

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Protocol for a mixed-methods study to optimise medication management for polymedicated home-dwelling older adults with multiple chronic conditions
AUTHORS	Pereira, Filipa; Roux, Pauline; Delefosse, Marie Santiago; Von-Gunten, Armin; Wernli, Boris; Martins, Maria Manuela; Verloo, Henk

VERSION 1 – REVIEW

REVIEWER	Pedro Simões University of Beira Interior, Covilhã, Portugal
REVIEW RETURNED	07-Apr-2019

GENERAL COMMENTS	<p>This is an important topic area because it is a serious problem and difficult to manage. There is a lack of information about the views of the older adults and their caregivers regarding the polymedication and what strategies they use to manage it. Therefore, it is good to see that you will use a mixed methods study.</p> <p>Below I leave some comments:</p> <p>Page 6 line 6: Is there more than one definition for "multiple chronic conditions"? What are the most used? Which coding lists are usually used?</p> <p>Page 11 line 27: What is the multiple chronic conditions definition you are going to use?</p> <p>Page 12 line 19: It is feasible interviews lasting an hour? Will older adults accept that? Aren't you worried that they can get tired and don't finish it? Who is collecting data? The researchers or a third party? How many interviewers will be present? Will be same interviewer for both interviews? Will you question the older adults if their opinion and preferences were taken into account in the treatment instituted? Will you question how he sees his medication (whether it is deemed necessary or whether it is excessive or even harmful)? These data may be important for the second interview because these may be the reasons for not adhering to treatment and using over-the-counter medications.</p> <p>The OAMCC will be interviewed alone - don't you think in some cases it would be important to have a caregiver present? To help</p>
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	<p>with communication? How will you deal with impaired cognitive status and hearing? What will you do if some older adults say to ask that information to the caregiver (namely when the caregiver is the spouse)?</p> <p>Page 13 line 38: When will the interview occur? During professional caregivers working time? What is the acceptance rate for this interview that you are expecting?</p>
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REVIEWER	Sam Kosari University of Canberra, Australia
REVIEW RETURNED	21-Apr-2019

GENERAL COMMENTS	<p>Thanks for the opportunity to review this manuscript. This is a study protocol for a mixed methods study to explore patient's medication records to identify the factors linked with hospitalization and other adverse outcomes, and to understand the medication management practices by polymedicated older adult individuals. This is an important area of research, since the pattern and trends of polypharmacy are changing due to advancement of our health care system and the advanced ageing of the population globally, thus, a greater attention to improve the medication management for the consumers is required.</p> <p>Major comments:</p> <p>Line 95-97, one of the aims is listed as making proposals for improving clinical and medication evidence-based pathways through an innovative and integrated model..... This seems to be the most important outcome of the study, however, there is no further information about this in 'methods'. Some further information about the 'proposed model' such as its components, metrics and etc will be critical.</p> <p>Abstract: the above also applies to the abstract</p> <p>Lines 165,6: in line with the previous comment, it is very helpful to provide more clarity and detail about the methods, how will this be achieved?</p> <p>The authors have explained different phases of the study reasonably well and in detail, however, there is a need for an additional information perhaps at the end of the methods, better explaining the connection and relevance of the 3 phases of the study (mainly phase 1 with 2 &3) and how they can contribute to proposals to improve the medication management system.</p> <p>Minor comments:</p> <p>Abstract, line 17: to introduce MRP</p> <p>Limitation listed are fairly generic and quite broad, it is recommended to more directly/specifically list the limitations. It is also worthwhile to comment on the extent of availability of RAI data if it is known, and the quality of data found in hospital charts. In the first phase of the study, authors planned to identify "Environmental-related factors" retrospectively from the hospital charts. The manuscript will be benefited from providing more clarity about these factors, what they are and to what extent they can be found from the hospital charts.</p>
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	<p>The manuscript will also benefit from information about sample size calculation and its relevance to the current national population of interest</p> <p>Line 179, authors have well introduced the RAI data, however, the relevance of this to qualitative interviews is unknown.</p> <p>To my knowledge the date of commencing the study is required by the journal</p> <p>It will be worthwhile to briefly explain the statistical methods that will be used in phase 1 to link different factors with hospitalizations and other adverse outcomes</p>
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REVIEWER	Wei Gao King's College London, UK
REVIEW RETURNED	17-Jul-2019

GENERAL COMMENTS	<p>This study combines the quantitative analysis of existing database and qualitative interviews to build evidence for a population that has highly complex care needs. It should offer scientific value to the field but clarity on some key aspects is required to assess if the study objectives can be achieved.</p> <ul style="list-style-type: none"> • Retrospective analysis of patients' hospital records: the authors need to describe more clearly the databases they are going to use. • It appeared that the research population will be "All home-dwelling OAMCC with somatic and/or mental health disorders who were hospitalised, rehospitalised or who consulted the emergency department at the partner hospital between 2015 and 2018 (estimated N= 50,000) will be included." If you only include all hospitalised patients, how can you identify what are at risk? Similarly, do you have a natural cohort of patients who are at-risk of emergency department visits? How do you define institutionalisation or early death? • There should be a theoretical framework to guide the retrospective analysis of patients' hospital records. • It needs to be clearer about the study outcomes. While in the Aim & objectives it stated several outcomes, in the methods/Data Analyses only two outcomes were mentioned.
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VERSION 1 – AUTHOR RESPONSE

Reviewers' 1 comments

Reviewer Name: Pedro Simões

Institution and Country: University of Beira Interior, Covilhã, Portugal

Reviewers' 1 comments	Response by authors	Location in text
This is an important topic area because it is a serious problem and difficult to manage. There is a lack of information about the views of the older adults and their caregivers regarding the poly medication and	We thank the reviewer for his support.	

<p>what strategies they use to manage it. Therefore, it is good to see that you will use a mixed methods study.</p>		
<p>Page 6 line 6:</p> <p>Is there more than one definition for "multiple chronic conditions"? What are the most used?</p> <p>Which coding lists are usually used?</p>	<p>We added a definition for "multiple chronic conditions", as per the World Health Organization (WHO, 2002).</p>	<p>Introduction</p> <p>Lines 55 to 59</p>
<p>Page 11 line 27:</p> <p>What is the multiple chronic conditions definition you are going to use?</p>	<p>Thank you for this relevant question. We added a reference to "Table 1. Phase 2 inclusion and exclusion criteria" to clarify our definition of multiple chronic conditions (WHO, 2002).</p>	<p>Line 247</p> <p>Table 1. Inclusion and exclusion criteria of phase 2</p>
<p>Page 12 line 19:</p> <p>It is feasible interviews lasting an hour? Will older adults accept that? Aren't you worried that they can get tired and don't finish it?</p>	<p>Thank you for this relevant question. According to our feasibility study, the interview duration was well accepted by our stakeholders, as was the time needed to collect relevant data. However, it could be necessary to break down the interview in two periods. We have completed the manuscript with the following sentence: "According to participants' levels of tiredness, it may be necessary to subdivide the interviews."</p> <p>Roux P, Pereira F, Santiago-Delefosse M, et al. Medication practices and experiences of older adults discharged home from hospital: a feasibility study protocol. <i>Patient Preference and Adherence</i> 2018;Volume 12:1055-63. doi: 10.2147/PPA.S160990</p>	
<p>Who is collecting data? The researchers or a third party? How many interviewers will be present? Will be same interviewer for both interviews?</p>	<p>To answer these questions, we replaced "the researcher" by "the principal investigator" who will be directly involved in data collection.</p>	<p>Participant recruitment and Data collection sections</p>
<p>Will you question the older adults if their opinion and preferences were taken into account in the treatment instituted?</p> <p>Will you question how he sees his medication (whether it is deemed necessary or whether it is excessive</p>	<p>Indeed, we intend to question participants on these points. Thus, we have completed the text as follows:</p> <p>"The first semi-structured interview will collect the perspectives of OAMCC with regards to their medication management (...) whether their opinions and</p>	<p>Lines 282-286</p>

<p>or even harmful)? These data may be important for the second interview because these may be the reasons for not adhering to treatment and using over-the-counter medications.</p>	<p>preferences were taken into account in the prescription of medications, and the informal and professional caregivers involved. (...)</p> <p>Participants will be asked to note their perceptions of and satisfaction with their treatment in a week-long medication journal."</p>	<p>Lines 293-294</p>
<p>The OAMCC will be interviewed alone - don't you think in some cases it would be important to have a caregiver present? To help with communication? How will you deal with impaired cognitive status and hearing? What will you do if some older adults say to ask that information to the caregiver (namely when the caregiver is the spouse)?</p>	<p>We agree that some OAMCC may not be able to participate in the first two interviews autonomously. Moreover, this was one of the findings of the feasibility study. For this reason, we have added the following statement:</p> <p>"OAMCCs will be interviewed alone or with an informal caregiver, if necessary."</p>	<p>Line 286</p>
<p>Page 13 line 38:</p> <p>When will the interview occur? During professional caregivers working time? What is the acceptance rate for this interview that you are expecting?</p>	<p>We completed the text as follows:</p> <p>"In agreement with the project's field partners and stakeholders, these interviews will take place in professionals' workplaces (Community Healthcare Centre, medical practice office or pharmacy), during working hours, (...)".</p>	<p>Line 320-323</p>

Reviewers' 2 comments

Reviewer Name: Sam Kosari

Institution and Country: University of Canberra, Australia

Reviewers' 2 comments	Response by authors	Location in text
<p>Thanks for the opportunity to review this manuscript. This is a study protocol for a mixed methods study to explore patient's medication records to identify the factors linked with hospitalization and other adverse outcomes, and to understand the medication management practices by polymedicated older adult individuals.</p> <p>This is an important area of research, since the pattern and trends of polypharmacy are changing due to the advancement of our health care system and the advanced ageing of the population globally, thus, a greater</p>	<p>We thank the reviewer for his support.</p>	

<p>attention to improve the medication management for the consumers is required.</p>		
<p>Major comments:</p> <p>Line 95-97, one of the aims is listed as making proposals for improving clinical and medication evidence-based pathways through an innovative and integrated model... This seems to be the most important outcome of the study, however, there is no further information about this in 'methods'. Some further information about the 'proposed model' such as its components, metrics and etc. will be critical.</p>	<p>We added an extra section to explain our intention to develop a Medication Management Model (phase 3 of the project):</p> <p>"Phase 3, Development of a Medication Management Model</p> <p>Connecting retrospective and prospective findings, - using an explanatory sequential design and participants' different perspectives, - will contribute to a deep understanding of the current state of medication management practices of polymedicated, home-dwelling OAMCC. This mixed-methods study corresponds to the "diagnostic" phase of the process of developing a Model of Care, as presented by the Agency for Clinical Innovation (ACI).⁴³ It will guide the "solution design" phase—the next step in the creation of an innovative, integrated model for supporting medication management and preventing adverse health outcomes.</p> <p>In addition to the ACI's framework, the development of a proposed Medication Management Model will consider the quadruple aim of enhancing the patient's experience, improving population health, reducing costs and improving the working lives of health care providers.⁴⁴</p> <p>Finally, our mixed-methods' research findings will be completed with those of an ongoing systematic review of Medication Management Models.⁴⁵"</p>	<p>Methods section</p> <p>Lines 343-355</p>
<p>Abstract: the above also applies to the abstract</p>	<p>We completed the abstract with an additional sentence:</p> <p><i>"Finally, the mixed-methods findings will enable the development of an innovative, integrated model of medication management based on the Agency for Clinical Innovation framework and Bodenheimer & Sinsky's quadruple aim."</i></p>	<p>Abstract</p>

<p>Lines 165,6: in line with the previous comment, it is very helpful to provide more clarity and detail about the methods, how will this be achieved?</p>	<p>We completed the "data analysis" of the retrospective investigation, specifying that our approach will use multivariate logistic regressions and multi-cluster analysis.</p>	<p>Lines 191-199</p>
<p>The authors have explained different phases of the study reasonably well and in detail, however, there is a need for an additional information perhaps at the end of the methods, better explaining the connection and relevance of the 3 phases of the study (mainly phase 1 with 2 &3) and how they can contribute to proposals to improve the medication management system.</p>	<p>The connection between phases 1 and 2 was improved in the "Study design" section (lines 138-141) and a new section was added and supported by new references to clarify how these two phases contribute to the main aim of the study (lines 343-355).</p>	<p>Lines 138-141 and 343-355.</p>
<p>Minor comments: Abstract, line 17: to introduce MRP</p>	<p>We introduced MRP at line 7 as suggested.</p>	<p>Line 7</p>
<p>Limitation listed are fairly generic and quite broad, it is recommended to more directly/specifically list the limitations. It is also worthwhile to comment on the extent of availability of RAI data if it is known, and the quality of data found in hospital charts.</p>	<p>We replaced one bullet point as follows: "Although patients' electronic hospital records and the RAI-HC data provide a broad range of patient-, medication- and environment-related information, they rarely highlight factors that may influence the occurrence of MRPs."</p>	<p>Lines 48-50</p>
<p>In the first phase of the study, authors planned to identify "Environmental-related factors" retrospectively from the hospital charts. The manuscript will be benefited from providing more clarity about these factors, what they are and to what extent they can be found from the hospital charts.</p>	<p>We thank the reviewer for this relevant comment. We completed "Data Collection" (Lines 153-173) and distinguished between patient-, medication- and environment-related factors (whole article).</p>	<p>Lines 166-175</p>
<p>The manuscript will also benefit from information about sample size calculation and its relevance to the current national population of interest</p>	<p>For the retrospective phase: "All home-dwelling OAMCC with somatic and/or mental health disorders who were hospitalised, rehospitalised or who consulted the emergency department (for MRPs or other reasons) at the partner hospital between 2015 and 2018 (estimated N = 50,000) will be included. The estimated sample of 50,000 older adults' electronic inpatient charts are part of the 40,000 yearly adult inpatients in acute care units and more than 40,000 adult emergency department</p>	<p>Lines 157-164</p>

	<p>consultations yearly at the partner hospital. To explore generalizability, we will compare the sociodemographic and health status characteristics with those of the national sample of the hospitalised older adults in Swiss hospitals for the same period."</p> <p>For the prospective phase: " Based on Guest et al., the principal investigator will recruit about 30 polymedicated OAMCC (until saturation of data), all recently hospitalised (within the last 90 days) and at risk of hospital readmission.^{32"}</p>	<p>Lines 231-233</p>
<p>Line 179, authors have well introduced the RAI data, however, the relevance of this to qualitative interviews is unknown.</p>	<p>We have clarified the usefulness of the RAI-HC Minimal Data Set (MDS) instrument in the qualitative phase as follows:</p> <p>"This instrument will provide information on the patient-, medication- and environment-related factors which may influence the occurrence of MRPs."</p> <p>"The MDS will aid interviews with OAMCC and the exploration of the facilitators and barriers to daily medication management."</p>	<p>Lines 220-223</p> <p>Lines 280-281</p>
<p>To my knowledge the date of commencing the study is required by the journal.</p>	<p>We added the beginning and end dates: " Two major phases will be conducted sequentially from February 2019 to January 2022"</p>	<p>Lines 128-129</p>
<p>It will be worthwhile to briefly explain the statistical methods that will be used in phase 1 to link different factors with hospitalizations and other adverse outcomes.</p>	<p>We completed the "data analysis" of the retrospective investigation, specifying that our approach will use multivariate logistic regressions analysis and multi-cluster analysis. Supplementary file 1 explains the statistical methods.</p>	<p>Lines 191-199</p>

Reviewers' 3 comments

Reviewer Name: Wei Gao

Institution and Country: King's College London, UK

Reviewers' 3 comments	Response by authors	Location in text
<p>This study combines the quantitative analysis of existing database and qualitative interviews to build evidence for a population that has highly complex care needs. It should offer scientific value to the field but clarity on some key aspects is required to assess if the study objectives can be achieved.</p>	<p>We thank the reviewer for his support.</p>	
<p>Retrospective analysis of patients' hospital records: the authors need to describe more clearly the databases they are going to use.</p>	<p>We have described more clearly the databases that will be used for retrospective analysis. Supplementary file 1 explains our retrospective analysis strategies.</p>	<p>Lines 166-175</p>
<p>It appeared that the research population will be "All home-dwelling OAMCC with somatic and/or mental health disorders who were hospitalised, rehospitalised or who consulted the emergency department at the partner hospital between 2015 and 2018 (estimated N= 50,000) will be included." If you only include all hospitalised patients, how can you identify what are at risk? Similarly, do you have a natural cohort of patients who are at-risk of emergency department visits?</p>	<p>We have adjusted the research population section as follows:</p> <p>"All home-dwelling OAMCC with somatic and/or mental health disorders who were hospitalised, rehospitalised or who consulted the emergency department (<u>for MRPs or other reasons</u>) (...)". Actually, we intend to distinguish between all home-dwelling OAMCC: those who were hospitalised, rehospitalised or consulted the emergency department for MRPs. The ED database contains the variable: "reason for ED consultation/admission" and allows us to make a connection with an MRP short list (see Supplementary file 1 for the list of variables in the ED database). Unfortunately, we do not have a follow-up cohort of older adults visiting the ED in the region.</p>	<p>Lines 158-159</p>
<p>How do you define institutionalisation or early death?</p>	<p>We have completed the text as follows:</p>	<p>Lines 147-148</p>

	" (...) institutionalisation in nursing homes, or early death (before the average age of death described by the Organisation for Economic Co-operation and Development in 2018). ²⁴ "	
There should be a theoretical framework to guide the retrospective analysis of patients' hospital records	The theoretical framework for this data analysis has indeed been developed. Please find the strategy in supplementary file 1.	Supplementary file 1
It needs to be clearer about the study outcomes. While in the Aim & objectives it stated several outcomes, in the methods/Data Analyses only two outcomes were mentioned.	In addition to the changes made in the "Methods" section to address previous comments, we have added Table 2 to summarise the outcomes for each study phase.	Line 358
<p>FORMATTING AMENDMENTS (if any)</p> <p>Required amendments will be listed here; please include these changes in your revised version:</p> <p>- Patient and Public Involvement:</p> <p>Authors must include a statement in the methods section of the manuscript under the sub-heading 'Patient and Public Involvement'.</p> <p>This should provide a brief response to the following questions:</p> <p>How was the development of the research question and outcome measures informed by patients' priorities, experience, and preferences?</p> <p>How did you involve patients in the design of this study?</p> <p>Were patients involved in the recruitment to and conduct of the study?</p> <p>How will the results be disseminated to study participants?</p>	We have completed the manuscript with a "Patient and Public Involvement" section.	Lines 360-374

<p>For randomised controlled trials, was the burden of the intervention assessed by patients themselves?</p> <p>Patient advisers should also be thanked in the contributorship statement/acknowledgements.</p> <p>If patients and or public were not involved please state this.</p>		
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VERSION 2 – REVIEW

REVIEWER	Sam Kosari University of Canberra
REVIEW RETURNED	03-Sep-2019
GENERAL COMMENTS	Authors have sufficiently addressed the comments of the reviewers