

# What's new for the clinician– summaries of recently published papers

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## 1. Does Vitamin D deficiency aggravate COVID-19 infection?- A systematic review and meta-analysis

The lack of a cure for COVID-19 infection has spawned a host of treatment and preventative approaches directed at either the virus, strengthening of the immune system or management of the signs and symptoms associated with the disease. Vitamin D is thought to play an effective role in immune system functioning, which can help in a satisfactory cellular response and in protecting against the severity of infections caused by microorganisms<sup>1</sup>. Vitamin D deficiency (25(OH)D below 50nmol/l) has also been associated with severe COVID-19 raising discussions about the benefits of supplementation of this vitamin when treating the illness caused by SARS-CoV-2. In Europe, an association has been identified between vitamin D deficiency in the population and higher COVID-19 mortality rates implying that that countries closer to the equator present lower COVID-19 mortality rates than those further from the equator<sup>1</sup>.

Pereira and colleagues (2021)<sup>1</sup> reported on a systematic review with meta-analysis that sought to evaluate the association between vitamin D deficiency and COVID-19 severity, via an analysis of the prevalence of vitamin D deficiency and insufficiency in people with the disease.

### METHODOLOGY

A search strategy was conducted by 3 independent reviewers in 5 electronic databases up until October 2020. The terms "Vitamin D" and "COVID-19" were used and the lists of bibliographical references of the relevant studies were examined in order to identify potentially eligible studies. No language limits were applied.

Using the PECO strategy (patient, exposure, comparison, outcome), only studies that met the following criteria were considered for inclusion:- (i) only involved individuals in the adult and elderly age group; (ii) involved individuals with COVID-19; (iii) compared the prevalence of vitamin D deficiency according to COVID-19 severity; (iv) classified the serum VitD concentration outcome in the study's participants: mean VitD (nmol/l; ng/ml), insufficiency, and

deficiency; and, (v) case series, cross-sectional, cohort, and case-control studies.

Studies were selected independently and any disagreements was resolved by consensus. Methodological quality was assessed according to the Research Triangle Institute Item Bank (RTI-Item Bank) scale, which assesses the risk of bias. The RTI-Item Bank contains 29 items for evaluating studies, of which seven were applied to observational studies included in this review. This tool considers the following issues: (1) clear inclusion and exclusion criteria; (2) uniformly distributed inclusion and exclusion criteria; (3) appropriate sample size; (4) whether the inclusion and exclusion criteria were applied using valid and reliable measures; (5) whether the results were analysed using valid and reliable measures, including all participants; and (6) whether important confounding and effect variables were considered in the study and/or analysis.

One point (yes) or zero (no) was scored for each item. The total score in all items can generate an overall quality index that ranges from 0 to 6. According to the scores, the risk of bias is classified as low risk (=6 points) or high risk (<6 points).

The main outcome was vitamin D deficiency and COVID-19 severity. The investigators compared the proportion of patients with vitamin D deficiency in those with mild versus severe COVID-19. Second, the occurrence of vitamin D deficiency and insufficiency and the association for vitamin D deficiency and the occurrence of infection, hospitalization, and mortality from COVID-19 was analysed.

### RESULTS

From the initial search, 1542 studies in the databases were identified and after the selection of studies protocol, 27 studies were selected for qualitative synthesis and 26 was included in the meta-analysis. All of the included studies were published in 2020 and presented 372332 participants with most studies set in Europe. There was a predominance of articles with a methodological quality classified as high risk of bias (n=23 out of 27, 74%). The meta-analysis included 8176 COVID-19 patients participating in 26 studies and the mean age was 58years old (95% CI = 54–62).

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The prevalence of vitamin D deficiency was 39% among individuals with COVID-19. Regarding the severity of the disease, it was recorded that individuals with severe COVID-19 present 65% (OR = 1.65; 95% CI = 1.30–2.09; I<sup>2</sup> = 35.7%) more vitamin D deficiency compared with mild cases of the disease. A vitamin D concentration of less than 75 nmol/L increased hospitalization for COVID-19 (OR = 1.81, 95% CI = 1.41–2.21; I<sup>2</sup> = 0.0%), and this deficiency was associated with COVID-19 mortality (OR = 1.82, 95% CI = 1.06–2.58; I<sup>2</sup> = 59.0%).

## CONCLUSIONS

The results of the meta-analysis confirm the high prevalence of vitamin D deficiency in people with COVID-19, especially the elderly. There was a positive association between vitamin D deficiency and the severity of the disease

### Implications for clinical practice:

The results of the meta-analysis suggest that vitamin D supplementation could be considered in patients with vitamin D deficiency and insufficiency, if they have COVID-19. However, there is no support for supplementation among groups with normal blood vitamin D values with the aim of prevention, prophylaxis or reducing the severity of the disease.

## REFERENCE

1. Pereira M, Dantas Damascena A, Galvão Azevedo LM, de Almeida Oliveira T, da Mota Santana J. Vitamin D deficiency aggravates COVID-19: systematic review and meta-analysis. *Critical reviews in food science and nutrition*. 2022 Mar 9;62(5):1308-16.

## 2. Plant-based diets and risk of disease mortality: a systematic review and meta-analysis of cohort studies

Plant-based diets (PBDs), focusing on a high intake of plant-based food products and low intake of animal-based products, have increasingly become popular in many settings that have promoted a healthier lifestyle. Depending on the definition, these diets may have diverse compositions- for example, a vegetarian diet, a type of PBD, includes vegan (no animal products), lacto-ovo-vegetarian (including dairy and eggs), lacto-vegetarian (including dairy products), pesco-vegetarian (eating fish and seafood), and semi-vegetarian (consuming meat infrequently) diets.

Dietary information is usually collected in the form of a food frequency questionnaire (FFQ), which is a list of foods and beverages with response categories to indicate usual frequency of consumption over the time period queried (usually the past 1 year). To assess the total diet, the number of foods and beverages assessed typically ranges from 80 to 120. To study the effects of the consumption of whole plant foods on health, researchers have developed the pro-vegetarian score or plant-based diet index (PDI) – a way of scoring the data collected from FFQs. This plant-based scoring system gives the consumption of plant foods positive marks and the consumption of any animal-derived foods negative markers. Unhealthy plant foods, such as refined grains and sugar and processed foods can also be given negative marks in what is termed an unhealthy plant-based diet index (uPDI).

Considering the variances in the composition of different PBDs, Jafari and colleagues (2021)<sup>1</sup> undertook a systematic review and meta-analysis of prospective cohort studies to investigate the association of a plant-based eating style with the risk of all-cause and cause-specific mortality in the general population.

### METHODOLOGY

This systematic review was completed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Four electronic databases were searched for publications related to the aim of the review using a structured search strategy up until October 2020. The search was performed without any restrictions. Moreover, the bibliography of relevant articles was meticulously examined to find potential missing studies. The researchers included prospective cohort studies that 1) were conducted in the general adult population ( $\geq 18$  years); 2) considered different types of plant-based eating style including PDI, and vegetarian, vegan, semi-, lacto-, lacto-ovo-, and pesco-vegetarian diets as exposure of interest; 3) reported all-cause, CVD, site-specific and total cancer mortalities as well as other causes of death; and 4) reported adjusted estimates including relative risk (RR), risk ratio, or hazard ratio (HR) and 95% confidence interval (CI) as the effect size.

Two reviewers independently applied the inclusion criteria and discrepancies were managed by a consensus

approach using a 3<sup>rd</sup> reviewer. The 9-point Newcastle–Ottawa assessment tool to assess the quality of the included studies.

The certainty of evidence was assessed by the use of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool which is also used in Cochrane Reviews. This tool grades the evidence as high, moderate, low, or very low quality.

### RESULTS

After the initial screening process, 22 relevant full-texts remained for review and consideration after which 10 were excluded (4 had incomplete data, 2 were not performed in the general population, 1 did not have a control and 1 did not report this review's outcome of interest). As a result, 12 prospective cohort studies with 42,697 cases and 508,861 participants were included.

The pooled results from the 12 trials showed that greater adherence to the PBDs (highest vs. lowest category) was significantly associated with a lower risk of all-cause mortality (HR: 0.90, 95% CI: 0.82, 0.99;  $I^2 = 90.7\%$ ,  $P_{heterogeneity} < .001$ ). The sensitivity analyses did not show changes in the significance of the results (HR range: 0.88–0.98) meaning that all subtypes of PBDs were significantly associated with a lower risk of all-cause mortality.

Further analyses based on types of PBDs showed significant inverse associations between Pesco-vegetarian diet (HR: 0.81, 95% CI: 0.70, 0.92), hPDI (HR: 0.92, 95% CI: 0.88, 0.96), and Pro-vegetarian diet (HR: 0.74, 95% CI: 0.55, 0.88) with the risk of all-cause mortality implying that the closer one adhered to these diets, the lower the risk of all-cause mortality.

Seven studies reported 5349 cases of mortality due to CVDs among 168,294 participants. The results of highest vs. lowest category did not show significant association between the PBDs and CVDs mortality (HR: 0.90, 95% CI: 0.79, 1.02;  $I^2 = 78\%$ ,  $P_{heterogeneity} < .001$ ). However, among different types of PBDs, only the vegetarian diet was significantly associated with lower risk of CVDs (HR: 0.92, 95% CI: 0.85, 0.99;  $I^2 = 0\%$ ,  $P_{heterogeneity} = .82$ ). Inverse significant results (HR: 0.77, 95% CI: 0.70, 0.86;  $I^2 = 36\%$ ,  $P_{heterogeneity} = .01$ ) were found with the meta-analysis on eight prospective cohort studies including 3168 deaths due to cardiac heart disease (CHD) among 234,202 participants. Analyses based on the type of diets showed inverse association between the vegetarian diet and lower risk of CHD (HR: 0.76, 95% CI: 0.68, 0.85;  $I^2 = 35\%$ ,  $P_{heterogeneity} = .16$ ) implying that the closer the adherence to a vegetarian diet resulted in a significantly lowered risk of CHD.

The pooled analysis of five cohort studies with 1088 cases of mortality due to cerebrovascular disease among 122,165 participants did not show any association

between adherence to vegetarian diet and risk of cerebrovascular mortality (HR: 0.93, 95% CI: 0.78, 1.10; I<sup>2</sup> = 45%, Pheterogeneity = .12)

Five prospective cohort studies including 2838 cases of mortality due to total cancer among 133,818 participants indicated that the highest vs. lowest category of vegetarian diet was not associated with total cancer mortality (HR: 0.96, 95% CI: 0.85, 1.08; I<sup>2</sup> = 28%, Pheterogeneity = .24). The meta-analyses on different cancer subtypes also did not show any associations between vegetarian diet and risk of mortality due to colorectal (HR: 1.01, 95% CI: 0.79, 1.29; I<sup>2</sup> = 0%, Pheterogeneity = .48), lung (HR: 0.96, 95% CI: 0.72, 1.29; I<sup>2</sup> = 0%, pheterogeneity = .44), female breast (HR: 0.92, 95% CI: 0.52, 1.64; I<sup>2</sup> = 72%, pheterogeneity = .01), prostate (HR: 0.89, 95% CI: 0.59, 1.34; I<sup>2</sup> = 18%, Pheterogeneity = .30), and gastric (HR: 1.06, 95% CI: 0.63, 1.77; I<sup>2</sup> = 27%, Pheterogeneity = .25) cancers. The reviewers also did not find any significant associations between the highest vs. lowest adherence to the vegetarian diet and risk of mortality due to mental and neurological (HR: 1.73, 95% CI: 0.98, 3.05; I<sup>2</sup> = 44%, pheterogeneity = .18), respiratory (HR: 1.18, 95% CI: 0.91, 1.54; I<sup>2</sup> = 30%, Pheterogeneity = .23), and gastrointestinal (HR: 0.93, 95% CI: 0.60, 1.44; I<sup>2</sup> = 0%, Pheterogeneity = .42) diseases.

The certainty of evidence was rated using the GRADE approach. The certainty of evidence was rated low for CHD mortality and very low for other outcomes, with various downgrades for serious imprecision and inconsistency

## CONCLUSIONS

This review found that there was an inverse association between the total PBDs and risk of all-cause and CHD mortality. Simply put, it implied that the “higher” the adherence to PBDs were, the “lower” the risk of all-cause and CHD mortality were.

### Implications for practice

Oral Health professionals are often required to offer dietary advice to their patients. These findings should assist clinicians in offering advice that benefits both oral and general health.

## REFERENCE

1. Jafari S, Hezaveh E, Jaliipiran Y, Jayedi A, Wong A, Safaiyan A, Barzegar A. Plant-based diets and risk of disease mortality: a systematic review and meta-analysis of cohort studies. *Critical Reviews in Food Science and Nutrition*. 2021 Apr 21:1-3.

## CPD questionnaire on page 374



The Continuous Professional Development (CPD) section provides for twenty general questions and five ethics questions. The section provides members with a valuable source of CPD points whilst also achieving the objective of CPD, to assure continuing education. The importance of continuing professional development should not be underestimated, it is a career-long obligation for practicing professionals.