Supplemental file

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2. Full details of the study eligibility criteria
3. List of studies excluded at full text review
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1. Full record of search

Medline (Ovid)

Search date: 06/05/2020
Database: Ovid MEDLINE(R) ALL <1946 to May 05, 2020>
Search Strategy:

1 exp Vitamin D/ (58492)
2 Vitamin D Deficiency/ (15552)
3 (vitamin D? or vit D? or D vitamin? or ergocalciferol or cholecalciferol or colecalciferol or calciferol or dihydroergocalciferol or sitocalciferol or dihydrotachysterol or dihydroxycholecalciferol? or dihydroxycholecalciferol? or "25(OH)D?" or 25OHD? or calcidiol or hydroxyergocalciferol or alfalcadiol or alphacalcidiol or "1,25(OH)2D" or hydroxyvitamin D? or dihydroxyvitamin D?).ab,kf,ti. (78232)
4 (paricalcitol or doxercalciferol or doxerocalciferol or calcifediol or calcitriol).ab,kf,ti. (5577)
5 hypovitaminosis D?.ab,kf,ti. (1775)
6 ((D or D2 or D3) adj3 supplement*).ab,kf,ti. (12158)
7 1 or 2 or 3 or 4 or 5 or 6 (92560)
8 coronavirus/ or betacoronavirus/ or betacoronavirus 1/ or coronavirus oc43, human/ or middle east respiratory syndrome coronavirus/ or sars virus/ (7431)
9 coronavirus infections/ or severe acute respiratory syndrome/ (10675)
10 (((corona* or corono*) adj1 (virus* or viral* or virinae*)) or coronavirus* or coronavirus* or coronaviirae* or Coronavirus* or Coronavirus* or Wuhan* or Hubei* or Huanan or "2019-nCoV" or 2019nCoV or nCoV2019 or "nCoV-2019" or "COVID-19" or COVID19 or "CORVID-19" or CORVID19 or "WN-CoV" or WNCoV or "HCoV-19" or HCoV19 or CoV or "2019 novel*" or Ncov or "n-cov" or "SARS-CoV-2" or "SARS-CoV-2" or "SARS-CoV2" or SARS-CoV19 or "SARS-Cov19" or "SARS-CoV-19" or "SARS-Cov-19" or Ncovor or Ncorona* or Ncoronavirus* or Ncoroine* or NcovWuhan* or NcovHubei* or NcovChina* or NcovChinese*).ab,kf,ti. (26891)
11 (severe acute respiratory syndrome or SARS or Middle East respiratory syndrome or MERS).ab,kf,ti. (16560)
12 (betacoronavirus* or betacoronaviirae*).ab,kf,ti. (280)
13 8 or 9 or 10 or 11 or 12 (37180)
14 7 and 13 (32)
15 exp Animals/ (23144176)
16  exp Humans/ (18448248)
17  15 not 16 (4695928)
18  14 not 17 (30)
19  limit 18 to yr="2002 -Current" (30)

Update
Search date: 10/6/2020
Actual databases searched: Ovid MEDLINE All <1946 to June 09, 2020>
Search strategy:
Re-ran search above plus...
20  limit 19 to ed=20200506-20200610 (8)
21  limit 19 to ep=20200506-20200610 (39)
22  limit 19 to dt=20200506-20200610 (43)
23  limit 19 to ez=20200506-20200610 (27)
24  20 or 21 or 22 or 23 (46)

Embase (Ovid)
Search date: 06/05/2020
Database: Embase <1974 to 2020 May 05>
Search Strategy:
--------------------------------------------------------------------------------
  1  exp vitamin D/ (139781)
  2  vitamin D deficiency/ (29333)
  3  (vitamin D? or vit D? or D vitamin? or ergocalciferol or cholecalciferol or colecalfcerol or
calciferol or dihydroergocalciferol or sitocalciferol or dihydrotachysterol or dihydroxycholecalciferol? or
hydroxycholecalciferol? or "25(OH)D?" or 25OHD? or calcidiol or hydroxyergocalciferol or
alfacalciol or alphacalcidiol or "1,25(OH)2D" or hydroxyvitamin D? or dihydroxyvitamin D?).ab,kw,ti. (112459)
  4  (paricalcitol or doxercalciferol or doxercalciol or calcifediol or calcitriol).ab,kw,ti. (8478)
  5  hypovitaminosis D?.ab,kw,ti. (3012)
  6  ((D or D2 or D3) adj3 supplement*).ab,kw,ti. (19177)
  7  1 or 2 or 3 or 4 or 5 or 6 (163395)
  8  betacoronavirus 1/ or betacoronavirus/ or human coronavirus oc43/ (696)
  9  Middle East respiratory syndrome coronavirus/ (2028)
 10  sars-related coronavirus/ or sars coronavirus/ (6354)
 11  Coronavirusae/ (2231)
 12  coronavirus infection/ or middle east respiratory syndrome/ or severe acute respiratory
syndrome/ (11950)
 13  (((corona* or corono*) adj1 (virus* or viral* or virinae*)) or coronavirus* or coronavirus* or
coronavirinae* or Coronavirus* or Coronavirus* or Wuhan* or Hubei* or Huanan or "2019-nCoV" or
2019nCoV or nCoV2019 or "nCoV-2019" or "COVID-19" or COVID19 or "CORVID-19" or CORVID19 or
"WN-CoV" or WNCov or "HCoV-19" or HCoV19 or CoV or "2019 novel**" or Ncov or "n-cov" or "SARS-
CoV-2" or "SARScov2" or "SARS-CoV2" or SARS-CoV2 or SARScov19 or "SARS-Cov19" or "SARS-CoV-19"
or "SARS-Cov-19" or "SARS-Cov-19" or Ncovor or Ncorona* or Ncorona* or NcovWuhan* or NcovHubei* or
NcovChina* or NcovChinese*).ab,kw,ti. (27686)
 14  (severe acute respiratory syndrome or SARS or Middle East respiratory syndrome or
MERS).ab,kw,ti. (17146)
 15  (betacoronavirus* or betacoronavirinae*).ab,kw,ti. (275)
 16  8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 (40716)
17 7 and 16 (61)
18 exp animal/ (25459151)
19 exp human/ (20834835)
20 18 not 19 (4624316)
21 17 not 20 (58)
22 limit 21 to yr="2002 -Current" (58)

Update
Search date: 10/6/2020
Actual databases searched: Ovid Embase <1974 to 2020 June 09>
Search strategy:
Re-ran search above plus...
22 limit 21 to yr="2002 -Current" (123)
23 limit 22 to dd=20200506-20200610 (39)
24 limit 22 to em=202005-202006 (0)
25 limit 22 to dc=20200506-20200610 (62)
26 23 or 24 or 25 (62)

MedRxiv (searched via Medrxivr https://mcguinlu.shinyapps.io/medrxivr/)

Search date: 07/05/2020
Search Strategy:

Topic 1:
[Vv]itamin D
[Vv]itamin D2
[Vv]itamin D3
calciferol
25OHD
25OHD3
[Hh]ypovitaminosis D

Topic 2:
[Cc]oronavirus
[Cc]orona\s||([[:graph:]]+\s){0,1}virus
[Cc]orovirinae
[Cc]ovid
COVID
nCoV
NCOV
Ncov
[Nn]-cov
N-COV
2019ncov
2019-ncov
ncov2019
ncov-2019
SARS
[Severe Acute Respiratory Syndrome
Middle East Respiratory Syndrome
MERS

Earliest record date
20190101
Latest record date
20200507
Remove older versions of the same record

6 results

Update
Search date: 10/6/2020
Re-ran search above changing record dates as follows:
Earliest record date
20200507
Latest record date
20200610
Remove older versions of the same record

11 results

BioRxiv
https://www.biorxiv.org/

Search date: 07/05/2020

65 Results
for abstract or title "vitamin D" (match phrase words)

22 Results
for full text or abstract or title "ergocalciferol cholecalciferol colecalciferol" (match whole any)

41 Results
for full text or abstract or title "25OHD 25OHD3" (match whole any)

Imported into EndNote and de-duplicated
92 results after deduplication

Searched in Endnote using the following search strategy:
coronavirus or corona or covid or SARS or MERS or betacoronavirus or ncov
Any Field

5 results

Update
Search date: 10/6/2020
1 Results
for abstract or title "vitamin D" (match phrase words) and posted between "07 May, 2020 and 10 Jun, 2020" – animal study (also in both results sets below) so not exported to EndNote

3 Results
for full text or abstract or title "ergocalciferol cholecalciferol colecalciferol" (match whole any) and posted between "07 May, 2020 and 10 Jun, 2020" - 2 animal studies and 1 on sertraline in TB

2 Results
for full text or abstract or title "25OHD 25OHD3" (match whole any) and posted between "07 May, 2020 and 10 Jun, 2020" - 1 animal study, 1 non-clinical / non-coronavirus

0 results relevant to coronaviruses

Cochrane Library

Search date: 08/05/2020

ID Search Hits
#1 MeSH descriptor: [Vitamin D] explode all trees 5224
#2 MeSH descriptor: [Vitamin D Deficiency] this term only 1226
#3 ((vitamin NEXT D?) or (vit NEXT D?) or (D NEXT vitamin?) or ergocalciferol or cholecalciferol or colecalciferol or calciferol or dihydroergocalciferol or sitocalciferol or dihydrotachysterol or dihydroxycholecalciferol? or hydroxycholecalciferol? or "25(OH)D" or "25(OH)D3" or 25OHD7 or calcidiol or hydroxyergocalciferol or alfacalcidol or alphacalcidol or "1,25(OH)2D" or (hydroxyvitamin NEXT D?) or (dihydroxyvitamin NEXT D?):ti,ab,kw 12959
#4 (paricalcitol or doxercalciferol or doxerocalciferol or calcifediol or calcitriol):ti,ab,kw 2417
#5 hypovitaminosis NEXT D? 303
#6 ((D OR D2 OR D3) NEAR/3 supplement*):ti,ab,kw 5633
#7 #1 or #2 or #3 or #4 or #5 or #6 14461
#8 MeSH descriptor: [Coronavirus] this term only 2
#9 MeSH descriptor: [Beta-coronavirus] this term only 2
#10 MeSH descriptor: [Betacoronavirus 1] this term only 0
#11 MeSH descriptor: [Coronavirus OC43, Human] this term only 0
#12 MeSH descriptor: [Middle East Respiratory Syndrome Coronavirus] explode all trees 1
#13 MeSH descriptor: [SARS Virus] this term only 9
#14 MeSH descriptor: [Coronavirus Infections] this term only 137
#15 MeSH descriptor: [Severe Acute Respiratory Syndrome] this term only 107
#16 ((corona* or corono*) near/1 (virus* or viral* or virinae*)) or coronavirus* or coronavirus* or coronavirinae* or Coronavirus* or Coronavirus* or Wuhan* or Hubei* or Huanan or "2019-nCoV" or 2019nCoV or nCoV2019 or "nCoV-2019" or "COVID-19" or COVID19 or "CORVID-19" or CORVID19 or "WN-CoV" or WNCov or "HCoV-19" or HCoV19 or CoV or "2019 novel*" or Ncov or "n-cov" or "SARS-CoV-2" or "SARS-CoV-2" or "SARS-CoV2" or SARS-CoV19 or "SARS-CoV19" or "SARS-CoV-19" or "SARS-CoV-19" or Ncovor or Ncorona* or Ncorono* or NcovWuhan* or NcovHubei* or NcovChina* or NcovChinese*:ti,ab,kw 614
#17 ("severe acute respiratory syndrome" or SARS or "Middle East respiratory syndrome" or MERS):ti,ab,kw 350
#18 (betacoronavirus* or betacoronavirinae*):ti,ab,kw 4
Update
Search date: 10/06/2020
Re-ran search exactly as above and retrieved 5 results, all from CENTRAL. All 5 results exported to EndNote for deduplication.

Database of publications (living map of evidence) on coronavirus disease (COVID-19) developed by the University of Bern

Living Evidence on COVID-19
Contributors: Michel Counotte, Hira Imeri, Mert Ipekci, Nicola Low

https://zika.ispm.unibe.ch/assets/data/pub/ncov/

Search date: 10/05/2020 (14,988 entries)

Search: Title, Abstract

Search:

- vitamin D 13
- vitamin D2 0
- vitamin D3 0
- ergocalciferol 0
- cholecalciferol 0
- colecalciferol 0
- 25(OH)D 0
- 25OHD 0
- 25(OH)D3 0
- 25OHD3 0
- hypovitaminosis D 1
- Vitamin D Deficiency 1

Oxford COVID-19 Evidence Service
https://www.cebm.net/oxford-covid-19-evidence-service/
The Centre for Evidence-Based Medicine (CEBM) The University of Oxford

Search date: 10/05/2020 (142 articles)

- vitamin D 1
- vitamin D2 0
- vitamin D3 0
- ergocalciferol 0
- cholecalciferol 0
- colecalciferol 0
- 25(OH)D 0
- 25OHD 0
25(OH)D3 0
25OHD3 0
hypovitaminosis D 0
Vitamin D Deficiency 0

Database of publications on coronavirus disease (COVID-19) developed by WHO

Search date: 10/05/2020 (15,253 entries)

Search: Title, Abstract, Subject

vitamin D 19
vitamin D2 0
vitamin D3 2
ergocalciferol 0
cholecalciferol 1
colecalciferol 0
25(OH)D 0
25OHD 0
25(OH)D3 0
25OHD3 0
hypovitaminosis D 1
Vitamin D Deficiency 2

Total: 25
After de-duplication: 20

Searches for systematic reviews, for reference checking

Medline

Search date: 19/05/2020
Database: Ovid MEDLINE(R) ALL <1946 to May 18, 2020>
Search Strategy:

1  exp Vitamin D/ (58577)
2  Vitamin D Deficiency/ (15588)
3  (vitamin D? or vit D? or D vitamin? or ergocalciferol or cholecalciferol or colecalciferol or calciferol or dihydroergocalciferol or sitocalciferol or dihydrocholcalciferol or dihydroxycholecalciferol? or hydroxycholecalciferol? or "25(OH)D?" or 25OHD? or calcidiol or hydroxyergocalciferol or alfalcacidol or alphacalcidol or "1,25(OH)2D" or hydroxyvitamin D? or dihydroxyvitamin D?).ab,kf,ti. (78395)
4  (paricalcitol or doxercalciferol or doxerocalciferol or calcifediol or calcitriol).ab,kf,ti. (5588)
5  hypovitaminosis D?.ab,kf,ti. (1780)
6  ((D or D2 or D3) adj3 supplement*).ab,kf,ti. (12198)
7  1 or 2 or 3 or 4 or 5 or 6 (92747)
coronavirus/ or betacoronavirus/ or betacoronavirus 1/ or coronavirus oc43, human/ or middle east respiratory syndrome coronavirus/ or sars virus/ (8161)
coronavirus infections/ or severe acute respiratory syndrome/ (11614)
(((corona* or corono*) adj1 (virus* or viral* or virinae*)) or coronavirus* or coronavirus* or coronavirinae* or Coronavirus* or Coronovirus* or Wuhan* or Hubei* or Huanan or "2019-nCoV" or 2019nCoV or nCoV2019 or "nCoV-2019" or "COVID-19" or COVID19 or "CORVID-19" or CORVID19 or "WN-CoV" or WNCov or "HCoV-19" or HCoV19 or CoV or "2019 novel*" or Ncov or "n-cov" or "SARS-CoV-2" or "SARS-CoV2" or SARS-CoV2 or SARS-CoV19 or "SARS-Cov19" or "SARS-Cov-19" or "SARS-Cov-19" or Ncovicor or Ncovor or Ncorona* or Ncorono* or NcovWuhan* or NcovHubei* or NcovChina* or NcovChinese*).ab,kf,ti. (31115)
(severe acute respiratory syndrome or SARS or Middle East respiratory syndrome or MERS).ab,kf,ti. (17795)
(betacoronavirus* or betacoronavirinae*).ab,kf,ti. (294)
exp Respiratory Tract Infections/ (356696)
(acute respiratory infection* or severe respiratory infection* or acute respiratory tract infection* or severe respiratory tract infection* or influenza or common cold or pneumonia or bronchitis).ab,kf,ti. (234266)
8 or 9 or 10 or 11 or 12 or 13 or 14 (503079)
7 and 15 (1062)
(metanaalys* or "meta analys*" or "meta-analys*").tw. (169008)
(systematic* adj3 review*).mp. (200684)
meta analysis.pt. (114746)
17 or 18 or 19 (301767)
16 and 20 (55)

Embase
Search date: 19/05/2020
Database: Embase Classic+Embase <1947 to 2020 Week 20>
Search Strategy:
--------------------------------------------------------------------------------
exp vitamin D/ (147053)
vitamin D deficiency/ (30106)
(vitamin D? or vit D? or D vitamin? or ergocalciferol or cholecalciferol or colecalciferol or calciferol or dihydroergocalciferol or sitocalciferol or dihydrotachysterol or dihydroxycholecalciferol? or hydroxycholecalciferol? or "25(OH)D?" or 25OHD? or calcidiol or hydroxyergocalciferol or alfalcacidol or alphacalcidol or "1,25(OH)2D" or hydroxyvitamin D? or dihydroxyvitamin D?).ab,kw,ti. (118981)
(paricalcitol or doxercalciferol or doxercalciferol or calcifediol or calcitriol).ab,kw,ti. (8485)
hypovitaminosis D?.ab,kw,ti. (3033)
(((D or D2 or D3) adj3 supplement*).ab,kw,ti. (19335)
1 or 2 or 3 or 4 or 5 or 6 (172654)
betacoronavirus 1/ or betacoronavirus/ or human coronavirus oc43/ (1085)
Middle East respiratory syndrome coronavirus/ (2082)
sars-related coronavirus/ or sars coronavirus/ (6062)
Coronavirinae/ (2060)
coronavirus infection/ or middle east respiratory syndrome/ or severe acute respiratory syndrome/ (12565)
13  (((corona* or corono*) adj1 (virus* or viral* or virinae*)) or coronavirus* or coronavirus* or corona-19-nCov or nCov2019 or "nCov-2019" or "COVID-19" or COVID19 or "CORVID-19" or CORVID19 or "WN-CoV" or WNCov or "HCoV-19" or HCoV19 or CoV or "2019 novel*" or Ncov or "n-cov" or "SARS-CoV-2" or "SARSCoV-2" or "SARSCoV2" or SARSCov19 or "SARS-Cov19" or SARSCov-19 or "SARS-CoV-19" or Ncovor or Ncorona* or Ncorono* or NcovWuhan* or NcovHubei* or NcovChina* or NcovChinese*).ab,kw,ti. (30532)
14  (severe acute respiratory syndrome or SARS or Middle East respiratory syndrome or MERS).ab,kw,ti. (17954)
16  exp respiratory tract infection/. (460049)
17  (acute respiratory infection* or severe respiratory infection* or acute respiratory tract infection* or severe respiratory tract infection* or influenza or common cold or pneumonia or bronchitis).ab,kw,ti. (329779)
18  8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 (674800)
19  7 and 18 (3315)
20  (metaanalysis* or "meta analys*" or "meta-analys*").mp. (294469)
21  (systematic* adj2 review*).mp. (330720)
22  20 or 21 (475492)
23  19 and 22 (219)
24  limit 19 to (meta analysis or "systematic review") (145)
25  23 or 24 (219)
26  limit 25 to (conference abstract or conference paper or "conference review" or editorial or letter) (41)
27  25 not 26 (178)

Cochrane Database of Systematic Reviews (Cochrane Library)

Search Name: Vitamin D Covid and Acute Respiratory Infections SRs
Date Run: 20/05/2020 18:30:28

Comment:
#13  MeSH descriptor: [SARS Virus] this term only 9
#14  MeSH descriptor: [Coronavirus Infections] this term only 137
#15  MeSH descriptor: [Severe Acute Respiratory Syndrome] this term only 107
#16  (((corona* or corono*) near/1 (virus* or viral* or virinae*)) or coronavirus* or coronovirus* or coronavirinae* or Coronavirus* or Coronavirus* or Wuhan* or Hubei* or Huanan or "2019-nCoV" or 2019nCoV or nCoV2019 or "nCoV-2019" or "COVID-19" or COVID19 or "CORVID-19" or CORVID19 or "WN-CoV" or WNCoV or "HCoV-19" or HCoV19 or CoV or "2019 novel*" or Ncov or "n-cov" or "SARS-CoV-2" or "SARSCoV-2" or "SARSCoV2" or SARS-CoV19 or "SARS-Cov19" or "SARS-Cov-19" or Ncovor or Ncorona* or Ncorono* or NcovWuhan* or NcovHubei* or NcovChina* or NcovChinese*:ti,ab,kw 616
#17  ("severe acute respiratory syndrome" or SARS or "Middle East respiratory syndrome" or MERS):ti,ab,kw 351
#18  (betacoronavirus* or betacoronavirinae*):ti,ab,kw 4
#19  MeSH descriptor: [Respiratory Tract Infections] explode all trees14360
#20  ((("acute respiratory" NEXT infection*) or ("severe respiratory" NEXT infection*) or ("acute respiratory tract" NEXT infection*) or ("severe respiratory tract" NEXT infection*) or influenza or "common cold" or pneumonia or bronchitis):ti,ab,kw 25944
#21  #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20
#22  #7 and #21 329

CDSR: 3

Expert consultation

One additional study identified:

## 2. Full details of the study eligibility criteria

<table>
<thead>
<tr>
<th>Include</th>
<th>Exclude</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>P - Population</strong></td>
<td>Animals studies, modelling studies</td>
</tr>
<tr>
<td>1) Patients acutely ill with Betacoronavirus infection [SARS-CoV, MERS-CoV, SARS-CoV-2]</td>
<td></td>
</tr>
<tr>
<td>2) or at risk of acute illness with Betacoronavirus infection</td>
<td></td>
</tr>
<tr>
<td><strong>I - Intervention/exposure</strong></td>
<td></td>
</tr>
<tr>
<td>1) Vitamin D supplementation</td>
<td></td>
</tr>
<tr>
<td>2) Low Serum Vitamin D</td>
<td></td>
</tr>
<tr>
<td><strong>O - Outcomes</strong></td>
<td></td>
</tr>
<tr>
<td>1) Betacoronavirus infection (to include serological evidence of infection or clinically confirmed symptomatic infection);</td>
<td></td>
</tr>
<tr>
<td>2) severity of Betacoronavirus infection (to include patients admitted to hospital or admitted to intensive care); mortality due to Betacoronavirus.</td>
<td></td>
</tr>
<tr>
<td>3) Mortality due to Betacoronavirus</td>
<td></td>
</tr>
<tr>
<td><strong>C - Comparator</strong></td>
<td></td>
</tr>
<tr>
<td>1) No Vitamin D supplementation</td>
<td></td>
</tr>
<tr>
<td>2) high or normal Serum Vitamin D</td>
<td></td>
</tr>
<tr>
<td><strong>S - Study design</strong></td>
<td></td>
</tr>
<tr>
<td>Randomised controlled trials and non-randomized studies will be eligible for inclusion in the review including, non randomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies, ecological studies, case reports and case series.</td>
<td>Qualitative studies, Non-primary research reviews, editorials etc, guidelines and non-systematic reviews.</td>
</tr>
<tr>
<td><strong>Subgroups</strong></td>
<td>Non-English language. Non peer reviewed publication.</td>
</tr>
<tr>
<td>1. Ethnicity characteristics (White British, All Other White, Mixed, Asian, Black, Other)</td>
<td></td>
</tr>
<tr>
<td>2. Age characteristics (population by five-year age groups)</td>
<td></td>
</tr>
</tbody>
</table>
3. List of studies excluded at full text review

<table>
<thead>
<tr>
<th>Excluded studies</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-eligible study design - e.g. review</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Non-eligible population</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Non-eligible intervention</strong></td>
<td></td>
</tr>
<tr>
<td><strong>No relevant outcome</strong></td>
<td></td>
</tr>
<tr>
<td><strong>No comparator group</strong></td>
<td></td>
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<tr>
<td></td>
<td>Study design - modelling</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Study ID</td>
<td>Title and Authors</td>
</tr>
<tr>
<td>----------</td>
<td>-------------------</td>
</tr>
<tr>
<td></td>
<td>Authors</td>
</tr>
<tr>
<td>---</td>
<td>-------------------------</td>
</tr>
<tr>
<td>34</td>
<td>Mitchell, F.</td>
</tr>
<tr>
<td>35</td>
<td>Molloy, E. J. and N. Murphy</td>
</tr>
<tr>
<td>37</td>
<td>Rabbitt, L. and E. Slattery</td>
</tr>
<tr>
<td>40</td>
<td>Silberstein, M.</td>
</tr>
</tbody>
</table>
4. Articles included at full text, but later excluded at time of narrative synthesis

<table>
<thead>
<tr>
<th>Citation record</th>
<th>Exclusion reason</th>
<th>Update performed 8th October 2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darling, A. L., et al. (2020). Vitamin D status, body mass index, ethnicity and COVID-19: Initial analysis of the first-reported UK Biobank COVID-19 positive cases (n 580) compared with negative controls (n 723). medRxiv.</td>
<td>Not peer reviewed publication at time of narrative synthesis</td>
<td>No update available</td>
</tr>
<tr>
<td>Reference</td>
<td>Summary</td>
<td>Status</td>
</tr>
<tr>
<td>--------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
<td>---------------------------</td>
</tr>
</tbody>
</table>
### Study details of the seven articles included at full text, but excluded at time of narrative synthesis

<table>
<thead>
<tr>
<th>Study</th>
<th>Design/setting</th>
<th>Population</th>
<th>Exposure/Intervention</th>
<th>Outcomes</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darling, A. L., et al. (2020)</td>
<td>Retrospective cohort study UK Biobank England cohort only</td>
<td>COVID-19 positive cases (n 580) Mean age 57.5 (SD 9.7) COVID-19 negative controls (n 723) Mean age 57.9 (SD 8.7)</td>
<td>Serum 25(OH)D status Median (IQR) nmol/L by gender (Male/Female), body mass index (Normal/underweight, overweight, obesity), ethnicity (Asian, Black, Mixed and Other; White)</td>
<td>COVID-19 test result</td>
<td>Serum 25(OH)D status similar in both groups: COVID-19 positive cases (median IQR) = 43.3 (32.1) nmol/L COVID-19 negative controls (median (IQR) 44.1 (31.2) nmol/L) for COVID-19. A logistic regression model suggests that being overweight (OR 1.51 CI 1.13-2.02) or obese (OR 1.67 CI 1.24-2.26); living in London (OR 1.45 CI 1.05-2.00); being male (OR 1.28 CI 1.01-1.61) and being of Asian, Black or Mixed ethnicity (OR 1.66 CI 1.08-2.54) is associated with a higher odds of testing positive for COVID-19.</td>
<td>UK Biobank baseline samples collected in 2006-2010.</td>
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<tr>
<td>De Smet, D., et al. (2020)</td>
<td>Retrospective observational study Central network hospital, West Flanders, Belgium</td>
<td>186 SARS-CoV-2 infected patients hospitalised from March 1, 2020 to April 7, 2020 (109 males [median age 68 years, IQR 53-79] 77 females [median age 71 years, IQR 65-74]) 25(OH)D in COVID-19 patients was compared a control group of 2717 patients with similar age distribution, sampled from March 1, 2019 to April 30, 2019. (999 males [median age 69 years, IQR 53-81] and 1718 females [median age 68 years, IQR 43-83]).</td>
<td>25(OH)D levels</td>
<td>SARS-CoV-2 infection</td>
<td>COVID-19 patients had a lower median 25(OH)D on admission (18.6 ng/mL, IQR 12.6-25.3) than controls (21.5 ng/mL, IQR 13.9-20.8, P=0.0016) and a higher percentage of vitamin D deficiency (defined as 25(OH)D &lt; 20ng/mL): 58.6% versus 45.2% (P=0.0005). In male COVID-19 patients, vitamin D deficiency was lower median 25(OH)D (17.6 ng/mL, IQR 12.7-24.0 versus 20.3 ng/mL, IQR 13.7-28.3, P=0.0234) and a higher deficiency rate (67.0% versus 49.2%, P=0.0006) than male controls.</td>
<td>The prevalence and age/sex/seasonal-distribution of vitamin D status was derived from the general population sampled from 16274 consecutive, unselected and unique patients from January 1, 2019 to December 31, 2019.</td>
</tr>
</tbody>
</table>
Lau, F. H., et al. (2020) ~
Retrospective observational study
A single, tertiary care academic (university) medical centre, Louisiana, New Orleans, USA

COVID-19 ICU patients (n 13)
Mean age 61.5 (SD 15.7)
COVID-19 floor patients (n 7)
Mean age 72.0 (SD 14.8)
Medical records of COVID-19 patients between March 27, 2020 and April 21, 2020
Vitamin D insufficiency (VDI) and COVID-19 metrics in ICU vs. floor patients
VDI: defined as serum 25(OH) D < 30 ng/mL
Serum 25(OH) D status Mean (SD) ng/mL
by gender (Male/Female), body mass index (Normal, obesity), race (African American), age (elderly>65 years), hypertension

COVID-19 metrics
Overall, few significant differences were identified between ICU and floor patients:
Lactate dehydrogenase was significantly higher among ICU patients (441.8 vs. 223.0, P=0.001).
Also, body mass index was significantly higher among ICU patients (35.2 vs. 24.5, P=0.02).
Among ICU subjects, 11 (84.6%) had VDI, vs. 4 (57.1%) of floor subjects. 100% of ICU patients less than 75 years old had VDI (n=11). Among these, 64.6% (n=7) had critically low 25(OH) D (<20 ng/mL) and 3 had <10 ng/mL.
VDI is highly prevalent in dark-skinned people (82.1% of African Americans vs. 41.6% overall).
Male/Female ratio was 1.24 and 1.44 for COVID-19 and VDI respectively.

Statistical analysis was limited by the small number of subjects.

Meltzer, D. O., et al. (2020)~
Retrospective cohort study
University of Chicago Medicine, USA

4,314 patients tested for COVID-19 from 3/3/2020 to 4/10/2020. Among these, 499 had a vitamin D level in the year before testing.
COVID-19 positive cases with vitamin D deficient (n 178)
Mean age 45.6
COVID-19 positive cases with not vitamin D deficient (n 321)
Mean age 50.7
Vitamin D deficiency: defined by the most recent 25(OH) D <20ng/ml or 1,25-dihydroxycholecalciferol <18pg/ml within 1 year before COVID-19 testing. Treatment: defined by the most recent vitamin D type and dose, and treatment changes between the time of the most recent vitamin D level and time of COVID-19 testing
Vitamin D deficiency and treatment changes were combined to categorize vitamin D status at the time of COVID-19 testing as:
1)Likely deficient (last-level-deficient/treatment-not-increased)

Testing positive for COVID-19
In multivariable analysis, testing positive for COVID-19 was associated with increasing age (RR (age<50)=1.05, P<0.021; RR (age≥50)=1.02, P<0.064)), non-white race (RR=2.54, P<0.01) and being likely vitamin D deficient (deficient/treatment-not-increased: RR=1.77, P<0.02) as compared to likely vitamin D sufficient (not-deficient/treatment-not-decreased), with predicted COVID-19 rates in the vitamin D deficient group of 21.6% (95%CI [14.0%-29.2%] ) vs 12.2% (95%CI [8.9%-15.4%]) in the vitamin D sufficient group.
Vitamin D deficiency declined with increasing vitamin D dose (especially of vitamin D3).
Vitamin D dose was not significantly associated with testing positive for COVID-19 (P=0.18).

The associations observed might not reflect causal effects of vitamin D deficiency on COVID-19. This is because vitamin D deficiency can reflect a range of chronic health conditions or behavioural factors which plausibly decrease the likelihood of treatment of vitamin D.
2) Likely sufficient (last-level-not-deficient/treatment-not-decreased)
3) Uncertain deficiency (last-level-deficient/treatment-increased or last-level-not-deficient/treatment-decreased)

by age (<50, ≥50), gender (Male/Female), race (White, other than White), ethnicity (Hispanic, not Hispanic), body mass index, employee status, comorbidity indicators (e.g. hypertension)

**Notari, A. and G. Torrieri (2020)**

<table>
<thead>
<tr>
<th>Correlational study</th>
<th>The number of cases follows in its early stages an almost exponential expansion. A starting point in each country was chosen: the first day with 30 cases and fitted for 12 days. Thus, capturing the early exponential growth. Countries with too small total population (less than 300 thousands inhabitants) were excluded.</th>
<th>They analysed risk factors correlated with the initial transmission growth rate of COVID-19. Average annual level of serum Vitamin D and the seasonal level. The seasonal level is defined as: the amount during March or during winter for northern hemisphere, or during summer for southern hemisphere or the annual level for countries with little seasonal variation.</th>
<th>Growth rate of COVID-19</th>
<th>They looked for linear correlations of the exponents with other variables, for a sample of 126 countries. They found a positive correlation, i.e. faster spread of COVID-19, with high confidence level with the following variables, with respective p-value: low Temperature (4.10^{-7}), high ratio of old vs. working-age people (3.10^{-4}), life expectancy (8.10^{-6}), number of international tourists (1.10^{-5}), earlier epidemic starting date di (2.10^{-5}), high level of physical contact in greeting habits (6.10^{-5}), lung cancer prevalence (6.10^{-5}), obesity in males (1.10^{-4}), share of population in urban areas (2.10^{-6}), cancer prevalence (3.10^{-4}), alcohol consumption (0.0019), daily smoking prevalence (0.0036), UV index (0.004, smaller sample, 73 countries), low Vitamin D serum levels (0.002-0.006, smaller sample, 50 countries). There is highly significant correlation also with blood type. Also, positive correlation with moderate CI (p-value of 0.02-0.03) with: CO2/SO emissions, type-1 diabetes in children, and low vaccination coverage for Tuberculosis (BCG).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Reference</td>
<td>Study Type</td>
<td>Study Details</td>
<td>Methods</td>
<td>Findings</td>
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<tr>
<td>Raisi-Estabragh, Z., et al. (2020)</td>
<td>Retrospective cohort study</td>
<td>UK Biobank: 4,510 UK participants tested for COVID-19. Latest data release (29/05/2020) includes test results from 16/03/2020 to 18/05/2020.</td>
<td>Serum 25(OH) D levels nmol/L. Multivariate logistic regression models by age, gender (Male/Female), ethnicity (Caucasian (any White background) and non-Caucasian: Black, Asian, Chinese) to test whether addition of: 1) cardio metabolic factors (e.g. hypertension, body mass index); 2) 25(OH)-vitamin D; 3) poor diet; 4) Townsend deprivation score; 5) housing; or 6) behavioural factors attenuated sex/ethnicity associations with COVID-19 status.</td>
<td>Vitamin D is not highly correlated with UV index due to different food consumption in different countries.</td>
</tr>
<tr>
<td>Tan, C. W., et al. (2020)</td>
<td>Cohort observational study</td>
<td>A tertiary academic hospital, Singapore: All 43 consecutive hospitalized COVID-19 patients aged 50 and above. Between 15 January and 15 April 2020.</td>
<td>DMB = a single daily oral dose of vitamin D3 1000 IU, magnesium 150mg and vitamin B12 500mcg for up to 14 days. Adjusted for age, gender and comorbidities</td>
<td>Deterioration post-DMB administration leading to any form of oxygen therapy and/or intensive care. Duration of therapy: days, Median 5 (IQR 4-7). Significantly fewer DMB patients than controls required initiation of oxygen therapy subsequently throughout their hospitalization (17.6% vs 61.5%, P=0.006). On univariate analysis, increasing age and presence of comorbidities were associated.</td>
</tr>
</tbody>
</table>

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| 17 patients received Vitamin D, Magnesium, Vitamin B12 (DMB): Mean age 58.4 (SD 7.0) | support for COVID-19 patients | with significantly higher OR for oxygen therapy, while exposure to DMB therapy was associated with a significantly improved OR 0.13 (95% CI: 0.03 – 0.59, P=0.008). On multivariate analysis, increasing age was associated with significantly higher OR for oxygen therapy, while exposure to DMB therapy was associated with a significantly improved OR 0.15 (95% CI: 0.025 – 0.93, P=0.041). |
| 26 patients did not: Mean age 64.1 (SD 7.9) | | |

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## 5. Risk of bias of included studies

Risk of bias assessment using the Downs and Black Checklist

<table>
<thead>
<tr>
<th>Study</th>
<th>Quality score</th>
<th>Reviewer notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hastie et al., 2020^9</td>
<td>14/20</td>
<td>Seven domains were not applicable and therefore not assessed, 2 reporting, 1 external validity and 1 internal validity (bias) and 1 internal validity (confounding). The study could not be scored for 3 questions as we were unable to determine; 1) the representativeness of the subjects who were prepared to participate from entire population from which they were recruited, 2) whether losses to follow-up were taken into account as patients lost to follow-up were not reported and 3) whether the study had sufficient power to detect a clinically important effect. The study did not score a point for 3 questions; 1) providing the number and a description of the characteristics of patients lost to follow-up, 2) stating whether study subjects in different intervention groups were recruited over the same period of time and 3) for assignment concealment as it was a non-randomised study. The study scored partially (only 1 point not two) for clearly described distributions of principal confounders in each group of subjects to be compared.</td>
</tr>
<tr>
<td>D’Avolio et al, 2020^10</td>
<td>13/15</td>
<td>Twelve domains were not applicable therefore not assessed, 3 reporting, 1 external validity, 4 internal validity (bias) and 4 internal validity (confounding). The study could not be scored for the ‘power’ domain as we were unable to determine from the article whether the study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%. The study did not score 1 point in the ‘external validity’ domain as those subjects who were prepared to participate were not representative of the entire population from which they were recruited.</td>
</tr>
<tr>
<td>Fasano et al, 2020 ^11</td>
<td>12/17</td>
<td>Ten domains were not applicable therefore not assessed, 3 reporting, 1 external validity, 4 internal validity (bias) and 2 internal validity (confounding). The study could not be scored for 4 items, the ‘power’ domain and one question in the ‘Internal validity - confounding (selection bias)’ as the study did not specify the time period over which patients were recruited. It could also not be scored for 2 questions in the ‘External validity domain’, 1) the representativeness of the subjects asked to participate in the study compared to the entire population from which they were recruited and 2) the representativeness of those subjects who were prepared to participate compared to the entire population from which they were recruited. The study did not score 1 point as the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses. The study scored two points for presentation of potential confounders.</td>
</tr>
</tbody>
</table>
Seven domains were not applicable and therefore not assessed, 1 reporting, 1 external validity, 3 internal validity (bias), 1 internal validity (confounding) and 1 for power. The study could not be scored for 9 questions. Two in the 'reporting' domain, 1) interventions of interest not clearly described, 2) the main findings of the study are not clearly described. Two ‘External validity’ questions 1) the representativeness of the subjects asked to participate in the study compared to the entire population from which they were recruited and 2) the representativeness of those subjects who were prepared to participate compared to the entire population from which they were recruited. Two ‘Internal validity – bias’ domain questions 1) all analyses that had not been planned at the outset of the study were not clearly indicated (results of the study based on “data dredging”, were not made clear), and 2) it was not clear is the statistical techniques used were appropriate to the data. Three ‘Internal validity - confounding (selection bias)’ domain questions, 1) no information provided concerning the source of patients included in the study 2) does not specify the time period over which patients were recruited, and 3) the numbers of patients lost to follow-up are not reported.

The study did not score 7 points for the following; 3 reporting issues 1) no description of the characteristics of participants included in the study 2) no description of the distributions of principal confounders in each group of subjects to be compared, and 3) no description of the characteristics of patients lost to follow-up. Two internal validity bias issues 1) differences in follow-up were ignored and 2) no evidence that the main measure used were accurate (valid and reliable).

Note: For each included study, the maximum possible quality score was dependent on which domains could be assessed based on the study design. The higher the score assigned to a study, the lower the risk of bias. For example, Hastie et al. 2020⁹ was assigned a score of 14 out of a maximum possible score of 20, suggesting good quality and therefore low risk of bias compared to the other studies.

References


8. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health* 1998;52(6):377-84. doi: 10.1136/jech.52.6.377


