

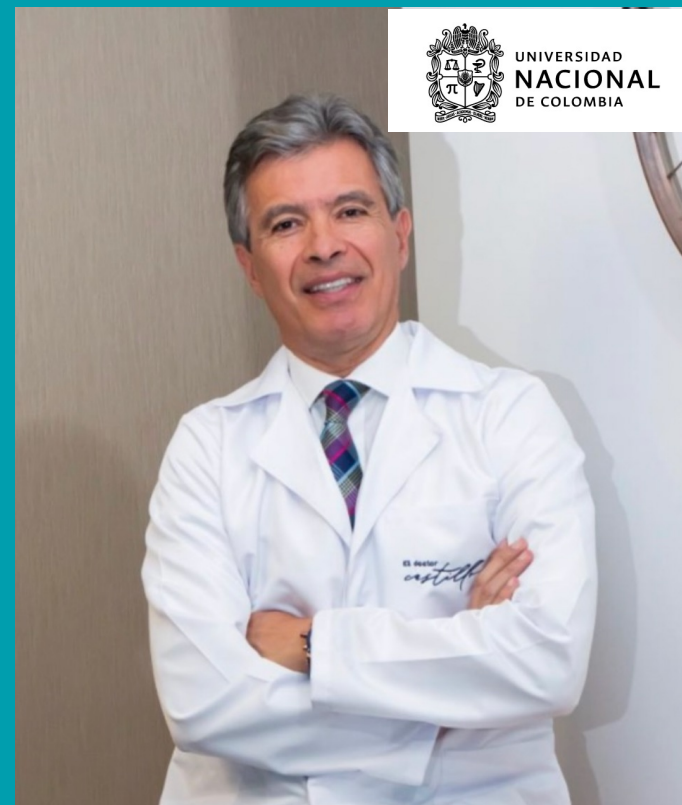
Vitamina D 50.000 UI:  
Corrección rápida y manejo  
inteligente

# Castillo

## Jorge

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Especialista en Endocrinología  
Los Cobos Medical Center  
Bogotá, Colombia



# Conflicto de interés

Conferencia disponible en

[www.eldoctorcastillo.com](http://www.eldoctorcastillo.com)

- ▶  Esta es una conferencia patrocinada por laboratorios **Procaps**
- ▶  Su contenido es producto de información científica no influenciada por el patrocinador
- ▶  He recibido honorarios como speaker de Amgen, Astra Zeneca, BD, Boeringher, Diabetrics, Euroetika, Gilead, Merck Serono, Merck Sharp and Dhome, Lilly, Novo Nordisk, Pharmatech, Pfizer, PTC, Procaps, Roche, Sanofi, Servier, Tecnofarma.

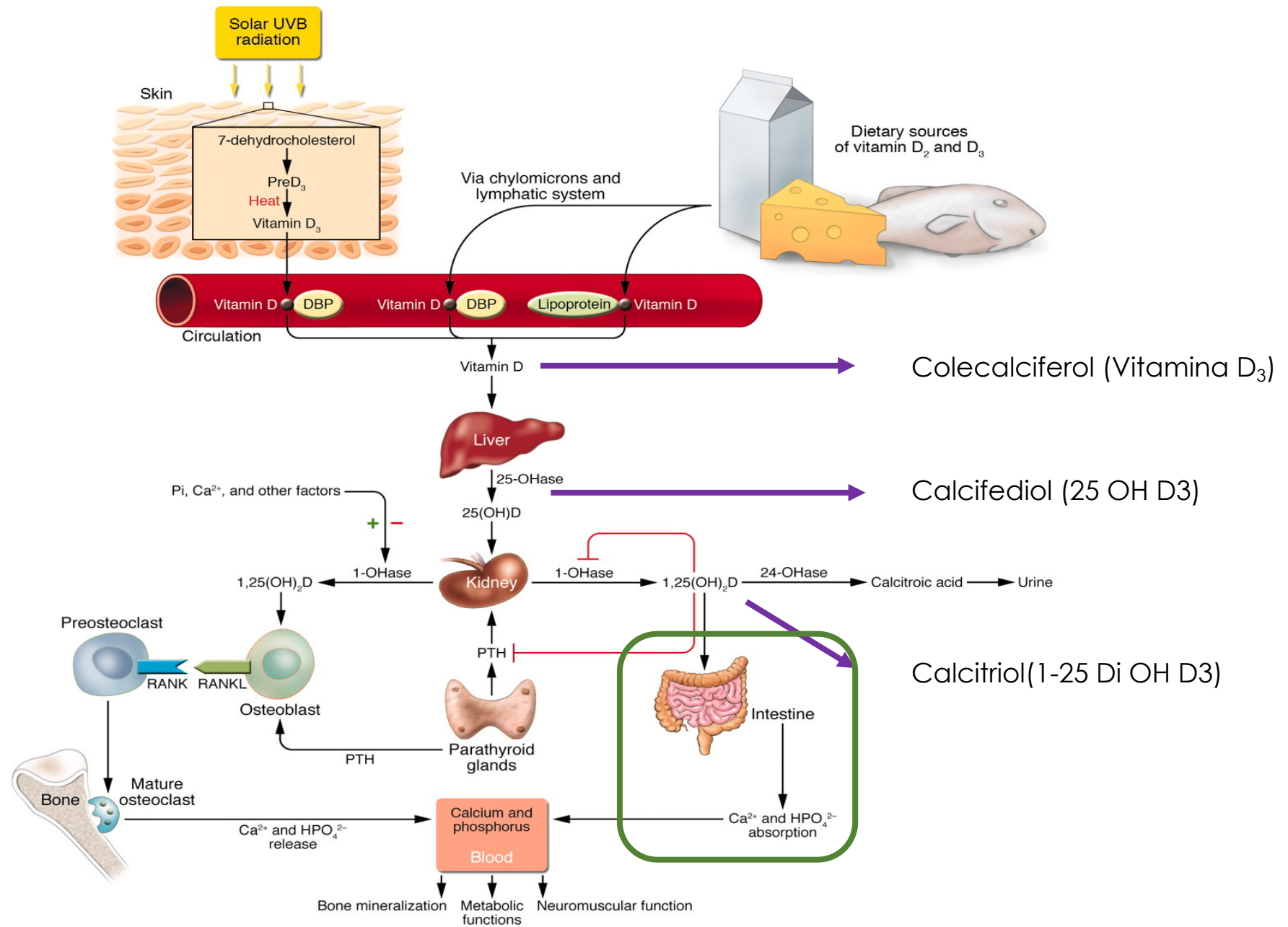
# Efectos de la Vitamina D



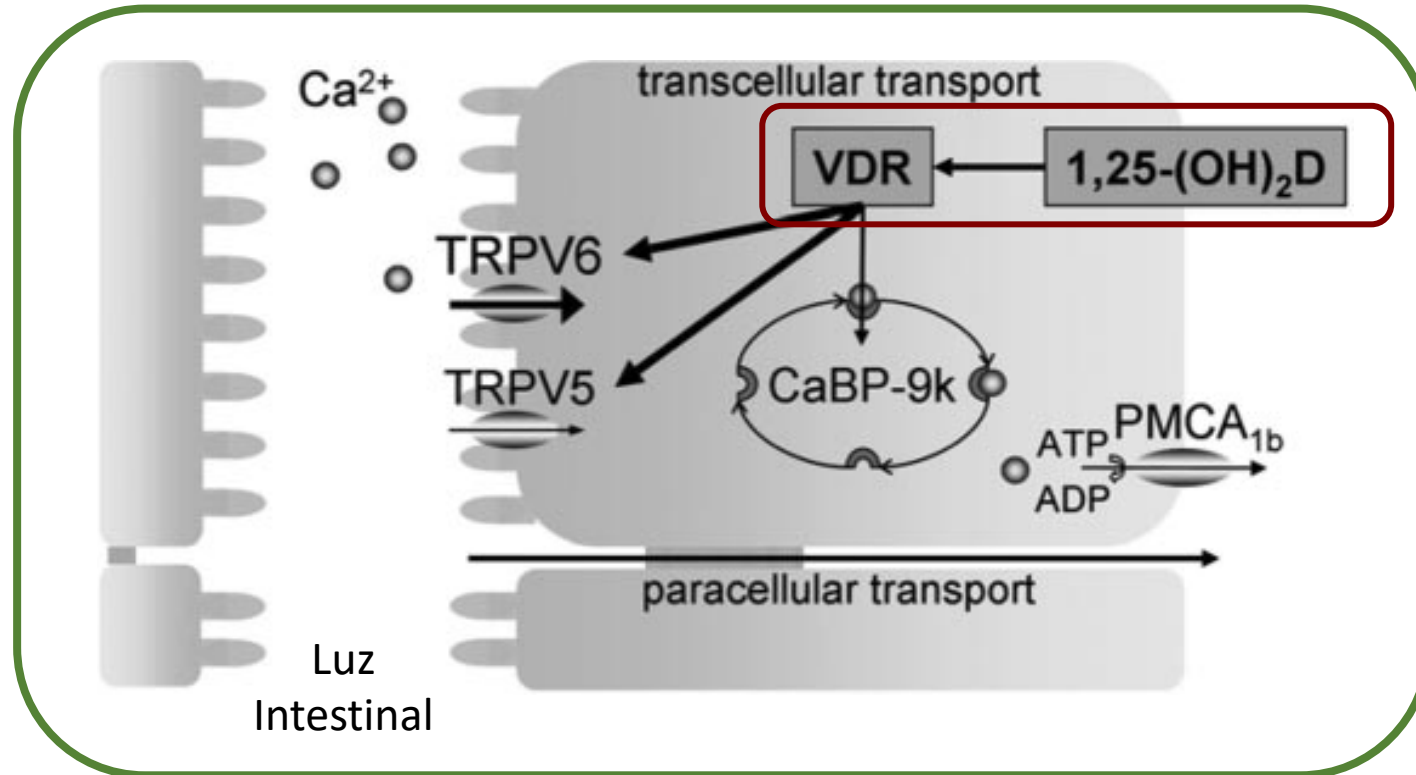
(1) Efecto genómico: El complejo 1,25 (OH) 2D3-receptor de vitamina D (VDR)-receptor de ácido retinoide X (RXR) formado se transloca del citoplasma al núcleo, donde se une al elemento de respuesta a la vitamina D (VDRE) en los genes diana. En consecuencia, el complejo regula la expresión de numerosos genes, hasta un total de cientos.

(2) Efecto no genómico: la activación del VDR de membrana inicia una rápida reacción de cebado de membrana, lo que desencadena vías de señalización que contribuyen a las respuestas biológicas.

(3) Efectos epigenéticos: estos efectos implican la regulación de los miRNA, la metilación del ADN, la acetilación/desacetilación de histonas y la metilación/desmetilación de histonas, que, en conjunto, inciden en la regulación de la expresión génica.

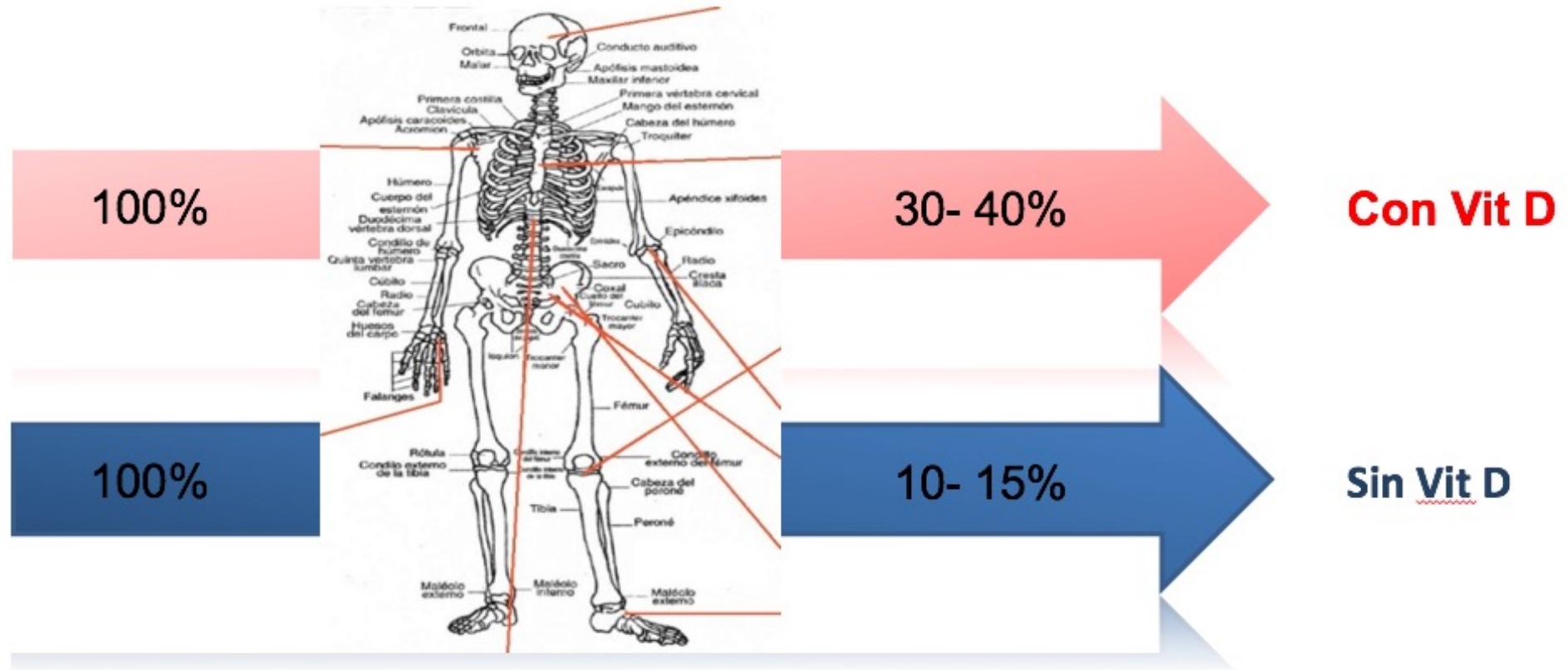


## Vitamin D and Human Health: Lessons from Vitamin D Receptor Null Mice



Entre las pocas células o tejidos que presentan una expresión baja o nula del receptor de vitamina D (VDR) se incluyen los glóbulos rojos, el músculo estriado maduro y algunas células cerebrales altamente diferenciadas, como las células de Purkinje del cerebelo.

# Absorción de Calcio



## CLINICAL GUIDELINE



**Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update From the American College of Physicians**

**COMPARATIVE BENEFITS OF TREATMENT VERSUS PLACEBO FOR REDUCING FRACTURES IN PATIENTS WITH OSTEOPOROSIS**

Calcium and vitamin D may be added as dietary supplements to osteoporosis treatment regimens, although the effectiveness of these regimens on fracture prevention is unclear.

**Table 2.** Summary of Evidence on Pharmacologic Treatments for Low Bone Density and Osteoporosis

Treatment	Effect on Fracture Risk in Osteoporotic Women and Evidence Quality			Adverse Events and Evidence Quality	Fair Price for 1-Day Supply*
	Vertebral	Nonvertebral	Hip		
Bisphosphonates	Summarized individually below	Summarized individually below	Summarized individually below	As a class: atypical subtrochanteric fracture, osteonecrosis of the jaw (low-quality)	Summarized individually below
Alendronate	Improves; high-quality	Improves; high-quality	Improves; high-quality	Mild upper GI symptoms (high-quality)	Generic: \$9 Brand-name (Fosamax): \$130
Ibandronate	Improves; high-quality	Uncertain	Uncertain	Mild upper GI symptoms (high-quality); myalgias, cramps and limb pain	Generic: \$60 Brand-name (Boniva): \$588
Risedronate	Improves; high-quality	Improves; high-quality	Improves; high-quality	Mild upper GI symptoms (high-quality)	Generic: \$136 Brand-name (Actonel): \$337
Zoledronic acid	Improves; high-quality Improves in osteoporotic men; moderate quality	Improves; high-quality	Improves; high-quality	Mild upper GI symptoms, hypocalcaemia, influenza-like symptoms (high-quality); atrial fibrillation; arthritis and arthralgias, headaches, uveitis	Generic: \$66 Brand-name (Reclast): \$1105
Denosumab (injectable)	Improves; high-quality	Improves; high-quality	Improves; high-quality	Mild upper GI symptoms (high-quality), infection (moderate-quality); rash	Brand-name (Prolia): \$1047
Teriparatide (injectable)	Improves; high-quality	Improves; high-quality	Unknown	Mild upper GI symptoms, headache, hypercalcemia (high-quality); hypercalciuria, renal adverse effects	Brand-name (Forteo): \$2767
Raloxifene	Improves; high-quality	No effect	No effect	Hot flashes, thromboembolic events (high-quality); pulmonary embolism, cerebrovascular death	Generic: \$2.40 Brand-name (Evista): \$70
Calcium and vitamin D	Uncertain	Uncertain	Uncertain	Increased risk for hypercalcemia	NA

- Amelioration of Osteoporosis and Hypovitaminosis D by Sunlight Exposure in Hospitalized, Elderly Women With Alzheimer's Disease: A Randomized Controlled Trial

- Mitate Hospital, Tagawa, Japan;

TABLE 3. BIOCHEMICAL INDICES OF BONE AND CALCIUM METABOLISM BEFORE AND AFTER THE 12-MONTH PERIOD IN THE 243 SUBJECTS WHO COMPLETED THE STUDY

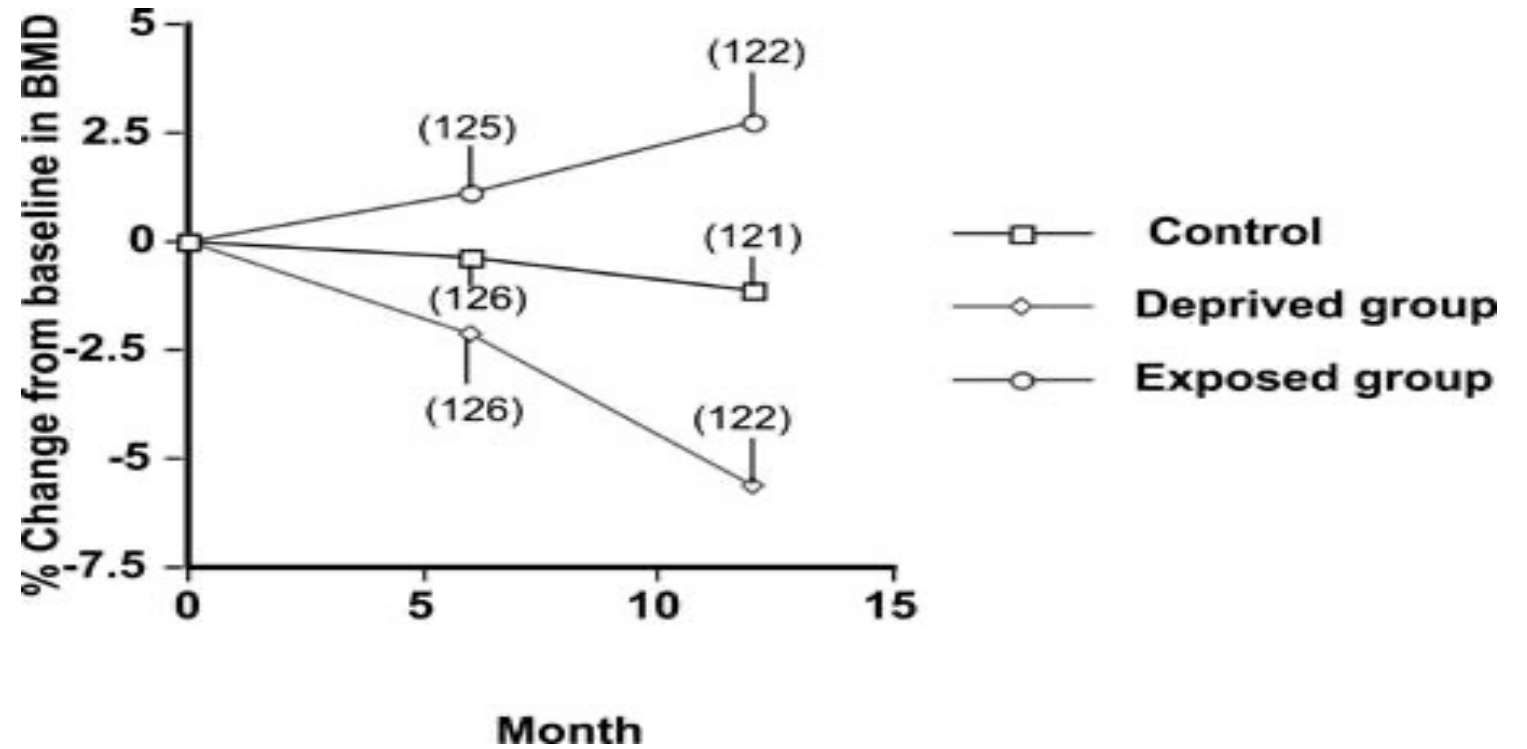
	<i>Deprived group</i>			<i>Exposed group</i>		
	<i>Before</i> ( <i>n</i> = 132)	<i>After</i> ( <i>n</i> = 121)	<i>p</i> *	<i>Before</i> ( <i>n</i> = 132)	<i>After</i> ( <i>n</i> = 122)	<i>p</i> *
Ionized calcium (mM)	1.15 ± 0.05	1.10 ± 0.051	<0.0001	1.15 ± 0.04	1.25 ± 0.05	<0.0001
Intact PTH (ng/liter)	55.8 ± 19.0	67.2 ± 13.8	<0.0001	55.1 ± 18.9	34.1 ± 11.0	<0.0001
25-OHD (nM)	24.0 ± 7.0	10.7 ± 5.2	<0.0001	24.0 ± 5.7	52.2 ± 9.7	<0.0001
1,25-(OH) <sub>2</sub> D (pM)	169.3 ± 52.0	214.5 ± 42.1	<0.0001	170.8 ± 50.0	141.2 ± 40.6	<0.0001
BGP (ng/ml)	15.5 ± 2.8	18.1 ± 3.5	<0.0001	15.8 ± 3.0	10.5 ± 2.2	<0.0001
Deoxyypyridinoline (μmol/mol creatinine)	10.7 ± 2.9	135 ± 3.4	<0.0001	10.7 ± 2.7	7.1 ± 2.2	<0.0001

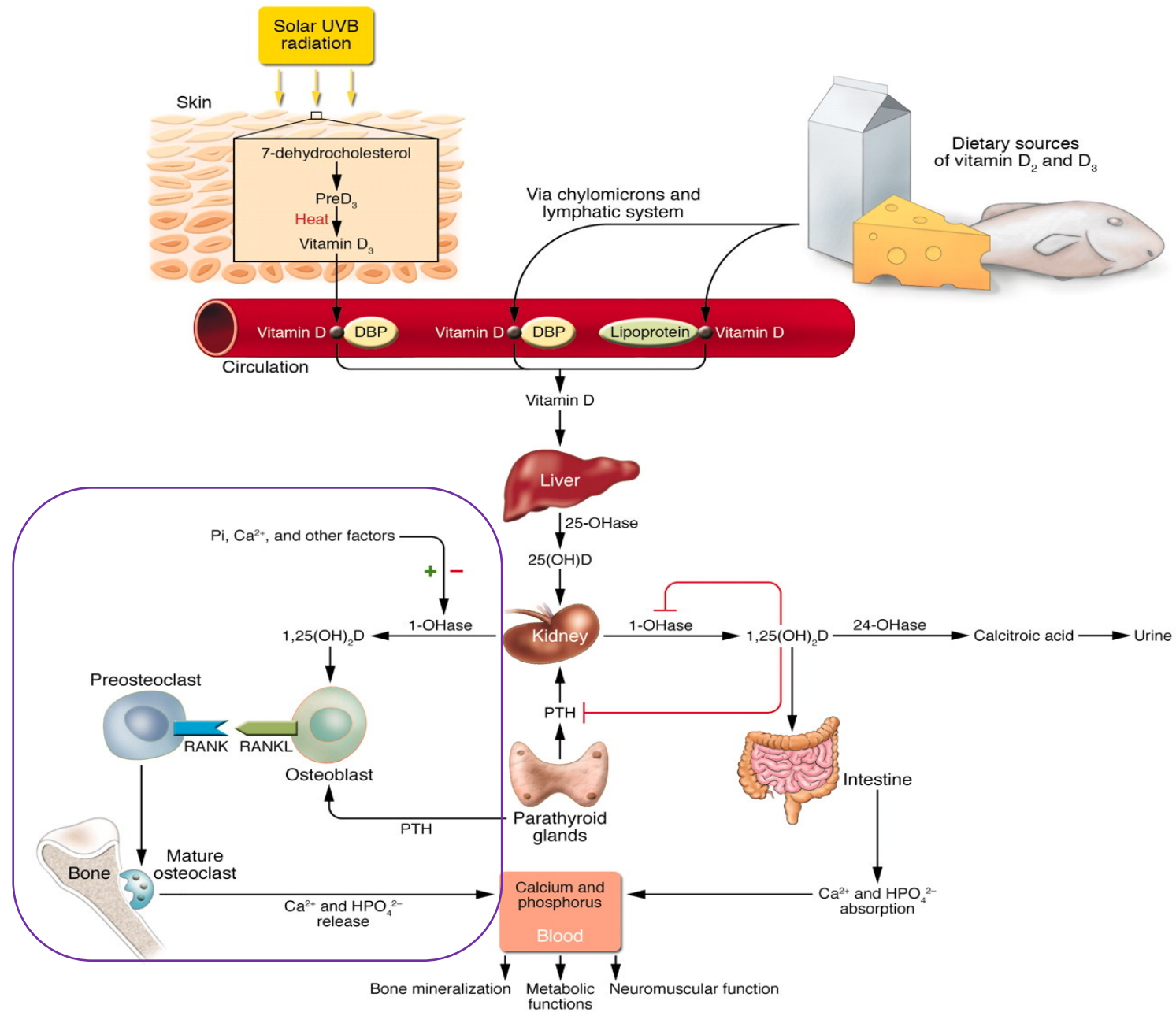
Values are the mean ± SD

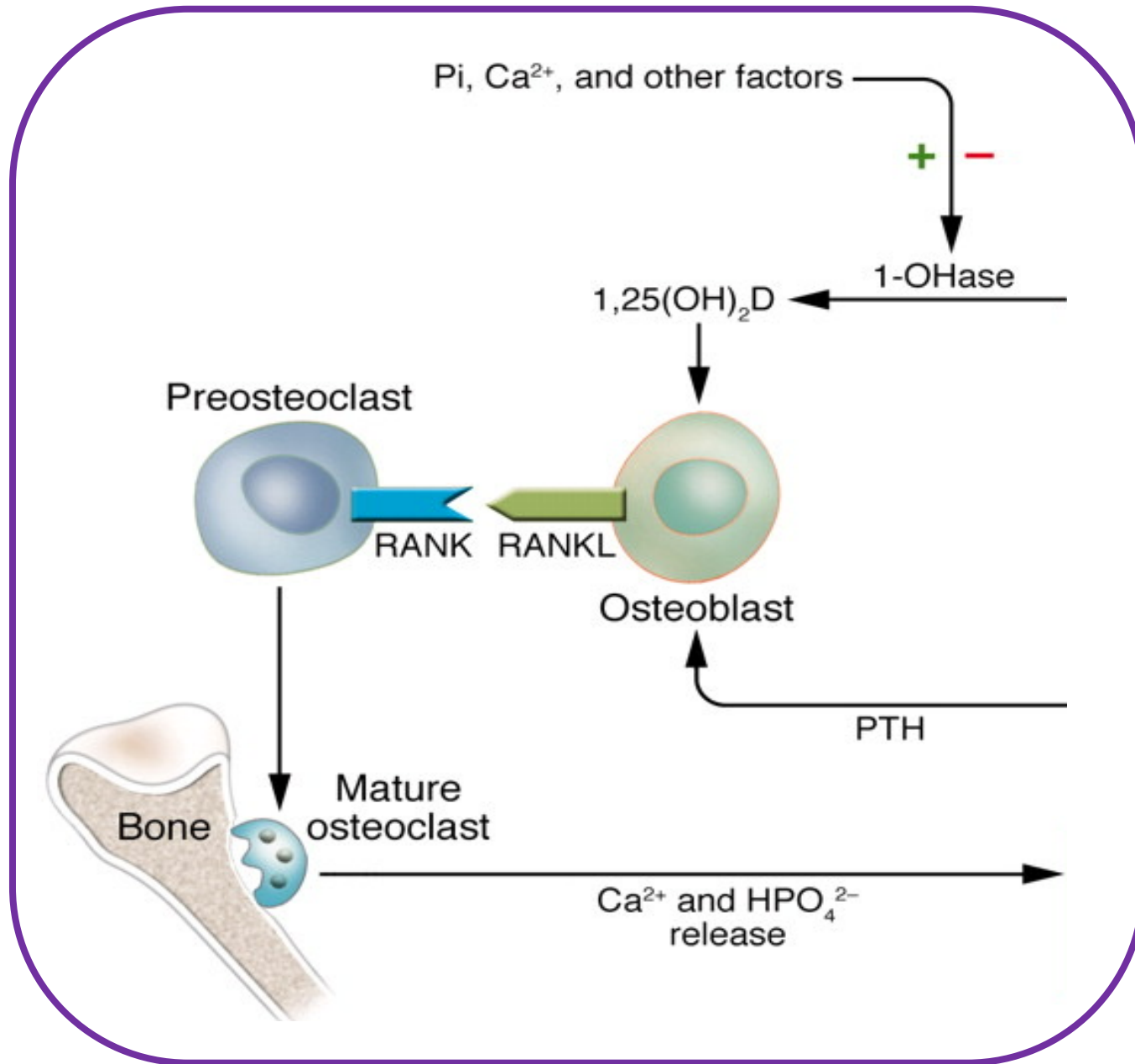
\* Paired *t*-test.



- Amelioration of Osteoporosis and Hypovitaminosis D by Sunlight Exposure in Hospitalized, Elderly Women With Alzheimer's Disease: A Randomized Controlled Trial
  - Mitate Hospital, Tagawa, Japan;







Article

# Vitamin D and Calcium Are Required during Denosumab Treatment in Osteoporosis with Rheumatoid Arthritis

Yukio Nakamura <sup>1,\*</sup>, Takako Suzuki <sup>1</sup>, Tomohiko Yoshida <sup>2</sup>, Hideshi Yamazaki <sup>3</sup> and Hiroyuki Kato <sup>1</sup>

Retrospective

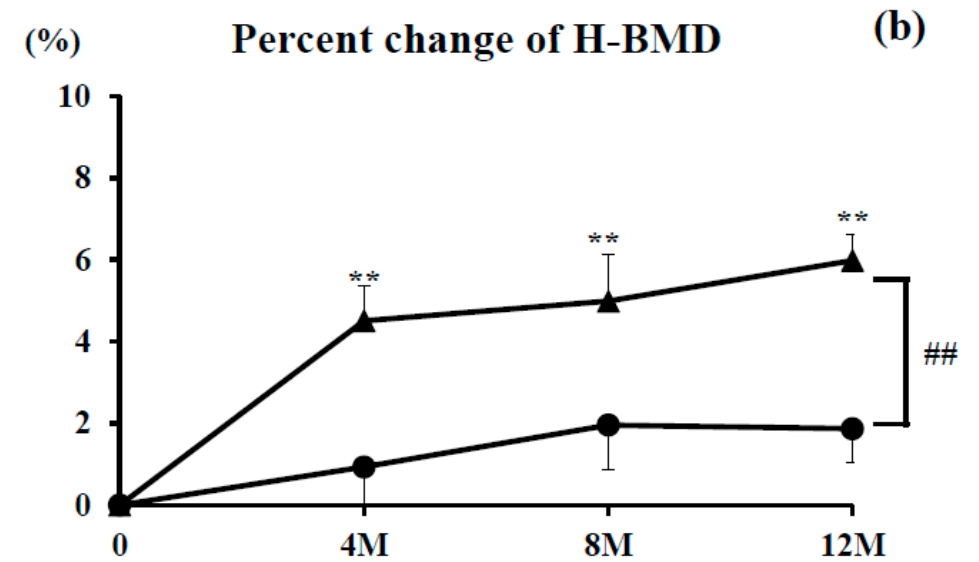
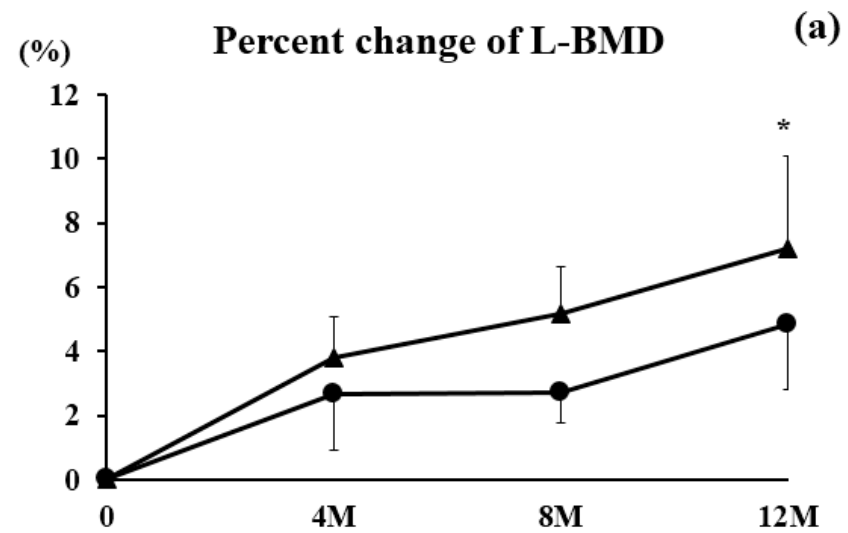
**Table 1.** Patient characteristics at baseline. Data are expressed as mean  $\pm$  standard error.

Characteristic	Denosumab ( <i>n</i> = 22)	Combination ( <i>n</i> = 21)	<i>p</i> -Value
Age (years)	70.9 $\pm$ 1.8	70.6 $\pm$ 2.3	0.9161
Gender (F:M)	22:0	21:00	
BMI (kg/m <sup>2</sup> )	20.8 $\pm$ 0.9	20.0 $\pm$ 0.9	0.5396
Serum corrected Ca (mg/dL)	9.4 $\pm$ 0.1	9.2 $\pm$ 0.1	0.2156
Serum P (mg/dL)	3.7 $\pm$ 0.1	3.5 $\pm$ 0.1	0.2378
Serum BAP ( $\mu$ g/L)	13.4 $\pm$ 0.6	13.8 $\pm$ 1.1	0.7631
Serum TRACP-5b (mU/dL)	302.9 $\pm$ 16.7	312.3 $\pm$ 29.7	0.7873
Urinary NTX (nmol BCE/mmol/CRE)	28.4 $\pm$ 2.5	26.7 $\pm$ 1.8	0.6015
1,25(OH)2D3 (pg/mL)	62.8 $\pm$ 4.9	60.7 $\pm$ 5.7	0.7847
P1NP ( $\mu$ g/L)	37.3 $\pm$ 4.2	36.0 $\pm$ 4.5	0.8239
Serum whole PTH (pg/dL)	29.7 $\pm$ 2.9	30.1 $\pm$ 4.2	0.9429
BP use, <i>n</i> (%)	22 (100)	21 (100)	
Period of BP use	5.8 $\pm$ 1.0	5.5 $\pm$ 1.0	0.8476
L-BMD (g/cm <sup>2</sup> )	0.71 $\pm$ 0.04	0.68 $\pm$ 0.02	0.4197
H-BMD (g/cm <sup>2</sup> )	0.487 $\pm$ 0.03	0.502 $\pm$ 0.02	0.6971
MTX, <i>n</i> (mg/week)	12 (6.7 $\pm$ 0.75)	10 (6.6 $\pm$ 0.85)	0.9536
PSL, <i>n</i> (mg/day)	2 (4.5 $\pm$ 0.5)	1 (5.0 $\pm$ 0.0)	
MMP-3	92.2 $\pm$ 22.2	94.3 $\pm$ 15.5	0.9392
Disease duration (years)	16.6 $\pm$ 2.9	18.5 $\pm$ 3.2	0.6815
DAS28-CRP	3.1 $\pm$ 0.3	3.0 $\pm$ 0.3	0.9090
SDAI	4.3 $\pm$ 1.0	4.7 $\pm$ 1.0	0.7987
HAQ-DI	0.44 $\pm$ 0.2	0.39 $\pm$ 0.2	0.8215

Each patient received denosumab (60 mg, s.c.) once every 6 months in both groups. In the combination group, we gave newly approved vitamin D supplementation tablets (762.5 mg of precipitated calcium carbonate, 200 IU of cholecalciferol, 59.2 mg of magnesium carbonate) twice daily to all patients after denosumab administration.



- ▲ Combinada
- Solo Denosumab



From Medscape Medical News

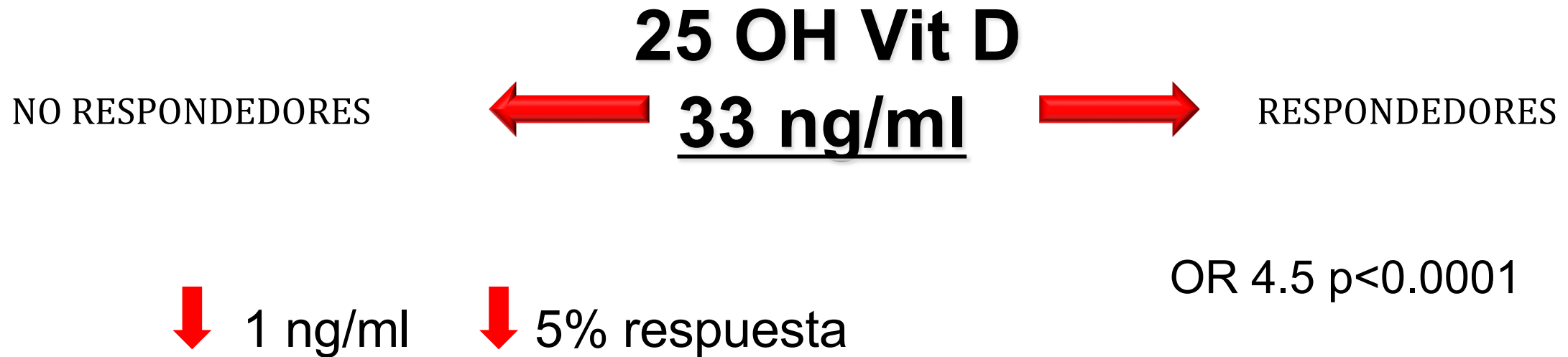
## Bisphosphonates Most Effective With Higher Vitamin D Levels

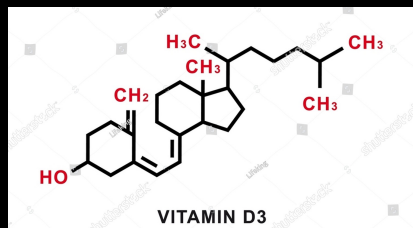
Nancy A. Melville

n= 210

Bisfosfonato por 5 años

AL: 50%; 25% RESD; 18% AZ





Entra fácilmente a las células (difusión pasiva)  
Se une a receptores intracelulares (VDR)  
Modula expresión génica

- Se almacena en **tejido adiposo y músculo**
- Permite una **reserva a largo plazo**

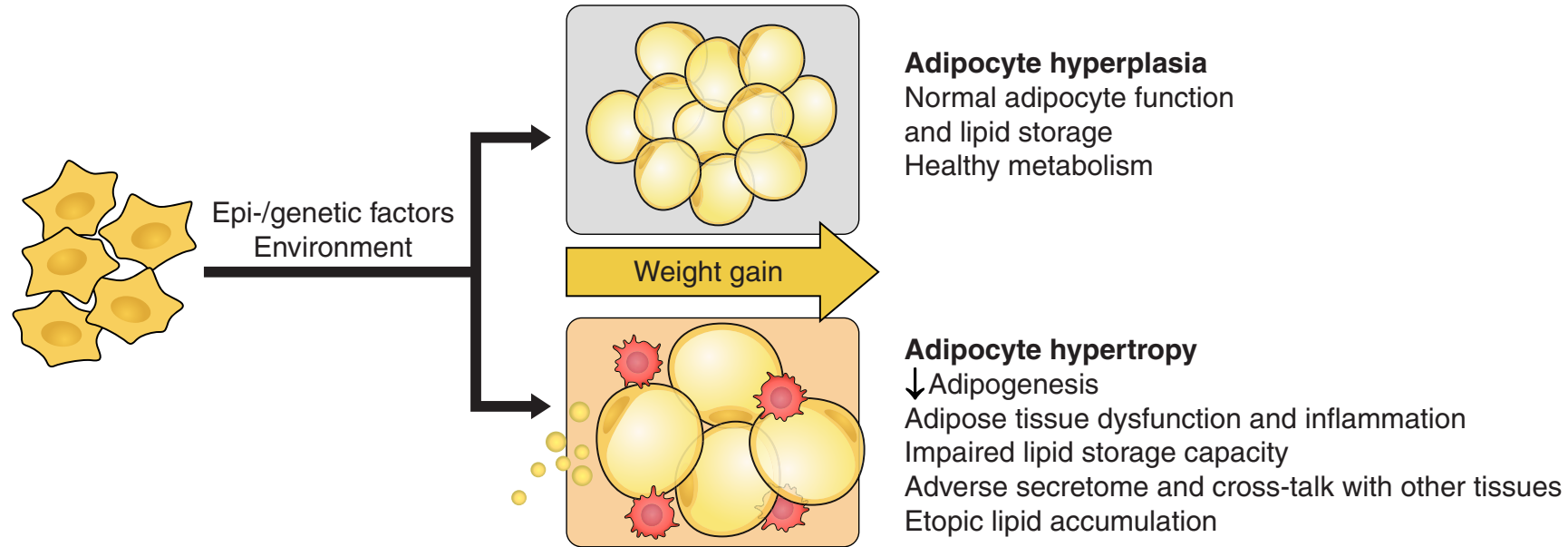
Esto es clave porque:

- La síntesis cutánea depende del sol (variable)
- La dieta suele ser insuficiente

Funciona como un “**buffer fisiológico**” para evitar deficiencia en periodos sin exposición solar.

• Por qué una vitamina que ayuda al hueso es liposoluble?

## Adipogénésis



**Adipocyte hyperplasia**  
Normal adipocyte function  
and lipid storage  
Healthy metabolism

**Adipocyte hypertrophy**  
↓ Adipogenesis  
Adipose tissue dysfunction and inflammation  
Impaired lipid storage capacity  
Adverse secretome and cross-talk with other tissues  
Etopic lipid accumulation

Sin R.I



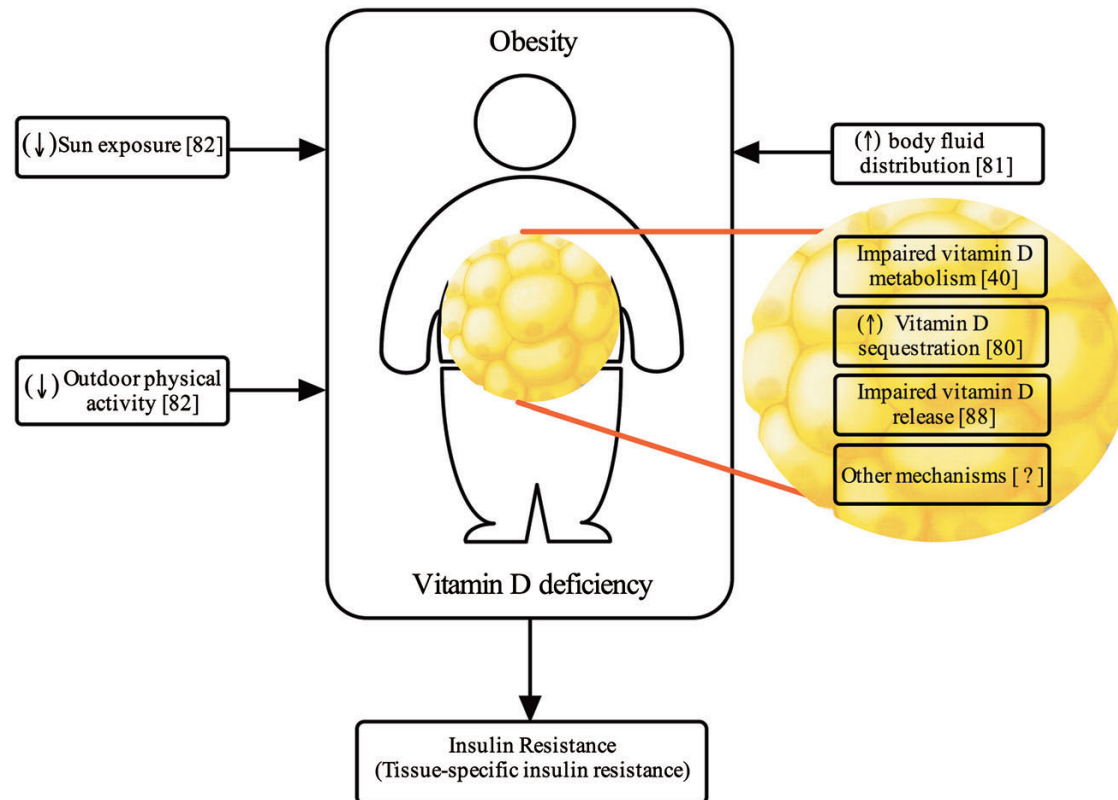
Con R.I



## Lipogénésis

## Vitamin D deficiency in the aetiology of obesity-related insulin resistance

Adriyan Pramono<sup>1,2</sup> | Johan W.E. Jocken<sup>1</sup> | Ellen E. Blaak<sup>1</sup>



VDR visceral > VDR s.c.



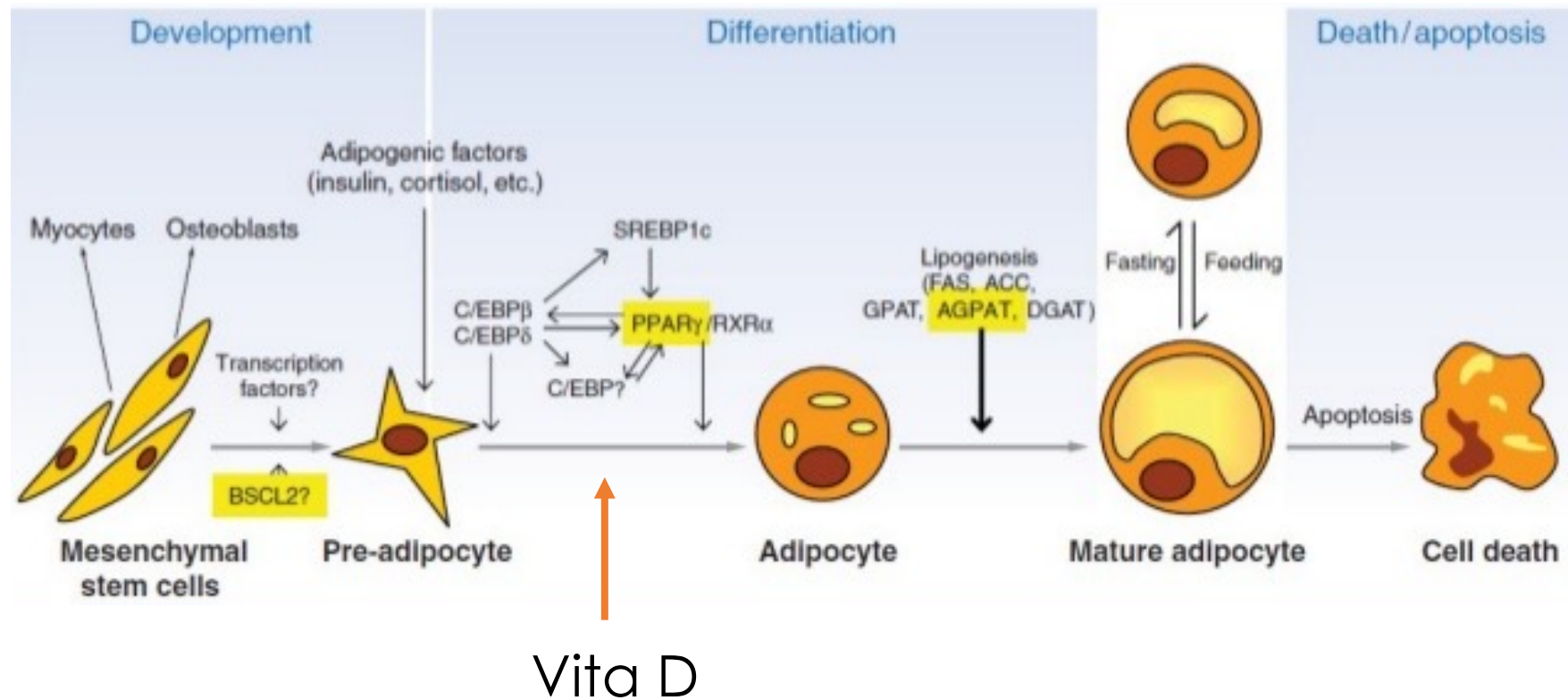
Review

Physiological functions of Vitamin D in adipose tissue

Manal A. Abbas



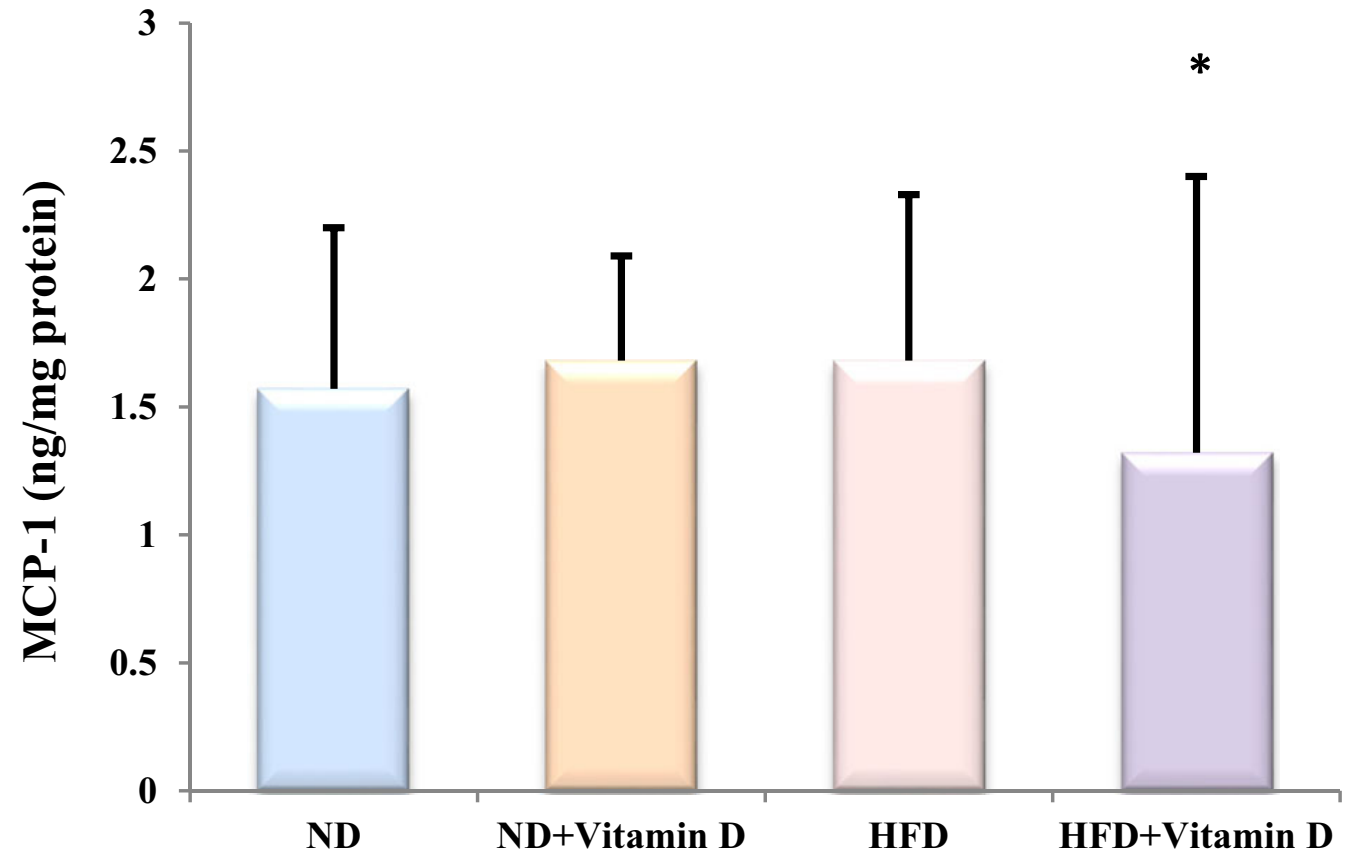
## Efecto de la Vitamina D en la Adipogenesis



## Adipose Tissue Inflammation and Oxidative Stress: the Ameliorative Effects of Vitamin D


Mahdieh Abbasalizad Farhangi,<sup>1,5</sup> Mehran Mesgari-Abbasi,<sup>1</sup> Ghazaleh Hajiluan,<sup>2</sup>  
Ghazaleh Nameni,<sup>3</sup> and Parviz Shahabi<sup>4</sup>

Monocyte Chemoattractant Protein (MCP)-1

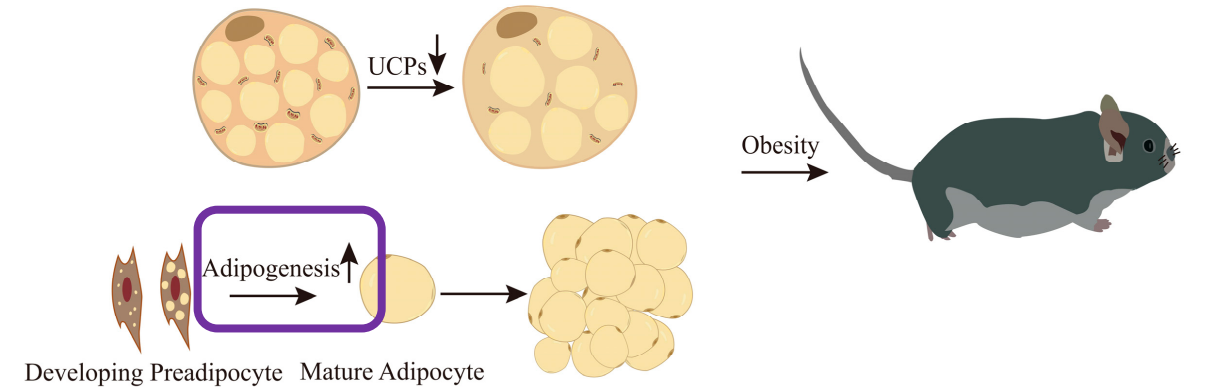


Review

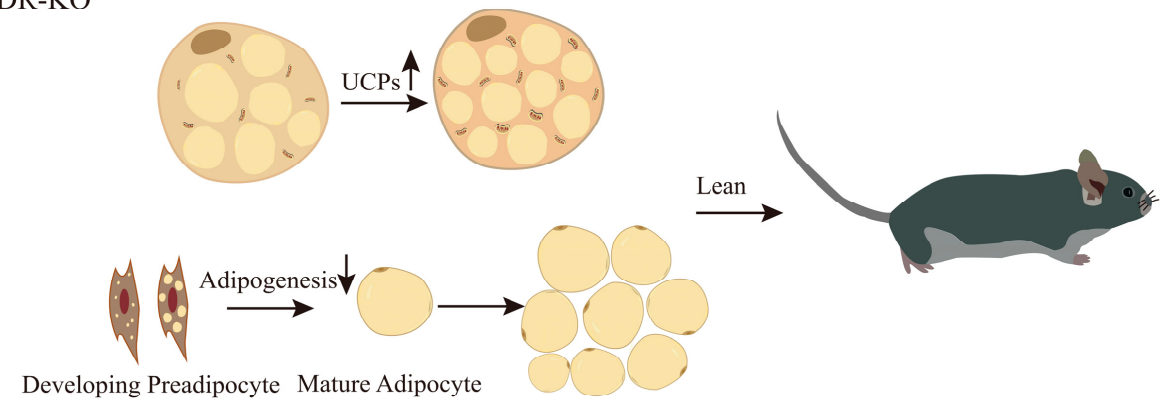
## Interplay between Vitamin D and Adipose Tissue: Implications for Adipogenesis and Adipose Tissue Function

Shiqi Lu and Zhen-Bo Cao \* 

VDR-Tg



VDR-KO



Article

**Vitamin D Insufficiency Exacerbates Adipose Tissue Macrophage Infiltration and Decreases AMPK/SIRT1 Activity in Obese Rats**

Eugene Chang and Yangha Kim \*

Mecanismos de protección celular de baja energía celular, para guardar exceso energía para futuras ocasiones



Mecanismos de protección celular de baja energía celular, para guardar exceso energía para futuras ocasiones

**mTOR**



a.a. Ramificados  
(leucina)

**ChREBP** **GOAT**



Glucosa



Ácidos Grasos  
Cadena media

**AMPK** **Sirtuínas**



Energía



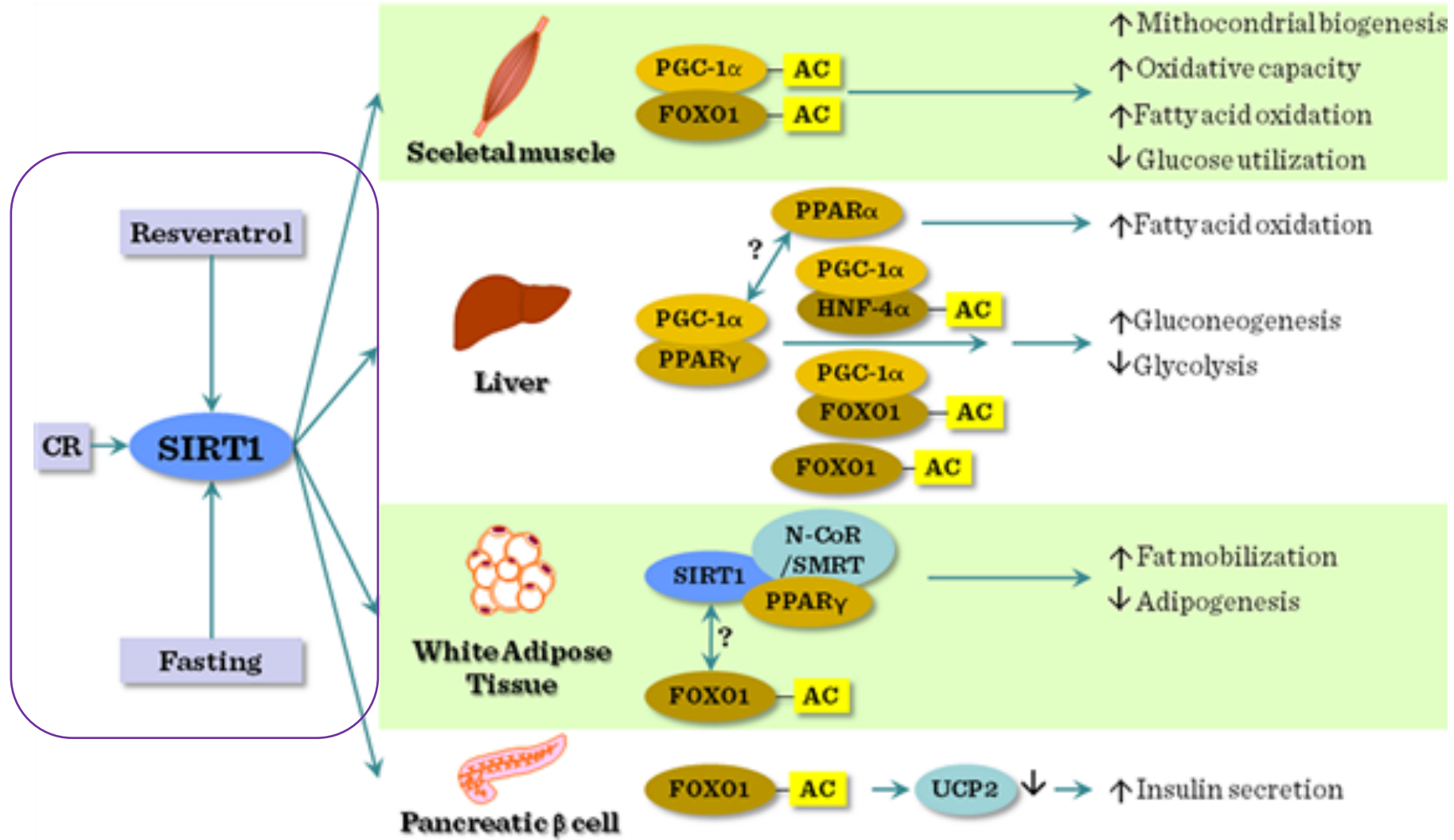
NAD<sup>+</sup>/NADH

Article

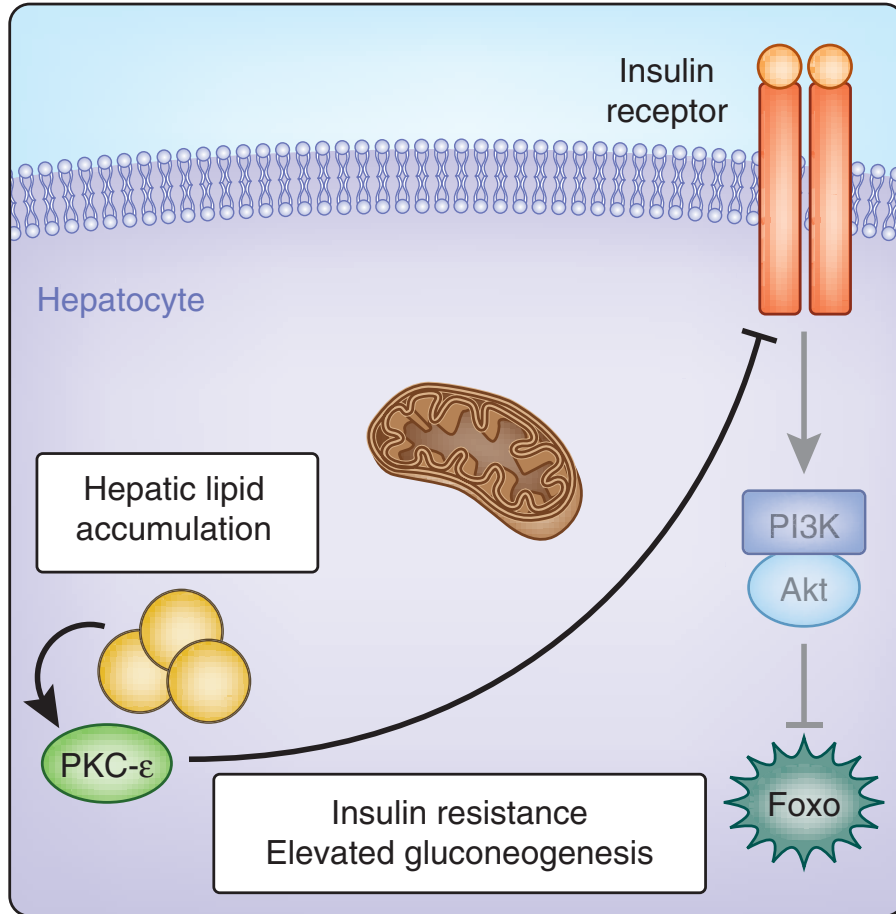
**Vitamin D Insufficiency Exacerbates Adipose Tissue Macrophage Infiltration and Decreases AMPK/SIRT1 Activity in Obese Rats**

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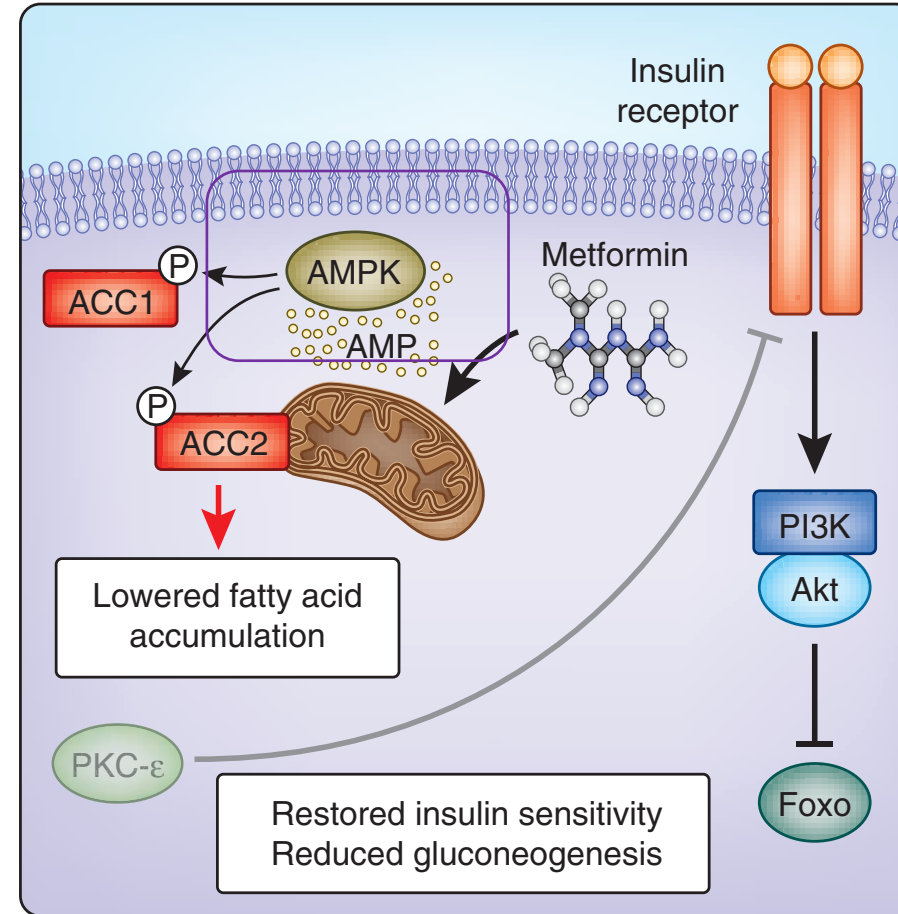
# Sirtuinas



### High-fat diet/obesity insulin resistance

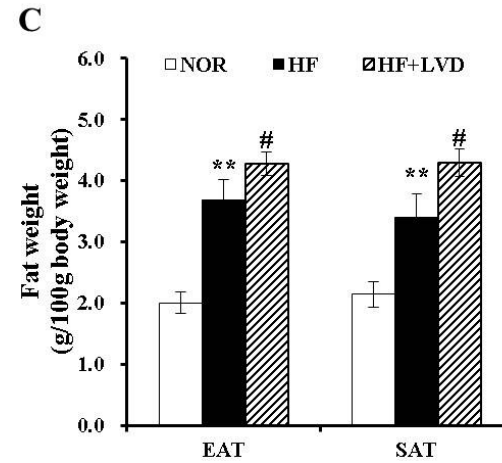
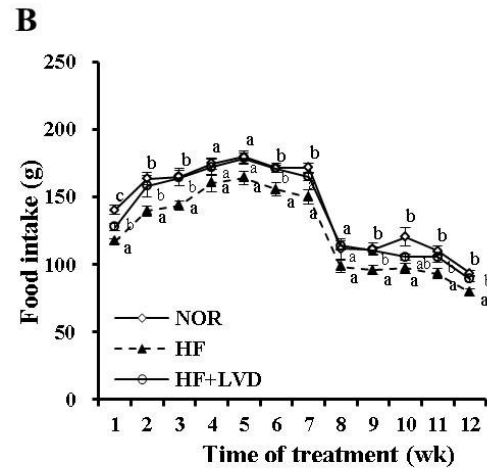
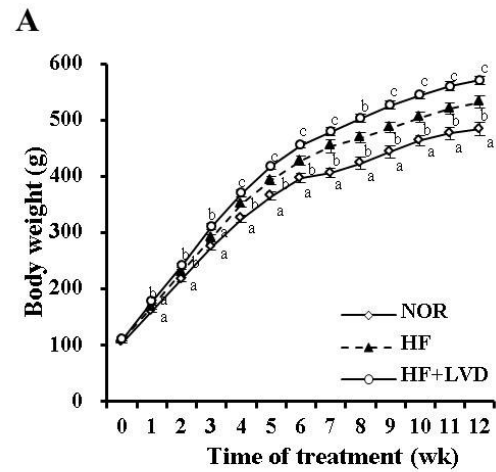


### Metformin-treated

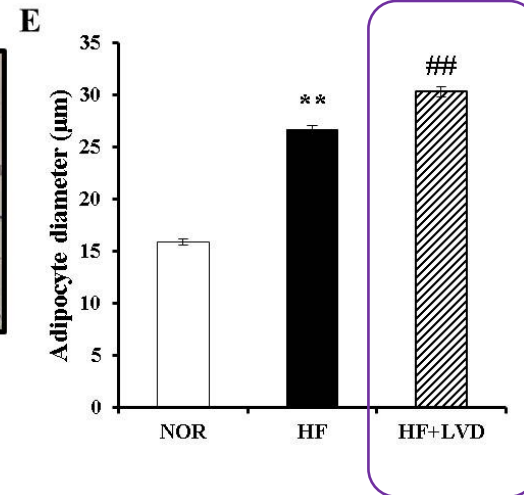
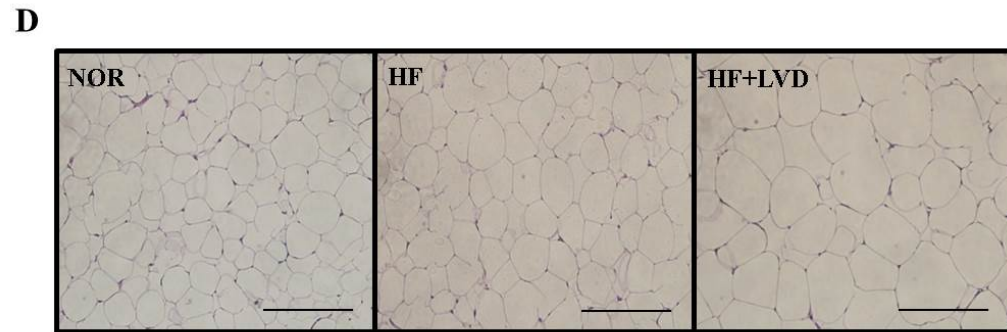


Article  
**Vitamin D Insufficiency Exacerbates Adipose Tissue Macrophage Infiltration and Decreases AMPK/SIRT1 Activity in Obese Rats**

Eugene Chang and Yangha Kim \*



1000 UI/Kg



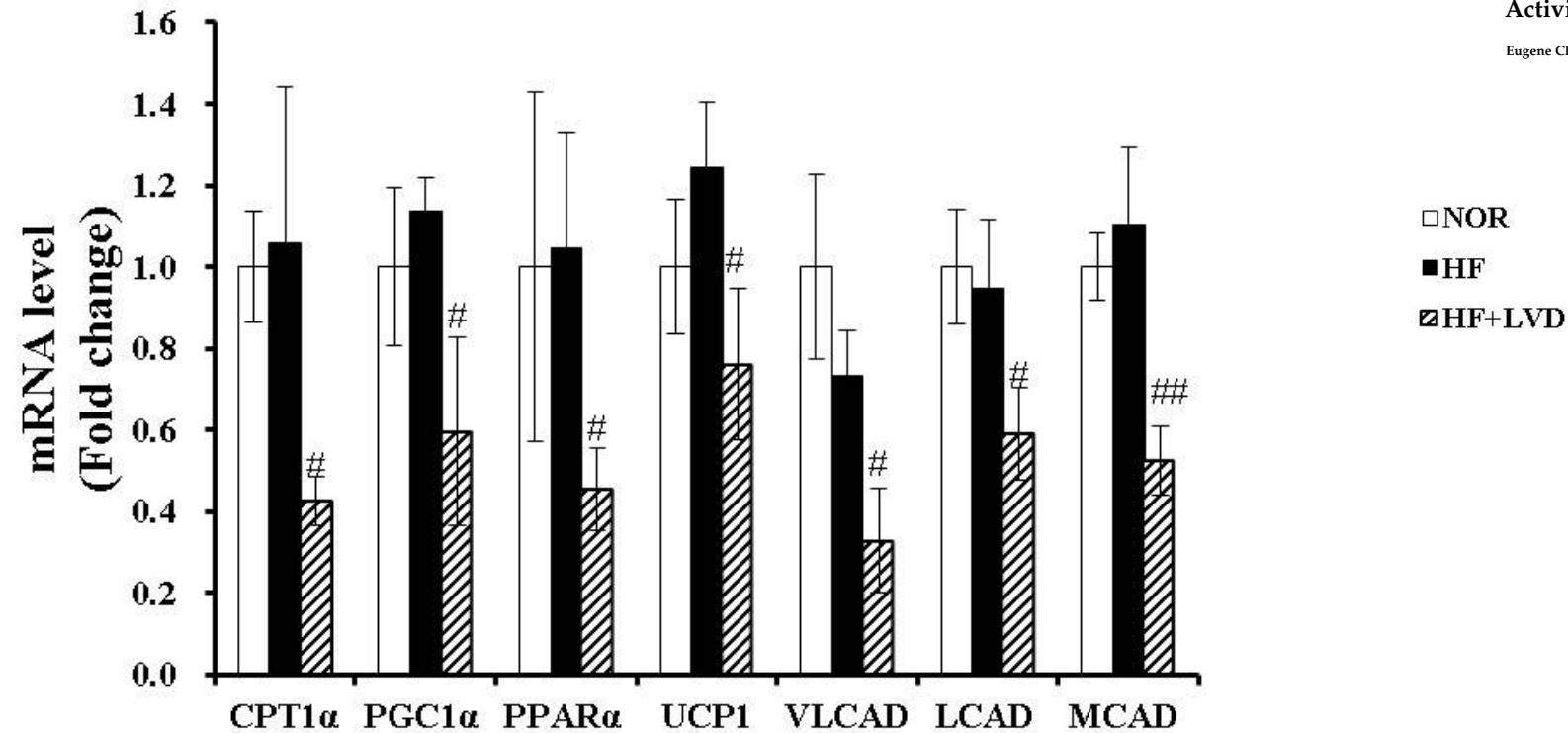
#*p*<0.05;##*p*<0.01 compared to HF

Article

## Vitamin D Insufficiency Exacerbates Adipose Tissue Macrophage Infiltration and Decreases AMPK/SIRT1 Activity in Obese Rats

Eugene Chang and Yangha Kim \*

### B. Fatty acid oxidation



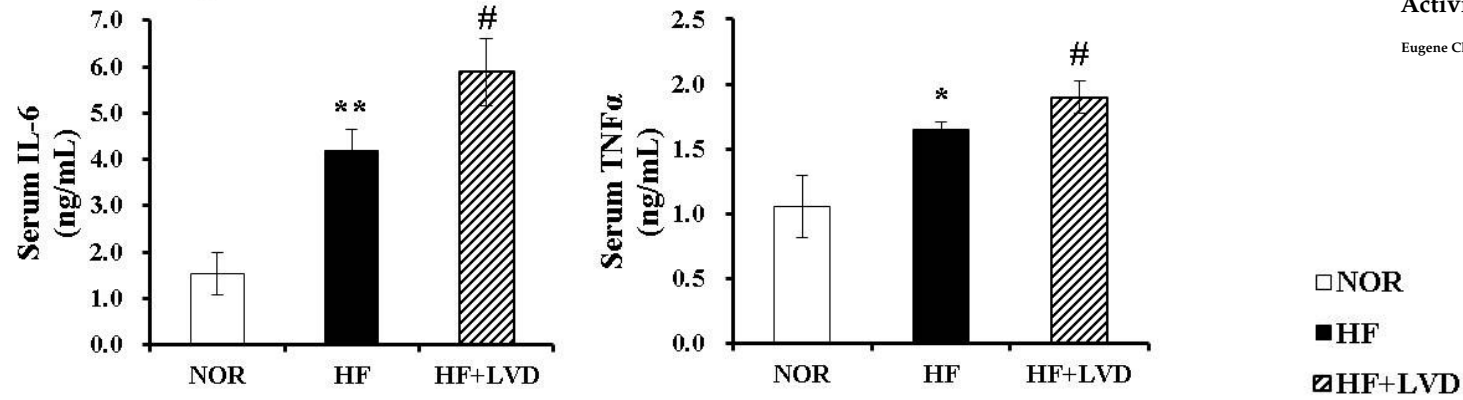
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Article

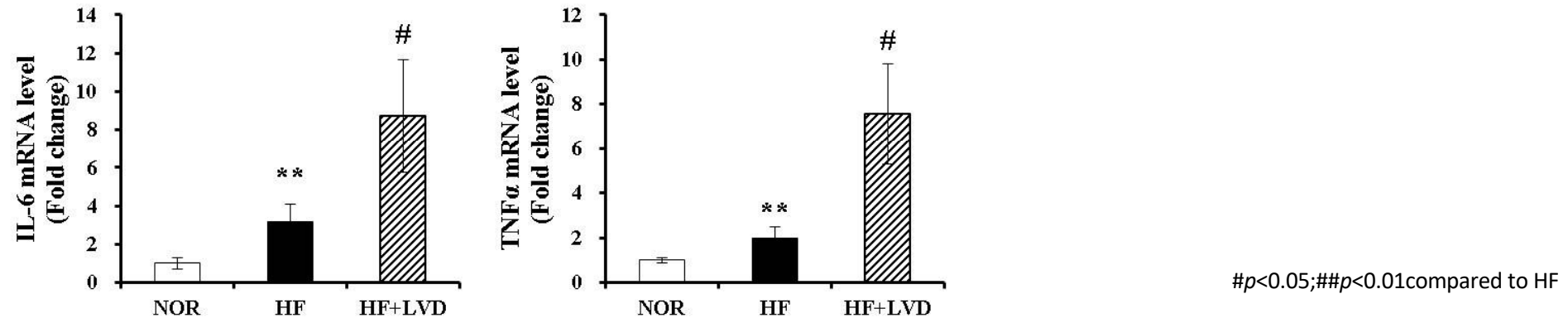
## Vitamin D Insufficiency Exacerbates Adipose Tissue Macrophage Infiltration and Decreases AMPK/SIRT1 Activity in Obese Rats

Eugene Chang and Yangha Kim \*

### A. Serum cytokine levels



### B. AT proinflammatory gene expression



## Crown-Like Structure (CLS) Quantification monoclonal anti-mouse F4/80 antibody

□ NOR  
■ HF  
▨ HF+LVD

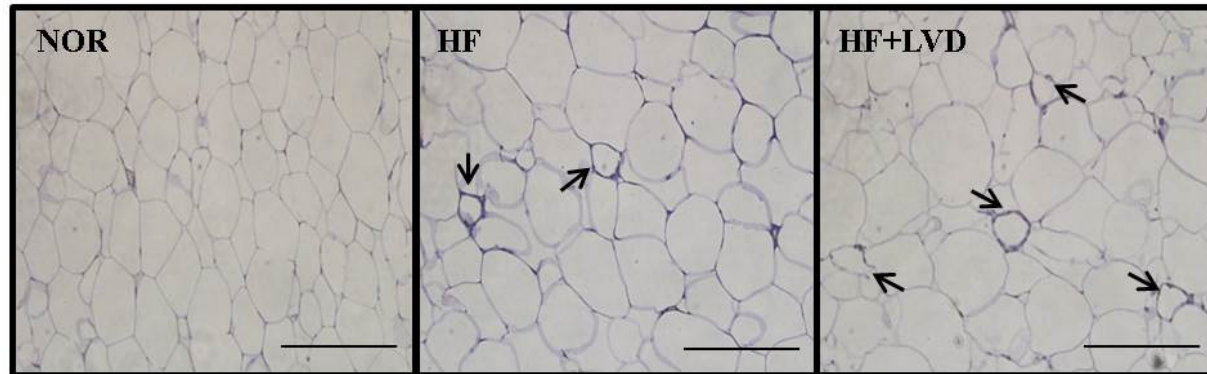


Article

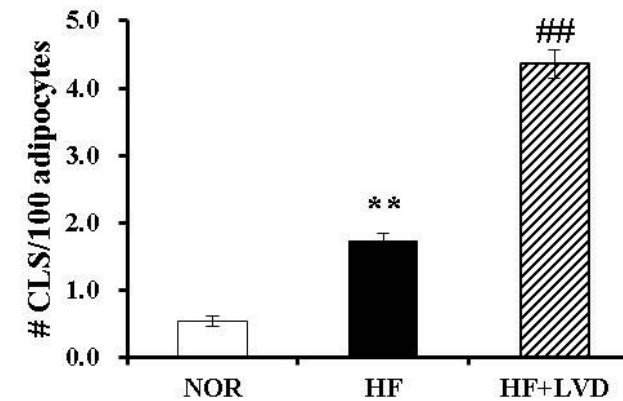
### Vitamin D Insufficiency Exacerbates Adipose Tissue Macrophage Infiltration and Decreases AMPK/SIRT1 Activity in Obese Rats

Eugene Chang and Yangha Kim \*

A



B



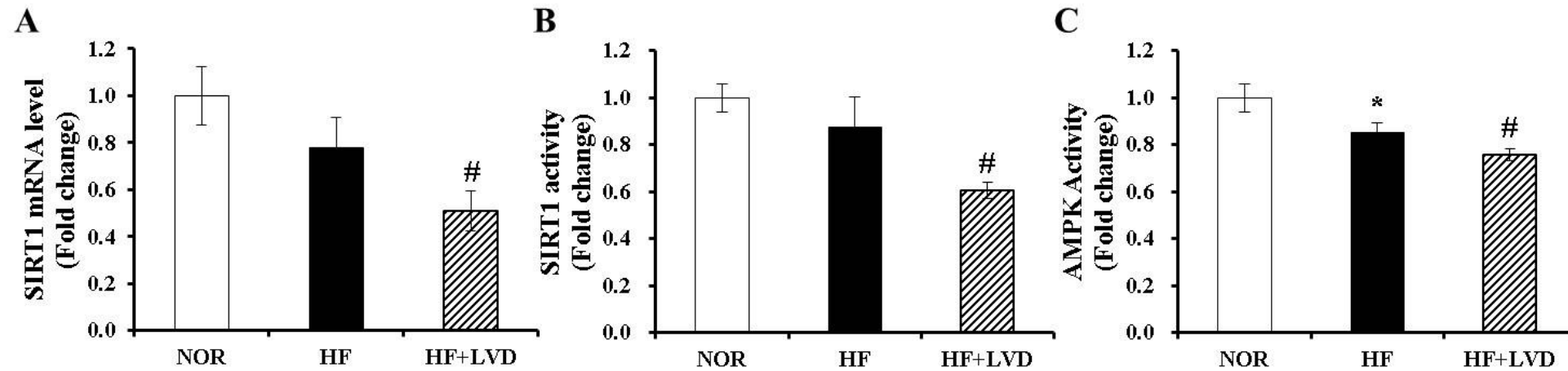
# $p < 0.05$ ; ## $p < 0.01$  compared to HF

Article

**Vitamin D Insufficiency Exacerbates Adipose Tissue Macrophage Infiltration and Decreases AMPK/SIRT1 Activity in Obese Rats**

Eugene Chang and Yangha Kim \*

□ NOR  
■ HF  
▨ HF+LVD

# $p < 0.05$ ; ## $p < 0.01$  compared to HF

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

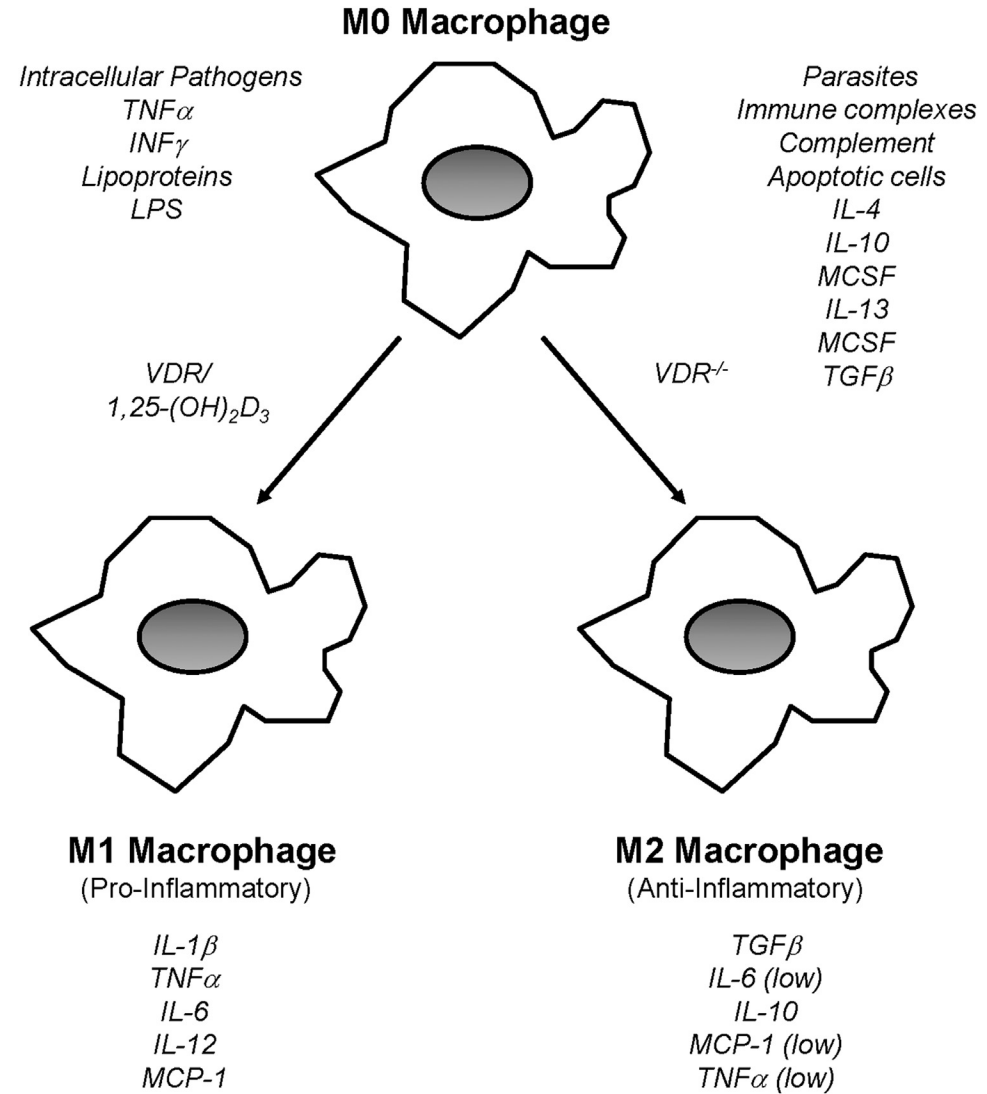
ScienceDirect

journal homepage: [www.elsevier.com/locate/NTR](http://www.elsevier.com/locate/NTR)

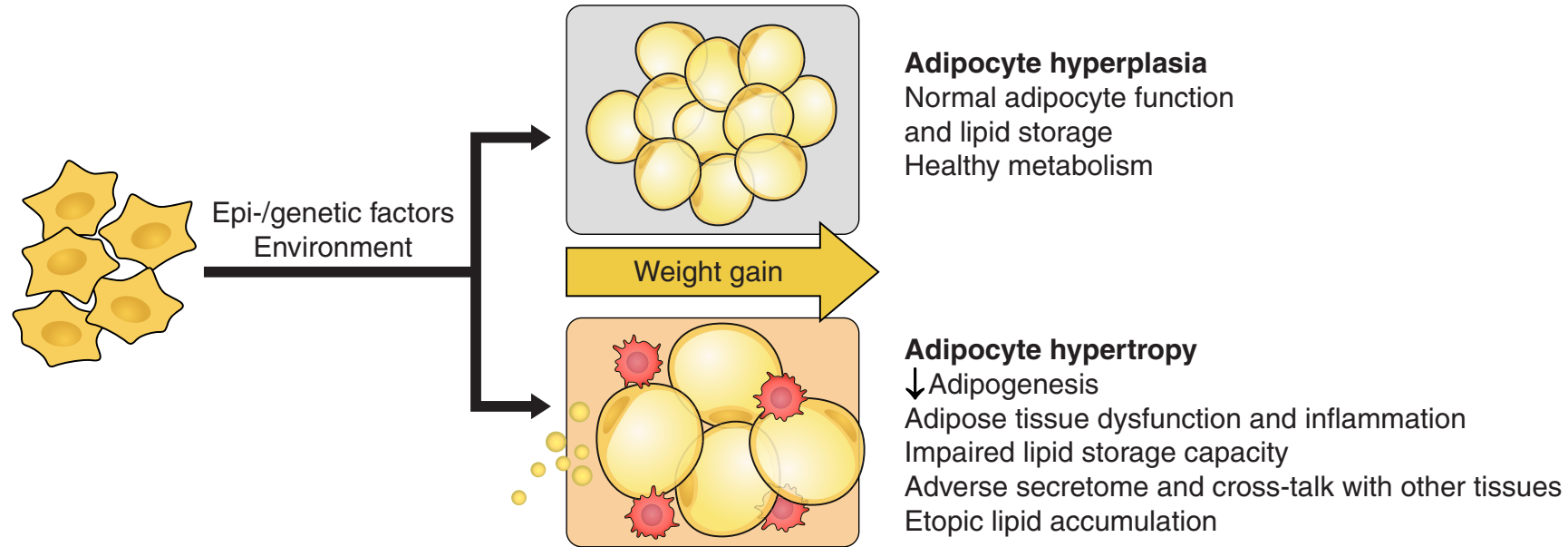
Review

## Vitamin D, immune function, and atherosclerosis. Where are we now?

Ailyn Rivero, Kent R. Wehmeier, Michael J. Haas\*, Arshag D. Mooradian



## Adipogénésis



**Adipocyte hyperplasia**  
Normal adipocyte function  
and lipid storage  
Healthy metabolism

**Adipocyte hypertrophy**  
↓ Adipogenesis  
Adipose tissue dysfunction and inflammation  
Impaired lipid storage capacity  
Adverse secretome and cross-talk with other tissues  
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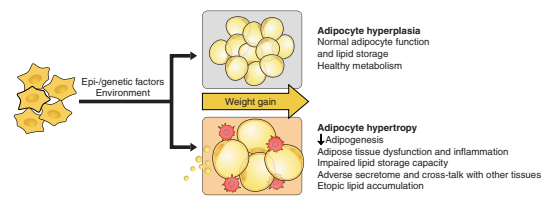
Sin R.I



Con R.I

## Lipogénésis

# Adipogénesis



# Lipogénesis

Sin R.I

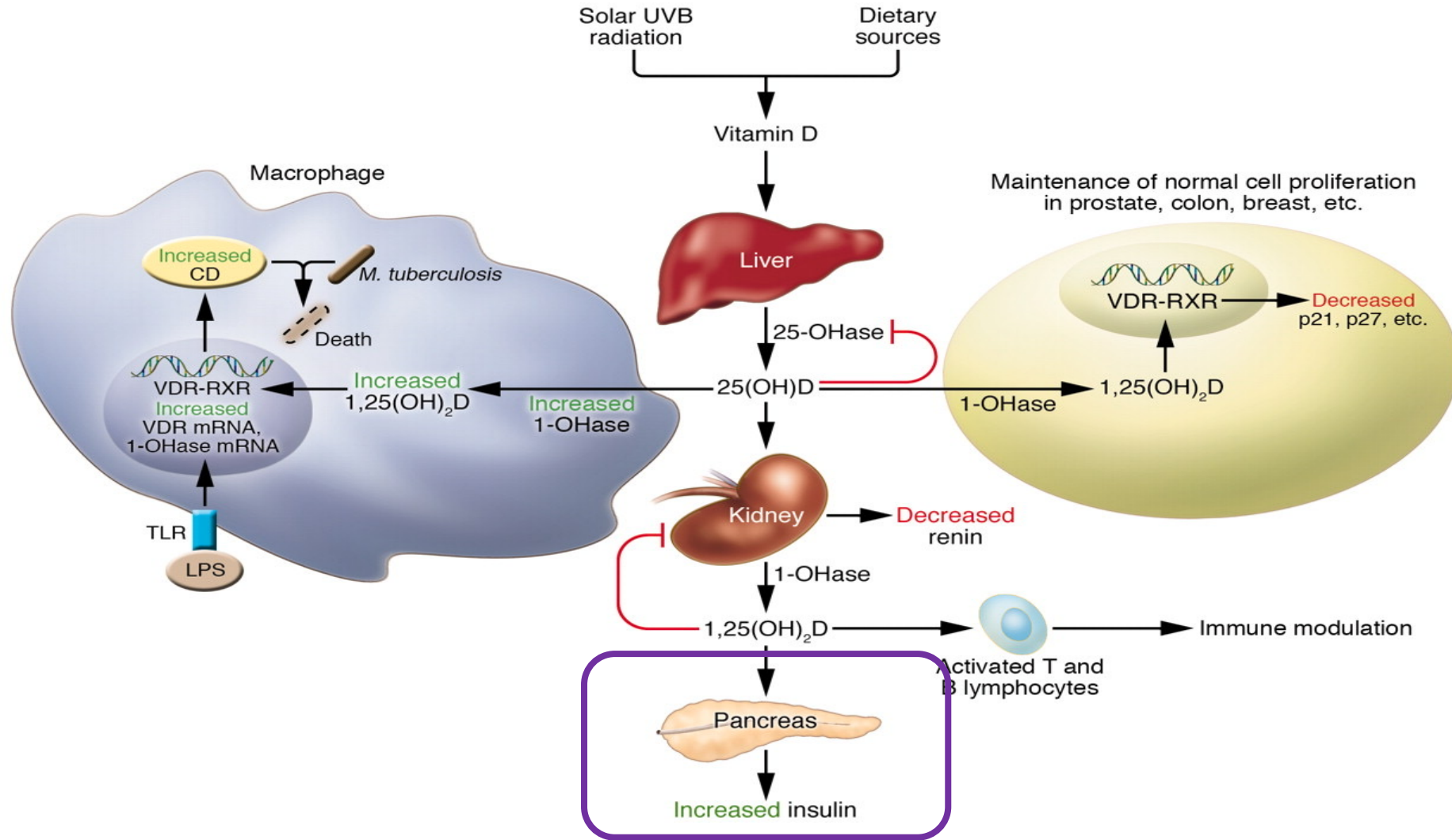


Vit D

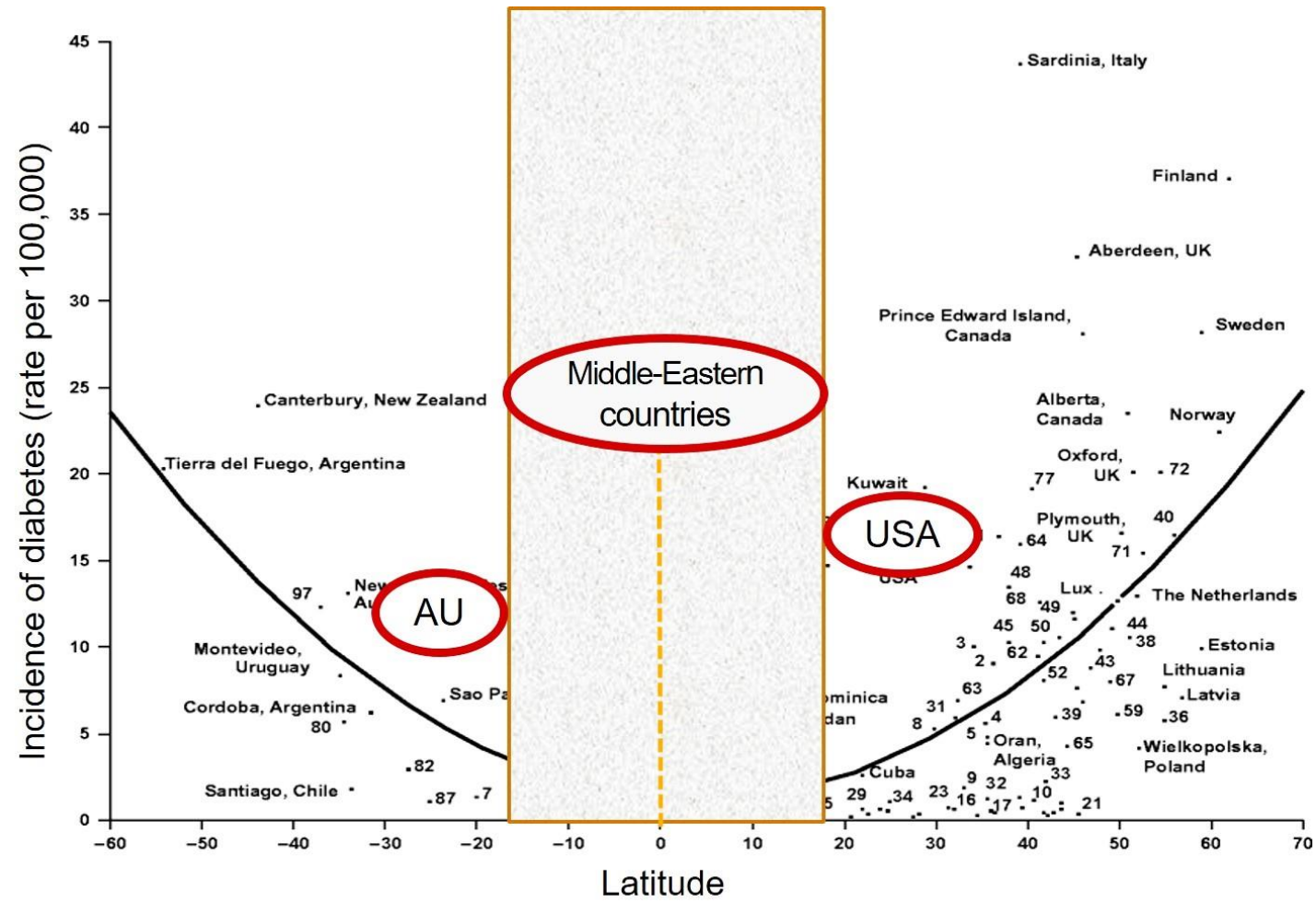
Con R.I



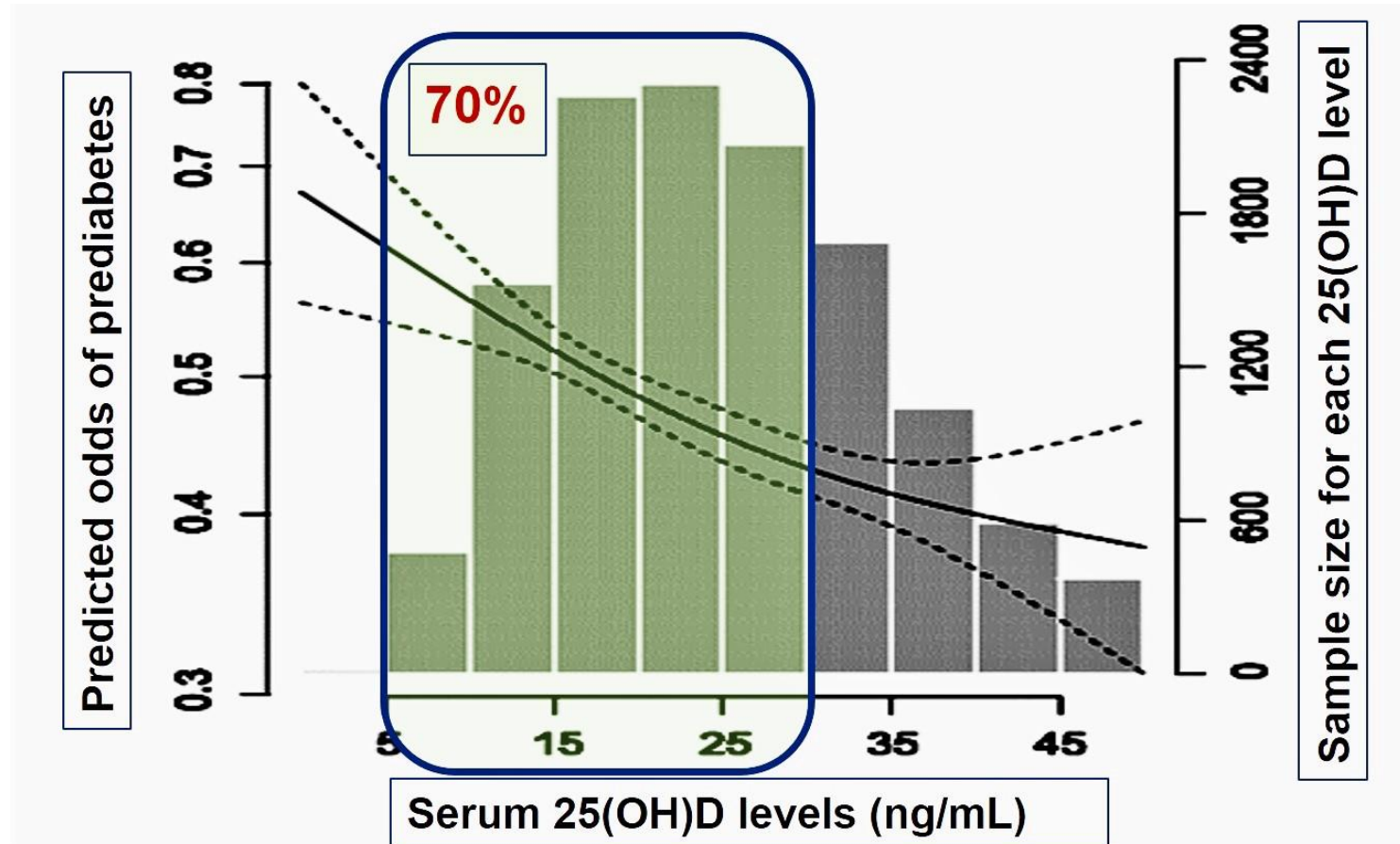
Vit D



# Incidencia de Diabetes tipo 2



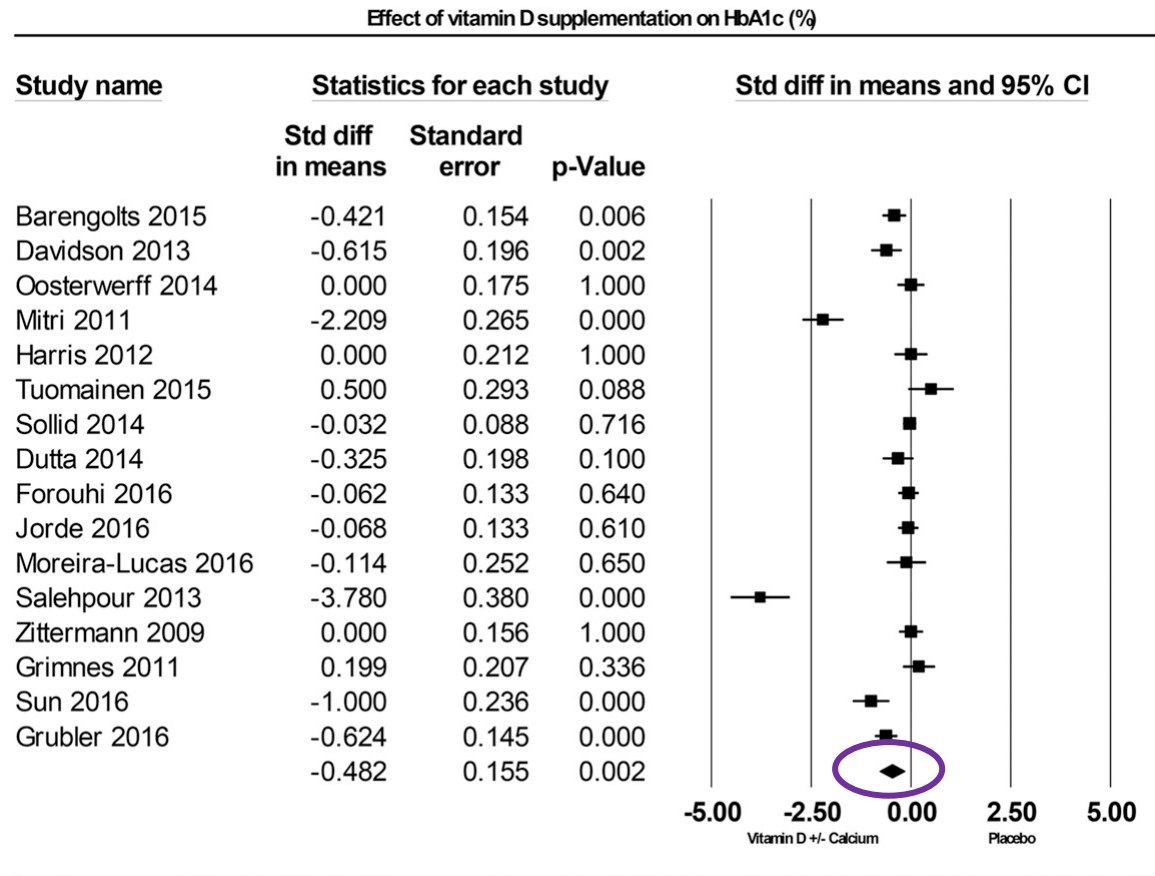
Las personas sanas con niveles bajos de 25(OH)D en suero presentan una mayor prevalencia de prediabetes.



## Vitamin D Supplementation, Glycemic Control, and Insulin Resistance in Prediabetics: A Meta-Analysis

Naghmeh Mirhosseini,<sup>1</sup> Hassanali Vatanparast,<sup>2</sup> Mohsen Mazidi,<sup>3,4</sup>  
and Samantha M. Kimball<sup>1,5</sup>

# HbA1c



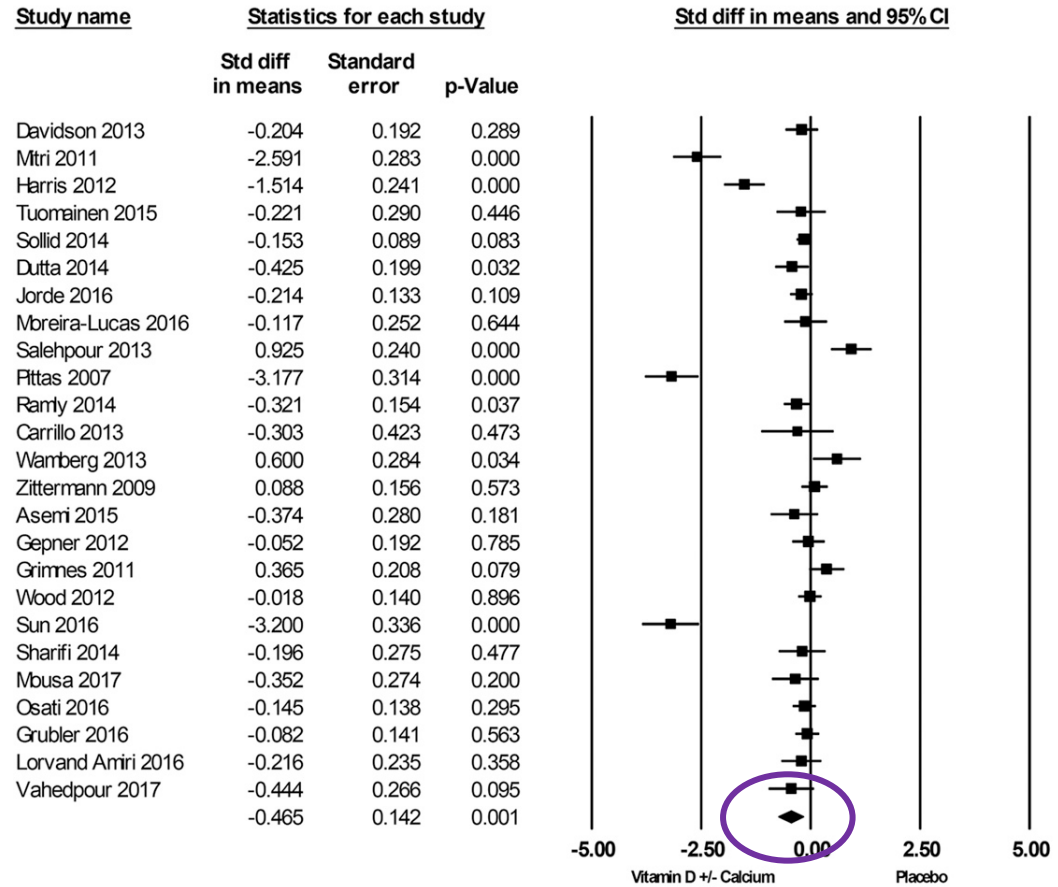
Meta Analysis

**Figure 3.** Forest plot of mean change from baseline in HbA1c (%) between vitamin D supplementation and control.

## Vitamin D Supplementation, Glycemic Control, and Insulin Resistance in Prediabetics: A Meta-Analysis

Naghmeh Mirhosseini,<sup>1</sup> Hassanali Vatanparast,<sup>2</sup> Mohsen Mazidi,<sup>3,4</sup>  
and Samantha M. Kimball<sup>1,5</sup>

# Glucosa ayunas



Meta Analysis

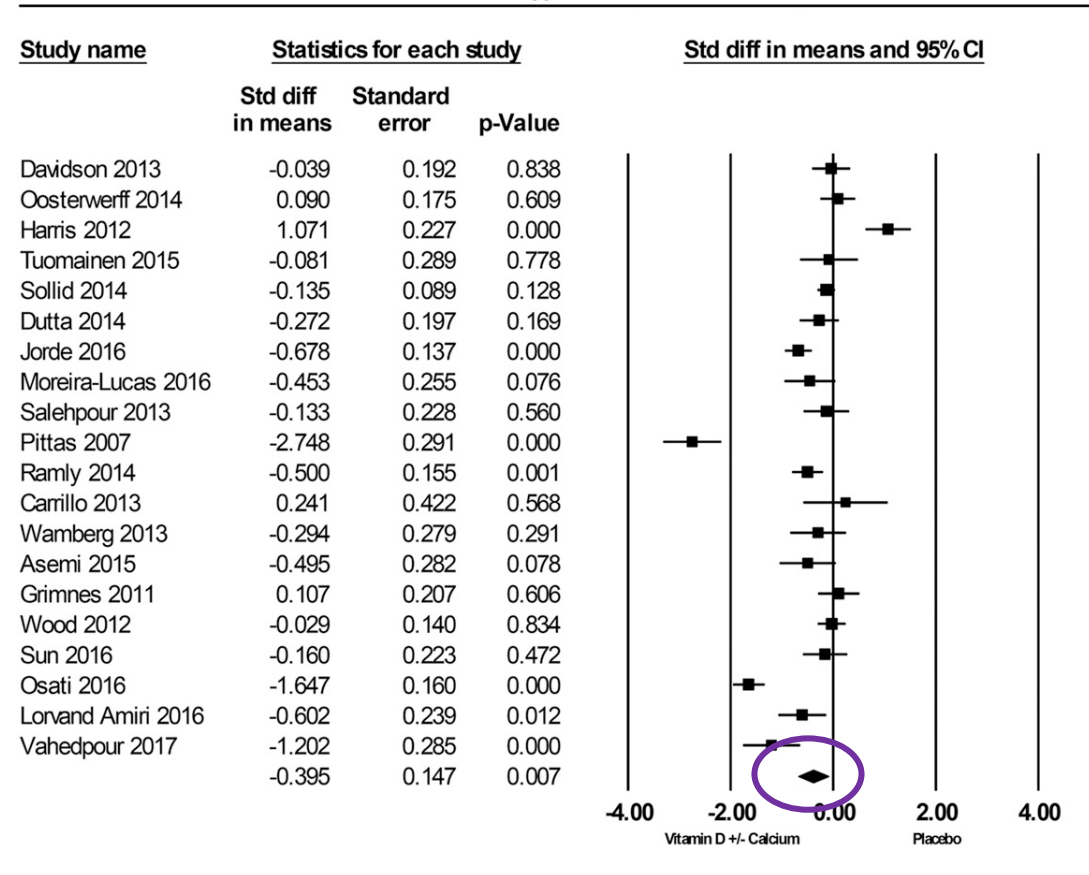
**Figure 4.** Forest plot of mean change from baseline in FPG (mmol/L) between vitamin D supplementation and control.

## Vitamin D Supplementation, Glycemic Control, and Insulin Resistance in Prediabetics: A Meta-Analysis

Naghmeh Mirhosseini,<sup>1</sup> Hassanali Vatanparast,<sup>2</sup> Mohsen Mazidi,<sup>3,4</sup>  
and Samantha M. Kimball<sup>1,5</sup>

# HOMA-IR

Effect of vitamin D supplementation on HOMA-IR



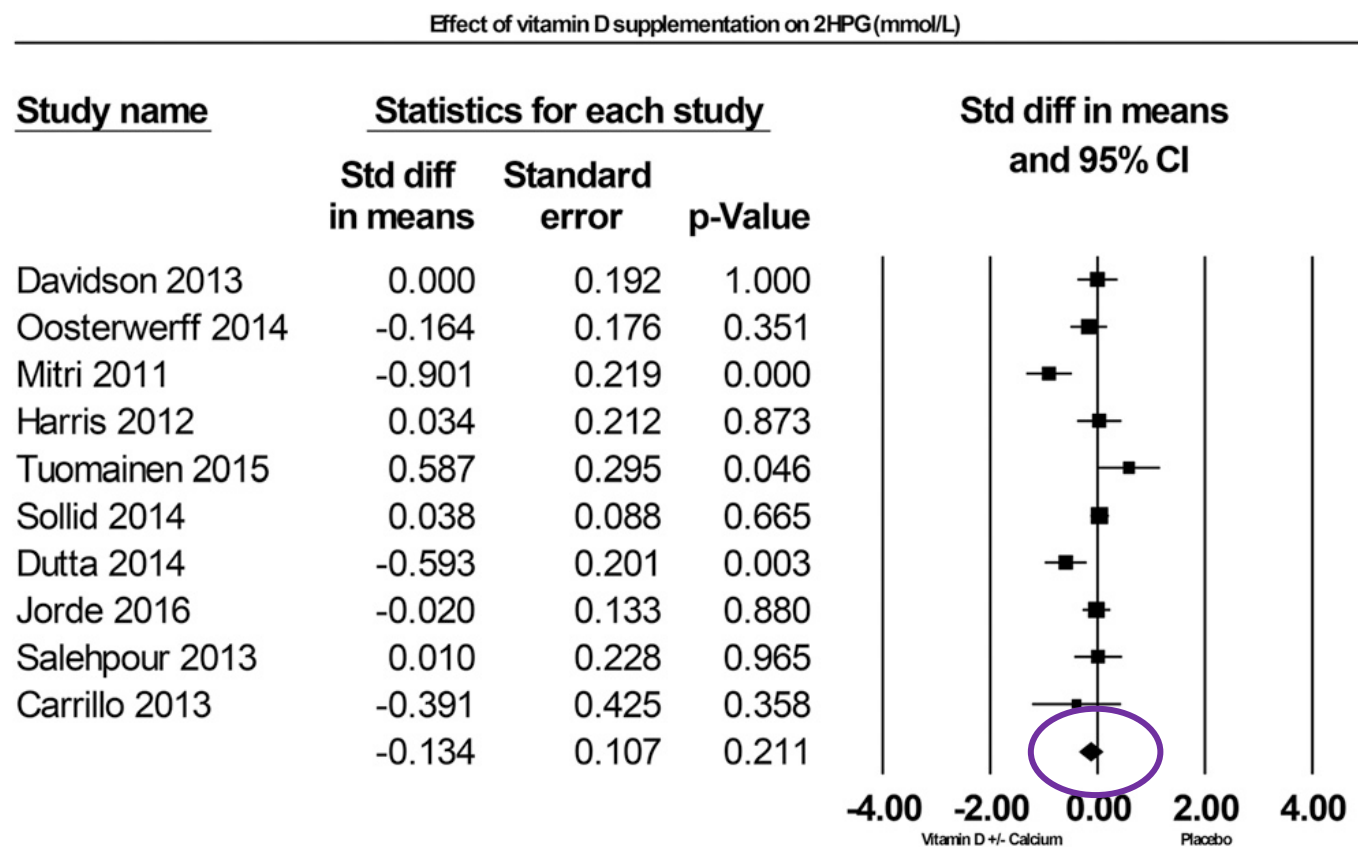
Meta Analysis

**Figure 5.** Forest plot of mean change from baseline in HOMA-IR between vitamin D supplementation and control.

## Vitamin D Supplementation, Glycemic Control, and Insulin Resistance in Prediabetics: A Meta-Analysis

Naghmeh Mirhosseini,<sup>1</sup> Hassanali Vatanparast,<sup>2</sup> Mohsen Mazidi,<sup>3,4</sup>  
and Samantha M. Kimball<sup>1,5</sup>

# Glucosa pos 2h



Meta Analysis

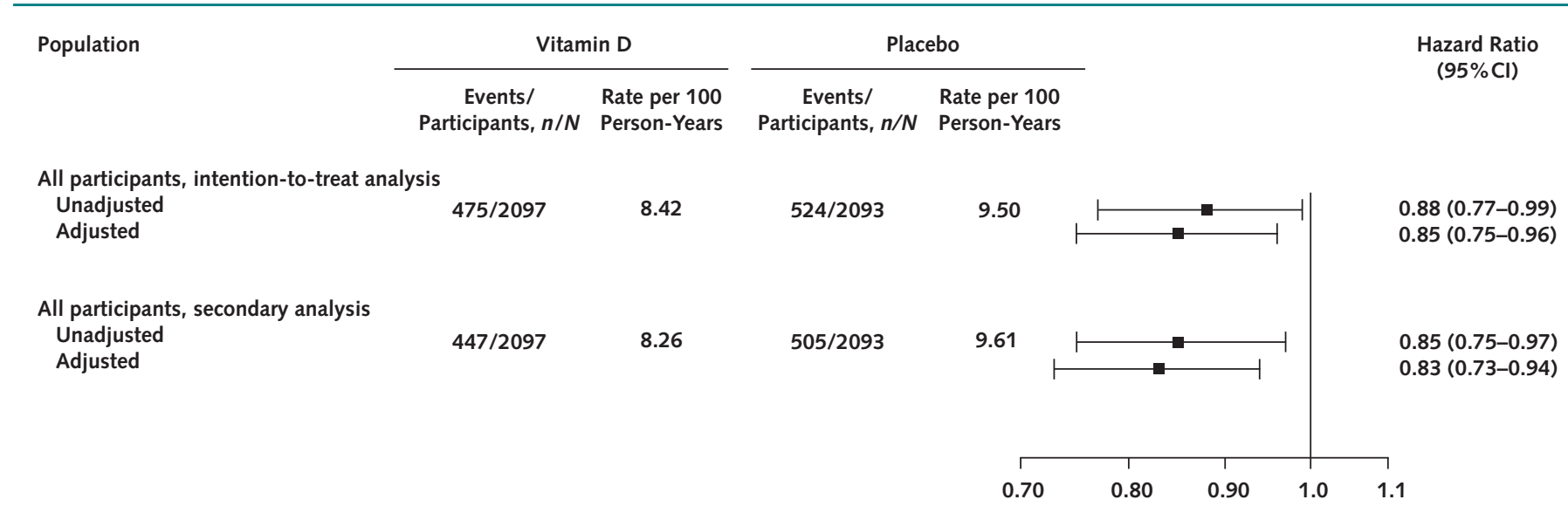
**Figure 6.** Forest plot of mean change from baseline in plasma glucose after 2HPG (mmol/L) between vitamin D supplementation and control.

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

### A Systematic Review and Meta-analysis of Individual Participant Data From 3 Randomized Clinical Trials

Anastassios G. Pittas, MD, MS; Tetsuya Kawahara, MD, PhD; Rolf Jorde, MD, PhD; Bess Dawson-Hughes, MD; Ellen M. Vickery, MS; Edith Angellotti, MD; Jason Nelson, MPH; Thomas A. Trikalinos, MD; and Ethan M. Balk, MD, MPH

**Figure 1.** Effect of vitamin D on new-onset diabetes among adults with prediabetes.



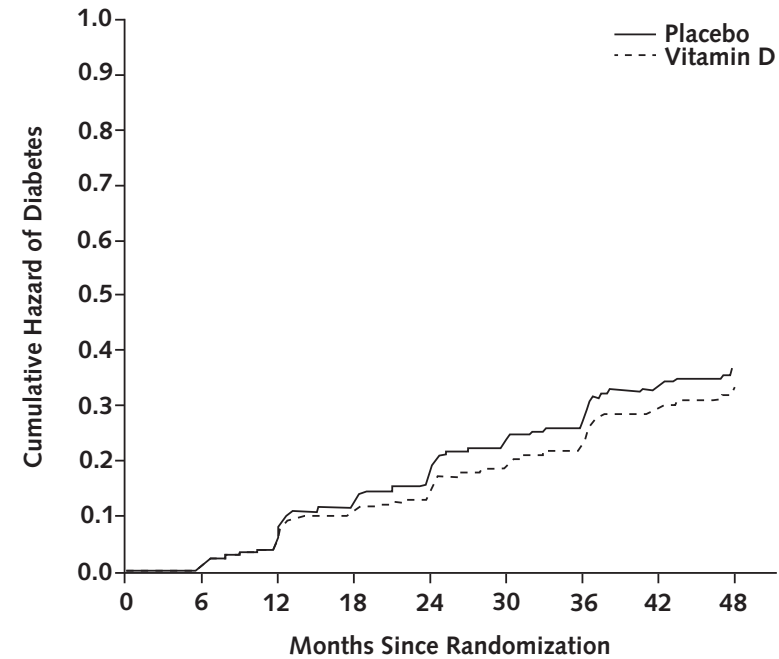
Secondary analyses censored follow-up when a participant stopped taking the trial pills, started using a diabetes or weight loss medication, or took vitamin D supplements at a dose above 1000 IU/d outside the study.

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

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**Figure 2.** Incidence curves for new-onset diabetes among adults with prediabetes: intention-to-treat analysis.



#### At risk, *n*

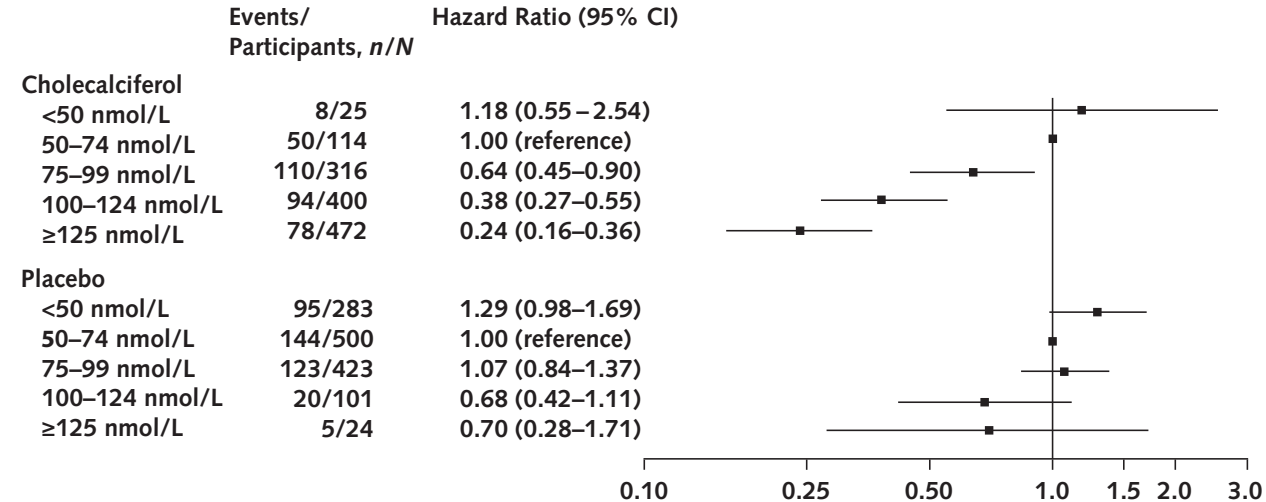
Vitamin D	2097	2040	1908	1745	1527	1298	1105	429	281
Placebo	2093	2032	1900	1714	1488	1239	1050	397	255

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

### A Systematic Review and Meta-analysis of Individual Participant Data From 3 Randomized Clinical Trials

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

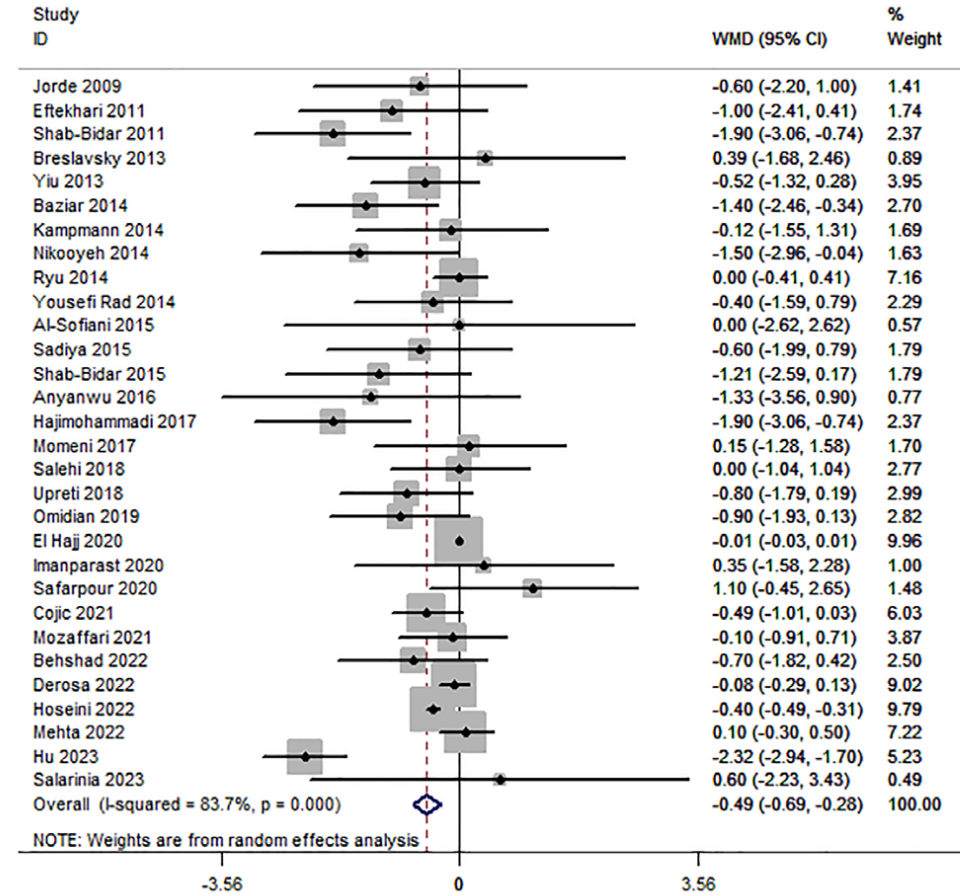


Analyses censored follow-up when a participant stopped taking the trial pills, started using a diabetes or weight loss medication, or took vitamin D supplements at a dose above 1000 IU/d outside the study. Details are provided in Supplement Methods 7 (available at [Annals.org](https://annals.org)).

## Efficacy of vitamin D supplementation on glycaemic control in type 2 diabetes: An updated systematic review and meta-analysis of randomized controlled trials

# Glucosa ayunas

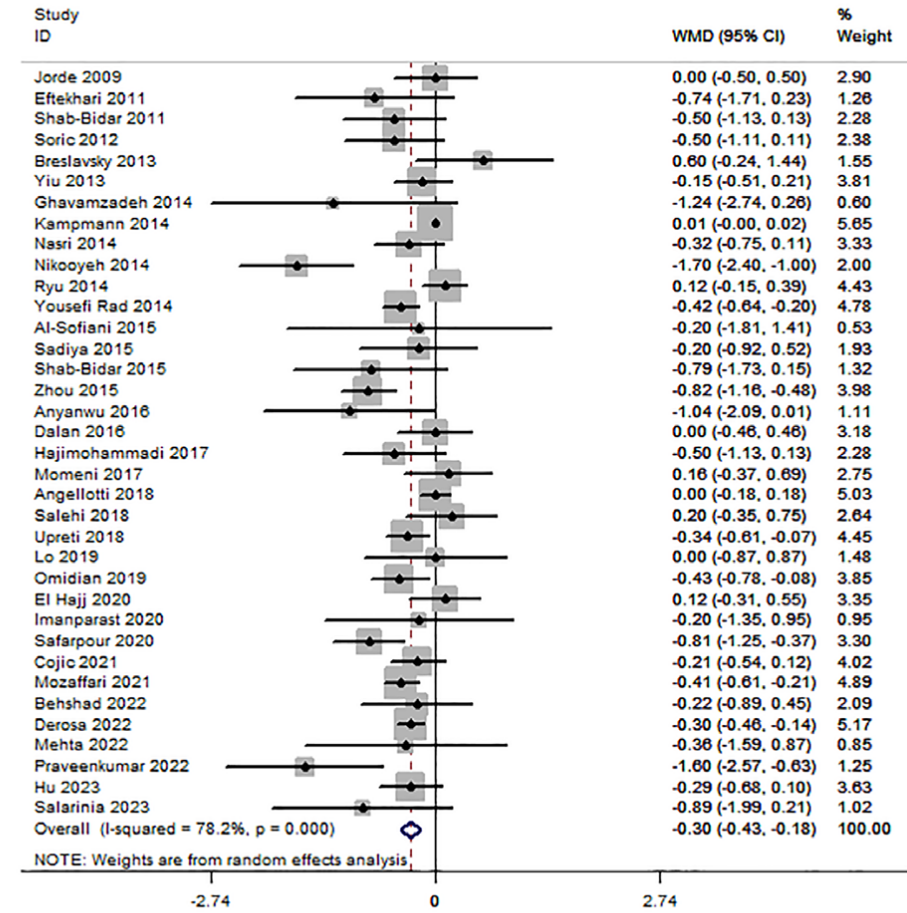
(A)  
FBG(mmol/L)



## Efficacy of vitamin D supplementation on glycaemic control in type 2 diabetes: An updated systematic review and meta-analysis of randomized controlled trials

# A1c

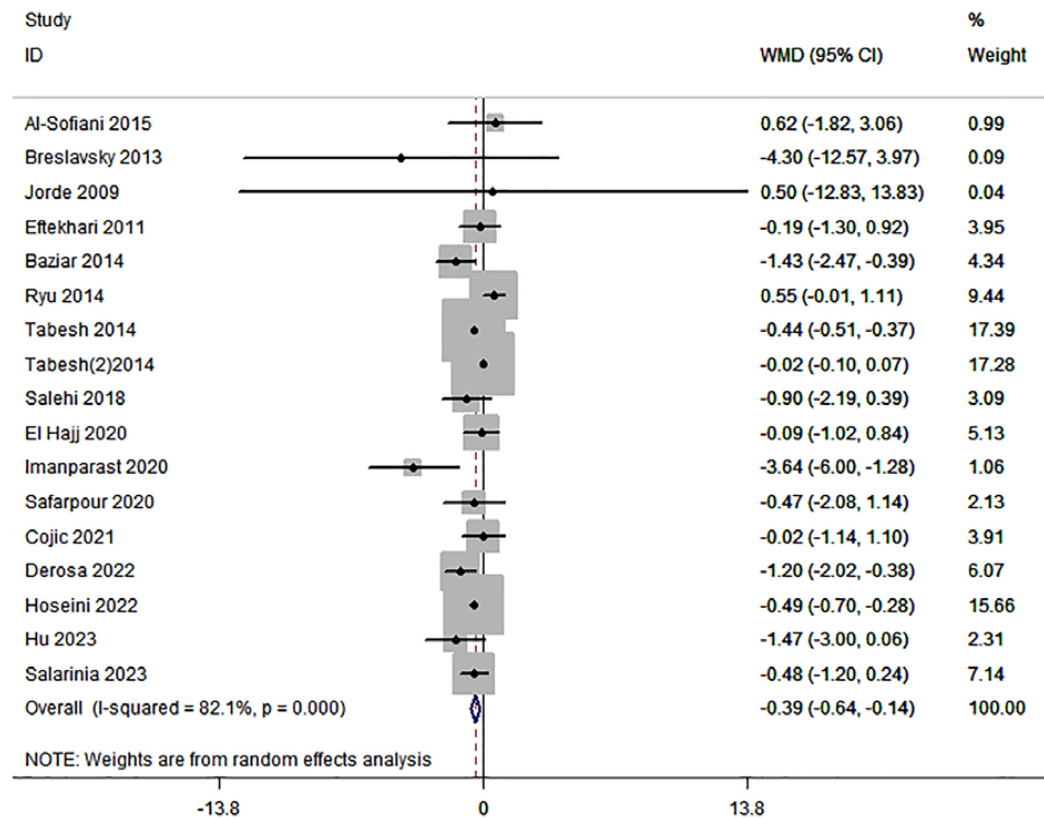
### (B) HbA1c



## Efficacy of vitamin D supplementation on glycaemic control in type 2 diabetes: An updated systematic review and meta-analysis of randomized controlled trials

# HOMA-IR

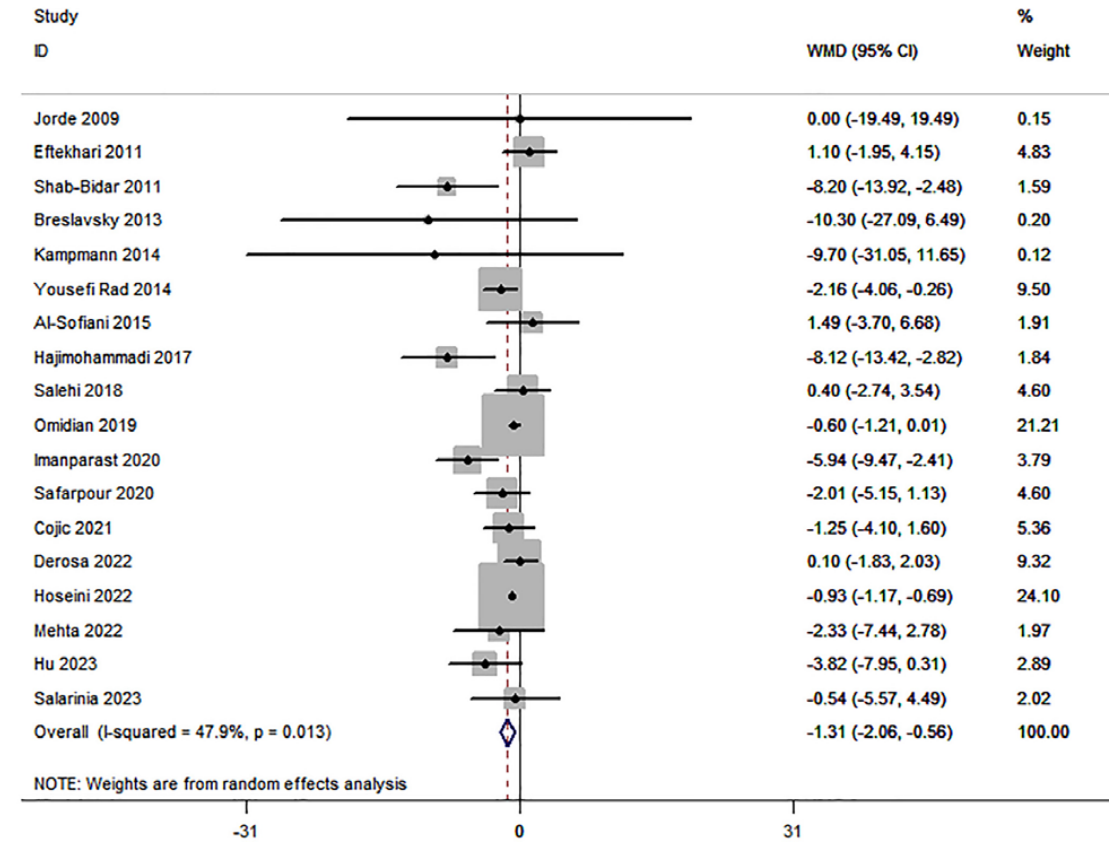
### (C) HOMA-IR



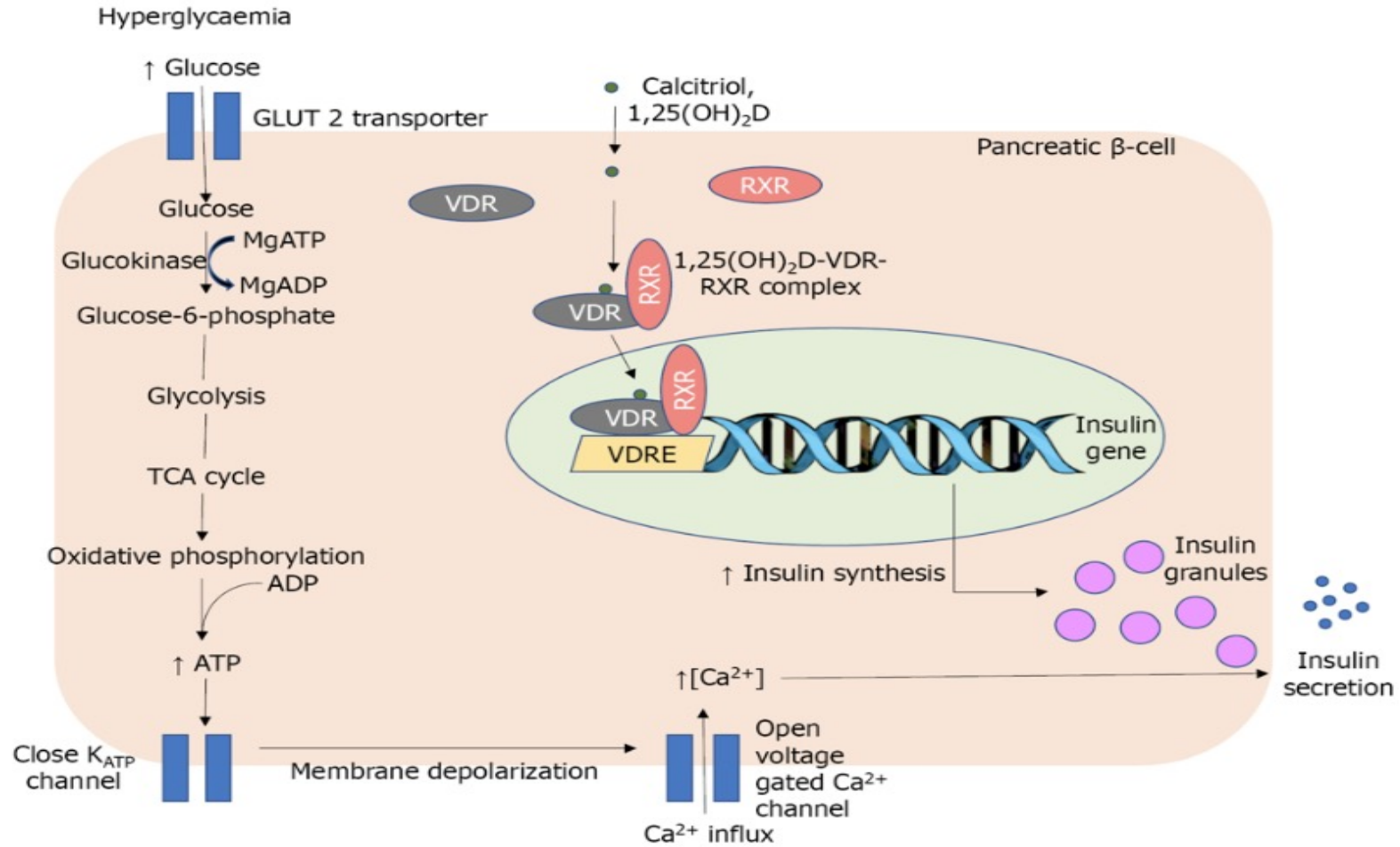
## Efficacy of vitamin D supplementation on glycaemic control in type 2 diabetes: An updated systematic review and meta-analysis of randomized controlled trials

# Insulina en ayunas

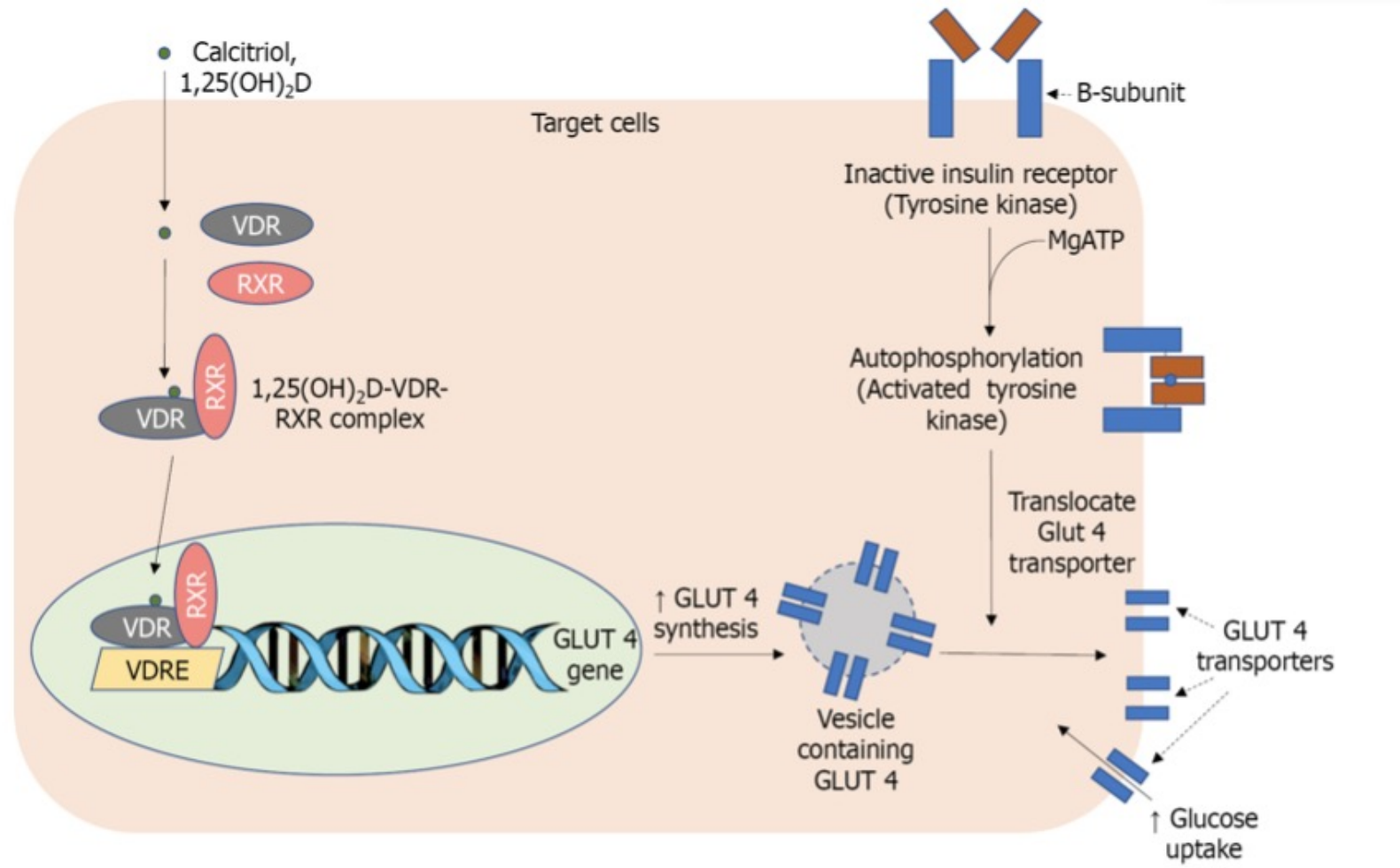
### (D) Fasting insulin( $\mu$ U/mL)

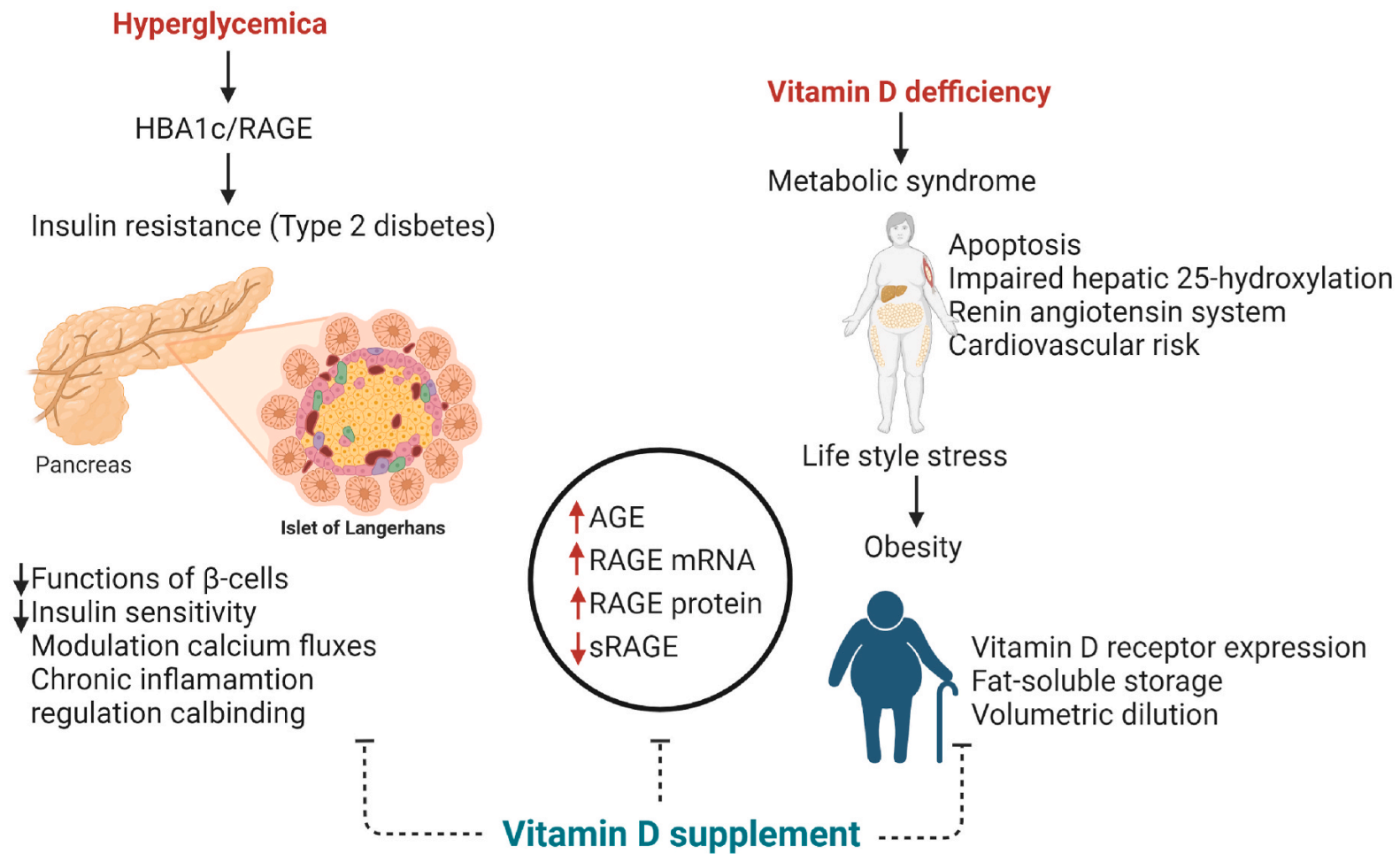


# VITAMINA D Y AUMENTO DE LA SECRECION DE INSULINA



# VITAMINA D Y AUMENTO DE LA SECRECION DE INSULINA

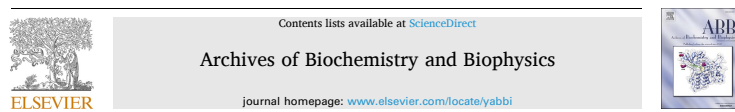




**Fig. 3.** Mechanisms relating to vitamin D insufficiency that led to dysregulation of glucose homeostasis.

## 7. Conclusions and future directions

## CRediT authorship contribution statement



Review article

Vitamin D supplementation modulates glycated hemoglobin (HBA1c) in diabetes mellitus

**Table 2**

25OHD serum levels and risk for Gestational Diabetes and Preeclampsia.

25OHD serum levels and risk for Gestational Diabetes (GD)				
Sample Size (GD/Controls)	Weeks of Gestation	25OHD	Risk for GD Development [Odds ratio (95 % CI)]	References
54/111	≥24	<37.5 nmol/L	2.66 (1.26–5.6)	[147]
68/1246	≥26	<25 nmol/L	3.6 (1.7–7.8)	[148]
81/226	13–26	<50 nmol/L	1.92 (0.89–4.17)	[149]
57/114	16	<50 nmol/L	3.74 (1.47–9.50)	[150]
116/219	≥15	<73.5 nmol/L	2.21 (1.19–4.13)	[151]
20/40	40	<50 nmol/L	30.78 (4.65–203.90)	[152]
200/200	≥26	<25 nmol/L	1.80 (1.209–2.678)	[153]
25OHD serum levels and risk for Preeclampsia				
Sample Size (Preeclampsia/Controls)	Weeks of Gestation	25OHD	Risk for Preeclampsia Development [Odds ratio (95 % CI)]	Reference
32/665	≥24	<50 nmol/L	3.24 (1.37–7.69)	[154]
51/204	≥15	<50 nmol/L	3.63 (1.52–8.65)	[155]
55/219	>20	<37.5 nmol/L	5.0 (1.7–14.1)	[156]
100/100	>24	<75 nmol/L	3.26 (1.12–9.54)	[157]
33/76	≥20	<5 nmol/L	3.9 (1.18–12.87)	[158]

## Pregunta 10

¿Se deben utilizar suplementos empíricos de vitamina D versus ningún suplemento de vitamina D para adultos con prediabetes (según criterios glucémicos)?

Para los adultos con prediabetes de alto riesgo, además de modificar el estilo de vida, sugerimos la suplementación empírica de vitamina D para reducir el riesgo de progresión a diabetes.

21 ⊕○○○

**Dosis promedio:  
2.000 UI**

### Vitamin D for the Prevention of Disease: An Endocrine Society Clinical Practice Guideline

Marie B. Demay,<sup>1</sup> Anastassios G. Pittas,<sup>2</sup> Daniel D. Bikle,<sup>3</sup> Dima L. Diab,<sup>4</sup> Mairead E. Kiely,<sup>5</sup> Marise Lazaretti-Castro,<sup>6</sup> Paul Lips,<sup>7</sup> Deborah M. Mitchell,<sup>8</sup> M. Hassan Murad,<sup>9</sup> Shelley Powers,<sup>10</sup> Sudhaker D. Rao,<sup>11,12</sup> Robert Scragg,<sup>13</sup> John A. Tayek,<sup>14,15</sup> Amy M. Valent,<sup>16</sup> Judith M. E. Walsh,<sup>17</sup> and Christopher R. McCartney<sup>18,19</sup>

# Conclusiones



Si bien la suplementación con vitamina D muestra beneficios potenciales en el manejo de la diabetes mellitus tipo 2 (DM2), estos efectos son complejos y pueden requerir enfoques individualizados.



Las **tendencias** observadas en la glucosa plasmática en ayunas (GA), los niveles de insulina, HOMA-IR, HOMA-B, HbA1c y PCR-as indican que la vitamina D puede influir en el control glucémico, la sensibilidad a la insulina y la inflamación; sin embargo, estos efectos suelen ser moderados y pueden disminuir con el tiempo.



La variabilidad en los resultados entre los estudios resalta la importancia de considerar factores como los niveles basales de vitamina D, la dosis, la duración del tratamiento y las características individuales de cada paciente.



Los regímenes de vitamina D en **dosis altas** podrían ser necesarios para una corrección rápida en ciertas poblaciones, mientras que las dosis de mantenimiento podrían mantener los beneficios a largo plazo.

## Concentrations of Serum Vitamin D and the Metabolic Syndrome Among U.S. Adults

EARL S. FORD, MD, MPH<sup>1</sup>  
UMED A. AJANI, MBBS, MPH<sup>1</sup>

LISA C. MCGUIRE, PHD<sup>1</sup>  
SIMIN LIU, MD, SCD<sup>2,3</sup>

medical examination clinic sampling weights to produce our weighted estimates and standard errors (17).



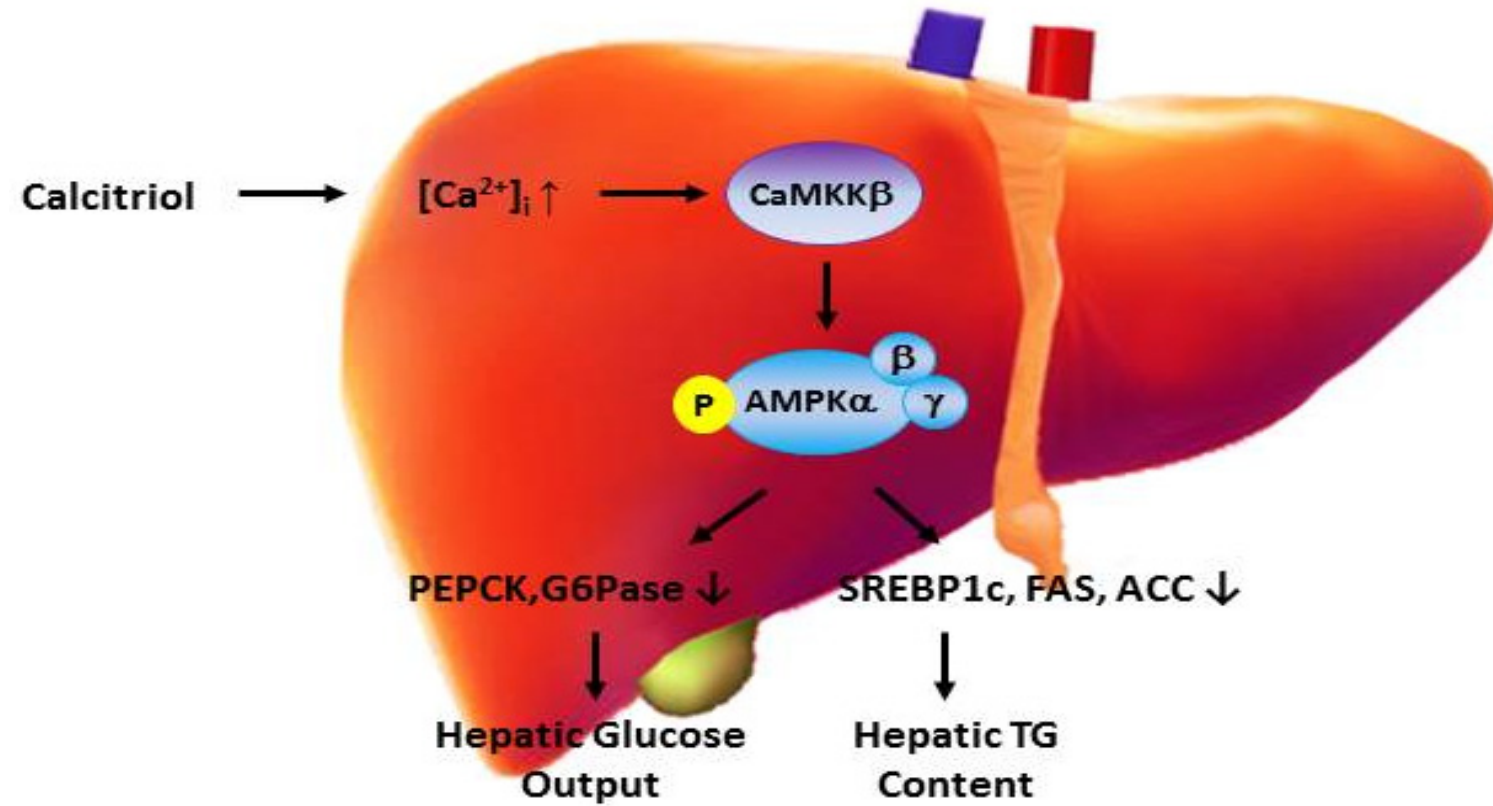
Table 1 —Unadjusted prevalence and adjusted odds ratios and 95% confidence limits of having the metabolic syndrome by quintiles of serum vitamin D concentration among 8,421 U.S. adults aged  $\geq 20$  years, NHANES III, 1988–1994

	Quintiles of vitamin D (nmol/l)					P*
	1 ( $\leq 48.4$ )	2 (48.5–63.4)	3 (63.5–78.1)	4 (78.2–96.3)	5 ( $\geq 96.4$ )	
Metabolic syndrome	<b>19</b>	<b>19–25</b>	<b>25–31</b>	<b>31–38</b>	<b>&gt; 38</b>	
Unadjusted prevalence†	27.5 (1.7)	26.6 (1.4)	23.3 (1.5)	18.7 (1.3)	13.5 (1.7)	<0.001
Model 1‡	1.00	0.91 (0.72, 1.17)	0.80 (0.62, 1.03)	0.65 (0.51, 0.83)	0.49 (0.37, 0.66)	<0.001
Model 2§	1.00	0.82 (0.60, 1.10)	0.75 (0.55, 1.02)	0.60 (0.44, 0.83)	0.46 (0.32, 0.67)	<0.001

Review

## The Potential Protective Action of Vitamin D in Hepatic Insulin Resistance and Pancreatic Islet Dysfunction in Type 2 Diabetes Mellitus

Po Sing Leung

CaMKK $\beta$  calcium/calmodulin protein kinase kinase beta

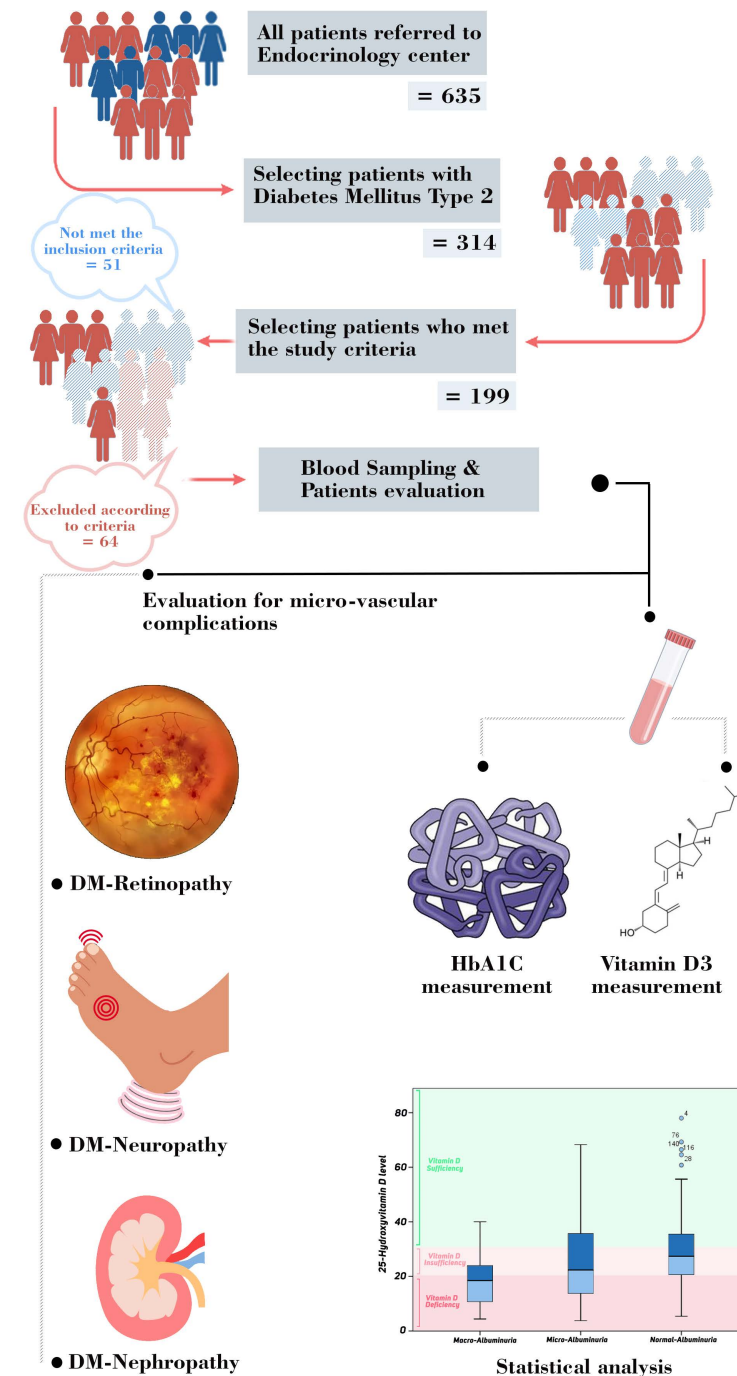
Y cómo lo hace



## RESEARCH ARTICLE

# Impact of vitamin D on glycemic control and microvascular complications in type 2 diabetes: A cross-sectional study

Salma Ahi<sup>1\*</sup>, Amirreza Reiskarimian<sup>2</sup>, Mohammad Aref Bagherzadeh<sup>1,3,4</sup>, Zhila Rahmanian<sup>1</sup>, Parisa Pilban<sup>2</sup>, Saeed Sobhanian<sup>1</sup>



## RESEARCH ARTICLE

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**Table 1. Clinical and laboratory characteristics of patients. Cell contents are expressed as a number, percentage, mean  $\pm$  s.d., or median (25<sup>th</sup> – 75<sup>th</sup> percentile). Normally distributed variables are shown as mean  $\pm$  s.d. nonparametric variables are shown as median (25<sup>th</sup> – 75<sup>th</sup> percentile).**

	Parameter	(N = 199)
Baseline Characteristics	Sex, F/M	126/73
	Age, years	56.79 $\pm$ 10.78
	BMI, kg/m <sup>2</sup>	28.91 (26.23–32.75)
	Duration, years	8 (3–15)
	Hypertension, yes%	114, 57.3%
	SBP, mmHg	125 (110–140)
	DBP, mmHg	80 (74–82)
	HbA <sub>1c</sub> , %	7.7 (6.5–8.9)
	FBS, mg/dL	134 (111–173)
	2HPP, mg/dL	198 (162–263)
	SCr, mg/dL	1 (0.9–1.2)
	25-OHD, ng/ml	24.3 (18–35.5)
	UACR, mg/g	22 (9.73–78)
Microvascular Complications	<b>Retinopathy, N(percent)</b>	51 (25.6%)
	<b>Neuropathy, N(percent)</b>	28 (14.1%)
	<b>Microalbuminuria (UACR* 30–300 mg/g)</b>	64 (32.2%)
	<b>Macroalbuminuria (UACR <math>\geq</math> 300 mg/g)</b>	16 (8%)
Vitamin D deficiency	<b>Vitamin D Deficiency (&lt; 20 ng/ml)</b>	58 (29.1%)
	<b>Vitamin D Insufficiency (20–30 ng/ml)</b>	68 (34.2%)
	<b>Vitamin D Sufficiency (<math>\geq</math> 30 ng/ml)</b>	73 (36.7%)

## RESEARCH ARTICLE

## Impact of vitamin D on glycemic control and microvascular complications in type 2 diabetes: A cross-sectional study

Salma Ahi<sup>1\*</sup>, Amirreza Reiskarimian<sup>2</sup>, Mohammad Aref Bagherzadeh<sup>1,3,4</sup>, Zhila Rahmanian<sup>1</sup>, Parisa Pilban<sup>2</sup>, Saeed Sobhanian<sup>1</sup>

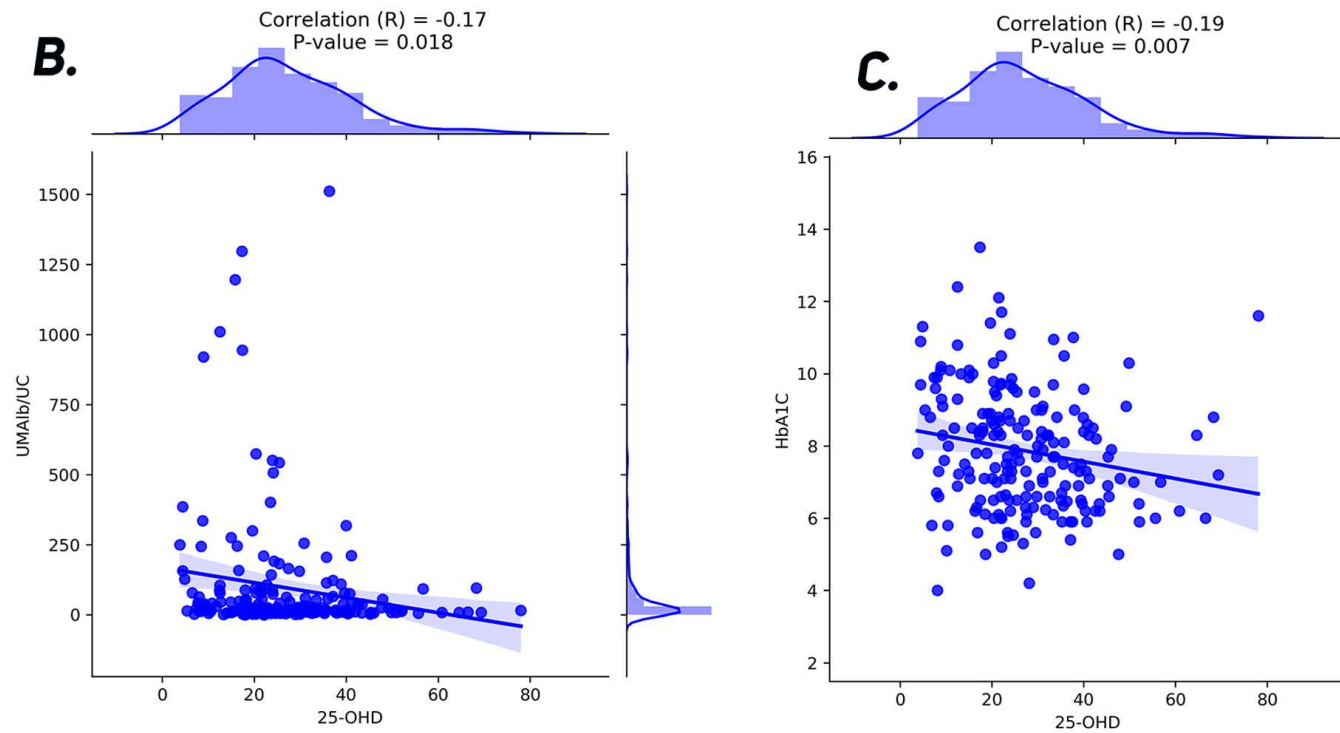
**Table 2. Distribution of patients based on the presence or absence of microvascular complications and vitamin D level.**

Vitamin D status	UACR			Retinopathy		Neuropathy	
	Macroalbuminuria (UACR* $\geq$ 300 mg/g)	Microalbuminuria (UACR 30–300 mg/g)	Neg.	No	Yes	No	Yes
Vitamin D Deficiency (< 20 ng/ml)	9	24	25	39	19	44	14
Vitamin D Insufficiency (20–30 ng/ml)	5	19	44	50	18	59	9
Vitamin D Sufficiency ( $\geq$ 30 ng/ml)	2	21	50	59	14	68	5
Vitamin D level	19.21 $\pm$ 9.76 ng/ml	24.66 $\pm$ 13.54 ng/ml	29.47 $\pm$ 13.6 ng/ml	27.96 $\pm$ 13.54 ng/ml	24.59 $\pm$ 13.77 ng/ml	27.74 $\pm$ 13.22 ng/ml	23.21 $\pm$ 15.7 ng/ml


## RESEARCH ARTICLE

## Impact of vitamin D on glycemic control and microvascular complications in type 2 diabetes: A cross-sectional study

Salma Ahi<sup>1\*</sup>, Amirreza Reiskarimian<sup>2</sup>, Mohammad Aref Bagherzadeh<sup>1,3,4</sup>, Zhila Rahmanian<sup>1</sup>, Parisa Pilban<sup>2</sup>, Saeed Sobhanian<sup>1</sup>



**Fig 3. Correlation of clinical and biochemical parameters; (A) Correlation matrix of clinical and biochemical parameters:** Pearson correlation coefficients (R) between age, weight, height, BMI, duration of type 2 diabetes (DMT2), fasting blood sugar (FBS), 2-hour postprandial blood sugar (2HPP), HbA1C, urinary albumin/creatinine ratio (UMA1b/UC), serum creatinine (S.Cr), and serum 25-hydroxyvitamin D (25-OHD). Significant

- 
- Entonces...  
por qué NO, una  
corrección rápida?

## Review

**Vitamin D<sub>3</sub> Distribution and Status in the Body**

Robert P. Heaney, MD, FACN, Ronald L. Horst, PhD, Diane M. Cullen, PhD, Laura A. G. Armas, MD  
 Creighton University, Omaha, Nebraska (R.P.H., D.M.C., L.A.G.A.), Heartland Assays, Inc., Ames, Iowa (R.L.H.)

1 nmol = 15.4 IU and 1 mcg = 40 IU



**70 Kg**

35% 25 OH Vitamina D

20% Músculo

30% Sérico

35% Grasa

15% Otros

65% Colecalciferol

$\frac{3}{4}$  Grasa

Conclusions: At total intakes on the order of 2000 IU/day, an adult has very little vitamin D reserve, despite intakes 10 x the current recommendations

- Data presented elsewhere suggest that daily utilization of vitamin D in humans at a serum 25(OH)D concentration of 32 ng/ml, is on the order of 4000 IU.



Brief communication

The effect of body mass index on adequacy of serum  
25-hydroxyvitamin D levels in US adults: the National  
Health and Nutrition Examination Survey 2001 to 2006

**Table 2**

Crude and adjusted prevalence ratios\* for serum 25(OH)D levels greater than or equal to 20 ng/mL by BMI categories among adults aged 18 years: NHANES 2001 to 2006

BMI categories (kg/m <sup>2</sup> )	Adequate status for vitamin D			
	Crude	Model 1	Model 2	Model 3
<18.5	0.96 (0.87 to 1.05)	0.96 (0.88 to 1.04)	0.96 (0.89 to 1.04)	0.97 (0.90 to 1.05)
18.5 to <25	1.00	1.00	1.00	1.00
25 to <30	0.92 (0.89 to 0.95)	0.93 (0.91 to 0.96)	0.93 (0.90 to 0.96)	0.93 (0.90 to 0.96)
≥30	0.74 (0.71 to 0.78)	0.79 (0.76 to 0.82)	0.78 (0.75 to 0.81)	0.79 (0.75 to 0.82)

26%



21%



Vitamina D 50.000 UI:  
**Corrección rápida y manejo  
inteligente**



THE PRESENT AND FUTURE

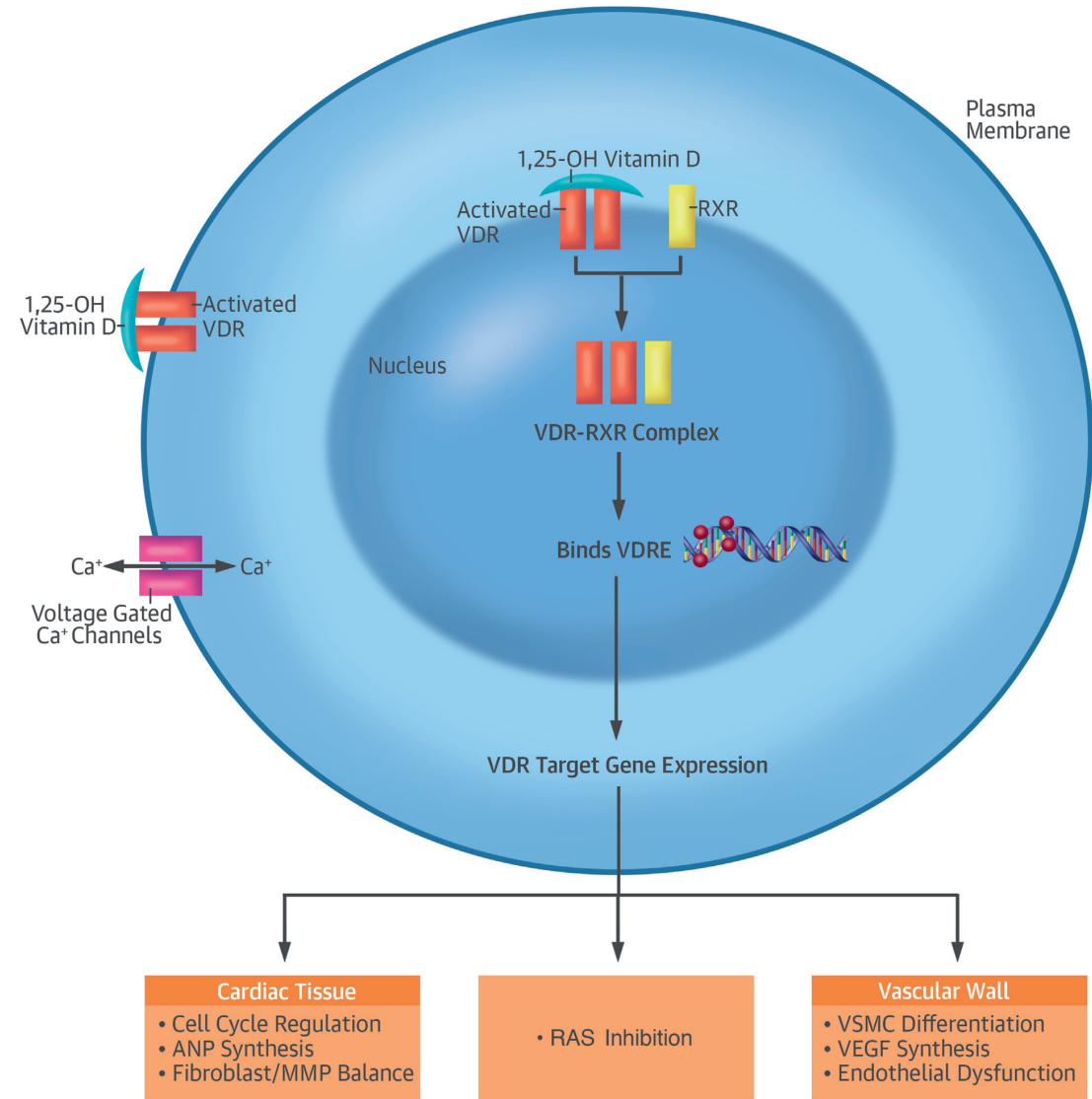
STATE-OF-THE-ART REVIEW

# Vitamin D and Cardiovascular Disease Controversy Unresolved

Ibhar Al Mheid, MD,<sup>a,b</sup> Arshed A. Quyyumi, MD<sup>a,b</sup>

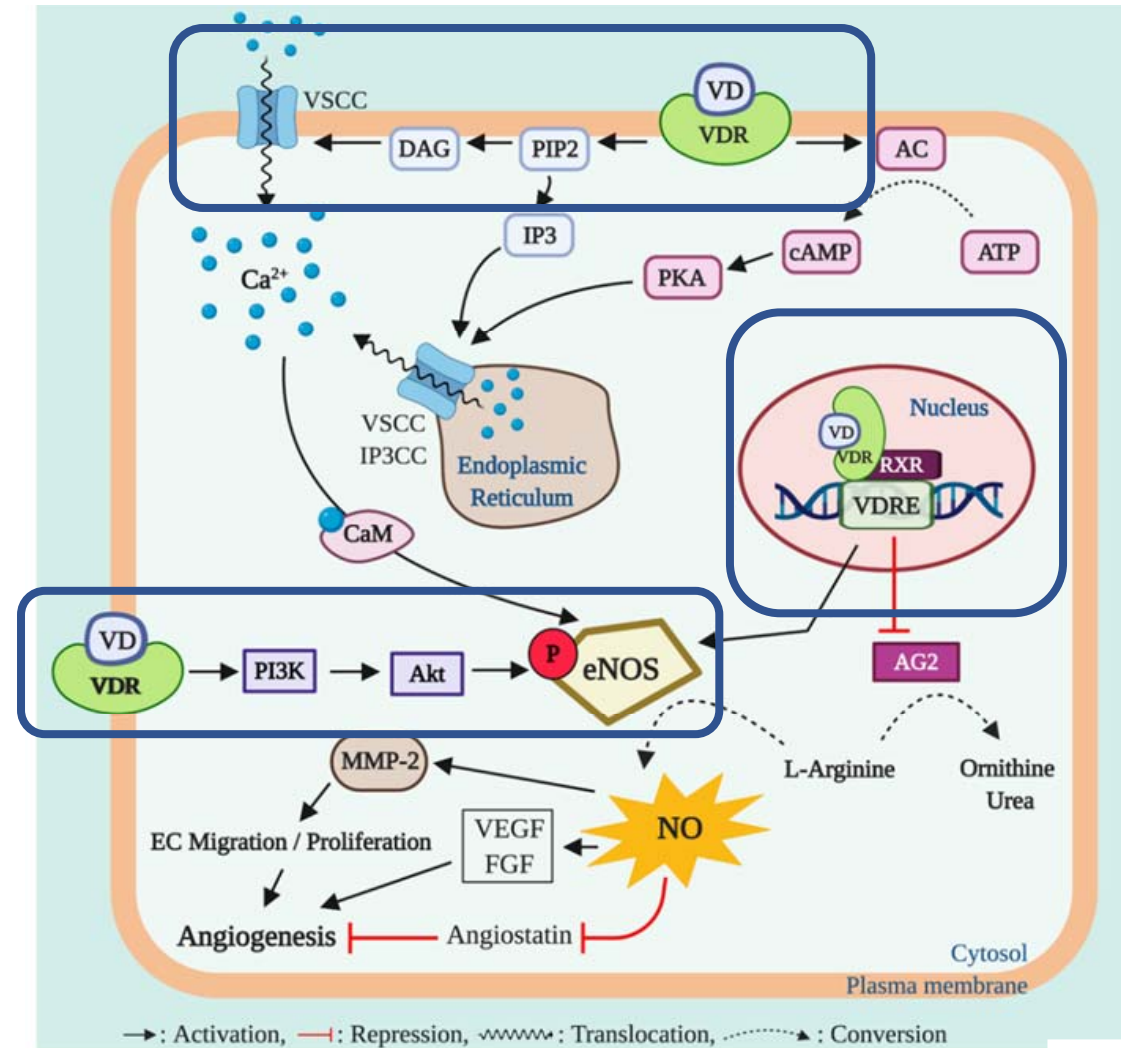


**CENTRAL ILLUSTRATION** Mechanisms by Which Vitamin D Deficiency May Confer Cardiovascular Risk



## Vitamin D and Endothelial Function

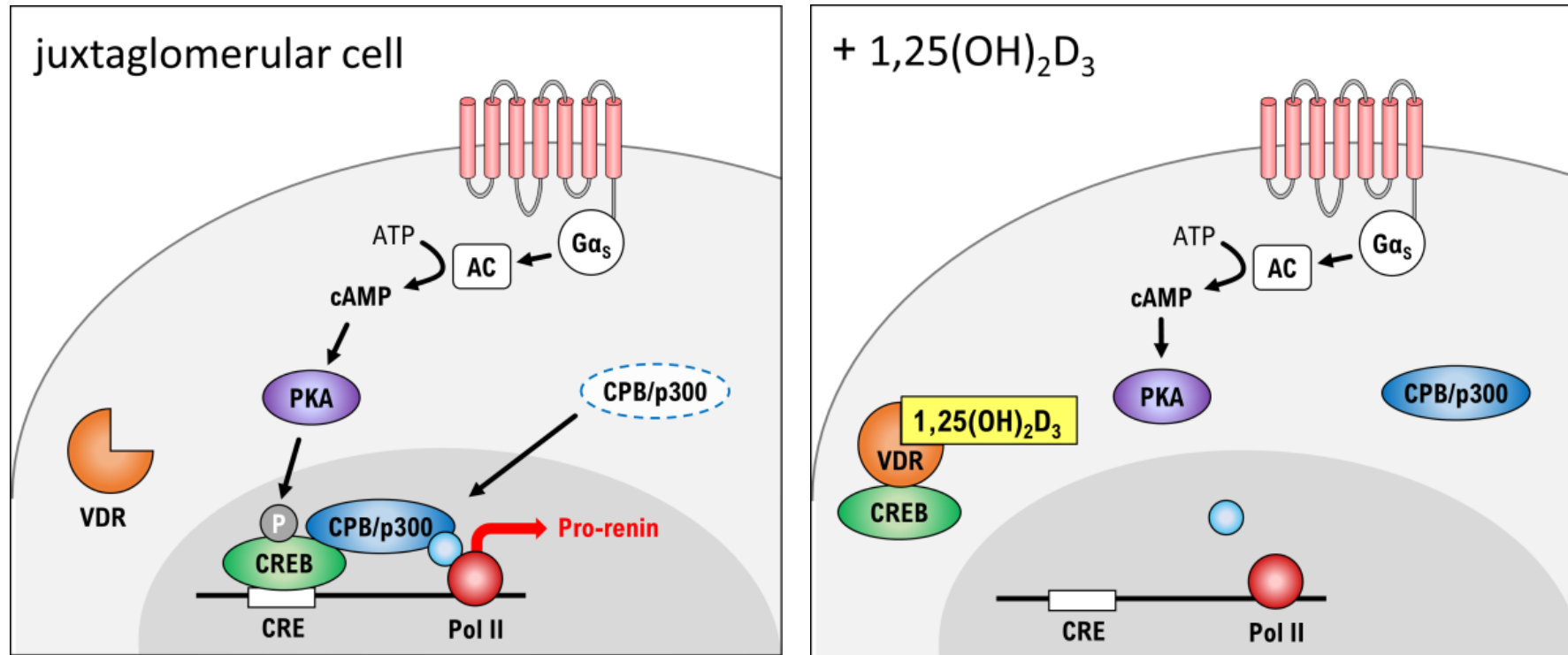
Do-Houn Kim <sup>1,2</sup>, Cesar A. Meza <sup>1</sup>, Holly Clarke <sup>1</sup>, Jeong-Su Kim <sup>1,2,3</sup> and Robert C. Hickner <sup>1,3,4,\*</sup>



Review

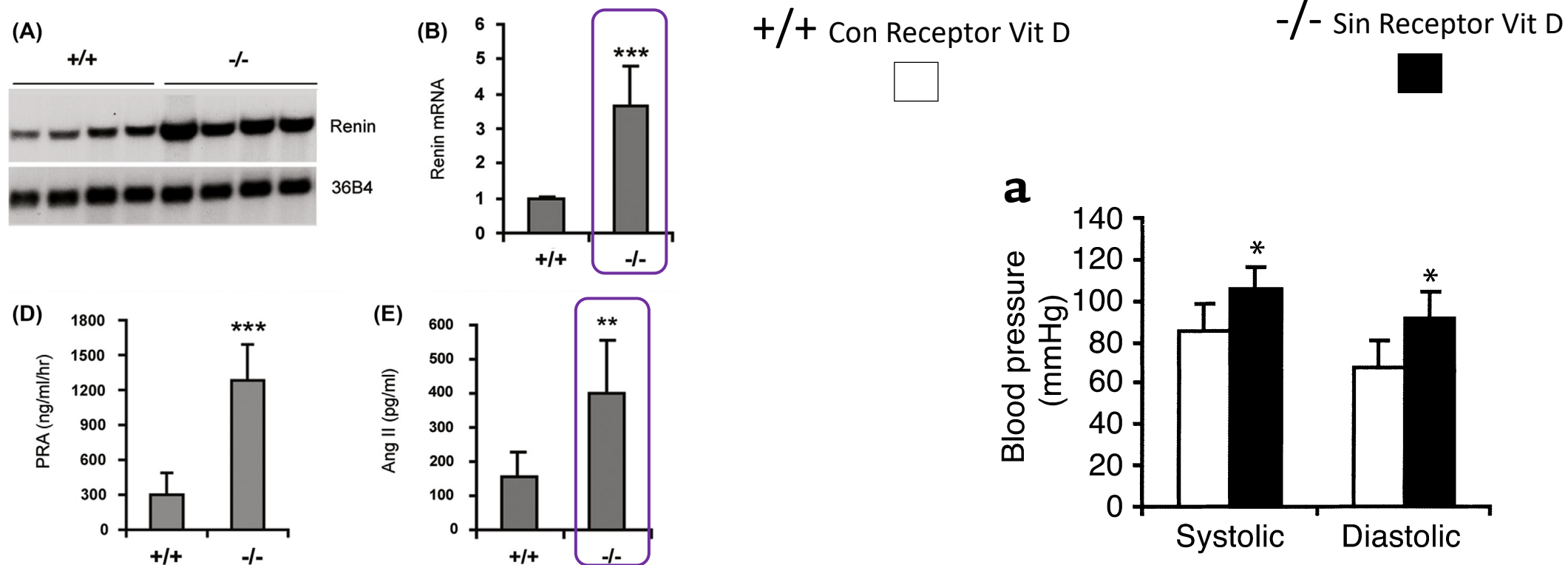
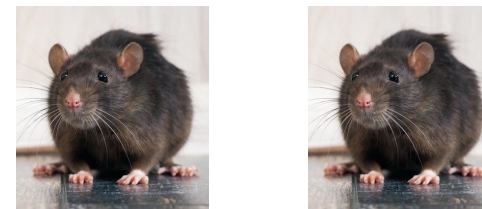
## The Impact of Vitamin D in the Treatment of Essential Hypertension

Christian Legarth<sup>1</sup>, Daniela Grimm<sup>1,\*</sup>, Markus Wehland<sup>2</sup>, Johann Bauer<sup>3</sup> and Marcus Krüger<sup>2</sup>



## 1,25-Dihydroxyvitamin D<sub>3</sub> is a negative endocrine regulator of the renin-angiotensin system

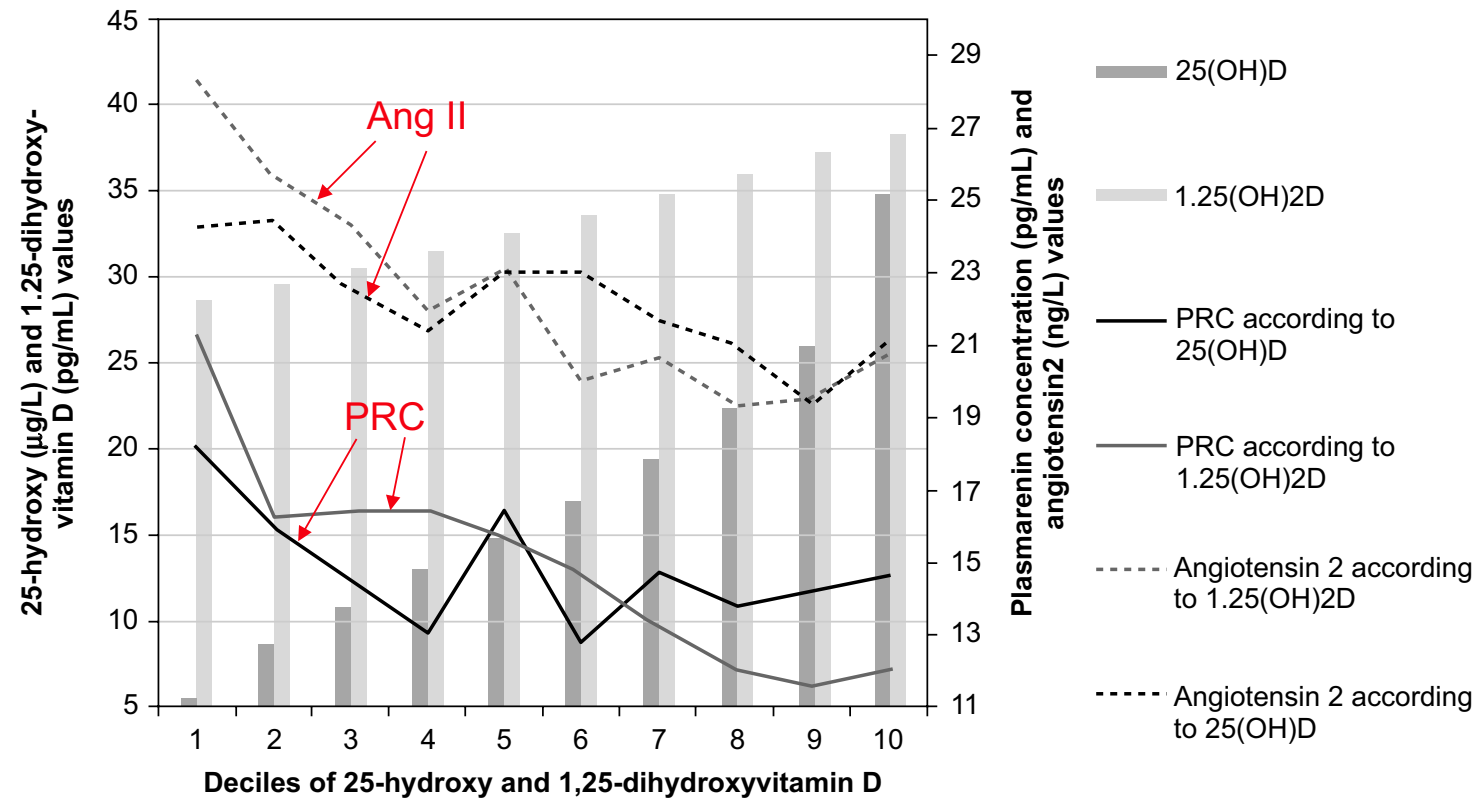
Yan Chun Li, ... , Shu Q. Liu, Li-Ping Cao



## Vitamin D and the Renin-Angiotensin System

Yan Chun Li

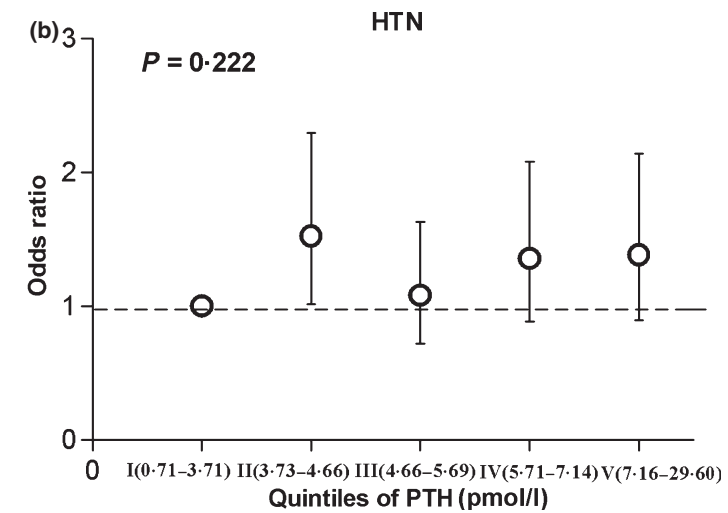
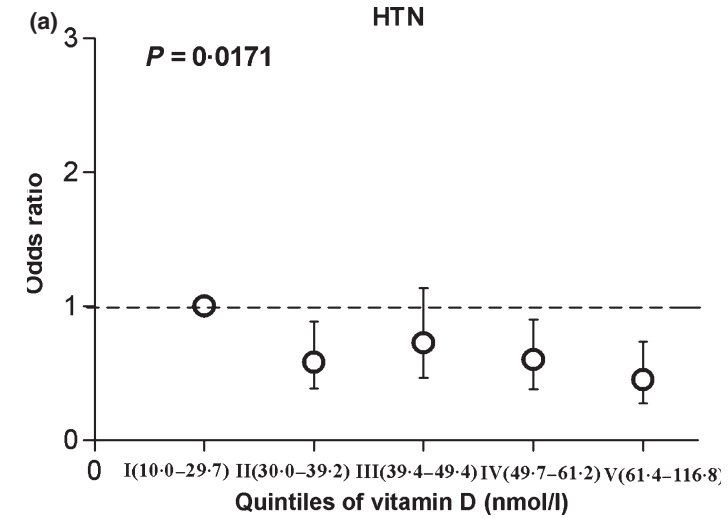
The University of Chicago, Chicago, IL, United States



## ORIGINAL ARTICLE

## The association of serum vitamin D level with presence of metabolic syndrome and hypertension in middle-aged Korean subjects

Mee K. Kim\*, Moo Il Kang\*, Ki Won Oht, Hyuk S. Kwon\*, Jin H. Lee‡, Won C. Lee‡, Kun-Ho Yoon\* and Ho Y. Son\*



## Clinical Trials

### Effect of Vitamin D Supplementation on Blood Pressure in Blacks

John P. Forman, Jamil B. Scott, Kimmie Ng, Bettina F. Drake, Elizabeth Gonzalez Suarez, Douglas L. Hayden, Gary G. Bennett, Paulette D. Chandler, Bruce W. Hollis, Karen M. Emmons, Edward L. Giovannucci, Charles S. Fuchs, Andrew T. Chan



1 ng/ml 25 OH VD

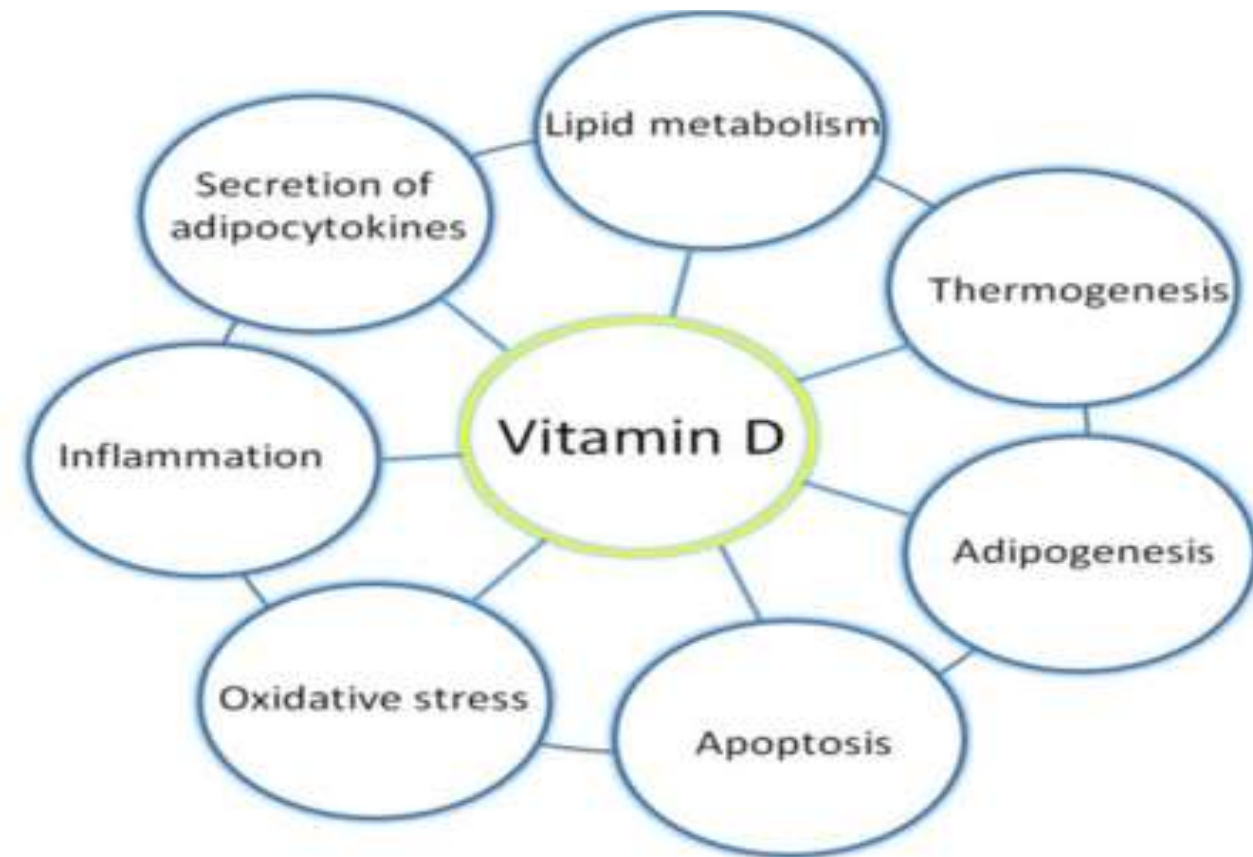


0.2% mm/Hg

**Table 2. Effect of Vitamin D Supplementation on Blood Pressure During the Treatment Period (Baseline to 3 mo)**

Parameter	Vitamin D Dose, IU/d				3 mo Change in BP per 1000 IU/d	P Value
	Placebo	1000	2000	4000		
n (at baseline)	72	68	73	70		
Baseline SBP, mean (SE)	122.2 (2.2)	124.7 (2.1)	122.8 (2.0)	130.4 (2.4)	-1.4 (0.7)	0.04
3 mo SBP, mean (SE)	124.9 (2.4)	122.5 (2.0)	120.0 (2.4)	126.6 (2.6)		
Difference SBP, mean (SE)	1.7 (2.1)	-0.66 (2.1)	-3.4 (2.0)	-4.0 (2.1)		
Baseline DBP, mean (SE)	78.0 (1.3)	79.8 (1.3)	77.6 (1.4)	79.8 (1.6)	-0.5 (0.5)	0.37
3 mo DBP, mean (SE)	78.9 (1.8)	78.0 (1.6)	76.0 (1.8)	78.0 (1.6)		
Difference DBP, mean (SE)	0.7 (1.6)	-2.5 (1.6)	-1.8 (1.4)	-1.8 (1.50)		

BP indicates blood pressure; DBP, diastolic blood pressure; IU, international unit; and SBP, systolic blood pressure.

**Effect of Vitamin D3 on Lipids Metabolism and Adipose Tissue Biology****Maha K. Ibrahim<sup>1</sup>, Eqbal Abdul-Aziz<sup>2</sup>, Zainab J. Abdulridha<sup>3</sup>, Ali A. Al-fahham<sup>4</sup>**<sup>1,2,3</sup> Biology department, College of Science, Basrah University, Basrah, Iraq,<sup>4</sup>Corresponding Author, Faculty of Nursing, University of Kufa, Iraq**Fig 4: The function of vitamin D in adipose tissue (Xiang et al.,2020).**



Osteoporos Int (2013) 24:2955–2959  
DOI 10.1007/s00198-013-2427-1

OPINION PAPER



## What's in a name revisited: should osteoporosis and sarcopenia be considered components of “dysmobility syndrome?”

N. Binkley · D. Krueger · B. Buehring

Interacción  
musculo/hueso

❑ Varias similitudes entre los dos tejidos

### FACTORES EXTRISECOS

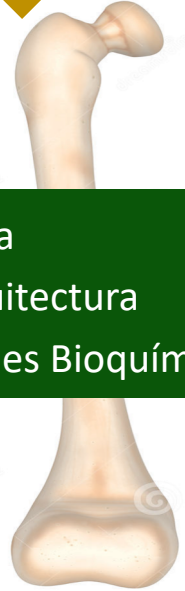
INACTIVIDAD

Factores  
Nutricionales

Tratamiento Medico

Estilo de vida

Deficiencia de  
Vitamina D



- ↓ Masa Osea
- Microarquitectura
- ↓ Propiedades Bioquímicas



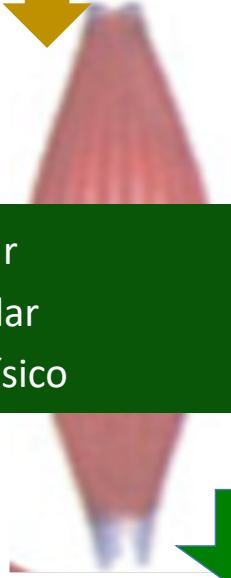
**Osteoporosis**

- Acidosis Metabólica
- Bajo grado de Inflamación
- Estrés Oxidativo
- Cambios Hormonales
- Lipotoxicidad

**INFLAMACION**

Disregulación Metabólica

- Factores Genéticos
- Deficiencia Hormonal (GH, Tiroides,)
- Insulino Resistencia
- Comorbilidades (Obesidad, diabetes, Cushing, caquexia)

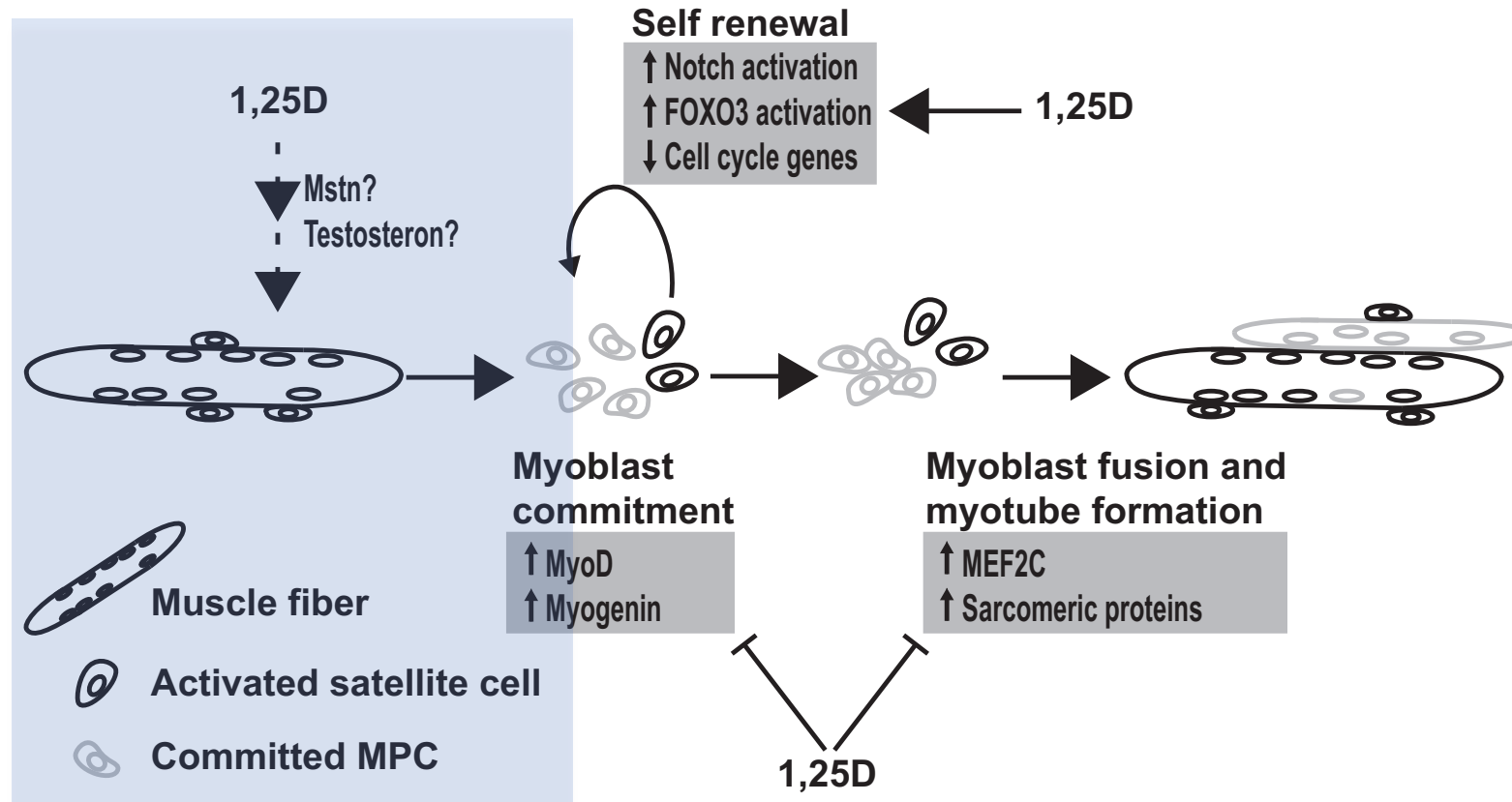


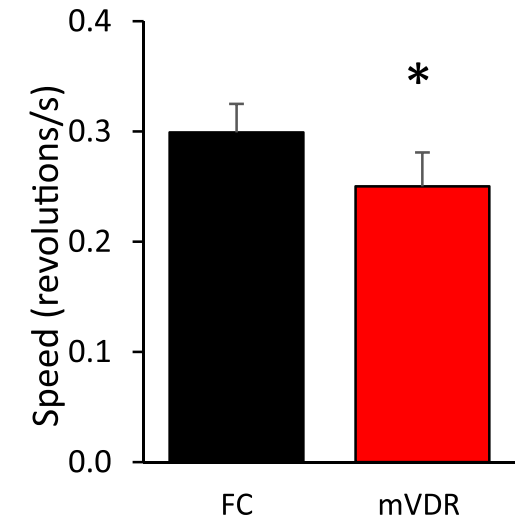
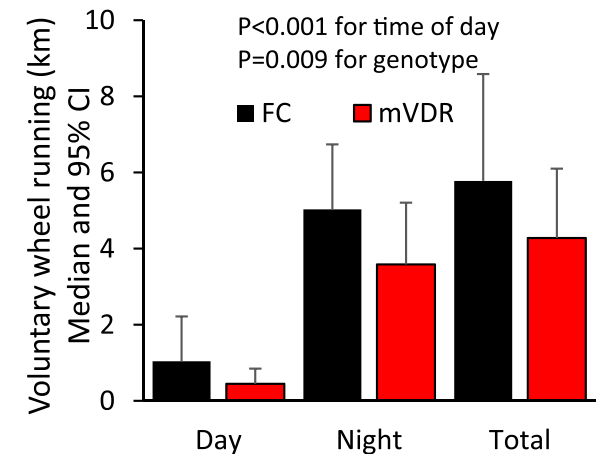
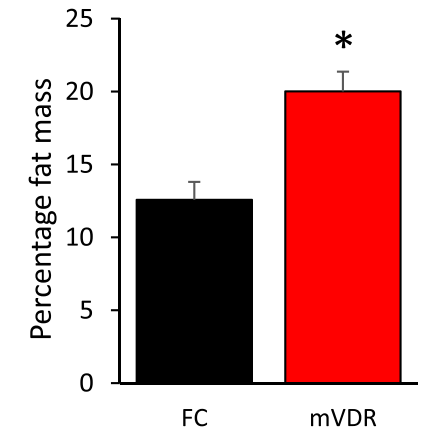
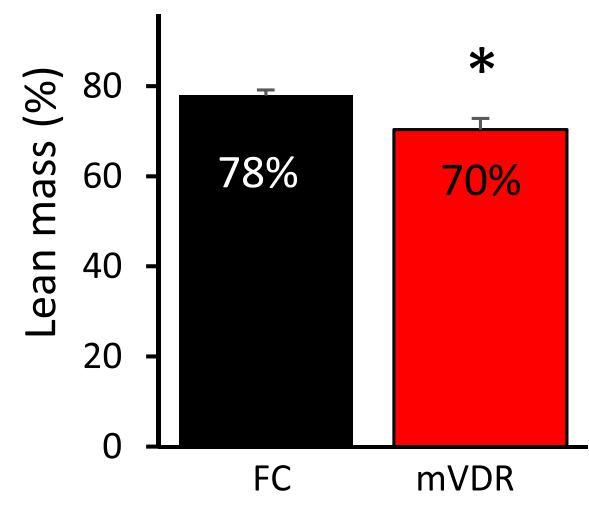
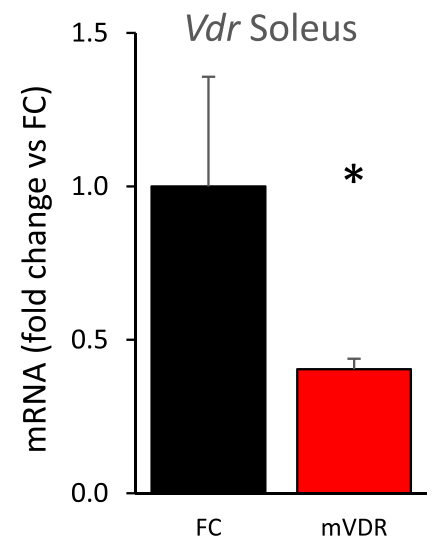
- ↓ Masa Muscular
- ↓ Fuerza Muscular
- ↓ Desempeño Físico



**Sarcopenia**

## Importancia de las células satelitales





Research Article

### Longitudinal Associations Between Vitamin D Metabolites and Sarcopenia in Older Australian men: The Concord Health and Aging in Men Project

Vasant Hirani,<sup>1,2</sup> Robert G. Cumming,<sup>2,3,4</sup> Vasi Naganathan,<sup>2</sup> Fiona Blyth,<sup>2</sup> David G. Le Couteur,<sup>6</sup> Benjamin Hsu,<sup>2,4,7</sup> David J. Handelsman,<sup>5</sup> Louise M. Waite,<sup>2</sup> and Markus J. Seibel<sup>8</sup>

The Concord Health and Aging in Men Project (CHAMP)

Masa magra  
apendicular



I.M.C.

Baja Masa Muscular  $\leq 0.789$

SARCOPENIA



## 25 OH VD

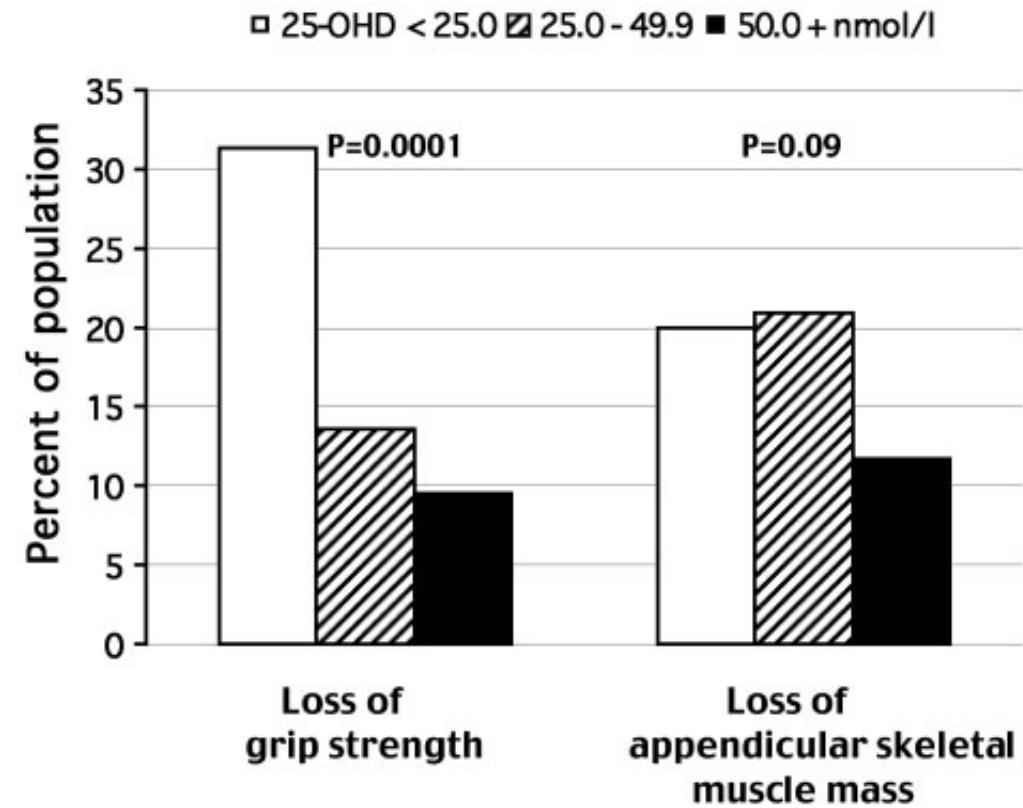
**Table 2.** Longitudinal Unadjusted and Multivariate Adjusted (Odds Ratios and 95% confidence interval) for GEE Analyses: 25D Status at Baseline, and Associations with Incidence of Sarcopenia at 2- and 5-year Follow-up (Reference Category is the Highest Quartile 25D  $\geq 68.9$  nmol/L)

<i>N</i> = 709	Serum 25D Lowest Quartile <40.0 nmol/L	Serum 25D Second Quartile 40–52.9 nmol/L	Serum 25D Third Quartile 53–68.9 nmol/L	Serum 25D Fourth Quartile $\geq 68.9$ nmol/L (Referent Category)
Model 1*	2.55 (1.33,4.90) <i>p</i> = .005	1.75 (0.91,3.39) <i>p</i> = .10	1.33 (0.69,2.58) <i>p</i> = .39	1
Model 2*	2.48 (1.27,4.85) <i>p</i> = .01	1.90 (0.97,3.73) <i>p</i> = .10	1.43 (0.74,2.78) <i>p</i> = .29	1
Model 3*	2.53 (1.14,5.64) <i>p</i> = .02	1.90 (0.89,4.10) <i>p</i> = .10	1.51 (0.73,3.12) <i>p</i> = .27	1
Model 4*	2.40 (1.02,5.64) <i>p</i> = .04	1.86 (0.83,4.15) <i>p</i> = .13	1.47 (0.68,3.16) <i>p</i> = .33	1
	16	16-21.2	21.2-27.6	$\geq 28$ ng/ml

## Low Vitamin D and High Parathyroid Hormone Levels as Determinants of Loss of Muscle Strength and Muscle Mass (Sarcopenia): The Longitudinal Aging Study Amsterdam

MARJOLEIN VISSER, DORLY J. H. DEEG, AND PAUL LIPS

Bajos niveles de Vit D:  
perdida de fuerza más que de masa





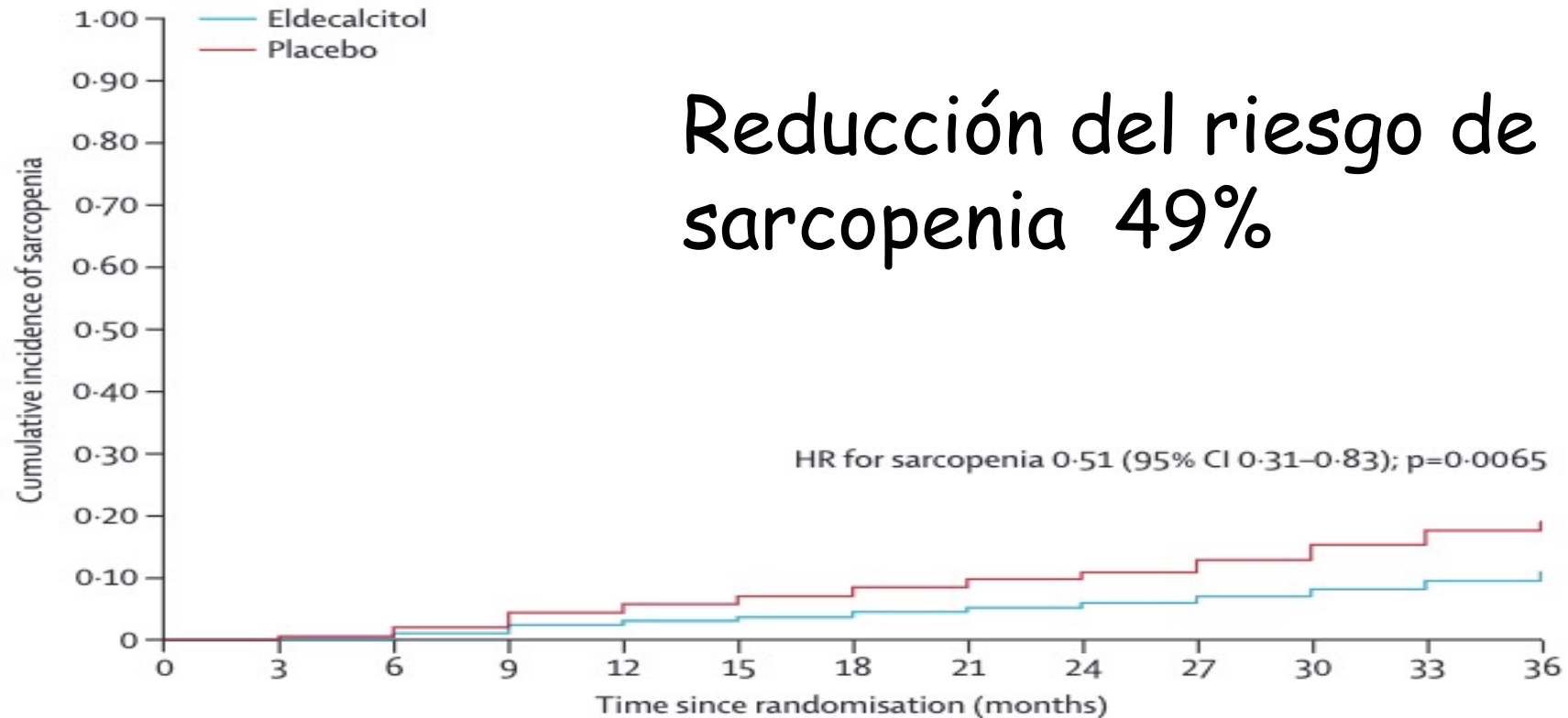
Active vitamin D treatment in the prevention of sarcopenia  
in adults with prediabetes (DPVD ancillary study):  
a randomised controlled trial



Tetsuya Kawahara, Gen Suzuki, Shoichi Mizuno, Naoki Tominaga, Mikio Toda, Nagahiro Toyama, Tetsuya Inazu, Chie Kawahara, Yosuke Okada, Yoshiya Tanaka



25 OH VIT D  
20± 6 ng/ml



Reducción del riesgo de  
sarcopenia 49%

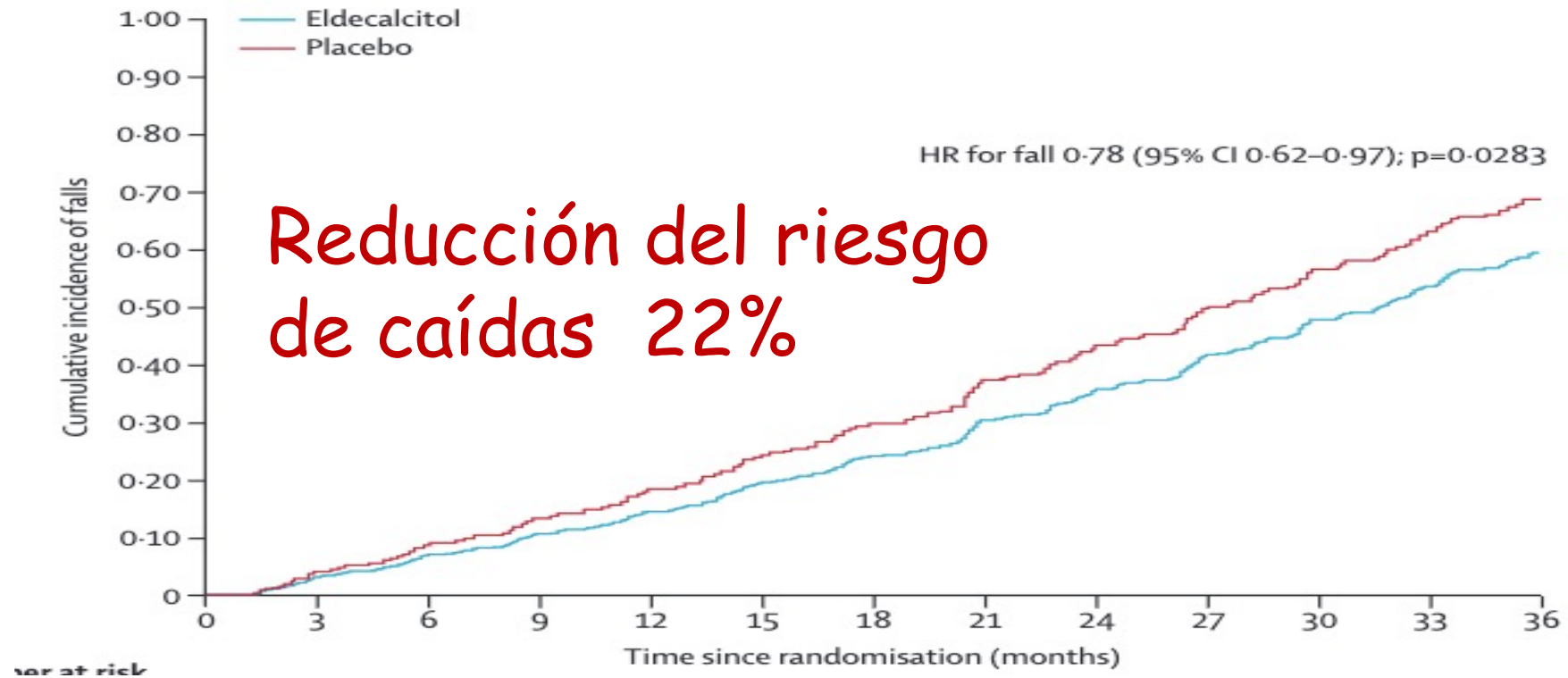
Active vitamin D treatment in the prevention of sarcopenia in adults with prediabetes (DPVD ancillary study): a randomised controlled trial



Tetsuya Kawahara, Gen Suzuki, Shoichi Mizuno, Naoki Tominaga, Mikio Toda, Nagahiro Toyama, Tetsuya Inazu, Chie Kawahara, Yosuke Okada, Yoshiya Tanaka



25 OH VIT D  
20± 6 ng/ml



Active vitamin D treatment in the prevention of sarcopenia in adults with prediabetes (DPVD ancillary study): a randomised controlled trial

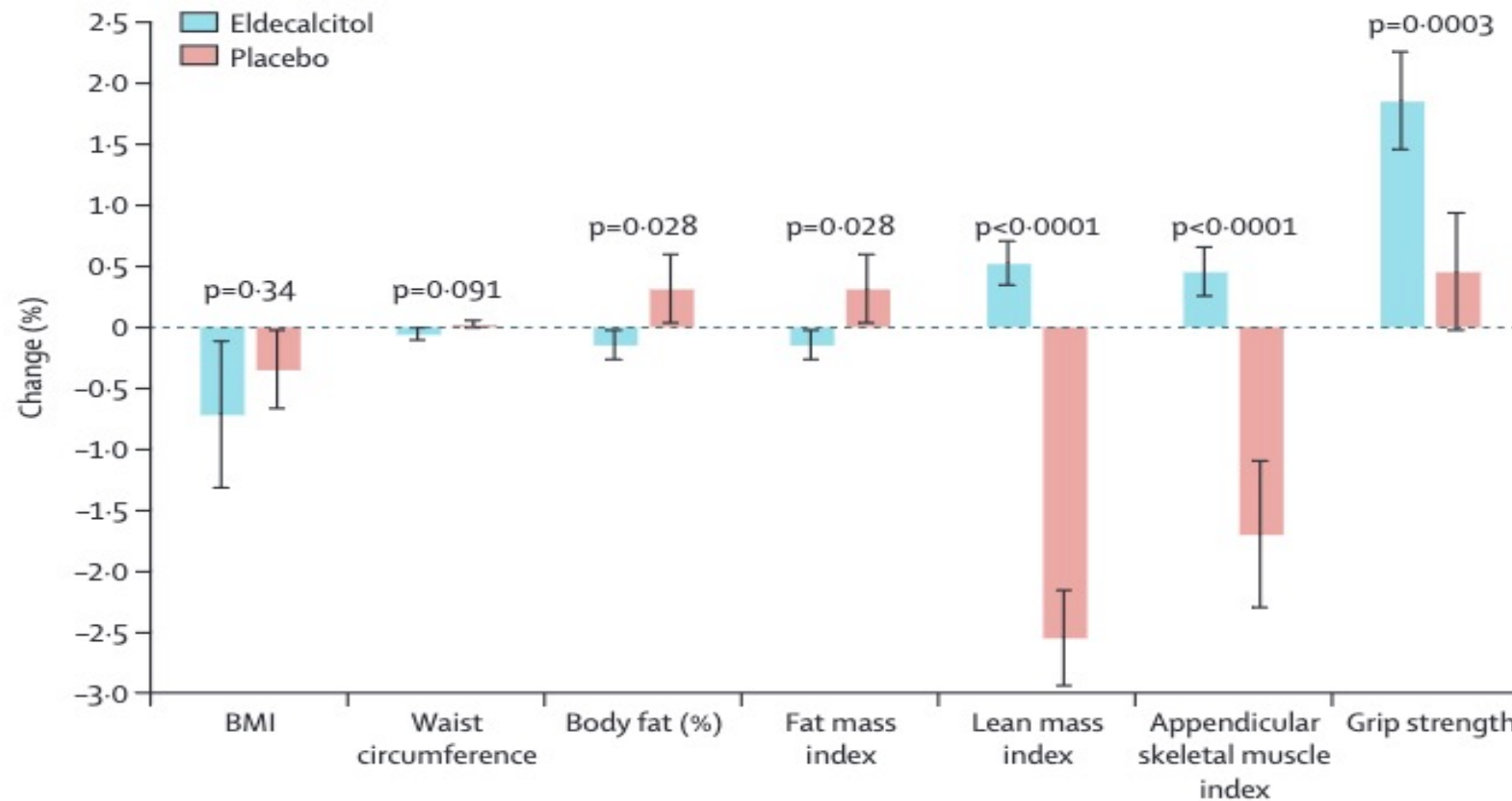


Tetsuya Kawahara, Gen Suzuki, Shoichi Mizuno, Naoki Tominaga, Mikio Toda, Nagahiro Toyama, Tetsuya Inazu, Chie Kawahara, Yosuke Okada, Yoshiya Tanaka



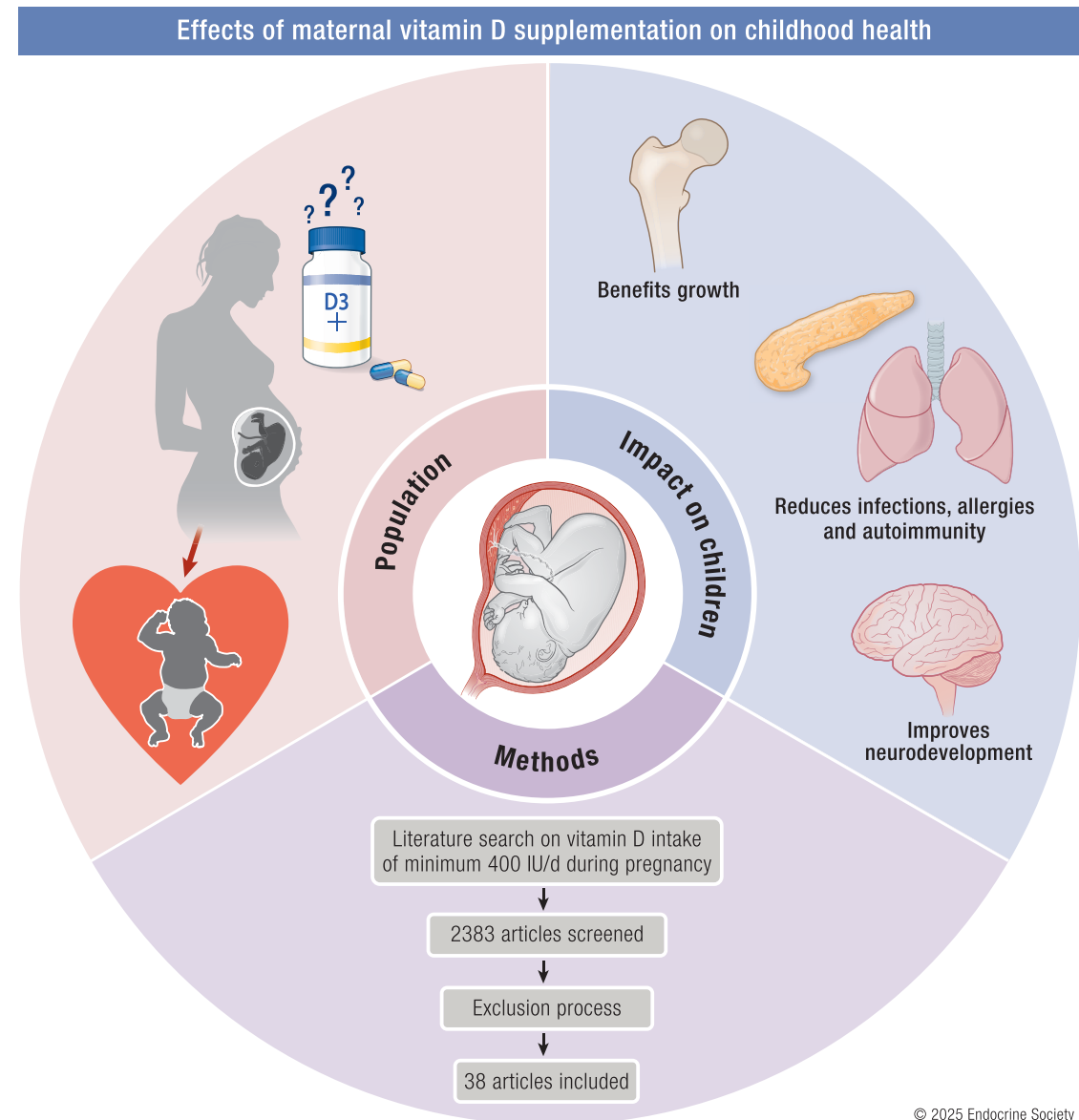
25 OH VIT D  
20± 6 ng/dl

Cambios en la composición corporal



## Effects of Maternal Vitamin D Supplementation on Childhood Health

Nanna S. Svensson,<sup>1,2</sup> Tabia Volqvartz,<sup>2</sup> Anna Louise Vestergaard,<sup>1,2</sup> Esben T. Vestergaard,<sup>2,3</sup> Agnete Larsen,<sup>2,4</sup> and Pinar Bor<sup>2,5</sup>



**Vitamina D 50.000 UI:**  
Corrección rápida y manejo  
inteligente

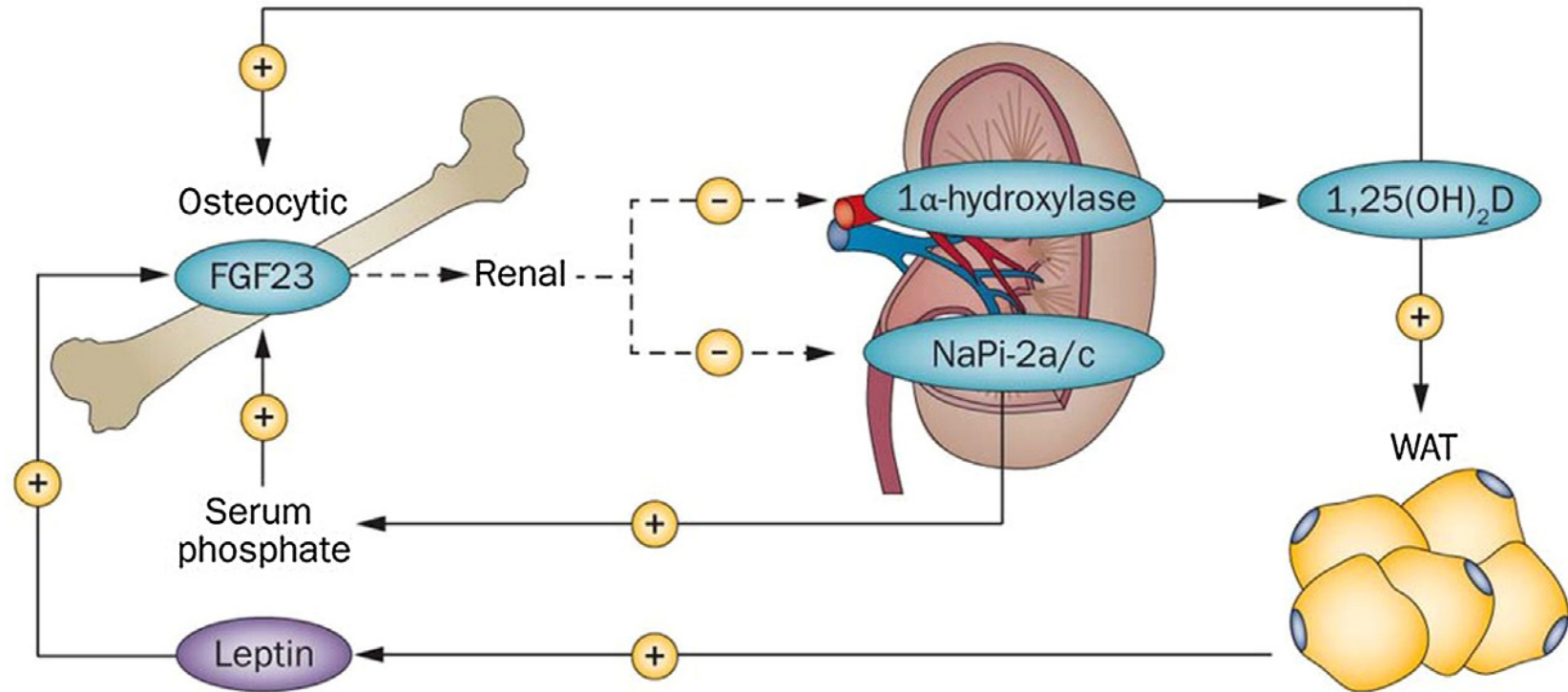




Review

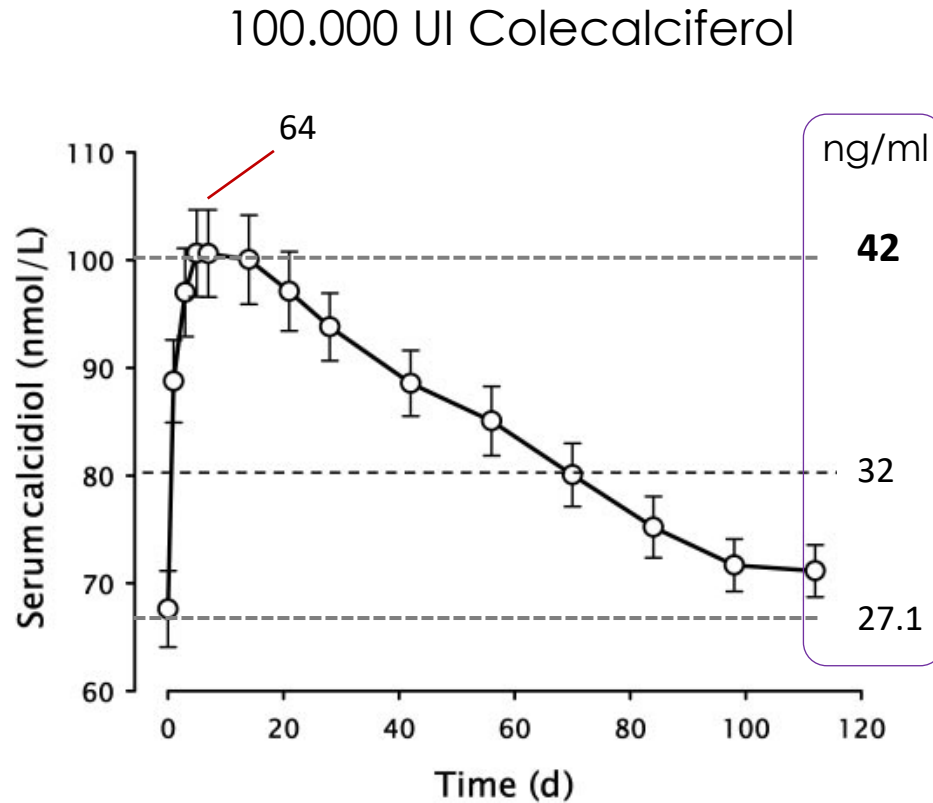
## Physiological functions of Vitamin D in adipose tissue

Manal A. Abbas



## Pharmacokinetics of a single, large dose of cholecalciferol<sup>1-3</sup>

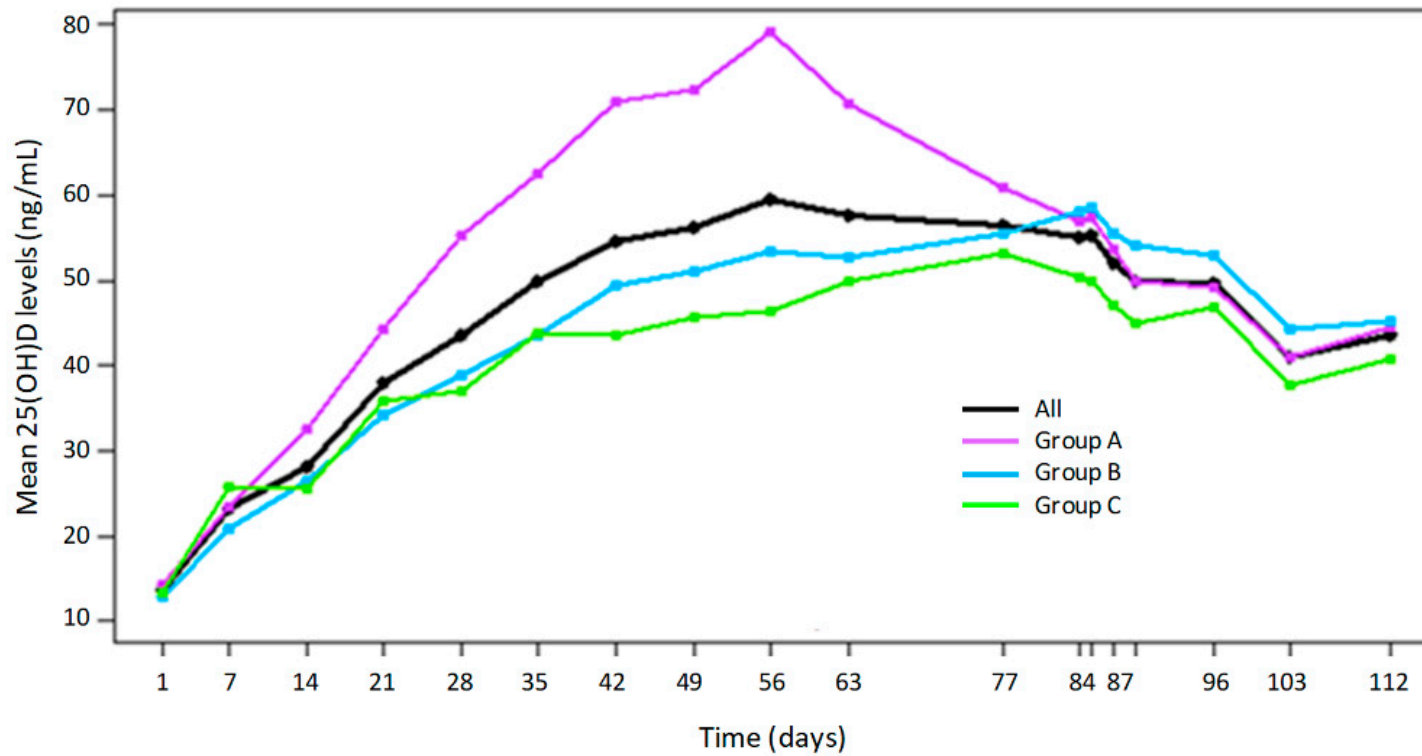
Marium Ilahi, Laura AG Armas, and Robert P Heaney



Serum calcium did not rise at any time point in either age group; in fact, a biologically small but statistically significant fall ( $-0.30 \pm 0.38$  mg/dL) occurred in serum calcium by 5 d after dosing. No subject experienced hypercalcemia at any of the measured time points.

Article

## Pharmacokinetics of Oral Cholecalciferol in Healthy Subjects with Vitamin D Deficiency: A Randomized Open-Label Study



A\_ 10.000 UI día  
B\_ 50.000 /wk  
C\_ 100.000 C/15D

## Pregunta 6

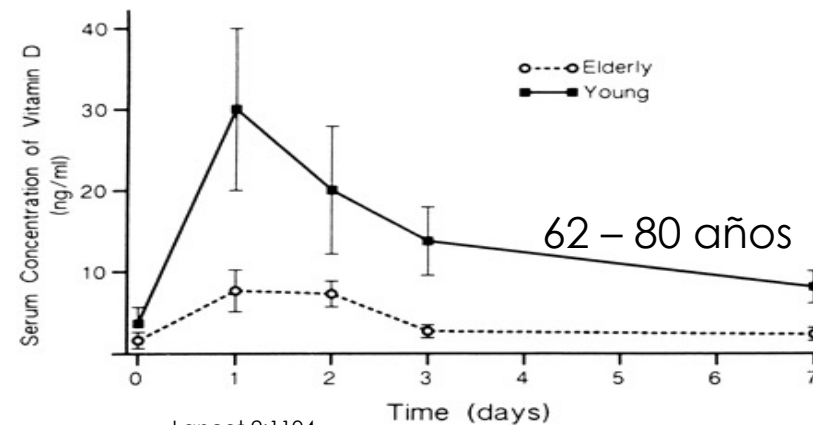
¿Deberían los adultos  $\geq 75$  años utilizar suplementos empíricos de vitamina D versus no suplementar empíricamente con vitamina D?

En la población general de 75 años o más, sugerimos la administración empírica de suplementos de vitamina D debido al potencial de reducir el riesgo de mortalidad.

2 | ⊕○○○

### Vitamin D for the Prevention of Disease: An Endocrine Society Clinical Practice Guideline

Marie B. Demay,<sup>1</sup> Anastassios G. Pittas,<sup>2</sup> Daniel D. Bikle,<sup>3</sup> Dima L. Diab,<sup>4</sup> Mairead E. Kiely,<sup>5</sup> Marise Lazaretti-Castro,<sup>6</sup> Paul Lips,<sup>7</sup> Deborah M. Mitchell,<sup>8</sup> M. Hassan Murad,<sup>9</sup> Shelley Powers,<sup>10</sup> Sudhaker D. Rao,<sup>11,12</sup> Robert Scragg,<sup>13</sup> John A. Tayek,<sup>14,15</sup> Amy M. Valent,<sup>16</sup> Judith M. E. Walsh,<sup>17</sup> and Christopher R. McCartney<sup>18,19</sup>



> 800 UI día

Lancet 2:1104–1105, 1989

# Recomendaciones

Deficiencia (<20 ng/mL):  
50.000 UI/semana × 6–8  
semanas

Insuficiencia (20–30 ng/mL):  
2.000–4.000 UI/día o  
esquemas intermedios

Mantenimiento: 1.000–  
2.000 UI/día (ajustado)

# Fundamento Fisiológico

Vitamina D liposoluble → secuestro en tejido adiposo

Vida media prolongada (25-OH vitamina D ~2–3 semanas)

Dosis bajas no generan gradiente de repleción

# Impacto Clínico

Corrección en 6–8 semanas vs meses con dosis bajas

Reduce riesgo de caídas y fracturas

Mejora función muscular

# Seguridad

50.000 UI/semana  $\approx$  7.000 UI/día

Amplio margen terapéutico

Toxicidad rara ( $<150$  ng/mL)

# Gracias

 @ eldoctorcastillo

[www.eldoctorcastillo.com](http://www.eldoctorcastillo.com)

[jorgecastillomd@hotmail.com](mailto:jorgecastillomd@hotmail.com)

