PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Protocol for a pragmatic randomised controlled trial of Body Brain Life – GP and a Lifestyle Modification Program to decrease dementia risk exposure in a primary care setting
AUTHORS	Kim, Sarang; McMaster, Mitchell; Torres, Susan; Cox, Kay L.; Lautenschlager, Nicola; Rebok, George; Pond, Dimity; D'Este, Catherine; McRae, Ian; Cherbuin, Nicolas; Anstey, Kaarin

VERSION 1 – REVIEW

REVIEWER	Deborah Barnes University of California, San Francisco, and San Francisco Veterans Affairs Health Care System, USA
REVIEW RETURNED	17-Sep-2017

GENERAL COMMENTS	This manuscript describes the protocol for a three-arm randomized, controlled trial of behavioral interventions to reduce dementia risk factors. Minor revisions are suggested to clarify study methods. • Consider describing this as a pragmatic trial and describing the pragmatic elements (see Ford and Norrie, NEJM 2016 or NIH Collaboratory on rethinking clinical trials: http://www.rethinkingclinicaltrials.org/ • The reference related to number of cases potentially prevented with 10-25% risk reduction incorrectly states that this is per annum. These numbers refer to the total number of cases. Please remove the words 'per annum' from the abstract and introduction • It would helpful to include a rationale for the inclusion criteria. Some of the conditions listed are not risk factors for dementia (e.g., osteoporosis). • Please specify the definition of a 'medium' effect size. • SPIRIT Checklist: o Please add the date and version for this study protocol (3). o Please add role of study sponsor (5c). o Please add statement regarding discontinuing or modifying allocated intervention (e.g., due to non-compliance or adverse event) (11b) o Please add explanation for why a Data Monitoring Committee is not needed (21a) o Please add information on interim analyses and stopping rules (e.g., under what conditions might the study be stopped early) (21b)? o Please add plans for auditing trial conduct and ensuring intervention fidelity (23) • It would be helpful to include information on the validity and

	reliability of the outcomes measures. • It would be helpful to have a Figure or Table comparing the intervention procedures for the 3 arms (e.g., frequency and type of contact)

REVIEWER	Shireen Sindi Karolinska Institute, Sweden
REVIEW RETURNED	22-Oct-2017

GENERAL COMMENTS	Bmjopen- 2017-019329 Title: Protocol for a randomised controlled trial of Body Brain Life – GP and a Lifestyle Modification dementia risk exposure in a primary care setting Program to decrease dementia risk exposure in a primary care setting This protocol article describes a randomized controlled trial to assess multidomain lifestyle interventions for dementia risk reduction in a primary care setting. The trial includes three arms: a 12 week online and face-to-face dementia risk reduction intervention; 2) a 6-week face-to-face group intervention; and 3) a 12-week email only program. This trial is ongoing, and its completion is anticipated for December 2018. This is an important trial, as there is a pressing need for such dementia prevention trials in primary care settings. The availability of such evidence-based programs would allow for wider implementation of dementia risk reduction interventions among individuals from different age groups. Overall this is a well-written protocol article, though a few areas need further clarifications / pieces of information. The comments are presented in the order they appear: Abstract: Methods and analysis: • What is the age range of participants? • It is difficult to understand what the different interventions are, when the abbreviations are not defined (BBL-GP) and (LMP). If space does not allow, then perhaps it would be better to remove these abbreviations and provide further information. For example it states that intervention #1 is a dementia risk reduction intervention, but this is not stated for interventions #2 and #3. Strengths and limitations of this study: • p.5 I understand that this section is meant to be brief, but for the first bullet point, it is important to clarify which programs when it states 'This study has been built on our dementia prevention research programs'. Stating the name of the program would be sufficient. Introduction: • p.6 Following the sentence: "Alzheimer's disease and cardiovascular disease share

	cardiometabolic and lifestyle risk factors….. reducing abnormally high blood pressure and cholesterol" (with the reference Santos et al., 2017), please clarify if these risk factors are described for midlife or late-life. For example high blood pressure and cholesterol are important in midlife, but not necessarily in late-life, and this differentiation is important to make. • p. 7 The reference 'Richard et al., 2009' is the protocol article. The trial results have been published last year. The following is the reference: van Charante, E. P. M., Richard, E., Eurelings, L. S., van Dalen, J. W., Ligthart, S. A., Van Bussel, E. F., ... & van Gool, W. A. (2016). Effectiveness of a 6-year multidomain vascular care intervention to prevent 2 dementia (preDIVA): a cluster-randomised controlled trial. The Lancet, 388(10046), 797- 805. • p.7 In the text, it is currently unclear how the current proposed intervention differs from the PreDIVA intervention conducted among older adults in primary care settings. Methods and analysis: • p. 8 Please provide reference(s) for the following: "we developed and have evaluated previously on volunteers and which has now been adapted for primary care" • This section would benefit from having a visual representation (e.g. Table) with the basic descriptive factors of the different interventions. Below is an example of how this may look: LMP BBL-GP Active control Previously tested: Yes, in primary care Yes, among volunteers, now adapted for primary care duration 6 weeks 12 weeks Number of sessions 12 ??? Format Face-to-face group sessions etc 1-hour individual session with dietician etc • The authors may also want to provide a diagram figure with the different trial arms, and the follow-up intervals. Participants: (p.9) • Might there be a bias when selecting participants who have renewed their membership (higher education levels, better health at baseline etc)? Please discuss this. • Although it is understandable that it is never 'too early' to adopt a healthy lifestyle, it may be difficult for readers to comprehend why the chosen minimum age for a dementia prevention programs is 18 years of age. Please elaborate on the motive for this.

	• "upon return of consent forms", was this via post? • There is an extra 'and', "unique identity numbers and as well as an online account". Inclusion criteria: (p.9) • Please revise the grammar in the sentence (to be able to bulk billed). • Please provide an explanation for why the person must be the only one in his/her household that is taking part in the study. • To be eligible for the study, participants were required to have a chronic health condition. What if despite having one chronic health condition, participants have healthy lifestyles at 3 baseline (in terms of nutrition, exercise)? what improvements might be expected as a result of the trial? Exclusion criteria: • How is cognitive impairment defined? • Are participants allowed to participate if they are already participating in other lifestyle intervention studies / trials? Sample size calculation: • What was the primary outcome for the "previous Body Brain Life Project"? • For which age group was the 33% attrition rate observed? Might the attrition rate differ for various age groups? How might this impact the available power for the analyses? Assessments: • Will the immediate follow-ups (at 7 weeks for LMP and 13 weeks for BBL-GP) be directly compared? If yes, are they considered directly comparable? • Will a cut-off be used for the Multidimensional Health Questionnaire at screening? Please include this information in the text. Primary outcome: • What if participants already have low scores on the ANU-ADRI-SF at baseline, what changes might be expected following the trial? Would it have been advantageous to have a cut-off to ensure that participants' risk score is sufficiently elevated to benefit from the interventions? Secondary outcomes: • Why were the cognitive tests limited to those mentioned, instead of including additional domains? The text can specify why those test & domains were chosen? Randomization How is the allocation sequence generated? Computer generated? Please provide more details. Who assigns the numbers to participants? How? Interventions: Group 1: Brain Body Life – GP • P.13 For which age group was this intervention intended? • P.14 It states, "the revised program was piloted with the general public. What were the results of the pilot? How were participants' experiences? What was the dropout rate?

	Adherence? 4 • P.14 The BBL-GP intervention is multidomain and consists of diet, exercise, cognitive activity, social activity, dementia literacy, risk factors etc., however; only physical activities and diet are described in more detail. Please also describe the other interventional domains. • p.15 How was diet measured at follow-up? Group 2: Lifestyle Modification Program (LMP). • On p.16 it states "designed to enhance general wellbeing and improve lifestyle to reduce the risk of chronic disease", whereas on p.17 it sates "designed to provide individuals with tools to help manage chronic disease". It is unclear whether the program is intended for dementia prevention, or management of existing chronic disease. Please clarify. Data Management and monitoring: • Is there an independent Data Monitoring Committee involved? Ethics and trial registration: • Please describe the process for obtaining informed consent. Adverse events: • Please comment on the definitions and reporting of Adverse Events and Serious Adverse events. Discussion: • Please comment on the feasibility of recruitment into the trial. Tables: • Table 1. It might be clearer if 'screening' is a column instead of a row • Table 2: Module 5: How does the program provide info. On the individual's specific chronic health conditions? • Table 2: Module 6: Please provide examples of the mentally stimulating activities.

VERSION 1 – AUTHOR RESPONSE

Editor Comments to Author:

- The referencing style is incorrect. Please use the Vancouver convention when referencing throughout your paper.

 The referencing style has changed to Vancouver

Reviewer: 1

Consider describing this as a pragmatic trial and describing the pragmatic elements (see Ford and Norrie, NEJM 2016 or NIH Collaboratory on rethinking clinical trials: http://www.rethinkingclinicaltrials.org/

 Thank you for your suggestion. We agree that our trial is a pragmatic trial and have revised the paper accordingly.

The reference related to number of cases potentially prevented with 10-25% risk reduction incorrectly states that this is per annum. These numbers refer to the total number of cases. Please remove the words 'per annum' from the abstract and introduction.

- This has been removed from the abstract (page 3) and the introduction (page 6).

It would be helpful to include a rationale for the inclusion criteria. Some of the conditions listed are not risk factors for dementia (e.g., osteoporosis).

- The inclusion criteria is pragmatic as the practice already had a criteria for referral to their LMP. In developing the protocol, it became clear that introducing a second set of inclusion criteria would make implementation difficult and reduce participant numbers. We therefore made a decision to use the principle that if a GP referred the patient to the LMP, then they would be eligible for the trial. This was a pragmatic feature of the current trial that significantly differs from our original BBL trial. The rationale has been updated on page 9.

Please specify the definition of a 'medium' effect size.

- A medium effect refers to 0.5 standard deviation. This has been added to page 10.

SPIRIT Checklist:
- Please add the date and version for this study protocol (3).
- Please add role of study sponsor (5c).
- Please add statement regarding discontinuing or modifying allocated intervention (e.g., due to non-compliance or adverse event) (11b)
- Please add explanation for why a Data Monitoring Committee is not needed (21a)
- Please add information on interim analyses and stopping rules (e.g., under what conditions might the study be stopped early) (21b)?
- Please add plans for auditing trial conduct and ensuring intervention fidelity (23)

- Thank you for pointing out missing information. Additional information and explanation have been added to the manuscript and page numbers are listed on the updated SPIRIT checklist.

It would be helpful to include information on the validity and reliability of the outcomes measures.

- Validity and reliability of the outcomes measures were added to page 12-13, demonstrating all measures have good reliability and validity.

It would be helpful to have a Figure or Table comparing the intervention procedures for the 3 arms (e.g., frequency and type of contact)

- Thank you for suggesting this. Table 2 comparing 3 intervention programs, in terms of duration and frequency of interventions, number of sessions, format or type of contact and whether the interventions have been previously applied, have been added on page 33.

Reviewer: 2
Abstract:
Methods and analysis:
What is the age range of participants?

- Anyone aged 18 and over can participate in this study. This information was added to page 3.

It is difficult to understand what the different interventions are, when the abbreviations are not defined (BBL-GP) and (LMP). If space does not allow, then perhaps it would be better to remove these abbreviations and provide further information. For example it states that intervention #1 is a dementia risk reduction intervention, but this is not stated for interventions #2 and #3.

- Thank you for pointing this out. A brief explanation was provided for LMP and active control just like it was provided for BBL-GP on page 3.

Strengths and limitations of this study:

p.5 I understand that this section is meant to be brief, but for the first bullet point, it is important to clarify which programs when it states 'This study has been built on our dementia prevention research programs'. Stating the name of the program would be sufficient.

- The words 'This study' has been replaced with 'BBL-GP program' to clarify which program it refers to on page 5.

Introduction:

p.6 Following the sentence: "Alzheimer's disease and cardiovascular disease share cardiometabolic and lifestyle risk factors….. reducing abnormally high blood pressure and cholesterol" (with the reference Santos et al., 2017), please clarify if these risk factors are described for midlife or late-life. For example high blood pressure and cholesterol are important in midlife, but not necessarily in late-life, and this differentiation is important to make.

- Thank you for highlighting this important point. Cholesterol, high blood pressure, and overweight/obesity are mid-life risk factors, all others apply to mid-life and late-life. We have now clarified this point on page 6.

p. 7 The reference 'Richard et al., 2009' is the protocol article. The trial results have been published last year. The following is the reference: van Charante, E. P. M., Richard, E., Eurelings, L. S., van Dalen, J. W., Ligthart, S. A., Van Bussel, E. F., ... & van Gool, W. A. (2016). Effectiveness of a 6-year multidomain vascular care intervention to prevent dementia (preDIVA): a cluster-randomised controlled trial. The Lancet, 388(10046), 797- 805.

- Thank you for providing this recent reference. The reference has been replaced with the suggested reference.

p.7 In the text, it is currently unclear how the current proposed intervention differs from the PreDIVA intervention conducted among older adults in primary care settings.

- The proposed intervention addresses not only cardiovascular risk factors, but also lifestyle related risk factors for adults aged 18 and older. This sentence has been revised on page 7.

Methods and analysis:

p. 8 Please provide reference(s) for the following: "we developed and have evaluated previously on volunteers and which has now been adapted for primary care"

- The reference for BBL study was added to page 8.

This section would benefit from having a visual representation (e.g. Table) with the basic descriptive factors of the different interventions. Below is an example of how this may look:

- Thank you for this suggestion. Table 2, describing and comparing interventions has been added to page 33.

The authors may also want to provide a diagram figure with the different trial arms, and the follow-up intervals.

- This is a great idea. Figure 1 has been added to give visual representation of the flow of study.

Participants: (p.9)

Might there be a bias when selecting participants who have renewed their membership (higher education levels, better health at baseline etc)? Please discuss this.

- NHC reported that those who are of lower-socioeconomic status renew more often because they use the medical services more frequently. There is also a re-joining fee that members have to pay if they let their membership lapse, which may have a significant impact on those with lower incomes. However, covariate such as education level will be examined when analysing data and appropriately screened for in future manuscripts.

Although it is understandable that it is never 'too early' to adopt a healthy lifestyle, it may be difficult for readers to comprehend why the chosen minimum age for a dementia prevention programs is 18 years of age. Please elaborate on the motive for this.

- We used a naturalistic approach in recruitment and therefore we used the inclusion criteria that is being used by the NHC. Moreover, risk factors for dementia exert their influence over decades and thus the earlier one decreases their risk exposure, the more impact it is likely to have over their lifespan. This is stated in the text on page 9.

"upon return of consent forms", was this via post?

- It was via email. This information has been added on page 9.

There is an extra 'and', "unique identity numbers and as well as an online account".

- The 'and' was removed from page 9.

Inclusion criteria: (p.9)
Please revise the grammar in the sentence (to be able to bulk billed).

- This has been rephrased to "for bulk billing eligibility" on page 10.

Please provide an explanation for why the person must be the only one in his/her household that is taking part in the study.

- This was to prevent a couple/family members from being randomly assigned to different groups and therefore receive different interventions. This might have introduced a bias if members of the same household shared information about their interventions with each other received. This additional information has been added to page 10.

To be eligible for the study, participants were required to have a chronic health condition.
What if despite having one chronic health condition, participants have healthy lifestyles at baseline (in terms of nutrition, exercise)? what improvements might be expected as a result of the trial?

- We agree that it is possible that using different selection criteria would lead to a greater effect but as this was a pragmatic trial, this was not possible. It also became clear that introducing a second set of inclusion criteria would make implementation difficult. We believe that if participants benefit from the LMP, they would benefit from the trial.

Exclusion criteria:
How is cognitive impairment defined?

- Cognitive impairment was assessed through self-report from the participants. However, cognitive impairment was again tested with MMSE during baseline assessment.

Are participants allowed to participate if they are already participating in other lifestyle intervention studies / trials?

- This is a good point. We did not exclude anyone if they are already participating in other intervention studies. However, as this is quite a unique intervention trial, we do not believe there will be too many similarities between our trial and the other trials participants might be participating in, if any.

Sample size calculation:
What was the primary outcome for the "previous Body Brain Life Project"?

- Primary outcome for the previous BBL was same as the current study, which is one's exposure to risk factors for Alzheimer's disease. This information has been added to page 10.

For which age group was the 33% attrition rate observed? Might the attrition rate differ for various age groups? How might this impact the available power for the analyses?

- The attrition rate was provided by NHC based on their experience of previous LMP programs that used the same inclusion and exclusion criteria and targeted the same age group (adults aged 18 and older). No difference in attrition between age groups was reported by NHC. This information has been added to page 11.

Assessments:
Will the immediate follow-ups (at 7 weeks for LMP and 13 weeks for BBL-GP) be directly compared? If yes, are they considered directly comparable?

- Yes, immediate follow ups will be directly compared between groups. Even though LMP was reduced to 6 weeks from the original 12 weeks, materials covered by the program have not been changed. In addition, LMP is a group based educational program where individual's progress/health and lifestyle changes are not followed through. Therefore, LMP's short duration should not make a difference in outcomes.

Will a cut-off be used for the Multidimensional Health Questionnaire at screening? Please include this information in the text.

- A cut-off will not be used for the Multidimensional Health Questionnaire as it is not being used for screening. It is a covariate for future analyses.

Primary outcome:
What if participants already have low scores on the ANU-ADRI-SF at baseline, what changes might be expected following the trial? Would it have been advantageous to have a cut-off to ensure that participants' risk score is sufficiently elevated to benefit from the interventions?

- Thank you for pointing out this potential bias. However, due to the inclusion criteria, we do not believe that participants will have low scores on the ANU-ADRI-SF. However, if the results suggest this when we analyse data, this will be addressed adequately and listed as a limitation. However, this is out of the scope of this paper.

Secondary outcomes:
Why were the cognitive tests limited to those mentioned, instead of including additional domains? The text can specify why those test & domains were chosen?

- This decision was made due to very limited resources and due to nurses at NHC conducting assessments. The trial is a pragmatic trial and in practice, they do not have capacity to administer the full research batter. In addition, previous research suggested that executive function is the most sensitive cognitive domain to physical activity interventions (Colombe & Kramer, 2003) and a decline in processing speed is associated with cardiovascular risk factors (Anstey, et al, 2014). Therefore, we made a decision to use only these cognitive tests. This information has been added to page 12.
- Colcombe S, Kramer AF. Fitness effects on the cognitive function of older adults: a meta-analytic study. Psychol Sci. 2003;14:125-130.
- Anstey KJ, Sargent-Cox K, Garde E, Cherbuin N, Butterworth P. Cognitive development over 8 years in midlife and its association with cardiovascular risk factors. Neuropsychology. 2014;28:653-665.

Randomization
How is the allocation sequence generated? Computer generated? Please provide more details.
Who assigns the numbers to participants? How?

- Allocation sequence was computer generated. The project manager who is not involved with conducting assessments assigns the participants accordingly. This additional information on randomization has been added to page 14.

Interventions:

Group 1: Brain Body Life – GP

P.13 For which age group was this intervention intended?

- BBL-GP is originally intended for middle aged adults. This information has been added to page 14. However, previous BBL was modified to target all adults to suit the current pragmatic trial. NHC does not restrict their referrals to LMP on the basis of age. Therefore, we had to adopt their practice to allow random allocation and be practical.

P.14 It states, "the revised program was piloted with the general public. What were the results of the pilot? How were participants' experiences? What was the dropout rate? Adherence?

- We received positive responses from participants with high adherence and low dropout rate. A separate paper with detailed information will be prepared for a publication on the pilot study.

P.14 The BBL-GP intervention is multidomain and consists of diet, exercise, cognitive activity, social activity, dementia literacy, risk factors etc., however; only physical activities and diet are described in more detail. Please also describe the other interventional domains.

- We purposely focused on physical activities and diet in detail as we provide extra support with changing exercise level and diet pattern for BBL-GP intervention. A brief explanation on other risk factors can be found in Table 3.

p.15 How was diet measured at follow-up?

- Diet is measured using the same questionnaire used for the baseline assessment. This information is shown in Table 1.

Group 2: Lifestyle Modification Program (LMP).

On p.16 it states "designed to enhance general wellbeing and improve lifestyle to reduce the risk of chronic disease", whereas on p.17 it sates "designed to provide individuals with tools to help manage chronic disease". It is unclear whether the program is intended for dementia prevention, or management of existing chronic disease. Please clarify.

- Thank you for noticing this inconsistency. These sentences have been revised on page 17 to clarify the intention of the LMP. LMP is not specifically designed to prevent dementia.

Data Management and monitoring:

Is there an independent Data Monitoring Committee involved?

- Yes, there is an independent Data Monitoring Committee. Additional information on DMC has been added to page 19.

Ethics and trial registration:

Please describe the process for obtaining informed consent.

- This information is provided under participants (page 9).

Adverse events:

Please comment on the definitions and reporting of Adverse Events and Serious Adverse events.

- A possible situation where an adverse event can occur has been added to page 20.

Discussion:

Please comment on the feasibility of recruitment into the trial.

- Recruitment is highly feasible because NHC has regular mail outs to approximately 13,000 members.

Tables:

Table 1. It might be clearer if 'screening' is a column instead of a row

 We considered changing format of the table 1. However, we were concerned that this might cause a confusion as all the measures/questionnaires are listed in a column instead of a row. We kept the Table 1 as it was.

Table 2: Module 5: How does the program provide info. On the individual's specific chronic health conditions?

 The program does not give information on the individual's specific chronic health condition. Instead, if a participant is classified as an at risk group by having one or more health conditions, they will not only receive general information on how these health conditions can be a risk factor for developing dementia, but will also receive advice on how to monitor and improve their health to reduce their risk.

Table 2: Module 6: Please provide examples of the mentally stimulating activities.

 Examples such as reading, doing crosswords and visiting museums, have been added to Table 3.

VERSION 2 – REVIEW

REVIEWER	Shireen Sindi Karolinska Institute, Sweden
REVIEW RETURNED	29-Dec-2017

GENERAL COMMENTS	Comment responses: • Reviewer: Are participants allowed to participate if they are already participating in other lifestyle intervention studies / trials? Authors: This is a good point. We did not exclude anyone if they are already participating in other intervention studies. However, as this is quite a unique intervention trial, we do not believe there will be too many similarities between our trial and the other trials participants might be participating in, if any. Reviewer: Thanks for the clarification. Please add a statement mentioning that those participating in other trials were not excluded (as this approach is different from most other trials, and it is important for readers to have this information). • Reviewer: P.14 It states, "the revised program was piloted with the general public. What were the results of the pilot? How were participants' experiences? What was the dropout rate? Adherence? Authors: We received positive responses from participants with high adherence and low dropout rate. A separate paper with detailed information will be prepared for a publication on the pilot study. Reviewer: The authors may want to add in brackets ('manuscript in preparation') to highlight that these previous results will be published. Tables: • Table 1. For some assessment measures, the acronym is provided (e.g. ANU-ADRI, MMSE), whereas for others a description

	is given (e.g. “Sleep Quality Assessment” instead of PSQI). Please ensure that these are consistent • Table 2. Row 5, column to the right, please provide a description of “12 emails”; what do the emails contain? • Table 2. Row 6, column to the right, “weekly emails containing health information” is vague. What type of health information? Manuscript: • Please specify the date on which recruitment began, and its duration. • In the literature, Framingham Coronary Heart Disease Risk tends to be written with capitals, please change this throughout the text. • p.12 The acronym IPAQ was never defined • Although the document stated “Figure 1. Study flowchart” on p.36, it was not there (or perhaps it was on a separate document”, but I could not find nor review this. • p.17 What is meant by a ‘fidelity test’? • The manuscript contains both British spelling (e.g. behaviour, randomise) and American spelling (e.g. organized, maximize), please revise the manuscript to ensure that it is consistent throughout. • Similarly, the manuscript most often uses the past tense (as the trial has already started and is ongoing), but it sometimes uses the future tense (p.19), giving the impression that the trial is in its planning phase. Please ensure consistency. • Since the acronym DMC (for Data Monitoring Committee) has already been used, please use it after its first definition, instead of spelling it out again (p.19).

VERSION 2 – AUTHOR RESPONSE

Reviewer 2
Comment responses:

• Reviewer: Are participants allowed to participate if they are already participating in other lifestyle intervention studies / trials?

• Authors: This is a good point. We did not exclude anyone if they are already participating in other intervention studies. However, as this is quite a unique intervention trial, we do not believe there will be too many similarities between our trial and the other trials participants might be participating in, if any.

• Reviewer: Thanks for the clarification. Please add a statement mentioning that those participating in other trials were not excluded (as this approach is different from most other trials, and it is important for readers to have this information).

 Authors: A statement stating that those participating in other trials were not excluded has been added to page 10. Those who have previously participated in LMP were however excluded.

• Reviewer: P.14 It states, "the revised program was piloted with the general public. What were the results of the pilot? How were participants' experiences? What was the dropout rate? Adherence?

• Authors: We received positive responses from participants with high adherence and low dropout rate. A separate paper with detailed information will be prepared for a publication on the pilot study.

• Reviewer: The authors may want to add in brackets ('manuscript in preparation') to highlight that these previous results will be published.

 Authors: 'Manuscript in preparation' was added to page 14.

Tables:

• Table 1. For some assessment measures, the acronym is provided (e.g. ANUADRI, MMSE), whereas for others a description is given (e.g. "Sleep Quality Assessment" instead of PSQI). Please ensure that these are consistent.

-> Table 1 was edited to ensure acronyms were used in a consistent manner.

• Table 2. Row 5, column to the right, please provide a description of "12 emails"; what do the emails contain?

-> Additional information was added to Table 2.

• Table 2. Row 6, column to the right, "weekly emails containing health information" is vague. What type of health information?

-> Additional information was added as an example of health information.

Manuscript:

• Please specify the date on which recruitment began, and its duration.

-> This information was added to page 9.

• In the literature, Framingham Coronary Heart Disease Risk tends to be written with capitals, please change this throughout the text.

-> This change was made throughout the text.

• p.12 The acronym IPAQ was never defined.

-> Full name of IPAQ was added to page 12.

• Although the document stated “Figure 1. Study flowchart” on p.36, it was not there (or perhaps it was on a separate document”, but I could not find nor review this.

-> Figure 1 was submitted as a separate file with the revised manuscript.

• p.17 What is meant by a ‘fidelity test’?

-> We meant a ‘fidelity test’ as a test to see if the intervention was delivered as it was intended. This sentence was reworded.

• The manuscript contains both British spelling (e.g. behaviour, randomise) and American spelling (e.g. organized, maximize), please revise the manuscript to ensure that it is consistent throughout.

-> Some American spellings were changed to British spelling throughout the manuscript.

• Similarly, the manuscript most often uses the past tense (as the trial has already started and is ongoing), but it sometimes uses the future tense (p.19), giving the impression that the trial is in its planning phase. Please ensure consistency.

-> Thank you for pointing this out to us. The manuscript was reviewed once again thoroughly to ensure consistency. Some sentences are however left in the future tense as this has not happened (e.g. data analyses).

• Since the acronym DMC (for Data Monitoring Committee) has already been used, please use it after its first definition, instead of spelling it out again (p.19).

-> This has been changed to DMC on page 19.

VERSION 3 – REVIEW

REVIEWER	Shireen Karolinska Institute
REVIEW RETURNED	07-Feb-2018

GENERAL COMMENTS	I would like to congratulate the authors for a well-written protocol article. I am very much looking forward to reading the results once they are published. A few very minor edits: - The acronym AD should be given in the first line of the introduction, and should be consistently used throughout the manuscript (instead of Alzheimer's disease). - p. 9 "Each participant is officially registered to the study and allocated a unique identity numbers". It is singular "number" - If the authors decide to use the acronym PA for physical activity, it

	should be used consistently throughout the manuscript - If dashes are used in 'face-to-face', this should be consistent throughout the manuscript

VERSION 3 – AUTHOR RESPONSE

A few very minor edits:

- The acronym AD should be given in the first line of the introduction, and should be consistently used throughout the manuscript (instead of Alzheimer's disease).

- p. 9 "Each participant is officially registered to the study and allocated a unique identity numbers". It is singular "number"

- If the authors decide to use the acronym PA for physical activity, it should be used consistently throughout the manuscript

- If dashes are used in 'face-to-face', this should be consistent throughout the manuscript