PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Quality improvement interventions to prevent the use of hospital services among nursing home residents: protocol for a systematic review and meta-analysis
AUTHORS	Basso, Ines; Gonella, Silvia; Bassi, Erika; Caristia, Silvia; Campagna, Sara; Dal Molin, Alberto

VERSION 1 – REVIEW

REVIEWER	Guion , Vincent Centre Hospitalier Universitaire de Toulouse Gerontopole
REVIEW RETURNED	26-May-2023

GENERAL COMMENTS	Thank you for submitting your research protocol. I have some comments/questions to the authors and found a few typos for which I could suggest a modification: 1- In the whole manuscript, did you mean effectiveness rather than efficacy of QI interventions? 2- In the introduction, you mention the general aim of reducing/preventing hospitalisations of nursing home residents. But some hospitalisations may benefit residents, and/or may be inevitable or appropriate. I would suggest balancing this general aim to striving for reducing/preventing inappropriate hospitalisations and making sure every remaining hospitalisation is appropriate. Could you please comment on that? 3-The defintiion of secondary outcomes (L191-195 + L226) is unclear to me, could you please rephrase and/or develop? 4- Phrasings L97-98 and L236-237 were unclear to me, could you please rephrase? 5- Ref 14 links to error 404. Please update reference Some typos: L55 : Quality improvement interventions (not QI improvement interventions) L63: completed L79: designs, tests and implements L89: healthcare interventions L97-98: unclear, please rephrase L166: residents L167: short and long-term L181: targeting L191-195: unclear, please rephrase. How will the secondary outcomes be defined? L203 eligibility?Plus L226: please detail L235-236: if the number of included studies is higher than 10

REVIEWER	Zanetti , Ermellina FONDAZIONE BRESCIA SOLIDALE
REVIEW RETURNED	27-May-2023

GENERAL COMMENTS	Older people living in Nursing Homes are a vulnerable, frail and complex population. They are more likely than people who reside in the community to become acutely unwell, present to the emergency department and require admission to hospital. For many, hospitalization carries with it risks. Importantly, evidence suggests that some admissions are avoidable. The aim of the systematic review and meta-analysis by Basso et al is strategic for organizations and professionals to identify which interventions are effective to reduce hospitalizations or emergency department visits among nursing home residents.

REVIEWER	Vossius, Corinna Stavanger Univ Hosp
REVIEW RETURNED	06-Jun-2023

GENERAL COMMENTS	Thank you for giving me the opportunity of reviewing this interesting study protocol. The protocol decribes a planned review of published studies about QI strategies to avoid unnecessary hospitalisations in longterm nursing home residents. My main concern is the scientific value of publishing a study report before performing a review. I am familiar with study protocols for large clinical studies, where data collection will be ongoin over a longer period of time and that will result in a number of publications of the results. However, I cannot see the scientific value in publishing a study protocol decribing the methods and analysis before performing the actual review. Further concerns: 1.The Introduction might be more to the point. How many hospitalisations, and what percentage is considered avoidable and why. What are strategies that might prevent hospitalisation? I miss advanced care planning as one important measure to avoid hospitalisations, not only care management. 2. The discussion is really a concluion. There is no discussion about the strenghts and weaknesses of the study protocol. 3. Language: The English is not always correct and needs some revision.

REVIEWER	Wilfling, Denise University of Lübeck, Institute of Family Medicine
REVIEW RETURNED	19-Jun-2023

GENERAL COMMENTS	Thank you for reviewing this study protocol 2023-074684 A very important topic will be addressed with this Review. Overall, the relevance, both for patients and the healthcare system, should be made clearer. What are the experiences from other settings about the effectiveness of QI interventions? Introduction Line 80: Please provide some examples of QI interventions. Please clarify the effectiveness of QI interventions. The benefit should be underlined. Why could help QI interventions especially for nursing home residents? What are possible interventions? What are QI interventions in other settings? Methods

	Line 142: When will the search be ran? Planed month and year would be helpful. I
	Line 145: What sources will be used to identify grey literature? Will the PICO Scheme used to develop the search strategy? This is unclear while in line 163 the eligibility criteria was mentioned, based on PICO.
	Line 147: What about MeSH-Terms?
	Line 191: Please clarify information about outcomes. Objective or subjective measured, what instruments….
	Line 229: What kind of software will be used to conduct the Meta-Analysis?
	Discussion
	What results are expected? What indications can be drawn from the evidence?

REVIEWER	Androulakis, Emmanouil
	University of Piraeus
REVIEW RETURNED	04-Jul-2023

| GENERAL COMMENTS | The aim of this systematic review and meta-analysis will be to assess the effectiveness of quality improvement interventions and the implementation strategies aimed at reducing hospital services use among nursing home residents. It is a well-defined protocol; however, my main concern corresponds to the heterogeneity assessment metrics. The authors mention that the chi-square and I^2 statistics will be applied. Concerning the former (corresponding to the Cochran's Q test), it is a well-accepted way of assessing whether a set of single studies are homogeneous or not. Cochran's Q increases both when the number of studies increases and when the sample size of a study increases. Therefore, Q and its significance highly depend on the size of the meta-analysis and the same applies to its statistical power. We should therefore not interpret the failure to reject the hypothesis of homogeneity as strong indication of its presence. In general, there is a strong debate regarding the scope of the Cochran's Q test utilization. For more details, you can see [1]. As an alternative, I^2 statistic can be applied, which is a proportion and not an absolute value, hence it cannot reveal how much the effects vary. There are alternative heterogeneity measures, which, in my opinion, are more preferred and the authors should also include them. See [1, 2, 3]. In addition, apart from the funnel plot, there are also additional plots in the literature in which the authors can be also based so as to explore heterogeneity, see for example [1, 4, 5]. |

[1] Stogiannis, D., Siannis, F., & Androulakis, E. (2023). Heterogeneity in metaanalysis: a comprehensive overview. The International Journal of Biostatistics, https://doi.org/10.1515/ijb-2022-0070.
[2] Lin, L., Chu, H., & Hodges, J. S. (2017). Alternative measures of between-study
heterogeneity in meta-analysis: reducing the impact of outlying studies. Biometrics,
73(1), 156-166.
[3] Ma, X., Lin, L., Qu, Z., Zhu, M., & Chu, H. (2018). Performance of between-study
heterogeneity measures in the Cochrane library. Epidemiology (Cambridge, Mass.),
29(6), 821.
[4] Anzures-Cabrera, J., & Higgins, J. P. (2010). Graphical displays for meta-analysis:
an overview with suggestions for practice. Research synthesis methods, 1(1), 66-80.
[5] Kossmeier, M., Tran, U. S., & Voracek, M. (2020). Charting the landscape of
graphical displays for meta-analysis and systematic reviews: a comprehensive review,
taxonomy, and feature analysis. BMC medical research methodology, 20(1), 1-24.

VERSION 1 – AUTHOR RESPONSE

Referee: 1	
Thank you for submitting your research protocol. I have some comments/questions to the authors and found a few typos for which I could suggest a modification	Thank you for the helpful evaluation of our manuscript and the constructive suggestions for improvement.
In the whole manuscript, did you mean effectiveness rather than efficacy of QI interventions?	You are right. The word efficacy has been changed in effectiveness throughout the entire manuscript
In the introduction, you mention the general aim of reducing/preventing hospitalisations of nursing home residents. But some hospitalisations may benefit residents, and/or may be inevitable or appropriate. I would suggest balancing this general aim to striving for reducing/preventing inappropriate hospitalisations and making sure every remaining hospitalisation is appropriate. Could you please comment on that?	Thank you for highlighting this concern that gives us the opportunity to better explain our point of view. We absolutely agree with you that a significant proportion of hospitalizations is appropriate and even needed. However, we chose to not introduce the concept of "inappropriate/avoidable hospitalizations" because most of the studies retrieved in the preliminary search assessed all-causes hospitalizations. Therefore, we will investigate potentially avoidable hospitalizations as secondary outcome. The following paragraph of the "Introduction" section has been modified as follow: *"Although a significant proportion of accesses to hospital services are helpful and necessary, international research suggests that up to 55% of hospitalizations in NHs can be avoided with appropriate*

	care (8). In fact, many conditions that result in admission or emergency department visit could be averted through proper prevention (e.g., exacerbation of chronic diseases or functional decline) or effective on-site management at an early stage (e.g., infection or dehydration) (9,10)."
3-The defintiion of secondary outcomes (L191-195 + L226) is unclear to me, could you please rephrase and/or develop?	As requested, the secondary outcome has been further discussed in page 6, lines 127-131. In this revised version of the manuscript, we have added: "In addition, given that the quality of QI interventions is often debated in the literature (37), the secondary aims are to assess the quality and rigor of QI interventions by evaluating whether the solutions tested consider the fundamental domains of a QI intervention, such as organizational readiness, implementation phase, sustainability, or adherence (38)"
4- Phrasings L97-98 and L236-237 were unclear to me, could you please rephrase?	The manuscript has been thoroughly revised by an English language expert and corrected for grammar mistakes.
5- Ref 14 links to error 404. Please update reference	We have corrected the website link
Some typos: L55 : Quality improvement interventions (not QI improvement interventions) L63: completed L79: designs, tests and implements L89: healthcare interventions L97-98: unclear, please rephrase L166: residents L167: short and long-term L181: targeting L191-195: unclear, please rephrase. How will the secondary outcomes be defined? L203 eligibility?Plus L226: please detail L235-236: if the number of included studies is higher than 10	We have corrected all the typos and added details where requested.
Reviewer 2 Older people living in Nursing Homes are a vulnerable, frail and complex population. They are more likely than people who reside in the community to become acutely unwell, present to the emergency department and require admission to hospital. For many, hospitalization	We really thank the Reviewer for the words of appreciation.

carries with it risks. Importantly, evidence suggests that some admissions are avoidable. The aim of the systematic review and meta-analysis by Basso et al is strategic for organizations and professionals to identify which interventions are effective to reduce hospitalizations or emergency department visits among nursing home residents.

Reviewer 3 Thank you for giving me the opportunity of reviewing this interesting study protocol. The protocol decribes a planned review of published studies about QI strategies to avoid unnecessary hospitalisations in longterm nursing home residents. My main concern is the scientific value of publishing a study report before performing a review. I am familiar with study protocols for large clinical studies, where data collection will be ongoin over a longer period of time and that will result in a number of publications of the results. However, I cannot see the scientific value in publishing a study protocol decribing the methods and analysis before performing the actual review. Further concerns:	The publication of the protocol of a systematic review is a best practice in evidence synthesis, to ensure the integrity and credibility of the review process. Firstly, it promotes transparency in the research process to reduce bias and enhances the overall trustworthiness of the review, by providing readers and researchers with a clear understanding of the review's objectives, methods, and planned analyses. Secondly, publishing the protocol of the review helps prevent duplication of effort and minimize research waste. Indeed, it allows researchers to decide whether to proceed with a similar review or explore other research questions, saving time and resources. Then, publishing the protocol minimizes bias, by ensuring that the review follows a predetermined set of methods, including study selection criteria, data extraction, and statistical analysis. Finally, sharing the protocol enables researchers to receive valuable input, suggestions, and improvements from the scientific community. We hope to have adequately clarify the importance to publish a systematic review protocol.
1. The Introduction might be more to the point. How many hospitalisations, and what percentage is considered avoidable and why. What are strategies that might prevent hospitalisation? I miss advanced care planning as one important measure to avoid hospitalisations, not only care management.	Thank you for your useful suggestions. We have added the following paragraph: *"Although a significant proportion of accesses to hospital services are helpful and necessary, international research suggests that up to 55% of hospitalizations in NHs can be avoided with appropriate care (8). In fact, many conditions that result in admission or emergency department visit could be averted through proper prevention (e.g., exacerbation of chronic diseases or functional decline) or effective on-site management at an early stage (e.g., infection or dehydration) (9,10). Improving the NH staff' skills in early recognition and management of acute change of conditions, and the use of standardized communication tools could prevent avoidable access to hospital*

	services (11). Similarly, promoting palliative care and advanced care planning enables healthcare professionals to be aligned with residents' preferences and values, ensuring the provision of respectful and patient-centred care (12)."
2. The discussion is really a concluion. There is no discussion about the strenghts and weaknesses of the study protocol.	In this revised version, the discussion/conclusion section has been removed because it is not part of journal formatting requirements for protocol articles
3. Language: The English is not always correct and needs some revision.	The manuscript has been thoroughly revised by an English language expert and corrected for grammar mistakes.
Reviewer 4 A very important topic will be addressed with this Review. Overall, the relevance, both for patients and the healthcare system, should be made clearer. What are the experiences from other settings about the effectiveness of QI interventions? Line 80: Please provide some examples of QI interventions. Please clarify the effectiveness of QI interventions. The benefit should be underlined. Why could help QI interventions especially for nursing home residents? What are possible interventions? What are QI interventions in other settings?	Thank you for your interesting questions that give us the opportunity to further explain these concepts. In according to the Reviewer comment, we have added the following paragraph: *"Previous experiences in hospital acute care setting found QI interventions beneficials in enhancing process care outcomes, such as organizational culture or teamwork, and improving patient care, by reducing the nosocomial infection rate, preventing falls, or improving surgical outcomes (21-24). Although previous studies have obtained encouraging results related to QI interventions, evidence of its effectiveness in NH remain limited (25,26) In particular, the INTERACT II intervention significantly reduced hospital admissions through a multi-component QI intervention aimed at training NH staff to identify and proactively manage major geriatric syndromes, encouraging advanced care planning, and promoting palliative care-oriented care. (27)"*
Line 142: When will the search be ran? Planed month and year would be helpful. I	We have included the planned search dates in the abstract and in the method section.
Line 145: What sources will be used to identify grey literature?	As indicated in page 7 (line 155), grey literature has been excluded.
Will the PICO Scheme used to develop the search strategy? This is unclear while in line 163 the eligibility criteria was mentioned, based on PICO.	Thank you for this comment. We have specified that the PICO scheme was employed to develop the search strategy by combining terms according to the PICO framework (page 7, lines 157-158)

Line 147: What about MeSH-Terms?	In response to the Reviewer's request, we make clearer that all the terms will be searched as controlled vocabulary and text words, as follow: *"The search strategy has been developed in collaboration with an expert librarian, by combining terms according to the PICO framework. All terms were searched as controlled vocabulary and text words with title and abstract field limiters, and combined with Boolean Operators (AND, OR). The research has been set from 2000, as no QI has been undertaken before this date (30) until December 31, 2022, and will be re-run on September 1, 2023. No language limitations will be applied. The full search strategy is available in the supplementary material".* The full search strategy has been reported as supplemental file.
Line 191: Please clarify information about outcomes. Objective or subjective measured, what instruments….	We have added the following paragraph: *"Both subjective (e.g., self-reported by NH staff) or objective measure (e.g., hospital database) of hospital service use will be collected."*
Line 229: What kind of software will be used to conduct the Meta-Analysis?	At page 12, we indicated that "All the analysis will be performed using STATA/SE17 version."
Discussion What results are expected? What indications can be drawn from the evidence?	In the revised version, the discussion/conclusion section has been removed because it is not part of journal formatting requirements for protocol articles
Reviewer 5 The aim of this systematic review and meta-analysis will be to assess the effectiveness of quality improvement interventions and the implementation strategies aimed at reducing hospital services use among nursing home residents. It is a well-defined protocol; however, my main concern corresponds to the heterogeneity assessment metrics. The authors mention that the chi-square and I2 statistics will be applied. Concerning the former (corresponding to the Cochran's Q test), it is a well-accepted way of assessing whether a set of single studies are homogeneous or not. Cochran's Q increases both when the number of studies increases and when the sample size of a study increases. Therefore, Q and its significance highly depend on the size of the meta-analysis and the same applies to its statistical power. We should therefore not interpret the failure to reject the hypothesis of homogeneity as strong indication of its	Thank you to the Reviewer for his important suggestions. We completely agree with the Reviewer about the debate on Cochran's Q (and others as R2 or Tau tests), however, considering the difficult interpretation of the former, we prefer to maintain the I2 statistics, because it has a precise cut-off to quantity heterogeneity. However, we recognized that I^2 can be inaccurate when the number of the included studies is less than 10. Given that, we have revised the manuscript as follow: *"Data from the included studies will be combined into a meta-analysis based on the outcomes. The results will be pooled by combining the natural logarithms of the rate ratio across studies, or by calculating the rate ratio using the generic inverse-variance method. We will use a permutation random-effect model to estimate meta-analysis effect. Heterogeneity will be assessed using the I^2 statistics and we will consider high level of heterogeneity an $I^2 > 75\%$; considering that the I^2 statistics is biased in small meta-analysis, we will test*

presence. In general, there is a strong debate regarding the scope of the Cochran's Q test utilization. For more details, you can see [1]. As an alternative, I2 statistic can be applied, which is a proportion and not an absolute value, hence it cannot reveal how much the effects vary. There are alternative heterogeneity measures, which, in my opinion, are more preferred and the authors should also include them. See [1, 2, 3].	*heterogeneity with the H^2 if it will be included less than 10 studies. We choose an acceptable level of H^2 under 1.88 with a confidence of 95% (48)."* 48) Mona P, Sada Nand D, SVS D, V Sreenivas, Bhaskar T. Which is the Preferred Measure of Heterogeneity in Meta-Analysis and Why? A Revisit. Biostat Biometrics Open Acc J. 2017;1(1): 555555. DOI: 10.19080/BBOAJ.2017.01.555555 020) Since we use the funnel plot to assess publication bias and not to explore heterogeneity, we did not fully understand the Reviewer's suggestion. We remain open to further evaluation, if needed.
In addition, apart from the funnel plot, there are also additional plots in the literature in which the authors can be also based so as to explore heterogeneity, see for example	

VERSION 2 – REVIEW

REVIEWER	Guion , Vincent Centre Hospitalier Universitaire de Toulouse Gerontopole
REVIEW RETURNED	19-Aug-2023

GENERAL COMMENTS	Thank you for your response and for adressing all my suggestions or comments.

REVIEWER	Wilfling, Denise University of Lübeck, Institute of Family Medicine
REVIEW RETURNED	26-Aug-2023

GENERAL COMMENTS	Thank you very much for your revised manuscript. Introduction: It is still not entirely clear what exactly QI interventions are or what exactly such an intervention could look like. You provide a definition, but please can you give some examples of interventions? Line 155: Please correct gray literature to grey literature

VERSION 2 – AUTHOR RESPONSE

Reviewer n 2 Thank you for your response and for adressing all my suggestions or comments.	Thank you for your revision.
Reviewer n 4 Thank you very much for your revised manuscript.	Thank you to give us the opportunity to improve the manuscript.
Introduction: It is still not entirely clear what exactly QI interventions are or what exactly such an intervention could look like. You provide a definition, but please can you give some examples of interventions?	As requested, we have added the following paragraph to make clearer what QI interventions are: *"QI interventions are planned as a cyclical process, starting with problem analysis to design a tailored intervention before implementation (16). Changes are constantly measured during and after implementation to understand the impact and adopt the required adjustments (16). The iterative cycle, also known as the plan-do-study-act (PDSA) method is the model used by several QI interventions, such as Total Quality Management, Lean and Six Sigma (17)."*
Please correct gray literature to grey literature	Done