Vitamin D for COVID-19: real-time meta analysis of 316 studies (120 treatment studies and 196 sufficiency studies)

@CovidAnalysis, Apr 26, 2024, Version 281
https://c19early.org/dmeta.html

Abstract

120 treatment studies show statistically significant lower risk for mortality, ICU admission, hospitalization, and cases. 62 studies from 58 independent teams in 22 countries show statistically significant lower risk.

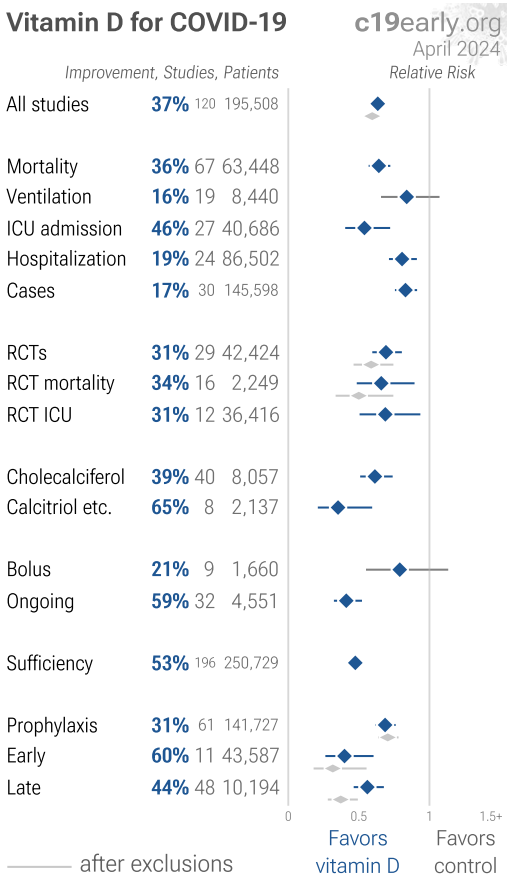
Random effects meta-analysis with pooled effects using the most serious outcome reported shows 60% [40-74%] and 37% [31-42%] lower risk for early treatment and for all studies. Results are similar for higher quality studies, peer-reviewed studies, and mortality: early treatment - 68% [45-82%], 57% [36-71%], 68% [39-84%]; all - 37% [31-42%], 41% [34-46%], 36% [28-43%].

Late stage treatment with calcitriol/calcifediol and analogs is more effective than cholecalciferol: 65% [41-79%] vs. 39% [26-49%].

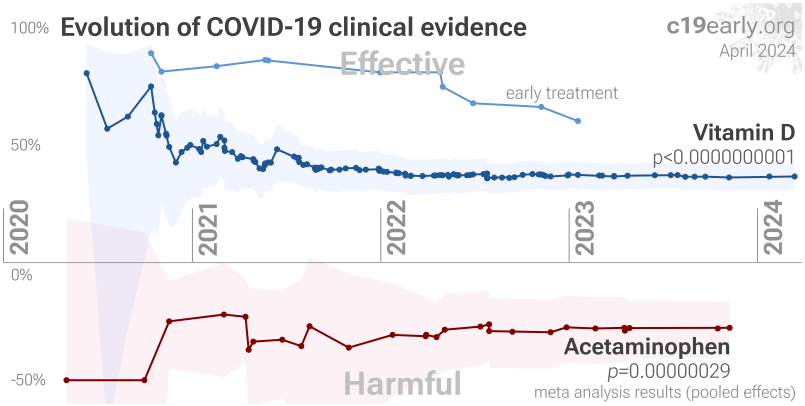
Ongoing treatment with multiple doses is more effective than single bolus doses: 59% [48-68%] vs. 21% [-13-45%]

196 sufficiency studies show a strong association between vitamin D sufficiency and outcomes, with 53% [49-56%] lower risk for higher levels.

No treatment or intervention is 100% effective. All practical, effective, and safe means should be used based on risk/benefit analysis. Multiple treatments are typically used in combination, and other treatments may be more effective. The quality of non-prescription supplements can vary widely *Crawford, Crighton*.



All data and sources to reproduce this paper are in the appendix. Other meta analyses show significant improvements with vitamin D treatment for mortality *Argano, Begum, D'Ecclesiis, Hariyanto, Hosseini, Jamilian, Nikniaz, Shah, Xie*, mechanical ventilation *Hariyanto, Meng, Shah, Xie*, ICU admission *Hariyanto, Hosseini, Meng, Sartini, Shah, Tentolouris, Xie*, hospitalization *Argano*, severity *D'Ecclesiis, Nikniaz, Varikasuvu, Xie*, and cases *Begum, Sartini, Varikasuvu*.



HIGHLIGHTS

Vitamin D reduces risk for COVID-19 with very high confidence for mortality, ICU admission, hospitalization, recovery, cases, viral clearance, and in pooled analysis, high confidence for progression, and very low confidence for ventilation.

8th treatment shown effective with ≥3 clinical studies in October 2020, now with $p < 0.00000000001$ from 120 studies, and recognized in 8 countries.

We show outcome specific analyses and combined evidence from all studies, incorporating treatment delay, a primary confounding factor for COVID-19.

Real-time updates and corrections, transparent analysis with all results in the same format, consistent protocol for 69 treatments.

Vitamin D COVID-19 early and late treatment studies

c19early.org
April 2024

	Improvement	RR [CI]		Treatment	Control	Dose (5d)	
Annweiler	89%	0.11 [0.03-0.48]	death	10/57	5/9	80,000IU	
Annweiler	63%	0.37 [0.06-2.21]	death	3/16	10/32	80,000IU	
Burahee	93%	0.07 [0.01-0.54]	death	0/12	2/2	400,000IU	
Asimi	97%	0.03 [0.00-0.44]	ventilation	0/270	9/86	10,000IU	CT[1]
Sánchez-Zuno (RCT)	89%	0.11 [0.01-0.91]	severe case	0/22	4/20	50,000IU	
Efird	49%	0.51 [0.23-1.17]	death	11/544	413/15,794	varies	
Valecha	87%	0.13 [0.01-2.43]	ICU	0/30	3/25	5,000IU	CT[1]
Khan (RCT)	33%	0.67 [0.37-1.19]	no recov.	10/25	15/25	1,800IU	CT[1]
Hunt	47%	0.53 [0.37-0.77]	death	43/1,019	1,569/25,489	n/a	
Said (RCT)	42%	0.58 [0.09-3.47]	recovery	30 (n)	30 (n)	10,000IU	
Din Ujjan (RCT)	29%	0.71 [0.50-1.03]	no recov.	15/25	21/25	1,800IU	CT[1]
Early treatment	60%	0.40 [0.26-0.60]		92/2,050	2,051/41,537		**60% lower risk**

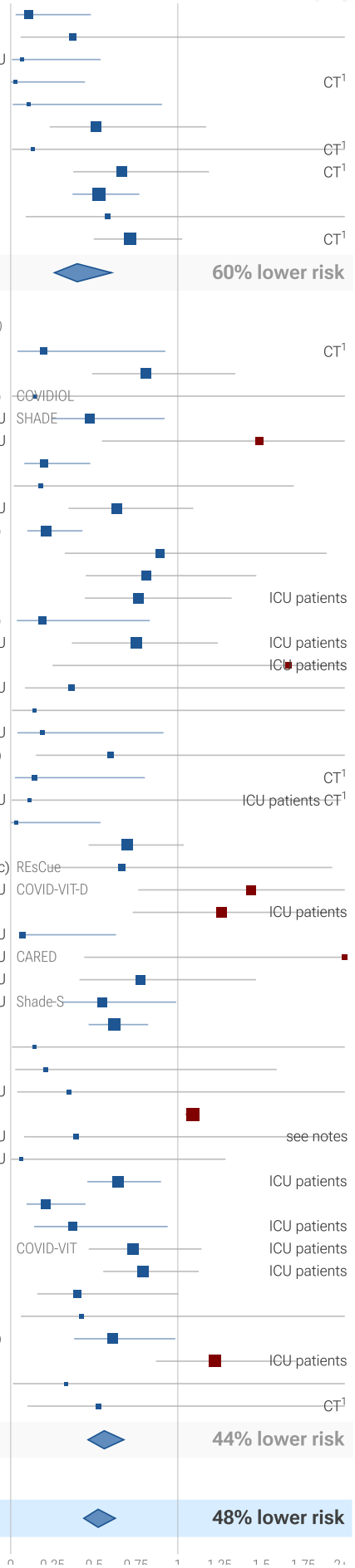
Tau^2 = 0.21, I^2 = 62.3%, p < 0.0001

	Improvement	RR [CI]		Treatment	Control	Dose (5d)	
Tan	80%	0.20 [0.04-0.93]	oxygen	3/17	16/26	5,000IU	CT[1]
Krishnan	19%	0.81 [0.49-1.34]	death	8/16	84/136	n/a	
Castillo (RCT)	85%	0.15 [0.01-2.93]	death	0/50	2/26	0.8mg (c)	COVIDIOL
Rastogi (RCT)	53%	0.47 [0.24-0.92]	viral+	6/16	19/24	300,000IU	SHADE
Murai (DB RCT)	-49%	1.49 [0.55-4.05]	death	9/119	6/118	200,000IU	
Ling	80%	0.20 [0.08-0.48]	death	73 (n)	253 (n)	40,000IU	
Jevalikar	82%	0.18 [0.02-1.69]	death	1/128	3/69	60,000IU	
Giannini	37%	0.63 [0.35-1.09]	death/ICU	14/36	29/55	400,000IU	
Nogués (QR)	79%	0.21 [0.10-0.43]	death	21/447	62/391	0.8mg (c)	
Lohia	11%	0.89 [0.32-1.89]	death	26 (n)	69 (n)	n/a	
Mazziotti	19%	0.81 [0.45-1.47]	death	116 (n)	232 (n)	varies	
Elhadi (ICU)	23%	0.77 [0.44-1.32]	death	7/15	274/450	n/a	ICU patients
Alcala-Diaz	81%	0.19 [0.04-0.83]	death	4/79	90/458	0.8mg (c)	
Güven (ICU)	25%	0.75 [0.37-1.24]	death	43/113	30/62	300,000IU	ICU patients
Assiri (ICU)	-66%	1.66 [0.25-7.87]	death	12/90	2/28	n/a	ICU patients
Soliman (RCT)	63%	0.37 [0.09-2.78]	death	7/40	3/16	200,000IU	
Elamir (RCT)	86%	0.14 [0.01-2.63]	death	0/25	3/25	2.5µg (t)	
Yildiz	81%	0.19 [0.04-0.91]	death	1/37	24/170	300,000IU	
Maghbooli (DB RCT)	40%	0.60 [0.15-2.38]	death	3/53	5/53	125µg (c)	
Leal-Martínez (RCT)	86%	0.14 [0.03-0.80]	death	1/40	7/40	20,000IU	CT[1]
Beigm.. (SB RCT)	89%	0.11 [0.01-1.98]	death	0/30	4/30	600,000IU	ICU patients CT[1]
Baguma	97%	0.03 [0.00-0.54]	death	23 (n)	458 (n)	n/a	
Mahmood	30%	0.70 [0.47-1.04]	death	45/238	31/114	varies	
Bishop (DB RCT)	34%	0.66 [0.23-1.92]	no recov.	5/65	8/69	1020µg (c)	REsCue
Cannata-An.. (RCT)	-44%	1.44 [0.76-2.72]	death	22/274	15/269	100,000IU	COVID-VIT-D
Zangeneh (ICU)	-26%	1.26 [0.73-2.16]	death	n/a	n/a	n/a	ICU patients
Fiore	93%	0.07 [0.07-0.63]	death	3/58	11/58	200,000IU	
Mariani (DB RCT)	-124%	2.24 [0.44-11.3]	death	5/115	2/103	500,000IU	CARED
Baykal	22%	0.78 [0.41-1.47]	death	7/18	28/56	300,000IU	
Singh (DB RCT)	45%	0.55 [0.31-0.99]	death	11/45	20/45	600,000IU	Shade-S
Shahid	38%	0.62 [0.47-0.82]	death	705 (n)	773 (n)	n/a	
Karonova (RCT)	86%	0.14 [0.01-2.66]	ICU	0/56	3/54	50,000IU	
Zurita-C.. (SB RCT)	79%	0.21 [0.03-1.59]	death	1/20	6/25	10,000IU	
De Niet (DB RCT)	65%	0.35 [0.04-3.10]	death	1/21	3/22	100,000IU	
Fairfield	-9%	1.09 [1.04-1.12]	death	population-based cohort		n/a	
Lakkireddy (RCT)	61%	0.39 [0.08-1.91]	death	2/44	5/43	300,000IU	see notes
Hafez	94%	0.06 [0.00-1.29]	death	0/7	12/30	150,000IU	
Saheb Shari.. (ICU)	36%	0.64 [0.46-0.90]	ICU	20 (n)	25 (n)	50,000IU	ICU patients
Karimpour-Razke..	79%	0.21 [0.10-0.45]	death	10/124	93/329	n/a	
Hafezi (ICU)	63%	0.37 [0.14-0.94]	death	8/43	12/37	50,000IU	ICU patients
Bychinin (DB RCT)	27%	0.73 [0.47-1.14]	death	19/52	27/54	80,000IU	COVID-VIT ICU patients
Domazet B.. (RCT)	21%	0.79 [0.55-1.13]	death	30/75	39/77	50,000IU	ICU patients
Salman (RCT)	60%	0.40 [0.16-1.00]	death	6/150	15/150	20,000IU	
Shamsi	58%	0.42 [0.06-2.95]	death	1/17	23/166	n/a	
Mingiano	39%	0.61 [0.38-0.99]	death	13/56	88/232	900µg (c)	
Al Sulaiman (ICU)	-22%	1.22 [0.87-1.71]	death	72/144	62/144	n/a	ICU patients
Ogasawara	67%	0.33 [0.01-8.01]	death	0/54	1/54	5µg (p)	
Seely (DB RCT)	48%	0.52 [0.10-2.71]	progression	2/42	4/44	55,000IU	CT[1]
Late treatment	44%	0.56 [0.46-0.68]		403/4,032	1,171/6,162		**44% lower risk**

Tau^2 = 0.22, I^2 = 79.9%, p < 0.0001

All studies	48%	0.52 [0.44-0.63]		495/6,082	3,222/47,699		**48% lower risk**

[1] CT



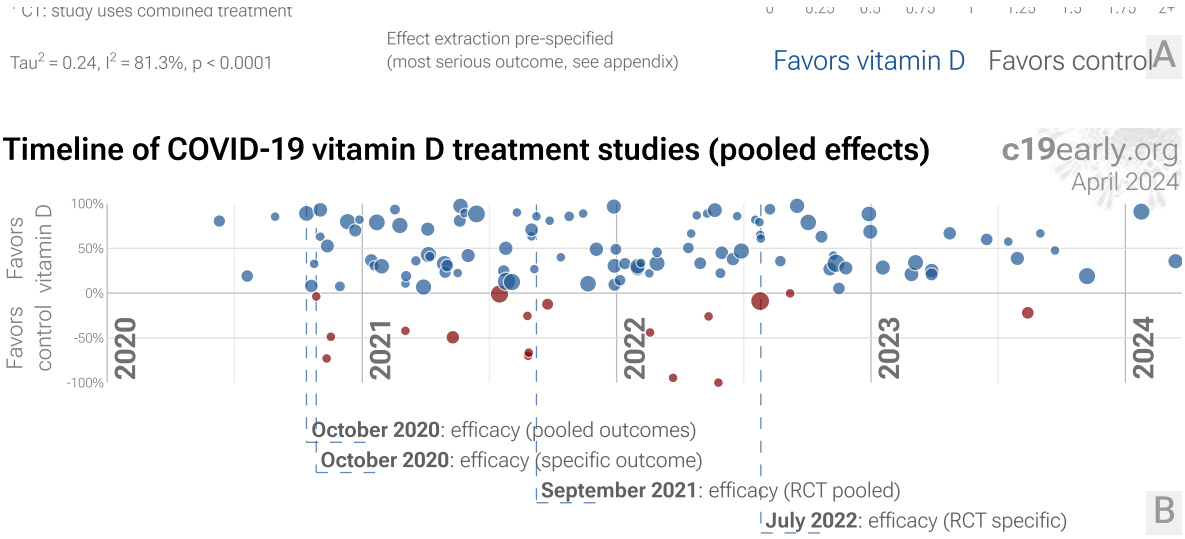


Figure 1. **A. Random effects meta-analysis of treatment studies.** This plot shows pooled effects, see the specific outcome analyses for individual outcomes. Analysis validating pooled outcomes for COVID-19 can be found below. Effect extraction is pre-specified, using the most serious outcome reported. Simplified dosages are shown for comparison, these are the total dose in the first five days for treatment, and the monthly dose for prophylaxis. Calcifediol, calcitriol, and paricalcitol treatment are indicated with (c), (t), and (p). For details of effect extraction and full dosage information see the appendix. **B. Timeline of results in vitamin D treatment studies.** The marked dates indicate the time when efficacy was known with a statistically significant improvement of ≥10% from ≥3 studies for pooled outcomes, one or more specific outcome, pooled outcomes in RCTs, and one or more specific outcome in RCTs. Efficacy based on RCTs only was delayed by 10.8 months, compared to using all studies. Efficacy based on specific outcomes in RCTs was delayed by 10.6 months, compared to using pooled outcomes in RCTs.

Introduction

Immediate treatment recommended. SARS-CoV-2 infection primarily begins in the upper respiratory tract and may progress to the lower respiratory tract, other tissues, and the nervous and cardiovascular systems, which may lead to cytokine storm, pneumonia, ARDS, neurological issues *Duloquin, Hampshire, Scardua-Silva, Sodagar, Yang*, cardiovascular complications *Eberhardt*, organ failure, and death. Minimizing replication as early as possible is recommended.

Many treatments are expected to modulate infection. SARS-CoV-2 infection and replication involves the complex interplay of 50+ host and viral proteins and other factors *Note A, Malone, Murigneux, Lv, Lui, Niarakis*, providing many therapeutic targets for which many existing compounds have known activity. Scientists have predicted that over 7,000 compounds may reduce COVID-19 risk *c19early.org*, either by directly minimizing infection or replication, by supporting immune system function, or by minimizing secondary complications.

Analysis. We analyze all significant controlled studies of vitamin D for COVID-19. Search methods, inclusion criteria, effect extraction criteria (more serious outcomes have priority), all individual study data, PRISMA answers, and statistical methods are detailed in Appendix 1. We perform random-effects meta analysis for all treatment studies, Randomized Controlled Trials, peer-reviewed studies, studies using cholecalciferol vs. calcifediol/calcitriol and analogs, studies using large bolus doses vs. ongoing treatment, higher quality studies, and for specific outcomes: mortality, mechanical ventilation, ICU admission, hospitalization, and case results. Results are presented for prophylaxis, early treatment, and late treatment. Separately, we perform random-effects meta analysis for studies that analyze outcomes based on vitamin D sufficiency (non-treatment studies).

Extensive supporting research. Vitamin D has been identified by the European Food Safety Authority (EFSA) as having sufficient evidence for a causal relationship between intake and optimal immune system function *EFSA, EFSA (B), Galmés, Galmés (B)*. Vitamin D inhibits SARS-CoV-2 replication *in vitro* *Campolina-Silva, Pickard*, mitigates lung inflammation, damage, and lethality in mice with an MHV-3 model for β-CoV respiratory infections *Campolina-Silva, Pickard*, reduces SARS-CoV-2 replication in nasal epithelial cells via increased type I interferon expression *Sposito*, downregulates proinflammatory cytokines IL-1β and TNF-α in SARS-CoV-2 spike protein-stimulated cells *Alcalá-Santiago*, attenuates

nucleocapsid protein-induced hyperinflammation by inactivating the NLRP3 inflammasome through the VDR-BRCC3 signaling pathway [Chen], may be neuroprotective by protecting the blood-brain barrier, reducing neuroinflammation, and via immunomodulatory effects [Gotelli], and improves regulatory immune cell levels and control of proinflammatory cytokines in severe COVID-19 [Saheb Sharif-Askari]. Symptomatic COVID-19 is associated with a lower frequency of natural killer (NK) cells and vitamin D has been shown to improve NK cell activity [Graydon, Oh].

Other infections. Studies have shown efficacy with vitamin D for influenza [Grant], RSV [Grant], and acute respiratory tract infections [Abioye, Martineau].

Vitamin D. Vitamin D is a steroid hormone that helps regulate the immune system by binding to specific receptors and activating genes involved in immune defense. It increases the production of antimicrobial proteins, like cathelicidin and defensins, which fight a variety of pathogens, including bacteria, viruses, and fungi. Vitamin D supports the immune system by boosting our natural defenses and promoting healthy cell connections. It helps clear respiratory pathogens through processes like apoptosis and autophagy and regulates toll-like receptors, which play a key role in immunity. Vitamin D also aids in immune cell maturation, balances inflammation, and reduces the production of proinflammatory cytokines. Vitamin D has been shown to downregulate angiotensin-converting enzyme-2 (ACE-2) receptors, which play a role in COVID-19 infection. By suppressing the production of ACE-2 and related molecules, vitamin D increases antioxidant and anti-inflammatory effects, enhances antimicrobial defenses, reduces cytokine storms, and promotes a protective immune response, all of which help decrease the severity of the disease. Vitamin D was first identified in relation to bone health, but is now known to have multiple functions, including an important role in the immune system [Carlberg, Martens]. For example, *Quraishi et al.* show a strong association between pre-operative vitamin D levels and hospital-acquired infections, as shown in Figure 2.

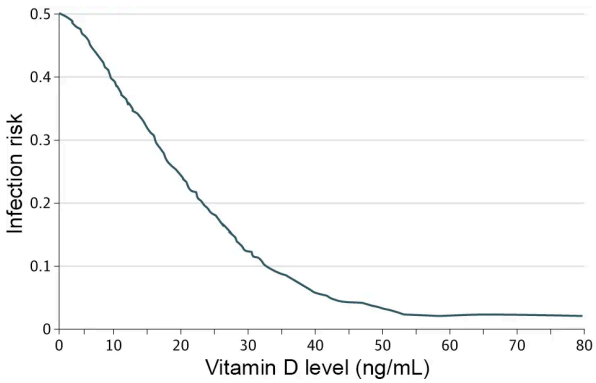


Figure 2. **Risk of hospital-acquired infections as a function of pre-operative vitamin D levels, from** *Quraishi et al.*

Conversion delays. Vitamin D undergoes two conversion steps before reaching the biologically active form as shown in Figure 3. The first step is conversion to calcidiol, or 25(OH)D, in the liver. The second is conversion to calcitriol, or 1,25(OH)2D, which occurs in the kidneys, the immune system, and elsewhere. Calcitriol is the active, steroid-hormone form of vitamin D, which binds with vitamin D receptors found in most cells in the body. There is a significant delay involved in the conversion from cholecalciferol, therefore calcifediol (calcidiol) or calcitriol may be preferable for treatment.

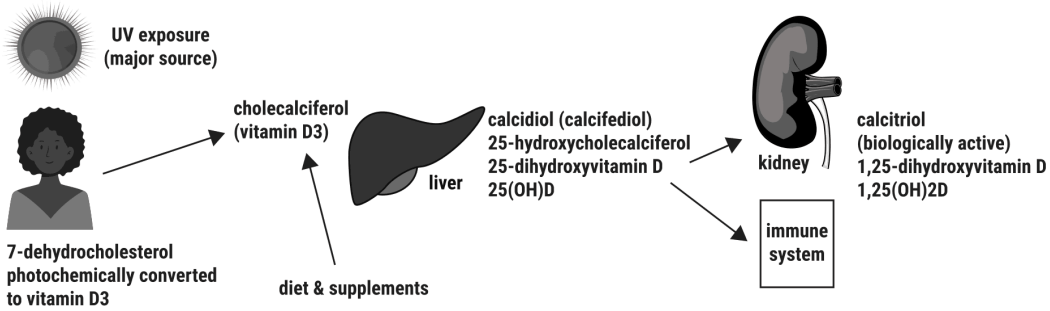


Figure 3. Simplified view of vitamin D sources and conversion.

Sufficiency. Many vitamin D studies analyze outcomes based on serum vitamin D levels which may be maintained via sun exposure, diet, or supplementation. We refer to these studies as sufficiency studies, as they typically present outcomes based on vitamin D sufficiency. These studies do not establish a causal link between vitamin D and outcomes. In general, low vitamin D levels are correlated with many other factors that may influence COVID-19 susceptibility and severity. Therefore, beneficial effects found in these studies may be due to factors other than vitamin D. On the other hand, if vitamin D is causally linked to the observed benefits, it is possible that adjustments for correlated factors could obscure this relationship. COVID-19 disease may also affect vitamin D levels *Silva*, suggesting additional caution in interpreting results for studies where the vitamin D levels are measured during the disease. For these reasons, we analyze sufficiency studies separately from treatment studies. We include all sufficiency studies that provide a comparison between two groups with low and high levels. Some studies only provide results as a function of change in vitamin D levels *Butler-Laporte, Gupta, Raisi-Estabragh*, which may not be indicative of results for deficiency/insufficiency versus sufficiency (increasing already sufficient levels may be less useful for example). Some studies show the average vitamin D level for patients in different groups, *Abdulameer, Aci, Al-Daghri, Alarslan, Azadeh, Beheshti, Chodick, D'Avolio, Desai, di Filippo, Ersöz, Hosseini (B), Jabbar, Jain, Kerget, Kumar, Latifi-Pupovci, Mansour, Mardani, Morad, Nicolescu, Pop-Kostova, Qu, Ranjbar, Rathod, Saeed, Saeed (B), Schmitt, Shannak, Sinnberg, Soltani-Zangbar, Takase, Vassiliou*, most of which show lower D levels for worse outcomes. Other studies analyze vitamin D status and outcomes in geographic regions, *Bakaloudi, Jayawardena, Marik, Papadimitriou, Rhodes, Sooriyaarachchi, Walrand, Yadav*, all finding worse outcomes to be more likely with lower D levels.

Sufficiency studies vary widely in terms of when vitamin D levels were measured, the cutoff level used, and the population analyzed (for example studies with hospitalized patients exclude the effect of vitamin D on the risk of hospitalization). We do not analyze sufficiency studies in more detail because there are many controlled treatment studies that provide better information on the use of vitamin D as a treatment for COVID-19. A more detailed analysis of sufficiency studies can be found in *Chiodini*. *Mishra* present a systematic review and meta analysis showing that vitamin D levels are significantly associated with COVID-19 cases.

Treatment. For studies regarding treatment with vitamin D, we distinguish three stages as shown in Figure 4. Prophylaxis refers to regularly taking vitamin D before being infected in order to minimize the severity of infection. Due to the mechanism of action, vitamin D is unlikely to completely prevent infection, although it may prevent infection from reaching a level detectable by PCR. Early Treatment refers to treatment immediately or soon after symptoms appear, while Late Treatment refers to more delayed treatment.

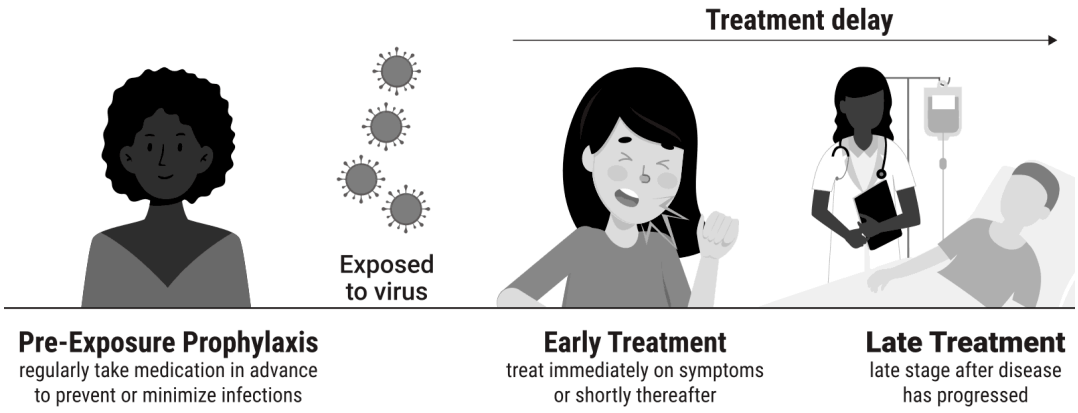


Figure 4. Treatment stages.

Preclinical Research

Vitamin D inhibits SARS-CoV-2 replication *in vitro* [Campolina-Silva, Pickard], mitigates lung inflammation, damage, and lethality in mice with an MHV-3 model for β-CoV respiratory infections [Campolina-Silva, Pickard], reduces SARS-CoV-2 replication in nasal epithelial cells via increased type I interferon expression [Sposito], downregulates proinflammatory cytokines IL-1β and TNF-α in SARS-CoV-2 spike protein-stimulated cells [Alcalá-Santiago], attenuates nucleocapsid protein-induced hyperinflammation by inactivating the NLRP3 inflammasome through the VDR-BRCC3 signaling pathway [Chen], and may be neuroprotective by protecting the blood-brain barrier, reducing neuroinflammation, and via immunomodulatory effects [Gotelli].

7 *In Silico* studies support the efficacy of vitamin D [Al-Mazaideh, Chellasamy, Mansouri, Morales-Bayuelo, Pandya, Qayyum, Song].

10 *In Vitro* studies support the efficacy of vitamin D [Alcalá-Santiago, Campolina-Silva, Chen, DiGuilio, Moatasim, Mok, Pickard, Rybakovsky, Sposito, Vargas-Castro].

3 *In Vivo* animal studies support the efficacy of vitamin D [Campolina-Silva, Chen, Fernandes de Souza].

Preclinical research is an important part of the development of treatments, however results may be very different in clinical trials. Preclinical results are not used in this paper.

Results

Table 1 summarizes the results for all stages combined, for Randomized Controlled Trials, for peer-reviewed studies, with different exclusions, for specific outcomes, and for sufficiency (non-treatment) studies. Table 2 shows results by treatment stage. Figure 5 and Figure 6 show individual results for treatment studies and sufficiency studies, and by treatment stage. Figure 7, 8, 9, 10, 11, 12, and 13 show forest plots for treatment studies with pooled effects, peer-reviewed studies, cholecalciferol studies, calcifediol/calcitriol studies, and for studies reporting mortality, mechanical ventilation, ICU admission, hospitalization, and case results only. Figure 14 shows a forest plot for random effects meta-analysis of sufficiency (non-treatment) studies.

	Improvement	*Studies*	*Patients*	*Authors*
All studies	**37%** [31-42%] p < 0.0001 ****	120	195,508	1,216
Exc. late treatment	**48%** [37-56%] p < 0.0001 ****	59	53,781	568
After exclusions	**41%** [34-46%] p < 0.0001 ****	84	171,477	888
Peer-reviewed studies	**37%** [31-42%] p < 0.0001 ****	113	193,688	1,145
Randomized Controlled Trials	**31%** [20-40%] p < 0.0001 ****	29	42,424	344
RCTs after exclusions	**41%** [26-54%] p < 0.0001 ****	20	41,101	256
Cholecalciferol	**35%** [29-41%] p < 0.0001 ****	106	186,169	1,045
Calcifediol/calcitriol	**50%** [30-64%] p < 0.0001 ****	14	9,339	171
Mortality	**36%** [28-43%] p < 0.0001 ****	67	63,448	656
Ventilation	**16%** [-7-34%] p = 0.16	19	8,440	216
ICU admission	**46%** [28-60%] p < 0.0001 ****	27	40,686	305
Hospitalization	**19%** [9-29%] p = 0.00059 ***	24	86,502	243
Recovery	**26%** [16-34%] p < 0.0001 ****	13	1,230	123
Cases	**17%** [9-24%] p = 0.00013 ***	30	145,598	338
Viral	**52%** [30-67%] p = 0.00014 ***	4	200	26
RCT mortality	**34%** [11-51%] p = 0.0075 **	16	2,249	185
RCT ventilation	**20%** [1-34%] p = 0.037 *	10	5,662	126
RCT ICU admission	**31%** [6-49%] p = 0.017 *	12	36,416	165
RCT hospitalization	**19%** [5-32%] p = 0.012 *	9	40,013	114
Sufficiency	**53%** [49-56%] p < 0.0001 ****	196	250,729	1,693

Table 1. **Random effects meta-analysis for all stages combined, for Randomized Controlled Trials, for peer-reviewed studies, with different exclusions, for specific outcomes, and for sufficiency (non-treatment) studies.** Results show the percentage improvement with treatment and the 95% confidence interval. * $p<0.05$ ** $p<0.01$ *** $p<0.001$ **** $p<0.0001$.

	Early treatment	*Late treatment*	*Prophylaxis*
All studies	**60%** [40-74%] ****	**44%** [32-54%] ****	**31%** [24-38%] ****
Exc. late treatment	**60%** [40-74%] ****	**44%** [32-54%] ****	
After exclusions	**68%** [45-82%] ****	**63%** [51-72%] ****	**30%** [22-36%] ****
Peer-reviewed studies	**57%** [36-71%] ****	**43%** [31-53%] ****	**32%** [24-39%] ****
Randomized Controlled Trials	**32%** [8-50%] *	**36%** [17-50%] ***	**25%** [-9-48%]
RCTs after exclusions	**65%** [-65-92%]	**50%** [31-64%] ****	**25%** [-9-48%]
Cholecalciferol	**60%** [40-74%] ****	**39%** [26-49%] ****	**31%** [23-38%] ****
Calcifediol/calcitriol		**65%** [41-79%] ***	**36%** [13-54%] **
Mortality	**68%** [39-84%] ***	**43%** [30-54%] ****	**23%** [9-34%] **
Ventilation	**97%** [56-100%] *	**7%** [-18-27%]	**38%** [-3-63%]
ICU admission	**87%** [-143-99%]	**46%** [24-62%] ***	**46%** [22-63%] **
Hospitalization	**90%** [-453-100%]	**18%** [8-28%] ***	**13%** [-4-27%]
Recovery	**31%** [7-49%] *	**26%** [13-37%] ***	
Cases			**17%** [9-24%] ***
Viral	**52%** [24-70%] **	**53%** [8-76%] *	
RCT mortality		**34%** [11-51%] **	
RCT ventilation		**20%** [2-35%] *	**-95%** [-3010-88%]
RCT ICU admission		**34%** [8-52%] *	**-0%** [-301-75%]
RCT hospitalization		**22%** [11-31%] ***	**-26%** [-92-17%]

Table 2. **Random effects meta-analysis results by treatment stage.** Results show the percentage improvement with treatment, the 95% confidence interval, and the number of studies for the stage. * $p<0.05$ ** $p<0.01$ *** $p<0.001$ **** $p<0.0001$.

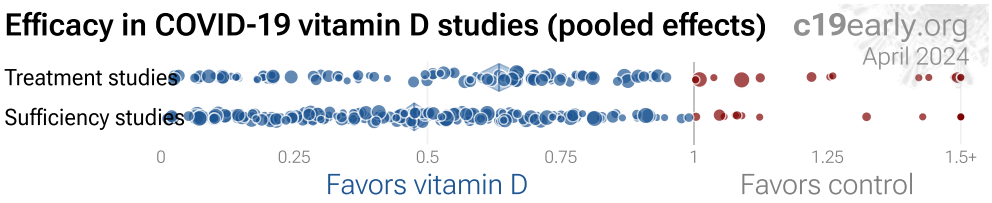


Figure 5. **Results for treatment and sufficiency studies.**

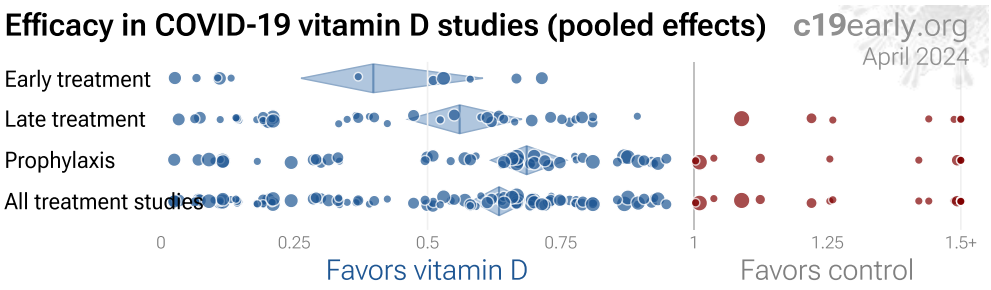


Figure 6. Results by treatment stage.

All 120 vitamin D COVID-19 treatment studies

c19early.org
April 2024

	Improvement, RR [CI]			Treatment	Control	Dose (5d)	
Annweiler	89%	0.11 [0.03-0.48]	death	10/57	5/9	80,000IU	
Annweiler	63%	0.37 [0.06-2.21]	death	3/16	10/32	80,000IU	
Burahee	93%	0.07 [0.01-0.54]	death	0/12	2/2	400,000IU	
Asimi	97%	0.03 [0.00-0.44]	ventilation	0/270	9/86	10,000IU	CT[1]
Sánchez-Zuno (RCT)	89%	0.11 [0.01-0.91]	severe case	0/22	4/20	50,000IU	
Efird	49%	0.51 [0.23-1.17]	death	11/544	413/15,794	varies	
Valecha	87%	0.13 [0.01-2.43]	ICU	0/30	3/25	5,000IU	CT[1]
Khan (RCT)	33%	0.67 [0.37-1.19]	no recov.	10/25	15/25	1,800IU	CT[1]
Hunt	47%	0.53 [0.37-0.77]	death	43/1,019	1,569/25,489	n/a	
Said (RCT)	42%	0.58 [0.09-3.47]	recovery	30 (n)	30 (n)	10,000IU	
Din Ujjan (RCT)	29%	0.71 [0.50-1.03]	no recov.	15/25	21/25	1,800IU	CT[1]
Early treatment	60%	0.40 [0.26-0.60]		92/2,050	2,051/41,537		**60% lower risk**

$Tau^2 = 0.21$, $I^2 = 62.3\%$, $p < 0.0001$

	Improvement, RR [CI]			Treatment	Control	Dose (5d)	
Tan	80%	0.20 [0.04-0.93]	oxygen	3/17	16/26	5,000IU	CT[1]
Krishnan	19%	0.81 [0.49-1.34]	death	8/16	84/136	n/a	
Castillo (RCT)	85%	0.15 [0.01-2.93]	death	0/50	2/26	0.8mg (c)	COVIDIOL
Rastogi (RCT)	53%	0.47 [0.24-0.92]	viral+	6/16	19/24	300,000IU	SHADE
Murai (DB RCT)	-49%	1.49 [0.55-4.05]	death	9/119	6/118	200,000IU	
Ling	80%	0.20 [0.08-0.48]	death	73 (n)	253 (n)	40,000IU	
Jevalikar	82%	0.18 [0.02-1.69]	death	1/128	3/69	60,000IU	
Giannini	37%	0.63 [0.35-1.09]	death/ICU	14/36	29/55	400,000IU	
Nogués (QR)	79%	0.21 [0.10-0.43]	death	21/447	62/391	0.8mg (c)	
Lohia	11%	0.89 [0.32-1.89]	death	26 (n)	69 (n)	n/a	
Mazziotti	19%	0.81 [0.45-1.47]	death	116 (n)	232 (n)	varies	
Elhadi (ICU)	23%	0.77 [0.44-1.32]	death	7/15	274/450	n/a	ICU patients
Alcala-Diaz	81%	0.19 [0.04-0.83]	death	4/79	90/458	0.8mg (c)	
Güven (ICU)	25%	0.75 [0.37-1.24]	death	43/113	30/62	300,000IU	ICU patients
Assiri (ICU)	-66%	1.66 [0.25-7.87]	death	12/90	2/28	n/a	ICU patients
Soliman (RCT)	63%	0.37 [0.09-2.78]	death	7/40	3/16	200,000IU	
Elamir (RCT)	86%	0.14 [0.01-2.63]	death	0/25	3/25	2.5µg (t)	
Yildiz	81%	0.19 [0.04-0.91]	death	1/37	24/170	300,000IU	
Maghbooli (DB RCT)	40%	0.60 [0.15-2.38]	death	3/53	5/53	125µg (c)	
Leal-Martínez (RCT)	86%	0.14 [0.03-0.80]	death	1/40	7/40	20,000IU	CT[1]
Beigm.. (SB RCT)	89%	0.11 [0.01-1.98]	death	0/30	4/30	600,000IU	ICU patients CT[1]
Baguma	97%	0.03 [0.00-0.54]	death	23 (n)	458 (n)	n/a	
Mahmood	30%	0.70 [0.47-1.04]	death	45/238	31/114	varies	
Bishop (DB RCT)	34%	0.66 [0.23-1.92]	no recov.	5/65	8/69	1020µg (c)	REsCue
Cannata-An.. (RCT)	-44%	1.44 [0.76-2.72]	death	22/274	15/269	100,000IU	COVID-VIT-D
Zangeneh (ICU)	-26%	1.26 [0.73-2.16]	death	n/a	n/a	n/a	ICU patients
Fiore	93%	0.07 [0.07-0.63]	death	3/58	11/58	200,000IU	
Mariani (DB RCT)	-124%	2.24 [0.44-11.3]	death	5/115	2/103	500,000IU	CARED
Baykal	22%	0.78 [0.41-1.47]	death	7/18	28/56	300,000IU	
Singh (DB RCT)	45%	0.55 [0.31-0.99]	death	11/45	20/45	600,000IU	Shade-S
Shahid	38%	0.62 [0.47-0.82]	death	705 (n)	773 (n)	n/a	
Karonova (RCT)	86%	0.14 [0.01-2.66]	ICU	0/56	3/54	50,000IU	
Zurita-C.. (SB RCT)	79%	0.21 [0.03-1.59]	death	1/20	6/25	10,000IU	
De Niet (DB RCT)	65%	0.35 [0.04-3.10]	death	1/21	3/22	100,000IU	
Fairfield	-9%	1.09 [1.04-1.12]	death	population-based cohort		n/a	
Lakkireddy (RCT)	61%	0.39 [0.08-1.91]	death	2/44	5/43	300,000IU	see notes
Hafez	94%	0.06 [0.00-1.29]	death	0/7	12/30	150,000IU	
Saheb Shari.. (ICU)	36%	0.64 [0.46-0.90]	ICU	20 (n)	25 (n)	50,000IU	ICU patients
Karimpour-Razke..	79%	0.21 [0.10-0.45]	death	10/124	93/329	n/a	
Hafezi (ICU)	63%	0.37 [0.14-0.94]	death	8/43	12/37	50,000IU	ICU patients
Bychinin (DB RCT)	27%	0.73 [0.47-1.14]	death	19/52	27/54	80,000IU	COVID-VIT ICU patients
Domazet B.. (RCT)	21%	0.79 [0.55-1.13]	death	30/75	39/77	50,000IU	ICU patients
Salman (RCT)	60%	0.40 [0.16-1.00]	death	6/150	15/150	20,000IU	
Shamsi	58%	0.42 [0.06-2.95]	death	1/17	23/166	n/a	
Mingiano	39%	0.61 [0.38-0.99]	death	13/56	88/232	900µg (c)	
Al Sulaiman (ICU)	-22%	1.22 [0.87-1.71]	death	72/144	62/144	n/a	ICU patients
Ogasawara	67%	0.33 [0.01-8.01]	death	0/54	1/54	5µg (p)	
Seely (DB RCT)	48%	0.52 [0.10-2.71]	progression	2/42	4/44	55,000IU	CT[1]
Late treatment	44%	0.56 [0.46-0.68]		403/4,032	1,171/6,162		**44% lower risk**

$Tau^2 = 0.22$, $I^2 = 79.9\%$, $p < 0.0001$

	Improvement, RR [CI]			Treatment	Control	Dose (1m)
Blanch-Rubió	8%	0.92 [0.63-1.36]	cases	62/1,303	47/799	n/a
Sainz-Amo	33%	0.67 [0.27-1.67]	severe case	case control		n/a
Hernández	-4%	1.04 [0.26-4.10]	death	2/19	20/197	varies

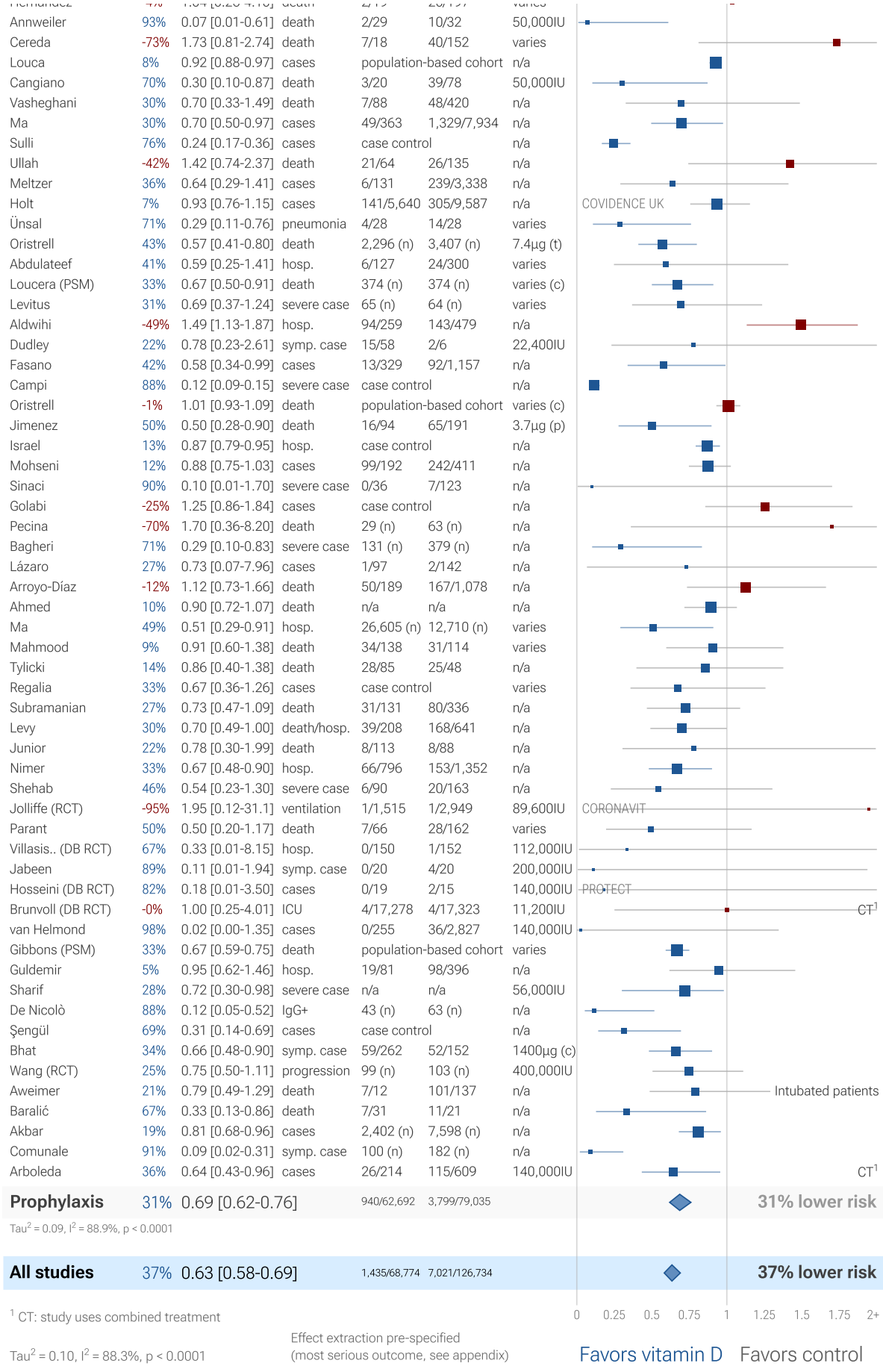


Figure 7. **Random effects meta-analysis for treatment studies.** Effect extraction is pre-specified, using the most serious outcome reported, see the appendix for details. Analysis validating pooled outcomes for COVID-19 can be found below.

All 113 vitamin D COVID-19 peer reviewed studies

c19early.org
April 2024

	Improvement, RR [CI]		Treatment	Control	Dose (5d)	
Annweiler	89%	0.11 [0.03-0.48] death	10/57	5/9	80,000IU	
Annweiler	63%	0.37 [0.06-2.21] death	3/16	10/32	80,000IU	
Burahee	93%	0.07 [0.01-0.54] death	0/12	2/2	400,000IU	
Sánchez-Zuno (RCT)	89%	0.11 [0.01-0.91] severe case	0/22	4/20	50,000IU	
Efird	49%	0.51 [0.23-1.17] death	11/544	413/15,794	varies	
Valecha	87%	0.13 [0.01-2.43] ICU	0/30	3/25	5,000IU	CT[1]
Khan (RCT)	33%	0.67 [0.37-1.19] no recov.	10/25	15/25	1,800IU	CT[1]
Hunt	47%	0.53 [0.37-0.77] death	43/1,019	1,569/25,489	n/a	
Said (RCT)	42%	0.58 [0.09-3.47] recovery	30 (n)	30 (n)	10,000IU	
Din Ujjan (RCT)	29%	0.71 [0.50-1.03] no recov.	15/25	21/25	1,800IU	CT[1]
Early treatment	57%	0.43 [0.29-0.64]	92/1,780	2,042/41,451		57% lower risk

$Tau^2 = 0.17$, $I^2 = 59.6\%$, $p < 0.0001$

	Improvement, RR [CI]		Treatment	Control	Dose (5d)	
Tan	80%	0.20 [0.04-0.93] oxygen	3/17	16/26	5,000IU	CT[1]
Krishnan	19%	0.81 [0.49-1.34] death	8/16	84/136	n/a	
Castillo (RCT)	85%	0.15 [0.01-2.93] death	0/50	2/26	0.8mg (c)	COVIDIOL
Rastogi (RCT)	53%	0.47 [0.24-0.92] viral+	6/16	19/24	300,000IU	SHADE
Murai (DB RCT)	-49%	1.49 [0.55-4.05] death	9/119	6/118	200,000IU	
Ling	80%	0.20 [0.08-0.48] death	73 (n)	253 (n)	40,000IU	
Jevalikar	82%	0.18 [0.02-1.69] death	1/128	3/69	60,000IU	
Giannini	37%	0.63 [0.35-1.09] death/ICU	14/36	29/55	400,000IU	
Nogués (QR)	79%	0.21 [0.10-0.43] death	21/447	62/391	0.8mg (c)	
Lohia	11%	0.89 [0.32-1.89] death	26 (n)	69 (n)	n/a	
Mazziotti	19%	0.81 [0.45-1.47] death	116 (n)	232 (n)	varies	
Elhadi (ICU)	23%	0.77 [0.44-1.32] death	7/15	274/450	n/a	ICU patients
Alcala-Diaz	81%	0.19 [0.04-0.83] death	4/79	90/458	0.8mg (c)	
Güven (ICU)	25%	0.75 [0.37-1.24] death	43/113	30/62	300,000IU	ICU patients
Assiri (ICU)	-66%	1.66 [0.25-7.87] death	12/90	2/28	n/a	ICU patients
Soliman (RCT)	63%	0.37 [0.09-2.78] death	7/40	3/16	200,000IU	
Elamir (RCT)	86%	0.14 [0.01-2.63] death	0/25	3/25	2.5µg (t)	
Yildiz	81%	0.19 [0.04-0.91] death	1/37	24/170	300,000IU	
Maghbooli (DB RCT)	40%	0.60 [0.15-2.38] death	3/53	5/53	125µg (c)	
Leal-Martínez (RCT)	86%	0.14 [0.03-0.80] death	1/40	7/40	20,000IU	CT[1]
Beigm.. (SB RCT)	89%	0.11 [0.01-1.98] death	0/30	4/30	600,000IU	ICU patients CT[1]
Mahmood	30%	0.70 [0.47-1.04] death	45/238	31/114	varies	
Bishop (DB RCT)	34%	0.66 [0.23-1.92] no recov.	5/65	8/69	1020µg (c)	REsCue
Cannata-An.. (RCT)	-44%	1.44 [0.76-2.72] death	22/274	15/269	100,000IU	COVID-VIT-D
Zangeneh (ICU)	-26%	1.26 [0.73-2.16] death	n/a	n/a	n/a	ICU patients
Fiore	93%	0.07 [0.07-0.63] death	3/58	11/58	200,000IU	
Mariani (DB RCT)	-124%	2.24 [0.44-11.3] death	5/115	2/103	500,000IU	CARED
Baykal	22%	0.78 [0.41-1.47] death	7/18	28/56	300,000IU	
Singh (DB RCT)	45%	0.55 [0.31-0.99] death	11/45	20/45	600,000IU	Shade-S
Shahid	38%	0.62 [0.47-0.82] death	705 (n)	773 (n)	n/a	
Karonova (RCT)	86%	0.14 [0.01-2.66] ICU	0/56	3/54	50,000IU	
Zurita-C.. (SB RCT)	79%	0.21 [0.03-1.59] death	1/20	6/25	10,000IU	
De Niet (DB RCT)	65%	0.35 [0.04-3.10] death	1/21	3/22	100,000IU	
Fairfield	-9%	1.09 [1.04-1.12] death	population-based cohort		n/a	
Lakkireddy (RCT)	61%	0.39 [0.08-1.91] death	2/44	5/43	300,000IU	see notes
Hafez	94%	0.06 [0.00-1.29] death	0/7	12/30	150,000IU	
Saheb Shari.. (ICU)	36%	0.64 [0.46-0.90] ICU	20 (n)	25 (n)	50,000IU	ICU patients
Karimpour-Razke..	79%	0.21 [0.10-0.45] death	10/124	93/329	n/a	
Hafezi (ICU)	63%	0.37 [0.14-0.94] death	8/43	12/37	50,000IU	ICU patients
Bychinin (DB RCT)	27%	0.73 [0.47-1.14] death	19/52	27/54	80,000IU	COVID-VIT ICU patients
Domazet B.. (RCT)	21%	0.79 [0.55-1.13] death	30/75	39/77	50,000IU	ICU patients
Salman (RCT)	60%	0.40 [0.16-1.00] death	6/150	15/150	20,000IU	
Shamsi	58%	0.42 [0.06-2.95] death	1/17	23/166	n/a	
Mingiano	39%	0.61 [0.38-0.99] death	13/56	88/232	900µg (c)	
Al Sulaiman (ICU)	-22%	1.22 [0.87-1.71] death	72/144	62/144	n/a	ICU patients
Ogasawara	67%	0.33 [0.01-8.01] death	0/54	1/54	5µg (p)	
Seely (DB RCT)	48%	0.52 [0.10-2.71] progression	2/42	4/44	55,000IU	CT[1]
Late treatment	43%	0.57 [0.47-0.69]	403/4,009	1,171/5,704		43% lower risk

$Tau^2 = 0.21$, $I^2 = 79.9\%$, $p < 0.0001$

	Improvement, RR [CI]		Treatment	Control	Dose (1m)
Blanch-Rubió	8%	0.92 [0.63-1.36] cases	62/1,303	47/799	n/a
Sainz-Amo	33%	0.67 [0.27-1.67] severe case	case control		n/a
Hernández	-4%	1.04 [0.26-4.10] death	2/19	20/197	varies
Annweiler	93%	0.07 [0.01-0.61] death	2/29	10/32	50,000IU
Cereda	-73%	1.73 [0.81-2.74] death	7/18	40/152	varies

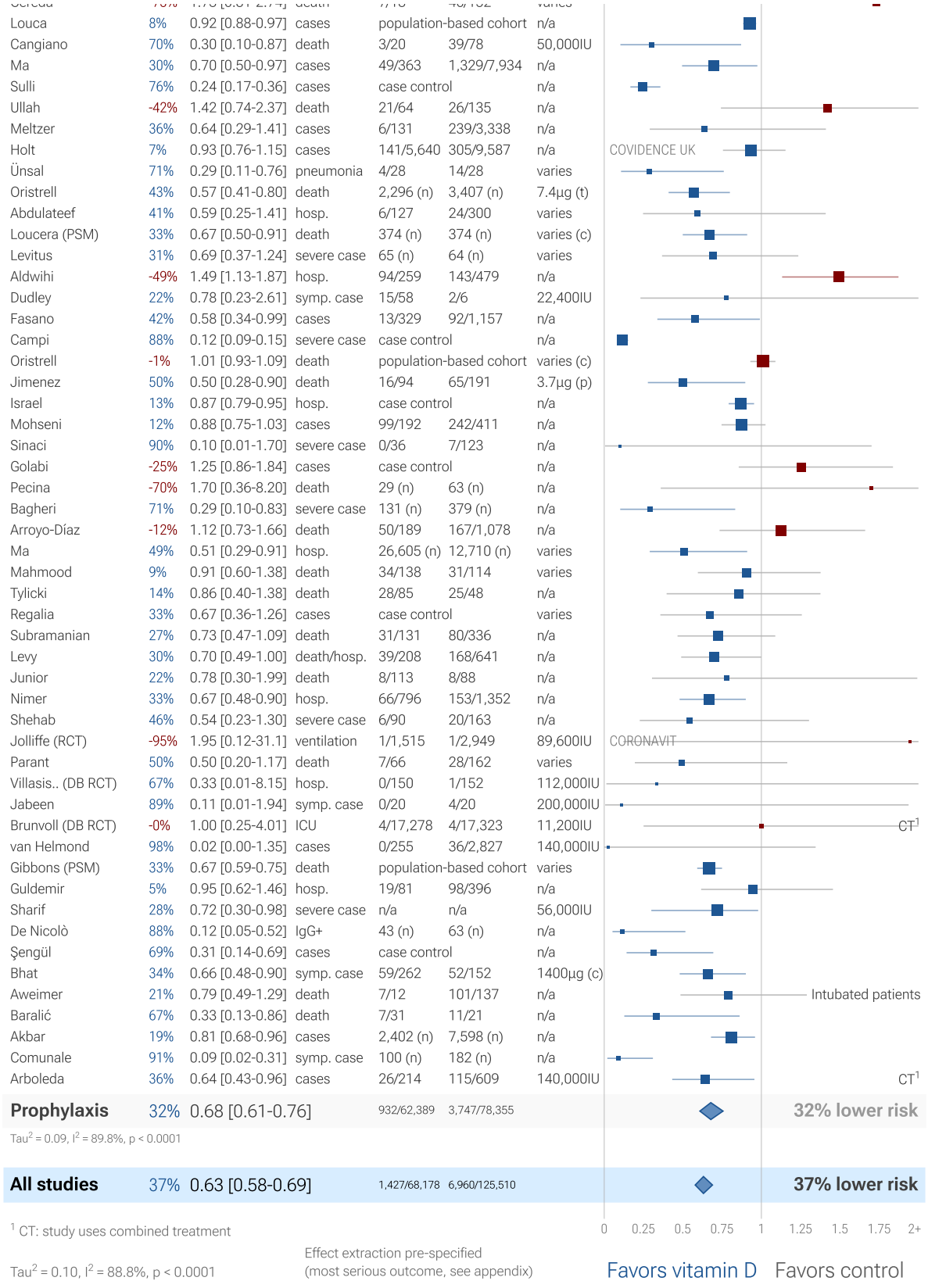


Figure 8. **Random effects meta-analysis for peer-reviewed treatment studies.** *Zeraatkar et al.* analyze 356 COVID-19 trials, finding no significant evidence that preprint results are inconsistent with peer-reviewed studies. They also show extremely long peer-review delays, with a median of 6 months to journal publication. A six month delay was equivalent to around 1.5 million deaths during the first two years of the pandemic. Authors recommend using preprint evidence, with appropriate checks for potential falsified data, which provides higher certainty much earlier. *Davidson et al.* also showed no important difference between meta analysis results of preprints and peer-reviewed publications for COVID-19, based on 37 meta analyses including 114 trials. Effect extraction is pre-specified, using the most serious outcome reported, see the appendix for details. Analysis validating pooled outcomes for COVID-19 can be found below.

All 67 vitamin D COVID-19 treatment mortality results

c19early.org
April 2024

	Improvement, RR [CI]	Treatment	Control	Dose (5d)	
Annweiler	89% 0.11 [0.03-0.48]	10/57	5/9	80,000IU	
Annweiler	63% 0.37 [0.06-2.21]	3/16	10/32	80,000IU	
Burahee	93% 0.07 [0.01-0.54]	0/12	2/2	400,000IU	
Efird	49% 0.51 [0.23-1.17]	11/544	413/15,794	varies	
Hunt	47% 0.53 [0.37-0.77]	43/1,019	1,569/25,489	n/a	
Early treatment	**68% 0.32 [0.16-0.61]**	67/1,648	1,999/41,326		**68% lower risk**

$Tau^2 = 0.34$, $I^2 = 73.1\%$, $p = 0.00067$

	Improvement, RR [CI]	Treatment	Control	Dose (5d)	
Krishnan	19% 0.81 [0.49-1.34]	8/16	84/136	n/a	
Castillo (RCT)	85% 0.15 [0.01-2.93]	0/50	2/26	0.8mg (c)	COVIDIOL
Murai (DB RCT)	-49% 1.49 [0.55-4.05]	9/119	6/118	200,000IU	
Ling	80% 0.20 [0.08-0.48]	73 (n)	253 (n)	40,000IU	
Jevalikar	82% 0.18 [0.02-1.69]	1/128	3/69	60,000IU	
Nogués (QR)	79% 0.21 [0.10-0.43]	21/447	62/391	0.8mg (c)	
Lohia	11% 0.89 [0.32-1.89]	26 (n)	69 (n)	n/a	
Mazziotti	19% 0.81 [0.45-1.47]	116 (n)	232 (n)	varies	
Elhadi (ICU)	23% 0.77 [0.44-1.32]	7/15	274/450	n/a	ICU patients
Alcala-Diaz	81% 0.19 [0.04-0.83]	4/79	90/458	0.8mg (c)	
Güven (ICU)	25% 0.75 [0.37-1.24]	43/113	30/62	300,000IU	ICU patients
Assiri (ICU)	-66% 1.66 [0.25-7.87]	12/90	2/28	n/a	ICU patients
Soliman (RCT)	63% 0.37 [0.09-2.78]	7/40	3/16	200,000IU	
Elamir (RCT)	86% 0.14 [0.01-2.63]	0/25	3/25	2.5µg (t)	
Yildiz	81% 0.19 [0.04-0.91]	1/37	24/170	300,000IU	
Maghbooli (DB RCT)	40% 0.60 [0.15-2.38]	3/53	5/53	125µg (c)	
Leal-Martínez (RCT)	86% 0.14 [0.03-0.80]	1/40	7/40	20,000IU	CT[1]
Beigm.. (SB RCT)	89% 0.11 [0.01-1.98]	0/30	4/30	600,000IU	ICU patients CT[1]
Baguma	97% 0.03 [0.00-0.54]	23 (n)	458 (n)	n/a	
Mahmood	30% 0.70 [0.47-1.04]	45/238	31/114	varies	
Cannata-An.. (RCT)	-44% 1.44 [0.76-2.72]	22/274	15/269	100,000IU	COVID-VIT-D
Zangeneh (ICU)	-26% 1.26 [0.73-2.16]	n/a	n/a	n/a	ICU patients
Fiore	93% 0.07 [0.07-0.63]	3/58	11/58	200,000IU	
Mariani (DB RCT)	-124% 2.24 [0.44-11.3]	5/115	2/103	500,000IU	CARED
Baykal	22% 0.78 [0.41-1.47]	7/18	28/56	300,000IU	
Singh (DB RCT)	45% 0.55 [0.31-0.99]	11/45	20/45	600,000IU	Shade-S
Shahid	38% 0.62 [0.47-0.82]	705 (n)	773 (n)	n/a	
Zurita-C.. (SB RCT)	79% 0.21 [0.03-1.59]	1/20	6/25	10,000IU	
De Niet (DB RCT)	65% 0.35 [0.04-3.10]	1/21	3/22	100,000IU	
Fairfield	-9% 1.09 [1.04-1.12]	population-based cohort		n/a	
Lakkireddy (RCT)	61% 0.39 [0.08-1.91]	2/44	5/43	300,000IU	see notes
Hafez	94% 0.06 [0.00-1.29]	0/7	12/30	150,000IU	
Karimpour-Razke..	79% 0.21 [0.10-0.45]	10/124	93/329	n/a	
Hafezi (ICU)	63% 0.37 [0.14-0.94]	8/43	12/37	50,000IU	ICU patients
Bychinin (DB RCT)	27% 0.73 [0.47-1.14]	19/52	27/54	80,000IU	COVID-VIT ICU patients
Domazet B.. (RCT)	21% 0.79 [0.55-1.13]	30/75	39/77	50,000IU	ICU patients
Salman (RCT)	60% 0.40 [0.16-1.00]	6/150	15/150	20,000IU	
Shamsi	58% 0.42 [0.06-2.95]	1/17	23/166	n/a	
Mingiano	39% 0.61 [0.38-0.99]	13/56	88/232	900µg (c)	
Al Sulaiman (ICU)	-22% 1.22 [0.87-1.71]	72/144	62/144	n/a	ICU patients
Ogasawara	67% 0.33 [0.01-8.01]	0/54	1/54	5µg (p)	
Late treatment	**43% 0.57 [0.46-0.70]**	373/3,780	1,092/5,865		**43% lower risk**

$Tau^2 = 0.23$, $I^2 = 80.5\%$, $p < 0.0001$

	Improvement, RR [CI]	Treatment	Control	Dose (1m)
Hernández	-4% 1.04 [0.26-4.10]	2/19	20/197	varies
Annweiler	93% 0.07 [0.01-0.61]	2/29	10/32	50,000IU
Cereda	-73% 1.73 [0.81-2.74]	7/18	40/152	varies
Cangiano	70% 0.30 [0.10-0.87]	3/20	39/78	50,000IU
Vasheghani	30% 0.70 [0.33-1.49]	7/88	48/420	n/a
Ullah	-42% 1.42 [0.74-2.37]	21/64	26/135	n/a
Oristrell	43% 0.57 [0.41-0.80]	2,296 (n)	3,407 (n)	7.4µg (t)
Loucera (PSM)	33% 0.67 [0.50-0.91]	374 (n)	374 (n)	varies (c)
Oristrell	-1% 1.01 [0.93-1.09]	population-based cohort		varies (c)
Jimenez	50% 0.50 [0.28-0.90]	16/94	65/191	3.7µg (p)
Pecina	-70% 1.70 [0.36-8.20]	29 (n)	63 (n)	n/a
Arroyo-Díaz	-12% 1.12 [0.73-1.66]	50/189	167/1,078	n/a
Ahmed	10% 0.90 [0.72-1.07]	n/a	n/a	n/a
Mahmood	9% 0.91 [0.60-1.38]	34/138	31/114	varies
Tylicki	14% 0.86 [0.40-1.38]	28/85	25/48	n/a
Subramanian	27% 0.73 [0.47-1.09]	31/131	80/336	n/a

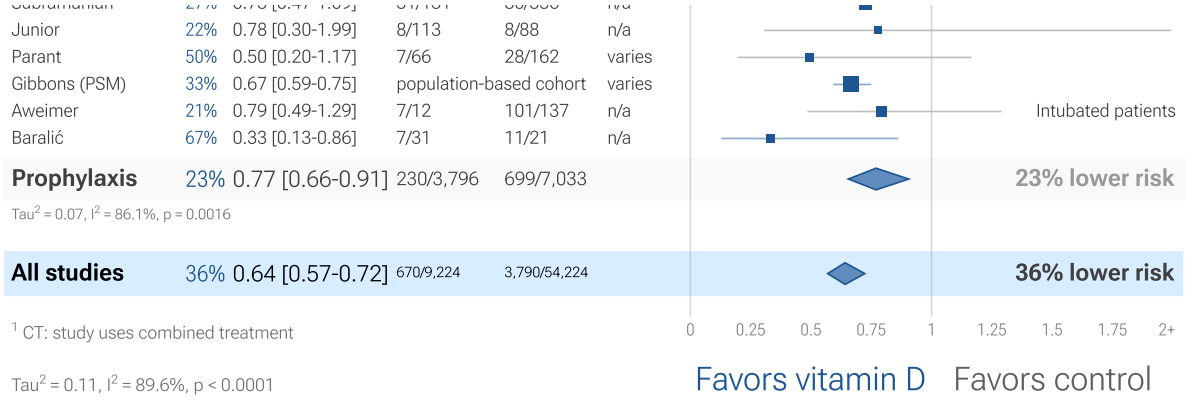


Figure 9. Random effects meta-analysis for treatment mortality results only.

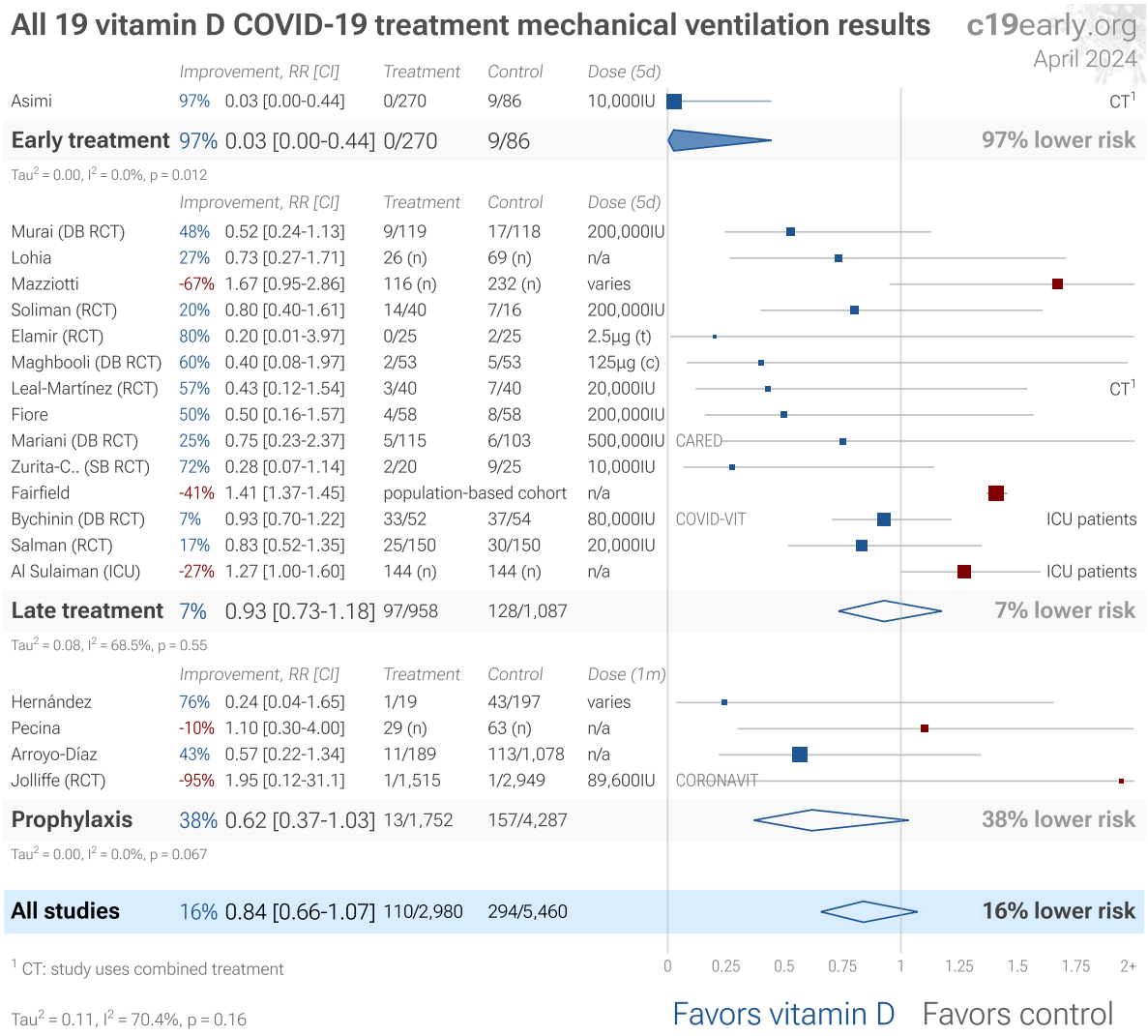


Figure 10. Random effects meta-analysis for treatment mechanical ventilation results only.

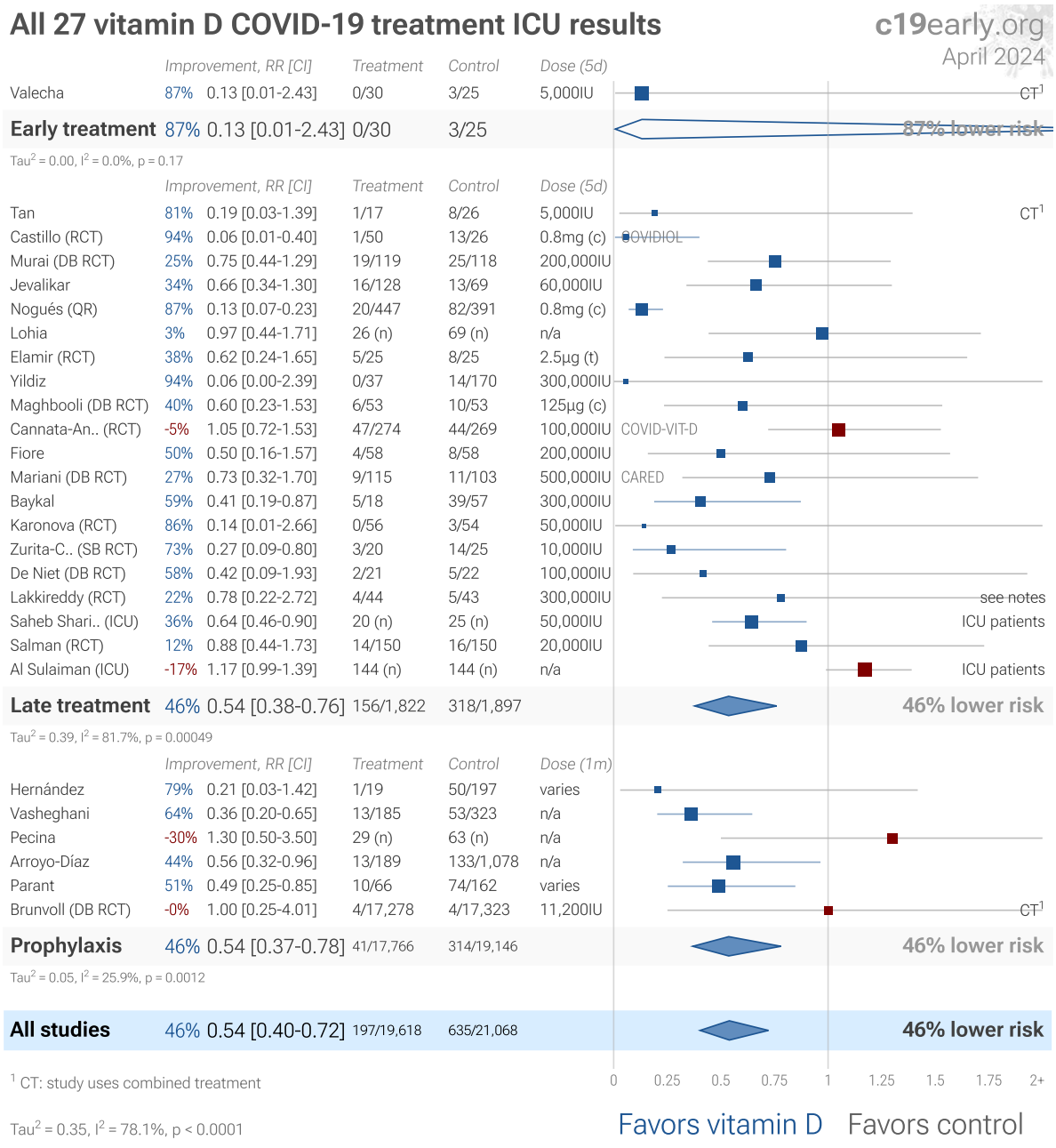


Figure 11. Random effects meta-analysis for treatment ICU admission results only.

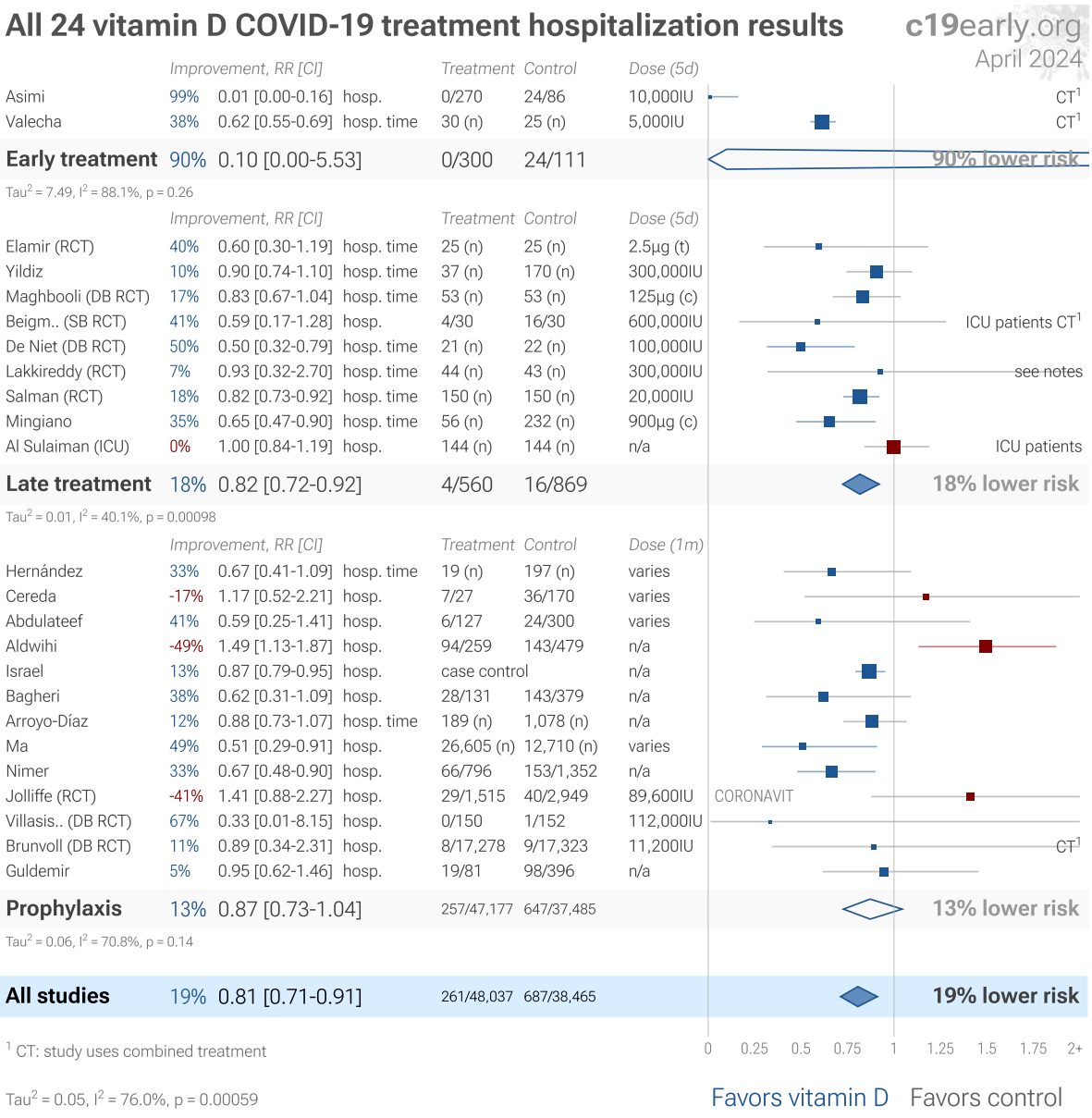


Figure 12. Random effects meta-analysis for treatment hospitalization results only.

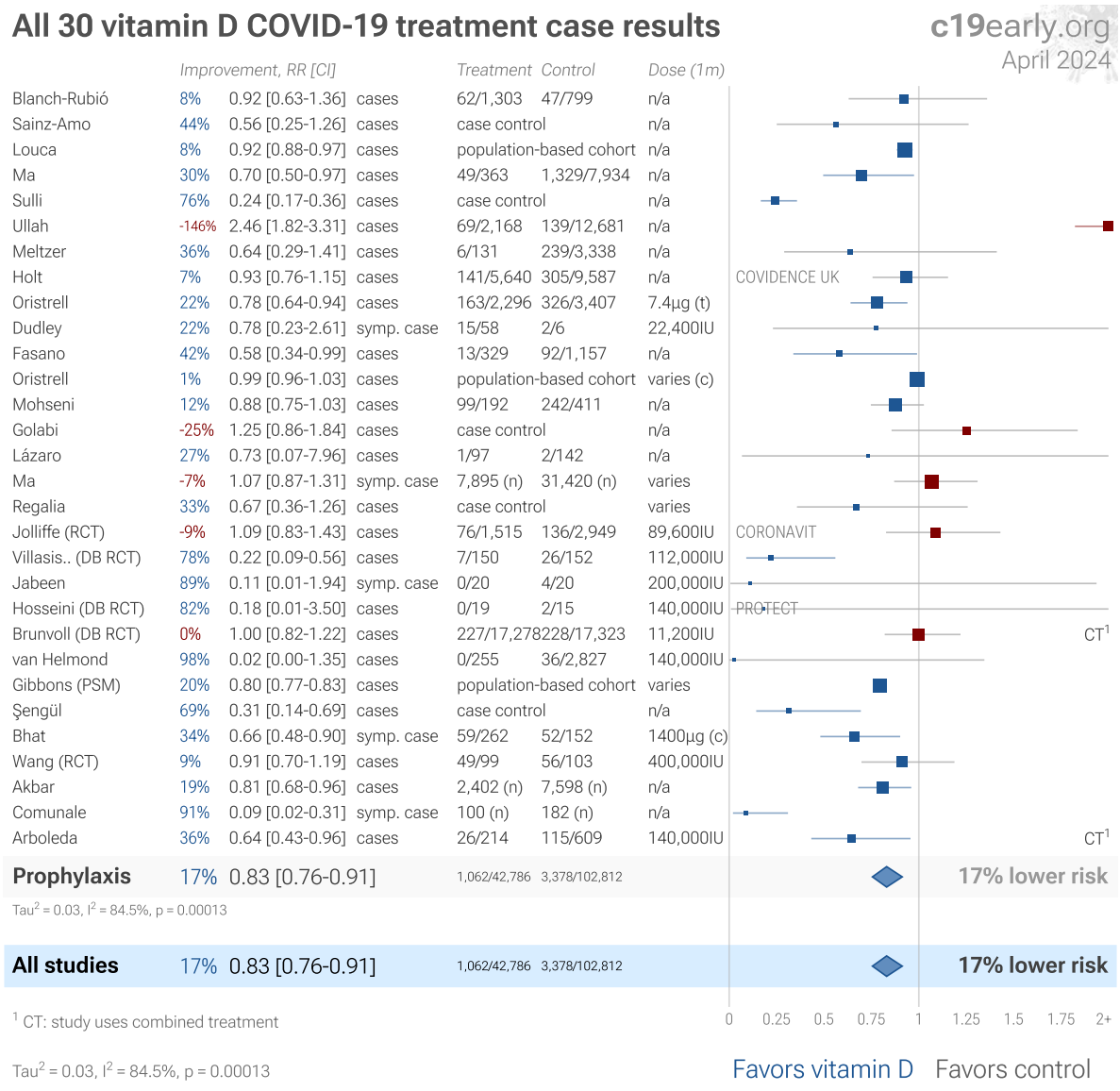
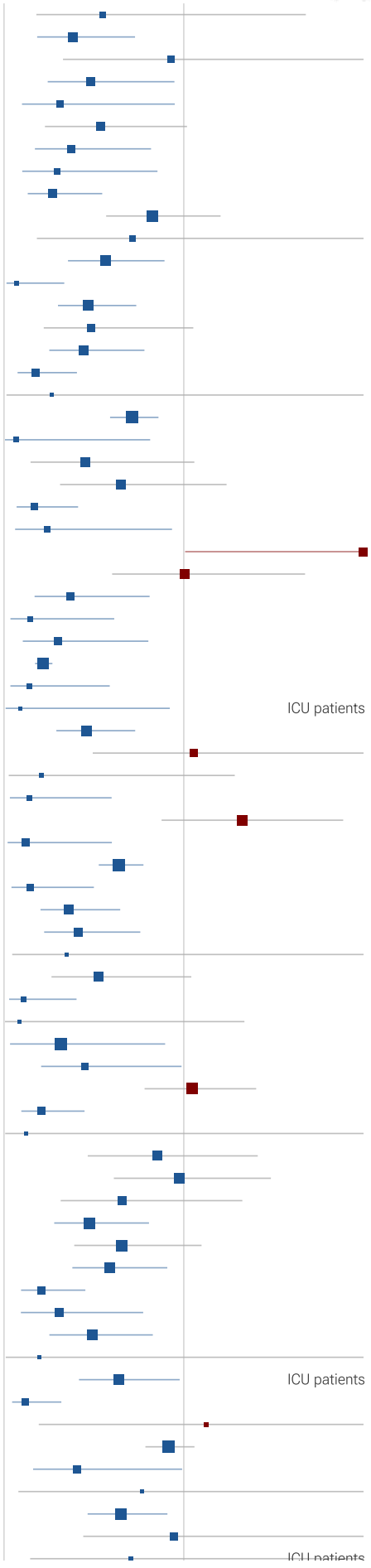


Figure 13. Random effects meta-analysis for treatment COVID-19 case results only.

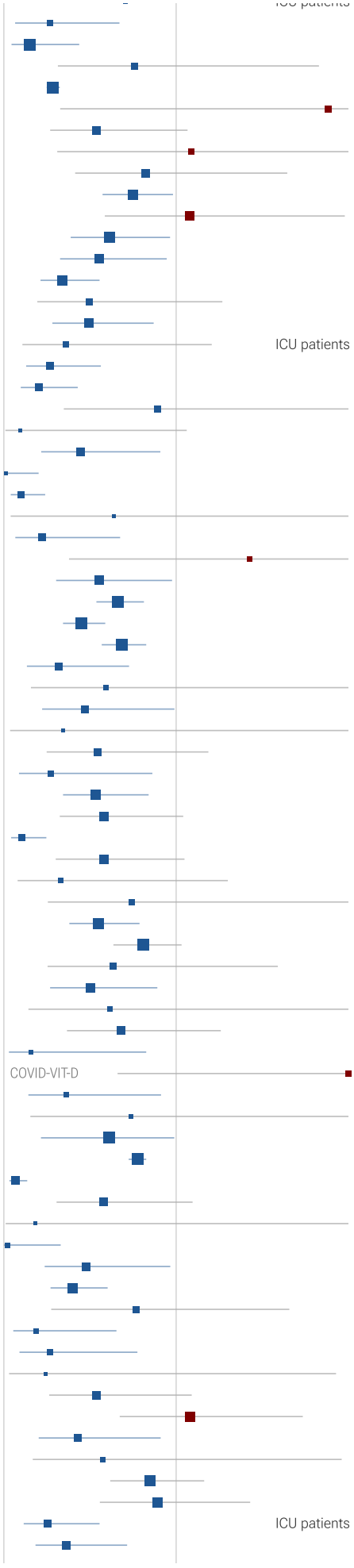
All 196 vitamin D COVID-19 sufficiency studies

c19early.org
April 2024

	Improvement	RR [CI]		High Levels	Low Levels
Lau	45%	0.55 [0.18-1.68]	ICU	2/5	11/15
Reyes Pérez	62%	0.38 [0.18-0.73]	death	21/137	14/35
Mendy	7%	0.93 [0.33-2.47]	death	21/600	5/89
Panagiotou	52%	0.48 [0.24-0.95]	ICU	8/44	34/90
Faul	69%	0.31 [0.10-0.95]	ventilation	4/21	8/12
Merzon	46%	0.54 [0.23-1.02]	hosp.	79 (n)	703 (n)
Anjum	62%	0.38 [0.17-0.82]	death	8/80	16/60
Carpagnano	71%	0.29 [0.10-0.85]	death	5/34	4/8
Im	73%	0.27 [0.13-0.55]	cases	case control	
Hastie	17%	0.83 [0.57-1.20]	death	population-based cohort	
Baktash	29%	0.71 [0.18-2.78]	death	4/31	6/39
Meltzer	44%	0.56 [0.36-0.89]	cases	39/317	32/172
Radujkovic	93%	0.07 [0.01-0.34]	death	144 (n)	12 (n)
Kaufman	53%	0.47 [0.30-0.74]	cases	12,321 (n)	39,190 (n)
Maghbooli	52%	0.48 [0.22-1.05]	death	7/72	27/134
Pepkowitz	56%	0.44 [0.25-0.78]	ICU	9/24	11/13
Karahan	83%	0.17 [0.08-0.41]	death	5/46	64/103
Yılmaz	73%	0.27 [0.01-5.14]	severe case	0/11	2/29
Faniyi	29%	0.71 [0.59-0.86]	seropositive	170/331	44/61
Ye	93%	0.07 [0.01-0.81]	hosp.	2/36	8/26
Macaya	55%	0.45 [0.15-1.06]	severe case	11/35	20/45
Tomasa-Irriguible	35%	0.65 [0.31-1.24]	ventilation	15/27	18/78
Hernández	83%	0.17 [0.07-0.41]	death/ICU	35 (n)	162 (n)
Abrishami	76%	0.24 [0.06-0.93]	death	3/47	9/26
Cereda	-120%	2.20 [1.01-3.22]	death	10/30	24/99
Walk	-0%	1.00 [0.60-1.67]	death/int.	48/110	10/23
Luo	63%	0.37 [0.17-0.81]	progression	335 (n)	560 (n)
Jain	85%	0.15 [0.04-0.61]	death	2/64	19/90
De Smet	70%	0.30 [0.10-0.80]	death	7/77	20/109
Katz	78%	0.22 [0.17-0.27]	cases	population-based cohort	
Alguwaihes	86%	0.14 [0.04-0.59]	death	111 (n)	328 (n)
Vassiliou (ICU)	91%	0.09 [0.01-0.92]	death	0/15	5/15
Abdollahi	54%	0.46 [0.29-0.73]	cases	108 (n)	294 (n)
Szeto	-6%	1.06 [0.49-2.26]	death	14/58	8/35
Karonova	79%	0.21 [0.03-1.28]	death	1/23	12/57
Ansari	86%	0.14 [0.03-0.60]	death	2/68	12/57
Amin	-32%	1.32 [0.88-1.89]	progression	population-based cohort	
Angelidi	88%	0.12 [0.02-0.60]	death	6/65	20/79
Li	36%	0.64 [0.53-0.78]	hosp.	population-based cohort	
Bennouar	86%	0.14 [0.04-0.50]	death	4/30	15/32
Vasheghani	64%	0.36 [0.20-0.65]	ICU	13/185	53/323
Orchard	59%	0.41 [0.22-0.76]	ICU	9/40	41/75
Barassi	65%	0.35 [0.05-2.69]	death	1/31	8/87
Tehrani	48%	0.52 [0.26-1.04]	death	34/180	9/25
Demir	89%	0.11 [0.03-0.40]	severe case	13 (n)	99 (n)
Susianti	91%	0.09 [0.01-1.34]	death	0/8	9/42
Basaran	69%	0.31 [0.03-0.90]	severe case	82/119	80/85
Infante	55%	0.45 [0.21-0.99]	death	4/19	55/118
Gavioli	-5%	1.05 [0.78-1.40]	death	80/260	52/177
Sulli	79%	0.21 [0.10-0.45]	cases	case control	
Ricci	88%	0.12 [0.01-2.28]	death	0/30	3/22
Lohia	15%	0.85 [0.47-1.41]	death	88 (n)	95 (n)
Mazziotti	2%	0.98 [0.61-1.48]	death	187 (n)	161 (n)
Charoenngam	34%	0.66 [0.32-1.33]	death	12/100	29/187
Vanegas-Cedillo	53%	0.47 [0.28-0.81]	death	95/494	21/57
Meltzer	35%	0.65 [0.39-1.10]	cases	61/1,097	118/1,251
Freitas	41%	0.59 [0.38-0.91]	death	23/179	68/311
Gaudio	79%	0.21 [0.09-0.45]	cases	case control	
Bayramoğlu	70%	0.30 [0.09-0.77]	severe case	10/60	24/43
Livingston	51%	0.49 [0.25-0.83]	cases	16/52	31/52
Ünsal	81%	0.19 [0.01-3.87]	death	0/29	2/27
Bychinin (ICU)	36%	0.64 [0.42-0.98]	death	16/38	31/47
Savitri	88%	0.12 [0.05-0.32]	symp. case	3/25	17/17
Davoudi	-12%	1.12 [0.19-6.52]	death	2/57	3/96
Li	9%	0.91 [0.79-1.06]	cases	610/13,650	290/4,498
AlSafar	59%	0.41 [0.16-0.99]	death	16/337	10/127
Reis	23%	0.77 [0.08-7.38]	death	198 (n)	16 (n)
Galaznik	35%	0.65 [0.47-0.91]	cases	13,903 (n)	2,384 (n)
Sánchez-Zuno	6%	0.94 [0.44-2.02]	severe case	4/8	18/34
Pimental (ICU)	29%	0.71 [0.15-3.43]	death	3/17	2/8



Diaz-Curiel	73%	0.27 [0.07-0.67]	ICU	3/214	91/1,017
Dror	85%	0.15 [0.04-0.44]	severe case	109/120	76/133
Campi	24%	0.76 [0.31-1.83]	death	6/39	13/64
Jude	72%	0.28 [0.25-0.32]	hosp.	n/a	n/a
Al-Jarallah	-88%	1.88 [0.33-6.97]	death	8/120	9/119
Zelzer	46%	0.54 [0.27-1.07]	death	24/121	10/27
Nasiri	-9%	1.09 [0.31-3.83]	death	238 (n)	43 (n)
Bianconi	18%	0.82 [0.41-1.65]	death	94 (n)	106 (n)
González-Estevez	25%	0.75 [0.57-0.98]	symp. case	6/8	32/32
Jimenez	-8%	1.08 [0.59-1.98]	death	50 (n)	110 (n)
Cozier	39%	0.61 [0.39-0.96]	cases	94/1,601	33/373
Al-Salman	44%	0.56 [0.33-0.95]	ICU	113 (n)	337 (n)
Matin	66%	0.34 [0.21-0.56]	cases	case control	
Nimavat	50%	0.50 [0.19-1.27]	death	13/131	5/25
Ribeiro	50%	0.50 [0.28-0.87]	cases	n/a	n/a
Eden (ICU)	64%	0.36 [0.11-1.21]	death	3/26	8/25
Alpcan	73%	0.27 [0.13-0.56]	cases	case control	
Sinaci	79%	0.21 [0.10-0.43]	m/s case	8/100	23/59
di Filippo	11%	0.89 [0.35-2.29]	death	5/28	12/60
Connolly	90%	0.10 [0.01-1.06]	death	65 (n)	49 (n)
Breslin	56%	0.44 [0.22-0.91]	progression	106 (n)	32 (n)
Parra-Ortega	99%	0.01 [0.00-0.20]	death	0/15	63/79
Golabi	90%	0.10 [0.04-0.24]	symp.	34 (n)	10 (n)
Pecina	36%	0.64 [0.04-6.25]	death	6/77	1/15
Karonova	78%	0.22 [0.07-0.67]	death	8/96	10/37
Zafar	-43%	1.43 [0.38-5.39]	death	12/42	2/10
Derakhshanian	45%	0.55 [0.30-0.98]	death	148 (n)	142 (n)
Israel	34%	0.66 [0.54-0.81]	severe case	case control	
Afaghi	55%	0.45 [0.34-0.59]	death	97/537	51/109
Ramirez-Sandoval	32%	0.68 [0.57-0.83]	death	2,337 (n)	571 (n)
Hurst	68%	0.32 [0.13-0.73]	death	68 (n)	191 (n)
Atanasovska	41%	0.59 [0.16-2.23]	death	2/9	9/24
Asghar	53%	0.47 [0.22-0.99]	death	73 (n)	18 (n)
Gönen	66%	0.34 [0.04-3.22]	death	1/80	3/82
Ramos	46%	0.54 [0.25-1.19]	cases	4/9	9/11
Asgari	73%	0.27 [0.09-0.86]	death	n/a	n/a
Seven	47%	0.53 [0.34-0.84]	severe case	n/a	n/a
Ranjbar	42%	0.58 [0.32-1.04]	death	16/163	26/154
Kaur	90%	0.10 [0.04-0.25]	death	5/64	13/17
Fatemi	42%	0.58 [0.30-1.05]	death	18/139	25/109
Ma	67%	0.33 [0.08-1.30]	hosp.	7,893 (n)	7,823 (n)
Putra	26%	0.74 [0.26-2.17]	hosp.	case control	
Seal	45%	0.55 [0.38-0.79]	death	n/a	n/a
Juraj	19%	0.81 [0.64-1.03]	death	127/283	41/74
Saponaro	36%	0.64 [0.25-1.59]	ARDS	5/32	15/61
Subramanian	50%	0.50 [0.27-0.89]	death	16/115	33/118
AlKhafaji	39%	0.61 [0.14-2.17]	death	2/76	13/127
Bushnaq	32%	0.68 [0.37-1.26]	ventilation	10/53	40/144
Junior	84%	0.16 [0.03-0.83]	ventilation	n/a	n/a
Cannata-Andía	-117%	2.17 [0.66-7.17]	death	87 (n)	96 (n)
Sanson	64%	0.36 [0.14-0.91]	death/vent.	2/9	37/60
Zidrou	26%	0.74 [0.15-3.52]	death	2/25	5/46
Rodríguez-Vidales	39%	0.61 [0.22-0.99]	severe case	89/265	27/32
Karonova	22%	0.78 [0.72-0.83]	severe case	n/a	n/a
Pande	93%	0.07 [0.03-0.14]	severe case	7/116	85/93
Ghanei	42%	0.58 [0.31-1.10]	cases	case control	
Ferrer-Sánchez	82%	0.18 [0.01-3.14]	ICU	0/9	4/73
Hafez	98%	0.02 [0.00-0.33]	death	6/116	3/10
Martínez-Rodríguez	52%	0.48 [0.24-0.97]	death	n/a	n/a
Kalichuran	60%	0.40 [0.27-0.60]	symp. case	56 (n)	44 (n)
Voelkle	23%	0.77 [0.28-1.66]	death/ICU	8/34	7/23
Nguyen	81%	0.19 [0.05-0.65]	death	n/a	n/a
Charkowick	73%	0.27 [0.09-0.78]	death	140 (n)	68 (n)
Kazemi	76%	0.24 [0.03-1.93]	death	1/75	7/127
Ozturk	46%	0.54 [0.26-1.09]	severe case	9/110	29/190
Baykal	-8%	1.08 [0.67-1.74]	death	11/20	28/55
Neves	57%	0.43 [0.20-0.91]	death	12/87	9/28
Alzahrani	43%	0.57 [0.17-1.96]	death	179 (n)	78 (n)
Bogliolo	15%	0.85 [0.62-1.16]	death	361 (all patients)	
Charla	11%	0.89 [0.56-1.43]	death	24/91	26/88
Gholi (ICU)	75%	0.25 [0.12-0.56]	death	157 (n)	38 (n)
Doğan	64%	0.36 [0.18-0.72]	cases	case control	



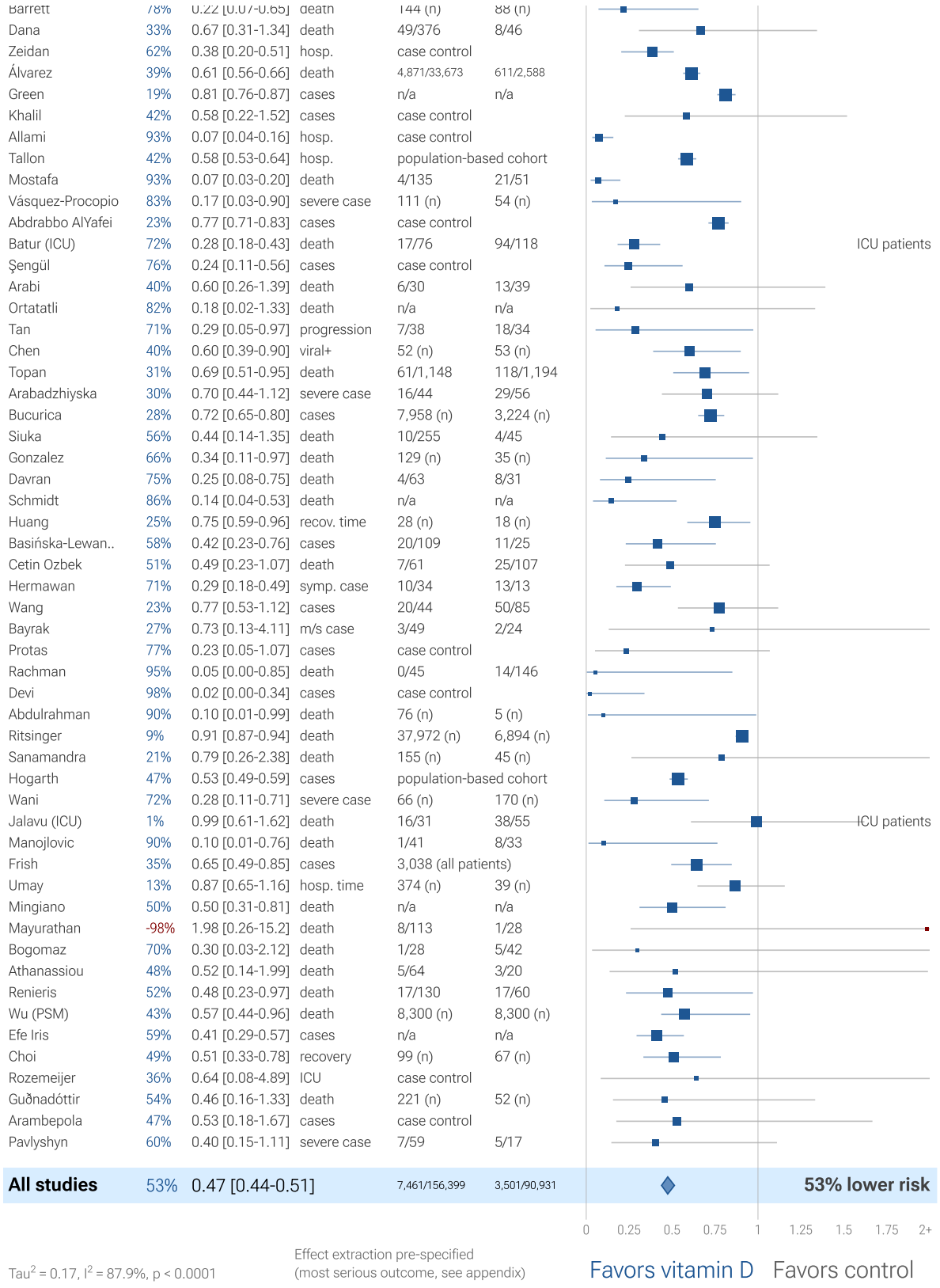


Figure 14. **Random effects meta-analysis for sufficiency studies.** This plot pools studies with different effects, different vitamin D cutoff levels and measurement times, and studies may be within hospitalized patients, excluding the risk of hospitalization. However, the prevalence of positive effects is notable.

Randomized Controlled Trials (RCTs)

Results restricted to Randomized Controlled Trials (RCTs), after exclusions, and for specific outcomes are shown in Figure 15, 16, 17, 18, and 19.

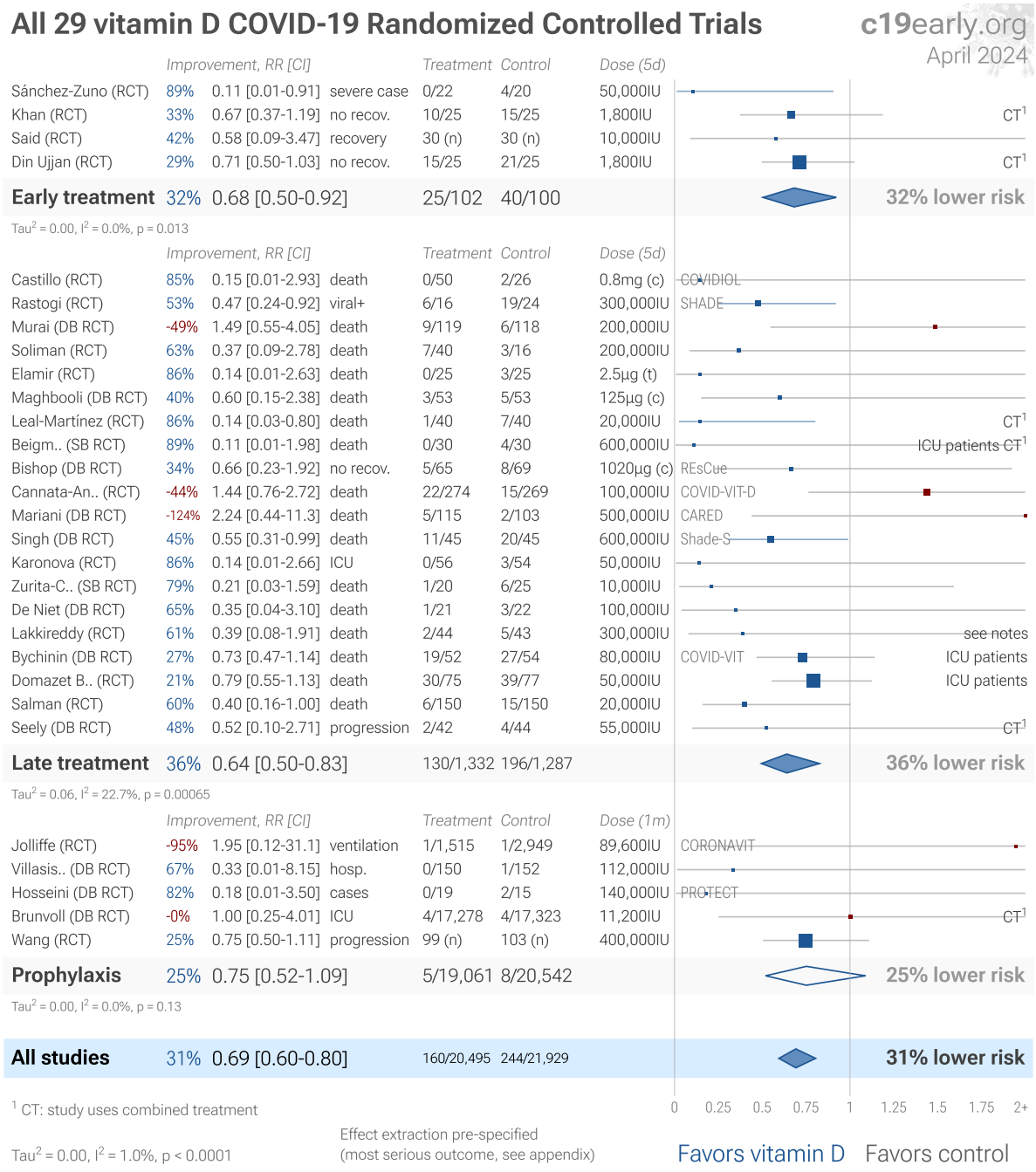


Figure 15. **Random effects meta-analysis for Randomized Controlled Trials only.** Effect extraction is pre-specified, using the most serious outcome reported, see the appendix for details. Analysis validating pooled outcomes for COVID-19 can be found below.

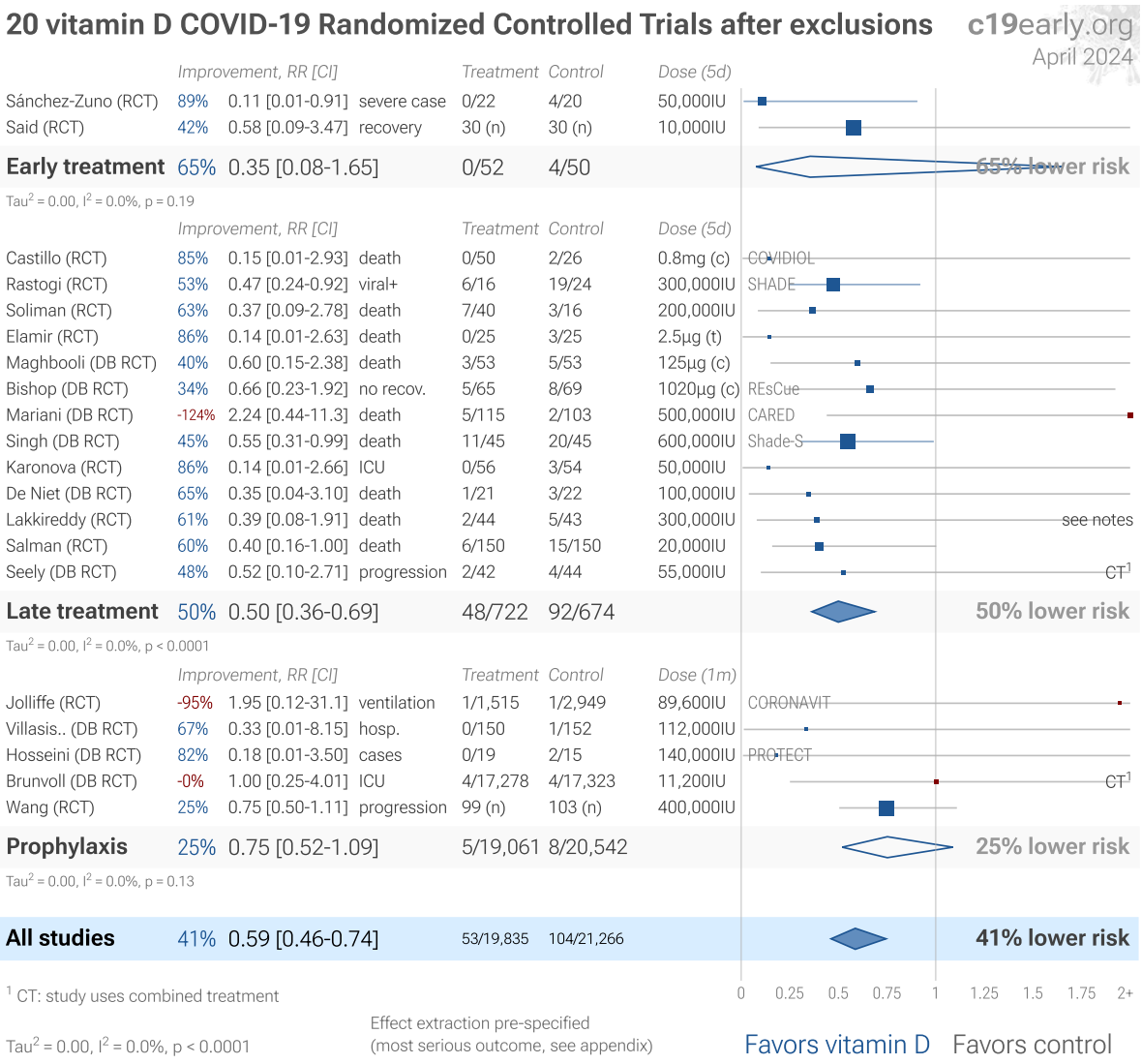


Figure 16. **Random effects meta-analysis for RCTs after exclusions.** Effect extraction is pre-specified, using the most serious outcome reported, see the appendix for details. Analysis validating pooled outcomes for COVID-19 can be found below.

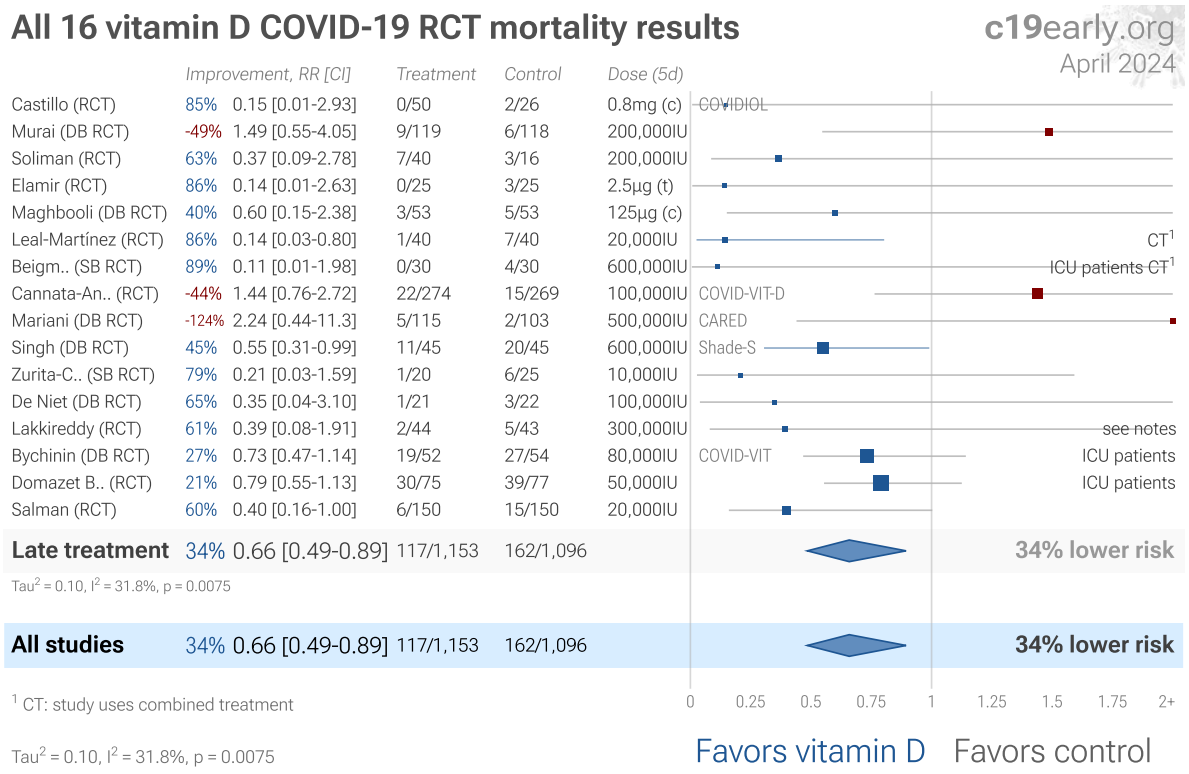


Figure 17. Random effects meta-analysis for RCT mortality results.

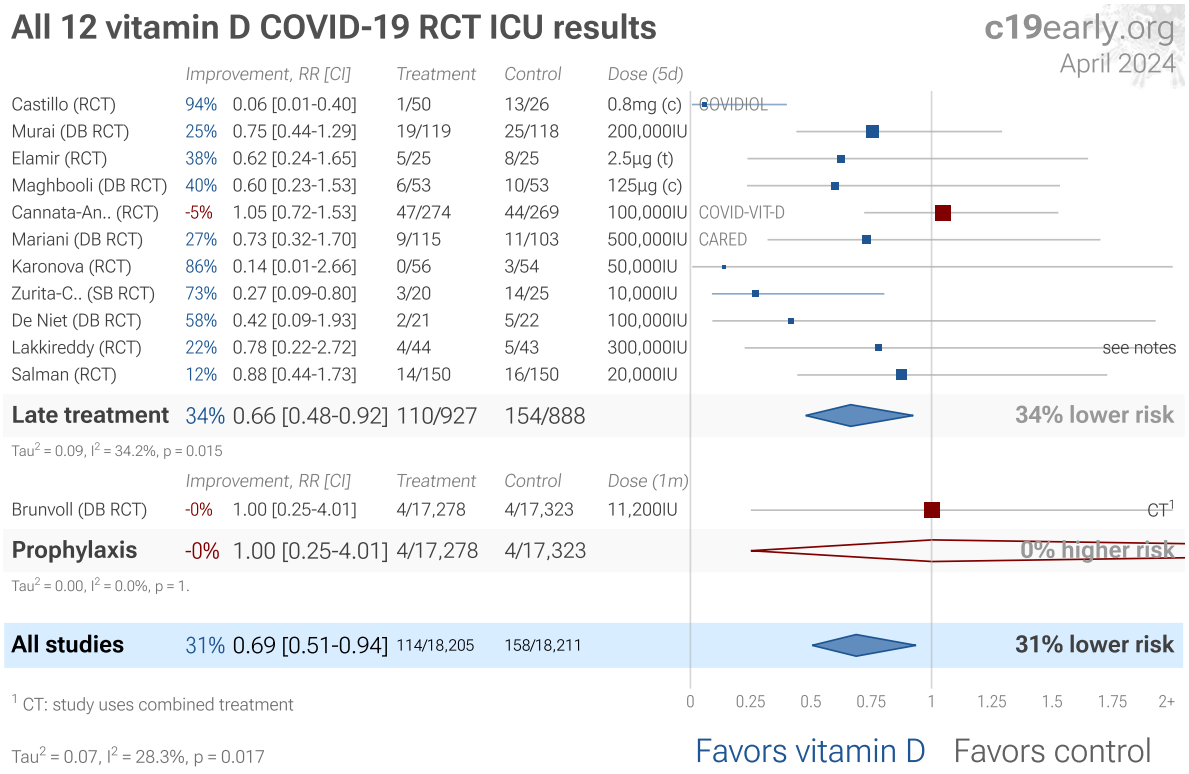


Figure 18. Random effects meta-analysis for RCT ICU admission results.

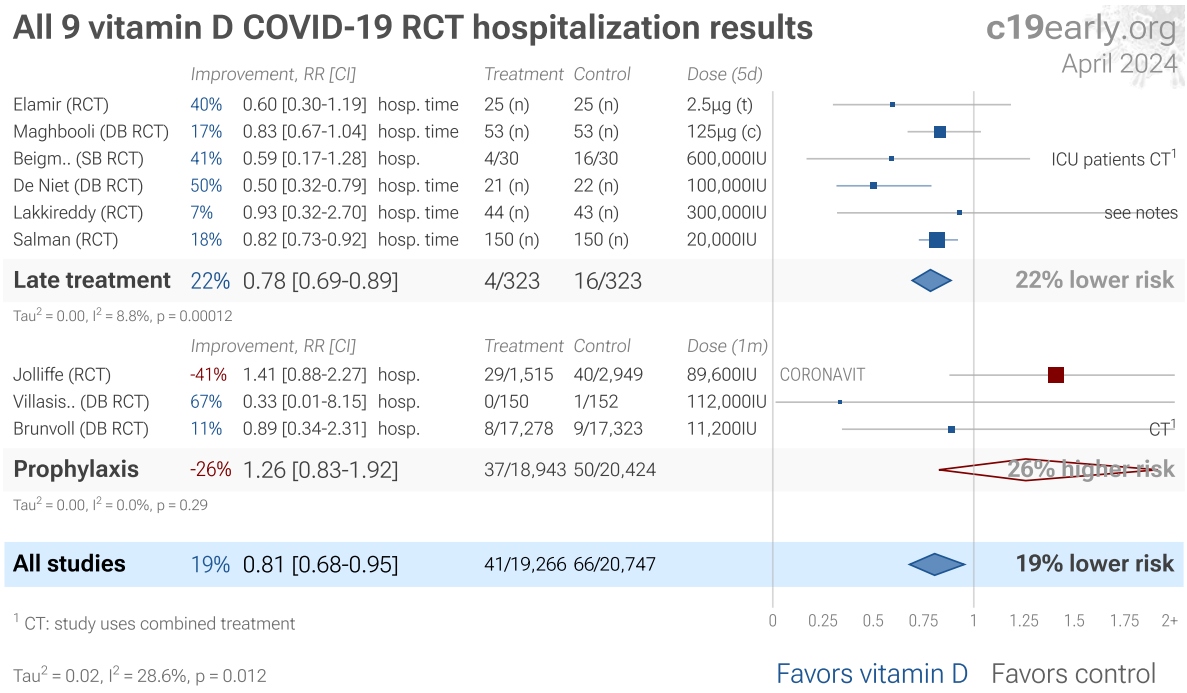


Figure 19. **Random effects meta-analysis for RCT hospitalization results.**

RCTs have many potential biases. RCTs help to make study groups more similar and can provide a higher level of evidence, however they are subject to many biases *Jadad*, and analysis of double-blind RCTs has identified extreme levels of bias *Gøtzsche*. For COVID-19, the overhead may delay treatment, dramatically compromising efficacy; they may encourage monotherapy for simplicity at the cost of efficacy which may rely on combined or synergistic effects; the participants that sign up may not reflect real world usage or the population that benefits most in terms of age, comorbidities, severity of illness, or other factors; standard of care may be compromised and unable to evolve quickly based on emerging research for new diseases; errors may be made in randomization and medication delivery; and investigators may have hidden agendas or vested interests influencing design, operation, analysis, reporting, and the potential for fraud. All of these biases have been observed with COVID-19 RCTs. There is no guarantee that a specific RCT provides a higher level of evidence.

Conflicts of interest for COVID-19 RCTs. RCTs are expensive and many RCTs are funded by pharmaceutical companies or interests closely aligned with pharmaceutical companies. For COVID-19, this creates an incentive to show efficacy for patented commercial products, and an incentive to show a lack of efficacy for inexpensive treatments. The bias is expected to be significant, for example *Als-Nielsen et al.* analyzed 370 RCTs from Cochrane reviews, showing that trials funded by for-profit organizations were 5 times more likely to recommend the experimental drug compared with those funded by nonprofit organizations. For COVID-19, some major philanthropic organizations are largely funded by investments with extreme conflicts of interest for and against specific COVID-19 interventions.

RCTs for novel acute diseases requiring rapid treatment. High quality RCTs for novel acute diseases are more challenging, with increased ethical issues due to the urgency of treatment, increased risk due to enrollment delays, and more difficult design with a rapidly evolving evidence base. For COVID-19, the most common site of initial infection is the upper respiratory tract. Immediate treatment is likely to be most successful and may prevent or slow progression to other parts of the body. For a non-prophylaxis RCT, it makes sense to provide treatment in advance and instruct patients to use it immediately on symptoms, just as some governments have done by providing medication kits in advance. Unfortunately, no RCTs have been done in this way. Every treatment RCT to date involves delayed treatment. Among the 69 treatments we have analyzed, 63% of RCTs involve very late treatment 5+ days after onset. No non-prophylaxis COVID-19 RCTs match the potential real-world use of early treatments. They may more accurately represent results for treatments that require visiting a medical facility, e.g., those requiring intravenous administration.

RCT bias for widely available treatments. RCTs have a bias against finding an effect for interventions that are widely available — patients that believe they need the intervention are more likely to decline participation and take the intervention. RCTs for vitamin D are more likely to enroll low-risk participants that do not need treatment to recover, making the results less applicable to clinical practice. This bias is likely to be greater for widely known treatments, and may be greater when the risk of a serious outcome is overstated. This bias does not apply to the typical pharmaceutical trial of a new drug that is otherwise unavailable.

Non-RCT studies have been shown to be reliable. Evidence shows that non-RCT studies can also provide reliable results. *Concato et al.* found that well-designed observational studies do not systematically overestimate the magnitude of the effects of treatment compared to RCTs. *Anglemyer et al.* summarized reviews comparing RCTs to observational studies and found little evidence for significant differences in effect estimates. *Lee et al.* showed that only 14% of the guidelines of the Infectious Diseases Society of America were based on RCTs. Evaluation of studies relies on an understanding of the study and potential biases. Limitations in an RCT can outweigh the benefits, for example excessive dosages, excessive treatment delays, or Internet survey bias may have a greater effect on results. Ethical issues may also prevent running RCTs for known effective treatments. For more on issues with RCTs see *Deaton, Nichol*.

Using all studies identifies efficacy 7+ months faster (8+ months for low-cost treatments). Currently, 44 of the treatments we analyze show statistically significant efficacy or harm, defined as ≥10% decreased risk or >0% increased risk from ≥3 studies. Of these, 28 have been confirmed in RCTs, with a mean delay of 7.0 months. When considering only low cost treatments, 23 have been confirmed with a delay of 8.4 months. For the 16 unconfirmed treatments, 3 have zero RCTs to date. The point estimates for the remaining 13 are all consistent with the overall results (benefit or harm), with 10 showing >20%. The only treatments showing >10% efficacy for all studies, but <10% for RCTs are sotrovimab and aspirin.

Summary. We need to evaluate each trial on its own merits. RCTs for a given medication and disease may be more reliable, however they may also be less reliable. For off-patent medications, very high conflict of interest trials may be more likely to be RCTs, and more likely to be large trials that dominate meta analyses.

Cholecalciferol vs. calcifidiol/calcitriol and analogs

Figure 20 shows the results for studies using cholecalciferol and studies using calcifediol/calcitriol and analogs. This shows late treatment studies as there are currently no early treatment studies using calcifediol/calcitriol and analogs. Calcifediol, calcitriol and analogs show improved results, as expected given the long conversion delays with cholecalciferol. However they were rarely used, despite wide availability.

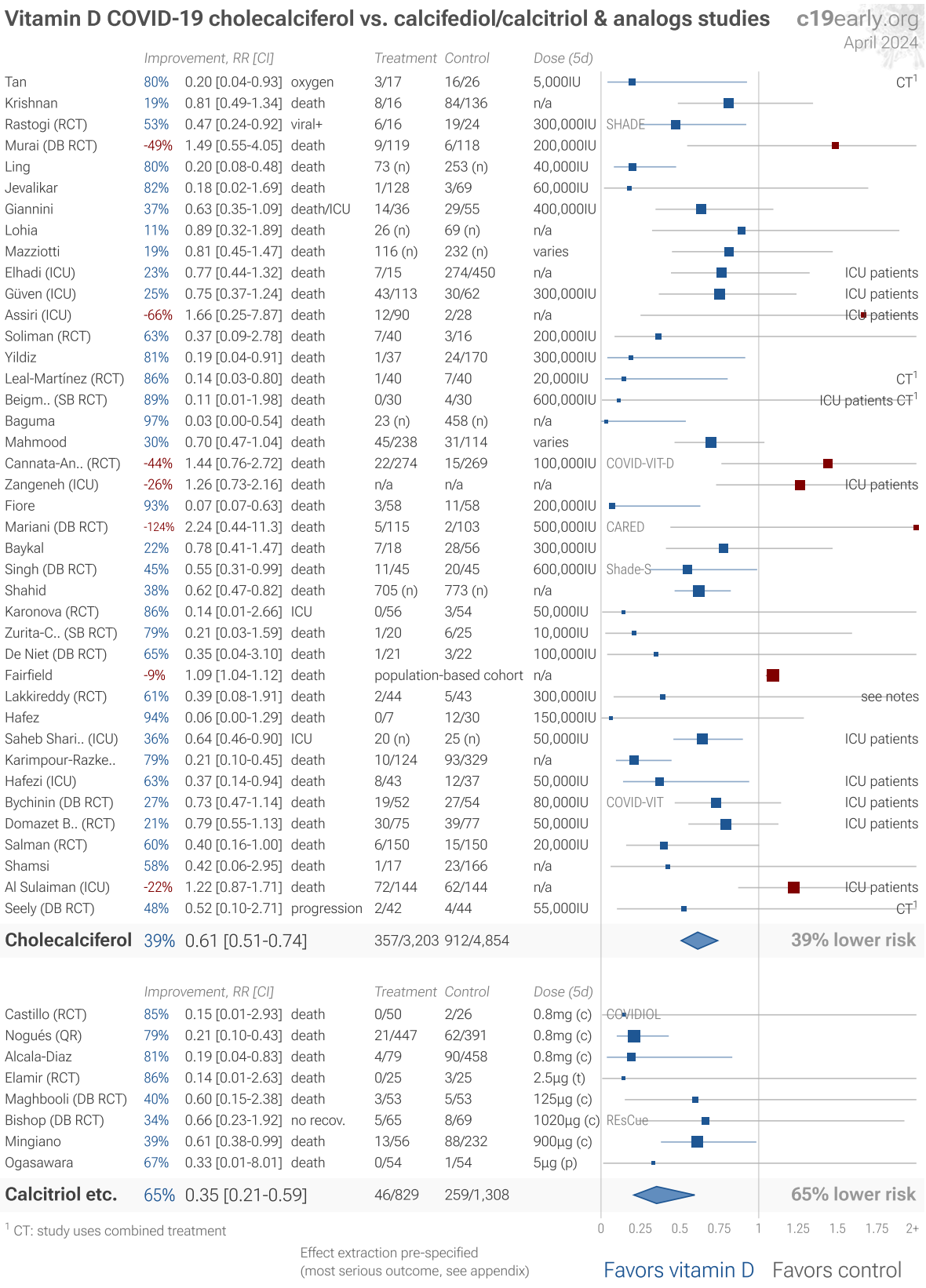


Figure 20. Comparison of cholecalciferol with calcifediol/calcitriol and analogs for late treatment studies, showing improved results with calcifediol/calcitriol and analogs.

Bolus dose vs. multiple doses

Pharmacokinetics and the potential side effects of high bolus doses suggest that ongoing treatment spread over time is more appropriate. One potential advantage of single dose treatment is patient compliance, however this does not apply to COVID-19 trials with ongoing medical care.

Research has shown that lower dose regular supplementation of vitamin D is more effective than intermittent high-dose bolus treatments for various conditions, including rickets and acute respiratory infections [Griffin, Martineau]. The biological mechanisms supporting these findings involve the induction of enzymes such as 24-hydroxylase and fibroblast growth factor 23 (FGF23) by high-dose bolus treatments. These enzymes play roles in inactivating vitamin D, which can paradoxically reduce levels of activated vitamin D and suppress its activation for extended periods post-dosage. Evidence indicates that 24-hydroxylase activity may remain elevated for several weeks following a bolus dose, leading to reduced levels of the activated form of vitamin D. Additionally, FGF23 levels can increase for at least three months after a large bolus dose, which also contributes to the suppression of vitamin D activation [Griffin].

Figure 21 shows the results for studies using a single bolus dose ≥100,000IU and for studies where treatment continues with multiple doses. Improved results are seen with multiple doses. This analysis is a simplification - for both bolus doses and ongoing treatment, individual trials may use doses that are significantly lower or higher than optimal.

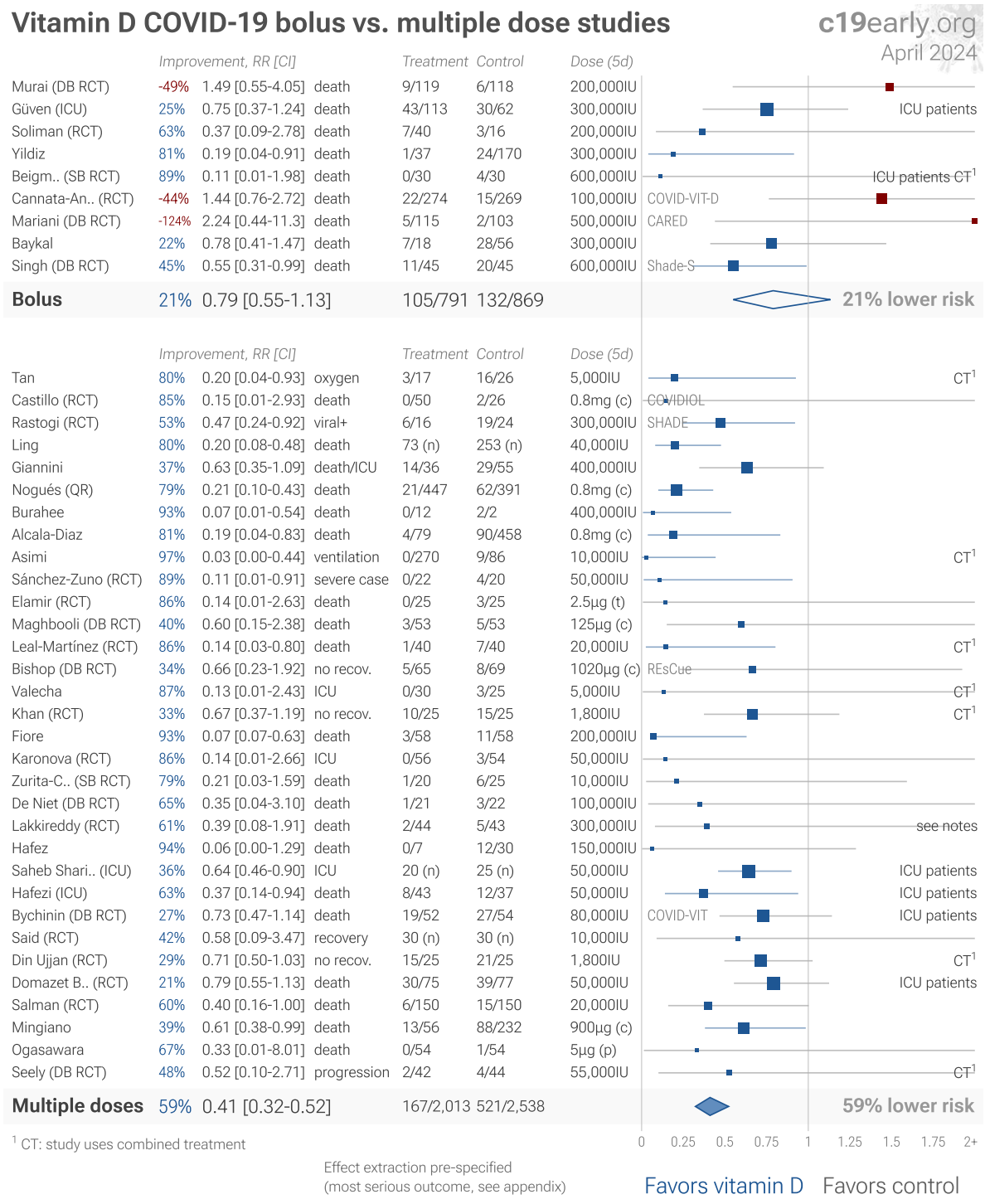


Figure 21. **Comparison of bolus vs. multiple dose studies, showing improved results with multiple doses.**

Exclusions

To avoid bias in the selection of studies, we include all studies in the main analysis, with the exception of *Espitia-Hernandez*. This study uses a combined protocol with another medication that shows high effectiveness when used alone. Authors report on viral clearance, showing 100% clearance with treatment and 0% for the control group. Based on the known mechanisms of action, the combined medication is likely to contribute more to the improvement.

Here we show the results after excluding studies with critical issues.

Murai is a very late stage study (mean 10 days from symptom onset, with 90% on oxygen at baseline), with poorly matched arms in terms of gender, ethnicity, hypertension, diabetes, and baseline ventilation, all of which favor the control group. Further, this study uses cholecalciferol, which may be especially poorly suited for such a late stage. *Cannata-Andía, Mariani* are also very late stage studies using cholecalciferol.

The studies excluded are as follows, and the resulting forest plot is shown in Figure 22.

Abdulateef, unadjusted results with no group details.

Al Sulaiman, very late stage study using cholecalciferol instead of calcifediol or calcitriol.

Arboleda, unadjusted results with no group details.

Asimi, excessive unadjusted differences between groups.

Assiri, unadjusted results with no group details.

Aweimer, unadjusted results with no group details.

Baykal, unadjusted results with no group details; significant confounding by time possible due to separation of groups in different time periods.

Beigmohammadi, very late stage study using cholecalciferol instead of calcifediol or calcitriol.

Bychinin, very late stage study using cholecalciferol instead of calcifediol or calcitriol.

Campi, significant unadjusted differences between groups.

Cannata-Andía, very late stage study using cholecalciferol instead of calcifediol or calcitriol.

Din Ujjan, based on dosages and previous research, combined treatments may contribute more to the effect seen.

Domazet Bugarin, very late stage study using cholecalciferol instead of calcifediol or calcitriol.

Elhadi, unadjusted results with no group details.

Fairfield, substantial unadjusted confounding by indication likely.

Guldemir, unadjusted results with no group details.

Güven, very late stage, ICU patients.

Hafezi, very late stage study using cholecalciferol instead of calcifediol or calcitriol.

Holt, significant unadjusted confounding possible.

Junior, unadjusted results with no group details.

Khan, based on dosages and previous research, combined treatments may contribute more to the effect seen.

Krishnan, unadjusted results with no group details.

Leal-Martínez, combined treatments may contribute more to the effect seen.

Lázaro, very few events; unadjusted results with no group details; minimal details provided.

Mahmood, unadjusted results with no group details; substantial unadjusted confounding by indication likely.

Mahmood, unadjusted results with no group details; substantial unadjusted confounding by indication likely.

Mohseni, unadjusted results with no group details.

Murai, very late stage, >50% on oxygen/ventilation at baseline; very late stage study using cholecalciferol instead of calcifediol or calcitriol.

Pecina, unadjusted results with no group details.

Saheb Sharif-Askari (B), very late stage study using cholecalciferol instead of calcifediol or calcitriol.

Shahid, minimal details provided.

Shamsi, unadjusted results with no group details.

Shehab, unadjusted results with no group details.

Ullah, significant unadjusted confounding possible.

Zangeneh, very late stage study using cholecalciferol instead of calcifediol or calcitriol.

Zurita-Cruz, randomization resulted in significant baseline differences that were not adjusted for.

84 vitamin D COVID-19 treatment studies after exclusions

c19early.org
April 2024

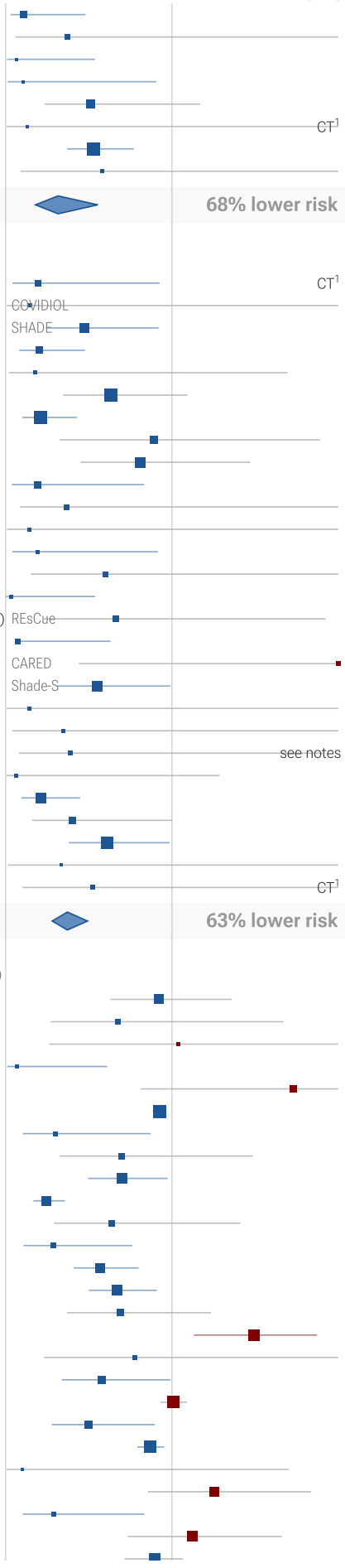
	Improvement, RR [CI]			Treatment	Control	Dose (5d)
Annweiler	89%	0.11 [0.03-0.48]	death	10/57	5/9	80,000IU
Annweiler	63%	0.37 [0.06-2.21]	death	3/16	10/32	80,000IU
Burahee	93%	0.07 [0.01-0.54]	death	0/12	2/2	400,000IU
Sánchez-Zuno (RCT)	89%	0.11 [0.01-0.91]	severe case	0/22	4/20	50,000IU
Efird	49%	0.51 [0.23-1.17]	death	11/544	413/15,794	varies
Valecha	87%	0.13 [0.01-2.43]	ICU	0/30	3/25	5,000IU
Hunt	47%	0.53 [0.37-0.77]	death	43/1,019	1,569/25,489	n/a
Said (RCT)	42%	0.58 [0.09-3.47]	recovery	30 (n)	30 (n)	10,000IU
Early treatment	68%	0.32 [0.18-0.55]		67/1,730	2,006/41,401	**68% lower risk**

$Tau^2 = 0.28$, $I^2 = 57.7\%$, $p < 0.0001$

	Improvement, RR [CI]			Treatment	Control	Dose (5d)
Tan	80%	0.20 [0.04-0.93]	oxygen	3/17	16/26	5,000IU
Castillo (RCT)	85%	0.15 [0.01-2.93]	death	0/50	2/26	0.8mg (c)
Rastogi (RCT)	53%	0.47 [0.24-0.92]	viral+	6/16	19/24	300,000IU
Ling	80%	0.20 [0.08-0.48]	death	73 (n)	253 (n)	40,000IU
Jevalikar	82%	0.18 [0.02-1.69]	death	1/128	3/69	60,000IU
Giannini	37%	0.63 [0.35-1.09]	death/ICU	14/36	29/55	400,000IU
Nogués (QR)	79%	0.21 [0.10-0.43]	death	21/447	62/391	0.8mg (c)
Lohia	11%	0.89 [0.32-1.89]	death	26 (n)	69 (n)	n/a
Mazziotti	19%	0.81 [0.45-1.47]	death	116 (n)	232 (n)	varies
Alcala-Diaz	81%	0.19 [0.04-0.83]	death	4/79	90/458	0.8mg (c)
Soliman (RCT)	63%	0.37 [0.09-2.78]	death	7/40	3/16	200,000IU
Elamir (RCT)	86%	0.14 [0.01-2.63]	death	0/25	3/25	2.5µg (t)
Yildiz	81%	0.19 [0.04-0.91]	death	1/37	24/170	300,000IU
Maghbooli (DB RCT)	40%	0.60 [0.15-2.38]	death	3/53	5/53	125µg (c)
Baguma	97%	0.03 [0.00-0.54]	death	23 (n)	458 (n)	n/a
Bishop (DB RCT)	34%	0.66 [0.23-1.92]	no recov.	5/65	8/69	1020µg (c)
Fiore	93%	0.07 [0.07-0.63]	death	3/58	11/58	200,000IU
Mariani (DB RCT)	-124%	2.24 [0.44-11.3]	death	5/115	2/103	500,000IU
Singh (DB RCT)	45%	0.55 [0.31-0.99]	death	11/45	20/45	600,000IU
Karonova (RCT)	86%	0.14 [0.01-2.66]	ICU	0/56	3/54	50,000IU
De Niet (DB RCT)	65%	0.35 [0.04-3.10]	death	1/21	3/22	100,000IU
Lakkireddy (RCT)	61%	0.39 [0.08-1.91]	death	2/44	5/43	300,000IU
Hafez	94%	0.06 [0.00-1.29]	death	0/7	12/30	150,000IU
Karimpour-Razke..	79%	0.21 [0.10-0.45]	death	10/124	93/329	n/a
Salman (RCT)	60%	0.40 [0.16-1.00]	death	6/150	15/150	20,000IU
Mingiano	39%	0.61 [0.38-0.99]	death	13/56	88/232	900µg (c)
Ogasawara	67%	0.33 [0.01-8.01]	death	0/54	1/54	5µg (p)
Seely (DB RCT)	48%	0.52 [0.10-2.71]	progression	2/42	4/44	55,000IU
Late treatment	63%	0.37 [0.28-0.49]		118/2,003	521/3,558	**63% lower risk**

$Tau^2 = 0.23$, $I^2 = 50.2\%$, $p < 0.0001$

	Improvement, RR [CI]			Treatment	Control	Dose (1m)
Blanch-Rubió	8%	0.92 [0.63-1.36]	cases	62/1,303	47/799	n/a
Sainz-Amo	33%	0.67 [0.27-1.67]	severe case	case control		n/a
Hernández	-4%	1.04 [0.26-4.10]	death	2/19	20/197	varies
Annweiler	93%	0.07 [0.01-0.61]	death	2/29	10/32	50,000IU
Cereda	-73%	1.73 [0.81-2.74]	death	7/18	40/152	varies
Louca	8%	0.92 [0.88-0.97]	cases	population-based cohort		n/a
Cangiano	70%	0.30 [0.10-0.87]	death	3/20	39/78	50,000IU
Vasheghani	30%	0.70 [0.33-1.49]	death	7/88	48/420	n/a
Ma	30%	0.70 [0.50-0.97]	cases	49/363	1,329/7,934	n/a
Sulli	76%	0.24 [0.17-0.36]	cases	case control		n/a
Meltzer	36%	0.64 [0.29-1.41]	cases	6/131	239/3,338	n/a
Ünsal	71%	0.29 [0.11-0.76]	pneumonia	4/28	14/28	varies
Oristrell	43%	0.57 [0.41-0.80]	death	2,296 (n)	3,407 (n)	7.4µg (t)
Loucera (PSM)	33%	0.67 [0.50-0.91]	death	374 (n)	374 (n)	varies (c)
Levitus	31%	0.69 [0.37-1.24]	severe case	65 (n)	64 (n)	varies
Aldwihi	-49%	1.49 [1.13-1.87]	hosp.	94/259	143/479	n/a
Dudley	22%	0.78 [0.23-2.61]	symp. case	15/58	2/6	22,400IU
Fasano	42%	0.58 [0.34-0.99]	cases	13/329	92/1,157	n/a
Oristrell	-1%	1.01 [0.93-1.09]	death	population-based cohort		varies (c)
Jimenez	50%	0.50 [0.28-0.90]	death	16/94	65/191	3.7µg (p)
Israel	13%	0.87 [0.79-0.95]	hosp.	case control		n/a
Sinaci	90%	0.10 [0.01-1.70]	severe case	0/36	7/123	n/a
Golabi	-25%	1.25 [0.86-1.84]	cases	case control		n/a
Bagheri	71%	0.29 [0.10-0.83]	severe case	131 (n)	379 (n)	n/a
Arroyo-Díaz	-12%	1.12 [0.73-1.66]	death	50/189	167/1,078	n/a
Ahmed	10%	0.90 [0.72-1.07]	death	n/a	n/a	n/a



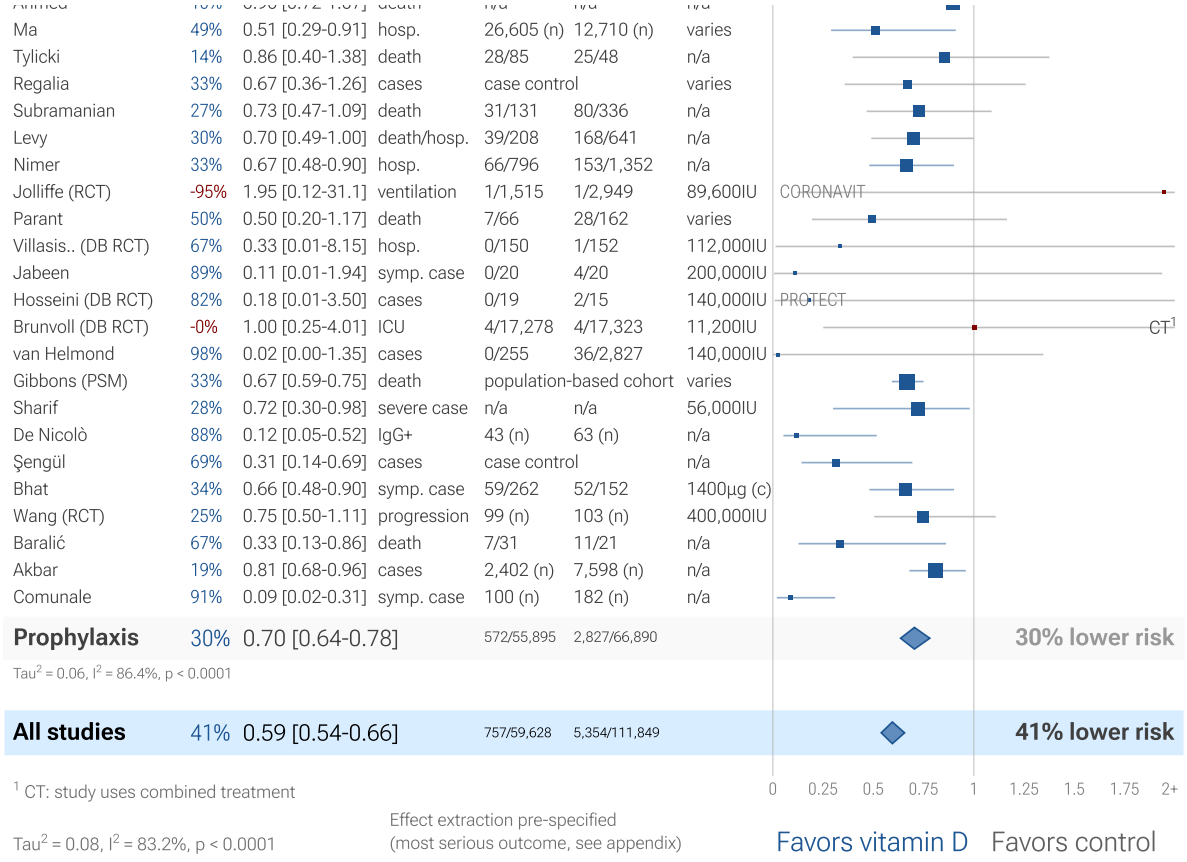


Figure 22. **Random effects meta-analysis excluding studies with significant issues.** Effect extraction is pre-specified, using the most serious outcome reported, see the appendix for details. Analysis validating pooled outcomes for COVID-19 can be found below.

Heterogeneity

Heterogeneity in COVID-19 studies arises from many factors including:

Treatment delay. The time between infection or the onset of symptoms and treatment may critically affect how well a treatment works. For example an antiviral may be very effective when used early but may not be effective in late stage disease, and may even be harmful. Oseltamivir, for example, is generally only considered effective for influenza when used within 0-36 or 0-48 hours *McLean, Treanor*. Baloxavir studies for influenza also show that treatment delay is critical — *Ikematsu et al.* report an 86% reduction in cases for post-exposure prophylaxis, *Hayden et al.* show a 33 hour reduction in the time to alleviation of symptoms for treatment within 24 hours and a reduction of 13 hours for treatment within 24-48 hours, and *Kumar (B) et al.* report only 2.5 hours improvement for inpatient treatment.

Treatment delay	*Result*
Post-exposure prophylaxis	86% fewer cases *Ikematsu*
<24 hours	-33 hours symptoms *Hayden*
24-48 hours	-13 hours symptoms *Hayden*
Inpatients	-2.5 hours to improvement *Kumar (B)*

Table 3. **Studies of baloxavir for influenza show that early treatment is more effective.**

Figure 23 shows a mixed-effects meta-regression of efficacy as a function of treatment delay in COVID-19 vitamin D studies, with group estimates for different stages when a specific value is not provided. For comparison, Figure 24 shows a meta-regression for all studies providing specific values across 69 treatments. Efficacy declines rapidly with treatment delay. Early treatment is critical for COVID-19.

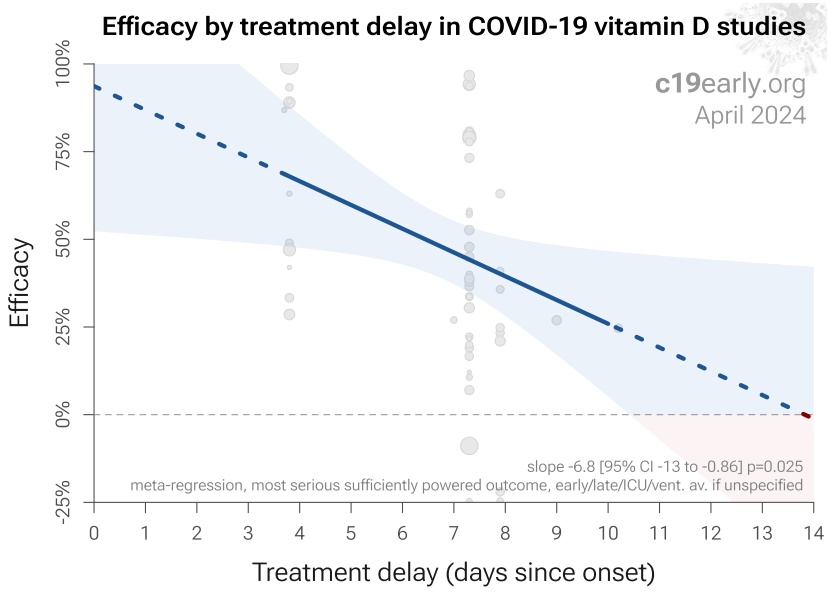


Figure 24. **Early treatment is more effective.** Meta-regression showing efficacy as a function of treatment delay in COVID-19 vitamin D studies.

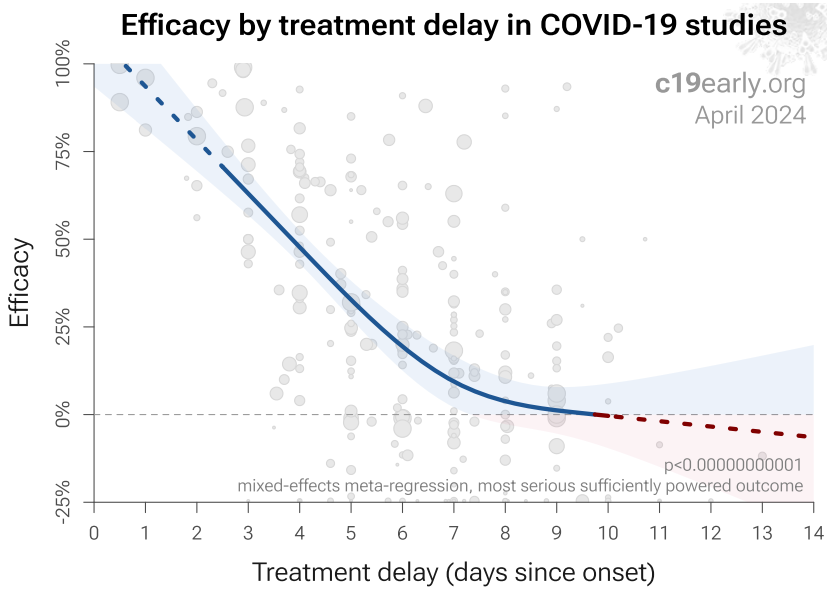


Figure 24. **Early treatment is more effective.** Meta-regression showing efficacy as a function of treatment delay in COVID-19 studies from 69 treatments.

Patient demographics. Details of the patient population including age and comorbidities may critically affect how well a treatment works. For example, many COVID-19 studies with relatively young low-comorbidity patients show all patients recovering quickly with or without treatment. In such cases, there is little room for an effective treatment to improve results, for example as in *López-Medina et al.*

Variants. Efficacy may depend critically on the distribution of SARS-CoV-2 variants encountered by patients. Risk varies significantly across variants [Korves], for example the Gamma variant shows significantly different characteristics [Faria, Karita, Nonaka, Zavascki]. Different mechanisms of action may be more or less effective depending on variants, for example the degree to which TMPRSS2 contributes to viral entry can differ across variants [Peacock, Willett].

Regimen. Effectiveness may depend strongly on the dosage, treatment regimen, and the form of vitamin D used (cholecalciferol, calcifediol, or calcitriol).

Other treatments. The use of other treatments may significantly affect outcomes, including supplements, other medications, or other interventions such as prone positioning. Treatments may be synergistic [Alsaidi, Andreani, De Forni, Fiaschi, Jeffreys, Jitobaom, Jitobaom (B), Ostrov, Said, Thairu, Wan], therefore efficacy may depend strongly on combined treatments.

Medication quality. The quality of medications may vary significantly between manufacturers and production batches, which may significantly affect efficacy and safety. *Williams et al.* analyze ivermectin from 11 different sources, showing highly variable antiparasitic efficacy across different manufacturers. *Xu et al.* analyze a treatment from two different manufacturers, showing 9 different impurities, with significantly different concentrations for each manufacturer. Non-prescription supplements may show very wide variations in quality [Crawford, Crighton].

Effect measured. Across all studies there is a strong association between different outcomes, for example improved recovery is strongly associated with lower mortality. However, efficacy may differ depending on the effect measured, for example a treatment may be more effective against secondary complications and have minimal effect on viral clearance.

Meta analysis. The distribution of studies will alter the outcome of a meta analysis. Consider a simplified example where everything is equal except for the treatment delay, and effectiveness decreases to zero or below with increasing delay. If there are many studies using very late treatment, the outcome may be negative, even though early treatment is very effective. All meta analyses combine heterogeneous studies, varying in population, variants, and potentially all factors above, and therefore may obscure efficacy by including studies where treatment is less effective. Generally, we expect the estimated effect size from meta analysis to be less than that for the optimal case. Looking at all studies is valuable for providing an overview of all research, important to avoid cherry-picking, and informative when a positive result is found despite combining less-optimal situations. However, the resulting estimate does not apply to specific cases such as early treatment in high-risk populations with a specific form and dosage of vitamin D. While we present results for all studies, we also present treatment time and individual outcome analyses, which may be more informative for specific use cases.

Vitamin D studies vary widely in all the factors above, which makes the consistently positive results even more remarkable. A failure to detect an association after combining heterogeneous studies does not mean the treatment is not effective (it may only work in certain cases), however the reverse is not true — an identified association is valid, although the magnitude of the effect may be larger for more optimal cases, and lower for less optimal cases. While we present results for all studies in this paper, the individual outcome, form of vitamin D, and treatment time analyses are more relevant for specific use cases.

Pooled Effects

Combining studies is required. For COVID-19, delay in clinical results translates into additional death and morbidity, as well as additional economic and societal damage. Combining the results of studies reporting different outcomes is required. There may be no mortality in a trial with low-risk patients, however a reduction in severity or improved viral clearance may translate into lower mortality in a high-risk population. Different studies may report lower severity, improved recovery, and lower mortality, and the significance may be very high when combining the results. *"The studies reported different outcomes"* is not a good reason for disregarding results.

Specific outcome and pooled analyses. We present both specific outcome and pooled analyses. In order to combine the results of studies reporting different outcomes we use the most serious outcome reported in each study, based on the thesis that improvement in the most serious outcome provides comparable measures of efficacy for a treatment. A critical advantage of this approach is simplicity and transparency. There are many other ways to combine evidence for different outcomes, along with additional evidence such as dose-response relationships, however these increase complexity.

Using more information. Another way to view pooled analysis is that we are using more of the available information. Logically we should, and do, use additional information. For example dose-response and treatment delay-response relationships provide significant additional evidence of efficacy that is considered when reviewing the evidence for a treatment.

Ethical and practical issues limit high-risk trials. Trials with high-risk patients may be restricted due to ethics for treatments that are known or expected to be effective, and they increase difficulty for recruiting. Using less severe outcomes as a proxy for more serious outcomes allows faster collection of evidence.

Improvement across outcomes. For many COVID-19 treatments, a reduction in mortality logically follows from a reduction in hospitalization, which follows from a reduction in symptomatic cases, which follows from a reduction in PCR positivity. We can directly test this for COVID-19.

Validating pooled outcome analysis for COVID-19. Analysis of the the association between different outcomes across studies from all 69 treatments we cover confirms the validity of pooled outcome analysis for COVID-19. Figure 25 shows that lower hospitalization is very strongly associated with lower mortality ($p < 0.000000000001$). Similarly, Figure 26 shows that improved recovery is very strongly associated with lower mortality ($p < 0.000000000001$). Considering the extremes, *Singh et al.* show an association between viral clearance and hospitalization or death, with $p = 0.003$ after excluding one large outlier from a mutagenic treatment, and based on 44 RCTs including 52,384 patients. Figure 27 shows that improved viral clearance is strongly associated with fewer serious outcomes. The association is very similar to *Singh et al.*, with higher confidence due to the larger number of studies. As with *Singh et al.*, the confidence increases when excluding the outlier treatment, from $p = 0.0000031$ to $p = 0.0000000067$.

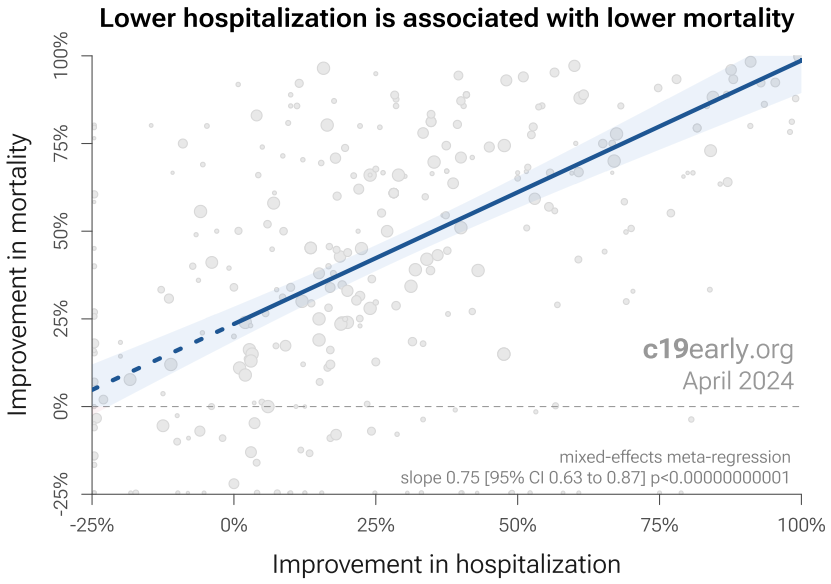


Figure 25. **Lower hospitalization is associated with lower mortality, supporting pooled outcome analysis.**

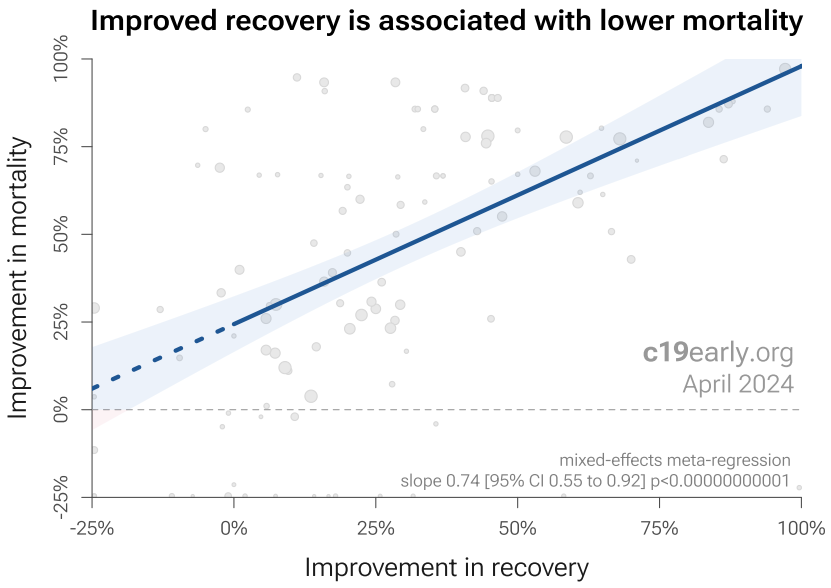


Figure 26. Improved recovery is associated with lower mortality, supporting pooled outcome analysis.

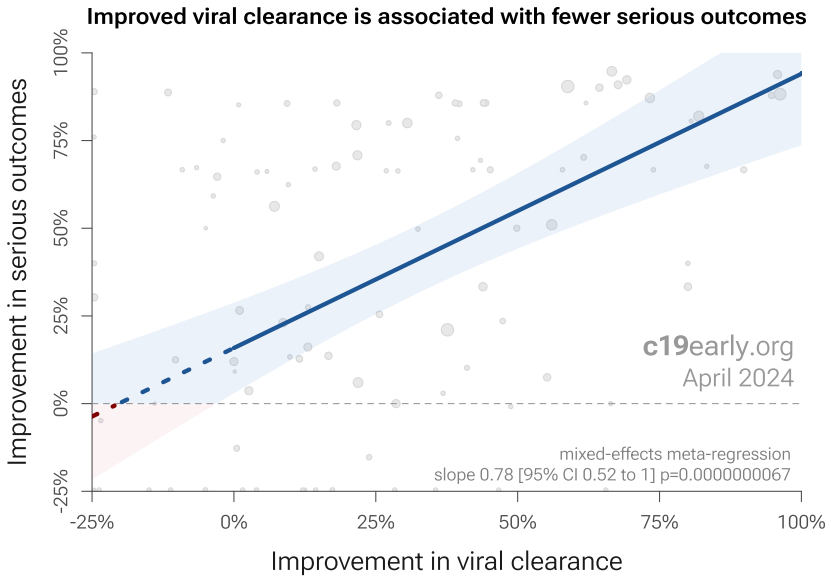


Figure 25. Improved viral clearance is associated with fewer serious outcomes, supporting pooled outcome analysis.

Pooled outcomes identify efficacy 5 months faster (6 months for RCTs). Currently, 44 of the treatments we analyze show statistically significant efficacy or harm, defined as ≥10% decreased risk or >0% increased risk from ≥3 studies. 88% of these have been confirmed with one or more specific outcomes, with a mean delay of 4.7 months. When restricting to RCTs only, 54% of treatments showing statistically significant efficacy/harm with pooled effects have been confirmed with one or more specific outcomes, with a mean delay of 5.5 months. Figure 28 shows when treatments were found effective during the pandemic. Pooled outcomes often resulted in earlier detection of efficacy.

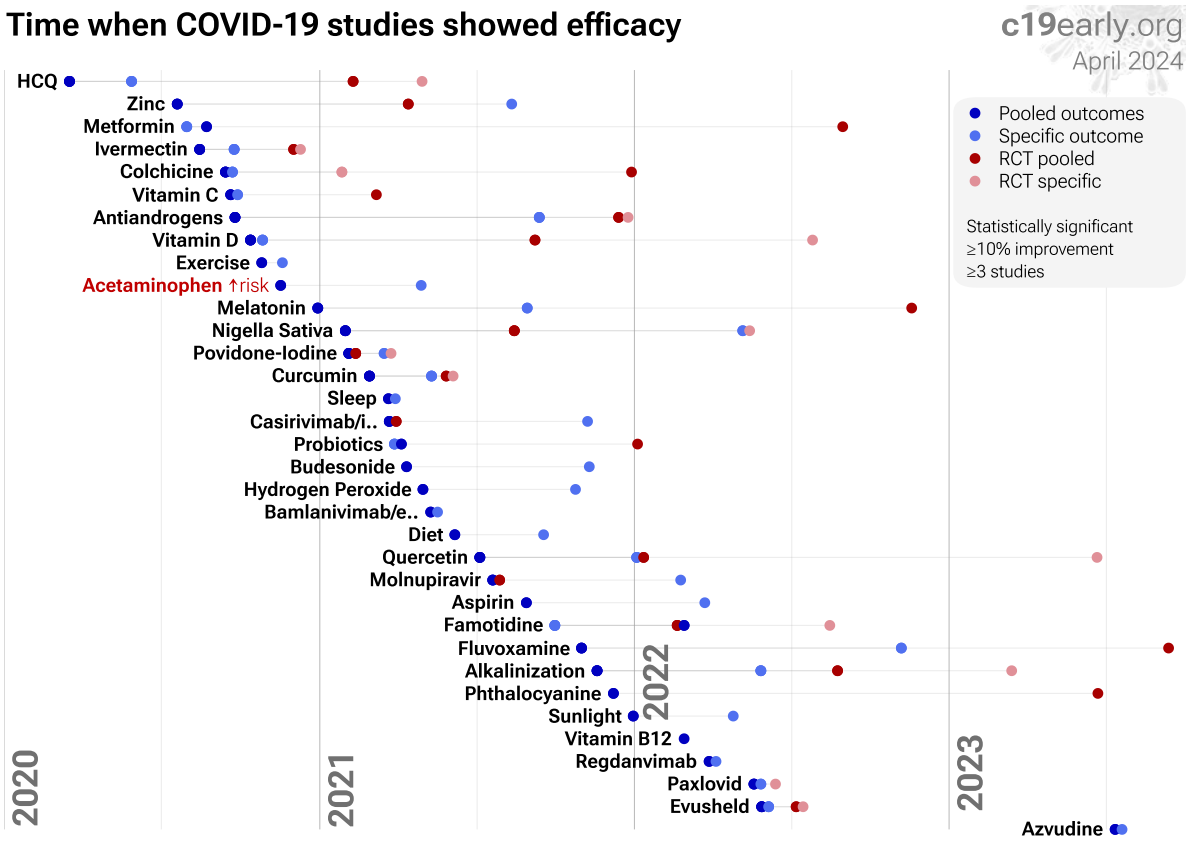


Figure 28. **The time when studies showed that treatments were effective, defined as statistically significant improvement of ≥10% from ≥3 studies.** Pooled results typically show efficacy earlier than specific outcome results. Results from all studies often shows efficacy much earlier than when restricting to RCTs. Results reflect conditions as used in trials to date, these depend on the population treated, treatment delay, and treatment regimen.

Limitations. Pooled analysis could hide efficacy, for example a treatment that is beneficial for late stage patients but has no effect on viral clearance may show no efficacy if most studies only examine viral clearance. In practice, it is rare for a non-antiviral treatment to report viral clearance and to not report clinical outcomes; and in practice other sources of heterogeneity such as difference in treatment delay is more likely to hide efficacy.

Summary. Analysis validates the use of pooled effects and shows significantly faster detection of efficacy on average. However, as with all meta analyses, it is important to review the different studies included. We also present individual outcome analyses, which may be more informative for specific use cases.

Discussion

Sufficiency studies. For sufficiency studies, different studies use different levels as the threshold of sufficiency, vitamin D levels were measured at different times, and some studies measure risk only within hospitalized patients, which excludes the risk of a serious enough case to be hospitalized. However, 183 of 196 studies present positive effects.

Sufficiency studies show a strong correlation between low vitamin D levels and worse COVID-19 outcomes, however they do not provide information on vitamin D treatment. Studies with vitamin D levels measured after admission may show lower levels because COVID-19 infection reduces vitamin D levels. Studies with levels measured before infection also show signficant benefit, however the cause could be one or more correlated factors. For example, sunlight exposure increases vitamin D levels, but also increases intracellular melatonin [Zimmerman], and melatonin shows significant benefit for COVID-19 [c19early.org (B)]. Sun exposure is also correlated with physical exercise, which also shows benefit for COVID-19 [c19early.org (C)].

Treatment studies. 103 of 120 treatment studies report positive effects. Studies vary significantly in terms of treatment delay, treatment regimen, patients characteristics, and (for the pooled effects analysis) outcomes, as reflected in the high degree of heterogeneity. However treatment consistently shows a significant benefit. The treatment studies not showing positive effects are mostly prophylaxis studies with unknown dosages. The only non-prophylaxis studies reporting negative effects are a small unadjusted retrospective *Assiri*, *Zangeneh* with no details of treatment, and *Cannata-Andía, Mariani, Murai* which are very late stage studies using cholecalciferol. For *Murai*, the result also has very low statistical significance due to the small number of events, and the other reported outcomes of ventilation and ICU admission, which have slightly more events and higher confidence, show benefits for vitamin D. Calcifediol or calcitriol, which avoids several days delay in conversion, may be more successful, especially with very late stage usage.

Acute treatment shows higher efficacy than long-term supplementation. Acute treatment shows greater efficacy than chronic prophylaxis for mortality (and in pooled analysis). One hypothesis is that long-term supplementation may affect normal biological processing. A key component of vitamin D processing is regulation via the enzyme CYP24A1, which breaks down active vitamin D. Long-term supplementation may lead to upregulation of CYP24A1, and potentially lower availability of active vitamin D where needed during infection. The prophylaxis RCTs to date *Jolliffe, Villasis-Keever* are consistent with this possibility, with the shorter-term supplementation in *Villasis-Keever* showing better results compared to the longer-term high adherence daily supplementation in *Jolliffe*. Specific forms and administration of vitamin D may minimize upregulation of CYP24A1 *Petkovich*. *Bader* performed an RCT showing high-dose cholecalciferol (50,000 IU/week) significantly increased IL-6, however other studies have shown no significant difference in IL-6 *El Hajj, Mousa* (30,000IU/wk and 100,000IU bolus + 4,000IU/day).

Other factors may be responsible for the observed lower efficacy in prophylaxis studies. For example, analysis of hospitalized patients is subject to selection bias because long-term accurate-dosage supplementing individuals may be significantly less likely to be hospitalized. Studies spanning higher-UV months are subject to confounding. Note that prophylaxis studies include case results, whereas we may expect vitamin D to be more effective against serious outcomes. Comparison of acute treatment versus long-term supplementation should use the specific outcome analyses rather than the pooled outcome analyses.

Publication bias. Publishing is often biased towards positive results, however evidence suggests that there may be a negative bias for inexpensive treatments for COVID-19. Both negative and positive results are very important for COVID-19, media in many countries prioritizes negative results for inexpensive treatments (inverting the typical incentive for scientists that value media recognition), and there are many reports of difficulty publishing positive results *Boulware, Meeus, Meneguesso, twitter.com*.

One method to evaluate bias is to compare prospective vs. retrospective studies. Prospective studies are more likely to be published regardless of the result, while retrospective studies are more likely to exhibit bias. For example, researchers may perform preliminary analysis with minimal effort and the results may influence their decision to continue. Retrospective studies also provide more opportunities for the specifics of data extraction and adjustments to influence results.

Figure 29 shows a scatter plot of results for prospective and retrospective treatment studies. Prospective studies show 50% [35-62%] improvement in meta analysis, compared to 32% [25-37%] for retrospective studies, suggesting possible negative publication bias, with a non-significant trend towards retrospective studies reporting lower efficacy. This gives us further confidence in the significant efficacy seen in all studies.

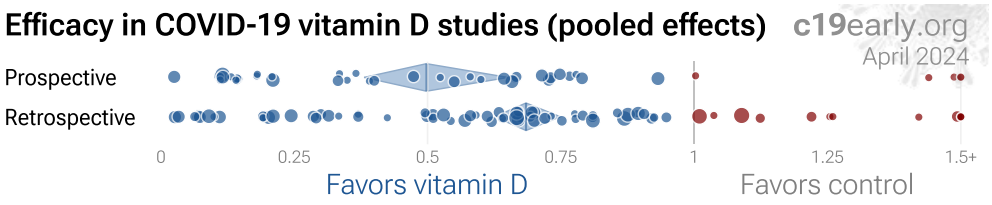


Figure 29. **Prospective vs. retrospective studies. The diamonds show the results of random effects meta-analysis.**

Genetic variants. Genetic variants have been shown to affect COVID-19 infection, severity, and mortality risk [Ren]. Patients with certain vitamin D receptor gene variants may potentially benefit more from vitamin D treatment [Abdollahzadeh, Abdulameer, Aci, Al-Anouti, Al-Gharrawi, Alhammadin, Kotur, Mamurova, Protas, Ren, Shawi Shawi, Zeidan].

Funnel plot analysis. Funnel plots have traditionally been used for analyzing publication bias. This is invalid for COVID-19 acute treatment trials — the underlying assumptions are invalid, which we can demonstrate with a simple example. Consider a set of hypothetical perfect trials with no bias. Figure 30 plot A shows a funnel plot for a simulation of 80 perfect trials, with random group sizes, and each patient's outcome randomly sampled (10% control event probability, and a 30% effect size for treatment). Analysis shows no asymmetry ($p > 0.05$). In plot B, we add a single typical variation in COVID-19 treatment trials — treatment delay. Consider that efficacy varies from 90% for treatment within 24 hours, reducing to 10% when treatment is delayed 3 days. In plot B, each trial's treatment delay is randomly selected. Analysis now shows highly significant asymmetry, $p < 0.0001$, with six variants of Egger's test all showing $p < 0.05$ [Egger, Harbord, Macaskill, Moreno, Peters, Rothstein, Rücker, Stanley]. Note that these tests fail even though treatment delay is uniformly distributed. In reality treatment delay is more complex — each trial has a different distribution of delays across patients, and the distribution across trials may be biased (e.g., late treatment trials may be more common). Similarly, many other variations in trials may produce asymmetry, including dose, administration, duration of treatment, differences in SOC, comorbidities, age, variants, and bias in design, implementation, analysis, and reporting.

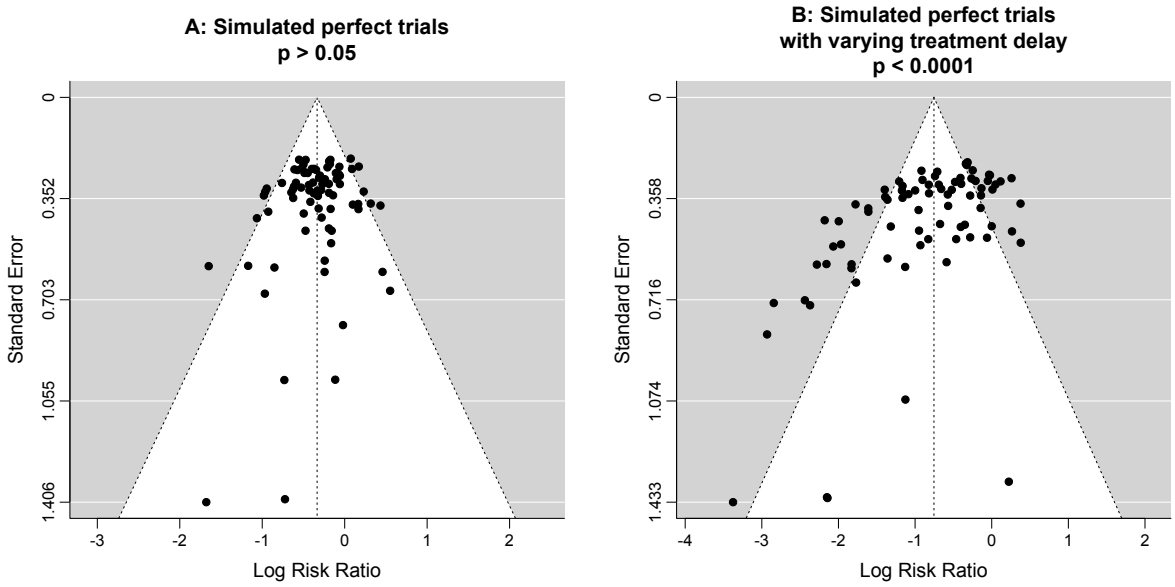


Figure 30. Example funnel plot analysis for simulated perfect trials.

Conflicts of interest. Pharmaceutical drug trials often have conflicts of interest whereby sponsors or trial staff have a financial interest in the outcome being positive. Vitamin D for COVID-19 lacks this because it is an inexpensive and widely available supplement. In contrast, most COVID-19 vitamin D trials have been run by physicians on the front lines with the primary goal of finding the best methods to save human lives and minimize the collateral damage caused by COVID-19. While pharmaceutical companies are careful to run trials under optimal conditions (for example, restricting patients to those most likely to benefit, only including patients that can be treated soon after onset when necessary, and ensuring accurate dosing), not all vitamin D trials represent the optimal conditions for efficacy.

Other meta analyses. Other meta analyses show significant improvements with vitamin D treatment for mortality [Argano, Begum, D'Ecclesiis, Hariyanto, Hosseini, Jamilian, Nikniaz, Shah, Xie], mechanical ventilation [Hariyanto, Meng, Shah, Xie], ICU admission [Hariyanto, Hosseini, Meng, Sartini, Shah, Tentolouris, Xie], hospitalization [Argano], severity [D'Ecclesiis, Nikniaz, Varikasuvu, Xie], and cases [Begum, Sartini, Varikasuvu].

Lakkireddy. The first version of *Lakkireddy* was censored based on incorrect claims from an anti-treatment researcher. For example, the author claims that the gender difference between arms (7/44 vs. 15/43 female) indicates randomization failure, however by simulation, using the group sizes and overall gender ratio, the difference between the number of female patients in each arm is expected to be ≥8 6.4% of the time (2.7% with ≥8 in the control arm, and 3.7% with ≥8 in the treatment arm).

Author claims that the difference in CRP would only happen about one in a billion times. This is incorrect. CRP is not normally distributed, and the observed values could be due to a very small number of outliers with very large CRP in one group.

A response from the study authors can be found at *c19early.org (D)*. The study was republished.

Limitations. Summary statistics from meta analysis necessarily lose information. As with all meta analyses, studies are heterogeneous, with differences in treatment delay, treatment regimen, patient demographics, variants, conflicts of interest, standard of care, and other factors. We provide analyses for specific outcomes and by treatment delay, and we aim to identify key characteristics in the forest plots and summaries. Results should be viewed in the context of study characteristics.

Some analyses classify treatment based on early or late administration, as done here, while others distinguish between mild, moderate, and severe cases. Viral load does not indicate degree of symptoms — for example patients may have a high viral load while being asymptomatic. With regard to treatments that have antiviral properties, timing of treatment is critical — late administration may be less helpful regardless of severity.

Details of treatment delay per patient is often not available. For example, a study may treat 90% of patients relatively early, but the events driving the outcome may come from 10% of patients treated very late. Our 5 day cutoff for early treatment may be too conservative, 5 days may be too late in many cases.

Comparison across treatments is confounded by differences in the studies performed, for example dose, variants, and conflicts of interest. Trials with conflicts of interest may use designs better suited to the preferred outcome.

In some cases, the most serious outcome has very few events, resulting in lower confidence results being used in pooled analysis, however the method is simpler and more transparent. This is less critical as the number of studies increases. Restriction to outcomes with sufficient power may be beneficial in pooled analysis and improve accuracy when there are few studies, however we maintain our pre-specified method to avoid any retrospective changes.

Studies show that combinations of treatments can be highly synergistic and may result in many times greater efficacy than individual treatments alone *Alsaidi, Andreani, De Forni, Fiaschi, Jeffreys, Jitobaom, Jitobaom (B), Ostrov, Said, Thairu, Wan*. Therefore standard of care may be critical and benefits may diminish or disappear if standard of care does not include certain treatments.

This real-time analysis is constantly updated based on submissions. Accuracy benefits from widespread review and submission of updates and corrections from reviewers. Less popular treatments may receive fewer reviews.

No treatment or intervention is 100% available and effective for all current and future variants. Efficacy may vary significantly with different variants and within different populations. All treatments have potential side effects. Propensity to experience side effects may be predicted in advance by qualified physicians. We do not provide medical advice. Before taking any medication, consult a qualified physician who can compare all options, provide personalized advice, and provide details of risks and benefits based on individual medical history and situations.

Reviews. Many reviews cover vitamin D for COVID-19, presenting additional background on mechanisms and related results, including *Andrade, Arora, Basha, Brenner, Cannell, Cutolo, DiGuilio (B), EFSA, EFSA (B), Foshati, Gotelli, Grant, Grant (B), Grant (C), Griffin, Kohlmeier, McCullough, Mercola, Nicoll, Palacios, Quesada-Gomez, Schloss, Shah Alam, Xu (B)*.

Physician case series results. Table 4 shows the reported results of physicians that use early treatments for COVID-19, compared to the results for a non-treating physician. The treatments used vary. Physicians typically use a combination of treatments, with almost all reporting use of ivermectin and/or HCQ, and most using additional

treatments, including vitamin D. These results are subject to selection and ascertainment bias and more accurate analysis requires details of the patient populations and followup, however results are consistently better across many teams, and consistent with the extensive controlled trial evidence that shows a significant reduction in risk with many early treatments, and improved results with the use of multiple treatments in combination.

LATE TREATMENT						
Physician / Team	*Location*	*Patients*	*Hospitalization*		*Mortality*	
Dr. David Uip (*)	Brazil	2,200	38.6% (850)	Ref.	2.5% (54)	Ref.
EARLY TREATMENT - 39 physicians/teams						
Physician / Team	*Location*	*Patients*	*Hospitalization*	*Improvement*	*Mortality*	*Improvement*
Dr. Roberto Alfonso Accinelli 0/360 deaths for treatment within 3 days	Peru	1,265			0.6% (7)	77.5%
Dr. Mohammed Tarek Alam patients up to 84 years old	Bangladesh	100			0.0% (0)	100.0%
Dr. Oluwagbenga Alonge	Nigeria	310			0.0% (0)	100.0%
Dr. Raja Bhattacharya up to 88yo, 81% comorbidities	India	148			1.4% (2)	44.9%
Dr. Flavio Cadegiani	Brazil	3,450	0.1% (4)	99.7%	0.0% (0)	100.0%
Dr. Alessandro Capucci	Italy	350	4.6% (16)	88.2%		
Dr. Shankara Chetty	South Africa	8,000			0.0% (0)	100.0%
Dr. Deborah Chisholm	USA	100			0.0% (0)	100.0%
Dr. Ryan Cole	USA	400	0.0% (0)	100.0%	0.0% (0)	100.0%
Dr. Marco Cosentino vs. 3-3.8% mortality during period; earlier treatment better	Italy	392	6.4% (25)	83.5%	0.3% (1)	89.6%
Dr. Jeff Davis	USA	6,000			0.0% (0)	100.0%
Dr. Dhanajay	India	500			0.0% (0)	100.0%
Dr. Bryan Tyson & Dr. George Fareed	USA	20,000	0.0% (6)	99.9%	0.0% (4)	99.2%
Dr. Raphael Furtado	Brazil	170	0.6% (1)	98.5%	0.0% (0)	100.0%
Dr. Heather Gessling	USA	1,500			0.1% (1)	97.3%
Dr. Ellen Guimarães	Brazil	500	1.6% (8)	95.9%	0.4% (2)	83.7%
Dr. Syed Haider	USA	4,000	0.1% (5)	99.7%	0.0% (0)	100.0%
Dr. Mark Hancock	USA	24			0.0% (0)	100.0%
Dr. Sabine Hazan	USA	1,000			0.0% (0)	100.0%
Dr. Mollie James	USA	3,500	1.1% (40)	97.0%	0.0% (1)	98.8%
Dr. Roberta Lacerda	Brazil	550	1.5% (8)	96.2%	0.4% (2)	85.2%
Dr. Katarina Lindley	USA	100	5.0% (5)	87.1%	0.0% (0)	100.0%
Dr. Ben Marble	USA	150,000			0.0% (4)	99.9%
Dr. Edimilson Migowski	Brazil	2,000	0.3% (7)	99.1%	0.1% (2)	95.9%
Dr. Abdulrahman Mohana	Saudi Arabia	2,733			0.0% (0)	100.0%
Dr. Carlos Nigro	Brazil	5,000	0.9% (45)	97.7%	0.5% (23)	81.3%
Dr. Benoit Ochs	Luxembourg	800			0.0% (0)	100.0%
Dr. Ortore	Italy	240	1.2% (3)	96.8%	0.0% (0)	100.0%
Dr. Valerio Pascua one death for a patient presenting on the 5th day in need of supplemental oxygen	Honduras	415	6.3% (26)	83.8%	0.2% (1)	90.2%
Dr. Sebastian Pop	Romania	300			0.0% (0)	100.0%
Dr. Brian Proctor	USA	869	2.3% (20)	94.0%	0.2% (2)	90.6%

Dr. Anastacio Queiroz	Brazil	700			0.0% (0)	100.0%
Dr. Didier Raoult	France	8,315	2.6% (214)	93.3%	0.1% (5)	97.6%
Dr. Karin Ried up to 99yo, 73% comorbidities, av. age 63	Turkey	237			0.4% (1)	82.8%
Dr. Roman Rozencwaig patients up to 86 years old	Canada	80			0.0% (0)	100.0%
Dr. Vipul Shah	India	8,000			0.1% (5)	97.5%
Dr. Silvestre Sobrinho	Brazil	116	8.6% (10)	77.7%	0.0% (0)	100.0%
Dr. Unknown	Brazil	957	1.7% (16)	95.7%	0.2% (2)	91.5%
Dr. Vladimir Zelenko	USA	2,200	0.5% (12)	98.6%	0.1% (2)	96.3%
Mean improvement with early treatment protocols		237,521	Hospitalization	94.1%	Mortality	94.7%

Table 4. **Physician results with early treatment protocols compared to no early treatment.** (*) Dr. Uip reportedly prescribed early treatment for himself, but not for patients *medicospelavidacovid19.com.br*.

NIH

NIH provides an analysis of vitamin D for COVID-19 *covid19treatmentguidelines.nih.gov*, concluding that there is insufficient evidence to recommend for or against use. However, they appear not to have looked at the majority of the evidence. For example, considering RCTs providing clinical results for COVID-19 and vitamin D, they reference only *Elamir, Mariani, Murai, Villasis-Keever*, and appear not to know about 25 other RCTs *Beigmohammadi, Bishop, Brunvoll, Bychinin, Cannata-Andía, Castillo, De Niet, Din Ujjan, Domazet Bugarin, Hosseini (C), Jolliffe, Karonova, Khan, Lakkireddy, Leal-Martínez, Maghbooli, Rastogi, Said, Salman, Seely, Singh (B), Soliman, Sánchez-Zuno, Wang, Zurita-Cruz* as shown in Figure 31. Notably, the NIH selection does not correspond to the most relevant and highest quality studies, for example including *Murai et al.*, which studies very late treatment (10 days from symptom onset, with 90% on oxygen at baseline) using cholecalciferol. Calcifediol or calcitriol, which avoids several days delay in conversion, may be more appropriate, especially with this very late stage usage. They include none of the early treatment RCTs.

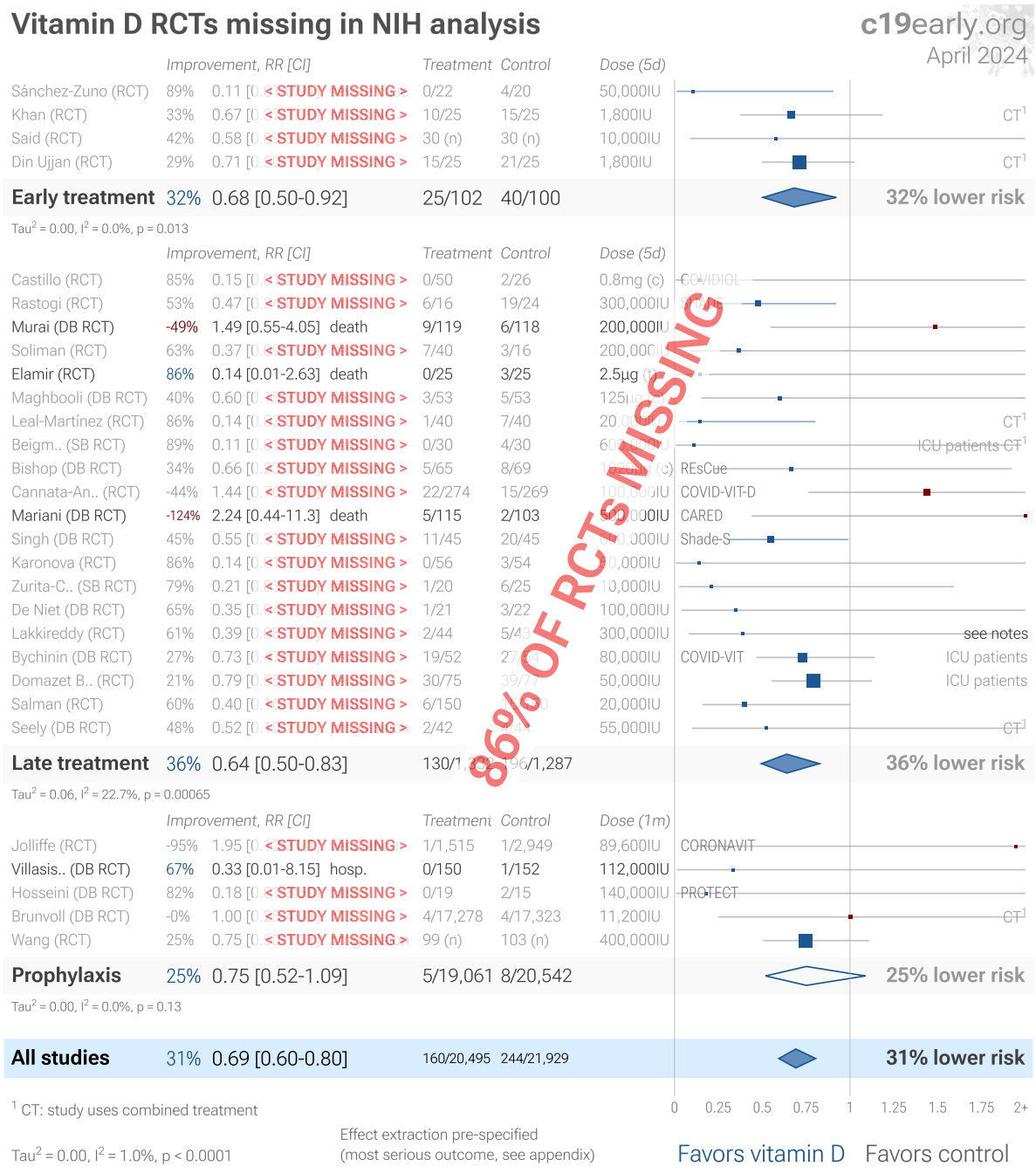


Figure 31. Analysis by NIH is missing 25 RCTs.

Perspective

Results compared with other treatments. SARS-CoV-2 infection and replication involves a complex interplay of 50+ host and viral proteins and other factors *Lui, Lv, Malone, Murigneux, Niarakis*, providing many therapeutic targets. Over 7,000 compounds have been predicted to reduce COVID-19 risk *c19early.org*, either by directly minimizing infection or replication, by supporting immune system function, or by minimizing secondary complications. Figure 32 shows an overview of the results for vitamin D in the context of multiple COVID-19 treatments, and Figure 33 shows a plot of efficacy vs. cost for COVID-19 treatments.

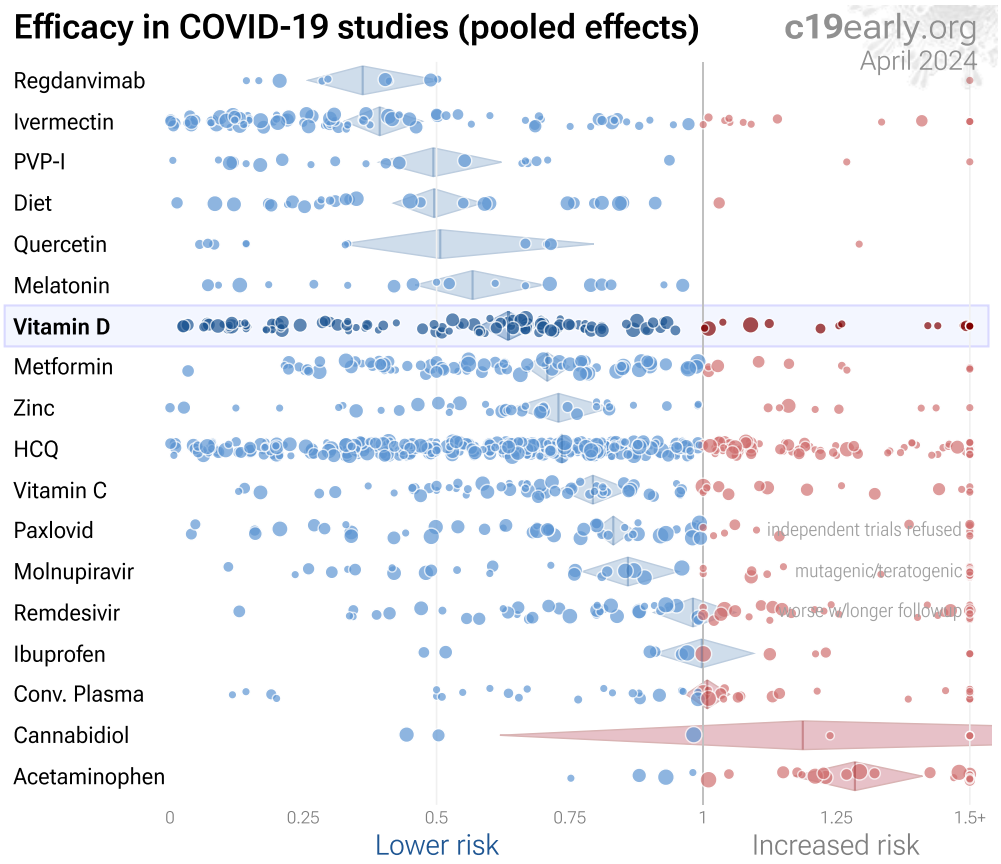


Figure 32. **Scatter plot showing results within the context of multiple COVID-19 treatments.** Diamonds shows the results of random effects meta-analysis. 0.6% of 7,000+ proposed treatments show efficacy *c19early.org (E)*.

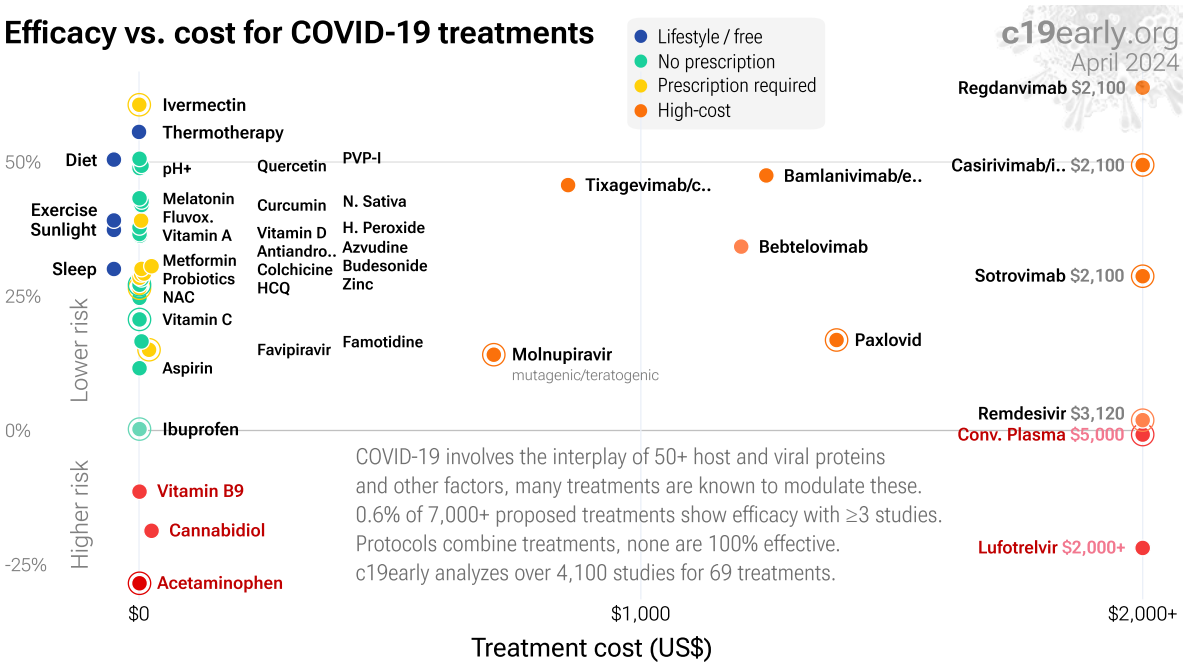


Figure 33. **Efficacy vs. cost for COVID-19 treatments.**

Conclusion

Random effects meta-analysis with pooled effects using the most serious outcome reported shows 60% [40-74%] and 37% [31-42%] lower risk for early treatment and for all studies. Results are similar for higher quality studies, peer-reviewed studies, and mortality: early treatment - 68% [45-82%], 57% [36-71%], 68% [39-84%]; all - 37% [31-42%], 41% [34-46%], 36% [28-43%].

120 treatment studies show statistically significant lower risk for mortality, ICU admission, hospitalization, and cases. 62 studies from 58 independent teams in 22 countries show statistically significant lower risk.

Acute treatment (early 60% [40-74%], late 44% [32-54%]) shows greater efficacy than chronic prophylaxis (31% [24-38%]).

Late stage treatment with calcitriol/calcifediol and analogs is more effective than cholecalciferol: 65% [41-79%] vs. 39% [26-49%].

Ongoing treatment with multiple doses is more effective than single bolus doses: 59% [48-68%] vs. 21% [-13-45%]

Other meta analyses show significant improvements with vitamin D treatment for mortality *Argano, Begum, D'Ecclesiis, Hariyanto, Hosseini, Jamilian, Nikniaz, Shah, Xie*, mechanical ventilation *Hariyanto, Meng, Shah, Xie*, ICU admission *Hariyanto, Hosseini, Meng, Sartini, Shah, Tentolouris, Xie*, hospitalization *Argano*, severity *D'Ecclesiis, Nikniaz, Varikasuvu, Xie*, and cases *Begum, Sartini, Varikasuvu*.

Revisions

This paper is data driven, all graphs and numbers are dynamically generated. Please submit updates and corrections at https://c19early.org/dmeta.html.

4/26: Updated discussion of bolus treatment.

4/25: We added *Chen*.

4/8: We added *Pavlyshyn*.

3/27: We added *Arambepola*, and updated discussion of pooled outcomes.

3/24: We added *Arboleda*.

3/13: We added *Guðnadóttir*.

3/11: We added *Devi*.

2/28: We added *Sartini*.

2/24: We added *Comunale*.

2/23: RCT discussion updates.

2/1: We added *Athanassiou*.

1/31: We updated *Singh (B)* to the journal version.

1/24: We added *Rozemeijer*.

1/24: We updated the introduction.

1/16: We added *Choi*.

1/9/2024: We added *Efe Iris*.

12/20: We added *Wu*.

12/15: Updated discussion of preclinical results.

11/27: We added *Renieris*.

11/9: We added *Akbar*.

10/2: We added *Bogomaz*.

9/24: We added *Seely (B)*.

9/8: We added *Ogasawara*.

8/29: We added *Shamsi*.

8/24: We added *Al Sulaiman*.

8/21: We added *Mayurathan*.

8/13: We added *Mingiano*.

8/10: We added *Connolly*.

8/5: We added analysis for RCT ICU outcomes.

6/24: We added *Frish*.

6/4: We added *Manojlovic*.

6/4: We added *Jalavu*.

6/4: We added *Wani*.

5/8: We added *Hogarth*.

5/6: We added *Ritsinger*.

5/5: We added *Regalia*.

5/2: We added *Sanamandra*.

4/25: We added *AlKhafaji, Baralić, Hafez*.

4/20: We added *Allami*.

4/19: We added *Cetin Ozbek, Zafar*.

4/16: We added *Rachman*.

4/12: We added *Basińska-Lewandowska*.

4/7: We added *Hermawan, Protas*.

4/6: We added *Bayrak*.

4/5: We added *Aweimer, Khalil, Wang*.

4/2: We added *Gonzalez*.

4/1: We added *Arabadzhiyska*.

3/28: We added *Schmidt*.

3/28: We added *Huang, Nasiri*.

3/23: We added *Davran*.

3/15: We added *Bucurica*.

3/15: We added *Topan*.

3/14: We added *Domazet Bugarin, Siuka*.

3/4: We added *Şengül*.

3/4: We added *Chen (B)*.

3/2: We added *Tan*.

2/18: We added *Ortatatli*.

2/8: We added *Arabi*.

1/28: We added *Batur*.

1/20: We added *Mostafa*.

1/19: We added *Din Ujjan*.

1/17: We added *Valecha*.

1/8: We updated *van Helmond* to the journal version.

1/7/2023: We updated discussion of acute treatment vs. long-term supplementation.

12/31: We added *De Nicolò*.

12/20: We added *Abdrabbo AlYafei*.

12/20: We updated the discussion of heterogeneity and RCTs.

12/12: We added *Vásquez-Procopio*.

12/3: We added *Tallon*.

11/27: We added *Guldemir (B)*.

11/26: We added *Sharif*.

11/13: We added *Gibbons*.

11/8: We added *Said*.

11/4: We added *Bychinin*.

10/28: We added *Álvarez*.

10/26: We added *Hafezi*.

10/15: We added *Charla*.

10/8: We added *Karimpour-Razkenari*.

10/1: We added *Singh (B)*.

9/20: We added *Shahid*.

9/19: We added *van Helmond*.

9/15: We added *Brunvoll*.

9/11: We added *Zeidan*.

8/25: We added *Hafez (B)*.

8/24: We added *Aldwihi, Saheb Sharif-Askari (B)*.

8/23: We added *Doğan*.

8/21: We added *Reyes Pérez*.

8/19: We added *Kalichuran*.

8/16: We updated *Lakkireddy* to the new version (post censorship of the previous version).

8/12: We added *Dana, Zurita-Cruz*.

8/10: We added *Barrett*.

8/5: We added *Bogliolo*.

8/3: We added *Alzahrani*.

7/27: We added *De Niet*.

7/26: We added *Neves*.

7/24: We added *Gholi*.

7/19: We added *Baykal*.

7/2: We added *Hunt*.

6/24: We added *Karonova*.

5/28: We added *Mariani*.

5/25: We added *Kazemi, Zangeneh*.

5/24: We added *Ghanei*.

5/23: We added *Fiore*.

5/20: We added *Hosseini (C)*.

5/19: We added *Jabeen*.

5/19: We added *Ozturk*.

5/8: We added *Charkowick*.

5/5: We added *Nguyen*.

5/1: We added *Khan*.

4/30: We added *Voelkle*.

4/24: We added *Davoudi*.

4/22: We added discussion of *Lakkireddy*.

4/18: We added *Villasis-Keever*.

4/17: We added a section on preclinical research.

4/15: We added *Parant*.

4/12: We added *Martínez-Rodríguez*.

4/5: We added preprint discussion based on *Zeraatkar*.

4/2: We added *Ferrer-Sánchez*.

3/31: We added *Ramos*.

3/27: We added *Pande*.

3/25: We added *Elhadi*.

3/23: We added *Jolliffe*.

3/20: We added *Bushnaq*.

3/19: We added *Shehab*.

3/7: We added *Rodríguez-Vidales*.

3/5: We added *Reis*.

3/4: We added *Nimer*.

3/3: We added *Karonova (B)*.

2/24: We added *Zidrou*.

2/20: We added *Sanson*.

2/19: We added *Cannata-Andía*.

2/18: We added *González-Estevez, Junior*.

2/17: We added *Mahmood*.

2/15: We updated *Vanegas-Cedillo* to the journal version.

2/11: We added *Bychinin (B)*.

2/8: We added *Subramanian*.

2/8: We added *Ranjbar*.

2/7: We added *Tylicki, Ullah*.

2/6: We added *Bishop*.

2/4: We added *Ahmed*.

2/4: We updated *Dror* to the journal version.

1/30: We updated *Leal-Martínez* to the journal version.

1/29: We added *Ansari*.

1/28: We added *Anjum*.

1/25: We added *Saponaro*.

1/23: We added *Juraj*.

1/14: We added *Baguma (B)*.

1/13: We updated *Israel* to the journal version.

1/8: We added *Seal*.

1/5: We added *Pepkowitz*.

1/3/2022: We added *Efird*.

12/26: We added *Abdulateef*.

12/21: We added *Beigmohammadi, Sainz-Amo*.

12/20: We added *Galaznik*.

12/17: We added *Seven*.

12/16: We added *Parra-Ortega*.

12/14: We added *Putra*.

12/9: We added analysis of the number of independent research groups reporting statistically significant positive results.

12/7: We added *Ma*.

12/5: We added *Asgari*.

12/3: We updated *Loucera* to the journal version.

12/3: We added *Fatemi*.

12/3: We added *Kaur*.

11/22: Added discussion related to sufficiency studies.

11/14: We added *Gönen*.

11/12: We added *Asghar*.

11/7: We added *Holt*.

11/3: We added *Atanasovska*.

11/2: We added *Al-Salman, Eden*.

11/1: We updated *Golabi* to the journal version.

10/31: We added *Assiri, Bianconi, Leal-Martínez*.

10/30: We added *Campi, Gaudio*.

10/27: We added *Hurst, Lázaro*.

10/19: We added *Jimenez*.

10/19: We added *Sinaci, Zelzer*.

10/18: We added *Mohseni*.

10/18: We added *Basaran, Dudley*.

10/16: We added a summary plot for all results.

10/15: We added *Ramirez-Sandoval*.

10/15: We added *Maghbooli*.

10/14: We added *Arroyo-Díaz, Burahee* and analysis of treatment mechanical ventilation, ICU admission, and hospitalization results.

9/28: We added *Yildiz*.

9/27: We added *Derakhshanian*.

9/22: We added *Bagheri*.

9/14: We added *Ribeiro*.

9/14: We updated *Vasheghani (B)* to the journal version of the article.

9/14: We added *Elamir*.

9/10: We added *Tomasa-Irriguible*.

9/7: We added *Karonova (C), Pecina*.

9/6: We added *Soliman*.

9/1: We added *Golabi*.

8/23: We corrected *Jain (B)* to include the mortality outcome.

8/15: We added *Nimavat*.

8/13: We added *di Filippo (B)* and updated *Louca* to the journal version of the article.

8/12: We added *Alpcan*.

8/10: We added discussion of the immune system and vitamin D.

8/2: We added *Matin*.

8/1: We added *Pimental*.

7/28: We added *Israel (B)*.

7/27: We added *Cozier*.

7/26: We added *Güven*.

7/25: We added *Asimi*.

7/24: We added *Orchard*.

7/21: We added *Savitri*.

7/19: We added *Oristrell*.

7/11: We added *Krishnan*.

6/25: We added *Cereda (B)*.

6/19: We added *Jude*.

6/16: We added *Campi*.

6/12: We added *Levitus*.

6/11: We updated *Oristrell (B)* to the journal version.

6/9: We added *Fasano*.

6/8: We updated *Nogués* to the journal version.

6/7: We added *Diaz-Curiel, Dror*.

5/29: We added *Sánchez-Zuno*.

5/22: We added analysis restricted to cholecalciferol studies.

5/21: We added *Alcala-Diaz, Li*.

5/20: We updated *Lakkireddy* to the journal version.

5/19: We added *AlSafar*.

5/10: We added additional information in the abstract.

5/9: We clarified terminology for prophylaxis and added discussion of heterogeneity.

5/8: We added analysis for treatment studies restricted to peer-reviewed articles.

4/30: We added *Loucera*.

4/29: We corrected the treatment group counts for the early treatment group in *Annweiler* (there was no change in the relative risk).

4/24: We added analysis restricted to RCT studies and to calcifediol/calcitriol studies. We have excluded *Espitia-Hernandez* in the treatment analysis because they use a combined protocol with another medication that shows high effectiveness when used alone.

4/14: We added *Blanch-Rubió*.

4/13: We added *Lohia, Oristrell (B)*.

4/12: We added *Barassi*.

4/10: We added *Szeto*.

4/9: We added *Ünsal*.

4/5: We added *Bayramoğlu, Livingston*.

4/4: We added event counts to the forest plots.

3/31: We added *Mendy*.

3/30: We added *Macaya*.

3/29: We added *Im*.

3/28: We added *Freitas*.

3/22: We added *Meltzer*.

3/15: We added *Vanegas-Cedillo*.

3/14: We added *Cereda*.

3/12: We added *Charoenngam*.

3/10: We added *Mazziotti*.

3/6: We added *Ricci*.

2/26: We added *Lakkireddy*.

2/25: We added *Sulli (B)*.

2/20: We added *Gavioli*.

2/20: We added *Infante*.

2/18: *Murai* was updated to the journal version of the paper.

2/17: We corrected an error in the effect extraction for *Angelidi*, and we added treatment case and viral clearance forest plots.

2/16: We added *Susianti*.

2/10: We added *Nogués*.

2/10: We added *Karonova (D)*.

2/9: We added *Karahan*.

2/7: We added *Li (B)*.

2/5: We added *Yılmaz*.

1/31: We added *Demir*.

1/30: We added *Ma (B)*.

1/22: We added *Giannini*.

1/21: We added *Bennouar*.

1/19: We added *Amin*.

1/18: We added *Vasheghani (B)*.

1/16: We moved the analysis with exclusions to the main text, and added additional commentary.

1/15: We added the effect measured for each study in the forest plots.

1/10: We added *Angelidi*.

1/7: We added direct links to the study details in the chronological plots.

1/5: We added direct links to the study details in the forest plots.

1/2/2021: We added dosage information and we added the number of patients to the forest plots.

12/31: We added additional details about the studies in the appendix.

12/28: We added *Jevalikar*.

12/27: We added the total number of authors and patients.

12/23: We added *Cangiano*.

12/17/2020: Initial revision.

Appendix 1. Methods and Data

We perform ongoing searches of PubMed, medRxiv, Europe PMC, ClinicalTrials.gov, The Cochrane Library, Google Scholar, Research Square, ScienceDirect, Oxford University Press, the reference lists of other studies and meta-analyses, and submissions to the site c19early.org, which regularly receives submissions of studies upon publication. Search terms are vitamin D, cholecalciferol, or calcitriol, and COVID-19 or SARS-CoV-2. Automated searches are performed twice daily, with all matches reviewed for inclusion. All studies regarding the use of vitamin D for COVID-19 that report a comparison with a control group are included in the main treatment analysis, and all studies comparing COVID-19 outcomes in groups of patients with low and high vitamin D levels are included in the sufficiency analysis. A few studies only provide results as a function of change in vitamin D levels, which may not be indicative of results for deficiency/insufficiency versus sufficiency (if levels are already sufficient then further increase may be less beneficial). Sensitivity analysis is performed, excluding studies with major issues, epidemiological studies, and studies with minimal available information. This is a living analysis and is updated regularly.

We extracted effect sizes and associated data from all studies. If studies report multiple kinds of effects then the most serious outcome is used in pooled analysis, while other outcomes are included in the outcome specific analyses. For example, if effects for mortality and cases are both reported, the effect for mortality is used, this may be different to the effect that a study focused on. If symptomatic results are reported at multiple times, we used the latest time, for example if mortality results are provided at 14 days and 28 days, the results at 28 days have preference. Mortality alone is preferred over combined outcomes. Outcomes with zero events in both arms are not used, the next most serious outcome with one or more events is used. For example, in low-risk populations with no mortality, a reduction in mortality with treatment is not possible, however a reduction in hospitalization, for example, is still valuable. Clinical outcomes are considered more important than viral test status. When basically all patients recover in both treatment and control groups, preference for viral clearance and recovery is given to results mid-recovery where available. After most or all patients have recovered there is little or no room for an effective treatment to do better, however faster recovery is valuable. If only individual symptom data is available, the most serious symptom has priority, for example difficulty breathing or low SpO_2 is more important than cough. When results provide an odds ratio, we compute the relative risk when possible, or convert to a relative risk according to *Zhang*. Reported confidence intervals and *p*-values

were used when available, using adjusted values when provided. If multiple types of adjustments are reported propensity score matching and multivariable regression has preference over propensity score matching or weighting, which has preference over multivariable regression. Adjusted results have preference over unadjusted results for a more serious outcome when the adjustments significantly alter results. When needed, conversion between reported *p*-values and confidence intervals followed *Altman, Altman (B)*, and Fisher's exact test was used to calculate *p*-values for event data. If continuity correction for zero values is required, we use the reciprocal of the opposite arm with the sum of the correction factors equal to 1 *Sweeting*. Results are expressed with RR < 1.0 favoring treatment, and using the risk of a negative outcome when applicable (for example, the risk of death rather than the risk of survival). If studies only report relative continuous values such as relative times, the ratio of the time for the treatment group versus the time for the control group is used. Calculations are done in Python (3.12.3) with scipy (1.13.0), pythonmeta (1.26), numpy (1.26.4), statsmodels (0.14.2), and plotly (5.21.0).

Forest plots are computed using PythonMeta *Deng* with the DerSimonian and Laird random effects model (the fixed effect assumption is not plausible in this case) and inverse variance weighting. Results are presented with 95% confidence intervals. Heterogeneity among studies was assessed using the I^2 statistic. Mixed-effects meta-regression results are computed with R (4.1.2) using the metafor (3.0-2) and rms (6.2-0) packages, and using the most serious sufficiently powered outcome. Forest plots show simplified dosages for comparison, these are the total dose in the first five days for treatment, and the monthly dose for prophylaxis. Calcifediol, calcitriol, and paricalcitol treatment are indicated with (c), (t), and (p). For full dosage details see below. For all statistical tests, a *p*-value less than 0.05 was considered statistically significant. Grobid 0.8.0 is used to parse PDF documents.

We have classified studies as early treatment if most patients are not already at a severe stage at the time of treatment (for example based on oxygen status or lung involvement), and treatment started within 5 days of the onset of symptoms. If studies contain a mix of early treatment and late treatment patients, we consider the treatment time of patients contributing most to the events (for example, consider a study where most patients are treated early but late treatment patients are included, and all mortality events were observed with late treatment patients).

We received no funding, this research is done in our spare time. We have no affiliations with any pharmaceutical companies or political parties.

A summary of study results is below. Please submit updates and corrections at https://c19early.org/dmeta.html.

Analysis of outcomes based on sufficiency

Effect extraction follows pre-specified rules as detailed above and gives priority to more serious outcomes. Only the first (most serious) outcome is used in pooled analysis, which may differ from the effect a paper focuses on. Other outcomes are used in outcome specific analyses.

Abdollahi, 12/12/2020, retrospective, Iran, peer-reviewed, 7 authors.	risk of case, 53.9% lower, RR 0.46, $p = 0.001$, high D levels 108, low D levels 294, >30ng/ml.
Abdrabbo AlYafei, 12/5/2022, retrospective, Qatar, peer-reviewed, mean age 19.0, 5 authors.	risk of case, 23.2% lower, OR 0.77, $p < 0.001$, cutoff 10ng/mL, adjusted per study, inverted to make OR<1 favor high D levels (≥10ng/mL), case control OR, severe deficiency vs. optimal, multivariable.
	risk of case, 21.5% lower, OR 0.78, $p < 0.001$, cutoff 20ng/mL, adjusted per study, inverted to make OR<1 favor high D levels (≥20ng/mL), case control OR, mild/moderate deficiency vs. optimal, multivariable.
Abdulrahman, 4/17/2023, retrospective, United Kingdom, peer-reviewed, mean age 69.0, 7 authors, study period April 2020 - May 2021.	risk of death, 90.1% lower, OR 0.10, $p = 0.048$, high D levels (≥25nmol/L) 76, low D levels (<25nmol/L) 5, adjusted per study, inverted to make OR<1 favor high D levels (≥25nmol/L), multivariable, RR approximated with OR.

	risk of progression, 82.5% lower, OR 0.18, $p = 0.09$, high D levels (≥25nmol/L) 76, low D levels (<25nmol/L) 5, adjusted per study, inverted to make OR<1 favor high D levels (≥25nmol/L), hospitalization, ICU, or death, multivariable, RR approximated with OR.
Abrishami, 10/30/2020, retrospective, Iran, peer-reviewed, mean age 55.2, 7 authors.	**risk of death, 75.9% lower, RR 0.24, $p = 0.04$**, high D levels (≥25ng/mL) 3 of 47 (6.4%), low D levels (<25ng/mL) 9 of 26 (34.6%), NNT 3.5, adjusted per study, inverted to make RR<1 favor high D levels (≥25ng/mL), Cox model 2.
Afaghi, 10/12/2021, retrospective, Iran, peer-reviewed, 7 authors.	**risk of death, 55.0% lower, RR 0.45, $p = 0.002$**, high D levels 97 of 537 (18.1%), low D levels 51 of 109 (46.8%), NNT 3.5, adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >20ng/mL, multivariate.
	risk of mechanical ventilation, 55.9% lower, RR 0.44, $p < 0.001$, high D levels 89 of 537 (16.6%), low D levels 41 of 109 (37.6%), NNT 4.8, >20ng/mL, unadjusted.
	risk of ICU admission, 34.1% lower, RR 0.66, $p < 0.001$, high D levels 211 of 537 (39.3%), low D levels 65 of 109 (59.6%), NNT 4.9, >20ng/mL, unadjusted.
Al-Salman, 7/29/2021, retrospective, Bahrain, peer-reviewed, 5 authors.	**risk of ICU admission, 44.4% lower, OR 0.56, $p = 0.03$**, high D levels (≥50nmol/L) 113, low D levels (<50nmol/L) 337, inverted to make OR<1 favor high D levels (≥50nmol/L), multinomial regression, RR approximated with OR.
Alguwaihes, 12/5/2020, retrospective, Saudi Arabia, peer-reviewed, 10 authors.	**risk of death, 85.7% lower, RR 0.14, $p = 0.007$**, high D levels 111, low D levels 328, inverted to make RR<1 favor high D levels, >12.5 nmol/L.
AlKhafaji, 1/31/2022, retrospective, Saudi Arabia, peer-reviewed, mean age 56.8, 16 authors, study period January 2021 - August 2021.	**risk of death, 38.6% lower, RR 0.61, $p = 0.50$**, high D levels (≥20ng/mL) 2 of 76 (2.6%), low D levels (<20ng/mL) 13 of 127 (10.2%), inverted to make RR<1 favor high D levels (≥20ng/mL), odds ratio converted to relative risk.
	risk of mechanical ventilation, 31.0% lower, RR 0.69, $p = 0.51$, high D levels (≥20ng/mL) 2 of 76 (2.6%), low D levels (<20ng/mL) 13 of 127 (10.2%), inverted to make RR<1 favor high D levels (≥20ng/mL), odds ratio converted to relative risk.
	risk of ICU admission, 41.8% lower, RR 0.58, $p = 0.20$, high D levels (≥20ng/mL) 2 of 76 (2.6%), low D levels (<20ng/mL) 13 of 127 (10.2%), inverted to make RR<1 favor high D levels (≥20ng/mL), odds ratio converted to relative risk.
Allami, 11/8/2022, retrospective, Iraq, peer-reviewed, 6 authors.	**risk of hospitalization, 92.5% lower, OR 0.07, $p < 0.001$**, high D levels (≥10ng/mL) 91, low D levels (<10ng/mL) 80, adjusted per study, inverted to make OR<1 favor high D levels (≥10ng/mL), case control OR, multivariable.
Alpcan, 8/10/2021, retrospective, Turkey, peer-reviewed, 3 authors.	**risk of case, 73.0% lower, OR 0.27, $p < 0.001$**, high D levels 42 of 75 (56.0%) cases, 66 of 80 (82.5%) controls, NNT 3.2, case control OR, >20ng/mL.

AlSafar, 5/19/2021, retrospective, United Arab Emirates, peer-reviewed, 8 authors.	risk of death, 59.3% lower, RR 0.41, $p = 0.048$, high D levels 16 of 337 (4.7%), low D levels 10 of 127 (7.9%), adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >=12ng/mL.
	risk of severe case, 33.2% lower, RR 0.67, $p = 0.005$, high D levels 337, low D levels 127, adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >=12ng/mL.
Alzahrani, 6/23/2022, retrospective, Saudi Arabia, peer-reviewed, mean age 54.3, 9 authors, study period March 2020 - July 2021.	risk of death, 42.5% lower, OR 0.57, $p = 0.46$, high D levels (≥25ng/mL) 179, low D levels (<25ng/mL) 78, adjusted per study, inverted to make OR<1 favor high D levels (≥25ng/mL), multivariable, RR approximated with OR.
	risk of ICU admission, 7.4% lower, OR 0.93, $p = 0.80$, high D levels (≥25ng/mL) 179, low D levels (<25ng/mL) 78, adjusted per study, inverted to make OR<1 favor high D levels (≥25ng/mL), multivariable, RR approximated with OR.
Al-Jarallah, 6/20/2021, retrospective, Kuwait, peer-reviewed, 20 authors.	risk of death, 88.3% higher, RR 1.88, $p = 0.45$, high D levels 8 of 120 (6.7%), low D levels 9 of 119 (7.6%), odds ratio converted to relative risk.
Amin, 1/7/2021, retrospective, population-based cohort, United Kingdom, peer-reviewed, 2 authors.	COVID-19 severity, 32.3% higher, RR 1.32, $p = 0.20$, high D levels 140,898, low D levels 35,079, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >=50nmol/L vs. <25nmol/L, MR Egger, baseline risk approximated with overall risk.
	risk of case, 7.6% higher, RR 1.08, $p = 0.14$, high D levels 140,898, low D levels 35,079, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >=50nmol/L vs. <25nmol/L, MR Egger, baseline risk approximated with overall risk.
Angelidi, 1/9/2021, retrospective, USA, peer-reviewed, 8 authors.	risk of death, 88.0% lower, RR 0.12, $p = 0.01$, high D levels 6 of 65 (9.2%), low D levels 20 of 79 (25.3%), NNT 6.2, adjusted per study, >30ng/mL, supplementary table 2, multivariable logistic regression model 5.
Anjum, 7/31/2020, prospective, Pakistan, peer-reviewed, 6 authors, study period March 2020 - June 2020, excluded in exclusion analyses: unadjusted results with no group details.	risk of death, 62.5% lower, RR 0.38, $p = 0.02$, high D levels (≥25nmol/L) 8 of 80 (10.0%), low D levels (<25nmol/L) 16 of 60 (26.7%), NNT 6.0.
Ansari, 12/31/2020, prospective, Pakistan, peer-reviewed, 6 authors, study period 1 March, 2020 - 31 August, 2020, excluded in exclusion analyses: unadjusted results with no group details.	risk of death, 86.0% lower, RR 0.14, $p = 0.02$, high D levels (≥25nmol/L) 2 of 68 (2.9%), low D levels (<25nmol/L) 12 of 57 (21.1%), NNT 5.5.
Arabadzhiyska, 2/28/2023, retrospective, Bulgaria, peer-reviewed, mean age 53.7, 2 authors, study period October 2021 - December 2021.	risk of severe case, 29.8% lower, RR 0.70, $p = 0.16$, high D levels (≥20ng/ml) 16 of 44 (36.4%), low D levels (<20ng/ml) 29 of 56 (51.8%), NNT 6.5.

Arabi, 1/22/2023, retrospective, Iran, peer-reviewed, 7 authors.	risk of death, 40.0% lower, RR 0.60, $p = 0.28$, high D levels (≥20ng/mL) 6 of 30 (20.0%), low D levels (<20ng/mL) 13 of 39 (33.3%), NNT 7.5.
	risk of ICU admission, 39.3% lower, RR 0.61, $p = 0.20$, high D levels (≥20ng/mL) 7 of 30 (23.3%), low D levels (<20ng/mL) 15 of 39 (38.5%), NNT 6.6.
	risk of AKI, 42.2% lower, RR 0.58, $p = 0.13$, high D levels (≥20ng/mL) 8 of 30 (26.7%), low D levels (<20ng/mL) 18 of 39 (46.2%), NNT 5.1.
Arambepola, 3/28/2024, retrospective, India, preprint, 6 authors.	risk of case, 47.4% lower, OR 0.53, $p = 0.27$, high D levels (≥50nmol/L) 17 of 104 (16.3%) cases, 30 of 104 (28.8%) controls, NNT 5.6, adjusted per study, inverted to make OR<1 favor high D levels (≥50nmol/L), case control OR.
Asgari, 11/21/2021, retrospective, Iran, peer-reviewed, 6 authors, study period 21 May, 2020 - 4 September, 2020.	risk of death, 72.5% lower, OR 0.27, $p = 0.03$, cutoff 25ng/mL, adjusted per study, inverted to make OR<1 favor high D levels (≥25ng/mL), RR approximated with OR.
	risk of progression, 65.6% lower, OR 0.34, $p = 0.02$, cutoff 25ng/mL, adjusted per study, inverted to make OR<1 favor high D levels (≥25ng/mL), RR approximated with OR.
Asghar, 11/10/2021, retrospective, Pakistan, peer-reviewed, 8 authors.	risk of death, 53.1% lower, HR 0.47, $p = 0.046$, high D levels (≥10ng/mL) 73, low D levels (<10ng/mL) 18, inverted to make HR<1 favor high D levels (≥10ng/mL), multivariate Cox regression.
	risk of mechanical ventilation, 19.4% lower, HR 0.81, $p = 0.32$, high D levels (≥10ng/mL) 5 of 73 (6.8%), low D levels (<10ng/mL) 6 of 18 (33.3%), NNT 3.8, adjusted per study, inverted to make HR<1 favor high D levels (≥10ng/mL), multivariate Cox regression.
	risk of ICU admission, 32.9% lower, HR 0.67, $p = 0.54$, high D levels (≥10ng/mL) 73, low D levels (<10ng/mL) 18, inverted to make HR<1 favor high D levels (≥10ng/mL), multivariate Cox regression.
Atanasovska, 11/2/2021, retrospective, North Macedonia, peer-reviewed, 8 authors.	risk of death, 40.7% lower, RR 0.59, $p = 0.68$, high D levels (≥30ng/mL) 2 of 9 (22.2%), low D levels (<30ng/mL) 9 of 24 (37.5%), NNT 6.5.
	risk of severe case, 59.0% lower, RR 0.41, $p = 0.13$, high D levels (≥30ng/mL) 2 of 9 (22.2%), low D levels (<30ng/mL) 13 of 24 (54.2%), NNT 3.1.
Athanassiou, 9/15/2023, prospective, Greece, peer-reviewed, 9 authors, excluded in exclusion analyses: unadjusted results with no group details.	risk of death, 47.9% lower, RR 0.52, $p = 0.39$, high D levels (≥10ng/mL) 5 of 64 (7.8%), low D levels (<10ng/mL) 3 of 20 (15.0%), NNT 14.
	risk of death, 43.0% lower, RR 0.57, $p = 0.70$, high D levels (≥20ng/mL) 2 of 31 (6.5%), low D levels (<20ng/mL) 6 of 53 (11.3%), NNT 21.

Baktash, 8/27/2020, prospective, United Kingdom, peer-reviewed, 8 authors.	risk of death, 28.6% lower, RR 0.71, $p = 0.50$, high D levels 4 of 31 (12.9%), low D levels 6 of 39 (15.4%), adjusted per study, inverted to make RR<1 favor high D levels, >30nmol/L.
Barassi, 1/25/2021, retrospective, Italy, peer-reviewed, 8 authors.	risk of death, 64.9% lower, RR 0.35, $p = 0.44$, high D levels 1 of 31 (3.2%), low D levels 8 of 87 (9.2%), NNT 17, >20ng/mL.
	risk of mechanical ventilation, 64.9% lower, RR 0.35, $p = 0.15$, high D levels 2 of 31 (6.5%), low D levels 16 of 87 (18.4%), NNT 8.4, >20ng/mL.
Barrett, 8/9/2022, prospective, Ireland, peer-reviewed, mean age 56.0, 19 authors, study period March 2020 - April 2021.	risk of death, 78.4% lower, OR 0.22, $p = 0.006$, high D levels (≥30nmol/L) 144, low D levels (<30nmol/L) 88, adjusted per study, inverted to make OR<1 favor high D levels (≥30nmol/L), multivariable, RR approximated with OR.
	risk of ICU admission, 15.3% lower, OR 0.85, $p = 0.63$, high D levels (≥30nmol/L) 144, low D levels (<30nmol/L) 88, adjusted per study, inverted to make OR<1 favor high D levels (≥30nmol/L), multivariable, RR approximated with OR.
	risk of progression, 52.6% lower, OR 0.47, $p = 0.12$, high D levels (≥30nmol/L) 144, low D levels (<30nmol/L) 88, adjusted per study, inverted to make OR<1 favor high D levels (≥30nmol/L), extended oxygen requirement, multivariable, RR approximated with OR.
Basaran, 2/12/2021, retrospective, Turkey, peer-reviewed, 6 authors.	risk of severe case, 68.6% lower, RR 0.31, $p = 0.005$, high D levels 82 of 119 (68.9%), low D levels 80 of 85 (94.1%), NNT 4.0, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >10µg/L, per standard deviation increase in levels.
Basińska-Lewandowska, 3/24/2023, retrospective, Poland, peer-reviewed, 5 authors, excluded in exclusion analyses: unadjusted results with no group details.	risk of case, 58.3% lower, RR 0.42, $p = 0.02$, high D levels (≥12ng/mL) 20 of 109 (18.3%), low D levels (<12ng/mL) 11 of 25 (44.0%), NNT 3.9.
Batur, 12/26/2022, retrospective, Turkey, peer-reviewed, 2 authors, study period March 2020 - June 2021, excluded in exclusion analyses: unadjusted differences between groups.	risk of death, 71.9% lower, RR 0.28, $p < 0.001$, high D levels (≥20ng/mL) 17 of 76 (22.4%), low D levels (<20ng/mL) 94 of 118 (79.7%), NNT 1.7.
	secondary infection, 23.3% lower, RR 0.77, $p = 0.03$, high D levels (≥20ng/mL) 40 of 76 (52.6%), low D levels (<20ng/mL) 81 of 118 (68.6%), NNT 6.2, growth in culture.
Baykal, 5/30/2022, retrospective, Turkey, peer-reviewed, 2 authors, study period 1 April, 2020 - 1 March, 2021, dosage 300,000IU single dose.	risk of death, 8.0% higher, RR 1.08, $p = 0.80$, high D levels (≥20ng/mL) 11 of 20 (55.0%), low D levels (<20ng/mL) 28 of 55 (50.9%), outcome based on serum levels.
	risk of ICU admission, 4.8% lower, RR 0.95, $p = 1.00$, high D levels (≥20ng/mL) 9 of 20 (45.0%), low D levels (<20ng/mL) 26 of 55 (47.3%), NNT 44, outcome based on serum levels.
	risk of progression, 6.1% lower, RR 0.94, $p = 0.77$, high D levels (≥20ng/mL) 14 of 20 (70.0%), low D levels (<20ng/mL) 41 of 55 (74.5%), NNT 22, severe/critical, outcome based on serum

	levels.
Bayrak, 4/5/2023, retrospective, Turkey, peer-reviewed, mean age 19.0, 8 authors, study period November 2020 - January 2021.	risk of moderate/severe case, 26.5% lower, RR 0.73, *p* = 1.00, high D levels (≥20ng/mL) 3 of 49 (6.1%), low D levels (<20ng/mL) 2 of 24 (8.3%), NNT 45.
	risk of case, 33.4% lower, OR 0.67, *p* = 0.23, high D levels (≥20ng/mL) 41 of 73 (56.2%) cases, 50 of 76 (65.8%) controls, NNT 9.9, case control OR.
Bayramoğlu, 3/31/2021, retrospective, Turkey, peer-reviewed, 7 authors.	risk of moderate/severe case, 69.5% lower, RR 0.30, *p* = 0.03, high D levels 10 of 60 (16.7%), low D levels 24 of 43 (55.8%), NNT 2.6, adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >12 ng/mL, multivariate logistic regression.
Bennouar, 1/12/2021, prospective, Algeria, peer-reviewed, 5 authors.	risk of death, 85.5% lower, RR 0.14, *p* = 0.002, high D levels 4 of 30 (13.3%), low D levels 15 of 32 (46.9%), NNT 3.0, adjusted per study, inverted to make RR<1 favor high D levels, >30µg/l vs. <10µg/l, proportional Cox regression.
	risk of death, 63.0% lower, RR 0.37, *p* = 0.10, high D levels 4 of 30 (13.3%), low D levels 14 of 35 (40.0%), NNT 3.7, adjusted per study, inverted to make RR<1 favor high D levels, >30µg/l vs. 10-19µg/l, proportional Cox regression.
	risk of death, 23.1% lower, RR 0.77, *p* = 0.73, high D levels 4 of 30 (13.3%), low D levels 4 of 23 (17.4%), NNT 25, adjusted per study, inverted to make RR<1 favor high D levels, >30µg/l vs. 20-29µg/l, proportional Cox regression.
Bianconi, 7/1/2021, prospective, Italy, peer-reviewed, 12 authors.	risk of death, 17.5% lower, HR 0.82, *p* = 0.58, high D levels (≥12ng/ml) 94, low D levels (<12ng/ml) 106, model 3, Table S2, Cox proportional hazards.
	risk of death, 13.9% lower, HR 0.86, *p* = 0.73, high D levels (≥20ng/ml) 40, low D levels (<20ng/ml) 160, model 3, Table S2, Cox proportional hazards.
	risk of death/ICU, 15.9% lower, HR 0.84, *p* = 0.53, high D levels (≥12ng/ml) 94, low D levels (<12ng/ml) 106, model 3, Cox proportional hazards.
	risk of death/ICU, 10.9% lower, HR 0.89, *p* = 0.73, high D levels (≥20ng/ml) 40, low D levels (<20ng/ml) 160, model 3, Cox proportional hazards.
Bogliolo, 7/5/2022, prospective, Italy, peer-reviewed, median age 73.0, 16 authors, study period March 2020 - August 2020.	risk of death, 15.3% lower, HR 0.85, *p* = 0.29, cutoff 20ng/mL, inverted to make HR<1 favor high D levels (≥20ng/mL).
Bogomaz, 8/24/2023, retrospective, Ukraine, peer-reviewed, median age 62.0, 2 authors.	risk of death, 70.0% lower, RR 0.30, *p* = 0.24, high D levels (≥30ng/ml) 1 of 28 (3.6%), low D levels (<30ng/ml) 5 of 42 (11.9%), NNT 12, inverted to make RR<1 favor high D levels (≥30ng/ml), odds ratio converted to relative risk.

	risk of mechanical ventilation, 75.0% lower, RR 0.25, $p = 0.23$, high D levels (≥30ng/ml) 1 of 28 (3.6%), low D levels (<30ng/ml) 6 of 42 (14.3%), NNT 9.3.
	risk of progression, 62.5% lower, RR 0.38, $p = 0.30$, high D levels (≥30ng/ml) 2 of 28 (7.1%), low D levels (<30ng/ml) 8 of 42 (19.0%), NNT 8.4, critical case.
	risk of oxygen therapy, 27.0% lower, RR 0.73, $p = 0.24$, high D levels (≥30ng/ml) 10 of 28 (35.7%), low D levels (<30ng/ml) 28 of 42 (66.7%), NNT 3.2, adjusted per study, inverted to make RR<1 favor high D levels (≥30ng/ml), odds ratio converted to relative risk, multivariable.
Breslin, 8/17/2021, retrospective, Ireland, peer-reviewed, 4 authors.	**risk of progression, 55.6% lower, OR 0.44, $p = 0.03$**, high D levels (≥30nmol/l) 106, low D levels (<30nmol/l) 32, adjusted per study, inverted to make OR<1 favor high D levels (≥30nmol/l), infiltrates on chest X-ray, multivariable, RR approximated with OR.
Bucurica, 3/6/2023, retrospective, Romania, peer-reviewed, mean age 55.2, 9 authors, study period 1 June, 2020 - 31 May, 2022.	**risk of case, 27.6% lower, OR 0.72, $p < 0.001$**, high D levels (≥20ng/mL) 7,958, low D levels (<20ng/mL) 3,224, inverted to make OR<1 favor high D levels (≥20ng/mL), RR approximated with OR.
	risk of case, 7.4% higher, OR 1.07, $p = 0.19$, high D levels (≥30ng/mL) 4,367, low D levels (<30ng/mL) 6,815, inverted to make OR<1 favor high D levels (≥30ng/mL), RR approximated with OR.
Bushnaq, 2/8/2022, retrospective, Saudi Arabia, peer-reviewed, 7 authors, excluded in exclusion analyses: unadjusted results with no group details.	**risk of mechanical ventilation, 32.1% lower, RR 0.68, $p = 0.27$**, high D levels (≥20ng/mL) 10 of 53 (18.9%), low D levels (<20ng/mL) 40 of 144 (27.8%), NNT 11, unadjusted.
	risk of ICU admission, 3.9% lower, RR 0.96, $p = 0.87$, high D levels (≥20ng/mL) 23 of 53 (43.4%), low D levels (<20ng/mL) 65 of 144 (45.1%), NNT 57, unadjusted.
Bychinin (B), 5/7/2021, retrospective, Russia, peer-reviewed, 5 authors, excluded in exclusion analyses: excessive unadjusted differences between groups.	**risk of death, 36.2% lower, RR 0.64, $p = 0.03$**, high D levels (≥10ng/mL) 16 of 38 (42.1%), low D levels (<10ng/mL) 31 of 47 (66.0%), NNT 4.2.
Campi, 6/14/2021, prospective, Italy, peer-reviewed, 21 authors, dosage not specified.	**risk of death for severe patients, 24.3% lower, RR 0.76, $p = 0.53$**, high D levels (≥20ng/ml) 6 of 39 (15.4%), low D levels (<20ng/ml) 13 of 64 (20.3%), NNT 20, hospitalized patients, outcome based on serum levels.
	risk of ICU for severe patients, 53.1% lower, RR 0.47, $p < 0.001$, high D levels (≥20ng/ml) 12 of 39 (30.8%), low D levels (<20ng/ml) 42 of 64 (65.6%), NNT 2.9, hospitalized patients, outcome based on serum levels.
Cannata-Andía, 2/18/2022, prospective, multiple countries, peer-reviewed, median age 59.0, 22 authors, study period 4 April, 2020 - 22 April, 2021, dosage 100,000IU single dose, trial NCT04552951	**risk of death, 117.0% higher, RR 2.17, $p = 0.20$**, high D levels 87, low D levels 96, >25 vs. ≤10 ng/mL, adjusted by demographics, comorbidities, and laboratory parameters, outcome based on serum levels.

(history) (COVID-VIT-D), excluded in exclusion analyses: very late stage study using cholecalciferol instead of calcifediol or calcitriol.	risk of ICU admission, 65.0% lower, RR 0.35, p = 0.04, high D levels 87, low D levels 96, >25 vs. ≤10 ng/mL, adjusted by demographics, comorbidities, and laboratory parameters, outcome based on serum levels.
	risk of progression, 79.0% lower, RR 0.21, p = 0.003, high D levels 87, low D levels 96, pulmonary involvment at admission, >25 vs. ≤10 ng/mL, adjusted by demographics, comorbidities, and laboratory parameters, outcome based on serum levels.
Carpagnano, 8/9/2020, retrospective, Italy, peer-reviewed, 10 authors.	**risk of death at day 26, 70.6% lower, RR 0.29, p = 0.0499**, high D levels 5 of 34 (14.7%), low D levels 4 of 8 (50.0%), NNT 2.8, >30 ng/mL.
	risk of death at day 10, 90.0% lower, RR 0.10, p = 0.02, high D levels 2 of 34 (5.9%), low D levels 4 of 8 (50.0%), NNT 2.3, adjusted per study, >30 ng/mL.
Cereda, 11/1/2020, prospective, Italy, peer-reviewed, 13 authors.	**risk of death, 120.0% higher, RR 2.20, p = 0.04**, high D levels 10 of 30 (33.3%), low D levels 24 of 99 (24.2%), inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >20ng/mL.
	risk of ICU admission, 86.7% lower, RR 0.13, p = 0.59, high D levels 0 of 30 (0.0%), low D levels 5 of 99 (5.1%), NNT 20, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm).
Cetin Ozbek, 3/24/2023, retrospective, Turkey, peer-reviewed, mean age 63.4, 6 authors, study period 1 August, 2021 - 31 October, 2021.	**risk of death, 50.9% lower, RR 0.49, p = 0.07**, high D levels (≥20ng/mL) 7 of 61 (11.5%), low D levels (<20ng/mL) 25 of 107 (23.4%), NNT 8.4.
	risk of death, 3.0% lower, OR 0.97, p = 0.32, adjusted per study, continuous values, multivariable, RR approximated with OR.
Charkowick, 5/5/2022, retrospective, USA, peer-reviewed, 10 authors, study period 1 January, 2020 - 5 February, 2021.	**risk of death, 73.4% lower, OR 0.27, p = 0.02**, high D levels 140, low D levels 68, adjusted per study, inverted to make OR<1 favor high D levels, multivariable, RR approximated with OR.
	risk of ICU admission, 67.2% lower, OR 0.33, p = 0.001, high D levels 140, low D levels 68, adjusted per study, inverted to make OR<1 favor high D levels, multivariable, RR approximated with OR.
Charla, 7/13/2022, retrospective, India, preprint, 8 authors, study period 1 April, 2020 - 30 April, 2021, excluded in exclusion analyses: excessive unadjusted differences between groups.	**risk of death, 10.7% lower, RR 0.89, p = 0.74**, high D levels (≥20ng/ml) 24 of 91 (26.4%), low D levels (<20ng/ml) 26 of 88 (29.5%), NNT 32.
Charoenngam, 3/8/2021, retrospective, USA, peer-reviewed, 6 authors.	**risk of death, 34.1% lower, RR 0.66, p = 0.26**, high D levels 12 of 100 (12.0%), low D levels 29 of 187 (15.5%), adjusted per study, odds ratio converted to relative risk, >=30ng/mL.
	risk of mechanical ventilation, 37.2% lower, RR 0.63, p = 0.17, high D levels 14 of 100 (14.0%), low D levels 34 of 187 (18.2%), adjusted per study, odds ratio converted to relative risk,

	>=30ng/mL.
	risk of ICU admission, 23.1% lower, RR 0.77, *p* = 0.28, high D levels 25 of 100 (25.0%), low D levels 56 of 187 (29.9%), NNT 20, adjusted per study, odds ratio converted to relative risk, >=30ng/mL.
	risk of death, 58.1% lower, RR 0.42, *p* = 0.05, high D levels 7 of 57 (12.3%), low D levels 25 of 79 (31.6%), NNT 5.2, adjusted per study, odds ratio converted to relative risk, >65 years old, >=30ng/mL.
Chen (B), 2/28/2023, retrospective, China, peer-reviewed, 9 authors, study period 1 June, 2022 - 5 July, 2022.	viral clearance, 40.0% improved, HR 0.60, *p* = 0.01, high D levels (≥41.07ng/mL) 52, low D levels (<27.5ng/mL) 53, adjusted per study, tertile 3 vs. tertile 1, multivariable, Cox proportional hazards.
Choi, 1/2/2024, retrospective, South Korea, peer-reviewed, mean age 55.7, 6 authors, study period April 2022 - December 2022.	risk of no recovery, 48.9% lower, HR 0.51, *p* = 0.002, high D levels (≥20ng/mL) 99, low D levels (<20ng/mL) 67, adjusted per study, multivariable.
	risk of PASC, 68.4% lower, HR 0.32, *p* = 0.001, high D levels (≥20ng/mL) 99, low D levels (<20ng/mL) 67, adjusted per study, inverted to make HR<1 favor high D levels (≥20ng/mL), multivariable.
	risk of hospitalization, 25.6% lower, RR 0.74, *p* = 0.48, high D levels (≥20ng/mL) 11 of 99 (11.1%), low D levels (<20ng/mL) 10 of 67 (14.9%), NNT 26, unadjusted.
Connolly, 8/17/2021, retrospective, Ireland, peer-reviewed, 8 authors, study period March 2020 - May 2020.	risk of death, 90.4% lower, OR 0.10, *p* = 0.06, high D levels (≥30nmol/l) 65, low D levels (<30nmol/l) 49, adjusted per study, inverted to make OR<1 favor high D levels (≥30nmol/l), multivariable, RR approximated with OR.
	risk of oxygen therapy, 73.3% lower, OR 0.27, *p* = 0.048, high D levels (≥30nmol/l) 65, low D levels (<30nmol/l) 49, adjusted per study, inverted to make OR<1 favor high D levels (≥30nmol/l), multivariable, RR approximated with OR.
Cozier, 7/27/2021, prospective, USA, peer-reviewed, 6 authors.	risk of case, 38.6% lower, RR 0.61, *p* = 0.04, high D levels 94 of 1,601 (5.9%), low D levels 33 of 373 (8.8%), NNT 34, adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >20ng/mL, multivariable.
Dana, 8/11/2022, retrospective, Iran, peer-reviewed, 16 authors, study period March 2020 - November 2020.	risk of death, 33.1% lower, RR 0.67, *p* = 0.29, high D levels (≥10ng/mL) 49 of 376 (13.0%), low D levels (<10ng/mL) 8 of 46 (17.4%), NNT 23, adjusted per study, inverted to make RR<1 favor high D levels (≥10ng/mL), odds ratio converted to relative risk, sufficiency vs. severe deficiency, multivariable.
	risk of death, 15.7% lower, RR 0.84, *p* = 0.44, high D levels (≥20ng/mL) 49 of 376 (13.0%), low D levels (<20ng/mL) 30 of 197 (15.2%), NNT 46, adjusted per study, inverted to make RR<1 favor high D levels (≥20ng/mL), odds ratio converted to relative risk, sufficiency vs. deficiency, multivariable.

	risk of severe case, no change, RR 1.00, $p = 1.00$, high D levels (≥10ng/mL) 59 of 376 (15.7%), low D levels (<10ng/mL) 7 of 46 (15.2%), adjusted per study, inverted to make RR<1 favor high D levels (≥10ng/mL), odds ratio converted to relative risk, sufficiency vs. severe deficiency, multivariable.
	risk of severe case, 11.6% lower, RR 0.88, $p = 0.45$, high D levels (≥20ng/mL) 59 of 376 (15.7%), low D levels (<20ng/mL) 35 of 197 (17.8%), NNT 48, adjusted per study, inverted to make RR<1 favor high D levels (≥20ng/mL), odds ratio converted to relative risk, sufficiency vs. deficiency, multivariable.
Davoudi, 5/18/2021, retrospective, Iran, peer-reviewed, 11 authors, study period February 2020 - March 2020, excluded in exclusion analyses: excessive unadjusted differences between groups.	risk of death, 12.3% higher, RR 1.12, $p = 1.00$, high D levels (≥30ng/mL) 2 of 57 (3.5%), low D levels (<30ng/mL) 3 of 96 (3.1%).
	risk of mechanical ventilation, 15.8% lower, RR 0.84, $p = 1.00$, high D levels (≥30ng/mL) 1 of 57 (1.8%), low D levels (<30ng/mL) 2 of 96 (2.1%), NNT 304.
	risk of ICU admission, 27.8% lower, RR 0.72, $p = 0.74$, high D levels (≥30ng/mL) 3 of 57 (5.3%), low D levels (<30ng/mL) 7 of 96 (7.3%), NNT 49.
	risk of severe case, 68.4% higher, RR 1.68, $p = 0.30$, high D levels (≥30ng/mL) 9 of 57 (15.8%), low D levels (<30ng/mL) 9 of 96 (9.4%).
Davran, 3/15/2023, retrospective, Turkey, peer-reviewed, mean age 53.6, 9 authors.	risk of death, 75.4% lower, RR 0.25, $p = 0.02$, high D levels (≥10ng/ml) 4 of 63 (6.3%), low D levels (<10ng/ml) 8 of 31 (25.8%), NNT 5.1.
De Smet, 11/25/2020, retrospective, Belgium, peer-reviewed, 5 authors.	risk of death, 70.1% lower, RR 0.30, $p = 0.02$, high D levels 7 of 77 (9.1%), low D levels 20 of 109 (18.3%), adjusted per study, odds ratio converted to relative risk, >20ng/mL.
Demir, 1/29/2021, retrospective, Turkey, peer-reviewed, 3 authors.	risk of severe case, 89.3% lower, RR 0.11, $p < 0.001$, high D levels 13, low D levels 99, ratio of the mean number of affected lung segments, >30ng/ml vs. <=10ng/mL.
	hospitalization time, 87.1% lower, relative time 0.13, $p < 0.001$, high D levels 13, low D levels 99, >30ng/ml vs. <=10ng/mL.
	risk of case, 24.2% lower, RR 0.76, $p = 0.18$, high D levels 13 of 31 (41.9%), low D levels 99 of 179 (55.3%), NNT 7.5, >30ng/ml vs. <=10ng/mL.
Derakhshanian, 9/19/2021, retrospective, Iran, peer-reviewed, 11 authors.	risk of death, 44.8% lower, RR 0.55, $p = 0.046$, high D levels 148, low D levels 142, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, control prevalance approximated with overall prevalence.
	risk of mechanical ventilation, 41.7% lower, RR 0.58, $p = 0.09$, high D levels 148, low D levels 142, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, control prevalance approximated with overall prevalence.

	risk of ICU admission, 37.3% lower, RR 0.63, p = 0.04, high D levels 148, low D levels 142, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, control prevalance approximated with overall prevalence.
Devi, 4/15/2023, retrospective, India, peer-reviewed, mean age 47.0, 4 authors, study period August 2020 - August 2022.	**risk of case, 98.0% lower, OR 0.02, p = 0.007**, high D levels (≥10ng/mL) 69 of 88 (78.4%) cases, 88 of 88 (100.0%) controls, NNT 1.8, case control OR.
	risk of case, 88.4% lower, OR 0.12, p < 0.001, high D levels (≥20ng/mL) 54 of 88 (61.4%) cases, 82 of 88 (93.2%) controls, NNT 2.2, case control OR.
di Filippo (B), 8/12/2021, retrospective, Italy, peer-reviewed, 8 authors.	**risk of death, 10.7% lower, RR 0.89, p = 1.00**, high D levels 5 of 28 (17.9%), low D levels 12 of 60 (20.0%), NNT 47, >20ng/mL.
	risk of ICU admission, 41.6% lower, RR 0.58, p = 0.22, high D levels 6 of 28 (21.4%), low D levels 22 of 60 (36.7%), NNT 6.6, >20ng/mL.
	risk of severe case, 39.6% lower, RR 0.60, p = 0.04, high D levels 11 of 28 (39.3%), low D levels 39 of 60 (65.0%), NNT 3.9, >20ng/mL.
Diaz-Curiel, 6/6/2021, retrospective, Spain, peer-reviewed, 8 authors.	**risk of ICU admission, 73.2% lower, RR 0.27, p = 0.02**, high D levels 3 of 214 (1.4%), low D levels 91 of 1,017 (8.9%), odds ratio converted to relative risk, >30ng/mL vs. <20ng/mL.
Doğan, 8/4/2022, prospective, Turkey, peer-reviewed, 5 authors, study period 1 July, 2021 - 30 October, 2021.	**risk of case, 63.7% lower, OR 0.36, p = 0.003**, high D levels (≥10ng/ml) 53 of 88 (60.2%) cases, 71 of 88 (80.7%) controls, NNT 4.1, case control OR.
Dror, 6/7/2021, retrospective, Israel, peer-reviewed, 18 authors.	**risk of severe or critical case, 84.8% lower, RR 0.15, p = 0.001**, high D levels 109 of 120 (90.8%), low D levels 76 of 133 (57.1%), adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >40ng/mL vs. <20ng/mL, multivariable.
Eden, 8/5/2021, retrospective, United Kingdom, peer-reviewed, 5 authors.	**risk of death, 63.9% lower, RR 0.36, p = 0.10**, high D levels (≥25nmol/L) 3 of 26 (11.5%), low D levels (<25nmol/L) 8 of 25 (32.0%), NNT 4.9.
	risk of death, 92.9% lower, RR 0.07, p = 0.18, high D levels (≥50nmol/L) 0 of 8 (0.0%), low D levels (<50nmol/L) 11 of 43 (25.6%), NNT 3.9, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm).
Efe Iris, 12/30/2023, retrospective, Turkey, peer-reviewed, mean age 46.9, 8 authors.	**risk of case, 59.2% lower, OR 0.41, p < 0.001**, cutoff 18.4ng/mL, inverted to make OR<1 favor high D levels (≥18.4ng/mL), RR approximated with OR.
Faniyi, 10/6/2020, prospective, United Kingdom, preprint, 10 authors.	**risk of seropositive, 28.8% lower, RR 0.71, p = 0.003**, high D levels 170 of 331 (51.4%), low D levels 44 of 61 (72.1%), NNT 4.8, >30nmol/L.

Fatemi, 11/30/2021, prospective, Iran, peer-reviewed, 5 authors, study period 1 October, 2020 - 31 May, 2021.	**risk of death, 42.0% lower, RR 0.58, p = 0.07**, high D levels 18 of 139 (12.9%), low D levels 25 of 109 (22.9%), NNT 10, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, vitamin D measured prior to COVID-19, multivariate.
	risk of death, 51.1% lower, RR 0.49, p = 0.02, high D levels 13 of 115 (11.3%), low D levels 30 of 133 (22.6%), NNT 8.9, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, vitamin D measured on admission, multivariate.
	risk of severe case, 37.9% lower, RR 0.62, p = 0.007, high D levels 38 of 139 (27.3%), low D levels 48 of 109 (44.0%), NNT 6.0, vitamin D measured prior to COVID-19.
	risk of severe case, 34.8% lower, RR 0.65, p = 0.02, high D levels 31 of 115 (27.0%), low D levels 55 of 133 (41.4%), NNT 6.9, vitamin D measured on admission.
Faul, 6/30/2020, retrospective, Ireland, peer-reviewed, 9 authors.	**risk of mechanical ventilation, 69.0% lower, RR 0.31, p = 0.03**, high D levels 4 of 21 (19.0%), low D levels 8 of 12 (66.7%), NNT 2.1, adjusted per study, >30nmol/L.
Ferrer-Sánchez, 3/26/2022, retrospective, Spain, peer-reviewed, 7 authors.	**risk of ICU admission, 81.8% lower, RR 0.18, p = 1.00**, high D levels (≥20ng/mL) 0 of 9 (0.0%), low D levels (<20ng/mL) 4 of 73 (5.5%), NNT 18, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), excluded in exclusion analyses: unadjusted results with no group details.
	risk of moderate/severe case, 88.7% lower, RR 0.11, p = 1.00, high D levels (≥20ng/mL) 0 of 9 (0.0%), low D levels (<20ng/mL) 7 of 73 (9.6%), NNT 10, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), excluded in exclusion analyses: unadjusted results with no group details.
	risk of case, 62.7% lower, OR 0.37, p = 0.01, cutoff 20ng/mL, adjusted per study, inverted to make OR<1 favor high D levels (≥20ng/mL), multivariable, RR approximated with OR.
Freitas, 3/27/2021, retrospective, Portugal, preprint, 36 authors.	**risk of death, 41.2% lower, RR 0.59, p = 0.02**, high D levels 23 of 179 (12.8%), low D levels 68 of 311 (21.9%), NNT 11, >20ng/mL.
Frish, 6/15/2023, retrospective, Israel, peer-reviewed, 7 authors, study period 1 February, 2020 - 31 December, 2020.	**risk of case, 35.5% lower, OR 0.65, p = 0.001**, cutoff 20ng/mL, adjusted per study, inverted to make OR<1 favor high D levels (≥20ng/mL), multivariable, RR approximated with OR.
Galaznik, 5/28/2021, retrospective, USA, preprint, 6 authors.	**risk of case, 35.1% lower, OR 0.65, p = 0.01**, high D levels 13,903, low D levels 2,384, adjusted per study, inverted to make OR<1 favor high D levels, breast cancer patients, logistic regression, RR approximated with OR.
	risk of case, 32.4% lower, OR 0.68, p = 0.045, high D levels 13,601, low D levels 1,318, adjusted per study, inverted to make OR<1 favor high D levels, prostate cancer patients, logistic regression, RR approximated with OR.

Gaudio, 3/27/2021, retrospective, Italy, peer-reviewed, 6 authors.	risk of case, 79.3% lower, OR 0.21, $p < 0.001$, high D levels 27 of 50 (54.0%) cases, 85 of 100 (85.0%) controls, NNT 2.7, case control OR.
Gavioli, 2/19/2021, retrospective, USA, peer-reviewed, 4 authors.	risk of death, 4.7% higher, RR 1.05, $p = 0.83$, high D levels 80 of 260 (30.8%), low D levels 52 of 177 (29.4%), >20ng/ml.
	risk of death, 44.8% lower, RR 0.55, $p < 0.001$, high D levels 102 of 376 (27.1%), low D levels 30 of 61 (49.2%), NNT 4.5, >10ng/ml.
	risk of oxygen therapy, 55.2% lower, RR 0.45, $p < 0.001$, high D levels 127 of 260 (48.8%), low D levels 116 of 177 (65.5%), NNT 6.0, adjusted per study, inverted to make RR<1 favor high D levels, >20ng/ml, multivariate.
	risk of hospitalization, 3.6% lower, RR 0.96, $p = 0.41$, high D levels 218 of 260 (83.8%), low D levels 154 of 177 (87.0%), NNT 32, >20ng/ml.
Ghanei, 3/23/2022, prospective, Iran, peer-reviewed, 6 authors, study period 20 March, 2020 - 20 January, 2021.	risk of case, 42.1% lower, OR 0.58, $p = 0.09$, high D levels (≥20ng/ml) 58 of 90 (64.4%) cases, 72 of 95 (75.8%) controls, NNT 7.4, case control OR.
Gholi, 7/19/2022, prospective, Iran, peer-reviewed, 4 authors.	risk of death, 74.7% lower, HR 0.25, $p < 0.001$, high D levels 157, low D levels 38, inverted to make HR<1 favor high D levels, >30ng/mL vs. <20ng/mL, model 2, day 45.
	risk of death, 39.8% lower, HR 0.60, $p = 0.05$, high D levels 157, low D levels 38, inverted to make HR<1 favor high D levels, >30ng/mL vs. <20ng/mL, ICU mortality, model 2.
	risk of mechanical ventilation, 44.9% higher, HR 1.45, $p = 0.27$, high D levels 157, low D levels 38, inverted to make HR<1 favor high D levels, >30ng/mL vs. <20ng/mL, model 2, day 45.
Golabi, 8/26/2021, retrospective, Iran, peer-reviewed, 10 authors.	odds of symptoms, 90.0% lower, OR 0.10, $p < 0.001$, high D levels 34, low D levels 10, >30ng/mL vs. <20ng/mL, GEE regression, RR approximated with OR.
	odds of symptoms, 81.0% lower, OR 0.19, $p = 0.006$, high D levels 34, low D levels 9, 20-30ng/mL vs. <20ng/mL, GEE regression, RR approximated with OR.
	risk of case, 71.7% lower, OR 0.28, $p = 0.07$, high D levels 34 of 44 (77.3%) cases, 36 of 39 (92.3%) controls, NNT 3.5, case control OR, >30ng/mL vs. <20ng/mL.
Gonzalez, 3/13/2023, retrospective, Argentina, peer-reviewed, 10 authors.	risk of death, 66.1% lower, OR 0.34, $p = 0.046$, high D levels (≥12ng/ml) 129, low D levels (<12ng/ml) 35, adjusted per study, inverted to make OR<1 favor high D levels (≥12ng/ml), multivariable, RR approximated with OR.
González-Estevez, 7/7/2021, retrospective, Mexico, peer-reviewed, 6 authors.	risk of symptomatic case, 25.0% lower, RR 0.75, $p = 0.04$, high D levels (≥30ng/mL) 6 of 8 (75.0%), low D levels (<30ng/mL) 32 of 32 (100.0%), NNT 4.0.

Green, 11/7/2022, retrospective, Israel, peer-reviewed, 9 authors, study period 1 February, 2020 - 31 December, 2020.	risk of case, 18.7% lower, OR 0.81, $p < 0.001$, cutoff 30ng/mL, adjusted per study, inverted to make OR<1 favor high D levels (≥30ng/mL), multivariable, RR approximated with OR.
Guðnadóttir, 3/4/2024, retrospective, Iceland, peer-reviewed, 4 authors, study period February 2020 - March 2021.	risk of death, 54.3% lower, OR 0.46, $p = 0.15$, high D levels (≥50nmol/L) 221, low D levels (<50nmol/L) 52, adjusted per study, inverted to make OR<1 favor high D levels (≥50nmol/L), multivariable, RR approximated with OR.
	risk of mechanical ventilation, 8.3% lower, OR 0.92, $p = 0.86$, high D levels (≥50nmol/L) 221, low D levels (<50nmol/L) 52, adjusted per study, inverted to make OR<1 favor high D levels (≥50nmol/L), multivariable, RR approximated with OR.
	risk of ICU admission, 28.1% lower, OR 0.72, $p = 0.43$, high D levels (≥50nmol/L) 221, low D levels (<50nmol/L) 52, adjusted per study, inverted to make OR<1 favor high D levels (≥50nmol/L), multivariable, RR approximated with OR.
Gönen, 11/12/2021, retrospective, Turkey, peer-reviewed, 20 authors, dosage varies.	risk of death, 65.8% lower, RR 0.34, $p = 0.62$, high D levels (≥12ng/mL) 1 of 80 (1.2%), low D levels (<12ng/mL) 3 of 82 (3.7%), NNT 42, retrospective study.
	risk of ICU admission, 16.9% lower, RR 0.83, $p = 1.00$, high D levels (≥12ng/mL) 4 of 77 (5.2%), low D levels (<12ng/mL) 5 of 80 (6.2%), NNT 95, retrospective study.
	hospital stay >8 days, 21.1% lower, RR 0.79, $p = 0.11$, high D levels (≥12ng/mL) 40 of 78 (51.3%), low D levels (<12ng/mL) 52 of 80 (65.0%), NNT 7.3, retrospective study.
Hafez, 3/29/2022, retrospective, United Arab Emirates, peer-reviewed, mean age 43.0, 11 authors.	risk of death, 97.7% lower, RR 0.02, $p = 0.02$, high D levels (≥12ng/mL) 6 of 116 (5.2%), low D levels (<12ng/mL) 3 of 10 (30.0%), NNT 4.0, adjusted per study, inverted to make RR<1 favor high D levels (≥12ng/mL), odds ratio converted to relative risk, multivariable, model 2.
	risk of death, 96.3% lower, RR 0.04, $p = 0.04$, high D levels (≥20ng/mL) 4 of 64 (6.2%), low D levels (<20ng/mL) 5 of 62 (8.1%), adjusted per study, inverted to make RR<1 favor high D levels (≥20ng/mL), odds ratio converted to relative risk, multivariable, model 3.
Hastie, 8/26/2020, retrospective, population-based cohort, database analysis, United Kingdom, peer-reviewed, 14 authors.	risk of death, 17.4% lower, RR 0.83, $p = 0.31$, cutoff 25nmol/L, adjusted per study, inverted to make RR<1 favor high D levels (≥25nmol/L), multivariable Cox.
	risk of hospitalization, 9.1% lower, RR 0.91, $p = 0.40$, cutoff 25nmol/L, adjusted per study, inverted to make RR<1 favor high D levels (≥25nmol/L), multivariable Cox.
Hermawan, 3/28/2023, retrospective, Indonesia, peer-reviewed, survey, 5 authors, study period March 2022 - July 2022.	risk of symptomatic case, 70.6% lower, RR 0.29, $p < 0.001$, high D levels (≥10ng/ml) 10 of 34 (29.4%), low D levels (<10ng/ml) 13 of 13 (100.0%), NNT 1.4.

	risk of symptomatic case, 45.6% lower, RR 0.54, $p = 0.42$, high D levels (≥20ng/ml) 2 of 7 (28.6%), low D levels (<20ng/ml) 21 of 40 (52.5%), NNT 4.2.
Hernández, 10/27/2020, retrospective, Spain, peer-reviewed, mean age 60.9, 12 authors.	**risk of combined death/ICU/ventilation, 83.0% lower, RR 0.17, $p < 0.001$**, high D levels 35, low D levels 162, >= 20ng/mL risk of hospitalization * risk of death/ICU/ventilation | hospitalization.
	risk of combined death/ICU/ventilation if hospitalized, 12.0% lower, RR 0.88, $p = 0.86$, high D levels 35, low D levels 162, >= 20ng/mL risk of death/ICU/ventilation | hospitalization.
	risk of hospitalization, 80.6% lower, RR 0.19, $p < 0.001$, >= 20ng/mL.
Hogarth, 5/3/2023, retrospective, USA, peer-reviewed, median age 56.0, 9 authors, study period 1 January, 2021 - 8 November, 2021.	**risk of case, 46.5% lower, OR 0.53, $p < 0.001$**, high D levels (≥20ng/mL) 96,894, low D levels (<20ng/mL) 13,486, adjusted per study, inverted to make OR<1 favor high D levels (≥20ng/mL), breakthrough case, multivariable, RR approximated with OR.
Huang, 3/24/2023, retrospective, China, peer-reviewed, 5 authors, study period 14 June, 2021 - 1 April, 2022.	**recovery time, 25.0% lower, relative time 0.75, $p = 0.02$**, high D levels (≥20ng/ml) 28, low D levels (<20ng/ml) 18, relative time until resolution of pneumonia.
Hurst, 10/22/2021, prospective, United Kingdom, peer-reviewed, 23 authors.	**risk of death, 68.4% lower, RR 0.32, $p = 0.005$**, high D levels 68, low D levels 191, odds ratio converted to relative risk, >50nmol/l, multivariable, Supplementary Table 2, control prevalance approximated with overall prevalence.
	risk of mechanical ventilation, 66.0% lower, RR 0.34, $p = 0.004$, high D levels 6 of 68 (8.8%), low D levels 61 of 191 (31.9%), NNT 4.3, odds ratio converted to relative risk, >50nmol/l, multivariable, Supplementary Table 2.
Im, 8/11/2020, retrospective, South Korea, peer-reviewed, 6 authors.	**risk of case, 73.1% lower, OR 0.27, $p < 0.001$**, high D levels 13 of 50 (26.0%) cases, 85 of 150 (56.7%) controls, NNT 4.3, case control OR.
Infante, 2/18/2021, retrospective, Italy, peer-reviewed, 11 authors.	**risk of death, 54.8% lower, RR 0.45, $p = 0.046$**, high D levels 4 of 19 (21.1%), low D levels 55 of 118 (46.6%), NNT 3.9, >20ng/mL.
Israel, 9/20/2021, retrospective, population-based cohort, Israel, peer-reviewed, 9 authors, study period 1 March, 2020 - 31 October, 2020.	**risk of severe case, 33.9% lower, OR 0.66, $p < 0.001$**, high D levels 423 of 1,036 (40.8%) cases, 509 of 934 (54.5%) controls, NNT 7.3, adjusted per study, inverted to make OR<1 favor high D levels, case control OR, >75 nmol/L vs. <30 nmol/L, multivariable.
	risk of case, 19.7% lower, OR 0.80, $p < 0.001$, high D levels 6,152 of 15,892 (38.7%) cases, 73,810 of 159,193 (46.4%) controls, NNT 39, adjusted per study, inverted to make OR<1 favor high D levels, case control OR, >75 nmol/L vs. <30 nmol/L, among COVID+ cases, multivariable.
Jain (B), 11/19/2020, prospective, India, peer-reviewed, 6 authors.	**risk of death, 85.2% lower, RR 0.15, $p = 0.001$**, high D levels 2 of 64 (3.1%), low D levels 19 of 90 (21.1%), NNT 5.6, >20ng/mL.

	risk of ICU admission, 95.4% lower, RR 0.05, $p < 0.001$, high D levels 2 of 64 (3.1%), low D levels 61 of 90 (67.8%), NNT 1.5, >20ng/mL.
Jalavu, 6/1/2023, prospective, South Africa, peer-reviewed, 16 authors, study period 29 October, 2020 - 10 February, 2021.	risk of death, 1.0% lower, HR 0.99, $p = 0.97$, high D levels (≥50nmol/L) 16 of 31 (51.6%), low D levels (<50nmol/L) 38 of 55 (69.1%), NNT 5.7, Kaplan–Meier.
Jimenez, 7/26/2021, retrospective, Spain, peer-reviewed, 21 authors, study period 12 March, 2020 - 21 May, 2020, dosage paricalcitol 0.9µg weekly, excluded in exclusion analyses: many patients received vitamin D treatment.	risk of death, 7.7% higher, OR 1.08, $p = 0.81$, high D levels 50, low D levels 110, >30 vs. <20ng/ml, RR approximated with OR, outcome based on serum levels.
	risk of mechanical ventilation, 47.5% lower, OR 0.53, $p = 0.56$, high D levels 50, low D levels 110, >30 vs. <20ng/ml, RR approximated with OR, outcome based on serum levels.
	risk of ICU admission, 12.2% lower, OR 0.88, $p = 0.87$, high D levels 50, low D levels 110, >30 vs. <20ng/ml, RR approximated with OR, outcome based on serum levels.
	risk of hospitalization, 0.8% lower, OR 0.99, $p = 0.98$, high D levels 50, low D levels 110, >30 vs. <20ng/ml, RR approximated with OR, outcome based on serum levels.
Jude, 6/17/2021, retrospective, United Kingdom, peer-reviewed, 5 authors.	risk of hospitalization, 71.6% lower, RR 0.28, $p < 0.001$, adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >25 nmol/L, control prevalence approximated with overall prevalence.
	risk of hospitalization, 57.9% lower, RR 0.42, $p < 0.001$, adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >50 nmol/L, control prevalence approximated with overall prevalence.
Junior, 2/17/2022, prospective, Brazil, peer-reviewed, 6 authors, dosage not specified.	risk of mechanical ventilation, 84.4% lower, OR 0.16, $p = 0.03$, cutoff 40ng/dl, inverted to make OR<1 favor high D levels (≥40ng/dl), risk of mechanical ventilation for vitamin D levels >40ng/ml, RR approximated with OR, outcome based on serum levels.
Juraj, 1/22/2022, retrospective, Slovakia, peer-reviewed, 13 authors, study period 1 November, 2020 - 30 April, 2021.	risk of death, 19.0% lower, RR 0.81, $p = 0.05$, high D levels (≥12ng/mL) 127 of 283 (44.9%), low D levels (<12ng/mL) 41 of 74 (55.4%), NNT 9.5.
Kalichuran, 4/26/2022, prospective, South Africa, peer-reviewed, survey, 4 authors, study period September 2020 - February 2021.	risk of symptomatic case, 60.0% lower, RR 0.40, $p < 0.001$, high D levels (≥20ng/mL) 56, low D levels (<20ng/mL) 44, inverted to make RR<1 favor high D levels (≥20ng/mL).
	risk of symptomatic case, 58.2% lower, RR 0.42, $p = 0.004$, inverted to make RR<1 favor high D levels, higher sunlight exposure vs. lower sunlight exposure.
Karahan, 10/5/2020, retrospective, Turkey, peer-reviewed, 2 authors.	risk of death, 82.5% lower, RR 0.17, $p < 0.001$, high D levels 5 of 46 (10.9%), low D levels 64 of 103 (62.1%), NNT 2.0, >20nmol/L.

Karonova (B), 3/2/2022, retrospective, Russia, peer-reviewed, 11 authors, study period 30 November, 2020 - 20 March, 2021.	**risk of severe case, 22.5% lower, OR 0.78, $p = 0.01$**, cutoff 11.4ng/mL, adjusted per study, inverted to make OR<1 favor high D levels (≥11.4ng/mL), multivariable, RR approximated with OR.
Karonova (C), 8/29/2021, retrospective, Russia, peer-reviewed, 8 authors, study period April 2020 - December 2020.	**risk of death, 77.8% lower, RR 0.22, $p = 0.006$**, high D levels 8 of 96 (8.3%), low D levels 10 of 37 (27.0%), NNT 5.3, adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >10ng/mL, logistic regression model 2.
	risk of death, 84.8% lower, RR 0.15, $p = 0.06$, high D levels 1 of 43 (2.3%), low D levels 17 of 90 (18.9%), NNT 6.0, adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >20ng/mL, logistic regression model 2.
	risk of severe case, 67.3% lower, RR 0.33, $p = 0.005$, high D levels 12 of 96 (12.5%), low D levels 13 of 37 (35.1%), NNT 4.4, adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >10ng/mL, logistic regression model 2.
	risk of severe case, 53.2% lower, RR 0.47, $p = 0.13$, high D levels 4 of 43 (9.3%), low D levels 21 of 90 (23.3%), NNT 7.1, adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >20ng/mL, logistic regression model 2.
Karonova (D), 12/31/2020, retrospective, Russia, peer-reviewed, 3 authors.	**risk of death, 79.4% lower, RR 0.21, $p = 0.11$**, high D levels 1 of 23 (4.3%), low D levels 12 of 57 (21.1%), NNT 6.0, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >20ng/ml.
	risk of severe case, 71.1% lower, RR 0.29, $p = 0.05$, high D levels 3 of 23 (13.0%), low D levels 22 of 57 (38.6%), NNT 3.9, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >20ng/ml.
Katz, 12/4/2020, retrospective, population-based cohort, USA, peer-reviewed, 3 authors.	**risk of case, 78.4% lower, RR 0.22, $p < 0.001$**, high D levels 85 of 101,175 (0.1%), low D levels 87 of 31,950 (0.3%), NNT 531, adjusted per study, inverted to make RR<1 favor high D levels.
Kaufman, 9/17/2020, retrospective, population-based cohort, USA, peer-reviewed, median age 54.0, 5 authors.	**risk of case, 53.0% lower, RR 0.47, $p < 0.001$**, high D levels 12,321, low D levels 39,190, >55 ng/mL vs. <20 ng/mL.
Kaur, 11/30/2021, prospective, India, peer-reviewed, 5 authors, excluded in exclusion analyses: unadjusted results with no group details.	**risk of death, 89.8% lower, RR 0.10, $p < 0.001$**, high D levels (≥10ng/mL) 5 of 64 (7.8%), low D levels (<10ng/mL) 13 of 17 (76.5%), NNT 1.5.
	risk of mechanical ventilation, 90.3% lower, RR 0.10, $p < 0.001$, high D levels (≥10ng/mL) 4 of 64 (6.2%), low D levels (<10ng/mL) 11 of 17 (64.7%), NNT 1.7.

Kazemi, 5/7/2022, retrospective, Iran, peer-reviewed, mean age 56.0, 4 authors.	risk of death, 75.8% lower, RR 0.24, $p = 0.26$, high D levels (≥30ng/mL) 1 of 75 (1.3%), low D levels (<30ng/mL) 7 of 127 (5.5%), NNT 24.
	risk of severe case, 4.8% higher, RR 1.05, $p = 1.00$, high D levels (≥30ng/mL) 13 of 75 (17.3%), low D levels (<30ng/mL) 21 of 127 (16.5%).
Khalil, 11/8/2022, retrospective, Iraq, peer-reviewed, 3 authors.	risk of case, 41.6% lower, OR 0.58, $p = 0.27$, high D levels (≥10ng/ml) 30 of 52 (57.7%) cases, 21 of 30 (70.0%) controls, NNT 8.2, case control OR.
Lau, 4/28/2020, retrospective, USA, preprint, 7 authors.	risk of ICU admission, 45.0% lower, RR 0.55, $p = 0.29$, high D levels 2 of 5 (40.0%), low D levels 11 of 15 (73.3%), NNT 3.0, >30ng/mL.
Li, 5/19/2021, retrospective, USA, peer-reviewed, 4 authors.	risk of case, 8.6% lower, RR 0.91, $p = 0.24$, high D levels 610 of 13,650 (4.5%), low D levels 290 of 4,498 (6.4%), adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >20ng/mL, Figure 2.
	risk of case, 12.4% lower, RR 0.88, $p = 0.07$, high D levels 289 of 7,272 (4.0%), low D levels 611 of 10,876 (5.6%), adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >30ng/mL, Figure 2.
Li (B), 1/11/2021, retrospective, population-based cohort, United Kingdom, peer-reviewed, 6 authors.	risk of hospitalization, 36.2% lower, RR 0.64, $p < 0.001$, NNT 932, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >25nmol/L.
	risk of case, 29.5% lower, RR 0.71, $p < 0.001$, NNT 823, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >25nmol/L.
Livingston, 4/2/2021, retrospective, United Kingdom, peer-reviewed, 7 authors.	risk of case, 50.9% lower, RR 0.49, $p = 0.02$, high D levels 16 of 52 (30.8%), low D levels 31 of 52 (59.6%), NNT 3.5, odds ratio converted to relative risk, >34.4nmol/L.
Lohia, 3/4/2021, retrospective, USA, peer-reviewed, 4 authors.	risk of death, 14.7% lower, RR 0.85, $p = 0.56$, high D levels 88, low D levels 95, odds ratio converted to relative risk, control prevalence approximated with overall prevalence, >30 ng/mL vs. <20 ng/mL, >30 ng/mL group size approximated.
	risk of mechanical ventilation, 18.9% lower, RR 0.81, $p = 0.48$, high D levels 88, low D levels 95, odds ratio converted to relative risk, control prevalence approximated with overall prevalence, >30 ng/mL vs. <20 ng/mL, >30 ng/mL group size approximated.
	risk of ICU admission, 28.5% lower, RR 0.72, $p = 0.17$, high D levels 88, low D levels 95, odds ratio converted to relative risk, control prevalence approximated with overall prevalence, >30 ng/mL vs. <20 ng/mL, >30 ng/mL group size approximated.
Luo, 11/13/2020, retrospective, China, peer-reviewed, median age 56.0, 5 authors.	risk of progression, 63.0% lower, RR 0.37, $p = 0.01$, high D levels 335, low D levels 560, >30nmol/L.

Ma, 12/3/2021, retrospective, USA, peer-reviewed, 16 authors, study period May 2020 - March 2021, dosage varies.	risk of hospitalization, 67.0% lower, OR 0.33, $p = 0.15$, high D levels 7,893, low D levels 7,823, adjusted per study, highest quintile vs. lowest quintile predicted vitamin D levels, model 3, supplemental table 3, multivariable, RR approximated with OR, outcome based on serum levels.
	risk of symptomatic case, 9.0% lower, OR 0.91, $p = 0.52$, high D levels 7,893, low D levels 7,823, adjusted per study, highest quintile vs. lowest quintile predicted vitamin D levels, model 3, supplemental table 3, multivariable, RR approximated with OR, outcome based on serum levels.
	risk of case, 52.0% lower, OR 0.48, $p = 0.01$, high D levels 7,893, low D levels 7,823, adjusted per study, highest quintile vs. lowest quintile predicted vitamin D levels, model 3, supplemental table 3, multivariable, RR approximated with OR, outcome based on serum levels.
Macaya, 10/21/2020, retrospective, Spain, peer-reviewed, 8 authors.	risk of severe case, 55.0% lower, RR 0.45, $p = 0.07$, high D levels 11 of 35 (31.4%), low D levels 20 of 45 (44.4%), NNT 7.7, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >20ng/mL.
Maghbooli (B), 9/25/2020, retrospective, Iran, peer-reviewed, 11 authors.	risk of death, 51.7% lower, RR 0.48, $p = 0.08$, high D levels 7 of 72 (9.7%), low D levels 27 of 134 (20.1%), NNT 9.6, age >40.
	risk of mechanical ventilation, 31.6% lower, RR 0.68, $p = 0.49$, high D levels 6 of 77 (7.8%), low D levels 18 of 158 (11.4%), NNT 28.
	risk of ICU admission, 32.0% lower, RR 0.68, $p = 0.33$, high D levels 11 of 77 (14.3%), low D levels 33 of 158 (20.9%), NNT 15, >30nmol/L.
Manojlovic, 6/15/2023, retrospective, Serbia, peer-reviewed, mean age 57.6, 11 authors, excluded in exclusion analyses: unadjusted differences between groups.	risk of death, 89.9% lower, RR 0.10, $p = 0.009$, high D levels (≥30nmol/l) 1 of 41 (2.4%), low D levels (<30nmol/l) 8 of 33 (24.2%), NNT 4.6.
Martínez-Rodríguez, 3/31/2022, retrospective, Mexico, peer-reviewed, 5 authors.	risk of death, 52.2% lower, OR 0.48, $p = 0.04$, cutoff 20ng/mL, adjusted per study, multivariable, RR approximated with OR.
Matin, 7/30/2021, retrospective, case control, Iran, peer-reviewed, 8 authors.	risk of case, 66.1% lower, OR 0.34, $p < 0.001$, inverted to make OR<1 favor high D levels, case control OR, >20ng/mL.
Mayurathan, 8/8/2023, retrospective, Sri Lanka, peer-reviewed, 11 authors.	risk of death, 98.2% higher, RR 1.98, $p = 0.69$, high D levels (≥20ng/mL) 8 of 113 (7.1%), low D levels (<20ng/mL) 1 of 28 (3.6%).
	risk of severe case, 67.3% higher, RR 1.67, $p = 0.32$, high D levels (≥20ng/mL) 27 of 113 (23.9%), low D levels (<20ng/mL) 4 of 28 (14.3%).
Mazziotti, 3/5/2021, retrospective, Italy, peer-reviewed, 11 authors, dosage varies.	risk of death, 2.4% lower, RR 0.98, $p = 0.91$, high D levels 187, low D levels 161, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >12ng/mL, control

	prevalance approximated with overall prevalence, outcome based on serum levels.
	risk of acute hypoxemic respiratory failure, 37.0% lower, RR 0.63, $p = 0.006$, high D levels 72 of 187 (38.5%), low D levels 97 of 161 (60.2%), NNT 4.6, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, >12ng/mL, outcome based on serum levels.
Meltzer, 3/19/2021, retrospective, database analysis, USA, peer-reviewed, 6 authors.	risk of case, 34.6% lower, RR 0.65, $p = 0.11$, high D levels 61 of 1,097 (5.6%), low D levels 118 of 1,251 (9.4%), NNT 26, adjusted per study, inverted to make RR<1 favor high D levels, >40ng/mL vs. <20ng/mL, Table 2, Model 2.
Meltzer (B), 9/3/2020, retrospective, USA, peer-reviewed, 6 authors.	risk of case, 43.5% lower, RR 0.56, $p = 0.02$, high D levels 39 of 317 (12.3%), low D levels 32 of 172 (18.6%), NNT 16, adjusted per study, inverted to make RR<1 favor high D levels, >20ng/mL.
Mendy, 6/27/2020, retrospective, USA, preprint, 4 authors.	risk of death, 7.0% lower, RR 0.93, $p = 0.89$, high D levels 21 of 600 (3.5%), low D levels 5 of 89 (5.6%), inverted to make RR<1 favor high D levels, odds ratio converted to relative risk.
	risk of death/ICU, 16.7% lower, RR 0.83, $p < 0.001$, high D levels 68 of 600 (11.3%), low D levels 23 of 89 (25.8%), NNT 6.9, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk.
	risk of ICU admission, 55.3% lower, RR 0.45, $p = 0.008$, high D levels 47 of 600 (7.8%), low D levels 18 of 89 (20.2%), NNT 8.1, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk.
	risk of hospitalization, 15.1% lower, RR 0.85, $p < 0.001$, high D levels 171 of 600 (28.5%), low D levels 45 of 89 (50.6%), NNT 4.5, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk.
Merzon, 7/23/2020, retrospective, Israel, peer-reviewed, 7 authors.	risk of hospitalization, 46.4% lower, RR 0.54, $p = 0.06$, high D levels 79, low D levels 703, odds ratio converted to relative risk, >30ng/mL.
	risk of case, 28.4% lower, RR 0.72, $p < 0.001$, high D levels 1,139, low D levels 6,668, odds ratio converted to relative risk, >30ng/mL.
Mingiano, 7/30/2023, retrospective, Italy, peer-reviewed, 11 authors, study period November 2020 - February 2021, dosage calcifediol 450µg days 1-2, patients with deficiency only.	risk of death, 49.8% lower, RR 0.50, $p = 0.005$, cutoff 10ng/mL, outcome based on serum levels.
	risk of death, 35.9% lower, RR 0.64, $p = 0.04$, cutoff 20ng/mL, outcome based on serum levels.
Mostafa, 11/30/2022, retrospective, Egypt, peer-reviewed, 10 authors, study period November 2020 - December 2021, excluded in exclusion analyses: categorical results are unadjusted with significant differences between groups.	risk of death, 92.8% lower, RR 0.07, $p < 0.001$, high D levels (≥20ng/mL) 4 of 135 (3.0%), low D levels (<20ng/mL) 21 of 51 (41.2%), NNT 2.6, unadjusted, normal vs. deficiency.

	risk of mechanical ventilation, 95.0% lower, RR 0.05, $p < 0.001$, high D levels (≥20ng/mL) 4 of 135 (3.0%), low D levels (<20ng/mL) 30 of 51 (58.8%), NNT 1.8, unadjusted, normal vs. deficiency.
	risk of ICU admission, 90.6% lower, RR 0.09, $p < 0.001$, high D levels (≥20ng/mL) 9 of 135 (6.7%), low D levels (<20ng/mL) 36 of 51 (70.6%), NNT 1.6, unadjusted, normal vs. deficiency.
Nasiri, 6/30/2021, retrospective, Iran, peer-reviewed, 3 authors.	risk of death, 8.9% higher, OR 1.09, $p = 0.89$, high D levels (≥30ng/mL) 238, low D levels (<20ng/mL) 43, inverted to make OR<1 favor high D levels (≥30ng/mL), RR approximated with OR.
Neves, 6/14/2022, retrospective, Brazil, peer-reviewed, mean age 62.1, 7 authors, study period July 2020 - December 2020, excluded in exclusion analyses: excessive unadjusted differences between groups.	risk of death, 57.1% lower, RR 0.43, $p = 0.046$, high D levels (≥50nmol/L) 12 of 87 (13.8%), low D levels (<50nmol/L) 9 of 28 (32.1%), NNT 5.4.
	risk of ICU admission, 19.5% higher, RR 1.20, $p = 0.81$, high D levels (≥50nmol/L) 26 of 87 (29.9%), low D levels (<50nmol/L) 7 of 28 (25.0%).
Nguyen, 5/3/2022, retrospective, USA, peer-reviewed, 11 authors, study period 15 July, 2020 - 15 October, 2020.	risk of death, 81.1% lower, OR 0.19, $p = 0.008$, cutoff 20ng/mL, adjusted per study, inverted to make OR<1 favor high D levels (≥20ng/mL), 25-OH-D3, multivariable, RR approximated with OR.
	risk of mechanical ventilation, 52.8% lower, OR 0.47, $p = 0.13$, cutoff 20ng/mL, adjusted per study, inverted to make OR<1 favor high D levels (≥20ng/mL), 25-OH-D3, multivariable, RR approximated with OR.
	risk of no hospital discharge, 74.0% lower, HR 0.26, $p < 0.001$, cutoff 20ng/mL, 25-OH-D3, Cox proportional hazards.
Nimavat, 8/5/2021, retrospective, India, peer-reviewed, 5 authors.	risk of death, 50.4% lower, RR 0.50, $p = 0.17$, high D levels 13 of 131 (9.9%), low D levels 5 of 25 (20.0%), NNT 9.9, >10ng/mL, within cases.
	risk of severe case, 67.6% lower, RR 0.32, $p = 0.003$, high D levels 17 of 131 (13.0%), low D levels 10 of 25 (40.0%), NNT 3.7, >10ng/mL, within cases.
Orchard, 1/19/2021, retrospective, United Kingdom, peer-reviewed, 7 authors.	risk of ICU admission, 58.8% lower, RR 0.41, $p = 0.001$, high D levels 9 of 40 (22.5%), low D levels 41 of 75 (54.7%), NNT 3.1, all hospitalized patients, >50 nmol/L.
	risk of death, 24.1% lower, RR 0.76, $p = 1.00$, high D levels 1 of 9 (11.1%), low D levels 6 of 41 (14.6%), NNT 28, ICU patients only, >50 nmol/L.
	risk of mechanical ventilation, 8.9% lower, RR 0.91, $p = 0.70$, high D levels 6 of 9 (66.7%), low D levels 30 of 41 (73.2%), NNT 15, ICU patients only, >50 nmol/L.
Ortatatli, 2/14/2023, prospective, Turkey, peer-reviewed, 9 authors, excluded in exclusion analyses: unadjusted results with no group details.	risk of death, 82.1% lower, RR 0.18, $p = 0.09$, cutoff 20ng/mL, inverted to make RR<1 favor high D levels (≥20ng/mL), 25(OH)D.

	risk of death, 73.7% lower, RR 0.26, *p* = 0.04, cutoff 1ng/mL, inverted to make RR<1 favor high D levels (≥1ng/mL), 1,25(OH)2D.
Ozturk, 5/16/2022, retrospective, Turkey, peer-reviewed, 6 authors, excluded in exclusion analyses: unadjusted results with no group details.	risk of severe case, 46.4% lower, RR 0.54, *p* = 0.10, high D levels (≥20ng/mL) 9 of 110 (8.2%), low D levels (<20ng/mL) 29 of 190 (15.3%), NNT 14.
Panagiotou, 6/30/2020, retrospective, United Kingdom, preprint, 12 authors.	risk of ICU admission, 52.0% lower, RR 0.48, *p* = 0.02, high D levels 8 of 44 (18.2%), low D levels 34 of 90 (37.8%), NNT 5.1, >50nmol/L.
Pande, 3/16/2022, retrospective, India, peer-reviewed, 7 authors, study period October 2020 - October 2021, excluded in exclusion analyses: unadjusted results with no group details.	risk of severe case, 93.4% lower, RR 0.07, *p* < 0.001, high D levels (≥20ng/ml) 7 of 116 (6.0%), low D levels (<20ng/ml) 85 of 93 (91.4%), NNT 1.2.
Parra-Ortega, 8/24/2021, prospective, Mexico, peer-reviewed, 9 authors, excluded in exclusion analyses: unadjusted results with no group details.	risk of death, 98.7% lower, RR 0.01, *p* < 0.001, high D levels (≥20ng/dL) 0 of 15 (0.0%), low D levels (<20ng/dL) 63 of 79 (79.7%), NNT 1.3, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), unadjusted.
Pavlyshyn, 4/5/2024, retrospective, Ukraine, peer-reviewed, 3 authors.	risk of severe case, 59.7% lower, RR 0.40, *p* = 0.13, high D levels (≥20ng/ml) 7 of 59 (11.9%), low D levels (<20ng/ml) 5 of 17 (29.4%), NNT 5.7, deficiency vs. other.
	risk of case, 89.0% lower, OR 0.11, *p* = 0.13, high D levels (≥20ng/ml) 59 of 76 (77.6%) cases, 15 of 15 (100.0%) controls, NNT 4.9, case control OR.
Pecina, 8/27/2021, retrospective, USA, peer-reviewed, 4 authors, dosage not specified.	risk of death, 35.9% lower, RR 0.64, *p* = 0.74, high D levels (≥20ng/mL) 6 of 77 (7.8%), low D levels (<20ng/mL) 1 of 15 (6.7%), inverted to make RR<1 favor high D levels (≥20ng/mL), odds ratio converted to relative risk, multivariable logistic regression, outcome based on serum levels.
	risk of mechanical ventilation, 56.9% lower, RR 0.43, *p* = 0.22, high D levels (≥20ng/mL) 8 of 15 (53.3%), low D levels (<20ng/mL) 4 of 15 (26.7%), inverted to make RR<1 favor high D levels (≥20ng/mL), odds ratio converted to relative risk, multivariable logistic regression, outcome based on serum levels.
	risk of ICU admission, 13.1% higher, RR 1.13, *p* = 0.57, high D levels (≥20ng/mL) 54 of 77 (70.1%), low D levels (<20ng/mL) 9 of 15 (60.0%), inverted to make RR<1 favor high D levels (≥20ng/mL), odds ratio converted to relative risk, multivariable logistic regression, outcome based on serum levels.
Pepkowitz, 9/29/2020, retrospective, USA, preprint, 7 authors.	risk of ICU admission, 55.8% lower, RR 0.44, *p* = 0.01, high D levels (≥20ng/mL) 9 of 24 (37.5%), low D levels (<20ng/mL) 11 of 13 (84.6%), NNT 2.1, inverted to make RR<1 favor high D levels (≥20ng/mL).
Pimental, 5/31/2021, retrospective, Brazil, peer-reviewed, 3 authors.	risk of death, 29.4% lower, RR 0.71, *p* = 1.00, high D levels 3 of 17 (17.6%), low D levels 2 of 8 (25.0%), NNT 14, >20ng/mL.

Protas, 4/6/2023, retrospective, Kazakhstan, peer-reviewed, survey, 6 authors, study period October 2022 - November 2022.	**risk of case, 76.6% lower, OR 0.23, $p = 0.06$**, high D levels (≥10ng/ml) 68 of 88 (77.3%) cases, 29 of 31 (93.5%) controls, NNT 4.8, case control OR.
	risk of case, 46.2% lower, OR 0.54, $p = 0.17$, high D levels (≥20ng/ml) 50 of 88 (56.8%) cases, 22 of 31 (71.0%) controls, NNT 8.8, case control OR.
Putra, 12/10/2021, retrospective, Indonesia, peer-reviewed, 3 authors, study period February 2020 - September 2020.	**risk of hospitalization, 25.6% lower, OR 0.74, $p = 0.59$**, high D levels 9 of 31 (29.0%) cases, 11 of 31 (35.5%) controls, NNT 14, case control OR.
Rachman, 4/13/2023, prospective, Indonesia, peer-reviewed, 4 authors, study period October 2021 - February 2022.	**risk of death, 94.8% lower, RR 0.05, $p = 0.04$**, high D levels (≥20ng/mL) 0 of 45 (0.0%), low D levels (<20ng/mL) 14 of 146 (9.6%), NNT 10, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm).
	risk of severe case, 77.6% lower, RR 0.22, $p = 0.01$, high D levels (≥20ng/mL) 2 of 45 (4.4%), low D levels (<20ng/mL) 29 of 146 (19.9%), NNT 6.5.
Radujkovic, 9/10/2020, prospective, Germany, peer-reviewed, 6 authors.	**risk of death, 93.2% lower, HR 0.07, $p = 0.001$**, high D levels 144, low D levels 12, >30nmol/L.
	risk of death/intubation, 84.0% lower, HR 0.16, $p < 0.001$, high D levels 144, low D levels 12, >30nmol/L.
Ramirez-Sandoval, 10/15/2021, retrospective, Mexico, peer-reviewed, 7 authors.	**risk of death, 31.5% lower, HR 0.68, $p < 0.001$**, high D levels 2,337, low D levels 571, adjusted per study, inverted to make HR<1 favor high D levels, >12.5ng/mL, 30 day in-hospital mortality.
	hospitalization time, 22.2% lower, relative time 0.78, $p < 0.001$, high D levels 2,337, low D levels 571.
Ramos, 11/15/2021, retrospective, Brazil, peer-reviewed, 11 authors.	**risk of case, 45.7% lower, RR 0.54, $p = 0.16$**, high D levels (≥20ng/mL) 4 of 9 (44.4%), low D levels (<20ng/mL) 9 of 11 (81.8%), NNT 2.7.
Ranjbar, 11/29/2021, retrospective, Iran, peer-reviewed, 27 authors, study period 16 February, 2020 - 21 March, 2020.	**risk of death, 41.9% lower, RR 0.58, $p = 0.07$**, high D levels (≥20ng/mL) 16 of 163 (9.8%), low D levels (<20ng/mL) 26 of 154 (16.9%), NNT 14.
Reis, 5/21/2021, prospective, Brazil, peer-reviewed, 19 authors.	**risk of death, 23.0% lower, HR 0.77, $p = 0.82$**, high D levels (≥10ng/mL) 198, low D levels (<10ng/mL) 16, model 2, Cox proportional hazards.
	risk of mechanical ventilation, 45.0% higher, HR 1.45, $p = 0.77$, high D levels (≥10ng/mL) 198, low D levels (<10ng/mL) 16, adjusted per study, model 2, multivariable, Cox proportional hazards.
	risk of no hospital discharge, 33.3% lower, HR 0.67, $p = 0.18$, high D levels (≥10ng/mL) 198, low D levels (<10ng/mL) 16, adjusted per study, inverted to make HR<1 favor high D levels

	(≥10ng/mL), model 2, multivariable, Cox proportional hazards.
	hospitalization time, 22.2% lower, relative time 0.78, $p = 0.06$, high D levels (≥10ng/mL) 191, low D levels (<10ng/mL) 15, model 2.
Renieris, 11/26/2023, retrospective, Greece, peer-reviewed, 10 authors, trial NCT04357366 (history).	risk of death, 52.4% lower, HR 0.48, $p = 0.04$, high D levels (≥20ng/mL) 17 of 130 (13.1%), low D levels (<20ng/mL) 17 of 60 (28.3%), NNT 6.6, inverted to make HR<1 favor high D levels (≥20ng/mL).
Reyes Pérez, 4/30/2020, retrospective, Mexico, peer-reviewed, 5 authors, excluded in exclusion analyses: unadjusted results with no group details.	risk of death, 61.7% lower, RR 0.38, $p = 0.006$, high D levels (≥8ng/mL) 21 of 137 (15.3%), low D levels (<8ng/mL) 14 of 35 (40.0%), NNT 4.1, inverted to make RR<1 favor high D levels (≥8ng/mL), odds ratio converted to relative risk.
Ribeiro, 8/5/2021, retrospective, Brazil, peer-reviewed, 8 authors.	risk of case, 50.5% lower, OR 0.50, $p = 0.01$, inverted to make OR<1 favor high D levels, >30ng/mL, multivariate, RR approximated with OR.
Ricci, 3/3/2021, retrospective, Italy, peer-reviewed, 15 authors.	risk of death, 87.6% lower, RR 0.12, $p = 0.07$, high D levels 0 of 30 (0.0%), low D levels 3 of 22 (13.6%), NNT 7.3, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), >10 ng/mL.
Ritsinger, 4/28/2023, retrospective, Sweden, peer-reviewed, mean age 79.8, 8 authors, study period 1 January, 2020 - 9 September, 2021.	risk of death, 9.1% lower, HR 0.91, $p < 0.001$, high D levels (≥50nmol/L) 37,972, low D levels (<50nmol/L) 6,894, inverted to make HR<1 favor high D levels (≥50nmol/L).
Rodríguez-Vidales, 2/24/2022, retrospective, Mexico, peer-reviewed, 8 authors, study period March 2020 - September 2020.	risk of severe case, 38.9% lower, RR 0.61, $p = 0.05$, high D levels (≥10ng/mL) 89 of 265 (33.6%), low D levels (<10ng/mL) 27 of 32 (84.4%), NNT 2.0, adjusted per study, inverted to make RR<1 favor high D levels (≥10ng/mL), odds ratio converted to relative risk, multivariable.
Rozemeijer, 1/29/2024, prospective, Netherlands, peer-reviewed, 9 authors.	risk of ICU admission, 35.7% lower, OR 0.64, $p = 0.67$, high D levels (≥50nmol/L) 6 of 20 (30.0%) cases, 2 of 5 (40.0%) controls, NNT 14, case control OR.
Sanamandra, 4/30/2023, prospective, India, peer-reviewed, 6 authors, study period August 2020 - March 2021.	risk of death, 20.9% lower, OR 0.79, $p = 0.67$, high D levels (≥10ng/mL) 155, low D levels (<10ng/mL) 45, inverted to make OR<1 favor high D levels (≥10ng/mL), RR approximated with OR.
	risk of mechanical ventilation, 15.3% lower, OR 0.85, $p = 0.73$, high D levels (≥10ng/mL) 155, low D levels (<10ng/mL) 45, inverted to make OR<1 favor high D levels (≥10ng/mL), RR approximated with OR.
	risk of severe case, 434.8% higher, OR 5.35, $p = 0.12$, high D levels (≥10ng/mL) 155, low D levels (<10ng/mL) 45, inverted to make OR<1 favor high D levels (≥10ng/mL), RR approximated with OR.
Sanson, 2/19/2022, prospective, Italy, peer-reviewed, 13 authors, study period March 2020 - September 2020, excluded in exclusion analyses: unadjusted results with no group details.	NIV/IMV/death, 64.0% lower, RR 0.36, $p = 0.03$, high D levels (≥30ng/mL) 2 of 9 (22.2%), low D levels (<30ng/mL) 37 of 60 (61.7%), NNT 2.5.

Saponaro, 1/24/2022, retrospective, Italy, peer-reviewed, 13 authors, study period March 2020 - May 2020.	risk of ARDS, 36.5% lower, RR 0.64, $p = 0.43$, high D levels (≥20ng/ml) 5 of 32 (15.6%), low D levels (<20ng/ml) 15 of 61 (24.6%), NNT 11, severe ARDS.
Savitri, 5/8/2021, retrospective, Indonesia, peer-reviewed, 5 authors.	risk of symptomatic case, 88.0% lower, RR 0.12, $p < 0.001$, high D levels 3 of 25 (12.0%), low D levels 17 of 17 (100.0%), NNT 1.1, >20ng/ml.
Schmidt, 3/22/2023, prospective, Poland, peer-reviewed, 4 authors, study period 4 February, 2021 - 31 December, 2021.	risk of death, 85.5% lower, OR 0.14, $p = 0.003$, cutoff 27ng/mL, inverted to make OR<1 favor high D levels (≥27ng/mL), RR approximated with OR.
Seal, 1/1/2022, retrospective, USA, peer-reviewed, 6 authors.	risk of death, 45.1% lower, RR 0.55, $p = 0.001$, adjusted per study, inverted to make RR<1 favor high D levels, 60ng/mL vs. 15 ng/mL.
	risk of death, 40.5% lower, RR 0.60, $p = 0.001$, adjusted per study, inverted to make RR<1 favor high D levels, 50ng/mL vs. 15 ng/mL.
	risk of death, 34.6% lower, RR 0.65, $p = 0.001$, adjusted per study, inverted to make RR<1 favor high D levels, 40ng/mL vs. 15 ng/mL.
	risk of death, 25.9% lower, RR 0.74, $p = 0.001$, adjusted per study, inverted to make RR<1 favor high D levels, 30ng/mL vs. 15 ng/mL.
	risk of death, 20.0% lower, RR 0.80, $p = 0.001$, adjusted per study, inverted to make RR<1 favor high D levels, 25ng/mL vs. 15 ng/mL.
	risk of death, 11.5% lower, RR 0.88, $p = 0.001$, adjusted per study, inverted to make RR<1 favor high D levels, 20ng/mL vs. 15 ng/mL.
	risk of hospitalization, 22.5% lower, RR 0.78, $p = 0.01$, adjusted per study, inverted to make RR<1 favor high D levels, 60ng/mL vs. 15 ng/mL.
	risk of hospitalization, 20.0% lower, RR 0.80, $p = 0.009$, adjusted per study, inverted to make RR<1 favor high D levels, 50ng/mL vs. 15 ng/mL.
	risk of hospitalization, 16.7% lower, RR 0.83, $p = 0.007$, adjusted per study, inverted to make RR<1 favor high D levels, 40ng/mL vs. 15 ng/mL.
	risk of hospitalization, 12.3% lower, RR 0.88, $p = 0.008$, adjusted per study, inverted to make RR<1 favor high D levels, 30ng/mL vs. 15 ng/mL.
	risk of hospitalization, 9.1% lower, RR 0.91, $p = 0.01$, adjusted per study, inverted to make RR<1 favor high D levels, 25ng/mL vs. 15 ng/mL.

	risk of hospitalization, 4.8% lower, RR 0.95, $p = 0.02$, adjusted per study, inverted to make RR<1 favor high D levels, 20ng/mL vs. 15 ng/mL.
Seven, 11/23/2021, prospective, Turkey, peer-reviewed, 6 authors, study period September 2020 - November 2020.	**risk of severe disease or poor prognostic factor, 46.5% lower, RR 0.53, $p = 0.006$**, cutoff 14.5ng/ml, inverted to make RR<1 favor high D levels (≥14.5ng/ml).
Sinaci, 8/11/2021, retrospective, Turkey, peer-reviewed, 10 authors, dosage not specified.	**risk of moderate/severe case, 79.5% lower, RR 0.21, $p < 0.001$**, high D levels (≥10ng/mL) 8 of 100 (8.0%), low D levels (<10ng/mL) 23 of 59 (39.0%), NNT 3.2, outcome based on serum levels.
	risk of case, 59.9% lower, RR 0.40, $p < 0.001$, high D levels (≥10ng/mL) 100 of 397 (25.2%), low D levels (<10ng/mL) 59 of 94 (62.8%), NNT 2.7, outcome based on serum levels.
Siuka, 3/9/2023, prospective, Slovenia, peer-reviewed, 7 authors, study period December 2020 - December 2021.	**risk of death, 55.9% lower, RR 0.44, $p = 0.24$**, high D levels (≥30nmol/L) 10 of 255 (3.9%), low D levels (<30nmol/L) 4 of 45 (8.9%), NNT 20.
	risk of ICU admission, 58.8% higher, RR 1.59, $p = 0.59$, high D levels (≥30nmol/L) 27 of 255 (10.6%), low D levels (<30nmol/L) 3 of 45 (6.7%).
	risk of severe case, 61.0% higher, RR 1.61, $p = 0.009$, high D levels (≥30nmol/L) 146 of 255 (57.3%), low D levels (<30nmol/L) 16 of 45 (35.6%).
Subramanian, 1/31/2022, prospective, United Kingdom, peer-reviewed, 16 authors, dosage not specified.	**risk of death, 49.7% lower, RR 0.50, $p = 0.02$**, high D levels 16 of 115 (13.9%), low D levels 33 of 118 (28.0%), NNT 7.1, adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, 50-74 nmol/L vs. <25nmol/L, multivariable, outcome based on serum levels.
	risk of death, 39.7% lower, RR 0.60, $p = 0.07$, high D levels 16 of 115 (13.9%), low D levels 38 of 157 (24.2%), NNT 9.7, adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, 50-74 nmol/L vs. 25-49nmol/L, multivariable, outcome based on serum levels.
Sulli, 2/24/2021, retrospective, Italy, peer-reviewed, 10 authors, dosage not specified.	**risk of case, 79.2% lower, OR 0.21, $p < 0.001$**, high D levels 28 of 65 (43.1%) cases, 51 of 65 (78.5%) controls, NNT 2.7, case control OR, >10ng/mL.
Susianti, 2/12/2021, retrospective, Indonesia, peer-reviewed, 8 authors.	**risk of death, 91.5% lower, RR 0.09, $p = 0.32$**, high D levels 0 of 8 (0.0%), low D levels 9 of 42 (21.4%), NNT 4.7, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), >49.92 nmol/L.
	risk of ICU admission, 90.5% lower, RR 0.10, $p = 0.32$, high D levels 0 of 8 (0.0%), low D levels 8 of 42 (19.0%), NNT 5.2, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), >49.92 nmol/L.

	risk of progression, 81.5% lower, OR 0.19, $p = 0.04$, high D levels 8, low D levels 42, inverted to make OR<1 favor high D levels, ISTH DIC>=5, >49.92 nmol/L, bivariate, RR approximated with OR.
	risk of progression, 44.4% lower, OR 0.56, $p = 0.03$, high D levels 8, low D levels 42, inverted to make OR<1 favor high D levels, increased D-dimer >2 mg/L, >49.92 nmol/L, multivariate, RR approximated with OR.
Szeto, 12/30/2020, retrospective, USA, peer-reviewed, 7 authors.	**risk of death, 5.6% higher, RR 1.06, $p = 1.00$**, high D levels 14 of 58 (24.1%), low D levels 8 of 35 (22.9%).
	risk of mechanical ventilation, 39.7% lower, RR 0.60, $p = 0.21$, high D levels 10 of 58 (17.2%), low D levels 10 of 35 (28.6%), NNT 8.8.
	risk of no hospital discharge, 26.7% higher, RR 1.27, $p = 0.50$, high D levels 21 of 58 (36.2%), low D levels 10 of 35 (28.6%).
Sánchez-Zuno (B), 5/28/2021, prospective, Mexico, peer-reviewed, 12 authors, dosage 10,000IU days 1-14.	**risk of severe case, 5.6% lower, RR 0.94, $p = 1.00$**, high D levels 4 of 8 (50.0%), low D levels 18 of 34 (52.9%), NNT 34, >30ng/mL, >4 symptoms.
Tallon, 11/15/2022, retrospective, USA, peer-reviewed, 17 authors.	**risk of hospitalization, 41.5% lower, OR 0.58, $p < 0.001$**, high D levels (≥30ng/mL) 113,143, low D levels (<30ng/mL) 3,227, adjusted per study, inverted to make OR<1 favor high D levels (≥30ng/mL), RR approximated with OR.
Tan, 2/27/2023, retrospective, Philippines, peer-reviewed, 3 authors.	**risk of progression, 71.5% lower, RR 0.29, $p = 0.04$**, high D levels (≥30ng/mL) 7 of 38 (18.4%), low D levels (<20ng/mL) 18 of 34 (52.9%), NNT 2.9, adjusted per study, inverted to make RR<1 favor high D levels (≥30ng/mL), odds ratio converted to relative risk, combined mortality and morbidity, multivariable.
	risk of death, 91.1% lower, RR 0.09, $p = 0.002$, high D levels (≥30ng/mL) 1 of 38 (2.6%), low D levels (<20ng/mL) 10 of 34 (29.4%), NNT 3.7, unadjusted.
	risk of ICU admission, 82.1% lower, RR 0.18, $p = 0.010$, high D levels (≥30ng/mL) 2 of 38 (5.3%), low D levels (<20ng/mL) 10 of 34 (29.4%), NNT 4.1, unadjusted.
Tehrani, 1/25/2021, retrospective, Iran, peer-reviewed, 5 authors.	**risk of death, 47.5% lower, RR 0.52, $p = 0.07$**, high D levels 34 of 180 (18.9%), low D levels 9 of 25 (36.0%), NNT 5.8, >10ng/ml.
Tomasa-Irriguible, 10/26/2020, retrospective, Spain, peer-reviewed, 7 authors, study period March 2020 - May 2020.	**risk of mechanical ventilation, 35.0% lower, RR 0.65, $p = 0.21$**, high D levels 15 of 27 (55.6%), low D levels 18 of 78 (23.1%), adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, ≥20 ng/mL, bivariate logistic regression.
	risk of ICU admission, 16.9% lower, RR 0.83, $p = 0.58$, high D levels 11 of 27 (40.7%), low D levels 17 of 78 (21.8%), adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk, ≥20 ng/mL, bivariate logistic

	regression.
Topan, 2/28/2023, retrospective, Romania, peer-reviewed, survey, 6 authors, study period April 2020 - May 2022.	risk of death, 30.6% lower, RR 0.69, $p = 0.02$, high D levels (≥20ng/mL) 61 of 1,148 (5.3%), low D levels (<20ng/mL) 118 of 1,194 (9.9%), adjusted per study, inverted to make RR<1 favor high D levels (≥20ng/mL), odds ratio converted to relative risk, multivariable.
	risk of severe case, 10.9% lower, RR 0.89, $p = 0.02$, high D levels (≥20ng/mL) 432 of 1,148 (37.6%), low D levels (<20ng/mL) 560 of 1,194 (46.9%), NNT 11, adjusted per study, inverted to make RR<1 favor high D levels (≥20ng/mL), odds ratio converted to relative risk, severe/critical case, multivariable.
Umay, 7/26/2023, retrospective, Turkey, peer-reviewed, 4 authors, study period 1 March, 2020 - 31 January, 2021.	hospitalization time, 13.5% lower, relative time 0.87, $p = 0.33$, high D levels 374, low D levels 39.
Vanegas-Cedillo, 3/14/2021, retrospective, Mexico, peer-reviewed, 15 authors.	risk of death, 52.6% lower, RR 0.47, $p = 0.006$, high D levels (≥12ng/mL) 95 of 494 (19.2%), low D levels (<12ng/mL) 21 of 57 (36.8%), NNT 5.7, adjusted per study, inverted to make RR<1 favor high D levels (≥12ng/mL).
Vasheghani, 1/18/2021, retrospective, Iran, preprint, 6 authors, dosage not specified.	risk of ICU admission, 63.8% lower, RR 0.36, $p = 0.009$, high D levels 13 of 185 (7.0%), low D levels 53 of 323 (16.4%), NNT 11, adjusted per study, inverted to make RR<1 favor high D levels, vitamin D levels >30ng/mL.
Vassiliou (B), 12/9/2020, prospective, Greece, peer-reviewed, 6 authors.	risk of death, 90.9% lower, RR 0.09, $p = 0.04$, high D levels 0 of 15 (0.0%), low D levels 5 of 15 (33.3%), NNT 3.0, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), >15.2ng/mL.
Voelkle, 4/30/2022, prospective, Switzerland, peer-reviewed, median age 67.0, 9 authors, study period 17 March, 2020 - 30 April, 2020.	risk of death/ICU, 23.4% lower, RR 0.77, $p = 0.55$, high D levels 8 of 34 (23.5%), low D levels 7 of 23 (30.4%), NNT 14, adjusted per study, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk.
Vásquez-Procopio, 12/2/2022, retrospective, Mexico, peer-reviewed, 12 authors.	risk of severe case, 82.8% lower, OR 0.17, $p = 0.04$, high D levels (≥20ng/mL) 111, low D levels (<20ng/mL) 54, adjusted per study, inverted to make OR<1 favor high D levels (≥20ng/mL), multivariable, RR approximated with OR.
Walk, 11/9/2020, retrospective, Netherlands, preprint, 5 authors.	risk of death/intubation, 0.4% higher, RR 1.00, $p = 1.00$, high D levels 48 of 110 (43.6%), low D levels 10 of 23 (43.5%), >25nmol/L.
Wang, 3/29/2023, prospective, China, preprint, median age 36.5, 23 authors, study period 18 December, 2022 - 20 February, 2023, dosage 200,000IU days 1, 14, trial NCT05673980 (history).	risk of case, 22.7% lower, RR 0.77, $p = 0.19$, high D levels (≥30ng/ml) 20 of 44 (45.5%), low D levels (<20ng/ml) 50 of 85 (58.8%), NNT 7.5, outcome based on serum levels.
Wani, 6/1/2023, retrospective, India, peer-reviewed, 5 authors, excluded in exclusion analyses: unadjusted results with no group details.	risk of severe case, 72.2% lower, OR 0.28, $p = 0.007$, high D levels (≥28ng/mL) 66, low D levels (<28ng/mL) 170, inverted to make OR<1 favor high D levels (≥28ng/mL), RR approximated with OR.

Wu, 12/19/2023, retrospective, multiple countries, peer-reviewed, 9 authors, study period 1 January, 2022 - 30 November, 2022.	**risk of death, 42.8% lower, HR 0.57, $p = 0.005$**, high D levels (≥20 ng/mL) 8,300, low D levels (<20 ng/mL) 8,300, inverted to make HR<1 favor high D levels (≥20 ng/mL), propensity score matching.
	risk of hospitalization, 18.7% lower, HR 0.81, $p < 0.001$, high D levels (≥20 ng/mL) 8,300, low D levels (<20 ng/mL) 8,300, inverted to make HR<1 favor high D levels (≥20 ng/mL), propensity score matching.
	ER visit, 10.2% lower, HR 0.90, $p = 0.03$, high D levels (≥20 ng/mL) 8,300, low D levels (<20 ng/mL) 8,300, inverted to make HR<1 favor high D levels (≥20 ng/mL), propensity score matching.
	risk of PASC, 2.0% higher, HR 1.02, $p = 0.93$, high D levels (≥20 ng/mL) 8,300, low D levels (<20 ng/mL) 8,300, inverted to make HR<1 favor high D levels (≥20 ng/mL), propensity score matching.
Ye, 10/13/2020, retrospective, China, peer-reviewed, 18 authors.	**risk of severe/critical COVID-19, 93.4% lower, RR 0.07, $p = 0.03$**, high D levels 2 of 36 (5.6%), low D levels 8 of 26 (30.8%), NNT 4.0, adjusted per study, inverted to make RR<1 favor high D levels, >50nmol/L.
Yılmaz, 10/5/2020, retrospective, Turkey, peer-reviewed, 2 authors.	**risk of severe case, 73.4% lower, RR 0.27, $p = 1.00$**, high D levels 0 of 11 (0.0%), low D levels 2 of 29 (6.9%), NNT 14, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), >20ng/ml.
	risk of moderate or severe case, 41.4% lower, RR 0.59, $p = 0.69$, high D levels 2 of 11 (18.2%), low D levels 9 of 29 (31.0%), NNT 7.8, >20ng/ml.
Zafar, 9/6/2021, retrospective, United Kingdom, peer-reviewed, median age 68.0, 37 authors.	**risk of death, 42.9% higher, RR 1.43, $p = 0.71$**, high D levels (≥25nmol/L) 12 of 42 (28.6%), low D levels (<25nmol/L) 2 of 10 (20.0%), COVID+ patients.
	risk of death, 6.0% lower, OR 0.94, $p = 0.68$, high D levels 42, low D levels 10, COVID+ patients, RR approximated with OR.
Zeidan, 9/9/2022, prospective, Egypt, peer-reviewed, median age 11.4, 38 authors.	**risk of hospitalization, 61.5% lower, OR 0.38, $p = 0.002$**, cutoff 20ng/mL, adjusted per study, inverted to make OR<1 favor high D levels (≥20ng/mL), case control OR, multivariable.
Zelzer, 6/22/2021, retrospective, Austria, peer-reviewed, 7 authors.	**risk of death, 46.4% lower, RR 0.54, $p = 0.08$**, high D levels 24 of 121 (19.8%), low D levels 10 of 27 (37.0%), NNT 5.8, >30nmol/L.
Zidrou, 2/19/2022, retrospective, Greece, peer-reviewed, 6 authors, study period August 2020 - October 2020.	**risk of death, 26.4% lower, RR 0.74, $p = 1.00$**, high D levels (≥20ng/ml) 2 of 25 (8.0%), low D levels (<20ng/ml) 5 of 46 (10.9%), NNT 35.
	radiographic changes, 18.2% lower, RR 0.82, $p = 0.26$, high D levels (≥20ng/ml) 16 of 25 (64.0%), low D levels (<20ng/ml) 36 of 46 (78.3%), NNT 7.0.

	hospitalization time, 37.7% lower, relative time 0.62, $p = 0.16$, high D levels (≥20ng/ml) 25, low D levels (<20ng/ml) 46.
Álvarez, 10/28/2022, retrospective, Spain, preprint, 1 author, study period March 2020 - March 2021, excluded in exclusion analyses: unadjusted results with no group details.	risk of death, 38.8% lower, RR 0.61, $p < 0.001$, high D levels 4,871 of 33,673 (14.5%), low D levels 611 of 2,588 (23.6%), NNT 11, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk.
	risk of ICU admission, 54.7% lower, RR 0.45, $p < 0.001$, high D levels 289 of 33,673 (0.9%), low D levels 49 of 2,588 (1.9%), NNT 97, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk.
	risk of hospitalization, 43.0% lower, RR 0.57, $p < 0.001$, high D levels 8,905 of 33,673 (26.4%), low D levels 1,202 of 2,588 (46.4%), NNT 5.0, inverted to make RR<1 favor high D levels, odds ratio converted to relative risk.
Ünsal, 4/5/2021, retrospective, Turkey, peer-reviewed, 10 authors.	risk of death, 80.6% lower, RR 0.19, $p = 0.23$, high D levels 0 of 29 (0.0%), low D levels 2 of 27 (7.4%), NNT 14, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), >=20ng/mL.
	risk of oxygen therapy, 73.4% lower, RR 0.27, $p = 0.07$, high D levels 2 of 29 (6.9%), low D levels 7 of 27 (25.9%), NNT 5.3, >=20ng/mL.
Şengül, 12/31/2022, retrospective, Turkey, peer-reviewed, 4 authors, study period March 2020 - December 2021, dosage not specified.	risk of case, 75.6% lower, OR 0.24, $p < 0.001$, high D levels (≥20ng/mL) 7 of 54 (13.0%) cases, 100 of 264 (37.9%) controls, NNT 6.4, case control OR, outcome based on serum levels.

Early treatment

Effect extraction follows pre-specified rules as detailed above and gives priority to more serious outcomes. Only the first (most serious) outcome is used in pooled analysis, which may differ from the effect a paper focuses on. Other outcomes are used in outcome specific analyses.

Annweiler, 11/2/2020, retrospective, France, peer-reviewed, 7 authors, dosage 80,000IU single dose.	risk of death, 63.0% lower, RR 0.37, $p = 0.28$, treatment 3 of 16 (18.8%), control 10 of 32 (31.2%), NNT 8.0, adjusted per study, supplementation after diagnosis.
Annweiler (B), 10/13/2020, retrospective, France, peer-reviewed, mean age 87.7, 6 authors, dosage 80,000IU single dose, 80,000IU either in the week following the suspicion or diagnosis of COVID-19, or during the previous month.	risk of death, 89.0% lower, RR 0.11, $p = 0.002$, treatment 10 of 57 (17.5%), control 5 of 9 (55.6%), NNT 2.6, adjusted per study.
Asimi, 5/22/2021, retrospective, Bosnia and Herzegovina, preprint, 3 authors, dosage 2,000IU daily, this trial uses multiple treatments in the treatment arm (combined with zinc and selenium) - results of individual treatments may vary, excluded in exclusion analyses: excessive unadjusted differences between groups.	risk of mechanical ventilation, 97.4% lower, RR 0.03, $p < 0.001$, treatment 0 of 270 (0.0%), control 9 of 86 (10.5%), NNT 9.6, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), unadjusted.
	risk of hospitalization, 99.0% lower, RR 0.010, $p < 0.001$, treatment 0 of 270 (0.0%), control 24 of 86 (27.9%), NNT 3.6, relative risk is not 0 because of continuity correction due to zero

	events (with reciprocal of the contrasting arm), unadjusted.
	risk of severe case, 99.5% lower, RR 0.005, $p < 0.001$, treatment 0 of 270 (0.0%), control 51 of 86 (59.3%), NNT 1.7, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), unadjusted.
Boukef, 2/28/2023, Double Blind Randomized Controlled Trial, placebo-controlled, Tunisia, trial NCT05670444 (history).	150 patient RCT with results unknown and over 1 year late.
Burahee, 2/17/2021, retrospective, United Kingdom, peer-reviewed, 4 authors, dosage 100,000IU days 1-4, additional 200000IU over four weeks if serum level insufficient.	risk of death, 93.3% lower, RR 0.07, $p = 0.01$, treatment 0 of 12 (0.0%), control 2 of 2 (100.0%), NNT 1.0, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm).
Din Ujjan, 1/18/2023, Randomized Controlled Trial, Pakistan, peer-reviewed, 6 authors, study period 21 September, 2021 - 21 January, 2022, dosage 360IU days 1-14, this trial uses multiple treatments in the treatment arm (combined with curcumin and quercetin) - results of individual treatments may vary, trial NCT04603690 (history), excluded in exclusion analyses: based on dosages and previous research, combined treatments may contribute more to the effect seen.	risk of no recovery, 28.6% lower, RR 0.71, $p = 0.11$, treatment 15 of 25 (60.0%), control 21 of 25 (84.0%), NNT 4.2, no symptoms, day 7.
	risk of no recovery, 71.4% lower, RR 0.29, $p < 0.001$, treatment 6 of 25 (24.0%), control 21 of 25 (84.0%), NNT 1.7, <= 1 symptom, day 7.
	risk of no recovery, 76.9% lower, RR 0.23, $p = 0.005$, treatment 3 of 25 (12.0%), control 13 of 25 (52.0%), NNT 2.5, <= 2 symptoms, day 7.
	risk of no recovery, 85.7% lower, RR 0.14, $p = 0.23$, treatment 0 of 25 (0.0%), control 3 of 25 (12.0%), NNT 8.3, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), <= 3 symptoms, day 7.
	risk of no viral clearance, 90.9% lower, RR 0.09, $p = 0.05$, treatment 0 of 25 (0.0%), control 5 of 25 (20.0%), NNT 5.0, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), day 14.
	risk of no viral clearance, 73.7% lower, RR 0.26, $p < 0.001$, treatment 5 of 25 (20.0%), control 19 of 25 (76.0%), NNT 1.8, day 7.
Efird, 12/31/2021, retrospective, USA, peer-reviewed, 10 authors, study period 1 March, 2020 - 10 September, 2020, dosage varies.	risk of death, 48.9% lower, RR 0.51, $p = 0.10$, treatment 11 of 544 (2.0%), control 413 of 15,794 (2.6%), adjusted per study, non-hospitalized patients, vitamin D + no corticosteroids vs. no vitamin D + no corticosteroids.
	risk of death, 54.5% lower, RR 0.45, $p = 0.02$, treatment 11 of 192 (5.7%), control 553 of 4,340 (12.7%), NNT 14, adjusted per study, hospitalized patients, vitamin D + no corticosteroids vs. no vitamin D + no corticosteroids.
Hunt, 6/29/2022, retrospective, USA, peer-reviewed, 8 authors, study period 1 March, 2020 - 10 September, 2020, dosage not specified.	risk of death, 47.0% lower, RR 0.53, $p < 0.001$, treatment 43 of 1,019 (4.2%), control 1,569 of 25,489 (6.2%), adjusted per study, day 30.

Khan, 5/1/2022, Randomized Controlled Trial, Pakistan, peer-reviewed, 7 authors, study period 2 September, 2021 - 28 November, 2021, dosage 360IU days 1-14, this trial uses multiple treatments in the treatment arm (combined with curcumin and quercetin) - results of individual treatments may vary, trial NCT05130671 (history), excluded in exclusion analyses: based on dosages and previous research, combined treatments may contribute more to the effect seen.	risk of no recovery, 33.3% lower, RR 0.67, $p = 0.15$, treatment 10 of 25 (40.0%), control 15 of 25 (60.0%), NNT 5.0.
	relative CRP reduction, 39.1% better, RR 0.61, $p = 0.006$, treatment 25, control 25.
	risk of no viral clearance, 50.0% lower, RR 0.50, $p = 0.009$, treatment 10 of 25 (40.0%), control 20 of 25 (80.0%), NNT 2.5.
Said, 11/8/2022, Randomized Controlled Trial, Egypt, peer-reviewed, 5 authors, study period 21 July, 2021 - 30 December, 2021, dosage 2,000IU daily, trial NCT04981743 (history).	risk of no recovery, 42.0% lower, OR 0.58, $p = 0.57$, treatment 30, control 30, adjusted per study, multivariable, dyspnea, RR approximated with OR.
	risk of no recovery, 89.0% lower, OR 0.11, $p = 0.01$, treatment 30, control 30, adjusted per study, vitamin D and nigella sativa, multivariable, dyspnea, RR approximated with OR.
	risk of no recovery, 52.0% lower, OR 0.48, $p = 0.16$, treatment 30, control 30, adjusted per study, multivariable, cough, RR approximated with OR.
	risk of no recovery, 77.0% lower, OR 0.23, $p = 0.01$, treatment 30, control 30, adjusted per study, vitamin D and nigella sativa, multivariable, cough, RR approximated with OR.
	risk of no recovery, 56.0% lower, OR 0.44, $p = 0.20$, treatment 30, control 30, adjusted per study, multivariable, fatigue, RR approximated with OR.
	risk of no recovery, 90.0% lower, OR 0.10, $p < 0.001$, treatment 30, control 30, adjusted per study, vitamin D and nigella sativa, multivariable, fatigue, RR approximated with OR.
	risk of no recovery, 33.0% lower, OR 0.67, $p = 0.67$, treatment 30, control 30, adjusted per study, multivariable, smell, RR approximated with OR.
	risk of no recovery, 67.0% lower, OR 0.33, $p = 0.23$, treatment 30, control 30, adjusted per study, vitamin D and nigella sativa, multivariable, smell, RR approximated with OR.
	risk of no recovery, 25.0% higher, OR 1.25, $p = 0.79$, treatment 30, control 30, adjusted per study, multivariable, taste, RR approximated with OR.
	risk of no recovery, 58.0% lower, OR 0.42, $p = 0.28$, treatment 30, control 30, adjusted per study, vitamin D and nigella sativa, multivariable, taste, RR approximated with OR.
	risk of no recovery, 56.0% lower, OR 0.44, $p = 0.36$, treatment 30, control 30, adjusted per study, multivariable, sore throat, RR approximated with OR.

	risk of no recovery, 86.0% lower, OR 0.14, p = 0.03, treatment 30, control 30, adjusted per study, vitamin D and nigella sativa, multivariable, sore throat, RR approximated with OR.
	risk of no recovery, 175.0% higher, OR 2.75, p = 0.13, treatment 30, control 30, adjusted per study, multivariable, headache, RR approximated with OR.
	risk of no recovery, 56.0% lower, OR 0.44, p = 0.21, treatment 30, control 30, adjusted per study, vitamin D and nigella sativa, multivariable, headache, RR approximated with OR.
	risk of no recovery, 87.0% lower, OR 0.13, p = 0.05, treatment 30, control 30, adjusted per study, multivariable, diarrhea, RR approximated with OR.
	risk of no recovery, 90.0% lower, OR 0.10, p = 0.03, treatment 30, control 30, adjusted per study, vitamin D and nigella sativa, multivariable, diarrhea, RR approximated with OR.
	risk of no viral clearance, 49.0% lower, OR 0.51, p = 0.20, treatment 30, control 30, day 14, RR approximated with OR.
	risk of no viral clearance, 23.0% lower, OR 0.77, p = 0.74, treatment 30, control 30, day 7, RR approximated with OR.
	risk of no viral clearance, 91.0% lower, OR 0.09, p < 0.001, treatment 30, control 30, vitamin D and nigella sativa, day 14, RR approximated with OR.
	risk of no viral clearance, 87.0% lower, OR 0.13, p = 0.003, treatment 30, control 30, vitamin D and nigella sativa, day 7, RR approximated with OR.
Sánchez-Zuno, 5/28/2021, Randomized Controlled Trial, Mexico, peer-reviewed, 12 authors, dosage 10,000IU days 1-14.	risk of severe case, 89.4% lower, RR 0.11, p = 0.04, treatment 0 of 22 (0.0%), control 4 of 20 (20.0%), NNT 5.0, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), risk of >3 symptoms at day 14.
	risk of no recovery, 80.8% lower, RR 0.19, p = 0.22, treatment 0 of 22 (0.0%), control 2 of 20 (10.0%), NNT 10.0, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), risk of fever at day 14, Table S1.
Tomasa-Irriguible (B), 11/30/2023, Double Blind Randomized Controlled Trial, placebo-controlled, Spain, trial NCT04751669 (history) (CoVIT).	Estimated 300 patient RCT with results unknown and over 4 months late.
Valecha, 4/26/2022, prospective, India, peer-reviewed, 1 author, average treatment delay 3.7 days, dosage 1,000IU daily, this trial uses multiple treatments in the treatment arm (combined with magnesium and vitamin B12) - results of individual treatments may vary.	risk of ICU admission, 86.8% lower, RR 0.13, p = 0.09, treatment 0 of 30 (0.0%), control 3 of 25 (12.0%), NNT 8.3, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm).

	hospitalization time, 38.5% lower, relative time 0.62, $p < 0.001$, treatment mean 11.2 (±2.8) n=30, control mean 18.2 (±1.21) n=25.

Late treatment

Effect extraction follows pre-specified rules as detailed above and gives priority to more serious outcomes. Only the first (most serious) outcome is used in pooled analysis, which may differ from the effect a paper focuses on. Other outcomes are used in outcome specific analyses.

Al Sulaiman, 8/14/2023, retrospective, Saudi Arabia, peer-reviewed, 25 authors, study period March 2020 - July 2021, dosage not specified, excluded in exclusion analyses: very late stage study using cholecalciferol instead of calcifediol or calcitriol.	risk of death, 22.0% higher, HR 1.22, $p = 0.25$, treatment 72 of 144 (50.0%), control 62 of 144 (43.1%).
	risk of mechanical ventilation, 27.0% higher, OR 1.27, $p = 0.046$, treatment 144, control 144, RR approximated with OR.
	risk of ICU admission, 17.0% higher, OR 1.17, $p = 0.07$, treatment 144, control 144, RR approximated with OR.
	risk of hospitalization, no change, OR 1.00, $p = 1.00$, treatment 144, control 144, RR approximated with OR.
Alcala-Diaz, 5/21/2021, retrospective, Spain, peer-reviewed, 17 authors, dosage calcifediol 0.5mg day 1, 0.27mg day 3, 0.27mg day 7, 0.27mg day 14, 0.27mg day 21, 0.27mg day 28.	risk of death, 80.8% lower, RR 0.19, $p = 0.04$, treatment 4 of 79 (5.1%), control 90 of 458 (19.7%), NNT 6.9, adjusted per study, odds ratio converted to relative risk, day 30, multivariate logistic regression.
Assiri, 8/28/2021, retrospective, Saudi Arabia, peer-reviewed, 8 authors, dosage not specified, excluded in exclusion analyses: unadjusted results with no group details.	risk of death, 66.5% higher, RR 1.66, $p = 0.60$, treatment 12 of 90 (13.3%), control 2 of 28 (7.1%), inverted to make RR<1 favor treatment, odds ratio converted to relative risk.
Baguma, 12/28/2021, retrospective, Uganda, preprint, 16 authors, study period March 2020 - October 2021, dosage not specified.	risk of death, 96.7% lower, RR 0.03, $p = 0.02$, treatment 23, control 458, adjusted per study, inverted to make RR<1 favor treatment, odds ratio converted to relative risk, multivariable, control prevalance approximated with overall prevalence.
Baykal, 5/30/2022, retrospective, Turkey, peer-reviewed, 2 authors, study period 1 April, 2020 - 1 March, 2021, dosage 300,000IU single dose, excluded in exclusion analyses: unadjusted results with no group details; significant confounding by time possible due to separation of groups in different time periods.	risk of death, 22.2% lower, RR 0.78, $p = 0.43$, treatment 7 of 18 (38.9%), control 28 of 56 (50.0%), NNT 9.0.
	risk of ICU admission, 59.4% lower, RR 0.41, $p = 0.005$, treatment 5 of 18 (27.8%), control 39 of 57 (68.4%), NNT 2.5.
Beigmohammadi, 11/14/2021, Single Blind Randomized Controlled Trial, Iran, peer-reviewed, 6 authors, study period April 2020 - July 2020, dosage 600,000IU single dose, this trial uses multiple treatments in the treatment arm (combined with vitamins A, B, C, E) - results of individual treatments may vary, trial IRCT20200319046819N1, excluded in exclusion analyses: very late stage study using cholecalciferol instead of calcifediol or calcitriol.	risk of death, 88.9% lower, RR 0.11, $p = 0.11$, treatment 0 of 30 (0.0%), control 4 of 30 (13.3%), NNT 7.5, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm).
	risk of hospitalization >7 days, 41.0% lower, RR 0.59, $p = 0.25$, treatment 4 of 30 (13.3%), control 16 of 30 (53.3%), NNT 2.5, adjusted per study, odds ratio converted to relative risk.

	relative SOFA score @day 7, 45.5% better, RR 0.55, $p < 0.001$, treatment 30, control 30.
Bishop, 2/5/2022, Double Blind Randomized Controlled Trial, placebo-controlled, USA, peer-reviewed, survey, 11 authors, study period 2 November, 2020 - 8 October, 2021, dosage calcifediol 300µg days 1-3, 60µg days 4-27, trial NCT04551911 (history) (REsCue).	risk of no recovery, 33.7% lower, RR 0.66, $p = 0.56$, treatment 5 of 65 (7.7%), control 8 of 69 (11.6%), NNT 26, day 21, mid-trial.
	risk of no recovery, 73.5% lower, RR 0.27, $p = 0.37$, treatment 1 of 65 (1.5%), control 4 of 69 (5.8%), NNT 23, day 35.
	risk of no recovery, 57.5% lower, RR 0.42, $p = 0.44$, treatment 2 of 65 (3.1%), control 5 of 69 (7.2%), NNT 24, day 28.
	risk of no recovery, 6.2% higher, RR 1.06, $p = 0.85$, treatment 17 of 65 (26.2%), control 17 of 69 (24.6%), day 14.
	risk of no recovery, 3.0% higher, RR 1.03, $p = 1.00$, treatment 33 of 65 (50.8%), control 34 of 69 (49.3%), day 7.
Bychinin, 11/3/2022, Double Blind Randomized Controlled Trial, placebo-controlled, Russia, peer-reviewed, 7 authors, study period 1 May, 2020 - 31 January, 2022, average treatment delay 9.0 days, dosage 60,000IU day 1, 5,000IU days 2-7, 8, 5,000IU days 9-14, 15, 5,000IU days 16-21, 22, 5,000IU days 23-28, trial NCT05092698 (history) (COVID-VIT), excluded in exclusion analyses: very late stage study using cholecalciferol instead of calcifediol or calcitriol.	risk of death, 26.9% lower, RR 0.73, $p = 0.18$, treatment 19 of 52 (36.5%), control 27 of 54 (50.0%), NNT 7.4.
	risk of mechanical ventilation, 7.4% lower, RR 0.93, $p = 0.68$, treatment 33 of 52 (63.5%), control 37 of 54 (68.5%), NNT 20.
Cannata-Andía, 2/18/2022, Randomized Controlled Trial, multiple countries, peer-reviewed, median age 59.0, 22 authors, study period 4 April, 2020 - 22 April, 2021, dosage 100,000IU single dose, trial NCT04552951 (history) (COVID-VIT-D), excluded in exclusion analyses: very late stage study using cholecalciferol instead of calcifediol or calcitriol.	risk of death, 44.0% higher, RR 1.44, $p = 0.31$, treatment 22 of 274 (8.0%), control 15 of 269 (5.6%).
	risk of ICU admission, 4.9% higher, RR 1.05, $p = 0.82$, treatment 47 of 274 (17.2%), control 44 of 269 (16.4%).
Castillo, 8/29/2020, Randomized Controlled Trial, Spain, peer-reviewed, 7 authors, study period May 2020 - June 2020, dosage calcifediol 0.5mg day 1, 0.27mg day 3, 0.27mg day 7, and then weekly until discharge or ICU admission, trial NCT04366908 (history) (COVIDIOL).	risk of death, 85.4% lower, RR 0.15, $p = 0.11$, treatment 0 of 50 (0.0%), control 2 of 26 (7.7%), NNT 13, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm).
	risk of ICU admission, 94.2% lower, RR 0.06, $p = 0.008$, treatment 1 of 50 (2.0%), control 13 of 26 (50.0%), NNT 2.1, odds ratio converted to relative risk.
De Niet, 7/26/2022, Double Blind Randomized Controlled Trial, placebo-controlled, Belgium, peer-reviewed, 16 authors, study period August 2020 - August 2021, dosage 25,000IU days 1-4, 11, 18, 25, trial NCT04636086 (history).	risk of death, 65.1% lower, RR 0.35, $p = 0.61$, treatment 1 of 21 (4.8%), control 3 of 22 (13.6%), NNT 11, COVID-19 mortality.
	risk of death, 39.7% higher, RR 1.40, $p = 0.70$, treatment 4 of 21 (19.0%), control 3 of 22 (13.6%), all cause including after discharge and non-COVID-19.
	risk of ICU admission, 58.1% lower, RR 0.42, $p = 0.41$, treatment 2 of 21 (9.5%), control 5 of 22 (22.7%), NNT 7.6.

	ICU time, 67.7% lower, relative time 0.32, p = 0.47, treatment 21, control 22.
	risk of no hospital discharge, 79.6% lower, RR 0.20, p = 0.49, treatment 0 of 21 (0.0%), control 2 of 22 (9.1%), NNT 11, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), day 36.
	risk of no hospital discharge, 85.4% lower, RR 0.15, p = 0.23, treatment 0 of 21 (0.0%), control 3 of 22 (13.6%), NNT 7.3, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), day 28.
	risk of no hospital discharge, 85.4% lower, RR 0.15, p = 0.23, treatment 0 of 21 (0.0%), control 3 of 22 (13.6%), NNT 7.3, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), day 21.
	risk of no hospital discharge, 65.1% lower, RR 0.35, p = 0.61, treatment 1 of 21 (4.8%), control 3 of 22 (13.6%), NNT 11, day 14.
	risk of no hospital discharge, 65.1% lower, RR 0.35, p = 0.03, treatment 4 of 21 (19.0%), control 12 of 22 (54.5%), NNT 2.8, day 7.
	recovery time, 45.4% lower, relative time 0.55, p = 0.06, treatment 21, control 22, fever.
	hospitalization time, 50.0% lower, relative time 0.50, p = 0.003, treatment 21, control 22.
Domazet Bugarin, 2/28/2023, Randomized Controlled Trial, Croatia, peer-reviewed, 9 authors, study period November 2021 - May 2022, dosage 10,000IU days 1-14, trial NCT05384574 (history), excluded in exclusion analyses: very late stage study using cholecalciferol instead of calcifediol or calcitriol.	risk of death, 21.0% lower, RR 0.79, p = 0.20, treatment 30 of 75 (40.0%), control 39 of 77 (50.6%), NNT 9.4, day 60.
	risk of death, 12.5% lower, RR 0.87, p = 0.61, treatment 23 of 75 (30.7%), control 27 of 77 (35.1%), NNT 23, day 28.
	risk of death, 28.9% lower, RR 0.71, p = 0.49, treatment 9 of 75 (12.0%), control 13 of 77 (16.9%), NNT 20, day 14.
Elamir, 9/8/2021, Randomized Controlled Trial, USA, peer-reviewed, 9 authors, study period September 2020 - December 2020, dosage calcitriol 0.5µg days 1-14.	risk of death, 85.7% lower, RR 0.14, p = 0.23, treatment 0 of 25 (0.0%), control 3 of 25 (12.0%), NNT 8.3, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm).
	risk of mechanical ventilation, 80.0% lower, RR 0.20, p = 0.48, treatment 0 of 25 (0.0%), control 2 of 25 (8.0%), NNT 12, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm).
	risk of ICU admission, 37.5% lower, RR 0.62, p = 0.33, treatment 5 of 25 (20.0%), control 8 of 25 (32.0%), NNT 8.3.
	hospitalization time, 40.5% lower, relative time 0.60, p = 0.14, treatment 25, control 25.

	relative Δ SaO_2/FiO_2, RR 0.14, p = 0.03, treatment 25, control 25, primary outcome.
Elhadi, 4/30/2021, prospective, Libya, peer-reviewed, 21 authors, study period 29 May, 2020 - 30 December, 2020, dosage not specified, excluded in exclusion analyses: unadjusted results with no group details.	risk of death, 23.4% lower, RR 0.77, p = 0.29, treatment 7 of 15 (46.7%), control 274 of 450 (60.9%), NNT 7.0.
Fairfield, 7/26/2022, retrospective, USA, peer-reviewed, 10 authors, study period 1 January, 2020 - 31 July, 2021, dosage not specified, excluded in exclusion analyses: substantial unadjusted confounding by indication likely.	risk of death, 8.9% higher, RR 1.09, p < 0.001, treatment 3,653 of 28,993 (12.6%), control 13,185 of 129,842 (10.2%), odds ratio converted to relative risk.
	risk of mechanical ventilation, 40.8% higher, RR 1.41, p < 0.001, treatment 4,897 of 28,993 (16.9%), control 15,520 of 129,842 (12.0%), odds ratio converted to relative risk.
Fiore, 5/22/2022, retrospective, matched cohort, Italy, peer-reviewed, mean age 62.5, 10 authors, dosage 100,000IU days 1-2.	risk of death, 92.7% lower, RR 0.07, p = 0.01, treatment 3 of 58 (5.2%), control 11 of 58 (19.0%), NNT 7.2, adjusted per study, odds ratio converted to relative risk, multivariable.
	risk of mechanical ventilation, 50.0% lower, RR 0.50, p = 0.36, treatment 4 of 58 (6.9%), control 8 of 58 (13.8%), NNT 14.
	risk of ICU admission, 50.0% lower, RR 0.50, p = 0.36, treatment 4 of 58 (6.9%), control 8 of 58 (13.8%), NNT 14.
	NIV, 47.8% lower, RR 0.52, p = 0.04, treatment 12 of 58 (20.7%), control 23 of 58 (39.7%), NNT 5.3.
Giannini, 1/14/2021, retrospective, Italy, peer-reviewed, 21 authors, dosage 200,000IU days 1-2.	risk of death/ICU, 36.6% lower, RR 0.63, p = 0.13, treatment 14 of 36 (38.9%), control 29 of 55 (52.7%), NNT 7.2, odds ratio converted to relative risk.
Güven, 7/23/2021, retrospective, Turkey, peer-reviewed, 2 authors, dosage 300,000IU single dose, excluded in exclusion analyses: very late stage, ICU patients.	risk of death, 24.8% lower, RR 0.75, p = 0.32, treatment 43 of 113 (38.1%), control 30 of 62 (48.4%), NNT 9.7, odds ratio converted to relative risk.
Hafez (B), 8/9/2022, retrospective, Egypt, peer-reviewed, 2 authors, study period April 2020 - June 2020, dosage 50,000IU days 1, 3, 5, 7, 9, 11, 13, 50,000IU every other day for two weeks or one intramuscular shot of 300,000IU.	risk of death, 93.7% lower, RR 0.06, p = 0.07, treatment 0 of 7 (0.0%), control 12 of 30 (40.0%), NNT 2.5, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), high dose, 50,000IU every other day for two weeks or one intramuscular shot of 300,000IU.
	risk of death, 58.3% lower, RR 0.42, p = 0.28, treatment 2 of 12 (16.7%), control 12 of 30 (40.0%), NNT 4.3, low dose, ≤10,000IU/day.
Hafezi, 10/22/2022, retrospective, United Arab Emirates, peer-reviewed, 8 authors, study period September 2020 - January 2021, dosage 50,000IU days 1, 8, 15, excluded in exclusion analyses: very late stage study using cholecalciferol instead of calcifediol or calcitriol.	risk of death, 63.0% lower, HR 0.37, p = 0.04, treatment 8 of 43 (18.6%), control 12 of 37 (32.4%), NNT 7.2, Cox proportional hazards, day 29.

Jevalikar, 12/28/2020, prospective, India, peer-reviewed, 8 authors, dosage 60,000IU single dose, median total dose.	**risk of death, 82.0% lower, RR 0.18, $p = 0.12$**, treatment 1 of 128 (0.8%), control 3 of 69 (4.3%), NNT 28.
	risk of ICU admission, 33.7% lower, RR 0.66, $p = 0.29$, treatment 16 of 128 (12.5%), control 13 of 69 (18.8%), NNT 16.
	risk of oxygen therapy, 31.7% lower, RR 0.68, $p = 0.06$, treatment 38 of 128 (29.7%), control 30 of 69 (43.5%), NNT 7.3.
Karimpour-Razkenari, 10/3/2022, retrospective, Iran, peer-reviewed, median age 58.5, 9 authors, study period 23 February, 2020 - 23 May, 2020, dosage not specified.	**risk of death, 79.0% lower, RR 0.21, $p < 0.001$**, treatment 10 of 124 (8.1%), control 93 of 329 (28.3%), NNT 4.9, adjusted per study, inverted to make RR<1 favor treatment, odds ratio converted to relative risk, multivariable.
Karonova, 6/23/2022, Randomized Controlled Trial, Russia, peer-reviewed, 12 authors, study period 30 November, 2020 - 20 March, 2021, dosage 50,000IU days 1, 8, trial NCT05166005 (history).	**risk of ICU admission, 85.9% lower, RR 0.14, $p = 0.11$**, treatment 0 of 56 (0.0%), control 3 of 54 (5.6%), NNT 18, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), day 9.
	risk of oxygen therapy, 7.0% lower, RR 0.93, $p = 0.85$, treatment 27 of 56 (48.2%), control 28 of 54 (51.9%), NNT 27, baseline oxygen supplementation was higher in the treatment group, 38 vs. 32, day 9.
Krishnan, 7/20/2020, retrospective, USA, peer-reviewed, 13 authors, dosage not specified, excluded in exclusion analyses: unadjusted results with no group details.	**risk of death, 19.0% lower, RR 0.81, $p = 0.42$**, treatment 8 of 16 (50.0%), control 84 of 136 (61.8%), NNT 8.5.
Lakkireddy, 7/27/2022, Randomized Controlled Trial, India, peer-reviewed, mean age 45.5, 9 authors, dosage 60,000IU days 1-8, 8 or 10 days depending on BMI.	**risk of death, 60.9% lower, RR 0.39, $p = 0.27$**, treatment 2 of 44 (4.5%), control 5 of 43 (11.6%), NNT 14.
	risk of ICU admission, 21.8% lower, RR 0.78, $p = 0.74$, treatment 4 of 44 (9.1%), control 5 of 43 (11.6%), NNT 39.
	hospitalization time, 7.1% lower, relative time 0.93, $p = 0.90$, treatment 44, control 43.
Leal-Martínez, 10/25/2021, Randomized Controlled Trial, Mexico, peer-reviewed, 7 authors, study period 1 September, 2020 - 28 February, 2021, dosage 4,000IU days 1-21, this trial uses multiple treatments in the treatment arm (combined with comprehensive nutritional support) - results of individual treatments may vary, trial NCT04507867 (history), excluded in exclusion analyses: combined treatments may contribute more to the effect seen.	**risk of death, 85.7% lower, RR 0.14, $p = 0.03$**, treatment 1 of 40 (2.5%), control 7 of 40 (17.5%), NNT 6.7.
	risk of mechanical ventilation, 57.1% lower, RR 0.43, $p = 0.31$, treatment 3 of 40 (7.5%), control 7 of 40 (17.5%), NNT 10.0.
Ling, 12/11/2020, retrospective, United Kingdom, peer-reviewed, 7 authors, dosage 40,000IU weekly, regimen varied with 77% receiving a total of 40,000IU/week.	**risk of death, 79.8% lower, RR 0.20, $p < 0.001$**, treatment 73, control 253, odds ratio converted to relative risk, primary cohort.
	risk of death, 55.5% lower, RR 0.44, $p = 0.02$, treatment 80, control 443, odds ratio converted to relative risk, validation cohort.

Lohia (B), 3/4/2021, retrospective, USA, peer-reviewed, 4 authors, dosage not specified.	risk of death, 10.7% lower, RR 0.89, *p* = 0.80, treatment 26, control 69, odds ratio converted to relative risk, <20 ng/mL, control prevalence approximated with overall prevalence.
	risk of mechanical ventilation, 26.9% lower, RR 0.73, *p* = 0.51, treatment 26, control 69, odds ratio converted to relative risk, <20 ng/mL, control prevalence approximated with overall prevalence.
	risk of ICU admission, 2.7% lower, RR 0.97, *p* = 0.93, treatment 26, control 69, odds ratio converted to relative risk, <20 ng/mL, control prevalence approximated with overall prevalence.
Maghbooli, 10/13/2021, Double Blind Randomized Controlled Trial, Iran, peer-reviewed, 12 authors, dosage calcifediol 25µg daily, mean daily dose.	risk of death, 40.0% lower, RR 0.60, *p* = 0.72, treatment 3 of 53 (5.7%), control 5 of 53 (9.4%), NNT 26.
	risk of mechanical ventilation, 60.0% lower, RR 0.40, *p* = 0.44, treatment 2 of 53 (3.8%), control 5 of 53 (9.4%), NNT 18.
	risk of ICU admission, 40.0% lower, RR 0.60, *p* = 0.42, treatment 6 of 53 (11.3%), control 10 of 53 (18.9%), NNT 13.
	ICU time, 36.4% lower, relative time 0.64, *p* = 0.20, treatment 53, control 53.
	hospitalization time, 16.7% lower, relative time 0.83, *p* = 0.10, treatment 53, control 53.
Mahmood, 12/29/2021, retrospective, United Kingdom, peer-reviewed, 4 authors, study period 23 March, 2020 - 31 December, 2020, dosage varies, excluded in exclusion analyses: unadjusted results with no group details; substantial unadjusted confounding by indication likely.	risk of death, 30.5% lower, RR 0.70, *p* = 0.10, treatment 45 of 238 (18.9%), control 31 of 114 (27.2%), NNT 12, started after admission, late treatment result.
Mariani, 5/27/2022, Double Blind Randomized Controlled Trial, placebo-controlled, Argentina, peer-reviewed, mean age 59.1, 33 authors, study period 14 August, 2020 - 22 June, 2021, average treatment delay 7.0 days, dosage 500,000IU single dose, trial NCT04411446 (history) (CARED).	risk of death, 124.0% higher, RR 2.24, *p* = 0.45, treatment 5 of 115 (4.3%), control 2 of 103 (1.9%).
	risk of mechanical ventilation, 25.0% lower, RR 0.75, *p* = 0.85, treatment 5 of 115 (4.3%), control 6 of 103 (5.8%), NNT 68.
	risk of ICU admission, 27.0% lower, RR 0.73, *p* = 0.62, treatment 9 of 115 (7.8%), control 11 of 103 (10.7%), NNT 35.
	risk of progression, 3.0% lower, OR 0.97, *p* = 0.82, treatment 115, control 103, Wilcoxon-Mann-Whitney, primary outcome, RR approximated with OR.
	risk of progression, 32.8% lower, RR 0.67, *p* = 0.71, treatment 3 of 115 (2.6%), control 4 of 103 (3.9%), NNT 78, Δ rSOFA 4.
	risk of progression, 79.1% higher, RR 1.79, *p* = 0.30, treatment 10 of 115 (8.7%), control 5 of 103 (4.9%), Δ rSOFA 3.
	risk of progression, 25.4% lower, RR 0.75, *p* = 0.76, treatment 5 of 115 (4.3%), control 6 of 103 (5.8%), NNT 68, Δ rSOFA 2.

	risk of progression, 16.0% lower, RR 0.84, $p = 0.70$, treatment 15 of 115 (13.0%), control 16 of 103 (15.5%), NNT 40, Δ rSOFA 1.
Mazziotti, 3/5/2021, retrospective, Italy, peer-reviewed, 11 authors, dosage varies.	**risk of death, 19.0% lower, OR 0.81, $p = 0.49$**, treatment 116, control 232, supplementation, RR approximated with OR.
	risk of mechanical ventilation, 67.0% higher, OR 1.67, $p = 0.08$, treatment 116, control 232, supplementation, RR approximated with OR.
Mingiano, 7/30/2023, retrospective, Italy, peer-reviewed, 11 authors, study period November 2020 - February 2021, dosage calcifediol 450µg days 1-2, patients with deficiency only.	**risk of death, 38.8% lower, RR 0.61, $p = 0.04$**, treatment 13 of 56 (23.2%), control 88 of 232 (37.9%), NNT 6.8.
	risk of oxygen therapy, 23.1% lower, RR 0.77, $p = 0.22$, treatment 18 of 56 (32.1%), control 97 of 232 (41.8%), NNT 10.
	hospitalization time, 34.6% lower, relative time 0.65, $p = 0.01$, treatment 56, control 232.
Murai, 11/17/2020, Double Blind Randomized Controlled Trial, Brazil, peer-reviewed, 17 authors, study period 2 June, 2020 - 27 August, 2020, average treatment delay 10.2 days, dosage 200,000IU single dose, trial NCT04449718 (history), excluded in exclusion analyses: very late stage, >50% on oxygen/ventilation at baseline; very late stage study using cholecalciferol instead of calcifediol or calcitriol.	**risk of death, 48.7% higher, RR 1.49, $p = 0.43$**, treatment 9 of 119 (7.6%), control 6 of 118 (5.1%).
	risk of mechanical ventilation, 47.5% lower, RR 0.52, $p = 0.09$, treatment 9 of 119 (7.6%), control 17 of 118 (14.4%), NNT 15.
	risk of ICU admission, 24.6% lower, RR 0.75, $p = 0.30$, treatment 19 of 119 (16.0%), control 25 of 118 (21.2%), NNT 19.
	risk of no hospital discharge, 6.5% lower, HR 0.93, $p = 0.63$, treatment 119, control 118, inverted to make HR<1 favor treatment.
Nogués, 1/22/2021, prospective quasi-randomized (ward), Spain, peer-reviewed, 16 authors, dosage calcifediol 0.5mg day 1, 0.27mg day 3, 0.27mg day 7, 0.27mg day 15, 0.27mg day 30.	**risk of death, 79.0% lower, RR 0.21, $p = 0.001$**, treatment 21 of 447 (4.7%), control 62 of 391 (15.9%), NNT 9.0, adjusted per study, ITT.
	risk of death, 48.0% lower, RR 0.52, $p = 0.001$, treatment 500, control 338, adjusted per study, including patients treated later.
	risk of ICU admission, 87.0% lower, RR 0.13, $p < 0.001$, treatment 20 of 447 (4.5%), control 82 of 391 (21.0%), NNT 6.1, adjusted per study, ITT.
Ogasawara, 9/1/2023, retrospective, Japan, peer-reviewed, 10 authors, study period April 2021 - September 2022, dosage alfacalcidol 1µg days 1-8, median duration, alfacalcidol and eldecalcitol used.	**risk of death, 66.7% lower, RR 0.33, $p = 1.00$**, treatment 0 of 54 (0.0%), control 1 of 54 (1.9%), NNT 54, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm).
	risk of progression, 77.8% lower, RR 0.22, $p = 0.05$, treatment 2 of 54 (3.7%), control 9 of 54 (16.7%), NNT 7.7, high-flow oxygen, mechanical ventilation, or mortality, primary outcome.
	risk of oxygen therapy, 75.0% lower, RR 0.25, $p = 0.09$, treatment 2 of 54 (3.7%), control 8 of 54 (14.8%), NNT 9.0.

Rastogi, 11/12/2020, Randomized Controlled Trial, India, peer-reviewed, 8 authors, dosage 60,000IU days 1-7, trial NCT04459247 (history) (SHADE).	risk of no viral clearance, 52.6% lower, RR 0.47, $p = 0.02$, treatment 6 of 16 (37.5%), control 19 of 24 (79.2%), NNT 2.4.
Saheb Sharif-Askari (B), 8/24/2022, retrospective, USA, peer-reviewed, 10 authors, dosage 50,000IU days 1, 8, 15, excluded in exclusion analyses: very late stage study using cholecalciferol instead of calcifediol or calcitriol.	ICU time, 35.7% lower, relative time 0.64, $p = 0.01$, treatment 20, control 25.
Salman, 6/16/2023, Randomized Controlled Trial, Pakistan, peer-reviewed, 6 authors, study period January 2021 - May 2021, dosage 4,000IU days 1-14.	risk of death, 60.0% lower, RR 0.40, $p = 0.07$, treatment 6 of 150 (4.0%), control 15 of 150 (10.0%), NNT 17.
	risk of mechanical ventilation, 16.7% lower, RR 0.83, $p = 0.55$, treatment 25 of 150 (16.7%), control 30 of 150 (20.0%), NNT 30.
	risk of ICU admission, 12.5% lower, RR 0.88, $p = 0.85$, treatment 14 of 150 (9.3%), control 16 of 150 (10.7%), NNT 75.
	hospitalization time, 18.2% lower, relative time 0.82, $p = 0.001$, treatment 150, control 150.
	recovery time, 22.2% lower, relative time 0.78, $p = 0.001$, treatment 150, control 150.
Seely, 9/22/2023, Double Blind Randomized Controlled Trial, placebo-controlled, Canada, peer-reviewed, mean age 39.9, 10 authors, study period September 2021 - April 2022, dosage 51,000IU day 1, 1,000IU days 2-21, this trial uses multiple treatments in the treatment arm (combined with vitamin C, D, K2, and zinc) - results of individual treatments may vary, trial NCT04780061 (history).	ER visit, 47.6% lower, RR 0.52, $p = 0.68$, treatment 2 of 42 (4.8%), control 4 of 44 (9.1%), NNT 23.
	relative mean cumulative symptom score, 13.8% better, RR 0.86, $p = 0.41$, treatment mean 166.3 (±92.3) n=34, control mean 192.9 (±153.6) n=24.
	EQ-VAS average score <80, 29.4% lower, RR 0.71, $p = 0.54$, treatment 7 of 34 (20.6%), control 7 of 24 (29.2%), NNT 12, average daily EQ-VAS score <80.
	relative EQ5D improvement, 28.6% better, RR 0.71, $p = 0.44$, treatment 32, control 31, relative improvement in EQ5D, week 1.
	relative EQ5D improvement, 14.3% better, RR 0.86, $p = 0.73$, treatment 33, control 30, relative improvement in EQ5D, week 2.
	relative EQ5D improvement, 50.0% better, RR 0.50, $p = 0.17$, treatment 32, control 33, relative improvement in EQ5D, week 3.
	relative EQ5D improvement, 12.5% worse, RR 1.12, $p = 0.47$, treatment 30, control 25, relative improvement in EQ5D, week 4.
	recovery time, 4.0% higher, relative time 1.04, $p = 0.81$, treatment 34, control 24.
	risk of PASC, 12.1% lower, RR 0.88, $p = 1.00$, treatment 3 of 33 (9.1%), control 3 of 29 (10.3%), NNT 80, 12 weeks.

	risk of PASC, 35.7% lower, RR 0.64, p = 0.69, treatment 3 of 35 (8.6%), control 4 of 30 (13.3%), NNT 21, 8 weeks.
	risk of PASC, 0.6% lower, RR 0.99, p = 1.00, treatment 6 of 35 (17.1%), control 5 of 29 (17.2%), NNT 1015, 4 weeks.
Shahid, 6/17/2022, retrospective, USA, peer-reviewed, 2 authors, dosage not specified, excluded in exclusion analyses: minimal details provided.	risk of death, 38.0% lower, RR 0.62, p < 0.001, treatment 705, control 773.
Shamsi, 7/17/2023, retrospective, Iran, peer-reviewed, 4 authors, study period 1 March, 2020 - 1 August, 2021, dosage not specified, excluded in exclusion analyses: unadjusted results with no group details.	risk of death, 57.5% lower, RR 0.42, p = 0.70, treatment 1 of 17 (5.9%), control 23 of 166 (13.9%), NNT 13.
Singh (B), 6/1/2022, Double Blind Randomized Controlled Trial, placebo-controlled, India, peer-reviewed, 15 authors, study period 1 August, 2021 - 10 December, 2021, dosage 600,000IU single dose, trial NCT04952857 (history) (Shade-S).	risk of death, 45.0% lower, RR 0.55, p = 0.046, treatment 11 of 45 (24.4%), control 20 of 45 (44.4%), NNT 5.0.
	risk of no recovery, 40.0% lower, RR 0.60, p = 0.01, treatment 45, control 45.
Soliman, 9/1/2021, Randomized Controlled Trial, placebo-controlled, Egypt, peer-reviewed, 3 authors, dosage 200,000IU single dose.	risk of death, 63.4% lower, RR 0.37, p = 0.21, treatment 7 of 40 (17.5%), control 3 of 16 (18.8%), adjusted per study, odds ratio converted to relative risk, logistic regression.
	risk of mechanical ventilation, 20.0% lower, RR 0.80, p = 0.56, treatment 14 of 40 (35.0%), control 7 of 16 (43.8%), NNT 11, unadjusted.
	risk of no recovery, 20.0% lower, RR 0.80, p = 0.56, treatment 14 of 40 (35.0%), control 7 of 16 (43.8%), NNT 11, unadjusted.
Tan (B), 6/10/2020, retrospective, Singapore, peer-reviewed, 14 authors, dosage 1,000IU daily, this trial uses multiple treatments in the treatment arm (combined with magnesium and vitamin B12) - results of individual treatments may vary.	risk of oxygen therapy, 80.5% lower, RR 0.20, p = 0.04, treatment 3 of 17 (17.6%), control 16 of 26 (61.5%), NNT 2.3, adjusted per study, multivariate.
	risk of ICU admission, 80.9% lower, RR 0.19, p = 0.07, treatment 1 of 17 (5.9%), control 8 of 26 (30.8%), NNT 4.0, no adjusted result available.
Yildiz, 9/27/2021, retrospective, Turkey, peer-reviewed, 5 authors, dosage 300,000IU single dose.	risk of death, 80.9% lower, RR 0.19, p = 0.04, treatment 1 of 37 (2.7%), control 24 of 170 (14.1%), NNT 8.8.
	risk of ICU admission, 94.5% lower, RR 0.06, p = 0.13, treatment 0 of 37 (0.0%), control 14 of 170 (8.2%), NNT 12, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm).
	hospitalization time, 9.6% lower, relative time 0.90, p = 0.32, treatment 37, control 170.
Zangeneh, 5/13/2022, retrospective, Iran, peer-reviewed, 3 authors, dosage not specified, excluded in exclusion analyses: very late stage study using cholecalciferol instead of calcifediol or calcitriol.	risk of death, 26.0% higher, HR 1.26, p = 0.40, Cox proportional hazards.

Zurita-Cruz, 7/25/2022, Single Blind Randomized Controlled Trial, Mexico, peer-reviewed, median age 12.0, 7 authors, study period 24 March, 2020 - 31 March, 2021, dosage 2,000IU daily, daily, 1,000IU for children <1 year, trial NCT04502667 (history), excluded in exclusion analyses: randomization resulted in significant baseline differences that were not adjusted for.	risk of death, 79.2% lower, RR 0.21, $p = 0.11$, treatment 1 of 20 (5.0%), control 6 of 25 (24.0%), NNT 5.3.
	risk of mechanical ventilation, 72.2% lower, RR 0.28, $p = 0.08$, treatment 2 of 20 (10.0%), control 9 of 25 (36.0%), NNT 3.8.
	risk of ICU admission, 73.2% lower, RR 0.27, $p = 0.006$, treatment 3 of 20 (15.0%), control 14 of 25 (56.0%), NNT 2.4.

Prophylaxis

Effect extraction follows pre-specified rules as detailed above and gives priority to more serious outcomes. Only the first (most serious) outcome is used in pooled analysis, which may differ from the effect a paper focuses on. Other outcomes are used in outcome specific analyses.

Abdulateef, 4/8/2021, retrospective, Iraq, peer-reviewed, 7 authors, study period July 2020 - August 2020, dosage varies, excluded in exclusion analyses: unadjusted results with no group details.	risk of hospitalization, 40.9% lower, RR 0.59, $p = 0.30$, treatment 6 of 127 (4.7%), control 24 of 300 (8.0%), NNT 31, unadjusted.
Ahmed, 11/21/2021, retrospective, USA, preprint, 5 authors, dosage not specified.	risk of death, 10.5% lower, RR 0.90, $p = 0.28$.
Akbar, 11/7/2023, retrospective, Qatar, peer-reviewed, mean age 40.3, 9 authors, study period March 2020 - September 2020, dosage not specified.	risk of case, 19.0% lower, OR 0.81, $p = 0.02$, treatment 2,402, control 7,598, adjusted per study, multivariable, model 2, RR approximated with OR.
Aldwihi, 5/11/2021, retrospective, Saudi Arabia, peer-reviewed, survey, mean age 36.5, 8 authors, study period August 2020 - October 2020, dosage not specified.	risk of hospitalization, 49.3% higher, RR 1.49, $p = 0.002$, treatment 94 of 259 (36.3%), control 143 of 479 (29.9%), adjusted per study, odds ratio converted to relative risk, multivariable.
Annweiler (C), 11/2/2020, retrospective, France, peer-reviewed, mean age 88.0, 7 authors, dosage 50,000IU monthly, dose varies - 50,000 IU/month, or 80,000IU/100,000IU every 2–3 months.	risk of death, 93.0% lower, RR 0.07, $p = 0.02$, treatment 2 of 29 (6.9%), control 10 of 32 (31.2%), NNT 4.1, adjusted per study, regular bolus supplementation.
Arboleda, 3/13/2024, prospective, Colombia, peer-reviewed, 4 authors, dosage 5,000IU daily, this trial uses multiple treatments in the treatment arm (combined with vitamin C) - results of individual treatments may vary, excluded in exclusion analyses: unadjusted results with no group details.	risk of case, 35.7% lower, RR 0.64, $p = 0.03$, treatment 26 of 214 (12.1%), control 115 of 609 (18.9%), NNT 15.
Arroyo-Díaz, 9/24/2021, retrospective, Spain, peer-reviewed, 11 authors, dosage not specified.	risk of death, 12.4% higher, RR 1.12, $p = 0.59$, treatment 50 of 189 (26.5%), control 167 of 1,078 (15.5%), adjusted per study, odds ratio converted to relative risk.
	risk of mechanical ventilation, 43.3% lower, RR 0.57, $p = 0.22$, treatment 11 of 189 (5.8%), control 113 of 1,078 (10.5%), NNT 21, adjusted per study, odds ratio converted to relative risk.

	risk of ICU admission, 44.2% lower, RR 0.56, p = 0.03, treatment 13 of 189 (6.9%), control 133 of 1,078 (12.3%), NNT 18, unadjusted.
	hospitalization time, 11.8% lower, relative time 0.88, p = 0.20, treatment 189, control 1,078, unadjusted.
Aweimer, 3/29/2023, retrospective, Germany, peer-reviewed, median age 67.0, 19 authors, study period 1 March, 2020 - 31 August, 2021, dosage not specified, excluded in exclusion analyses: unadjusted results with no group details.	risk of death, 20.9% lower, RR 0.79, p = 0.31, treatment 7 of 12 (58.3%), control 101 of 137 (73.7%), NNT 6.5.
Bagheri, 9/1/2021, retrospective, Iran, peer-reviewed, 6 authors, dosage not specified.	risk of severe case, 70.9% lower, OR 0.29, p = 0.02, treatment 131, control 379, adjusted per study, multinomial logistic regression, RR approximated with OR.
	risk of hospitalization, 37.9% lower, RR 0.62, p = 0.11, treatment 28 of 131 (21.4%), control 143 of 379 (37.7%), NNT 6.1, adjusted per study, inverted to make RR<1 favor treatment, odds ratio converted to relative risk, binary logistic regression.
Baralić, 4/24/2023, prospective, France, peer-reviewed, 15 authors, study period March 2020 - September 2022, dosage not specified.	risk of death, 66.8% lower, HR 0.33, p = 0.02, treatment 7 of 31 (22.6%), control 11 of 21 (52.4%), NNT 3.4, Cox proportional hazards.
Bhat, 3/6/2023, prospective, placebo-controlled, India, peer-reviewed, 13 authors, dosage calcifediol 50µg days 1-180, trial CTRI/2021/08/035709.	risk of symptomatic case, 34.2% lower, RR 0.66, p = 0.01, treatment 59 of 262 (22.5%), control 52 of 152 (34.2%), NNT 8.6.
Blanch-Rubió, 10/20/2020, retrospective, Spain, peer-reviewed, mean age 66.4, 11 authors, dosage not specified.	risk of case, 8.0% lower, RR 0.92, p = 0.68, treatment 62 of 1,303 (4.8%), control 47 of 799 (5.9%), adjusted per study.
Brunvoll, 9/7/2022, Double Blind Randomized Controlled Trial, placebo-controlled, Norway, peer-reviewed, mean age 44.9, 15 authors, study period 10 November, 2020 - 2 June, 2021, dosage 400IU daily, this trial uses multiple treatments in the treatment arm (combined with cod liver oil) - results of individual treatments may vary, trial NCT04609423 (history).	risk of ICU admission, 0.3% higher, RR 1.00, p = 1.00, treatment 4 of 17,278 (0.0%), control 4 of 17,323 (0.0%).
	risk of hospitalization, 10.9% lower, RR 0.89, p = 1.00, treatment 8 of 17,278 (0.0%), control 9 of 17,323 (0.1%), NNT 17692.
	risk of severe case, 20.0% higher, RR 1.20, p = 0.17, treatment 121 of 17,278 (0.7%), control 101 of 17,323 (0.6%).
	risk of case, no change, RR 1.00, p = 0.98, treatment 227 of 17,278 (1.3%), control 228 of 17,323 (1.3%), NNT 42377.
Campi, 6/14/2021, prospective, Italy, peer-reviewed, 21 authors, dosage not specified, excluded in exclusion analyses: significant unadjusted differences between groups.	risk of severe case, 88.4% lower, OR 0.12, p < 0.001, treatment 31 of 103 (30.1%) cases, 41 of 52 (78.8%) controls, NNT 2.3, case control OR, vitamin D supplementation, hospitalized patients vs. controls.
Cangiano, 12/22/2020, retrospective, Italy, peer-reviewed, 14 authors, dosage 25,000IU 2x per month.	risk of death, 70.0% lower, RR 0.30, p = 0.04, treatment 3 of 20 (15.0%), control 39 of 78 (50.0%), NNT 2.9.

Cereda (B), 11/11/2020, retrospective, Italy, peer-reviewed, mean age 68.8, 7 authors, dosage varies.	risk of death, 73.0% higher, RR 1.73, $p = 0.14$, treatment 7 of 18 (38.9%), control 40 of 152 (26.3%), odds ratio converted to relative risk, >=25,000IU/month for at least 3 months.
	risk of hospitalization, 17.3% higher, RR 1.17, $p = 0.68$, treatment 7 of 27 (25.9%), control 36 of 170 (21.2%), odds ratio converted to relative risk.
Comunale, 1/24/2024, retrospective, USA, peer-reviewed, 6 authors, study period November 2020 - May 2021, dosage not specified, trial NCT04639375 (history).	risk of symptomatic case, 91.0% lower, OR 0.09, $p < 0.001$, treatment 100, control 182, adjusted per study, multivariable, RR approximated with OR.
	risk of case, 88.0% lower, OR 0.12, $p = 0.001$, treatment 100, control 182, adjusted per study, multivariable, RR approximated with OR.
De Nicolò, 12/29/2022, prospective, Italy, peer-reviewed, 11 authors, study period January 2021 - April 2021, dosage not specified.	risk of IgG positive, 88.4% lower, OR 0.12, $p = 0.002$, treatment 43, control 63, adjusted per study, multivariable, RR approximated with OR.
Dudley, 5/18/2021, retrospective, United Kingdom, peer-reviewed, 5 authors, dosage 800IU daily.	risk of symptomatic case, 22.4% lower, RR 0.78, $p = 0.65$, treatment 15 of 58 (25.9%), control 2 of 6 (33.3%), NNT 13, positive test.
Fasano, 6/2/2021, retrospective, Italy, peer-reviewed, 7 authors, dosage not specified.	risk of case, 42.0% lower, RR 0.58, $p = 0.048$, treatment 13 of 329 (4.0%), control 92 of 1,157 (8.0%), NNT 25, odds ratio converted to relative risk.
Gibbons, 11/12/2022, retrospective, USA, peer-reviewed, 7 authors, dosage varies.	risk of death, 33.3% lower, HR 0.67, $p < 0.001$, treatment 5,315 of 199,498 (2.7%), control 6,591 of 199,498 (3.3%), D3, propensity score matching, Cox proportional hazards.
	risk of death, 23.5% lower, HR 0.77, $p = 0.10$, treatment 716 of 33,216 (2.2%), control 987 of 33,216 (3.0%), NNT 123, D2, propensity score matching, Cox proportional hazards.
	risk of case, 20.3% lower, HR 0.80, $p < 0.001$, treatment 462 of 199,498 (0.2%), control 689 of 199,498 (0.3%), D3, propensity score matching, Cox proportional hazards.
	risk of case, 28.0% lower, HR 0.72, $p < 0.001$, treatment 65 of 33,216 (0.2%), control 86 of 33,216 (0.3%), NNT 1582, D2, propensity score matching, Cox proportional hazards.
Golabi (B), 8/26/2021, retrospective, Iran, peer-reviewed, 10 authors, dosage not specified.	risk of case, 25.4% higher, OR 1.25, $p = 0.56$, treatment 28 of 53 (52.8%) cases, 25 of 53 (47.2%) controls, case control OR.
Guldemir, 11/16/2022, retrospective, Turkey, peer-reviewed, 3 authors, study period 30 March, 2020 - 23 September, 2020, dosage not specified, excluded in exclusion analyses: unadjusted results with no group details.	risk of hospitalization, 5.2% lower, RR 0.95, $p = 0.89$ (Fisher's exact test), treatment 19 of 81 (23.5%), control 98 of 396 (24.7%), NNT 77.
Hernández (B), 10/27/2020, retrospective, Spain, peer-reviewed, mean age 60.9, 12 authors, dosage varies.	risk of death, 3.7% higher, RR 1.04, $p = 1.00$, treatment 2 of 19 (10.5%), control 20 of 197 (10.2%).

	risk of mechanical ventilation, 75.9% lower, RR 0.24, *p* = 0.13, treatment 1 of 19 (5.3%), control 43 of 197 (21.8%), NNT 6.0.
	risk of ICU admission, 79.3% lower, RR 0.21, *p* = 0.05, treatment 1 of 19 (5.3%), control 50 of 197 (25.4%), NNT 5.0.
	hospitalization time, 33.3% lower, relative time 0.67, *p* = 0.11, treatment 19, control 197.
Holt, 3/30/2021, prospective, United Kingdom, peer-reviewed, 34 authors, study period 1 May, 2020 - 5 February, 2021, dosage not specified, trial NCT04330599 (history) (COVIDENCE UK), excluded in exclusion analyses: significant unadjusted confounding possible.	risk of case, 6.8% lower, RR 0.93, *p* = 0.53, treatment 141 of 5,640 (2.5%), control 305 of 9,587 (3.2%), adjusted per study, odds ratio converted to relative risk, fully adjusted, group sizes approximated.
Hosseini (C), 7/19/2022, Double Blind Randomized Controlled Trial, placebo-controlled, Canada, preprint, mean age 39.5, 9 authors, study period 8 February, 2021 - 4 May, 2021, dosage 100,000IU day 1, 10,000IU day 7, 10,000IU day 14, 10,000IU day 21, 10,000IU day 28, 100,000IU cholecalciferol at baseline, 10,000IU weekly for 16 weeks, trial NCT04483635 (history) (PROTECT).	risk of case, 81.9% lower, RR 0.18, *p* = 0.19, treatment 0 of 19 (0.0%), control 2 of 15 (13.3%), NNT 7.5, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm).
Israel (B), 7/27/2021, retrospective, Israel, peer-reviewed, 10 authors, dosage not specified.	risk of hospitalization, 13.1% lower, OR 0.87, *p* = 0.003, treatment 737 of 6,953 (10.6%) cases, 1,669 of 13,906 (12.0%) controls, NNT 33, case control OR, PCR+, cohort 2.
Jabeen, 5/11/2022, prospective, Pakistan, peer-reviewed, 7 authors, dosage 200,000IU single dose.	risk of symptomatic case, 88.9% lower, RR 0.11, *p* = 0.11, treatment 0 of 20 (0.0%), control 4 of 20 (20.0%), NNT 5.0, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm).
Jimenez, 7/26/2021, retrospective, Spain, peer-reviewed, 21 authors, study period 12 March, 2020 - 21 May, 2020, dosage paricalcitol 0.9µg weekly.	risk of death, 50.1% lower, HR 0.50, *p* = 0.02, treatment 16 of 94 (17.0%), control 65 of 191 (34.0%), NNT 5.9, adjusted per study, paricalcitol treatment, multivariate Cox regression.
	risk of death, 50.7% lower, HR 0.49, *p* = 0.003, all vitamin D derivatives, univariate.
Jolliffe, 3/23/2022, Randomized Controlled Trial, United Kingdom, peer-reviewed, median age 60.2, 25 authors, study period December 2020 - June 2021, dosage 3,200IU daily, daily, trial NCT04579640 (history) (CORONAVIT).	risk of mechanical ventilation, 94.7% higher, RR 1.95, *p* = 1.00, treatment 1 of 1,515 (0.1%), control 1 of 2,949 (0.0%), 3200IU/day.
	risk of mechanical ventilation, 94.7% higher, RR 1.95, *p* = 1.00, treatment 1 of 1,515 (0.1%), control 1 of 2,949 (0.0%), 800IU/day.
	risk of hospitalization, 41.1% higher, RR 1.41, *p* = 0.16, treatment 29 of 1,515 (1.9%), control 40 of 2,949 (1.4%), 3200IU/day.
	risk of hospitalization, 16.8% higher, RR 1.17, *p* = 0.60, treatment 24 of 1,515 (1.6%), control 40 of 2,949 (1.4%), 800IU/day.

	risk of case, 8.8% higher, RR 1.09, *p* = 0.55, treatment 76 of 1,515 (5.0%), control 136 of 2,949 (4.6%), 3200IU/day.
	risk of case, 24.5% higher, RR 1.25, *p* = 0.11, treatment 87 of 1,515 (5.7%), control 136 of 2,949 (4.6%), 800IU/day.
	risk of case, 12.3% higher, RR 1.12, *p* = 0.56, treatment 45 of 1,515 (3.0%), control 78 of 2,949 (2.6%), confirmed, 3200IU/day.
	risk of case, 37.3% higher, RR 1.37, *p* = 0.08, treatment 55 of 1,515 (3.6%), control 78 of 2,949 (2.6%), confirmed, 800IU/day.
Junior, 2/17/2022, prospective, Brazil, peer-reviewed, 6 authors, dosage not specified, excluded in exclusion analyses: unadjusted results with no group details.	**risk of death, 22.1% lower, RR 0.78, *p* = 0.61**, treatment 8 of 113 (7.1%), control 8 of 88 (9.1%), NNT 50.
	risk of progression, 30.8% lower, RR 0.69, *p* = 0.26, treatment 16 of 113 (14.2%), control 18 of 88 (20.5%), NNT 16, respiratory failure.
Levitus, 5/3/2021, retrospective, USA, peer-reviewed, 9 authors, dosage varies.	**risk of severe case, 30.8% lower, RR 0.69, *p* = 0.25**, treatment 65, control 64, odds ratio converted to relative risk, ≥1,000IU, control prevalence approximated with overall prevalence.
	risk of severe case, 40.0% lower, RR 0.60, *p* = 0.15, treatment 65, control 64, odds ratio converted to relative risk, ≥5,000IU, control prevalence approximated with overall prevalence.
	risk of severe case, no change, RR 1.00, *p* = 0.92, treatment 65, control 64, odds ratio converted to relative risk, ≥50,000IU, control prevalence approximated with overall prevalence.
Levy, 1/31/2022, retrospective, Israel, peer-reviewed, 10 authors, dosage not specified.	**risk of death/hospitalization, 30.0% lower, HR 0.70, *p* = 0.05**, treatment 39 of 208 (18.8%), control 168 of 641 (26.2%), NNT 13, adjusted per study, multivariable, Cox proportional hazards, day 40.
Louca, 11/30/2020, retrospective, population-based cohort, United Kingdom, peer-reviewed, mean age 49.6, 26 authors, dosage not specified.	**risk of case, 7.5% lower, RR 0.92, *p* < 0.001**, odds ratio converted to relative risk, United Kingdom, all adjustment model.
Loucera, 4/29/2021, retrospective, propensity score matching, Spain, peer-reviewed, 11 authors, dosage varies (calcifediol).	**risk of death, 33.0% lower, HR 0.67, *p* = 0.009**, treatment 374, control 374, calcifediol, <15 days before hospitalization, Cox model with inverse propensity weighting.
	risk of death, 27.0% lower, HR 0.73, *p* = 0.02, treatment 439, control 439, calcifediol, <30 days before hospitalization, Cox model with inverse propensity weighting.
	risk of death, 25.0% lower, HR 0.75, *p* = 0.005, treatment 570, control 570, cholecalciferol, <15 days before hospitalization, Cox model with inverse propensity weighting.
	risk of death, 12.0% lower, HR 0.88, *p* = 0.11, treatment 802, control 802, cholecalciferol, <30 days before hospitalization, Cox model with inverse propensity weighting.

Lázaro, 9/5/2021, retrospective, Spain, preprint, 9 authors, dosage not specified, excluded in exclusion analyses: very few events; unadjusted results with no group details; minimal details provided.	risk of case, 26.8% lower, RR 0.73, $p = 1.00$, treatment 1 of 97 (1.0%), control 2 of 142 (1.4%), NNT 265.
Ma, 12/3/2021, retrospective, USA, peer-reviewed, 16 authors, study period May 2020 - March 2021, dosage varies.	risk of hospitalization, 49.0% lower, OR 0.51, $p = 0.04$, treatment 26,605, control 12,710, adjusted per study, supplementation ≥400 IU/day, model 3, supplemental table 3, multivariable, RR approximated with OR.
	risk of symptomatic case, 7.0% higher, OR 1.07, $p = 0.25$, treatment 7,895, control 31,420, adjusted per study, supplementation ≥2000 IU/day vs. <400 IU/day, model 3, supplemental table 3, multivariable, RR approximated with OR.
	risk of case, 17.0% lower, OR 0.83, $p = 0.07$, treatment 7,895, control 31,420, adjusted per study, supplementation ≥2000 IU/day vs. <400 IU/day, model 3, supplemental table 3, multivariable, RR approximated with OR.
Ma (B), 1/29/2021, retrospective, United Kingdom, peer-reviewed, 4 authors, dosage not specified.	risk of case, 30.0% lower, RR 0.70, $p = 0.03$, treatment 49 of 363 (13.5%), control 1,329 of 7,934 (16.8%), adjusted per study, odds ratio converted to relative risk.
Mahmood, 12/29/2021, retrospective, United Kingdom, peer-reviewed, 4 authors, study period 23 March, 2020 - 31 December, 2020, dosage varies, excluded in exclusion analyses: unadjusted results with no group details; substantial unadjusted confounding by indication likely.	risk of death, 9.4% lower, RR 0.91, $p = 0.67$, treatment 34 of 138 (24.6%), control 31 of 114 (27.2%), NNT 39, prescribed by GP.
Meltzer (C), 3/19/2021, retrospective, database analysis, USA, peer-reviewed, 6 authors, dosage not specified.	risk of case, 36.0% lower, RR 0.64, $p = 0.38$, treatment 6 of 131 (4.6%), control 239 of 3,338 (7.2%), NNT 39, >=2,000IU/d.
	risk of case, 31.1% lower, RR 0.69, $p = 0.16$, treatment 15 of 304 (4.9%), control 239 of 3,338 (7.2%), NNT 45, >=1,001IU/d.
	risk of case, 8.9% lower, RR 0.91, $p = 0.56$, treatment 60 of 920 (6.5%), control 239 of 3,338 (7.2%), NNT 157, >=1IU/d.
Mohseni, 8/4/2021, retrospective, Iran, peer-reviewed, 4 authors, dosage not specified, excluded in exclusion analyses: unadjusted results with no group details.	risk of case, 12.4% lower, RR 0.88, $p = 0.09$, treatment 99 of 192 (51.6%), control 242 of 411 (58.9%), NNT 14.
Nimer, 2/28/2022, retrospective, Jordan, peer-reviewed, survey, 4 authors, study period March 2021 - July 2021, dosage not specified.	risk of hospitalization, 33.3% lower, RR 0.67, $p = 0.001$, treatment 66 of 796 (8.3%), control 153 of 1,352 (11.3%), NNT 33, adjusted per study, odds ratio converted to relative risk, multivariable.
	risk of severe case, 29.0% lower, RR 0.71, $p = 0.01$, treatment 81 of 796 (10.2%), control 179 of 1,352 (13.2%), NNT 33, adjusted per study, odds ratio converted to relative risk, multivariable.

Oristrell, 7/17/2021, retrospective, population-based cohort, Spain, peer-reviewed, 8 authors, dosage varies (calcifediol).	**risk of death, 1.0% higher, RR 1.01, $p = 0.91$**, calcifediol, univariate.
	risk of death, 4.0% lower, RR 0.96, $p = 0.37$, cholecalciferol, univariate.
	risk of case, 1.0% lower, RR 0.99, $p = 0.65$, NNT 3499, calcifediol, univariate.
	risk of case, 5.0% lower, RR 0.95, $p = 0.004$, cholecalciferol, multivariate.
Oristrell (B), 4/6/2021, retrospective, Spain, peer-reviewed, 10 authors, dosage calcitriol 0.3µg daily, mean daily dose.	**risk of death, 43.0% lower, HR 0.57, $p = 0.001$**, treatment 2,296, control 3,407, multivariate, patients with CKD stages 4-5.
	risk of severe case, 43.0% lower, HR 0.57, $p < 0.001$, treatment 2,296, control 3,407, multivariate, patients with CKD stages 4-5.
	risk of case, 22.0% lower, HR 0.78, $p = 0.01$, treatment 163 of 2,296 (7.1%), control 326 of 3,407 (9.6%), NNT 40, multivariate, patients with CKD stages 4-5.
Parant, 4/14/2022, retrospective, France, peer-reviewed, median age 78.0, 12 authors, study period 1 March, 2020 - 30 June, 2020, dosage varies, trial NCT04877509 (history).	**risk of death, 50.5% lower, RR 0.50, $p = 0.11$**, treatment 7 of 66 (10.6%), control 28 of 162 (17.3%), adjusted per study, odds ratio converted to relative risk, multivariable.
	risk of ICU admission, 51.2% lower, RR 0.49, $p = 0.008$, treatment 10 of 66 (15.2%), control 74 of 162 (45.7%), NNT 3.3, adjusted per study, odds ratio converted to relative risk, multivariable.
	risk of severe case, 38.7% lower, RR 0.61, $p = 0.01$, treatment 19 of 66 (28.8%), control 86 of 162 (53.1%), NNT 4.1, adjusted per study, odds ratio converted to relative risk, multivariable.
Pecina, 8/27/2021, retrospective, USA, peer-reviewed, 4 authors, dosage not specified, excluded in exclusion analyses: unadjusted results with no group details.	**risk of death, 70.0% higher, OR 1.70, $p = 0.52$**, treatment 29, control 63, supplementation, unadjusted, RR approximated with OR.
	risk of mechanical ventilation, 10.0% higher, OR 1.10, $p = 0.89$, treatment 29, control 63, supplementation, unadjusted, RR approximated with OR.
	risk of ICU admission, 30.0% higher, OR 1.30, $p = 0.61$, treatment 29, control 63, supplementation, unadjusted, RR approximated with OR.
Regalia, 1/13/2022, retrospective, Italy, peer-reviewed, 10 authors, dosage varies.	**risk of case, 33.0% lower, OR 0.67, $p = 0.21$**, treatment 32 of 60 (53.3%) cases, 75 of 119 (63.0%) controls, NNT 11, case control OR, vitamin D supplementation for ≥3 months in the last year.
Sainz-Amo, 10/24/2020, retrospective, Spain, peer-reviewed, mean age 74.5, 13 authors, dosage not specified.	**risk of severe case, 32.7% lower, OR 0.67, $p = 0.45$**, treatment 5 of 29 (17.2%) cases, 43 of 182 (23.6%) controls, NNT 23, case control OR.

	risk of case, 43.7% lower, OR 0.56, p = 0.23, treatment 6 of 39 (15.4%) cases, 42 of 172 (24.4%) controls, NNT 13, case control OR.
Sharif, 11/26/2022, retrospective, Bangladesh, peer-reviewed, 14 authors, study period 13 December, 2020 - 4 February, 2021, dosage 2,000IU daily.	**risk of severe case, 28.0% lower, OR 0.72, p = 0.001**, adjusted per study, multivariable, RR approximated with OR.
	risk of severe case, 97.0% lower, OR 0.03, p = 0.005, adjusted per study, combined use of vitamin C, vitamin D, and zinc, multivariable, RR approximated with OR.
Shehab, 2/28/2022, retrospective, multiple countries, peer-reviewed, survey, 7 authors, study period September 2020 - March 2021, dosage not specified, excluded in exclusion analyses: unadjusted results with no group details.	**risk of severe case, 45.7% lower, RR 0.54, p = 0.20**, treatment 6 of 90 (6.7%), control 20 of 163 (12.3%), NNT 18, unadjusted, severe vs. mild cases.
Sinaci, 8/11/2021, retrospective, Turkey, peer-reviewed, 10 authors, dosage not specified.	**risk of severe case, 90.0% lower, RR 0.10, p = 0.35**, treatment 0 of 36 (0.0%), control 7 of 123 (5.7%), NNT 18, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), supplementation.
	risk of moderate/severe case, 18.8% higher, RR 1.19, p = 0.64, treatment 8 of 36 (22.2%), control 23 of 123 (18.7%), supplementation.
Subramanian, 1/31/2022, prospective, United Kingdom, peer-reviewed, 16 authors, dosage not specified.	**risk of death, 27.3% lower, RR 0.73, p = 0.12**, treatment 31 of 131 (23.7%), control 80 of 336 (23.8%), adjusted per study, odds ratio converted to relative risk, prescribed supplement use, multivariable.
Sulli (B), 2/24/2021, retrospective, Italy, peer-reviewed, 10 authors, dosage not specified.	**risk of case, 75.6% lower, OR 0.24, p < 0.001**, treatment 22 of 65 (33.8%) cases, 44 of 65 (67.7%) controls, NNT 3.0, case control OR, vitamin D supplementation.
Tylicki, 1/6/2022, retrospective, Poland, peer-reviewed, 10 authors, study period 6 October, 2020 - 28 February, 2021, dosage not specified.	**risk of death, 14.4% lower, RR 0.86, p = 0.61**, treatment 28 of 85 (32.9%), control 25 of 48 (52.1%), NNT 5.2, adjusted per study, odds ratio converted to relative risk, multivariable.
Ullah, 3/4/2021, retrospective, United Kingdom, peer-reviewed, 3 authors, dosage not specified, excluded in exclusion analyses: significant unadjusted confounding possible.	**risk of death, 42.1% higher, RR 1.42, p = 0.34**, treatment 21 of 64 (32.8%), control 26 of 135 (19.3%), adjusted per study, odds ratio converted to relative risk.
	risk of case, 146.0% higher, RR 2.46, p < 0.001, treatment 69 of 2,168 (3.2%), control 139 of 12,681 (1.1%), adjusted per study, odds ratio converted to relative risk.
van Helmond, 9/17/2022, prospective, USA, peer-reviewed, 14 authors, study period 27 October, 2020 - 31 January, 2021, dosage 5,000IU daily, trial NCT04596657 (history).	**risk of case, 97.5% lower, RR 0.02, p = 0.07**, treatment 0 of 255 (0.0%), control 36 of 2,827 (1.3%), NNT 79, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm).
Vasheghani (B), 1/18/2021, retrospective, Iran, preprint, 6 authors, dosage not specified.	**risk of death, 30.4% lower, RR 0.70, p = 0.45**, treatment 7 of 88 (8.0%), control 48 of 420 (11.4%), NNT 29, vitamin D supplementation.

	risk of ICU admission, 63.8% lower, RR 0.36, *p* = 0.009, treatment 13 of 185 (7.0%), control 53 of 323 (16.4%), NNT 11, adjusted per study, inverted to make RR<1 favor treatment, vitamin D levels >30ng/mL.
Villasis-Keever, 4/18/2022, Double Blind Randomized Controlled Trial, placebo-controlled, Mexico, peer-reviewed, 16 authors, study period 15 July, 2020 - 30 December, 2020, dosage 4,000IU daily.	risk of hospitalization, 66.5% lower, RR 0.33, *p* = 1.00, treatment 0 of 150 (0.0%), control 1 of 152 (0.7%), NNT 152, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), ITT.
	risk of case, 78.0% lower, RR 0.22, *p* = 0.001, treatment 7 of 150 (4.7%), control 26 of 152 (17.1%), NNT 8.0, adjusted per study, multivariable, Table 3.
Wang, 3/29/2023, Randomized Controlled Trial, China, preprint, median age 36.5, 23 authors, study period 18 December, 2022 - 20 February, 2023, dosage 200,000IU days 1, 14, trial NCT05673980 (history).	risk of progression, 25.2% lower, RR 0.75, *p* = 0.15, treatment 99, control 103, combined symptoms.
	risk of progression, 4.0% higher, RR 1.04, *p* = 1.00, treatment 5 of 99 (5.1%), control 5 of 103 (4.9%), risk of severe case, fever.
	risk of progression, 7.5% lower, RR 0.92, *p* = 1.00, treatment 8 of 99 (8.1%), control 9 of 103 (8.7%), NNT 152, risk of severe case, sore throat.
	risk of progression, 42.2% lower, RR 0.58, *p* = 0.41, treatment 5 of 99 (5.1%), control 9 of 103 (8.7%), NNT 27, risk of severe case, rhinorrhea or congestion.
	risk of progression, 66.2% lower, RR 0.34, *p* = 1.00, treatment 0 of 99 (0.0%), control 1 of 103 (1.0%), NNT 103, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), risk of severe case, diarrhea.
	risk of progression, 66.2% lower, RR 0.34, *p* = 1.00, treatment 0 of 99 (0.0%), control 1 of 103 (1.0%), NNT 103, relative risk is not 0 because of continuity correction due to zero events (with reciprocal of the contrasting arm), risk of severe case, vomiting.
	risk of progression, 13.3% lower, RR 0.87, *p* = 0.82, treatment 10 of 99 (10.1%), control 12 of 103 (11.7%), NNT 65, risk of severe case, cough.
	risk of progression, 48.0% lower, RR 0.52, *p* = 0.13, treatment 8 of 99 (8.1%), control 16 of 103 (15.5%), NNT 13, risk of severe case, muscle/joint aches.
	risk of progression, 56.1% higher, RR 1.56, *p* = 0.68, treatment 3 of 99 (3.0%), control 2 of 103 (1.9%), risk of severe case, taste/smell.
	risk of case, 9.0% lower, RR 0.91, *p* = 0.57, treatment 49 of 99 (49.5%), control 56 of 103 (54.4%), NNT 21.
	risk of case, 12.3% higher, RR 1.12, *p* = 0.56, treatment 41 of 99 (41.4%), control 38 of 103 (36.9%), first two weeks.

	risk of case, 53.8% lower, RR 0.46, p = 0.06, treatment 8 of 99 (8.1%), control 18 of 103 (17.5%), NNT 11, last two weeks.
Ünsal (B), 4/5/2021, retrospective, Turkey, peer-reviewed, 10 authors, dosage varies.	risk of pneumonia, 71.4% lower, RR 0.29, p = 0.009, treatment 4 of 28 (14.3%), control 14 of 28 (50.0%), NNT 2.8, average 800-1000IU/day cholecalciferol.
Şengül, 12/31/2022, retrospective, Turkey, peer-reviewed, 4 authors, study period March 2020 - December 2021, dosage not specified.	risk of case, 68.5% lower, OR 0.31, p = 0.004, treatment 8 of 54 (14.8%) cases, 94 of 264 (35.6%) controls, NNT 7.4, case control OR.

Footnotes

a. Viral infection and replication involves attachment, entry, uncoating and release, genome replication and transcription, translation and protein processing, assembly and budding, and release. Each step can be disrupted by therapeutics.

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