Ο ΡΟΛΟΣ ΤΟΥ ΑΣΒΕΣΤΙΟΥ ΚΑΙ ΤΗΣ ΒΙΤΑΜΙΝΗΣ D ΣΤΟ ΜΥΟΣΚΕΛΕΤΙΚΟ ΣΥΣΤΗΜΑ

ΓΙΩΡΓΟΣ ΤΡΟΒΑΣ
ΕΝΔΟΚΡΙΝΟΛΟΓΟΣ
ΕΡΓΑΣΤΗΡΙΟ ΕΡΕΥΝΑΣ ΜΥΟΣΚΕΛΕΤΙΚΩΝ ΠΑΘΗΣΕΩΝ <Θ.ΓΑΡΟΦΑΛΙΔΗΣ>
ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ

"It is better to understand little than to misunderstand a lot."

-Anatole France

There are more published meta-analyses of trials of vitamin D and fracture risk (>20) than there are individual trials. It is time to stop torturing these data until new trial results emerge.

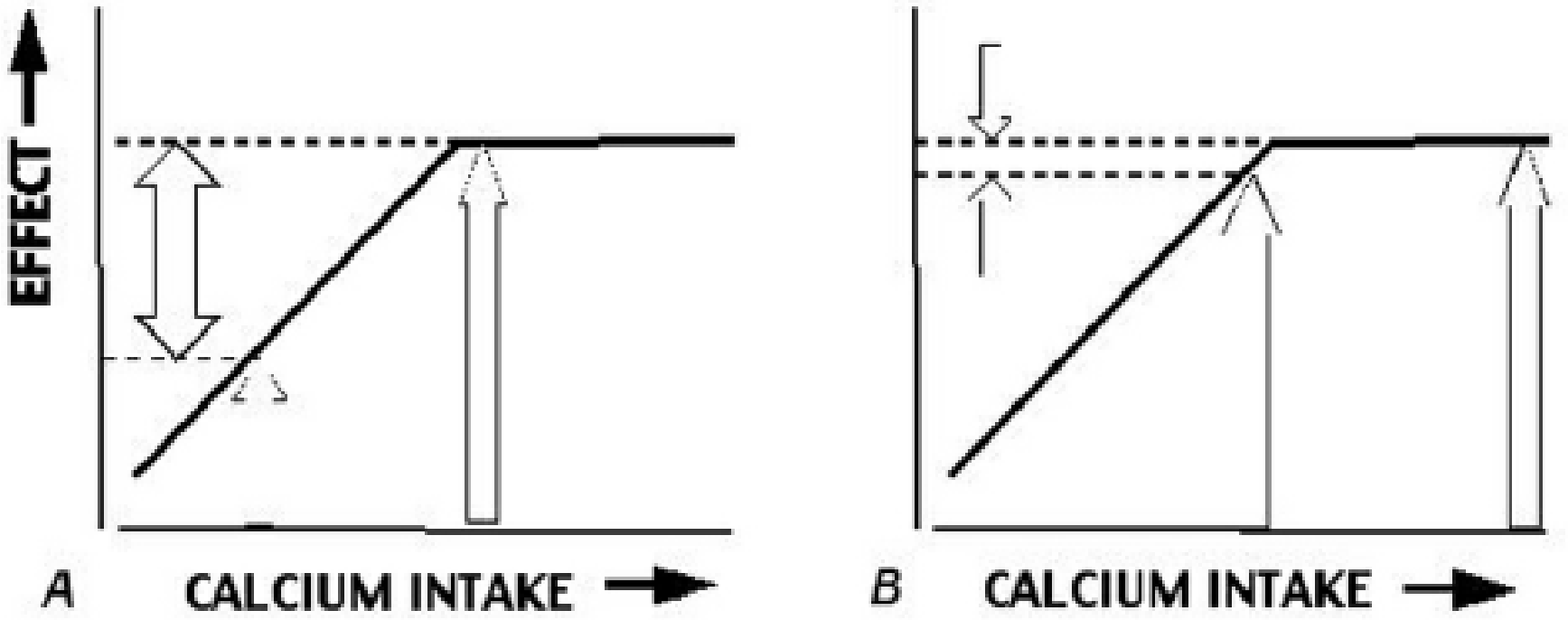
What Do We Tell Our Patients about Calcium and Vitamin D Supplementation?

Sundeep Khosla

Division of Endocrinology and Metabolism, College of Medicine, Mayo Clinic, Rochester, Minnesota 55905

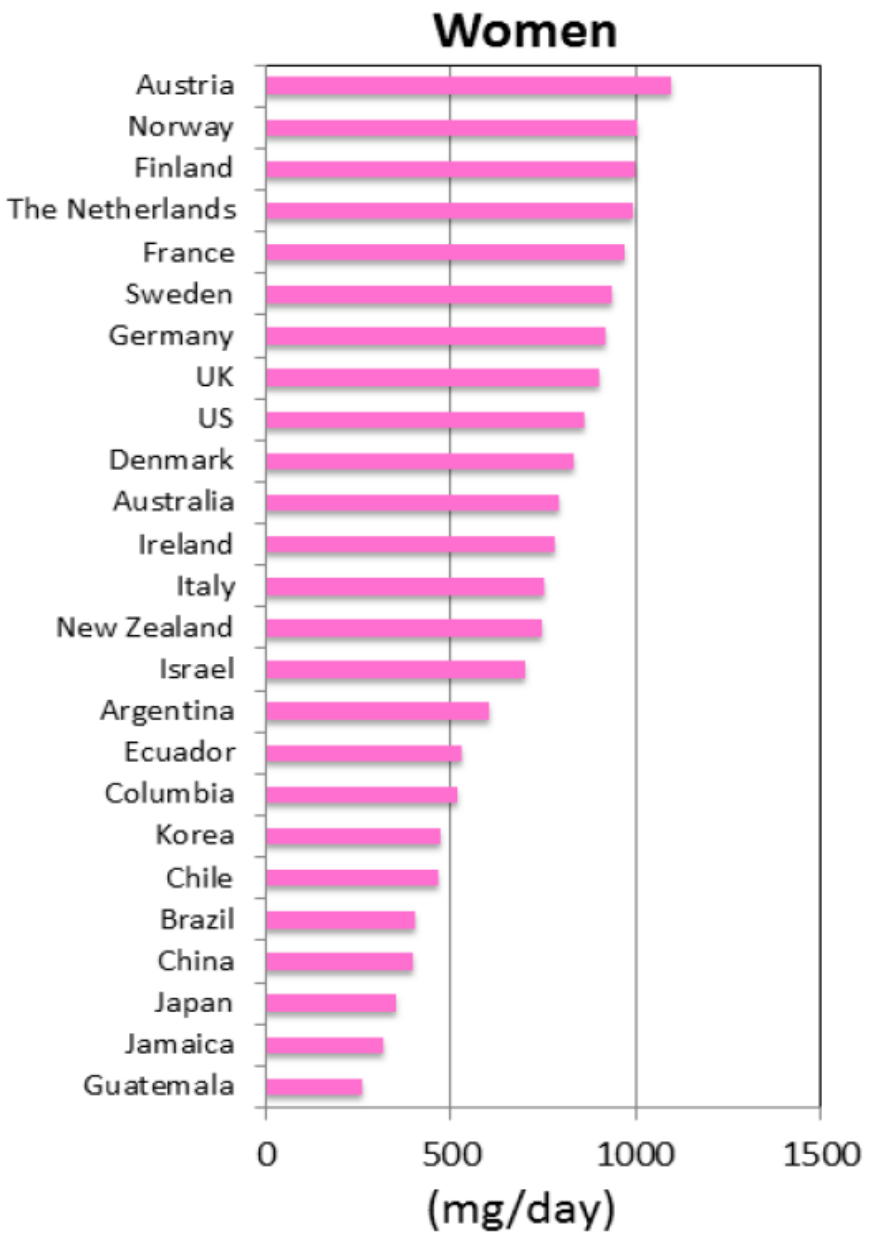
Πρόσφατα είδα μια γυναίκα στην οποία μεταξύ των άλλων στο παρελθόν της είχα συστήσει 800 μον D και 1200 mg Ca ημερησίως. Στη συζήτηση μαζί της διαπίστωσα ότι παίρνει από διάφορα συμπληρώματα 6000 μον D ημερησίως και έχει διακόψει το συμπλήρωμα του ασβεστίου. Όταν την ρώτησα γιατί έκανε αυτές τις αλλαγές μου είπε ότι έχει πληροφορίες από διάφορες πηγές ότι η βιταμίνη D είναι καλή γιατί προλαμβάνει τα κατάγματα ,τον καρκίνο και τις καρδιοπάθειες ενώ το ασβέστιο προκαλεί καρδιακά επεισόδια.

Ενώ στην αρχή εκνευρίστηκα κατάλαβα ότι από την πλευρά της προσπαθούσε να είναι μια ενημερωμένη ασθενής και (έκτος από το γεγονός ότι δεν με ρώτησε για τις αλλαγές αυτές) αυτή ήταν η αντίδραση της σε ένα κατακλυσμό από πληροφορίες που δέχονται οι ασθενείς καθημερινά για διάφορα ιατρικά θέματα.



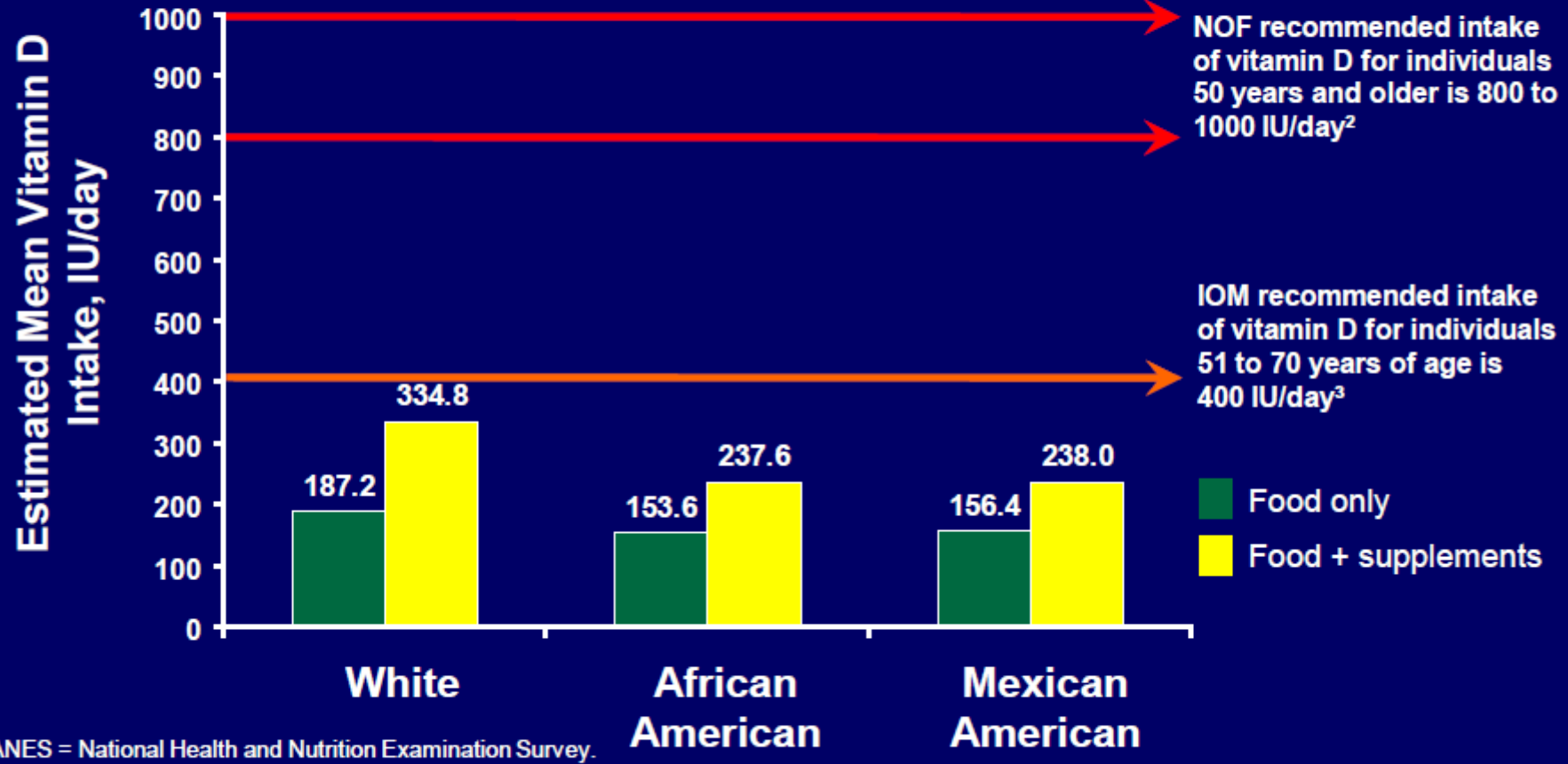
R.Heaney Am J Clin Nutr 2006

ΠΑΓΚΟΣΜΙΑ ΚΑΤΑΝΟΜΗ ΤΗΣ ΠΡΟΣΛΗΨΗΣ ΑΣΒΕΣΤΙΟΥ



Vitamin D Intake Did Not Reach 400 IU/day for Women 50 Years and Older, Even With Supplementation

NHANES III Population[1]



NHANES = National Health and Nutrition Examination Survey.

1. Calvo MS et al. *Am J Clin Nutr.* 2004;80(suppl):1710S–1716S.
2. National Osteoporosis Foundation. National Osteoporosis Foundation's Updated Recommendations for Calcium and Vitamin D_3 Intake. Available at: http://www.nof.org/prevention/calcium_and_VitmaminD.htm. Accessed April 24, 2007.
3. Institute of Medicine of the National Academies. Dietary reference intakes (DRIs): recommended intakes for individuals. Available at: http://www.iom.edu/?id=21381. Accessed April 24, 2007.

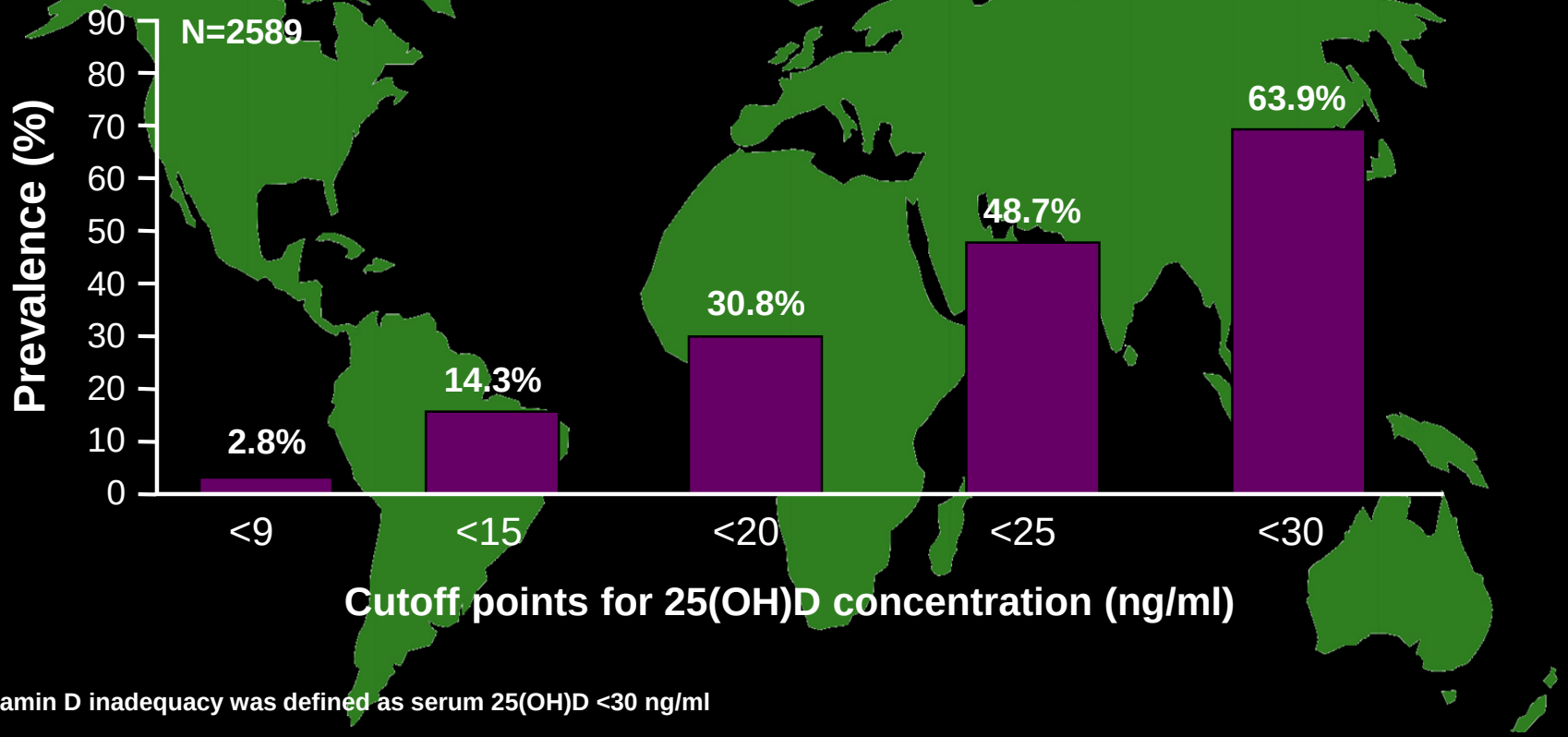
35-80% ΠΑΙΔΙΩΝ ΕΧΟΥΝ ΧΑΜΗΛΑ ΕΠΙΠΕΔΑ ΒΙΤΑΜΙΝΗΣ D

- Σαουδική Αραβία
- Ινδία
- Τουρκία
- Νέα Ζηλανδία
- Ισραήλ
- Αίγυπτος
- Λίβανος
- Χονγκ-Κονγκ
- Κίνα
- Λιβύη
- Ισπανία
- Αυστραλία
- Σαν Ντιέγκο
- Βορειοανατολική Αμερική

According to a recent study,

Almost Two-Thirds of Postmenopausal Women Have Vitamin D Inadequacy*

In a cross-sectional, observational, international study in 2589 postmenopausal women with osteoporosis



Vitamin D inadequacy was defined as serum 25(OH)D <30 ng/ml

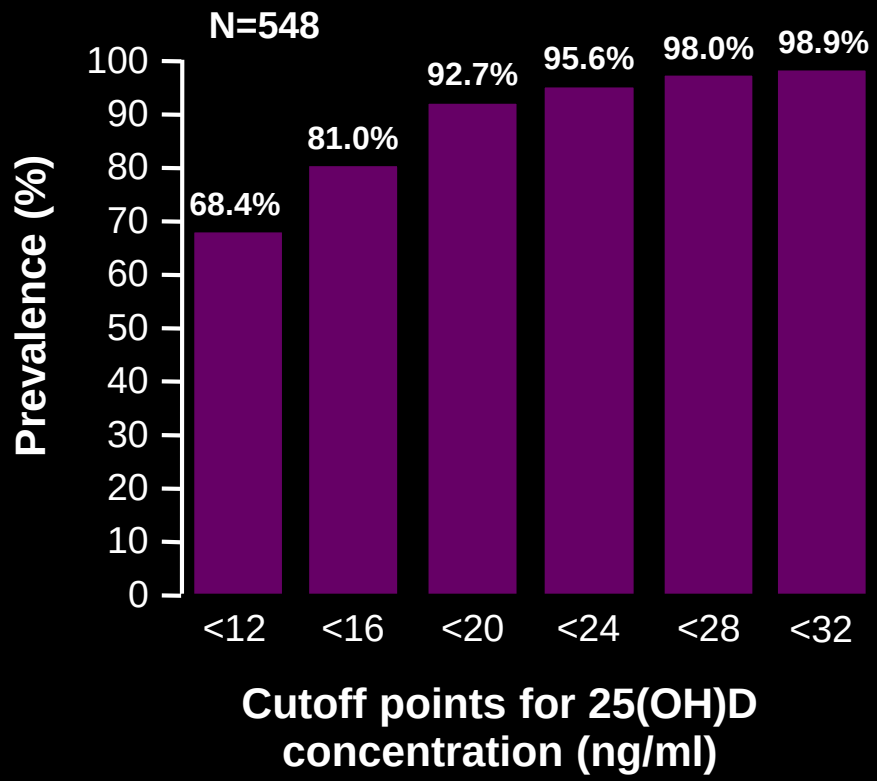
Lips P et al. Poster presented at ASBMR, Nashville, TN, USA, September 23–27, 2005

Vitamin D Deficiency in Older Men

Eric Orwoll, Carrie M. Nielson, Lynn M. Marshall, Lori Lambert, Kathleen F. Holton, Andrew R. Hoffman, Elizabeth Barrett-Connor, James M. Shikany, Tien Dam, and Jane A. Cauley, for the Osteoporotic Fractures in Men (MrOS) Study Group

J Clin Endocrinol Metab 94: 1214–1222, 2009)

Virtually All Patients Hospitalized for Nontraumatic Fractures Had Vitamin D Inadequacy*—Retrospective Arm



- Patients >60 years old hospitalized for nontraumatic fractures
- Serum 25(OH)D< 30 ng/ml in 97.8%
- Patients had no vitamin D supplementation

ΠΡΟΣΛΗΨΗ ΑΣΒΕΣΤΙΟΥ ΣΕ ΔΕΙΓΜΑ ΕΛΛΗΝΙΚΟΥ ΠΛΗΘΥΣΜΟΥ

Ε. ΓΡΗΓΟΡΙΟΥ[1] *, Γ. ΤΡΟΒΑΣ[2], Σ. ΤΟΥΡΝΗΣ[2], Κ. ΚΑΤΣΑΛΗΡΑ[2], Α. ΓΑΛΑΝΟΣ[2], Γ. ΔΕΔΟΥΣΗΣ[1], Ν. ΠΑΠΑΙΩΑΝΝΟΥ[2]

1. ΕΡΓΑΣΤΗΡΙΟ ΒΙΟΛΟΓΙΑΣ, ΒΙΟΧΗΜΕΙΑΣ, ΦΥΣΙΟΛΟΓΙΑΣ ΤΟΥ ΑΝΘΡΩΠΟΥ ΚΑΙ ΤΩΝ ΜΙΚΡΟΟΡΓΑΝΙΣΜΩΝ, ΤΜΗΜΑ ΕΠΙΣΤΗΜΗΣ ΔΙΑΤΡΟΦΗΣ ΚΑΙ ΔΙΑΙΤΟΛΟΓΙΑΣ, ΧΑΡΟΚΟΠΕΙΟΥ ΠΑΝΕΠΙΣΤΗΜΙΟΥ
2. ΕΡΓΑΣΤΗΡΙΟ ΕΡΕΥΝΑΣ ΠΑΘΗΣΕΩΝ ΜΥΟΣΚΕΛΕΤΙΚΟΥ ΣΥΣΤΗΜΑΤΟΣ "Θ.ΓΑΡΟΦΑΛΙΔΗΣ", ΙΑΤΡΙΚΗ ΣΧΟΛΗ, ΕΘΝΙΚΟ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ

ΕΙΣΑΓΩΓΗ: Το ασβέστιο και η βιταμίνη D είναι στοιχεία - κλειδιά για την πρόληψη και αντιμετώπιση της οστεοπόρωσης, αν η πρόσληψη τους είναι επαρκής.

Διάφορες μελέτες έχουν δείξει ότι το ισοζύγιο του ασβεστίου στον ανθρώπινο οργανισμό είναι βέλτιστο όταν η ημερήσια πρόσληψη είναι 1000 με 1200mg.

Σκοπός της παρούσης μελέτης είναι να εκτιμηθεί η ημερήσια πρόσληψη ασβεστίου σε γυναίκειο Ελληνικό πληθυσμό.

ΜΕΘΟΔΟΙ: Στα πλαίσια των εξορμήσεων του συλλόγου υποστήριξης ασθενών με οστεοπόρωση για την ανίχνευση παραγόντων κίνδυνου που επιδρούν στο σκελετό καταγράφηκαν τα δημογραφικά χαρακτηριστικά και μέσω ερωτηματολογίου έγινε υπολογισμός της ημερησίας πρόσληψης ασβεστίου σε ελληνίδες γυναίκες από όλες σχεδόν τις περιοχές της Ελλάδος αγροτικές και αστικές.

ΑΠΟΤΕΛΕΣΜΑΤΑ: Ρωτήθηκαν 10216 άτομα μέσης ηλικίας 58.77 ετών (εύρος 18-97) με Βάρος 71.06 ±12.51(μέση τιμή±ΤΑ),΄Υψος 1.61±0.07 και ΔΜΣ=27.50±4.84. Η ανάλυση ανά κατηγορία πρόσληψης ασβεστίου έδειξε: <400mg στο 21,8%, 400-800mg στο 28,1%, 800-1200mg στο 21.4% και >1200 στο 28.7% του συνόλου των ερωτηθέντων. Περαιτέρω ανάλυση ανά ηλικιακή ομάδα κατέδειξε ότι το 24.7% των ατόμων κάτω των 40 ετών είχαν πρόσληψη μικρότερη των 400mg ημερησίως ενώ το αντίστοιχο ποσοστό σε άτομα άνω των 80 ετών ήταν 16.4%.

ΣΥΜΠΕΡΑΣΜΑΤΑ: Περίπου το 50% των ερωτηθέντων είχαν ημερήσια πρόσληψη ασβεστίου κάτω από 800mg με τα άτομα κάτω των 40 ετών να έχουν υψηλότερο ποσοστό κάτω των 400mg σε σύγκριση με τις γυναίκες άνω των 80ετων.

Σχεδιασμός μελέτης OSTEOS II

- **Σκοπός μελέτης:**

Επιπολασμός ανεπάρκειας βιταμίνης D στον ελληνικό πληθυσμό

- **Πληθυσμός μελέτης**

N= 973 υγιείς 836 γυναίκες & 134 άνδρες

Ηλικία > 18 ετών

Στρατολόγηση: εκδηλώσεις που οργανώνει Σύλλογος Υποστήριξης Ασθενών με Οστεοπόρωση στο νομό Αττικής και σε διάφορους νομούς της χώρας

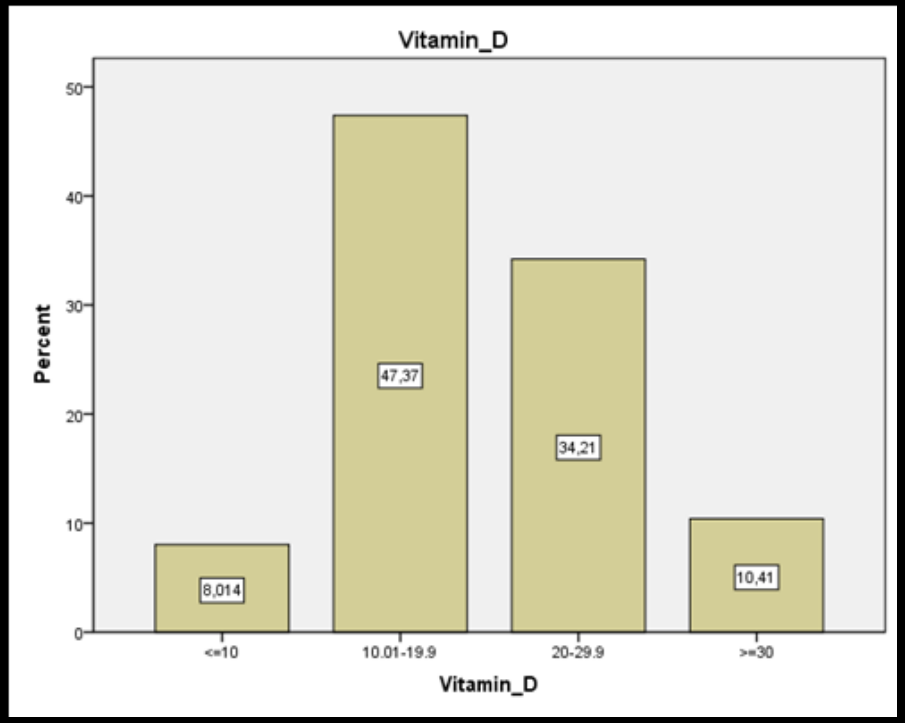
- **Υλικά και Μεθοδοι**

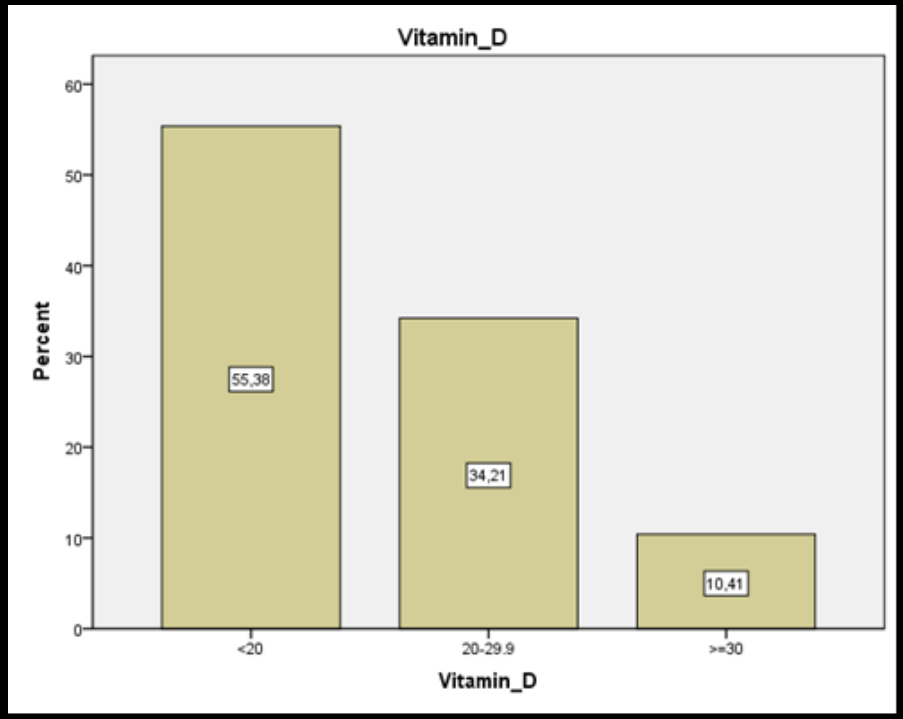
12ώρη νηστεία

10mL φλεβικού αίματος σε φιαλίδιο χωρίς αντιπηκτικό (άμεση απομόνωση ορού), για μέτρηση **βιοχημικών δεικτών** (25(OH)D, Ολικό μόριο παραθορμόνης , Ολικό ασβέστιο, Φωσφόρος, Οστικό κλάσμα αλκαλικής φωσφατάσης, κρεατινίνη

Αποτελέσματα

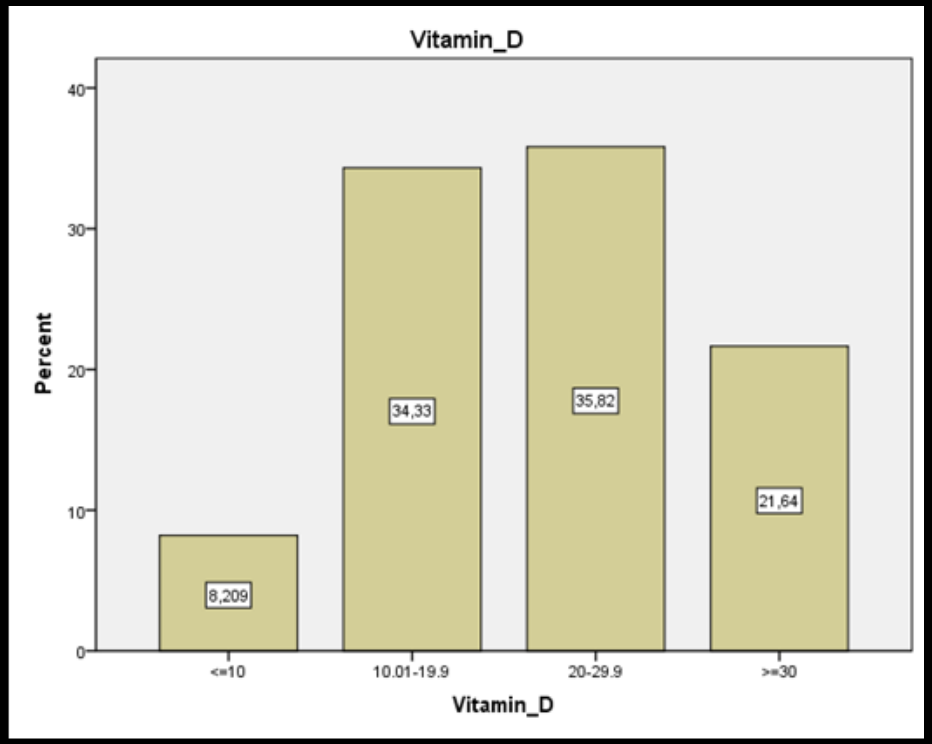
N=836 γυναίκες

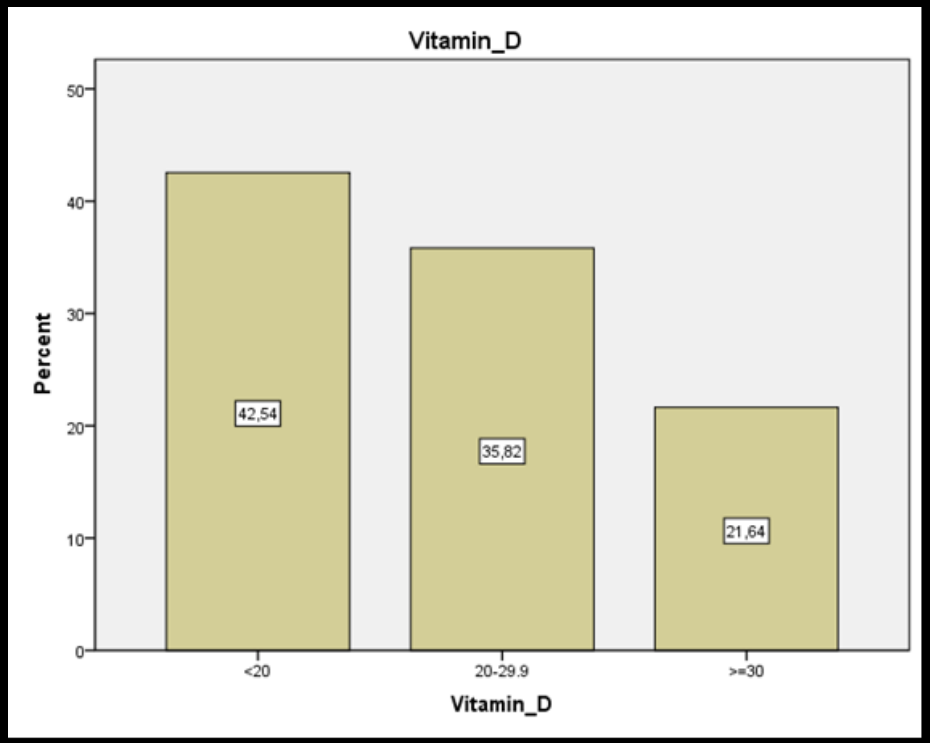




Αποτελέσματα

N=134 άνδρες

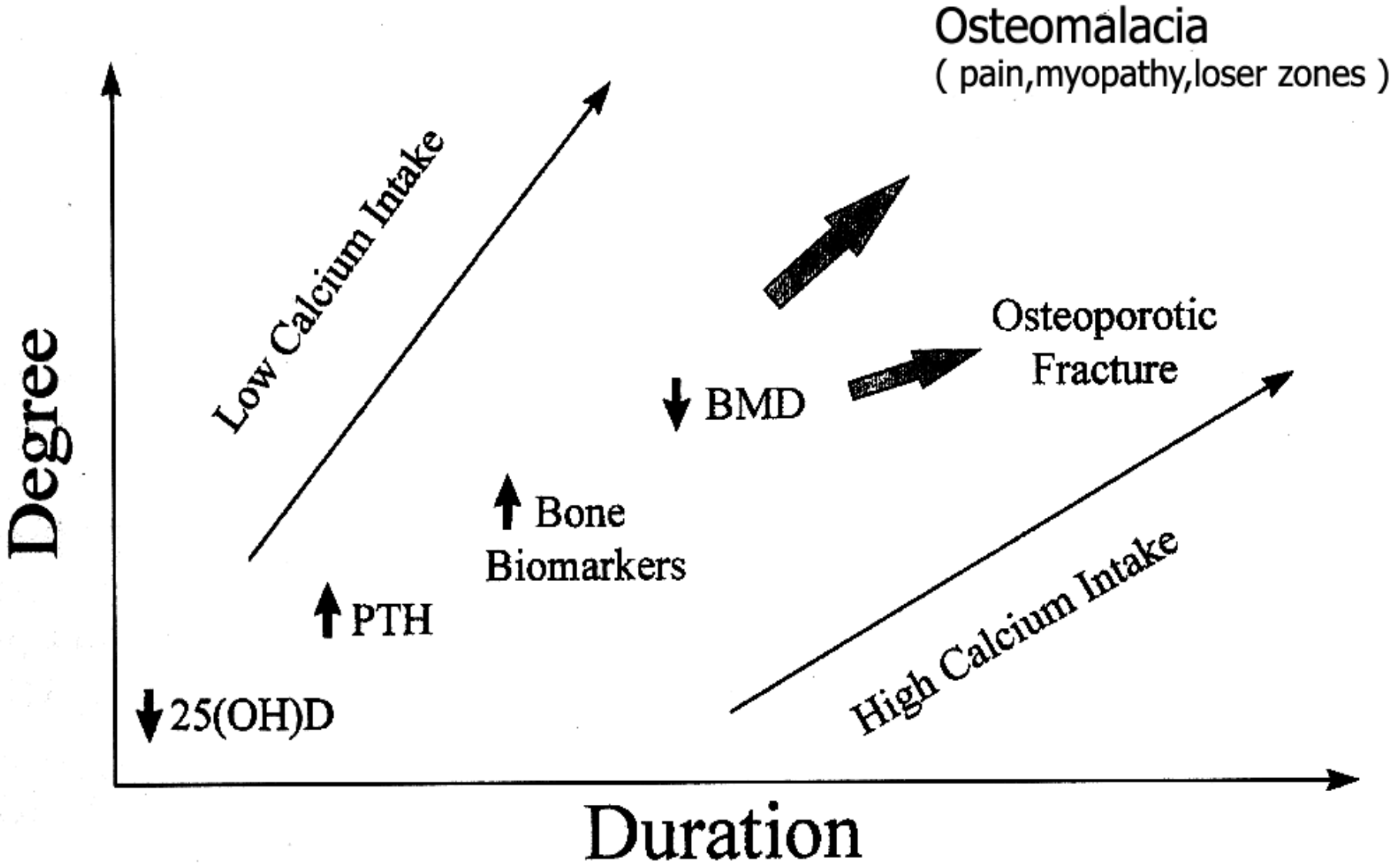


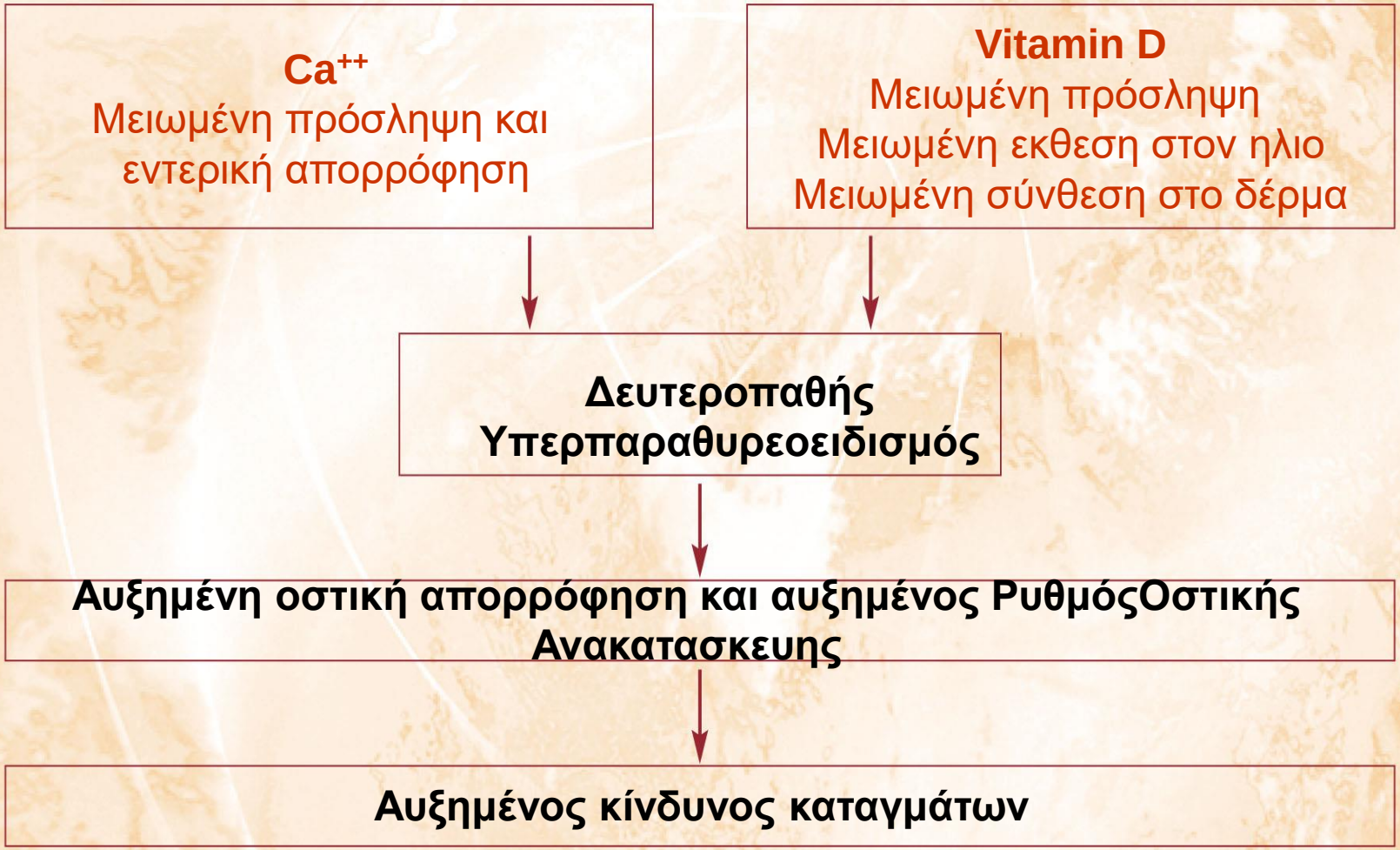


Οστεοπάθεια της υποβιταμίνωσης D

M. Parfitt

Vitamin D Deficiency in the Elderly





Fardellone P et al. Am J Clin Nutr 1998; 67:1273-78

Table 2. Vitamin D (25-(OH)D) levels and their impact on bone health.

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

*25 nmol/L is equivalent to 10 ng/mL, 50 nmol/L to <20 ng/mL, and 75 nmol/L to 30 ng/mL.

ESCEO 2013

ΕΠΙΠΕΔΑ ΒΙΤΑΜΙΝΗΣ D ΚΑΙ ΚΑΤΑΓΜΑΤΑ ΤΟΥ ΙΣΧΙΟΥ

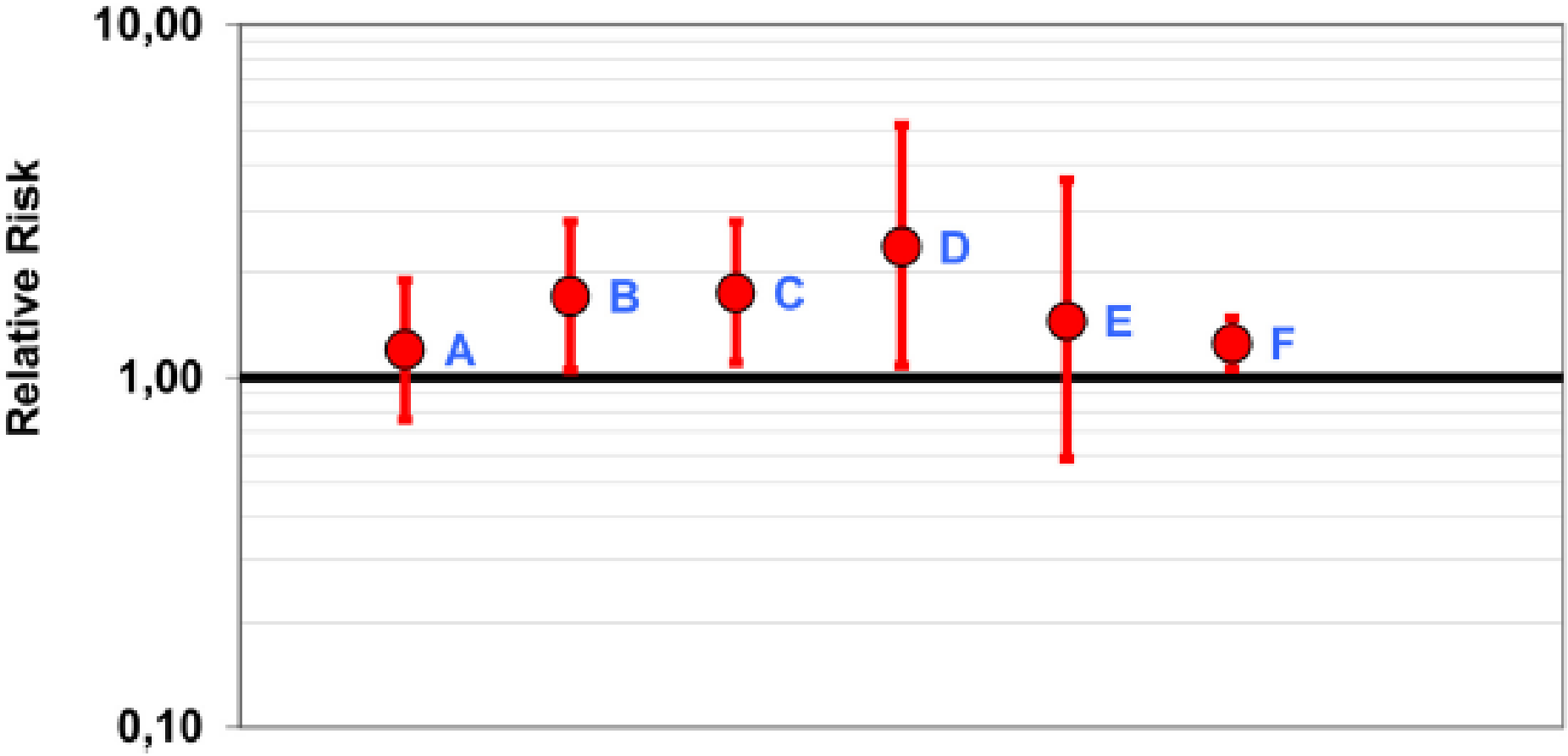


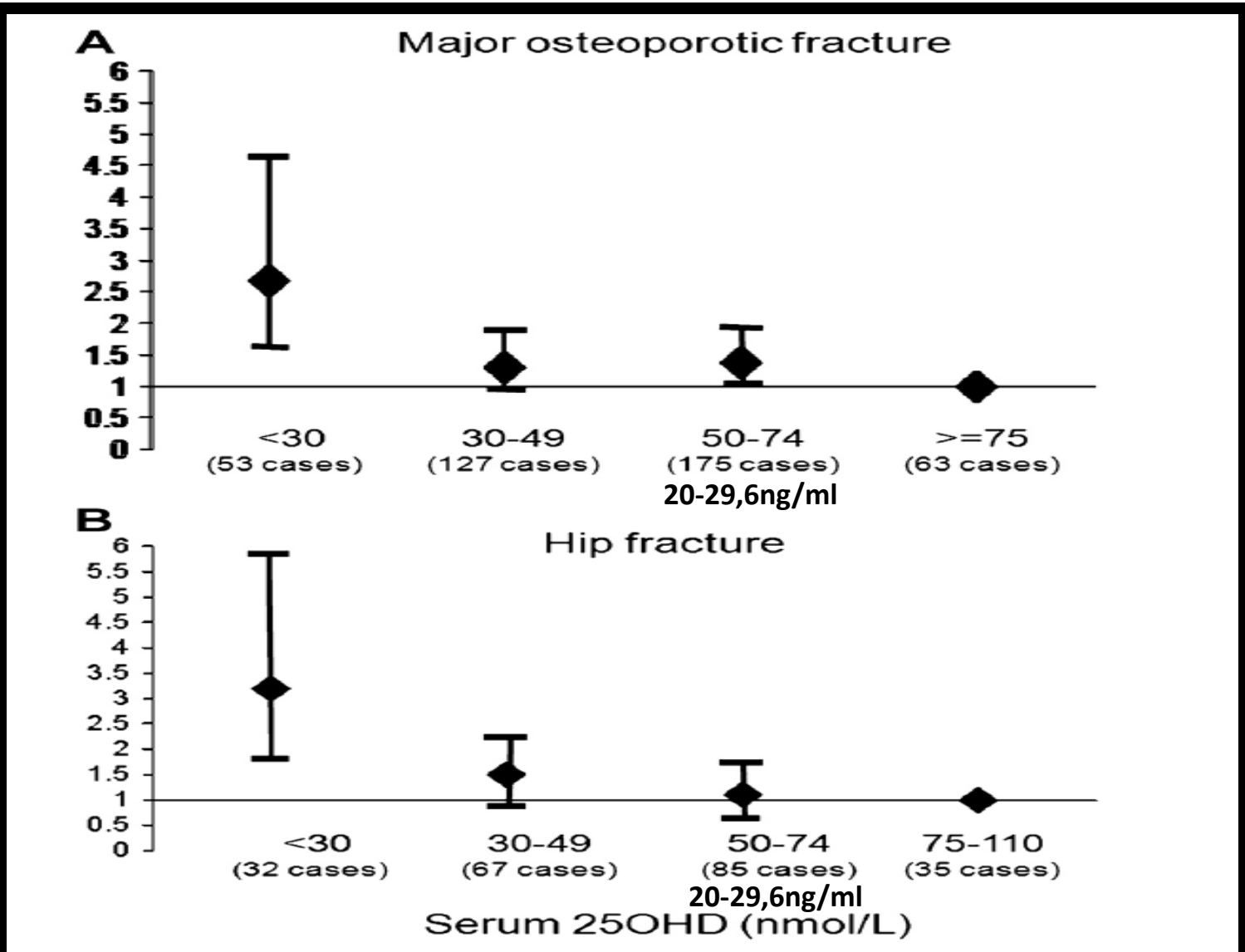
Figure 3. Relative risk estimates with 95% confidence intervals for hip fracture at plasma 25(OH)D of less than 50 nmol/L in prospective studies.

Original Article

Serum 25-hydroxyvitamin D and risk of major osteoporotic fractures in older U.S. adults[1†]

Anne C. Looker, Ph.D

National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville MD



JBMR 2012

ΕΊΝΑΙ ΑΠΟΤΕΛΕΣΜΑΤΙΚΗ Η ΧΟΡΗΓΗΣΗ ?

Calcium and Vitamin D Supplementation in Postmenopausal Women

John F. Aloia, Ruban Dhaliwal, Albert Shieh, Mageda Mikhail, Shahidul Islam, and James K. Yeh

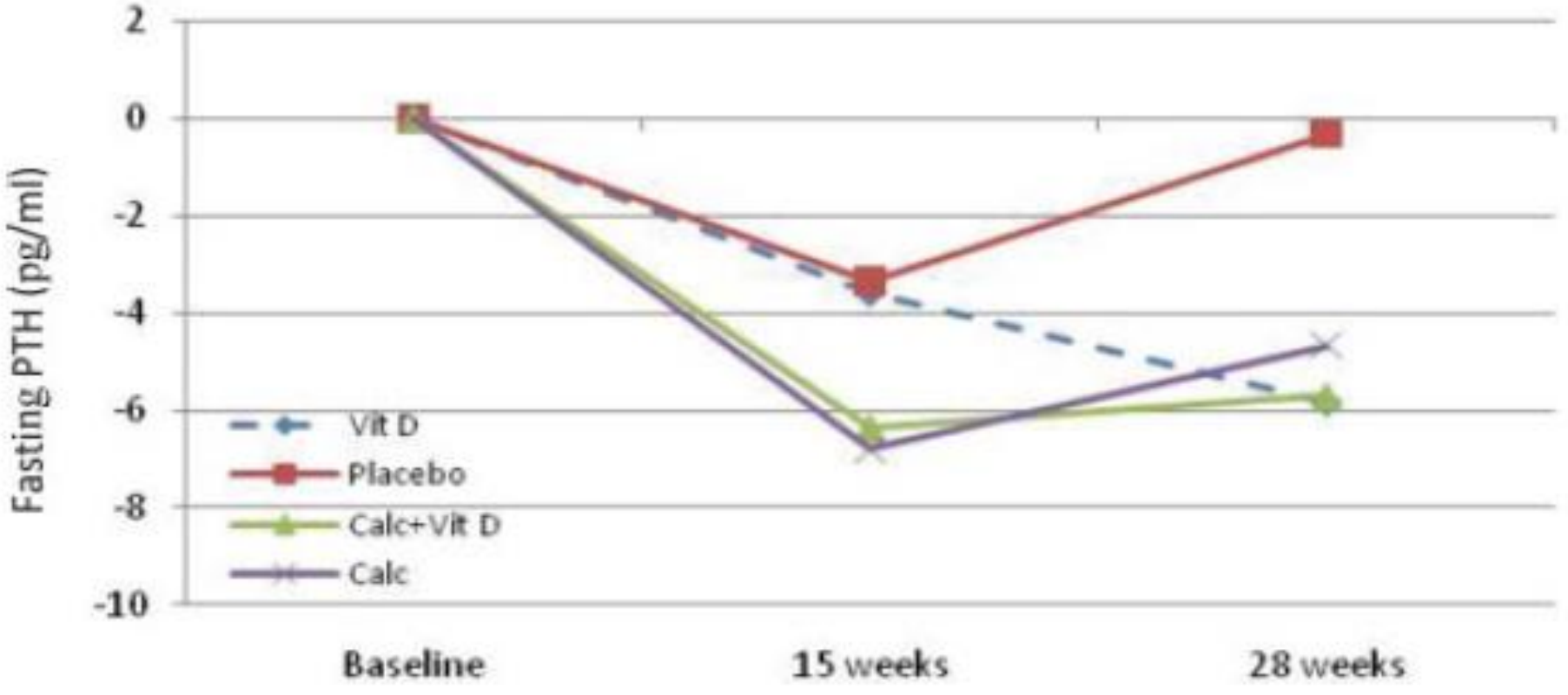
Winthrop University Hospital, Bone Mineral Research Center, Mineola, New York 11501

J Clin Endocrinol Metab, November 2013, 98(11):E1702–E1709

Table 1. Baseline Characteristics[a]

Variable	Randomization Group			
	Vitamin D	Calcium and Vitamin D	Calcium	Placebo
Age, y	59.7 (7.1)	57.6 (7.1)	60 (8.)5	58.6 (6.7)
BMI, kg/m^2	26.9 (3.6)	27.4 (3.9)	26.7 (3.3)	26.8 (3.9)
Dietary vitamin D, IU/d	180 (163)	158 (105)	185 (140)	215 (205)
Dietary Ca, mg/d	876 (310)	907 (288)	906 (320)	890 (259)
PTH, pg/mL	37.4 (16)	33.5 (13)	39.1 (17)	35.7 (15)
P1NP, μg/L	55.8 (21)	52.5 (18)	53.8 (21)	56.3 (21)
CTX, ng/mL	0.53 (0.21)	0.47 (0.17)	0.54 (0.25)	0.51 (0.21)
1,25D, pmol/L	113 (42)	108 (37)	115 (29)	113 (34)
25(OH)D, nmol/L	64 (16)	69 (17)	66 (19)	67 (17)
Urinary Ca/Cr	0.11 (0.07)	0.12 (0.06)	0.10 (0.07)	0.11 (0.07)

[a] Reference laboratory ranges are as follows: PTH, 17–72 pg/mL; P1NP, 16–96 μg/L; CTX, 0.142–1.351 ng/mL; 1,25(OH)$_2$D, 39–193 pmol/L; 25(OH)D, 50–125 nmol/L; urinary Ca/Cr, <0.37



Conclusions: Fasting PTH declines with vitamin D supplementation. PTH declines after calcium intake. Supplementation of the diet with 1200 mg calcium/d reduces bone turnover markers, whereas supplementation with up to100 μg vitamin D_3/d does not. (***J Clin Endocrinol Metab*** **98: E1702–E1709, 2013)**

Supplemental file 4. Meta-analyses of the anti-fracture efficacy of vitamin D (alone of in combination with calcium)

Bischoff-Ferrari 2005 (282)	*Combined calcium and vitamin D (700-800 IU/d) supplementation reduces the risk of hip fractures compared with placebo*
Boonen 2007 (99)	*Vitamin D alone (independent of dose 400IU/d or more) does not reduce the risk of hip fractures.* *combined vitamin D and vitamin D supplementation reduces the risk of non-vertebral fractures and hip fractures compared with placebo, and reduces the risk of hip fractures compared with vitamin D alone.*
Jackson 2007 (283)	Vitamin D alone does not reduce the risk of vertebral fractures.
Tang 2007 (103)	*Combined calcium and vitamin D supplementation reduces the risk of any fractures.* *Calcium alone is equally effective to reduce the risk of any fractures compared with combined supplementation.*
Cranney 2007 (284)	*Combined calcium (500-1200mg) and vitamin D (700-800 IU/d) supplementation reduces the risk of fractures, primarily in institutionalized elderly women, compared with placebo.*
Reid 2008 (285)	*Combined calcium and vitamin D supplementation reduced the risk of hip fractures.* *Calcium alone increases the risk of hip fractures.*
Avenell 2009 (101)	*Vitamin D alone does not reduce the risk of any fractures, hip fractures and vertebral fractures.* *Combined calcium and vitamin D supplementation reduces the risk of hip fractures compared with placebo.*
Bischoff-Ferrari 2009 (106)	Vitamin D (>400 IU/d) reduces the risk of non-vertebral fractures and hip fractures. No benefit of additional calcium on fracture risk
Chung 2009 (129)	*Inconsistent evidence for an association between vitamin D alone and the risk of fractures.* *Combined calcium and vitamin D supplementation reduces the disk of any fractures and hip fractures compared with placebo.*
Dipart group 2010 (100)	*Vitamin D alone (400-800 IU/d) does not reduce the risk of any fractures, hip fractures and vertebral fractures.* *Combined calcium and vitamin D supplementation reduces the risk of any fractures and hip fractures compared with placebo.*
Bergman 2010 (286)	*Combined calcium and vitamin D (≥800 IU/d) supplementation reduces the risk of non-vertebral fractures and hip fractures compared with placebo, and reduces the risk of non-vertebral non-hip fractures compared with calcium alone*
Lai 2010 (287)	Vitamin D alone (independent of dose < or > 800 IU/d) does not reduce the risk of hip fractures
Chung 2012 (108)	*Combined calcium and vitamin D supplementation reduces the risk of fractures in institutionalized elderly compared with placebo.*
Bischoff-Ferrari 2012 (107)	Vitamin D (792-2000 IU/d) reduces the risk of non-vertebral fractures and hip fractures. No benefit of additional calcium on fracture risk.

Calcium + vitamin D studies shown in italic

Calcium plus vitamin D supplementation and risk of fractures: an updated meta-analysis from the National Osteoporosis Foundation

Osteoporos Int Published online: 28 October 2015

C. M. Weaver[1] · D. D. Alexander[2] · C. J. Boushey[3] · B. Dawson-Hughes[4] · J. M. Lappe[5,6] · M. S. LeBoff[7] · S. Liu[8] · A. C. Looker[9] · T. C. Wallace[10,11] · D. D. Wang[12]

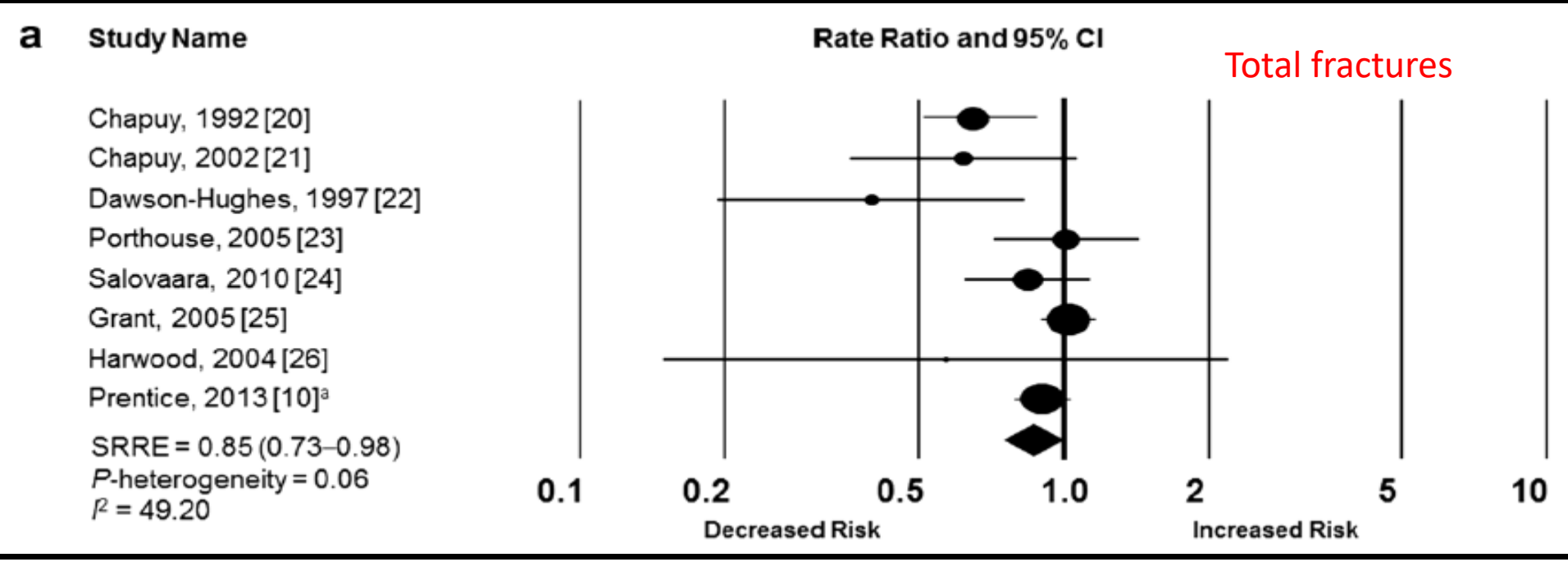
Table 1 Summary of meta-analysis results for calcium plus vitamin D supplementation versus placebo and fracture risk

Reference	Status	Vitamin D (IU/day)	Calcium (mg/day)	No. of total fracture events/total			No. of hip fracture events/total		
				RR (95 % CI)	Treatment	Control	RR (95 % CI)	Treatment	Control
Chapuy et al. [20]	Institutionalized	800	1200	0.74 (0.56–0.97)	80/1387	110/1403	0.74 (0.56–0.97)	21/1387	37/1403
Chapuy et al. [21]	Institutionalized	800	1200	0.62 (0.36–1.07)	27/393	21/190	0.62 (0.36–1.07)	27/393	21/190
Dawson-Hughes et al. [22]	Community-dwelling	700	500	0.46 (0.23–0.90)	11/187	26/202	0.36 (0.01–8.77)	0/187	1/202
Porthouse et al. [23]	Community-dwelling	800	1000	1.01 (0.71–1.43)	58/1321	91/1993	0.75 (0.31–1.80)	8/1321	17/1993
Prentice et al. [10][a]	Community-dwelling	400	1000	0.90 (0.78–1.03)	405/7530[b]	458/7801[b]	0.55 (0.32–0.97)	19/7530[b]	35/7406[b]
Salovaara et al. [24]	Community-dwelling	800	1000	0.83 (0.61–1.12)	78/1586	94/1609	2.02 (0.37–11.02)	4/1586	2/1609
Grant et al. [25]	Community-dwelling with history of fracture	800	1000	1.02 (0.89–1.16)	387/2649	377/2643	ND	ND	ND
Harwood et al. [26]	Community-dwelling with history of fracture	800	1000	0.57 (0.15–2.19)	3/39	5/37	ND	ND	ND

CI confidence interval, *ND* no data, *RR* relative risk, *WHI* Women's Health Initiative

[a] Data analyzing the WHI for adherence to assigned pills and no personal use of supplements from Table 6 in Prentice et al. [10]

[b] Data provided from WHI investigators


a
Study Name
Rate Ratio and 95% CI
Total fractures
Chapuy, 1992 [20]
Chapuy, 2002 [21]
Dawson-Hughes, 1997 [22]
Porthouse, 2005 [23]
Salovaara, 2010 [24]
Grant, 2005 [25]
Harwood, 2004 [26]
Prentice, 2013 [10]a
SRRE = 0.85 (0.73–0.98)
P-heterogeneity = 0.06
I² = 49.20
0.1
0.2
0.5
1.0
2
5
10
Decreased Risk
Increased Risk

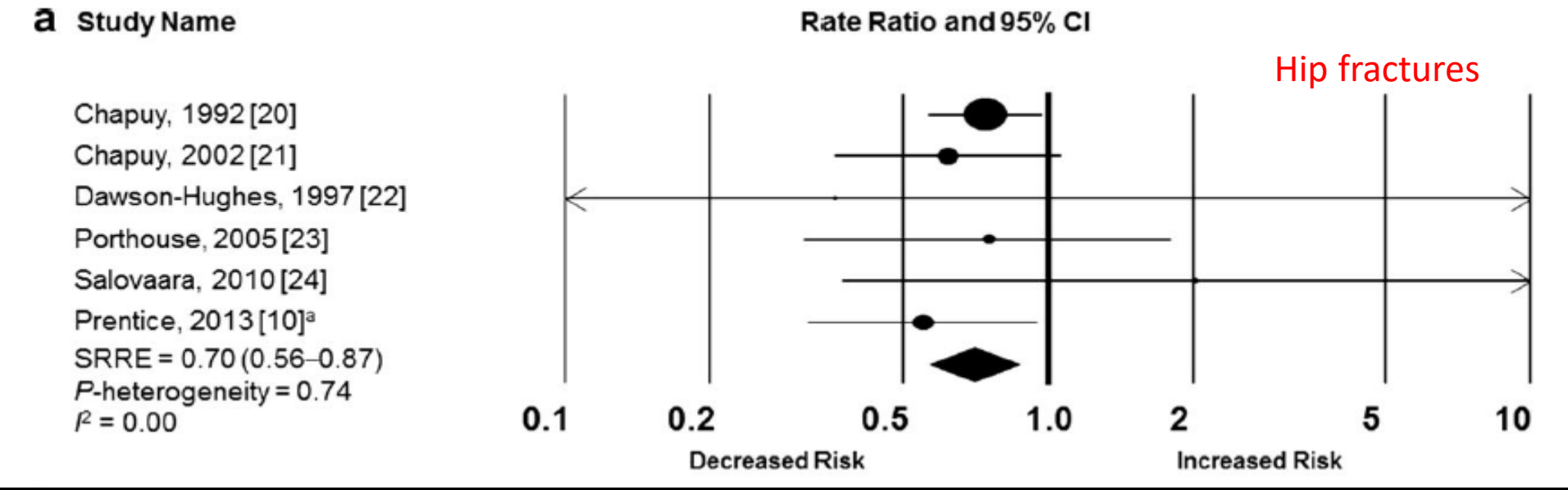

a
Study Name
Rate Ratio and 95% CI
Hip fractures
Chapuy, 1992 [20]
Chapuy, 2002 [21]
Dawson-Hughes, 1997 [22]
Porthouse, 2005 [23]
Salovaara, 2010 [24]
Prentice, 2013 [10]a
SRRE = 0.70 (0.56–0.87)
P-heterogeneity = 0.74
I² = 0.00
0.1
0.2
0.5
1.0
2
5
10
Decreased Risk
Increased Risk

Table 2. Author's interpretation of current evidence base from controlled intervention studies.

	Calcium alone	Vitamin D alone	CaD combined
BMD	Small gain	No effect	Small gain
Fractures	No effect	Conflicting evidence	Small risk reduction in the elderly
Cardiovascular events	Conflicting evidence	Conflicting evidence	Conflicting evidence
All-cause mortality	No effect	No effect	Small risk reduction in the elderly

BMD, bone mineral density; CaD, calcium and vitamin D.

Bo Abrahamsen

Ther Adv Musculoskel Dis
2017, Vol. 9(5) 107–114

The role of calcium supplementation in healthy musculoskeletal ageing

An expert consensus meeting of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) and the International Foundation for Osteoporosis (IOF)

Published online: 20 October 2016

N. C. Harvey[1,2] · E. Biver[3] · J.-M. Kaufman[4] · J. Bauer[5] · J. Branco[6] · M. L. Brandi[7] · O. Bruyère[8] · V. Coxam[9,10] · A. Cruz-Jentoft[11] · E. Czerwinski[12] · H. Dimai[13] · P. Fardellone[14] · F. Landi[15] · J.-Y. Reginster[16] · B. Dawson-Hughes[17] · J. A. Kanis[18,19] · R. Rizzoli[3] · C. Cooper[1,2,20]

- Ο συνδυασμός Ca-D έχει μια ήπια αντικαταγματική δράση σε άτομα που ζουν σε ιδρύματα όπως και στην κοινότητα.
- Η δράση αυτή δεν έχει αποδεδειχθεί για όλες τις ομάδες καταγμάτων ξεχωριστά ούτε για το Ασβέστιο μόνο του.
- Η αποτελεσματικότητα της συγχορήγησης είναι πιο εύρωστη στα άτομα υψηλού κινδύνου για έλλειψη (Ca-D).

Indications for vitamin D screening

- Bone diseases
  (e.g., rickets, osteomalacia, osteoporosis, nontraumatic fracture, or hyperparathyroidism)
- Old age
- (particularly in case of history of falls or nontraumatic fracture)
- Dark skin
  (e.g., Africans, African-Americans, Hispanics, or Asians)
- Obesity
  (e.g., adults with body mass index $>30\ kg/m^2$ and obese children with other risk factors or symptoms)
- Pregnancy or lactation (with risk factors)
  (e.g., dark-skinned or overweight, gestational diabetes, or very low exposure to sunlight, and no vitamin D supplementation)
- Sports athletes (especially indoor sports)
- Chronic kidney disease
- Liver failure
- Malabsorption syndromes
  (e.g., cystic fibrosis, inflammatory bowel disease, Crohn's disease, bariatric surgery, or radiation enteritis)
- Medications
  (e.g., antiepileptic drugs, glucocorticoids, AIDS drugs, antifungals, or cholestyramine)
- Granuloma-forming diseases
  (e.g., sarcoidosis, tuberculosis, histoplasmosis, coccidiomycosis, or berylliosis)

ΜΥΙΚΟ ΣΥΣΤΗΜΑ-ΠΤΩΣΕΙΣ

Figure 4.

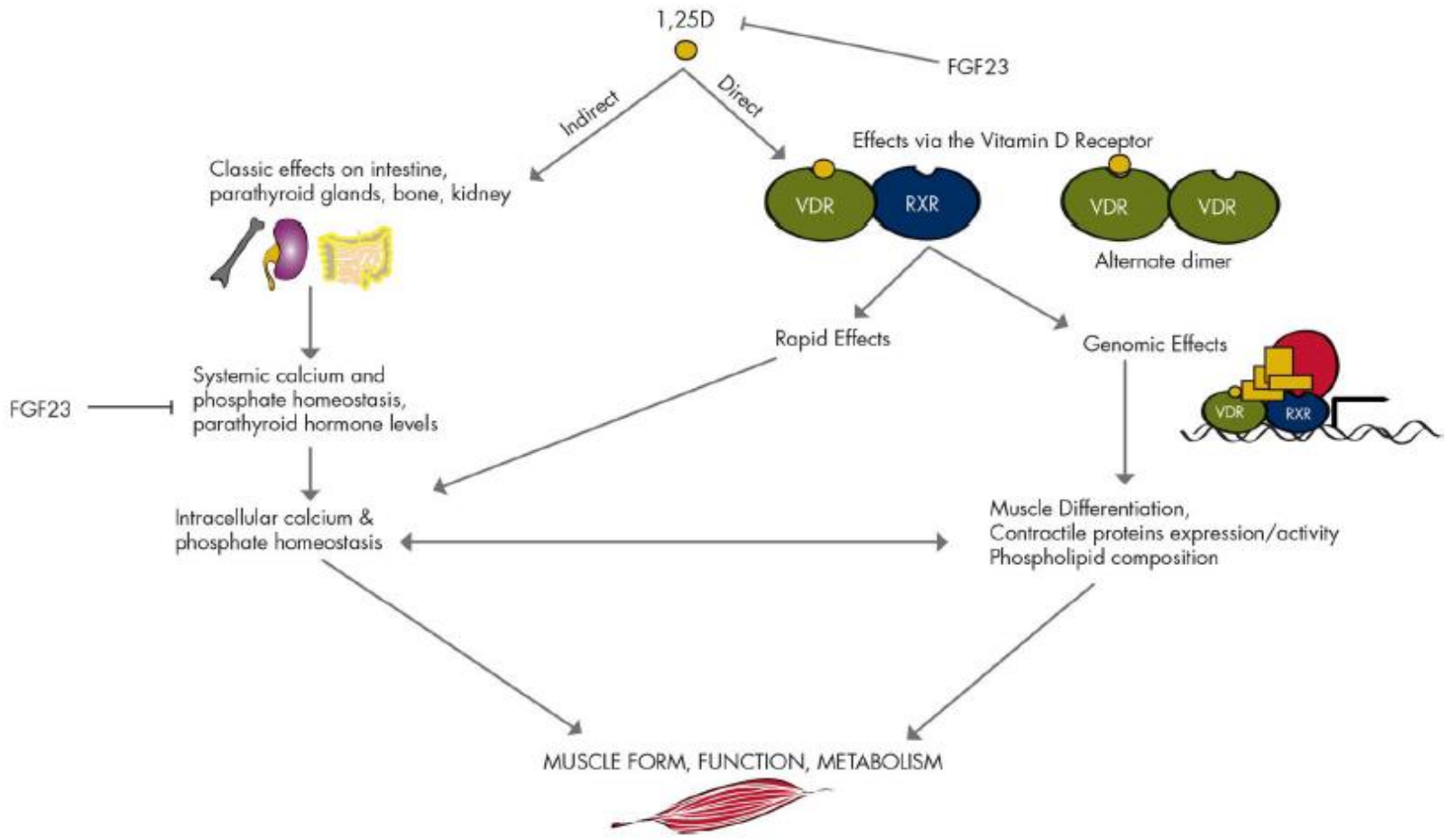


Figure 4. Direct and indirect effects of vitamin D on muscle. Data on direct effects come predominantly from *in vitro* studies and are yet to be confirmed *in vivo*, where the presence of the VDR is currently under debate.

Endocrine Reviews, February 2013, 34(1):0000–0000

Hypovitaminosis D Myopathy Without Biochemical Signs of Osteomalacic Bone Involvement

H.Glerup et al Calcif Tissue Int 2000

Table 2 Meta-analyses on vitamin D and fall prevention

Meta-analysis	Number of trials	Intervention	Control	Fall prevention effect size 95 % CI	Heterogeneity in subgroup analyses			
					Calcium supplements co-administration	Baseline vitamin D levels	Achieved vitamin D levels	Vitamin D dose effect
Bischoff-Ferrari, JAMA 2004 [33]	5 RCT	Vit D (+active D) ± calcium	Placebo ± calcium	0.78 (0.64–0.92)	No	–	–	–
Jackson, Q J Med 2007 [34]	5 RCT	Vit D ± calcium	Placebo ± calcium	0.88 (0.78–1.00)	–	–	–	–
O'Donnel, J Bone Miner Metab 2008 [39]	2 RCT	Calcitriol and alfacalcidol	Placebo	0.66 (0.44–0.98)	–	–	–	–
Richy, Calcif Tissue Int 2008 [40]	14 RCT (3 open-label trials)	Vit D (+active D) ± calcium	Placebo/control ± calcium	0.92 (0.86–0.98)	–	–	–	–
Bischoff-Ferrari, BMJ 2009 [32]	8 RCT	Vit D (+active D) ± calcium	Placebo ± calcium	0.87 (0.77–0.99)	–	–	Yes (≥60 nmol/l)	Yes (700–1000 IU/day)
Kalyani, J Am Geriatr Soc 2010 [35]	10 RCT	Vit D (+active D) ± calcium	Placebo ± calcium	0.86 (0.79–0.93)	Yes	–	–	Yes (≥ 800 IU/day)
Michael, Ann Intern Med 2010 [37]	9 RCT	Vit D (+active D) ± calcium	Placebo ± calcium	0.83 (0.77–0.89)	No	–	–	–
Murad, J Clin Endocrinol Metab 2011 [38]	26 RT	Vit D (+active D) ± calcium	Placebo/nothing ± calcium	0.86 (0.77–0.96)	Yes	Yes. Low level: risk ratio 0.53 [0.39, 0.72]	–	–
Cameron, Cochrane review 2012 [41, 42]	6 RCT in care facilities and hospitals	Vit D ± calcium	Placebo ± calcium	0.99 (0.90–1.08)	No	–	–	–
Gillespie, Cochrane review 2012 [45, 46]	11 RCT in the community	Vit D (+active D) ± calcium	Placebo/control ± calcium	0.96 (0.89–1.03)	–	Yes. Low level: risk ratio 0.70 [0.56, 0.87]	–	–
Bolland, Lancet Diabetes Endocrinol 2014 [43]	20 RCT	Vit D ± calcium	Placebo/control ± calcium	0.96 (0.91–1.01)	No	No	No (≥50 nmol/l)	–
LeBlanc, JAMA Internal Medicine 2015 [36]	11 RCT	Vit D (+active D) ± calcium	Placebo ± calcium	0.89 (0.82–0.97)	No	Yes. Low level: risk ratio 0.85 (0.73–0.98)	–	–

RCT randomised controlled trial, *RT* randomised trial, *CI* confidence interval, – not tested

- 9 από τις 12 έδειξαν μείωση του κινδύνου πτώσεων.
- Μεγάλη ετερογένεια λόγω διαφορετικών πληθυσμών, παρέμβαση (φυσική D η μεταβολίτες),μεθοδολογία ανίχνευσης πτώσεων, βασικά επίπεδα βιταμίνης D,επίπεδα που επιτυχαίνονται με την παρέμβαση .
- Αν και το ασβέστιο εμπλέκεται στην φυσιολογία των μυών οι κλινικές μελέτες δείχνουν ότι η χορήγηση της βιταμίνης D παρά του ασβεστίου οδηγεί σε μείωση των πτώσεων.

Annual High-Dose Oral Vitamin D and Falls and Fractures in Older Women

A Randomized Controlled Trial

Table 3. Incidence Rate Ratio for Falls and Fractures and Analysis Adjusted by Calcium Intake

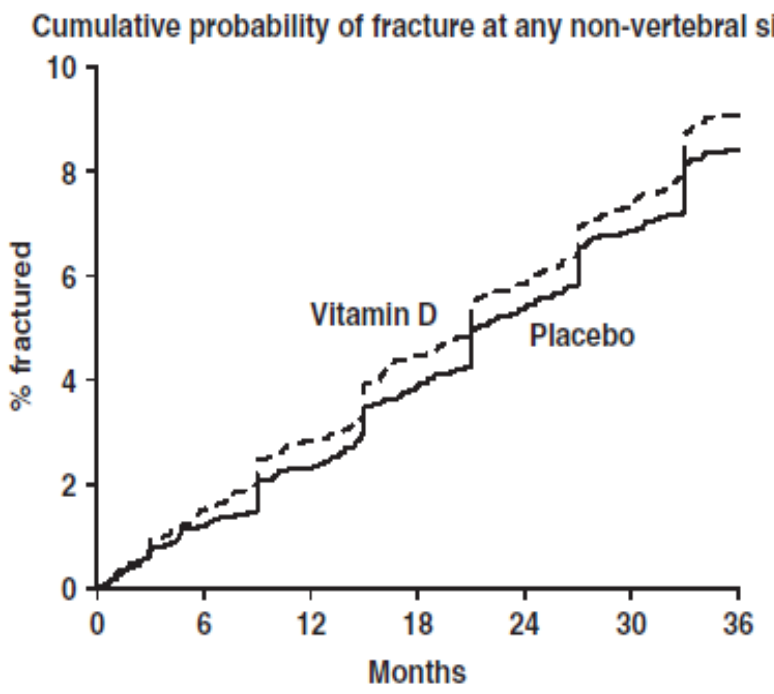
	Incidence Rate Ratio for Vitamin D Group, Estimate (95% Confidence Interval)	*P* Value
No adjustment, No.		
Falls	1.15 (1.02-1.30)	.03
Fractures	1.26 (1.00-1.59)	.047
Nonvertebral fractures	1.28 (1.00-1.65)	.06
Adjusted for calcium intake, No.		
Falls adjusted	1.16 (1.03-1.31)	.02
Fractures adjusted	1.25 (0.99-1.58)	.06
Nonvertebral fractures	1.27 (0.98-1.65)	.08

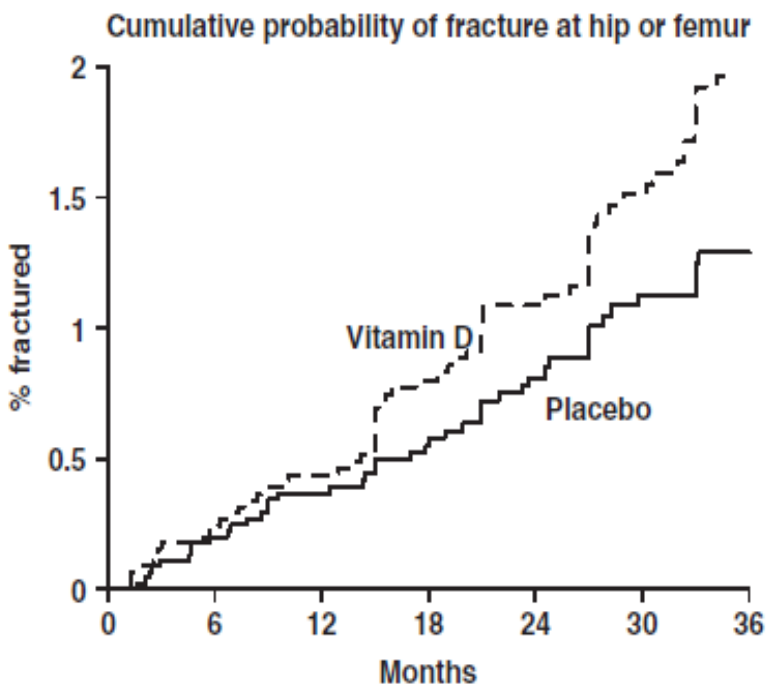
Intervention 500 000 IU of cholecalciferol or placebo.

JAMA, May 12, 2010—Vol 303, No. 18

Effect of annual intramuscular vitamin D on fracture risk in elderly men and women—a population-based, randomized, double-blind, placebo-controlled trial

H. Smith, F. Anderson[1], H. Raphael, P. Maslin, S. Crozier[2] and C. Cooper[2]





300 000 IU intramuscular (i.m.) vitamin D_2 (ergocalciferol) injection

Rheumatology 2007;46:1852–1857

Original Investigation | LESS IS MORE

Monthly High-Dose Vitamin D Treatment for the Prevention of Functional Decline
A Randomized Clinical Trial

JAMA Intern Med. 2016;176(2):175-183.

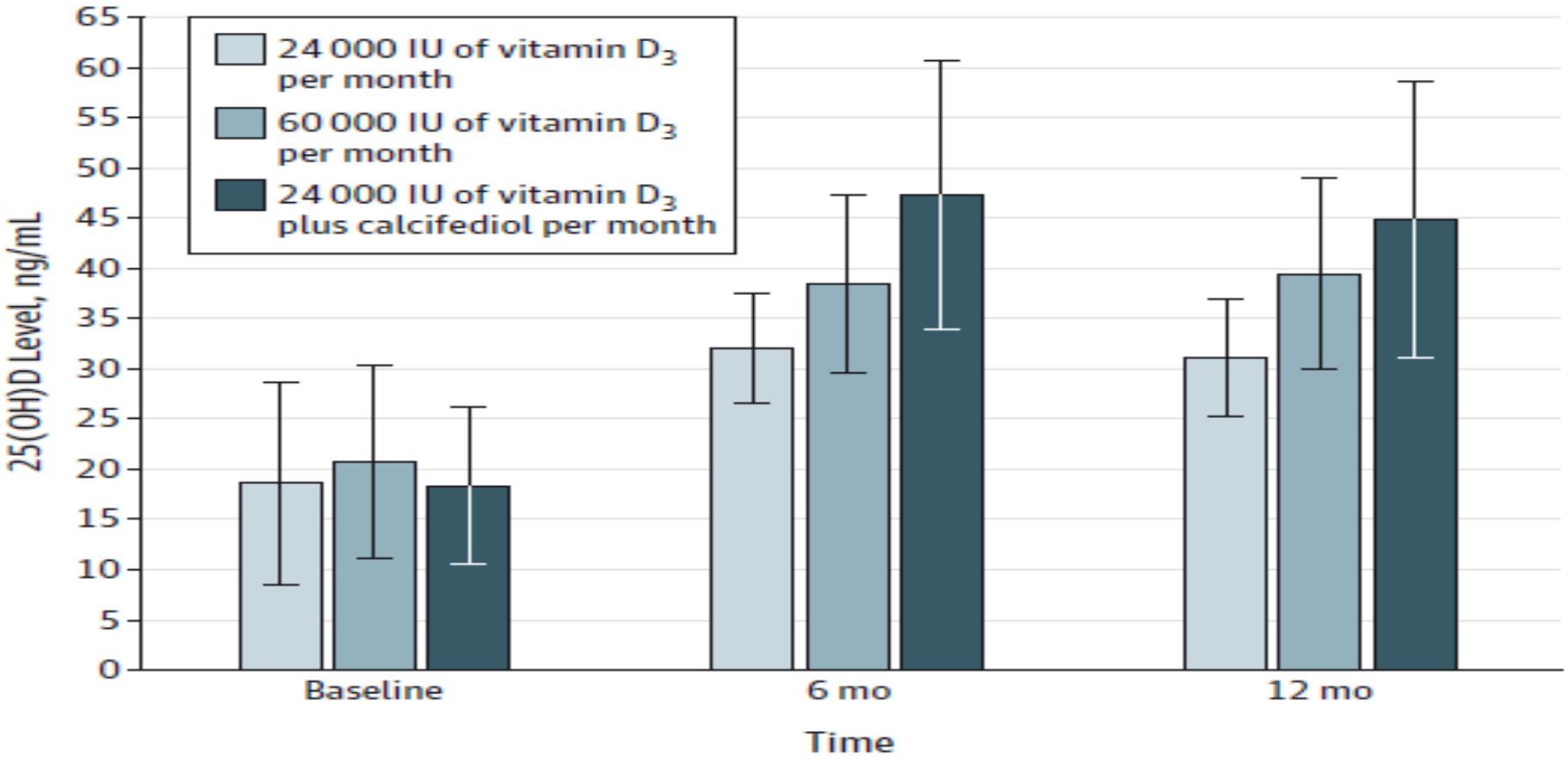
Heike A. Bischoff-Ferrari, MD, DrPH; Bess Dawson-Hughes, MD; E. John Orav, PhD; Hannes B. Staehelin, MD; Otto W. Meyer, MD; Robert Theiler, MD; Walter Dick, MD; Walter C. Willett, MD, DrPH; Andreas Egli, MD

INTERVENTIONS Three study groups with monthly treatments, including a low-dose control group receiving 24 000 IU of vitamin D_3 (24 000 IU group), a group receiving 60 000 IU of vitamin D_3 (60 000 IU group), and a group receiving 24 000 IU of vitamin D_3 plus 300 µg of calcifediol (24 000 IU plus calcifediol group).

Intent-to-treat analyses showed that, while 60 000 IU and 24 000 IU plus calcifediol were more likely than 24 000 IU to result in 25-hydroxyvitamin D levels of at least 30 ng/mL (P = .001), they were not more effective in improving lower extremity function, which did not differ among the treatment groups.

over the 12-month follow-up, the incidence of falls differed significantly among the treatment groups, with higher incidences in the 60 000 IU group (66.9%; 95% CI, 54.4%to 77.5%) and the 24 000 IU plus calcifediol group (66.1%; 95%CI, 53.5%-76.8%) group compared with the 24 000 IU group (47.9%; 95%CI, 35.8%-60.3%) (P = .048).

Figure 2. Unadjusted 25(OH)D Levels by Treatment at Baseline, 6 Months, and 12 Months

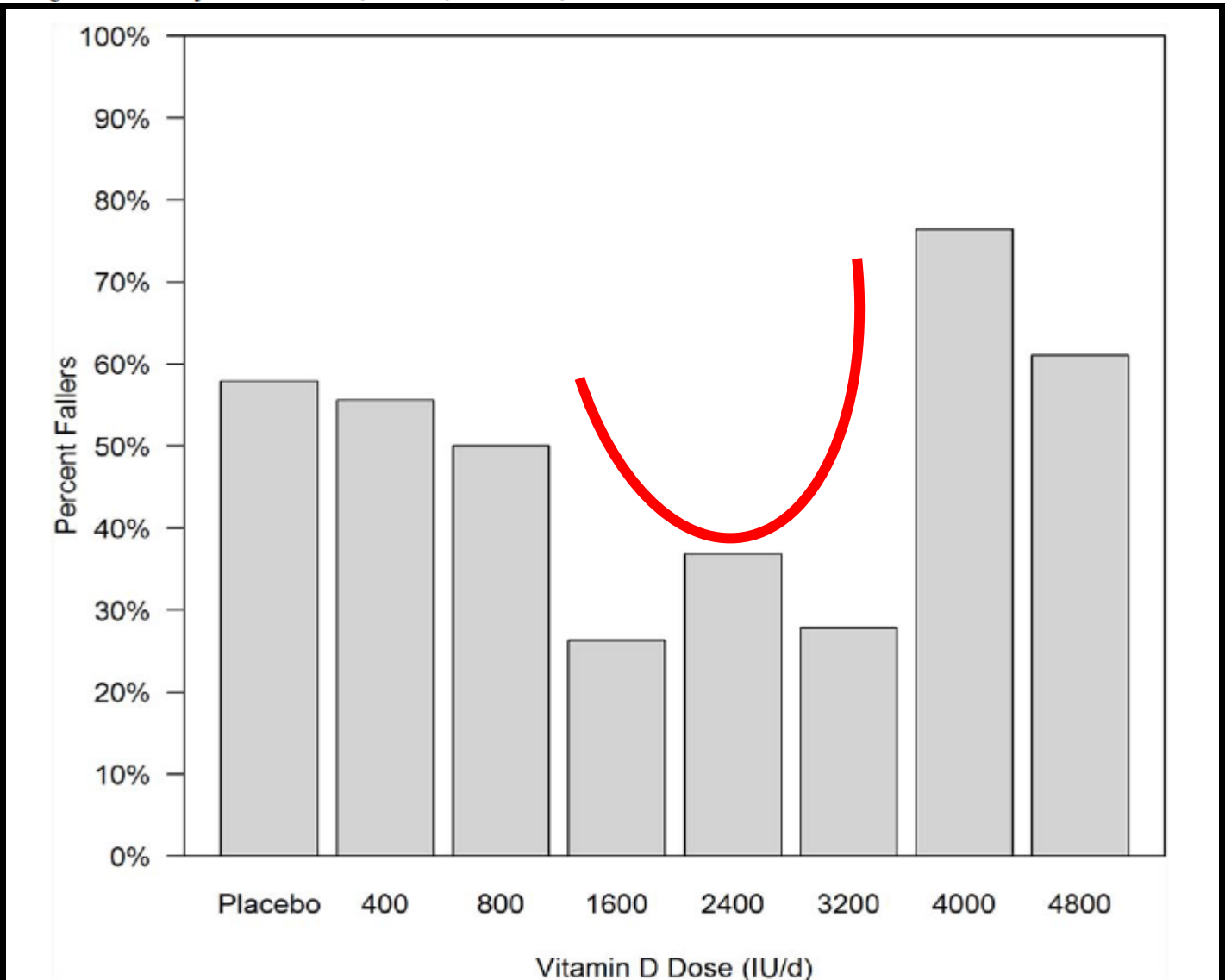


Medium doses of daily vitamin D decrease falls and higher doses of daily vitamin D3 increase falls: A randomized clinical trial

Lynette M. Smith[a], J. Christopher Gallagher[b,*], Corinna Suiter[b]

[a] *Biostatistics, Public Health Department, University Nebraska Medical Center, Omaha, NE 68198, United States*
[b] *Endocrinology, Creighton University Medical School, Omaha, NE 68131, United States*

Accepted 17 March 2017



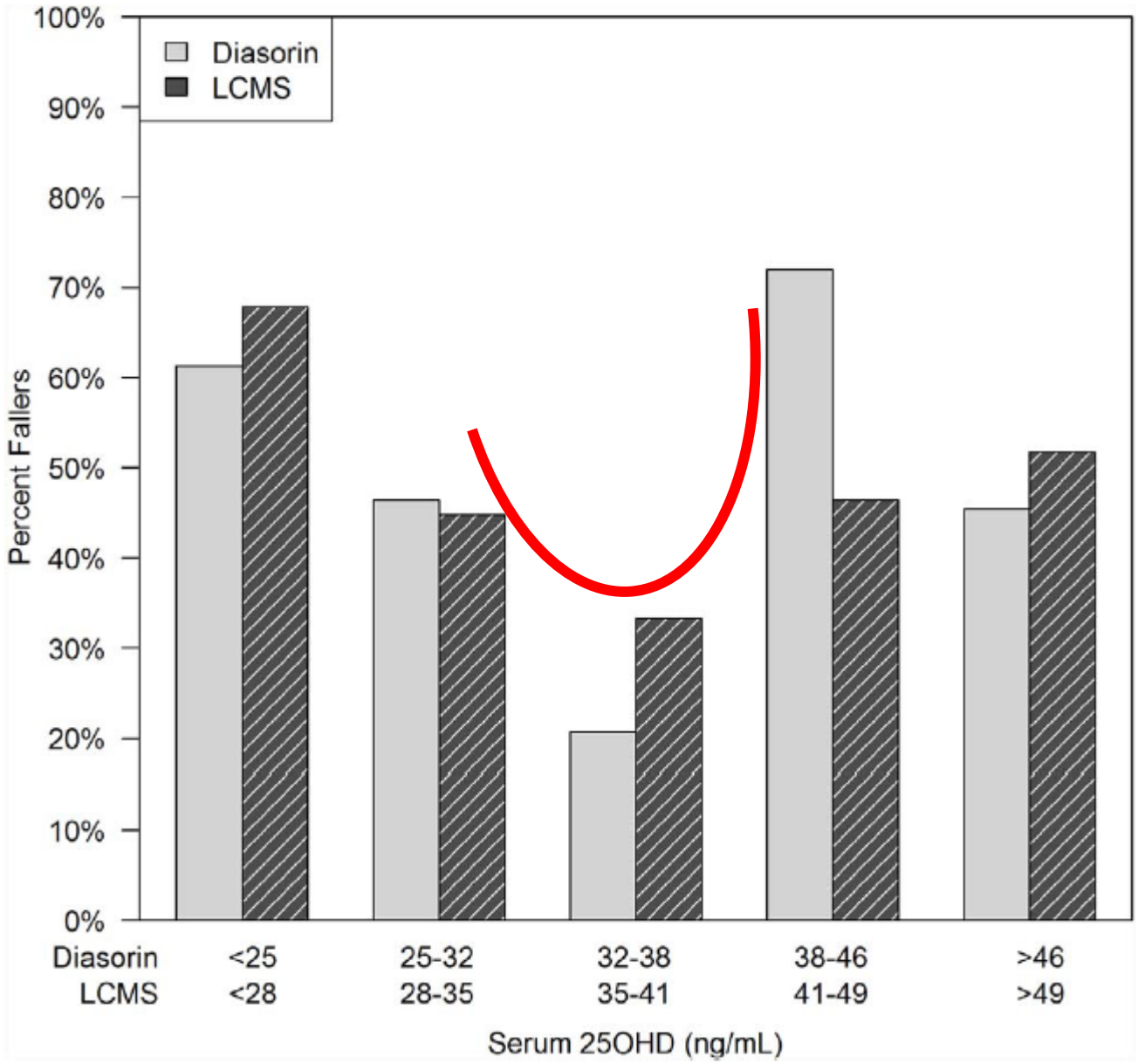


Fig. 4. Faller rates by serum 25OHD quintiles measured by Diasorin and LCMS assay. Serum 25OHD quintiles measured by Diasorin and LCMS assays showed a significant quadratic trend in faller rate ($p = 0.033$ and $p = 0.005$ respectively).

ΣΥΜΠΕΡΑΣΜΑΤΙΚΑ

- Η Συσχέτιση των επιπέδων της 25OHD3 του ορού >40-45 ng/ml με αυξημένο ρυθμό πτώσεων σε 3 διαφορετικές μελέτες είναι μια νέα παρατήρηση και αποτελεί μια ανεπιθύμητη απάντηση στη χορήγηση βιτ.D.
- Αν και οι 60.000 μον./μ bolus ισοδυναμούν με 2000μον /ημ η εφάπαξ χορήγηση αυξάνει τις πτώσεις (67%) ενώ η ημερήσια των 2000μον τις μειώνει κατά 30% υποδηλώνοντας ότι η εφάπαξ χορήγηση είναι επιζήμια γιατί αυξάνει πολύ τα επίπεδα της 25OHD3 και 1,25OHD3 του ορού.

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

Rheumatology Unit, Department of Medicine, University of Verona, 37134 Verona, Italy

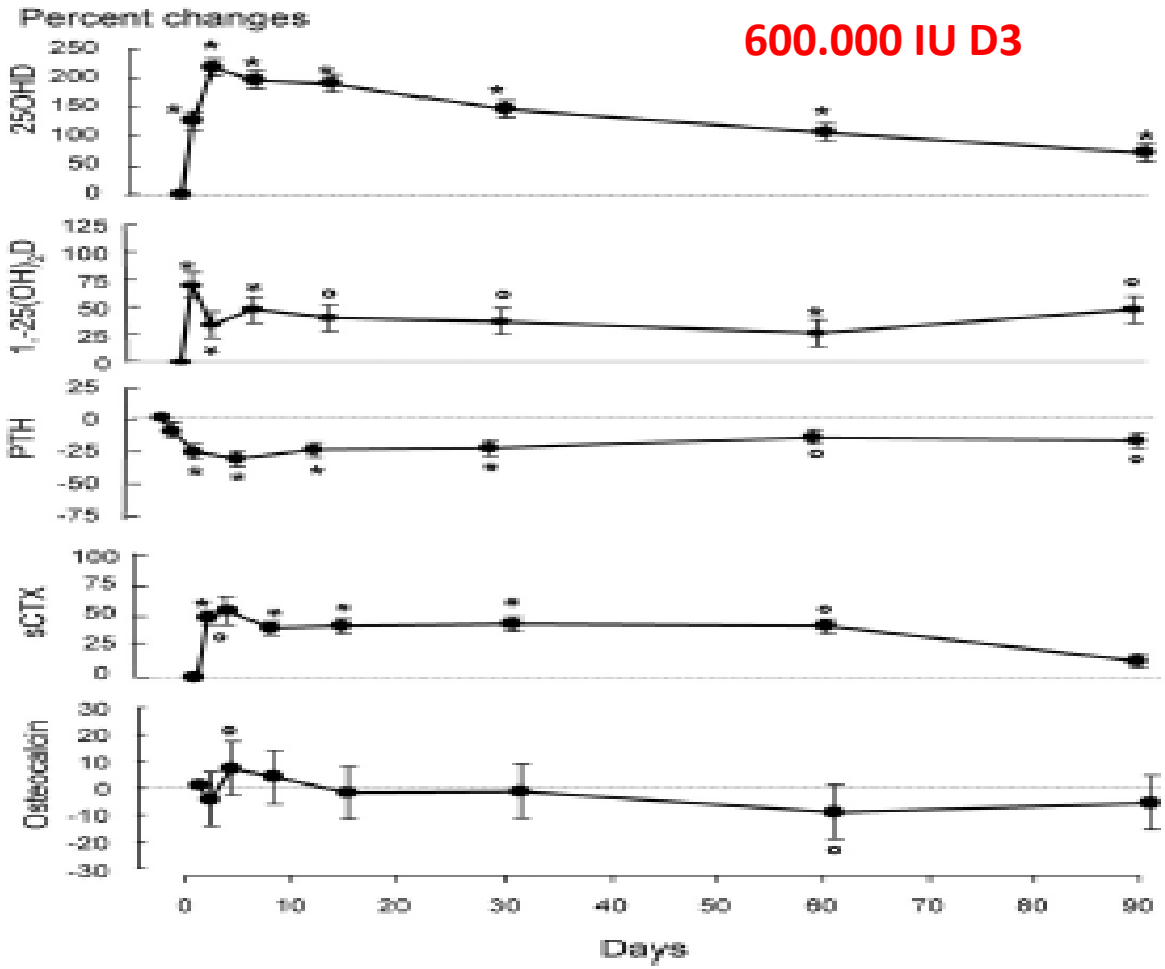
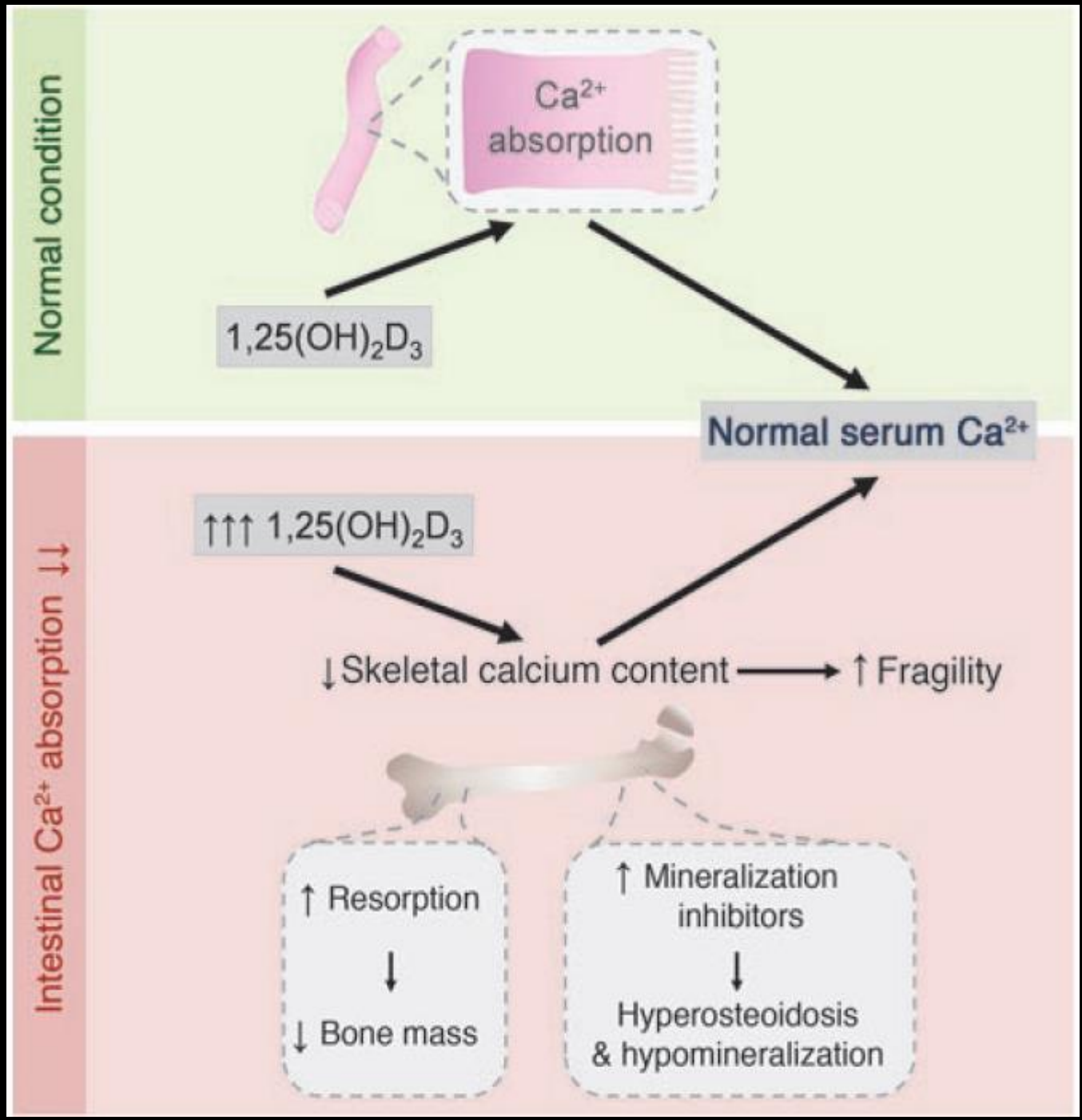


FIG. 1. Effects (percent changes ± SEM vs. baseline) of a single oral bolus of 600,000 IU vitamin D_3 on 25OHD, $1,25(OH)_2D$, PTH, sCTX, and osteocalcin serum levels. *, $P < 0.01$; °, $P < 0.05$.

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


Normal condition
Ca2+ absorption
1,25(OH)2D3
Normal serum Ca2+
Intestinal Ca2+ absorption ↓↓
↑↑↑ 1,25(OH)2D3
↓Skeletal calcium content
↑ Fragility
↑ Resorption
↓ Bone mass
↑ Mineralization inhibitors
Hyperosteoidosis & hypomineralization

ΑΣΦΑΛΕΙΑ

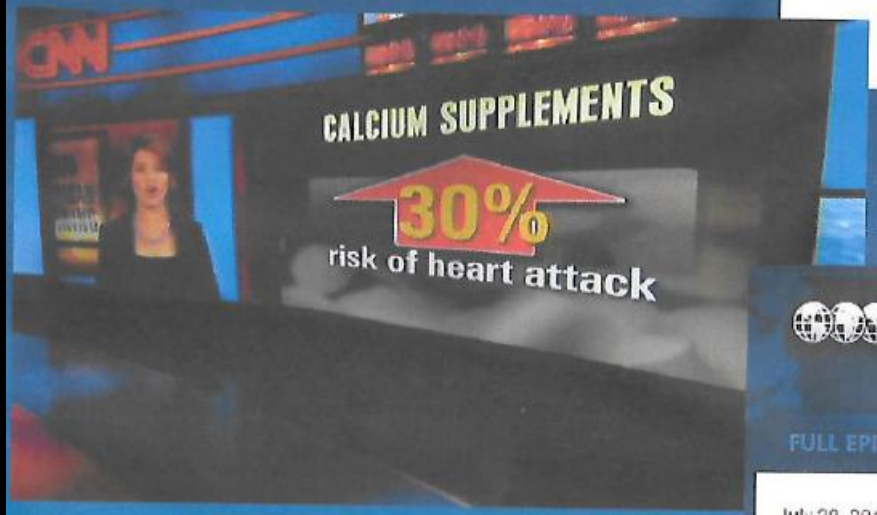
- Ανεπιθύμητες Ενέργειες (από το γαστρεντερικό)
- Ναυτία
- Δυσκοιλιότητα
- Επιγαστραλγία

ΑΣΒΕΣΤΙΟ-ΝΕΦΡΟΛΙΘΙΑΣΗ

- Πρόσληψη ασβεστίου με τις τροφές συσχετίζεται αρνητικά με την επίπτωση της νεφρολιθίασης πιθανά λόγο ελάττωσης της απορρόφησης των οξαλικών απο το έντερο.
- Τα σκευάσματα ασβεστίου συσχετίστηκαν με μια μικρή αύξηση της νεφρολιθίασης.(ΣΚ 1.17 -2100mg συνολική ημερησία πρόσληψηWHI-Στην υποομάδα των ατόμων που δεν έπαιρναν από μόνοι τους ασβέστιο ο κίνδυνος ήταν 1.08 (CI 0.88-1.32).

Curhan etalNEJM1992(ανδρες)- Curhan et al Ann InterMed1997(γυναικες) - Burtis etal AmJClinNutr1994-Heller J AmCollNutr1999

Media Reports:



BMJ

RESEARCH

Effect of calcium supplements on risk of myocardial infarction and cardiovascular events: meta-analysis

Mark J Bolland, senior research fellow,[1] Alison Avenell, clinical senior lecturer,[2] John A Baron, professor,[3] Andrew Grey, associate professor,[1] Graeme S MacLennan, senior research fellow,[2] Greg D Gamble, research fellow,[1] Ian R Reid, professor[1]

CBS EVENING NEWS with SCOTT PELLEY

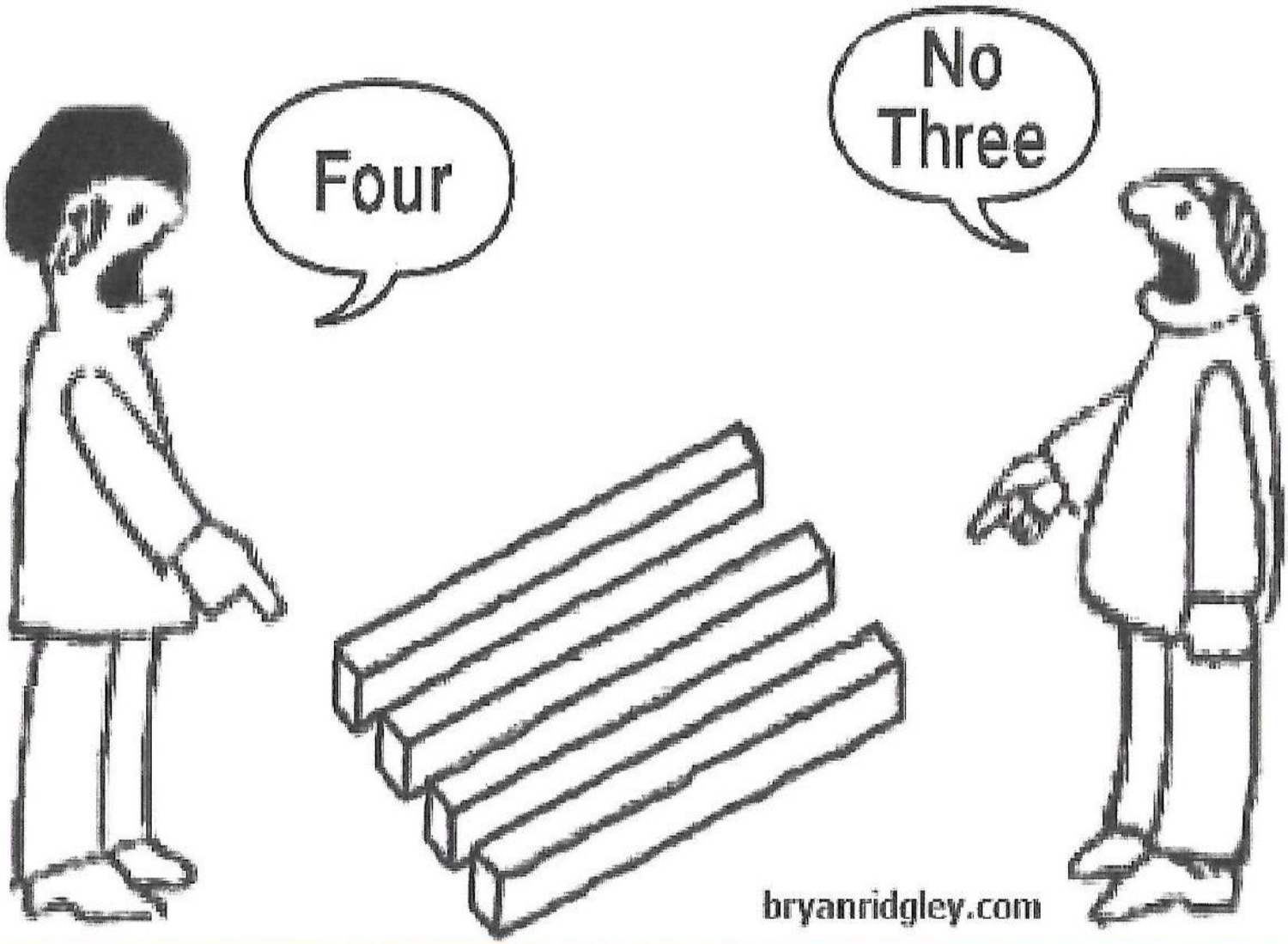
FULL EPISODES ON THE ROAD THE TEAM ABOUT US

July 29, 2010 8:56 PM

PRINT TEXT

Calcium Supplements Linked to Heart Attacks

Reality can be so complex that equally valid observations from differing perspectives can appear to be contradictory.



Abs #1008: Nguyen et al. Calcium plus Vitamin D Supplementation, Fracture, and Cardiovascular Outcomes

Background and Question: Calcium and Vitamin D Supplementation: good or bad for fracture and/or cardiovascular outcomes

Design:

11 Primary RCTS (n=56569) on Fx risk; 7 post-hoc analyses of RTCs on CVD (n=46526);

Bayesian approach to analysis of the RCTs

Results:

Abs #1008: Nguyen et al. Calcium plus Vitamin D Supplementation, Fracture, and Cardiovascular Outcomes

Results:

Outcome	5-yr incidence[1]	Relative risk	Utility[2]	NNT or NNH
Total fracture	0.093	0.85	0.90	NNT = 68
Myocardial infarction	0.017	1.05	0.75	NNH = 1176
Stroke	0.018	1.03	0.72	NNH = 1851

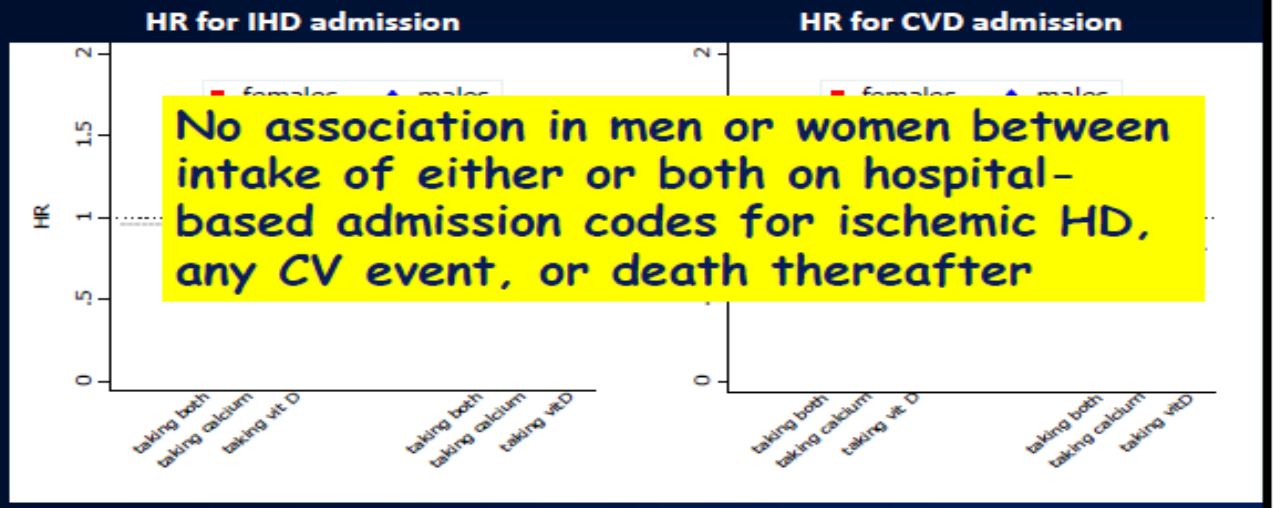
Abs #1108: Harvey et al. Calcium and/or Vitamin D supplementation are not Associated with Ischemic Heart Disease

Background and Question: Calcium ± Vitamin D Supplementation: increased risk of MI?

Design: UK biobank cohort (n= 502,664) age 40-69; prospective over 7 yrs

Results: # self-reporting calcium, 6.9%; vitamin D, 3.9%; both, 2.1%.

Abs #1108: Harvey et al. Calcium and/or Vitamin D supplementation are not Associated with Ischemic Heart Disease



HR and 95%CI

Position Statement :

National Osteoporosis Foundation (NOF) and American Society for Preventive Cardiology (ASPC)

Lack of evidence linking calcium with or without vitamin D supplementation to cardiovascular disease in generally healthy adults

Stephen L. Kopecky, MD[1]; Douglas C. Bauer, MD[2]; Martha Gulati, MD[3]; Jeri W. Nieves, PhD[4]; Andrea J. Singer, MD[5]; Peter P. Toth, MD, PhD[6]; James A. Underberg, MD[7]; Taylor C. Wallace, PhD[8,9]; Connie M. Weaver, PhD[10]

[1]Cardiology, Mayo Clinic; [2] Med and Epi & Biostat, UCSF [3] Cardiology, U of Arizona-Phoenix; [4]Mailman School of Public Health, Columbia University; [5]Ob/Gyn, Georgetown University ; Ciccarone Center Johns Hopkins; [7]Medicine, NYU; [8]NOF; [9]Nutrition and Food Studies, George Mason University; [10]Nutritional Sciences, Purdue University

In Press : Annals of Internal Medicine 2016

Annals of Internal Medicine

REVIEW

Calcium Intake and Cardiovascular Disease Risk

An Updated Systematic Review and Meta-analysis

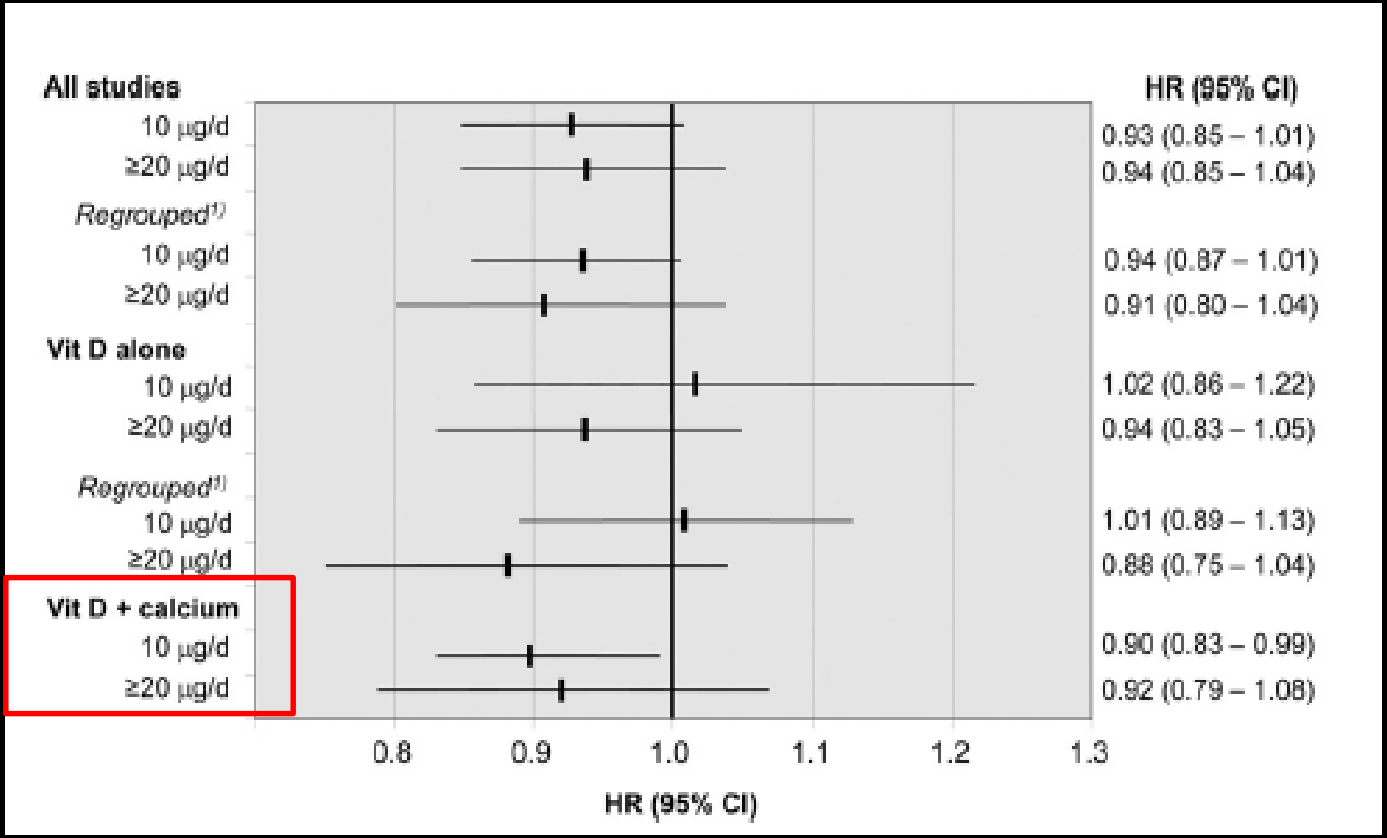
Mei Chung, MPH, PhD; Alice M. Tang, SCM, PhD; Zhuxuan Fu, MPH; Ding Ding Wang, MPH; and Sydne Jennifer Newberry, MS, PhD

This article was published at www.annals.org on 25 October 2016.

Conclusion: Calcium intake within tolerable upper intake levels (2000 to 2500 mg/d) is not associated with CVD risk in generally healthy adults.

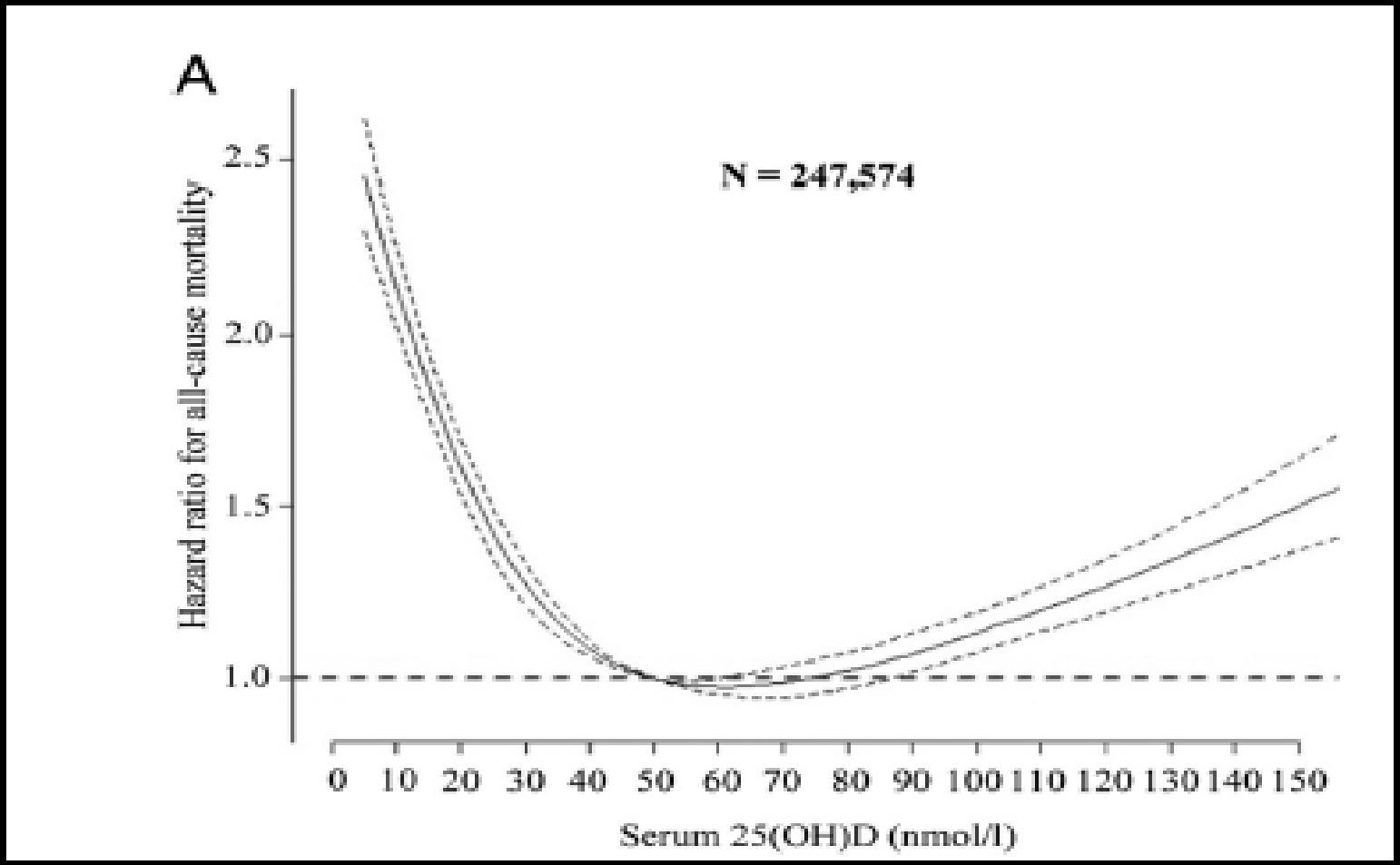
Vitamin D with Calcium Reduces Mortality: Patient Level Pooled Analysis of 70,528 Patients from Eight Major Vitamin D Trials

Lars Rejnmark, Alison Avenell, Tahir Masud, Frazer Anderson, Haakon E. Meyer, Kerrie M. Sanders, Kari Salovaara, Cyrus Cooper, Helen E. Smith, Elizabeth T. Jacobs, David Torgerson, Rebecca D. Jackson, JoAnn E. Manson, Kim Brixen, Leif Mosekilde, John A. Robbins, Roger M. Francis, and Bo Abrahamsen*



J Clin Endocrinol Metab, August 2012, 97(8):2670–2681

ΘΝΗΣΙΜΟΤΗΤΑ



J Clin Endocrinol Metab, August 2012, 97(8):2644–2652

NUTRITION

New guidelines on vitamin D-ficiency —clear or confusing?

Kevin D. Cashman and Mairead Kiely

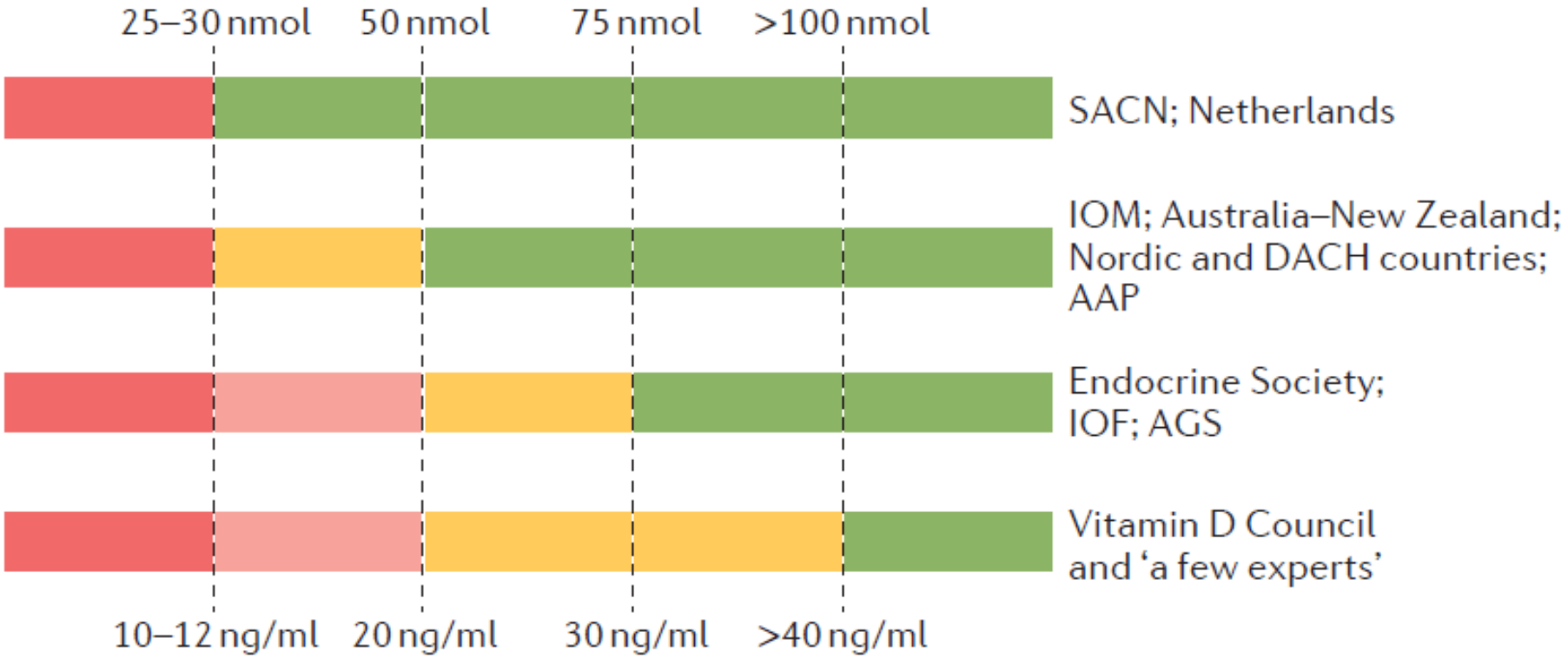


Figure 3 | **Recommendations for interpreting serum levels of 25OHD.** A schematic representation of how different agencies and countries interpret serum levels of 25-hydroxyvitamin D is shown. Colour code: red denotes a state of severe deficiency (danger) that has to be corrected without exception; orange denotes a state of mild deficiency (modest concern), in which intervention is desirable; green denotes a state of sufficient supply that does not benefit from additional supplementation. AAP, American Academy of Pediatrics; AGS, American Geriatrics Society; DACH, Deutschland (Germany), Austria and Confoederatio Helvetica (Switzerland); IOF, International Osteoporosis Foundation; IOM, Institute of Medicine; SACN, Scientific Advisory Committee on Nutrition.

Υπάρχει παραπάνω όφελος εάν αυξηθούν τα επίπεδα της 25OHD3 από 20ng/ml σε 30 ng/ml ;

Table 1 25-Hydroxyvitamin D participants in DEQAS January 2012

Method	Number participating	CV for samples analyzed (%)
Diasorin Liaison total	401	9.6–13.7
IDS EIA	136	10.2–11.8
IDS-iSYS	131	8.1–12.9
LC-MS/MS	125	8.9–14.9
Automated IDS EIA	106	8.6–10.2
Roche total 25OHD	61	8.2–16.9
Siemens ADVIA Centaur	46	14.0–19.6
Abbott Architect	34	6.8–10.7
HPLC	31	15.4–35.6
Diasorin RIA	26	14.1–20.7
IDS RIA	11	5.2–15.3
Unknown	4	9.5–24.3
Roche $25OHD_3$	3	7.1–39.7
DIAsource	2	7.6–36.7
Diazyme 25OHVitD	1	NA
Chromatographic ligand	1	NA
Binding assay		

NA not available

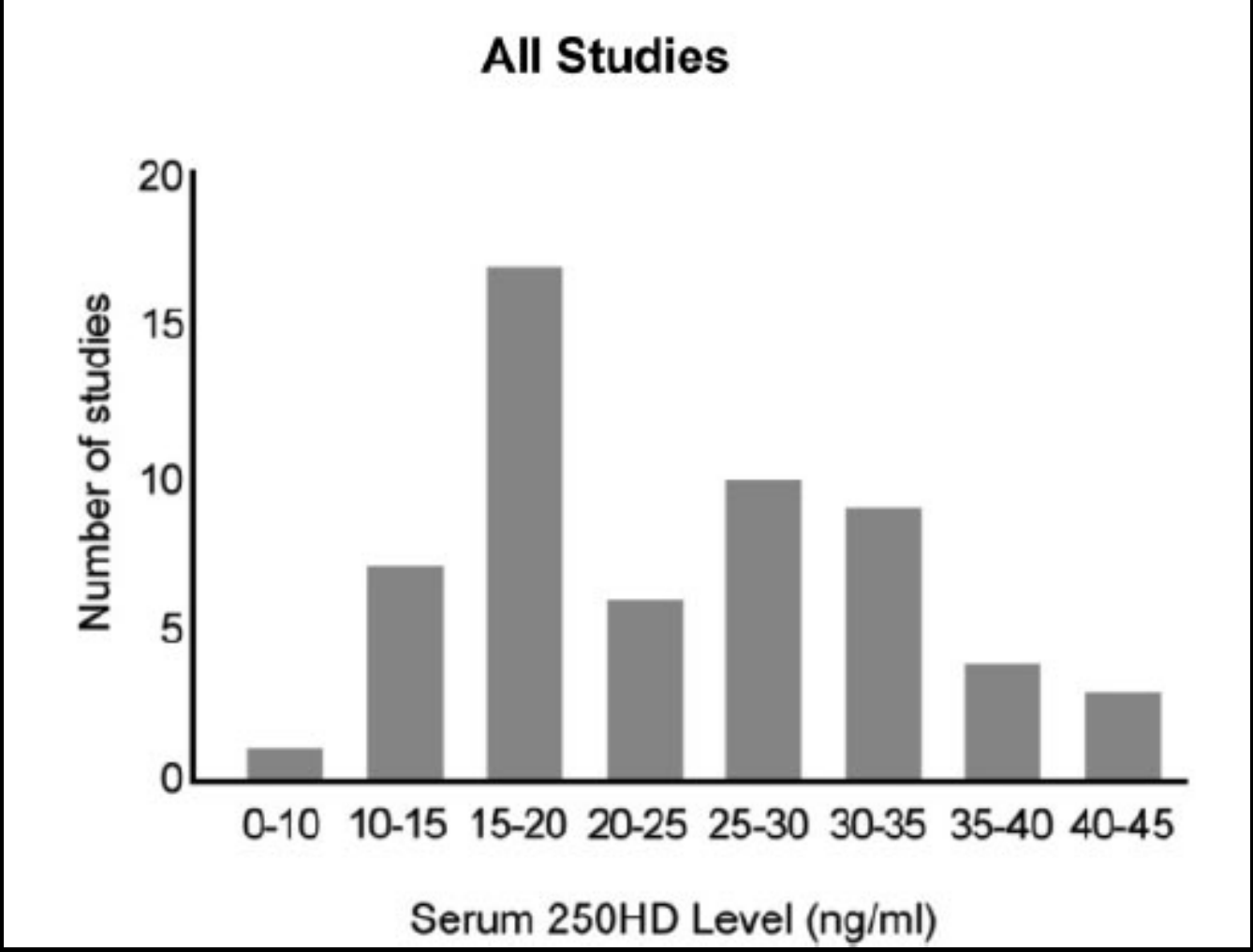
The Effect of Vitamin D on Calcium Absorption in Older Women

J. Christopher Gallagher, Vinod Yalamanchili, and Lynette M. Smith

Bone Metabolism Unit (J.C.G., V.Y.), Creighton University Medical Center, Omaha, Nebraska 68131; and Department of Public Health (L.M.S.), University of Nebraska Medical Center, Omaha, Nebraska 68198

Conclusions: There was no evidence of a threshold for reduced calcium absorption in the serum 25OHD range of 10–66 ng/ml (25–165 nmol/liter). The increase in absorbed calcium of 6% on high doses of vitamin D is so small that the same amount could be obtained from half a glass of milk (100 ml) or 100 mg elemental calcium. The results challenge assumptions about the value of adding vitamin D to increase calcium absorption except when serum 25OHD is very low that is less than 10 ng/ml (25 nmol/liter). (*J Clin Endocrinol Metab* 97: 3550–3556, 2012)

Επίπεδα 25OHD3 στα οποία υπάρχει plateau η καταστέλλεται η PTH



ΑΓΩΓΗ ΜΕ ΒΙΤΑΜΙΝΗ D

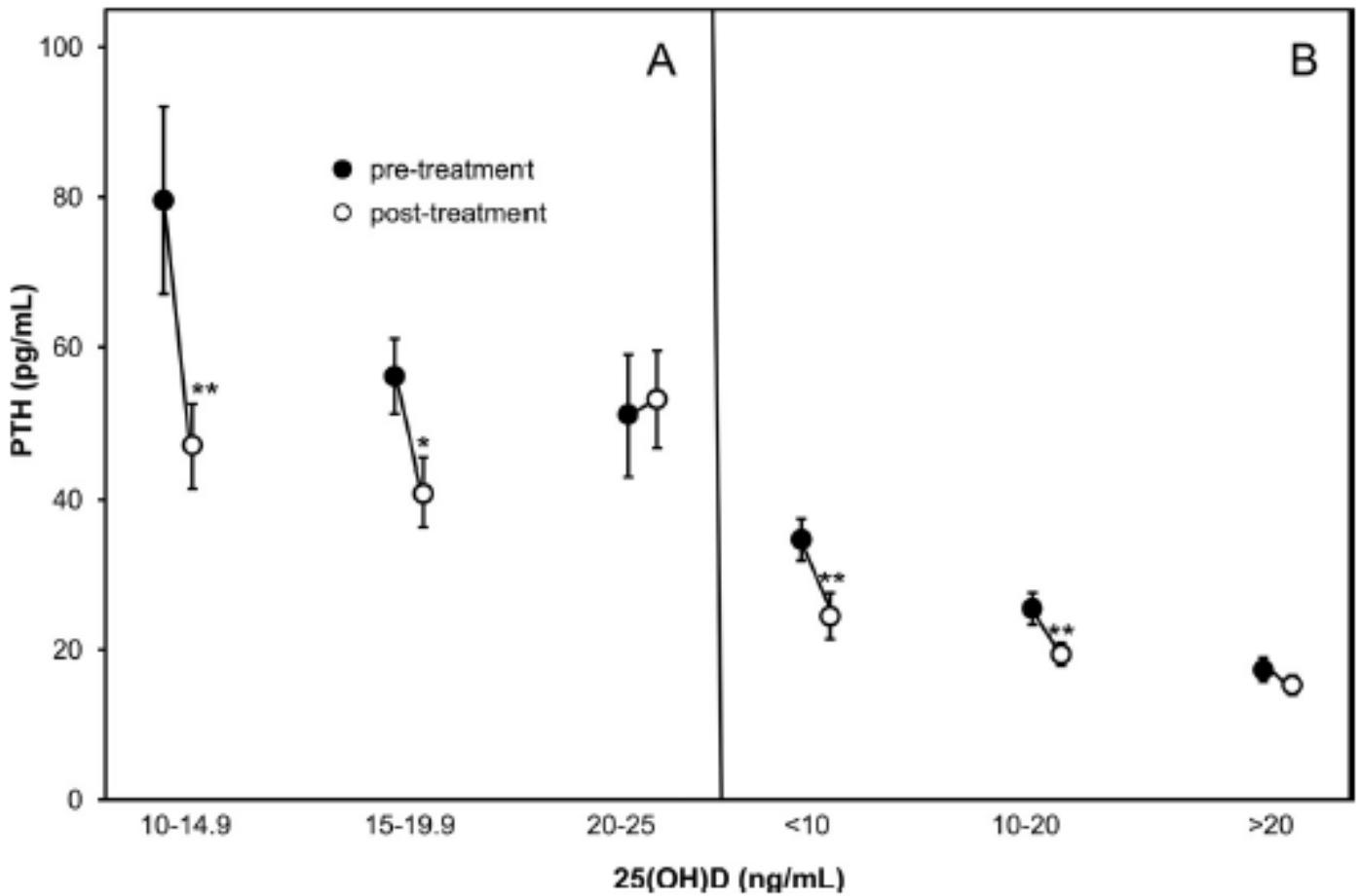


Figure 1. Changes in serum PTH concentrations (mean ± SE) in response to vitamin D supplementation of adults, according to baseline serum 25OHD concentrations. Adapted from Refs. 67 (A) and 68 (B). *, $P < .02$; **, $P < .001$.

The effect of high-dose vitamin D on bone mineral density and bone turnover markers in postmenopausal women with low bone mass—a randomized controlled 1-year trial

G. Grimnes · R. Joakimsen · Y. Figenschau · P. A. Torjesen · B. Almås · R. Jorde

Conclusions One year treatment with 6,500 IU vitamin D_3/day was not better than 800 IU/day regarding BMD in vitamin D-replete postmenopausal women with reduced bone mass and was less efficient in reducing bone turnover.

OI 2012

Effect of Vitamin D_3 and Calcium on Fracture Risk in 65- to 71-Year-Old Women: A Population-Based 3-Year Randomized, Controlled Trial—The OSTPRE-FPS

Kari Salovaara,[1,2] Marjo Tuppurainen,[1,3] Matti Kärkkäinen,[1] Toni Rikkonen,[1] Lorenzo Sandini,[1,4] Joonas Sirola,[1,2] Risto Honkanen,[1] Esko Alhava,[1,5] and Heikki Kröger[1,2]

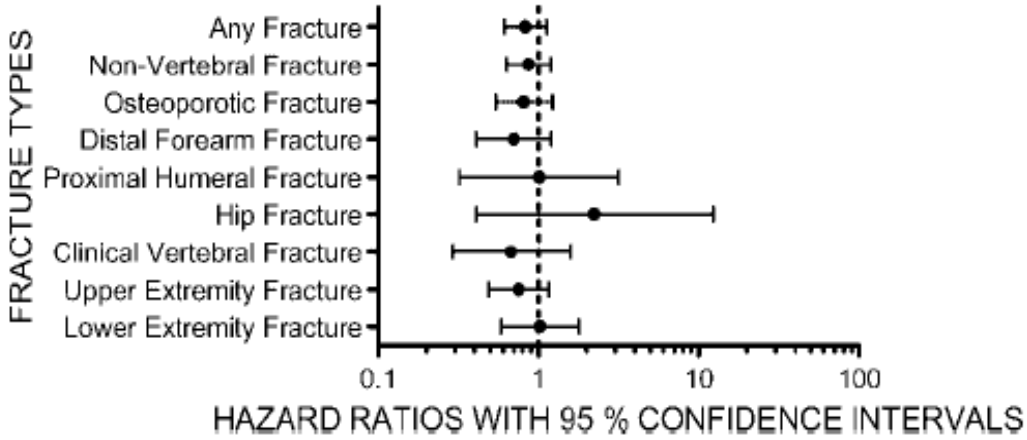


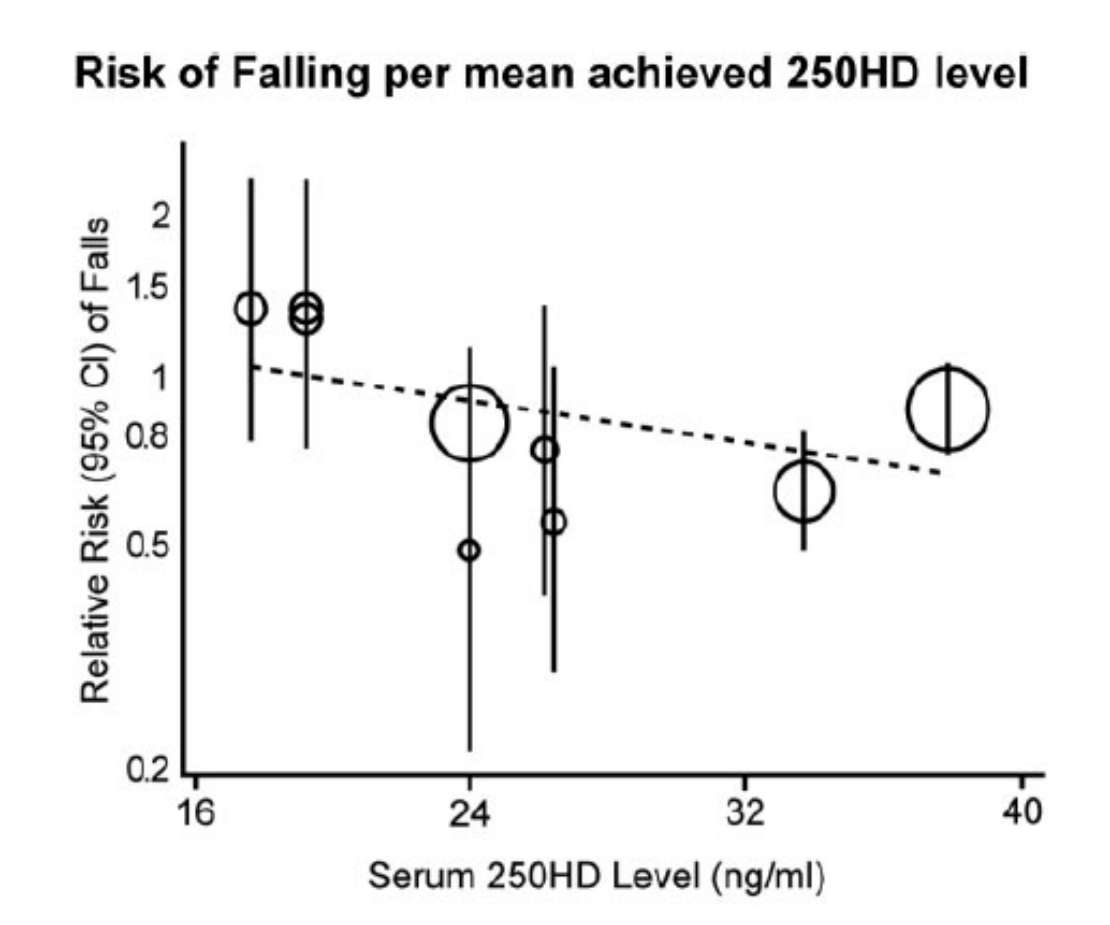
Fig. 2. Adjusted[a] hazard ratios (•) of different fracture types with 95% confidence intervals (*bars*). [a]Adjusted for age, BMI, background fracture, parental hip fracture, smoking, use of alcohol, glucocorticoid use, and diagnosed rheumatoid arthritis and secondary osteoporosis.

Serum 25(OH)D levels

In the intervention group, the mean baseline 25(OH)D level of 50.0 nmol/L (SD 18.7 nmol/L) was elevated by 49% to 74.6 (21.9) nmol/L ($p < .001$) during follow-up. In the control group, the change by 14% from a baseline of 49.1 (17.7) nmol/L to 55.9 (21.9) nmol/L was remarkably smaller but statistically significant ($p < .001$).

Journal of Bone and Mineral Research, Vol. 25, No. 7, July 2010, pp 1487–1495

IOM ΑΝΑΛΥΣΗ


Risk of Falling per mean achieved 250HD level
Relative Risk (95% CI) of Falls
2
1.5
1
0.8
0.5
0.2
16
24
32
40
Serum 250HD Level (ng/ml)

D2 H D3;

Comparison of vitamin D_2 and vitamin D_3 supplementation in raising serum 25-hydroxyvitamin D status: a systematic review and meta-analysis[1–3]

Laura Tripkovic, Helen Lambert, Kathryn Hart, Colin P Smith, Giselda Bucca, Simon Penson, Gemma Chope, Elina Hyppönen, Jacqueline Berry, Reinhold Vieth, and Susan Lanham-New

Study or Subgroup	D3 Mean	D3 SD	D3 Total	D2 Mean	D2 SD	D2 Total	Weight	Mean Difference IV, Random, 95% CI
Biancuzzo 2010-1 (7)	23.3	17.8	20	27	14.8	16	11.2%	-3.70 [-14.35, 6.95]
Biancuzzo 2010-2 (7)	32	25.3	18	26.5	18	17	9.9%	5.50 [-8.99, 19.99]
Binkley 2011-1 (15)	23	33.8	16	15.3	16.5	16	8.6%	7.70 [-10.73, 26.13]
Binkley 2011-2 (15)	22.3	18.3	15	9	14.3	16	10.9%	13.30 [1.69, 24.91]
Glendenning 2009 (16)	40	24.7	17	26	11.2	20	10.5%	14.00 [1.27, 26.73]
Heaney 2011 (17)	98.4	29.1	17	57.4	22	16	8.9%	41.00 [23.46, 58.54]
Holick 2008 (6)	23.3	17.8	20	24.8	8	16	11.8%	-1.50 [-10.23, 7.23]
Romagnoli 2008-1 (5)	70.2	20.8	8	25.5	16.9	8	8.6%	44.70 [26.13, 63.27]
Romagnoli 2008-2 (5)	65.4	30.3	8	23.1	13.8	8	7.2%	42.30 [19.23, 65.37]
Trang 1998 (4)	23.3	15.7	55	13.7	11.4	17	12.3%	9.60 [2.77, 16.43]
Total (95% CI)			**194**			**150**	**100.0%**	**15.23 [6.12, 24.34]**

Heterogeneity: $Tau^2 = 162.74$; $Chi^2 = 47.10$, df = 9 ($P < 0.00001$); $I^2 = 81\%$

Test for overall effect: $Z = 3.28$ ($P = 0.001$)

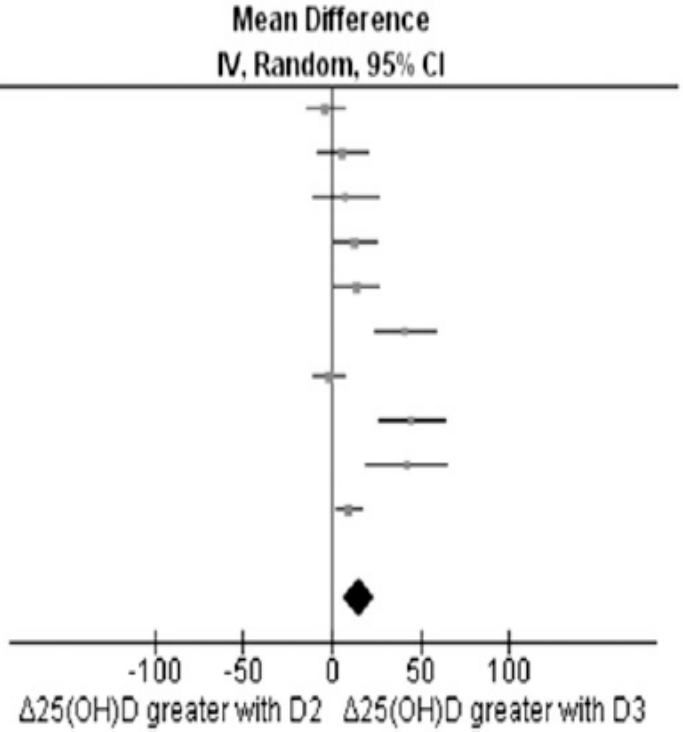


FIGURE 2. Random-effects meta-analysis comparing the effects of daily and bolus supplementation of D3 with that of D2 on net changes in serum 25(OH)D concentrations. The forest plot indicates that the absolute change in 25(OH)D from baseline favored the D3 intervention. In the figure, "Δ25(OH)D" denotes the change in serum 25(OH)D concentrations from baseline (net change), squares denote mean differences [with 95% CIs (lines)], and "Total" denotes the cumulative *n* from all included studies. With the use of a random-effects model, overall, there was a significantly greater effect in the raising of serum 25 (OH)D concentrations over time for D3 supplementation than for D2 supplementation (mean difference: 15.23; 95% CI: 6.12, 24.34; $P = 0.001$). D2, vitamin D_2; D3, vitamin D_3; IV, inverse variance; 25(OH)D, 25-hydroxyvitamin D.

Am J Clin Nutr 2012;95:1357–64.

ΣΥΜΠΕΡΑΣΜΑΤΙΚΑ

- Υπάρχουν διαφορές στα επίπεδα της βιταμίνης D που επιτυγχάνονται στον ορό με παρόμοιες δόσεις σκευασμάτων D λόγω αναλυτικής και βιολογικής διακύμανσης.
- Αν και η D2και D3 είναι αποτελεσματικές στην αντιμετώπιση της ανεπαρκείας της βιταμίνηςD η D3 έχει ένα πλεονέκτημα εξ αιτίας της μεγαλύτερης διάρκειας δράσης.

ΑΠΌ ΤΟΥ ΣΤΟΜΑΤΟΣ Η ΕΝΔΟΜΥΙΚΑ;

- Υπάρχουν φαρμακοκινητικές διαφορές
- Με την per os χορήγηση τα επίπεδα της 25OHD στον ορό αυξάνουν μέσα σε 3 ημέρες ενώ ενδομυϊκά η βιταμίνη D παγιδεύεται στο μυϊκό και λιπώδη ιστό και μετά απελευθερώνεται σταδιακά στη κυκλοφορία.

	Preventive and Maintenance Measures to Avoid Deficiency	Treatment of Deficiency
Adults		
Inadequate sun exposure[7,15] or supplementation,[7-20] decreased 7-dehydrocholesterol in skin because of aging (over 50 yr)[7]	800–1000 IU of vitamin D_3/day,[1-3,8,16,21,42] 50,000 IU of vitamin D_2 every 2 wk or every mo,[7,9] sensible sun exposure[7,15,109,110] or use of tanning bed or other UVB radiation device (e.g., portable Sperti lamp),[111-114] up to 10,000 IU of vitamin D_3/day is safe for 5 mo,[27] maintenance dose is 50,000 IU every 2 wk or every mo[7,9]‡	50,000 IU of vitamin D_2 every wk for 8 weeks[9]; repeat for another 8 wk if 25-hydroxyvitamin D <30 ng/ml‡

Michael F. Holick, M.D., Ph.D. N Engl J Med 2007;357:266-81.

ΣΥΜΠΕΡΑΣΜΑΤΙΚΑ ΤΟ ΒΕΛΤΙΣΤΟ STATUS VIT D ΓΙΑ ΚΛΑΣΣΙΚΟΥΣ ΣΤΟΧΟΥΣ ΕΠΙΤΥΓΧΑΝΕΤΑΙ

ΕΠΙΠΕΔΑ $25OHD_3$>20ng/ml

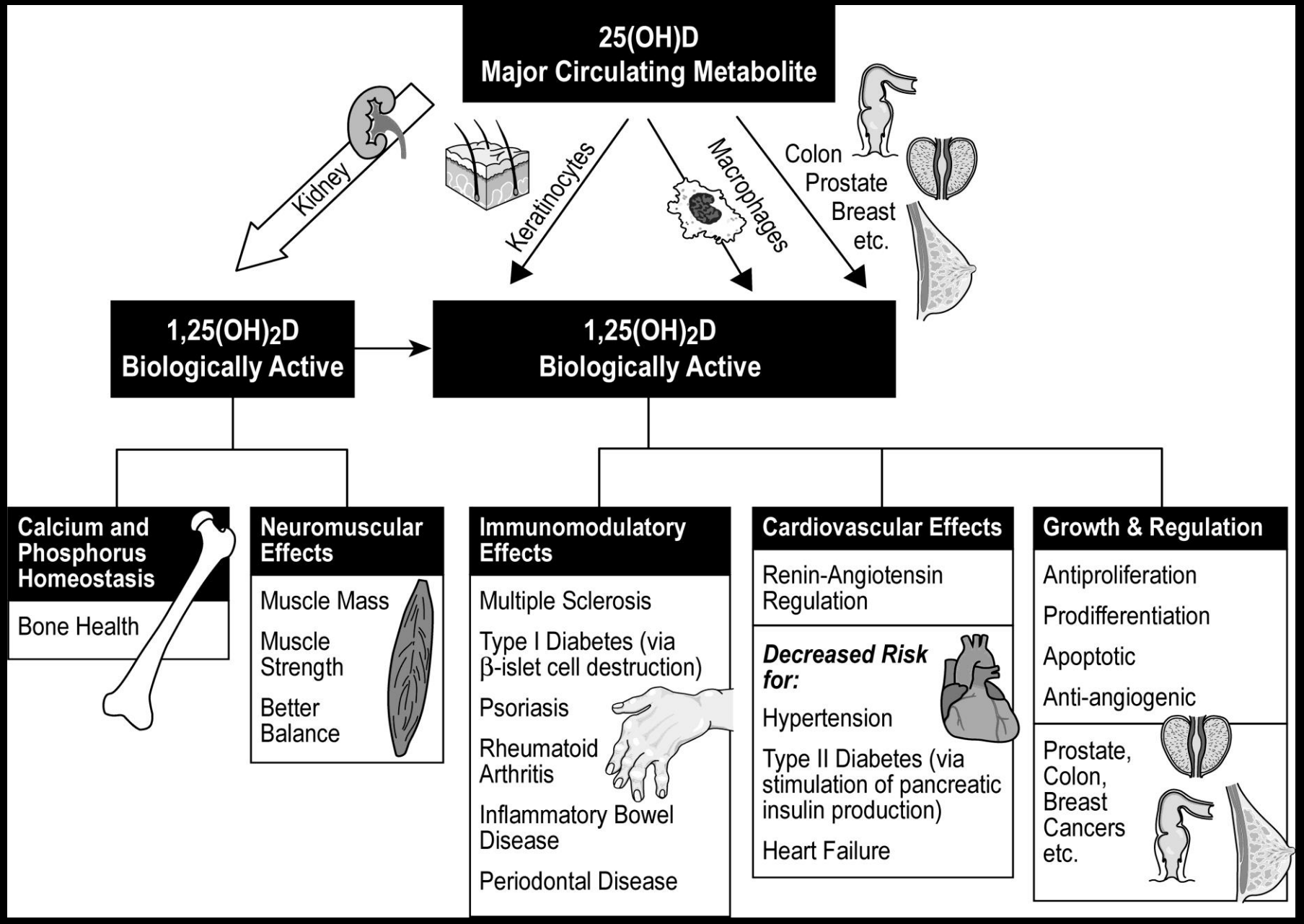
- Διατηρούν σε φυσιολογικά όρια την PTH και την 1,25,OHD3 ορού.
- Βελτιώνουν την εντερική απορρόφηση του Ca.
- Μειώνουν τα κατάγματα του ισχίου.

ΗΜΕΡΗΣΙΑ ΣΥΜΠΛΗΡΩΜΑΤΑ 700-800 μονάδων

- Αυξάνουν ήπια την ΟΠ
- Μειώνουν τον κίνδυνο πτώσεων και καταγμάτων στους ηλικιωμένους.
- Οι δόσεις αυτές αναμένεται να αυξήσουν τα επίπεδα της 25OHD3 στα 20ng/ml στη πλειοψηφία του πληθυσμού στόχου.

Table 1: Factors influencing dose response to vitamin D supplementation [17,18]

Baseline serum 25(OH)D levels
Age
Race/ethnicity
Body composition (obesity)
Renal function
Geographic locations
Sex
Calcium/phosphorus status
Genetics
Oestrogen use
Supplement use of vitamin D_2 or D_3


25(OH)D
Major Circulating Metabolite
Kidney
Keratinocytes
Macrophages
Colon
Prostate
Breast
etc.
1,25(OH)2D
Biologically Active
1,25(OH)2D
Biologically Active
Calcium and Phosphorus Homeostasis
Bone Health
Neuromuscular Effects
Muscle Mass
Muscle Strength
Better Balance
Immunomodulatory Effects
Multiple Sclerosis
Type I Diabetes (via β-islet cell destruction)
Psoriasis
Rheumatoid Arthritis
Inflammatory Bowel Disease
Periodontal Disease
Cardiovascular Effects
Renin-Angiotensin Regulation
Decreased Risk for:
Hypertension
Type II Diabetes (via stimulation of pancreatic insulin production)
Heart Failure
Growth & Regulation
Antiproliferation
Prodifferentiation
Apoptotic
Anti-angiogenic
Prostate, Colon, Breast Cancers etc.

IOM

- The proposed extraskeletal indicators

  were rejected for the purpose of DRI development because of insufficient evidence of causality, inconsistency in the evidence, or inability to develop a dose-response relationship.

The Nonskeletal Effects of Vitamin D: An Endocrine Society Scientific Statement

Clifford J. Rosen, John S. Adams, Daniel D. Bikle, Dennis M. Black, Marie B. Demay, JoAnn E. Manson, M. Hassan Murad, and Christopher S. Kovacs

Although observational studies support a strong case for an association between vitaminD and musculoskeletal, cardiovascular, neoplastic, and metabolic disorders, there remains a paucity of large-scale and long-term randomized clinical trials. Thus, at this time, more studies are needed to definitively conclude that vitamin D can offer preventive and therapeutic benefits across a wide range of physiological states and chronic nonskeletal disorders.

Endocrine Reviews, June 2012, 33(3):456–492

Ongoing large trials for vitamin D supplementation

Randomized, controlled trial	Location	Sample size/ recruitment status	Mean active study period (years)	Study end	Main inclusion criteria	Intervention doses	Cardiovascular end points
VITAL* (Pradhan et al.[203,210])	USA	25,875/ completed	5	2017[#]	≥50 years (men), ≥55 years (women)	2,000 IU per day	Cardiovascular disease
ViDa[‡] (Scragg et al.[154,211])	New Zealand	5,110/ completed	4	2016	50–84 years	100,000 IU per month	Cardiovascular disease
FIND* (Tuomainen et al.[204])	Finland	2,500[§]/ completed	5	2018	≥60 years (men), ≥65 years (women)	1,600 IU per day 3,200 IU per day	Cardiovascular disease
D-Health[‖] (Neale et al.[205])	Australia	25,000/ completed	5	2019	60–79 years	60,000 IU per month	Cardiovascular events
DO-HEALTH* (Bischoff-Ferrari et al.[206])	Western Europe	2,152/ completed	3	2017	≥70 years	2,000 IU per day	Cardiovascular events, cardiovascular mortality
VIDAL[¶] feasibility study (Pete et al.[207])	UK	1,600/ completed	2	2017	65–84 years	100,000 IU per month	Cause-specific mortality
EVITA* (Zittermann et al.[208])	Germany	400/ completed	3	2016	18–79 years, 25(OH)D ≤75 nmol/l, congestive heart failure	4,000 IU per day	Event-free survival[#]

Pilz S et al., Nat Rev Cardiology 2016

Clinicaltrials.gov or www.ncbi.nlm.nih.gov/pubmed

- **Currently, far too many people do not receive the amount of vitamin D that they need, despite updated guidelines for intake of vitamin D in many countries.**
- **In addition, a small group of people and ‘addicts’ take too much vitamin D as a result of the misconception that ‘more of a good thing should be better'.**
- **experience with other micronutrients has amply proved that such high dosages are not necessarily more efficient or even safe.**

Roger Bouillon

Skin β-endorphin mediates addiction to ultraviolet light

Gillian L. Fell[1,†,4], Kathleen C. Robinson[1,4], Jianren Mao[2], Clifford J. Woolf[3], and David E. Fisher[1,*]

Cell. 2014 June 19; 157(7): 1527–1534.

ΕΥΧΑΡΙΣΤΩ