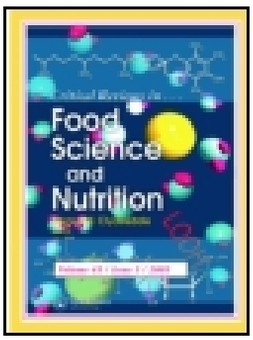

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# Rebuttal to the letter "Plant-based diets do not prevent most chronic diseases" of Fenton et al.

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## TO THE EDITOR

We read with great interest the letter of Fenton & Gillis regarding our recent publication in the Journal (1). Despite recognizing several strengths within our study, Fenton & Gillis raised few concerns about our meta-analysis. First, they pointed out that our paper, and the Abstract in particular, suffers from selective reporting of results. They claimed that over-stated cause-and-effect statements are present and that we did not mention the results of non-significant associations between vegetarian and vegan diets and chronic diseases. The Authors should know that, as with all the published papers, space constraints imposed by all the Journals limit the amount of details that can be included in the Abstract. As usual, in fact, only the most relevant results are reported. In the 'Results' section, all the results are reported and we clearly stated that no significant association was evidenced for total cardiovascular and cerebrovascular diseases, all-cause mortality, cancer mortality and specific types of cancer incidence/mortality.

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Second, Fenton & Gillis correctly observed that the health differences noted in this systematic review should not be attributed solely to the diets, as vegetarians tend to be more conscious for the health aspects, slimmer, and in better health when compared with omnivores. We fully agree with this observation as we have already highlighted this aspect in the 'Introduction' section. In addition, as also reported by the Authors of the letter, we discussed in the 'Discussion' section the fact that the observed difference between Adventists and non-Adventists reinforce the hypothesis that the studies coming from Adventist cohorts present a low degree of generalizability when compared to other cohorts. Meta-analysis is not an instrument to solve problems, but to raise questions within the scientific literature, and residual confounding coming from risk factors represents a common and intrinsic limitation in the investigation of dietary exposures and risk of diseases among cohort prospective studies. In our meta-analysis, every effort has been made to explore and mitigate heterogeneity, considering pre-specified covariates as potential confounders in meta-regression analysis, using a more conservative random model in risk ratio calculations, and performing subgroup analyses limited to the more homogeneous subgroup of subjects.

Third, Fenton & Gillis claimed that we should have used a more reasonable P-value, and that the risk ratio should be at least reduced to one half to have a true and important effect. These observations are in part true, but somewhat specious. If these observations were to be applied to the whole scientific literature, most of the scientific papers would be considered null. A P-value of 0.05 is usually selected by all the studies as the standard level of significance to justify a claim of a statistically significant, and most of the associations found between risk factors (including also non-dietary factors) and diseases are modest, even in larger studies. The results need to be

always interpreted with caution and, in our paper, we have repeatedly stated it especially regarding the vegan diet, because of the very small sample size and the low number of studies available.

In conclusion, we appreciate the interest of Fenton & Gillis in our work and we are grateful for the opportunity they gave us to further clarify it. However, taking into account their criticisms we believe that they are not able to influence the main results as well as the global message of our study.

**Conflict of interest:** Nothing to report.

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**Plant-based diets do not prevent most chronic diseases**

We are concerned about the selective reporting, over-stated cause-and-effect statements and lack of mentioning the 10 results of no associations between vegetarian and vegan diets and chronic diseases in the recent paper (1).

The abstract reports on only the three statistically significant results from the cohort study analyses and did not mention the 10 results of no associations. Findings of no association are of interest as well as findings of associations, as both increase knowledge and understanding. The authors should have noted that a vegan diet lifestyle was not associated with lower all-cause mortality. There were also no differences between the vegetarians and those who ate an omnivorous diet regarding all-cause mortality, cardiovascular diseases, cerebrovascular diseases, cancer mortality, breast

cancer incidence, breast cancer mortality, colorectal mortality, prostate cancer mortality and lung cancer mortality.

Individuals who eat vegetarian or vegan diets are predominantly young female educated physically active non-smokers (2); these were controlled for by most but not all of the included studies in this systematic review. They also have more nutrition knowledge, are more concerned about their health and eat more balanced diets that include more whole grains and vegetables (3) and spend less time watching television (4); these variables were not controlled for in the included studies. Since it is not possible to disentangle health effects between the diet effects and the effects of these other health-promoting behaviors, the health differences noted in this systematic review should not be attributed solely to the diets as the authors stated that the diets conferred “a protective effect”.

The authors used the *P*-value of 0.05 for 44 tests to indicate statistical significance, giving a high probability of wrongly concluding that some of the tests were significant due to chance alone. Conducting multiple tests raises the risk of Type I errors. If they had used a more reasonable *P*-value, such as <0.004 (based approximately on a Bonferroni correction (5) for their 13 cohort study tests), only 2 of the 3 relationships would remain statistically significant, readers could have much more confidence in their findings.

The risk ratios of 0.75 to 0.92 were modest in this study. The authors noted a reduction of 25% of ischemic heart disease. GRADE (Grades of Recommendation, Assessment,

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Development, and Evaluation) recommends that to have confidence that you have identified a true and important effect from observational studies the risk ratio should be at least reduced to one half, that is a risk ratio of <0.5, for a reduced risk to 50% or less (6). The reason for this caution is that observational studies usually have residual confounding by unmeasured or unknown determinants of health that are different between the comparison groups (6).

The finding that the relationships for all-cause mortality and breast cancer mortality were stronger between vegetarian eating for the Adventists compared to the non-Adventist suggests that the benefits were likely due to other Adventist lifestyle factors rather than the vegetarian diets alone (1).

Strengths within this systematic review (1) include the authors defining their research question and inclusion criteria *a priori*; having two reviewers independently extract the data and assess methodological quality; performed a comprehensive literature search of five sources; and performed subgroup analyses to gain better understanding of the results' heterogeneity. An additional weakness was not searching for unpublished data (known as the grey literature), which is a measure of thoroughness of systematic reviews.

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