PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

Title (Provisional)

Timely short-term specialised palliative home care for older people with frailty and their family: a mixed-methods pilot randomised controlled trial and process evaluation

Authors

De Nooijer , Kim; Van Den Noortgate, Nele; Pype, Peter; trial group , Frailty+; Pivodic, Lara; Van den Block , Lieve

---

VERSION 1 - REVIEW

Reviewer	**1**
Name	**Green, Richard**
Affiliation	**University of Surrey, School of Health Sciences**
Date	**24-Jul-2023**
COI	**Lieve Van den Block, an author for this paper, is a member of a steering advisory group for the PALLUP study, which I previously worked on as a research fellow. I have had previous contact with Lieve in this capacity, but otherwise no other contact with Lieve or any other author for this paper.**

My thanks to the authors for this well-written and engaging article outlining valuable findings from your pilot RCT and process evaluation for a short-term specialised palliative care intervention for older people with frailty and their family in primary care. This paper provides useful insights into some of the barriers to, and in turn possible future directions for, implementing this style of intervention, a question of interest to geriatric care and palliative care professionals internationally. Below are some very minor suggestions for changes pertaining to clarity of expression that you may wish to make:

Introduction - great, very clear

Pg. 7 line 3- what structured measures?

Pg. 7 Line 47-

and asked them whether they agree that researchers come and introduce the

study. ----- could or can come?

Inclusion criteria - well justified

Pg. 8 Frailty+

the service is initiated in a timely manner, i.e., when the patient's complex care needs cannot be addressed by generalist providers alone. ----- how is this decided, at MDT?

Pg. 9 Line 20-

as they needed to hire additional staff --- assumedly on a temporary basis, hire in more people for certain days? If on a bigger scale, are the new staff delivering this intervention, or existing staff?

Pg. 13, line 45

GPs

Pg. 16, line 22

Nurses reported having provided psychosocial support during the first home visit for 16 of the 19 patients, --- might be worth reiterating this is for the intervention group here

---

Reviewer	**2**
Name	**Alharbi, Khulud**
Affiliation	**The University of Manchester Faculty of Medical and Human Sciences**
Date	**03-Jan-2024**
COI	**No**

---

clearly state the limitation in your study,

In the result: you can simplify your explanation by mentioning only the important number and referring to the table or figure.

In the discussion, you repeat the same information from the research; the reader needs to know what your study added to the current literature and what other areas need to be explored in the future.

Reviewer	**3**
Name	**Crippa, Matteo**
Affiliation	**Fondazione Floriani**
Date	**04-Mar-2024**
COI	**No competing interests**

The manuscript deals with one of the most important topics of the moment in palliative care sector: how to adapt palliative care services and practices to a growing demand of care from frail population. This requires new models of care, new knowledge, and new “lenses” to look at the patient and his/her family. Integration between geriatric and palliative care should be nowadays a common practice, even if only a few entities are concretely committed to carrying forward this effort. I appreciate the choice of looking at the frailty and complex conditions (becoming needs) instead of a diagnosis as a selection criteria. Looking at the affiliations of the authors of the manuscript, I valued also their different professional background and their integration efforts. Authors did a very good job in writing the manuscript, designing the service (the short-term specialized palliative care service) and providing evidence of it. Moreover, I sincerely appreciate the clarity of the authors displaying the limits and the implications of the evidence for future research and service implementation.

Here some minor comments.

- I suggest to better describe the differences between generalist, specialized and the short-term specialized PC service provided. Authors did it in the “introduction” section, but since palliative care is not propagated equally in different country, I would suggest articulating more to better highlights appropriateness of the intervention according to the different trajectories and needs of patients and their families.

- On the topic of the previous comment I wonder how many patients in control group actually received PC as usual care (If I didn’t get wrong, patients receiving usual PC have been excluded from intervention group and enrolled in control group): since there are only small differences between intervention and control group (Table 4), I would look into confounder effects of usual Palliative Care (generalist or specialist).

- Premising that I don't know in detail the context within which the research was carried out (Flanders - Belgium), I found marginal the involvement of the GPs, which may play an important role in providing palliative care at home to frailty patients. Could the authors provide an explanation of this choice, which could be only derived from healthcare sector organization?

- Authors cited a distress protocol, which I presume it would be activated if research have provided distress to patients/caregiver, and the fact that none of the participants needed the distress protocol activated. I would suggest to add a reference or explanation about the nature of such protocol (for instance: Whitney, C., & Evered, J. A. (2022). The Qualitative Research Distress Protocol: A Participant-Centered Tool for Navigating Distress During Data Collection. International Journal of Qualitative Methods, 21. https://doi-org.unimib.idm.oclc.org/10.1177/16094069221110317).

Reviewer **4**

Name **Robinson-Reilly, Melissa**

Affiliation	**University of Newcastle School of Nursing and Midwifery**
Date	**07-Mar-2024**
COI	**No competing interests to declare.**

Thank you for the opportunity to review this manuscript. It is noted that the most recent citation/reference is 2022.

Introduction: The opening statement in the Introduction is based on literature from 2012 and could not be considered contemporary to support a study aligning to develop best practice.

Page 4 (5 of 43) - Line 31; refers to literature from 2013 and requires review as to whether this remains current in 2024. As does the citation to support line 35 claim -This is particularly needed in the setting where most older people reside, i.e. at home (Davies & Higginson, 2004). If this is in reference to the location of the study, then requires clarification rather than generalised to the wider cohort. Line 54, second last statement is supported by 2008 citation – and although this does have relevance -as a reader it would be important to discuss any changes since.

To clearly support the introduction and set the stance for the need to investigate, current literature is important for the reader to agree that this issue still is continuing or identified globally today. It is also noted this study is supported from previous 1st author publications.

Page (12 of 43) Line 15 states outcomes were measure using validated questionnaires in a structured interview format, though there is no example of this. There is a lot of detail within this paragraph and suggest a table or chart to ensure the information is clearly presented and linked.

Justification of the findings is in line with the objectives and is written clearly.

All the best.

Reviewer	**5**
Name	**Kalra, Saurabh**
Affiliation	**Rutgers University, Health Behavior Society and policy**
Date	**12-Mar-2024**
COI	**None**

Thank you for writing this manuscript about the importance of timely and short-term specialized palliative care for older people with frailty, emphasizing the need for interventions that address complex care needs in various domains.

I would like to suggest some suggestions and give comments to improve the manuscript.

1. I am not convinced with the justification of Intervention:

References are old. Have you done a literature on similar studies done recently. What is the novelty of doing this RCT. Are you reinforcing the evidence for short term palliative care?

2. What phase is the study presently in? Did you do any followup RCT etc?

3. How did you define frality?

The manuscript mentions that frailty is a common condition in older people but does not provide a clear definition or operationalization of frailty. This lack of clarity could affect the reproducibility and comparability of the study findings.

4. Other terms such as "timely-initiated," "short-term," and "specialized palliative care" were used with definitions and intermittently changing. Use consistent language.

5. add a limitation about reproducibility and generalizability as study setting is limited to Flanders, Belgium, which may limit the generalizability of the findings to other settings or populations.

6. add discussions of potential biases and their implications for the interpretation of the findings is essential for the validity and reliability of the study.

7. do you think patients had access to other forms of palliative care or mental health access that may affect study results.

8.The conclusion restates some key findings but could be strengthened by summarizing the main implications of the study and offering actionable recommendations for practitioners and policymakers.

9. The challenges that authors faced during implementations, it is okay to use them in the results and conclusions, but, how do you think they affected the validity or reliability of the study?

Reviewer	**6**
Name	**Martin, James**
Affiliation Research	**University of Birmingham, Institute of Applied Health**
Date	**08-May-2024**
COI	**None**

This is a pilot/feasibility study that looks at the appropriateness of an intervention (Frailty+) in older adults with frailty.

There seems to be an interchange between pilot and feasibility study. Whilst they are quite similar, they generally have slightly different aims. A feasibility study is identifying whether something can be done, and if so, how. A pilot study may ask similar questions, but is essentially conducting a definitive trial, but on a smaller scale. You may want to look at the following paper for guidance: "Eldridge SM, Lancaster GA, Campbell MJ, Thabane L, Hopewell S, Coleman CL, Bond CM. Defining feasibility and pilot studies in preparation for randomised controlled trials: development of a conceptual framework. PloS one. 2016 Mar 15;11(3):e0150205."

Given this is a pilot/feasibility study, I would expect the primary objectives and the primary outcome to be related to feasibility. Whilst objectives 1 and 2 do focus on the implementation and feasibility aspects, the third objective is looking at the effect of the intervention and the primary outcome is a change in a clinical outcome. Whilst it is important to collect clinical outcomes that are likely to be the primary outcome in a definitive randomised trial, the focus should be on a summary of them, the response rate and the feasibility of collecting these outcomes.

You included patients whose frailty score was 5 to 7 on the Clinical Frailty Scale. Was the person who did the recruitment the same person who did this assessment? (As this can result in bias). Also, what was the rationale for excluding those with a score of 8 or 9?

Were there any exclusion criteria involving patients with dementia?

What was the rationale for the inclusion criteria of: "admitted to a hospital and about to be discharged home". Is this likely to be differences in this patient population than the wider community that could be classified as frail?

The description of the randomisation is okay, and seems to have been done correctly. Its not clear whether this would be the planned method of randomisation for a definitive trial or whether a constrained randomisation would be used to ensure balance on patient characteristics.

I understand that masking of patients was not possible, but was it possible to blind people taking outcomes from the patients? If so, was this done? (It is not clear if this was the study investigators or not).

The description of doing a "difference in mean change from baseline to follow-up" is quite different from the methods described – which seem to describe a difference in outcome at follow-up, after an allowance for baseline.

For this type of data (with observations on participants at baseline and follow-up), there are three possible analysis options: 1) ANCOVA approach, whereby a model is fitted to the follow-up outcome and the baseline outcome is a covariate in the model; 2) a model with treatment arm, time, and its interaction; 3) a model with time and its interaction with treatment arm. It would be interesting to know why you chose to do approach 2 here, as I think generally approaches 1 and 3 are recommended.

Given this patient population, were there are monitoring of harms during the study period?

I would perhaps expect to see more feasibility aspects related to outcome collection, such as response rates, completion rates, ability to collect information at planned time, etc. But there is no real mention of these in the methods section.

VERSION 1 - AUTHOR RESPONSE

REVIEWER 1		
1) My thanks to the authors for this well-written and engaging article outlining valuable findings from your pilot RCT and process evaluation for a short-term specialised palliative care intervention for older people with frailty and their family in primary care. This paper provides useful insights into some of the barriers to, and in turn possible future directions for, implementing this style of intervention, a question of interest to geriatric care and palliative care professionals internationally. Below are some very minor suggestions for changes pertaining to clarity of expression that you may wish to make.	Thank you for confirming the value of our manuscript on specialised palliative home care for older people.	
2) Introduction - great, very clear	Thank you.	
3) Pg. 7 line 3- what structured measures?	We have explained this in the manuscript.	p.6, Study design To test the preliminary effects of Frailty+, we used quantitative data collected through structured measures **(the measures are described in the section Data collection and outcomes).**
4) Pg. 7 Line 47- and asked them whether they agree that researchers come and introduce the study. ----- could or can come?	We have clarified the sentence in the manuscript.	p.6, Participants and recruitment process In the other hospital, researchers were not allowed to attend the meetings. **Instead,** the geriatricians and mobile geriatric teams identified patients and asked them whether **the researchers could come to introduce the study.**
5) Inclusion criteria - well justified	Thank you.	
6) Pg. 8 Frailty+	Indeed, during the weekly staff	

the service is initiated in a timely manner, i.e., when the patient's complex care needs cannot be addressed by generalist providers alone. ----- how is this decided, at MDT?	meetings at the two collaborating hospitals, potentially eligible patients were identified. We had explained this in the participants and recruitment process section (p. 6).	
7) Pg. 9 Line 20- as they needed to hire additional staff --- assumedly on a temporary basis, hire in more people for certain days? If on a bigger scale, are the new staff delivering this intervention, or existing staff?	We gave the specialised palliative care teams the freedom to use the resources as they wished, as long as they could provide the intervention as planned. Although we do not know whether the new staff members were hired on temporary or permanent contracts, we do know that both existing as well as new staff members delivered the Frailty+ intervention. We have added this information in the manuscript.	p. 9, The Frailty+ intervention The specialised palliative care teams were paid from the research project for their participation in the study next to their usual tasks, as they needed to hire additional staff. **Both existing staff members and new staff members delivered Frailty+.**
8) Pg. 13, line 45 GPs	Unfortunately, we were not sure which sentence the reviewer referred to, but we have checked the language of the manuscript again.	

9) Pg. 16, line 22 Nurses reported having provided psychosocial support during the first home visit for 16 of the 19 patients, --- might be worth reiterating this is for the intervention group here	We have clarified this in the manuscript.	p. 15, Implementation of the Frailty+ intervention Nurses reported having provided psychosocial support during the first home visit for 16 of the 19 patients **in the intervention group**, introduction/information concerning the specialised palliative home care service for 15/19, coordination/practical help for 12/19, pain control, symptom control and comfort care for 10/19 and life and existential questions support for 6/19.
REVIEWER 2		
1) Clearly state the limitation in your study	Please see our answer on comment 7 of reviewer 5.	
2) In the result: you can simplify your explanation by mentioning only the important number and referring to the table or figure.	We have simplified the results where possible.	
3) In the discussion, you repeat the same information from the research; the reader needs to know what your study added to the current literature and what other areas need to be explored in the future.	We have added a paragraph in which we compare the findings from our study with a previously conducted timely and short-term palliative care intervention in the UK. In addition, we have clarified the recommendations in the Discussion and Conclusion section.	p. 20 - 22, Discussion and Conclusion **Still, we recommend for future research** even more intensive processes of co-design **and co-creation of the intervention** with patients, families and stakeholders in primary and secondary **care.** **Comparing our results to a previously conducted short-term specialised palliative care intervention for older people in the UK, we identified considerably different findings. For**

		instance, the UK intervention was effective in reducing symptom distress in older people.(19) A possible explanation for this difference might be the different healthcare contexts in which the intervention was implemented, which might have influenced the implementation of the intervention. For instance, there might be closer existing collaborations and co-creation between the researchers and the professional stakeholders in the UK enabling a stronger engagement in the study.(47) To further our understanding of the mechanisms essential to bringing about change in clinical practice, a comparative case study focusing on commonalities and differences in the implementation strategies and processes of both studies could be useful. Our findings highlight that considerable organisational and cultural changes are required **to ensure timely-initiated and short-term specialised palliative care for** older people. Furthermore, **we recommend striving for more co-creation between researchers, practitioners and**

		policymakers in the development and implementation of such complex interventions, in which we need to establish agreement on complex needs-based referral criteria for older people and to define roles and tasks of specialised palliative care nurses in addressing these complex needs.
REVIEWER 3		
1) The manuscript deals with one of the most important topics of the moment in palliative care sector: how to adapt palliative care services and practices to a growing demand of care from frail population. This requires new models of care, new knowledge, and new "lenses" to look at the patient and his/her family. Integration between geriatric and palliative care should be nowadays a common practice, even if only a few entities are concretely committed to carrying forward this effort. I appreciate the choice of looking at the frailty and complex conditions (becoming needs) instead of a diagnosis as a selection criteria. Looking at the affiliations of the authors of the manuscript, I valued also their different professional background and their integration efforts. Authors did a very good job in writing the manuscript, designing the service (the short-term specialized palliative care service) and providing evidence of it. Moreover, I sincerely appreciate the clarity of the authors displaying the limits and the implications of the evidence for future research and service implementation.	Thank you very much for your positive feedback on our study.	
2) - I suggest to better describe the differences between generalist, specialized and the short-term specialized PC service provided. Authors did it in the "introduction" section, but since palliative care is not propagated equally in different country, I would suggest articulating more to better highlights appropriateness of the intervention according to the different trajectories and needs of patients and their families.	We have provided an explanation of the concepts in the introduction. In the Methods section, we have clarified the organization of palliative care in Belgium.	p. 6, Study setting These services consist of multidisciplinary teams comprising nurses, psychologists, and palliative care physicians. In Belgium, these services are typically involved in the last days or weeks of life of patients with serious symptoms or problems. (9, 10, 12) **Next to the provision of specialised**

		palliative care, generalist palliative care is, for most patients, provided by their general practitioner (GP). According to Belgian law, the GP needs to initiate the involvement of the specialised palliative care service. Regarding the recruitment of the participants for our study, patients were recruited upon discharge from the acute geriatrics department and via the multidisciplinary mobile geriatric teams of two public hospitals.
3) - On the topic of the previous comment I wonder how many patients in control group actually received PC as usual care (If I didn't get wrong, patients receiving usual PC have been excluded from intervention group and enrolled in control group): since there are only small differences between intervention and control group (Table 4), I would look into confounder effects of usual Palliative Care (generalist or specialist).	If patients in the control group were referred to the specialised palliative care service, they would be excluded from the study. However, none of the patients in the control group were referred to the specialised palliative care service in the follow-up period. Regarding the potential confounding effects of general palliative care, we have no data available to test this hypothesis, even though is it plausible. We have therefore included a	p. 21, Discussion This preliminary analysis is limited by the sample size of this pilot trial, but the lack of effects is also likely a consequence of the implementation problems we encountered. A future large-scale trial therefore needs to pay particular attention to implementation to ensure that useful effectiveness data are obtained. **Another possible explanation for the small differences in primary and secondary outcomes, is that the needs of the patients in the control group could have been addressed by their GP. Our process evaluation showed that almost all patients had contact with their GP**

	section on this in the discussion.	**during the study at least once. However, we do not exactly know which care was delivered during these consultations. For future studies, we would advise to also carefully describe and evaluate care as usual in the control group.**
4) - Premising that I don't know in detail the context within which the research was carried out (Flanders - Belgium), I found marginal the involvement of the GPs, which may play an important role in providing palliative care at home to frailty patients. Could the authors provide an explanation of this choice, which could be only derived from healthcare sector organization?	Unfortunately, we were not completely sure what the reviewer meant with the 'explanation of this choice'. We think that the reviewer refers to why we chose to focus primarily on specialised palliative care services, with relatively less emphasis on the involvement of GPs. In the Belgian context, the general practitioner is the main provider of palliative care, and specialised palliative care services are only initiated when needed. However, older people often receive specialised palliative care late in the illness trajectory. Therefore, in the Frailty+ intervention, we have chosen to	

	focus specifically on the earlier initiation of the specialised palliative care service based on patients' complex care needs.	
5) Authors cited a distress protocol, which I presume it would be activated if research have provided distress to patients/caregiver, and the fact that none of the participants needed the distress protocol activated. I would suggest to add a reference or explanation about the nature of such protocol (for instance: Whitney, C., & Evered, J. A. (2022). The Qualitative Research Distress Protocol: A Participant-Centered Tool for Navigating Distress During Data Collection. International Journal of Qualitative Methods, 21. https://doi-org.unimib.idm.oclc.org/10.1177/16094069221110317).	The reference seems very interesting, however, it was not available at the time we wrote our protocol so we cannot refer to it. We have explained the procedures of our distress protocol in the study protocol of the Frailty+ study (de Nooijer et al., 2021). We have therefore added the reference of the protocol.	p. 15 Mechanisms of Change The distress protocol was not activated during the study period **(more information about the distress protocol can be found in the study protocol of Frailty+ (42).**
REVIEWER 4		
1) Thank you for the opportunity to review this manuscript. It is noted that the most recent citation/reference is 2022.	Thank you, we have updated the article with more recent references.	
2) Introduction: The opening statement in the Introduction is based on literature from 2012 and could not be considered contemporary to support a study aligning to develop best practice.	We have added a more recent study on the prevalence of frailty in community-dwelling older people.	p. 4 Introduction An estimated **12%** of people living in the community are frail.(2)
3) Page 4 (5 of 43) - Line 31; refers to literature from 2013 and requires review as to whether this remains current in 2024.	We have checked this in the literature and have changed the reference in the manuscript.	p. 4 Introduction Furthermore, older people, and particularly those with non-cancer conditions, are less likely to receive palliative care**.(13-16)**

4) As does the citation to support line 35 claim -This is particularly needed in the setting where most older people reside, i.e. at home (Davies & Higginson, 2004). If this is in reference to the location of the study, then requires clarification rather than generalised to the wider cohort.	We have updated the reference. In the introduction we describe the current situation and therefore refer to the wider cohort.	p. 4, Introduction This is particularly **relevant at their home, as this is the setting where most of them live.(17)**
5) Line 54, second last statement is supported by 2008 citation – and although this does have relevance -as a reader it would be important to discuss any changes since.	We have updated the reference with the last version of the UK MRC framework.	p. 5, Introduction This is particularly relevant for complex interventions such as specialised palliative care, where multiple intervention components interact with a given context to produce the desired outcomes**.(20)**
6) To clearly support the introduction and set the stance for the need to investigate, current literature is important for the reader to agree that this issue still is continuing or identified globally today. It is also noted this study is supported from previous 1st author publications.	We fully agree and have therefore updated the references where possible.	
7) Page (12 of 43) Line 15 states outcomes were measure using validated questionnaires in a structured interview format, though there is no example of this. There is a lot of detail within this paragraph and suggest a table or chart to ensure the information is clearly presented and linked.	We have made a table in which the information regarding the outcomes and outcome measures is presented.	p. 10 – 11, Preliminary effects of the Frailty+ intervention (Objective 3) We collected data at baseline (T0) and 8-weeks after baseline (T1). **One exploratory outcome, namely patient's healthcare utilisation (i.e. number and length of hospital admissions and number of GP visits), was only assessed at 8-weeks post-baseline through a telephone interviews with the patient's GP.** The primary outcome was mean change on a sum score based on five key palliative care symptoms experienced by the older person (i.e. breathlessness, pain,

		anxiety, constipation, drowsiness) from baseline to 8-weeks, measured by the Integrated Palliative Care Outcome Scale (IPOS).(41) **The outcomes are presented in Table 2.** p. 32 – 33, Table 2. **Primary, secondary and exploratory outcomes and related measures.**
8) Justification of the findings is in line with the objectives and is written clearly.	Thank you.	
REVIEWER 5		
1) Thank you for writing this manuscript about the importance of timely and short-term specialized palliative care for older people with frailty, emphasizing the need for interventions that address complex care needs in various domains. I would like to suggest some suggestions and give comments to improve the manuscript.	Thank you for your thorough evaluation.	
2) I am not convinced with the justification of Intervention: References are old. Have you done a literature on similar studies done recently. What is the novelty of doing this RCT. Are you reinforcing the evidence for short term palliative care?	We have conducted a search in the literature to see whether recent RCTs have been published on timely short-term specialised palliative care for older people with frailty and complex care needs. However, to the best of our knowledge, we did not identify other RCTs than those we have referred to in the Introduction section (i.e. the one conducted in the UK in 2021). Our study is reinforcing this first valuable	

	evidence as several gaps in evidence still exist, such as insights into the specific intervention components and the implementation of such interventions in practice. We had reported this in the Introduction section.	
3) What phase is the study presently in? Did you do any followup RCT etc?	We have not yet continued with testing/adapting Frailty+. As we concluded in the article, considerable organizational and cultural changes are required to successfully implement such an intervention. We will therefore first focus on revising the current intervention to ensure a better fit with clinical practice. The current context in Belgium for such an intervention study is also not ideal as the government is planning a large reform in the sector.	
4) How did you define frailty? The manuscript mentions that frailty is a common condition in older people but does not provide a clear definition or operationalization of frailty. This lack of clarity could affect the reproducibility and comparability of the study findings.	We have added the definition that we used in the study.	p. 4, Introduction **Following the definition by Clegg et al., 2013, frailty is defined as 'a health**

		state of increased vulnerability to poor resolution of homoeostasis after a stressor event, which increases the risk of adverse outcomes, including falls, delirium, and disability'.(1)
5) Other terms such as "timely-initiated," "short-term," and "specialized palliative care" were used with definitions and intermittently changing. Use consistent language.	We have checked this throughout the manuscript and clarified where needed.	
6) add a limitation about reproducibility and generalizability as study setting is limited to Flanders, Belgium, which may limit the generalizability of the findings to other settings or populations.	We had a limitation regarding generalizability of our findings in the Discussion section and the statement section.	
7) add discussions of potential biases and their implications for the interpretation of the findings is essential for the validity and reliability of the study.	We have added discussions of potential biases in the Limitations section.	p. 22, Discussion We cannot exclude recall bias, as the process evaluation data from healthcare professionals were collected after recruitment was completed. **There might also be detection bias, as the data managers and researcher were not blinded. A Cochrane review showed that there might be an overestimation of the effects of the intervention in non-blinded trials.(50) Finally, there could be selection bias, because in one hospital, researchers were not allowed to attend the staff meetings and hospital**

		care staff were gatekeepers in the recruitment of potential participants. They might have selected patients that were in better health considering this was a trial in timely short-term specialised palliative care. Hence, our sample might represent a group with a lower symptom burden compared to the wider population. p. 3, Strengths and limitations of this study **Detection bias cannot be excluded in this study, as data managers and researcher involved in outcome assessment were not blinded.**
8) do you think patients had access to other forms of palliative care or mental health access that may affect study results.	We would like to refer to our answer on comment 3 of reviewer 3 in which a similar question was posed.	
9) The conclusion restates some key findings but could be strengthened by summarizing the main implications of the study and offering actionable recommendations for practitioners and policymakers.	We have added the main implications of the study in the conclusion section.	p. 22 -23, Discussion Our findings highlight that considerable organisational and cultural changes are required **to ensure timely-initiated and short-term specialised palliative care for older people.** Furthermore, **we recommend striving for more co-creation between researchers, practitioners and policymakers in the development and implementation of such complex**

		interventions, in which we need to establish agreement on complex needs-based referral criteria for older people and to define roles and tasks of specialised palliative care nurses in addressing these complex needs.
10) The challenges that authors faced during implementations, it is okay to use them in the results and conclusions, but, how do you think they affected the validity or reliability of the study?	We have described the potential biases and its implications in our answer to comment 7.	
REVIEWER 6		
1) This is a pilot/feasibility study that looks at the appropriateness of an intervention (Frailty+) in older adults with frailty.	Thank you for your thorough evaluation.	
2) There seems to be an interchange between pilot and feasibility study. Whilst they are quite similar, they generally have slightly different aims. A feasibility study is identifying whether something can be done, and if so, how. A pilot study may ask similar questions, but is essentially conducting a definitive trial, but on a smaller scale. You may want to look at the following paper for guidance: "Eldridge SM, Lancaster GA, Campbell MJ, Thabane L, Hopewell S, Coleman CL, Bond CM. Defining feasibility and pilot studies in preparation for randomised controlled trials: development of a conceptual framework. PloS one. 2016 Mar 15;11(3):e0150205."	We have checked the paper of Eldridge. In our study, we have followed their concept of randomized pilot studies (i.e. those in which the future RCT is conducted on a smaller scale) in which we assessed the feasibility of the RCT methods and procedures (as described in Objective 2). We have checked the manuscript for consistency in terminology.	
3) Given this is a pilot/feasibility study, I would expect the primary objectives and the primary outcome to be related to feasibility. Whilst objectives 1 and 2 do focus on the implementation and feasibility aspects, the third objective is looking at the effect of the intervention and the primary outcome is a change in a clinical outcome. Whilst it is important	We fully agree with the reviewer that the main focus of a pilot RCT should be related to	

to collect clinical outcomes that are likely to be the primary outcome in a definitive randomised trial, the focus should be on a summary of them, the response rate and the feasibility of collecting these outcomes.	feasibility. We only assessed preliminary effects in the third aim, as these outcomes might be selected as primary outcome in the full-scale RCT. Our first two aims therefore focus on implementation of the intervention as well as on the feasibility of the RCT methods and procedures.	
4) You included patients whose frailty score was 5 to 7 on the Clinical Frailty Scale. Was the person who did the recruitment the same person who did this assessment? (As this can result in bias). Also, what was the rationale for excluding those with a score of 8 or 9?	The persons who recruited participants for the study were two data managers (KE and AJ) and a researcher (KdN), the same persons conducted the outcome measurement. We do agree that this might have resulted in bias, we have therefore added this to the limitations of the study. Patients were selected if they had a frailty score of 5 to 7 on the Clinical Frailty Scale (mild to severe frailty). The reason that we excluded participants who had a score of 8	p. 22, Discussion **There might also be detection bias, as the data managers and researcher were not blinded. A Cochrane review showed that there might be an overestimation of the effects of the intervention in non-blinded trials.(50)**

	or 9 (very severe to terminally ill) is because these patients should receive specialised palliative care, and it is therefore not ethical to randomize them.	
5) Were there any exclusion criteria involving patients with dementia?	Patients with dementia could be included, as they form a large group of older people living in primary care. We had explained this in the section Participants and recruitment process on page 7 of the manuscript. We included 37 patients in our study, including 8 adults lacking capacity (see also Figure 1 for the flow chart of recruitment and retention).	
6) What was the rationale for the inclusion criteria of: "admitted to a hospital and about to be discharged home". Is this likely to be differences in this patient population than the wider community that could be classified as frail?	We acknowledge that, through our recruitment in the hospitals, the included population might differ from the population in the wider community. We have chosen to recruit via the hospitals mainly for reasons of feasible recruitment. However this	p.22, Discussion **Also important to note, we recruited patients who were specifically admitted to the hospital and about to be discharged home, therefore the included population might not be representative for the wider population of older people with frailty and complex care needs in the community.**

	can be considered a limitation of our study. We have therefore added this to the limitation section.	
7) The description of the randomisation is okay, and seems to have been done correctly. Its not clear whether this would be the planned method of randomisation for a definitive trial or whether a constrained randomisation would be used to ensure balance on patient characteristics.	We used a permuted block randomization technique to randomize patients to the intervention group or the control group. The same type of randomization technique would be used for a definitive trial to ensure balance on patient characteristics.	
8) I understand that masking of patients was not possible, but was it possible to blind people taking outcomes from the patients? If so, was this done? (It is not clear if this was the study investigators or not).	Those assessing the outcomes from patients were the same persons as whom conducted recruitment, and this might have led to biased results. Blinding would not be possible as some questions in the follow-up measurement of those in the intervention group were specifically about the specialised palliative care service. Also, during the follow-up measurement, patients could have told whom	p. 22, Discussion **There might also be detection bias, as the data managers and researcher were not blinded. A Cochrane review showed that there might be an overestimation of the effects of the intervention in non-blinded trials.(50)**

	from the specialised palliative care service visited them.	
9) The description of doing a "difference in mean change from baseline to follow-up" is quite different from the methods described – which seem to describe a difference in outcome at follow-up, after an allowance for baseline.	We have described in the Methods section that we assessed the differences in mean change from baseline to follow-up at 8-weeks between the intervention and control group, in which we used the baseline measure as an outcome measure and not as a covariate. We have explained in comment 10 why we have chosen to conduct a model with treatment arm, time, and its interaction rather than the ANCOVA approach or a model with time and its interaction with treatment arm.	
10) For this type of data (with observations on participants at baseline and follow-up), there are three possible analysis options: 1) ANCOVA approach, whereby a model is fitted to the follow-up outcome and the baseline outcome is a covariate in the model; 2) a model with treatment arm, time, and its interaction; 3) a model with time and its interaction with treatment arm. It would be interesting to know why you chose to do approach 2 here, as I think generally approaches 1 and 3 are recommended.	We have analysed our data using a generalized linear mixed model with treatment, time and its interaction as fixed effects. We have chosen this type of analysis as for the ANCOVA approach, it is not sure whether	

	the gain in efficiency still holds in the presence of missing data. ANCOVA assumes missingness completely at random because an observation is not included in the analysis if a baseline or a follow-up value is missing. Not including observations in the analysis would also be a violation of the intention-to-treat principle, i.e. not all observations would be used for this type of analysis. It is then possible to use multiple imputation to include all observations, and weaken the missingness mechanisms assumption to only missing at random, but then the question is if this approach would still be preferrable to a simpler approach (such as those described as approach 2 and 3). As for approach 3, we made the judgement that leaving out the main effect of treatment arm would be less	

	intuitive for some readers. This judgement is ofcourse subjective.	
11) Given this patient population, were there are monitoring of harms during the study period?	We have developed a distress protocol for the study (detailed description of the distress protocol has been presented in the study protocol of this study (de Nooijer et al, 2021)). We have monitored the harms mainly through this protocol. We have added the reference to this protocol in the results section. The distress protocol was not activated during the study period.	p. 15 Mechanisms of Change The distress protocol was not activated during the study period **(more information about the distress protocol can be found in the study protocol of Frailty+ (42)).**
12) I would perhaps expect to see more feasibility aspects related to outcome collection, such as response rates, completion rates, ability to collect information at planned time, etc. But there is no real mention of these in the methods section.	We agree with the reviewer that there are more feasibility aspects related to the outcome collection however, we have chosen to focus in this pilot RCT on a selection of important data collection aspects such as the number of patients and families who completed the baseline measurement, next to the other feasibility aspects which	

	we assessed in this pilot RCT (i.e. recruitment, randomization, and retention).	

VERSION 2 - REVIEW

Reviewer	**4**
Name	**Robinson-Reilly, Melissa**
Affiliation	**University of Newcastle School of Nursing and Midwifery**
Date	**24-Sep-2024**
COI	

Thank you for the opportunity to review this manuscript.

Palliative care is a progressive discipline globally, and noted are the changes which have been addressed for this manuscript. Reflected is the stigma still around palliative care and overcoming gatekeepers during recruitment to the RCT.

A minor word change is suggested - the use of "mentioned" - (16 times) - replacing would strengthen the context associated where used - stated, acknowledged, voiced - for example as an alternative. Another word change is "furthermore" (6 times) as detracts from the flow of the dialogue.

All the best.

Reviewer	**5**
Name	**Kalra, Saurabh**
Affiliation	**Rutgers University, Health Behavior Society and policy**
Date	**20-Sep-2024**
COI	

Thank you for resolving my comments/concerns.

Reviewer	**6**
Name	**Martin, James**

Affiliation	**University of Birmingham, Institute of Applied Health Research**
Date	**30-Sep-2024**
COI	

Thank you for submitting this revised paper, and for your responses to the reviewers' comments. I have some additional comments and queries related to the manuscript below:

On Table 2 (primary, secondary and exploratory outcome measures), this gives the indication that the primary outcome of the pilot study is a comparison between arms of a palliative care composite outcome. Whilst I appreciate this is just for the "preliminary effects" part of the objectives, it currently reads as though this is the primary outcome of the whole pilot study. Since this is a pilot study, the primary outcome should not be a comparison between arms, as this study is not powered to detect a difference in outcomes. The primary outcome should be related to understanding prevalence/drop-out rate/ability to recruit and randomise, or something related to the pilot part of the design.

The methods describe the outcomes that are relevant for objective 2, but there is no description in the methods of how this will be calculated or reported. More generally, I would like to see a clearer description of the methods for each of the aims of the pilot study.

Further, it should be clearer how these outcomes help inform the future definitive trial. I worry that it otherwise looks as though you are trying to do a definitive trial without the required sample size, since the focus seems to be on the "preliminary effects".

The methods for the statistical analysis of objective 3 are very detailed. There is more focus here though on finding a difference between groups, rather than reporting the completeness of them, or reporting the mean outcome – which might be useful to help guide the sample size for a definitive trial.

That being said, I found part of the preliminary effects under data analysis to be a little confusing. From the outcomes, it seemed that the outcome was a continuous outcome. Yet you have modelled it as a count outcome and allowed for over-dispersion. But there is not anything mentioned about this.

On Table 2, you use several acronyms. Can these please be explained in a caption under the table.

On Table 3, the rows for "How many people outside the household have given any kind of personal care or practical help" don't quite match up (the numbers and % are one row lower down).

In Table 5 and supplementary Table 1, it is unclear why you had reported mean and 95% confidence intervals and not mean and SD.

VERSION 2 - AUTHOR RESPONSE

REVIEWER 5		
1) Thank you for resolving my comments/concerns.	Thank you.	
REVIEWER 4		
1) Thank you for the opportunity to review this manuscript. Palliative care is a progressive discipline globally, and noted are the changes which have been addressed for this manuscript. Reflected is the stigma still around palliative care and overcoming gatekeepers during recruitment to the RCT.	Thank you for emphasizing the key messages of the study.	
2) A minor word change is suggested - the use of "mentioned" - (16 times) - replacing would strengthen the context associated where used - stated, acknowledged, voiced - for example as an alternative. Another word change is "furthermore" (6 times) as detracts from the flow of the dialogue.	Thank you for noticing. We have made some changes to these words throughout the manuscript.	
REVIEWER 6		
1) Thank you for submitting this revised paper, and for your responses to the reviewers' comments. I have some additional comments and queries related to the manuscript below:	Thank you for your comprehensive evaluation of the manuscript.	
2) On Table 2 (primary, secondary and exploratory outcome measures), this gives the indication that the primary outcome of the pilot study is a comparison between arms of a palliative care composite outcome. Whilst I appreciate this is just for the "preliminary effects" part of the objectives, it currently reads as though this is the primary outcome of the whole pilot study. Since this is a pilot study, the primary outcome should not be a comparison between arms, as this study is not powered to detect a difference in outcomes. The primary outcome should be related to understanding prevalence/drop-out rate/ability to recruit and randomise, or something related to the pilot part of the design.	We fully agree with this. The primary outcomes of this pilot RCT were related to the feasibility of the trial methodology as well as to the implementation of the intervention in practice. The secondary outcomes were then the family and patient outcomes, which we divided in primary, secondary and exploratory outcomes for potential use in a future full-scale RCT, if the study proves to be feasible and implementable. However, we understand the confusion this might have raised to the reader. We have therefore adapted the language throughout the manuscript.	<u>p.2, Abstract: Objective</u> Objective: **The primary study aims were to evaluate** the implementation, mechanisms, and context of a timely short-term specialised palliative care intervention for older people with frailty (Frailty+ intervention) **as well as to assess** the feasibility of a randomised controlled trial to evaluate Frailty+. **Our secondary aim was to describe any preliminary effects of Frailty+.** <u>p.2, Abstract: Outcome measures</u> The primary outcome **to be used in a potential full-**

The methods describe the outcomes that are relevant for objective 2, but there is no description in the methods of how this will be calculated or reported. More generally, I would like to see a clearer description of the methods for each of the aims of the pilot study.	Most of the outcome descriptions the reviewer is asking were included in the tables but not in the text. We have now elaborated on outcome reporting and calculation for the primary and secondary outcomes in the text, as well as added extra details. In addition, we have rearranged the paragraphs to first mention the outcomes measured followed by the explanation of the data collection procedures.	**scale trial if the study is feasible and implementable** was mean change in five palliative care symptoms over 8 weeks. p.2, Abstract: Results The baseline mean score on the **five palliative care symptoms** was 6.0 and 5.6 in intervention and control group, respectively; and 4.5 and 4.1 at 8 weeks (adjusted ratio 1.0, i.e. no effects on symptoms). p.5, Introduction We conducted a pilot RCT with an embedded process evaluation with the **primary** aim**s** to: 1) evaluate the implementation, underlying mechanisms of change, and the contextual factors potentially affecting implementation and outcomes of the Frailty+ intervention **and;** 2) assess the feasibility of the methods and procedures of the pilot RCT, specifically recruitment and randomisation procedures, retention, and missing data. **The secondary aim was to:** 3) test the preliminary effects of the Frailty+ intervention in older people with frailty and their family carers. p.9, Methods: Implementation, mechanisms of change and contextual factors **(Primary aim)** **The primary outcomes of this study included the 'dose' of the intervention components that were**

		delivered as well as the adaptations that were made to the initial intervention description, the experiences with the intervention of the stakeholders, including the unexpected events, and the factors that influenced the outcomes and implementation of the intervention according to the stakeholders. An overview of the collected data, methods, and timing of data collection is given in Table 1. This data was collected in the intervention group only. p.10, Methods: Feasibility of the RCT methods **(Primary aim)** **The other primary outcomes of this study were related to** the feasibility of the RCT methods. **More specifically, we assessed the recruitment and randomisation procedures by reporting the following: 1) number of eligible, approached, enrolled and randomised patients and family carers; 2) number and characteristics of eligible patients and family carers not approached or not enrolled, and reasons for not approaching them or for patients' or family carers' refusal to participate; 3) patients', families' and GPs' views of the information letter and informed consent procedure; 4) mobile geriatric teams' and geriatricians' views of and experiences with the inclusion criteria and their application, and with the procedure of**

		introducing the study to patients and; 5) patients', family carers' and GPs' views of and experiences with the randomisation procedure. The recruitment rate was calculated as the number of participants randomised divided by the number of approached participants. We also evaluated the study retention and data collection procedures by reporting the following: 1) number of patients, family carers and GPs who dropped out of the study, and reasons for dropping out (if stated); 2) number of patients and family carers who completed the baseline /follow-up assessment or reasons for not completing it (if stated) and; 3) patients' and family carers' views of and experiences with completing baseline and follow-up assessments. We calculated the retention rate as the number of participants who completed the follow-up assessment divided by the number of randomised participants. p.10, Methods: Preliminary effects of the Frailty+ intervention **(Secondary aim)** **The** secondary aim of this pilot RCT was to evaluate **preliminary** effects of the Frailty+ intervention. This is considered a preliminary effects study, as this pilot RCT is not statistically powered to determine the effectiveness of Frailty+. All **secondary** outcomes **related to the preliminary**

		effects evaluation were identified through stakeholder input and previous literature (21). The research team then classified **them** as primary, secondary, or exploratory **outcomes for potential use in a future full-scale RCT if the study is considered as feasible and implementable (outcomes are described in Table 2).** p. 17, Results: Participant flow, recruitment **and retention** However, as the foreseen sample size for this pilot RCT whose main aim was to test the feasibility of the trial methods **as well as to assess the implementation of the intervention in practice**, was not based on a statistical power calculation, we performed the data analyses as planned with 37 patients. We were convinced that this number would allow us to determine the main strengths, **issues and challenges** in feasibility and **implementation,** as well as to describe any preliminary intervention effects. p.17, Results: Preliminary effects of Frailty+ As this was a pilot RCT, we evaluated preliminary effects of the Frailty+ intervention. The estimated mean sum score on the primary outcome **to be used in a potential full-scale RCT if the study proves to be feasible and implementable** (five key IPOS palliative care symptoms; range 0 – 20) was 6.0 in the intervention

		group and 5.6 in the control group at baseline, and 4.5 in the intervention group and 4.1 in the control group 8-weeks post-baseline (adjusted ratio 1.0, i.e. no effect of Frailty+ over time on the mean sum score compared to standard care alone) (Table 5). p.21, Discussion Our analysis of **preliminary** effects of Frailty+ showed no effects on primary or secondary outcomes **potentially to be used in a full-scale trial.** p. 28, Table 1. Process evaluation: Data collected, methods and timing of data collection **(Primary aim)** p.30, Table 2. **Preliminary effects evaluation: outcomes, measures and respondents (Secondary aim)** Primary outcome **potentially to be used in a full-scale RCT** Secondary outcomes **potentially to be used in a full-scale RCT** Exploratory outcomes **potentially to be used in a full-scale RCT** p. 36, Table 5. Estimated mean changes in primary and secondary outcomes **potentially to be used in a full-scale RCT** from baseline to 8-weeks Primary outcome **potentially to be used in a full-scale RCT** Secondary outcomes **potentially to be used in a full-scale RCT**

		Supplementary Table 1. Estimated mean changes exploratory endpoints **potentially to be used in a full-scale RCT** from baseline to 8-weeks Patient exploratory outcomes **potentially to be used in a full-scale RCT** Family carer exploratory outcomes **potentially to be used in a full-scale RCT**
3) Further, it should be clearer how these outcomes help inform the future definitive trial. I worry that it otherwise looks as though you are trying to do a definitive trial without the required sample size, since the focus seems to be on the "preliminary effects".	We fully agree that it was not clear how these outcomes then helped to inform the future definitive trial. We have chosen not to use specific criteria or quantitative measures only to decide whether to continue with a full-scale RCT, but the research team provided an integrated understanding of the qualitative and quantitative findings to inform the definitive trial. We have explained this in the Data analysis section.	p. 11, Methods: Data analysis **The researchers discussed the qualitative and quantitative findings during several research meetings to come to an integrated understanding and decision about whether, and how, to continue with a full-scale RCT.**
4) The methods for the statistical analysis of objective 3 are very detailed. There is more focus here though on finding a difference between groups, rather than reporting the completeness of them, or reporting the mean outcome – which might be useful to help guide the sample size for a definitive trial.	We have focused on data collection completion in the feasibility aim. We assessed various quantitative and qualitative aspects related to this, for instance the number of participants who completed the baseline measurement and the experiences of participants with completing the baseline measurement. In the data analysis section of the preliminary effects evaluation, we indeed describe in detail that differences between the intervention- and controlgroup were tested using generalized linear mixed model analysis. However, we also reported that we calculated the mean outcomes, which could be useful for the sample size calculation in a full-scale RCT.	

5) That being said, I found part of the preliminary effects under data analysis to be a little confusing. From the outcomes, it seemed that the outcome was a continuous outcome. Yet you have modelled it as a count outcome and allowed for over-dispersion. But there is not anything mentioned about this.	We have clarified in the preliminary effects analysis section of the manuscript that, dependent on the endpoint, a negative binomial distribution or a normal distribution with identity link was used.	p. 11, Methods: Data analysis **Depending on the endpoint, a normal distribution with identity link or a** negative binomial distribution with log link was used.
6) On Table 2, you use several acronyms. Can these please be explained in a caption under the table.	We have explained the acronyms used in the tables in captions below each respective table.	p. 29, Table 1 **GP, general practitioner** p. 31, Table 2 **IPOS, Integrated Palliative Care Outcome Scale: ICECAP-SCM, ICEpop CAPability measure for supportive care: GP, general practitioner** p. 35, Table 4 **GP, general practitioner** p. 37, Table 5 **CI, confidence interval: IPOS, Integrated Palliative Care Outcome Scale: ICECAP-SCM, ICEpop CAPability measure for supportive care: SEC-P, Sense of Security in Care – Patients: SEC-R, Sense of Security in Care – Relatives: FACQ-PC, Family Appraisal of Caregiving Questionnaire for Palliative Care**
7) On Table 3, the rows for "How many people outside the household have given any kind of personal care or practical help" don't quite match up (the numbers and % are one row lower down).	We have clarified this in Table 3.	p. 32-33, Table 3 7 (36.8) 4 (21.**1)** 0 2 (10.5) 6 (31.6)
8) In Table 5 and supplementary Table 1, it is unclear why you had reported mean and 95% confidence intervals and not mean and SD.	We decided, in consultation with the statistician (and as reported in the statistical analysis plan of Frailty+), to calculate and report the mean	

	and the 95% confidence intervals in Table 5 and the appendix Table 1 as these were needed to answer our research question related to the preliminary effects of the Frailty+ intervention. This way of reporting has also been described in the CONSORT 2010 statement extension to pilot and feasibility trials (item 12a), namely *"typically, any estimate of effect using participant outcomes … would be reported as estimates with 95% confidence intervals"* (Eldridge et al., 2016).	

Additional changes:
p.12, Results: Participant flow, recruitment **and retention** Of these, 37 (25%) were randomised to standard care plus Frailty+ (19 patients) or standard care alone (18 patients). Ultimately, 28 patients **(76%)** completed measurements after eight weeks (intervention n=16 and control n=12).