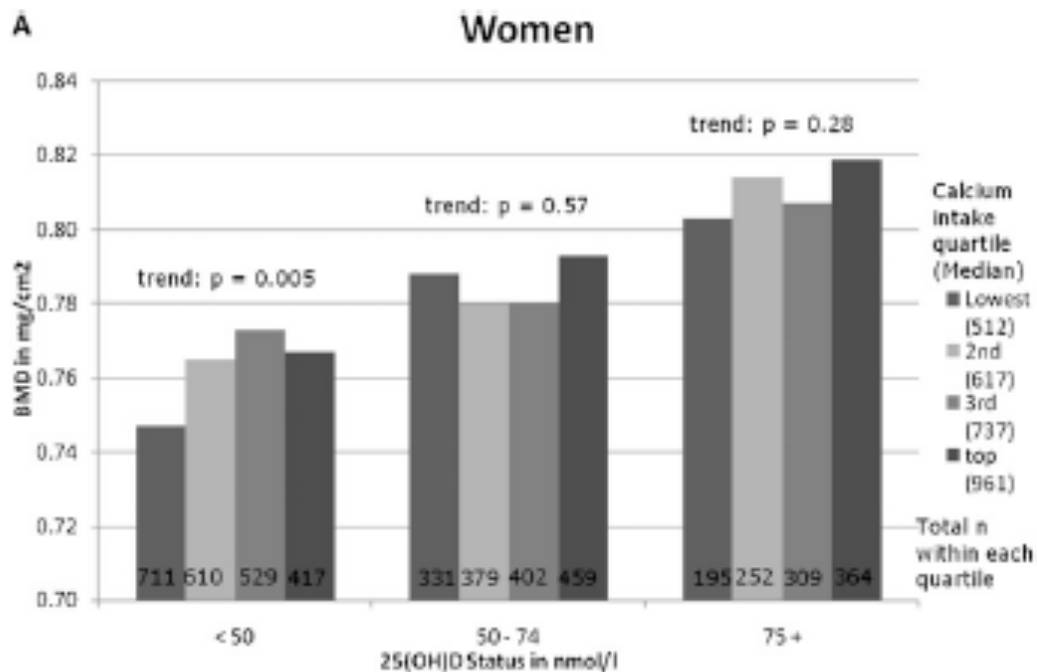
Volume 24, Number 5, 2009

Published online on December 29, 2008; doi: 10.1359/JBMR.081242

© 2009 American Society for Bone and Mineral Research

Dietary Calcium and Serum 25-Hydroxyvitamin D Status in Relation to BMD Among U.S. Adults

Heike A. Bischoff-Ferrari,^{1,2,3} Douglas P. Kiel,⁴ Bess Dawson-Hughes,⁵ John E. Orav,⁶ Ruifeng Li,^{6,7}
Donna Spiegelman,^{5,6} Thomas Dietrich,⁸ and Walter C. Willett²



Bischoff-Ferrari et al
2009

Osteoporos Int (2014) 25:2359–2381

DOI 10.1007/s00198-014-2794-2

POSITION PAPER

Clinician's Guide to Prevention and Treatment of Osteoporosis

**F. Cosman • S. J. de Beur • M. S. LeBoff • E. M. Lewiecki •
B. Tanner • S. Randall • R. Lindsay**

Table 1 Conditions, diseases, and medications that cause or contribute to osteoporosis and fractures

Lifestyle factors		
Alcohol abuse	Excessive thinness	Excess vitamin A
Frequent falling	High salt intake	Immobilization
Inadequate physical activity	Low calcium intake	Smoking (active or passive)
Vitamin D insufficiency		
Genetic diseases		
Cystic fibrosis	Ehlers-Danlos	Gaucher's disease
Glycogen storage diseases	Hemochromatosis	Homocystinuria
Hypophosphatasia	Marfan syndrome	Menkes steely hair syndrome
Osteogenesis imperfecta	Parental history of hip fracture	Porphyria
Riley-Day syndrome		
Hypogonadal states		
Androgen insensitivity	Anorexia nervosa	Athletic amenorrhea
Hyperprolactinemia	Panhypopituitarism	Premature menopause (<40 years)
Turner's and Klinefelter's syndromes		
Endocrine disorders		
Central obesity	Cushing's syndrome	Diabetes mellitus (types 1 and 2)
Hyperparathyroidism	Thyrotoxicosis	
Gastrointestinal disorders		
Celiac disease	Gastric bypass	Gastrointestinal surgery
Inflammatory bowel disease	Malabsorption	Pancreatic disease
Primary biliary cirrhosis		
Hematologic disorders		
Hemophilia	Leukemia and lymphomas	Monoclonal gammopathies
Multiple myeloma	Sickle cell disease	Systemic mastocytosis
Thalassemia		
Rheumatologic and autoimmune diseases		
Ankylosing spondylitis	Other rheumatic and autoimmune diseases	
Rheumatoid arthritis	Systemic lupus	
Neurological and musculoskeletal risk factors		
Epilepsy	Multiple sclerosis	Muscular dystrophy
Parkinson's disease	Spinal cord injury	Stroke
Miscellaneous conditions and diseases		
AIDS/HIV	Amyloidosis	Chronic metabolic acidosis
Chronic obstructive lung disease	Congestive heart failure	Depression
End-stage renal disease	Hypercalciuria	Idiopathic scoliosis
Post-transplant bone disease	Sarcoidosis	Weight loss
Medications		
Aluminum (in antacids)	Anticoagulants (heparin)	Anticonvulsants
Aromatase inhibitors	Barbiturates	Cancer chemotherapeutic drugs
Depo-medroxyprogesterone (premenopausal contraception)	Glucocorticoids (≥ 5 mg/day prednisone or equivalent for ≥ 3 months)	GnRH (gonadotropin-releasing hormone) agonists
Lithium cyclosporine A and tacrolimus	Methotrexate	Parental nutrition
Proton pump inhibitors	Selective serotonin reuptake inhibitors	
Tamoxifen® (premenopausal use)	Thiazolidinediones (such as Actos® and Avandia®)	Thyroid hormones (in excess)

Age and Ageing 2014; **43**: 592–595
doi: 10.1093/ageing/afu093
Published electronically 28 July 2014

© The Author 2014. Published by Oxford University Press on behalf of the British Geriatrics Society.
All rights reserved. For Permissions, please email: journals.permissions@oup.com

CLINICAL GUIDELINE

National Osteoporosis Society Vitamin D Guideline Summary

TERRY J. ASPRAY^{1,2}, CLAIRE BOWRING³, WILLIAM FRASER⁴, NEIL GITTOES⁵, M. KASSIM JAVAID⁶,
HELEN MACDONALD⁷, SANJEEV PATEL⁸, PETER SELBY⁹, NUTTAN TANNA¹⁰, ROGER M. FRANCIS²

Recommendations

- (1) Measurement of serum 25OHD is the best way of estimating vitamin D status.
- (2) Serum 25OHD measurement is recommended for
 - patients with bone diseases that may be improved with vitamin D treatment;
 - patients with bone diseases, prior to specific treatment where correcting vitamin D deficiency is appropriate and
 - patients with musculoskeletal symptoms that could be attributed to vitamin D deficiency.
- (3) Routine vitamin D testing may be unnecessary in patients with osteoporosis or fragility fracture, who may be co-prescribed vitamin D supplementation with an oral antiresorptive treatment.

Trattamento con Vitamina D nell'osteoporosi

REVIEW

Management of osteoporosis of the oldest old

**R. Rizzoli • J. Branco • M.-L. Brandi • S. Boonen • O. Bruyère • P. Cacoub • C. Cooper •
A. Diez-Perez • J. Duder • R. A. Fielding • N. C. Harvey • M. Hiligsmann • J. A. Kanis •
J. Petermans • J. D. Ringe • Y. Tsouderos • J. Weinman • J.-Y. Reginster**

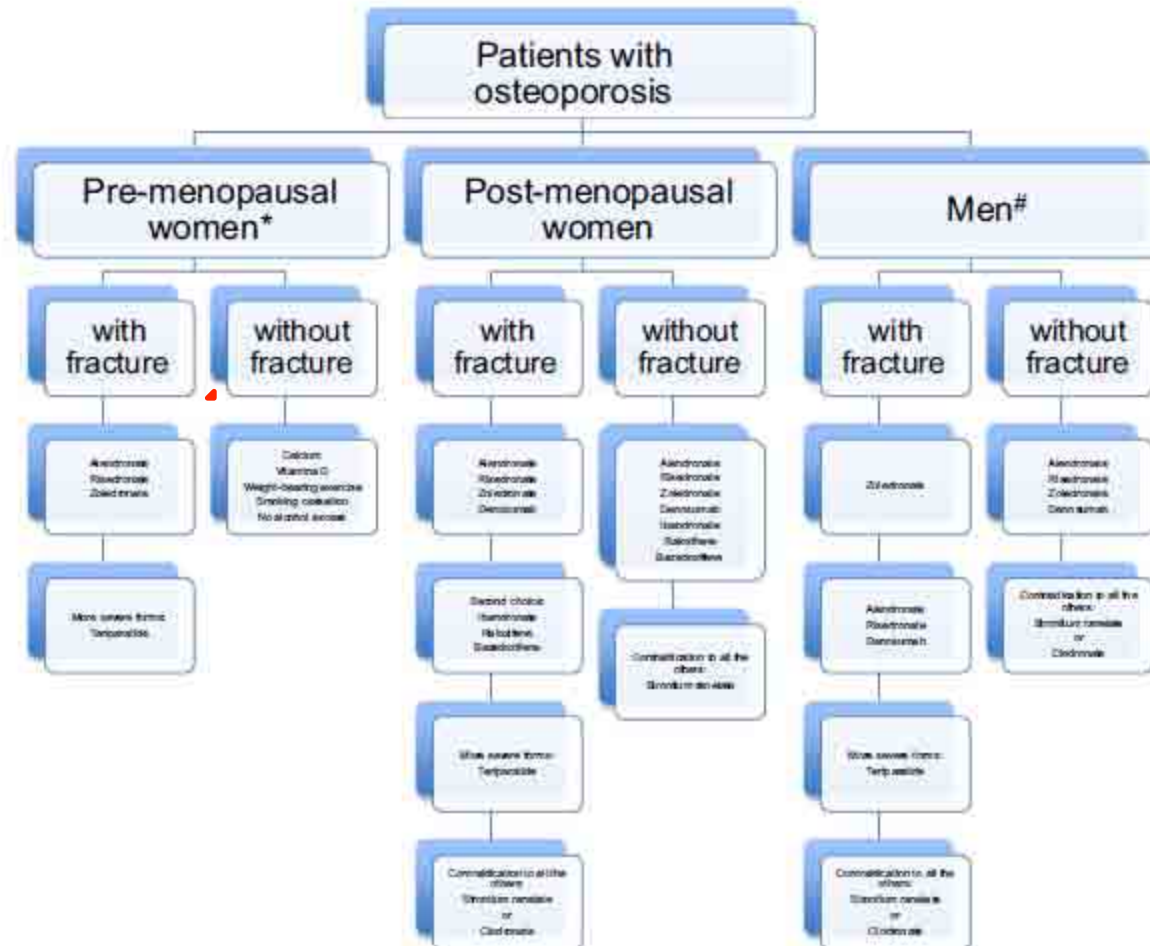
**Therapeutic approaches to osteoporosis: nutritional
supplementation and vitamin D**

CONSENSUS STATEMENT

Italian association of clinical endocrinologists (AME) position statement: drug therapy of osteoporosis

F. Vescini¹ · R. Attanasio² · A. Balestrieri³ · F. Bandeira⁴ · S. Bonadonna⁵ ·
V. Camozzi⁶ · S. Cassibba⁷ · R. Cesareo⁸ · I. Chiodini⁹ · C. Maria Francucci^{10,11} ·
L. Gianotti¹² · F. Grimaldi¹ · R. Guglielmi¹³ · B. Madeo¹⁴ · C. Marocchi¹⁵ ·
A. Palermo¹⁶ · A. Scillitani¹⁷ · E. Vignali¹⁸ · V. Rochira¹⁹ · M. Zini²⁰

Received: 28 September 2015 / Accepted: 22 January 2016
© The Author(s) 2016. This article is published with open access at Springerlink.com



The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., *Editor*

Postmenopausal Osteoporosis

Dennis M. Black, Ph.D., and Clifford J. Rosen, M.D.

Patients who have had recent osteoporotic fractures are at particularly high risk for additional fractures. One strategy for identifying such patients is the use of a fracture liaison service targeted to patients with recent fractures that provides a consultative approach with advice and recommendations for the clinician about diagnosis and treatment; such a service has been shown to be cost-effective.¹⁰ Other high-risk patients are those with secondary osteoporosis due to hyperparathyroidism, multiple myeloma, malabsorption, diabetes mellitus (with or without low BMD), or inflammatory bowel disease. In patients with low BMD or a previous fracture or those being considered for anti-osteoporosis therapy, a single evaluation for vitamin D status is recommended, even in those who take vitamin D supplements.

MANAGEMENT

Nonpharmacologic Options

Physical Activity and Modifiable Risk Factors

Resistance and weight-bearing exercise can increase muscle mass and can transiently increase BMD.¹¹ Although data from randomized trials are lacking to show that weight-bearing physical activity reduces the risk of fractures, longitudinal studies involving high-resolution computed tomography have shown beneficial effects on skeletal microarchitecture in association with some forms of regular physical activity.¹² Fractures result from falls, and the number of falls and the proportion of falls that result in fractures increase with age. Exercise and balance programs (e.g., yoga and tai chi) may result in

improved balance and an increase in muscle tone and may secondarily reduce the risk of falls among some elderly persons. Besides exercise, assessment of the home for hazards, withdrawal of psychotropic medications (when possible), and the use of a multidisciplinary program to assess risk factors are prudent strategies for potentially reducing the risk of falls. Other measures should include counseling about cigarette smoking (which is linked to reduced BMD) and about excess alcohol intake (which can increase the risk of falls).

Calcium and Vitamin D

The efficacy of calcium and vitamin D treatment for the prevention of osteoporotic fractures is controversial.¹³ In a large randomized trial by the Women's Health Initiative (WHI) investigators involving more than 36,000 postmenopausal women, calcium (1000 mg of elemental calcium supplementation daily) plus vitamin D (400 IU daily) did not have a significant effect on fractures, although there was evidence of benefit in post hoc subgroup analyses among women 60 years of age or older and among those who were adherent to the assigned regimen.¹⁴ Subsequent meta-analyses of several large trials of both calcium and vitamin D supplementation have shown a small reduction in fracture risk, particularly among the institutionalized elderly or those with a low intake of calcium or vitamin D.¹⁵ However, vitamin D supplementation alone has not been shown to reduce the risk of fractures or increase BMD, although smaller trials have suggested that daily supplementation (but not intermittent high-dose supplementation) may

CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., *Editor*

Postmenopausal Osteoporosis

Dennis M. Black, Ph.D., and Clifford J. Rosen, M.D.

Standard recommendations for most postmenopausal women with osteoporosis support a total calcium intake of 1000 to 1500 mg per day (through diet, supplements, or both) and a total vitamin D intake of 600 to 800 IU per day.

Quale Vitamina D utilizzare?

- D2: ergocalciferolo
- D3: colecalciferolo
- 25(OH)D3: calcifediolo

How to select the doses of vitamin D in the management of osteoporosis

H. A. Bischoff-Ferrari

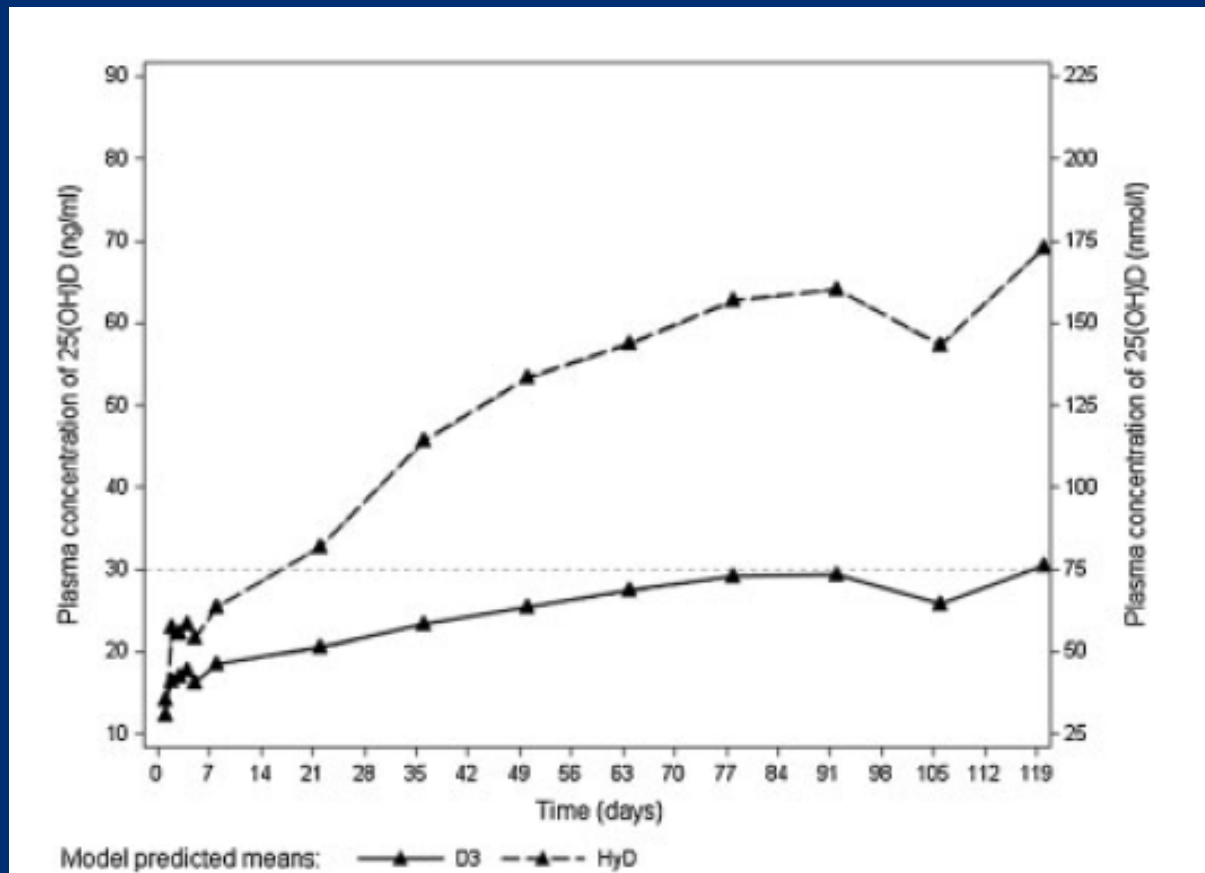
Table 1 Different vitamin D regimens, achieved 25(OH)D serum concentrations, and fall and fracture efficacy

Application	Expected mean 25(OH)D serum concentrations	Anti-fall efficacy	Anti-fracture efficacy
Oral daily 400 IU cholecalciferol [36, 37]	60 to 65 nmol/l	No	No
Oral daily 700–800 IU cholecalciferol [2]	74 to 110 nmol/l	Yes	Yes
Oral 100,000 IU cholecalciferol every 4 months [38]	74 nmol/l	?	Yes
Annual 300,000 IU ergocalciferol [33, 35]	45 to 65 nmol/l	No	No*

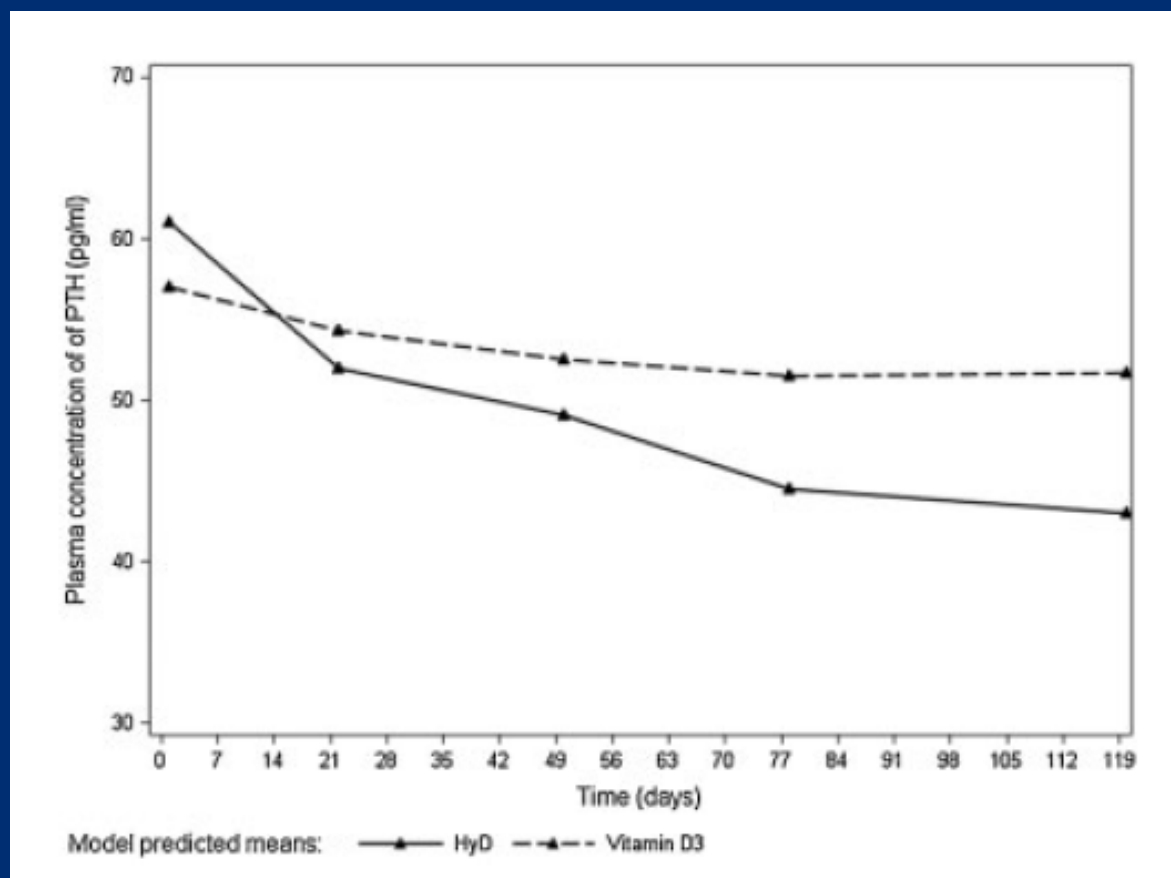
The data presented in the table assume adherence to treatment of at least 80%.

*As discussed in the text, two trials have been performed with conflicting results

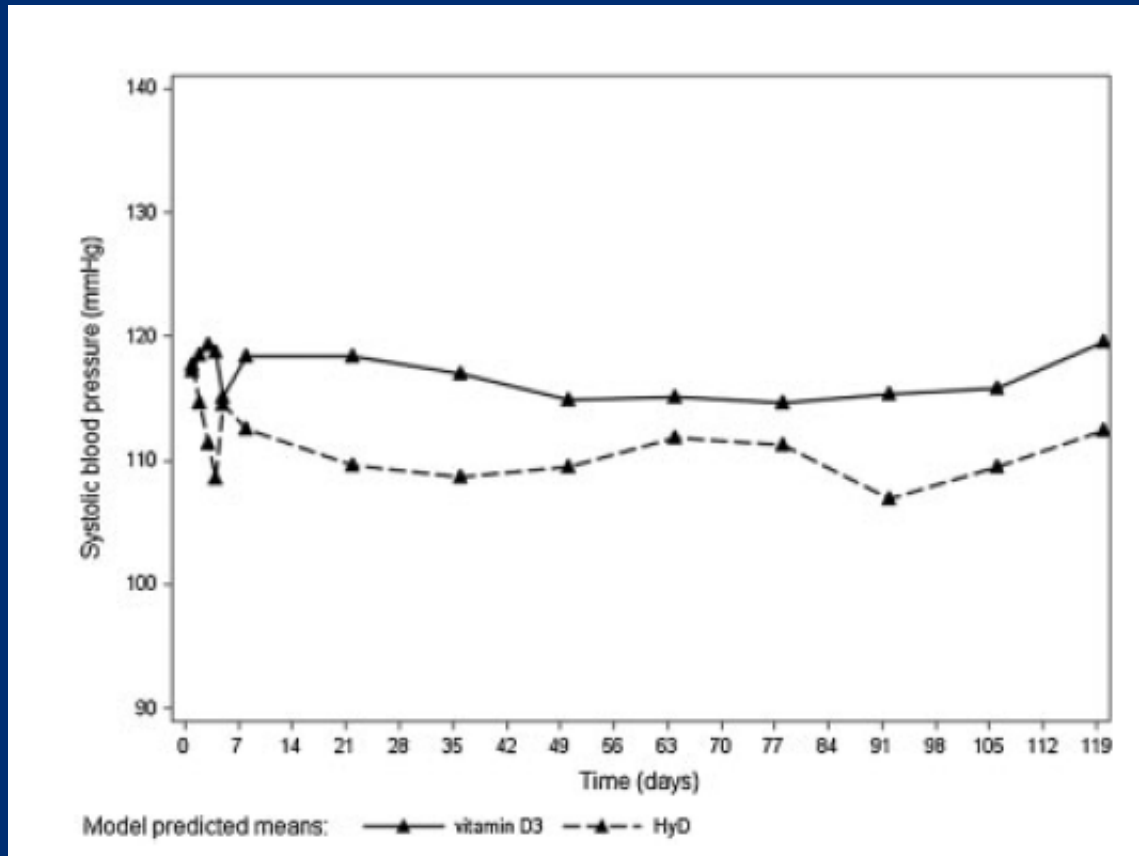
Variazioni plasmatiche di 25OHD in pazienti trattate con calcifediolo o colecalciferolo

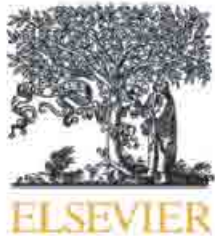


Variazioni plasmatiche di PTH in pazienti trattate con calcifediolo o colecalciferolo



Variazioni della pressione arteriosa sistolica in pazienti trattate con calcifediolo o colecalciferolo

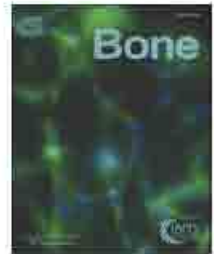




Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

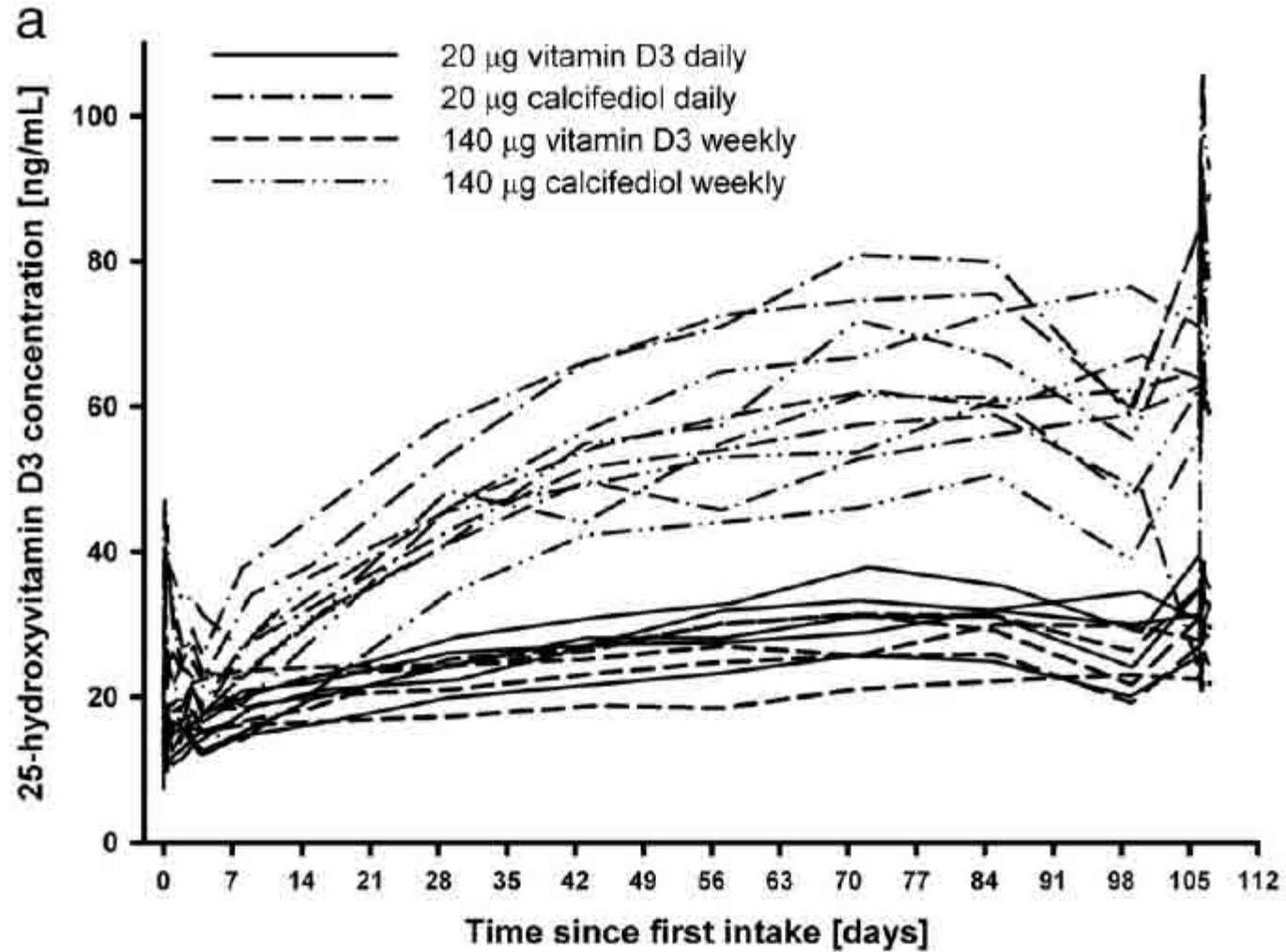


Original Full Length Article

Pharmacokinetics of oral vitamin D₃ and calcifediol[☆]



Alexander Jetter^a, Andreas Egli^{b,c,1}, Bess Dawson-Hughes^d, Hannes B. Staehelin^e, Elisabeth Stoecklin^f, Richard Goessl^g, Jana Henschkowski^{b,c}, Heike A. Bischoff-Ferrari^{b,g,*}



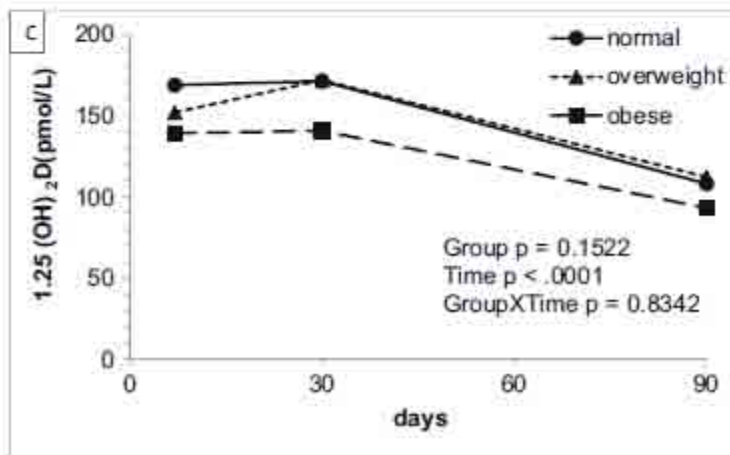
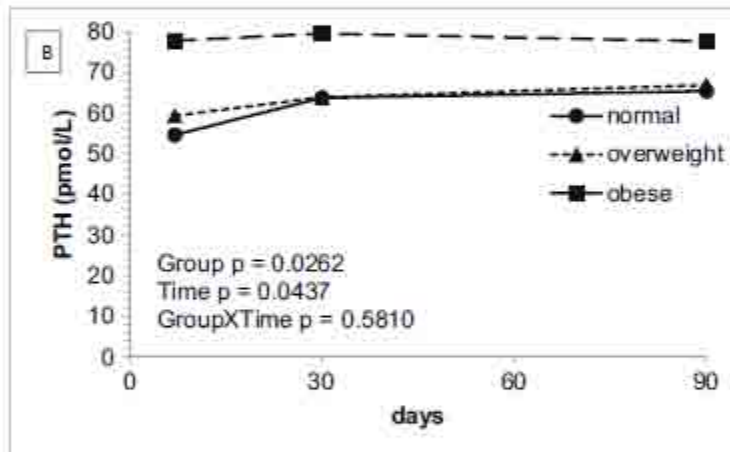
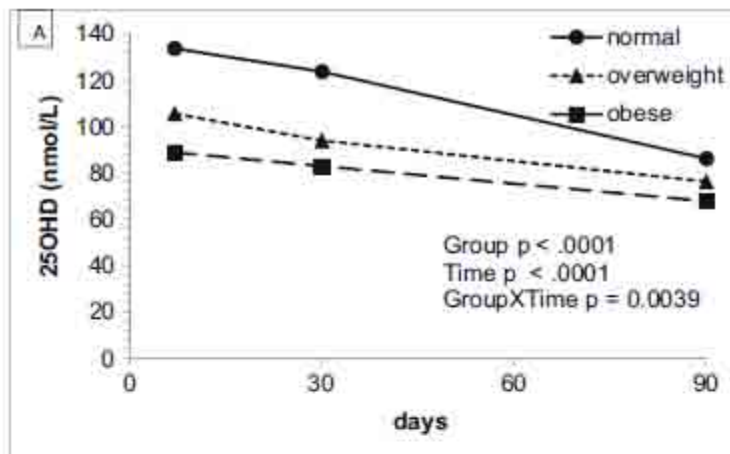


ORIGINAL ARTICLE

25-Hydroxycholecalciferol response to single oral cholecalciferol loading in the normal weight, overweight, and obese

V. Camuzzi¹ · A. C. Frigo² · M. Zaninotto³ · E. Sanguin¹ · M. Plebani³ · M. Boscaro¹ ·
L. Schiavon¹ · G. Luisetto¹

Received: 15 July 2015 / Accepted: 14 March 2016
© International Osteoporosis Foundation and National Osteoporosis Foundation 2016

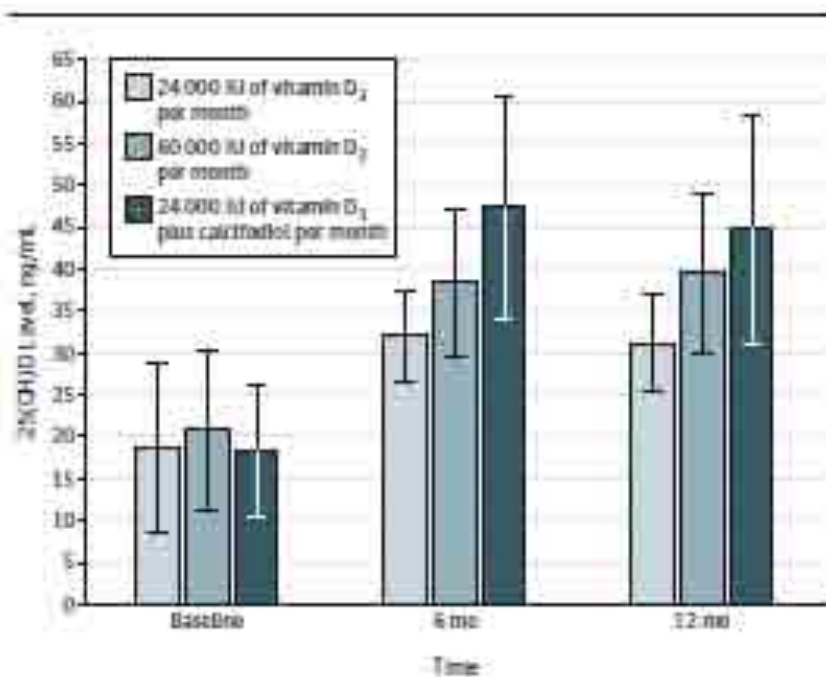


Camozzi et al, 2016

Monthly High-Dose Vitamin D Treatment for the Prevention of Functional Decline

A Randomized Clinical Trial

Helke A. Bischoff-Ferrari, MD, DrPH; Bess Dawson-Hughes, MD; E. John Orav, PhD; Hannes B. Staehelin, MD; Otto W. Meyer, MD; Robert Theller, MD; Walter Dick, MD; Walter C. Willett, MD, DrPH; Andreas Egli, MD



At the 6-month and 12-month follow-ups, the mean 25(OH)D levels differed significantly by treatment ($P < .001$). 25(OH)D indicates 25-hydroxyvitamin D; error bars, SD. To convert 25(OH)D level to nanomoles per liter, multiply by 2.496.

ORIGINAL RESEARCH

Dose-Dependent Short-Term Effects of Single High Doses of Oral Vitamin D₃ on Bone Turnover Markers

Maurizio Rossini · Silvano Adami · Ombretta Viapiana ·
Elena Fracassi · Luca Idolazzi · Maria Rosaria Povino ·
Davide Gatti

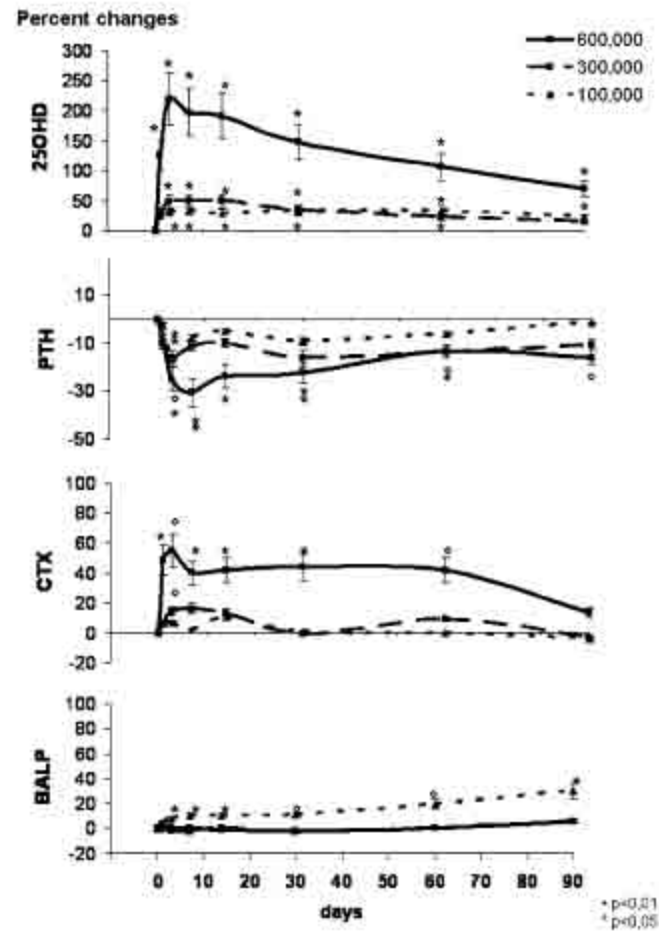


Fig. 1 Effects (percent changes $\pm$ SD vs. baseline) of the three single oral boluses of 600,000, 300,000, and 100,000 IU vitamin D₃ on 25OHD, PTH, CTX, and BALP serum levels. * $p < 0.01$, ° $p < 0.05$

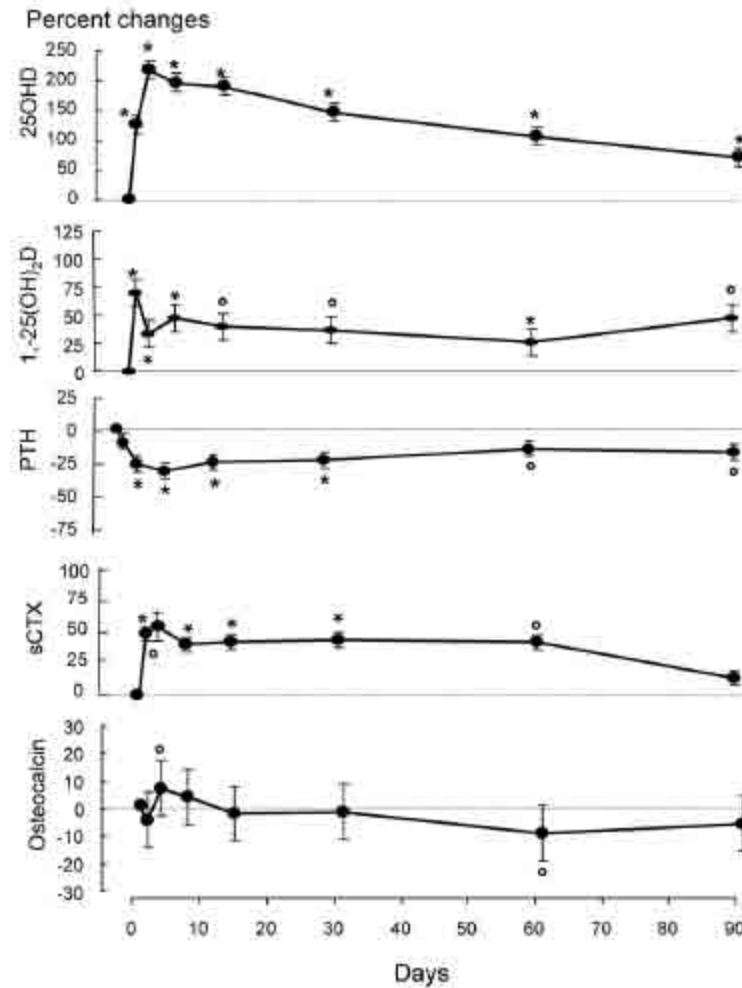


FIG. 1. Effects (percent changes $\pm$ SEM vs. baseline) of a single oral bolus of 600,000 IU vitamin D₃ on 25OHD, 1,25(OH)₂D, PTH, sCTX, and osteocalcin serum levels. *, $P < 0.01$; °, $P < 0.05$.

Trattamento con Vitamina D nell'osteoporosi

Elementi da considerare

- Caratteristiche del paziente (possibile carenza di Vit D – dosaggio ematico?)
- Dose : in media, 600-800 U/die
- (Obiettivo: portare la concentrazione di Vit D a livelli di sufficienza)
- Aderenza alla restante terapia in caso di concomitante trattamento
- Caratteristiche del preparato di Vit D che si intende utilizzare
- Compliance del paziente
- Stile di vita del paziente- anche nell'anziano

