SYSTEMATIC REVIEW

Changes in 25-hydroxyvitamin D levels post-vitamin D supplementation in people of Black and Asian ethnicities and its implications during COVID-19 pandemic: A systematic review

Megan Vaughan | Mike Trott | Raju Sapkota | Gurmel Premi | Justin Roberts | Jaspal Ubhi | Lee Smith | Shahina Pardhan

Abstract

Background: People of Black and Asian ethnicities have a higher infection rate and mortality as a result of COVID-19. It has also been reported that vitamin D deficiency may play a role in this, possibly because of the multi-gene regulatory function of the vitamin D receptor. As a result, increased dietary intake and/or supplementation to attain adequate 25-hydroxyvitamin D (25(OH)D) levels could benefit people in these ethnicities. The present study aimed to review the literature examining the changes in 25(OH)D in different types of vitamin D supplementation from randomised controlled trials in this population.

Methods: This systematic review was conducted using the PRISMA guidelines. Electronic databases were systematically searched using keywords related to vitamin D supplementation in Black and Asian ethnicities.

Results: Eight studies were included in the review. All the included studies found that supplementation of vitamin D (D2 and D3), regardless of dosage, increased 25(OH)D levels compared to a placebo. All trials in which participants were vitamin D deficient at baseline showed increased 25(OH)D levels to a level considered adequate. Two studies that used food fortification yielded smaller 25(OH)D increases compared to similar studies that used oral supplementation (10.2 vs. 25.5 nmol L⁻¹, respectively). Furthermore, vitamin D2 supplementation yielded significantly lower 25(OH)D increases than vitamin D3 supplementation.

Conclusions: Oral vitamin D supplementation may be more efficacious in increasing 25(OH)D levels than food fortification of Black and Asian ethnicities, with vitamin D2 supplementation possibly being more efficacious than vitamin D3. It is recommended that people with darker skin supplement their diet with vitamin D3 through oral tablet modes where possible, with recent literature suggesting a daily intake of 7000–10,000 IU to be potentially protective from unfavourable COVID-19 outcomes. As a result of the paucity of studies, these findings should be treated as exploratory.

KEYWORDS

ethnicity, nutrients, social groups, study design and analysis, systematic review, vitamins

Highlights

• Oral vitamin D supplementation could be more efficacious than food fortification in Black and Asian populations.
• Vitamin D3 is more efficacious than vitamin D2.
• It is recommended that people with darker skin supplement their diet with vitamin D3.
VITAMIN D SUPPLEMENTATION IN BLACK AND ASIAN ETHNICITIES AND COVID-19

INTRODUCTION

Vitamin D is a major contributor to the regulation of calcium and phosphate in the body and can potentially play a role in preventing many diseases. Moreover, insufficient concentrations of vitamin D have been reported as a significant risk factor of mortality. Although the majority of vitamin D is synthesized in the human body via sunlight, this may not be sufficient in some people; for example, if the inability to go outdoors (such as in the elderly) is impaired, or as a result of opaque clothes that cover up the majority of the skin. Furthermore, it is known that people with darker skin do not convert vitamin D from ultraviolet radiation as effectively as people with lighter skin types. Moreover, it has been reported that people with darker skin are more prone to vitamin D deficiency in countries where the majority of the population is of the Fitzpatrick skin type V or VI, such as Afghanistan, India, Mongolia, Pakistan and Tunisia. Indeed, it has been reported that people with darker skin require almost three times the exposure of sunlight than Caucasians to attain similar changes in serum 25-hydroxyvitamin D (25(OH)D) levels and therefore may need to increase dietary intake of vitamin D, thus increasing serum 25(OH)D levels, to reduce the likelihood of deficiency. Moreover, it has also been reported that 25(OH)D levels are positively associated with several health outcomes in African Americans, including Alzheimer’s disease and multiple sclerosis.

Historically, several studies have examined the efficacy of vitamin D supplementation in participants of Black and Asian ethnicities. Of these, several randomised controlled trials (RCTs) have reported that vitamin D supplementation can minimise the likelihood of deficiency, and have examined serum 25(OH)D changes for several dosages and intervention lengths. A number of these studies have also compared changes in serum 25(OH)D levels following vitamin D supplementation in people of different skin colours, reporting significant improvements.

The influence of vitamin D has received interest in the light of the COVID-19 pandemic in people of Black and Asian ethnicities. COVID-19 has been found to disproportionately affect people of Black and Asian ethnicities. Primary studies have yielded conflicting results associations between vitamin D and COVID-19 outcomes. For example, a recent large, nationally representative study reported non-significant associations between vitamin D levels, COVID-19 infection and COVID-19 mortality in adjusted models, whereas others have found significant associations. Furthermore, recent systematic reviews have concluded that there is insufficient evidence to conclude whether vitamin D levels are conclusively associated with COVID-19. When stratifying by ethnicity, reports suggest that people of Black and/or Asian ethnicities consistently yield significant associations between low circulating vitamin D concentrations and poor COVID-19 outcomes, with policy-makers recommending vitamin D supplementation as a possible protective measure for COVID-19. Because people of Black and Asian ethnicities have been reported to yield significant associations between vitamin D status and poor COVID-19 outcomes, it is important to understand to what extent vitamin D supplementation increases serum 25(OH)D levels.

To date, no studies have systematically reviewed RCTs exploring the efficacy of different dosages, modes of entry and duration of vitamin D supplementation in Black and Asian communities. The present exploratory study therefore aimed to review all of the available literature examining the efficacy of vitamin D supplementation (via changes in 25(OH)D levels) in Black or Asian participants. The results obtained have the potential to inform future research, identify gaps in the current literature and inform COVID-19 related nutrition advice, especially regarding the general efficacy of vitamin D supplementation in this potentially vulnerable population.

METHODS

Study registration

The present study was registered with the international prospective register of systematic reviews (the full protocol can be found on PROSPERO; Protocol ID: CRD4202 1239233) and was conducted in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines.

Search strategy

Electronic databases were searched from inception to 31 July 2021, including PubMed, Scopus, Web of Science and EMBASE. Searching methodology included terms and synonyms relating to vitamin D supplementation in Black and Asian populations:

\[
\text{(Vitamin D* OR 25 – hydroxyvitamin D OR hypovitaminosis D) AND (Black OR Asia* OR Ethnic*) AND (Therap* OR treatment)}
\]

The results from the searches were imported into a bibliographic database (Covidence) and duplicates were automatically removed. Titles and abstracts of studies were screened for inclusion by two independent investigators (MV and GP) using criteria for inclusion as outlined below.

Population

Healthy adults with Black or Asian ethnicity were included. Children <18 years, studies with pregnant women and animal studies were excluded.
Intervention

Any intervention designed to increase vitamin D levels including oral tablets, injection and food fortification.

Control

Control groups were defined as a placebo treatment with no vitamin D supplementation.

Outcomes

Studies had to report the efficacy of the respective vitamin D deficiency treatment in terms of changes in serum concentration of 25(OH)D in both populations.

Study design

Only RCTs were included.

Following title and abstract screening, full texts of potential papers were reviewed independently by the same two investigators (MV and GP) using the same inclusion criteria. Any discrepancies between the reviewers were resolved by discussion and consultation with a third senior investigator (SP) if required.

Data extraction

A bespoke data extraction form was created according to the requirements of the review. Two of the investigators piloted the data extraction form in a random sample of studies to ensure that the relevant information was selected by the reviewers. The data were independently extracted by two investigators (MV and RS) and included: first author, year of study, country, number of participants, outcomes, inclusion and exclusion criteria, method of assessing vitamin D levels, details of randomisation, quality of study, limitations and conclusions. Where information was missing or variables of interest were not reported in the paper, or clarification was required, the corresponding authors of a study were contacted. If no response was received within a 2-week window, these studies were excluded.

Quality assessment

The risk of bias was assessed by two independent investigators (MV and RS) with the Joanna Briggs Institute (JBI) checklist for randomised control trials, comprising a non-scoring appraisal tool for assessing the validity of articles, which requires the identification of whether or not relevant information is present in each article using a yes, no, unclear or not applicable rating. Any discrepancies between the reviewers over the risk of bias in particular studies was made by consensus, with the involvement of a third investigator (SP) where necessary.

RESULTS

In total, 9178 studies were initially identified from the database searches. After the removal of 3890 duplicates, 5105 studies were excluded based on their title and abstract. This left 183 studies selected for full-text review. Of these studies screened, 164 were excluded (full exclusion reasons are broken down and can be seen in PRISMA flow diagram) (Figure 1), and one study was added from the reference lists, leaving eight studies included in the review.
| Study | Country | Treatment group | Treatment type | Ethnicity | N participants baseline | N participants follow-up | Mean age (SD) | Percentage female | Method of vitamin D measurement | Follow-up |
|-------|---------|----------------|----------------|-----------|------------------------|-------------------------|---------------|------------------|--------------------------------|-----------|
| Chandler** | USA | Placebo | Placebo tablets (200 mg calcium carbonate day⁻¹) | African-American | 81 | 71 | 51 (44–58) b | 66.7 | Blood sample a | 3 months a |
| Treatment Group 1 | 1000 IU (25 μg) vitamin D₃ + 200 mg calcium carbonate day⁻¹ | 81 | 67 | 51 (43–60) b | 72.8 |
| Treatment Group 2 | 2000 IU (50 μg) vitamin D₃ + 200 mg calcium carbonate day⁻¹ | 83 | 76 | 50 (44–58) b | 66.3 |
| Treatment Group 3 | 4000 IU (100 μg) vitamin D₃ + 200 mg calcium carbonate day⁻¹ | 83 | 78 | 51 (44–60) b | 65.1 |
| Goswami (2012) | India | Double Placebo | Lactose tablets and sachets | Indian | 43 | 37 | 22 (4.9) | 100 | Blood sample a | 6 months a |
| Treatment Group 1 | Lactose sachets and calcium carbonate tablets (1 g day⁻¹) | 42 | 38 | 22 (4.4) | 100 |
| Treatment Group 2 | Vitamin D₃ sachets (60,000 IU/week for first 8 weeks followed by 60,000 IU twice/month for 4 months) and lactose tablets | 42 | 39 | 21 (3.2) | 100 |
| Treatment Group 3 | Vitamin D₃ sachets (60,000 IU/week for first 8 weeks followed by 60,000 IU twice/month for 4 months) and calcium carbonate tablets (1 g day⁻¹ for 6 months) | 43 | 39 | 22 (3.5) | 100 |
| Grønborg (2020) | Denmark | Placebo | Unfortified food supplements | Pakistani | 37 | 31 | 36 (9) | 100 | Blood sample a | 12 weeks a |
| Treatment Group 1 | Fortified food supplements (approximately 20 μg day⁻¹ vitamin D₃) | 35 | 33 | 36 (10) | 100 |
| Islam (2010) | Bangladesh | Placebo | Placebo tablets 1 day⁻¹ | Bangladeshi | 50 | 35 | 23 (3.9) | 100 | Blood sample a | 1 year a |
| Treatment Group 1 | 10 μg vitamin D day⁻¹ | 50 | 40 | 22 (3.9) | 100 |
| Treatment Group 2 | 10 μg of vitamin D₃ + 600 mg of calcium lactate day⁻¹ | 50 | 41 | 23 (3.6) | 100 |
| Treatment Group 3 | Multiple micronutrients +10 μg of VD + 600 mg of calcium lactate day⁻¹ | 50 | 37 | 22 (3.3) | 100 |
| Study          | Country     | Treatment group | Treatment type                                           | Ethnicity          | \(N\) participants baseline | \(N\) participants follow-up | Mean age (SD) | Percentage female | Method of vitamin D measurement | Follow-up |
|---------------|-------------|-----------------|----------------------------------------------------------|--------------------|------------------------------|-----------------------------|----------------|--------------------|---------------------------------|-----------|
| Kim (2020)    | USA         | Placebo         | Placebo tablets (200 mg calcium carbonate day⁻¹)          | African-American   | NR                          | 61                          | 30-80⁺          | NR                 | Blood sample                   | 3 months⁺ |
|               |             | Treatment Group 1| 1000 IU (25 μg) vitamin D₃ + 200 mg calcium carbonate day⁻¹ |                    | NR                          | 65                          | NR             | NR                 |                                 |           |
|               |             | Treatment Group 2| 2000 IU (50 μg) vitamin D₃ + 200 mg calcium carbonate day⁻¹ |                    | NR                          | 61                          | NR             | NR                 |                                 |           |
|               |             | Treatment Group 3| 4000 IU (100 μg) vitamin D₃ + 200 mg calcium carbonate day⁻¹ |                    | NR                          | 63                          | NR             | NR                 |                                 |           |
| Kim (2020)    |             | Placebo         | Placebo tablets (200 mg calcium carbonate day⁻¹)          | African-American   | NR                          | 31                          |                 | 77⁺                |                                 |           |
|               |             | Treatment Group 1| 1000 IU (25 μg) vitamin D₃ + 200 mg calcium carbonate day⁻¹ |                    | NR                          | 36                          | NR             | NR                 |                                 |           |
|               |             | Treatment Group 2| 2000 IU (50 μg) vitamin D₃ + 200 mg calcium carbonate day⁻¹ |                    | NR                          | 33                          | NR             | NR                 |                                 |           |
|               |             | Treatment Group 3| 4000 IU (100 μg) vitamin D₃ + 200 mg calcium carbonate day⁻¹ |                    | NR                          | 41                          | NR             | NR                 |                                 |           |
| Kim (2020)    |             | Placebo         | Placebo tablets (200 mg calcium carbonate day⁻¹)          | African-American   | NR                          | 30                          |                 | 58⁺                |                                 |           |
|               |             | Treatment Group 1| 1000 IU (25 μg) vitamin D₃ + 200 mg calcium carbonate day⁻¹ |                    | NR                          | 29                          | NR             | NR                 |                                 |           |
|               |             | Treatment Group 2| 2000 IU (50 μg) vitamin D₃ + 200 mg calcium carbonate day⁻¹ |                    | NR                          | 28                          | NR             | NR                 |                                 |           |
|               |             | Treatment Group 3| 4000 IU (100 μg) vitamin D₃ + 200 mg calcium carbonate day⁻¹ |                    | NR                          | 22                          | NR             | NR                 |                                 |           |
| Kuwabara (2009)| Japan      | Placebo         | 200 mg calcium day⁻¹                                      | Japanese           | 30                          | 30                          | 86 (8.5)       | 67                 | Blood sample                   | 30 days   |
|               |             | Treatment Group 1| 200 mg calcium + 800 IU vitamin D₃ (20 μg) day⁻¹           |                    | 32                          | 32                          | 84 (7.6)        | 74                 |                                 |           |

(Continues)
TABLE 1  (Continued)

| Study                  | Country    | Treatment group | Treatment type                                         | Ethnicity          | N participants baseline | N participants follow-up | Mean age (SD) | Percentage female | Method of vitamin D measurement | Follow-up |
|------------------------|------------|-----------------|--------------------------------------------------------|--------------------|-------------------------|--------------------------|---------------|------------------|----------------------------------|-----------|
| Tripkovic (2017) UK    | Placebo    | Placebo juice and placebo biscuit day<sup>−1</sup>  | South Asian     | 17                  | 14                      | 44. (12)<sup>c</sup>    | 100           |                  | Blood sample<sup>e</sup>           | 12 weeks  |
|                        | Treatment  | Juice fortified with 600 IU (15 μg) vitamin D<sub>2</sub> and placebo biscuit |              | 18                  | 13                      | 44 (11)<sup>c</sup>     |              |                  |                                  |           |
|                        | Group 1    | Placebo juice and biscuit fortified with 600 IU (15 μg) vitamin D<sub>2</sub> |              | 17                  | 14                      | 43 (13)<sup>c</sup>     |              |                  |                                  |           |
|                        | Treatment  | Juice fortified with 600 IU (15 μg) vitamin D<sub>3</sub> and placebo biscuit |              | 19                  | 11                      | 43 (13)<sup>c</sup>     |              |                  |                                  |           |
|                        | Group 3    | Placebo juice and biscuit fortified with 600 IU (15 μg) vitamin D<sub>3</sub> |              | 19                  | 11                      | 44 (13)<sup>c</sup>     |              |                  |                                  |           |
| von Hurst (2010) New Zealand (pre-menopausal) | Placebo    | 4 placebo capsules day<sup>−1</sup>                  | 91% Indian; 6% Sri Lankan; 3% Pakistani<sup>a</sup> | 106<sup>a</sup>    | 29                      | >20<sup>a</sup>         | 100<sup>a</sup> |                  | Blood sample<sup>e</sup>           | 6 months<sup>a</sup> |
|                        | Treatment  | 4 × 1000 IU (100 μg) vitamin D<sub>3</sub> capsules day<sup>−1</sup> |              |                     |                         |                          |              |                  |                                  |           |
|                        | Group 1    | Placebo        | 13                      |                     |                          |                          |              |                  |                                  |           |
| von Hurst (2010) New Zealand (post-menopausal) | Placebo    | 4 placebo capsules day<sup>−1</sup>                  |                | 13                  | 13                      |                          |              |                  |                                  |           |
|                        | Treatment  | 4 × 1000 IU (100 μg) vitamin D<sub>3</sub> capsules day<sup>−1</sup> |              |                     |                         |                          |              |                  |                                  |           |
|                        | Group 1    | Placebo        | 13                      |                     |                          |                          |              |                  |                                  |           |

<sup>a</sup>Statistics for the whole cohort; stratified characteristics not reported.

<sup>b</sup>Median (interquartile range).

<sup>c</sup>Mean ages are for both South Asian and White European cohorts.
Full characteristics of included studies can be found in Table 1. In brief, all studies were published in the years 2010–2020, with a total of 1108 participants at follow-up (baseline number of participants was incomplete). Study follow-up ranged from 30 days to 1 year. There were two studies with an African American population, one with an Indian population, one with a Bangladeshi population, one with a Pakistani population, one with a Japanese population and one with a non-South Asian population, with the one remaining study’s population being mixed. All included studies were placebo-controlled, with the placebo group being the same ethnicity as the treatment group. Two studies investigated the effect of food/drink fortification, two studies investigated the effect of an increasing dosage (1000, 2000 and 4000 IU) of vitamin D3 combined with 200 mg calcium carbonate day−1, one study investigated the effect of vitamin D3 sachets in combination with lactose or calcium carbonate tablets, one study investigated the difference between 10 μg vitamin D day−1, 10 μg of vitamin D3 or 600 mg of calcium lactate day−1 and multiple micronutrients + 10 μg of vitamin D3 + 600 mg of calcium lactate day−1, one study investigated a combination of calcium (200 mg day−1) and vitamin D3 (800 IU day−1), and one study investigated 4 × 1000 IU capsules of vitamin D3 per day. Of the eight included studies, one had a five-arm placebo-controlled method and four had used a four-arm placebo-controlled method, whereas three studies used a placebo and single-arm assessment group. All studies used 25(OH)D assays using plasma/serum samples at baseline and follow-up. All eight studies were evaluated with the JBI RCT checklist and were considered of sufficient quality to be included. Full scoring information is provided in the Supporting information (Table S1).

Regarding baseline vitamin D status, there were three studies where the baseline population had a 25(OH)D of <25 nmol L−1. Of these studies, all treatment groups (regardless of dosage or duration) showed significant 25(OH)D increases compared to the placebo group(s), and mean 25(OH)D levels of all treatment groups increased to >25 nmol L−1 (range 47.2–118.75 nmol L−1). Furthermore, all but two studies reported follow-up levels for treatment group of 25(OH)D at >50 nmol L−1 (Table 2).

DISCUSSION

In this systematic review, we have summarised the outcomes of eight RCTs (1108 participants) relating to the relative efficacy of vitamin D supplementation in people of Black and/or Asian ethnicities.

In the trials in which participants had 25(OH)D levels of <25 nmol L−1 at baseline, the intervention, regardless of dosage, mode of delivery or duration, increased the levels to >25 nmol L−1. In all but two studies, the intervention increased 25(OH)D levels to >50 nmol L−1 effectively lifting them out of VD deficient status. The study with the smallest intervention dosage (400 IU; 10 μg day−1) reported that all of their participants were no longer vitamin deficient, indicating that a high dosage may not be necessary to increase 25(OH)D levels above 50 nmol L−1. It is worth noting that the study with the shortest duration of treatment (30 days) did not increase the serum 25(OH)D levels to >50 nmol L−1; therefore, it is likely that higher dosages may be required in Black and Asian populations especially when sun exposure does not contribute to allow sufficient vitamin D synthesis. Whether this would be sustainable after sufficient vitamin D levels were attained requires further investigation. In participants who had a baseline 25(OH)D of >25 nmol L−1, significant increases in 25(OH)D levels were also observed in their respective treatment groups, regardless of dosage, duration or modality of supplementation.

Modality of vitamin D supplementation

The modality of intake makes a difference. One study that used foods fortified with vitamin D3 as a mode of supplementation yielded much smaller changes in 25(OH)D levels than another included study (10.2 vs. 25.5 nmol L−1, respectively) in which participants received similar dosages and durations (approximately 20 μg/800 IU vs. 25 μg/1000 IU, respectively) of oral vitamin D3, suggesting that oral vitamin D3 supplementation may be more efficacious than food fortification. It has been argued that food fortification may be an easier way to add vitamin D to the diet than other modes, particularly for some South Asian populations who have a vegan or vegetarian diet, because vitamin D is primarily present in animal sources such as meat and poultry. Furthermore, it has been reported that food fortification can have a significant role in increasing serum 25(OH)D levels in other ethnicities as well, and it is ranked as a priority intervention to reduce malnutrition in Southeast Asians and also internationally. The results of this review, however, suggest that, compared to oral supplementation, food fortification may be less efficacious. Further research to confirm or refute this is warranted.

South Asian vs. populations with lighter skin

The two studies that used food fortification as a vitamin D delivery mode were also the only ones to directly compare the results for different skin types (in other arms of their respective RCTs). Grønborg et al. found that, although both populations (Danish vs. Pakistani) significantly increased 25(OH)D levels, the Danish group’s 25(OH)D levels increased more than the Pakistani group. However, the it was argued that adherence to the fortified foods was higher amongst the Danish group, which may go towards explaining their findings. Tripkovic et al. found no
| Ethnicity          | Study                        | Intervention duration | Placebo Pre | Placebo Post | Treatment group 1 Pre | Treatment group 1 Post | Treatment group 2 Pre | Treatment group 2 Post | Treatment group 3 Pre | Treatment group 3 Post | Treatment group 4 Pre | Treatment group 4 Post |
|-------------------|------------------------------|-----------------------|-------------|-------------|------------------------|-------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|-------------------------|
| African-American  | Kim et al. \(^{12a}\) (all) | 3 months              | 40          | 34          | 44                     | 70                      | 41                     | 91                     | 45                     | 119                    | NA                     |                         |
|                   |                              |                       | (23)        | (19)**      | (23)                   | (23)**                  | (23)                   | (28)**                 | (23)                   | (25)**                 | NA                     |                         |
|                   | Kim et al. \(^{12a}\) (obese only) |                       | 39          | 32          | 45                     | 71                      | 38                     | 88                     | 46                     | 113                    | NA                     |                         |
|                   |                              |                       | (22)        | (18)        | (21)                   | (15)**                  | (23)                   | (20)**                 | (23)                   | (25)**                 | NA                     |                         |
|                   | Kim et al. \(^{12a}\) (non-obese only) |                       | 42          | 36          | 44                     | 69                      | 45                     | 95                     | 44                     | 131                    | NA                     |                         |
|                   |                              |                       | (25)        | (21)        | (25)                   | (29)**                  | (22)                   | (35)**                 | (23)                   | (22)**                 | NA                     |                         |
|                   | Chandler et al. \(^{13a,b}\) | 3 months              | 38          | 34          | 41                     | 74                      | 35                     | 87                     | 39                     | 115                    | NA                     |                         |
|                   |                              |                       | (26–59)     | (18–47)     | (28–57)                | (64–82)**               | (24–56)                | (72–103)**             | (28–58)               | (99–138)**             | NA                     |                         |
| Japanese          | Kuwabara et al. \(^{30a}\)  | 30 days               | 24          | 28          | 24                     | 48                      | NA                     |                        |                        |                        |                        |                         |
|                   |                              |                       | (9.0)       | (11)        | (7)                    | (10)**                  |                        |                        |                        |                        |                        |                         |
| South Asian       | Goswami et al. \(^{28a}\)   | 6 months              | 22          | 19          | 25                     | 20                      | 23                     | 75                     | 24                     | 68                     | NA                     |                         |
|                   |                              |                       | (8.2)       | (9.1)       | (8.4)                  | (7.3)                   | (8.5)                  | (52)*                  | (8.7)                  | (24)*                  | NA                     |                         |
|                   | Von Hurst et al. \(^{31}\) (pre-menopausal) | 6 months              | 18          | 30          | 20                     | 75                      | NA                     |                        |                        |                        |                        |                         |
|                   |                              |                       | (NR)        | (NR)*       | (NR)                  | (NR)**                  |                        |                        |                        |                        |                        |                         |
|                   | Von Hurst et al. \(^{31}\) (post-menopausal) |                       | 32          | 40          | 31                     | 74                      | NA                     |                        |                        |                        |                        |                         |
|                   |                              |                       | (NR)        | (NR)        | (NR)                  | (NR)*                   |                        |                        |                        |                        |                        |                         |
|                   | Islam et al. \(^{29}\)      | 1 year                | 35          | 36          | 37                     | 69                      | 38                     | 70                     | 37                     | 65                     | NA                     |                         |
|                   |                              |                       | (9.4)       | (NR)        | (12)                  | (NR)**                  | (11)                   | (NR)*                  | (13)                   | (NR)**                 | NA                     |                         |
|                   | Grønborg et al\(^{11}\)     | 12 weeks              | 49          | 37          | 45                     | 55                      | NA                     |                        |                        |                        |                        |                         |
|                   |                              |                       | (23)        | (16)        | (21)                  | (18)                    |                        |                        |                        |                        |                        |                         |
|                   | Tripkovic et al\(^{14a,b}\) | 12 weeks              | 31          | 23          | 30                     | 47                      | 31                     | 49                     | 27                     | 60                     | 21                     | 53                     |
|                   |                              |                       | (18–43)     | (13–33)     | (17–42)               | (37–57)                 | (18–43)                | (39–59)                | (16–39)                | (50–71)                | (8.7–32)               | (43–63)               |

**Notes:** The unit of measurement in all data is reported in nmol L\(^{-1}\); data reported as the mean (SD) unless otherwise stated. NA, not available.

\(^{a}\)Original data were in ngmL\(^{-1}\) and have been converted to nmol L\(^{-1}\) post hoc.

\(^{b}\)Data reported as the median and interquartile range.

\(^{*}\)p < 0.05; \(^{**}\)p < 0.001.
interaction effects between 25(OH)D changes and ethnicity; however, they also reported that fewer South Asian women increased their 25(OH)D levels to $>50\text{ nmol L}^{-1}$, predominantly because their baseline 25(OH)D levels were much lower.

**Vitamin D$_2$ vs. vitamin D$_3$ supplementation**

A comparison of the type of vitamin D supplementation showed that, although vitamin D$_2$ supplementation did increase 25(OH)D levels, there was significantly less change than the group who received vitamin D$_3$ supplementation, regardless of ethnicity. This concurs with the previous literature suggesting that vitamin D$_2$ is less efficacious than vitamin D$_3$ with respect to increasing serum 25(OH)D levels.\textsuperscript{39-41} One possible mechanism is the enhanced ability of vitamin D$_3$ to bind to the vitamin D receptor after the formation of 1,24,25(OH)$_3$ in the kidneys.\textsuperscript{42}

**Vitamin D, COVID-19 and supplementation recommendations**

With reference to COVID-19, several studies have reported negative associations between serum 25(OH)D levels and disease severity,\textsuperscript{20,43} resulting in recommendations that policy-makers should include dietary intake/supplementation as a potential protective measure against the infection and mortality.\textsuperscript{20,21,25,44} Vitamin D has been advocated to reduce viral replication rates and expression of pro-inflammatory cytokines.\textsuperscript{20,45} Specific ‘one-size fits all’ vitamin D dosages and treatment lengths are difficult to recommend, partly as a result of the potential effect of vitamin D receptor gene activation on the responsiveness of vitamin D supplementation in African Americans,\textsuperscript{46} as well as general human variability. Grimes \textit{et al}.\textsuperscript{47} have recommended a dosage of 75–125 $\mu$g (7000–10,000 IU) per day for adults who are people ‘of colour’ to attain a potential protective effect against COVID-19, which is a much higher dosage than any of the included studies in this review. Our review suggests that oral supplementation may be more beneficial than food fortification in people with darker skin and that vitamin D$_3$ is more efficacious than vitamin D$_2$ and therefore may therefore provide better protection against adverse COVID-19 outcomes. Further RCTs to test these hypotheses are required.

Although this is the first systematic review to assess the efficacy of vitamin D supplementation for Black and Asian populations, the results should be considered within the study’s limitations. First, there was a paucity of studies found, making robust conclusions challenging. More RCTs in Black and Asian populations are needed to confirm or refute these purely preliminary findings. Second, the studies were highly heterogeneous, with different treatment durations, dosages and populations, making any direct comparison of the results challenging. In particular, the baseline levels of 25(OH)D and intervention lengths were highly heterogeneous. Future studies should robustly examine previous literature to ascertain comparability of results in the future, which would enable future reviews to use established nutrient review guidelines.\textsuperscript{48} Lastly, because of limitations in translation resources, only studies published in English were included, which could mean that relevant information may not be included based on language barriers.

**CONCLUSIONS**

Our review suggests that oral vitamin D supplementation could be more efficacious than food fortification in Black and Asian populations, and also that vitamin D$_3$ is more efficacious than VD$_2$. It is recommended that people with darker skin supplement their diet with vitamin D$_3$ through oral modes aiming to reduce the risk of adverse outcomes of COVID-19, with the current literature suggesting a dosage of 7000–10,000 IU for people of Black or Asian ethnicity. Further studies that aim to determine differences between supplementation in different ethnicities are warranted.

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**CONFLICT OF INTERESTS**

The authors declare that there are no conflicts of interest.

**AUTHOR CONTRIBUTIONS**

Megan Vaughan: Conceptualisation; literature search; data collection; writing. Mike Trott: Literature search; data collection; data analysis; writing; supervision. Raju Sapkota: Conceptualisation; literature search; writing. Gurmel Premi: Conceptualisation; literature search; data collection. Justin Roberts: Data analysis; writing; critical appraisal. Jaspal Ubhi: Writing; critical appraisal. Lee Smith: Data analysis; writing; critical appraisal. Shahina Pardhan: Conceptualisation; writing; critical appraisal; supervision.

**ETHICAL APPROVAL**

As all included data in this study was from previously published literature, and, therefore, no ethical approval was required.

**TRANSPARENCY DECLARATION**

The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported. The reporting of this work is compliant with PRISMA guidelines. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained.

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PEER REVIEW

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**SUPPORTING INFORMATION**
Additional supporting information may be found in the online version of the article at the publisher’s website.

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