VITAMIN D

RECOMMENDATION

There is insufficient evidence to recommend the use of Vitamin D supplementation as adjunct treatment for patients with COVID-19 infection. *(Very low quality of evidence)*

Consensus Issues

There were no issues raised during the panel meeting.

EVIDENCE SUMMARY

Should Vitamin D supplements be used as adjunct treatment for COVID-19?

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Key Findings

Three RCTs were found on the use of vitamin D as adjunct treatment for patients with COVID-19. The effect of vitamin D supplements as adjunct treatment for patients with COVID-19 for the outcomes of mortality (pooled RR 0.58, 95% CI [0.05 to 7.18]; p=0.67; I2=64%; n=283, 2 RCTs), progression of oxygen support (RR 0.52, 95% CI [0.24 to 1.13]; p=0.10; n=237 1 RCT) and ICU admission (pooled RR 0.20, 95% CI [0.01 to 4.26], p=0.30 I2=89%; n=313, 2 RCTs) was inconclusive. Across these outcomes, the studies were found to have low to very low certainty because of serious risk of bias (from unclear randomization and lack of blinding), inconsistency and imprecision. More patients supplemented with vitamin D had virologic clearance by day 21 (RR 0.47, 95% CI [0.24 to 0.92], p=0.03; n=40, 1 RCT; very low certainty of evidence due to high imprecision and low event rate. No significant difference was found with duration of hospital length of stay (MD 0 days, 95% CI [-1.33 to 1.33]), and duration of mechanical ventilation (MD 2.2 days, 95% CI [-8.4 to 12.8]). Based on indirect evidence, vitamin D in excessive amounts may cause gastrointestinal complaints, hypercalcemia, hypercalciuria, and increased renal stone formation.

Introduction

SARS-CoV-2 virus upregulates renin and angiotensin- converting enzyme (ACE2) expression. This leads to a buildup of angiotensin II causing inflammation, enhanced lung permeability, and acute respiratory distress syndrome via the angiotensin 1 receptor pathway. Recent studies suggest that vitamin D lowers the risk of COVID-19 complications by attenuating the cytokine storm through lowering renin and angiotensin-converting enzyme expression. Vitamin D also lowers inflammation, fibrosis, and apoptosis [1-3]. Currently, it is unknown whether vitamin D can also reduce the severity and deaths due to COVID-19 when used as adjunct treatment.

Review Methods

MEDLINE, Cochrane library, and gray literature in MedRxIV, and BioRxIV (search date up to December 25, 2020) were searched using the following keywords and MeSH terms: “vitamin D”, “ergocalciferol”, “cholecalciferol”, and COVID-19 related terms. Ongoing trials were searched in Clinicaltrials.gov and NMA-COVID-19 registry. NICE Guidance (https://www.nice.org.uk/guidance), COVID-19 Open Living Evidence Synthesis to Inform Decision (https://covid-nma.com/), National COVID-19 Clinical Evidence Taskforce Living Guidelines (https://covid19evidence.net.au/) and WHO Living CPG (https://www.who.int/publications/i/item/therapeutics-and-covid-19-living-guideline) were also searched.

The study selection criteria included articles that met the PICO criteria, as follows:

Population: Adult COVID-19 patients, with any comorbidities, any severity
Intervention: vitamin D supplements as adjunctive therapy for an active or standard treatment
Comparator: Placebo, any active control, no intervention
Outcomes: Mortality, clinical deterioration/ development of ARDS, need for mechanical ventilation, hospital length of stay, time to clinical improvement/ recovery, improvement in chest CT Scan/ X-ray, virologic clearance by PCR test, adverse effects
Study design: randomized controlled trials (RCTs)

Results

Three RCTs (N=356) were found that used vitamin D as adjunct treatment among hospitalized patients with COVID-19 in Brazil, India and Spain, with sample size ranging from 40 to 240. The first study [5] included patients with mild to severe COVID-19, while the second study [4] included patients who required hospitalization due to respiratory illness. The third study [6] included both asymptomatic and mildly asymptomatic patients with vitamin D deficiency, but excluded those requiring invasive mechanical ventilation and with significant comorbidities. Two different preparations of vitamin D were given as adjunct treatment: calcifediol capsules (532 micrograms on day 1 and 266 micrograms on days 3, 7, 14, 21, 28 or until discharge) and vitamin D3 (cholecalciferol), as a single dose of 200,000 IU) and as a daily dose for 7 days (oral nano-liquid droplets 60,000 IU) [4-6]. Two studies were placebo-controlled [5-6] (Appendix 1, Characteristics of Included Studies). Standard of care consisted of hydroxychloroquine and azithromycin with ceftriaxone for those with pneumonia in one study [4] but was not specified in the two other studies [5-6].

The pooled treatment effects of vitamin D on mortality (pooled RR 0.58, 95% CI [0.05 to 7.18]; p=0.67; I2=64%; n=313, 2 RCTs), progression to O2 support (RR 0.52, 95% CI [0.24 to 1.13]; p=0.10; n=237 1 RCT), ICU admission (pooled RR 0.20, 95% CI [0.01 to 4.26], p=0.30 I2=89%; n=313, 2 RCTs) were inconclusive (Appendix 2: GRADE Evidence Profile Table) [5]. More patients supplemented with vitamin D tested COVID-19 negative on day 21 (RR 0.47, 95% CI [0.24 to 0.92], p=0.03; n=40, 1 RCT) but there was very low certainty of evidence due to high imprecision and low event rate. Only one study [5] showed no significant difference in terms of hospital length of stay (MD 0 days, 95% CI [-1.33 to 1.33]) and duration of mechanical ventilation (MD 2.2 days, 95% CI [-8.4 to 12.8]).

Among the three trials that enrolled COVID-19 patients, only one patient who received vitamin D3 was reported to have vomiting. We found no reports of adverse events directly attributable to

vitamin D supplementation among COVID-19 patients. However, based on indirect evidence, a review by Kearns et al. found that single high dose vitamin D supplementation (300,000 IU – 600,000 IU D3) was associated with gastrointestinal complaints, hypercalciuria and increased urine magnesium excretion [7]. A Cochrane systematic review reported that supplemental forms of vitamin D (D3 and D2) had no statistically significant effect on the risk of hypercalcemia (RR 1.36, 95% CI [0.85 to 2.18], p=0.21, I2=0%; n=11,323) but if combined with calcium may significantly increase the risk of nephrolithiasis (RR 1.17, 95% CI [1.02 to 1.34], p=0.02, I2=0%; n=42,876). The risk of other adverse events with Vitamin D was not statistically significant (e.g., hypercalciuria, renal insufficiency, cardiovascular effects, gastrointestinal disorders, psychiatric disorders, skin disorders, and cancer). In summary, indirect evidence suggests that hypercalcemia is the most common adverse event associated with Vitamin D supplementation. Risk of hypercalciuria, renal stone formation and gastrointestinal symptoms are also increased with intake of Vitamin D.

Recommendations from Other Groups

The US National Institutes of Health found insufficient data to recommend either for or against the use of vitamin D for the prevention or treatment of COVID-19. Both NICE guidelines (December 17,2020; evidence searched up to October 7, 2020) and Australian Living CPG (NC19CET) do not recommend vitamin D supplement to treat COVID-19, except as part of a clinical trial [9-11].

Ongoing Studies

There are 26 ongoing clinical trials on the efficacy of vitamin D supplementation as adjunct treatment for COVID-19 (Appendix 4: Characteristics of Ongoing Studies).

References

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controlled study (SHADE study). Postgrad Med J. 2020;0:1-4. doi:10.1136/postgradmedj-2020-139065.
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Appendix 1: Characteristics of Included Studies

No.	Clinical Trial ID/ Title	Population	Intervention	Comparator	Outcomes	Sample Size
1	Murai 2020 Effect of vitamin D3 Supplementation vs Placebo on Hospital Length of Stay in Patients with Severe COVID-19: A Multicenter, Double-blind, Randomized Controlled Trial	Patients hospitalized with COVID-19 infection (mild to severe) Adults aged 18>yrs Positive for SARS-CoV-2 PCR or positive CT scan findings compatible with COVID-19	200,000 IU of vitamin D 3 given on day of admission (N=120) Plus standard of care	Placebo (N=120) Plus standard of care	Hospital length of stay Mortality ICU admission Need for mechanical ventilator Vitamin D levels	N=240
2	Castillo 2020 Effect of Calcifediol Treatment and best Available Therapy versus best Available Therapy on Intensive Care Unit Admission and Mortality Among Patients Hospitalized for COVID-19: A Pilot Randomized Clinical study	Patients hospitalized with COVID-19 infection clinical picture of acute respiratory infection confirmed by a radiographic pattern of viral pneumonia positive SARS-CoV-2 PCR with CURB65 severity scale (recommending hospital admission in case of total score > 1).	Day of admission: 2 capsules of calcifediol (266 µg/cap). 1 capsule on days 3, 7, 14, 21, 28 until discharge or ICU admission. Plus standard of care (N=50)	Standard of care (N=26) defined as: 1) Hydroxychloroquine 400mg every 12 hours on first day and 200 mg every 12 hours for the following 5 days 2) Azithromycin 500 mg orally for 5 days, 3) For patients with pneumonia and NEWS score >5, Ceftriaxone 2 g intravenously every 24 hours was given for 5 days.	ICU admission Death Hospital discharge	N=76
3	Rastogi 2020 Short term, high-dose vitamin D supplementation for COVID-19 disease: a randomized,	Consecutive hospitalized patients with SARS-COV2 infection (mildly symptomatic or asymptomatic with or without co-morbidities (hypertension, diabetes	Daily 60000 IU of cholecalciferol (5 ml oral solution in nano droplet form) for 7 days with the aim to achieve 25 (OH)D level>50 ng/ml (N=16) Subsequently, 25(OH)D levels were assessed at day 7 and a weekly	Placebo (5 ml distilled water) Plus standard of care	SARS-CoV-2 RNA detection (OP swabs) at days 5, 7, 10, 14,18 and 21 (real-time PCR, CFX-	N=40

No.	Clinical Trial ID/ Title	Population	Intervention	Comparator	Outcomes	Sample Size
	placebo-controlled, study (SHADE study)	mellitus, chronic obstructive airway disease, chronic liver disease, chronic kidney disease) Excluded those requiring invasive ventilation ; with vitamin D deficiency defined as 25 (OH)D level<20 ng/ml	supplementation of 60000IU provided to those with 25(OH)D >50 ng/ml or else continued on daily vitamin D 60,000 IU supplementation for another 7 days up until day-14 in partici-pants with 25(OH)D <50 ng/ml Plus standard of care		96 IVD, Bio-Rad)	

Appendix 2: GRADE Evidence Profile

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Should Vitamin D supplements	placebo	Relative (95% CI)	Absolute (95% CI)		
Mortality												
2	randomised trials	not serious	serious [a]	not serious	very serious [b]	none	9/169 (5.3%)	8/144 (5.6%)	**RR 0.58** (0.05 to 7.18)	**23 fewer per 1,000** (from 53 fewer to 343 more)	⨁◯◯◯ VERY LOW	
O2 support												
1	randomised trials	not serious	not serious	not serious	very serious [b]	none	9/119 (7.6%)	17/118 (14.4%)	**RR 0.52** (0.24 to 1.13)	**69 fewer per 1,000** (from 109 fewer to 19 more)	⨁⨁◯◯ LOW	
ICU admission												
2	randomised trials	serious [c]	very serious [d]	not serious	very serious [b]	none	20/169 (11.8%)	38/144 (26.4%)	**RR 0.20** (0.01 to 4.26)	**211 fewer per 1,000** (from 261 fewer to 860 more)	⨁◯◯◯ VERY LOW	
Virologic Clearance												
1	randomised trials	serious [e]	not serious	not serious	very serious [b]	none	10/16 (62.5%)	5/24 (20.8%)	**RR 0.47** (0.24 to 0.92)	**110 fewer per 1,000** (from 158 fewer to 17 fewer)	⨁◯◯◯ VERY LOW	
Hospital length of stay												
1	randomised trials	not serious	not serious	not serious	very serious [f]	none	119	118	-	MD **0 days** (1.33 lower to 1.33 higher)	⨁⨁◯◯ LOW	
Duration of Mechanical Ventilation												
1	randomised trials	not serious	not serious	not serious	very serious [f]	none	119	118	-	MD **2.2 days higher** (8.4 lower to 12.8 higher)	⨁⨁◯◯ LOW	
Adverse Events												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Should Vitamin D supplements	placebo	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	not serious	not serious	not serious	very serious [b]	none	1/114 (0.9%)	0/118 (0.0%)	not estimable		⨁⨁◯◯ LOW	

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

Explanations

a. Inconsistency downgraded by 1 level: I^2=61%
b. Imprecision downgraded by 2 levels: due to very wide confidence interval consistent with the possibility for benefit and the possibility for harm and low number of events and participants.
c. Risk of bias downgraded by 1 level: some concerns regarding adequate randomization, open-label, non-blinded RCT
d. Inconsistency downgraded by 2 level: I^2=89%
e. Risk of bias downgraded by 1 level: some concerns due to unclear randomization and allocation concealment, and lack of blinding in participants and personnel.
f. imprecision, wide confidence interval

Appendix 3: Forest Plots

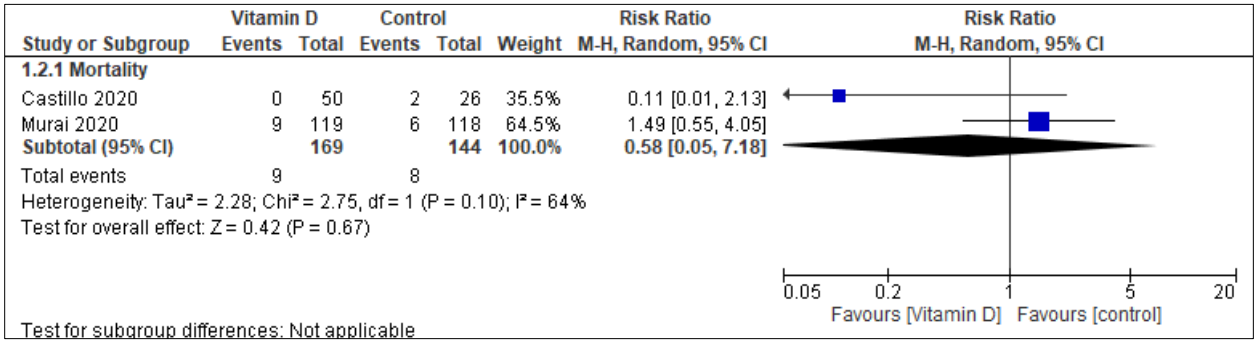

Figure 1. Forest plot comparing vitamin D and Control for the outcome of mortality

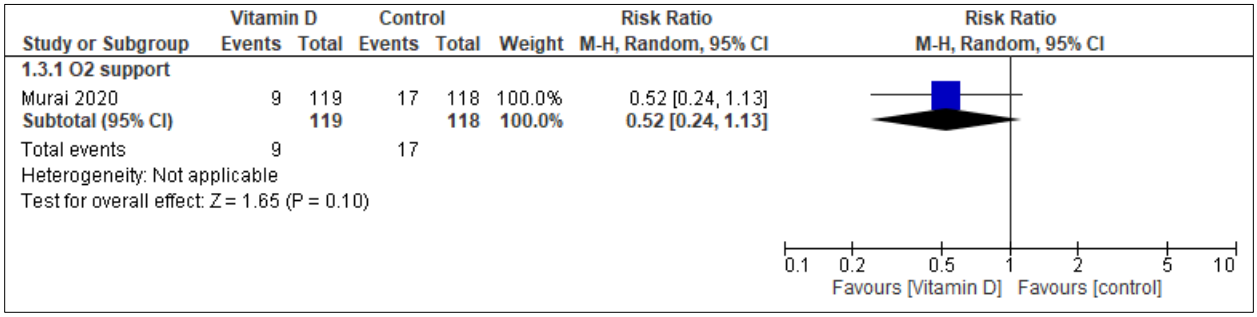

Figure 2. Forest plot comparing vitamin D and Control for the outcome of progression of O2 support

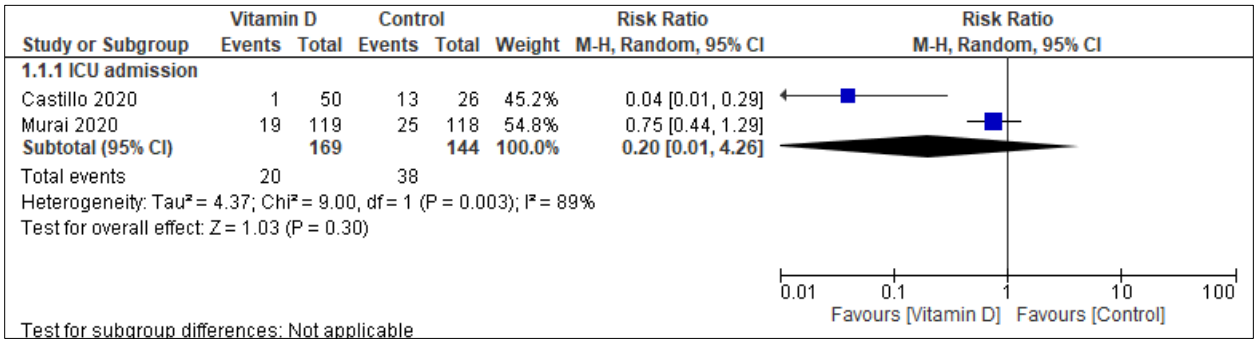

Figure 3. Forest plot comparing vitamin D and Control for the outcome of ICU admission

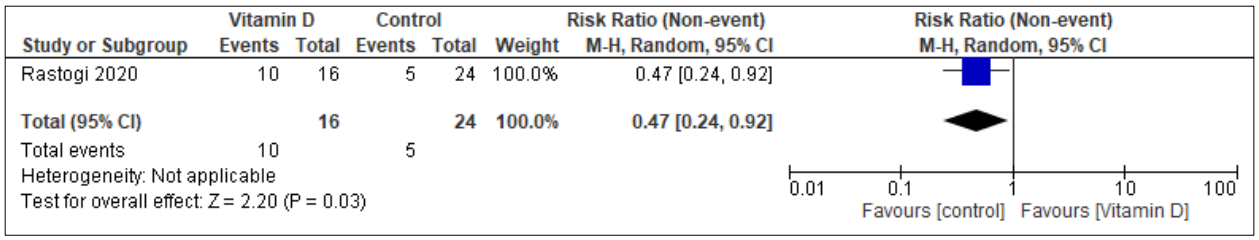

Figure 4. Forest plot comparing vitamin D and Control for the outcome of proportion of patients showing virologic clearance at day 21

Appendix 4: Characteristics of Ongoing Studies

	Clinical Trial ID / Title	Population	Intervention Group(s)	Comparison Group(s)	Outcomes
1	NCT04489628 / Tele-health Enabled Clinical Trial for COVID-19: vitamin D as an Immunomodulator to Prevent Complications and Reduce Resource Utilization in Outpatients	COVID-19 patients ages 18 and up being treated on an outpatient basis	8 capsules of cholecalciferol 50,000 IU	Placebo	Patients requiring admission or experiencing death
2	NCT04525820 / High Dose vitamin-D Substitution in Patients With COVID-19: a Randomized Controlled, Multi-Center Study	COVID-19 patients ages 18 and up with vitamin D deficiency being treated on an inpatient basis	Single high dose of vitamin D (140'000) in addition to daily 800 IU of vitamin D.	Single dose of placebo, orally administered and then treatment as usual (daily 800 IU of vitamin D, orally administered)	Primary Outcome Measures (1) Length of hospitalization Secondary Outcome Measures (1) Need of intensive care (2) Length of intensive care treatment (3) Overall mortality (4) Development of vitamin D levels (5) Development of sepsis
3	NCT04536298 / A Cluster-Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy of vitamin D3 Supplementation to Reduce Disease Severity in Persons with Newly Diagnosed COVID-19 Infection and to Prevent Infection in Household Members	COVID-19 patients ages 30 years or older	Daily vitamin D3 (9600 IU/day on days 1 and 2; 3200 IU/day on days 3 through 28)	Placebo	Primary Outcome Measure: hospitalization or death in index cases Secondary Outcome Measures: (1) Disease severity (2) Time to hospitalization or death in index cases (3) ICU admission/ventilation support in index cases (4) SARS-CoV-2 infection in close household contacts (5) Self-reported disease severity in close household contacts
4	NCT04552951 / Estudio Destinado a Valorar la Utilidad de vitamina D Sobre Morbilidad y Mortalidad de la infección Por Virus SARS-COV-2 (COVID-19) en el Hospital Universitario Central de Asturias	COVID-19 patients ages 18 years old or older	1 dose of 100.000 iu of Cholecalciferol when the COVID 19 Disease is diagnosed	No vitamin D	Primary Outcome Measures: (1) mortality (2) admission to ICU (3) time of hospitalization (4) clinical changes (5) radiological changes

	Clinical Trial ID / Title	Population	Intervention Group(s)	Comparison Group(s)	Outcomes
5	NCT04621058 / Efficacy of Treatment With vitamin D in Patients Diagnosed With COVID-19 Who Presenting vitamin D Deficiency and Pneumonia.	COVID-19 patients of all ages	If vitamin D deficiency (< 30 ng/ml) treatment with 2 capsules of 0.266 mg If vitamin D deficiency (< 40 ng/ml): treatment with 1 capsule of 0.266 mg	Placebo	Primary Outcome Measure: mortality Secondary Outcome Measures: (1) ICU admissions
6	NCT04636086 / vitamin D Supplementation and Covid-19: a Randomized, Double- Blind, Controlled Study	COVID-19 patients ages 18 years old or older	Ampoule for enteral use containing 25,000 IU/mL of cholecalciferol taken a total of 9 times	Placebo	Primary Outcome Measure: vitamin D serum concentration Secondary Outcome Measures (1) Clinical improvement (2) Hospital length of stay (3) ICU length of stay (4) Supplemental oxygen, non-invasive or invasive ventilation or organ support (5) Duration of supplemental oxygen, non-invasive or invasive ventilation or organ support (6) Absence of fever (7) Time until negative laboratory SARS-CoV-2 test (8) Mortality all causes (9) Mortality related to COVID-19
7	NCT04641195 / A Randomized Trial to Determine the Effect of vitamin D and Zinc Supplementation for Improving Treatment Outcomes Among COVID-19 Patients in India	COVID-19 patients ages 18 years old or older	(1) 180,000 international units (IU) of vitamin D3 at enrollment, followed by 2000 IU once per day from enrollment to 8 weeks (2) 40mg of zinc gluconate taken once per day from enrollment to 8 weeks (3) 180,000 IU of vitamin D3 at enrollment, followed by 2000 IU of vitamin D3 and 40mg of zinc gluconate once per day from enrollment to 8 weeks	Placebo vitamin D bolus at enrollment followed by placebo daily vitamin D maintenance doses and placebo daily zinc supplements.	Primary Outcome Measure: Time to recovery Secondary Outcome Measures: All-cause mortality Necessity for assisted ventilation

	Clinical Trial ID / Title	Population	Intervention Group(s)	Comparison Group(s)	Outcomes
8	EUCTR2020-001960-28-ES / Efficacy of vitamin D treatment in patients diagnosed with pneumonia who require hospital admission and have vitamin D deficiency and a positive diagnosis for SARS-Cov-2 (COVID-19)	COVID-19 patients ages 18 years old or older with vitamin D deficiency	vitamin D supplements	Placebo	Evolution of respiratory syndrome Virological clearance by PCR Days in ICU Clinical symptoms Mortality
9	EUCTR2020-002312-43 / Clinical trial, PHASE III, randomized, open-label, to evaluate the efficacy of administering high-dose cholecalciferol orally alongside standard therapy in patients with COVID-19 pneumonia (COVID-19 HUSO).	COVID-19 patients ages 18 years old or older with vitamin D deficiency	high-dose cholecalciferol orally alongside standard therapy in patients with COVID-19 pneumonia	Placebo	Progression to respiratory failure Increased oxygen requirements Need for mechanical ventilation Radiological progression of the disease Average hospital stay ICU admission Mortality
10	NCT04411446 / Randomized Controlled Trial of High Dose of vitamin D as Compared With Placebo to Prevent Complications Among COVID-19 Patients	COVID-19 patients ages 45 or older, or with co-morbidities	5 capsules of 100.000 UI vitamin D orally given all at once. One dose.	5 capsules containing placebo orally given all at once. One dose.	admission to ICU invasive mechanical ventilation hospital length of stay
11	NCT04449718 / vitamin D Supplementation in Patients With COVID-19: A Randomized, Double-blind, Placebo-controlled Trial	COVID-19 patients ages 18 years old or older	200,000 IU of vitamin D3 on admission + conventional care	Placebo	Length of hospitalization Mortality Admission to ICU Length of use of mechanical ventilator
12	IRCT20110726007117N11 / Effect of vitamin D supplementation in diagnosed cases of 2019 Novel Coronavirus; a randomized clinical trial	COVID-19 patients ages 30 to 60 years old with vitamin D deficiency	The 50000 International Unit (IU) vitamin D supplement weekly 5000 IU vitamin D supplement daily	None	Length of stay Chest x-ray findings

	Clinical Trial ID / Title	Population	Intervention Group(s)	Comparison Group(s)	Outcomes
			1000 IU vitamin D supplement daily		
13	NCT04459247 / Short Term, High Dose vitamin D Supplementation for COVID-19 Disease: Double Blind, Controlled, Study	Asymptomatic COVID-19 patients ages 18 years old or older	vitamin D: Oral liquid formulation of 60000 IU	Placebo	Virus negativity
14	EUCTR2020-001903-17 / A randomized clinical trial (IIIb) of efficacy of a single dose of Tocilizumab or a combination of Tocilizumab plus vitamin D (single i.m. dose) for the treatment of the COVID-19 hyperimmune complication. Assessment of IL-6.	Moderate-severe COVID-19 patients needing oxygen therapy	Combination of Tocilizumab plus vitamin D (single i.m. dose)	Single dose of Tocilizumab	Mortality Time to get to ICU Time to discharge from ICU Time to get rid from oxygen therapy
15	NCT04482673 / The Role of vitamin D in Mitigating COVID-19 Infection Severity: Focusing on Reducing Health Disparities in South Carolina	Adults aged 50 years or older presenting for COVID-19 testing	Bolus 20,000 IU vitamin D3 daily for 3 days 6000 IU vitamin D3 daily	Placebo	Change in SARS-CoV-2 antibody titers Respiratory symptoms
16	NCT04334005 / Effect of vitamin D Administration on Prevention and Treatment of Mild Forms of Suspected Covid-19	non-severe symptomatic COVID-19 patients aged 40 to 70 years	25000 UI of vitamin D supplement in addition to usual care	Usual care	Mortality Necessity of assisted ventilation ICU admission Hospital admission
17	CTRI/2020/12/030083	COVID-19 patients ages 18 years old or older	1. Uncomplicated illness-3,60,000-6,00,000IU 6-10days Once a day 2. Mild Pneumonia-3,60,000-6,00,000IU 6-10days Once a day 3. Severe Pneumonia-3,60,000-6,00,000IU 3-5days Twice a day	standard treatment	Duration of symptoms Time taken for double negative RT-PCR Time of hospital stay ICU admission Mortality

	Clinical Trial ID / Title	Population	Intervention Group(s)	Comparison Group(s)	Outcomes
18	IRCT20200324046850N1/ Comparison of vitamin D3 and N-acetylcysteine prescription in COVID19 patients and their effect on recovery process	COVID-19 patients that have positive PCR test of nasopharyngeal sample or have positive CT Scan for COVID-19.	vitamin D3 ampoules of 50,000 units once a week and N-acetylcysteine placebo tablets every 12 hours 600mg N-acetylcysteine tablet every 12 hours and vitamin D3 placebo once a week 600mg N-acetylcysteine tablets every 12 hours and 500,000 units of vitamin D3 once a week	Placebo	Time to clinical improvement
19	IRCT20200401046909N1 / The efficacy of oral 25-hydroxyvitamin D3 on COVID-19 treatment in adults: A Randomized, Controlled Double-Blind Clinical Trial.	COVID-19 patients aged 18 to 75 years	1000 IUs of 25(OH)D daily for 8 wks.	Placebo	Infection duration Severity of disease
20	NCT04344041 / COvid-19 and vitamin D Supplementation: a Multicenter Randomized Controlled Trial of High Dose Versus Standard Dose vitamin D3 in High-risk COVID-19 Patients (CoVitTrial)	COVID-19 patients aged 65 or older	vitamin D supplementation of 400,000 IU in a single oral dose.	vitamin D supplementation of 50,000 IU in a single oral dose	Mortality Clinical evolution
21	NCT04363840 / The LEAD COVID-19 Trial: Low-risk, Early Aspirin and vitamin D to Reduce COVID-19 Hospitalizations	COVID-19 patients aged 18 or older	(1) vitamin D 50,000 IU to be taken orally once weekly for 2 weeks + Aspirin 81 mg to be taken orally once daily for 14 days. (2) Aspirin 81 mg to be taken orally once daily for 14 days.	Observation	
22	EUCTR2020-001717-20 / Prevention and treatment with Calcifediol of Coronavirus COVID-19-induced acute respiratory syndrome (SARS)	COVID-19 patients aged 18 to 90 years	treatment with Calcifediol	n/a	admission to ICU mortality

	Clinical Trial ID / Title	Population	Intervention Group(s)	Comparison Group(s)	Outcomes
23	NCT04385940 / Improving vitamin D Status in the Management of COVID-19	COVID-19 patients aged 17 years or older	50,000 IU, Oral vitamin D3	vitamin D3 1000IU	Symptoms recovery Hospitalization Duration of mechanical ventilation ICU admission
24	IRCT20140305016852N4/ Comparison of three methods of treatment in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with and without coronavirus positive test (Kovid-19)	COVID-19 patients aged 15 years or older	(1) Taking vitamin D supplements and routine treatment (2) Taking vitamin C supplements and routine treatment	Routine treatment	RT-PCR results CX-Ray findings Vital signs Respiratory symptoms
25	NCT04386850 / Preventive and Therapeutic Effects of Oral 25-hydroxyvitamin D3 on Coronavirus (COVID-19) in Adults	COVID-19 patients aged 18 to 75 years	25 mcg of 25(OH)D3 once daily	Placebo	COVID-19 infection Severity of COVID-19 Hospitalization Mortality
26	EUCTR2020-002274-28 / Usefulness of vitamin D on morbidity and mortality of SARS-COV-2 virus infection (Covid-19) at the Central University Hospital of Asturias	COVID-19 patients aged 18 years or older being treated on an inpatient basis	vitamin D	n/a	Negative SARS-CoV-2 viral load Clinical symptoms and time during hospitalization Average stay in ICU Admission to ICU Mortality during follow-up