Vitamina D y COVID 19

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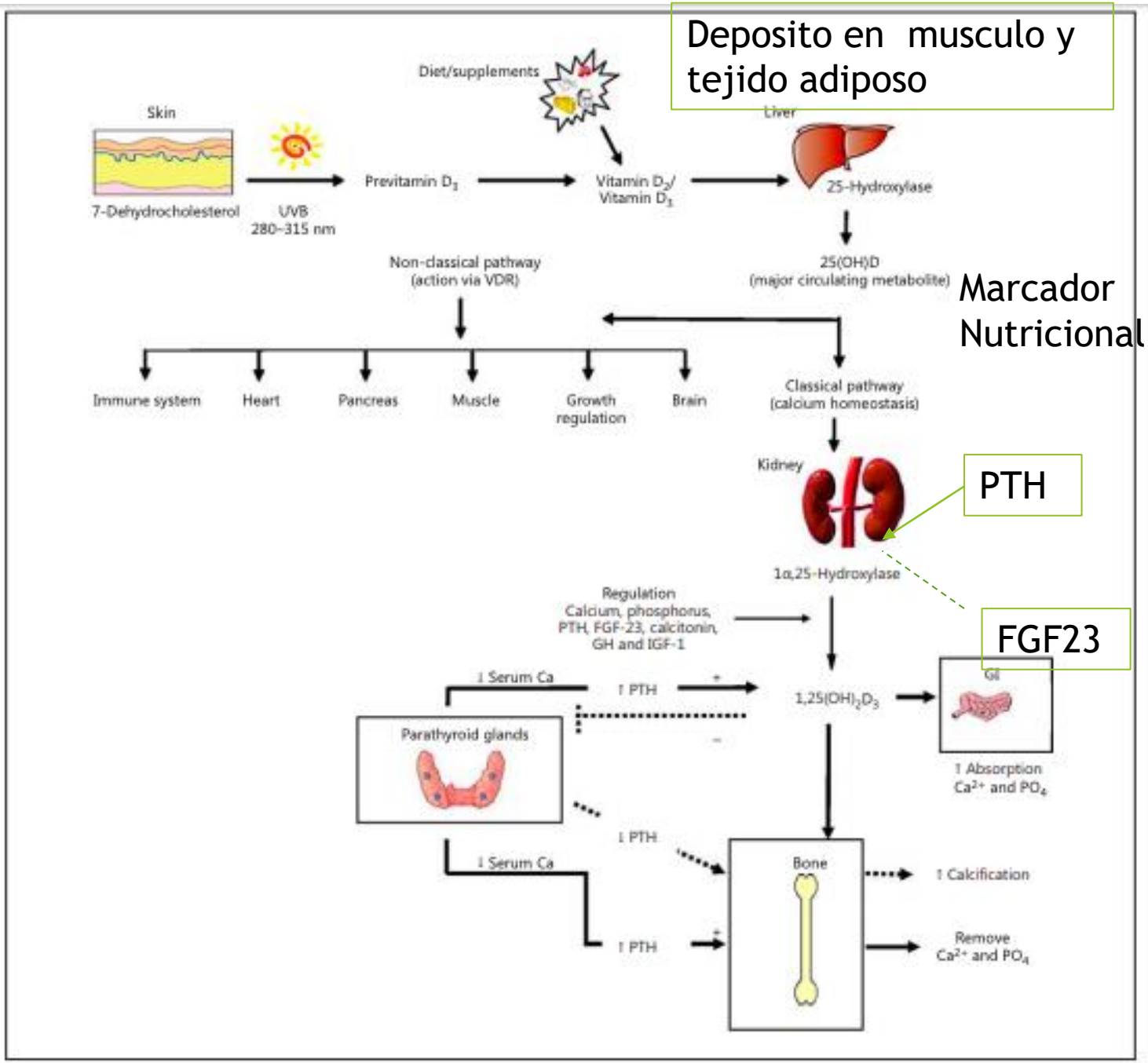
Deposito en musculo y tejido adiposo



Marcador Nutricional

PTH

FGF23

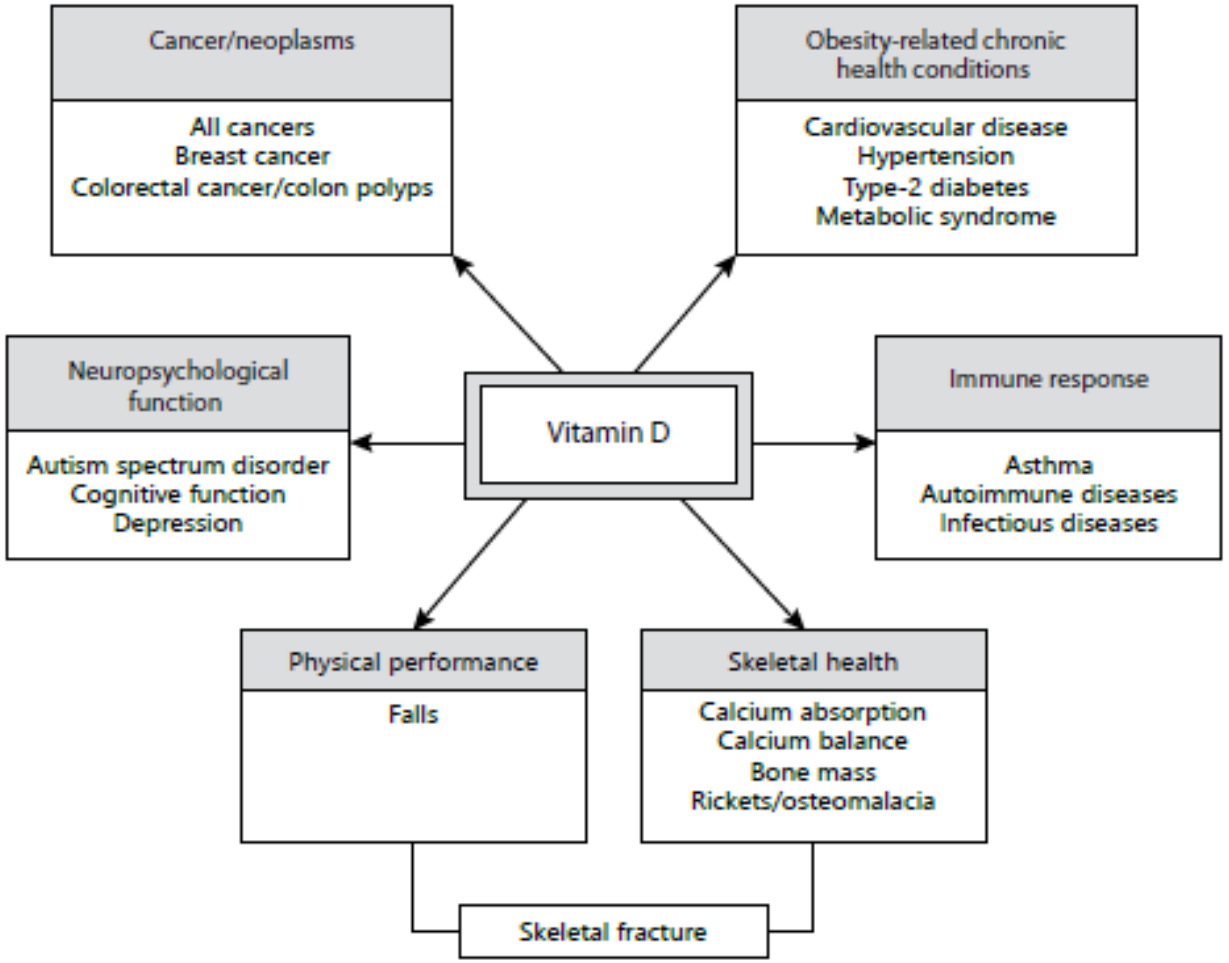
Horm Res Paediatr 2014;81:363–378

Factores que contribuyen

- Externos
  - Latitud
  - Estacion del año
  - Temperatura
  - Polucion
- Personal
  - Edad
  - Pigmentacion de la piel
  - Vestimenta
  - Exposicion solar
  - Geneticas

Niveles optimos de vitamina D

Task force endocrine society 2011 /fasen 2011 /IOF 2010/ IOM 2011 imagen modificada fondo nacional de salud



Giustina A, Bilezikian JP (eds): Vitamin D in Clinical Medicine.
Front Horm Res. Basel, Karger, 2018, vol 50, pp 42–65 (DOI: 10.1159/000486065)

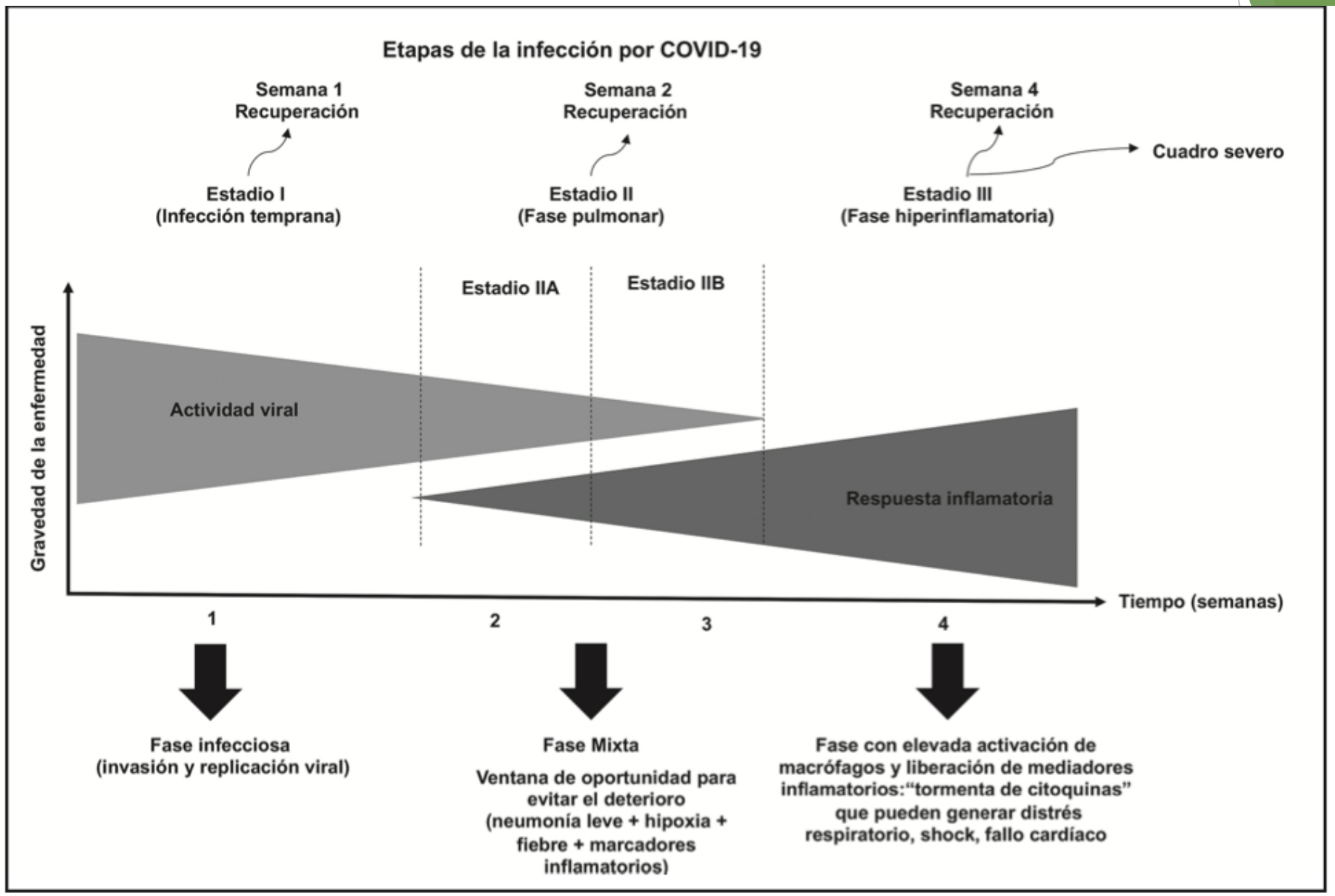
Covid 19

ARN actua como Patron molecular asociado al patógeno (PAMPS)

Union Rs Toll like

Destrucción del alveolo

Activa neutrófilos


Etapas de la infección por COVID-19
Semana 1
Recuperación
Semana 2
Recuperación
Semana 4
Recuperación
Cuadro severo
Estadio I
(Infección temprana)
Estadio II
(Fase pulmonar)
Estadio III
(Fase hiperinflamatoria)
Estadio IIA
Estadio IIB
Gravedad de la enfermedad
Actividad viral
Respuesta inflamatoria
Tiempo (semanas)
1
2
3
4
Fase infecciosa
(invasión y replicación viral)
Fase Mixta
Ventana de oportunidad para evitar el deterioro (neumonía leve + hipoxia + fiebre + marcadores inflamatorios)
Fase con elevada activación de macrófagos y liberación de mediadores inflamatorios:"tormenta de citoquinas" que pueden generar distrés respiratorio, shock, fallo cardíaco

Antecedentes .

Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data

- Es de utilidad
- 25 ensayos controlados aleatorios elegibles (un total de 11 321 participantes, con edades entre 0 y 95 años).
- La suplementación con vitamina D redujo el riesgo de infección aguda del tracto respiratorio entre todos los participantes (odds ratio ajustado 0.88, intervalo de confianza del 95% 0.81 a 0.96; P para heterogeneidad <0.001).

Table 1 | Characteristics of the 25 eligible trials and their participants

Reference	Setting (study duration)	Participants (male:female)	Mean (SD) age, years (range)	25(OH)D			No in intervention: control group	Oral dose of vitamin D_3	ARTI		No entering primary analysis/No randomised (%)
				Assay, EQA scheme	Mean (SD) baseline level, nmol/L (range)	Baseline level <25 nmol/L (%)			Definition	Outcome type	
Li-Ng 2009[41]	USA (3 months)	Healthy adults (34:128)	57.9 (13.6) (21.4-80.6)	RIA (DiaSorin), DEQAS	63.7 (25.5) (16.0-156.0)	3/150 (2.0)	84:78	50 µg daily, placebo	URTI: ≥2 URTI symptoms in absence of allergy symptoms	Primary	157/162 (96.9)
Urashima 2010[27]	Japan (4 months)	Schoolchildren (242:188)	10.2 (2.3) (6.0-15.0)	--	ND	--	217:213	30 µg daily, placebo	URTI: influenza A/B diagnosed by RIDT or RIDT-negative ILI	Primary	334/430 (77.7)
Manaseki-Holland 2010[42]	Afghanistan (3 months)	Preschool children with pneumonia (257:196)	1.1 (0.8) (0.1-3.3)	--	ND	--	224:229	2.5 mg bolus once, placebo	LRTI: repeat episode of pneumonia—age-specific tachypnoea without wheeze	Secondary	453/453 (100.0)
Laaksi 2010[37]	Finland (6 months)	Military conscripts (164:0)	19.1 (0.6) (18.0-21.0)	EIA (IDS OCTEIA)	75.9 (18.7) (41.9-129.0)	0/73 (0.0)	80:84	10 µg daily, placebo	ARTI: medical record diagnosis	Primary	164/164 (100.0)
Majak 2011[43]	Poland (6 months)	Children with asthma (32:16)	10.9 (3.3) (6.0-17.0)	RIA (BioSource Europe), RIQAS	88.9 (38.2) (31.5-184.7)	0/48 (0.0)	24:24	12.5 µg daily, placebo	ARTI: self report	Secondary	48/48 (100.0)
Trilok-Kumar 2011[44]	India (6 months)	Low birthweight infants (970:1109)	0.1 (0.0) (0.0-0.3)	--	ND	ND	1039:1040	35 µg weekly, placebo	ARTI: medical record diagnosis of events resulting in hospital admission	Secondary	2064/2079 (99.3)
Lehouck 2012[15]	Belgium (1 year)	Adults with COPD (145:37)	67.9 (8.3) (48.0-86.0)	RIA (Diasorin), DEQAS	49.8 (29.2) (9.0-159.7)	31/182 (17.0)	91:91	2.5 mg bolus monthly, placebo	URTI: self report	Secondary	175/182 (96.2)
Manaseki-Holland 2012[35]	Afghanistan (1.5 years)	Infants (1591:1455)	0.5 (0.3) (0.0-1.0)	--	ND	ND	1524:1522	2.5 mg bolus 3-monthly, placebo	LRTI: pneumonia confirmed by chest radiography	Primary	3011/3046 (98.9)
Camargo 2012[21]	Mongolia (7 weeks)	3rd/4th grade schoolchildren (129:118)	10.0 (0.9) (7.0-12.7)	LC-MS/MS, DEQAS	18.9 (9.7) (3.3-61.2)	192/245 (78.4)	143:104	7.5 µg daily, placebo	ARTI: parent reported "chest infections or colds"	Secondary	244/247 (98.8)
Murdoch 2012[22]	New Zealand (1.5 years)	Healthy adults (81:241)	48.1 (9.7) (18.0-67.6)	LC-MS/MS, DEQAS	72.1 (22.1) (13.0-142.0)	5/322 (1.6)	161:161	2×5 mg bolus monthly then 2.5 mg bolus monthly, placebo	URTI: assessed with symptom score	Primary	322/322 (100.0)
Bergman 2012[45]	Sweden (1 year)	Adults with increased susceptibility to ARTI (38:102)	53.1 (13.1) (20.0-77.0)	CLA (DiaSorin), DEQAS	49.3 (23.2) (8.0-135.0)	15/131 (11.45)	70:70	100 µg daily, placebo	URTI: assessed with symptom score	Secondary	124/140 (88.6)
Marchisio 2013[46]	Italy (6 months)	Children with recurrent acute otitis media	2.8 (1.0) (1.3-4.8)	CLA (DiaSorin), ISO9001	65.3 (17.3) (24.7-120.6)	2/116 (1.7)	58:58	25 µg daily, placebo	URTI: doctor diagnosed acute otitis media	Primary	116/116 (100.0)

Table 3 | One step individual participant data meta-analysis, proportion of participants experiencing at least one acute respiratory tract infection (ARTI): overall and by subgroup, stratified by dosing frequency

	Bolus dosing						Daily or weekly dosing					
Variables	No of trials*	Proportion with ≥1 ARTI, control group (%)	Proportion with ≥1 ARTI, intervention group (%)	Adjusted odds ratio (95% CI)†	P value	P value for interaction	No of trials*	Proportion with ≥1 ARTI, control group (%)	Proportion with ≥1 ARTI, intervention group (%)	Adjusted odds ratio (95% CI)†	P value	P value for interaction
Overall	10	994/2786 (35.7)	1097/3014 (36.4)	0.97 (0.86 to 1.10)	0.67	--	15	1210/2439 (49.6)	1206/2694 (44.8)	0.81 (0.72 to 0.91)	0.001	--
Baseline 25(OH)D (nmol/L):												
<25	8	73/142 (51.4)	77/162 (47.5)	0.82 (0.51 to 1.33)	0.43	0.42	6	64/107 (59.8)	40/127 (31.5)	0.30 (0.17 to 0.53)	<0.001	0.006
≥25	8	550/910 (60.4)	663/1121 (59.1)	1.02 (0.83 to 1.24)	0.87		11	477/729 (65.4)	516/874 (59.0)	0.75 (0.60 to 0.95)	0.02	
Daily dose equivalent (µg):												
<20	.	.	.	.	.	0.56	5	629/1321 (47.6)	619/1435 (43.1)	0.80 (0.68 to 0.94)	0.006	0.82
20-50	3	467/1931 (24.2)	542/2127 (25.5)	0.95 (0.81 to 1.10)	0.50		6	478/865 (55.3)	481/950 (50.6)	0.81 (0.66 to 1.01)	0.06	
≥50	7	527/855 (61.6)	555/887 (62.6)	1.03 (0.83 to 1.28)	0.81		4	103/253 (40.7)	106/309 (34.3)	0.85 (0.58 to 1.24)	0.39	
Age (years):												
≤1	2	321/1634 (19.6)	322/1637 (19.7)	0.99 (0.83 to 1.19)	0.93	0.72	2	511/1110 (46.0)	532/1190 (44.7)	0.91 (0.77 to 1.08)	0.30	0.37
1.1-15.9	1	50/100 (50.0)	35/93 (37.6)	0.62 (0.35 to 1.11)	0.11		7	191/413 (46.2)	159/473 (33.6)	0.59 (0.45 to 0.79)	<0.001	
16-65	8	432/678 (63.7)	466/716 (65.1)	1.15 (0.90 to 1.48)	0.27		9	422/781 (54.0)	419/876 (47.8)	0.79 (0.63 to 0.99)	0.04	
>65	8	191/374 (51.1)	274/568 (48.2)	0.85 (0.65 to 1.12)	0.25		3	86/135 (63.7)	96/155 (61.9)	0.88 (0.52 to 1.52)	0.66	
Body mass index (kg/m²):												
<25	8	215/372 (57.8)	231/417 (55.4)	1.01 (0.72 to 1.40)	0.97	0.70	11	757/1571 (48.2)	725/1657 (43.8)	0.82 (0.71 to 0.95)	0.009	>0.99
≥25	8	406/677 (60.0)	509/867 (58.7)	1.00 (0.80 to 1.25)	0.98		9	253/358 (70.7)	245/367 (66.8)	0.83 (0.59 to 1.17)	0.30	
Asthma:												
No	5	303/484 (62.6)	323/523 (61.8)	0.95 (0.71 to 1.28)	0.75	0.40	6	215/524 (41.0)	197/578 (34.1)	0.74 (0.58 to 0.95)	0.02	0.40
Yes	4	224/371 (60.4)	232/364 (63.7)	1.18 (0.85 to 1.65)	0.32		7	72/163 (44.2)	53/178 (29.8)	0.60 (0.37 to 0.98)	0.04	
COPD:												
No	5	410/632 (64.9)	436/656 (66.5)	--‡	--‡	--‡	2	67/131 (51.1)	57/135 (42.2)	--‡	--‡	--‡
Yes	4	117/223 (52.5)	119/231 (51.5)	--‡	--‡	--‡	2	5/7 (71.4)	1/7 (14.3)	--‡	--‡	--‡
Influenza vaccination												
No	5	119/163 (73.0)	121/178 (68.0)	--‡	--‡	--‡	5	136/210 (64.8)	132/229 (57.6)	--‡	--‡	--‡
Yes	5	286/396 (72.2)	294/421 (69.8)	.	.	.	5	278/383 (72.6)	283/405 (69.9)			

25(OH)D=25-hydroxyvitamin D; COPD=chronic obstructive pulmonary disease; 1 µg vitamin D_3=40 international units (IU).

*Some trials did not contribute data to a given subgroup, either because individuals within that subgroup were not represented or because data relating to the potential effect modifier were not recorded; accordingly the number of trials represented varies between subgroups.

†Adjusted for age, sex, and study duration.

‡Values could not be estimated as models did not converge.

Table 2 | One step individual participant data meta-analysis, proportion of participants experiencing at least one acute respiratory tract infection (ARTI): overall and by subgroup

Variables	No of trials*	Proportion with ≥1 ARTI, control group (%)	Proportion with ≥1 ARTI, intervention group (%)	Adjusted odds ratio (95% CI)†	P value	P value for interaction
Overall	25	2204/5225 (42.2)	2303/5708 (40.3)	0.88 (0.81 to 0.96)	0.003	--
Baseline 25(OH)D (nmol/L):						
<25	14	137/249 (55.0)	117/289 (40.5)	0.58 (0.40 to 0.82)	0.002	0.01
≥25	19	1027/1639 (62.7)	1179/1995 (59.1)	0.89 (0.77 to 1.04)	0.15	
Dosing regimen type:						
Bolus dose ≥30 000 IU given	10	994/2786 (35.7)	1097/3014 (36.4)	0.97 (0.86 to 1.10)	0.67	0.05
Bolus dose not given	15	1210/2439 (49.6)	1206/2694 (44.8)	0.81 (0.72 to 0.91)	<0.001	
Daily dose equivalent (µg):						
<20	5	629/1321 (47.6)	619/1435 (43.1)	0.80 (0.68 to 0.94)	0.006	0.12
20-50	9	945/2796 (33.8)	1023/3077 (33.2)	0.90 (0.79 to 1.01)	0.08	
≥50	11	630/1108 (56.9)	661/1196 (55.3)	0.98 (0.81 to 1.18)	0.84	
Age (years):						
≤1	4	832/2744 (30.3)	854/2827 (30.2)	0.94 (0.83 to 1.06)	0.33	0.61
1.1-15.9	8	241/513 (47.0)	194/566 (34.3)	0.60 (0.46 to 0.77)	<0.001	
16-65	17	854/1459 (58.5)	885/1592 (55.6)	0.93 (0.79 to 1.10)	0.41	
>65	11	277/509 (54.4)	370/723 (51.2)	0.86 (0.67 to 1.09)	0.21	
Body mass index (kg/m^2):						
<25	19	972/1943 (50.0)	956/2074 (46.1)	0.85 (0.74 to 0.97)	0.02	0.29
≥25	17	659/1039 (63.4)	754/1235 (61.1)	0.95 (0.79 to 1.14)	0.58	
Asthma:						
No	11	518/1008 (51.4)	520/1101 (47.2)	0.82 (0.68 to 0.99)	0.04	0.48
Yes	11	296/534 (55.4)	285/542 (52.6)	0.95 (0.73 to 1.25)	0.73	
COPD:						
No	7	477/763 (62.5)	493/791 (62.3)	1.00 (0.80 to 1.26)	0.98	0.38
Yes	6	122/230 (53.0)	120/238 (50.4)	0.84 (0.57 to 1.24)	0.38	
Influenza vaccination:						
No	10	255/373 (68.4)	253/407 (62.2)	0.74 (0.52 to 1.03)	0.08	0.51
Yes	10	564/779 (72.4)	577/826 (69.9)	0.86 (0.68 to 1.09)	0.22	

25(OH)D=25-hydroxyvitamin D; COPD=chronic obstructive pulmonary disease; 1 µg vitamin D_3=40 international units (IU).
*Some trials did not contribute data to a given subgroup, either because individuals within that subgroup were not represented or because data relating to the potential effect modifier were not recorded; accordingly the number of trials represented varies between subgroups.
†Adjusted for age, sex, and study duration.

SISTEMA INMUNE

Innate immunity and barrier function

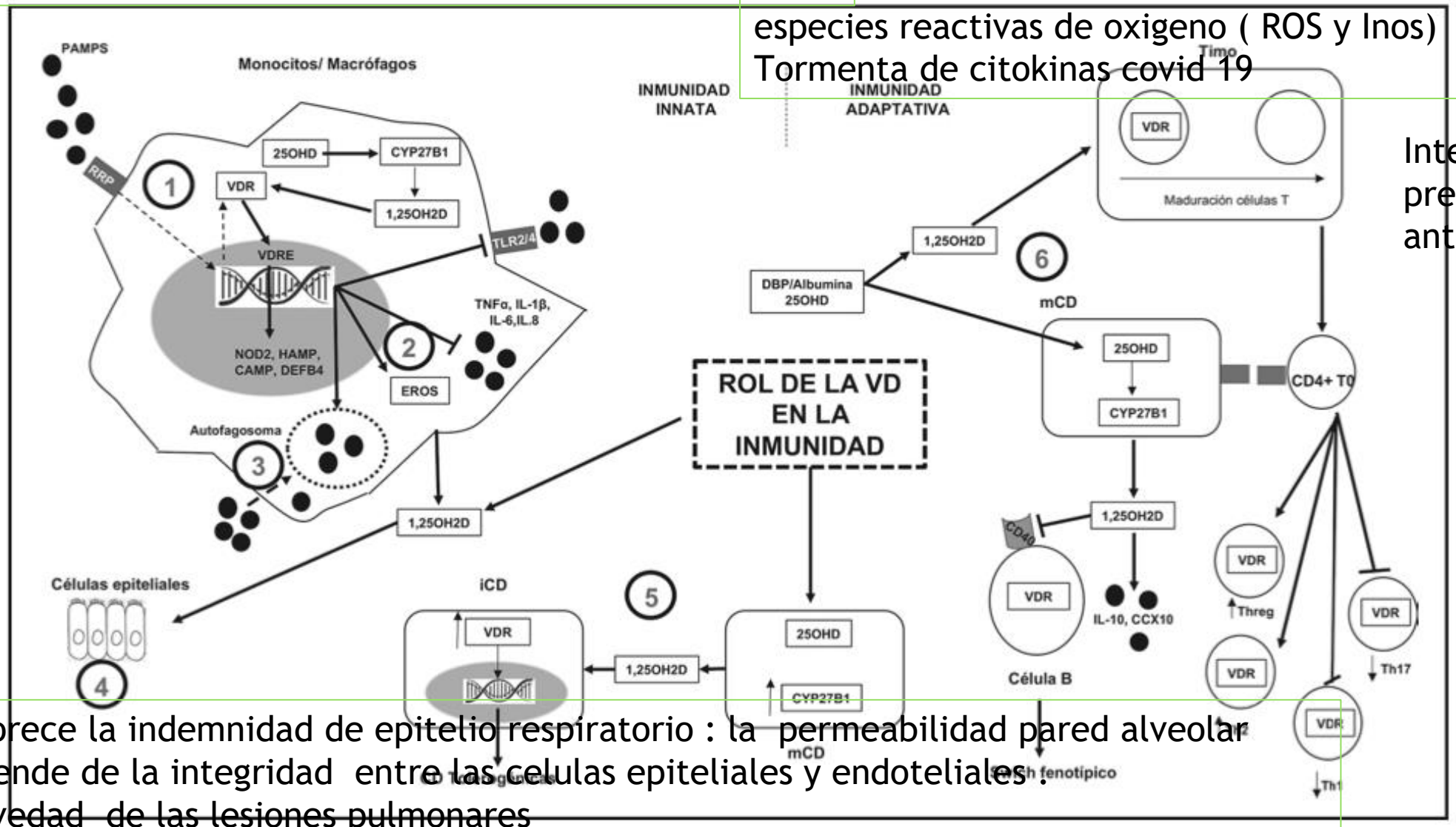
- Maintaining barrier integrity, intracellular functions and cell communication
- ↑ Production and expression of AMPs such as cathelicidin and α defensins from epithelial cells, macrophages and neutrophils
- Recruitment of immune cells, enhance phagocytosis
- ↓ Expression of TLR2 and TLR4 in monocytes
- ↑ Cytolytic activity and number of NK cells
- ↑ Wound healing
- Decrease cytokine inflammatory response

Levis 2018

Mecanismos de acción de la VD implicados en la defensa del organismo en relación con COVID-19

Estimula la Inmunidad Innata = diferenciacion de monocitos a macrofagos y mejora sus capacidad fagocitica y quimiotactica

Favorece la homeostasis en la oxidacion y reduccion celular (redox): Mantienen la funcion mitocondrial normal e inhibir las vias de estrés oxidativos modulando asi la produccion de especies reactivas de oxigeno (ROS y Inos)
Tormenta de citokinas covid 19

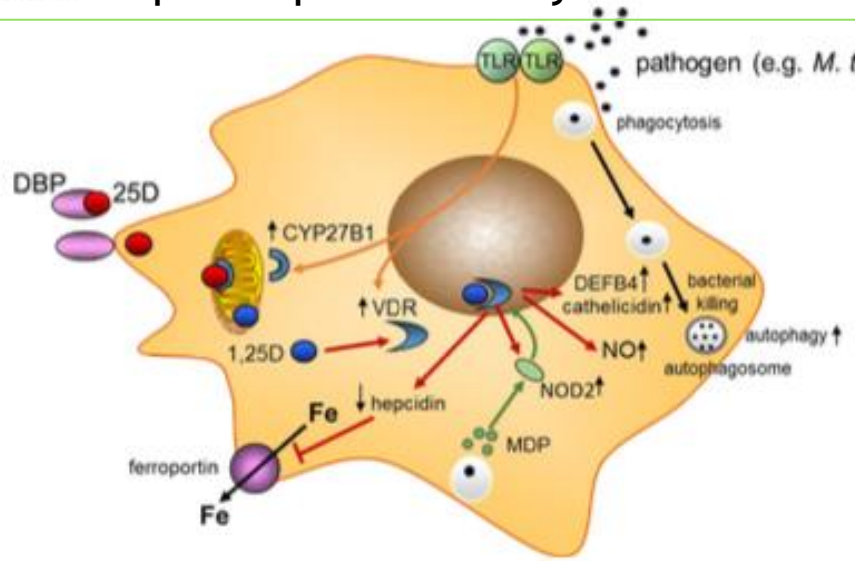


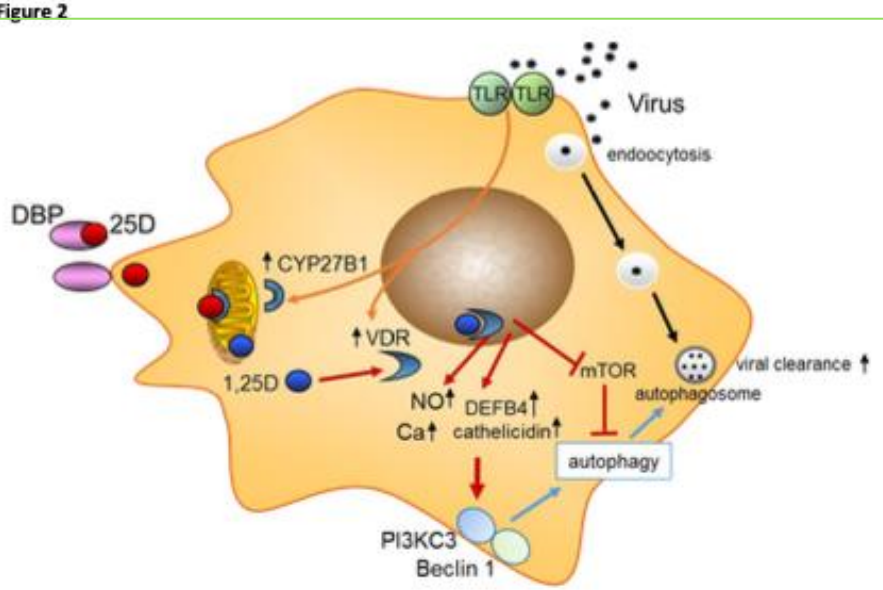
Intermediaria presentacion de antigenos

Favorece la indemnidad de epitelio respiratorio : la permeabilidad pared alveolar depende de la integridad entre las celulas epiteliales y endoteliales :
Gravedad de las lesiones pulmonares
Vit D y Gap

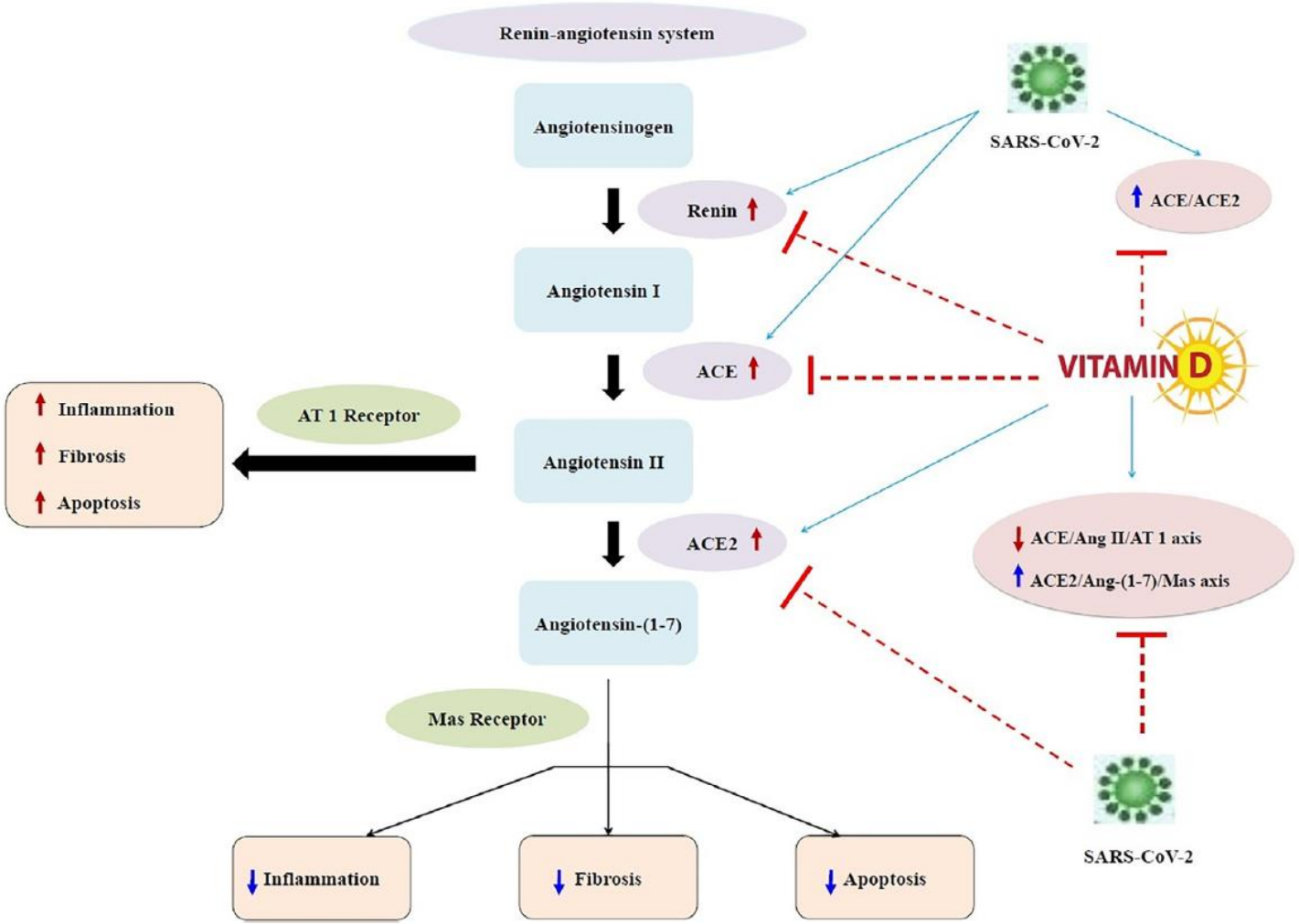
Actualizaciones en osteologia . Oliveri 2020

Promueve el mecanismos de autofagia : mecanismo de degradacion celular que remueve proteinas y organelas dañadas
Vit d : puede inducir autofagia
Covid 19 bloquea estre proceso SKP2
Vit D podria bloquear spk2 disminuyendo el mecanismo de replicacion viral





Bilezikian 2020 Vitamina d and covid 19


Renin-angiotensin system
Angiotensinogen
Renin
Angiotensin I
ACE
Angiotensin II
ACE2
Angiotensin-(1-7)
Mas Receptor
AT 1 Receptor
Inflammation
Fibrosis
Apoptosis
Inflammation
Fibrosis
Apoptosis
SARS-CoV-2
ACE/ACE2
VITAMIN D
ACE/Ang II/AT 1 axis
ACE2/Ang-(1-7)/Mas axis
SARS-CoV-2

Causalidad

- **Plausibilidad biológica**: ¿tiene sentido biológico?
- **Consistencia:** si ***a*** es causa de ***b*** entonces la asociación ***ab*** debe haber sido hallada por distintosinvestigadores en distintos lugares.
- **Temporalidad**: si ***a*** es causa de ***b*** entonces ***a*** es previa a ***b***.
- **Especificidad**: si ***a*** es causa de ***b*** la presencia de ***a*** debe ocasionar ***b*** y ***b*** debe darse solo en presencia de ***a***.
- **Fuerza de asociación:** a mayor intensidad del estímulo mayor intensidad de respuesta

Brunetto 2011

Datos clinicos actuales

Table 2. How vitamin D is related to the clinical and epidemiological findings for incidence and case-fatality rates.

Characteristics	Relation to 25(OH)D	Reference
Clinical		

nutrients

MDPI

Review

Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths

William B. Grant [1,*], Henry Lahore [2], Sharon L. McDonnell [3], Carole A. Baggerly [3], Christine B. French [3], Jennifer L. Aliano [3] and Harjit P. Bhattoa [4]

Higher CFR for cardiovascular disease	Lower 25(OH)D associated with increased risk of incidence and death	[87]
Higher CFR for chronic respiratory disease	For COPD patients, 25(OH)D inversely correlated with risk, severity, and exacerbation	[88]
Found at higher rates in regions with elevated air pollution	Air pollution associated with lower 25(OH)D concentrations	[89]

Note: 25-hydroxyvitamin D ((25(OH)D); acute respiratory distress syndrome (ARDS); community-acquired pneumonia (CAP); case-fatality rate (CFR); interleukin 6 (IL-6); chronic obstructive pulmonary disease (COPD); C-reactive protein (CRP); vitamin D deficiency (VDD).

Table 3. How vitamin D supplementation is related to the clinical and epidemiological findings for treatment.

Clinical Characteristics	Findings from Vitamin D Supplementation Trials	Reference
Treatment of CAP with vitamin D	Did not significantly result in complete resolution. Baseline 25(OH)D was 20 ng/ml. Achieved 25(OH)D in the treatment arm was 40 ng/mL.	[90]
Increased production of pro-inflammatory cytokines such as IL-6	Reduces concentration of IL-6	[11]
Increased CRP	Reduces CRP in diabetic patients	[91]
Increased risk of sepsis	No reduction in mortality rate found for adults with sepsis supplemented with vitamin D. Most trials included participants with 25(OH)D <20 ng/mL; vitamin D_3 doses between 250 and 600 thousand IU.	[92]
Risk of ARDS	Vitamin D deficiency contributes to development of ARDS	[77,93]

Acute respiratory distress syndrome (ARDS); community-acquired pneumonia (CAP); case-fatality rate (CFR); interleukin 6 (IL-6); chronic obstructive pulmonary disease (COPD); C-reactive protein (CRP); vitamin D deficiency (VDD).

- Aunque el grado de protección generalmente aumenta a medida que aumenta la concentración de 25 (OH) D, el rango óptimo parece estar en el rango de 40-60 ng / mL (100-150 nmol / l).
- Sobre la base de estudios observacionales
- HIPOTESIS : Durante la epidemia de COVID-19, todas las personas en el hospital, incluidos los pacientes y el personal, deben tomar suplementos de vitamina D para aumentar las concentraciones de 25 (OH) D como un paso importante para prevenir la infección y la propagación.

Dosis

Por lo tanto, de la literatura, es razonable sugerir tomar 10,000 UI / d durante un mes, lo que es efectivo para aumentar rápidamente los niveles circulantes de 25 (OH) D en el rango preferido de 40-60 ng / ml. Para mantener ese nivel después de ese primer mes, la dosis puede reducirse a 5000 UI / d

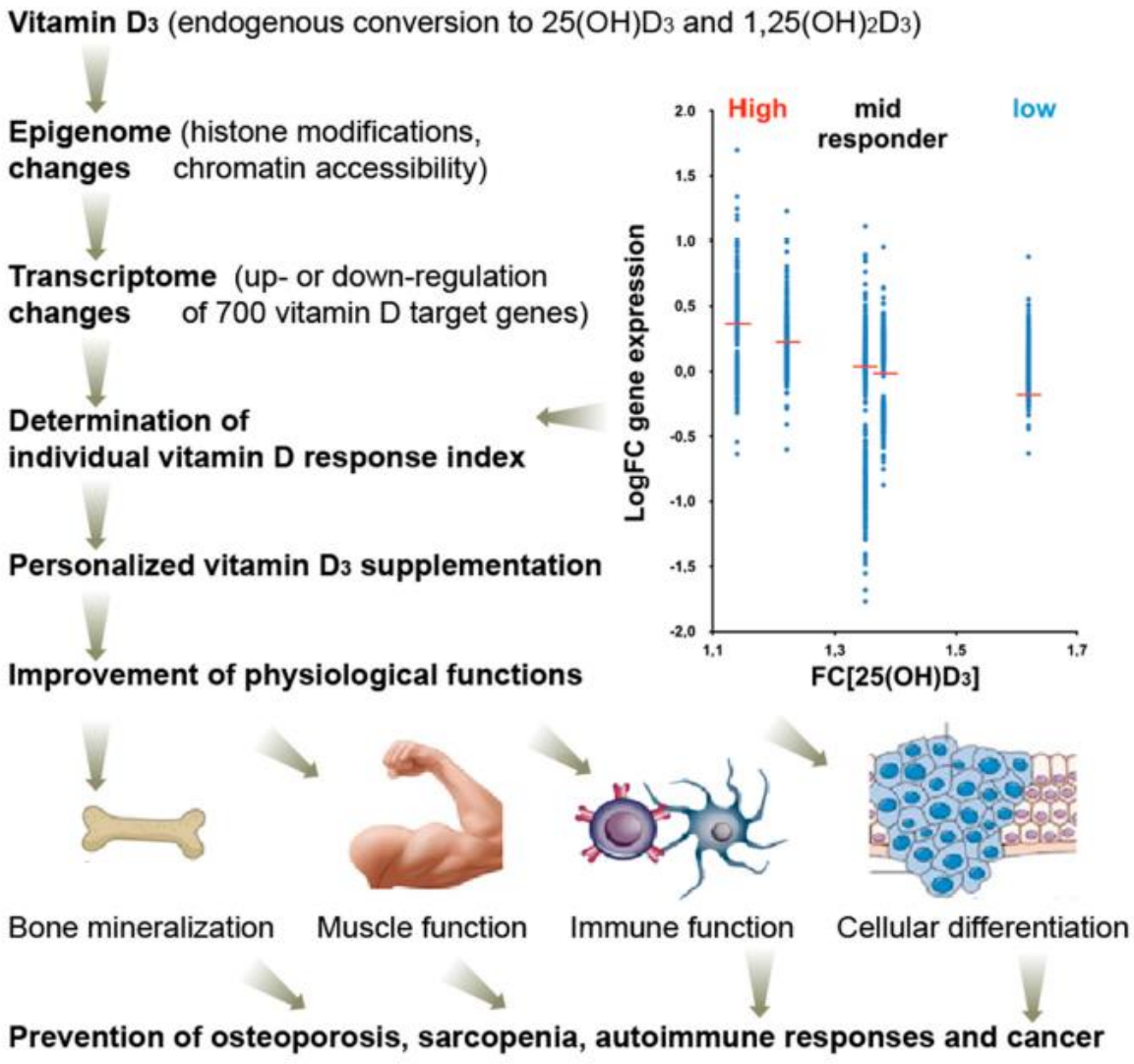
Cuando se toman altas dosis de vitamina D, los suplementos de calcio no deben ser altos para reducir el riesgo de hipercalcemia.

Una revisión reciente sugirió utilizar dosis de carga de vitamina D de 200,000 a 300,000 UI en cápsulas de 50,000 UI para reducir el riesgo y la gravedad de COVID

Seguridad

- La eficacia y seguridad de la suplementación con altas dosis de vitamina D se ha demostrado en un hospital psiquiátrico en Cincinnati, Ohio .
- El rango de edad fue de 18 a 90 años. La mitad de los pacientes eran negros y casi la mitad eran blancos. **Todos** los pacientes que ingresaron desde 2011 recibieron suplementos de 5000 o 10,000 UI / d de vitamina D3. Para 36 pacientes que recibieron 5000 UI / día durante 12 meses o más, la concentración media de 25 (OH) D en suero aumentó de 24 a 68 ng / ml, mientras que para los 78 pacientes que recibieron 10,000 UI / día, las concentraciones medias aumentaron de 25 a 96 ng / ml. No se informaron casos de hipercalcemia inducida por vitamina D
- Un ensayo en el que participaron pacientes canadienses con **cáncer de mama** con metástasis óseas tratadas con bifosfonatos pero sin afecciones comórbidas informó que las dosis de 10.000 UI / día de vitamina D3 durante un período de cuatro meses no mostraron efectos adversos, pero desenmascararon dos casos de **hiperparatiroidismo primario**
- **Necesitamos clinical trials**

Efectos clínicos de la vitamina D



Calberg 2019

Vitamin D supplementation could possibly improve clinical outcomes of patients infected with Coronavirus-2019 (Covid-2019)

Mark M. Alipio

Table 1. Descriptive statistics

Variables	Overall N (%)	Clinical Outcomes				
		Mild	Ordinary	Severe	Critical	p-value
Overall N (%)	212 (100.0)	49 (23.1)	59 (27.8)	56 (26.4)	48 (22.6)	
Serum (OH)D, ng/ml	23.8	31.2	27.4	21.2	17.1	<0.001
Vitamin D status						
Normal	55 (25.9)	47 (85.5)	4 (7.3)	2 (3.6)	2 (3.6)	<0.001
Insufficient	80 (37.7)	1 (1.3)	35 (43.8)	23 (28.8)	21 (26.3)	
Deficient	77 (36.3)	1 (1.4)	20 (26.0)	31 (40.3)	25 (32.5)	

Table 2. Multinomial logistic regression analysis

Predictor	Mild	OR	p-value
Serum (OH)D, ng/ml	Ordinary	0.614	0.007
	Severe	0.126	<0.001
	Critical	0.051	<0.001

Note: OR = odds ratio associated with the effect of a one standard deviation increase in the predictor.

Open Access Brief Report

25-Hydroxyvitamin D Concentrations Are Lower in Patients with Positive PCR for SARS-CoV-2

by Antonio D'Avolio [1,*], Valeria Avataneo [1], Alessandra Manca [1], Jessica Cusato [1], Amedeo De Nicolò [1], Renzo Lucchini [2], Franco Keller [2] and Marco Cantù [2]

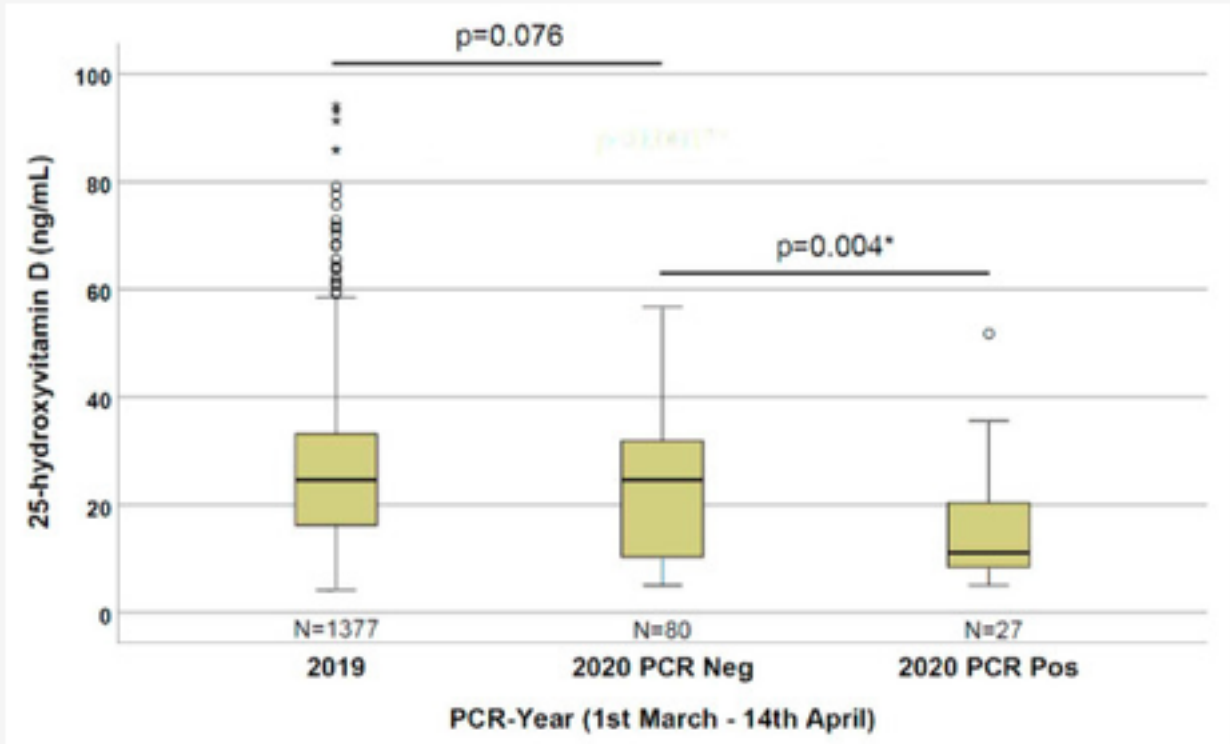


Figure 1

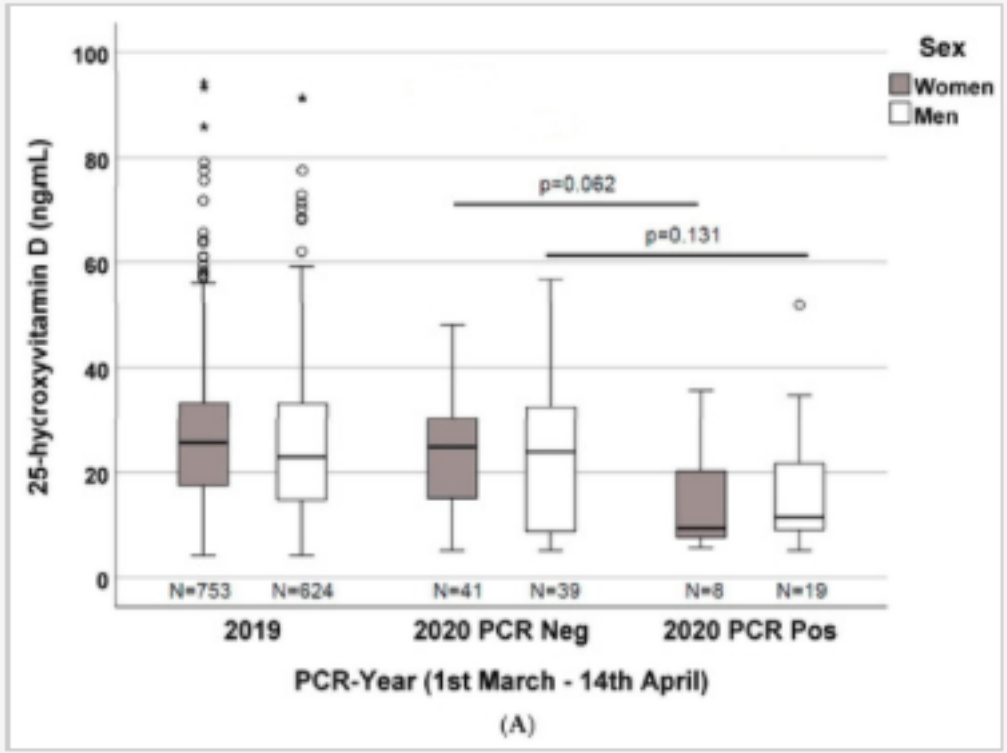


Figure 2

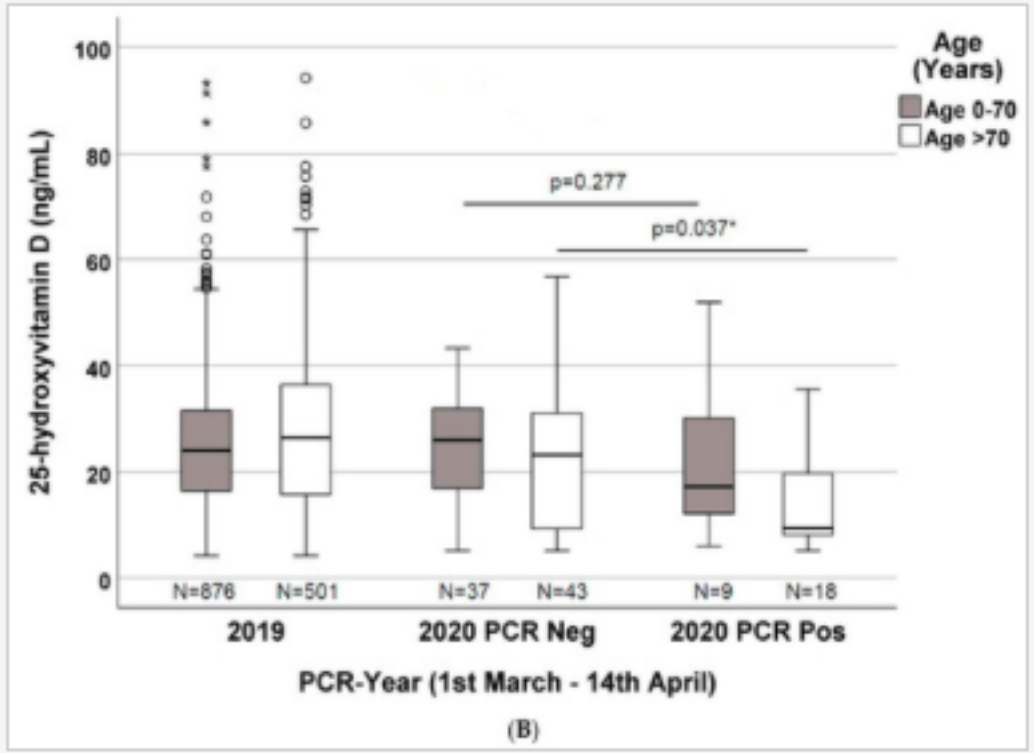


Figure 2 Cont.

RESEARCH ARTICLE

SARS-CoV-2 positivity rates associated with circulating 25-hydroxyvitamin D levels

Harvey W. Kaufman[1], Justin K. Niles[1], Martin H. Kroll[1], Caixia Bi[1], Michael F. Holick[2]*

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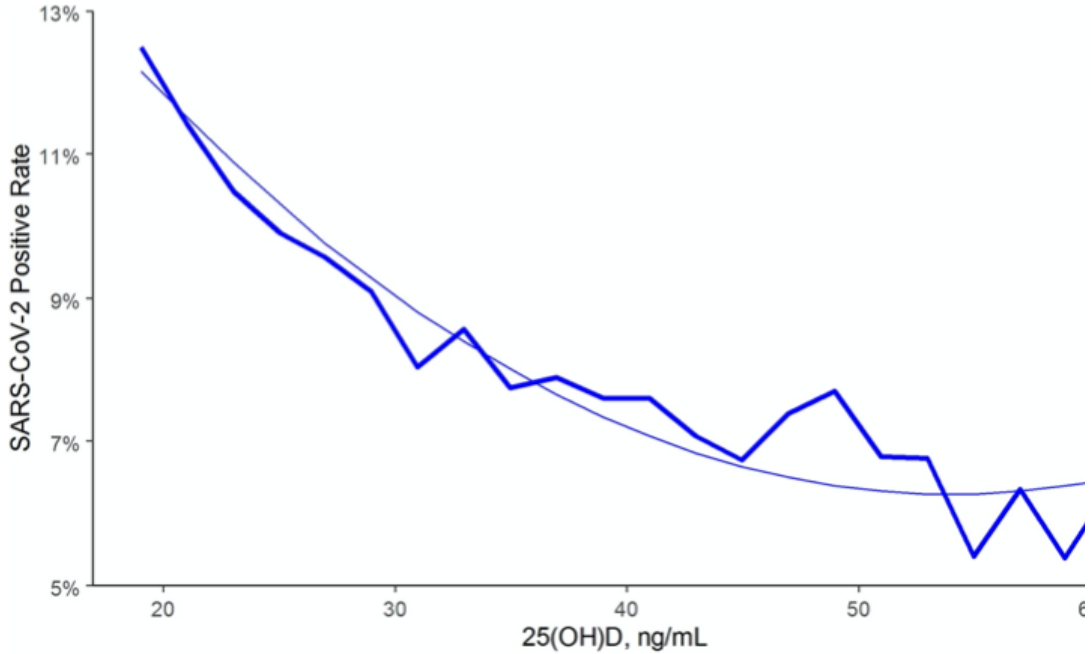
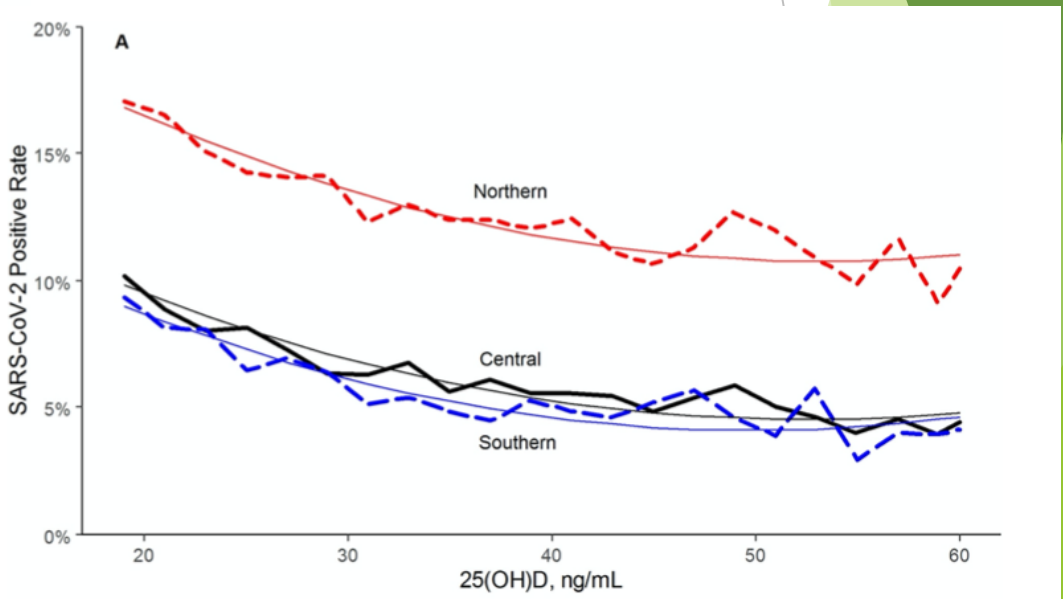
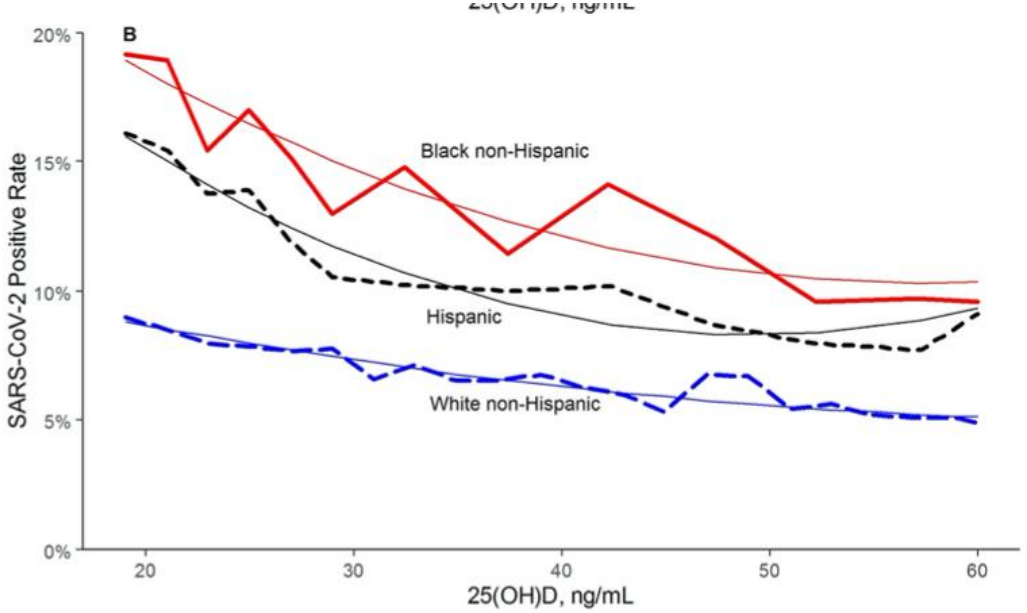
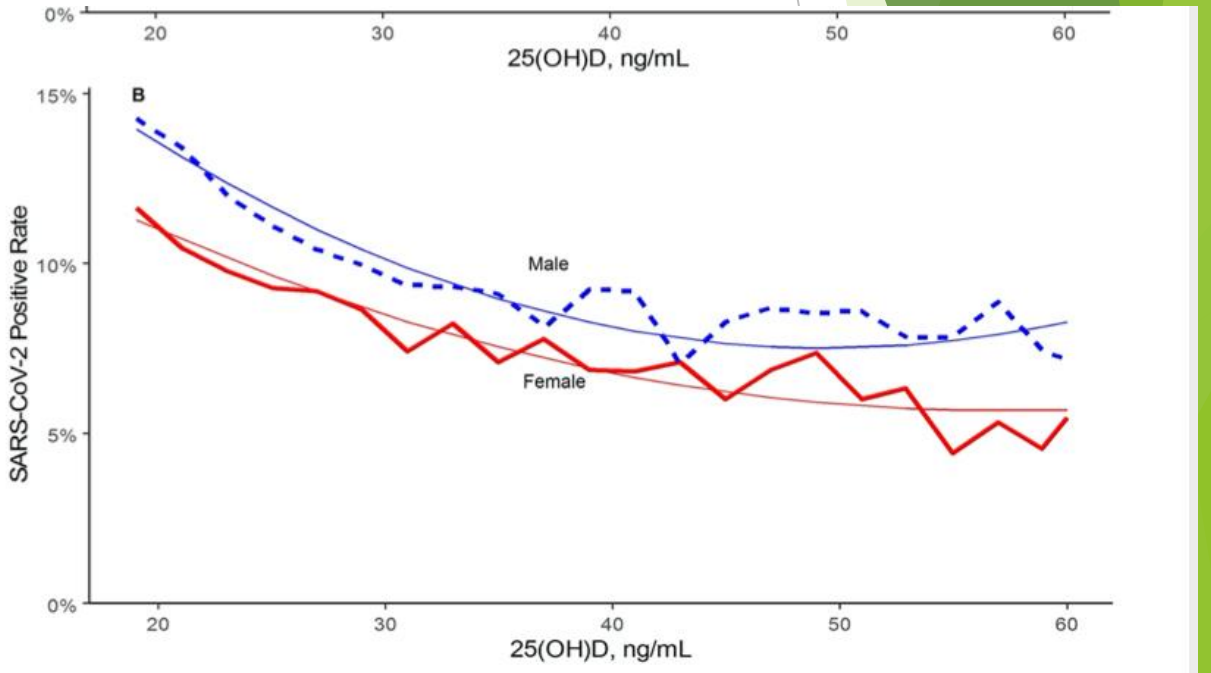
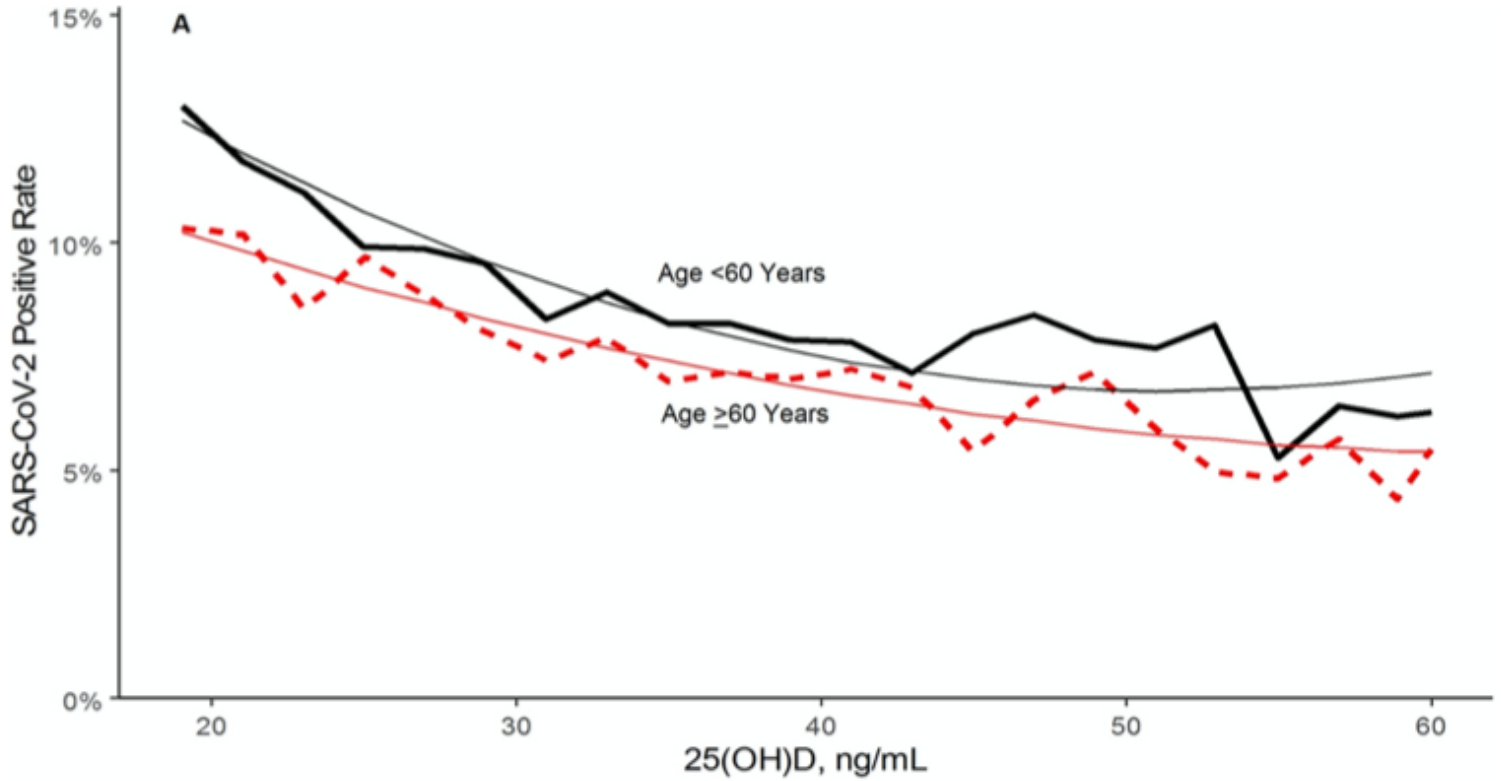


Fig 1. SARS-CoV-2 NAAT positivity rates and circulating 25(OH)D levels in the total population. Smooth line represents the weighted second order polyno regression fit to the data associating circulating 25(OH)D levels (x) and SARS-CoV-2 positivity rates (y) where: $y = 0.2029–0.0052^{*}x + 4.8e\text{-}05^{*}x^2$; $R^2 = 0.96$. SI conversion factor: 1 ng/mL = 0.400641 nmol/L.




B
20%
15%
10%
5%
0%
SARS-CoV-2 Positive Rate
Black non-Hispanic
Hispanic
White non-Hispanic
20
30
40
50
60
25(OH)D, ng/mL


0%
20
30
40
50
60
25(OH)D, ng/mL
B
15%
10%
5%
0%
SARS-CoV-2 Positive Rate
Male
Female
20
30
40
50
60
25(OH)D, ng/mL


A
15%
10%
5%
0%
SARS-CoV-2 Positive Rate
Age <60 Years
Age ≥60 Years
20
30
40
50
60
25(OH)D, ng/mL

- En la actualidad ya se encuentran en realización protocolos de suplementación de VD controlados con placebo en pacientes con COVID-19, cuyos resultados no han sido publicados a la fecha.

	Title	Status	Study Results	Conditions	Interventions	Locations
1	COvid-19 and Vitamin D Supplementation: a Multicenter Randomized Controlled Trial of High Dose Versus Standard Dose Vitamin D3 in High-risk COVID-19 Patients (CoVitTrial)	Recruiting	No Results Available	·Coronavirus	·Drug: cholecalciferol 200,000 IU ·Drug: cholecalciferol 50,000 IU	·CHU Angers, Angers, France ·CHU Bordeaux, Bordeaux, France ·CH Le Mans, Le Mans, France ·CHU Lille, Lille, France ·CHU Limoges, Limoges, France ·CHU Nantes, Nantes, France ·CHU Nice, Nice, France ·CHU Saint Etienne, Saint Etienne, France ·CH Saumur, Saumur, France ·CHU Tours, Tours, France
2	Investigating the Role of Vitamin D in the Morbidity of COVID-19 Patients	Not yet recruiting	No Results Available	·COVID-19 ·Vitamin D Deficiency		·Tameside Hospital NHS Foundation Trust, Ashton-under-Lyne, Greater Manchester, United Kingdom
3	BREATH: Vitamin D Polymorphisms and Severity of COVID-19 Infection	Not yet recruiting	No Results Available	·COVID-19	·Other: Exposure	·Cardiovascular Center at Universidade de Lisboa, Lisbon, Lisboa, Portugal ·Centro Hospitalar Universitário Lisboa Norte, Lisbon, Lisboa, Portugal ·Centro Hospitalar de São João, Oporto, Portugal
4	Vitamin D and COVID-19 Management	Not yet recruiting	No Results Available	·COVID-19	·Dietary Supplement: Ergocalciferol ·Dietary Supplement: Vitamin D3	
5	Vitamin D on Prevention and Treatment of COVID-19	Not yet recruiting	No Results Available	·Patients Infected With COVID-19	·Dietary Supplement: Vitamin D	·Universidad de Granada, Granada, Andalucia, Spain ·Medicine Faculty, Granada, Spain
6	The LEAD COVID-19 Trial: Low-risk, Early Aspirin and Vitamin D to Reduce COVID-19 Hospitalizations	Not yet recruiting	No Results Available	·COVID ·Vitamin D Deficiency ·Coagulopathy ·Disseminated Intravascular Coagulation	·Drug: Aspirin 81 mg ·Dietary Supplement: Vitamin D	
7	Impact of Zinc and Vitamin D3 Supplementation on the Survival of Aged Patients Infected With COVID-19	Not yet recruiting	No Results Available	·SARS-CoV 2	·Dietary Supplement: Zinc gluconate ·Dietary Supplement: 25-OH cholecalciferol	
8	A Study of Hydroxychloroquine, Vitamin C, Vitamin D, and Zinc for the Prevention of COVID-19 Infection	Not yet recruiting	No Results Available	·COVID-19 ·Coronavirus Infection ·Sars-CoV2 ·Corona Virus Infection ·COVID ·Coronavirus ·Coronavirus-19 ·Coronavirus 19	·Drug: Hydroxychloroquine ·Dietary Supplement: Vitamin C ·Dietary Supplement: Vitamin D ·Dietary Supplement: Zinc	·ProgenaBiome, Ventura, California, United States
9	Oral 25-hydroxyvitamin D3 and COVID-19	Recruiting	No Results Available	·COVID 19	·Drug: Oral 25-Hydroxyvitamin D3	·Tehran University of Medical Sciences, Tehran, Iran, Islamic Republic of

Características generales de los estudios

- Problemas de diseño (adultos-niños)
- Falta de registro niveles previos de vitamina D
- Diferentes dosis /vía
- Factores confusores /sesgos

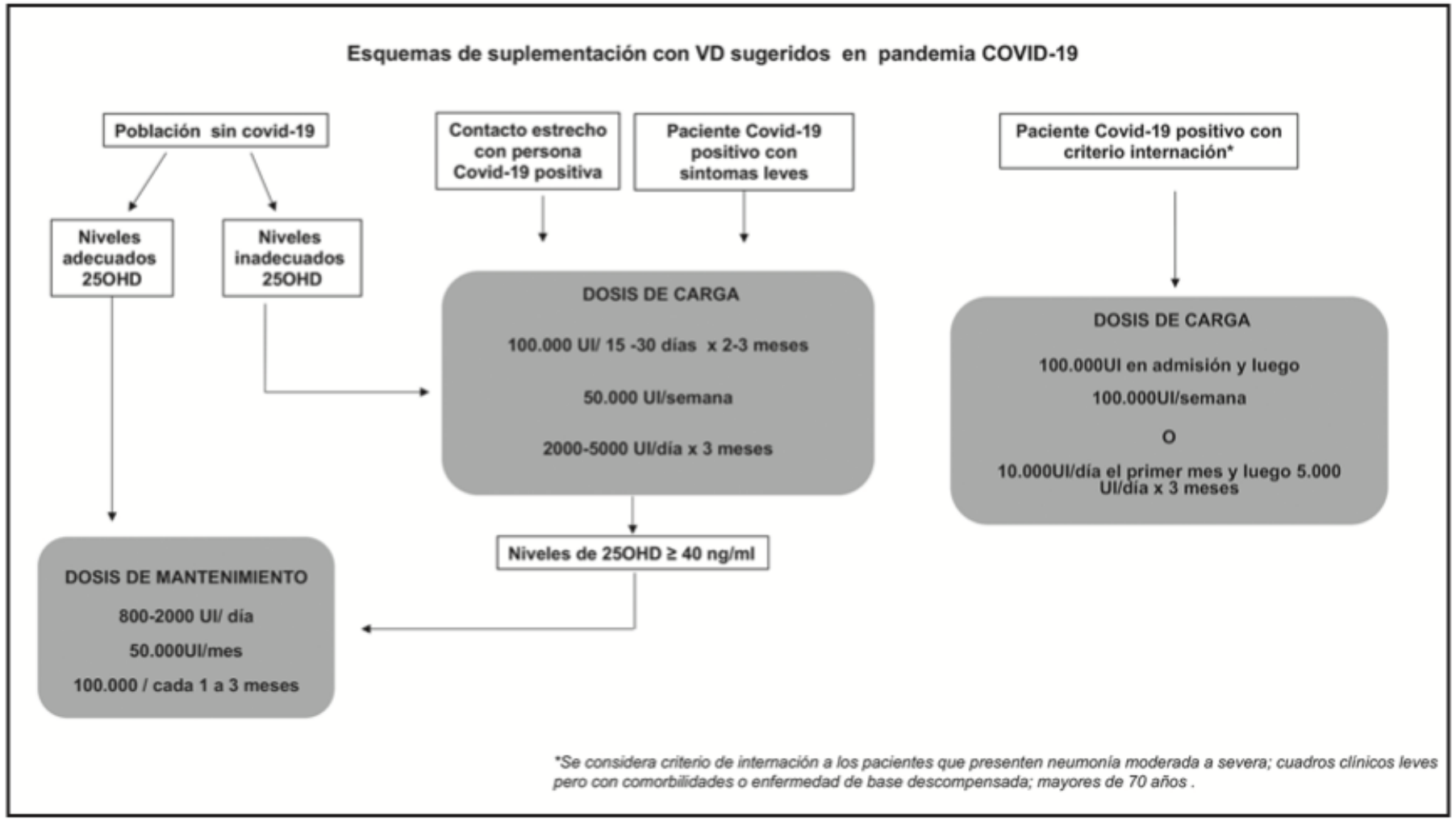


Figura 4. Esquema de suplementación con VD propuesto para la pandemia por COVID-19 en los diferentes grupos poblacionales.

Conclusiones

- Los datos clínicos disponibles, en resumen, son todavía muy preliminares con respecto al estado de vitamina D y la enfermedad COVID-19.
- Muchos informes, hasta la fecha, se han publicado sin una rigurosa revisión por pares, son retrospectivos y solo asociativos. Por tanto, es necesario tener precaución al interpretar los datos. No obstante, las publicaciones recientes muestran de forma consistente una mayor prevalencia de deficiencia de vitamina D en pacientes que presentan formas graves de COVID-19 .
- Además, los supuestos mecanismos que subyacen al papel de la vitamina D en la inmunidad y las acciones no esqueléticas proporcionarían apoyo a la hipótesis planteada de que la deficiencia de vitamina D es un factor de riesgo para la enfermedad y / o su resultado adverso. Por otro lado, en países como India y Lituania donde la deficiencia de vitamina D está generalizada, la incidencia de la enfermedad COVID-19 no es tan alta como cabría esperar . Claramente, hay otros factores a considerar que incluyen no solo los factores de riesgo establecidos sino también las medidas locales de salud pública que se toman para controlar la propagación del virus SARS-CoV-2.
- Se está registrando un número creciente de ensayos clínicos para investigar el efecto de la suplementación con vitamina D o los niveles de 25-OHD en varios resultados de COVID-19 . Hasta que se conozcan los resultados de estos ensayos, una medida de salud general prudente es garantizar la suficiencia de vitamina D. Para la mayoría de las personas en todo el mundo, esta recomendación viene con la necesidad de suplementos de vitamina D para mantener niveles circulantes adecuados de 25-OHD.

Gracias por su atención