Online Supplementary Material

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Supplementary Material 1: Search Strategy

This review looks at how malnutrition in all its forms (undernutrition, micronutrient deficiencies and overnutrition) may influence both susceptibility to, and progression of, COVID-19. We synthesise information on the following 13 nutrition-related components and their potential interactions with COVID-19:

i) Protein-energy malnutrition
ii) Overweight, obesity and diabetes
iii) Anaemia
iv) Iron
v) Vitamin A
vi) Vitamin C
vii) Vitamin D
viii) Vitamin E
ix) Poly-Unsaturated Fatty Acids
x) Selenium
xi) Zinc
xii) Anti-oxidants
xiii) Nutritional support

Each section follows the following structure:

1. **Landscape review of other pertinent evidence**

This section does not require a systematic search. Coverage is limited to: a) very brief description of nutrient/condition vis-à-vis infection/immunity; b) evidence of any role in other viral infections (especially of respiratory tract); c) possible mechanisms; d) possible utility in treatment.

2. **Systematic review of published literature and pre-prints**

a) PUBMED – see example search string in **Supplementary Material 2**
b) EMBASE - see example search string below **Supplementary Material 2**
c) Pre-print servers: see search terms in **Supplementary Material 2**
    i. WHO Global literature on coronavirus disease: https://search.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/
    ii. The Lancet COVID-19 Resource Centre: https://www.thelancet.com/coronavirus
    iii. The JAMA network Coronavirus Resource site: https://jamanetwork.com/collections/46099/coronavirus-covid19
    iv. The New England Journal of Medicine Coronavirus Resource site: https://www.nejm.org/coronavirus
    v. The bioRxiv preprint server: https://www.biorxiv.org
    vi. The medRxiv preprint server: https://www.medrxiv.org
    vii. The ChinaXiv preprint server: http://chinaxiv.org/home.htm
    viii. The ChemRxiv preprint server: https://chemrxiv.org/

ix. The Preprints server: https://www.preprints.org
x. The Research Square preprint site: https://www.researchsquare.com
xi. The LitCovid hub: https://www.ncbi.nlm.nih.gov/research/coronavirus/
xii. The WHO Global research database: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov
xiii. The Cell Press Coronavirus Resource Hub: https://www.cell.com/2019-nCOV
xiv. The Nature Research Coronavirus collection: https://www.nature.com/collections/hajgidghjb
xv. Science Coronavirus collection: https://www.sciencemag.org/collections/coronavirus
xvi. The COVID-19 Primer: https://covid19primer.com/dashboard

Inclusion criteria

- Human studies
- **PubMed & EMBASE:** related to COVID-19, MERS-CoV or SARS-CoV AND disease susceptibility / progression AND nutrient exposure of interest.
- **Pre-print servers:** related to COVID-19 AND disease susceptibility / progression AND nutrient exposure of interest.
- All original studies of any design
- Systematic reviews (to check bibliography)
- Published in English language

Exclusion criteria

- Comments, letters, opinions, non-systematic reviews

3. **Systematic review of the following clinical trial registers:**

a) ClinicalTrials.gov: https://clinicaltrials.gov/
b) ISRCTN Registry: https://www.isrctn.com/
c) EU Clinical Trials Register: https://www.clinicaltrialsregister.eu/
d) Pan African Clinical Trials Registry: https://pactr.samrc.ac.za/
e) India Clinical Trials Registry: http://ctri.nic.in/Clinicaltrials/login.php
f) Chinese Clinical Trial Registry: http://www.chictr.org.cn/enIndex.aspx

Inclusion criteria: trials related to COVID-19 AND nutrient exposure of interest, human trials, protocols in English language.

See **Supplementary Material 2** for simplified search terms.

Supplementary Material 2: Search terms

Search terms for PubMed and EMBASE databases

	Concept 1 AND	**(Concept 2 OR**	**Concept 3)**	**AND Concept 4**
Key concepts	Coronavirus **AND**	(Disease susceptibility **OR**	Disease progression)	**AND** Terms specific to sub-section
Free text terms	coronavir* OR “coronavirus infections” OR covid* OR ncov*OR 2019-ncov OR 2019ncov OR “2019-novel CoV” OR HCoV* OR cov2 OR “cov 2” OR OC43 OR NL63 OR 229E OR HKU1 OR “sars coronavirus 2” OR “sars-like coronavirus” OR “Severe Acute Respiratory Syndrome” OR SARS OR sars-cov* OR sarscov* OR “Middle East Respiratory Syndrome” OR MERS OR MERS-CoV	“adaptive immunity” OR “acquired immunity” OR “innate immunity” OR “cell-mediated immunity” OR “humoral immunity” OR “antibody formation” OR immunosuppression OR immunodepression OR “immunity impairment” OR “immune dysfunction” OR “lymphocyte function” OR “macrophage activity” OR “oxidative stress” OR “host defence” OR “immune response” OR inflammation OR “immune pathology” OR immunopathology OR "Macrophage activation syndrome” OR “MAS” OR “cytokine storm”	“viral load” OR “viral pathogen*” OR “viral replication” OR “viral mutation” OR “viral transmission” OR “acute respiratory distress OR syndrome” OR “ARDS” OR “hemophagocytic lymphohistiocytosis” OR “HLH” OR pneumonia OR bronchitis OR bronchiolitis OR “asthma exacerbation*” OR seizure* OR diarrhoea OR diarrhea OR “acute gastroenteritis” or dehydration or “electrolyte imbalance” OR “renal failure” OR “kidney failure” OR “multi-organ failure*” OR “multiple organ failure*” OR encephalomyelitis OR “Kawasaki disease” OR “Kawasaki syndrome” OR “Mucocutaneous Lymph Node Syndrome” OR coagulopathy OR death OR mortality	e.g. Vit C Ascorbic acid

	Concept 1 AND	(Concept 2 OR	Concept 3)	AND Concept 4
Controlled vocabulary terms / Subject terms MeSH terms	"Coronavirus Infections"[Mesh] OR "Coronavirus"[Mesh] OR "COVID-19"[Supplementary Concept] OR "Severe Acute Respiratory Syndrome"[Mesh] OR "severe acute respiratory syndrome coronavirus 2" [Supplementary Concept] OR "Middle East Respiratory Syndrome Coronavirus"[Mesh]	"Immune System Phenomena"[Mesh] OR "T-Lymphocytes, Regulatory"[Mesh] OR "Inflammation"[Mesh] OR "Immunosuppression"[Mesh] OR "Oxidative Stress"[Mesh] OR "Macrophage Activation Syndrome"[Mesh]	"Viral Load"[Mesh] OR "Virus Physiological Phenomena"[Mesh] OR "Respiratory Distress Syndrome, Adult"[Mesh] OR "Respiratory Tract Infections"[Mesh] OR "Gastrointestinal Diseases"[Mesh] OR "Gastroenteritis"[Mesh] OR "Seizure"[Mesh] OR "Diarrhea"[Mesh] OR "Dehydration"[Mesh] OR "Water-Electrolyte Imbalance"[Mesh] OR "Kidney Failure, Chronic"[Mesh] OR "Shock"[Mesh] OR "Encephalomyelitis"[Mesh] OR "Mucocutaneous Lymph Node Syndrome"[Mesh] OR "Blood Coagulation Disorders"[Mesh] OR "Mortality"[Mesh]	e.g. "Ascorbic Acid"[Mesh]
Controlled vocabulary terms / Subject terms Emtree terms	exp Coronavirus/ exp Coronaviridae infection/ exp severe acute respiratory syndrome/ exp SARS coronavirus/ exp Middle East respiratory syndrome coronavirus/	exp immune system/ exp T lymphocyte/ exp inflammation/ exp immune deficiency/ exp oxidative stress/ exp macrophage activation/ exp cytokine storm/	exp virus load/ exp virus transmission/ exp virus shedding/ exp virus virulence/ exp virus characterization/ exp virus immunity/ exp virus infection/ exp virus cell interaction/ exp virus transcription/ exp virus inhibition/ exp respiratory tract infection/	exp ascorbic acid/

	Concept 1 AND	(Concept 2 OR	Concept 3)	AND Concept 4
			exp gastrointestinal infection/ exp pneumonia/ exp virus pneumonia/ exp bronchitis/ exp bronchiolitis/ exp viral bronchiolitis/ exp asthma/ exp seizure/ exp diarrhea/ exp gastroenteritis/ exp viral gastroenteritis/ exp dehydration/ exp electrolyte disturbance/ exp kidney failure/ exp multiple organ failure/ exp encephalomyelitis/ exp mucocutaneous lymph node syndrome/ exp blood clotting disorder/ exp mortality/	

Vitamin C example

Example search string in PubMed

(coronavir* OR “coronavirus infections” OR covid* OR ncov* OR “2019-ncov” OR “2019ncov” OR “2019-novel CoV” OR HCoV* OR cov2 OR “cov 2” OR OC43 OR NL63 OR 229E OR HKU1 OR “sars coronavirus 2” OR “sars-like coronavirus” OR “Severe Acute Respiratory Syndrome” OR SARS OR sars-cov* OR sarscov* OR “Middle East Respiratory Syndrome” OR MERS OR “MERS-CoV” OR "Coronavirus Infections"[Mesh] OR “Coronavirus”[Mesh] OR “COVID-19"[Supplementary Concept] OR "Severe Acute Respiratory Syndrome"[Mesh] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "Middle East Respiratory Syndrome Coronavirus"[Mesh])

AND

((“adaptive immunity” OR “acquired immunity” OR “innate immunity” OR “cell-mediated immunity” OR “humoral immunity” OR “antibody formation” OR immunosuppression OR immunodepression OR “immunity impairment” OR “immune dysfunction” OR “lymphocyte function” OR “macrophage activity” OR “oxidative stress” OR “host defence” OR “immune response” OR inflammation OR “immune pathology” OR immunopathology OR "Macrophage activation syndrome” OR “MAS” OR “cytokine storm” OR "Immune System Phenomena"[Mesh] OR "T-Lymphocytes, Regulatory"[Mesh] OR "Inflammation"[Mesh] OR "Immunosuppression"[Mesh] OR "Oxidative Stress"[Mesh] OR "Macrophage Activation Syndrome"[Mesh])

OR

(“viral load” OR “viral pathogen*” OR “viral replication” OR “viral mutation” OR “viral transmission” OR “acute respiratory distress syndrome” OR “ARDS” OR “hemophagocytic lymphohistiocytosis” OR “HLH” OR “pneumonia” OR “bronchitis” OR “bronchiolitis” OR “asthma exacerbation*” OR “seizure*” OR “diarrhoea” OR “diarrhea” OR “acute gastroenteritis” or “dehydration” or “electrolyte imbalance” OR “renal failure” OR “kidney failure” OR “multi-organ failure*” OR “multiple organ failure*” OR “encephalomyelitis” OR “Kawasaki disease” OR “Kawasaki syndrome” OR “Mucocutaneous Lymph Node Syndrome” OR “coagulopathy” OR “death” OR “mortality” OR “Viral Load”[Mesh] OR “Virus Physiological Phenomena”[Mesh] OR "Respiratory Distress Syndrome, Adult"[Mesh] OR "Respiratory Tract Infections"[Mesh] OR "Gastrointestinal Diseases"[Mesh] OR "Gastroenteritis"[Mesh] OR "Seizures"[Mesh] OR "Diarrhea"[Mesh] OR "Dehydration"[Mesh] OR "Water-Electrolyte Imbalance"[Mesh] OR "Kidney Failure, Chronic"[Mesh] OR "Shock"[Mesh] OR "Encephalomyelitis"[Mesh] OR "Mucocutaneous Lymph Node Syndrome"[Mesh] OR "Blood Coagulation Disorders"[Mesh] OR "Mortality"[Mesh]))

AND

(“vitamin C” OR “ascorbic acid” OR "Ascorbic Acid"[Mesh])

Example search string in EMBASE

((coronavir* OR "coronavirus infections" OR covid* OR ncov* OR 2019-ncov OR 2019ncov OR "2019-novel CoV" OR HCoV* OR cov2 OR "cov 2" OR OC43 OR NL63 OR 229E OR HKU1 OR "sars coronavirus 2" OR "sars-like coronavirus" OR "Severe Acute Respiratory Syndrome" OR SARS OR sars-cov* OR sarscov* OR "Middle East Respiratory Syndrome" OR MERS OR MERS-CoV).ti,ab,kw. OR exp Coronavirus/ OR exp Coronaviridae infection/ OR exp severe acute respiratory syndrome/ OR exp SARS coronavirus/ OR exp Middle East respiratory syndrome coronavirus/)

AND

(((("adaptive immunity" OR "acquired immunity" OR "innate immunity" OR "cell-mediated immunity" OR "humoral immunity" OR "antibody formation" OR immunosuppression OR immunodepression OR "immunity impairment" OR "immune dysfunction" OR "lymphocyte function" OR "macrophage activity" OR "oxidative stress" OR "host defence" OR "immune response" OR inflammation OR "immune pathology" OR immunopathology OR "Macrophage activation syndrome" OR MAS OR "cytokine storm").ti,ab,kw. OR exp immune system/ OR exp T lymphocyte/ OR exp inflammation/ OR exp immune deficiency/ OR exp oxidative stress/ OR exp macrophage activation/ OR exp cytokine storm/)

OR

(("viral load" OR "viral pathogen*" OR "viral replication" OR "viral mutation" OR "viral transmission" OR "acute respiratory distress syndrome" OR ARDS OR "hemophagocytic lymphohistiocytosis" OR HLH OR pneumonia OR bronchitis OR bronchiolitis OR "asthma exacerbation*" OR seizure* OR diarrhoea OR diarrhea OR "acute gastroenteritis" or dehydration or "electrolyte imbalance" OR "renal failure" OR "kidney failure" OR "multi-organ failure*" OR "multiple organ failure*" OR encephalomyelitis OR "Kawasaki disease" OR "Kawasaki syndrome" OR "Mucocutaneous Lymph Node Syndrome" OR coagulopathy OR death OR mortality).ti,ab,kw. OR exp virus load/ OR exp virus transmission/ OR exp virus shedding/ OR exp virus virulence/ OR exp virus characterization/ OR exp virus immunity/ OR exp virus infection/ OR exp virus cell interaction/ OR exp virus transcription/ OR exp virus inhibition/ OR exp respiratory tract infection/ OR exp gastrointestinal infection/ OR exp pneumonia/ OR exp virus pneumonia/ OR exp bronchitis/ OR exp bronchiolitis/ OR exp viral bronchiolitis/ OR exp asthma/ OR exp seizure/ OR exp diarrhea/ OR exp gastroenteritis/ OR exp viral gastroenteritis/ OR exp dehydration/ OR exp electrolyte disturbance/ OR exp kidney failure/ OR exp multiple organ failure/ OR exp encephalomyelitis/ OR exp mucocutaneous lymph node syndrome/ OR exp blood clotting disorder/ OR exp mortality/))

AND

(("vitamin C" OR "ascorbic acid").ti,ab,kw. OR exp ascorbic acid/)

Search terms for specific sections (used in concept 4)

Section	PubMed search terms	EMBASE search terms
Protein-energy Malnutrition	“protein energy malnutrition” OR “protein-energy malnutrition” OR “childhood undernutrition” OR “severe acute malnutrition” OR marasmus OR kwashiorkor OR “bilateral pitting oedema” OR “bilateral pitting edema” OR “elderly undernutrition” OR “low body mass index” OR “low BMI” OR sarcopenia OR (undernutrition AND elderly) OR “adult malnutrition” OR “adult undernutrition” OR "Protein-Energy Malnutrition"[Mesh] OR "Sarcopenia"[Mesh] OR "Severe Acute Malnutrition"[Mesh]	("protein energy malnutrition" OR "protein-energy malnutrition" OR "childhood undernutrition" OR "severe acute malnutrition" OR marasmus OR kwashiorkor OR "bilateral pitting oedema" OR "bilateral pitting edema" OR "elderly undernutrition" OR "low body mass index" OR "low BMI" OR sarcopenia OR (undernutrition AND elderly) OR "adult malnutrition" OR "adult undernutrition").ti,ab,kw. OR exp malnutrition/ OR exp kwashiorkor/ OR exp marasmus/ OR exp muscle atrophy/ OR exp sarcopenia/
Overweight, obesity, diabetes	overweight OR obes* OR “high body mass index” OR “high BMI” OR diabetes OR diabetic OR prediabetes OR "Obesity"[Mesh] OR "Overweight"[Mesh] OR "Diabetes Mellitus"[Mesh]	(overweight OR obes* or "high body mass index" OR "high BMI" OR diabetes OR prediabetes).ti,ab,kw. OR exp obesity/ OR exp morbid obesity/ OR exp obesity management/ OR exp diet induced obesity/ OR exp abdominal obesity/ OR exp diabetic obesity/ OR exp maternal obesity/ OR exp diabetes mellitus/ OR exp impaired glucose tolerance/
Anaemia	anaemia OR anemia OR "Anemia"[Mesh]	(anaemia OR anemia).ti,ab,kw. OR exp megaloblastic anemia/ or exp microcytic anemia/ or exp iron deficiency anemia/ or exp normochromic normocytic anemia/ or exp sideroblastic anemia/ or exp hemolytic anemia/ or exp aplastic anemia/ or exp anemia/ or exp macrocytic anemia/ or exp pernicious anemia/
Vit A	“vitamin A” OR retinol OR carotenoid* OR “xerophthalmia” OR "Vitamin A"[Mesh] OR "Vitamin A Deficiency"[Mesh]	("vitamin A" OR retinol OR carotenoid* OR xerophthalmia).ti,ab,kw. OR exp retinol/ OR exp carotenoid/ OR exp retinol deficiency/
Vit C	“vitamin C” OR “ascorbic acid” OR "Ascorbic Acid"[Mesh]	("vitamin C" OR "ascorbic acid").ti,ab,kw. OR exp ascorbic acid/
Vit D	“Vitamin D” OR “vitamin D2” OR “vitamin D3” OR “cholecalciferol” OR “ergocalciferol” OR “25 hydroxyvitamin D”	("vitamin D" OR "cholecalciferol" OR "ergocalciferol" OR "25 hydroxyvitamin D").ti,ab,kw. OR exp vitamin D/
Vit E	“Vitamin E” OR “alpha tocopherol” OR "Vitamin E"[Mesh]	("vitamin E" OR "alpha tocopherol").ti,ab,kw. OR exp alpha tocopherol/
PUFAs	“PUFA” OR “polyunsaturated fatty acid” OR "eicosapentaenoic acid" OR “EPA” OR “docosahexaenoic acid” OR “DHA” OR “gamma linolenic acid” OR “GLA” OR “fish oil”[Mesh]	("PUFA" OR "polyunsaturated fatty acid" OR "eicosapentaenoic acid" OR "EPA" OR "docosahexaenoic acid" OR "DHA" OR "gamma linolenic acid" OR "GLA" OR "fish oil").ti,ab,kw. OR

		exp polyunsaturated fatty acid/ OR exp eicosapentaenoic acid/ OR exp docosahexaenoic acid/ OR exp gamma linolenic acid/ OR exp N-3 fatty acid/
Iron	iron OR ferrous OR ferric OR hepcidin OR ferritin OR transferrin OR Tsat OR heme OR haem OR hypoferremia OR hemochromatosis OR (("Ferritins"[Mesh] OR "Transferrins"[Mesh]) OR "Hepcidins"[Mesh]) OR "Receptors, Transferrin"[Mesh] OR "Iron Metabolism Disorders"[Mesh] OR "Iron, Dietary"[Mesh]	(iron OR ferrous OR ferric OR hepcidin OR ferritin OR transferrin OR Tsat OR heme OR haem OR hypoferremia OR hemochromatosis).ti,ab,kw. OR exp iron storage/ OR exp iron chelation/ OR exp iron/ OR exp iron overload/ OR exp iron metabolism disorder/ OR exp iron intake/ OR exp iron responsive element/ OR exp iron chelate/ OR exp iron deficiency anemia/ OR exp iron depletion/ OR exp iron therapy/ OR exp iron transport/ OR exp iron homeostasis/ OR exp iron chelating agent/ OR exp iron absorption/ OR exp iron deficiency/ OR exp iron metabolism/ OR exp iron binding capacity/ OR exp iron restriction/ OR exp iron balance/ OR exp iron blood level/ OR exp transferrin receptor/ OR exp transferrin receptor 2/ OR exp transferrin blood level/ OR exp transferrin/ OR exp hepcidin/ OR exp ferritin/
Selenium	selenium OR "Selenium"[Mesh]	(selenium).ti,ab,kw. OR exp selenium/
Zinc	zinc OR "Zinc"[Mesh]	(zinc).ti,ab,kw. OR exp zinc/
Anti-oxidants	“anti-oxidant*” OR “anti oxidant*” OR hydroxytyrosol OR lycopene OR lutein OR carotene OR carotenoid* OR polyphenol* OR resveratrol OR "Antioxidants"[Mesh] OR "Resveratrol"[Mesh] OR "Carotenoids"[Mesh]	("anti-oxidant*" OR "anti oxidant*" OR hydroxytyrosol OR lycopene OR lutein OR carotene OR carotenoid OR polyphenol* OR resveratrol).ti,ab,kw. OR exp antioxidant/ OR exp lycopene/ OR exp carotenoid/ OR exp polyphenol/ OR exp resveratrol/)
Nutritional support	“nutritional support” OR “enteral nutrition” OR “parenteral nutrition” OR "Nutritional Support"[Mesh]	("nutritional support" OR "enteral nutrition" OR "parenteral nutrition").ti,ab,kw. OR exp nutritional support/ OR exp enteric feeding/ OR exp parenteral nutrition/

Searches on clinical trial registries and pre-print servers are restricted to COVID-19 related studies, and use simplified search terms as below:

Section	Disease	Nutritional exposure
Protein-energy Malnutrition	coronavirus AND	"Protein-energy malnutrition" Undernutrition Sarcopenia "Severe acute malnutrition
Overweight, obesity, diabetes	coronavirus AND	Overweight Obesity Obese Diabetes
Anemia	coronavirus AND	Anemia Anaemia
Vit A	coronavirus AND	"Vitamin A" Retinol Carotenoid
Vit C	coronavirus AND	"Vitamin C" "Ascorbic Acid"
Vit D	coronavirus AND	"Vitamin D" Cholecalciferol Ergocalciferol "25 hydroxyvitamin D"
Vit E	coronavirus AND	"Vitamin E" Tocopherol
PUFAs / anti-inflammatories	coronavirus AND	"Polyunsaturated fatty acids" PUFA Omega-3 Eicosapentaenoic Acid
Iron	coronavirus AND	Iron Ferritin Hepcidin Transferrin
Selenium	coronavirus AND	Selenium
Zinc	coronavirus AND	Zinc

Anti-oxidants	coronavirus AND	Antioxidants “Anti oxidants” Anti-oxidants “Free radical”
Nutritional support	coronavirus AND	“nutritional support” “enteral nutrition” “Parenteral nutrition”

Supplementary Material 3: RCT results narrative

1. Protein-energy Malnutrition (PEM)

The clinical trials registry search identified three on-going studies in the US, Spain and France related to PEM, none of which are in children (Supplementary Material 3). All of these are observational studies. The US study (NCT04350073) seeks to undertake a detailed evaluation of the longitudinal energy expenditure and metabolic effects in COVID-19 adult patients, admitted to a single intensive care unit (ICU) with respiratory failure, using indirect calorimetry, cardiac assessment, body composition, and muscle and ultrasound measures. This is to guide the metabolic and nutritional care of these high-risk patients, optimise their care and ultimately improve outcomes. In Spain, the study (NCT04346212) seeks to assess the prevalence of oropharyngeal dysphagia among COVID-19 adult patients post discharge from one ICU and to describe their associated nutritional status, requirements for nutritional supplements and adaptations, in order to design strategies to optimise their care and clinical outcomes. The study in France (NCT04386460) seeks to explore the associated risks of dental health/isolation/ anorexia with malnutrition among elderly patients and evaluate the impact of dentists referring these at-risk patients to physicians on malnutrition prevention. The results of these studies are eagerly awaited as they will be key to informing the design of targeted nutritional interventions to both prevent and manage PEM in the context of COVID-19.

Whilst not a registered trial, Caccialanza *et al.*' (1) published the rationale and suggested protocol for early nutritional supplementation with high-calorie dense diets combined with intravenous infusion of multivitamin, multimineral trace elements solutions for non-critically ill patients hospitalized for COVID-19 disease.

2. Overweight, obesity and diabetes mellitus

Searches of clinical trials databases revealed 13 planned or ongoing studies related to overweight/obesity or diabetes and COVID-19 (Supplementary Material 3). Of these nine were observational studies and four RCTs (two in the USA, one in Israel and one in Italy). Three of the RCTs evaluate the efficacy of the use of dipeptidyl peptidase 4 (DPP4) inhibitors (oral hypoglycemic agents: Linagliptin and Sitagliptin respectively) whilst another uses an antiviral nucleotide analogue (AT-527) on COVID-19 outcomes. All three studies using oral hypoglycemic agents evaluate their efficacy, compared with standard care, on clinical outcomes defined as lung disease in two studies and changes in glucose levels in one. The study using AT-527 seeks to assess its effect on progression to respiratory insufficiency, compared with a matching placebo, in moderate COVID-19 patients aged 45 to 80 years who are obese, or with a history of diabetes and hypertension.

3. Anaemia

The search of clinical trial registries did not identify any ongoing clinical studies specifically evaluating the effects of anaemia, or treatment of anaemia, on COVID-19 prognosis.

4. Iron

The clinical trial screen returned 134 trials. Amongst these 124 were identified owing to inclusion of ferritin concentration amongst clinical outcomes. No clinical trials pertaining to iron supplementation, or investigations of baseline iron status on COVID-19 susceptibility or progression were identified. However, three clinical trials were identified aimed at targeting iron during COVID-19 infection (Supplementary Material 3): each proposes to examine the effect of deferoxamine (Desferal®) on COVID-19 disease course and mortality, an approach discussed in a recent review (2). The rationale was not described in two of the three trials; in the third, a rationale of reducing iron-induced lung toxicity was proposed. Iron chelation can reduce replication of viruses including HIV-1 in vitro (2), yet its effect on viral pathogenesis in vivo is less clear. Given the emerging importance of iron in immune function and the uncharacterised role of iron in the SARS-CoV2 life cycle, outcomes of trials of iron sequestration in the context of COVID-19 are awaited with interest.

5. Vitamin A

Two small sized randomized clinical trials involving vitamin A in the treatment of COVID-19 patients were identified from the clinical trials registries search. One of the trials, targeting 30 hospitalised patients (15 in the intervention arm) involves the use of an oral nutrient supplement (anti-inflammatory/antioxidant nutrients and vitamins) as supportive care for COVID-19 and includes 2840 IU vitamin A daily among other nutrients in the supplement for 14 days (NCT04323228). The reason for using anti-inflammatory or anti-oxidant nutrients in COVID-19 patients in this trial is to modulate the cytokine storm associated with the disease on the lungs. The other trial, targeting 80 hospitalised (non-ICU) patients (NCT04360980) uses an unspecified amount of vitamin A as part of a combination of nutrients given to the control group or standard of care (n=40).

6. Vitamin C

The search of clinical trials registers in June 2020 yielded 27 entries involving vitamin C. Three were observational studies, and 8 used vitamin C as a placebo (reportedly because vitamin C tablets are a similar size and appearance to the hydroxychloroquine tablets used in all these trials). Of the remaining 16 trials where vitamin C was, or was part of, the active compound under test, 2 did not clearly state dose or mode of administration. Four trials involved dietary supplements of vitamin C

combined with other micronutrients, herbal remedies or in one case methylene blue and n-acetyl cysteine. These trials target 1220 participants at various stages of SARS-CoV-2 infection; usually in mild disease or testing the prophylactic value in healthcare workers. Based upon prior trials of HDIVC in patients with pneumonia, sepsis and cancers, 10 trials involve the intravenous administration of vitamin C.

The 10 currently-registered trials of HDIVC for COVID involve a target of 2,758 adult patients hospitalised with significant-to-critical COVID disease. They range from Phase 1 to 4. Three studies involve single-day bolus treatments with 10-20g vitamin C (for a 70kg individual). The remaining studies use doses ranging from 14 to 66g per day over 3-8 days with total doses amounting to between 56 and 327g of vitamin C (again for a 70kg individual). The rationale for these mega-doses is mixed, with claims of both anti-oxidant and pro-oxidant mechanisms, sometimes within the same rationale statements. Note that these doses are between 150 and 730 times higher than the recommended daily intake, and 7 to 33 times higher than the US Institute of Medicine's Tolerable Upper Limits for vitamin C (3). These should be viewed as pharmaceutical trials having no reference to vitamin C's normal physiological functions. Based upon the paucity of prior evidence the investment in such trials is questionable.

7. Vitamin D

Searches of clinical trials databases revealed 21 planned or ongoing studies related to vitamin D and COVID-19. Of these four were observational studies. The remaining 17 focussed on treatment (including disease progression) (n=12), prevention (n=2) or both prevention and treatment (n=2). Of the four prevention studies, vitamin D is registered as the main intervention for one trial, whilst two use vitamin D as an adjuvant with hydroxycholoroquine and one as a placebo. Of the remaining 13 trials, four use vitamin D in all groups, two as an adjuvant to the main treatment and seven either vitamin D3 (between 25 µg daily to single, bolus dose of 10 mg), vitamin D2 (1.25 mg twice weekly) or 25OHD (0.266 mg daily) as the primary intervention (one in combination with zinc). Study size ranges from 64 to 3140 participants.

8. Vitamin E

The search of clinical trials registers yielded a single entry (NCT04323228) involving a very small study (n=30) in Saudi Arabia with vitamin E administered to 15 patients as part of a broad antioxidant cocktail.

9. Poly-unsaturated fatty acids (PUFAs)

The search of trial registers yielded three trials that had PUFA in the active intervention arm (see Supplementary Material 3). The two trials in hospitalized patients in the USA are testing eicosapentaenoic acid (EPA). One of the trials combines the EPA with docosahexaenoic acid (DHA) and gamma linolenic acid (GLA) plus additional antioxidant micronutrients. The third trial, in Latin American countries, will test whether icosapent ethyl (IPE) will prevent occurrence of COVID in at-risk health providers. Severity of disease will also be compared against placebo.

10. Selenium

The search of trial registers yielded two listed trials. In one of these small doses of selenium are included in the control arm. The other was a very small Phase 4 trial in which low dose selenium forms part of an antioxidant cocktail administered to both arms. There were no listed trials of intravenous selenium, suggesting that the null or very marginal results from previous trials in ICU patients have discouraged further endeavours.

11. Zinc

A screen of registered trials revealed 16 studies of potential relevance. On review, three were removed; one was an observational case-control study and in a further two studies zinc was not included in any of the experimental arms. Of the remaining 13 trials, only a single trial (USA, n=520) is designed to fully assess the impact of zinc, in a four-arm trial of outpatients who test positive for SARS-CoV-2 and comparing vitamin C (8000mg/d) vs zinc (50mg/d) vs vitamin C + zinc (doses as before) vs standard of care (NCT04342728). In a further treatment trial among SARS-CoV-2 patients in Senegal (n=384), zinc (20mg/d) is being used as the control arm in a trial of HQ plus azithromycin (two arms with differing dosing regimens) (PACTR202005622389003). In four trials, zinc (at doses ranging from 15 to 250mg/d) is being administered in combination with other antiviral drugs including HQ, HC and azithromycin, HC and doxycycline or favipiravir. In the remaining seven trials, zinc is being provided in combination with single or multiple other micronutrients, including vitamin C, and vitamin B12 and, therefore, the potential therapeutic benefits of zinc as a single micronutrient cannot be established.

12. Antioxidants

The search of clinical trials registers yielded eight entries involving antioxidants (that were not vitamins A, C or E) (Supplementary Material 3). Of the eight trials, three involved dietary supplements containing a mixture of antioxidants and other molecules. The remaining five are testing the following molecules: Reservatrol, Silymarin, Quercetin, N-acetyl cysteine and melatonin. These trials target participants at various stages of SARS-CoV2 infection.

13. Nutritional support

Sixteen clinical trials were identified through our search and two were relevant to nutritional support (Supplementary Material 3). One has not yet started recruitment and aims to describe nutritional consequences of COVID-19 in patients discharged from hospital (based in France). The other aims to validate the use of a nutrition scoring tool “NUTRIC” in Chinese ICU patients diagnosed with COVID-19, results pending.

References

1 Caccialanza R, Laviano A, Lobascio F, *et al.* Early nutritional supplementation in non-critically ill patients hospitalized for the 2019 novel coronavirus disease (COVID-19): Rationale and feasibility of a shared pragmatic protocol. *Nutrition* 2020; **74**: 110835.

2 Liu W, Zhang S, Nekhai S, Liu S. Depriving Iron Supply to the Virus Represents a Promising Adjuvant Therapeutic Against Viral Survival. *Curr Clin Microbiol Reports* 2020; **7**: 13–9.

3 Institute of Medicine. Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids. Washington, D.C.: National Academies Press, 2000 DOI:10.17226/9810.

Supplementary Material 4: Ferritin and inflammation in the context of COVID-19

Ferritin was included as a systematic review search term since low serum ferritin is frequently used in diagnosis of iron deficiency (1, 2). The initial screen returned 22 papers, 9 preprints and 124 clinical trials mentioning ferritin, none of which related to iron status assessment. Instead, elevated ferritin (hyperferritinaemia) was consistently reported in COVID-19 patients, with levels highest in critical disease (see meta-analyses (3, 4)). While serum ferritin is upregulated in response to increased iron, it is also induced during inflammation by IL-1β and TNF-α, often correlating with inflammatory markers such as C reactive protein (CRP); as such, inflammation is a well-known confounder of ferritin-based iron status assessment (1, 5). Given that severe COVID-19 disease is characterised by hyperinflammation, reminiscent of other syndromes with macrophage activation-related hyperferritineamia (5, 6), serum ferritin levels will not reflect iron levels in the majority of COVID-19 patients. However, it does show potential as a prognostic biomarker given its association with COVID-19 disease severity (3, 4). Whether or not ferritin plays an active role in disease pathogenesis, or merely reflects the degree of inflammation and macrophage activation warrants further attention.

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Supplementary Table 1: Detailed Search Results per section

	Vit A	Vit C	Vit D	Vit E	Iron	Anae-mia	Selen-ium	Zinc	Anti-oxidants	PUFAs	Over-weight	PEM	Nutrit-ional Support	TOTAL
Pubmed and Embase searches														
PUBMED search date	18/05/2020	06/05/2020	22/05/2020	26/06/2020	16/05/2020	11/08/2020	04/06/2020	21/05/2020	01/06/2020	30/07/2020	04/06/2020	16.05.2020	02/06/2020	
No. of hits	9	18	28	13	54	118	6	9	53	19	522	9	36	894
EMBASE search date	18/05/2020	06/05/2020	22/05/2020	26/06/2002	16/05/2020	11/08/2020	04/06/2020	21/05/2020	01/06/2020	30/07/2020	04/06/2020	16.05.2020	02/06/2020	
No. of hits	35	36	49	26	95	380	13	68	159	26	809	101	41	1838
PUBMED + EMBASE hits	44	54	77	39	149	498	19	77	212	45	1331	110	77	2732
No. of duplicates	5	11	18	9	39	91	7	8	69	8	384	0	12	661
No. taken forwards to title / abstract screen	39	43	59	30	110	407	12	69	143	37	947	110	65	2071
No. ineligible	36	39	50	24	65	398	10	63	99	32	832	87	48	1783
No. taken to full text screen	3	4	9	6	45	9	2	6	44	5	115	23	17	288
No. ineligible: not related to COVID-19, SARS-CoV or MERS-CoV	1	0	3	0	10	0	0	0	9	0	1	8	3	35
No. ineligible: not related to disease susceptibility or progression	*0*	0	0	0	1	0	0	3	*7*	0	12	10	1	34
No. ineligible: not related to nutrient / condition in your section	0	0	0	0	25	6	0	1	6	0	2	2	3	45
No. ineligible: other reasons (e.g. not English, not human, reviews)	2	4	4	6	9	1	2	2	22	5	82	3	10	152
FINAL included in review	**0**	**0**	**2**	**0**	**0**	**2**	**0**	**0**	**0**	**0**	**18**	**0**	**0**	**22**
Clinical trial registries (searches 21-22/05/2020)														
clinicaltrials.gov	9	24	18	1	86	11	2	12	43	5	70	28	13	322
ISRCTN Registry	0	0	0	0	3	0	0	0	0	0	26	1	0	30
EU Clinical Trials Register	0	0	5	5	45	1	0	2	0	1	13	0	1	73
Pan African Clinical Trials Registry	0	0	0	0	0	0	0	1	0	0	0	0	2	3
India Clinical Trials Registry:	0	1	0	0	0	0	0	1	0	0	0	0	0	2
Chinese Clinical Trial Registry:	0	2	1	0	0	0	0	0	0	0	0	0	0	3
Total hits	9	27	24	6	134	12	2	16	43	6	109	29	16	433
Total no. sent to author	9	27	24	6	134	12	2	16	43	6	109	29	16	433
No. ineligible at author check	7	17	3	5	131	12	2	3	35	3	96	26	14	354
Total included in review	**2**	**10**	**21**	**1**	**3**	**0**	**0**	**13**	**8**	**3**	**13**	**3**	**2**	**79**
Pre-print servers (searches 25-28/05/2020)														

	Vit A	Vit C	Vit D	Vit E	Iron	Anae-mia	Selen-ium	Zinc	Anti-oxidants	PUFAs	Over-weight	PEM	Nutrit-ional Support	TOTAL
WHO Global literature on coronavirus disease	1	14	34	1	37	18	4	19	4	2	431	5	26	596
The Lancet COVID-19 Resource Centre	10	3	6	1	30	8	0	2	1	0	104	7	4	176
The JAMA network Coronavirus Resource site	2	1	1	1	0	6	0	2	3	2	54	0	7	79
The New England Journal of Medicine Coronavirus Resource site	0	0	0	0	2	2	0	0	0	0	22	0	1	27
The bioRxiv preprint server	1	0	0	0	0	0	1	0	0	1	8	0	0	11
The medRxiv preprint server	54	54	56	48	138	62	0	21	22	2	770	39	37	1303
The ChinaXiv preprint server	14	4	1	1	0	0	0	1	1	3	0	7	1	33
The ChemRxiv preprint server	4	0	9	3	1	0	1	2	2	0	1	0	0	23
The Preprints server	9	11	9	8	0	0	0	2	7	4	5	22	3	80
The Research Square preprint site	0	0	4	5	2	0	0	0	5	0	9	17	0	42
The LitCovid hub	46	48	47	46	32	14	3	11	69	2	376	12	178	884
The WHO Global research database	33	8	30	12	29	0	4	14	5	2	326	0	4	467
The Cell Press Coronavirus Resource Hub	0	0	0	0	0	0	0	0	1	0	0	0	0	1
The Nature Research Coronavirus collection	15	10	6	9	29	8	1	15	15	1	99	9	13	230
Science Coronavirus collection	2	2	2	1	3	0	0	7	2	1	27	3	0	50
The COVID-19 Primer	0	0	0	0	68	4	0	0	1	0	89	0	0	162
Total hits from pre-print servers	191	**155**	**205**	**136**	**371**	**122**	**14**	**96**	**138**	**20**	**2321**	**121**	**274**	**4164**
No. ineligible from simple screen	190	138	152	132	330	118	6	83	132	19	2037	117	254	3708
No. of duplicates across servers	0	4	15	0	17	0	4	3	0	0	130	0	5	178
Total no. of citations sent to author	**1**	**13**	**38**	**4**	**24**	**4**	**4**	**10**	**6**	**1**	**154**	**4**	**15**	**278**
No. ineligible at author check: not related to COVID-19	0	0	15	0	0	2	0	0	0	0	1	0	0	18
No. ineligible at author check: not related to disease susceptibility or progression	0	0	0	0	0	0	0	0	0	0	14	0	0	14
No. ineligible at author check: not related to nutrient / condition in your section	1	0	3	0	8	2	2	0	0	0	15	0	3	34
No. ineligible at author check: other reason for exclusion (e.g. not in English), reviews	0	13	14	4	16	0	2	9	6	1	95	2	12	173

	Vit A	Vit C	Vit D	Vit E	Iron	Anae-mia	Selen-ium	Zinc	Anti-oxidants	PUFAs	Over-weight	PEM	Nutrit-ional Support	TOTAL
Total included in review (data extraction)	**0**	**0**	**6**	**0**	**0**	**0**	**0**	**1**	**0**	**0**	**29**	**2**	**0**	**39**

Supplementary Table 2: Systematic Review data extraction

Section	Reference	Study design	Country	Sample size	Population details	Nutritional exposure	Disease susceptibility / progression	Outcomes: as defined by authors
EMBASE and PubMed searches								
Vitamin D	D'Avolio A *et al.* (1)	Retrospective cohort study (Observational)	Switzerland	107 patients with SARS-CoV-2 PCR test and 1377 patients without PCR test.	Of the 107 patients with PCR test, 27 were positive and 80 negative, 54% were male; median age was 73 years old (IQR 63–81). Of the 1377, 45% were male; median age was 63 years old (IQR 46 - 76).	Vitamin D status within 7 weeks of SARS-CoV-2 PCR results.	COVID-19 susceptibility	COVID-19 positive group had significantly lower 25-hydroxyvitamin D (25(OH)D)(P=0.004). When split by gender, it was not significant. When split by age, vitamin D status is associated with COVID-19 susceptibility in patients >70 years only (P=0.037).
Vitamin D	Ilie P *et al.* (2)	Cross-sectional	European countries	20 countries	Mean level of vitamin D, cases of COVID-19/1 M and deaths caused by COVID-19 (8th April 2020) for 20 European countries	Vitamin D status	COVID-19 susceptibility and severity	Inverse correlation between population mean vitamin D status and COVID-19 cases and deaths (both P=0.05).
Anemia	Hadadi A *et al.* (3)	Case study	Iran	1	80 years old man	Iron deficiency anemia	COVID-19 progression	Attenuation of attenuate respiratory distress syndrome, using antiviral treatment plus recombinant human erythropoietin to treat severe anemia.
Anemia	Bellmann-Weiler R *et al.* (4)	Retrospective cohort study (Observational)	Austria	259	Patients with PCR-confirmed SARS-CoV-2 infection needing hospitalization. 24.7% were anemic	Iron deficiency anemia	COVID-19 progression	Anemia was associated with a significantly higher in-hospital mortality (OR =3.729; 95%CI 1.739–7.995), P= 0.001) but not an increased frequency of intensive care unit admission or need for

Section	Reference	Study design	Country	Sample size	Population details	Nutritional exposure	Disease susceptibility / progression	Outcomes: as defined by authors
					and 80.0% had functional iron deficiency on admission.			mechanical ventilation. Functional iron deficiency was associated with more advanced inflammation and longer hospital stay.
Found in Preprint scan								
Vitamin D	Cuñat T *et al.* (5)	Retrospective transversal study (Observational)	Spain	17	Adult patients with COVID-19 in ICU.	25(OH)D concentration	COVID-19 severity	13/17 had 25(OH)D < 31 nmol/L
Vitamin D	De Smet D *et al.*(6)	Retrospective observational study	Belgium	186 cases; 2717 age/season-matched controls	Hospitalized patients	25(OH)D concentration	Association with infection	COVID-19 patients showed lower median 25(OH)D (18.6 ng/mL, IQR 12.6-25.3, versus 21.5 ng/mL, IQR 13.9-30.8; P=0.0016) and higher vitamin D deficiency rates (58.6% versus 45.2%, P=0.0005).
Vitamin D	Hastie C *et al.* (7)	Prospective cohort study (Observational)	UK	348598	UK Biobank participants	25(OH)D concentration	COVID-19 susceptibility	Associated with COVID-19 infection univariably (OR 0.99; 95% CI 0.99 - 0.999; p=0.013 but not after adjusting for confounders (OR= 1.0; 95% CI 0.998 - 1.01; P=208).
Vitamin D	Lau F *et al.* (8)	Retrospective observational study	USA	20	COVID-19 cases (13 in ICU, 7 floor patients), mean age 65.2+/-16.2 years old, 45% male	25(OH)D concentration	COVID-19 severity	No evidence of association between vitamin D deficiency and COVID-19 severity; greater vitamin D insufficiency (<75nmol/L) in ICU patients compared to floor patients.
Vitamin D	Meltzer D *et al.* (9)	Retrospective cohort study (Observational)	USA	499	Patients tested for SARS-CoV-2with vitamin D result from within the past year.	25(OH)D predicted status (likely deficient or sufficient at the moment of SARS-CoV-2 testing, based on results from previous year)	COVID-19 susceptibility	No effect of vitamin D deficiency (< 50 nmol/L), P=0.11). Being "likely vitamin D deficient" was associated with a greater risk of infection (RR=1.77, P<0.02) compared to being "likely vitamin D sufficient".
Vitamin D	Pinzon R *et al.* (10)	Case series (Observational)	Indonesia	10	COVID-19 cases 9 in Bethesda hospital Yogyakarta,	25(OH)D concentration	COVID-19 susceptibility and severity	9/10 patients had 25(OH)D < 50 nmol/L; 4/10 had 25(OH)D < 25nmol/L.

Section	Reference	Study design	Country	Sample size	Population details	Nutritional exposure	Disease susceptibility / progression	Outcomes: as defined by authors
					Indonesia, mean age 49.6 years old, 50% male.			
Protein Energy Malnutrition	Caccialanza R *et al.* (11)	Pragmatic intervention study protocol	Italy	Not stated in protocol	All hospitalized patients with COVID-19 (non-ICU).	Body mass index (BMI) <22 kg/m^2 , weight loss in past 3 months, reduced or expected to reduce food intake in the next few days.	COVID-19 severity	COVID-19 clinical outcomes.
Protein Energy Malnutrition	Li T *et al*. (12)	Cross-sectional study	China	182	Hospitalized elderly ≥65 with COVID-19	Mini nutritional assessment (MNA). Based on MNA scores, patients were divided into non-malnutrition group (MNA ≥ 24), the group with risk of malnutrition (MNA 17–23.5) and malnutrition group (MNA score < 17).	COVID-19 severity	"Combined diabetes (OR= 2.12; 95% CI 1.92–3.21), low calf circumference (OR=2.42; 95% CI 2.29–3.53), and low albumin (OR= 2.98; 95% CI 2.43–5.19) were independent risk factors for malnutrition".
Protein Energy Malnutrition	Liu G *et al.* (13)	Retrospective analysis of clinical cases	China	141	Hospitalized elderly >65 years with COVID-19	Four nutritional risk screening (NRS) tools: Nutrition Risk Screening 2002 (NRS 2002), Malnutrition Universal Screening Tool (MUST), Mini Nutrition Assessment Shortcut (MNA-sf), and Nutrition Risk Index (NRI).	COVID-19 severity	Nutritional risk was associated with "longer length of stay, higher hospital expenses, worse disease severity, and more weight change (in kg) than the normal group as assessed by the NRS 2002, MNA-sf, and NRI tools (P<0.05)". MUST only demonstrated that "patients with nutritional risk had less appetite and more weight change (kg) (P<0.05)".

Section	Reference	Study design	Country	Sample size	Population details	Nutritional exposure	Disease susceptibility / progression	Outcomes: as defined by authors
Zinc	Carlucci P *et al.* (14)	Retrospective observational	USA	932	Hospitalized patients with at least one positive test for SARS-CoV-2, "received hydroxychloroquine and azithromycin, and had either been discharged from the hospital, transitioned to hospice, or expired."	NA - patients categorized according to exposure to hydroxychloroquine and azithromycin alone or with zinc sulphate (50mg zinc twice daily for 5 days).	COVID-19 severity	"The addition of zinc sulfate did not impact the length of hospitalization, duration of ventilation, or ICU duration. In univariate analyses, zinc sulfate increased the frequency of patients being discharged home, and decreased the need for ventilation, admission to the ICU, and mortality or transfer to hospice for patients who were never admitted to the ICU. After adjusting for the time at which zinc sulfate was added to our protocol, an increased frequency of being discharged home (OR= 1.53; 95% CI 1.12-2.09) reduction in mortality or transfer to hospice remained significant (OR=0.449; 95% CI 0.271-0.744)".

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Supplementary Table 3: Results from Clinical Trial Registries Search

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Vitamin A	NCT04323228	Saudi Arabia	Double blind RCT	30	Hospitalized COVID-19 patients	237 mL ONS enriched in EPA, GLA and antioxidants (including 2,840 IU vitamin A)	Isocaloric placebo	Serum ferritin level, cytokine storm parameters (IL-6, TNF-α, and MCP1), CRP, total leukocyte count, differential lymphocytic count and neutrophil to lymphocyte ratio.
Vitamin A	NCT04360980	Iran	Double blind RCT	80	Hospitalized non-ICU COVID-19 patients	Colchicine tablets: 1.5 mg loading then 0.5 mg twice a day PO	Standard of care including daily (vitamin C 3 g, 400 mg Thiamin, Selenium, Omega-3 500 mg daily, Vitamin A, Vitamin D, Azithromycin, Ceftriaxone, Kaletra 400 twice a day). Some doses not specified.	CRPxN/R ratio change, clinical deterioration by the WHO definition including change in fever or O_2 Saturation, PCR Viral load change in RT-PCR, CT severity involvement index change in CT involvement.
Vitamin D	NCT04372017	USA	Prospective, double-blind, randomized, placebo-controlled trial	1,739	Healthcare workers and high-risk participants	HCQ: 800 mg on day 1 followed by 400 mg on days 2-5.	Vitamin D: 1,600 IU on day 1 and 800 IU on days 2-5	COVID-19 status
Vitamin D	NCT04335084	USA	Double-blind, randomized, placebo-controlled phase-IIa trial	600	Medical workers	HCQ, vitamin C, vitamin D, Zn	Vitamin C, vitamin D, Zn	Prevention of COVID-19 symptoms
Vitamin D	EUCTR: 2020-001363-85	Denmark	RCT	206	Nursing home residents >65 y, not previously infected	200 mg HCQ + unknown doses of vitamin D and Zn	Not stated	Prevention of COVID-19 symptoms

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Vitamin D	EUCTR: 2020-002274-28	Spain	Non-blind, randomized, two-arm, no-control trial	60	COVID-19 positive cases admitted to hospital >18 y	Vitamin D (Videsil 100,000 IU)	Not stated	Progression and clinical outcomes
Vitamin D	NCT04363840	USA	Non-blind, randomized, two-arm, no-control trial	1,080	Newly diagnosed COVID-19 patients	**Group 1:** Aspirin (81 mg once a day for 14 days) & **Group 2:** Aspirin (81 mg once daily for 14 days) + vitamin D (50,000 IU once a week for 2 weeks)	Observation only	Hospitalization for COVID-19
Vitamin D	NCT04360980	Iran	Double blind RCT	80	Hospitalized non-ICU COVID-19 patients	Colchicine tablets: 1.5 mg loading then 0.5 mg twice a day PO	Standard of care including daily (vitamin C 3 g, 400 mg Thiamin, Selenium, Omega-3 500 mg daily, Vitamin A, Vitamin D, Azithromycin, Ceftriaxone, Kaletra 400 twice a day). Some doses not specified.	CRPxN/R ratio change, clinical deterioration by the WHO definition including change in fever or O_2 Saturation, PCR Viral load change in RT-PCR, CT severity involvement index change in CT involvement.
Vitamin D	NCT04334512	USA	Randomized, Double-Blind, Placebo-Controlled Phase II intervention trial	600	Adults with diagnosis of COVID-19	HCQ, azithromycin, vitamin C, vitamin D, Zn	Vitamin C, vitamin D, Zn	Rate of recovery, reduction of symptomatic days
Vitamin D	NCT04399746	Mexico	Non-blind, non-randomized, control trial	30	Adults with confirmed COVID-19 (mild symptoms)	6 mg of Ivermectin once a day in days 0,1,7 and 8, 500 mg of azithromycin once a day for 4 days; 400 IU of cholecalciferol twice a day for 30 days	Observation only	Viral clearance, symptoms duration, O_2 saturation

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Vitamin D	NCT04400890	USA	Randomized Double-Blind Placebo-Controlled Trial	200	Adults >45 y with mild COVID-19 symptoms	Resveratrol (unknown dose) + vitamin D (cholecalciferol 100,000 IU on day 1)	Vitamin D (cholecalciferol 100,000 IU on day 1)	Hospitalization for COVID-19
Vitamin D	NCT04344041	France	Non-blinded RCT	260	Adults >=70 y with COVID-19	High dose vitamin D (400,000 IU)	Low dose vitamin D (50,000 IU)	Number of deaths
Vitamin D	NCT04366908	Spain	Non-blinded RCT	1,008	Adults 18-90 with PCR confirmed COVID-19	Vitamin D (cholecalciferol: 524 µg on day 1; 266 µg on days 3, 7, 14, 21 and 28) + best available treatment (combination of drugs included in the current protocol of the Ministry of Health and/or complementary notes issued by the AEMPS)	Best available treatment (combination of drugs included in the current protocol of the Ministry of Health and/or complementary notes issued by the AEMPS)	Admission to ICU, death
Vitamin D	NCT04351490	France	Non-blinded RCT	3,140	Institutiona-lized Adults >60 y	Zn (2x15 mg per day for 2 months), 25-hydroxycholecalciferol (2,000 IU per day for 2 months)	Usual treatment	Survival rate
Vitamin D	NCT04385940	Canada	Double-blinded, randomized, intervention trial	64	>17 y with COVID-19	High dose vitamin D (50,000 IU)	Low dose vitamin D (1,000 IU)	Symptom recovery
Vitamin D	NCT04334005	Spain	Double-blind, randomized, intervention trial	200	40-70 y with mild respiratory infection	25,000 IU of vitamin D (single dose) + usual treatment (NSAIDs, ACE2 inhibitor, ARB or thiazolidinediones)	Usual treatment (NSAIDs, ACE2 inhibitor, ARB or thiazolidinediones)	Mortality

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Vitamin D	EUCTR: 2020-001960-28	Spain	Randomized Double-Blind Placebo-Controlled Trial	108	Hospital admission with positive COVID-19, >18 y	0,266 mg of cholecalciferol (unknown frequency)	Placebo	Progression and mortality
Vitamin D	NCT04395768	Australia	Single-blinded RCT	200	>18 y with active COVID-19	**Inpatients**: Vitamin C (sodium ascorbate): 50 mg/kg every 6 h on day 1 followed by 100 mg/kg every 6 h (4 times per day; 400 mg/kg/d) for 7 days (average 28 g/d; maximum dose of 50 g/24 h for those weighing more than 125 kg) + standard treatment & **Outpatients**: Vitamin C (sodium ascorbate): 200 mg/kg x1 IV, then 1 g PO three times per day for 7 days + standard treatment	Standard treatment: HCQ 400 mg (2x200 mg) PO for 1 day, followed by 200 mg PO per day for 6 days azithromycin 500 mg PO on day 1 followed by 250 mg PO once daily for 4 days Zn citrate 30 mg elemental Zn PO daily cholecalciferol 5,000 IU PO daily for 14 days vitamin B-12 (methylcobalamin) 500 µg PO daily for 14 days	Symptoms, duration of hospital stay, ventilation, mortality

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Vitamin D	NCT04386850	Iran	Multicenter randomized double-blinded placebo-controlled clinical trial	1,500	18-75 y, **Intervention 1:** patients diagnosed with COVID-19 & **Intervention 2:** health care providers, hospital workers and close relatives of COVID-19 patients that have tested negative	25 g of 25-hydroxycholecalciferol once per day for 2 months	Placebo for 2 months	Infection, severity, hospitalization, disease duration, death, O_2 support
Vitamin D	NCT04394390	Turkey	Prospective cohort study (2 months follow-up)	100	Children and adults	N/A: measured "exposure" is vitamin D levels in positive COVID-19 patients	N/A	Disease severity
Vitamin D	NCT04386044	UK	Cross-sectional (hospitalized patients) & prospective cohort study (6 months follow-up of participants recruited from GP practice)	1,800	Adults, infected and uninfected	N/A: measured "exposure" is vitamin D levels in positive COVID-19 patients & vitamin D levels in GP patients	N/A	Cross sectional: Death, O_2 therapy - Cohort: Infection with COVID-19
Vitamin D	NCT04370808	Portugal	Prospective cohort study	500	>18 y with active COVID-19	N/A: measured "exposure" is vitamin D levels/genetic variants in vitamin D-related genes	N/A	COVID-19 severity and death

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Vitamin D	ChiCTR2000031163	China	Prospective cohort study	80	0.1-85 y males	N/A: measured "exposure" is vitamin D deficiency	N/A	Progression, treatment outcome and prognosis of COVID-19
Iron	NCT04389801	Egypt	Single-blind, placebo-controlled RCT	200	Hospitalized COVID-19 with chest tightness	Deferoxamine (desferal), Initial 1000 mg at 15 mg/kg/h (1 g) Subsequent 500 mg at 125 mg/h (0.5 g)	5% glucose	14-day mortality
Iron	NCT04361032	Tunisia	Open-label, Multicentric, Comparative, Randomized Study	260	ARDS ICU COVID-19, (18-80 y)	Deferoxamine (desferal), 40 mg/kg/d for 14 days (2.8 g)	Tocilizumab, 8 mg/kg/d	90-day mortality
Iron	NCT04333550	Iran	Double-blind, RCT	50	Mild, moderate or severe pneumonia COVID-19 (3-99 y)	Deferoxamine (desferal), dose not stated	Standard treatment	20-day mortality
Zinc	EudraCT Number: 2020-001449-38 NCT04373733	UK	Randomized non-blinded randomized trial	450	London >18 y COVID-19 patients	**Intervention 1** Favipiravir (1800 mg twice per day on day 1, 800 mg twice per day on days 2-10) + standard care & **Intervention 2** HCQ (400 mg twice per day on day 1, 200 mg twice per day on days 2-10) + azithromycin (250 mg once per day on days 1-3), Zn-sulphate: (125 mg twice per day on days 1-10) + standard care	Standard care	Time to clinical improvement

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Zinc	NCT04377646	Tunisia	Double blind randomized placebo-controlled trial with 3 arms	660	18-65 y, COVID-19 negative	HCQ (400 mg at days 1-2, then a weekly dose of 400 mg up to 2 months) + Zn (15 mg at daily dose up to 2 months)	Double placebo of HCQ and Zn	Frequency of confirmed SARS-CoV-2 infection
Zinc	NCT04335084	USA	Randomized, Double-Blind, Placebo-Controlled Phase IIa Study	600	Medical workers who are exposed to COVID-19 and as such are at higher risk of infection	No information on dosing levels. HCQ, vitamin C, vitamin D, Zn	Vitamin C, vitamin D, Zn	Prevention of COVID-19 symptoms over 24 weeks
Zinc	NCT04334512	USA	Randomized, Double-Blind, Placebo-Controlled Phase II Study	600	>18 y with COVID-19 diagnosis	No information on dosing levels. HCQ azithromycin, vitamin C, vitamin D, Zn	Vitamin C, vitamin D, Zn	Rate of recovery of mild or moderate COVID-19
Zinc	NCT04323228	Saudi Arabia	Randomized, Double-Blind, Placebo-Controlled trial	30	18-65 y; confirmed COVID-19 but stable condition	Daily ONS enriched in EPA, GLA and antioxidants. The composition of one can (237 mL) of the intervention-ONS includes: 14.8 g protein, 22.2 g fat, 25 g carbohydrate, 355 Kcal, 1.1 g EPA, 450 mg DHA, 950 mg GLA, 2840 IU vitamin A as 1.2 mg β-carotene, 205 mg vitamin C, 75 IU vitamin E, 18 ug selenium, and 5.7 mg Zn	Isocaloric-isonitrogenous product (by the same manufacture) and served in cans with the same color and shape.	Nutrition risk screening and biochemical markers

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Zinc	NCT04342728	USA	Randomized open label trial	520	>18 y; outpatients who test positive for COVID-19	**Intervention 1:** 8000 mg of ascorbic acid divided into 2-3 doses/d with food. **Intervention 2:** 50 mg of Zn gluconate to be taken daily at bedtime. **Intervention 3**: 8000 mg of ascorbic acid divided into 2-3 doses/d with food and 50 mg of Zn gluconate to be taken daily at bedtime.	Standard care	Symptom reduction over 28 days
Zinc	NCT04384458	Brazil	Open non-blinded randomized trial	400	Healthcare workers aged 18-70 y without COVID-19	HCQ: 400 mg PO twice a day on day 1, one 400 mg tablet on days 2-5, followed by one 400 mg tablets every 5 days until day 50, combined with 20 mg of active zinc taken twice daily for 45 consecutive days	Oral ivermectin dosage based on body weight, once per day for 2 consecutive days. This dose schedule is repeated every 14 days for 45 days, combined with 20 mg of active zinc taken twice daily.	Proportion of participants in whom there was a clinical finding of COVID-19 or number of symptomatic COVID-19 infections
Zinc	EudraCT Number: 2020-001363-85	Denmark	Randomized controlled Open trial	206	Nursing home residents >65 y	HCQ 200 mg, vitamin D and Zn (dose not stated)		Severity of the disease, hospitalization rate, and death in nursing home residents
Zinc	CTRI/2020/05/025215	India	Randomized, parallel Group Trial	50 per group	COVID-19 patients aged 18-55 y	Kabasura Kudineer 60 mL bd for 14 days	Vitamin C (60,000 IU OD for 14 days) + Zn (100 mg OD for 14 days)	Reduction in incidence of clinical symptoms of COVID-19

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Zinc	NCT04370782	USA	Randomized, non-blinded two arm (no control) clinical trial	750	>30 y; high initial clinical suspicion of COVID-19	**Intervention 1:** HCQ (400 mg twice a day on day 1, followed by 200 mg twice a day for days 2-5) + azithromycin (500 mg on day 1, followed by 250 mg once daily for days 2-5) + Zn sulphate (220 mg once daily for 5 days) **Intervention 2:** HCQ (400 mg twice a day on day 1, followed by 200 mg twice a day for days 2-5) + doxycycline (200 mg once daily for days 2-5) + Zn sulphate (220 mg once daily for 5 days)	N/A	Time to resolution of symptoms (day 5, 14 and 21), number of participants hospitalized, ICU length of stay, ventilator time frame
Zinc	PACTR202005622389003	Senegal	Randomized open label-controlled trial	384/128 per group	Patients 18-65 y with confirmed COVID-19	**Intervention 1**: 200 mg HCQ will be given 3 times a day for 6 days. Azithromycin will be administered on a single daily dose: 500 mg the first day followed by 250 mg from days 2-5. **Intervention 2**: HCQ will be given on 2 times daily (200mg - 200 mg) for 6 days. Azithromycin will be administered on a single daily dose: 500 mg the first day followed by 250 mg from days 2-5.	Zn (20 mg/d)	Death at day 7, time to first negative PCR after treatment initiation, biochemical parameters, hematological parameters, ECG abnormalities

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Zinc	NCT04351490	France	Randomized open label	3,140	>60 y	Zn gluconate capsule (2x15 mg per day for 2 months) + 25-hydroxycholecalciferol (2000 IU per day for 2 months)	Usual treatment	Survival rate in asymptomatic subjects at inclusion
Zinc	NCT04395768	Australia	Multi-center, International, single - blinded Randomized Trial	200	>18 y with active diagnosis	**Inpatients:** IV vitamin C (sodium ascorbate) 50 mg/kg every 6 h on day 1 followed by 100 mg/kg every 6 h (4 times per day; 400 mg/kg/d) for 7 days (average 28 g/d; maximum dose of 50 g/24 h for those weighing more than 125 kg). Can be converted to 1 g three times per day PO on hospital discharge. **Outpatients**: 200 mg/kg x1 IV vitamin C, then 1 g PO three times per day for 7 days	HCQ (400 mg PO twice a day for 1 day, followed by 200 mg PO two times a day for 6 days) + azithromycin (500 mg PO on day 1 followed by 250 mg PO once daily for 4 days) + Zn citrate (30 mg elemental Zn PO daily) + cholecalciferol (5,000 IU PO daily for 14 days) + vitamin B-12 (methylcobalamin 500 µg PO daily for 14 days)	Symptoms, length of hospital stay, invasive mechanical ventilation
Nutritional support	NCT04365816	France	Prospective cohort	403	Patients discharged from hospital after admission with COVID-19	N/A	N/A	Food intake at 1-month post discharge; weight variation during the infection; factors limiting food intake; implemented nutritional strategy; pre-existing chronic disorders; COVID-19 repercussions

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Nutritional support	NCT04274322	China	Prospective cohort	117	ICU patients	N/A	N/A	Validate the use of NUTRIC score nutritional risk assessment tool in Chinese ICU patients with COVID-19, 28-day all-cause mortality, all cause infection, rate of complications, length of ICU-stay, duration of mechanical ventilation
Vitamin C	NCT03680274	Canada	Double-blind RCT	800	Septic ICU (including COVID-19)	HDIVC 200 mg/kg/d for 4 days (56 g)	Dextrose 5% in water (D5W) or normal saline (0.9% NaCl).	28-day mortality
Vitamin C	NCT04264533	China	Double-blind RCT	140	Severe viral pneumonia	HDIVC 340 mg/kg/d for 7 days (168 g)	50 mL water for injection	28-day ventilator free days
Vitamin C	NCT04323514	Italy	Open label non-randomized trial	500	COVID-19 pneumonia	Diet + HDIVC 140 mg/kg/d for 1 day (10 g)	N/A (Single group assignment).	3-day mortality
Vitamin C	NCT04344184	USA	Double-blind RCT	200	COVID-19 pneumonia	HDIVC 300 mg/kg/d for 3 d (63 g)	Dextrose 5% Water	28-day ventilator free days
Vitamin C	NCT04357782	USA	Open label non-randomized trial	20	Mild/severe deoxygena-tion	HDIVC 200 mg/kg/d for 4 days (56 g)	N/A (Single group assignment)	Incidence of adverse events
Vitamin C	NCT04363216	USA	Open label randomized trial	66	Hospitalized COVID-19	Escalating dose of vitamin C 300, 600 and 900 mg/kg/d for 6 days (126/252/378 g)	Routine care	3-day clinical improvement (50% reduction in the highest flow rate of oxygen during the 72-hour period or 50% reduction in the most frequent use of bronchodilators within a 12-hour window within the 72-hour period or hospital discharge).
Vitamin C	NCT04395768	Australia	Double-blind RCT	200	COVID-19	200 mg/kg/d for 1 day + 400 mg/kg/d for 7 days (210 g)	No vitamin C	15-day symptoms since enrolment.

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Vitamin C	NCT04401150	Canada	Double-blind RCT	800	Hospitalized COVID-19	HDIVC 200 mg/kg/d for 4 days (56 g)	Normal saline (0.9% NaCl) or dextrose 5% in water (D5W) in a volume to match the vitamin C.	28-day mortality or persistent organ dysfunction
Vitamin C	ChiCTR 2000032716	China	RCT	12	Severe/critical COVID-19 pneumonia	HDIVC, dose not stated	Not stated	CRP, lymphocytes, CD4+ T helper cells
Vitamin C	ChiCTR 2000032717	China	RCT	60	Mild/severe COVID	Bolus HDIVC 166 mg/kg/d for 1 day	Not stated	Recovery time
PUFAs and antioxidants	NCT04323228	Saudi Arabia	Double-blind RCT	30	Hospitalized COVID-19	EPA, GLA and antioxidants PO: 1.1g EPA, 450 mg DHA, 950 mg GLA, 2840 IU vitamin A as 1.2 mg β-carotene, 205 mg vitamin C, 75 IU vitamin E, 18 ug selenium, 5.7 mg Zn	Placebo	3-month change in score of NRS-2002
PUFAs	NCT04335032	USA	Open label non-randomized trial	240	Hospitalized COVID-19	EPA gastro-resistant capsules (2 g daily EPA FFA)	N/A (Single group assignment)	Time to treatment failure within 28 days
PUFAs	NCT04460651	Latin America	Double-blind RCT	1,500	Healthcare providers at risk of COVID-19	IPE. 8 g IPE on days 1-3 4 g IPE on days 4-60	Placebo	PCR or IgG positive for SARS-CoV-2 by day 60
Overweight/ obesity/DM	NCT04396106	USA	Double-blind RCT	190	Moderate COVID-19 patients with history of obesity (BMI>30 kg/m^2), DM and hypertension age 45-80 y	AT-527 at 550 mg tablets on day 1 and twice every day for 5 days	Placebo	14-day proportions (active vs placebo) of subjects with progressive respiratory insufficiency

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Overweight/ obesity/DM	NCT04391738	France	Retrospective cohort	1,200	Patients admitted to ICU with SARS-CoV-2	N/A	N/A	3-month relationship between BMI and SARS-CoV-2
Overweight/ obesity/DM	NCT04391686	France	Observational Cohort	90	COVID-19 patients admitted at ICU with BMI>30 kg/m^2	N/A	N/A	The resting energy expenditure (in Kcal/24 h) measured by indirect calorimetry during the stay in intensive care (3 months after baseline).
Overweight/ obesity/DM	NCT04390555	Switzerland	Observational Cohort	1,500	Hospitalized COVID-19 patients with pre-existing cardiovascular diseases and/or cardiovascular risk factors (DM, arterial hypertension and/or dyslipidemia)	N/A	Patients with COVID-19 without pre-existing cardiac involvement	30-day in-hospital mortality
Overweight/ obesity/DM	NCT04390074	Sweden	Case-control	9,905	ICU patients	N/A	Age- and sex-matched controls are drawn from all residents of Sweden by Statistics Sweden	Odds of intensive care treatment for COVID-19 for patients treated with drugs for DM1, DM2, obesity and other co-morbidities (drug dispensation within 6 months prior to enrolment). Odds of intensive care treatment for COVID-19 for patients diagnosed with a range of comorbidities.

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Overweight/ obesity/DM	NCT04384471	Canada	Cross-sectional	384	People living with DM1 in Quebec and are registered on the BETTER registry	N/A	N/A	Self-reported acute-DM complication. Severe hypoglycemia and diabetic ketoacidosis
Overweight/ obesity/DM	NCT04382794	Italy	Case-control	338	DM2 hospitalized patients with COVID-19 diagnosis	Sitagliptin	Not treated with Sitagliptin	Clinical parameter of acute lung disease
Overweight/ obesity/DM	NCT04371978	Israel	Open label randomized trial	100	Hospitalized COVID-19 patients with DM	Linagliptin (5 mg PO once a day)	Standard of care	Time to clinical change (within 28 days)
Overweight/ obesity/DM	NCT04365634	China	Case-control	306	Hospitalized COVID-19 patients with and without DM	N/A	N/A	The predictive factors associated with hospitalized death of patients with COVID-19 (timeframe of 28 days)
Overweight/ obesity/DM	NCT04365517	Italy	Open label randomized trial	170	Patients hospitalized for COVID-19 and suffering from DM2	Sitagliptin at an adjusted dosage for estimated glomerular filtrate: 100 mg once a day (estimated glomerular filtration rate less than or equal to 45 mL/min/1.73 m^2) or 50 mg (estimated glomerular filtration rate 30-45 mL/min/1.73 m^2) in combination or not with insulin	Standard of care	Time to clinical improvement, clinical and biochemical parameters of acute lung disease
Overweight/ obesity/DM	NCT04341935	USA	Open label randomized trial	20	Hospitalized for COVID-19 with DM2	5 mg Linagliptin PO once per daily	Standard of care	Changes in glucose levels up to 2 weeks

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Overweight/ obesity/DM	NCT04324736	France	Retrospective cohort	5,497	DM patients treated for COVID-19 in a hospital center and non-DM patients treated for COVID-19	N/A	N/A	Assess the prevalence of severe forms among hospitalized patients with DM and COVID-19 within 1 month.
Overweight/ obesity/DM	NCT04324684	Italy	Case-control	198	Subjects hospitalized for COVID-19 pneumonia presenting with complications including DM and obesity.	N/A	N/A	Time to improvement within 3 weeks
Antioxidants	NCT04400890	USA	Double-blind RCT	200	Mild COVID-19 with symptoms <7 days	Resveratrol four times a day for 15 days	Placebo	Hospitalization 21 days from randomization
Antioxidants	NCT04394208	Egypt	Double-blind RCT	50	Patients with COVID-19 pneumonia	420 mg/d Silymarin in 3 divided doses	Placebo	Time to clinical improvement (7-28 days)
Antioxidants	NCT04382040	Israel	Double-blind RCT	50	COVID-19+; in stable to moderate condition (not requiring ICU admission)	6 mg Artemisinin, 20 mg Curcumin, 15 mg Frankincense and 60 mg vitamin C given daily in two divided doses, on days 1 and 2.	Placebo	Time to clinical improvement, percent of patients with adverse events (24 hours)

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
Antioxidants	NCT04377789	Turkey	Non-randomized	50	At moderate-high risk for COVID-19 (prophylaxis group), COVID-19+ (treatment group)	500 (prophylaxis group) or 1000 mg (treatment group) Quercetin. Time of treatment unclear.	Placebo	Prevalence of COVID-19 (prophylaxis group). Mortality rate (treatment group)
Antioxidants	NCT04374461	USA	Non-randomized	86	COVID-19+, **Intervention 1:** Admission to an ICU; **Intervention 2:** Hospital admission but not requiring mechanical ventilation or admission to an ICU	N-acetylcysteine IV 6 g/d	None	**Intervention 1:** number of patients who are successfully extubated and/or transferred out of critical care due to clinical improvement. **Intervention 2:** number of patients who are discharged from the hospital due to clinical improvement
Antioxidants	NCT04353128	Spain	Double blind RCT	450	COVID-19 negative healthcare workers	Melatonin 2 mg/d for 12 weeks	Placebo	SARS-CoV-2 infection rate up to 12 weeks.
Antioxidants	NCT04370288	Iran	Single blind RCT	20	COVID-19 hospitalized patients	Methylene Blue (1 mg/kg) + vitamin C (1500 mg/kg) + N-acetylcysteine (1500 mg/kg) PO or IV	Standard of care	Proportion of patients remaining free of need for mechanical ventilation

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
PEM	NCT04386460	France		100	Nice University Hospital - adult patients attending dental clinic and referred to their Physician for assessment and nutritional care	N/A	N/A	BMI evolution from baseline at 1 and 3 months
PEM	NCT04350073	USA		120	Duke University ICU, Group 1: COVID-19 patients with respiratory failure admitted to the ICU, Group 2 (controls) Non-COVID-19 respiratory failure patients requiring mechanical ventilation >48 h receiving similar ICU standards of care at Duke	Q-NRG Metabolic Cart Device; MuscleSound Ultrasound Multifrequency Bioimpedance Spectroscopy	Standard of care	Metabolic and nutritional needs of COVID-19 Patients, Cardiac output and cardiac measures (non-invasive) in COVID-19 patients

Section	Registry ID	Country	Trial design	Sample size	Population	Intervention	Comparator	Outcomes
PEM	NCT04346212	Spain		100	*Hospital de Mataró*. Patients infected by SARS-CoV-2 at *Hospital de Mataró*, *Hospital de Sant Jaume i Santa Magdalena* and other medicalized facilities in *Mataró*.	N/A	N/A	Prevalence of oropharyngeal dysphagia according to a clinical assessment tool, the Volume-Viscosity Swallowing Test (V-VST)

Abbreviations: ACE2, angiotensin-converting enzyme 2; AEMPS, Spanish Agency of Medicines and Health Products; ARB, angiotensin 2 receptor blocker; ARDS, Acute respiratory distress syndrome; BMI, body mass index; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; DHA, docosahexaenoic acid; DM, diabetes mellitus; DM1, type 1 diabetes; DM2, type 2 diabetes; EPA, eicosapentaenoic acid; FFA, free fatty acids; GLA, gamma-linoleic acid; GP, general practitioner; HDIVC, High dose intravenous vitamin C; HCQ, Hydroxychloroquine; ICU, intensive care unit; IgG, Immunoglobulin G; IL-6, interleukin-6; IPE, Icosapent ethyl; IU, international units; IV, intravenous; MCP1, monocyte chemoattractant protein 1; n-3, omega-3; NRS-2002, Nutrition risk screening-2002; NSAID, nonsteroidal anti-inflammatory drug; NUTRIC, Nutrition Risk in Critically ill; O_2, oxygen; OD, overdose; ONS, oral nutrient supplement; PCR, polymerase chain reaction; PEM, Protein/energy malnutrition; PO, orally (from Latin *per os*); PUFA, polyunsaturated fatty acid; RCT, randomized-controlled trial; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TNF-α, Tumor necrosis factor-α; UK, United Kingdom; USA, United States of America; Zn, zinc.