Vitamin D for COVID-19: real-time meta analysis of 89 treatment and 137 sufficiency studies

Covid Analysis, Sep 11, 2022, Version 191

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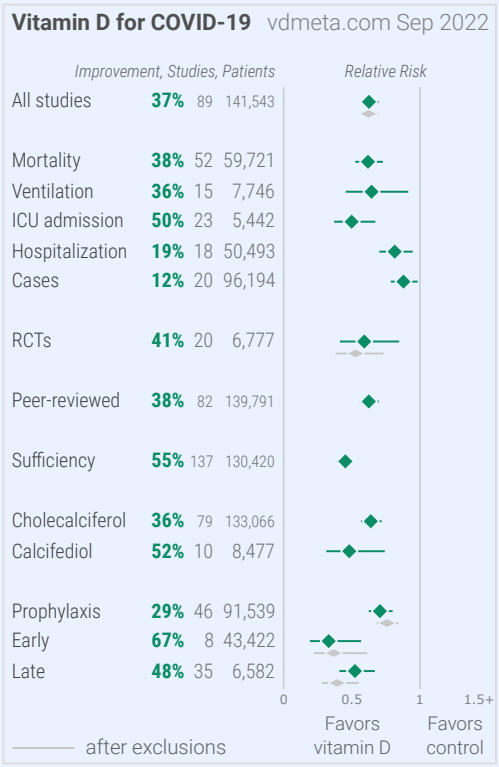
- Statistically significant improvements are seen in treatment studies for mortality, ventilation, ICU admission, hospitalization, and cases. 43 studies from 40 independent teams in 18 different countries show statistically significant improvements in isolation (29 for the most serious outcome).
- Random effects meta-analysis with pooled effects using the most serious outcome reported shows 67% [43-81%] and 37% [30-44%] improvement for early treatment and for all studies. Results are similar after restriction to 82 peer-reviewed studies: 63% [39-78%] and 38% [30-44%], and for the 52 mortality results: 68% [39-84%] and 38% [27-48%].
- Acute treatment (early 67% [43-81%], late 48% [33-59%]) shows greater efficacy than chronic prophylaxis (29% [20-38%]), suggesting that long-term supplementation may not be ideal.
- Late stage treatment with calcifediol/calcitriol shows greater improvement compared to cholecalciferol: 73% [57-83%] vs. 40% [24-53%].



- Sufficiency studies show a strong association between vitamin D sufficiency and outcomes. Meta analysis of the 137 studies using the most serious outcome reported shows 55% [50-59%] improvement.
- While many treatments have some level of efficacy, they do not replace vaccines and other measures to avoid infection. Only 13% of vitamin D treatment studies show zero events in the treatment arm.
- No treatment, vaccine, or intervention is 100% available and effective for all variants. All practical, effective, and safe means should be used. Denying the efficacy of treatments increases mortality, morbidity, collateral damage, and endemic risk.
- All data to reproduce this paper and the sources are in the appendix.

	Improvement	Studies	Authors	Patients
Treatment RCTs	**41%** [15-59%]	20	247	6,777
Treatment studies	**37%** [30-44%]	89	909	141,543
Cholecalciferol treatment	**36%** [28-43%]	79	787	133,066
Calcifediol/calcitriol treatment	**52%** [26-69%]	10	122	8,477

Treatment mortality	**38%** [27-48%]	52	499	59,721
Sufficiency studies	**55%** [50-59%]	137	1,210	130,420

HIGHLIGHTS

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

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

Real-time updates and corrections, transparent analysis with all results in the same format, consistent protocol for 46 treatments.

All 89 vitamin D COVID-19 treatment studies

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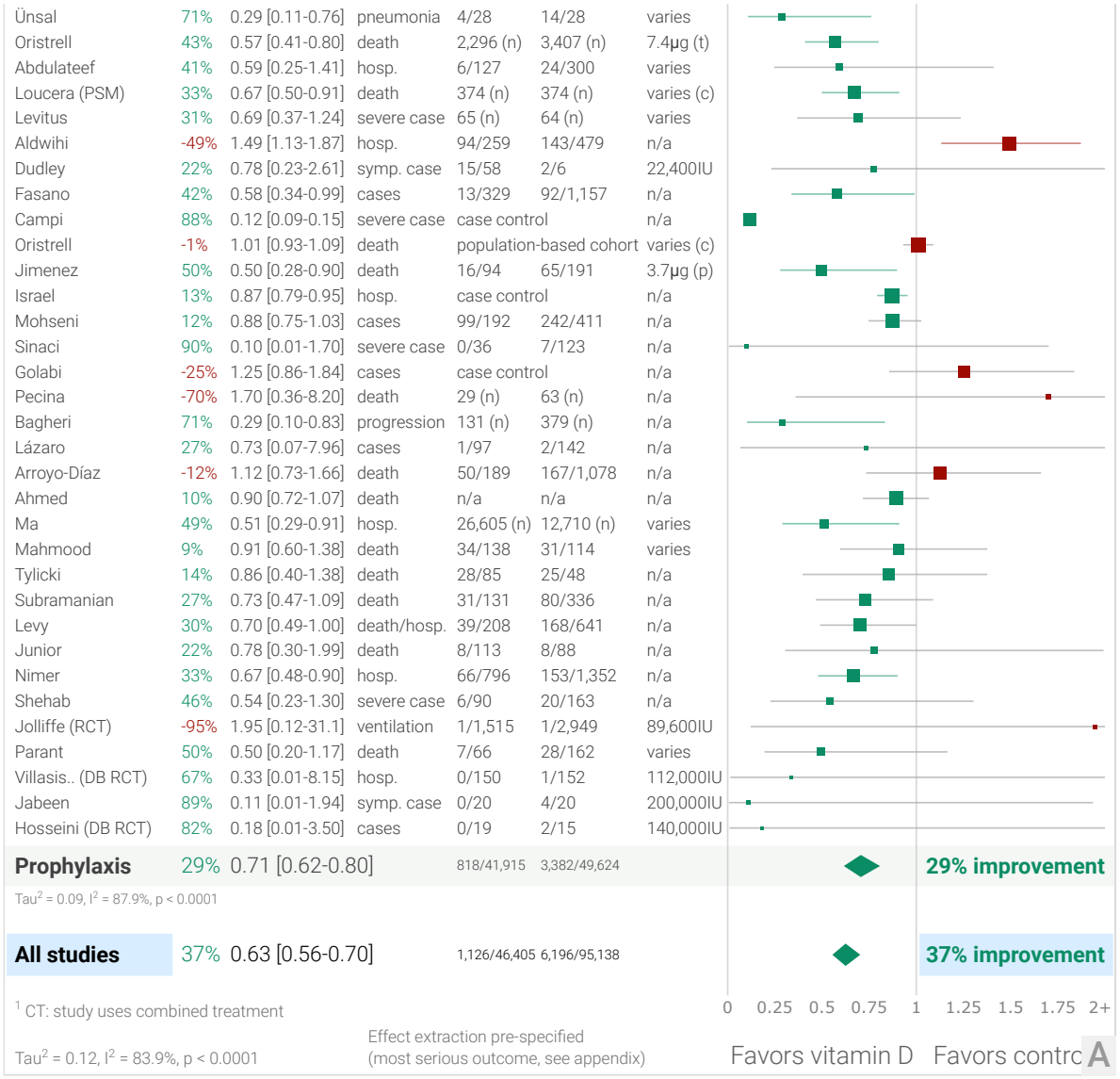
	Improvement	RR [CI]		Treatment	Control	Dose (5d)	
Annweiler	89%	0.11 [0.03-0.48]	death	10/57	5/9	80,000IU	
Annweiler	63%	0.37 [0.06-2.21]	death	3/16	10/32	80,000IU	
Burahee	93%	0.07 [0.00-1.06]	death	0/12	2/2	400,000IU	
Asimi	97%	0.03 [0.00-0.44]	ventilation	0/270	9/86	10,000IU	CT[1]
Sánchez-Zuno (RCT)	89%	0.11 [0.01-1.86]	severe case	0/22	4/20	50,000IU	
Efird	49%	0.51 [0.23-1.17]	death	11/544	413/15,794	varies	
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	
Early treatment	67%	0.33 [0.19-0.57]		77/1,965	2,027/41,457		**67% improvement**

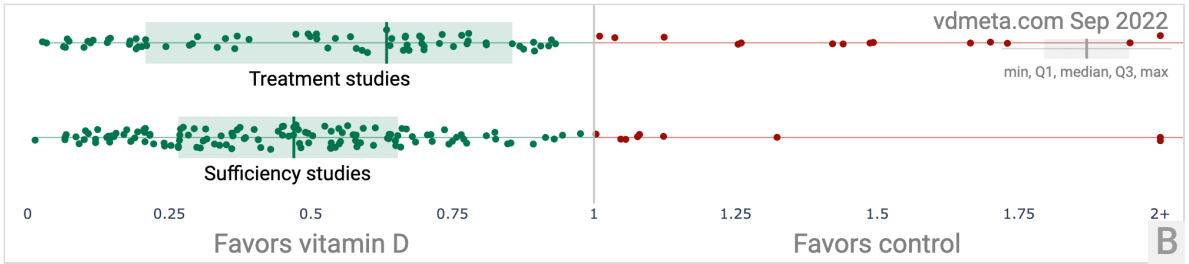
Tau^2 = 0.30, I^2 = 67.4%, p < 0.0001

	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)	
Rastogi (RCT)	53%	0.47 [0.24-0.92]	viral+	6/16	19/24	300,000IU	
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 [0.03-1.37]	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)	
Cannata-An.. (RCT)	-44%	1.44 [0.76-2.72]	death	22/274	15/269	100,000IU	
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	
Baykal	22%	0.78 [0.41-1.47]	death	7/18	28/56	300,000IU	
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	
Lakkireddy (RCT)	61%	0.39 [0.08-1.91]	death	2/44	5/43	300,000IU	see notes
Hafez	94%	0.06 [0.00-0.96]	death	0/7	12/30	150,000IU	
Sharif-Askari (ICU)	36%	0.64 [0.46-0.90]	ICU	20 (n)	25 (n)	50,000IU	ICU patients
Late treatment	48%	0.52 [0.41-0.67]		231/2,525	787/4,057		**48% improvement**

Tau^2 = 0.25, I^2 = 63.3%, 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
Ullah	-42%	1.42 [0.74-2.37]	death	21/64	26/135	n/a
Meltzer	36%	0.64 [0.29-1.41]	cases	6/131	239/3,338	n/a
Holt	7%	0.93 [0.76-1.15]	cases	141/5,640	305/9,587	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)
Abdulateef 41% 0.59 [0.25-1.41] hosp. 6/127 24/300 varies
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
Campi 88% 0.12 [0.09-0.15] severe case case control 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
Mohseni 12% 0.88 [0.75-1.03] cases 99/192 242/411 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
Pecina -70% 1.70 [0.36-8.20] death 29 (n) 63 (n) n/a
Bagheri 71% 0.29 [0.10-0.83] progression 131 (n) 379 (n) n/a
Lázaro 27% 0.73 [0.07-7.96] cases 1/97 2/142 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
Ma 49% 0.51 [0.29-0.91] hosp. 26,605 (n) 12,710 (n) varies
Mahmood 9% 0.91 [0.60-1.38] death 34/138 31/114 varies
Tylicki 14% 0.86 [0.40-1.38] death 28/85 25/48 n/a
Subramanian 27% 0.73 [0.47-1.09] death 31/131 80/336 n/a
Levy 30% 0.70 [0.49-1.00] death/hosp. 39/208 168/641 n/a
Junior 22% 0.78 [0.30-1.99] death 8/113 8/88 n/a
Nimer 33% 0.67 [0.48-0.90] hosp. 66/796 153/1,352 n/a
Shehab 46% 0.54 [0.23-1.30] severe case 6/90 20/163 n/a
Jolliffe (RCT) -95% 1.95 [0.12-31.1] ventilation 1/1,515 1/2,949 89,600IU
Parant 50% 0.50 [0.20-1.17] death 7/66 28/162 varies
Villasis.. (DB RCT) 67% 0.33 [0.01-8.15] hosp. 0/150 1/152 112,000IU
Jabeen 89% 0.11 [0.01-1.94] symp. case 0/20 4/20 200,000IU
Hosseini (DB RCT) 82% 0.18 [0.01-3.50] cases 0/19 2/15 140,000IU
Prophylaxis 29% 0.71 [0.62-0.80] 818/41,915 3,382/49,624 29% improvement
Tau² = 0.09, I² = 87.9%, p < 0.0001
All studies 37% 0.63 [0.56-0.70] 1,126/46,405 6,196/95,138 37% improvement
[1] CT: study uses combined treatment
Tau² = 0.12, I² = 83.9%, p < 0.0001
Effect extraction pre-specified
(most serious outcome, see appendix)
0 0.25 0.5 0.75 1 1.25 1.5 1.75 2+
Favors vitamin D
Favors contrc
A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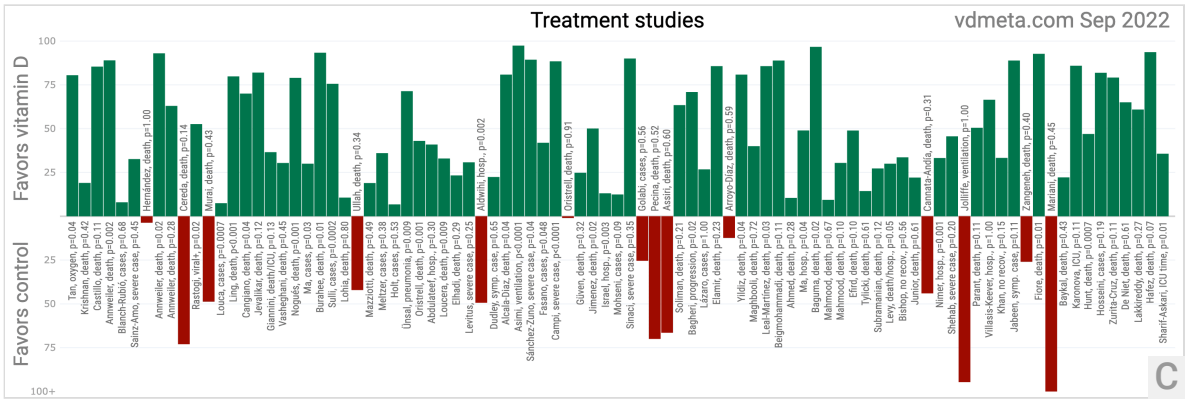
min, Q1, median, Q3, max
Treatment studies
Sufficiency studies
0 0.25 0.5 0.75 1 1.25 1.5 1.75 2+
Favors vitamin D
Favors control
B



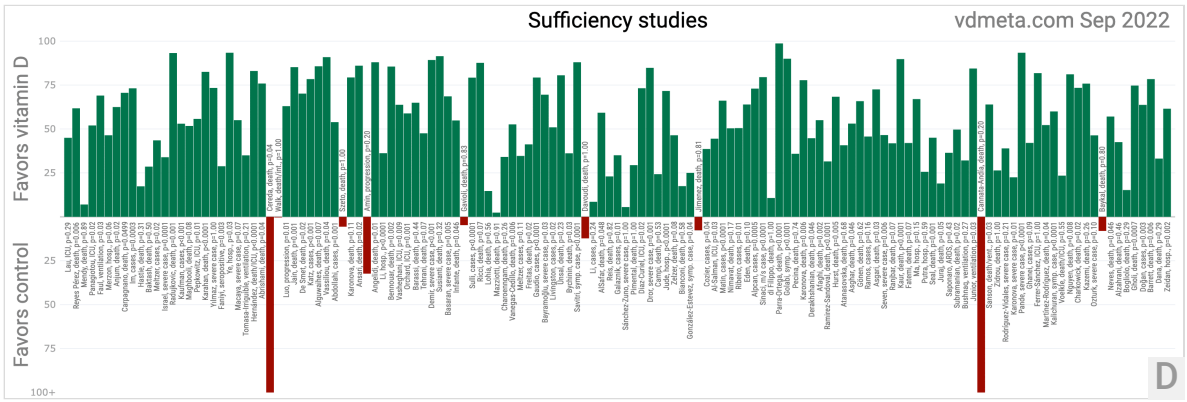


Figure 1. *A. Random effects meta-analysis of treatment studies. This plot shows pooled effects, analysis for individual outcomes is below, and more details on pooled effects can be found in the heterogeneity section. Effect extraction is pre-specified, using the most serious outcome reported. Simplified 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.*** *Scatter plot showing the distribution of effects reported in serum level analysis (sufficiency) studies and treatment studies (the vertical lines and shaded boxes show the median and interquartile range).* ***C and D.*** *Chronological history of all reported effects for treatment studies and sufficiency studies.*

Introduction

We analyze all significant studies regarding vitamin D and 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 present random-effects meta-analysis results for studies analyzing outcomes based on sufficiency, for all treatment studies, for mortality results only, and for treatment studies within each treatment stage.

Vitamin D. Vitamin D undergoes two conversion steps before reaching the biologically active form as shown in Figure 2. 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. 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]*** show a strong association between pre-operative vitamin D levels and hospital-acquired infections, as shown in Figure 3. There is a significant delay involved in the conversion from cholecalciferol, therefore calcifediol (calcidiol) or calcitriol may be preferable for treatment.

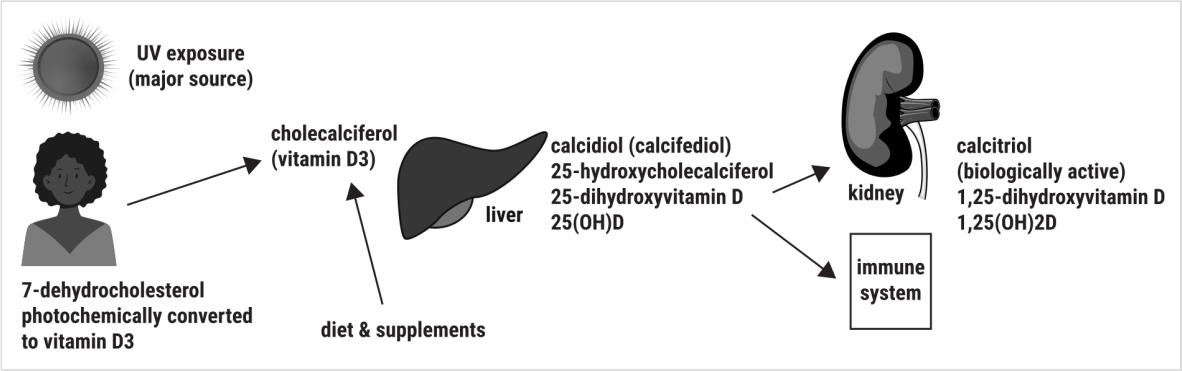


Figure 2. *Simplified view of vitamin D sources and conversion.*

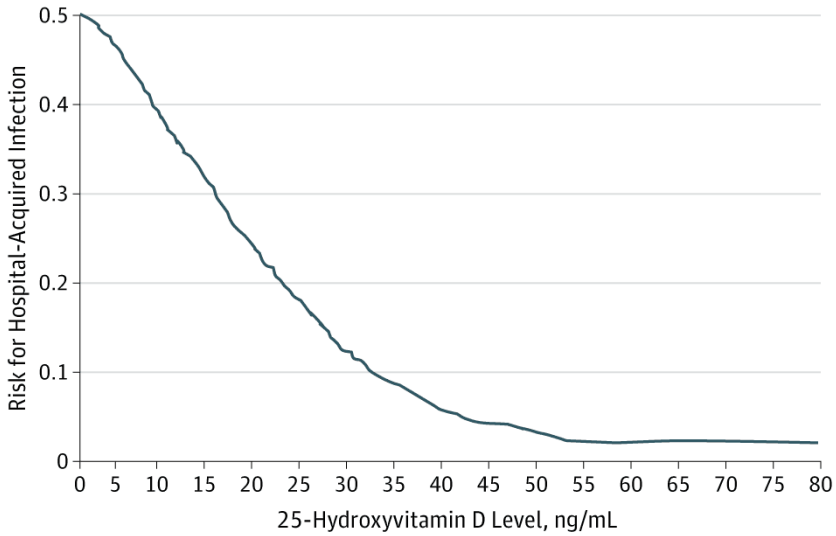


Figure 3. *Risk of hospital-acquired infections as a function of pre-operative vitamin D levels, from* ***[Quraishi]****.*

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. A few 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). A few studies show the average vitamin D level for patients in different groups ***[Al-Daghri, Alarslan, Azadeh, Chodick, D'Avolio, Desai, Ersöz, Jabbar, Kerget, Latifi-Pupovci, Mardani, Ranjbar, Saeed, 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.

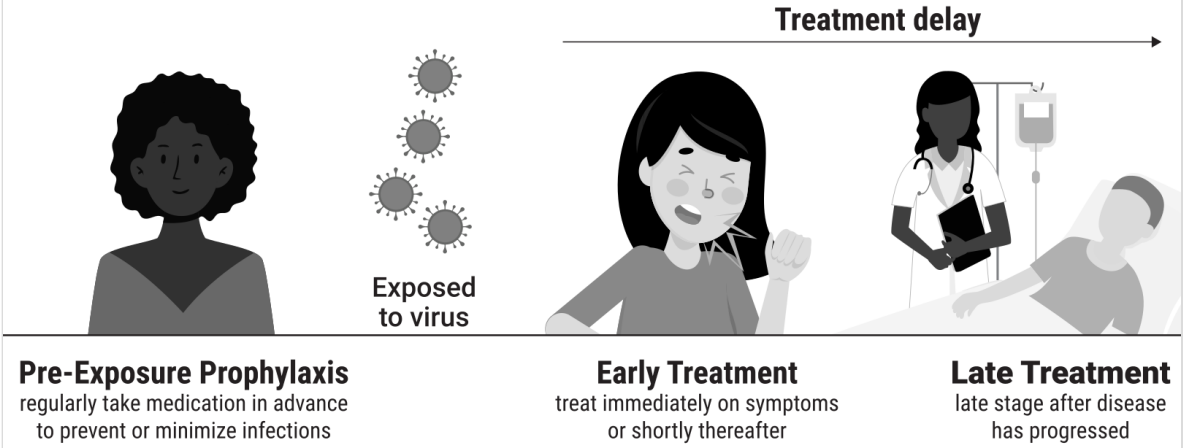


Figure 4. *Treatment stages.*

Preclinical Research

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

2 *In Vitro* studies support the efficacy of vitamin D ***[Mok, Pickard]***.

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

Figure 5 shows a visual overview of the results. Figure 1 shows a forest plot for all treatment studies, and the effects reported in sufficiency studies and treatment studies. Figure 6 and 7 show results by treatment stage. Figure 8 shows a forest plot for random effects meta-analysis of sufficiency studies, while Figure 9, 10, 11, 12, 13, 14, 15, 16, and 17 show forest plots for all treatment studies with pooled effects, cholecalciferol studies, calcifediol/calcitriol studies, and for studies reporting mortality, mechanical ventilation, ICU admission, hospitalization, and case results only. Table 1 summarizes the results.

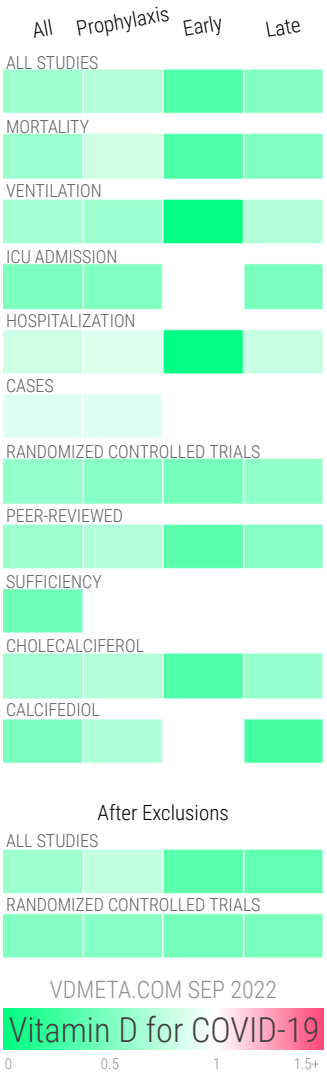


Figure 5. *Overview of results.*

Study type	Number of studies reporting positive results	Total number of studies	Percentage of studies reporting positive results	Random effects meta-analysis results
Analysis of outcomes based on sufficiency	128	137	**93.4%**	**55%** improvement RR 0.45 [0.41-0.50] p < 0.0001
Early treatment	8	8	**100%**	**67%** improvement RR 0.33 [0.19-0.57] p < 0.0001
Late treatment	30	35	85.7%	48% improvement RR 0.52 [0.41-0.67] p < 0.0001
Prophylaxis	37	46	80.4%	29% improvement RR 0.71 [0.62-0.80] p < 0.0001
All treatment studies	75	89	84.3%	37% improvement RR 0.63 [0.56-0.70] p < 0.0001

Table 1. *Results.*

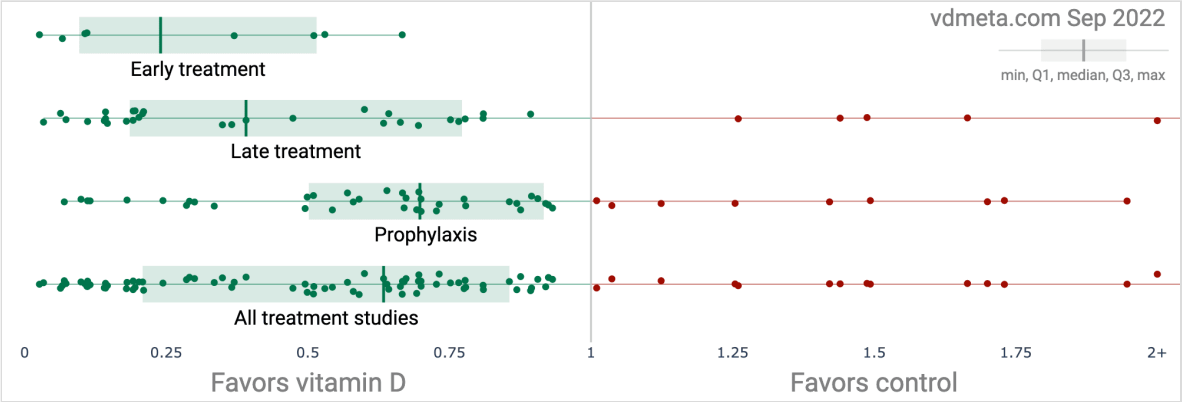


Figure 6. *Results by treatment stage.*

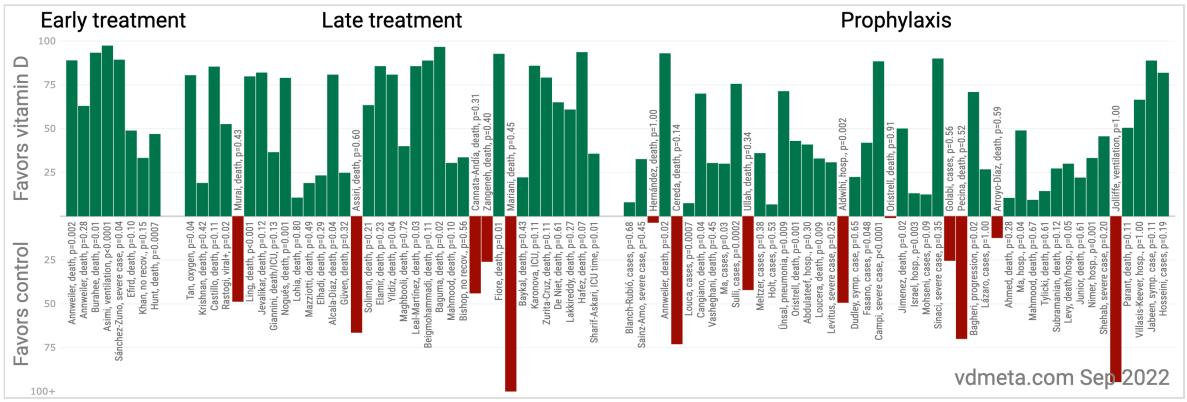


Figure 7. *Results by treatment stage.*

All 137 vitamin D COVID-19 sufficiency studies

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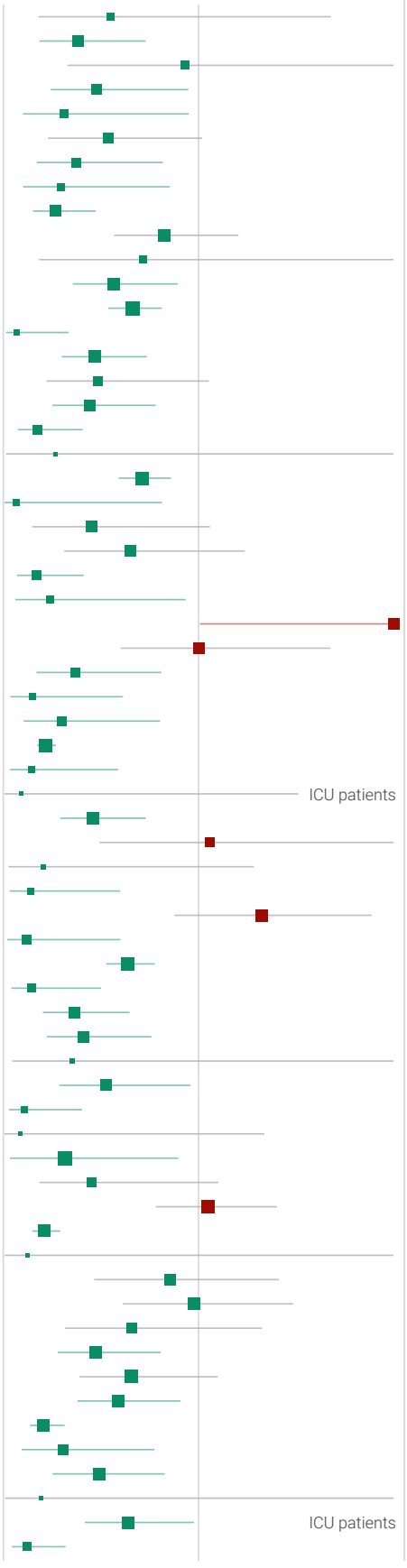
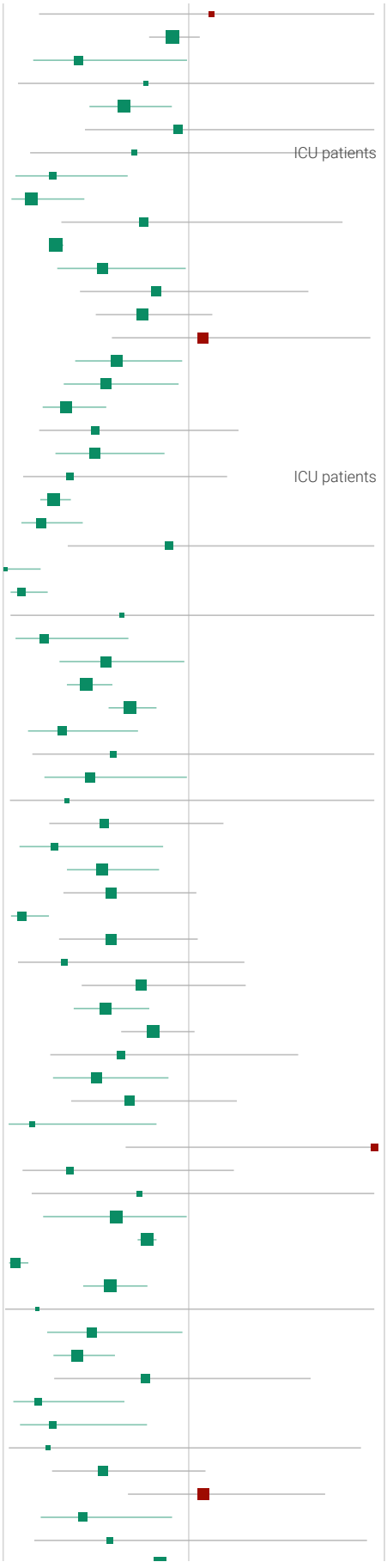
	Improvement	RR [CI]		High Levels	Low Levels
Lau	45%	0.55 [0.18-1.68]	ICU	2/5	11/15
Reyes Pérez	62%	0.38 [0.18-0.73]	death	21/137	14/35
Mendy	7%	0.93 [0.33-2.47]	death	21/600	5/89
Panagiotou	52%	0.48 [0.24-0.95]	ICU	8/44	34/90
Faul	69%	0.31 [0.10-0.95]	ventilation	4/21	8/12
Merzon	46%	0.54 [0.23-1.02]	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 [0.15-0.47]	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
Israel	34%	0.66 [0.54-0.81]	severe case	case control	
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 [0.01-1.51]	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 [0.29-0.96]	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 [0.19-1.10]	death	4/19	55/118
Gavioli	-5%	1.05 [0.78-1.40]	death	80/260	52/177
Sulli	79%	0.21 [0.15-0.29]	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 [0.14-0.31]	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	ICU patients
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	
Zelzer	46%	0.54 [0.29-0.98]	death	24/121	10/27	
Bianconi	18%	0.82 [0.41-1.65]	death	94 (n)	106 (n)	
González-Estevez	25%	0.75 [0.50-1.13]	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	ICU patients
Alpcan	73%	0.27 [0.20-0.36]	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	
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	
Derakhshanian	45%	0.55 [0.30-0.98]	death	148 (n)	142 (n)	
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 [0.42-1.31]	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	
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 [0.10-1.24]	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 [0.43-0.78]	cases	case control		
Ferrer-Sánchez	82%	0.18 [0.01-3.14]	ICU	0/9	4/73	
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)	



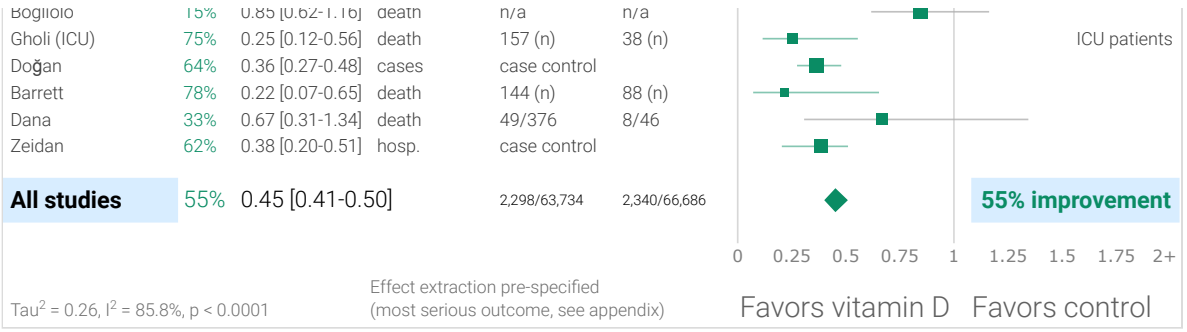


Figure 8. *Random effects meta-analysis for sufficiency studies. This plot pools studies with different effects, different vitamin D cutoff levels and measurement times, and studies may be within hospitalized patients, excluding the risk of hospitalization. However, the prevalence of positive effects is notable.*

All 89 vitamin D COVID-19 treatment studies

vdmeta.com Sep 2022

	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 [0.00-1.06]	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 [0.01-1.86]	severe case	0/22	4/20	50,000IU	
Efird	49%	0.51 [0.23-1.17]	death	11/544	413/15,794	varies	
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	
Early treatment	67%	0.33 [0.19-0.57]		77/1,965	2,027/41,457		**67% improvement**

Tau^2 = 0.30, I^2 = 67.4%, 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)	
Rastogi (RCT)	53%	0.47 [0.24-0.92]	viral+	6/16	19/24	300,000IU	
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 [0.03-1.37]	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)	
Cannata-An.. (RCT)	-44%	1.44 [0.76-2.72]	death	22/274	15/269	100,000IU	
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	
Baykal	22%	0.78 [0.41-1.47]	death	7/18	28/56	300,000IU	
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	
Lakkireddy (RCT)	61%	0.39 [0.08-1.91]	death	2/44	5/43	300,000IU	see notes
Hafez	94%	0.06 [0.00-0.96]	death	0/7	12/30	150,000IU	
Sharif-Askari (ICU)	36%	0.64 [0.46-0.90]	ICU	20 (n)	25 (n)	50,000IU	ICU patients
Late treatment	48%	0.52 [0.41-0.67]		231/2,525	787/4,057		**48% improvement**

Tau^2 = 0.25, I^2 = 63.3%, 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
Ullah	-42%	1.42 [0.74-2.37]	death	21/64	26/135	n/a
Meltzer	36%	0.64 [0.29-1.41]	cases	6/131	239/3,338	n/a
Holt	7%	0.93 [0.76-1.15]	cases	141/5,640	305/9,587	n/a

Figure 9. *Random effects meta-analysis for treatment studies. Effect extraction is pre-specified, using the most serious outcome reported, see the appendix for details.*

All 82 vitamin D COVID-19 peer reviewed trials

vdmeta.com Sep 2022

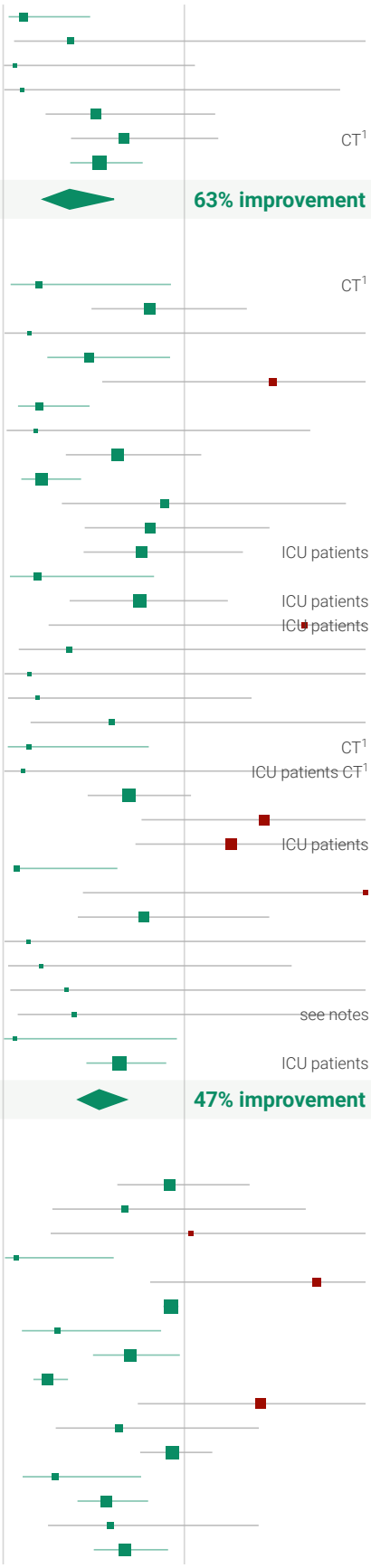
	Improvement	RR [CI]		Treatment	Control	Dose (5d)	
Annweiler	89%	0.11 [0.03-0.48]	death	10/57	5/9	80,000IU	
Annweiler	63%	0.37 [0.06-2.21]	death	3/16	10/32	80,000IU	
Burahee	93%	0.07 [0.00-1.06]	death	0/12	2/2	400,000IU	
Sánchez-Zuno (RCT)	89%	0.11 [0.01-1.86]	severe case	0/22	4/20	50,000IU	
Efird	49%	0.51 [0.23-1.17]	death	11/544	413/15,794	varies	
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	
Early treatment	63%	0.37 [0.22-0.61]		77/1,695	2,018/41,371		**63% improvement**

Tau² = 0.25, I² = 65.8%, p = 0.00014

	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)	
Rastogi (RCT)	53%	0.47 [0.24-0.92]	viral+	6/16	19/24	300,000IU	
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 [0.03-1.37]	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	
Cannata-An.. (RCT)	-44%	1.44 [0.76-2.72]	death	22/274	15/269	100,000IU	
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	
Baykal	22%	0.78 [0.41-1.47]	death	7/18	28/56	300,000IU	
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	
Lakkireddy (RCT)	61%	0.39 [0.08-1.91]	death	2/44	5/43	300,000IU	see notes
Hafez	94%	0.06 [0.00-0.96]	death	0/7	12/30	150,000IU	
Sharif-Askari (ICU)	36%	0.64 [0.46-0.90]	ICU	20 (n)	25 (n)	50,000IU	ICU patients
Late treatment	47%	0.53 [0.41-0.68]		226/2,437	779/3,530		**47% improvement**

Tau² = 0.25, I² = 63.8%, 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
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
Ullah	-42%	1.42 [0.74-2.37]	death	21/64	26/135	n/a
Meltzer	36%	0.64 [0.29-1.41]	cases	6/131	239/3,338	n/a
Holt	7%	0.93 [0.76-1.15]	cases	141/5,640	305/9,587	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)
Abdulateef	41%	0.59 [0.25-1.41]	hosp.	6/127	24/300	varies
Loucera (PSM)	33%	0.67 [0.50-0.91]	death	374 (n)	374 (n)	varies (c)



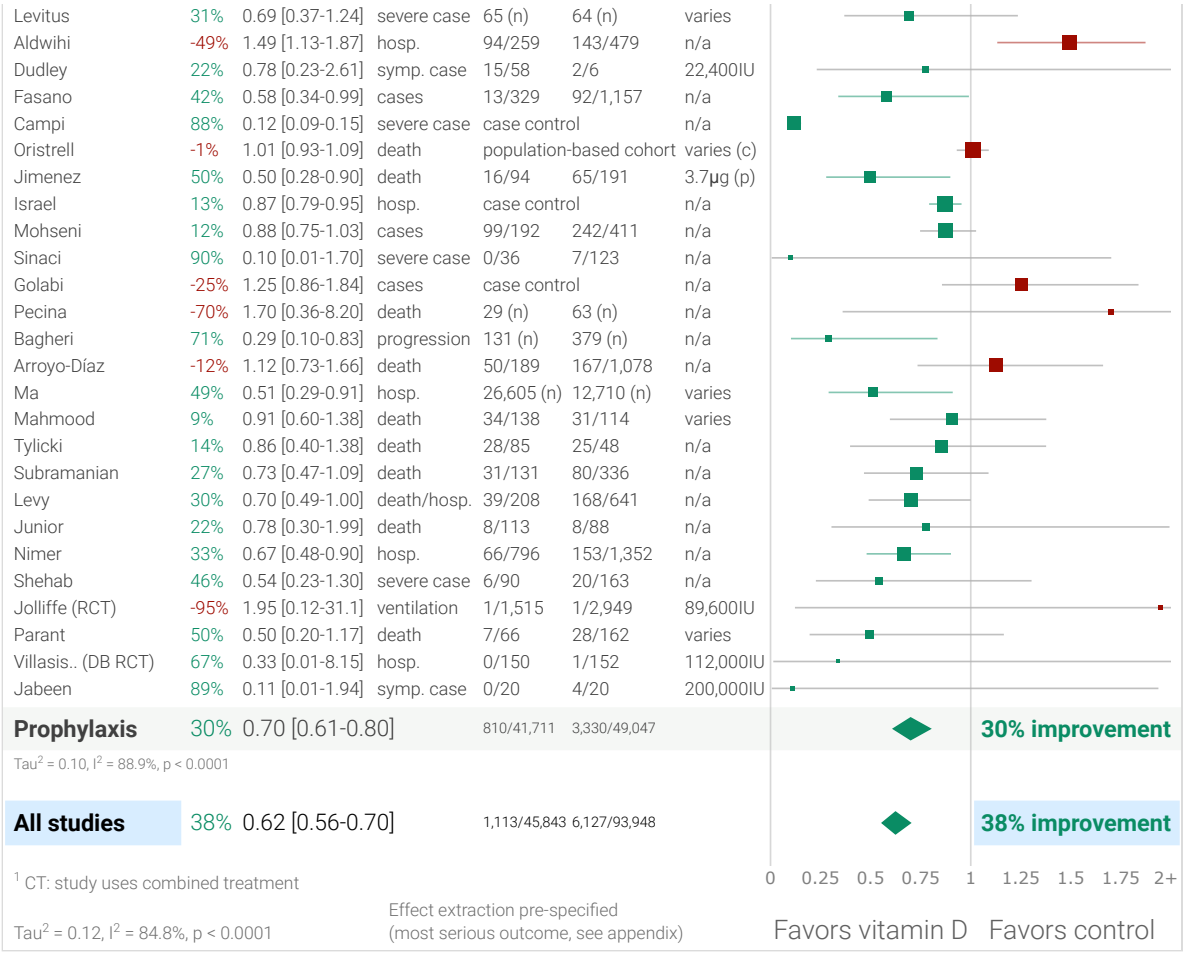


Figure 10. *Random effects meta-analysis for peer-reviewed treatment studies.* ***[Zeraatkar]*** *analyze 356 COVID-19 trials, finding no significant evidence that peer-reviewed studies are more trustworthy. They also show extremely slow review times during a pandemic. Authors recommend using preprint evidence, with appropriate checks for potential falsified data, which provides higher certainty much earlier. Effect extraction is pre-specified, using the most serious outcome reported, see the appendix for details.*

All 79 cholecalciferol COVID-19 studies

vdmeta.com Sep 2022

	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 [0.00-1.06]	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 [0.01-1.86]	severe case	0/22	4/20	50,000IU	
Efird	49%	0.51 [0.23-1.17]	death	11/544	413/15,794	varies	
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	
Early treatment	67%	0.33 [0.19-0.57]		77/1,965	2,027/41,457		**67% improvement**

$Tau^2 = 0.30$, $I^2 = 67.4\%$, $p < 0.0001$

	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	
Rastogi (RCT)	53%	0.47 [0.24-0.92]	viral+	6/16	19/24	300,000IU	
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	
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
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	
Yildiz	81%	0.19 [0.03-1.37]	death	1/37	24/170	300,000IU	
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	
Cannata-An.. (RCT)	-44%	1.44 [0.76-2.72]	death	22/274	15/269	100,000IU	
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	
Baykal	22%	0.78 [0.41-1.47]	death	7/18	28/56	300,000IU	
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	
Lakkireddy (RCT)	61%	0.39 [0.08-1.91]	death	2/44	5/43	300,000IU	see notes
Hafez	94%	0.06 [0.00-0.96]	death	0/7	12/30	150,000IU	
Sharif-Askari (ICU)	36%	0.64 [0.46-0.90]	ICU	20 (n)	25 (n)	50,000IU	ICU patients
Late treatment	40%	0.60 [0.47-0.76]		198/1,806	617/3,035		**40% improvement**

$Tau^2 = 0.17$, $I^2 = 55.8\%$, $p < 0.0001$

	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
Ullah	-42%	1.42 [0.74-2.37]	death	21/64	26/135	n/a
Meltzer	36%	0.64 [0.29-1.41]	cases	6/131	239/3,338	n/a
Holt	7%	0.93 [0.76-1.15]	cases	141/5,640	305/9,587	n/a
Ünsal	71%	0.29 [0.11-0.76]	pneumonia	4/28	14/28	varies
Abdulateef	41%	0.59 [0.25-1.41]	hosp.	6/127	24/300	varies
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

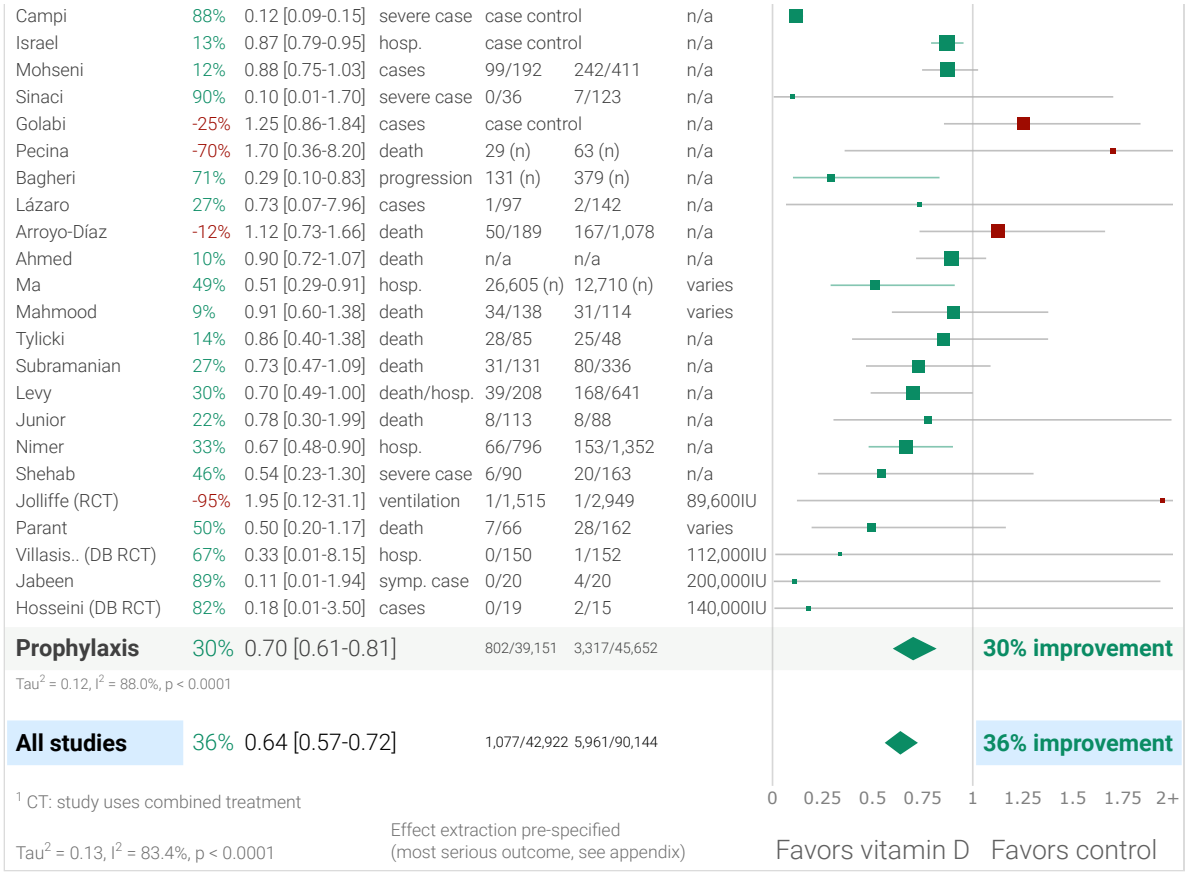


Figure 11. *Random effects meta-analysis for cholecalciferol treatment studies. Effect extraction is pre-specified, using the most serious outcome reported, see the appendix for details.*

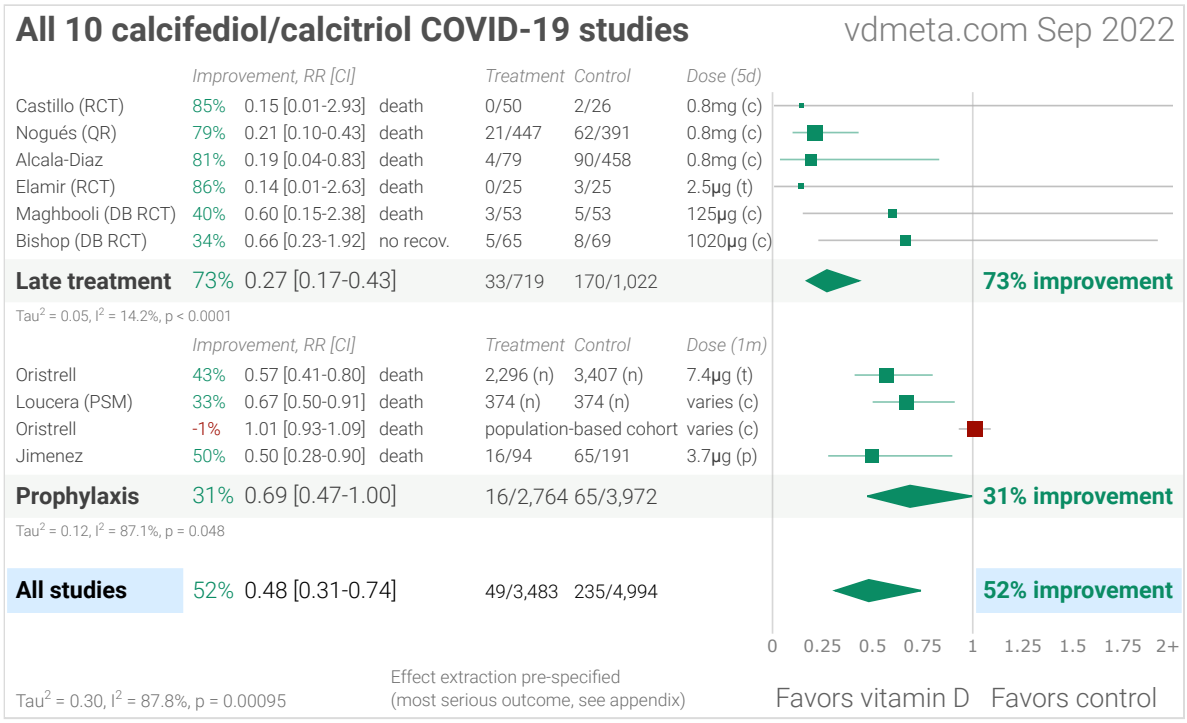


Figure 12. *Random effects meta-analysis for calcifediol/calcitriol treatment studies. Effect extraction is pre-specified, using the most serious outcome reported, see the appendix for details.*

All 52 vitamin D COVID-19 treatment mortality results vdmeta.com Sep 2022

	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 [0.00-1.06]	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% improvement**

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

	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)	
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 [0.03-1.37]	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	
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	
Baykal	22% 0.78 [0.41-1.47]	7/18	28/56	300,000IU	
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	
Lakkireddy (RCT)	61% 0.39 [0.08-1.91]	2/44	5/43	300,000IU	see notes
Hafez	94% 0.06 [0.00-0.96]	0/7	12/30	150,000IU	
Late treatment	49% 0.51 [0.38-0.70]	203/2,315	712/3,804		**49% improvement**

$Tau^2 = 0.35$, $I^2 = 67.6\%$, $p < 0.0001$

	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	
Junior	22% 0.78 [0.30-1.99]	8/113	8/88	n/a	
Parant	50% 0.50 [0.20-1.17]	7/66	28/162	varies	
Prophylaxis	19% 0.81 [0.68-0.96]	216/3,753	587/6,875		**19% improvement**

$Tau^2 = 0.06$, $I^2 = 68.8\%$, $p = 0.014$

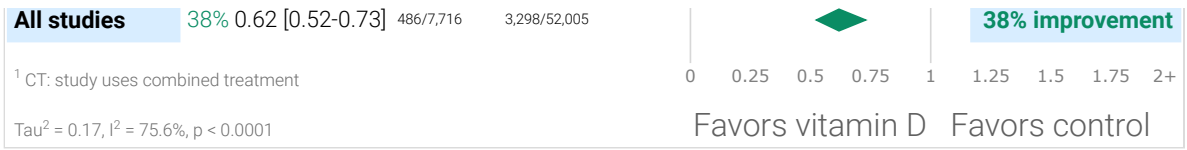


Figure 13. *Random effects meta-analysis for treatment mortality results only.*

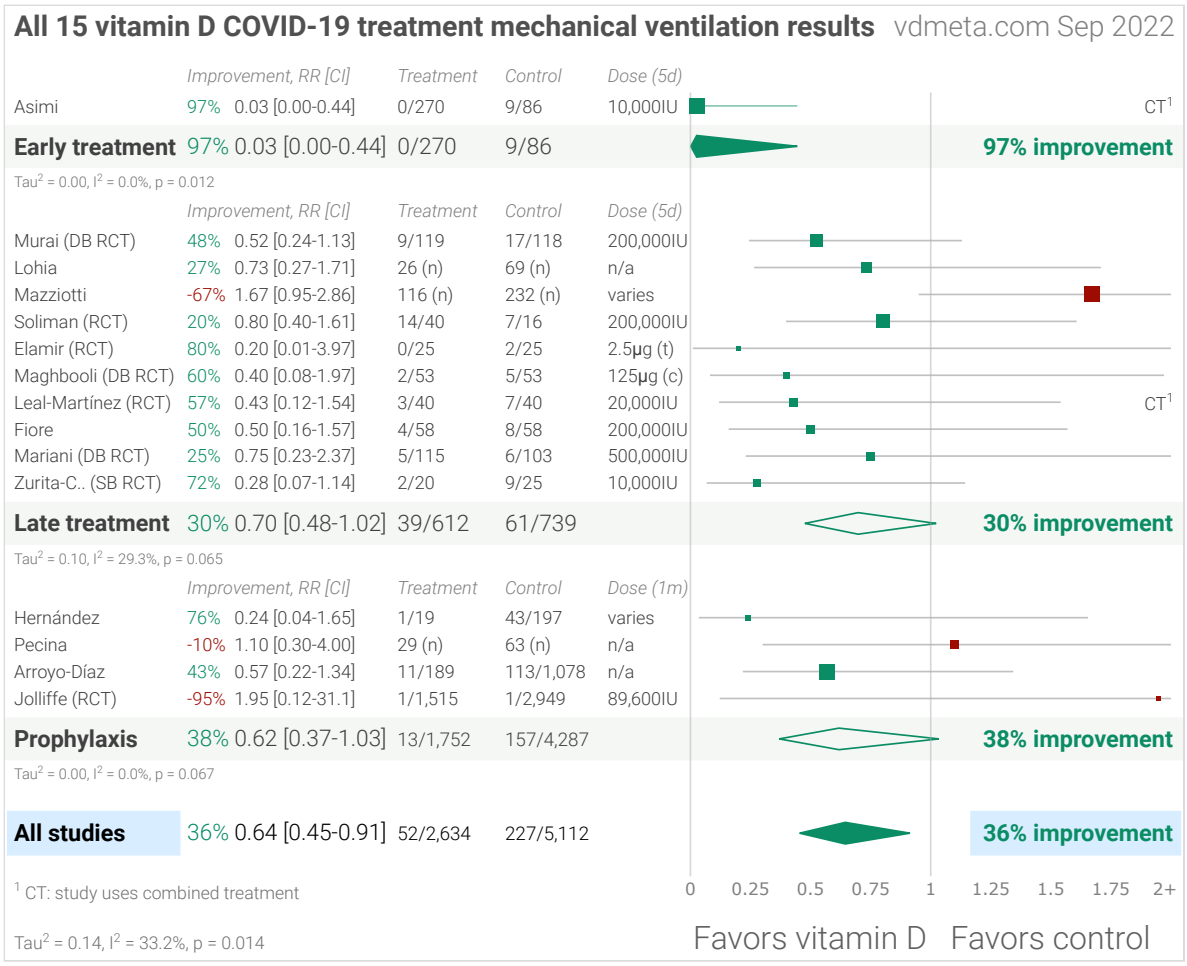


Figure 14. *Random effects meta-analysis for treatment mechanical ventilation results only.*

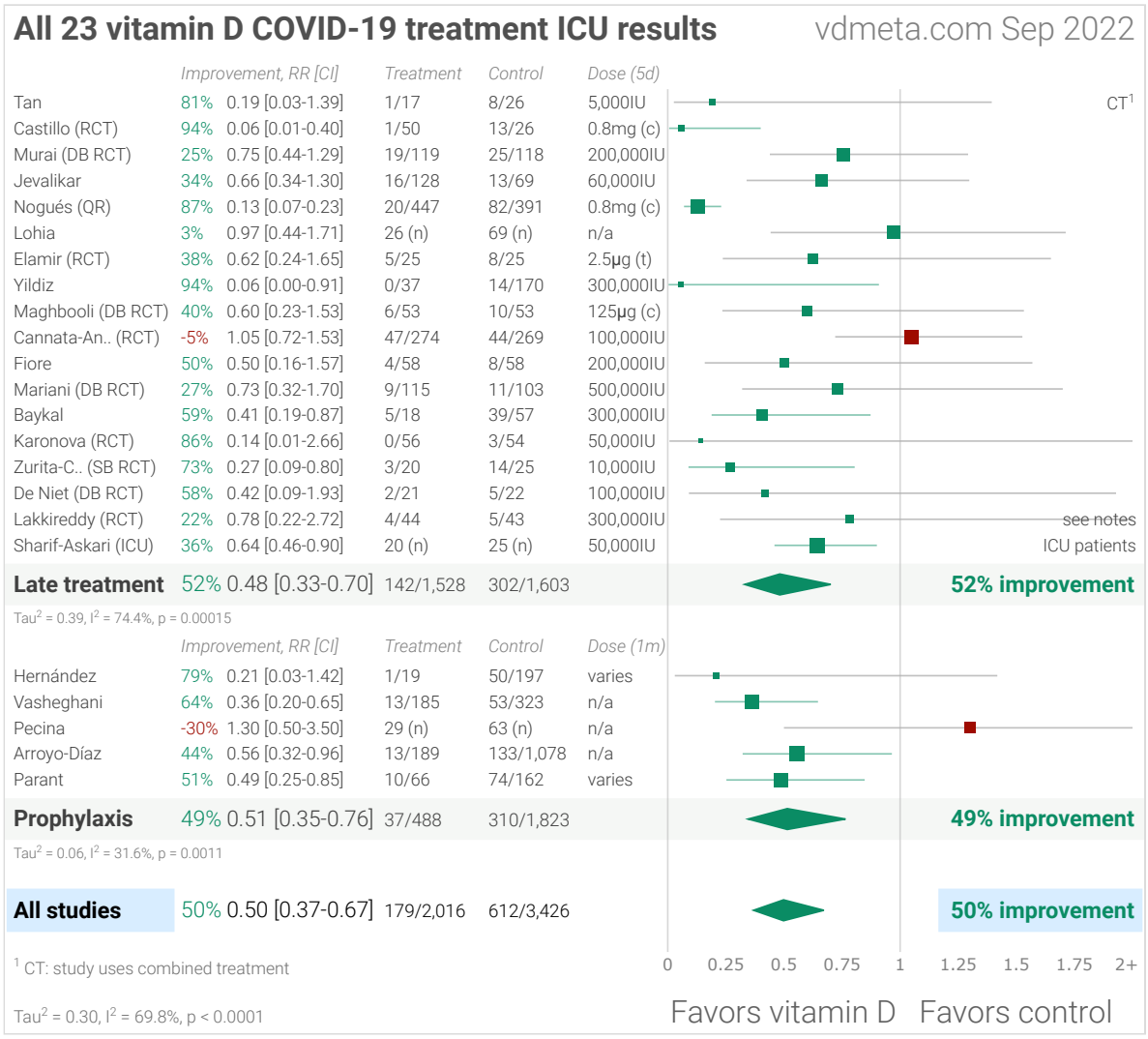


Figure 15. *Random effects meta-analysis for treatment ICU admission results only.*

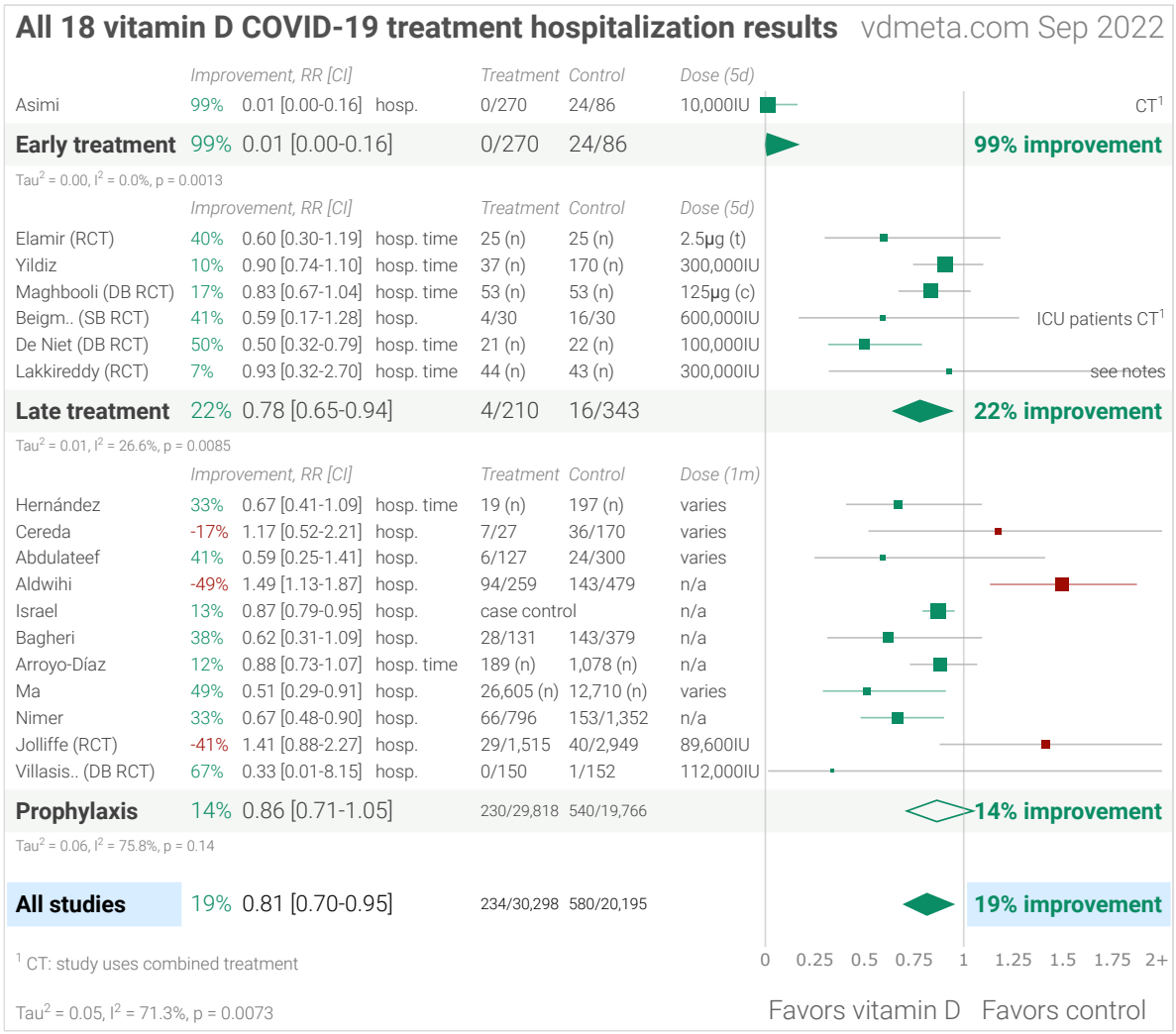


Figure 16. *Random effects meta-analysis for treatment hospitalization results only.*

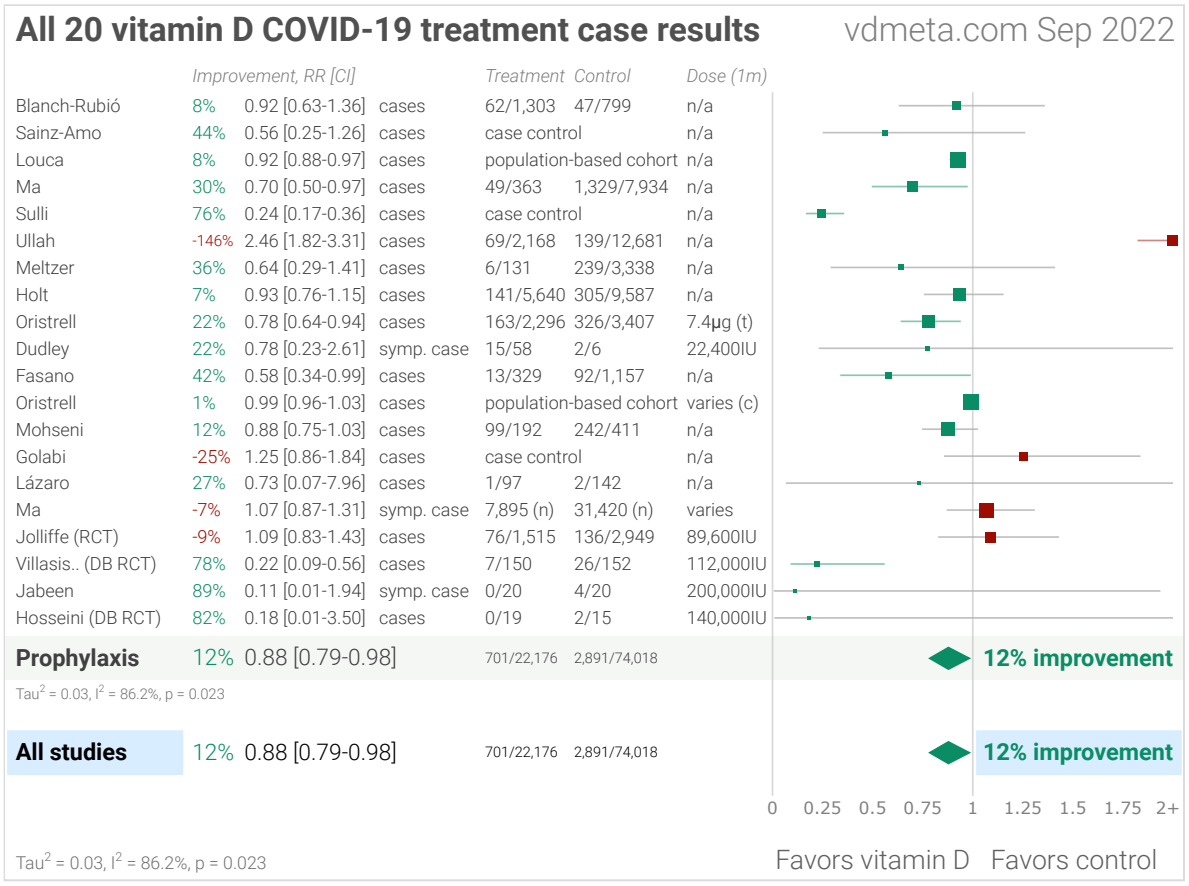


Figure 17. *Random effects meta-analysis for treatment COVID-19 case results only.*

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 18.

[Abdulateef], unadjusted results with no group details.

[Asimi], excessive unadjusted differences between groups.

[Assiri], 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.

[Campi], significant unadjusted differences between groups.

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

[Elhadi], unadjusted results with no group details.

[Güven], very late stage, ICU patients.

[Holt], significant unadjusted confounding possible.

[Junior], unadjusted results with no group details.

[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.

[Shehab], unadjusted results with no group details.

[Ullah], significant unadjusted confounding possible.

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

68 vitamin D COVID-19 treatment studies after exclusions vdmeta.com Sep 2022

	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 [0.00-1.06]	death	0/12	2/2	400,000IU	
Sánchez-Zuno (RCT)	89%	0.11 [0.01-1.86]	severe case	0/22	4/20	50,000IU	
Efird	49%	0.51 [0.23-1.17]	death	11/544	413/15,794	varies	
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	
Early treatment	63%	0.37 [0.22-0.61]		77/1,695	2,018/41,371		**63% improvement**

Tau² = 0.25, I² = 65.8%, p = 0.00014

	Improvement, RR [CI]			Treatment	Control	Dose (5d)	
Tan	80%	0.20 [0.04-0.93]	oxygen	3/17	16/26	5,000IU	CT[1]
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 [0.03-1.37]	death	1/37	24/170	300,000IU	
Maghbooli (DB RCT)	40%	0.60 [0.15-2.38]	death	3/53	5/53	125µg (c)	
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	
Bishop (DB RCT)	34%	0.66 [0.23-1.92]	no recov.	5/65	8/69	1020µg (c)	
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	
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	see notes
Hafez	94%	0.06 [0.00-0.96]	death	0/7	12/30	150,000IU	
Sharif-Askari (ICU)	36%	0.64 [0.46-0.90]	ICU	20 (n)	25 (n)	50,000IU	ICU patients
Late treatment	61%	0.39 [0.28-0.55]		76/1,582	304/2,759		**61% improvement**

Tau² = 0.35, I² = 63.9%, 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
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]	progression	131 (n)	379 (n)	n/a

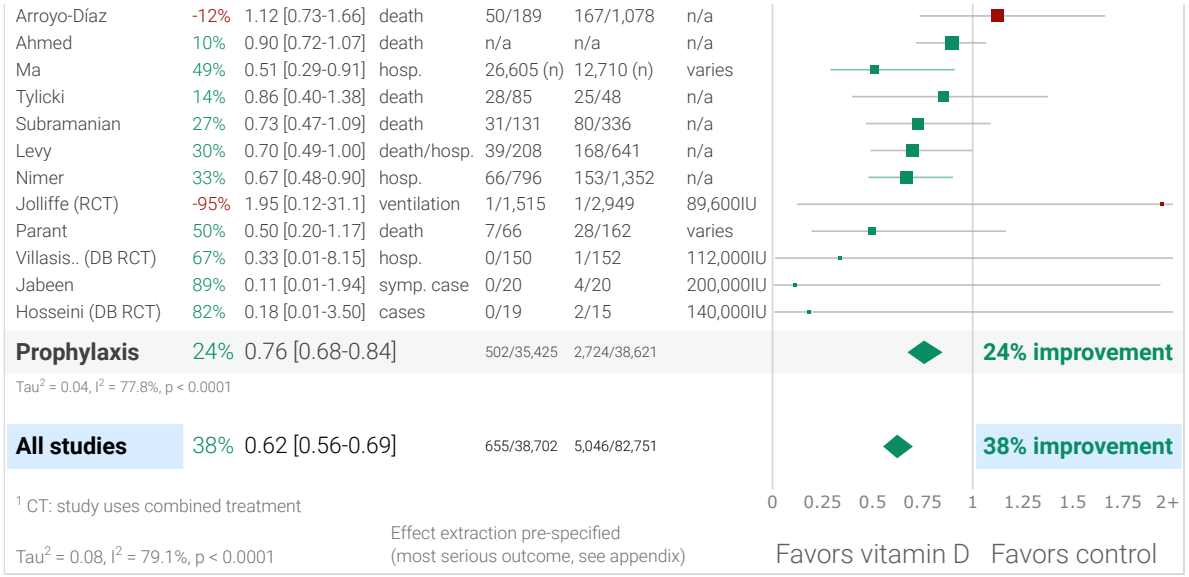


Figure 18. *Random effects meta-analysis excluding studies with significant issues. Effect extraction is pre-specified, using the most serious outcome reported, see the appendix for details.*

Randomized Controlled Trials (RCTs)

Results restricted to Randomized Controlled Trials (RCTs), after exclusions, and after restriction to mortality results are shown in Figure 19, 20, and 21.

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. This is illustrated with the extreme example of an RCT showing no significant differences for use of a parachute when jumping from a plane ***[Yeh]***. 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 well-known treatments such as vitamin D. Note that this bias does not apply to the typical pharmaceutical trial of a new drug that is otherwise unavailable.

Evidence shows that non-RCT trials can also provide reliable results. ***[Concato]*** find that well-designed observational studies do not systematically overestimate the magnitude of the effects of treatment compared to RCTs. ***[Anglemyer]*** summarized reviews comparing RCTs to observational studies and found little evidence for significant differences in effect estimates. ***[Lee]*** shows 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 could 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]***.

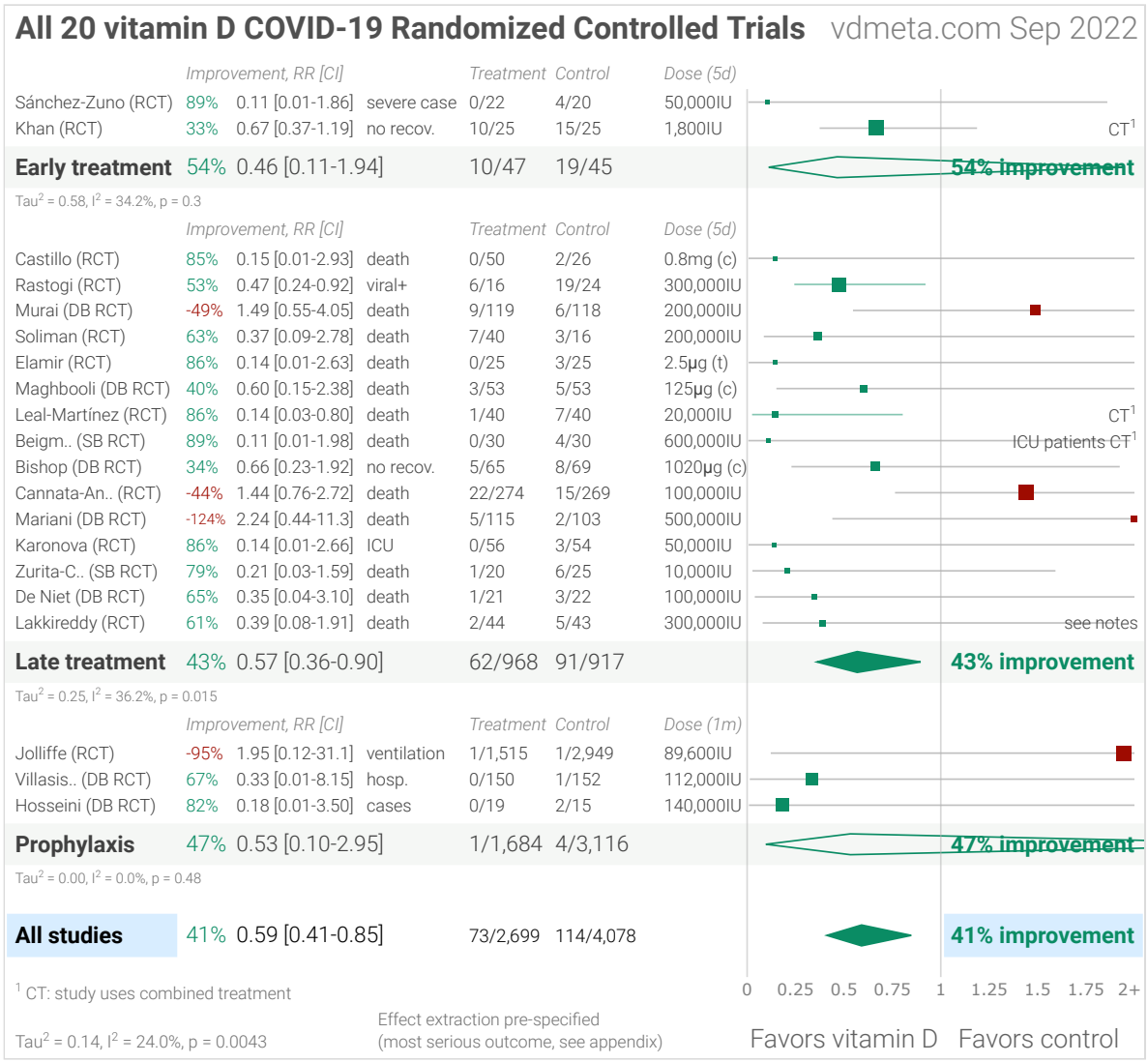


Figure 19. *Random effects meta-analysis for Randomized Controlled Trials only. Effect extraction is pre-specified, using the most serious outcome reported, see the appendix for details.*

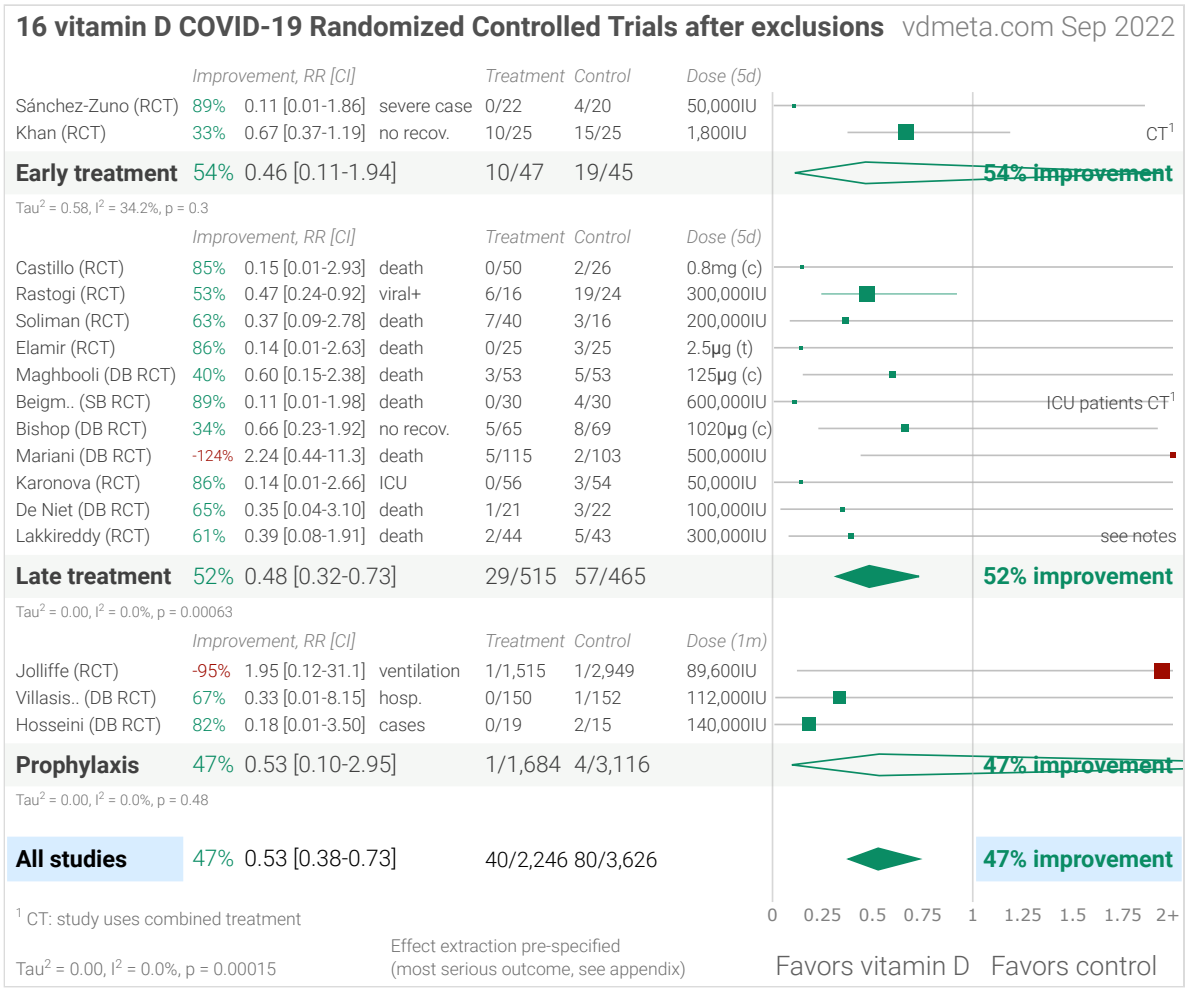


Figure 20. *Random effects meta-analysis for RCTs after exclusions. Effect extraction is pre-specified, using the most serious outcome reported, see the appendix for details.*

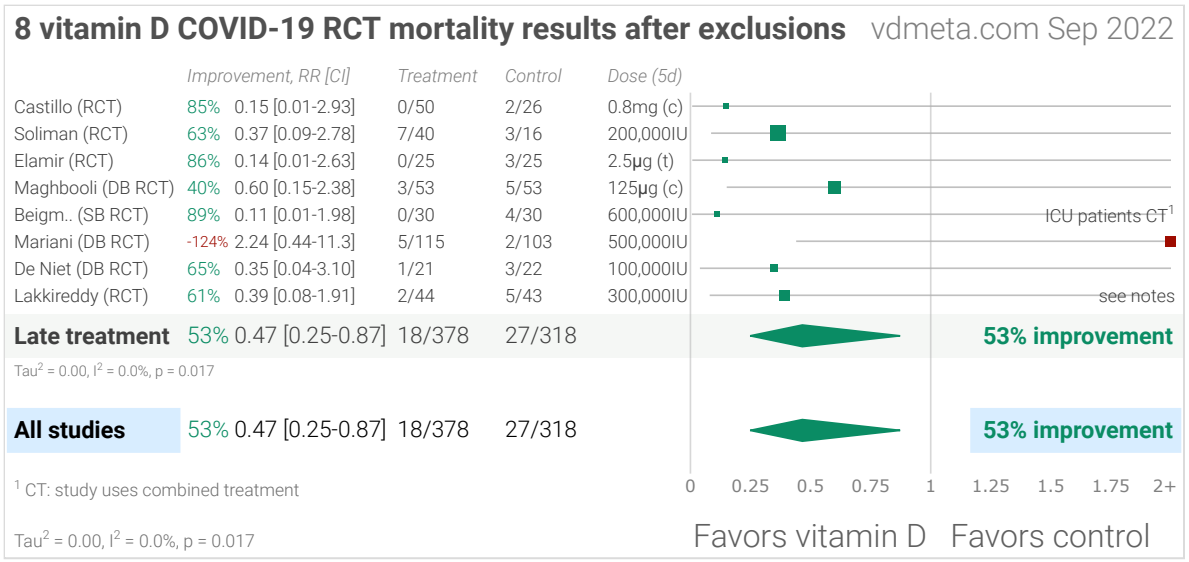


Figure 21. *Random effects meta-analysis for RCT mortality results after exclusions.*

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]***. Figure 22 shows a mixed-effects meta-regression for efficacy as a function of treatment delay in COVID-19 studies from 46 treatments, showing that efficacy declines rapidly with treatment delay. Early treatment is critical for COVID-19.

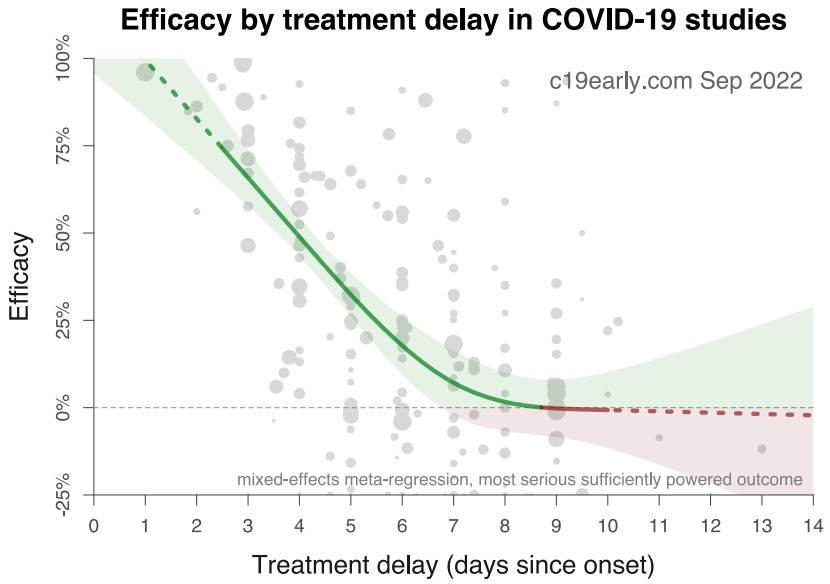


Figure 22. *Meta-regression showing efficacy as a function of treatment delay in COVID-19 studies from 46 treatments. Early treatment is critical.*

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 (as in ***[López-Medina]***).

Effect measured. Efficacy may differ significantly depending on the effect measured, for example a treatment may be very effective at reducing mortality, but less effective at minimizing cases or hospitalization. Or a treatment may have no effect on viral clearance while still being effective at reducing mortality.

Variants. There are many different variants of SARS-CoV-2 and efficacy may depend critically on the distribution of variants encountered by the patients in a study. 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 viral entry process for the omicron variant has moved towards TMPRSS2-independent fusion, suggesting that TMPRSS2 inhibitors may be less effective ***[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 anything from supplements, other medications, or other kinds of treatment such as prone positioning.

Medication quality. The quality of medications may vary significantly between manufacturers and production batches, which may significantly affect efficacy and safety. ***[Williams]*** analyze ivermectin from 11 different sources, showing highly variable antiparasitic efficacy across different manufacturers. ***[Xu]*** analyze a treatment from two different manufacturers, showing 9 different impurities, with significantly different concentrations for each manufacturer.

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 the treatment may be very effective when used earlier.

In general, by combining heterogeneous studies, as all meta analyses do, we run the risk of obscuring an effect by including studies where the treatment is less effective, not effective, or harmful.

When including studies where a treatment is less effective we expect the estimated effect size to be lower than that for the optimal case. We do not *a priori* expect that pooling all studies will create a positive result for an effective treatment. 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 pooled results for all studies, we also present individual outcome and treatment time analyses, which are more relevant 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.

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, 128 of 137 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 ***[c19melatonin.com]***. Sun exposure is also correlated with physical exercise, which also shows benefit for COVID-19 ***[c19early.com]***.

Treatment studies. 75 of 89 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.

Long-term supplementation may not be ideal. Acute treatment (early 67% [43-81%], late 48% [33-59%]) shows greater efficacy than chronic prophylaxis (29% [20-38%]).

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. If correct, this may suggest more judicious use of supplementation. 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]***.

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]***.

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.

52% of retrospective studies report a statistically significant positive effect for one or more outcomes, compared to 39% of prospective studies, consistent with a bias toward publishing positive results. The median effect size for retrospective studies is 33% improvement, compared to 64% for prospective studies, suggesting a potential bias towards publishing results showing lower efficacy. Figure 23 shows a scatter plot of results for prospective and retrospective treatment studies.

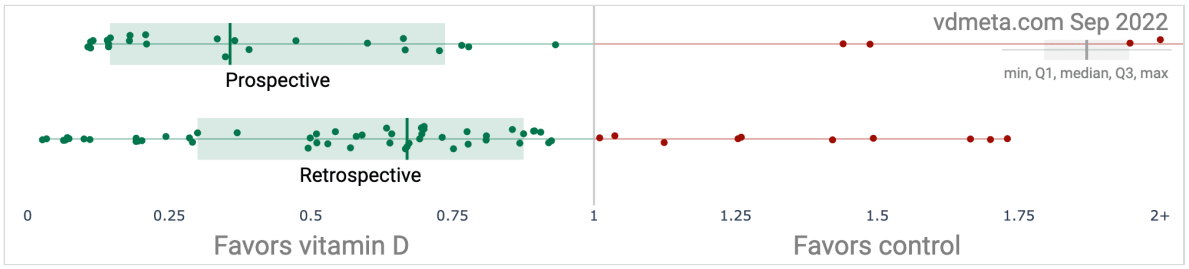


Figure 23. *Prospective vs. retrospective studies.*

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 24 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.

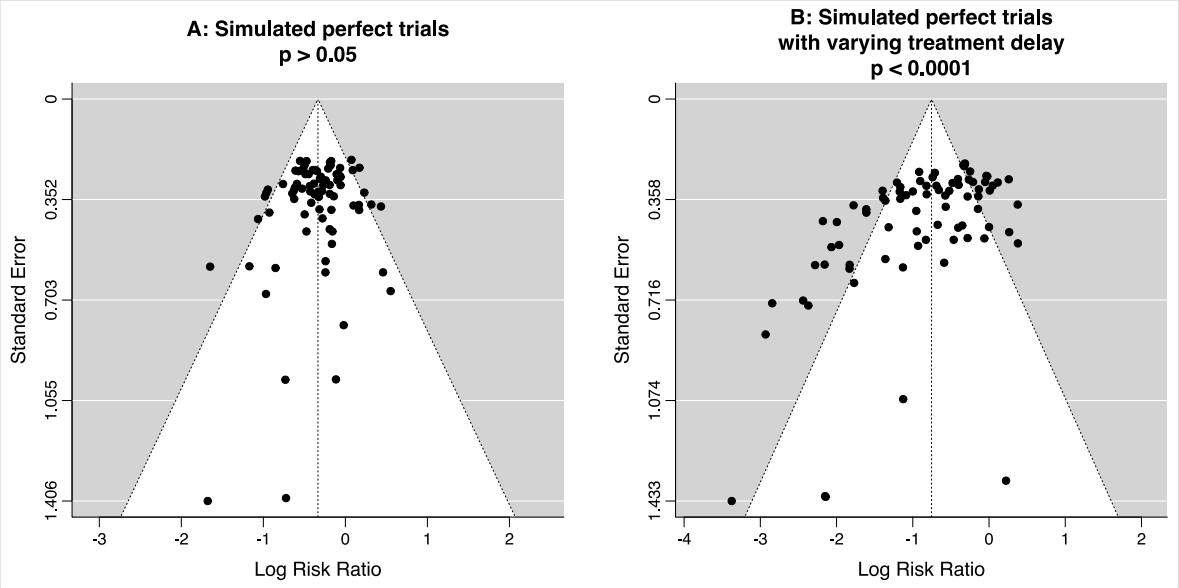


Figure 24. *Example funnel plot analysis for simulated perfect trials.*

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 for vitamin D treatment studies can be found in ***[D'Ecclesiis, Hosseini, Nikniaz, Shah, Varikasuvu]***, showing significant improvements for cases, severity, mortality, mechanical ventilation, and ICU admission.

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 *[c19vitamind.com]*. The study was republished.

Physician case series results. Table 2 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. A more detailed analysis requires information on the patient populations, however results are 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 - 35 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	4,375	0.2% (9)	99.5%	0.1% (3)	97.2%
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. 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. Vladimir Zelenko	USA	2,200	0.5% (12)	98.6%	0.1% (2)	96.3%
Mean improvement with early treatment protocols		219,653	Hospitalization	**94.7%**	Mortality	**94.3%**

Table 2. *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]****.*

Conclusion

Random effects meta-analysis with pooled effects using the most serious outcome reported shows 67% [43-81%] and 37% [30-44%] improvement for early treatment and for all studies. Results are similar after restriction to 82 peer-reviewed studies: 63% [39-78%] and 38% [30-44%], and for the 52 mortality results: 68% [39-84%] and 38% [27-48%].

Statistically significant improvements are seen in treatment studies for mortality, ventilation, ICU admission, hospitalization, and cases. 43 studies from 40 independent teams in 18 different countries show statistically significant improvements in isolation (29 for the most serious outcome).

Acute treatment (early 67% [43-81%], late 48% [33-59%]) shows greater efficacy than chronic prophylaxis (29% [20-38%]), suggesting that long-term supplementation may not be ideal.

Late stage treatment with calcifediol/calcitriol shows greater improvement compared to cholecalciferol: 73% [57-83%] vs. 40% [24-53%].

Responses

GMK response. An influential anti-treatment Twitter personality, journalist, and epidemiologist is known for being against many COVID-19 treatments including vitamin D. Of the 89 treatment studies, author suggests only one trial is worth looking at ***[Murai]***. This makes it easy to examine potential bias. ***[Murai]*** is a small trial providing no statistically significant effects (mortality p = 0.43, other outcomes are positive while also not significant). Author acknowledges that the trial is too small for a conclusion. More importantly, this trial provides no information about whether vitamin D reduces the risk of a serious COVID-19 case, because the patients in this trial already had a serious COVID-19 case (90% already on oxygen treatment at baseline). Author does not mention this. The trial also has poorly matched arms in terms of gender, ethnicity, hypertension, diabetes, and baseline ventilation, all favoring the control group. Further, this study uses an inappropriate form of vitamin D — cholecalciferol. In reality physicians would use calcifediol or calcitriol with late stage treatment, because they avoid a very long delay for conversion. We are unaware of a reason to use cholecalciferol in this case (other than to produce a null result). In summary, author's chosen study is the study providing the least useful information from the 89 studies to date, suggesting biased analysis.

*Update: author has now also covered **[Jolliffe (B)]** which presents null results for prophylaxis. Author continues to disregard the large number of positive studies, including **[Villasis-Keever]**, a prophylaxis RCT with very positive results.*

Revisions

This paper is data driven, all graphs and numbers are dynamically generated. We will update the paper as new studies are released or with any corrections. Please submit updates and corrections at https://vdmeta.com/.

9/11: We added ***[Zeidan]***.

8/25: We added ***[Hafez]***.

8/24: We added ***[Aldwihi, Sharif-Askari]***.

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 (D)]***.

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 (B)]***.

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]*.

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]***.

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]***.

10/29: We added discussion of GMK's vitamin D analysis.

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 (B)]***.

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 (B), Pecina]***.

9/6: We added ***[Soliman]***.

9/1: We added ***[Golabi]***.

8/23: We corrected ***[Jain]*** to include the mortality outcome.

8/15: We added ***[Nimavat]***.

8/13: We added ***[di Filippo]*** 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 (B)]*.

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 (C)]*.

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 performed ongoing searches of PubMed, medRxiv, ClinicalTrials.gov, The Cochrane Library, Google Scholar, Collabovid, Research Square, ScienceDirect, Oxford University Press, the reference lists of other studies and meta-analyses, and submissions to the site c19vitamind.com. Search terms were vitamin D, cholecalciferol, and calcitriol, and COVID-19 or SARS-CoV-2. Automated searches are performed every hour with notification of new matches. All studies that report a result for vitamin D treatment of COVID-19 patients compared to a control group, and all studies comparing COVID-19 outcomes in groups of patients with low and high vitamin D levels are included. 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 useful). 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 are used. Mortality alone is preferred over combined outcomes. Outcomes with zero events in both arms were not used (the next most serious outcome is used — no studies were excluded). 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 outcome is considered more important than PCR testing 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 no room for an effective treatment to do better). 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 computed the relative risk when possible, or converted 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 including propensity score matching (PSM), the PSM results are used. Adjusted primary outcome 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 (3.10.6) with scipy (1.9.1), pythonmeta (1.26), numpy (1.23.2), statsmodels (0.13.2), and plotly (5.10.0).

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. 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.

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

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).

A summary of study results is below. Please submit updates and corrections at https://vdmeta.com/.

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.
[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.
[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.
[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	**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

2020 - June 2020, excluded in exclusion analyses: unadjusted results with no group details.	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.
[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 RR<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 RR<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 RR<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.
[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.
[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.
[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, 4 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 RR<1 favor high D levels (≥20ng/mL).
[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], 5/7/2021, retrospective, Russia, peer-reviewed, 5 authors, excluded in exclusion analyses: excessive unadjusted differences	**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.

between groups.	
[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, dosage 100,000IU single dose, trial NCT04552951 (history), excluded in exclusion analyses: very late stage study using cholecalciferol instead of calcifediol or calcitriol.	**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.
	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).
[Charkowick], 5/5/2022, retrospective, USA, peer-reviewed, 10 authors, study period 1	**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

January, 2020 - 5 February, 2021.	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.
[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.
[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%).
[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.
[di Filippo], 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).
[Faniyi], 10/6/2020, prospective, United	**risk of seropositive, 28.8% lower, RR 0.71, *p* = 0.003**, high

Kingdom, preprint, 10 authors.	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.

[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 RR<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 RR<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 RR<1 favor high D levels, >30ng/mL vs. <20ng/mL, model 2, day 45.
[Golabi], 8/26/2021, retrospective, Iran, peer-	**odds of symptoms, 90.0% lower, OR 0.10, p < 0.001**, high

reviewed, 10 authors.	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.
[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.
[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.
[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.
[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.

[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], 9/10/2020, 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], 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.
[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], 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 (B)], 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 (C)], 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 = 0.07, 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-	**risk of death, 75.8% lower, RR 0.24, p = 0.26**, high D levels

reviewed, mean age 56.0, 4 authors.	(≥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%).
[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], 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.
[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.

[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, 3 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.

[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.
[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.
[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.
[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.
[Radujkovic], 9/10/2020, prospective,	**risk of death, 93.2% lower, HR 0.07, $p = 0.001$**, high D

Germany, peer-reviewed, 6 authors.	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 RR<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 RR<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.
[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.
[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* = 0.21**, 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.
[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.
[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.
[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], 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.
[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.	**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.
[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.
[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.
[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.
[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.
[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.

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,	**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.

80,000IU either in the week following the suspicion or diagnosis of COVID-19, or during the previous month.	
[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.
[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).
[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	**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.

(combined with curcumin and quercetin) - results of individual treatments may vary, trial NCT05130671 (history).	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.
[Sánchez-Zuno (B)], 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.

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.

[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, 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.	**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, preprint, 11 authors, study period 2 November, 2020 - 27 August, 2021, dosage calcifediol 300µg day 1, 60µg days 4-27, trial NCT04551911 (history).	**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.
[Cannata-Andía], 2/18/2022, Randomized Controlled Trial, multiple countries, peer-reviewed, median age 59.0, 22 authors, dosage 100,000IU single dose, trial NCT04552951 (history), 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, dosage calcifediol 0.5mg day 1, 0.27mg day 3, 0.27mg day 7, and then weekly until discharge or ICU admission.	**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.
[Elamir], 9/8/2021, Randomized Controlled Trial, USA, peer-reviewed, 9 authors, 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.
[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], 8/9/2022, retrospective, Egypt, peer-	**risk of death, 93.7% lower, RR 0.06, p = 0.07**, treatment 0

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.	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.
[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.
[Karonova (D)], 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	**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.

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 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 (B)], 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	**risk of death, 30.5% lower, RR 0.70, *p* = 0.10**, treatment

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.	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.
[Murai], 11/17/2020, Double Blind Randomized Controlled Trial, Brazil, peer-reviewed, 17 authors, average treatment delay 10.2 days,	**risk of death, 48.7% higher, RR 1.49, *p* = 0.43**, treatment 9 of 119 (7.6%), control 6 of 118 (5.1%).

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 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.
[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.
[Rastogi], 11/12/2020, Randomized Controlled Trial, India, peer-reviewed, 8 authors, dosage 60,000IU days 1-7.	**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.
[Sharif-Askari], 8/24/2022, retrospective, USA, peer-reviewed, 10 authors, dosage 50,000IU days 1, 8, 15.	**ICU time, 35.7% lower, relative time 0.64, p = 0.01**, treatment 20, control 25.
[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], 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-	**risk of death, 80.9% lower, RR 0.19, p = 0.04**, treatment 1

reviewed, 5 authors, dosage 300,000IU single dose.	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.	**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**.
[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	**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

authors, dosage 50,000IU monthly, dose varies - 50,000 IU/month, or 80,000IU/100,000IU every 2–3 months.	per study, regular bolus supplementation.
[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.
[Bagheri], 9/1/2021, retrospective, Iran, peer-reviewed, 6 authors, dosage not specified.	**risk of progression, 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 being in the hospitalized vs. outpatient group, 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.
[Blanch-Rubió], 10/20/2020, retrospective, Spain, peer-reviewed, mean age 66.4, 10 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.
[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.
[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.
[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.
[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 (B)], 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,	**risk of hospitalization, 13.1% lower, OR 0.87, *p* = 0.003**,

peer-reviewed, 10 authors, dosage not specified.	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, 24 authors, study period December 2020 - June 2021, dosage 3,200IU daily, daily, trial NCT04579640 (history).	**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,	**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.

excluded in exclusion analyses: unadjusted results with no group details.	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,	**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.

excluded in exclusion analyses: unadjusted results with no group details.	
[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.
[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.
[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-	**risk of death, 14.4% lower, RR 0.86, p = 0.61**, treatment

reviewed, 10 authors, study period 6 October, 2020 - 28 February, 2021, dosage not specified.	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.
[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.
[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.

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