



The effect of physical activity on vitamin D: A systematic review and meta-analysis of intervention studies in humans

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ABSTRACT

Objectives: Cross-sectional studies demonstrate a positive association between higher physical activity and serum 25-hydroxyvitamin D (25(OH)D) concentration. However, whether this association is causal is unclear. We conducted a systematic review to identify intervention studies that examined the effect of physical activity on serum 25(OH)D concentration in humans.

Study design: Systematic review and meta-analysis.

Methods: We searched PubMed, Scopus and Web of Science to identify full-text peer-reviewed articles published in English from inception until January 2023. Eligible studies were randomised controlled trials or quasi-experimental studies. We used random effects meta-analysis to calculate the weighted mean difference (WMD) in the change in 25(OH)D concentration between physical activity and control groups. We used the revised Cochrane risk-of-bias tool for randomized trials (RoB 2) to assess the methodological quality of included studies.

Results: We included 32 articles in the systematic review and 24 in the meta-analysis. The intervention varied from resistance and weight-bearing exercises (n = 13) to aerobic exercises (n = 10), moderate and moderate-to-vigorous exercises (n = 5), aquatic exercise (n = 2), and multicomponent traditional exercises (n = 2) (Tai Chi and Yijinjing). The WMD in 25(OH)D in the physical activity and control groups was 9.51 and 4.87, respectively (between-group mean difference 4.64, p = 0.002). However, the difference was only evident in studies that implemented the intervention outdoors (n = 3; between-group mean difference 17.33, p < 0.0001); when the intervention was indoors there was no significant effect of physical activity on 25(OH)D (n = 16; between-group mean difference 1.80, p = 0.113).

Conclusions: This meta-analysis of physical activity interventions in humans showed that physical activity does not lead to increased 25(OH)D independently of time outdoors. However, most studies were under-powered, in many the exercise was low intensity, and vitamin D was not the primary outcome.

1. Introduction

Vitamin D can be synthesised in the skin following exposure to ultraviolet (UV) B radiation from sunlight. It can also be obtained from dietary sources or from vitamin D supplements. Vitamin D is hydroxylated in the liver to form 25-hydroxyvitamin D (25(OH)D), the serum concentration of which is used as the clinical indicator of vitamin D status. The role of vitamin D in maintaining bone health is well-established [1]. Observational studies, randomised controlled trials,

and Mendelian randomisation studies suggest that vitamin D may also play a role in a wide range of other health outcomes such as cancer mortality [2], risk and severity of infection [3,4], and autoimmune diseases [5,6].

It is possible that physical activity could influence serum 25(OH)D concentration. Fat-soluble vitamins, including vitamin D, are stored in adipose tissues. Higher body fat mass is associated with a lower rise in 25(OH)D concentration following supplementation, probably caused by vitamin D accumulation in adipose tissue [7]. It has been suggested that

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exercise can increase serum 25(OH)D concentration by stimulating its release from adipose tissue due to lipolysis [8].

A narrative review of observational, cross-sectional and cohort studies found that 25(OH)D concentration was higher in those who undertook more physical activity, irrespective of whether it occurred indoors or outdoors [9]. Several cross-sectional studies published subsequent to the review have reported similar findings [10–17]. However, the positive association between physical activity and vitamin D from these observational studies may be due to confounding by other factors such as body mass index, overall health status, and vitamin D intake from food and supplements.

In light of the potential importance of physical activity in avoiding vitamin D deficiency, and inclusion of advice about the benefits of physical activity for vitamin D in existing guidelines [18], we aimed to systematically review and meta-analyse data from intervention studies that reported the effect of a physical activity intervention on serum 25(OH)D concentration.

2. Methods

We conducted a systematic review and meta-analysis according to the PRISMA updated guideline for reporting systematic reviews [19]. The protocol for this review was registered with the International Prospective Register of Systematic Reviews (PROSPERO; CRD42020171025; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=171025).

2.1. Data sources

We searched PubMed, Scopus and Web of Science to identify eligible articles published between database inception and January 2023. We searched reference and citation lists of included studies and reviews to capture any publications missed through our search. We did not search for unpublished studies or other literature. The search terms are presented in [Supplement A](#).

2.2. Inclusion and exclusion criteria

The inclusion criteria were: published in English; included human participants of any age or sex; reported the effect of a physical activity intervention (either indoors or outdoors) on serum/plasma 25(OH)D concentration. We excluded studies that also provided vitamin D supplementation as part of the intervention protocol, unless the same supplement dose was provided to the intervention and control groups. Studies were excluded from the meta-analysis if the pre- and post-intervention data were not presented or were not able to be extracted from the published figures. However, these studies were included in the systematic review if a description of the difference between the intervention and control groups was reported.

2.3. Data extraction

Two reviewers (SRK, REN) screened the title and abstract of studies identified, excluded those that were clearly irrelevant and reviewed the full text of all potentially eligible studies. Any disagreements were resolved by consensus or by consulting a third reviewer (AK). SRK and MC independently extracted data from the included studies. We extracted: year of publication; author; study design; country of origin; characteristics of the study population (i.e., recruitment framework, age, sex); details of the intervention (i.e., intervention design, type and components of the intervention, location of the intervention (indoors, outdoors, not stated but presumed indoors, not reported), length of the intervention, whether the intervention was supervised, use of vitamin D supplement); and outcome (i.e., serum 25(OH)D concentration and associated measure of variability before and after the intervention, 25(OH)D assay technique used). If the location of the intervention was not

explicitly stated, we inferred the location, where possible, from the description of the intervention. Where we were unable to determine the location, the study location was labelled as ‘not reported.’

For all studies, the mean, standard deviation (SD) (or equivalent), and number of participants for baseline and post-intervention measurement of serum 25(OH)D were recorded. Serum 25(OH)D concentration presented as nanograms per millilitre was converted to nanomoles per litre. If necessary, we calculated SDs from the standard error of the mean or 95% confidence interval (CI).

2.4. Risk of bias assessment

Two reviewers (SRK, MC) independently assessed the methodological quality of the articles using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2) [20]. All five domains from the tool were used to assess the quality of the studies: randomisation process, effect of assignment to intervention, missing outcome data, measurement of the outcome, and selection of the reported result. The questions in each domain that were addressed to assess each study can be found in [Supplement B](#). Each domain was scored as low, some concerns, or high risk of bias; the tool algorithm was then used to reach a judgement of the overall risk-of-bias across domains. Any disagreement between the two reviewers were resolved through discussion with REN.

2.5. Statistical analyses

The primary outcome was the difference in the change in 25(OH)D concentration (nmol/L) from pre- to post-intervention between the intervention and control groups. The SD of the change (i.e., post – pre) was obtained by using the formula:

$$SD_{change} = \sqrt{SD_{pre}^2 + SD_{post}^2 - 2 \times \rho \times SD_{pre} \times SD_{post}}$$

where SD_{pre} represents the SD of the baseline (i.e., pre-intervention) measure, SD_{post} represents the SD of post-intervention measure, and ρ represents the correlation coefficient between pre- and post-intervention measures. Given the unavailability of ρ values, we assumed $\rho = 0.50$, as used elsewhere [21].

We used random-effects meta-analysis using inverse variance models to calculate the pooled unstandardised weighted mean difference (WMD) in the change in serum 25(OH)D concentration from baseline to post-intervention between the physical activity and control groups. Statistical heterogeneity was assessed by calculating I^2 statistics. In addition to our overall meta-analysis, we estimated the effects of physical activity on serum 25(OH)D concentration according to whether the physical activity intervention occurred indoors or outdoors. Studies where the location was not reported were excluded from the subgroup analysis. If the studies contained multiple intervention and control arms (e.g., one arm performed physical activity outdoors and one arm performed indoors), they were treated as separate studies for the purposes of the meta-analysis.

3. Results

3.1. Search results

We identified 946 articles through our database searches and three additional articles were identified through reference list searches. After removing duplicates, the titles and abstracts of 667 articles were screened; 123 full-text articles were assessed for eligibility, 32 were included in the review [22–53] and 24 in the meta-analysis [22–26,29,31–38,40–43,45–49,51] ([Fig. 1](#)).

3.2. Characteristics of included studies

Thirty-one studies were randomised controlled trials (RCTs) and one

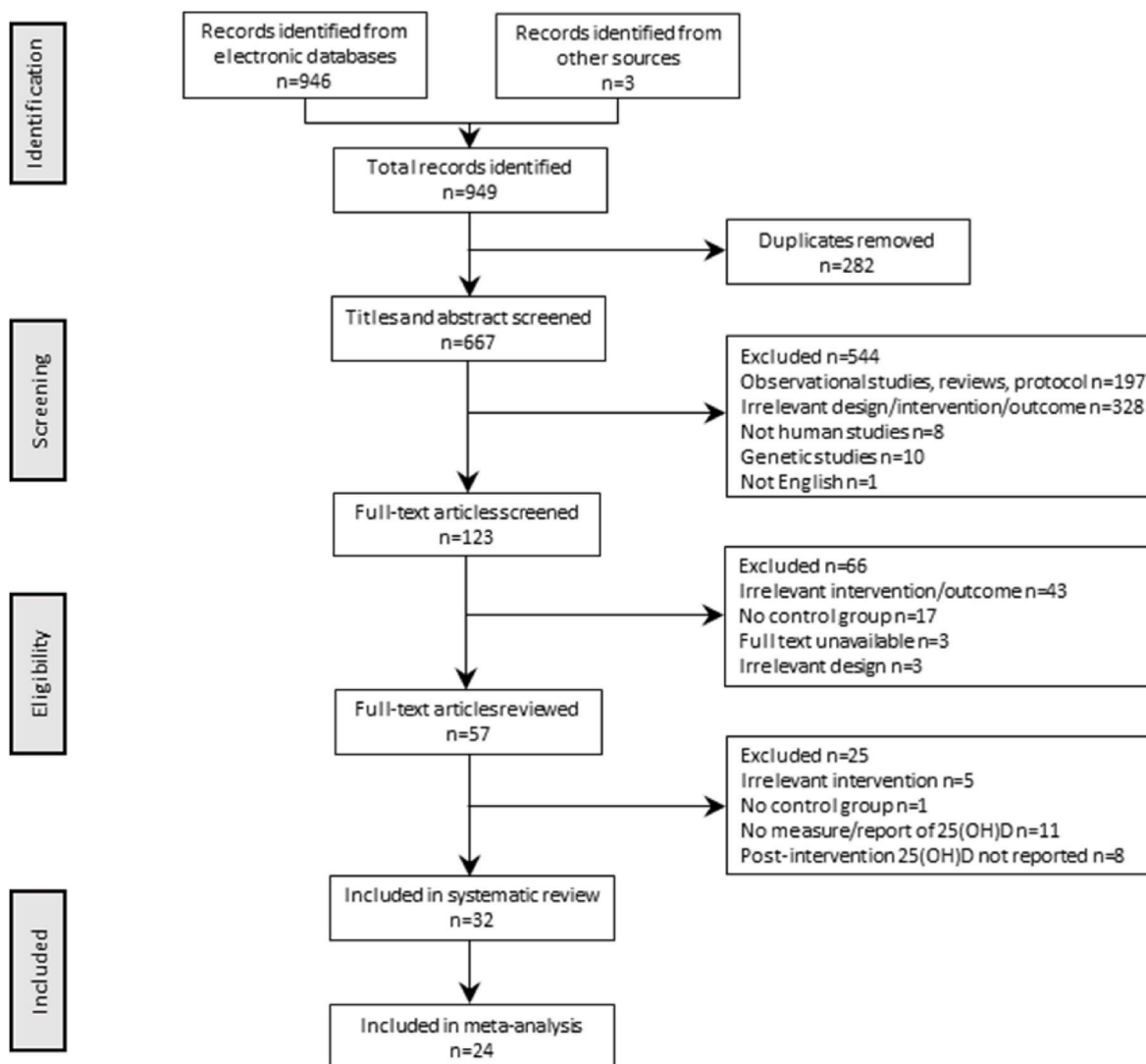


Fig. 1. PRISMA flow diagram for study inclusion.

was a quasi-experimental study [29]. The included studies were conducted between 1999 and 2022. Ten studies were conducted in Europe, 10 in the Asia-Pacific region, seven in the Middle East, three in Brazil and two in the United States. Table S1 presents the characteristics of the included studies.

3.3. Participant characteristics

The total number of participants per study varied from 13 [28] to 855 [39]. Only five studies recruited more than 100 participants [24,27,39,44,46]. Twelve studies recruited only female participants and six only male participants. Population groups included pregnant women, breast cancer survivors, post-menopausal women, pre-menopausal women, healthy men, athletes, and people with specific medical diagnoses (adults and children with obesity, children with autism spectrum disorder, cystic fibrosis, adults with type II diabetes, multiple sclerosis, people with metabolic syndrome, haemodialysis patients, and acute hip fracture patients).

3.4. Intervention details

The physical activity interventions varied widely. The interventions were reported as moderate or moderate-to-vigorous intensity ($n = 5$); aerobic ($n = 10$); resistance training and weight-bearing ($n = 13$);

aquatic ($n = 2$); Dynamic Flamingo (DF) exercise: standing on one leg for 1 min three times per day, Tai Chi and walking ($n = 1$); and Yijinjing (traditional Chinese mind-body exercise) combined with resistance training ($n = 1$).

In most studies the physical activity interventions were supervised but two home-based physical activity programs were unsupervised [26, 40] and two studies had both supervised training sessions and unsupervised home-based sessions [39,44]. Six studies did not clearly state whether the physical activity sessions were supervised or not [36,38, 46–48,52]. The frequency of the physical activity interventions ranged from once a week to once daily, with the length of each session ranging from 30 to 75 min. Four studies clearly stated that the physical activity sessions were carried out indoors, and we were able to infer that the physical activity was conducted indoors for an additional 11 studies. However, for six studies we were unable to deduce the location of intervention from the description given. One study had separate intervention arms for indoors and outdoors physical activity [31] and two studies specifically designed the intervention to take place outdoors [36, 48]. In one study, participants were encouraged to be moderately physically active and were supplied with a pedometer; however, no information was included in the paper about the location of their activity. The participants in this study also had access to a supervised session at a fitness centre [44].

Thirty studies had one intervention and one control arm. One study

had two separate intervention arms – indoors physical activity and outdoors physical activity – and one control arm [31]. Another study in athletes included three separate intervention and three control arms, for each of three separate sports (6 arms in total) [35].

The interventions in the control group were: no intervention (n = 16); vitamin D or vitamin D and calcium (n = 9; the intervention group received the same dose); placebo tablets of vitamin D (n = 2); non-exercise intervention (n = 3) such as health education classes, sham exercise training (breathing and stretching) combined with nutrition counselling, and cognitive training. In one study, the control group were encouraged to maintain a lifestyle based on standard medical care for diabetic patients that included a minimum of 150 min per week exercise [52]. One study maintained usual medical care in bariatric surgery patients in the control group [45].

3.5. Risk-of-bias

No studies were assessed to have an overall low risk-of-bias; 29 studies had some concerns and three had high risk-of-bias (Table S2).

3.6. Effect of physical activity on 25(OH)D concentration

The meta-analysis included 24 studies in total, representing 27 different intervention groups (Fig. 2). Three of the interventions occurred outdoors, 18 indoors or presumed to be indoors and six were not reported. The pre- and post-intervention serum 25(OH)D concentrations reported for each study are presented in Table S3. Overall, the intervention group had an average of 4.64 nmol/L greater increase in 25(OH)D concentration from baseline to post-intervention compared to the control group (95% CI: 1.76 to 7.52; p = 0.002); the heterogeneity was 88.5% (p < 0.0001). In studies where the physical activity intervention took place indoors or was presumed to be indoors there was minimal

difference between the intervention and control groups (between-group mean difference 1.80; 95% CI: -0.43 to 4.02; p = 0.113), whereas there was a large, statistically significant difference when the intervention took place outdoors (between-group mean difference 17.33; 95% CI: 14.59 to 20.07; p < 0.0001). However, only three studies designed the intervention to take place outdoors and the sample sizes in these studies were small (45, 30 and 37, respectively) [31,36,48].

Eight studies were not included in the meta-analysis due to the way the results were presented. Four of these, all of which were conducted indoors or indoors-presumed, reported that the change in 25(OH)D concentration from baseline to post-intervention differed minimally between the intervention and control groups [27,50,52,53]. Three studies found a greater change in the intervention group compared with the control group [30,39,44]. Of these, one was carried out indoors and possibly outdoors and found a significantly higher increase in 25(OH)D concentration in the intervention group compared to the control group (p = 0.009) [44]. Two others took place indoors; one reported a slightly greater increase in 25(OH)D concentration in the intervention group (1.9 nmol/L; p = 0.048) [39] and the other reported a 6.25 nmol/L increase in 25(OH)D concentration in the intervention group and a 2.5 nmol/L decrease in the control group post-intervention [30]. One study, presumably conducted indoors, reported a decrease in 25(OH)D concentration in both intervention and control groups. However, the decrease was much larger in the intervention group than the control group (55 nmol/L vs 35 nmol/L, respectively) [28].

4. Discussion

In this systematic review and meta-analysis of intervention studies we found that physical activity does not influence serum 25(OH)D concentration independently of time outdoors. However, there was considerable variability across the physical activity intervention in

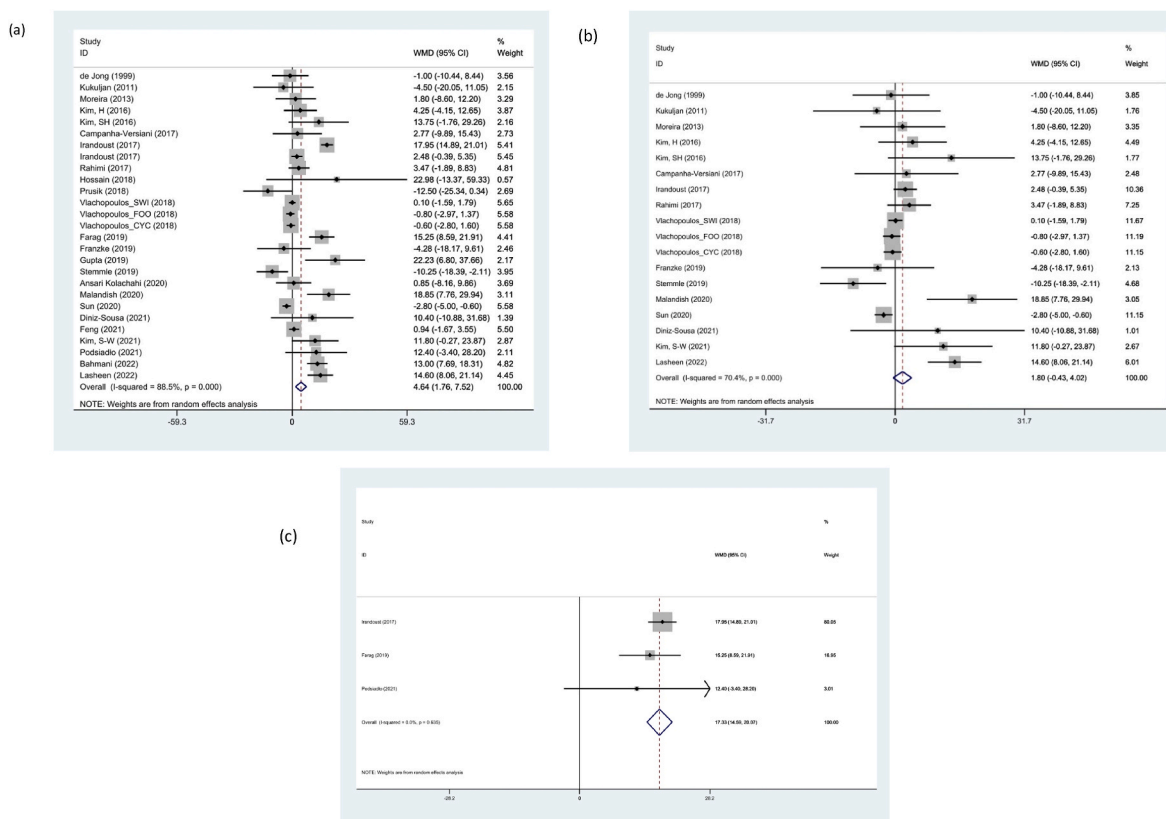


Fig. 2. Random effects meta-analysis of: (a) all studies; (b) studies conducted indoors or indoor-presumed; and (c) studies conducted outdoors. The estimate is the weighted mean difference in the change in serum 25(OH)D concentration between the intervention and control groups.

terms of the type and frequency of exercise and the length of the intervention; few studies explored the effect of high-intensity exercise.

It has been hypothesised that physical activity might influence serum 25(OH)D concentration by increasing fat metabolism, leading to the release of vitamin D and/or its metabolites from adipose tissue [58]. This hypothesis has been supported by the many observational studies that have shown positive effects of physical activity on 25(OH)D concentration or vitamin D status [54–57]. However, observational data are difficult to interpret due to the challenges in controlling for confounding factors including time outdoors. Some observational studies have found that the effect persists after controlling for sun exposure [54], and that both indoor and outdoor physical activity lead to increased 25(OH)D concentration after mutual adjustment [57]. However, time outdoors is extremely difficult to measure, and the dose of UV radiation received while outdoors is difficult to measure [59], limiting the ability to control for confounders. Some studies have concluded that much of the effects of physical activity on vitamin D is attributable to time outdoors. For example, one study reported effects of physical activity on 25(OH)D concentration in the months when there was sufficient UV-B radiation to manufacture vitamin D, but not in those months with limited UV-B radiation [56]; if physical activity has an independent effect on vitamin D this difference would not have been observed. Given the somewhat intractable problem of controlling for confounding, experimental evidence is needed to determine whether physical activity, independently of time outdoors or sun exposure, influences vitamin D.

Our findings suggest that it is unlikely that physical activity, in the absence of time outdoors, has any clinically meaningful effect on vitamin D status. However, many of the studies were in people with a clinical condition, and for the most part the exercise regimen administered was relatively modest. It is plausible that high dose (frequency and length) and intensity of physical activity would lead to increased 25(OH)D concentration. In addition, the baseline 25(OH)D concentration was in the sufficient range in many studies, and there is some evidence that physical activity may only be beneficial in the presence of vitamin D deficiency [58]. Nevertheless, as vitamin D deficiency is a clinical condition warranting rapid correction through supplementation, this question is of limited clinical relevance.

This analysis has strengths and limitations. Despite our comprehensive review of the literature, it is possible that we might have failed to identify some studies that reported on the effect of physical activity on 25(OH)D concentration. For most studies, change in 25(OH)D concentration was not the primary or secondary outcome, frequently being reported incidentally, making it challenging to identify all relevant publications. Most studies recruited people from selected population subgroups, limiting generalisability to the wider population, and most had small sample size, and were statistically under-powered. There was variability in the laboratory assays used to determine 25(OH)D concentration and not all laboratories were taking part in a quality assurance program; measurement error may have reduced the ability of studies to detect the effect of a physical activity intervention. The quality of the included studies was moderate, with no studies classified as having low risk of bias. Not all studies described whether the physical activity intervention occurred indoors or outdoors; in some, but not all, we were able to infer the location from the description of the intervention. Finally, participants were not blinded to whether they were in the intervention or control group, and it is plausible that being randomised to a physical activity intervention could have resulted in other changes that could have influenced 25(OH)D concentration.

The studies of indoors physical activity interventions suggest that there is minimal effect of physical activity on 25(OH)D concentration. There was a large effect when physical activity interventions were delivered outdoors, but this was based on only three small studies, and increased sun exposure is most likely responsible for this effect. Regular physical activity clearly has a range of physical and psychological benefits, so it is vital that campaigns continue to promote this as an effective health promotion measure. However, physical activity indoors should

not be promoted specifically as a measure to mitigate the risk of vitamin D deficiency. This should be reflected as existing guidelines are updated.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.puhip.2024.100495>.

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