

# Conceptual Interpretation and Clinical Validity of Meta-analysis on Vegetarian-Based Dietary Patterns and Their Relation with Inflammatory and Immune Biomarkers

Dear Editor:

We read with great interest the article by Craddock and colleagues in which they describe a systematic review and meta-analysis of vegetarian dietary patterns and their relation with inflammatory and immune biomarkers (1).

## Excellent Research Approach

The study is of great relevance, compounding recent developments in the field of nutrition and health. Craddock et al. present a thorough and detailed analysis; however, a few valid points of improvement are suggested to advance further and enhance the study's potential for informing clinical practice.

## Interpretation of Estimated Effect Size or Statistical Significance of the Pooled Outcome Measure Derived from Meta-analysis

Craddock et al. concluded, "Pooled effects of vegetarian-based dietary patterns were associated with significantly lower concentrations of C-reactive protein, fibrinogen, and total leukocyte compared with those following non-vegetarian dietary patterns in observational studies." However, it is important to note that statistical significance is not sufficient as an independent parameter for assessing the pooled effect estimate results of the meta-analysis, as it is binary in its interpretation. Using the effect size metric as part of the assessment of outcomes or results, is therefore, as it presents a nuanced approach to the analysis of pooled results (2).

## Essential Publication Bias Indicators of the Included Studies

Although the authors followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for their systematic review and meta-analysis, they did not perform analysis of publication bias (3). Publication bias is inherent to all meta-analysis studies as it is a byproduct of the overall publication process (Table 1). The inclusion of a funnel plot, Orwin and Classic fail-safe N test, Begg and Mazumdar Rank correlation test, Egger's regression, and

Duval and Tweedie's Trim and Fill would give a clear picture of possible publication bias from small or missing studies, as these are the customary tests used for assessment of bias. Therefore, it is integral to the study's integrity that the extent to which this bias affects the results is assessed and estimated (4-7).

## Conceptual Interpretation of the Concluding Findings from the Literature-Based Meta-analysis

We would also like to suggest that the concluding statement presented by Craddock et al. should better reflect the uncertainty of a literature-based review or a meta-analysis. In which case, stating that "vegetarian-based dietary patterns are associated with lowered serum C-reactive protein, fibrinogen, and total leukocyte concentrations," should preferably be replaced by "vegetarian-based dietary patterns could be/may be/are likely associated with lowered serum C-reactive protein, fibrinogen, and total leukocyte concentrations."

## Future Research Directions

We comprehend that it may not be conceivable to retroactively add the recommendations we have projected to the systematic review and meta-analysis study as has already been published. Nevertheless, it will most undoubtedly benefit any future systematic review and meta-analysis studies conducted in a similar research field. Therefore, we firmly believe that the aforementioned key points are relevant to both the authors of the original study and other future researchers working in this field to publish higher-quality systematic reviews and meta-analyses for future scientific *Advances in Nutrition*.

## Publication Bias Indicators

Classic and Orwin fail-safe N tests display the likelihood that studies are absent from the current meta-analysis and that these studies if included in the analysis, would shift the estimated effect size of the weighted mean differences (WMDs) for each outcome variable between vegetarian and nonvegetarian groups toward the null.

Begg and Mazumdar rank order correlation advises the estimated or computed Kendall's  $\tau$  b between the WMDs and the standard error (which is driven primarily by sample size) of vegetarian and nonvegetarian groups.

Duval and Tweedie's Trim and Fill test imputes the missing studies that are likely to fall, adds them to the analysis, and then recomputes the combined WMDs for each outcome variable between vegetarian and nonvegetarian groups.

These parameters are integral to any literature based meta-analysis given that this meta-analysis on vegetarian-based

**TABLE 1** Publication bias of “Vegetarian-Based Dietary Patterns and Their Relation with Inflammatory and Immune Biomarkers”

Serial numbers	Groups	Classic fail-safe N		Orwin fail-safe N		Begg and Mazumdar		Egger's regression		Dual and Tweedie (random effects)				
		Z value	P value	Std diff in observed studies	Std diff in mean in missing studies	$\tau$ value	Z value	P value	Intercept	P value	df	Observed	Adjusted	Q value
1	Difference in C-reactive protein values	-5.07447	0	-0.5188	0	-0.156	0.90906	0.36332	-0.7083	0.8325	16	0.0486	0.0486	1363.9
2	Difference in fibrinogen values	-2.4934	0.012	-0.3312	0	-0.666	1.04447	0.2962	-10.32	0.2555	1	-0.352	-0.352	3.6384
3	Difference in leukocytes	-11.71	0	-0.413	0	-0.29	1.2456	0.2129	-9.427	0.0828	9	-1.101	-1.101	477.34
4	Difference in thrombocytes	1.6799	0.092	0.1153	0	0	0	1	-0.2737	0.8589	5	0.1148	0.1148	8.6567

dietary patterns and their relation with inflammatory and immune biomarkers is based on published literature, not on vegetarian and nonvegetarian cohorts.

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