PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Implementation of a virtual community of practice to promote the empowerment of middle-aged people with multimorbidity: Study protocol of a randomized controlled trial.
AUTHORS	Campillejo, Alba; Gefaell-Larrondo, Ileana; Ramos-García, Vanesa; Koatz, Débora; Santos-Álvarez, Anthea; Barrio-Cortes, Jaime; Gómez-Rueda, Sara; Calderón-Larrañaga, Amaia; Cifuentes, Patricia; Company-Sancho, Consuelo; Domínguez-Coello, Santiago; García-García, Francisco Javier; Garrido-Elustondo, Sofía; González de León, Beatriz; Ramón-Vazquez, José; Martín, Candelaria; Suárez-Fernández, Carmen; Parra-Caballero, Pedro; Vicente-Rabaneda, Esther F.; Quiroga-Colina, Patricia; Ramírez-Puerta, Ana; Ruíz-López, Marta; Tello-Bernabé, María-Eugenia; Sanchez-Gamborino, Estrella; Ugalde-Abiega, Beatriz; Vall-Roqué, Helena; Duarte-Díaz, Andrea; Abt-Sacks, Analía; Hernández-Yumar, Aránzazu; Torres-Castaño, Alezandra; Álvarez-Pérez, Yolanda; Muth, Christiane; van den Akker, Marjan; Montori, Victor; Orrego, Carola; Perestelo-Pérez, Lilisbeth; González-González, Ana Isabel

VERSION 1 – REVIEW

REVIEWER	Howard, Michelle McMaster University, Dept of Family Medicine
REVIEW RETURNED	03-Mar-2024

GENERAL COMMENTS	This is a protocol of an RCT to evaluate the effectiveness of a virtual community of practice for middle-age people living with multimorbidity. This review was done following the SPIRIT checklist to ensure completeness of the protocol description. Overall it is complete and clearly described. I have some minor suggestions for further clarification. Introduction: It would be helpful to mention how this trial will add to the literature on patient self-management and multi-morbidity. Presumably passive online education has not been highly effective, however the more resource intensive community of practice intervention has not been tested to determine the added value. Outcome: It may be of interest to provide a statement of how patient activation has been related in the literature to other outcomes such as improved adherence to recommended care and improved health outcomes. Per SPIRIT checklist 12.2, state how the detectable difference of 4 points was chosen for the sample size calculation.

	Statistical analysis: How will the per-protocol population be determined – will there be a minimum level of engagement with the platforms required to be included in this population? Allocation concealment: After the investigator receives the allocation, how will this be conveyed to the participant? Outcome measurement: how will this be collected? Is all data collection self-administered on the platforms? Consent for publication: I believe this refers to individual participant consent for the publication of any identifiable information in a manuscript, rather than consent for study participation. Best of luck with this important study.

REVIEWER	Kabir, Alamgir University of New South Wales - Kensington Campus
REVIEW RETURNED	16-Mar-2024

GENERAL COMMENTS	The increasing life expectancy worldwide has led to a rising prevalence of multimorbidity among the older population, posing significant challenges to healthcare systems globally. Addressing self-management and prevention of multimorbidity has become imperative to alleviate its burden on healthcare systems and enhance the quality of life for affected individuals. The study protocol proposed by Campillejo-Garcia et al. presents a significant opportunity to contribute to the evidence base regarding the self-management of multimorbidity. The trial aims to assess the efficacy of online self-management programs for chronic diseases, administered either through Virtual Communities of Practice (VCoP) (Intervention) or individually (control). The simplicity and feasibility of the intervention hold promise for reducing the burden on healthcare systems and improving the quality of life for individuals with multimorbidity. Based on the potential impact of the study, I strongly advocate for its publication. The manuscript is well-written; however, I have provided some minor comments for the authors to consider. 1. Secondary Outcomes: While the investigators have appropriately considered secondary outcomes such as depression, anxiety, treatment burden, and health-related quality of life, it would be beneficial to include additional healthcare-related outcomes, such as the number of General Practice (GP) visits, hospital admissions, or Emergency Department (ED) presentations could provide valuable insights. 2. Sample Size Calculation: Given the multicentric nature of the study, it would be prudent for the investigators to clarify whether they accounted for design effects in the sample size calculation. I commend the authors for their dedication to addressing this pertinent research question. I am grateful for the opportunity to review this protocol paper and contribute to advancing knowledge in the field of multimorbidity management. Overall, I recommend the publication of this study, anticipating its potential to significantly impact healthcare practices and improve outcomes for individuals with multimorbidity.

VERSION 1 – AUTHOR RESPONSE

Revisions (R) made according to BMJ Open Editor's comments by queries (Q)

Q1 - Please revise the 'Strengths and limitations of this study' section of your manuscript (after the abstract). This section should contain up to five short bullet points, no longer than one sentence each, that relate specifically to the methods. The novelty, aims, results or expected impact of the study should not be summarized here.
R1 - We appreciate the suggestion and proceeded accordingly as follows:
Strengths and limitations of the study (lines 87 to 95):
"Strengths
• Pragmatic, multicentre design enhances the generalizability of the findings.
• Comprehensive measures, including patient activation, mental health, and quality of life.
• Longitudinal follow-up over 18 months to assess interventions' sustained effects.

Limitations
• Restricted to internet-accessible participants, impacting representativeness.
• Dependent on participants' engagement willingness in online communities."

Q2 - Please confirm the trial registration status. The details of the NCT06046326 entry suggest that your trial was prospectively registered while you selected 'no' for this detail in the meta-data of your submission.
R2 - Thank you for the observation. We have proceeded to update the trial status and correct the error: https://clinicaltrials.gov/study/NCT06046326?id=NCT06046326&rank=1&tab=table
Q3 - Please clarify which outcomes are for the aim of assessing cost-effectiveness?
R3 - Thank you so much for noticing. We have addressed both the outcome variables related to cost-effectiveness and the statistical analysis. We have added the following paragraph in the variables section (lines 309-310):
● "Loss of productivity: Self-administered questionnaire about work absences related to the illness."
In the statistical analysis section, we have also added the following paragraph (lines 352-365):
"We will conduct a cost-effectiveness analysis of the VCoP over 18 months, comparing it to standard care with educational access for middle-aged patients with multimorbidity. This analysis will include both direct healthcare costs and indirect costs like productivity losses. Costs for each patient will be calculated using healthcare resources and the indirect costs will be assessed based on productivity impacts. The study will also include the initial costs of developing and implementing the VCoP, and any costs incurred during the follow-up period.
The primary measure will be the cost per QALY gained. We will derive QALY estimates from the EQ-5D-5L questionnaire completed by patients at the study's start and each follow-up. The results will be presented as the incremental cost-effectiveness ratio (ICER), which compares cost and health outcomes differences between the VCoP and standard care. We will use robust statistical methods to ensure reliable ICER estimates and conduct sensitivity analyses to evaluate the effects of various factors on the results. The analysis will help determine whether the VCoP is a cost-effective option within our health system."
Q4 - The discussion section is optional for protocols and if present, we would like it to focus on discussing the study's strengths and weaknesses. Please consider removing it. Alternatively, please revise appropriately.
R4 – Many thanks for the suggestion. We have removed it.

Revisions (R) made according to BMJ Open Reviewer 1 report by queries (Q)
Q5 - This is a protocol of an RCT to evaluate the effectiveness of a virtual community of practice for middle-aged people living with multimorbidity. This review was done following the SPIRIT checklist to

ensure completeness of the protocol description. Overall, it is complete and clearly described. I have some minor suggestions for further clarification.
R5 – We thank Reviewer 1 for the thorough reading of our protocol and for all the suggestions provided.
Q6 - Introduction: It would be helpful to mention how this trial will add to the literature on patient self-management and multi-morbidity. Presumably passive online education has not been highly effective; however, the more resource intensive community of practice intervention has not been tested to determine the added value.
R6 – We have modified the last paragraph of the introduction (lines 156-157) according to Koatz et al. article about the added value of virtual communities of practice:
“Unlike passive educational strategies, key benefits of VCoPs encompass receiving and providing information, offering social support, boosting patient optimism, improving coping skills, brightening mood, reducing anxiety, and managing stress more effectively (15,16).”
Q7 - Outcome: It may be of interest to provide a statement of how patient activation has been related in the literature to other outcomes such as improved adherence to recommended care and improved health outcomes. Per SPIRIT checklist 12.2, state how the detectable difference of 4 points was chosen for the sample size calculation.
R7 – According to the suggestion, the following paragraph has been added in the primary outcome section (lines 241-243):
“Higher levels of patient activation, as measured by the PAM are linked to greater patient satisfaction, better quality of life, and enhanced physical and mental functional status (18).”
And another paragraph has been added in the sample size section (lines 367-371):
“To detect a mean difference of 4 points (SD = 10) in the PAM between the intervention and control groups, with individual randomization, 100 patients per group are required. This threshold of 4 points (SD = 10) was selected to capture clinically meaningful changes in patient activation (18). For this calculation, an alpha error of 0.05 and a power of 80% are assumed. This size is increased by the estimate of 20% loss, making a total of 240 patients.”
Q8 - Statistical analysis: How will the per-protocol population be determined – will there be a minimum level of engagement with the platforms required to be included in this population?
R9 - We have proposed a per-protocol analysis in addition to an intention-to-treat analysis. The intention-to-treat analysis includes all randomized subjects in their originally assigned groups, regardless of their compliance with all study requirements. For the per-protocol analysis, only participants who have fully complied with the study protocol will be included. We have not yet defined what constitutes full compliance with the protocol. This might be defined as attending all follow-up visits, or at least completing up to visit 12.
Q9 - Allocation concealment: After the investigator receives the allocation, how will this be conveyed to the participant?
R9 - We have proceeded to clarify the paragraph related to allocation concealment accordingly. Randomization and blinding (lines 329-334): "The STATA 17.0 software will generate a random sequence used by an investigator to allocate participants to different platform groups and notify them via email, after they have provided written consent. The allocation of interventions will be blinded to participants, clinicians, and data analysts."
Q10 -Outcome measurement: how will this be collected? Is all data collection self-administered on the platforms?
R10 - We have added an explanation that was missing in the original text. We appreciate the observation.
Description of material and outcome measures (lines 314-316): “All the outcome measures will be collected online from a patient self-reported questionnaire that the research team will elaborate. VCoP use data will be collected through the platform database.”
Q11 -Consent for publication: I believe this refers to individual participant consent for the publication of any identifiable information in a manuscript, rather than consent for study participation.
R11 - You are totally right. We modified the statement as follows:

Consent for publication (line 678): “All authors read, approved the final manuscript and gave their consent for publication”
Q12 - Best of luck with this important study.
R12 – Many thanks for your encouraging message.

Revisions (R) made according to BMJ Open Reviewer 2 report by queries (Q)

Q13 - The increasing life expectancy worldwide has led to a rising prevalence of multimorbidity among the older population, posing significant challenges to healthcare systems globally. Addressing self-management and prevention of multimorbidity has become imperative to alleviate its burden on healthcare systems and enhance the quality of life for affected individuals.
The study protocol proposed by Campillejo-Garcia et al. presents a significant opportunity to contribute to the evidence base regarding the self-management of multimorbidity. The trial aims to assess the efficacy of online self-management programs for chronic diseases, administered either through Virtual Communities of Practice (VCoP) (Intervention) or individually (control). The simplicity and feasibility of the intervention hold promise for reducing the burden on healthcare systems and improving the quality of life for individuals with multimorbidity.
Based on the potential impact of the study, I strongly advocate for its publication. The manuscript is well-written; however, I have provided some minor comments for the authors to consider.
R13 – We truly thank Reviewer 2 for the suggestions that will for sure improve our protocol, and for the positive words provided.
Q14 - Secondary Outcomes: While the investigators have appropriately considered secondary outcomes such as depression, anxiety, treatment burden, and health-related quality of life, it would be beneficial to include additional healthcare-related outcomes, such as the number of General Practice (GP) visits, hospital admissions, or Emergency Department (ED) presentations could provide valuable insights.
R14 – Many thanks for the suggestion. In lines 269-270, we have included:
“● Use of resources: Primary care (PC) visits, visits to the emergency department, visits to specialists, number of hospitalizations, lengths of stay.”
Q15 - Sample Size Calculation: Given the multicentric nature of the study, it would be prudent for the investigators to clarify whether they accounted for design effects in the sample size calculation.
R15 - We did not account for design effects. We assessed that it was not necessary for our specific study design.
Q16 - I commend the authors for their dedication to addressing this pertinent research question. I am grateful for the opportunity to review this protocol paper and contribute to advancing knowledge in the field of multimorbidity management.
Overall, I recommend the publication of this study, anticipating its potential to significantly impact healthcare practices and improve outcomes for individuals with multimorbidity.
R16 – We thank again Reviewer 2 for the motivating words.