IV CONGRESSO NAZIONALE

SOCIETÀ ITALIANA
G.U.I.D.A.
PER LA GESTIONE UNIFICATA E INTERDISCIPLINARE DEL DOLORE MUSCOLO-SCHELETRICO E DELL'ALGODISTROFIA

Centro Congressi Unione Industriali

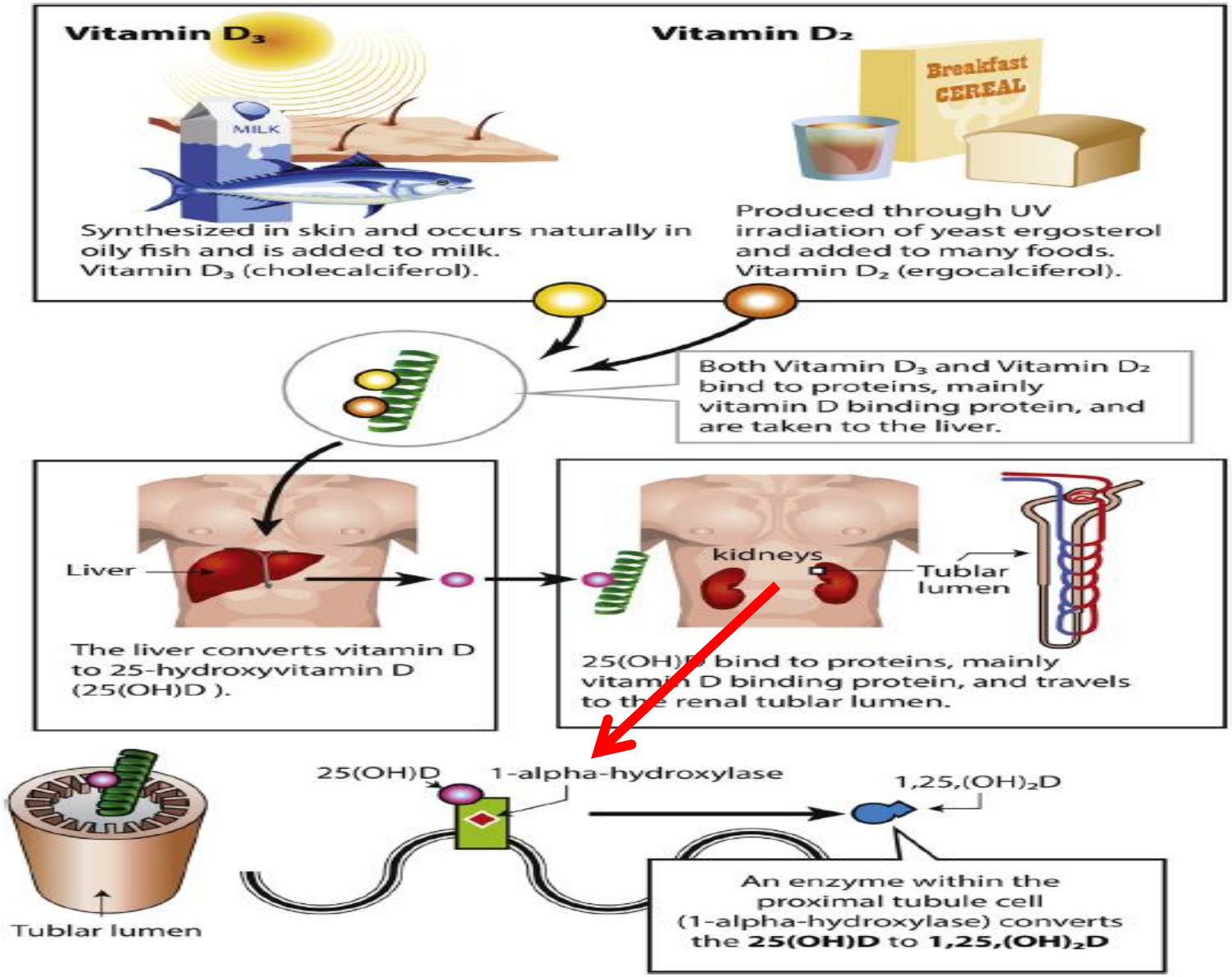
TORINO 11-13 MAGGIO 2023

Relatore	Sandro Giannini

Titolo

Vitamina D e salute muscolo-scheletrica

Vitamin D metabolism: an overview

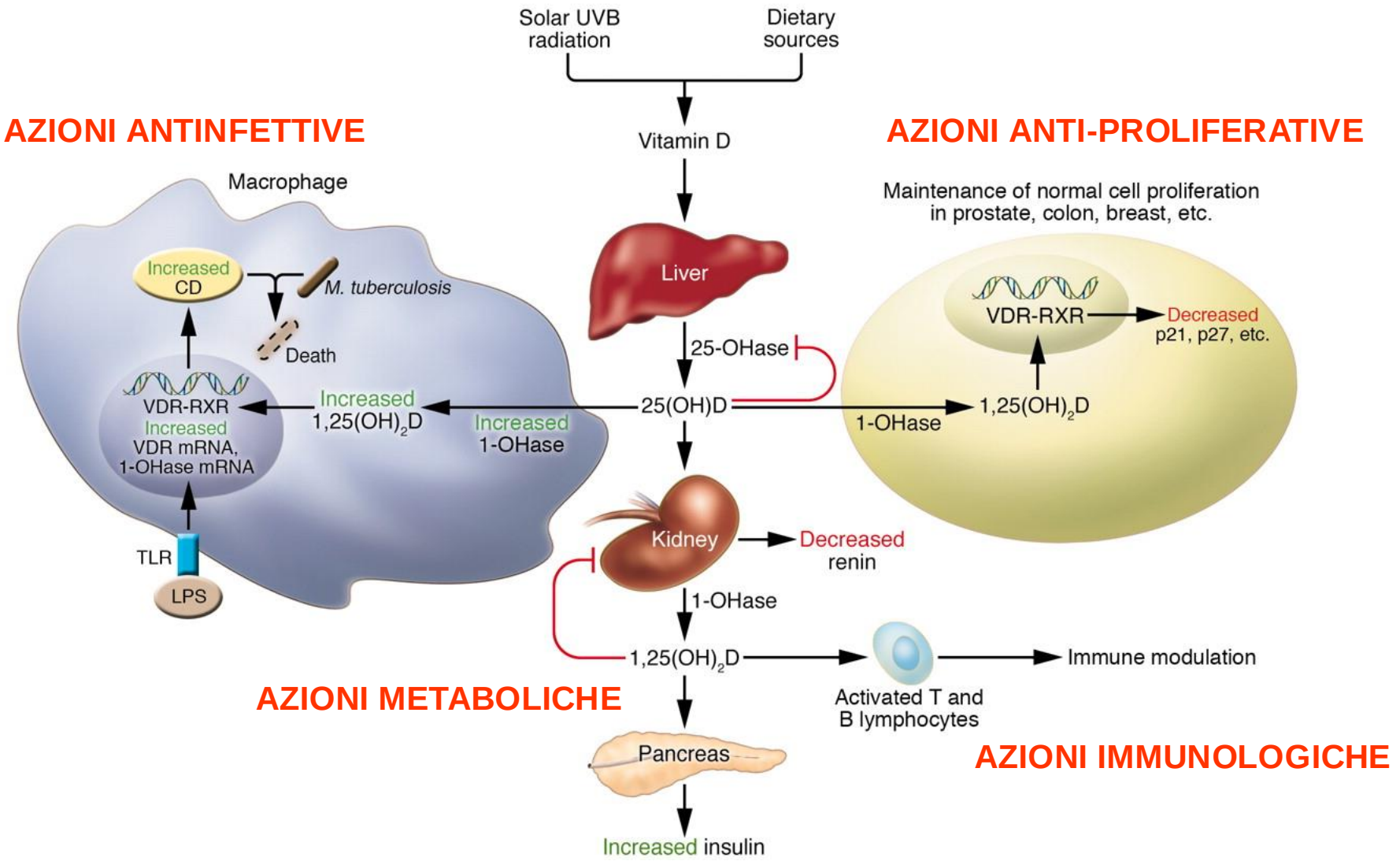


Kramer H et al., AJKD 2014

Tessuti e funzioni influenzati dalla vitamina D

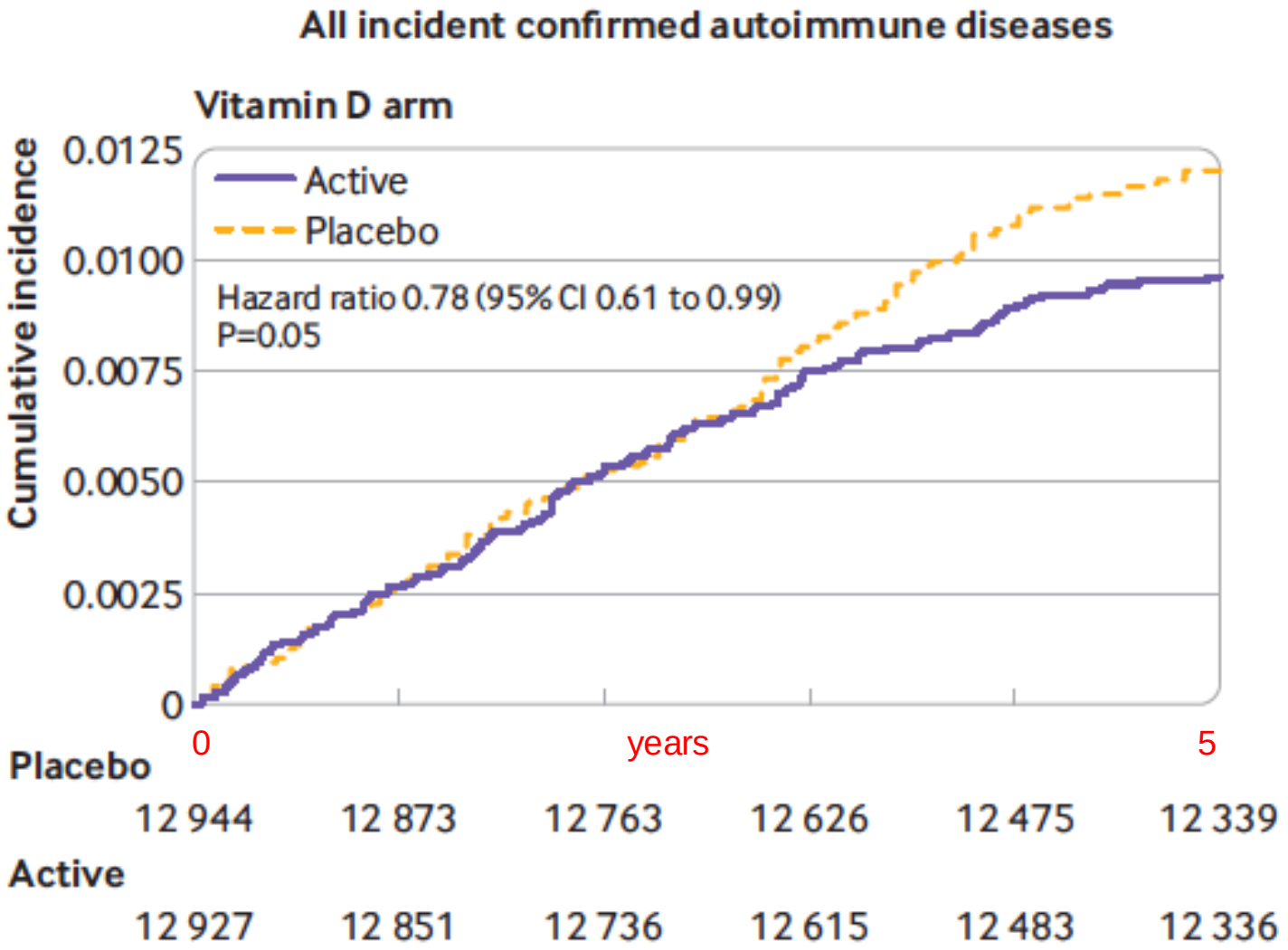
- Sistema scheletrico
- Sistema muscolare
- Crescita e differenziazione cellulare
- Funzione immunitaria
- Secrezione insulinica
- Progressione dell’osteoartrite
- Sistema cardiovascolare
- Gonadi e riproduzione
- ……..

Noncalcemic functions



Holick, M. F. J. Clin. Invest. 2006;116:2062-2072

Vitamin D and marine omega 3 fatty acid supplementation and incident autoimmune disease: VITAL randomized controlled trial

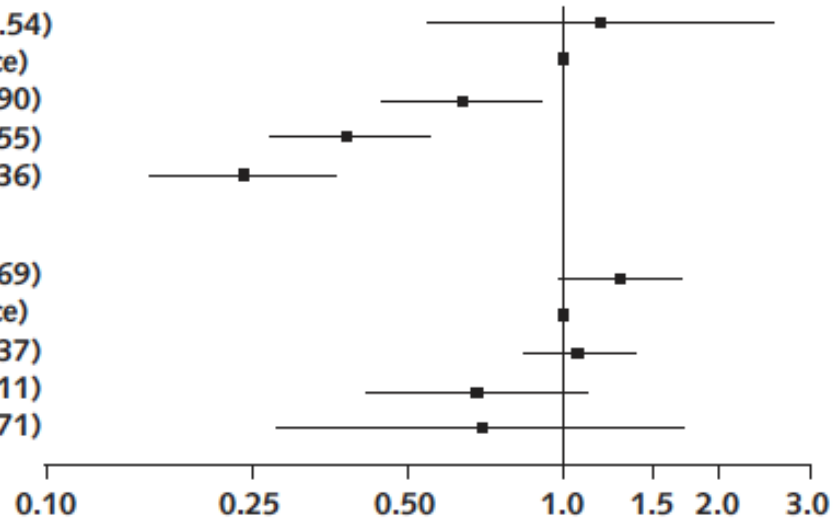


Hahn J et al.,. BMJ 2022

Vitamin D and Risk for Type 2 Diabetes in People With Prediabetes

Figure 3. Effect of cholecalciferol on new-onset diabetes among adults with prediabetes according to intratrial cumulative mean serum 25-hydroxyvitamin D level.

	Events/ Participants, *n*/*N*	Hazard Ratio (95% CI)
Cholecalciferol		
<50 nmol/L	8/25	1.18 (0.55–2.54)
50–74 nmol/L	50/114	1.00 (reference)
75–99 nmol/L	110/316	0.64 (0.45–0.90)
100–124 nmol/L	94/400	0.38 (0.27–0.55)
≥125 nmol/L	78/472	0.24 (0.16–0.36)
Placebo		
<50 nmol/L	95/283	1.29 (0.98–1.69)
50–74 nmol/L	144/500	1.00 (reference)
75–99 nmol/L	123/423	1.07 (0.84–1.37)
100–124 nmol/L	20/101	0.68 (0.42–1.11)
≥125 nmol/L	5/24	0.70 (0.28–1.71)



Pittas AG et al., Ann Int Med 2023

Tessuti e funzioni influenzati dalla vitamina D

- Sistema scheletrico
- Sistema muscolare
- Crescita e differenziazione cellulare
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- Gonadi e riproduzione
- ……

Vitamin D: Brief History

Mid 1600s

- Rickets identified as major health problem
- People moving from rural to urban areas, lifestyles change, decreased sun exposure

Early 1800s

- Rickets incidence escalates with Industrial Revolution, becoming epidemic in northern Europe and in industrialized northern regions of the United States.

Vitamin D: Brief History

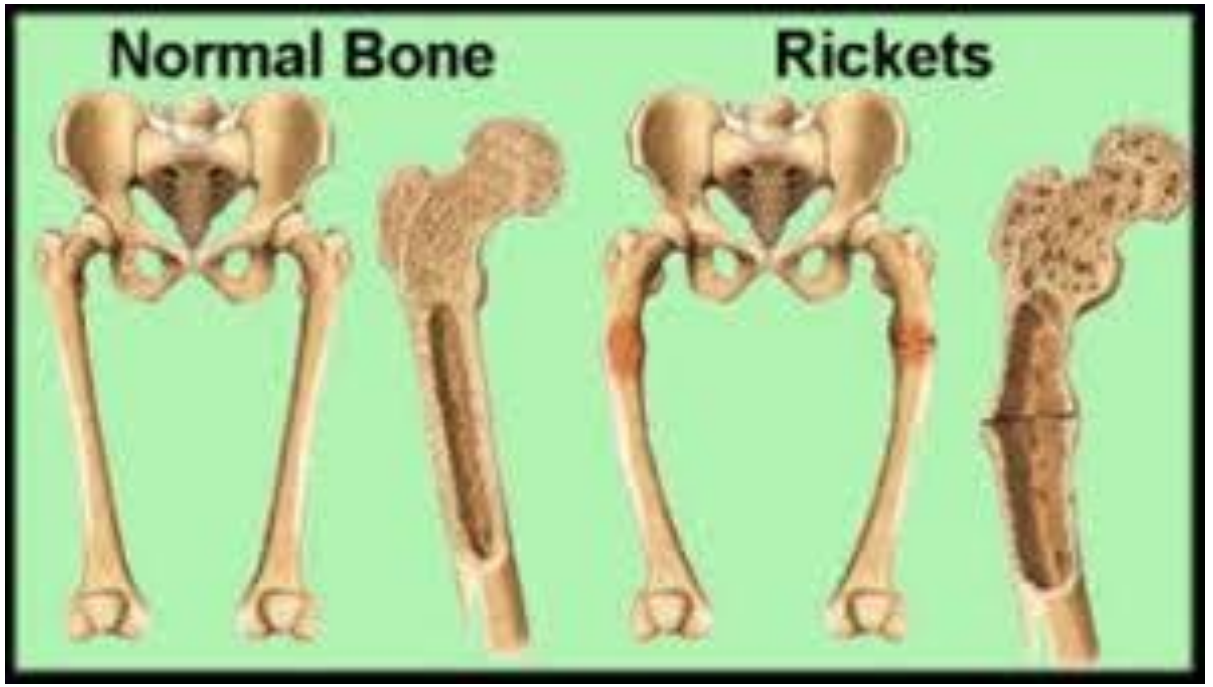
1824

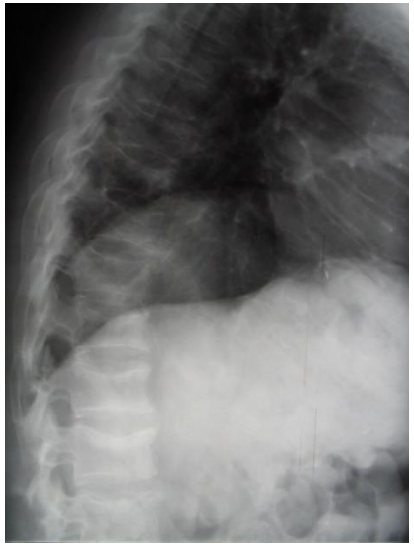
- First report on the use of cod liver oil to prevent rickets
  - Schutte D. Beobachtungen Uber den Nutzen des Berger Leberthrans (Oleum jecoris Aseli, von Gadus asellus L) Arch Med Erfahr. 1824;2:79–92.

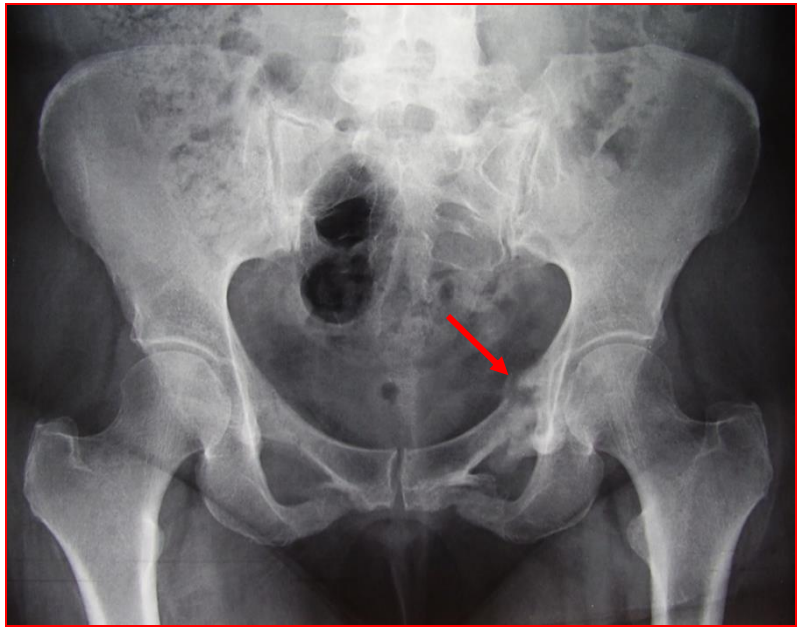
1922

- McCollum coined term "vitamin D" to describe antirachitic factor in cod liver oil
  - McCollum EV, Simmonds N, Becker JE, Shipley PG. J Biol Chem. 1922;53:293–312.
- Antirachitic properties of UV light demonstrated in rats
  - Hess AF. Lancet. 1922;ii:367. Reprinted in: Hess AF. *Collected Writings*. Vol 2. Springfield, Ill: Charles C. Thomas; 1936:5–14.

Miopatia in rachitismo vitamina D-dipendente


Normal Bone
Rickets





Tessuti e funzioni influenzati dalla vitamina D

- Sistema scheletrico
- **Sistema muscolare**
- Crescita e differenziazione cellulare
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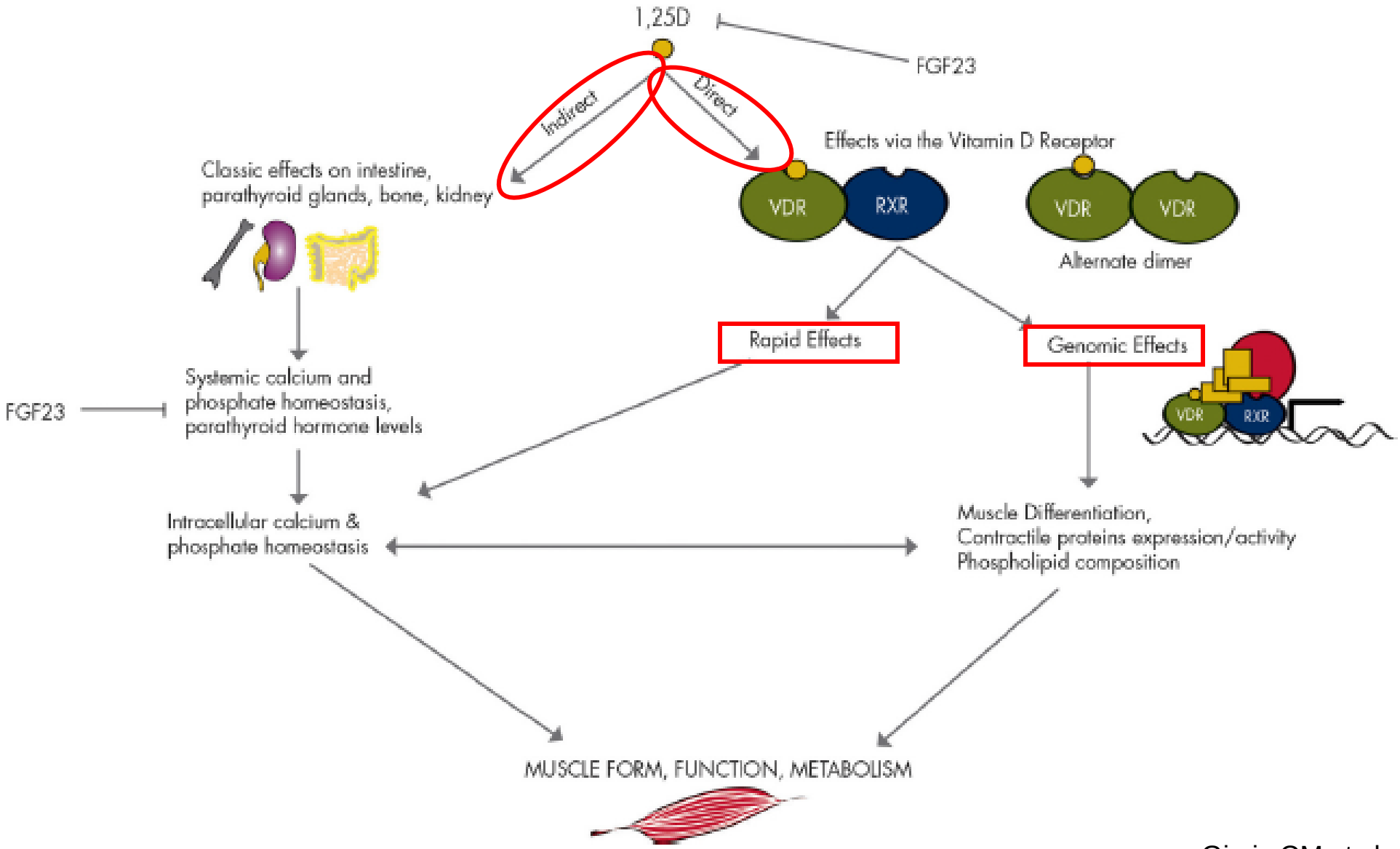
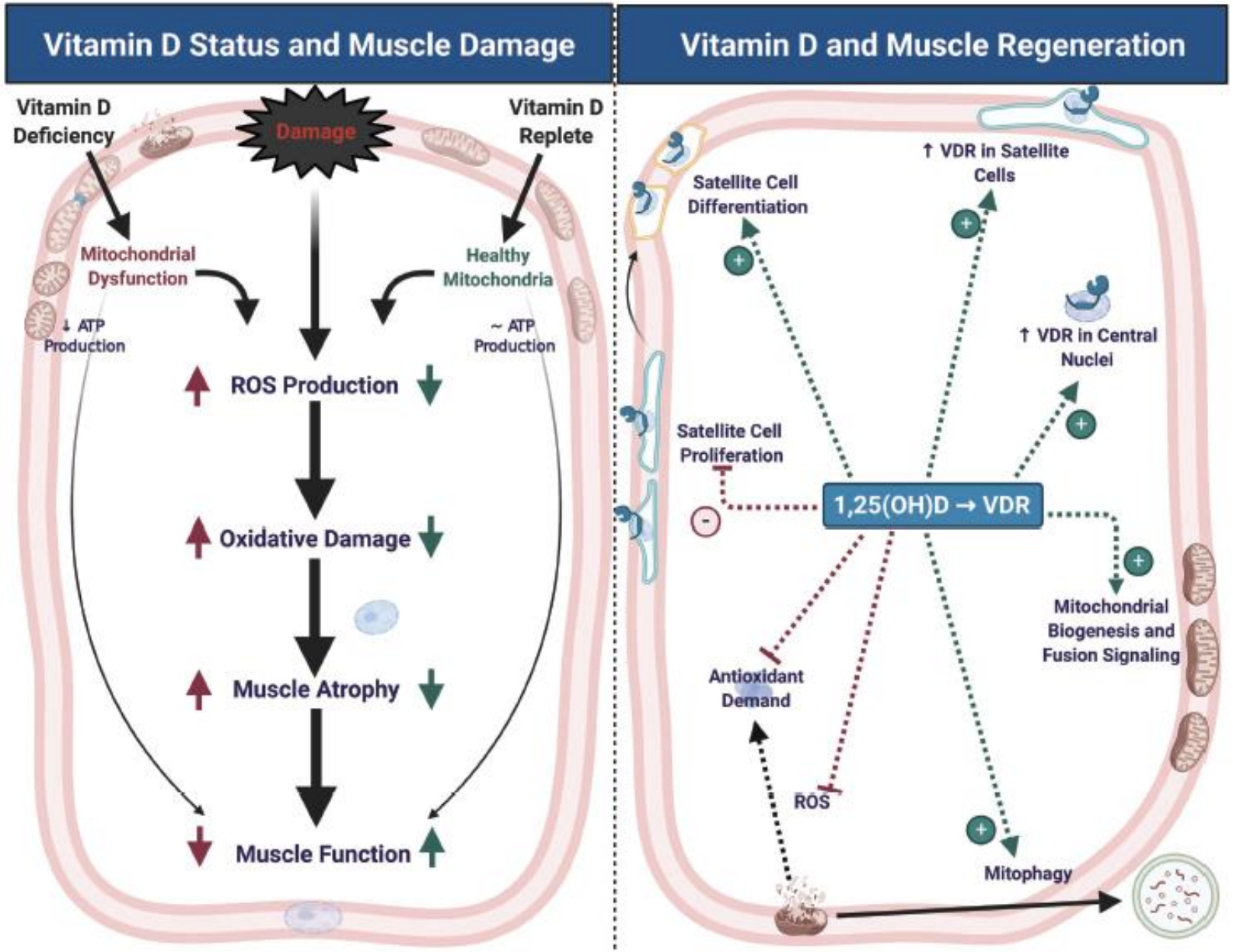
The Roles of Vitamin D in Skeletal Muscle



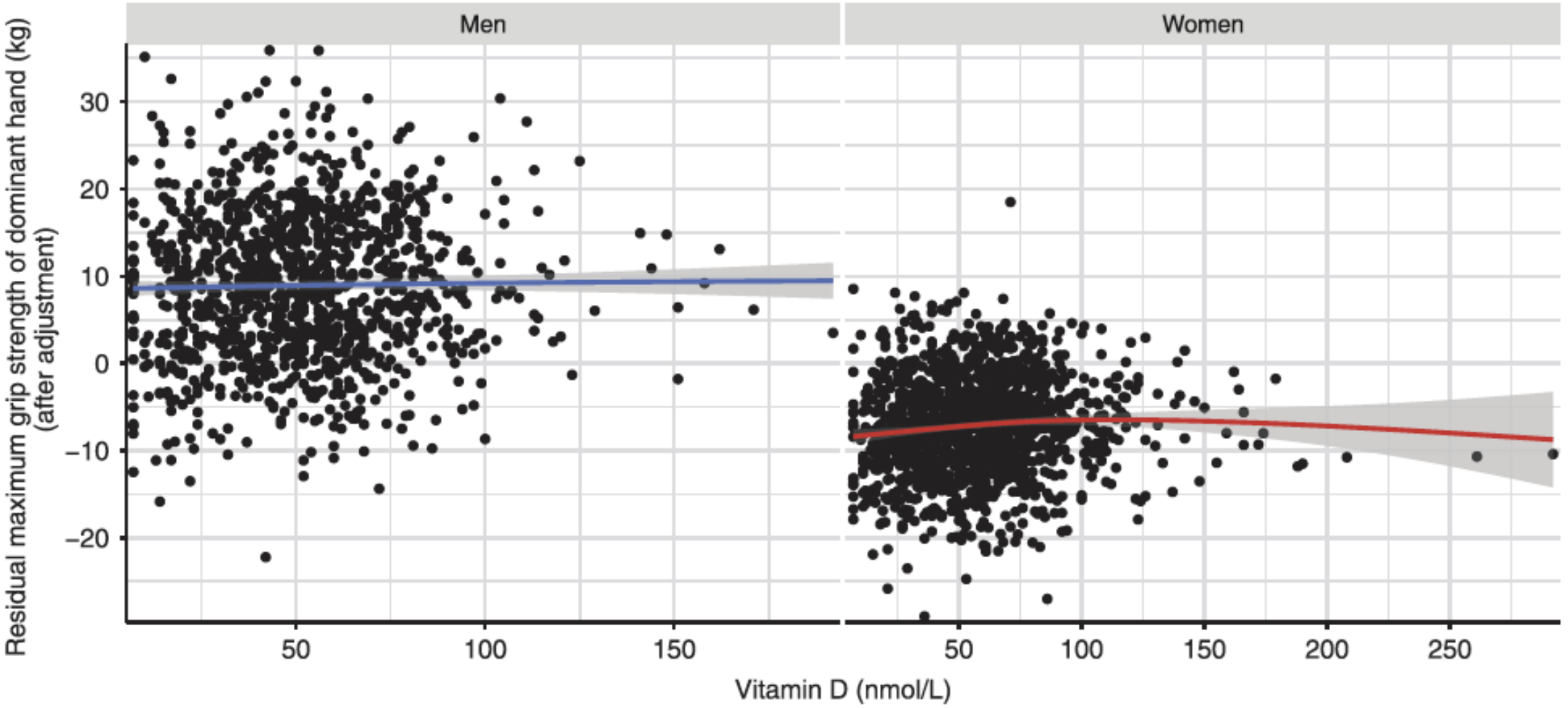
Girgis CM et al., Endocr Rev. 2013



Vitamin D Promotes Mitochondrial Health and Muscle Regeneration

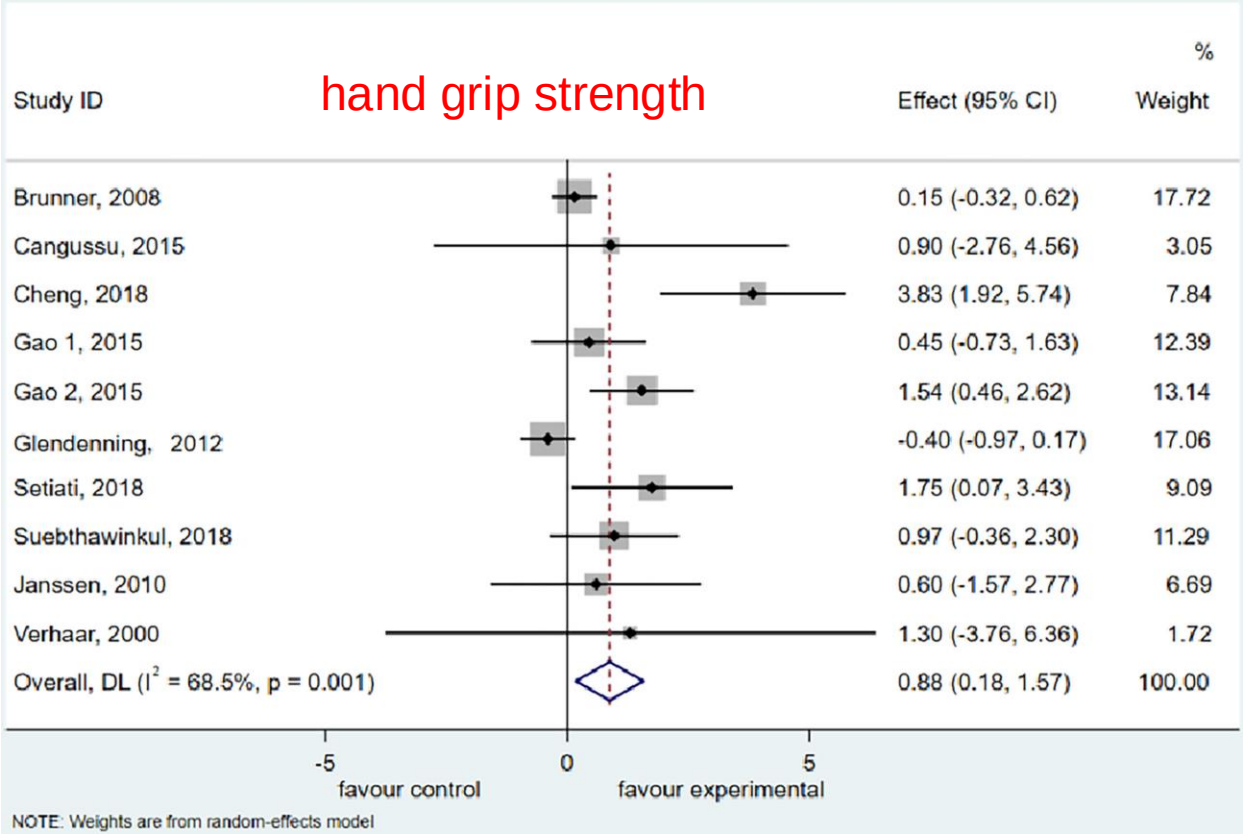
Latham CM et al., Front Physiol 2021

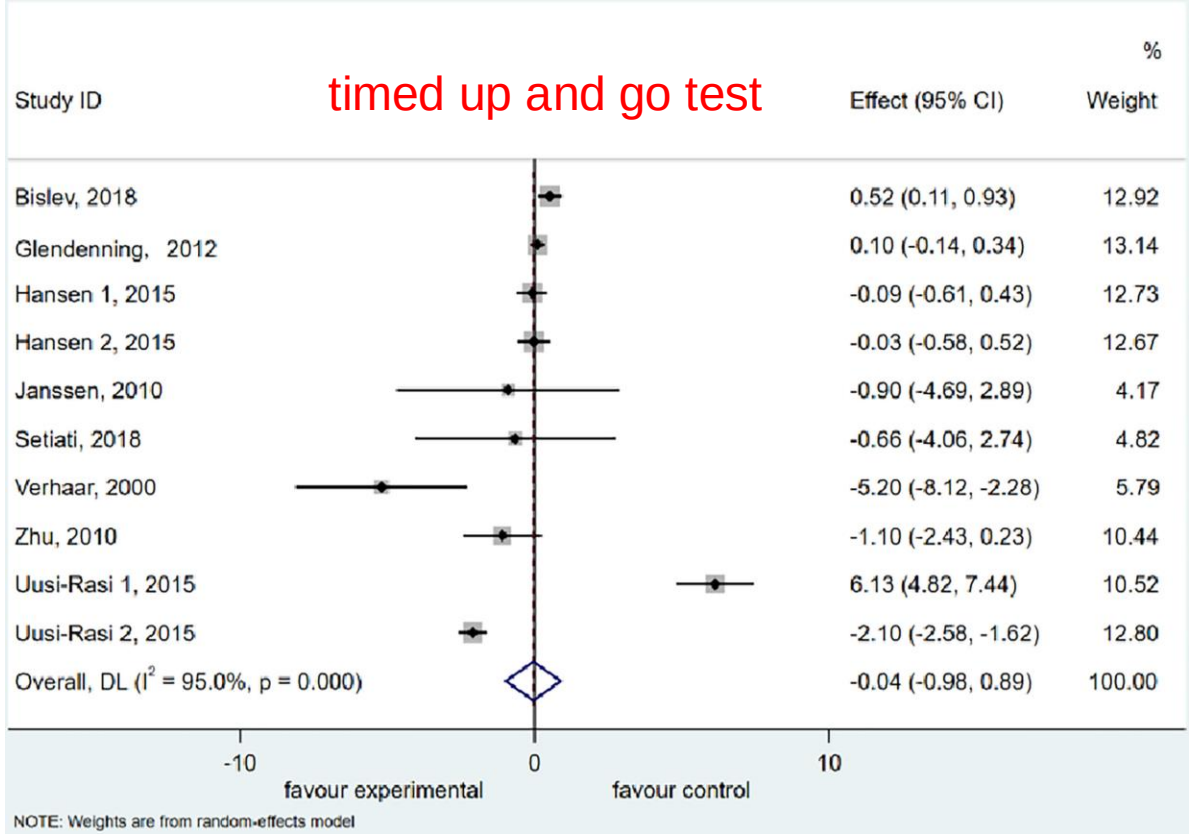
25-hydroxyvitamin D level is associated with greater grip strength across adult life span: apopulation-based cohort study



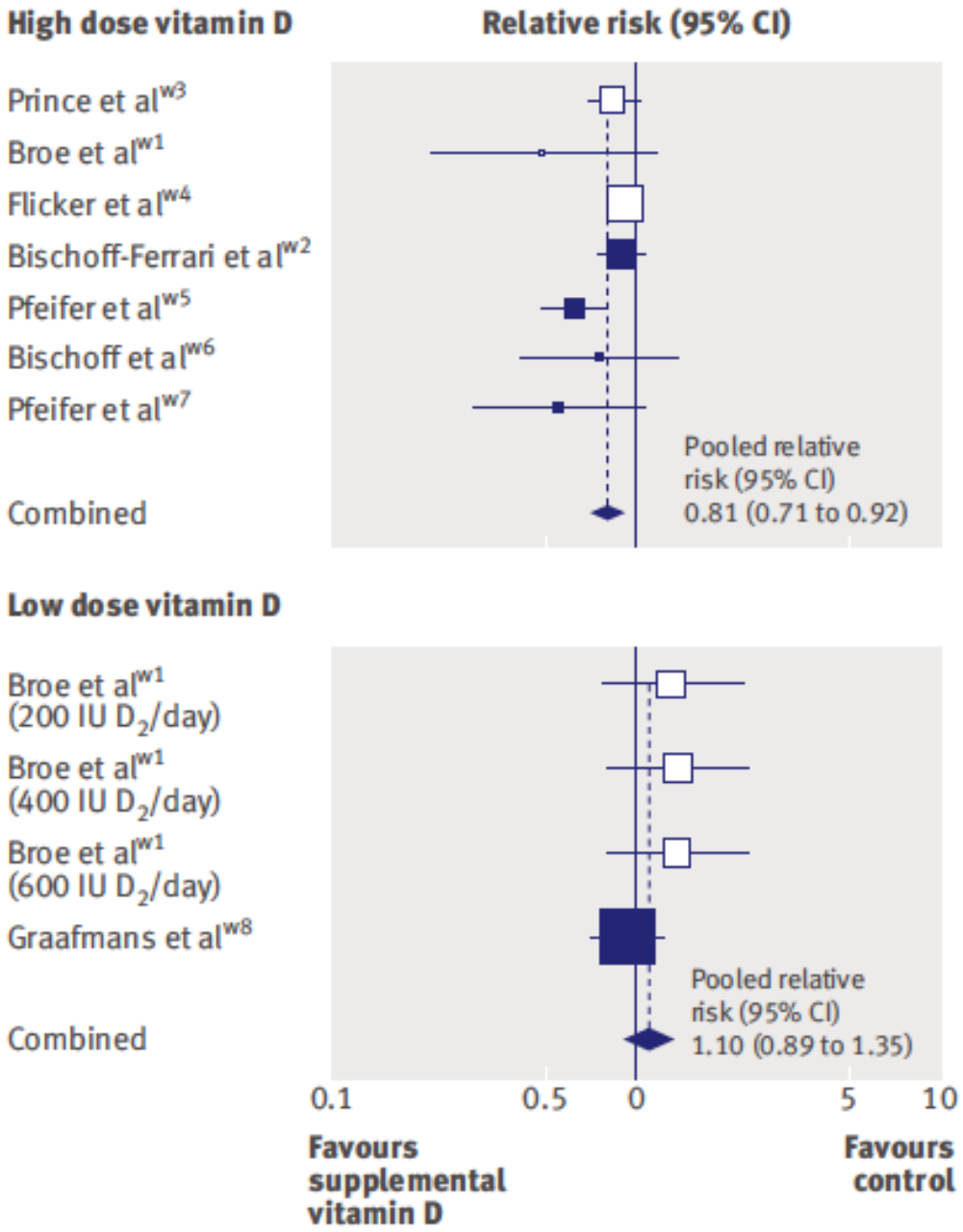
Fox FAU et al., Endocr Connect 2023

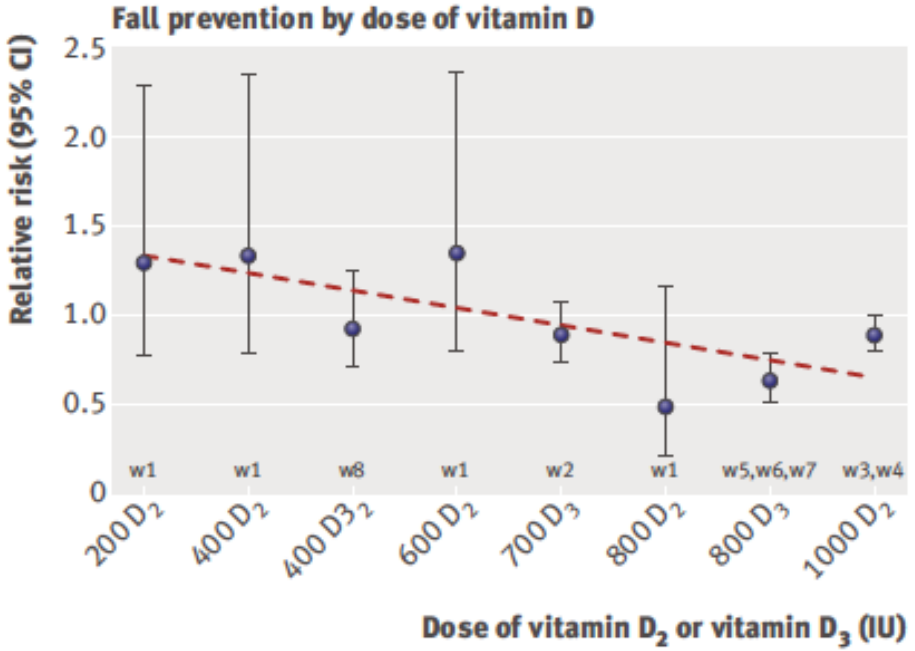
Vitamin D Supplementation Improves Handgrip Strength in Postmenopausal Women

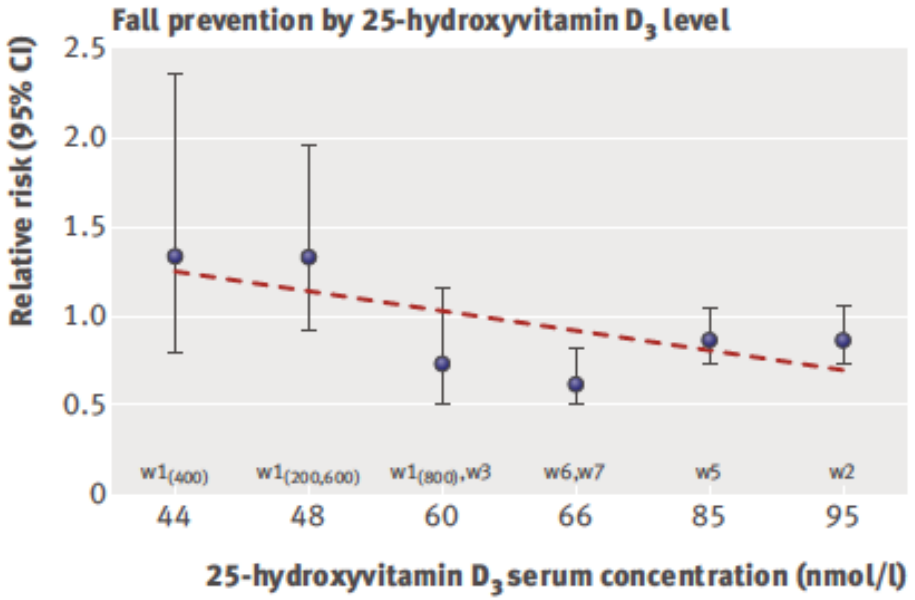




Zhang JL et al., Front Endocrinol 2022







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

Bischoff-Ferrari HA et al., BMJ 2009

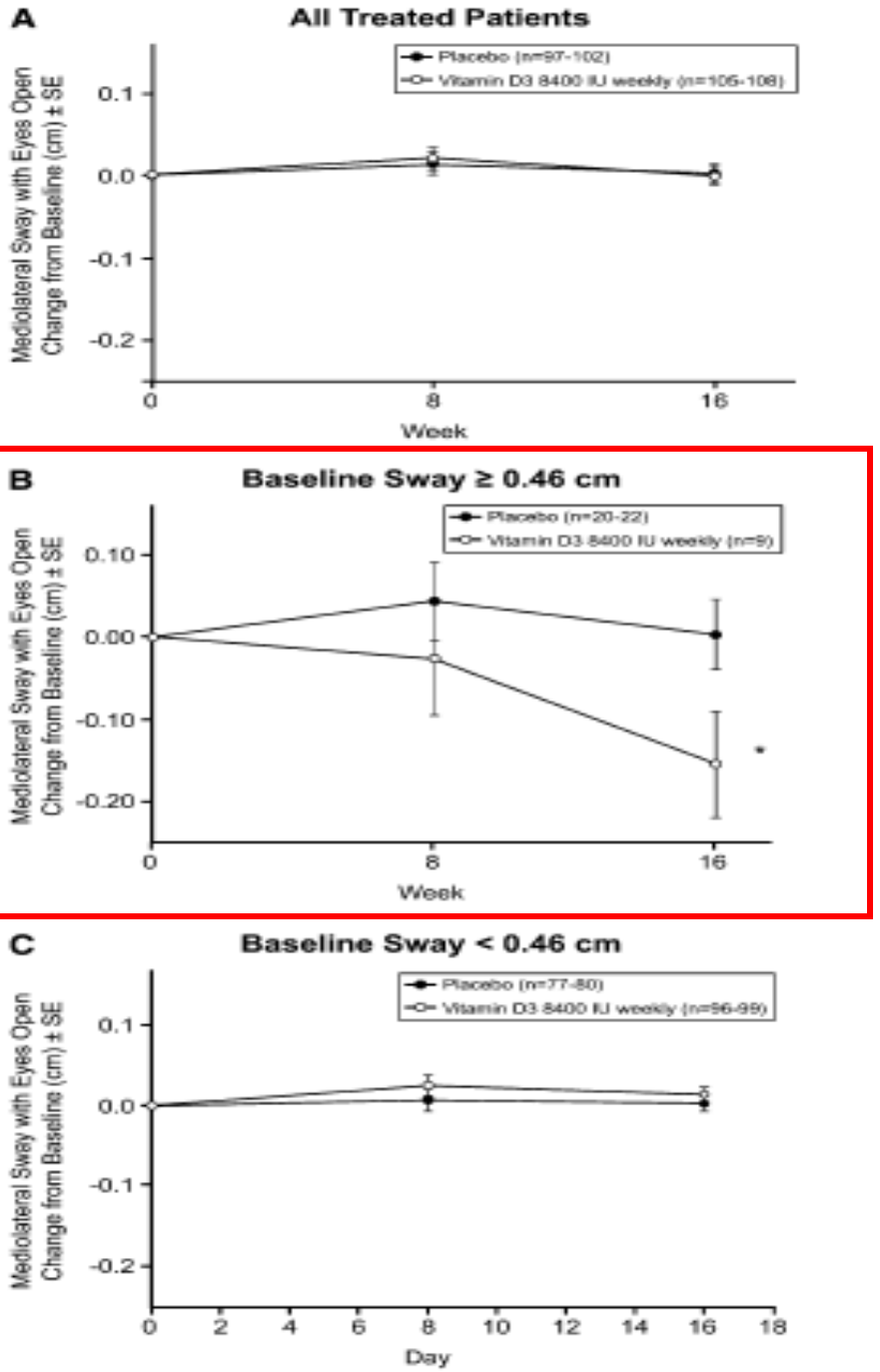
Once-weekly dose of 8400 IU vitamin D_3 compared with placebo: effects on neuromuscular function and tolerability in older adults with vitamin D insufficiency[1–3]

Paul Lips, Neil Binkley, Michael Pfeifer, Robert Recker, Suvajit Samanta, Dosinda A Cohn, Julie Chandler, Elizabeth Rosenberg, and Dimitris A Papanicolaou

Baseline characteristics of subjects[1]

Characteristic	Placebo (n = 112)	Vitamin D_3 (n = 114)
Age (y)	77.6 ± 6.6[2]	78.5 ± 6.2
Height (cm)	161.9 ± 10.3	162.3 ± 10.7
Weight (kg)	73.8 ± 17.0	72.3 ± 15.2
Mediolateral sway with eyes open (cm)		
All patients	0.349 ± 0.150	0.306 ± 0.123
Subgroups by baseline 25(OH)D concentration		
≤15 ng/mL	0.355 [68][3]	0.303 [75]
>15 ng/mL	0.340 [43]	0.313 [38]
Serum 25(OH)D concentration (ng/mL)		
All patients	14.1 ± 5.5	13.7 ± 4.4

Conclusions: Weekly treatment with 8400 IU vitamin D_3 raised 25(OH)D concentrations in elderly, vitamin D–insufficient individuals. Treatment with 8400 IU vitamin D_3 did not reduce mediolateral sway significantly compared with treatment with placebo in this population, although in post hoc analysis, treatment with 8400 IU vitamin D_3 reduced sway in the subgroup of patients who had elevated sway at baseline. Weekly treatment with 8400 IU vitamin D_3 was well tolerated. This trial was registered at clinicaltrials.gov as NCT00242476. *Am J Clin Nutr* 2010;91:985–91.



Influence of vitamin D on sarcopenia pathophysiology: A longitudinal study in humans and basic research in VDR knockout mice

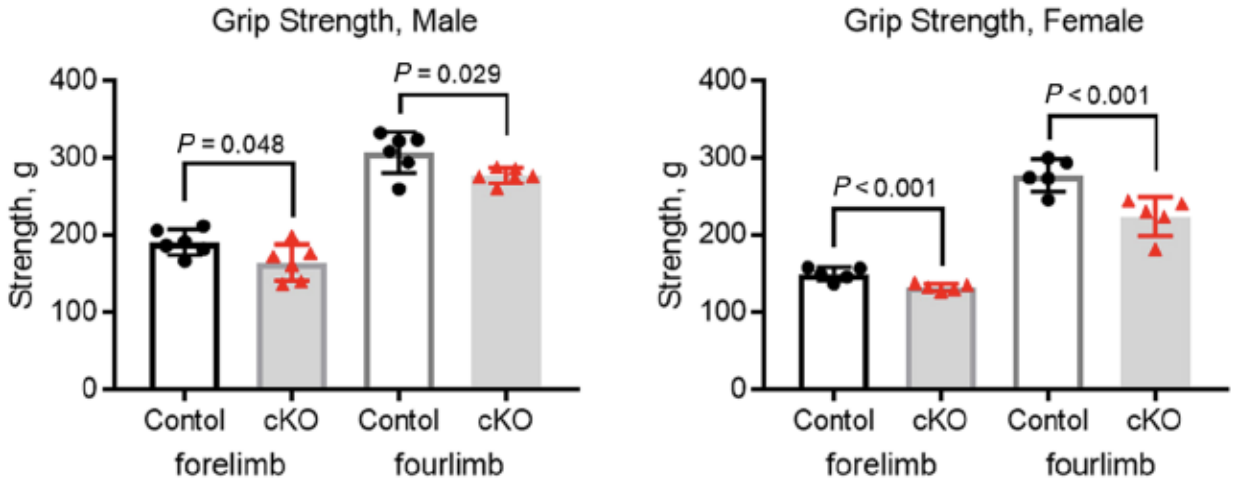
Table 2 Comparison of sarcopenia-related changes in the two groups

		Vitamin D non-deficient	Vitamin D deficient	
		384	384	*P* value
Grip 7th (kg)		28.55 ± 9.14	27.83 ± 9.25	0.278
ASM 7th (kg)		16.67 ± 4.24	16.37 ± 3.99	0.307
SMI 7th (kg/m^2)		6.55 ± 1.13	6.48 ± 1.03	0.367
Grip		−1.13 ± 2.47	−1.55 ± 2.47	**0.019**
ASM		−0.01 ± 0.74	−0.05 ± 0.79	0.423
SMI		0.02 ± 0.29	0.02 ± 0.29	0.743
Sarcopenia classification 7th (%)	Normal	266 (69.3)	263 (68.5)	0.299
	Dynapenia	26 (6.8)	29 (7.6)	
	Presarcopenia	75 (19.5)	64 (16.7)	
	Sarcopenia	14 (3.6)	26 (6.8)	
	Severe sarcopenia	3 (0.8)	2 (0.5)	
New dynapenia (%)		17 (4.4)	15 (3.9)	0.857
New presarcopenia (%)		19 (4.9)	13 (3.4)	0.367
New sarcopenia (%)		5 (1.3)	15 (3.9)	**0.039**
New severe sarcopenia (%)		3 (0.8)	2 (0.5)	1.000

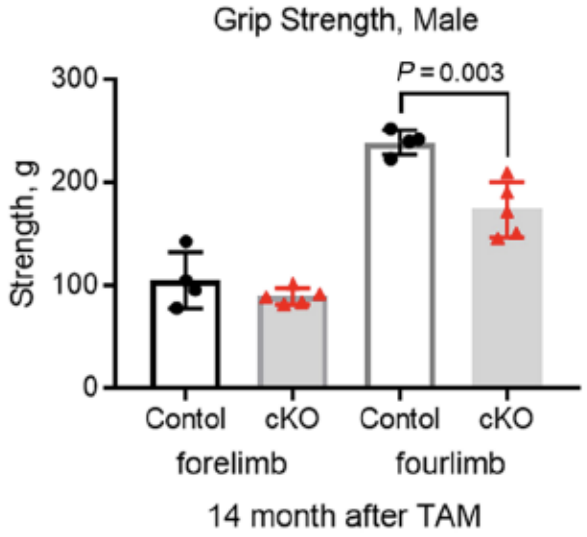
ASM, appendicular skeletal muscle mass; SMI, skeletal muscle mass.
Values are expressed as number (%).
Mean ± standard deviation.
P values were obtained using the *t*-test for continuous data and Fisher's exact test for categorical data.

Mizuno T et al., Journal of Cachexia, Sarcopenia and Muscle 2022

(A)



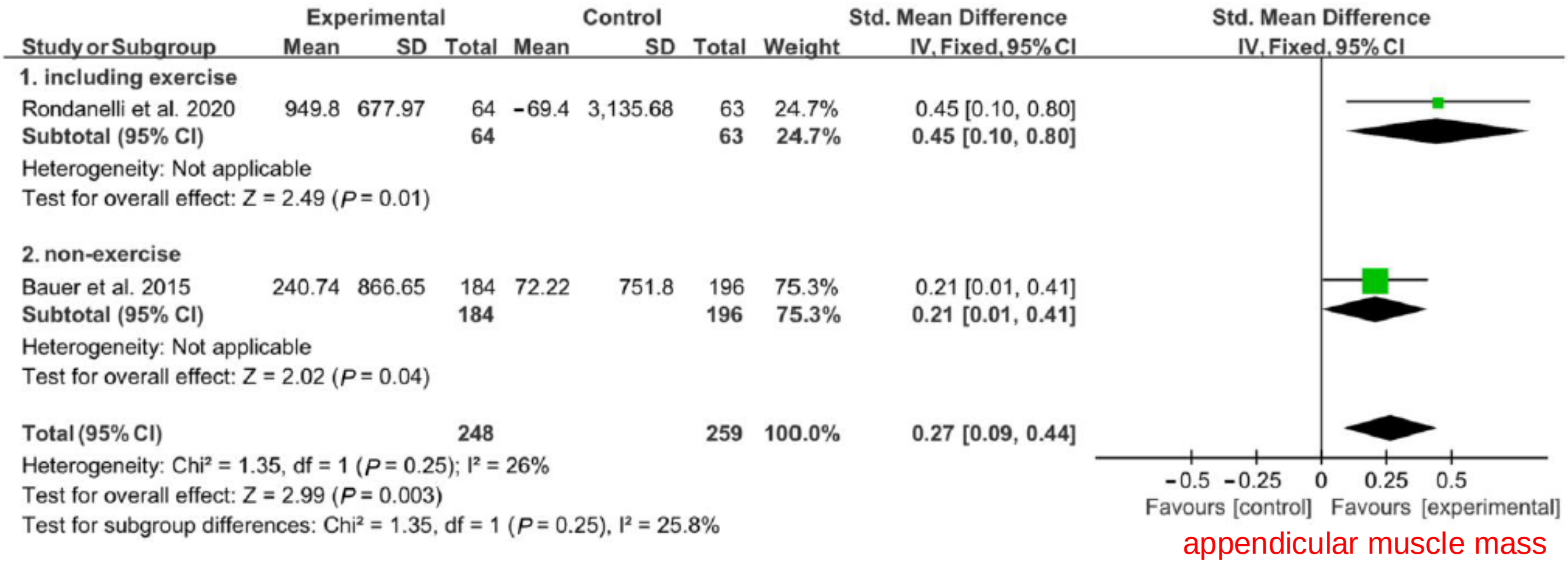
(B)



Influence of vitamin D on sarcopenia pathophysiology: A longitudinal study in humans and basic research in VDR knockout mice

Mizuno T et al., Journal of Cachexia, Sarcopenia and Muscle 2022

Effects of Whey Protein, Leucine, and Vitamin D Supplementation in Patients with Sarcopenia: A Systematic Review and Meta-Analysis

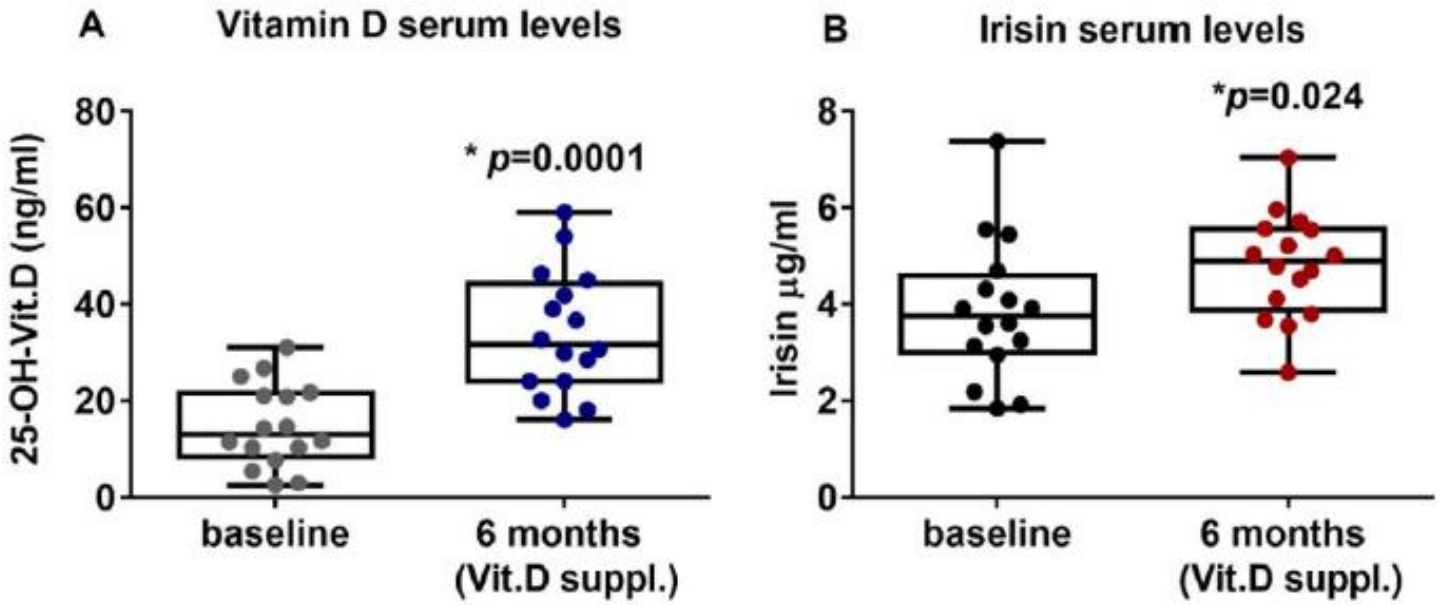


appendicular muscle mass

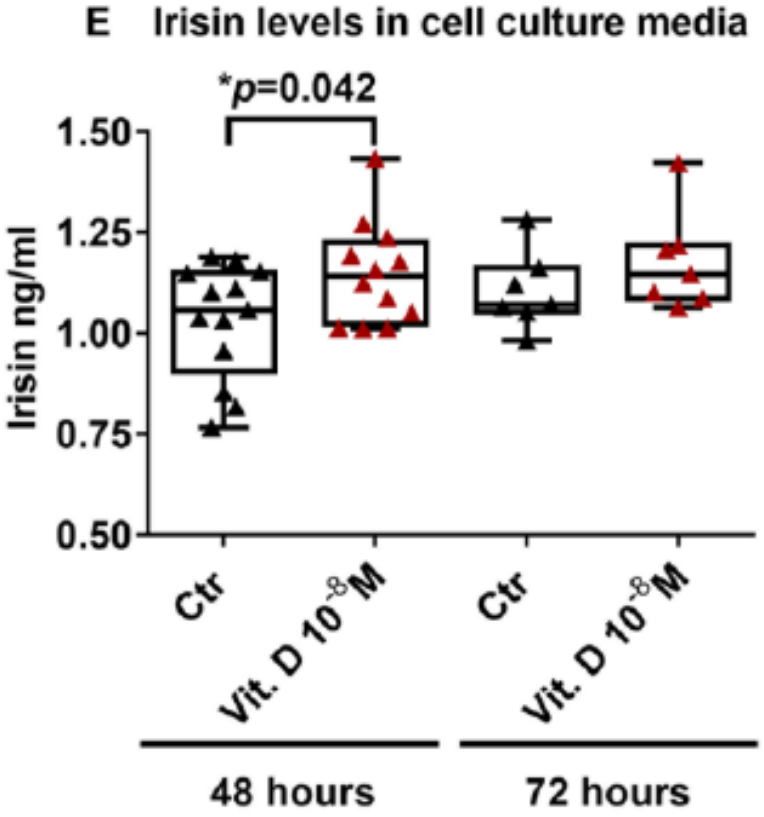
Chang M.C & Choo YJ, Nutrients 2023

Vitamin D Increases Irisin Serum Levels and the Expression of Its Precursor in Skeletal Muscle

In vivo in humans



In vitro



Sanesi, L. et al., Int J Mol Sci 2023

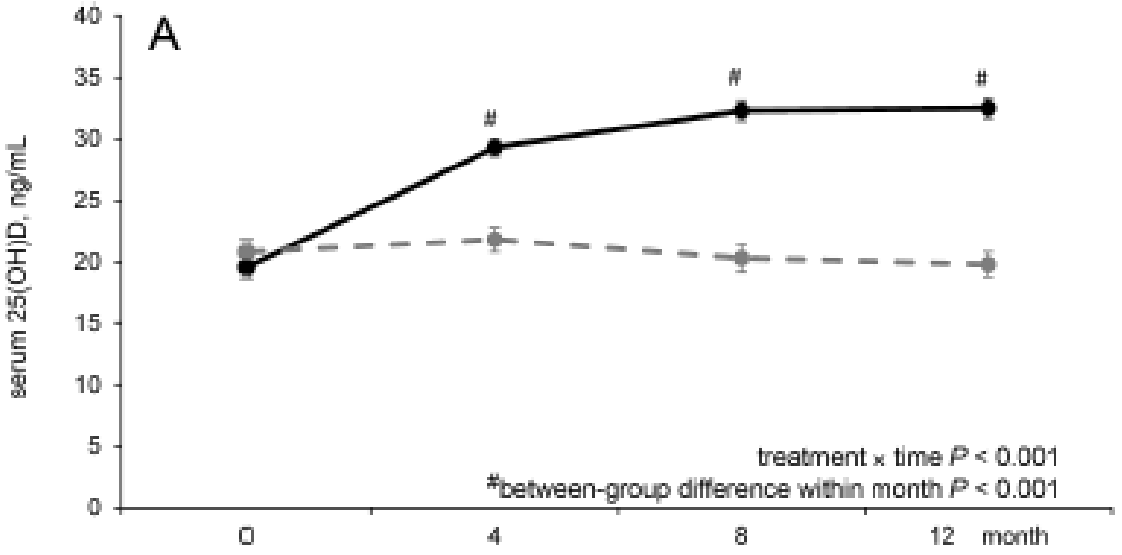
The effect of vitamin D supplementation on lower-extremity power and function in older adults: a randomized controlled trial

M Kyla Shea, Roger A Fielding, and Bess Dawson-Hughes

Methods: This was a single-center, double-blind, randomized, placebo-controlled trial that included 100 community-dwelling men and women ≥60 y old who had serum 25(OH)D ≤20 ng/mL at screening and a mean ± SD serum 25(OH)D of 20.2 ± 6.7 ng/mL at baseline. Participants were randomly assigned to 800 IU vitamin D_3/d (intervention) or placebo. Those in the intervention group whose serum 25(OH)D was <28 ng/mL after 4 mo were given an additional 800 IU vitamin D_3/d, whereas all other participants received placebo as an additional pill.

Results: After 12 mo, the mean ± SD serum 25(OH)D was 32.5 ± 5.1 ng/mL in the intervention group and 19.8 ± 7.3 ng/mL in the control group (treatment × time $P < 0.001$). The change in leg press power, function, and strength did not differ between the 2 groups over 12 mo (all treatment × time $P \geq 0.60$), nor did the change in lean mass (treatment × time $P \geq 0.89$).

Conclusion: Increasing serum 25(OH)D to >32 ng/mL (on average) over 12 mo did not affect lower-extremity power, strength, or lean mass in older community-dwelling adults. This trial was registered at clinicaltrials.gov as NCT02293187. *Am J Clin Nutr* 2019;109:369–379.



Journal of Cachexia, Sarcopenia and Muscle 2022; **13**: 1642–1652
Published online 8 March 2022 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/jcsm.12976

Effect of vitamin D monotherapy on indices of

Table 1 Study and participant characteristics of the included studies in the meta-analysis

			Vitamin D[a]			Placebo					
Study, year	Country	Study design	*n* (M/F)	Age	Baseline 25(OH)D[b]	*n* (M/F)	Age	Baseline 25(OH)D[b]	Treatmentdose	Treatment duration	Sarcopenia outcomes
Shea, 2019	USA	Double-blind RCT	49 (32/17)	70.1 (±7.4)	19.6 (6.6)	51 (32/19)	69.2 (±6.2)	20.8 (6.9)	853 IU/day	12 months	HGS SPPB SCT
Aloia, 2019	USA	Double-blind RCT	130 (0/130)	67.8 (65.1–71.5)	21.5 (6.5)	130 (0/130)	69 (65.4–73.4)	22.2 (6.9)	3490 IU/day[c]	36 months	HGS SPPB
Levis, 2016	USA	Double-blind crossover RCT	66 (66/0)	71.8 (±6.3)	23.1 (5.0)	64 (64/0)	73.0 (±7.3)	22.6 (5.3)	4000 IU/day	9 months	HGS SPPB GST CST
Hansen, 2015	USA	Double-blind RCT	79 (0/79)	60.0 (±5.0)	21.0 (3.0)	76 (0/76)	61.0 (±6.0)	21.0 (3.0)	50 000 IU/month	12 months	TUG ALM CST
Cangussu, 2015	Brazil	Double-blind RCT	80 (0/80)	58.8 (±6.6)	15.0 (7.5)	80 (0/80)	59.3 (±6.7)	16.9 (6.7)	1000 IU/day	9 months	HGS CST ALM
Pirotta, 2015	Australia	Double-blind RCT	13 (5/8)	66.1 (±4.0)	18.6 (4.6)	13 (8/5)	71.5 (±5.7)	19.4 (4.5)	2000 IU/day	10 weeks	KET TUG
Ceglia, 2013	USA	Double-blind RCT	9 (0/9)	76.0 (± 4.0)	43.6 (10.3)	12 (0/12)	80.0 (±5.0)	48.3 (8.8)	4000 IU/day	4 months	SPPB
Glendenning, 2012	Australia	Double-blind RCT	353 (0/353)	76.9 (± 4.0)	26.0 (7.1)	333 (0/333)	76.5 (±4.0)	26.6 (10.9)	150 000 IU/3 months	9 months	HGS TUG
Lips, 2010	Europe and North America	Double-blind RCT	114 (NA)	78.5 (±6.2)	13.7 (4.4)	112 (NA)	77.6 (±6.6)	14.1 (5.5)	8400 IU/week	16 weeks	SPPB GST
Grady, 1991	USA	Double-blind RCT	50 (27/23)	79.4 (±5.4)	24.2 (14.1)	48 (22/26)	78.9 (±5.4)	26.3 (20.6)	0.5 μg/day	6 months	HGS

Conclusions Vitamin D supplementation did not improve any sarcopenia indices in community-dwelling older adults and may compromise some aspects of physical performance. Future studies are warranted to investigate the impact of vitamin D supplementation on individual indices of SPPB, including mobility and balance, in older adults.

The American Journal of Clinical Nutrition

Available online 19 April 2023

In Press, Journal Pre-proof What's this?

Original Research Article

Vitamin D supplementation and muscle power, strength and physical performance in older adults: a randomized controlled trial ☆

Denise K. Houston [a], Anthony P. Marsh [b], Rebecca H. Neiberg [a], Jamehl L. Demons [a], Claudia L. Campos [a], Stephen B. Kritchevsky [a], Osvaldo Delbono [a], Janet A. Tooze [a]

Conclusions

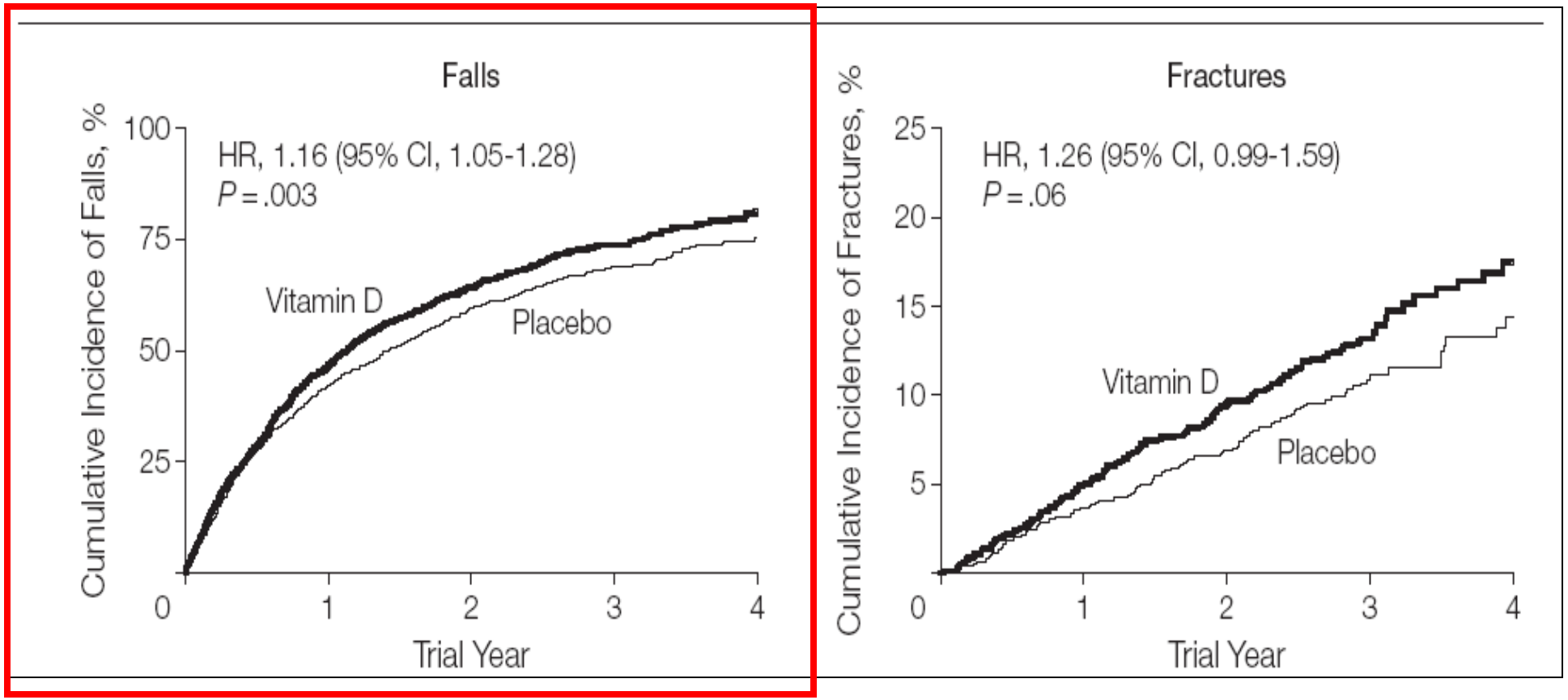
In low-functioning older adults with 25(OH)D concentrations of 18 to <30 ng/mL, randomization to 2000 IU/day vitamin D_3 did not result in improvements in leg power, strength, or physical performance or muscle fiber composition and contractile properties.

Kerrie M. Sanders, PhD
Amanda L. Stuart, BappSc
Elizabeth J. Williamson, MA, PhD
Julie A. Simpson, PhD
Mark A. Kotowicz, MBBS, FRACP
Doris Young, MD, MBBS, FRACGP
Geoffrey C. Nicholson, PhD, FRACP

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

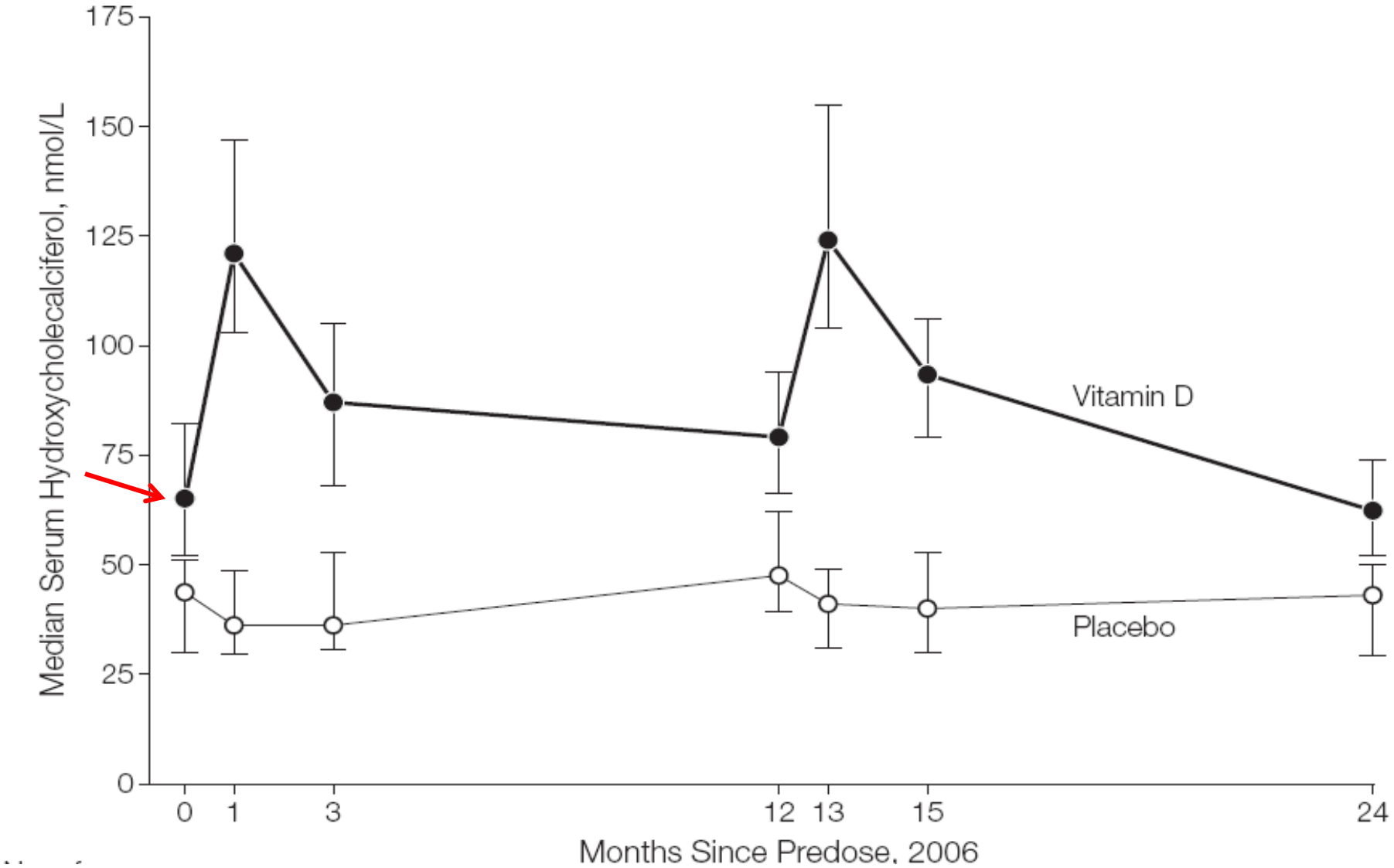
A Randomized Controlled Trial

Double-blind, placebo controlled trial of 2256 community-dwelling women, aged >70 years
500000 IU of D3, orally, in autumn or winter



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

25OHD before and after annual oral high-dose



Sanders KM et al., JAMA 2010

Effect of monthly high-dose vitamin D supplementation on falls and non-vertebral fractures: secondary and post-hoc outcomes from the randomised, double-blind, placebo-controlled ViDA trial

Kay-Tee Khaw, Alistair W Stewart, Debbie Waayer, Carlene M M Lawes, Les Toop, Carlos A Camargo Jr, Robert Scragg

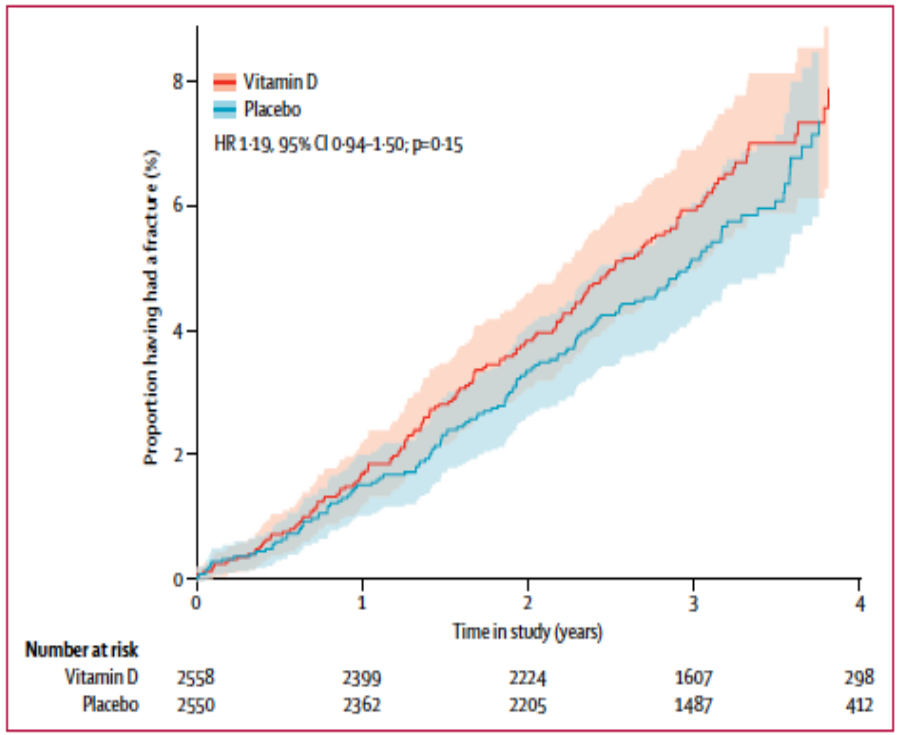
Lancet Diabetes Endocrinol 2017; 5: 438–56
Published Online April 28, 2017

Summary

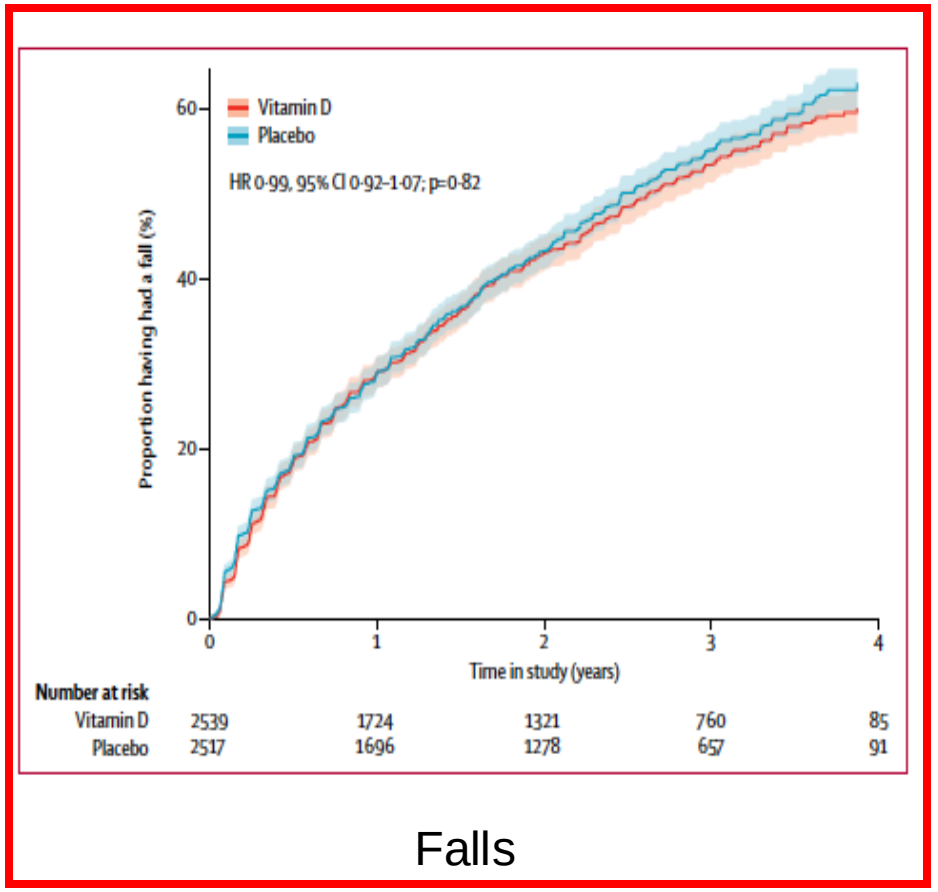
Background Adults with low concentrations of 25-hydroxyvitamin D (25[OH]D) in blood have an increased risk of falls and fractures, but randomised trials of vitamin D supplementation have had inconsistent results. We aimed to assess the effect of high-dose vitamin D supplementation on fractures and falls.

- 100 000 IU cholecalciferol capsule or identical placebo every month from 2011 to 2015.
- 5108 participants

Cox proportional hazards model of fractures and falls recorded during follow-up. Lines depict the proportion of participants having a fracture or a fall during follow-up



Fractures



Falls

Khaw KT et al., Lancet Diabetes Endocrinol 2017

Effect of monthly high-dose vitamin D supplementation on falls and non-vertebral fractures: secondary and post-hoc outcomes from the randomised, double-blind, placebo-controlled ViDA trial

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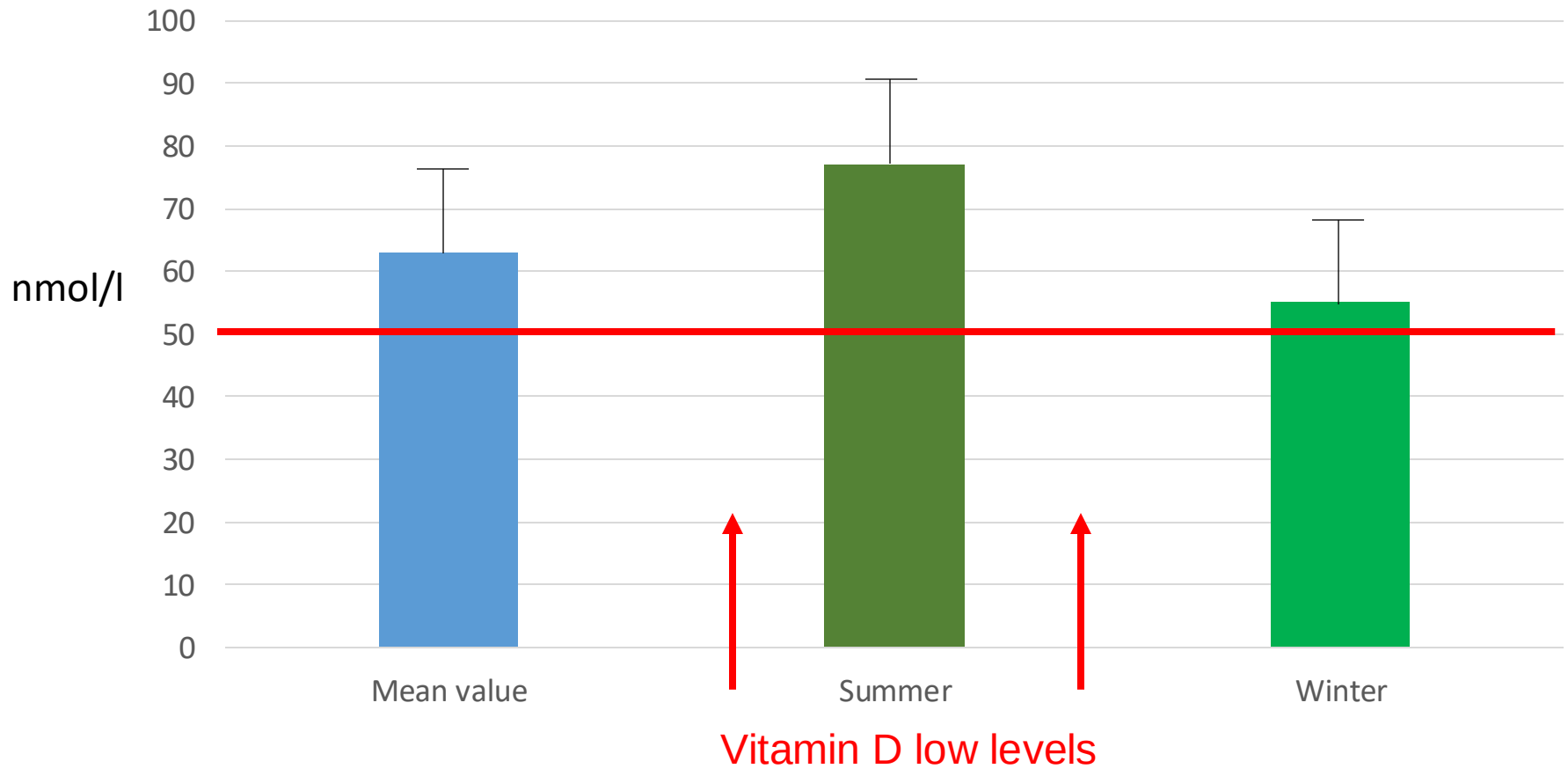
- 5108 participants

Base-line 25(OH)D serum levels



Khaw KT et al., Lancet Diabetes Endocrinol 2017

Tessuti e funzioni influenzati dalla vitamina D

- **Sistema scheletrico**
- Sistema muscolare
- Crescita e differenziazione cellulare
- Funzione immunitaria
- Secrezione insulinica
- Progressione dell’osteoartrite
- Sistema cardiovascolare
- Gonadi e riproduzione
- ……

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 28, 2022 VOL. 387 NO. 4

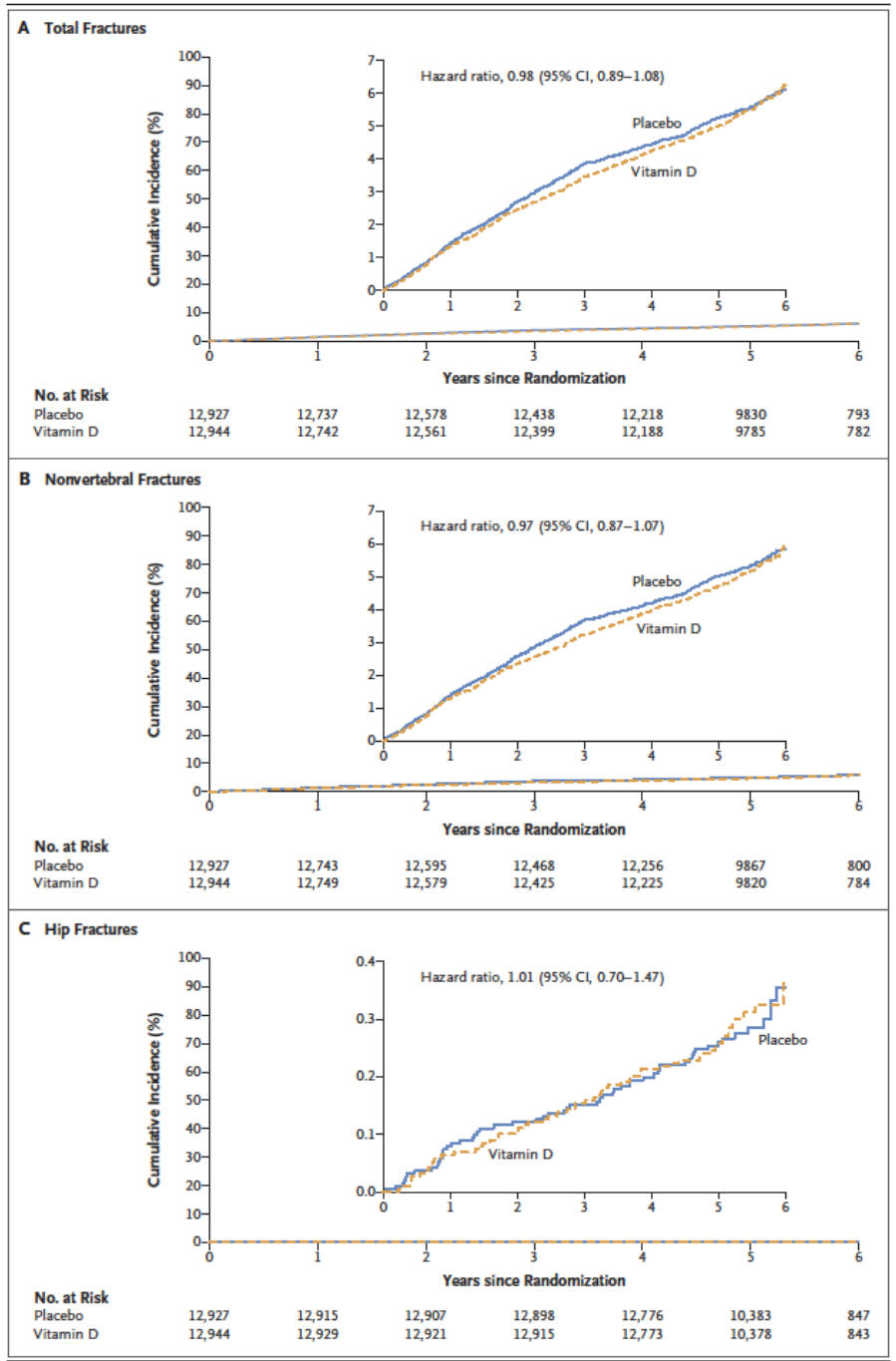
Supplemental Vitamin D and Incident Fractures in Midlife and Older Adults

Meryl S. LeBoff, M.D., Sharon H. Chou, M.D., Kristin A. Ratliff, B.A., Nancy R. Cook, Sc.D., Bharti Khurana, M.D., Eunjung Kim, M.S., Peggy M. Cawthon, Ph.D., M.P.H., Douglas C. Bauer, M.D., Dennis Black, Ph.D., J. Chris Gallagher, M.D., I-Min Lee, M.B., B.S., Sc.D., Julie E. Buring, Sc.D., and JoAnn E. Manson, M.D., Dr.P.H.

Vitamin D 2000 IU/daily

Table 1. Characteristics of the Participants at Baseline, According to Randomized Assignment to Vitamin D or Placebo.*

Characteristic	Total (N=25,871)	Vitamin D Group (N=12,927)	Placebo Group (N=12,944)
Female sex — no. (%)	13,085 (50.6)	6,547 (50.6)	6,538 (50.5)
Age — yr	67.1±7.1	67.1±7.0	67.1±7.1
Race or ethnic group — no./total no. (%)†			
Non-Hispanic White	18,046/25,304 (71.3)	9,013/12,647 (71.3)	9,033/12,657 (71.4)
Black	5,106/25,304 (20.2)	2,553/12,647 (20.2)	2,553/12,657 (20.2)
Non-Black Hispanic	1,013/25,304 (4.0)	516/12,647 (4.1)	497/12,657 (3.9)
Asian or Pacific Islander	388/25,304 (1.5)	188/12,647 (1.5)	200/12,657 (1.6)
American Indian or Alaskan Native	228/25,304 (0.9)	118/12,647 (0.9)	110/12,657 (0.9)
Other or unknown	523/25,304 (2.1)	259/12,647 (2.0)	264/12,657 (2.1)
Body-mass index‡	28.1±5.7	28.1±5.7	28.1±5.8
Diabetes — no./total no. (%)	3,537/25,824 (13.7)	1,804/12,900 (14.0)	1,733/12,924 (13.4)
Parental history of hip fracture — no./total no. (%)	3,704/23,979 (15.4)	1,809/11,970 (15.1)	1,895/12,009 (15.8)
Rheumatoid arthritis — no./total no. (%)	1,118/25,512 (4.4)	556/12,749 (4.4)	562/12,763 (4.4)
History of fragility fracture — no./total no. (%)	2,578/25,023 (10.3)	1,287/12,513 (10.3)	1,291/12,510 (10.3)
Unintentional fall in the past year — no./total no. (%)	6,921/25,715 (26.9)	3,521/12,848 (27.4)	3,400/12,867 (26.4)
Current use of osteoporosis medication — no./total no. (%)§	1,240/25,690 (4.8)	609/12,835 (4.7)	631/12,855 (4.9)
Current smoker — no./total no. (%)	1,835/25,488 (7.2)	921/12,732 (7.2)	914/12,756 (7.2)
Current use of supplemental vitamin D — no. (%)¶	11,030 (42.6)	5,497 (42.5)	5,533 (42.7)
Current use of glucocorticoids — no./total no. (%)	461/25,427 (1.8)	239/12,705 (1.9)	222/12,722 (1.7)
Servings of milk per day	0.71±0.91	0.71±0.89	0.72±0.92
Baseline 25-hydroxyvitamin D level — ng/ml‖	30.7±10.0	30.7±10.0	30.7±10.0
Baseline calcium level — mg/dl**	9.00±1.61	9.00±1.61	9.00±1.61



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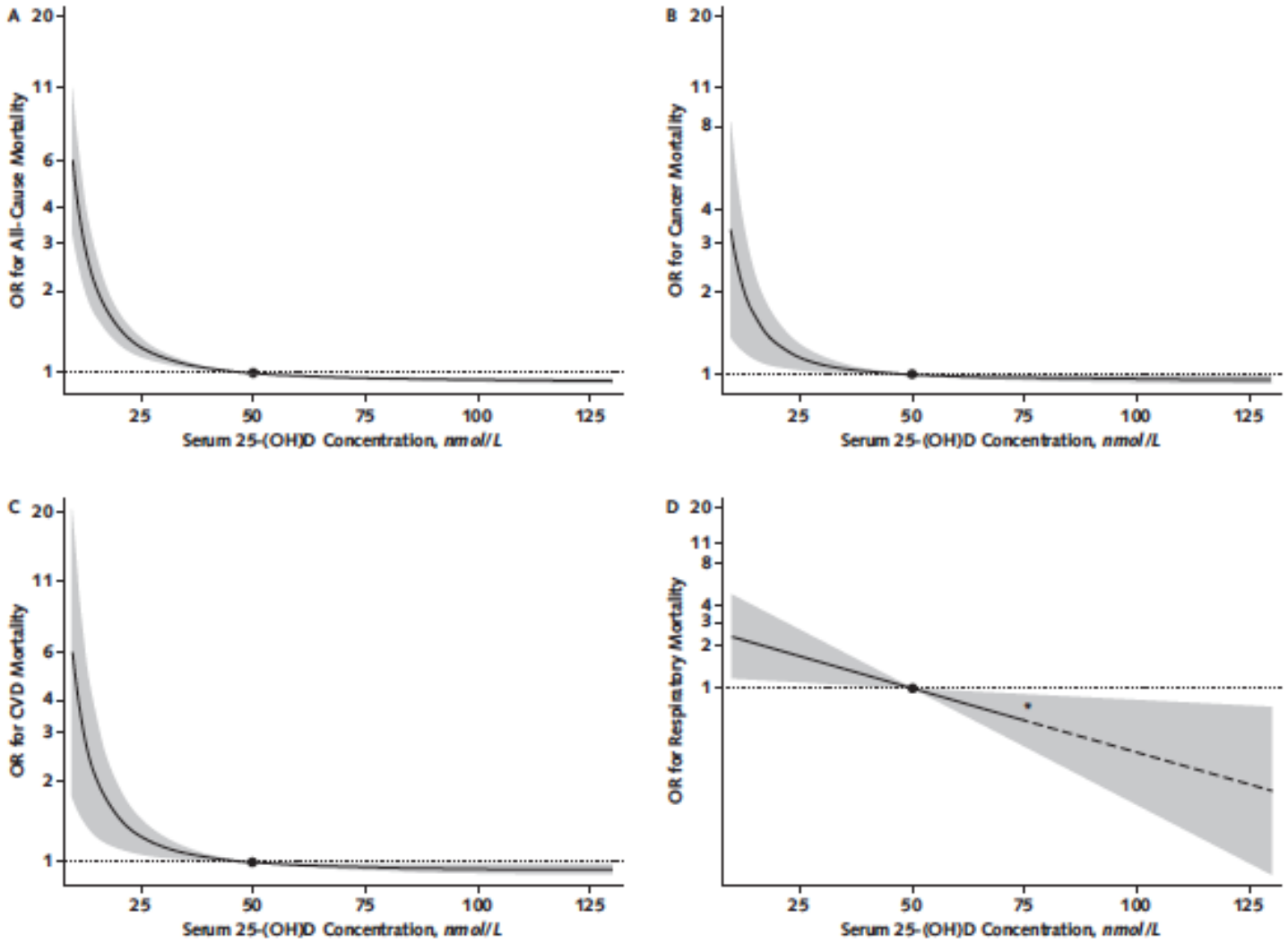
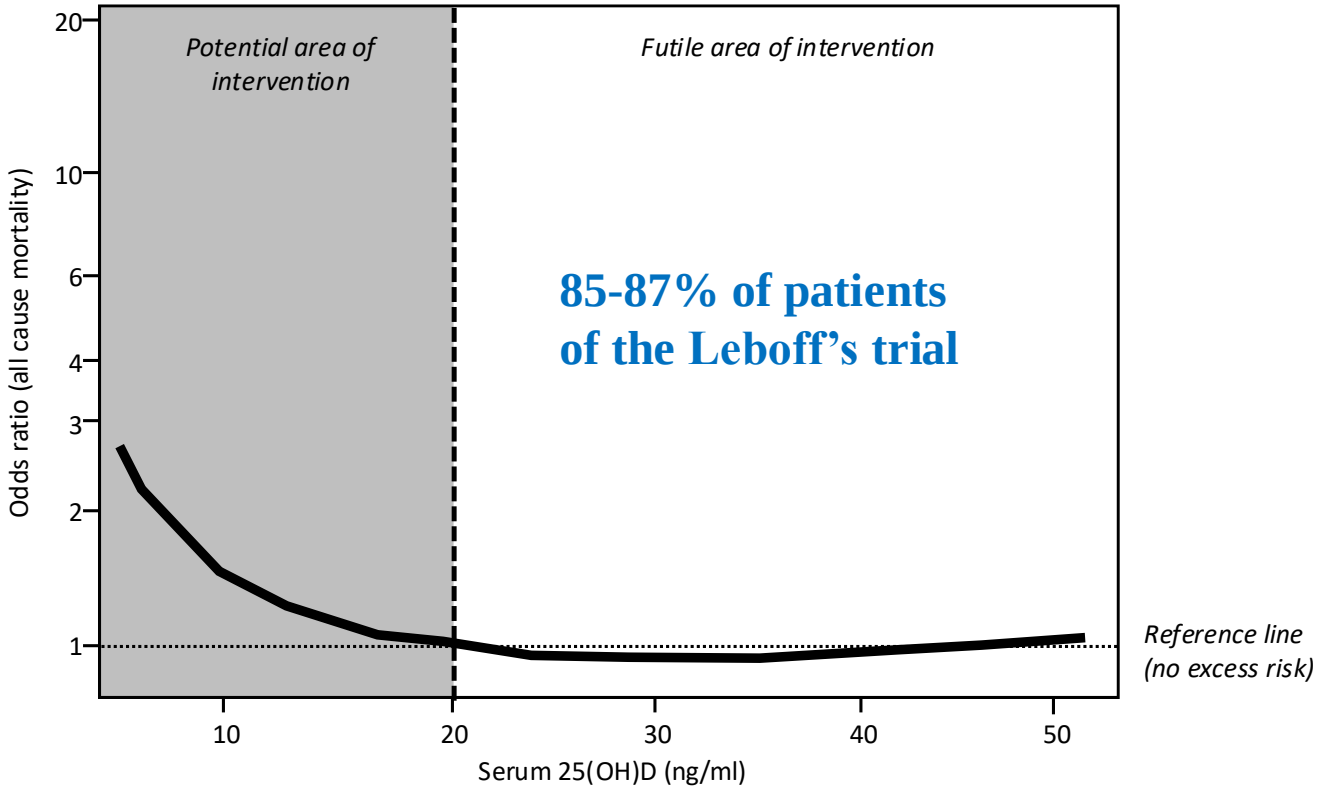
Nonlinear (A, B, and C) and linear (D) Mendelian randomization analyses for the association of genetically predicted 25-(OH)D with all-cause (A), cancer (B), CVD (C), and respiratory (D) mortality in the UK Biobank, projected on the measured 25-(OH)D scale.



Sutherland JP et al., Ann Int Med 2022

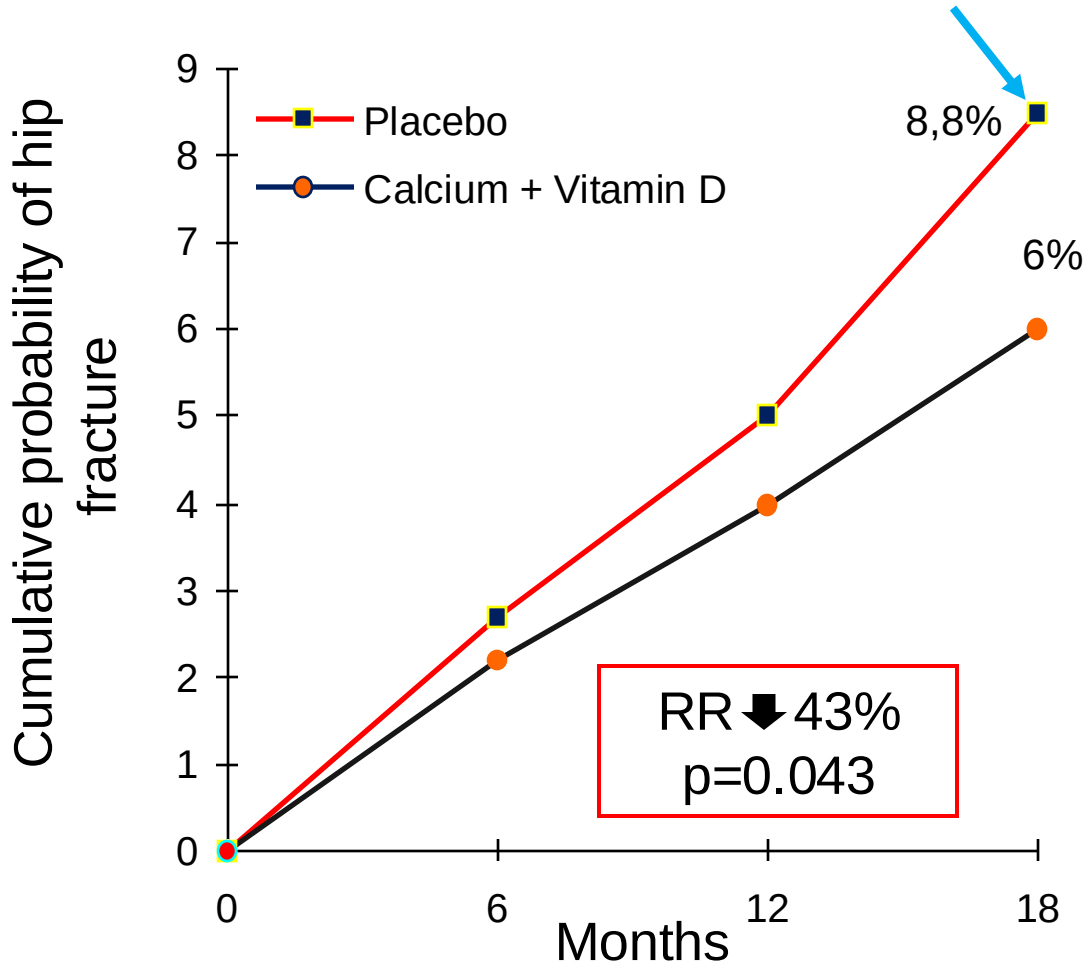
Evaluating benefit from vitamin D supplementation: defining the area for treatment



Nella popolazione generale!!

Tripepi G et al., Osteoporos Int 2023, accepted

Risk of hip fracture in a RCT comparing the effects of cholecalciferol D and calcium vs placebo



3270 healthy ambulatory women, (mean age, 84 yrs years) treated with calcium 1000 mg and cholecalciferol 800 IU/d

Chapuy MC et al., NEJM 1992

Serum Biochemical Values in the Vitamin D_3—Calcium and Placebo Groups at Base Line and after 6, 12, and 18 Months of Follow-up

Table 5. Serum Biochemical Values in the Vitamin D_3—Calcium and Placebo Groups at Base Line and after 6, 12, and 18 Months of Follow-up.*

Serum Index and Group†	Base Line	Follow-up		
		6 mo	12 mo	18 mo
Calcium (mg/dl)†				
Vitamin D_3—calcium	9.17±0.36	9.28±0.35	9.20±0.33	9.21±0.39
Placebo	9.15±0.40	9.15±0.36	9.00±0.39‡	9.00±0.35‡
PTH (pg/ml)§				
Vitamin D_3—calcium	54±37	35±21¶	33±23¶	30±14¶
Placebo	50±24	50±23	60±30‡	56±29‡
25(OH)D (ng/ml)‖				
Vitamin D_3—calcium	16±11	40±11¶	42±9¶	42±9¶
Placebo	13±9	13±9	10±8‡	11±7
1,25$(OH)_2$D (pg/ml)**				
Vitamin D_3—calcium	26±10	ND	ND	27±9
Placebo	29±10	ND	ND	26±9
Alkaline phosphatase (U/liter)				
Vitamin D_3—calcium	69±25	60±22¶	62±20‡	67±22
Placebo	72±22	72±27	79±32††	89±27‡
Osteocalcin (μg/liter)‡‡				
Vitamin D_3—calcium	8±3	8±3	7±3	7±2
Placebo	8±3	9±3	7±3	8±3

*Plus–minus values are means ±SD. Normal ranges for adults 40 to 70 years of age: calcium, 9.2 to 10.2 mg per deciliter; parathyroid hormone (PTH), 11 to 55 pg per milliliter; 25(OH)D, 15 to 50 ng per milliliter; 1,25$(OH)_2$D, 23 to 45 pg per milliliter; and osteocalcin, 7 to 12 μg per liter. ND denotes not determined. Values are for 73 women in the vitamin D_3—calcium group and 69 in the placebo group, except for 1,25$(OH)_2$D (19 in the vitamin D_3—calcium group and 21 in the placebo group).

†To convert serum values to millimoles per liter, multiply by 0.25.

‡$P<0.01$ for the comparison with the base-line value.

§To convert values to picomoles per liter, multiply by 0.11.

¶$P<0.001$ for the comparison with the base-line value.

‖To convert values to nanomoles per liter, multiply by 2.5.

**To convert values to picomoles per liter, multiply by 2.5.

††$P<0.05$ for the comparison with the base-line value.

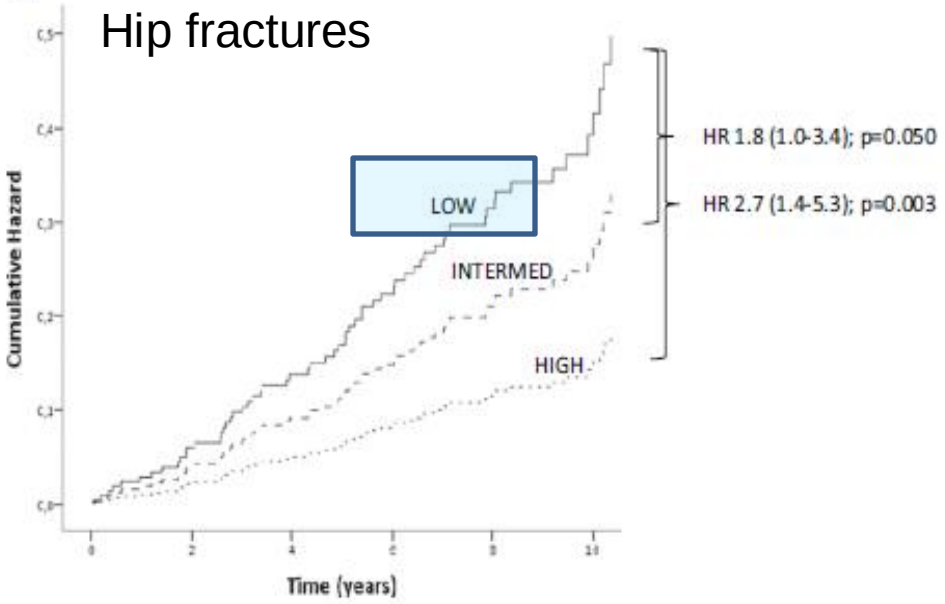
‡‡To convert values to nanomoles per liter, multiply by 0.17.

Chapuy MC et al. N Engl J Med 1992

Vitamin D insufficiency over 5 years is associated with increased fracture risk

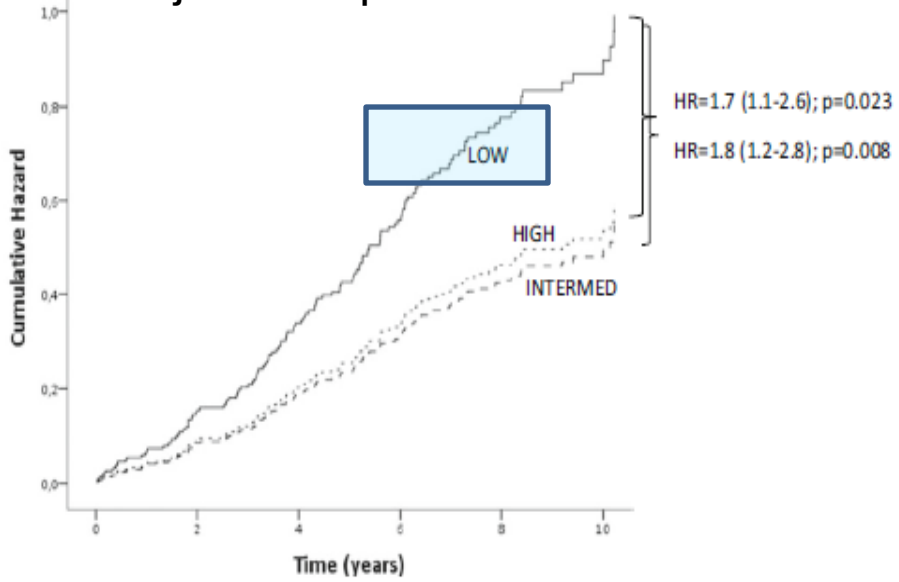
a

Hip fractures



b

Major osteoporotic fractures



- **Low = < 50 nmol/l**
- Intermediate = 50-75 nmol/l
- High = > 75 nmol/l

Buchebner D et al., Osteoporos Int 2014

Nelle Popolazioni «Speciali», invece……

NOTA 96
PER LA PRESCRIZIONE DI FARMACI A BASE DI VITAMINA D

Farmaci inclusi nella Nota AIFA: • colecalciferolo • colecalciferolo/sali di calcio • calcifediolo	La prescrizione a carico del SSN dei farmaci inclusi nella Nota con indicazione **"prevenzione e trattamento della carenza di vitamina D"** nell'adulto (≥18 anni) è limitata alla prevenzione e al trattamento della carenza di vitamina D nei seguenti scenari clinici: **A. indipendentemente dalla determinazione della 25(OH)D** • persone istituzionalizzate • persone con gravi deficit motori o allettate che vivono al proprio domicilio • donne in gravidanza o in allattamento • persone affette da osteoporosi da qualsiasi causa non candidate a terapia remineralizzante (vedi Nota 79) **B. previa determinazione della 25(OH)D** (vedi Allegato 1) • persone con livelli sierici di 25(OH)D **<12 ng/mL (o <30 nmol/L)** e sintomi attribuibili a ipovitaminosi (astenia intensa, mialgie, dolori diffusi o localizzati, frequenti cadute immotivate) • persone asintomatiche con rilievo occasionale di 25(OH)D **<12 ng/mL (o <30 nmol/L)** • persone con 25(OH)D **<20 ng/mL (o <50 nmol/L)** in terapia di lunga durata con farmaci interferenti col metabolismo della vitamina D • persone con 25(OH)D **<20 ng/mL (o <50 nmol/L)** affette da malattie che possono causare malassorbimento nell'adulto • persone con 25(OH)D **<30 ng/mL (o 75 nmol/L)** con diagnosi di iperparatiroidismo (primario o secondario) • persone con 25(OH)D **<30 ng/mL (o 75 nmol/L)** affette da osteoporosi di qualsiasi causa o osteopatie accertate candidate a terapia remineralizzante per le quali la correzione dell'ipovitaminosi dovrebbe essere propedeutica all'inizio della terapia * * Le terapie remineralizzanti dovrebbero essere iniziate dopo la correzione della ipovitaminosi D.

Per una guida alla determinazione appropriata dei livelli di 25OH vitamina D e la conseguente prescrizione terapeutica è possibile fare riferimento alla flowchart allegata (Allegato 1).

NOTA 96
PER LA PRESCRIZIONE DI FARMACI A BASE DI VITAMINA D

Farmaci inclusi nella Nota AIFA:	La prescrizione a carico del SSN dei farmaci inclusi nella Nota con indicazione **"prevenzione e trattamento della carenza di vitamina D"** nell'adulto (≥18 anni) è limitata alla prevenzione e al trattamento della carenza di vitamina D nei seguenti scenari clinici:
• colecalciferolo • colecalciferolo/sali di calcio • calcifediolo	**A. indipendentemente dalla determinazione della 25(OH)D** • persone istituzionalizzate • persone con gravi deficit motori o allettate che vivono al proprio domicilio • donne in gravidanza o in allattamento • persone affette da osteoporosi da qualsiasi causa non candidate a terapia remineralizzante (vedi Nota 79) **B. previa determinazione della 25(OH)D** (vedi Allegato 1) • persone con livelli sierici di 25(OH)D **<12 ng/mL (o <30 nmol/L)** e sintomi attribuibili a ipovitaminosi (astenia intensa, mialgie, dolori diffusi o localizzati, frequenti cadute immotivate) • persone asintomatiche con rilievo occasionale di 25(OH)D **<12 ng/mL (o <30 nmol/L)** • persone con 25(OH)D **<20 ng/mL (o <50 nmol/L)** in terapia di lunga durata con farmaci interferenti col metabolismo della vitamina D • persone con 25(OH)D **<20 ng/mL (o <50 nmol/L)** affette da malattie che possono causare malassorbimento nell'adulto • persone con 25(OH)D **<30 ng/mL (o 75 nmol/L)** con diagnosi di iperparatiroidismo (primario o secondario) • persone con 25(OH)D **<30 ng/mL (o 75 nmol/L)** affette da osteoporosi di qualsiasi causa o osteopatie accertate candidate a terapia remineralizzante per le quali la correzione dell'ipovitaminosi dovrebbe essere propedeutica all'inizio della terapia * * Le terapie remineralizzanti dovrebbero essere iniziate dopo la correzione della ipovitaminosi D.

Per una guida alla determinazione appropriata dei livelli di 25OH vitamina D e la conseguente prescrizione terapeutica è possibile fare riferimento alla flowchart allegata (Allegato 1).

NOTA 96
PER LA PRESCRIZIONE DI FARMACI A BASE DI VITAMINA D

Farmaci inclusi nella Nota AIFA:	La prescrizione a carico del SSN dei farmaci inclusi nella Nota con indicazione **"prevenzione e trattamento della carenza di vitamina D"** nell'adulto (≥18 anni) è limitata alla prevenzione e al trattamento della carenza di vitamina D nei seguenti scenari clinici:
• colecalciferolo • colecalciferolo/sali di calcio • calcifediolo	**A. indipendentemente dalla determinazione della 25(OH)D** • persone istituzionalizzate • persone con gravi deficit motori o allettate che vivono al proprio domicilio • donne in gravidanza o in allattamento • persone affette da osteoporosi da qualsiasi causa non candidate a terapia remineralizzante (vedi Nota 79)

NOTA 96
PER LA PRESCRIZIONE DI FARMACI A BASE DI VITAMINA D

Farmaci inclusi nella Nota AIFA:	La prescrizione a carico del SSN dei farmaci inclusi nella Nota con indicazione **"prevenzione e trattamento della carenza di vitamina D"** nell'adulto (≥18 anni) è limitata alla prevenzione e al trattamento della carenza di vitamina D nei seguenti scenari clinici:
• colecalciferolo • colecalciferolo/sali di calcio • calcifediolo	**A. indipendentemente dalla determinazione della 25(OH)D** • persone istituzionalizzate • persone con gravi deficit motori o allettate che vivono al proprio domicilio • donne in gravidanza o in allattamento • persone affette da osteoporosi da qualsiasi causa non candidate a terapia remineralizzante (vedi Nota 79) **B. previa determinazione della 25(OH)D** (vedi Allegato 1) • persone con livelli sierici di 25(OH)D **<12 ng/mL (o <30 nmol/L)** e sintomi attribuibili a ipovitaminosi (astenia intensa, mialgie, dolori diffusi o localizzati, frequenti cadute immotivate) • persone asintomatiche con rilievo occasionale di 25(OH)D **<12 ng/mL (o <30 nmol/L)** • persone con 25(OH)D **<20 ng/mL (o <50 nmol/L)** in terapia di lunga durata con farmaci interferenti col metabolismo della vitamina D • persone con 25(OH)D **<20 ng/mL (o <50 nmol/L)** affette da malattie che possono causare malassorbimento nell'adulto • persone con 25(OH)D **<30 ng/mL (o 75 nmol/L)** con diagnosi di iperparatiroidismo (primario o secondario) • persone con 25(OH)D **<30 ng/mL (o 75 nmol/L)** affette da osteoporosi di qualsiasi causa o osteopatie accertate candidate a terapia remineralizzante per le quali la correzione dell'ipovitaminosi dovrebbe essere propedeutica all'inizio della terapia * * Le terapie remineralizzanti dovrebbero essere iniziate dopo la correzione della ipovitaminosi D.

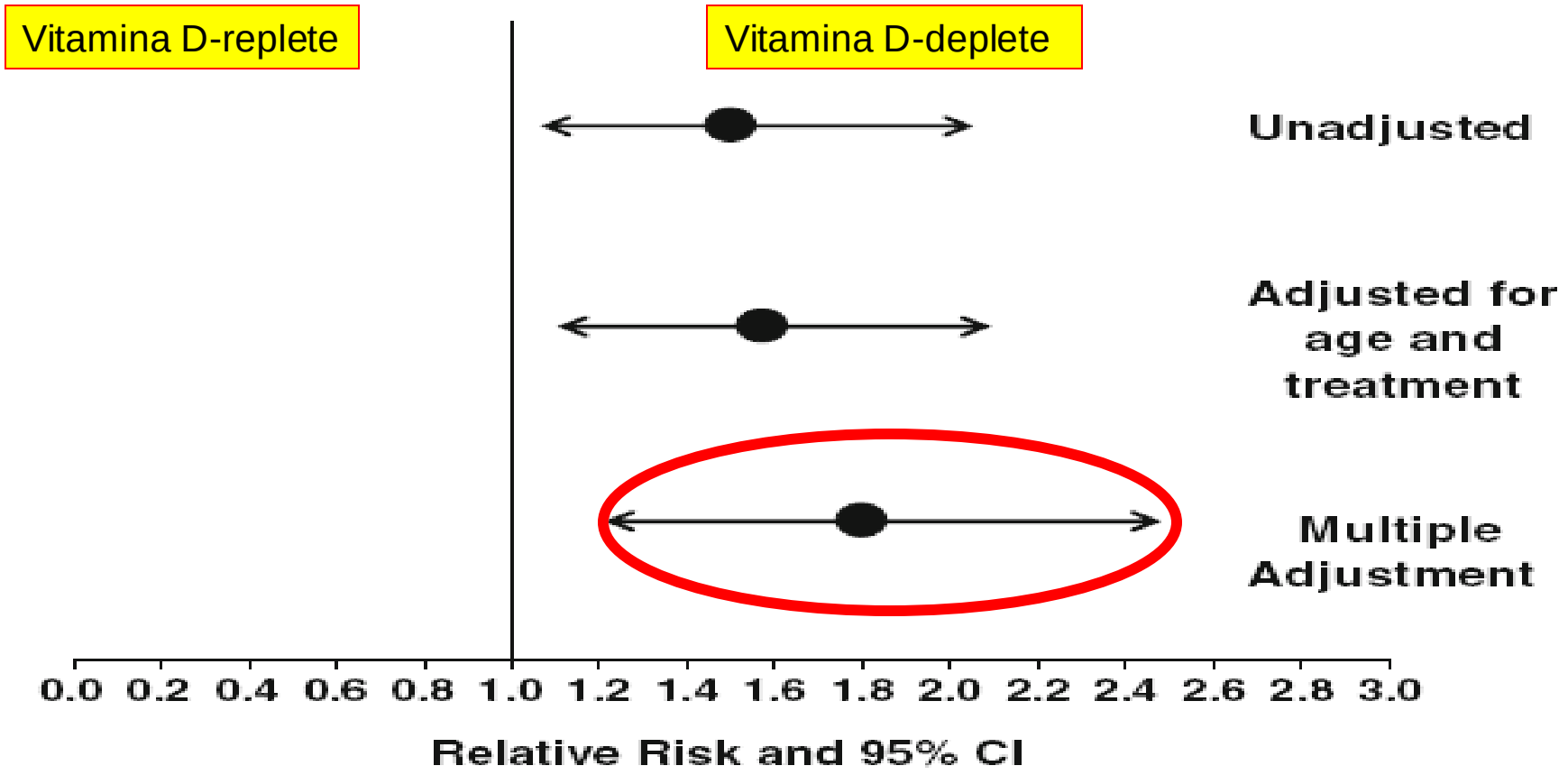
Per una guida alla determinazione appropriata dei livelli di 25OH vitamina D e la conseguente prescrizione terapeutica è possibile fare riferimento alla flowchart allegata (Allegato 1).

B. previa determinazione della 25(OH)D
(vedi Allegato 1)

- persone con livelli sierici di 25(OH)D **<12 ng/mL (o <30 nmol/L)** e sintomi attribuibili a ipovitaminosi (astenia intensa, mialgie, dolori diffusi o localizzati, frequenti cadute immotivate)
- persone asintomatiche con rilievo occasionale di 25(OH)D **<12 ng/mL (o <30 nmol/L)**
- persone con 25(OH)D **<20 ng/mL (o <50 nmol/L)** in terapia di lunga durata con farmaci interferenti col metabolismo della vitamina D
- persone con 25(OH)D **<20 ng/mL (o <50 nmol/L)** affette da malattie che possono causare malassorbimento nell'adulto
- persone con 25(OH)D **<30 ng/mL (o 75 nmol/L)** con diagnosi di iperparatiroidismo (primario o secondario)
- persone con 25(OH)D **<30 ng/mL (o 75 nmol/L)** affette da osteoporosi di qualsiasi causa o osteopatie accertate candidate a terapia remineralizzante per le quali la correzione dell'ipovitaminosi dovrebbe essere propedeutica all'inizio della terapia *

* Le terapie remineralizzanti dovrebbero essere iniziate dopo la correzione della ipovitaminosi D.

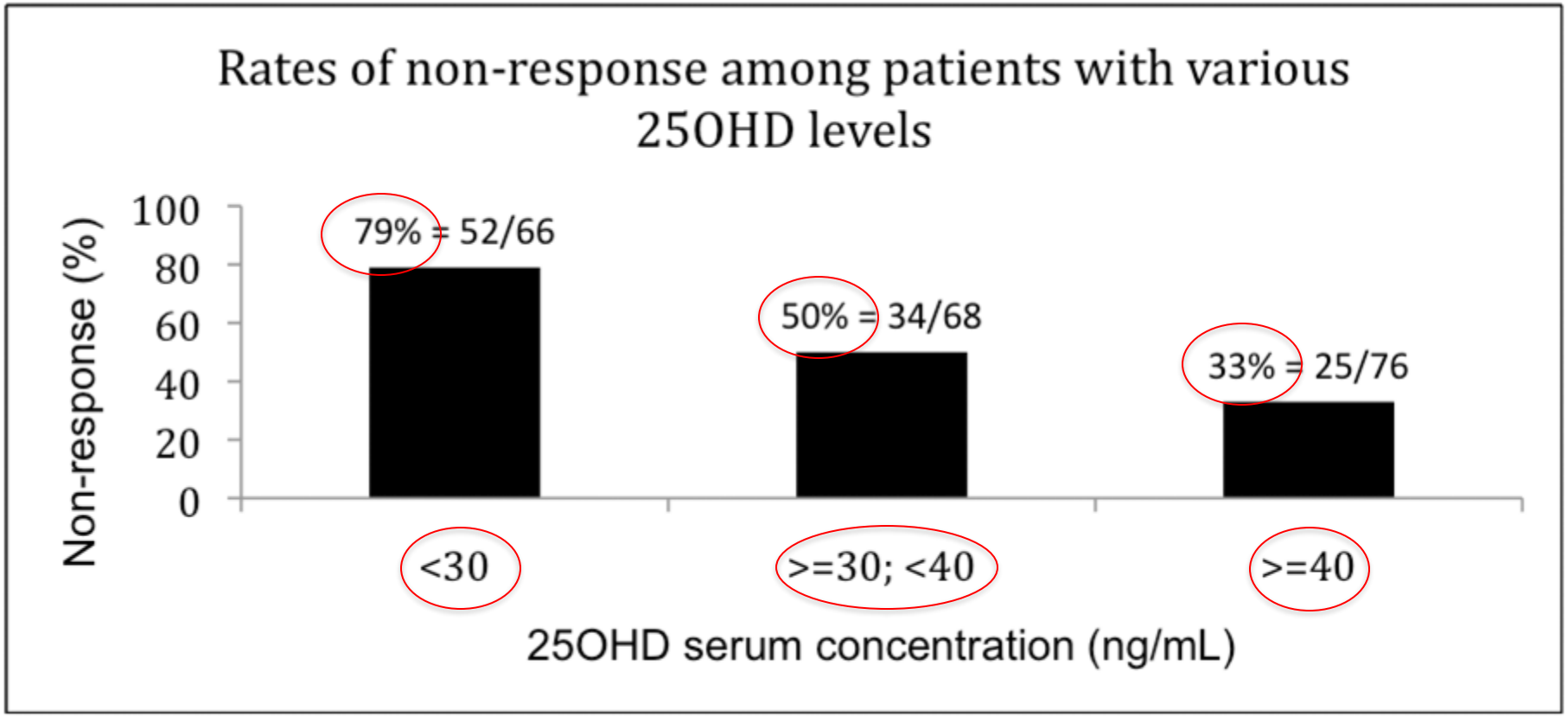
Il rischio di frattura è più elevato in donne osteoporotiche in trattamento con alendronato, risedronato o raloxifene ma deplete di vitamina D (vs replete)



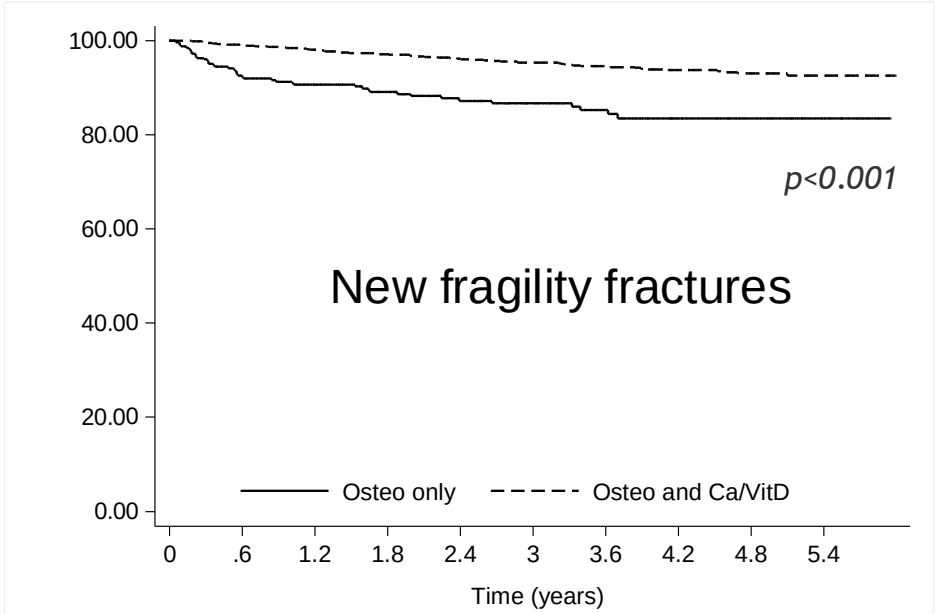
RR corretto per tipo di trattamento, età, precedenti fratture, durata del follow-up ed intake di calcio

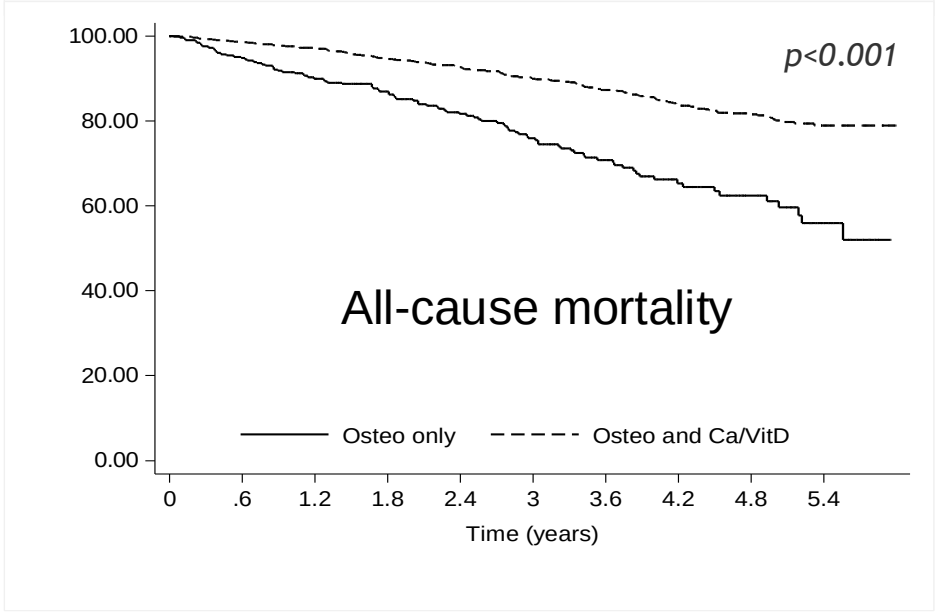
Adami S, Giannini S et al., Osteoporos Int 2008

Association between 25OHD level and bisphosphonate response



Carmel AS et al., Osteoporos Int 2012





Osteoporosis treatment with and without Calcium/Vitamin D in patients with fragility fractures: risk of subsequent fractures and mortality in the real life

Degli Esposti L et al., Endocrine 2018

Conclusioni

- Il sistema endocrino della vitamina D svolge funzioni assai importanti per tessuto muscolare ed osseo
- L’ipovitaminosi D si associa a danno osseo e muscolare
- Il trattamento con vitamina D si associa a beneficio sulla robustezza ossea e la funzione muscolare nei soggetti che ne sono carenti