PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Implementation of a strategy involving a multidisciplinary mobile unit team to prevent hospital admission in nursing home residents: protocol of a quasi-experimental study (MMU-1 Study)
AUTHORS	Nouvenne, Antonio; Caminiti, Caterina; Diodati, Francesca; Iezzi, Elisa; Prati, Beatrice; Lucertini, Stefano; Schianchi, Paolo; Pascale, Federica; Starcich, Bruno; Manotti, Pietro; Brianti, Ettore; Fabi, Massimo; Ticinesi, Andrea; Meschi, Tiziana

VERSION 1 – REVIEW

REVIEWER	Véronique Provencher Université de Sherbrooke, Canada Research Center on Aging, Canada
REVIEW RETURNED	18-Nov-2019

GENERAL COMMENTS	Thank you for the opportunity to review this clinically-relevant manuscript. However, some issues pertaining to the literature review and the method need clarification. • Introduction / Literature review: - I would recommend the authors to describe the intervention and argue that their intervention is based on best current knowledge (what works). I might be wrong, but I do not see how the post hospital supported discharge (page 5) is related to MMU-1 intervention (if so, please make it explicit). Moreover, the authors mentioned “Although the majority of the studies reported reductions in hospitalizations (in the form of either ED presentations or hospital admissions), only six obtained statistically significant findings, of which none were RCTs”. As the study is not a RCT, the argument does not support the rationale for the study. It would seem more appropriate to detail these 6 studies and describe their strength and limitations. - Please merge 1st and 2nd paragraph. • Design: - The authors mentioned that it is “a prospective, pragmatic, multicenter, 18-month quasi-experimental study (sequential design with two cohorts)”. Please clarify if the study used a cluster-multicenter design. If not, please detail the rationale for the design in terms of internal / external validity. Are there any risks of “contamination” between intervention/ control nursing homes (same staff)? To help support the feasibility of the study, how many residents in each nursing home?

	- "All residents of the participating nursing homes are eligible, regardless of their clinical status. Residents who do not provide informed consent will be excluded". Please clarify that the family member / proxy can provide consent (page 9). - The Ethic section can be shorten (page 12) - I would recommend merging the cost analysis section in the outcome or statistical analysis section.

REVIEWER	Scott Dresden Northwestern University Feinberg School of Medicine, USA
REVIEW RETURNED	26-Nov-2019

GENERAL COMMENTS	General Comments: This is an interesting manuscript on an important topic. It will be important however for the authors to clearly describe how their study is different from previously reported results. Specifically, I am interested in the decision to use a non-randomized parallel cluster trial rather than a randomized trial such as a step wedged design. Given the quasi-experiential design, it is important to understand details of the nursing homes, significant differences between the intervention and control nursing homes would be a major limitation of this study. I have described multiple areas where additional detail or clarification would be helpful, particularly in the methods section. Specifically, more detail regarding data collection would be beneficial. There is no discussion section. A short discussion on the potential impact of this research would be helpful to put this manuscript in context with the existing literature. Specific Issues: Introduction: Page 7 Line 16: The introduction nicely describes the previous literature and summarizes the Santosaputri systematic review. However, it does not make it clear how the described study protocol differs from previous studies. Methods: Page 7 Line 52: Though the hospital initiatives are interesting background, it is not immediately clear how they relate the to study you are proposing. Consider making the connection more explicit, or removing the section regarding other interventions at your hospital. Page 8 Line 16: Spell out (and consider translating) C.R.A. Page 8 Line 14: Additional description of the nursing homes involved would be helpful to clarify the environment in which this study is being performed. Page 8 Line 25: Spell out and consider describing MRC

	Page 8 Line 42: cite the "data from qualitative interviews" or describe the qualitative interview process if these were performed at your institution and have not yet been published. Page 8 Line 52: the section describing the differences between your study and the Schippinger and Diaz-Gegundez studies goes back and forth between describing the differences and justifying those differences. Clarification in the writing would be helpful. Perhaps simplify the language to something like, "based on the Schippinger and Diaz-Gegundez studies, we created a mobile physician service. Unlike those studies we did not use a nurse, because the participating facilities have nursing staff available 24 hours a day, and we used medical hospital staff because …" Page 10 Line 6: how is the "expert hospital physician" chosen? Are there specific clinical situations where one physician is chosen over another? Page 12 Line 22: are there pre-defined adverse events which will be monitored? How will those be determined? Page 12 Line 33: it is unclear if all data are routinely collected at the nursing home and hospital. Are any data being collected from the MMU activation protocol? Page 12 Line 58: Details as to where the cost data will be obtained are lacking. How are staff time and costs being recorded? Details of the DRG system or references to articles using the DRG system will be helpful to understand how costs will be measured. Discussion: There is no discussion section. A short discussion on the potential impact of this research would be helpful to put this manuscript in context with the existing literature.

VERSION 1 – AUTHOR RESPONSE

ANSWERS TO REVIEWER #1

"Thank you for the opportunity to review this clinically-relevant manuscript. However, some issues pertaining to the literature review and the method need clarification."

R: Thank you very much for the positive comment and suggestions on our manuscript. We have revised the manuscript in accordance with your indications, with particular attention on literature review and methodology.

"Introduction / Literature review: I would recommend the authors to describe the intervention and argue that their intervention is based on best current knowledge (what works). I might be wrong, but I do not see how the post hospital supported discharge (page 5) is related to MMU-1 intervention (if so, please make it explicit). Moreover, the authors mentioned "Although the majority of the studies reported reductions in hospitalizations (in the form of either ED presentations or hospital admissions), only six obtained statistically significant findings, of which none were RCTs". As the study is not a RCT, the argument does not support the rationale for the study. It would seem more appropriate to detail these 6 studies and describe their strength and limitations."

R: Thank you for the wise comment. We have updated the introduction to make the background and rationale of our study clearer. The key innovative elements of our proposed intervention have been introduced in this part of the text, highlighting how they differ from previous research (page 5 lines 13-17). We also explained how the intervention was developed, integrating literature evidence, best current knowledge and experience in our institution (page 5 lines 18-24).

Moreover, we have revised the discussion of the existing literature, which was basically set up on the findings of the systematic review by Santosaputri et al (now reference 13). In this review, the authors examined the existing interventions led by hospital-based staff towards nursing home residents, with the aim of reducing Emergency Department visits and hospitalizations. Some of these interventions were actually performed after an hospital admission, in form of post-hospital supported discharge, to prevent further readmissions. So, they are briefly discussed as a possible alternative approach to reach the same goal as the MMU-1 Study intervention. The paragraph has been rephrased to make this connection clearer (page 4 line 24-26).

Finally, in accordance with the suggestion, we also detailed the design, type of intervention, strengths and limitations of the six studies where statistically significant findings were obtained (from page 4 line 27 to page 5 line 8). The circumstance that none of them was a RCT is not mentioned in this new version, because, as rightly pointed out, this is not an argument supporting the MMU-1 Study, which is not a RCT.

“Please merge 1st and 2nd paragraph.”

R: The first and second paragraphs have been merged and shortened, to keep the introduction length acceptable (page 4 lines 2-8).

“Design: The authors mentioned that it is “a prospective, pragmatic, multicenter, 18-month quasi-experimental study (sequential design with two cohorts)”. Please clarify if the study used a cluster-multicenter design. If not, please detail the rationale for the design in terms of internal / external validity.”

R: Thank you for the important comment. We have now specified, in the Study Design paragraph (from page 9 line 17 to page 10 line 2), that the study uses a multicenter/cluster design and detailed the reason for this choice. We have also justified the choice of the quasi-experimental over the randomized design and indicated the reasons for not using a stepped-wedge design. For the latter, in fact, we estimated that approximately 2000 residents would be necessary.

“Are there any risks of “contamination” between intervention/ control nursing homes (same staff)?”

R: The nursing homes participating in the study share no staff member. So, the risk of “contamination” is limited (page 6 line 11-12).

“To help support the feasibility of the study, how many residents in each nursing home?”

R: Each participating nursing home has between 90 and 100 residents; this information has been added (page 6 line 9 and page 12 line 4-5). Therefore, the study appears to be feasible.

““All residents of the participating nursing homes are eligible, regardless of their clinical status. Residents who do not provide informed consent will be excluded”. Please clarify that the family member / proxy can provide consent (page 9).”

R: The informed consent will be collected from patients or, for those unable to plead, from their proxies/legal representatives, in conformity with the current European Union law. The sentence has been rephrased in the new version of the manuscript (page 10 line 5-7).

“The Ethic section can be shorten (page 12)”

R: Thank you for the suggestion. The section has been completely revised, to retain the essential information (see page 13 line 6-15).

“I would recommend merging the cost analysis section in the outcome or statistical analysis section.”

R: The section on cost analysis has been merged with the statistical analysis section, in accordance with your suggestion (from page 12 line 18 to page 13 line 2). We have also introduced more details on the sources of data used for cost analysis, as suggested by another reviewer.

ANSWERS TO REVIEWER #2

“This is an interesting manuscript on an important topic. It will be important however for the authors to clearly describe how their study is different from previously reported results.”

R: Thank you for the positive comment on our manuscript. We acknowledge that, in the previous version, the introduction section did not fully explain how the proposed model of intervention differs from that described in previous studies. To help readers put our proposed intervention in the framework of previous research, we completely revised the introduction section, describing in more detail the existing studies that gave statistically significant results (page 4 and 5) and better outlining the key innovative elements of our study (page 5 lines 9-17).

“Specifically, I am interested in the decision to use a non-randomized parallel cluster trial rather than a randomized trial such as a step wedged design.”

R: We are grateful for this comment, a point also raised by Reviewer 1. We have now specified, in the Study Design paragraph, that the study uses a multicenter/cluster design and detailed the reason for this choice (please see page 9 from line 17 onwards). We have also justified the choice of the quasi-experimental over the randomized design and indicated the reasons for not using a stepped-wedge design. For the latter, in fact, we estimated that approximately 2000 residents would be necessary.

“Given the quasi-experiential design, it is important to understand details of the nursing homes, significant differences between the intervention and control nursing homes would be a major limitation of this study.”

R: As described in the Study Setting paragraph, participating nursing homes have similar sizes and standards of care, and the role of distance to the hospital was considered. We have now added in the text the approximate number of residents, the same for all facilities (page 6 line 9-13).

“I have described multiple areas where additional detail or clarification would be helpful, particularly in the methods section. Specifically, more detail regarding data collection would be beneficial.”

R: Thank you for the comment. We have addressed all the specific comments, as detailed below. We have enriched the paragraph on data collection with more information on data sources used for each study outcome (page 22 lines 6-22).

“There is no discussion section. A short discussion on the potential impact of this research would be helpful to put this manuscript in context with the existing literature.”

R: Thank you for the suggestion. We have included a discussion section, where strengths and limitations of the study are critically discussed in the light of the existing literature (from page 13 line 17 to page 14 line 15).

"Introduction: Page 7 Line 16: The introduction nicely describes the previous literature and summarizes the Santosaputri systematic review. However, it does not make it clear how the described study protocol differs from previous studies."

R: Thank you for the comment. The introduction has been completely revised, to include more details on previous literature and better explain how the care model proposed in this study differs from previous experiences (page 5 line 9-17).

"Methods: Page 7 Line 52: Though the hospital initiatives are interesting background, it is not immediately clear how they relate the to study you are proposing. Consider making the connection more explicit, or removing the section regarding other interventions at your hospital."

R: The hospital initiatives mentioned in the text are the clinical and cultural background that allowed the MMU project to be developed and implemented. All these initiatives involved the Internal Medicine and Critical Subacute Care unit, which is the hospital unit where the MMU team is based. This is the relationship with the study protocol proposed in the manuscript. This part of the text has been revised to improve comprehension of the relationship between these initiatives and the MMU study (page 6 line 3-8).

"Page 8 Line 16: Spell out (and consider translating) C.R.A."

R: CRA is the acronym for "Casa Residenza Anziani", the official name given to nursing homes by the Emilia-Romagna Region Health Authority. The text has been revised accordingly (page 6 line 14).

"Page 8 Line 14: Additional description of the nursing homes involved would be helpful to clarify the environment in which this study is being performed."

R: Thank you for the comment. Please see the response above and page 6 line 9-13.

"Page 8 Line 25: Spell out and consider describing MRC"

R: MRC has been spelled out in the new version of the manuscript (page 6 line 19).

"Page 8 Line 42: cite the "data from qualitative interviews" or describe the qualitative interview process if these were performed at your institution and have not yet been published."

R: Thank you for the comment. Our considerations were mainly based on previously published literature (see references 24 and 25 of the novel version of the manuscript and the discussion of the Santosaputri review, reference 13). In these papers, the authors conclude that the decision to transfer nursing home residents to Emergency Departments depends critically on the staffing and skill mix in the nursing home care team, availability of diagnostic resources and communication with the patient proxies. These elements are critical also in our experience with the Italian Health Care System, and were considered as critical also by the nursing homes staff contacted, though in an unstructured way, during the feasibility phase. The paragraph has been rephrased to improve comprehension (from page 6 line 28 to page 7 line 4).

"Page 8 Line 52: the section describing the differences between your study and the Schippinger and Diaz-Gegundez studies goes back and forth between describing the differences and justifying those differences. Clarification in the writing would be helpful. Perhaps simplify the language to something like, "based on the Schippinger and Diaz-Gegundez studies, we created a mobile physician service. Unlike those studies we did not use

a nurse, because the participating facilities have nursing staff available 24 hours a day, and we used medical hospital staff because …""

R: Thank you for the useful suggestion. The paragraph has been completely re-written in accordance with your comment (page 7 line 5-8).

"Page 10 Line 6: how is the "expert hospital physician" chosen? Are there specific clinical situations where one physician is chosen over another?"

R: As detailed in the text (page 8 line 7-11), when the MMU team is activated by phone, the flow manager triages the clinical problem and, if the MMU visit is deemed necessary, activates the team by choosing the available physician with the clinical skill more appropriate to the specific clinical problem. For example, in case of abdominal pain and constipation, a gastroenterologist is activated. In case of dyspnea, an internist with certification in chest ultrasound is activated.

"Page 12 Line 33: it is unclear if all data are routinely collected at the nursing home and hospital. Are any data being collected from the MMU activation protocol?"

R: Please see the response above. We have now included more details on data collection and sources (page 11 lines 7-22).

"Page 12 Line 22: are there pre-defined adverse events which will be monitored? How will those be determined?"

R: Since the range of situations requiring MMU activation cannot be pre-determined (Table 1 provides only an example of the alleged most common situations), possible adverse events following MMU activation cannot be pre-defined as well. Thus, we define as "adverse event" any unexpected clinical worsening of the patient requiring urgent or emergent hospital admission that occurs in the first 48 hours following MMU visit. The text has been revised accordingly (page 11 line 1-3).

"Page 12 Line 58: Details as to where the cost data will be obtained are lacking. How are staff time and costs being recorded? Details of the DRG system or references to articles using the DRG system will be helpful to understand how costs will be measured."

R: We have added more details both in the Data Collection and Statistical Analysis sections (please see page 11 lines 6-22 and from page 12 line 18 to page 13 line 2).

"There is no discussion section. A short discussion on the potential impact of this research would be helpful to put this manuscript in context with the existing literature."

R: Please see the response above and from page 13 line 17 to page 14 line 15.

VERSION 2 – REVIEW

REVIEWER	Véronique Provencher Université de Sherbrooke Research Center on Aging Québec, Canada
REVIEW RETURNED	07-Jan-2020

GENERAL COMMENTS	We thank the authors for the revisions made, which improve the manuscript. Minor comments:

	- Page 4: I would revise the last point (limitation) by adding "individual" randomization and by underlying the strength of your design. - Page 6: I would recommend adding a reference to support lines 12-16. - To support the relevance of keeping the "Post-hospital supported discharge interventions" in the literature review, I would recommend adding a sentence in the rationale (at the end of the first paragraph on page 5) about the adverse effects of transitions for nursing home patients (your intervention aims to bring ED to nursing home, and thus avoids hospital discharge and its potential adverse effects). - If the two nursing homes received the pilot intervention, please clarify why the design is "sequential", while not a step-wedge (a figure might be useful). Please also add on page 10 (line 1) that the pilot intervention was conducted in the two nursing homes. - Please add in parenthesis "current study" beside "evaluation phase" (page 10), so that we understand that the development and the pilot are "past studies". - Please mention all your outcomes in your objectives (page 10): "crude all-cause mortality, hospital mortality, length of stay and healthcare-related costs". - Page 10: please mention the options instead of only referring to "d) and e)" - I would recommend adding the rationale for not using the step-wedge design only in the study limitations. Minor edits: - Page 5: I would remove "designed" (or developed) for more clarity.

REVIEWER	Scott M Dresden Northwestern University Feinberg School of Medicine USA
REVIEW RETURNED	17-Jan-2020

GENERAL COMMENTS	The authors have done a good job of satisfying my initial concerns. Particularly in describing why the study design was chosen. I have provided specific comments below: Introduction: Though I asked for more information in my previous review, now the introduction has become very long. Consider moving editing to make the introduction more concise. Methods: The methods are very clear and detailed. They do a good job of explaining this complex intervention Page 7 line 7: MMU should be spelled out Page 8 line 5: why were the Schippinger and Diaz-Gegundez studies chosen to emulate? A brief statement stating that they were previously effective would likely suffice to prevent the reader from having to look up both studies. Page 12 line 1: how are "unexpected worsening of clinical conditions" going to be defined? Page 12: line 25: has initiation started in November 2019 as expected?

	Discussion: The addition of a discussion section helps to put the study into context with prior literature Page 14 line 12: consider directly addressing how this study will be better than the Schippinger and Diaz-Gegundez studies which you have referenced in the methods section

VERSION 2 – AUTHOR RESPONSE

ANSWERS TO REVIEWER #1
"Page 4: I would revise the last point (limitation) by adding "individual" randomization and by underlying the strength of your design."
R: Thank you for the suggestion. We have added a fifth bullet point underlying the strength of our study design, especially in terms of transferability of results into clinical practice. We have also added "individual" to "randomization" in the fourth bullet point, as recommended.

"Page 6: I would recommend adding a reference to support lines 12-16."
R: Appropriate references have been added in the updated version of the manuscript (number 7 and 20).

"To support the relevance of keeping the "Post-hospital supported discharge interventions" in the literature review, I would recommend adding a sentence in the rationale (at the end of the first paragraph on page 5) about the adverse effects of transitions for nursing home patients (your intervention aims to bring ED to nursing home, and thus avoids hospital discharge and its potential adverse effects)."
R: Thank you for the suggestion. We added a sentence at the end of the first paragraph of the Introduction, to highlight the possible adverse events related to care transition between hospital and nursing home (page 4 lines 8-9).

"If the two nursing homes received the pilot intervention, please clarify why the design is "sequential", while not a step-wedge (a figure might be useful). Please also add on page 10 (line 1) that the pilot intervention was conducted in the two nursing homes."
R: The study design has been defined as "sequential" because all subjects staying in the participating nursing homes at the moment of study initiation will be eligible for inclusion, irrespective of the date of admission. Moreover, all patients newly admitted to the same nursing homes during the period of the study until its conclusion will be eligible for inclusion too. Thus, the design has some elements of longitudinal designs and some elements of cross-sectional designs, and the definition of "sequential" seems appropriate. These aspects have been made explicit by rephrasing the first sentence of the "Study population" paragraph (page 10 lines 1-2). We have also made explicit that the pilot intervention was conducted in the two nursing homes participating to the study as intervention arm (page 8 lines 28-29).

"Please add in parenthesis "current study" beside "evaluation phase" (page 10), so that we understand that the development and the pilot are "past studies"."
R: Done (page 9 lines 9).

"Please mention all your outcomes in your objectives (page 10): "crude all-cause mortality, hospital mortality, length of stay and healthcare-related costs"."
R: Thank you for the suggestion. The sentence has been rephrased accordingly (page 9 lines 13-15).

"Page 10: please mention the options instead of only referring to "d) and e)""

R: The text was modified following the suggestion (page 10 line 18).

“I would recommend adding the rationale for not using the step-wedge design only in the study limitations.”
R: We have merged the sentence previously added to the “Study design” paragraph with the study limitation paragraph in the discussion (page 14 lines 7-12).

“Page 5: I would remove “designed” (or developed) for more clarity.”
R: Thank you for the advice. The term “designed” was removed (page 4 line 11).

ANSWERS TO REVIEWER #2
“Introduction: Though I asked for more information in my previous review, now the introduction has become very long. Consider moving editing to make the introduction more concise.”
R: We are aware that the introduction is long and we have further revised it in the novel version of the manuscript, eliminating unnecessary words and rephrasing some sentences in a more concise way. Unfortunately, the rationale of the study is very complex and we think it is necessary to bring it entirely to the audience to make them fully understand the study.

“Methods: The methods are very clear and detailed. They do a good job of explaining this complex intervention”
R: Thank you for the positive comment.

“Page 7 line 7: MMU should be spelled out.”
R: MMU means “Multidisciplinary Mobile Unit”. The acronym is now spelled out in the text (page 6 line 5).

“Page 8 line 5: why were the Schippinger and Diaz-Gegundez studies chosen to emulate? A brief statement stating that they were previously effective would likely suffice to prevent the reader from having to look up both studies.”
R: The two studies by Diaz-Gegundez and Schippinger were chosen because they were effective in reducing hospital admissions of nursing home residents. The text has been modified accordingly (see page 7 line 3-4).

“Page 12 line 1: how are “unexpected worsening of clinical conditions” going to be defined?”
R: It is defined as sudden alteration of vital signs (page 10 line 26).

“Page 12: line 25: has initiation started in November 2019 as expected?”
R: The study has been initiated in January 2020, as reported in the ClinicalTrials.gov page (NCT 04085679). The text has been modified accordingly (page 11 lines 20-21).

“Discussion: The addition of a discussion section helps to put the study into context with prior literature. Page 14 line 12: consider directly addressing how this study will be better than the Schippinger and Diaz-Gegundez studies which you have referenced in the methods section”
R: A sentence has been added to the discussion section explaining why the present study has the potential of being better than the previous ones by Schippinger and Diaz-Gegundez (page 14 lines 4-6).