

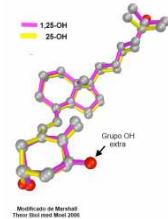
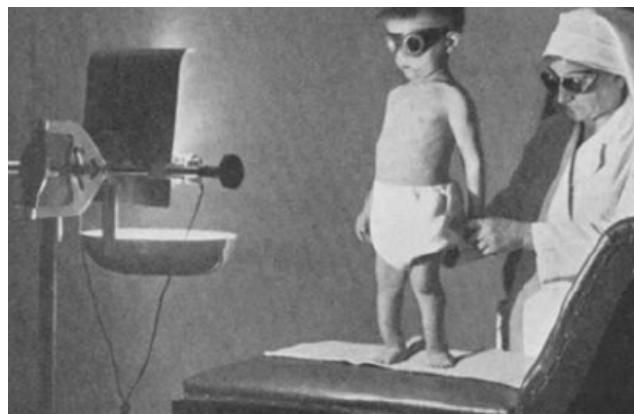
NIVELES DE VITAMINA D: La historia interminable

Isidoro Cano

LA VITAMINA D

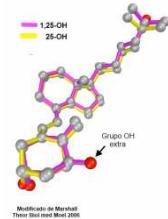


Rickets



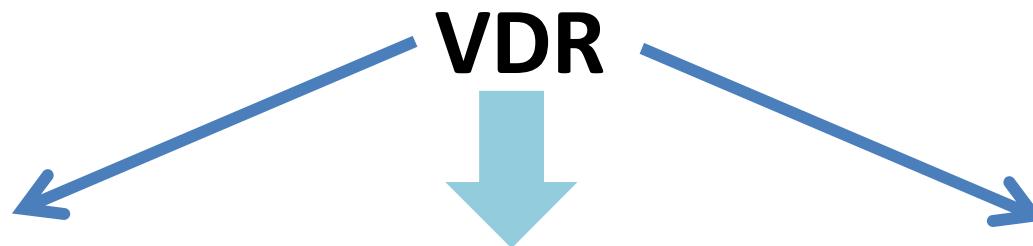
McCollum EF, Simmonds N, Becker JE, et al. J Biol Chem 1922;53:293–312.

Vitamina D como hormona

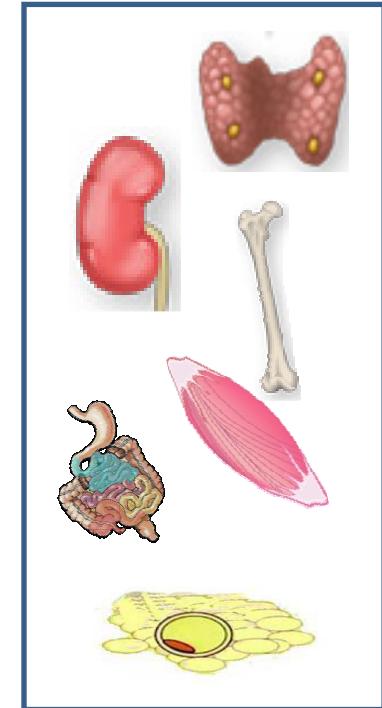
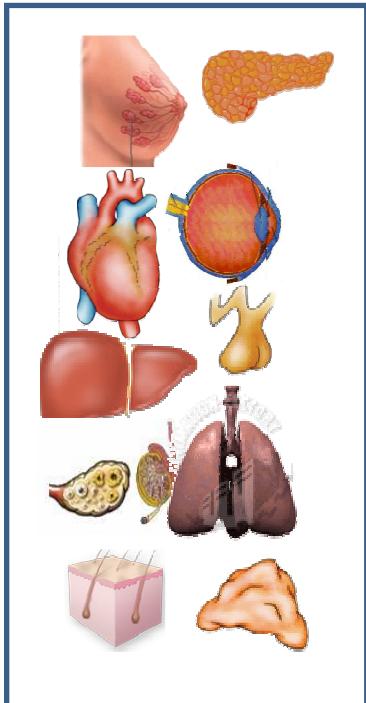


Vit D-25

Vit D-1,25



+ 913 genes
(3% del genoma)

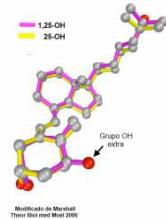


Acciones esqueléticas

Modula el sistema inmune

Regula la proliferación y diferenciación celular

Regula la secreción hormonal (insulina, PTH, renina)



MUSCULOESQUELÉTICO

OSTEODISTROFIA, CAIDAS OSTEOPOROSIS, OSTEOMALACIA

CÁNCER
LEUCEMIA, COLON
PROSTATICO, Mama

CARDIOVASCULAR
HTA,
F. RIESGO

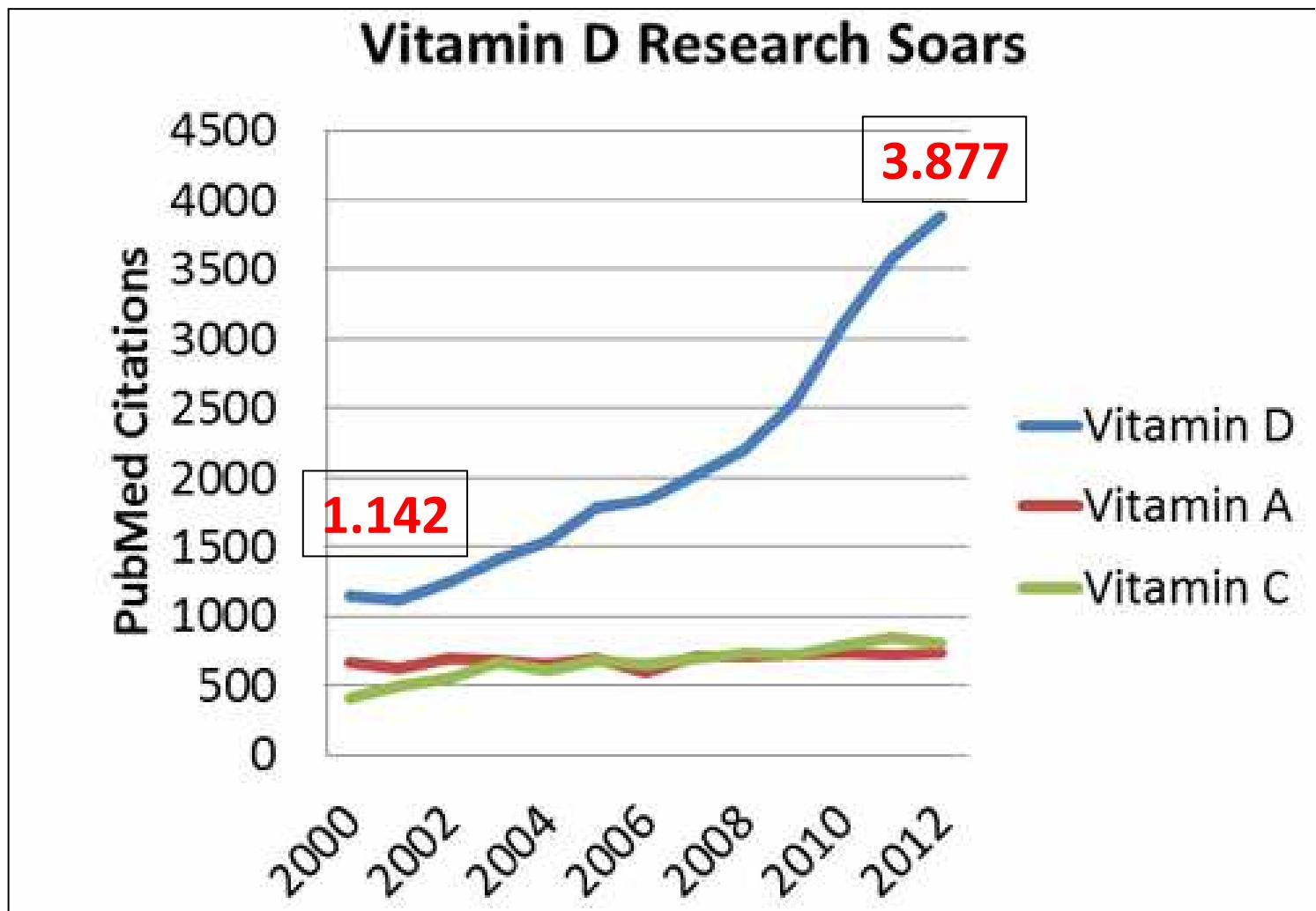
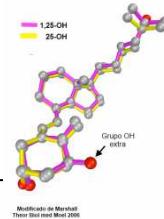
Estudios RCT
Observacionales
VITAMINA D

PIEL
PSORIASIS,
ALOPECIA

ENDOCRINO
HPT2º,
DIABETES 2
F. GONADAL

SISTEMA INMUNE
LUPUS ,DIABETES 1, Esclerosis, EII

Publicaciones Vitamina D Febrero 2013



Finn et al Medscape Feb 2013

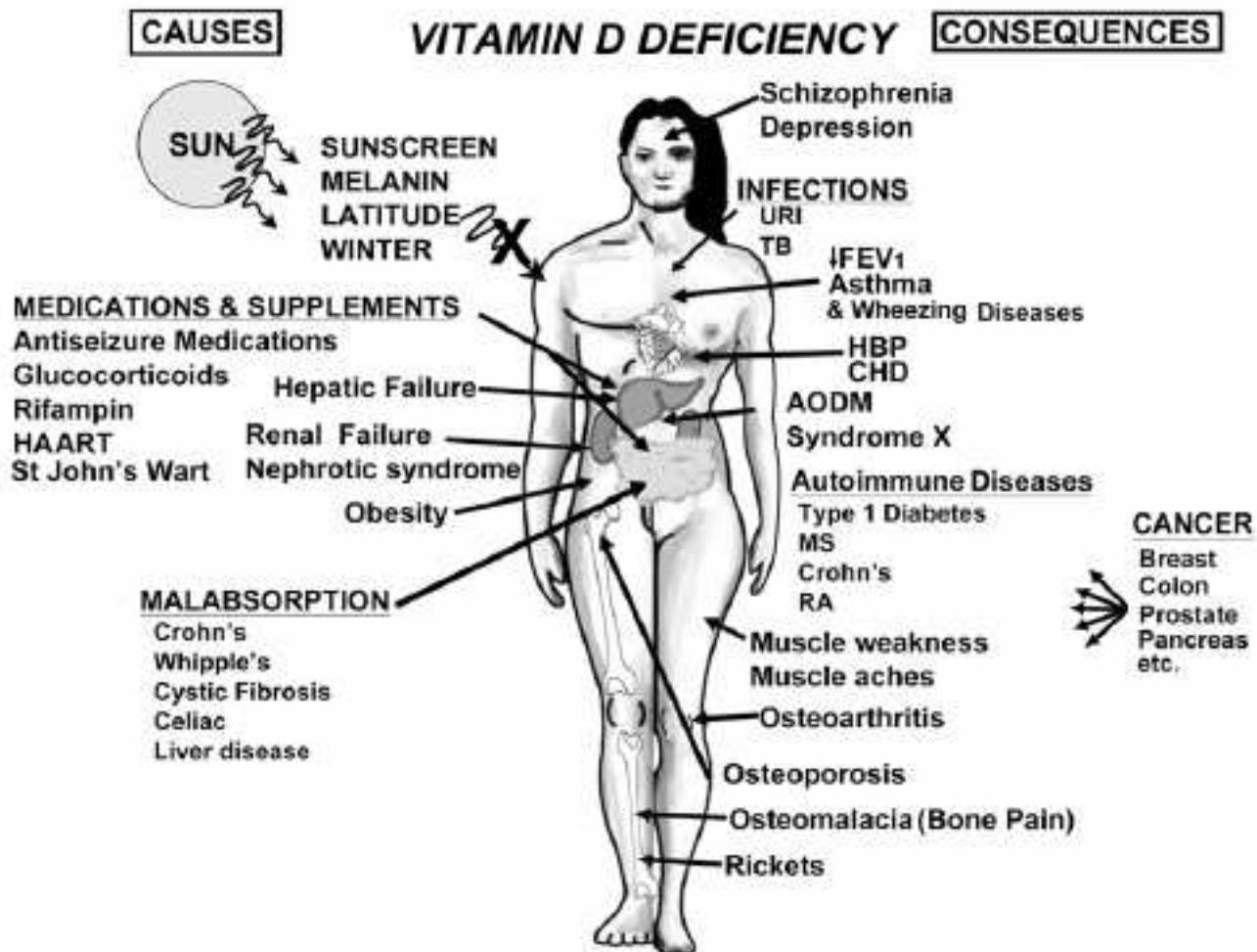
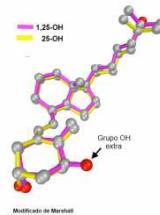
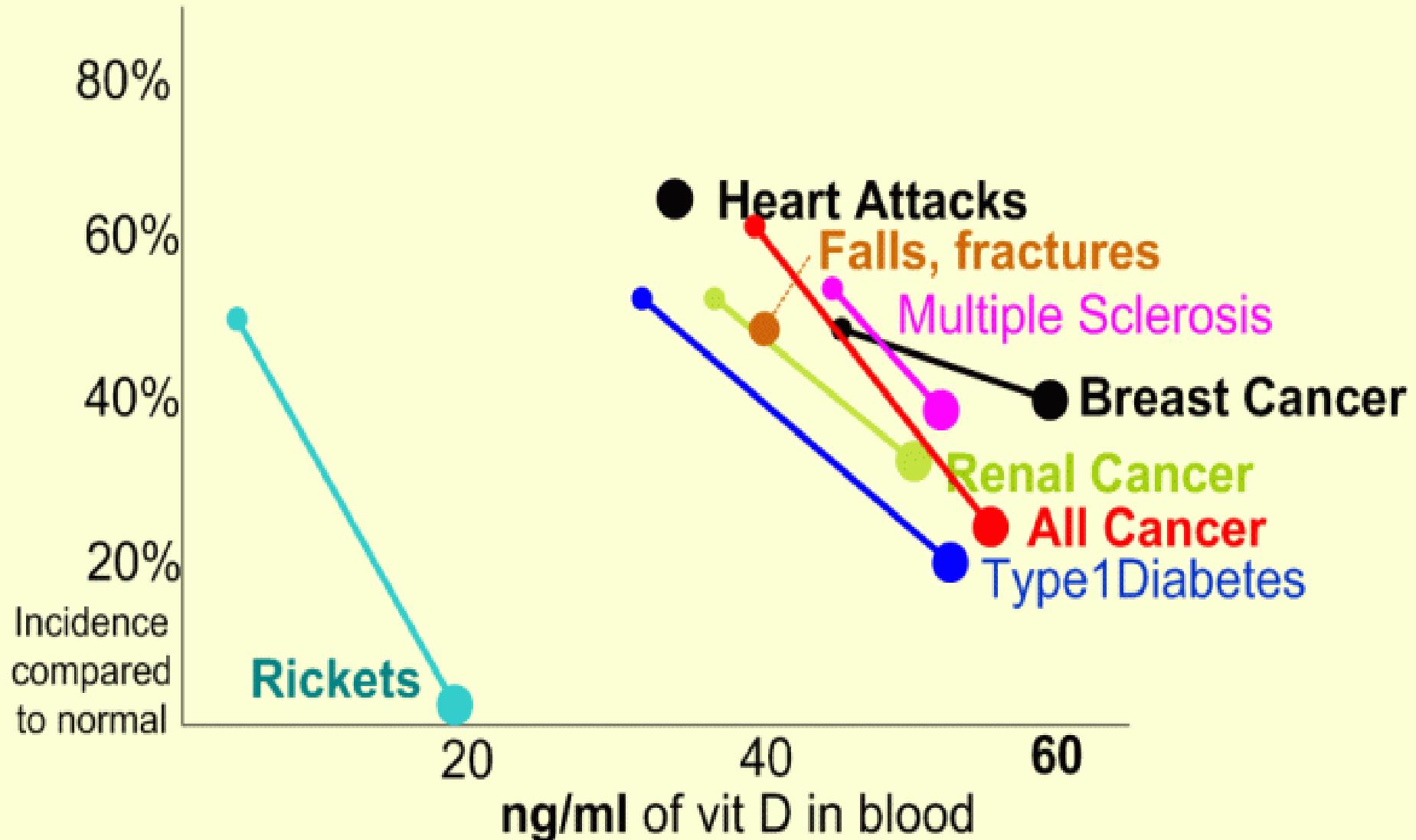
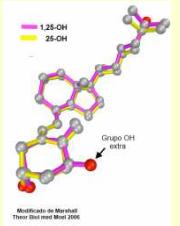
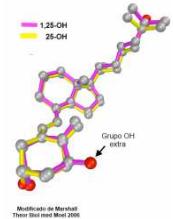


Fig. 8. Major Causes of vitamin D deficiency and potential health consequences. (Courtesy of Michael F. Holick, PhD, MD; Copyright © 2007.)

More Vitamin D in blood reduces incidence of major health problems



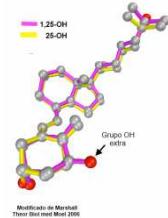
Lahore August 2010 using data of Garland and Baggerly 2010



“With the help of a good word from talk show host **Oprah Winfrey**, who told her viewers that adequate intake of **vitamin D could be five times** current recommended levels, **market growth** has **reached triple digits!**”.

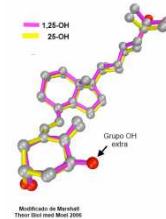
Markets: Global vitamin D boom
Guy Montague-Jones, 25-Mar-2010

NUTRA
ingredients.com



“Using 2009 prices as a base, the market research firm said **vitamin D sales** have grown **from \$141.1m** in 2005 to **\$366.3m** in 2009”

And Euromonitor expects **vitamin D** to continue its onward march in the US with CAGR **growth tipped** to be **11.2 per cent** in the country between 2009 and 2014.



Vitamin D: Health Unlimited

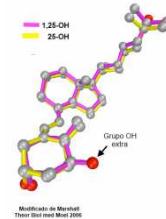
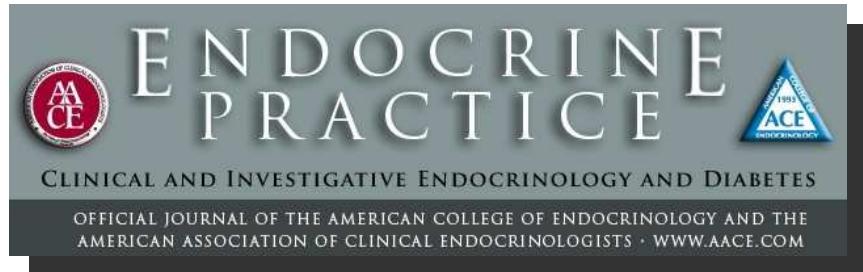
Vitamin D is a well-known ingredient in the bone health sector. Often known as calciferol, it contributes to the maintenance of normal levels of calcium and phosphorus in the bloodstream, which are required for healthy bones. **Vitamin D** is frequently used in combination with calcium. Plethora of clinical evidence illustrates the bone health benefits of **vitamin D**. Bone Health Ingredient Recently

Published: 18 Mar 2010

Market Insights

Frost & Sullivan said **vitamin D supplement sales increased by a massive 127 per cent in 2008, and by 117 per cent in the first quarter of 2009.**

"Regulatory standards are undoubtedly the primary factor holding back the potential boom of the vitamin D market"



Is vitamin D the fountain of youth?

Binkley N. 2009 Endocr Pract 15:590-596.

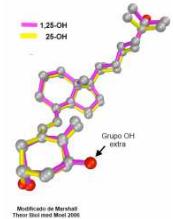
Medscape Diabetes & Endocrinology
NEWS

Vitamin D: Is It The Best Thing Under The Sun

Robert Finn; Deborah Flapan; Darbe Rotach

Medscape Feb 2013

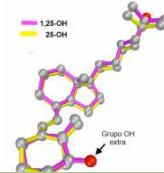
TOP de los Productos Milagrosos



**BÁLSAMO DE
FIERABRAS**

**AGUA DE
LOURDES**

VITAMINA D3



Dietary Reference Intakes for Calcium and Vitamin D.

The National Academies Press, DC, USA (2010) IOM
(Institute of Medicine).

http://www.nap.edu/catalog.php?record_id=13050

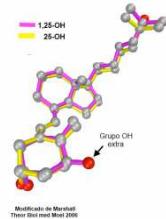
A. Catharine Ross, Christine L. Taylor, Ann L. Yaktine, and Heather B. Del Valle,



The 2011 Report on Dietary Reference Intakes for Calcium and Vitamin D from the Institute of Medicine: What Clinicians Need to Know

A. Catharine Ross, JoAnn E. Manson, Steven A. Abrams, John F.
Aloia, Patsy M. et al .

J Clin Endocrinol Metab, January 2011, 96(1):0000–0000



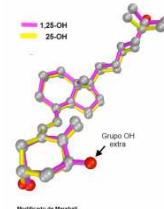
JCEM



Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine society clinical practice guideline.

Holick MF, Binkley NC, Bischoff-Ferrari HA et al.

J. Clin. Endocrinol. Metab. 2011 9, 1911–1930



New guidelines on vitamin D-ficiency clear or confusing?

Kevin D. Cashman and Mairead Kiely

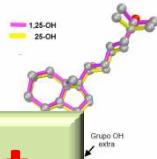
Nat. Rev. Endocrinol 2011: 7, 566–568



The 2011 Report on Dietary Reference Intake for Vitamin D: Where Do We Go From Here?

John F. Aloia

J Clin Endocrinol Metab, October 2011, 96(10):2987–2996



Vitamin D and Calcium Supplementation to Prevent Fractures in Adults: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, MPH on behalf of the U.S. Preventive Services Task Force* www.annals.org on line first 26 February 2013.

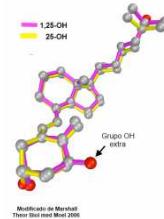


Vitamin D supplementation in elderly or postmenopausal women: a 2013 update of the 2008 recommendations from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO)

R. Rizzoli et al Curr Med Res & Op. 29. 4: 2013, 1–9

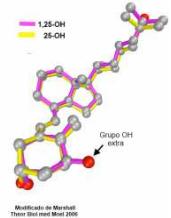
Concordancia

2011 Report IOM vs Guideline 2011 Endocrine Society vs US TASK Force vs ESCEO update



- La vitamina D **eficaz** en la prevención de **fracturas***
- La vitamina D **eficaz** en la prevención de **caídas**
- El nivel de 25-OH- D como el marcador de estado
- **No existen datos** que sustenten beneficios de la suplementación con Vitamina D en:
 - Enfermedad Cardiovascular
 - Prevención de Neoplasias
 - Prevención de infecciones
 - Prevención de enfermedades metabólicas
 - Disminución de la mortalidad global

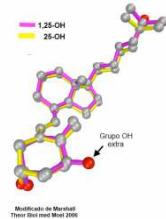
* No según USTASK force



Discordancia

2011 Report IOM vs Guideline 2011 Endocrine Society

- Dintel de normalidad según valor 25-OHD
- Niveles de toxicidad
- Dosis de vitamina D3 recomendadas

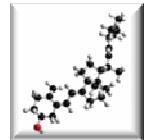


Discordancia

2011 Report IOM vs Guideline 2011 Endocrine Society

IMPLICACIONES

Valores de 25-OH-D ng/ml	IOM	End Soc
Deficiencia	<12	<20
Riesgo de deficiencia	<16	-----
Insuficiencia	-----	<30
Adecuado	>20	>30
Tóxico	>50	>100

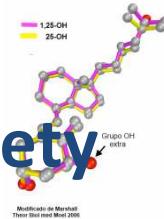


Conceptos para cuantificar ingesta de nutrientes

	Concepto	Definition
AI	Average Intake	Requerimiento medio individual.
EAR	Estimated Average Requirement	Ingesta media de nutrientes que cumple más del 50% de población sana del grupo a estudio (mediana)
RDA	Recommended Dietary Allowance	Ingesta media que cubre el 97,5% de un determinado grupo(EAR+2sd)
DRI	Dietary Reference Intake	50% de la población según un modelo probabilístico de riesgo
UL	Tolerable Upper Intake level	El valor medio más alto sin riesgo para el 100% de la población

Discordancia

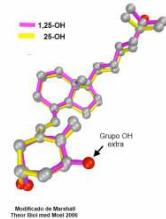
2011 Report IOM vs Guideline 2011 Endocrine Society



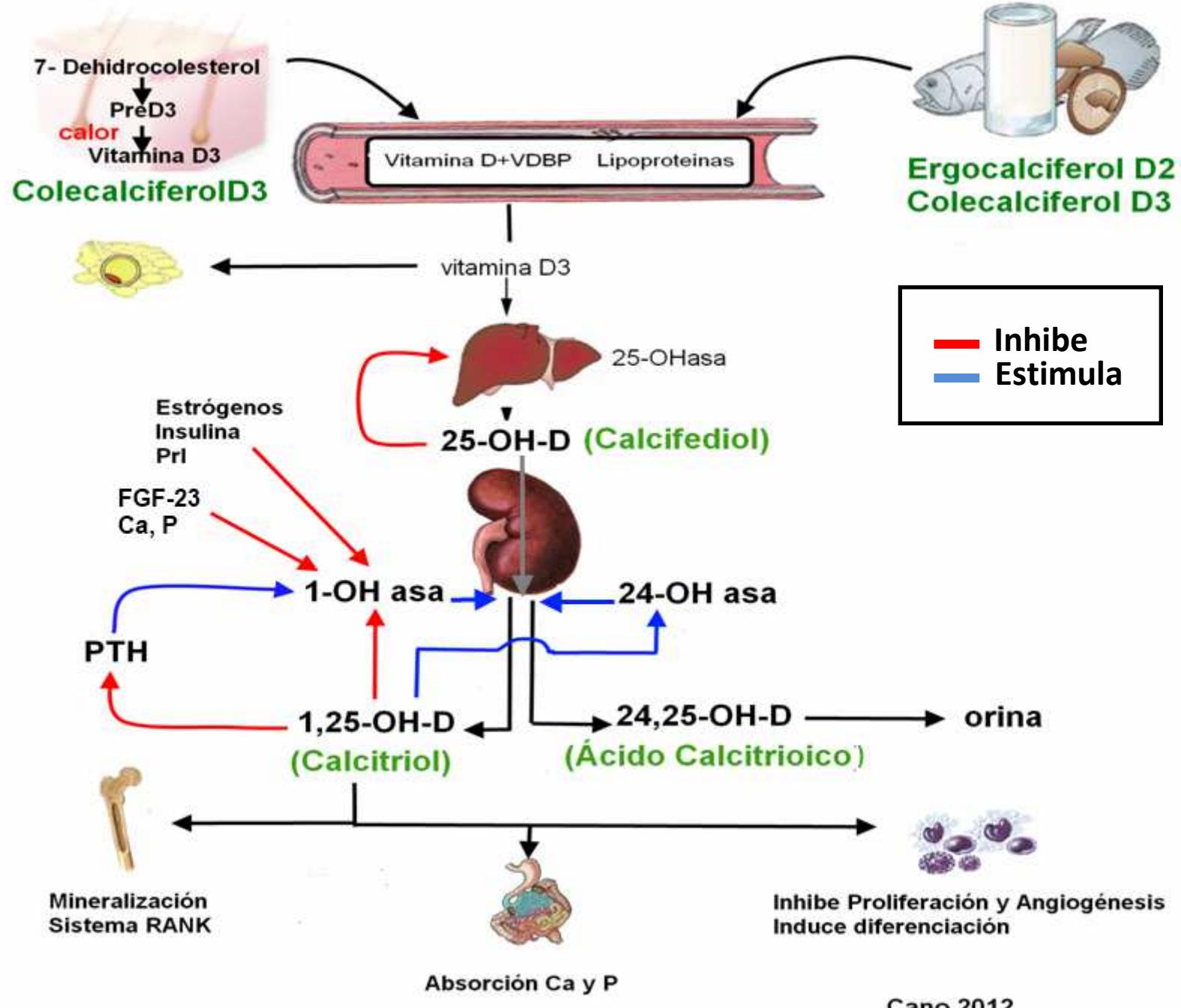
IMPLICACIONES

	IOM		E.S.	
	DRI *	UI	Diaria UI	UI
Población				
1-18 a.	400	4.000	600-1.000	4.000
18-70 a.	400	4.000	1.500-2.000	10.000
>70 a.	400	4.000	1.500-2.000	10.000
Gesta/lact.				
14-18 a.	400	4.000	600-1000	4.400
19-50 a.	400	4.000	1.500-2.000	10.000

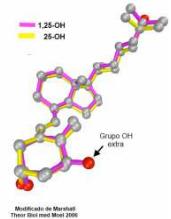
* Con exposición solar. Sin exposición :800UI/d



¿ Qué parámetro refleja mejor el
Estado corporal de la vitamina D
25-OH-D o 1,25-OH-D ?

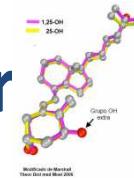


Cano 2012



¿ Cuál es el valor óptimo de 25-OH-D?

Factores implicados en la construcción del valor



Marcadores
de
normalidad

Metabolismo

Nivel PTH
Absorción de Ca

Salud ósea

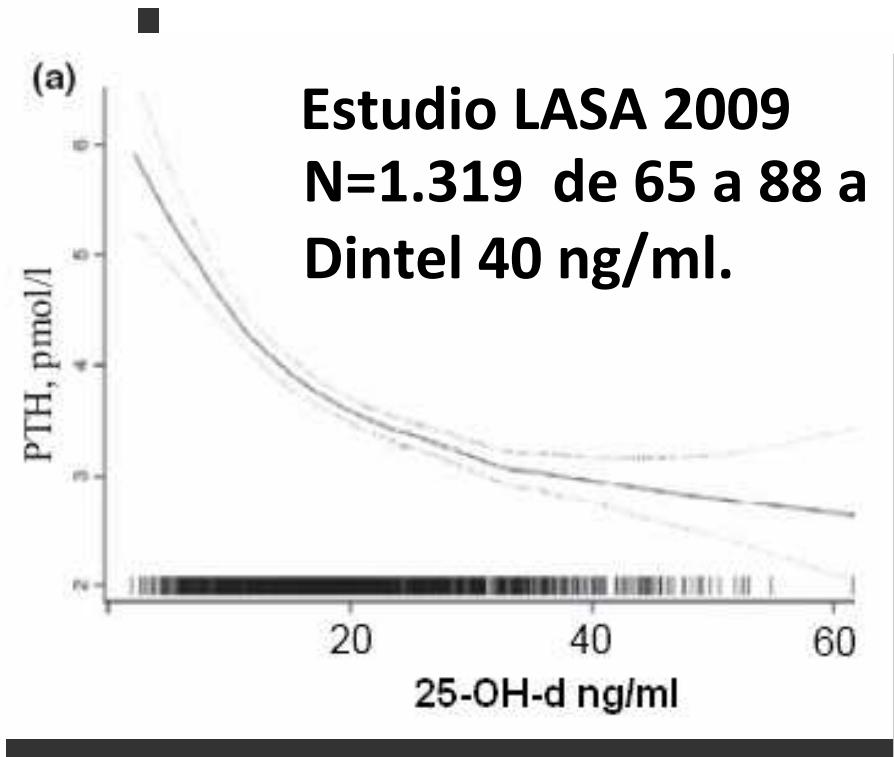
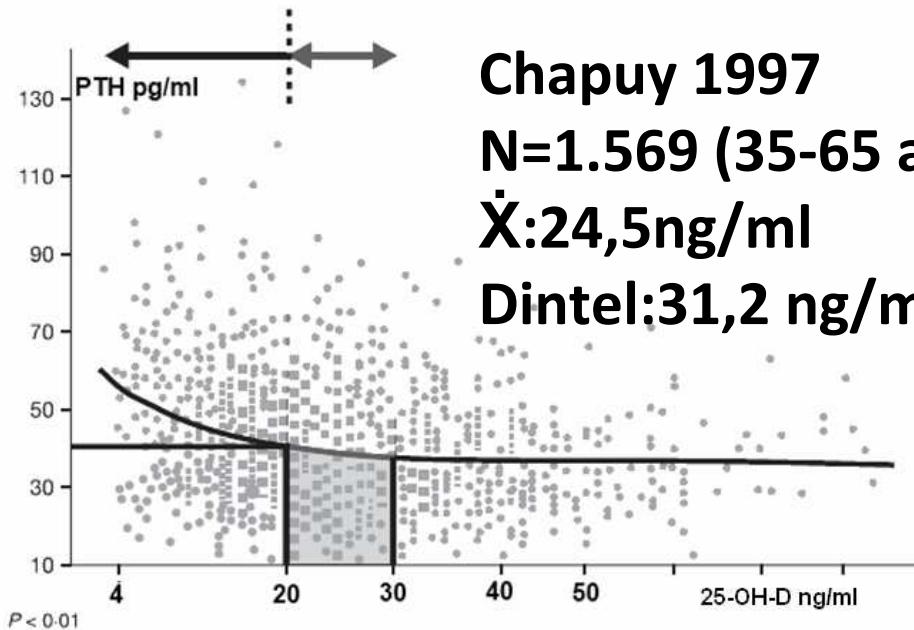
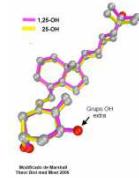
Masa ósea
Riesgo de fracturas
Mineralización

Capacidad física muscular: caídas
Prevención de enfermedades

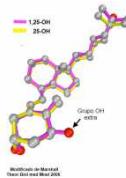
Marcadores
de exceso

Hipercalcemia, hipercalciuria y nefrolitiasis
Calcificación de tejidos blandos
Causa de mortalidad

RELACIÓN VITAMINA D25 y PTH



25-OH-D ng/ml Malbanan 1998	PTH ↓
10-16	35%
16-20	26%
>20	Sin cambios

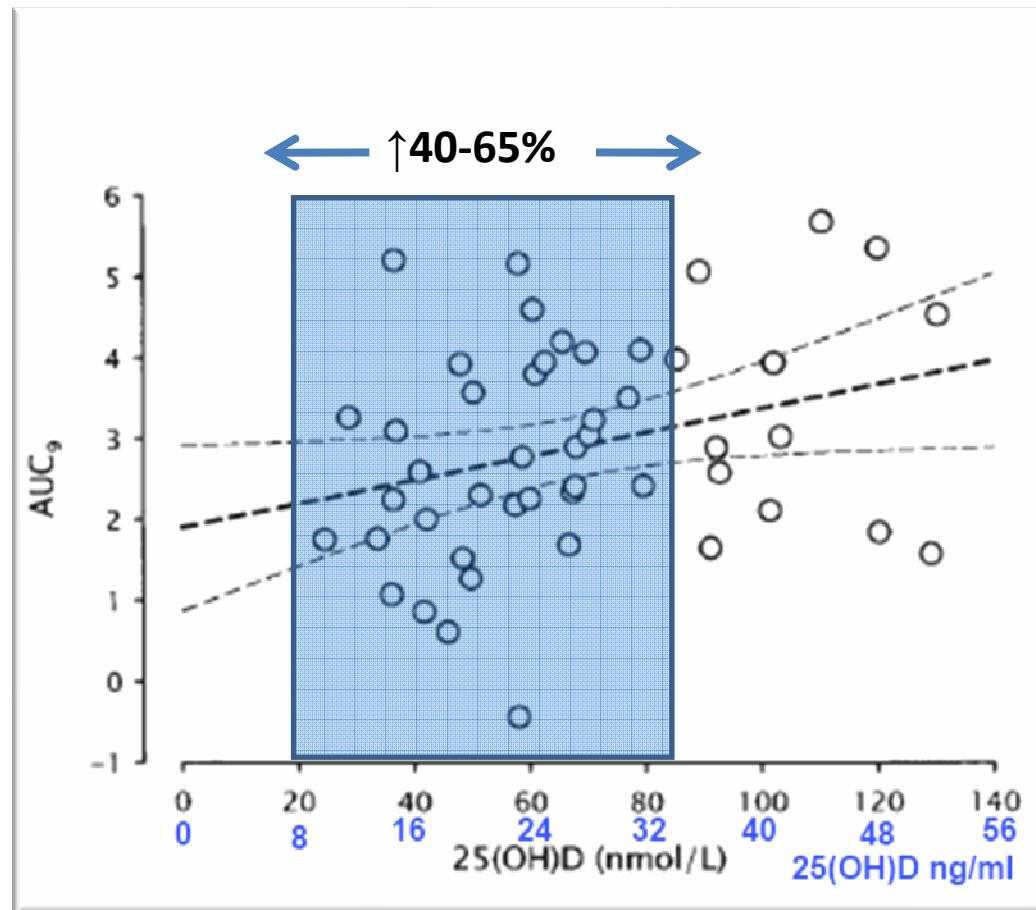


Calcium Absorption Varies within the Reference Range for Serum 25-Hydroxyvitamin D

Robert P. Heaney, MD, FACN, M. Susan Dowell, PhD, Cecilia A. Hale, PhD, and Adrienne Bendich, PhD, FACN

Creighton University, Omaha, Nebraska (R.P.H., M.S.D.), GlaxoSmithKline, Parsippany, New Jersey (C.A.H., A.B.)

Journal of the American College of Nutrition (2003)



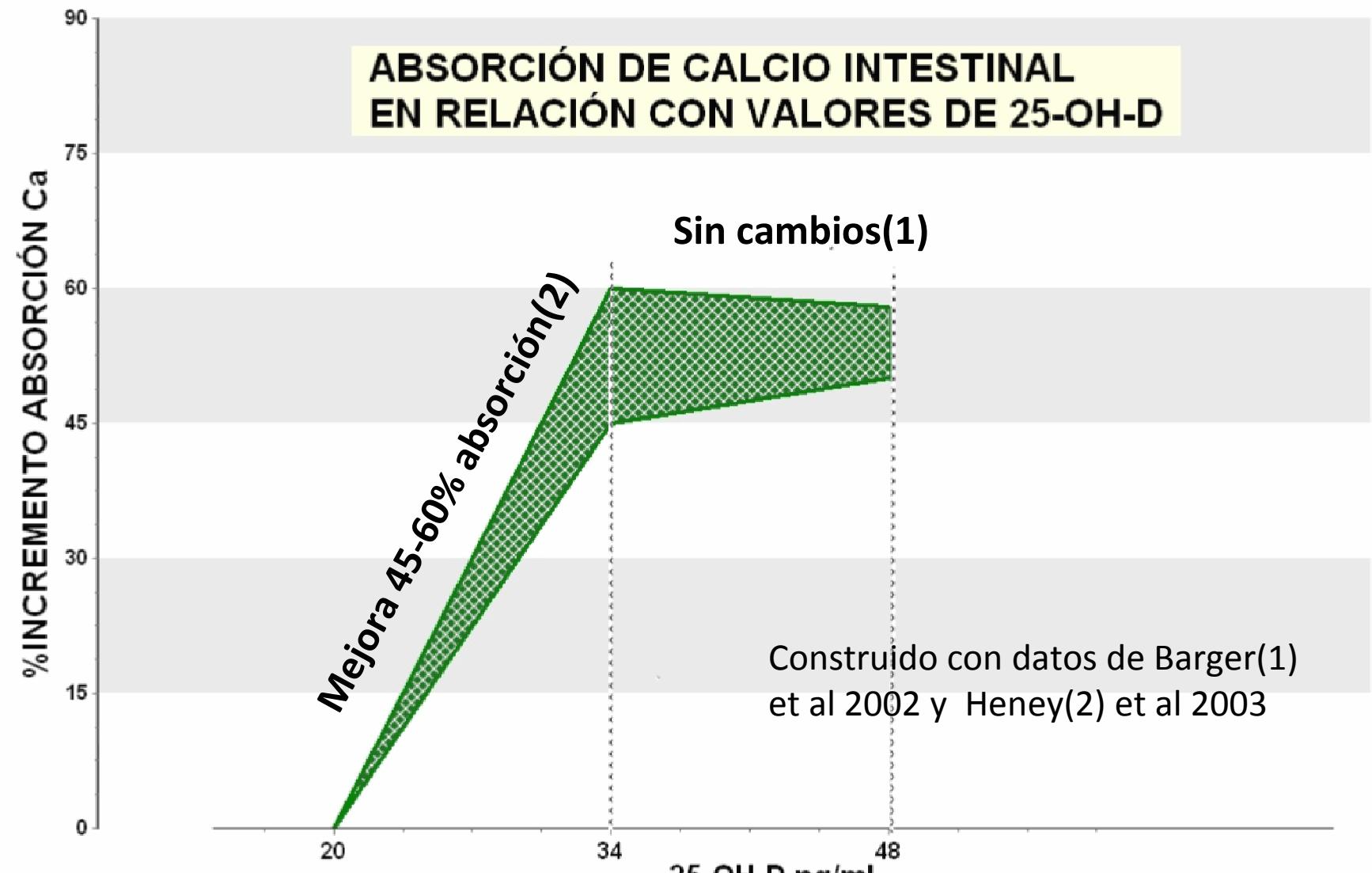
34 determinaciones en
48 postmenopausia.

Conclusiones:

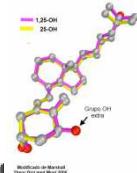
- Correlación Ca y 25OH-D
- Gran variabilidad



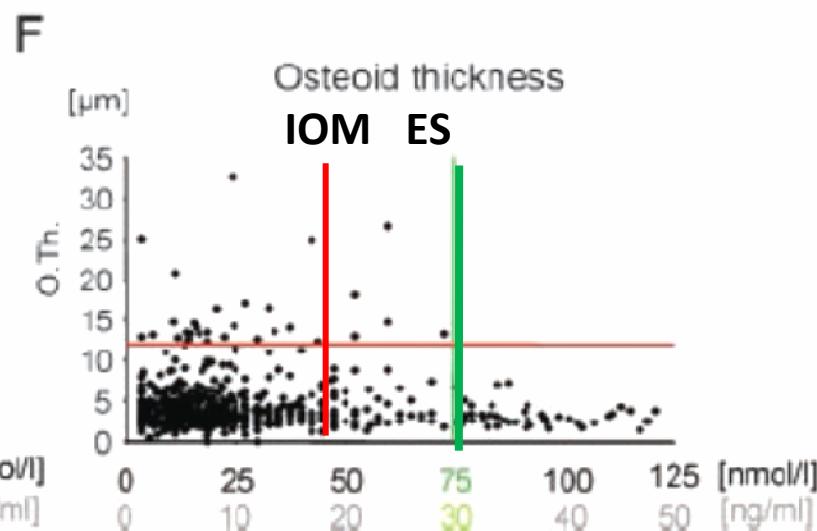
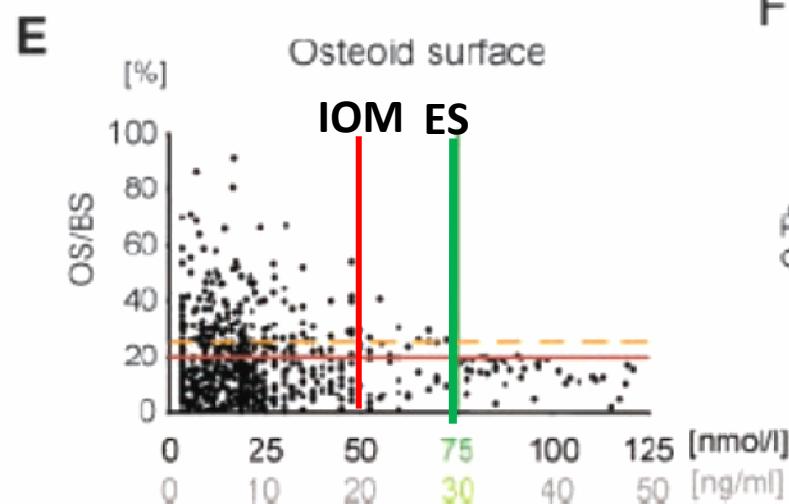
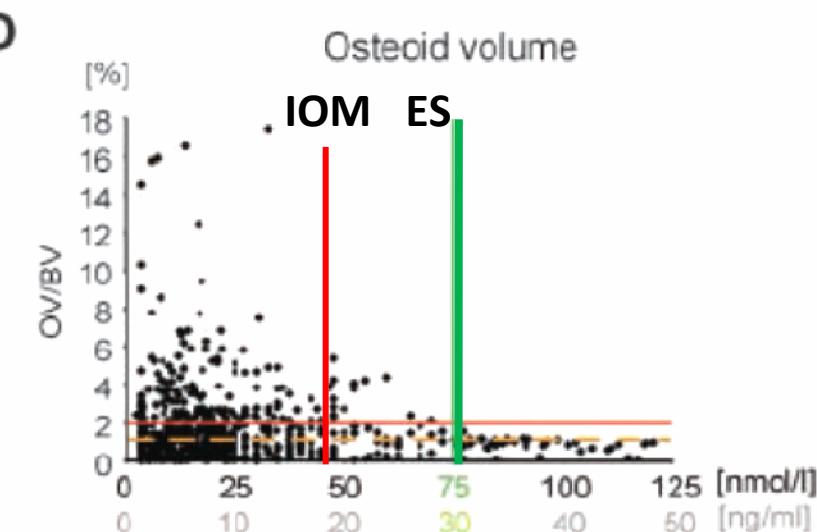
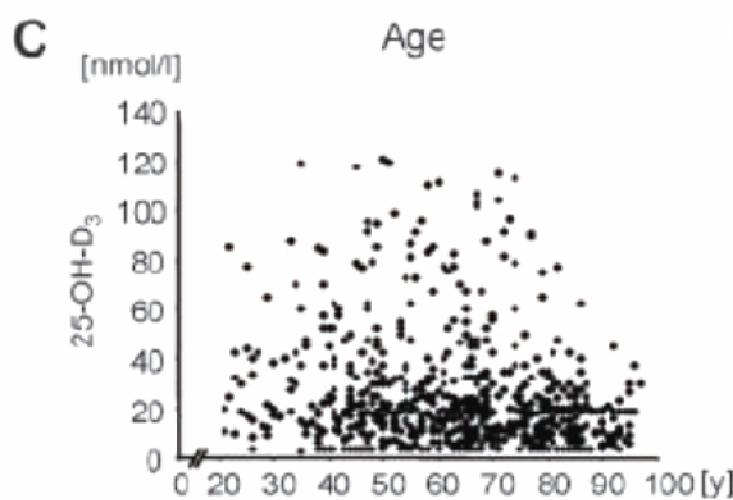
ABSORCIÓN DE CALCIO INTESTINAL EN RELACIÓN CON VALORES DE 25-OH-D



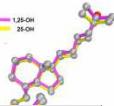
Relación entre 25-OH y calidad ósea



as
a.
a.

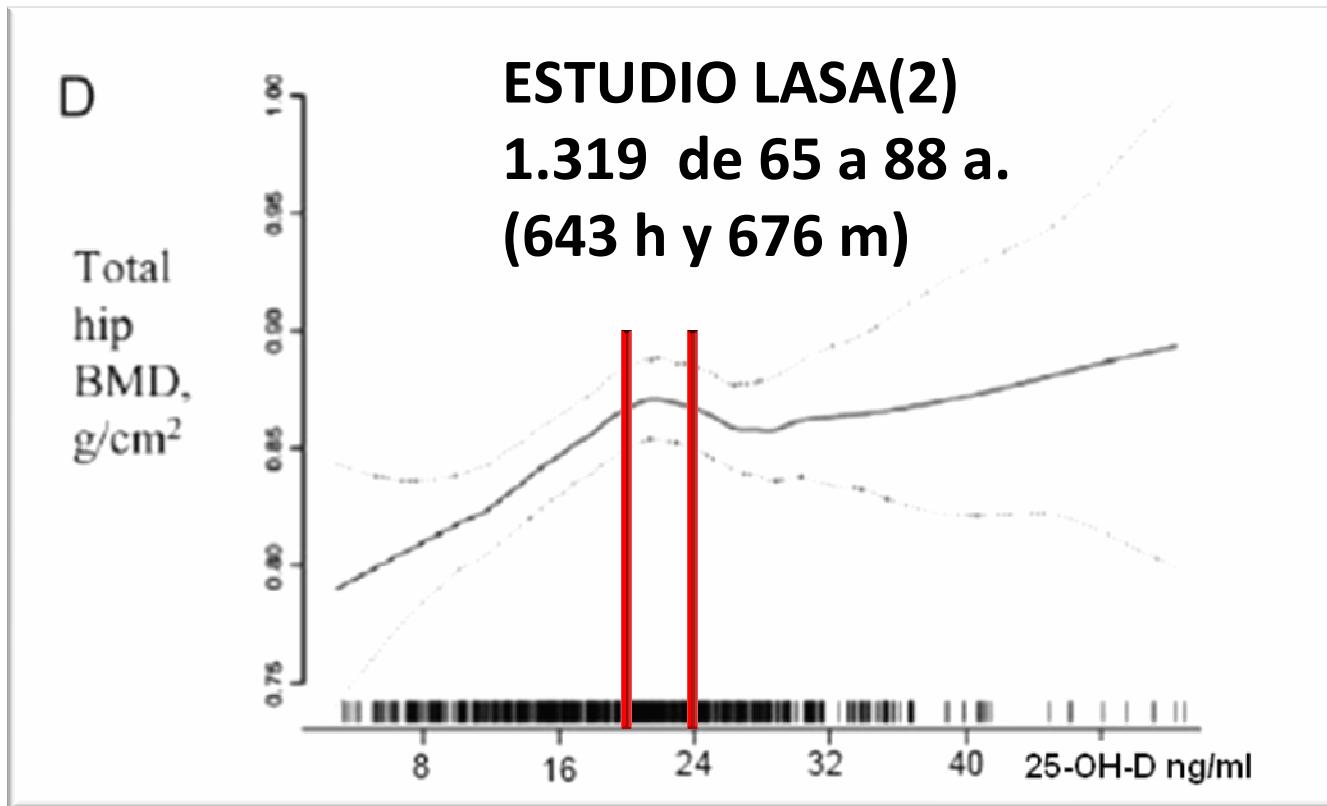


Relación entre 25-OH y DMO



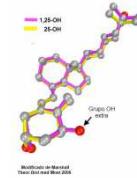
NHANES III(1)

- 13.432 sujetos > 20 años.
- Relación positiva en el rango de 10 a 38ng/ml
- Deterioro de DMO <20ng/ml y sin cambios >34ng/ml



(1)Bischoff-Ferrari Am J Med 2004 (2)Kuchuk Estudio LASA JCEM 2009

Relación entre 25-OH y DMO



Hipótesis:

Valores bajos de 25-OH-D se asocian con mayor pérdida de masa ósea de cadera en varones ancianos

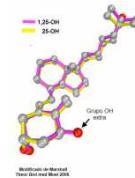
Tipo	Prospectivo
Edad	>69
género	✓
Nº	1.279
DMO cadera total	Basal y 4 años

25-OH ng/dl	DMO%
<15	↓0,59*
<20	↓0,54*
<30	↓0,35
>30	↓0,37

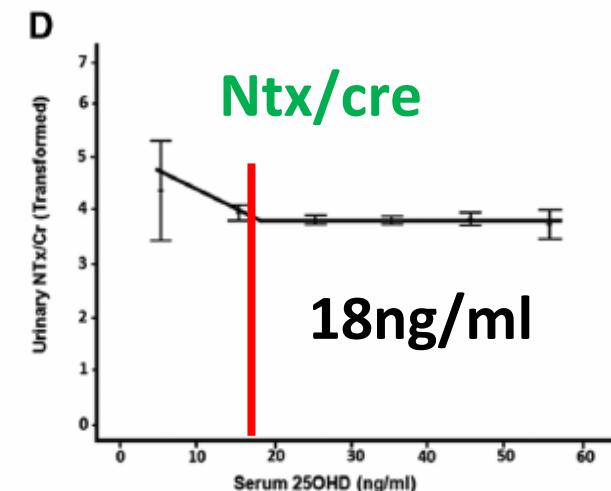
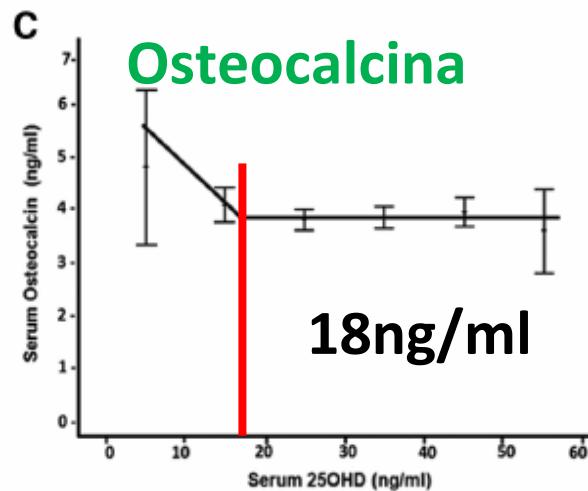
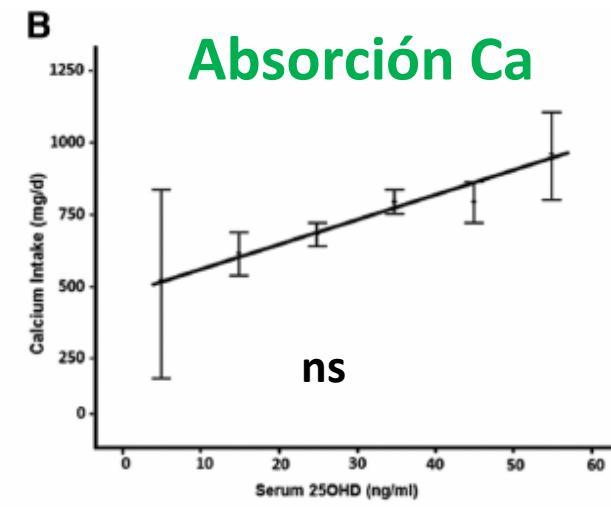
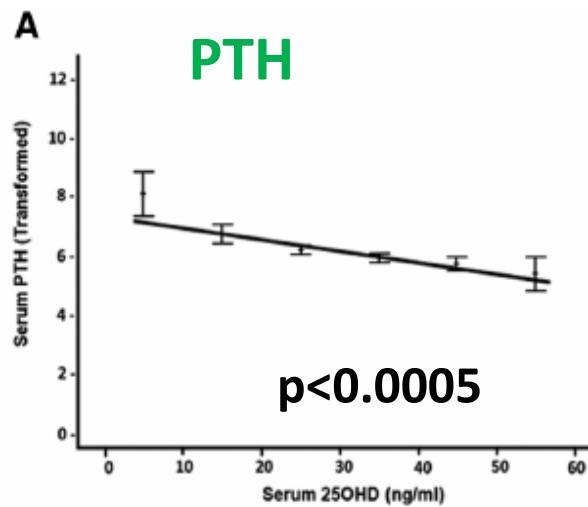
La evidencia es fuerte >75a.(p<0.005) pero no <75a.(P<0.55)

Ensrud KE J Clin Endocrinol Metab, August 2009, 94(8):2773–2780

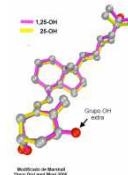
Relación entre 25-OH y marcadores óseos



**488 mujeres
Edad: 71a
Transversal**



Relationships of Serum 25-Hydroxyvitamin D to Bone Mineral Density and Serum Parathyroid Hormone and Markers of Bone Turnover in Older Persons



Natalia O. Kuchuk, Saskia M. F. Pluijm, Natasja M. van Schoor, Caspar W. N. Loosman, Johannes H. Smit, and Paul Lips

(*J Clin Endocrinol Metab* 94: 1244–1250, 2009)

N: 1.509 mujeres entre 55-85 años

TABLE 2. Differences in the mean values of bone markers, BMD, and physical performance in different serum 25(OH)D level groups

Parameter	Serum 25(OH)D (nmol/liter) ^a				P value ^b
	<25 (n = 136)	25–50 (n = 451)	50–75 (n = 419)	>75 (n = 227)	
25(OH)D (nmol/liter)	18.7 (1.0)***	38.1 (0.7)***	60.0 (0.7)***	89.6 (0.9)	<0.001
PTH (pmol/liter)	5.1 (0.10)***	3.9 (0.11)***	3.3 (0.11)	3.1 (0.16)	<0.001
OC (nmol/liter)	2.5 (0.09)	2.1 (0.05)	2.2 (0.05)	2.2 (0.07)	0.13
DPD/Cr (nmol/mmol)	6.7 (0.21)***	5.5 (0.11)	5.3 (0.11)	5.4 (0.16)	<0.001
BUA (dB/MHz)	68.8 (1.5)	70.4 (0.8)	71.7 (0.8)	71.0 (1.2)	0.42
SOS (m/sec)	1619 (4.1)	1620 (2.2)	1623 (2.2)	1627 (3.2)	0.30
Physical performance score (range 0–10)	5.9 (0.2)***	6.8 (0.1)**	7.2 (0.1)	7.3 (0.2)	<0.001

<10 ng/ml 10-20 20-30 >30

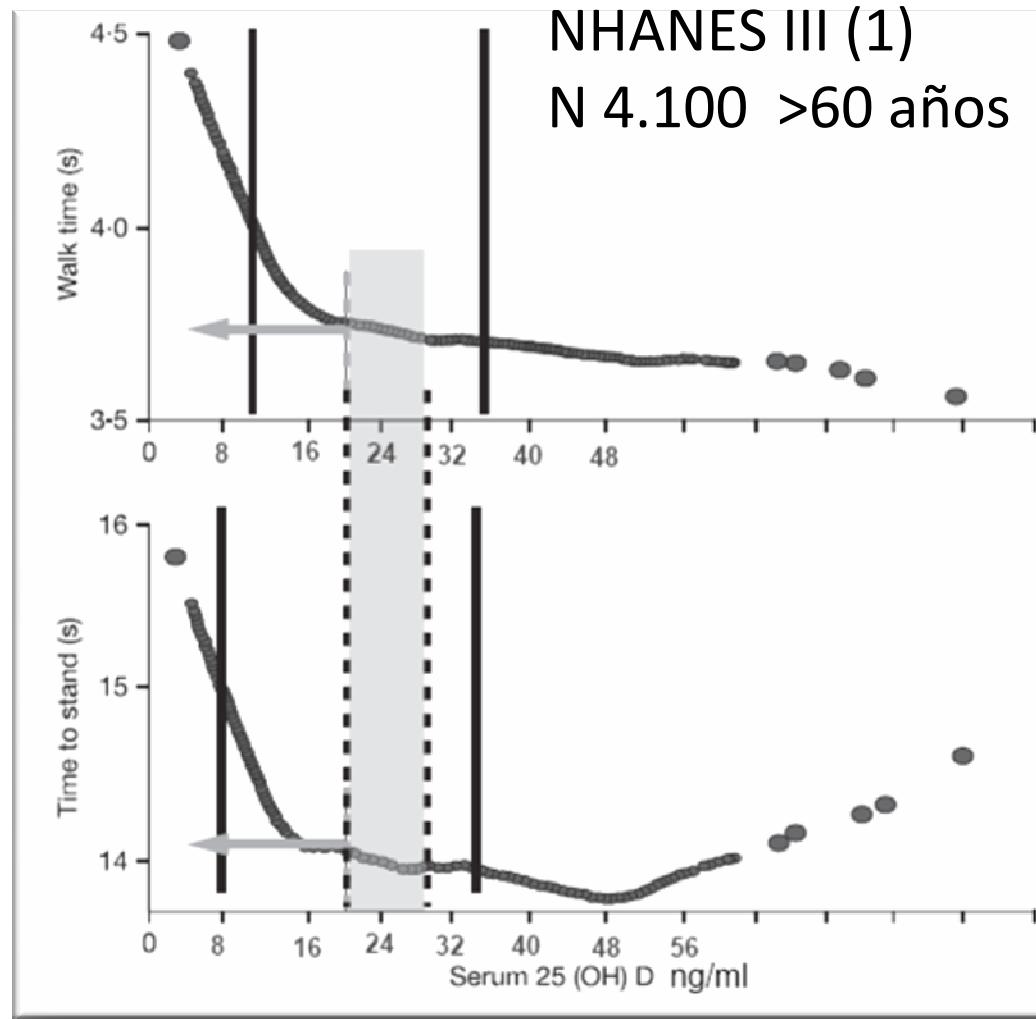
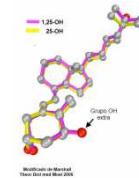
Values are presented as mean \pm SD. For conversion of 25(OH)D from nmol/liter to ng/ml, divide by 2.496; for conversion of PTH from pmol/liter to pg/ml, multiply by 11.1.

^a Adjusted for age, sex, level of education, level of urbanization, BMI, number of chronic diseases, level of Cr, smoking, and season of vitamin D determination.

^b Overall results of covariance analysis.

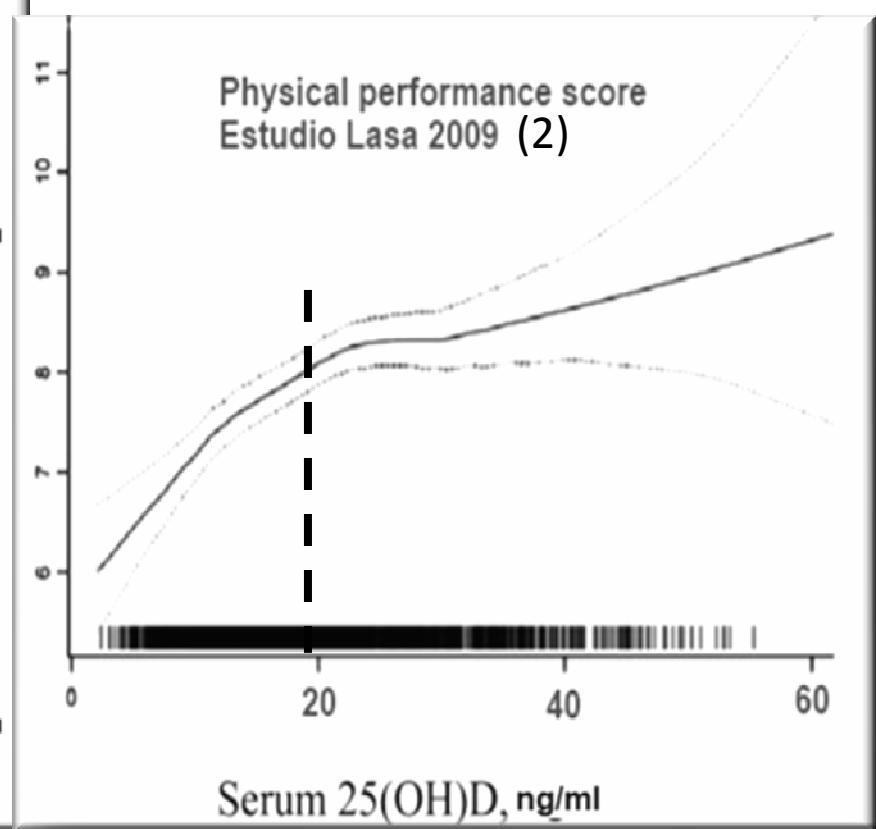
* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$, as compared to the reference category (>75 nmol/liter).

Relación 25-OH-D y funcionalidad muscular



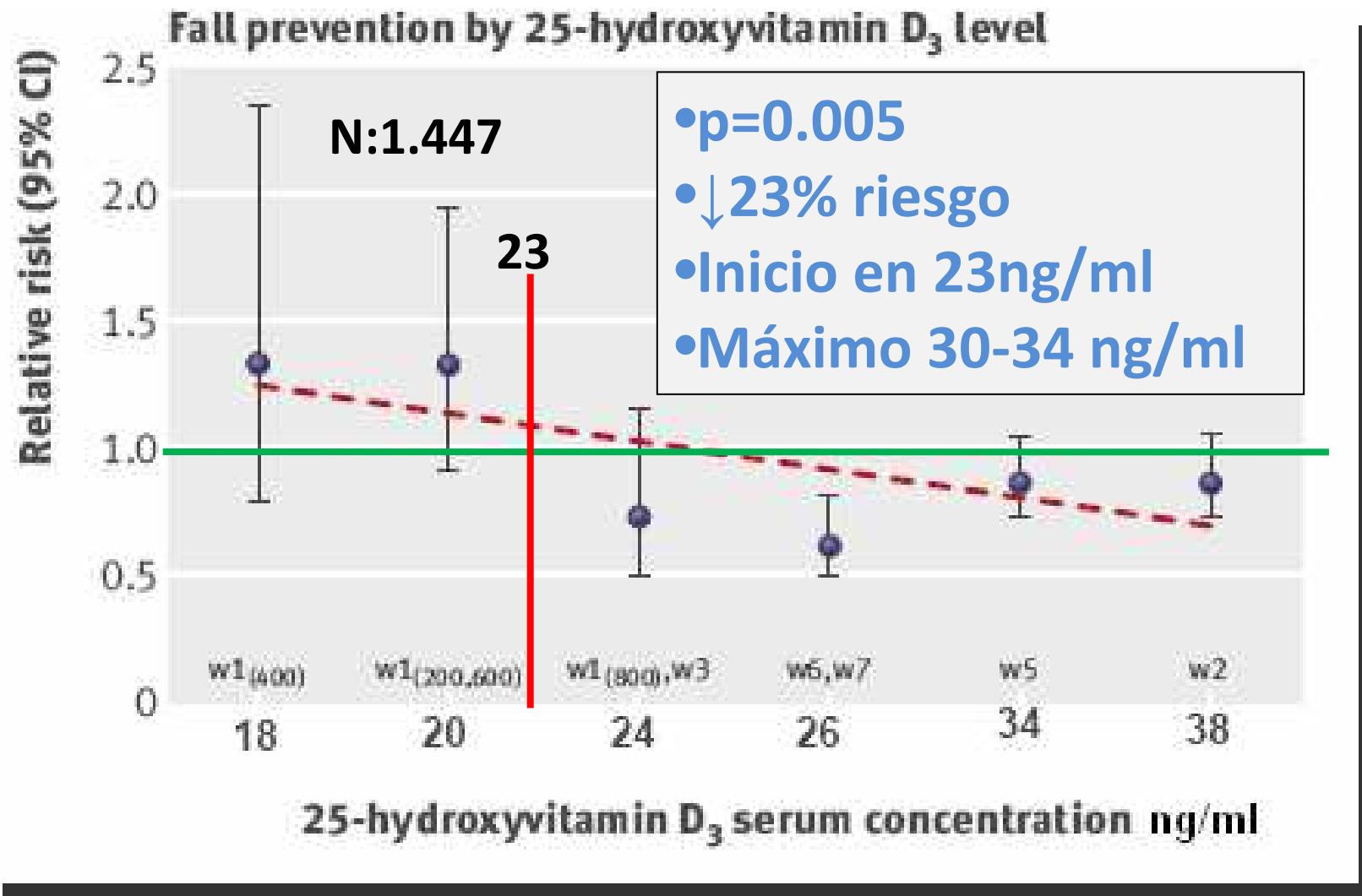
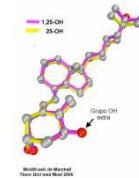
(1) Bischoff-Ferrari et al J Clin Nut 2004

Máxima con
20-30ng/ml



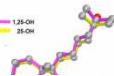
(2) Kuchuk N et al JCEM 2009

Relación entre 25-OH y Caídas



Bisofh-Ferrari et al BMJ 2009

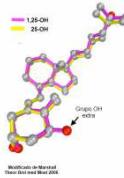
Relación 25-OH y Fracturas óseas



	MROS Cauley 2010	WHI Cauley 2008	NHANES Looker 2008	Gerbhem 2005	Melhus 2010	Hernández 2013
	Fx cadera	Fx cadera	Fx cadera	Fx cadera	Fx cadera	Fx vertebral
Ed.	73	71	>65	75	71	51
G	V	M	V,M	M	V	M
Nº	1.608	800	1.917	986	1.194	820
Nivel 25-OH ng/ml						
<15	-----	-----	60%	-----	58%	-----
<20	+100%	71%	45%	100%	BASE	97%
<30	BASE	BASE	36%	BASE		BASE
>30	ns	ns	13%			

Influence of Vitamin D Status on Vertebral Fractures, Bone Mineral Density, and Bone Turnover Markers in Normocalcemic Postmenopausal Women With High Parathyroid Hormone Levels

Cohorte Camargo



José L. Hernández, José M. Olmos, Emilio Pariente, Daniel Nan,
Josefina Martínez, Javier Llorca, Carmen Valero, Eduardo Obregón,
and Jesús González-Macías

Objetivo:

Relación entre nivel de PTH y prevalencia de fracturas según el status de vitamina D

Vitamina D, PTH y Fracturas vertebrales

Cohorte Camargo

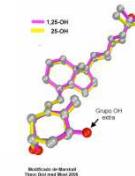
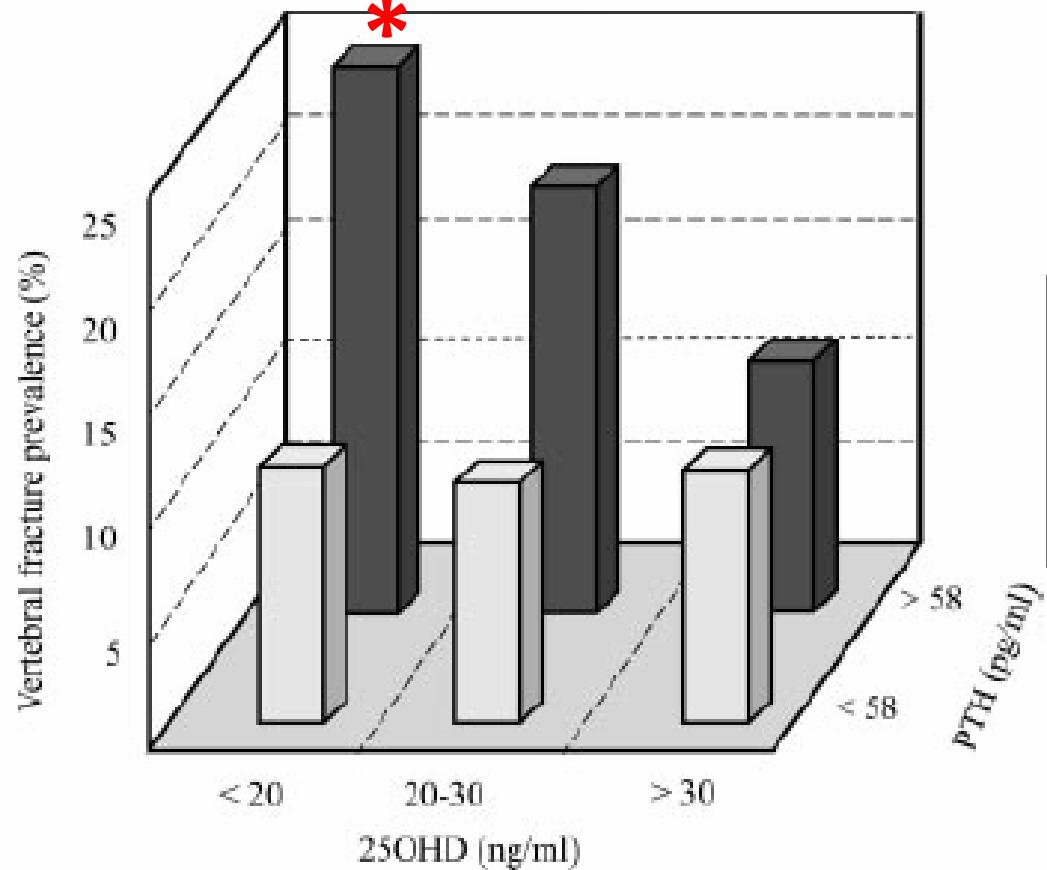
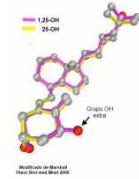


Table 1. Baseline Characteristics of the Overall Sample, Grouped by PTH Levels

Parameter	PTH ≤ 58 pg/mL	PTH > 58 pg/mL	P
n	551	269	
Age, y	57 [53–62]	61 [56–70]	<.0001
Years since menopause	7 [3–14]	11 [5–21]	<.0001
Weight, kg	68.7 ± 12.7	71.2 ± 11.8	.008
BMI, kg/m ²	28.1 ± 4.9	29.3 ± 4.8	.001
Family history of hip fracture, n (%)	97 (18)	50 (19)	.8
Dairy calcium intake, mg/d	650 [450–900]	600 [450–900]	.1
Education, y	8 [8–10]	8 [8–8]	.4
Smoking, n (%)	116 (21)	21 (8)	<.0001
Vitamin D supplements, n (%)	30 (5)	20 (7)	.3
Alcohol, n (%)	67 (12)	36 (13)	.7
Corrected calcium, mg/dL	9.1 ± 0.3	9.1 ± 0.4	.4
Phosphate, mg/dL	3.6 [3.3–3.9]	3.4 [3.0–3.4]	<.0001
GFR (MDRD)	71 [66–80]	73 [66–81]	.6
25OHD, ng/mL	23.8 ± 8.1	19.0 ± 7.1	<.0001
PTH, pg/mL	43 [37–49]	67 [62–78]	<.0001
PINP, ng/mL	46.0 [34.9–60.3]	46.2 [36.3–63.2]	.3
CTX, ng/mL	0.363 [0.248–0.508]	0.393 [0.277–0.525]	.01
Exercise, n (%)			
Sedentary	10 (2)	7 (3)	.8
Moderate	241 (44)	154 (58)	.001
High	296 (54)	107 (40)	.001
Previous fracture (>40 yr), n (%)	67 (12)	45 (17)	.08
BMD, g/cm ²			
Lumbar spine	0.932 ± 0.135	0.916 ± 0.154	.1
Femoral neck	0.746 ± 0.115	0.721 ± 0.118	.001
Total hip	0.869 ± 0.122	0.846 ± 0.123	.004
Prevalent vertebral fracture, n (%)	51 (9)	55 (20)	<.0001

Abbreviation: MDRD, Modification of Diet in Renal Disease. Quantitative variables are expressed as mean ± SD. Variables non-normally distributed are expressed as median [interquartile range].

Vitamina D, PTH y Fracturas vertebrales

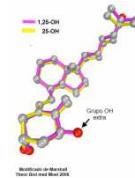


* p<0.04

Asociación Fracturas

- PTH(p<0.004)
- 25-OH-D (p<0.025)

A Pooled Analysis of Vitamin D Dose Requirements for Fracture Prevention



Heike A. Bischoff-Ferrari et al NEJM 2012

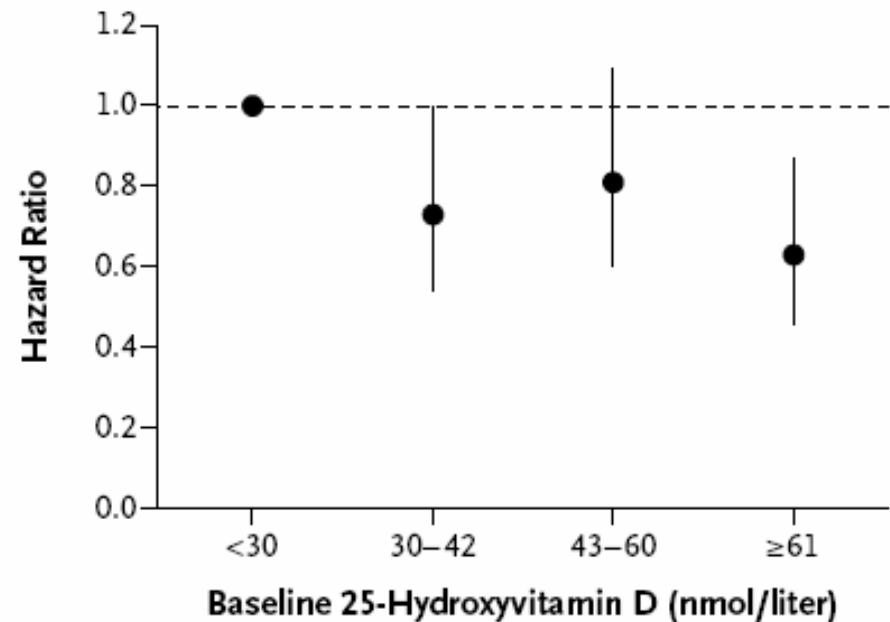
12 RCT con 31.022 personas (Edad: 76a y 91%m)

Fx Cadera: ↓Riesgo 37% (p<0.002)*

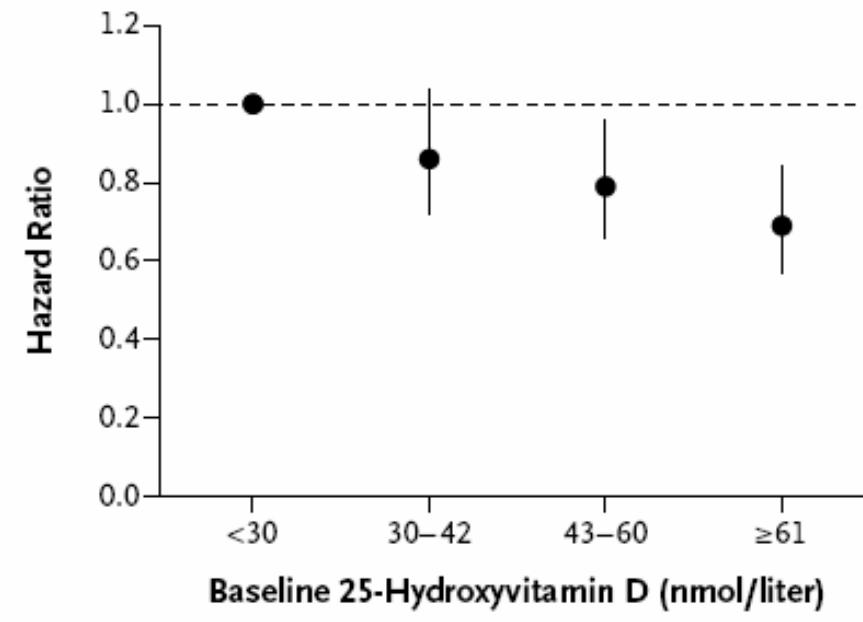
Fx vertebral: ↓Riesgo 31% (p<0.001)*

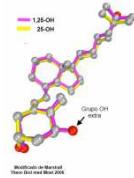
*>24ng/ml vs 12ng/ml

A Hip-Fracture Events (N=313)



B Nonvertebral-Fracture Events (N=914)

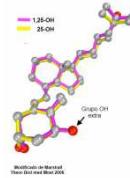




La administración de vitamina D:

- ¿Tiene efecto?
- ¿Cuál es la dosis óptima?

Relación Consumo Vitamina D y Caídas

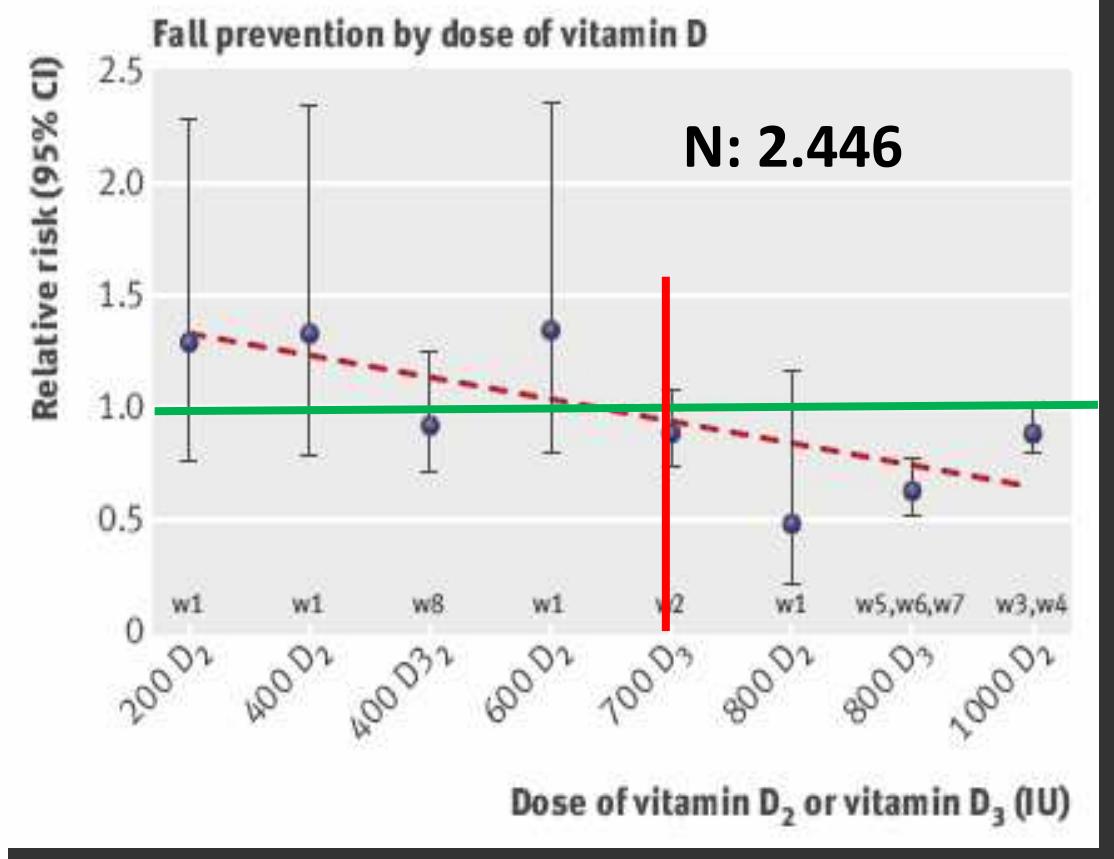


Objetivo: Eficacia en caídas

Metodología: Metaanálisis de 9

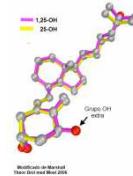
RCT

- Dosis/caída $p < 0.02$
- Inicio > 700UI/d
- ↓ RR 19%
- NNT : 11



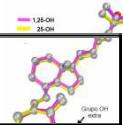
Bisofh-Ferrari et al BMJ 2009

Relación Consumo Vitamina D y Fracturas

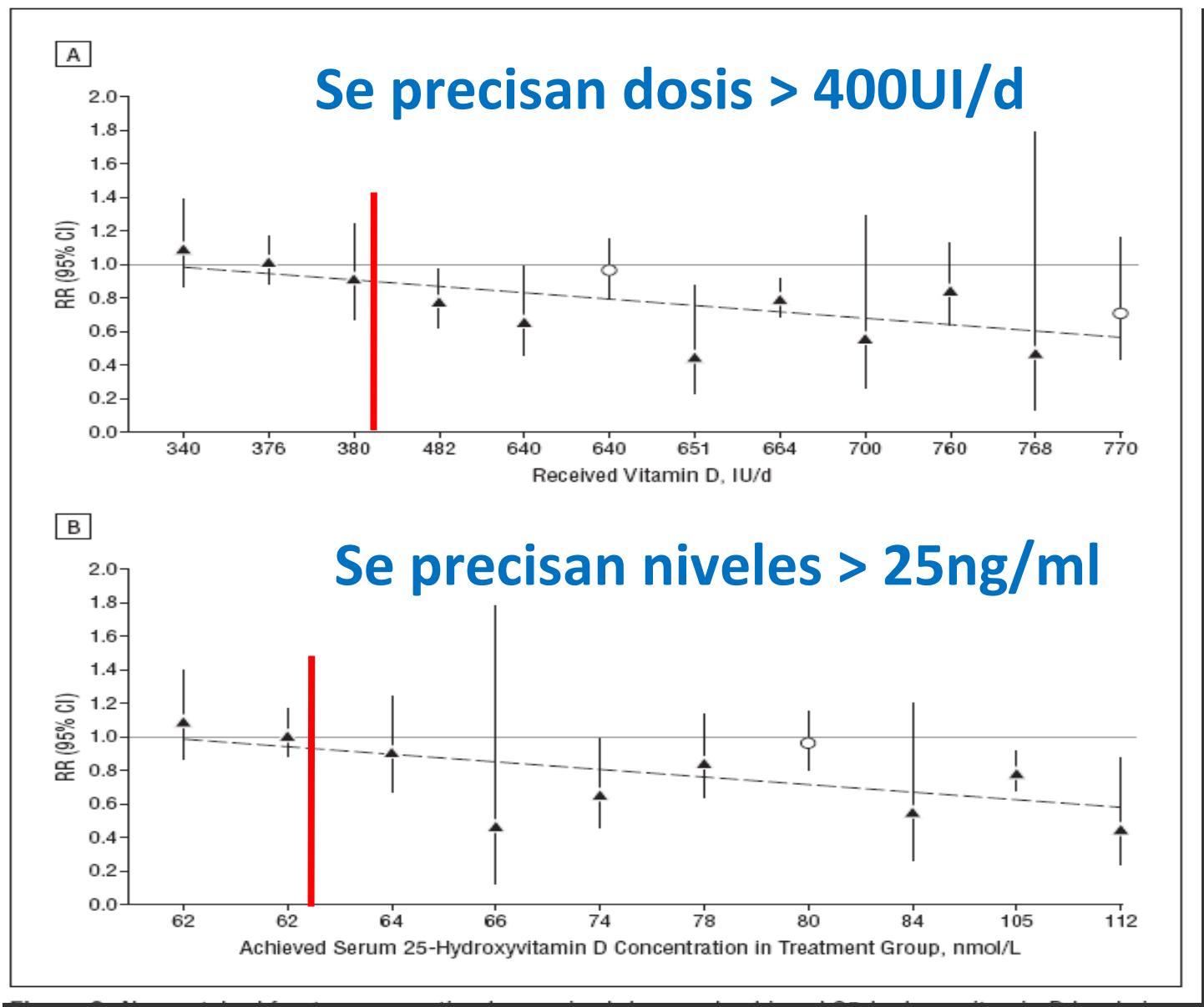
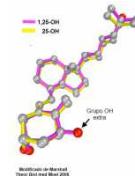


RCT Vitamina D y eficacia Fracturas							Riesgo fractura
	Pacientes	Vitamin D	Ca mg/day	25(OH) ng/d	PTH	DMO	
Lips 96	2578	400 IU		21,6	-15%	+2.2%	Cadera: NS No Vert: NS
Meyer 02	1144	400 IU					Cadera: NS, No Vert: NS
Larsen 04	7073	400 IU	1000	18,8	-15%		No Vert: -16%*
Jackson 03	36.282	400 IU	1000			1%	Cadera: NS, total fr: NS
Dawson-Hughes 97	389	700 IU	500	39,6	-15%	1%	No Vert: -50%*
Chapuy 1992	2303	800 IU	1200	28,4	-44%	6%	cadera: -43%* No Vert: -23%*
Chapuy 02	583	800 IU	1200	32	-40%	5%	No Vert: P = 0.07
Harwood 04	76	800 IU	1000	20,8	-30%	3%	No Vert: NS
Record 05	5292	800 IU	1000	24,8	-20%		Cadera: NS, No Vert: NS
Porthouse 05	3314	800 IU	1000				Cadera: NS No Vert: NS
Pfeifer 09	242	800 IU	1000	33,6	-20%		No Vert: NS
Lyons 07	3440	100.000 IU/4 months		32	-25%		Nonvert: NS
Trivedi 03	2686	100.000 IU/4 months		29,6	-6%		No Vert: -22%*
Flicker 05	625	1000 IU	600				No Vert: NS
Grant 05	387	800	1000				No totales

Vitamina D y fracturas	Conclusiones metaanálisis
Bischoff-Ferrari et al 2005	800 UI mejor que 400 UI
Boonen et al 07	Vitamina D sola no es efectiva Vitamina D con Calcio si lo es -18%
Tang et al 2007	Mejor en instituciones Mejor con Calcio Mejor 800UI vs 400UI Mejor con adherencia >80%
Avenell et al 2009	Mejor respuesta en institucionalizados
Bischoff-Ferrari 2009	RR: -14% No vertebrales RR:-9% cadera Vitamina > 400 RR:-18% cadera Dosis dependiente No sustenta el uso de 1-alfa-25
Chung et al 2011	Vitamina D con Calcio ↓ RR Mejor efecto en institucionalizados ¿Régimen de administración?

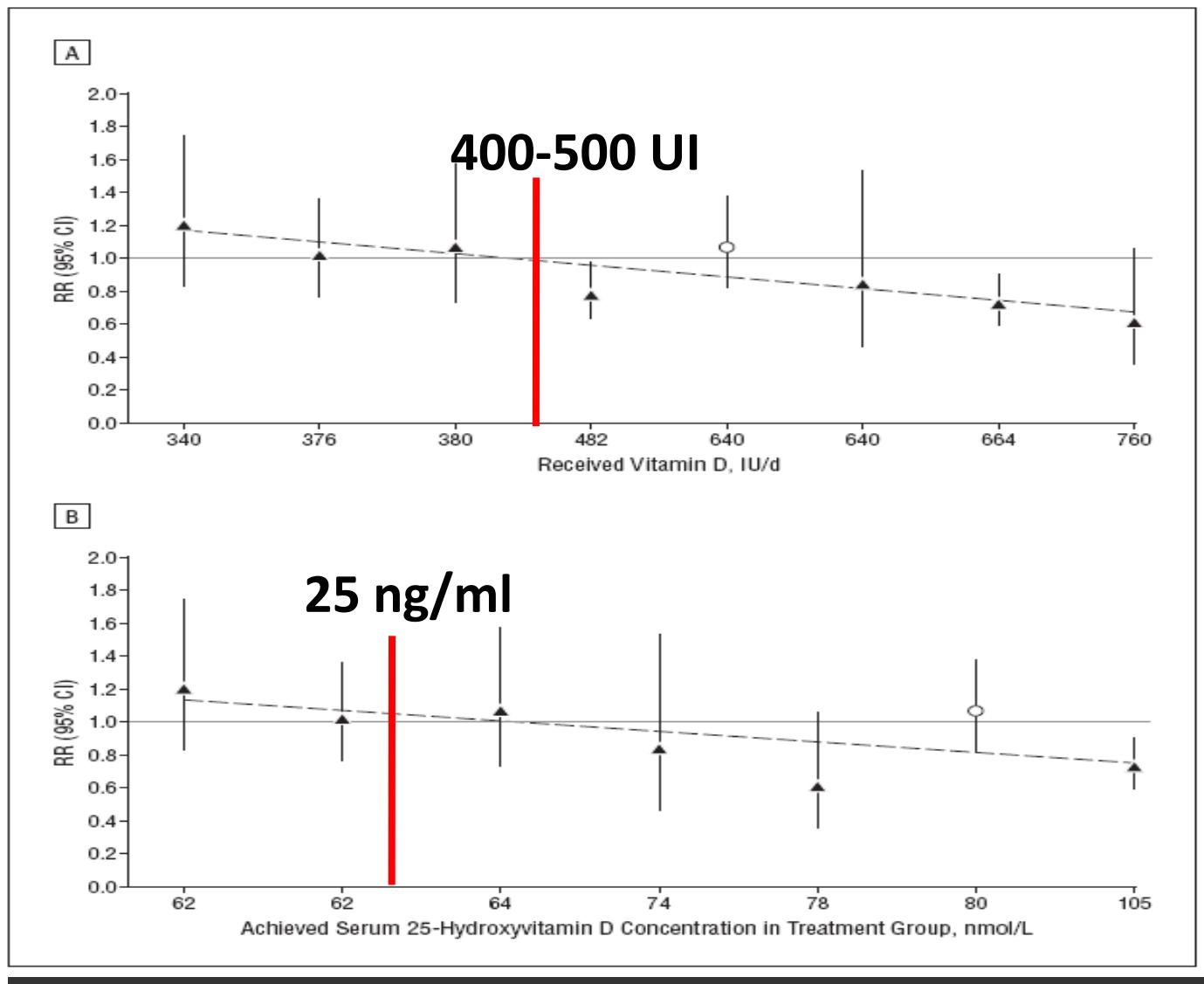
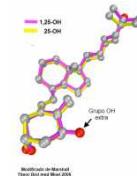


Relación Vitamina D y Fr. No vertebrales



Bisofh-Ferrari et al BMJ 2009

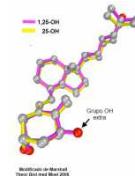
Relación Vitamina D y Fr. de Cadera



Bisofh-Ferrari et al BMJ 2009

A Systematic Review: Influence of Vitamin D Supplementation on Serum 25-Hydroxyvitamin D Concentration

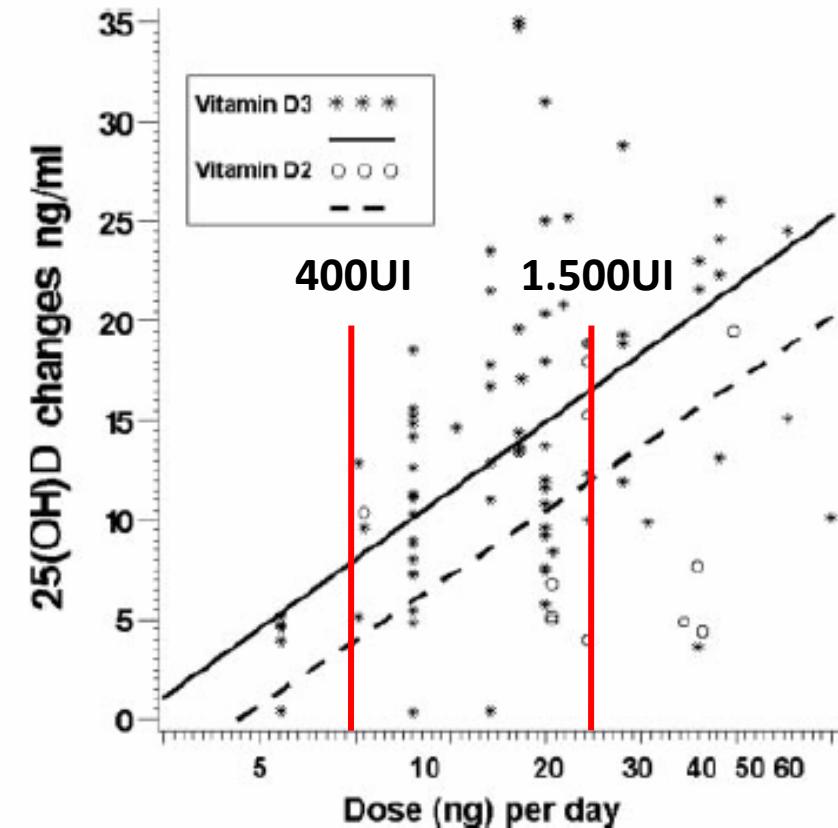
Autier et al JCEM 2012, 97(8):0000–0000



- Mayores de 50 años
- 76 estudios 1984-2011
- 6.207 sujetos
- Dosis 5-530 mcg/d
- Mediana 20mcg/d

Resultados

- Gran dispersión/dosis
- $\Delta : 0,78 \text{ ng/ml} / 1 \text{ mcg o } 60 \text{ UI}$



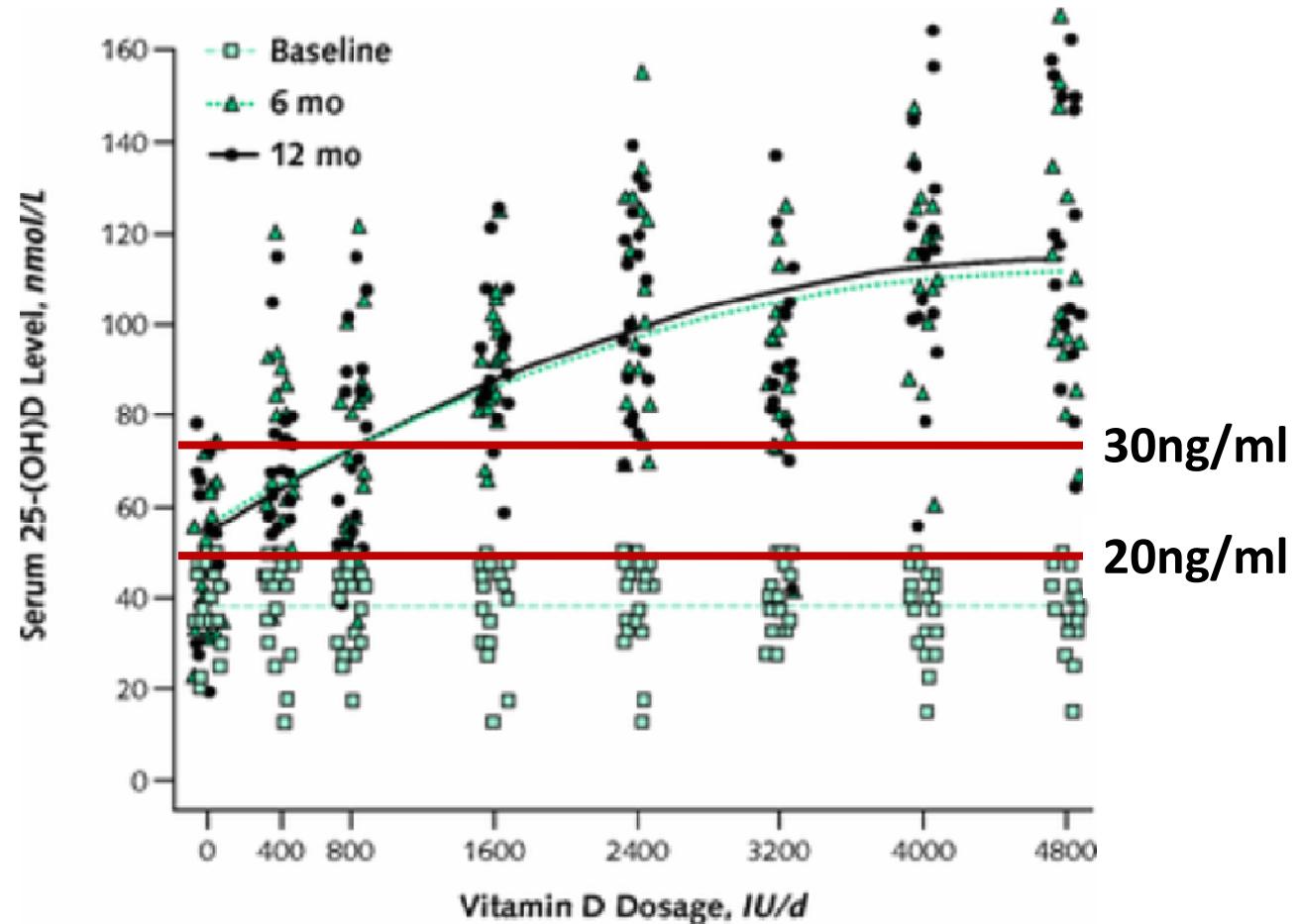
Conclusión:

Las recomendaciones de ingesta o los RCT deben considerar si se cumplen los objetivos de niveles para 25-OH.

Dose Response to Vitamin D Supplementation in Postmenopausal Women: A Randomized Trial

Annals of Internal Medicine
ESTABLISHED IN 1927 BY THE AMERICAN COLLEGE OF PHYSICIANS

- 163 Mujeres
 - 57-90 año
 - Invi/Primav
- Se incluyen**
- 25-OH> 5ng/ml
 - 25-OH<20ng/ml

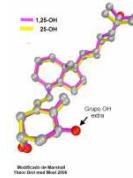


800 UI/d el 97,5% con >20ng/ml

800-1.600 UI/d el 50% con >30 ng/ml y 3.000UI el 97% con >30ng/ml

Gallagher et al. Ann Intern Med. 2012;156(6):425-437.

A Pooled Analysis of Vitamin D Dose Requirements for Fracture Prevention

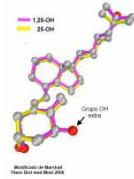


Heike A. Bischoff-Ferrari et al NEJM 2012

12 RCT con 31.022 personas (Edad:76a y 91% mujeres)

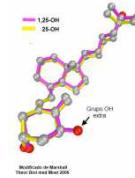
Analysis	No. of Participants	Hip Fracture			Any Nonvertebral Fracture		
		No. of Fractures	Relative Risk (95% CI)	P Value	No. of Fractures	Relative Risk (95% CI)	P Value
Actual-intake analysis:							
Control	15,495	586	1.00		1948	1.00	
0–360 IU/day	3,935	100	1.00 (0.79–1.26)	0.99	425	0.96 (0.86–1.07)	0.44
361–637 IU/day	3,836	110	1.03 (0.83–1.29)	0.78	520	1.01 (0.91–1.12)	0.85
638–791 IU/day	3,790	164	1.01 (0.83–1.23)	0.92	419	0.90 (0.80–1.01)	0.08
792–2000 IU/day	3,966	151	0.70 (0.58–0.86)	<0.001	458	0.86 (0.76–0.96)	0.007
Sensitivity analysis							
Control	15,495	586	1.00		1948	1.00	
0–337 IU/day	3,353	84	1.01 (0.79–1.30)	0.91	465	1.06 (0.95–1.17)	0.32
338–360 IU/day	5,652	114	0.83 (0.66–1.05)	0.11	619	0.89 (0.80–0.98)§	0.02
361–699 IU/day	2,640	180	1.14 (0.93–1.41)	0.21	326	1.05 (0.91–1.22)	0.52
700–2000 IU/day	3,882	147	0.71 (0.58–0.87)	0.001	412	0.81 (0.72–0.91)	<0.001

↓30% R Fx cadera y ↓14% R Fx no vertebral
25-OH>24ng/ml dintel fractura



¿Cuál es la dosis máxima de vitamina D?

Valores de vitamina D y Toxicidad



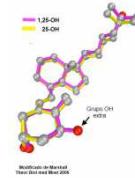
- 10.000 UI/d durante 5 meses sin cambios en Ca sangre u orina(1)
- 3.000UI/d durante 6 años sin evidencia de toxicidad(2)
- La hipercalcemia tóxica se asocia con valores entre 100-400 ng/ml de 25-OH-D(3)

(1)Heaney RP et al Am J Clin Nutr 2003

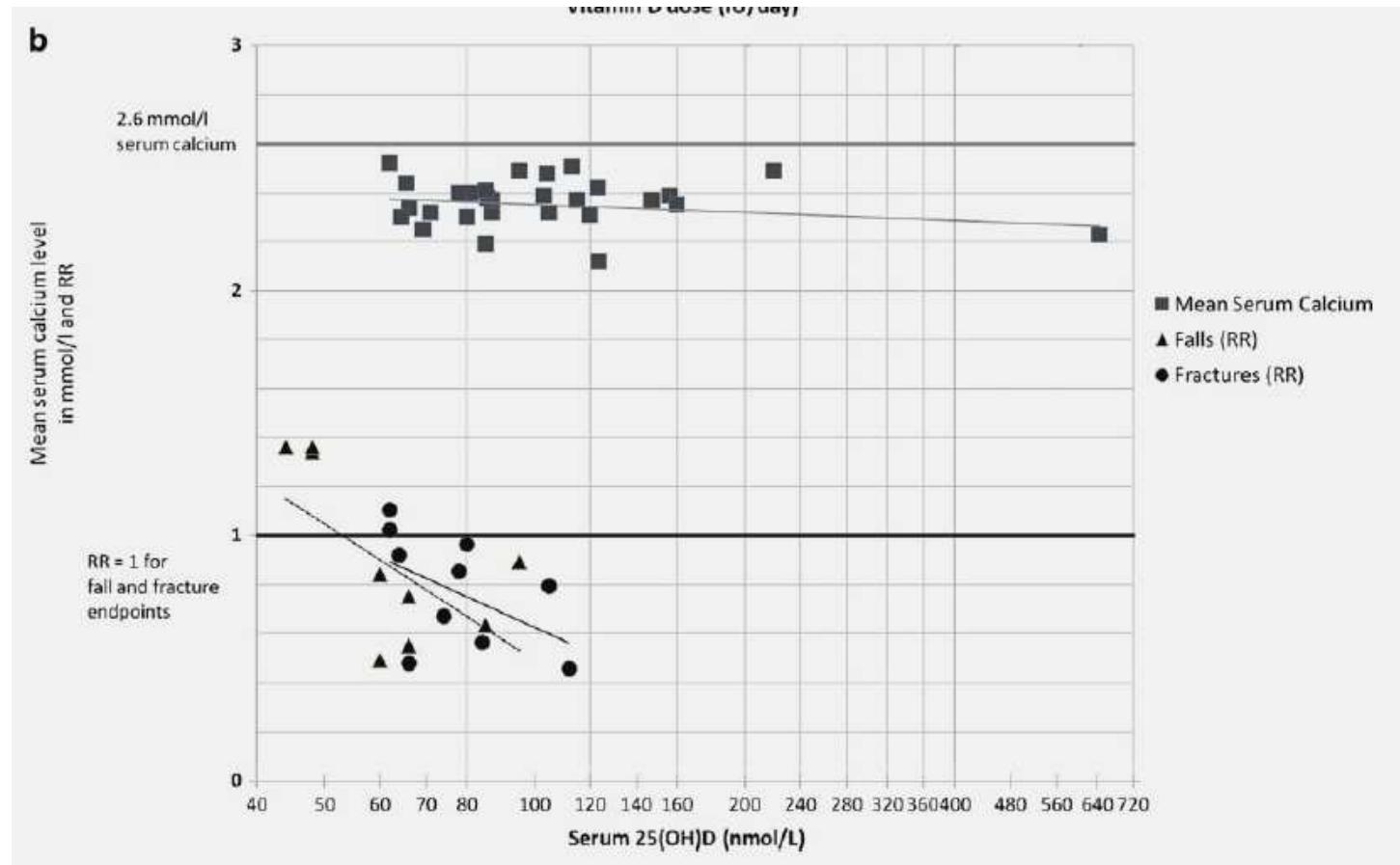
(2)Pietras SM et al Arch Intern Med 2009

(3)De Luca. Arch. Biochem. Biophys (2011).

Valores de vitamina D/Hipercalcemia



Metaanálisis de 24 RCT

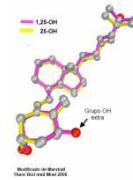


No se detecta hipercalcemia con valores de 70ng/ml

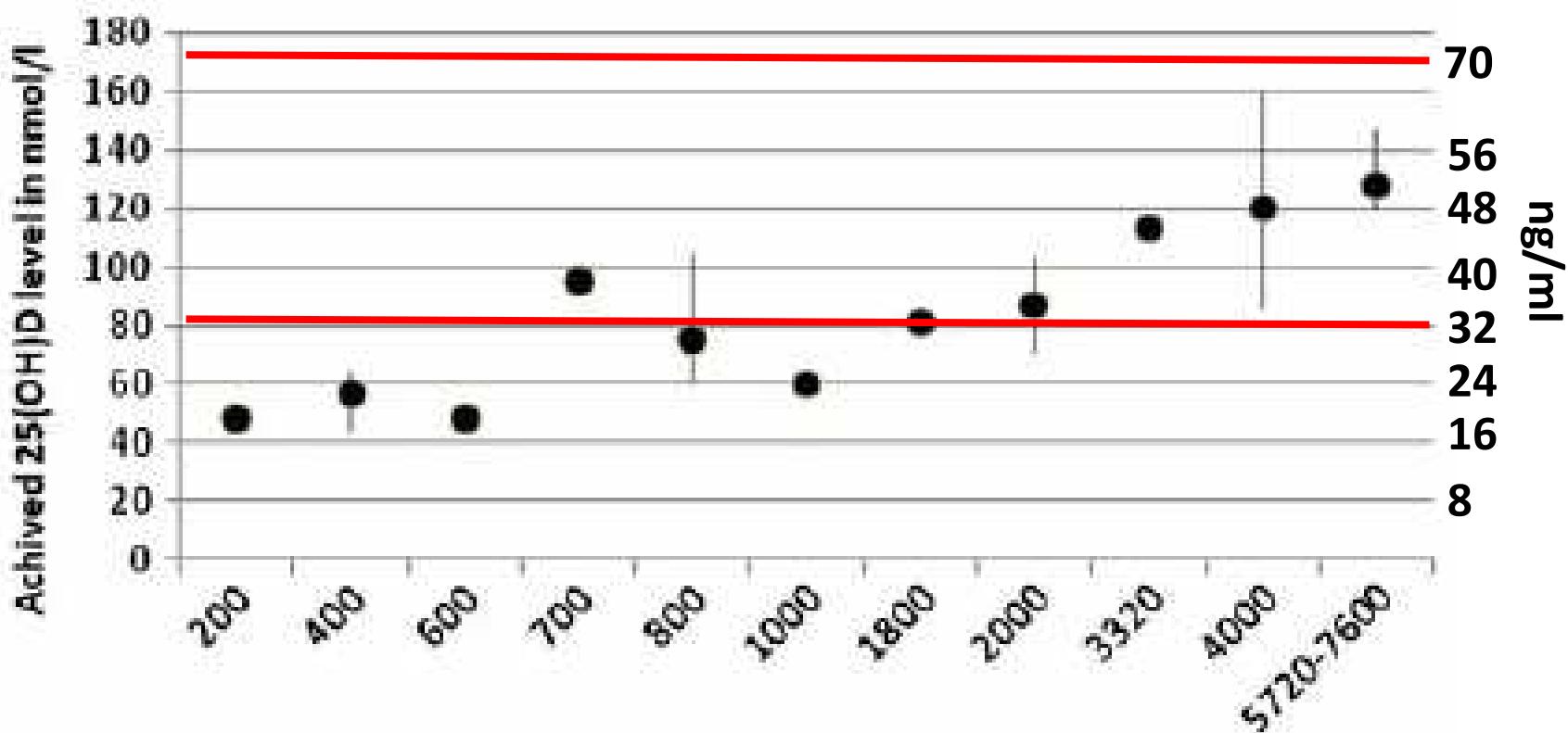
Bischoff-Ferrari Osteoporos Int 2010

Benefit–risk assessment of vitamin D supplementation

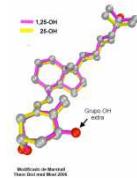
H. A. Bischoff-Ferrari • A. Shao • B. Dawson-Hughes •
J. Hathecock • E. Giovannucci • W. C. Willett



Osteoporos Int (2010) 21:1121–1132
Metaanálisis de 22 RCT

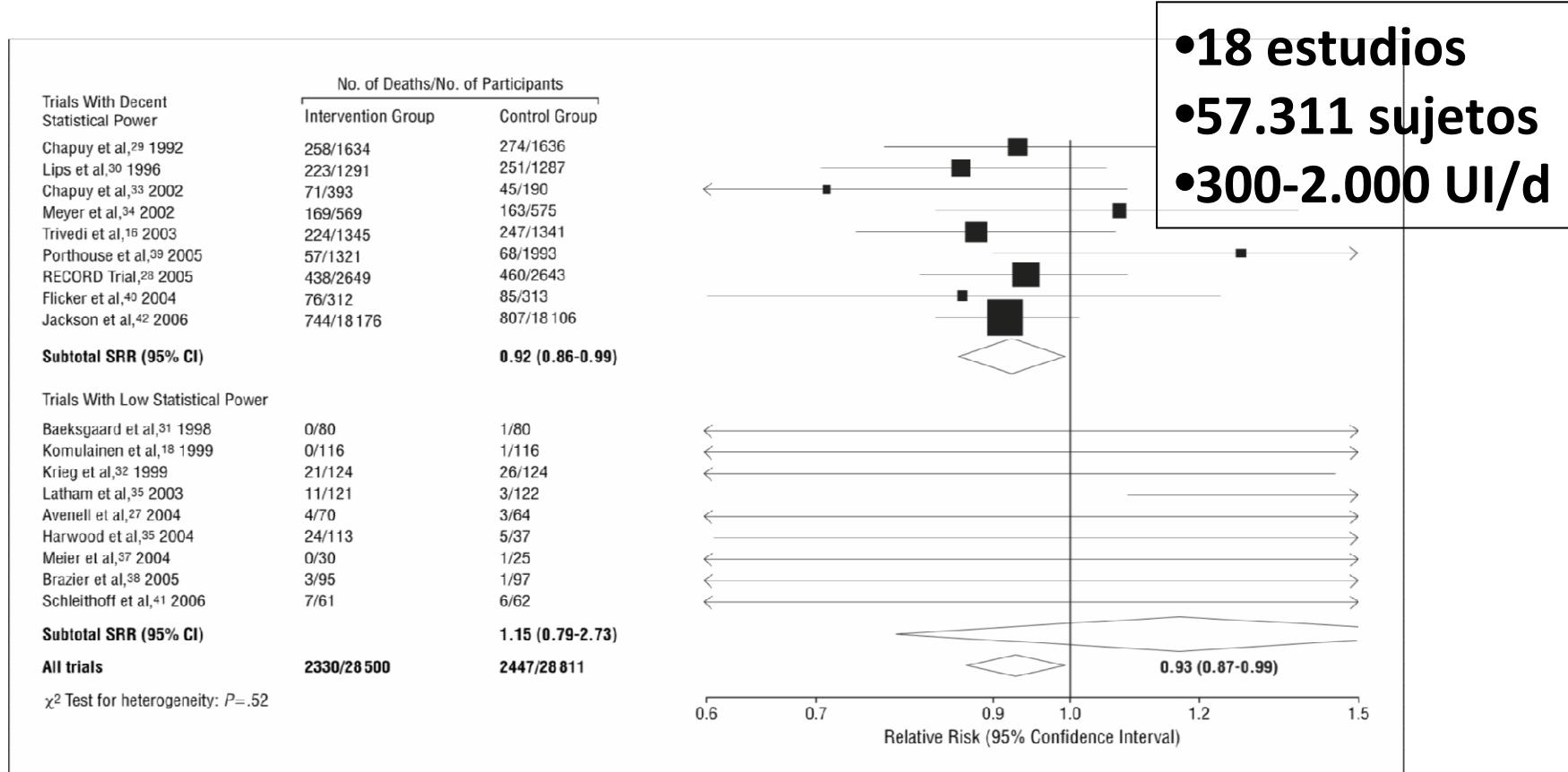


Para alcanzar niveles superiores a 32 ng/ml
se precisan dosis continuadas >2.000UI/d



Vitamin D Supplementation and Total Mortality: A Meta-analysis of Randomized Controlled Trials

Autier 2007 Arch Intern Med. 2007;167(16):1730-1737. doi:10.1001/archinte.167.16.1730

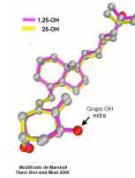


Conclusión:

La ingesta de vitamina D a las dosis habituales parece disminuir la mortalidad

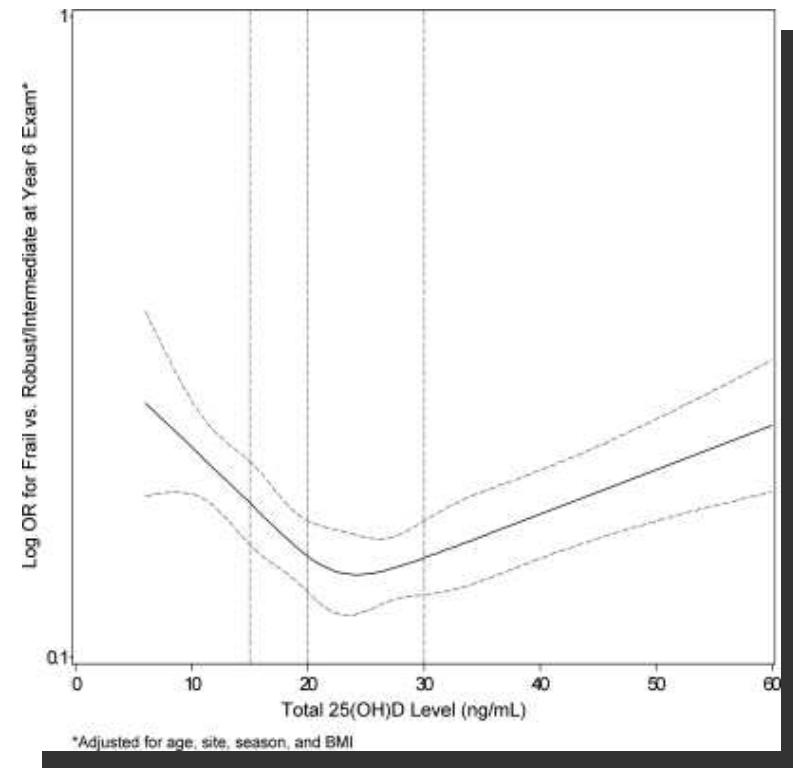
Niveles de 25-OHD y Fragilidad.

Study of Osteoporotic Fractures Research Group



- 6.307 mujeres
- >69 años
- Seguimiento 4,5 años
- Objetivo: fragilidad y mortalidad

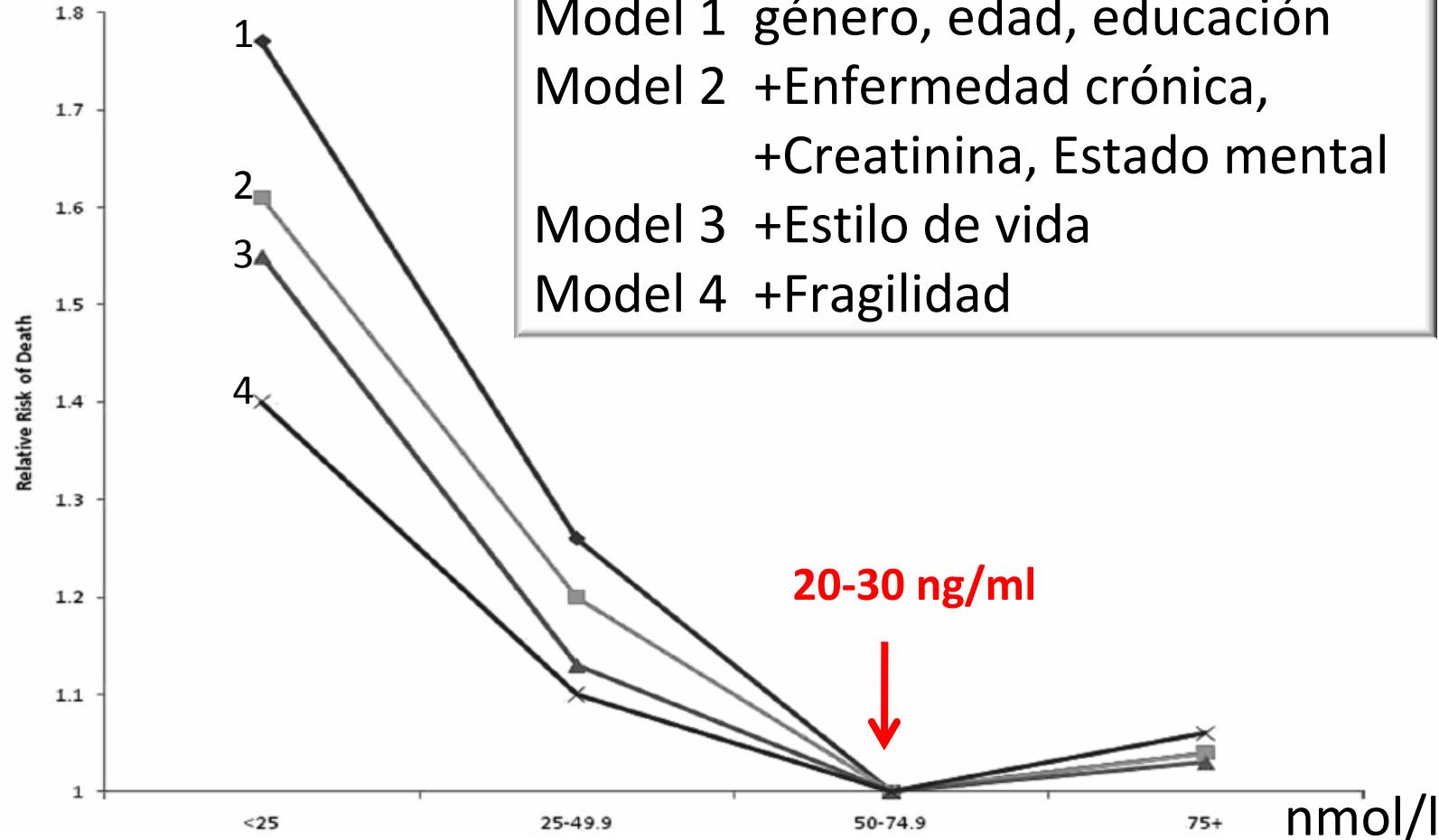
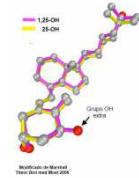
25-OH ng/ml	Multivariate Odds Ratio
<15	1.47 (95% CI 1.19-1.82)
15-19.9	1.24 (95% CI 0.99-1.54)
20.0-29.9	control
>30	1.32 (95% CI 1.06-1.63)



[Ensrud KE J Clin Endocrinol Metab. 2010 December; 95\(12\): 5266–5273.](#)

doi: 10.1210/jc.2010-2317

Valores de vitamina D y Toxicidad

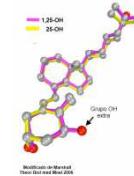


Dietary Reference Intakes for Calcium and Vitamin D.
The National Academies Press, DC, USA (2010) IOM (Institute of Medicine).

http://www.nap.edu/catalog.php?record_id=13050

A. Catharine Ross, Christine L. Taylor, Ann L. Yaktine, and Heather B. Del Valle

Long-Term Follow-Up for Mortality and Cancer in a Randomized Placebo-Controlled Trial of Vitamin D₃ and/or Calcium (RECORD Trial)



Avenell et al J Clin Endocrinol Metab 2012 97: 614–622

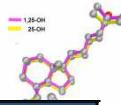
N: 5.922 seguidos 6,2 años ; 4 grupos: Ca, D, Ca+D y Pbo
15,2 ng/ml de 25-OH-D al inicio; 800UI vit D y 1.200mg de Ca

TABLE 3. HR for mortality, vascular disease mortality, cancer mortality, and cancer: ITT analysis

	With vitamin D ₃ or calcium			Without vitamin D ₃ or calcium			HR (95% CI): ITT estimate	P value
	Events	No. of participants	% with event	Events	No. of participants	% with event		
Vitamin D₃								
All deaths	836	2649	31.6	881	2643	33.3	0.93 (0.85–1.02)	0.132
Vascular deaths	350	2649	13.2	376	2643	14.2	0.91 (0.79–1.05)	0.175
Cancer deaths	151	2649	5.7	178	2643	6.7	0.85 (0.68–1.06)	0.157
Cancer incidence	338	2649	12.8	315	2643	11.9	1.07 (0.92–1.25)	0.376
Calcium								
All deaths	862	2617	32.9	855	2675	32.0	1.03 (0.94–1.13)	0.460
Vascular deaths	371	2617	14.2	355	2675	13.3	1.07 (0.92–1.24)	0.333
Cancer deaths	173	2617	6.6	156	2675	5.8	1.13 (0.91–1.40)	0.249
Cancer incidence	329	2617	12.6	324	2675	12.1	1.06 (0.91–1.23)	0.485

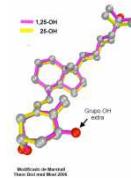
Suplementar con 800 UI de vitamina D
no produce beneficio/perjuicio en las variables estudiadas

ESTADO CORPORAL DE VITAMINA D

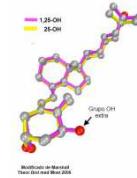


Estado	25-OH ng/ml	Asociación Clínica
Deficiente	<16* <20**	Raquitismo /Osteomalacia Enfermedad periodontal Osteoide ↑↑ PTH ↑↑ Absorción Ca ↓↓
Adecuada poblacional* Insuficiente clínica**	20-30	↑ Riesgo de fracturas y caídas Osteoide ↑ PTH ↑ Absorción Ca ↓
Suficiente	>30	Dintel de fracturas y caídas No osteoide PTH Normal Absorción Ca Máxima
¿Terapéutico? ¿Tóxico?	> 50* >100**	Sin datos claros Hipercalcemia

* IOM ** Endocrine Society ¿?Posible valor de prevención



¿Son fiables las determinaciones de la vitamina D?

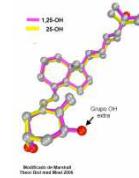


Evaluación del Estado Corporal en vitamina D

Determinación de 25OHD

- Competición proteica (CBP).
- Radioinmunoanálisis (RIA)
- Ensayo inmunoabsorbente ligado a enzimas (ELISA)
- HPLC, acoplada a espectrometría de masas UV;LC-MS/MS

Current status of clinical 25-hydroxyvitamin D measurement: An assessment of between-laboratory agreement



Objetivo:

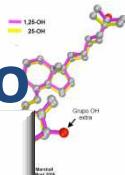
Variabilidad en las determinaciones de 25-OH-D

Métodos:

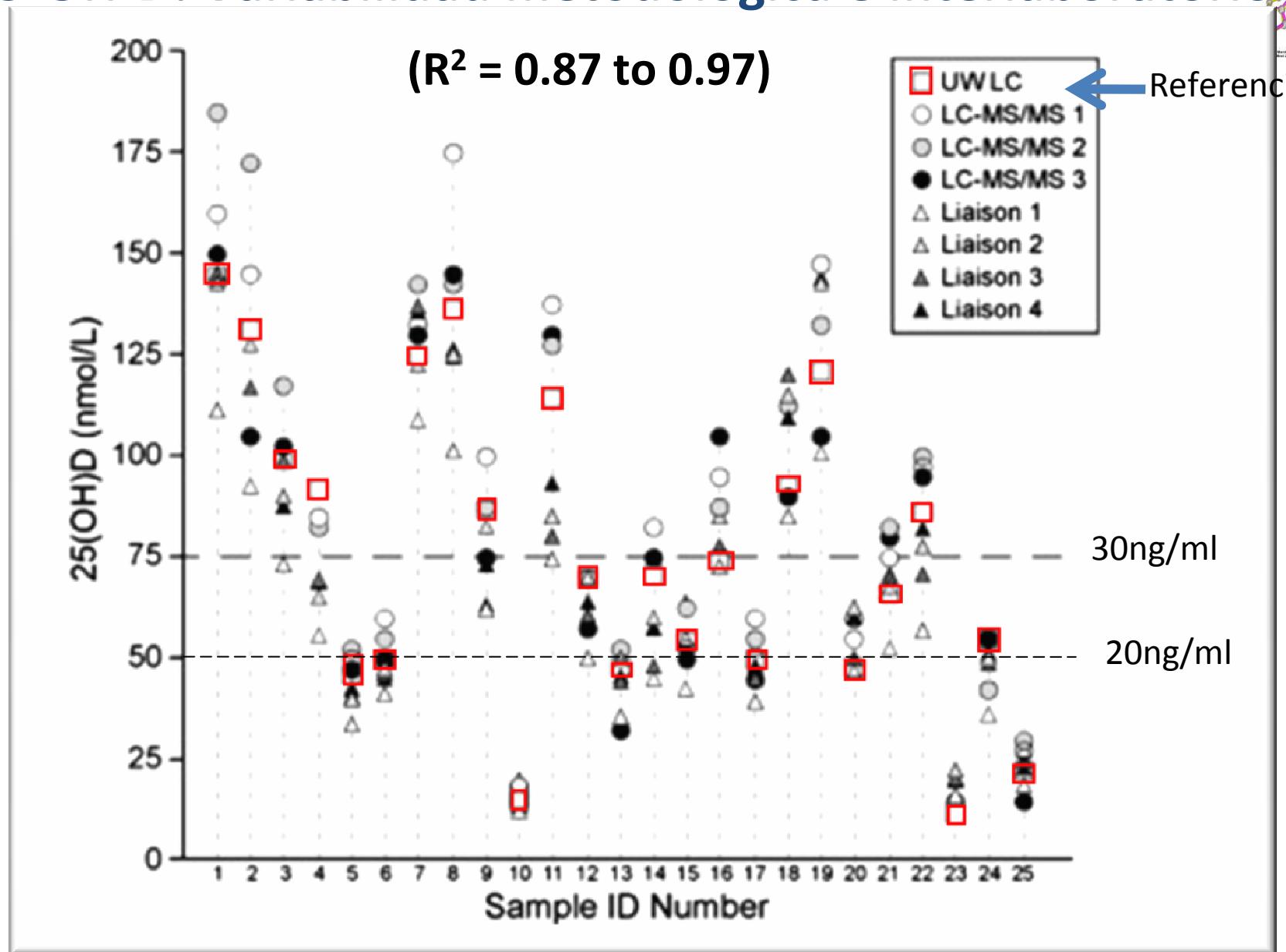
- 25 muestras con (25-OH-D₂ y 25-OH-D₃)
- Concentraciones de 25-OH-D desde 5 a 60ng/ml
- 8 laboratorios de referencia en USA
- Métodos: HPLC-UV (1); HPLC-MS/MS(3); Inmunoanálisis(4)

Binkley et al Clin Chim Act 2010. 411: 1976–1982

25-OH-D: Variabilidad metodológica e interlaboratorio



Referencia



25-OH-D: Variabilidad metodológica/interlaboratorio

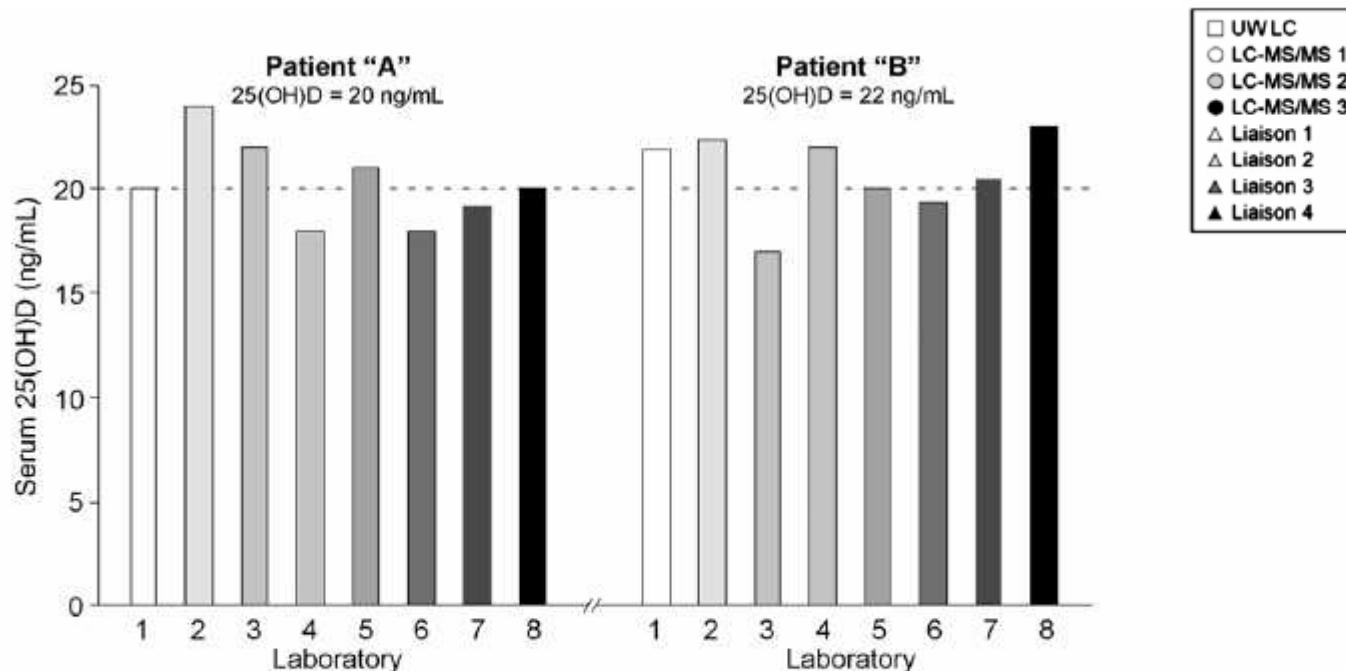
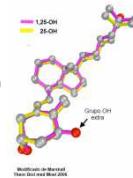
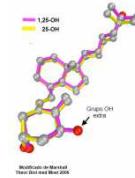


Fig. 2. Examples of between-laboratory variability in 25(OH)D measurement. In these 2 examples (patient "A" and "B"), serum aliquots were sent to 8 different clinical laboratories. Laboratory 1 served as the reference standard using high-performance liquid chromatography methodology that compares extremely well with the National Institute of Standards and Technology standards. Despite excellent overall agreement between these 8 laboratories, it is apparent that applying a simple "cutpoint" approach (depicted here as the dotted line at 20 ng/mL), will lead individual patients to be told that their vitamin D status is "normal" or "low" based on the laboratory used. Data from Binkley et al (18).



HOUSTON
JUNE 23-26



Holmes at al.

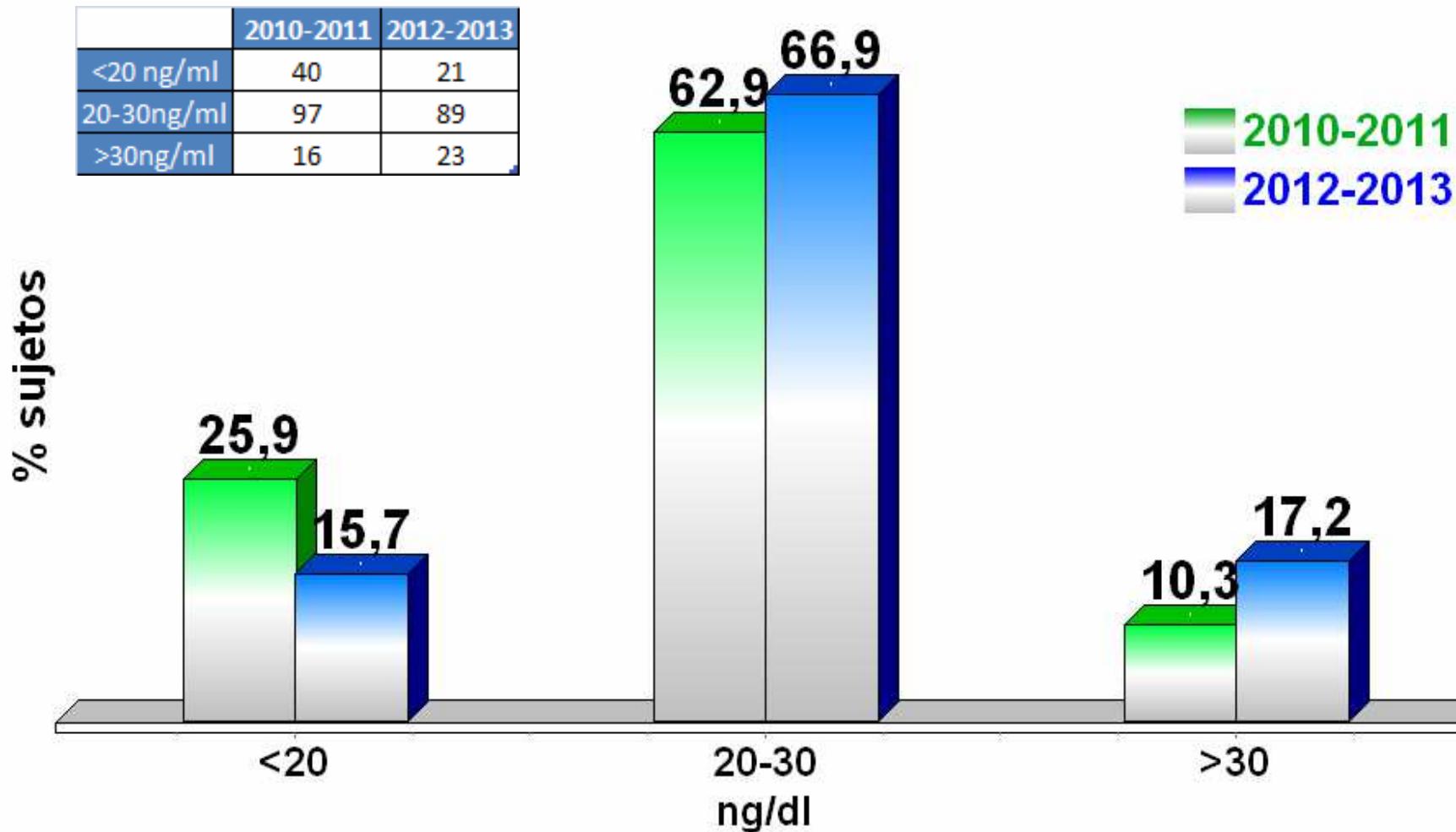
Estudiados 163 pacientes

- 33 con deficiencia HPLC-SPM (referencia)
- 45 con deficiencia Abbot Architect
- 71 con deficiencia Siemens Centaur

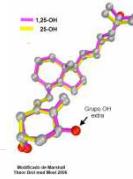
40% muestras con fluctuaciones >25% Abbot Architect

48% muestras con fluctuaciones >25% Simens Centaur

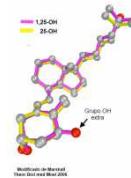
Valores de vitamina D Noviembre/Diciembre/Enero



Conclusiones

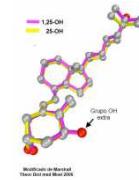


- En la actualidad no existen datos para sustentar o descartar un efecto de la vitamina D terapéutico o preventivo en la enfermedad extraesquelética.
- Las dosis de 400-800Ui/d son adecudas para la mayoría de las personas.
- La protección contra caídas y fracturas está en el rango 26-32 ng/ml de 25-OHD y con dosis superiores a 800UI/d
- Para muchos pacientes son precisas 1.000-2.000 UI/d para mantener un nivel de 25-OH de 30ng/dl
- Por ahora es preciso utilizar las recomendaciones junto con el juicio clínico ante un paciente concreto .



¿La vitamina D es causa o consecuencia?

Modelo deficiencia/Enfermedad (Vitamina D como Causa de enfermedad)



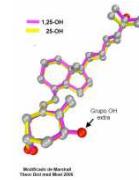
PREMISAS:

- Valores Vit. D bajos en sujetos con E. Autoinmune
- Tomar Vit. D ↓ frecuencia de E. Autoinmune

CONCLUSIÓN:

Los niveles bajos de vitamina D son causa de enfermedad y su suplementación es beneficiosa

Modelo Enfermedad/Deficiencia (Vitamina D como consecuencia)



PREMISAS:

- El proceso inflamatorio ↓ los valores de 25-OH
- La toma de Vit. D normaliza marcadores de Enfermedad

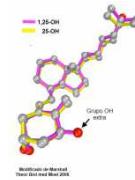
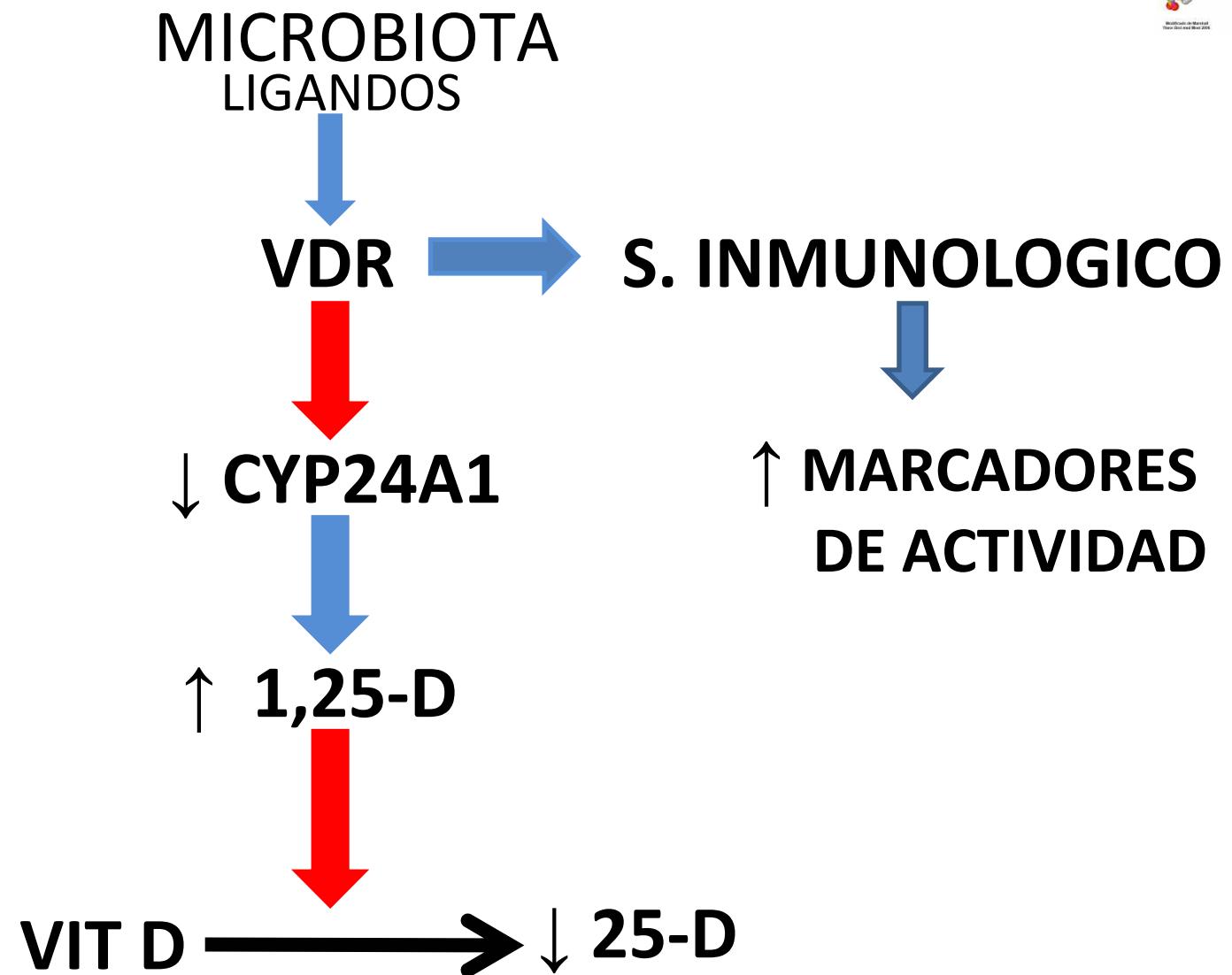
Conclusión:

Los valores de 25-OH son marcadores de enfermedad y la toma de Vit. D puede no ser beneficiosa.

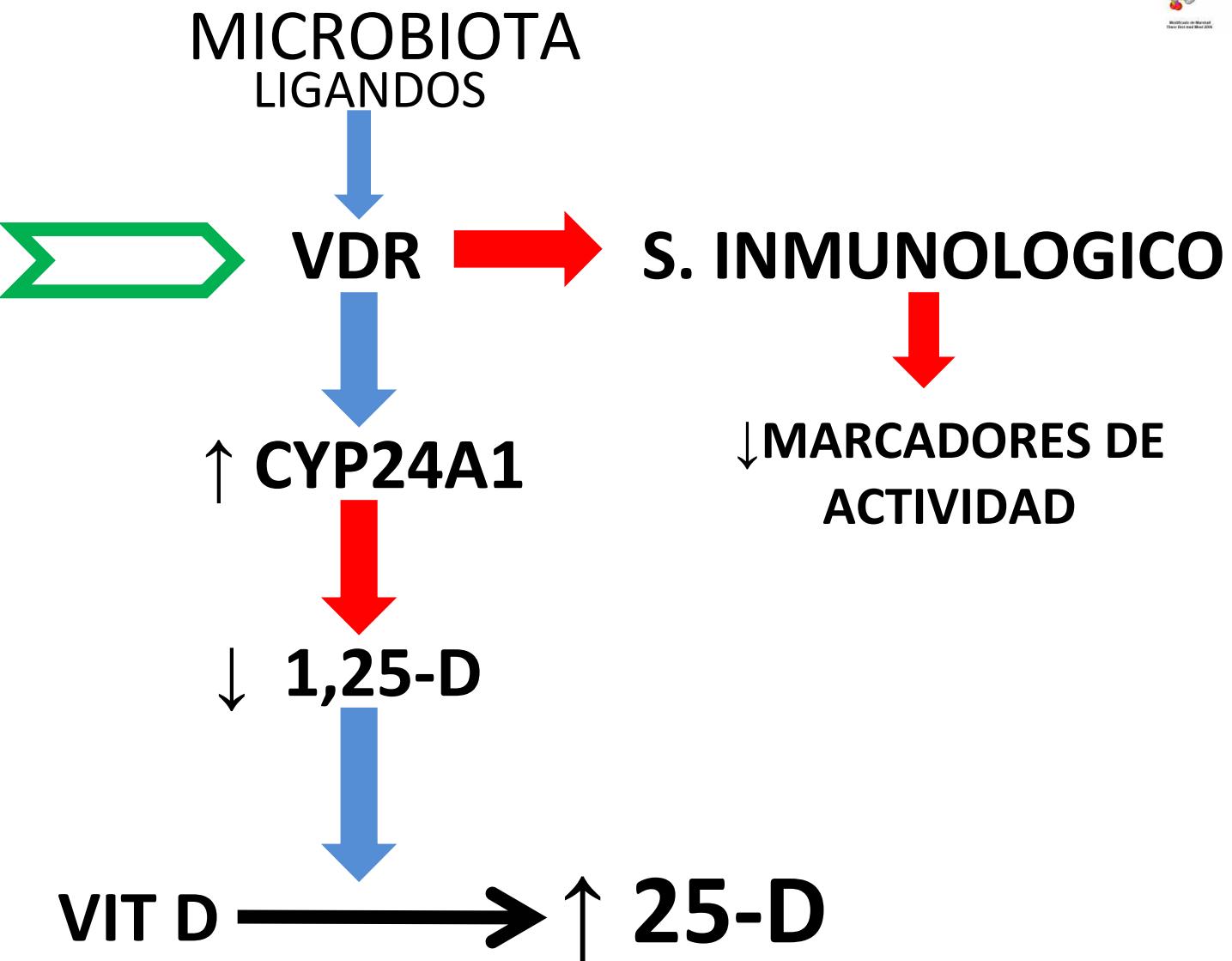
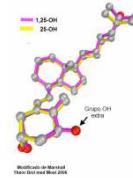
Hipótesis Alternativa de Paul J. Albert.
Autoimmunity Reviews 8 (2009) 639–644



HIPOTESIS ALTERNATIVA

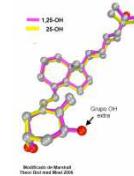


HIPOTESIS ALTERNATIVA



Paul J. Albert. Autoimmunity Reviews 8 (2009) 639–644

Niveles de 25-OH-D: ¿ Causa o Consecuencia?



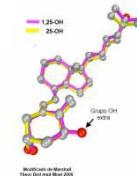
Vitamin D: a negative acute phase reactant

Table 1 Biochemical data in 30 patients before and 48 h after elective knee or hip surgery

Analyte	Preoperative	Postoperative	p Value
Serum CRP (mg/l)	5.0 (5.5)	116.0 (81.2)	<0.0001
Serum 25-(OH)D (nmol/l)	56.2 (30.3)	46 (27.6)	0.0006
Serum VDBP (mg/l)	334 (43)	298 (37)	<0.0001
Serum albumin (g/l)	46 (2.2)	39 (2.6)	<0.0001
Serum creatinine (μ mol/l)	76 (15)	78 (24)	0.4633
Serum adjusted calcium (mmol/l)	2.26 (0.11)	2.26 (0.07)	0.7624
Urine VDBP/creatinine (pg/mmol)	8 (9)	20 (25)	0.0004
Urine ACR (mg/mmol)	0.85 (1.03)	2.10 (2.60)	0.0040

Results are mean (SD).

25-(OH)D, 25-hydroxy-vitamin D; ACR, albumin to creatinine ratio (microalbumin); CRP, C reactive protein; VDBP, vitamin D binding protein.



The relation between acute changes in the systemic inflammatory response and plasma 25-hydroxyvitamin D concentrations after elective knee arthroplasty^{1–4}

David Reid, Barry J Toole, Susan Knox, Dinesh Talwar, Johann Harten, Denis St J O'Reilly, Scott Blackwell, John Kinsella, Donald C McMillan, and A Michael Wallace

TABLE 2

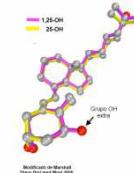
Perioperative measurements of vitamin D metabolism after elective surgery for knee arthroplasty ($n = 33$)¹

	Preoperative	6–12 h	Day 1	Day 2	Day 3	Day 4	Day 5 ²	P value ³
CRP (mg/L)	2.8 (0.6–9.3)	—	56 (5–105)**	164 (74–298)**	189 (61–296)**	136 (36–284)**	113 (25–234)**	<0.001
Estimated GFR (mL · min ⁻¹ · 1.73 m ⁻²)	81 (39–110)	—	81 (39–110)	80 (2.7–112)	79 (29–115)	83 (38–120)	76.5 (42–115)	0.505
Adjusted calcium (mmol/L)	2.3 (1.81–2.47)	2.10 (0.94–2.35)**	2.11 (1.52–2.32)**	2.13 (1.84–2.30)**	2.15 (1.72–2.31)**	2.15 (1.75–2.38)**	2.19 (1.64–2.36)*	<0.001
PTH (pmol/L)	6.3 (3.4–25.3)	7.7 (3.8–32.3)	7.2 (3.9–29.9)	6.5 (4.0–30.1)	6.9 (3.8–27.3)	7.3 (4.0–28.0)	6.9 (3.3–24.5)	0.063
25(OH)D (nmol/L)	40 (12–124)	26 (8–93)**	23 (8–95)**	23 (8–79)**	25 (7.5–70)**	28 (8–72)**	29 (8–76)**	<0.001
Albumin (g/L)	39 (24–48)	—	33 (25–38)**	32 (23–39)**	31 (24–36)**	30 (27–36)**	31 (24–34)**	<0.001
VDBP (μmol/L)	7.5 (5.6–10.6)	6.6 (2.8–9.2)*	6.9 (3.8–9.3)*	7.1 (4.3–25)	—	—	7.9 (4.1–10.9)	<0.001
Molar ratio	6.9 (1.5–26.9)	5.4 (1.1–36.6)*	4.2 (1.0–27.0)**	4.8 (0.7–19.8)**	—	—	4.0 (0.9–15.0)	<0.001
Free 25(OH)D (pmol/L)	9.04 (1.94–34.90)	—	5.41	6.40	—	—	6.09 (1.20–18.96)**	<0.001

¹ All values are medians; ranges in parentheses. CRP, C-reactive protein; GFR, glomerular filtration rate; 25(OH)D, 25-hydroxyvitamin D; PTH, parathyroid hormone; VDBP, vitamin D-binding protein. ***Significantly different from preoperative values (Wilcoxon's signed-rank test); * $P < 0.01$, ** $P < 0.001$.

² $n = 23$.

³ Friedman's test.



LETTERS

VITAMIN D DEFICIENCY

Position statements on vitamin D deficiency are no substitute for well designed studies

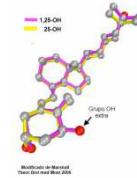
Stephen S Nussey *professor of endocrinology*

St George's Hospital Medical School, London SW17 0RE, UK

NIVELES DE VITAMINA D: La historia interminable

*Gracias
por su
atención*

¿Cuál es la dosis de vitamina D recomendada?



INSTITUCIÓN	RECOMENDACIÓN UI/d
 U.S. Preventive Services TASK FORCE	+400
 INSTITUTE OF MEDICINE OF THE NATIONAL ACADEMIES	600-800
 International Osteoporosis Foundation	800-1.000
	800-1.000
	1.500-2.000