Reviewer's report

Title: A randomised controlled trial investigating the effects of Mediterranean diet and aerobic exercise on cognition in cognitively healthy older people living independently within aged care facilities: the Lifestyle Intervention in Independent Living Aged Care (LIILAC) study protocol

Version: 2

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Reviewer: Colin Rehm

Reviewer's report:

Review

This paper describes the protocol for an interesting RCT examining the effect of walking and Mediterranean diet on reducing the impact of age-related cognitive declines. The rationale for the study is well-described and the brief review at the beginning of the protocol is helpful for researchers not intimately involved in this area of research. The background and review should be carefully edited prior by the authors as there were a number of minor grammatical/formatting errors and some awkward sentences. This is particularly important as this journal does not provide any text editing. Some comments and minor issues follow.

Major Compulsory Revisions

It would be helpful to put the power calculation in the context of the primary study outcome to aide in interpretability. Also, please comment on any issues in using the effect sizes for exercise->cognitive function rather than the effects of Mediterranean diet (though such data are not available). Does this sample size seem reasonable given the existing evidence for an association between Mediterranean diet and cognitive function? Some post hoc calculations might be useful as this is a limitation.

It is implied, but please explicitly note that all participants, regardless of intervention arm will complete the same questionnaires. This is implied in the flow diagram, but should be noted somewhere in the main text.

Secondary outcomes: These are currently written as aims, and should be revised.

Analysis approach: Given that this is a factorial trial it is unclear whether the investigators will take advantage of this design by evaluating synergy/antagonism and evaluating the mean/rate difference for the Mediterranean diet by pooling data from the diet-alone and diet+walking arm and comparing to the mean/rate difference from the walking and control arm. Please provide a few more details regarding the analytical approach. In addition, will synergy be evaluated quantitatively or qualitatively?
Including couples whom live together in the same intervention arm certainly makes sense; however, it may introduce some correlated data, which should be accounted for in the analysis. Please comment on how you will account for correlated data or whether you do not need to account for it (the only reason being if there are very few cohabitating couples included in the study).

As a related note, what steps will be taken to reduce the likelihood of “contamination” beyond families?

Secondary outcomes: There are a large number of secondary outcomes. The authors mention that these will be treated as secondary outcomes, but it is unclear what this means. Were there intentions of accounting for multiple comparisons? I do not know if this is necessary, but the authors should comment.

The collection of numerous secondary outcomes/mediators is a strength of this study, though it is unclear how such data are to be used. For example, early in the paper the authors discuss traditional CVD risk factors as potential mediators of any PA/diet association with cognitive function, but do not discuss how the data collected here will be used to empirically test this? This is likely beyond the scope of the protocol, but some mention of how the secondary data are to be used would be helpful. This particular issue is brought up by the authors at the top of page 7, but is not revisited in the design/methodology section.

Minor Essential Revisions

Abstract, background, last line: delete “significant” or use a different clause. The significance of the interventional study should be determined by others, not the authors themselves.

When discussing costs of cognitive impairment, please specify if these are Australian dollars, US dollars, or some other currency.

Page 5, “A high consumption of…serum carotenoids”: Serum carotenoids are not consumed, rather they are a marker of consumption of carotenoids.

Page 5-6; a 1-point increase in Mediterranean diet means very little; please revise. Perhaps comparison of extreme quintiles would be more helpful. In the next sentence, the authors mention “grains”, do they specifically mean “whole grains”. Refined grains are certainly not a cornerstone of the Mediterranean diet.

How exactly will participants be randomized? Please include the method to be used in greater detail.

About how many aged care facilities will be involved in this study? This is important information to provide even if the exact number is not known. If the number is very large, concerns of contamination become less pronounced.

Page 8, please define irregular vitamin/supplement use.
Page 8, I know it is discussed later, but when mentioning GP approval, please note that this approval will be received prior to randomization.

Page 10, when discussed earlier an MMSE #24 is used but <25 here. Not all people will know that MMSE scores are rounded to the nearest whole integer, so I would recommend using consistent definitions.

For the collection of blood, please clarify whether the participants will be under any instruction to not engage in physical activity, take supplements/drugs or fast, as such behaviors immediately before collection of blood could impact the measurement.

Editorial issues

Please be sure to define each acronym upon first use; for example, see MCI on page 5.

There were many sentences throughout the paper that did not have a period, specifically when the sentence ended in a reference, please check carefully as this journal does not provide copy editing.

Page 3, “It is considered that memory”: is awkwardly written.

Page 5, “the nutritional impact of diet”: confusing and somewhat redundant as written.

Page 6, “These findings of these studies”: confusing and awkward as written.

Page 6, “cardio-vascular” should be “cardiovascular”.

Page 11, change “conducted the residents’ medical practitioners” to “conducted by the residents’ medical practitioners”.

Page 12, please delete either “compliance” or “adherence” when discussing adherence to the Med diet.

References: for some of the references there is a box (see #19, 22, for example)

Discretionary Revisions

Alcohol and Mediterranean diet: Perhaps the authors should note “moderate” intake of alcohol rather than lower intake of alcohol. Many of the observational studies evaluating the health effects of the Mediterranean diet include moderate alcohol consumption in the score.

A table summarizing all of the outcome measures/mediators, their methods of assessment and any relevant citations would be a useful, but not necessary addition.

Quality of written English: Needs some language corrections before being published
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.