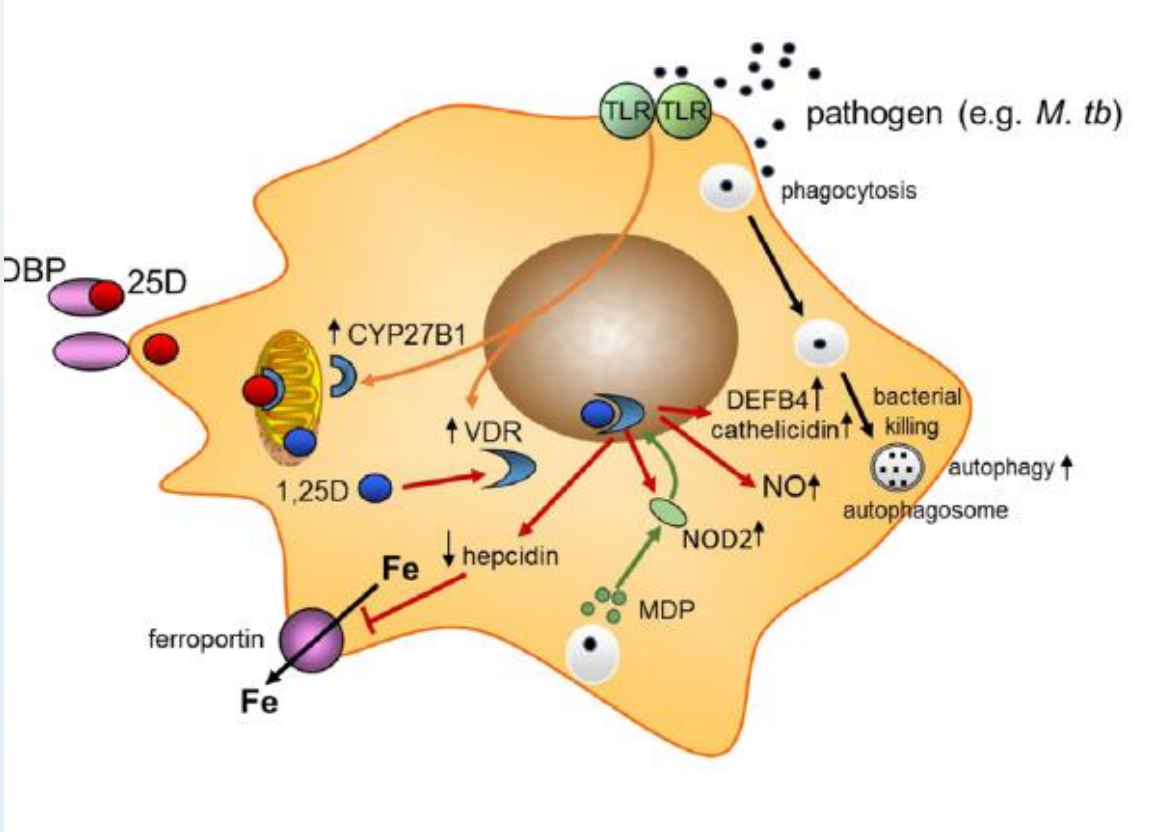
COVID 19 και βιταμίνη D

Ελευθεριάδου Φοίβη Αντιγόνη
Ρευματολόγος

Vitamin D and COVID-19

John P Bilezikian[1], Daniel Bikle[2], Martin Hewison[3], Marise Lazaretti-Castro[4], Anna Maria Formenti[5], Aakriti Gupta[6,7,8], Mahesh V Madhavan[6,7], Nandini Nair[1], Varta Babalyan[9], Nicholas Hutchings[10], Nicola Napoli[11,12], Domenico Accili[1], Neil Binkley[13], Donald W Landry[14] and **Andrea Giustina[5]**

Αντιμικροβιακή δράση της βιταμίνης D

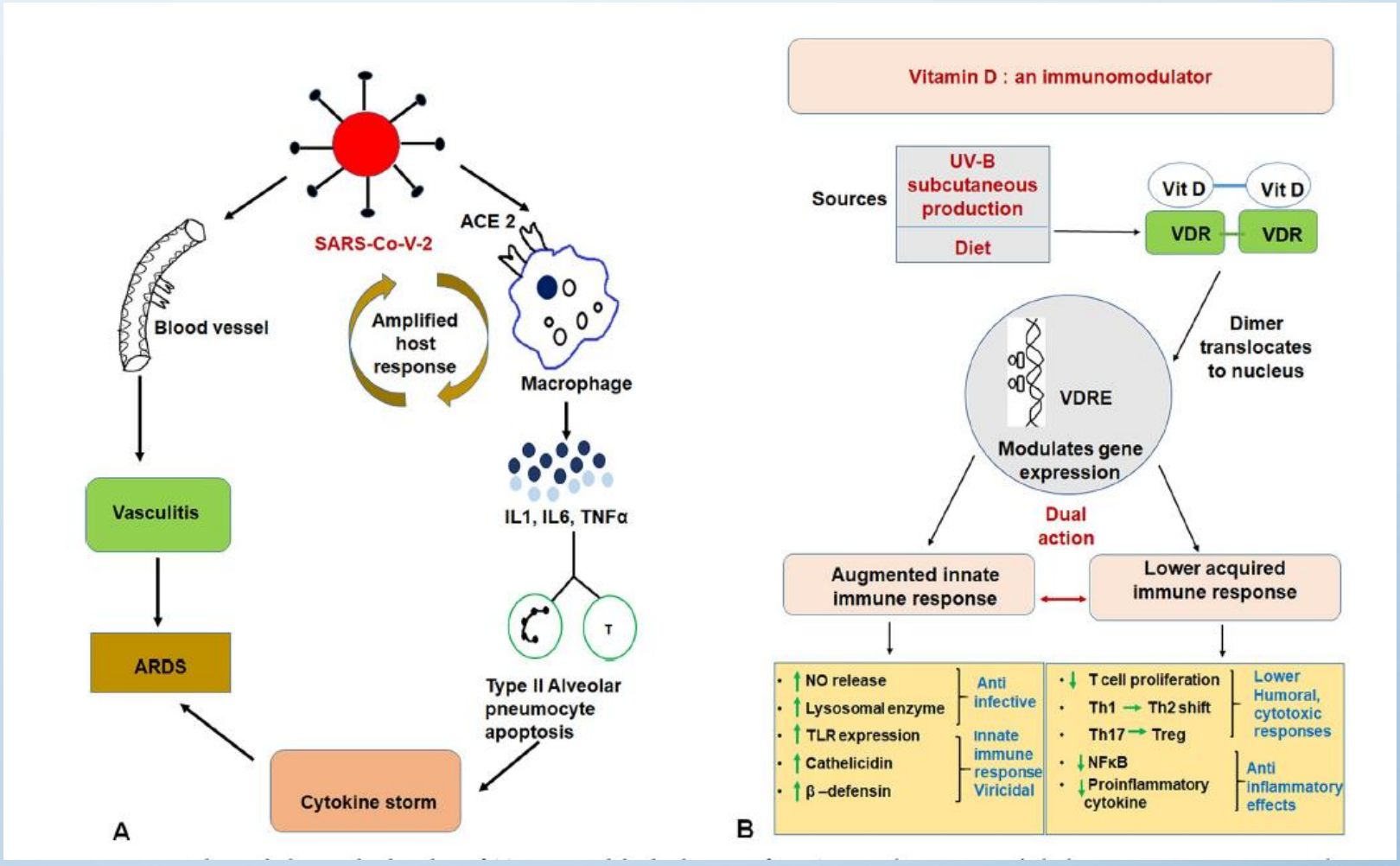


European journal of endocrinology 2020

Exploring links between vitamin D deficiency and COVID-19

Mradul Mohan[1☯], Jerin Jose Cherian[2☯], Amit Sharma[1,3*]

1 Parasite-Host Biology Group, National Institute of Malaria Research, New Delhi, India, 2 Division of Basic Medical Sciences, Indian Council of Medical Research, New Delhi, India, 3 Structural Parasitology Group, International Centre for Genetic Engineering and Biotechnology, New Delhi, India



Vitamin D and survival in COVID-19 patients: A quasi-experimental study

Cédric Annweiler [a,b,c,*], Bérangère Hanotte [d], Claire Grandin de l'Eprevier [e], Jean-Marc Sabatier [f], Ludovic Lafaie [d], Thomas Célarier [d,g,h]

- Μία δόση από το στόμα 80000 IU vitD μέχρι ένα μήνα πριν την διάγνωση Covid 19
- Ομάδα σύγκρισης χωρίς συμπλήρωμα
- Σκοπός : θνητότητα , κλινική ανταπόκριση
- Επιβίωση: 82.5 % από την ομάδα παρέμβασης, 44.4% ομάδα σύγκρισης
- Συμπέρασμα: η χορήγηση βιταμίνης D σχετιζόταν με λιγότερο σοβαρή νόσο και καλύτερη επιβίωση

Vitamin D Status and COVID-19 Clinical Outcomes in Hospitalized Patients

Betsy Szeto, Jason E. Zucker, Elijah D. LaSota, Mishaela R. Rubin, Marcella D. Walker, Michael T. Yin & Adi Cohen

- 93 ασθενείς θετικοί στον ιό είχαν μετρήσει την βιταμίνη d μέχρι ένα χρόνο πριν.
- Ανεπάρκεια 25(OH)D < 20 ng/ml
- Πρωτεύοντα καταληκτικά σημεία: κατάσταση εξόδου, θνητότητα, ημέρες νοσηλείας, διασωλήνωση, νεφρική λειτουργία.
- Δευτερογενή καταληκτικά σημεία: δείκτες φλεγμονής

- Περισσότερες συννοσυρότητες στην ομάδα που είχε μέτρηση της d
- 37.6% είχαν vitd <20 ng/ml
- Ανεπάρκεια σε μικρότερη ηλικία και χωρίς προηγούμενη πνευμονική προσβολή

- Δεν βρέθηκε συσχέτιση μεταξύ βιταμίνης D και κλινικής έκβασης

COVID-19 fatalities, latitude, sunlight, and vitamin D

Paul B. Whittemore PhD *

- Ο αριθμός των θανάτων αυξάνεται όσο απομακρύνεται μια χώρα από τον Ισημερινό
- Υπόθεση: πληθυσμός με μεγαλύτερη έκθεση στον ήλιο έχει λιγότερη ανεπάρκεια σε βιταμίνη και άρα μικρότερη πιθανότητα θανάτου από τον covid

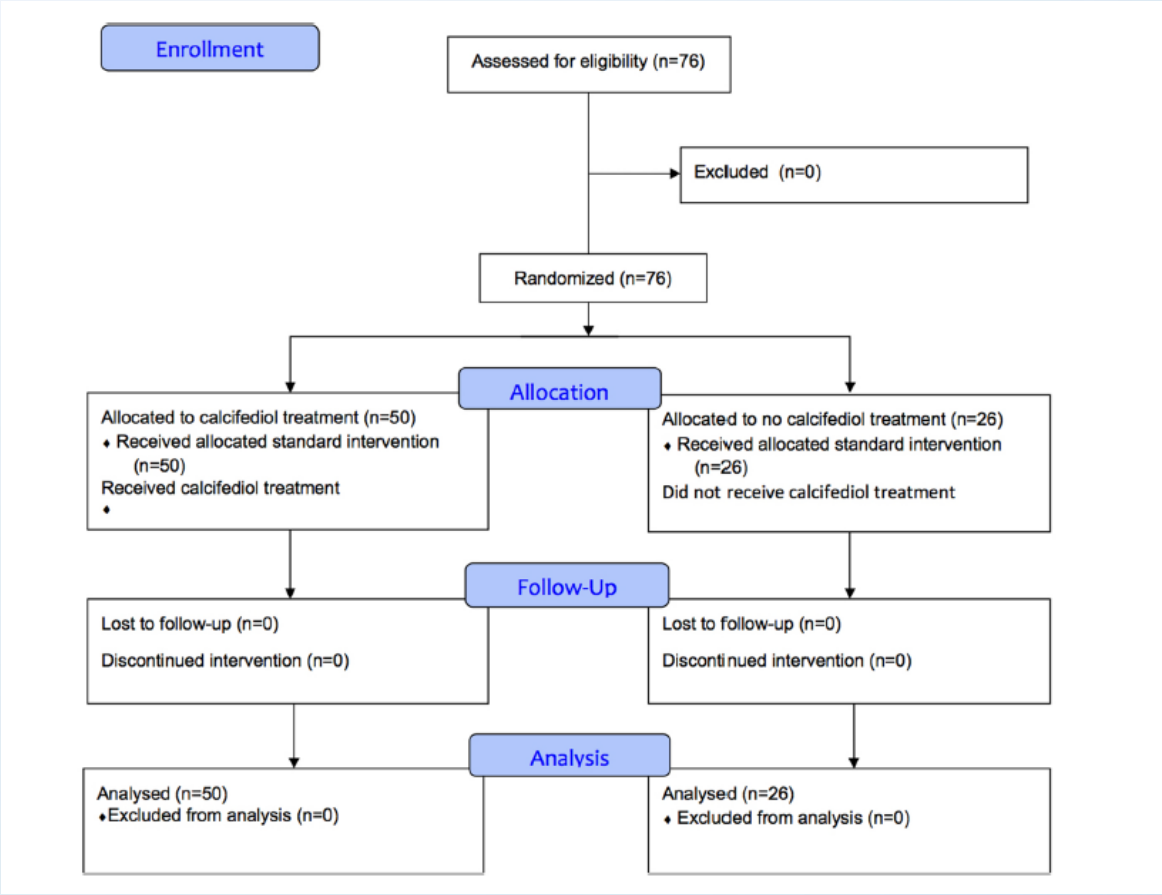
- Γεωγραφικό πλάτος της πρωτεύουσας κάθε χώρας (88 χώρες)
  - Ιταλία, Κίνα εξαίρεση

- Στατιστικά σημαντική συσχέτιση μεταξύ γεωγραφικού πλάτους και θνητότητα από τον covid 19

American Journal of Infection Control 2020

"Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among patients hospitalized for COVID-19: A pilot randomized clinical study"

Marta Entrenas Castillo [a], Luis Manuel Entrenas Costa [a,*], José Manuel Vaquero Barrios [a], Juan Francisco Alcalá Díaz [b], José López Miranda [b], Roger Bouillon [c], José Manuel Quesada Gomez [d]



"Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among patients hospitalized for COVID-19: A pilot randomized clinical study"

Marta Entrenas Castillo [a], Luis Manuel Entrenas Costa [a,*], José Manuel Vaquero Barrios [a], Juan Francisco Alcalá Díaz [b], José López Miranda [b], Roger Bouillon [c], José Manuel Quesada Gomez [d]

Table 3
Requirements for admission to the Intensive Care Unit, in patients hospitalized with COVID-19 (treated or not with calcifediol).

	Without Calcifediol Treatment (n = 26)	With Calcifediol Treatment (n = 50)	p value (1d712;2) Fischer Test
Need for ICU			<0.001
Not requiring ICU, n (%)	13 (50)	49 (98)	
Requiring ICU, n (%)	13 (50)	1 (2)	

Short term, high-dose vitamin D supplementation for COVID-19 disease: a randomised, placebo-controlled, study (SHADE study)

Ashu Rastogi,[1] Anil Bhansali,[1] Niranjan Khare,[2] Vikas Suri,[2] Narayana Yaddanapudi,[3] Naresh Sachdeva,[1] G D Puri,[3] Pankaj Malhotra [2]

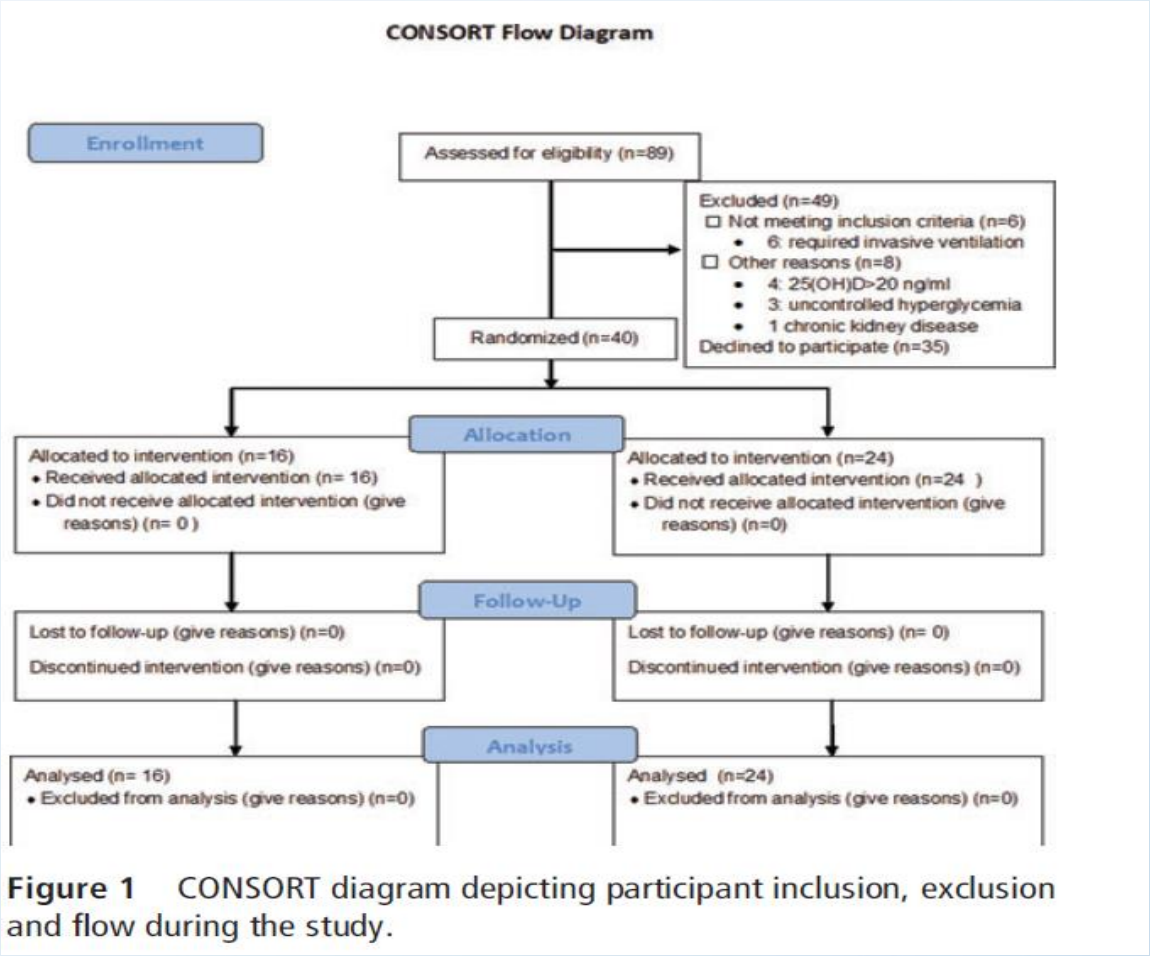


Figure 1 CONSORT diagram depicting participant inclusion, exclusion and flow during the study.

Short term, high-dose vitamin D supplementation for COVID-19 disease: a randomised, placebo-controlled, study (SHADE study)

Ashu Rastogi,[1] Anil Bhansali,[1] Niranjan Khare,[2] Vikas Suri,[2] Narayana Yaddanapudi,[3] Naresh Sachdeva,[1] G D Puri,[3] Pankaj Malhotra [2]

Table 2 Change in the levels of serum inflammatory markers in the two groups during follow up

	Intervention group (N=16)	Control group (N=24)	P-value
Δ Vitamin D (ng/ml)	42.4 (39 to 48.8)	5.1 (0 to 12.3)	<0.001*
Δ D-dimer(g/L)	–80.0 (–308.0 to 13.2)	–31.2 (–202 to 0)	0.241
Δ Fibrinogen (ng/ml)	–0.9 (–2.0 to –1.0)	–0.04 (–1.02 to 0.0)	0.001*
ΔCRP(ng/ml)	–0.3 (–1.4 to 0.2)	0.0 (–0.9 to 0.3)	0.507
Δ Procalcitonin (mg/L)	0.00 (–0.2 to 0.7)	–0.1 (–0.60 to 0.04)	0.260

*p<0.05 considered significant.
Data represented as median (Inter-quartile range).
Δ: Last available value-Baseline value.
CRP, C-reactive protein.

Covid 19 και βιταμίνη D

Εγκυμοσύνη

Vitamin D status is not associated with clinical severity of COVID-19 in pregnant women

Arzu Bilge Tekin[1] · Murat Yassa[1] · Pınar Birol[1] · Sakine Nisa Unlu[1] · Turan Sahin[1] · Ayca Miray Buran[1] · Esra Ayanoglu[1] · Niyazi Tug[1]

Table 2 The characteristics of pregnant women with COVID-19 and primary outcomes according to vitamin D status

	Vitamin D deficiency (< 50 nmol/L) (n = 111)		Adequate vitamin D (≥ 50 nmol/L) (n = 36)		
	Mean	SD	Mean	SD	p
Age (year)	27.81	5.32	28.50	4.57	0.487[a]
BMI (kg/m^2)	28.18	4.84	29.27	4.78	0.237[a]
Gestational week	27.32	9.49	28.47	8.20	0.513[a]
Hospitalization (days)	9.97	4.70	10.05	3.73	0.924[a]

	Exist (n(%))	Absent (n(%))	Exist (n(%))	Absent (n (%))	p (χ^2)
Comorbidity	11 (9.9)	100 (90.1)	5 (13.9)	31 (86.1)	0.505[b] (0.444)

	1st	2nd	3rd	1st	2nd	3rd	p (χ^2)
Trimesters	15 (13.5%)	35 (31.5%)	61 (55%)	2 (5.6%)	11 (30.6%)	23 (63.9%)	0.391[b] (1.877)

	Exist (n (%))	Absent (n (%))	Exist (n (%))	Absent (n (%))	p (χ^2)
Pulmonary involvement	100 (90.1%)	11 (9.9%)	34 (94.4%)	2 (5.6%)	0.424[b] (0.639)

	O_2 not required (mild to moderate)	Received O_2 (severe to critical)	O_2 not required (mild to moderate)	Received O_2 (severe to critical)	p (χ^2)
Clinical severity	90 (81.1%)	21 (18.9%)	24 (66.7%)	12 (33.3%)	0.072[b] (3.244)
Clinical severity (excluding those with supplementation, n = 90)	50 (83.3%)	10 (16.7%)	22 (73.3%)	8 (26.7%)	0.264[b] (1.250)

SD standard deviation, *IQR* interquartile range, *BMI* body mass index

[a]Independent samples *T* test

[b]Pearson Chi-square test

COVID 19 και Βιταμίνη D

Παιδιά

Is vitamin D deficiency a risk factor for COVID-19 in children?

Kamil Yılmaz[1] | Velat Şen[2]

Material and Methods: This study includes 40 patients who were diagnosed to have COVID-19 and hospitalized with the real-time reverse transcription polymerase chain reaction method, 45 healthy matched control subjects with vitamin D levels. The age of admission, clinical and laboratory data, and 25-hydroxycholecalciferol (25-OHD) levels were recorded. Those with vitamin D levels which are below 20 ng/ml were determined as Group 1 and those with ≥20 ng/ml as Group 2.

Results: Patients with COVID-19 had significantly lower vitamin D levels 13.14 μg/L (4.19–69.28) than did the controls 34.81 (3.8–77.42) μg/L ($p < .001$). Patients with COVID-19 also had significantly lower serum phosphorus (4.09 ± 0.73 vs. 5.06 ± 0.93 vs. (U/L) ($p < .001$)) values compared with the controls. The symptom of fever was significantly higher in COVID- 19 patients who had deficient and insufficient vitamin D levels than in patients who had sufficient vitamin D levels ($p = .038$). There was a negative correlation found between fever symptom and vitamin D level ($r = -0.358$, $p = .023$).

Vitamin D, Covid-19 and Children

E.J. Molloy[1-4], N. Murphy[5,6]

- Τα παιδιά στην εντατική είχαν χαμηλότερη βιταμίνη D σε πιθανή σήψαιμία.
- Ανεπάρκεια βιταμίνης d συσχετίζεται με επιβεβαιωμένη σηψαιμία και κακή πρόγνωση.
- Επιπεδα αλβουμίνης , πρωτείνες σύζευξης και αιμοδιάλυση, ελεύθεροι μεταβολίτες της d
- Επάρκεια βιταμίνης D. Μεγαλύτερες δόσεις βιταμίνης δεν έχει αποδειχτεί ότι είναι οφέλιμες

Ir Med J; Vol 113; No 4; P59

Μετα αναλύσεις

Vitamin D deficiency aggravates COVID-19: systematic review and meta-analysis

Marcos Pereira, Alialdo Dantas Damascena, Laylla Mirella Galvão Azevedo, Tarcio de Almeida Oliveira & Jerusa da Mota Santana

- Μετα-ανάλυση μελετών παρατήρησης
- Καταληκτικό σημείο : ανεπάρκεια βιταμίνης D και βαρύτητα νόσου Covid 19
- Ασθενείς με σοβαρή νόσο είχαν 65% περισσότερη ανεπάρκεια βιταμίνης d σε σχέση με ασθενείς με πιο ήπια νόσο.
- Ειδικότερα στους ηλικιωμένους
- Αναπνευστικά προβλήματα συσχέτιση με ανεπάρκεια βιταμίνης D

Critical Reviews in Food Science and Nutrition 2020

Vitamin D deficiency aggravates COVID-19: systematic review and meta-analysis

Marcos Pereira, Alialdo Dantas Damascena, Laylla Mirella Galvão Azevedo, Tarcio de Almeida Oliveira & Jerusa da Mota Santana

- Δεν παρατηρήθηκε συσχέτιση μεταξύ έλλειψης βιταμίνης d και κινδύνου νόσησης από Covid 19

- Επαρκή διατροφή είναι απαραίτητη για την υγεία
- Διόρθωση της ανεπάρκειας είναι σημαντική για την υγεία ανεξάρτητα από συνοσηρότητες

Critical Reviews in Food Science and Nutrition
2020

Low vitamin D levels do not aggravate COVID-19 risk or death, and vitamin D supplementation does not improve outcomes in hospitalized patients with COVID-19: a meta-analysis and GRADE assessment of cohort studies and RCTs

Jie Chen[1†], Kaibo Mei[2†], Lixia Xie[3], Ping Yuan[4], Jianyong Ma[5], Peng Yu[6], Wengen Zhu[7], Chunhua Zheng[1*] and Xiao Liu[8,9,10*]

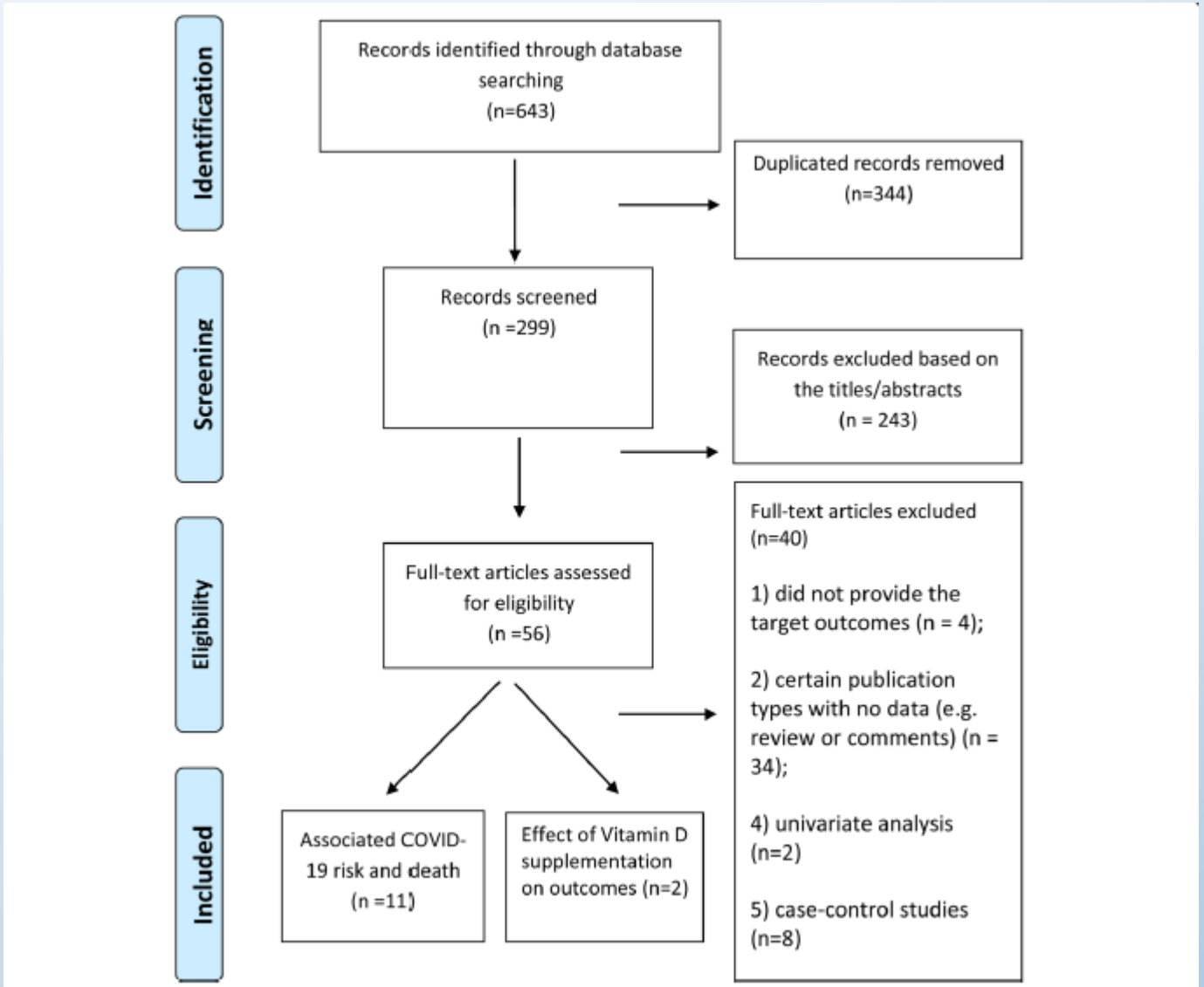


Fig. 1 Flow chart of study selection in this meta-analysis

Low vitamin D levels do not aggravate COVID-19 risk or death, and vitamin D supplementation does not improve outcomes in hospitalized patients with COVID-19: a meta-analysis and GRADE assessment of cohort studies and RCTs

Jie Chen[1†], Kaibo Mei[2†], Lixia Xie[3], Ping Yuan[4], Jianyong Ma[5], Peng Yu[6], Wengen Zhu[7], Chunhua Zheng[1*] and Xiao Liu[8,9,10*]

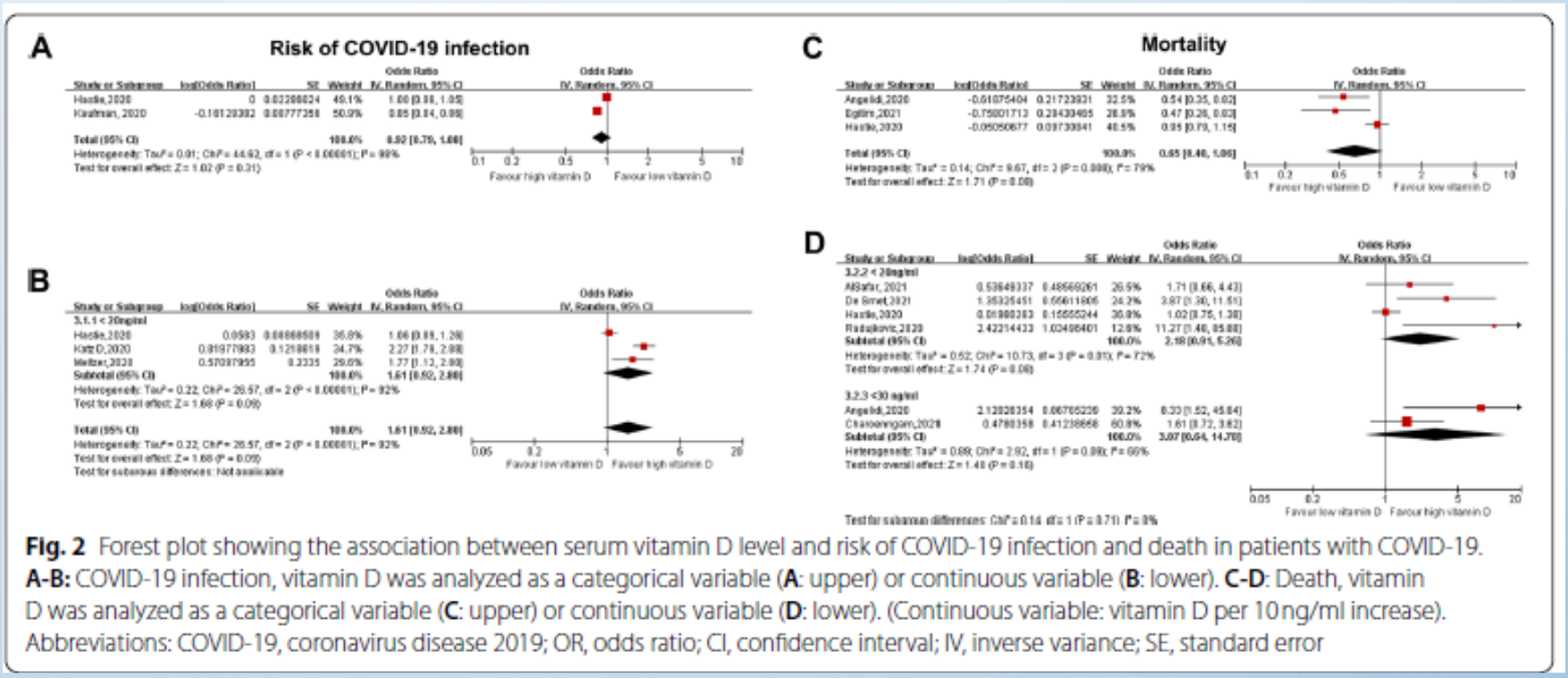


Fig. 2 Forest plot showing the association between serum vitamin D level and risk of COVID-19 infection and death in patients with COVID-19. **A-B:** COVID-19 infection, vitamin D was analyzed as a categorical variable (**A**: upper) or continuous variable (**B**: lower). **C-D**: Death, vitamin D was analyzed as a categorical variable (**C**: upper) or continuous variable (**D**: lower). (Continuous variable: vitamin D per 10 ng/ml increase). Abbreviations: COVID-19, coronavirus disease 2019; OR, odds ratio; CI, confidence interval; IV, inverse variance; SE, standard error

Low vitamin D levels do not aggravate COVID-19 risk or death, and vitamin D supplementation does not improve outcomes in hospitalized patients with COVID-19: a meta-analysis and GRADE assessment of cohort studies and RCTs

Jie Chen[1†], Kaibo Mei[2†], Lixia Xie[3], Ping Yuan[4], Jianyong Ma[5], Peng Yu[6], Wengen Zhu[7], Chunhua Zheng[1*] and Xiao Liu[8,9,10*]

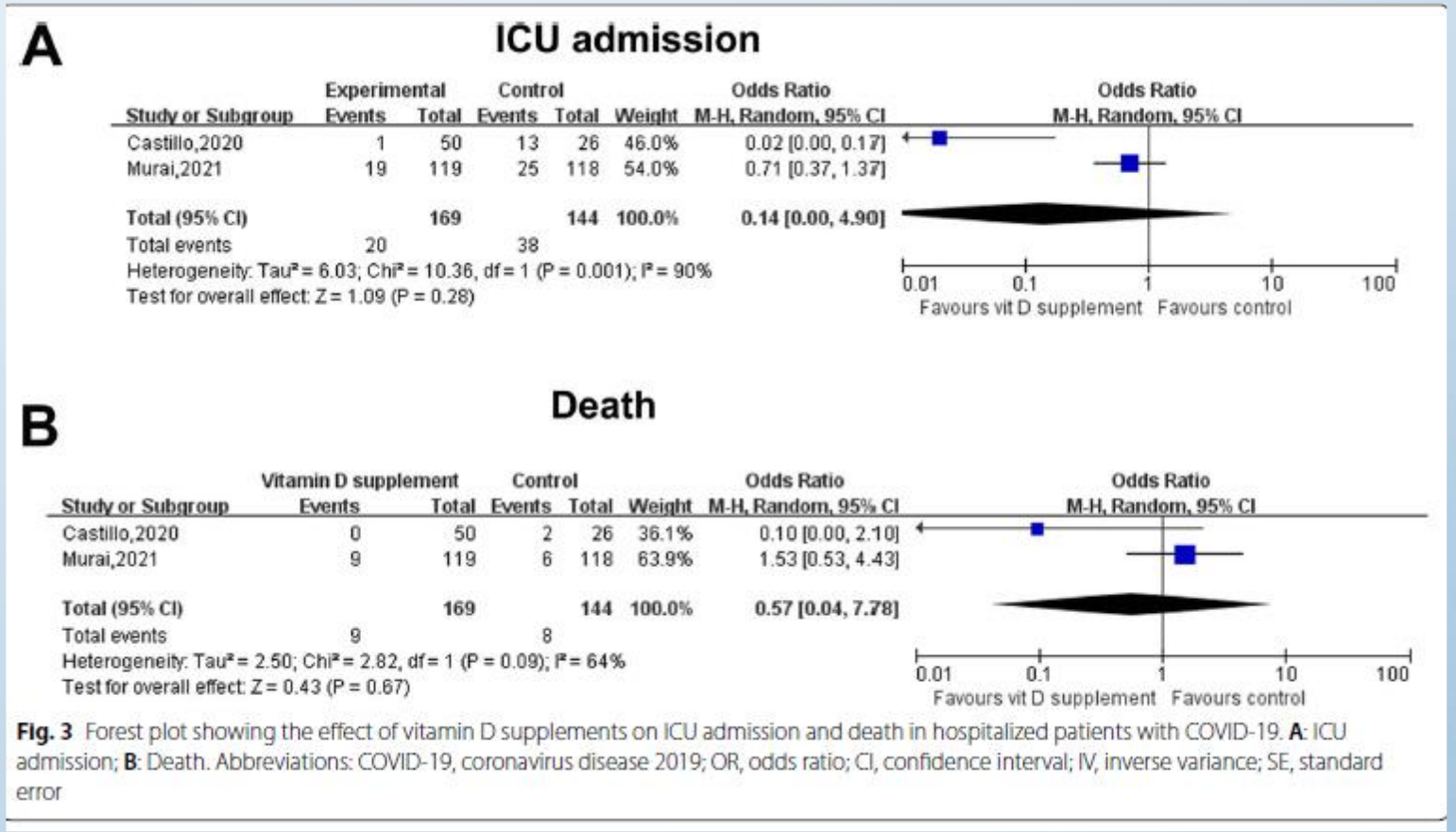
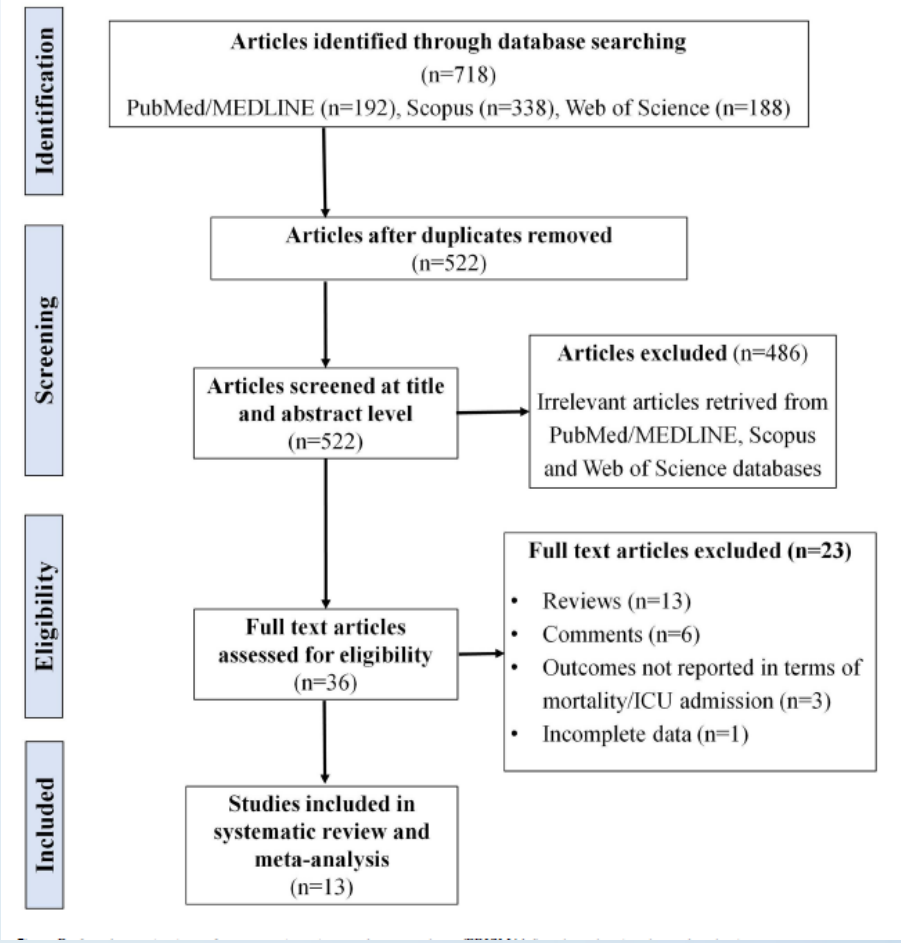


Fig. 3 Forest plot showing the effect of vitamin D supplements on ICU admission and death in hospitalized patients with COVID-19. **A**: ICU admission; **B**: Death. Abbreviations: COVID-19, coronavirus disease 2019; OR, odds ratio; CI, confidence interval; IV, inverse variance; SE, standard error

- The present study showed that: (i) vitamin D deficiency (< 20 ng/ml) or insufficiency (< 30 ng/ml) was not associated with a significantly increased risk of COVID-19 infection or in-hospital death ($P = 0.56$). (ii) A 10 ng/ml increase in serum vitamin D was not significantly linked to an increased risk of COVID-19 infection or in-hospital death. (iii) Vitamin D supplements did not improve clinical outcomes in patients with COVID-19. Overall, our study suggested no significant association between vitamin D level, COVID-19 infection, and outcomes and no benefit of vitamin D supplementation in hospitalized patients with COVID-19.

Vitamin D supplementation and clinical outcomes in COVID-19: a systematic review and meta-analysis

R. Pal[1] · M. Banerjee[2] · S. K. Bhadada[1] · A. J. Shetty[1] · B. Singh[3] · A. Vyas[4]



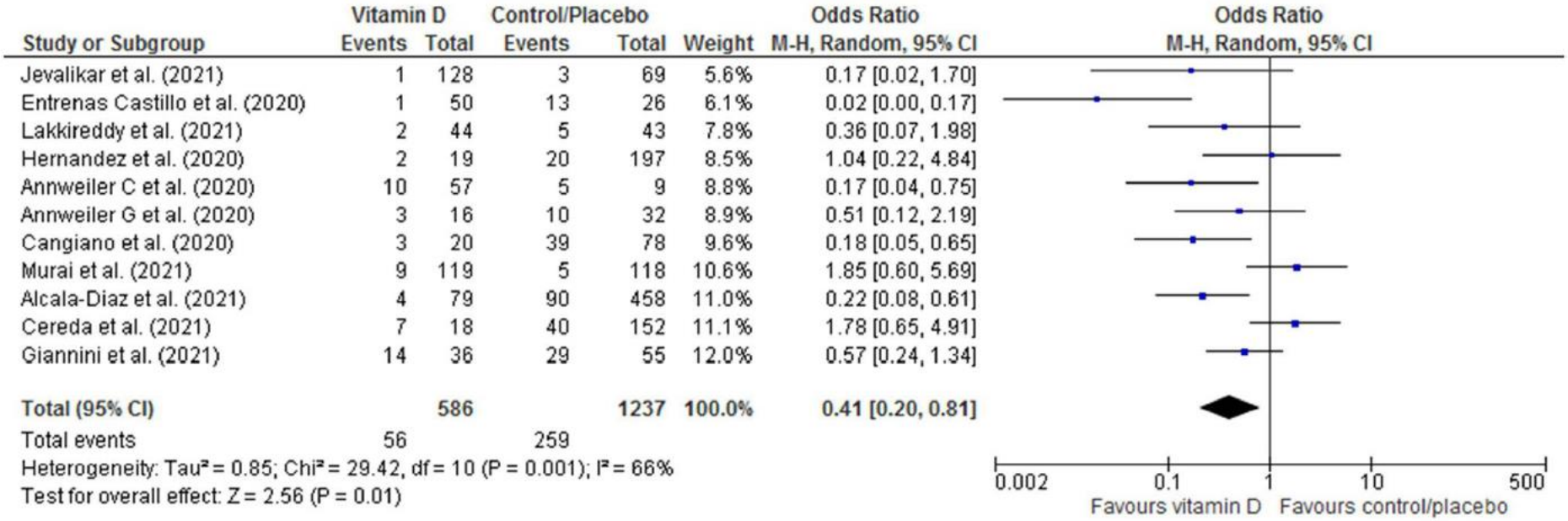


Fig. 2 Forest plot showing the effect (unadjusted) of vitamin D supplementation on clinical outcomes (intensive care unit admission and/or mortality) in patients with COVID-19 as compared to non-use of vitamin D

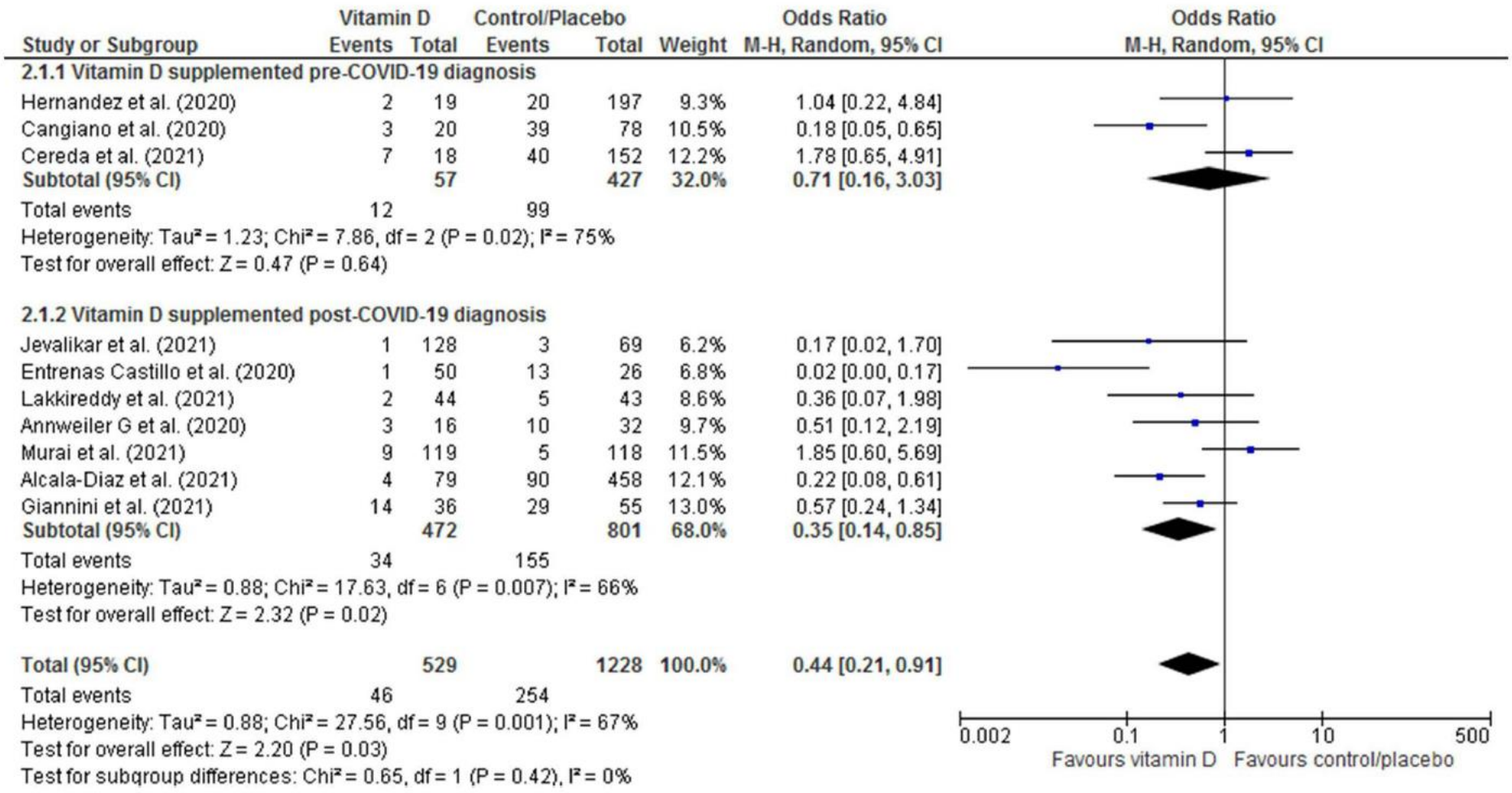
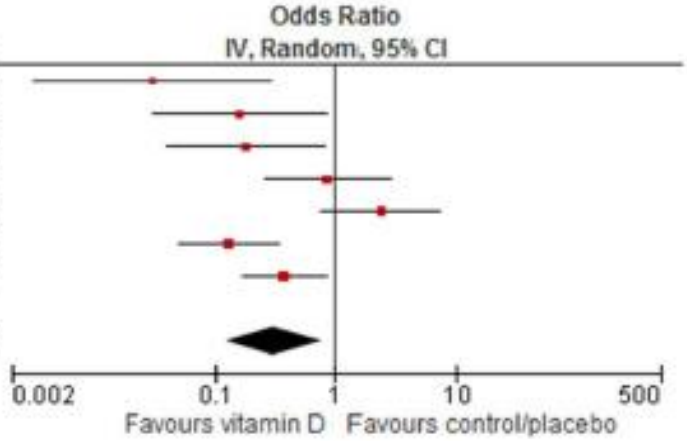


Fig. 3 Forest plot with subgroup analysis (based on the use of vitamin D pre- or post-COVID-19 diagnosis) showing the effect (unadjusted) of vitamin D supplementation on clinical outcomes (intensive care unit admission and/or mortality) in patients with COVID-19 as compared to non-use of vitamin D

A

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Entrenas Castillo et al. (2020)	-3.5066	1.1748	9.0%	0.03 [0.00, 0.30]
Alcala-Diaz et al. (2021)	-1.8326	0.8541	12.2%	0.16 [0.03, 0.85]
Giannini et al. (2021)	-1.7148	0.7674	13.3%	0.18 [0.04, 0.81]
Lohia et al. (2021)	-0.1508	0.6103	15.2%	0.86 [0.26, 2.84]
Cereda et al. (2021)	0.8502	0.5738	15.7%	2.34 [0.76, 7.21]
Ling et al. (2020) (Primary cohort)	-2.0402	0.4875	16.8%	0.13 [0.05, 0.34]
Ling et al. (2020) (Validation cohort)	-0.9676	0.4104	17.7%	0.38 [0.17, 0.85]
Total (95% CI)			**100.0%**	**0.31 [0.12, 0.78]**

Heterogeneity: Tau² = 1.09; Chi² = 23.25, df = 6 (P = 0.0007); I² = 74%
Test for overall effect: Z = 2.48 (P = 0.01)



B

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
Annweiler G et al. (2020)	-0.9943	0.9282	33.8%	0.37 [0.06, 2.28]
Annweiler C et al. (2020)	-2.2073	0.6629	66.2%	0.11 [0.03, 0.40]
Total (95% CI)			**100.0%**	**0.17 [0.06, 0.48]**

Heterogeneity: Chi² = 1.13, df = 1 (P = 0.29); I² = 12%
Test for overall effect: Z = 3.33 (P = 0.0009)

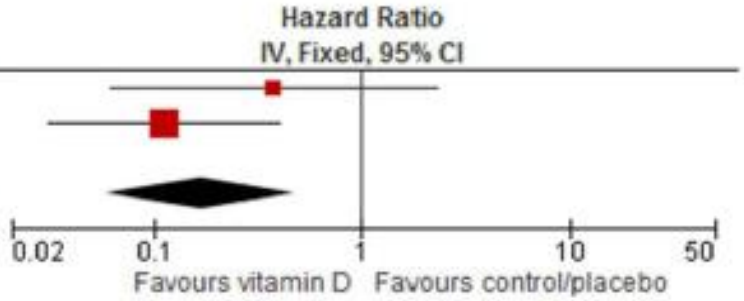


Fig. 4 Forest plots showing the effect (adjusted) of vitamin D supplementation on clinical outcomes (intensive care unit admission and/or mortality) in patients with COVID-19 as compared to non-use of vitamin D expressed either as pooled odds ratio (**A**) or pooled hazard ratio (**B**)

- Vitamin D supplementation might be associated with improved clinical outcomes, especially when administered after the diagnosis of COVID-19. However, issues regarding the appropriate dose, duration, and mode of administration of vitamin D remain unanswered and need further research.