PEER REVIEW HISTORY

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

ARTICLE DETAILS

TITLE (PROVISIONAL)	Improvement of perioperative care of the elderly patient (PeriAge): protocol of a controlled interventional feasibility study
AUTHORS	Olotu, Cynthia; Lebherz, Lisa; Härter, Martin; Mende, Anna; Plümer, Lili; Goetz, Alwin E; Zöllner, Christian; Kriston, Levente; Kiefmann, Rainer

VERSION 1 – REVIEW

REVIEWER	Patricia Tejedor Queen Alexandra Hospital, Portsmouth, UK.
REVIEW RETURNED	26-Jun-2019

GENERAL COMMENTS	I would like to congratulate the authors, as the study and the methodology are well desinged and explained. The objective is clear and addresses a common concern when operating elderly population. I have some minor comments: - The abstract is not clear enough. You mentioned a program based on different interventions, but I am not certain what kind of interventions you mean by reading only the abstract. It would be nice to explain a bit more about the PeriAge protocol here. - Figure 1 is not very clear as it is. I would rather delete it or modify in a way everybody can understand the risks factors you are actually mention. - Are the patients including in the study under an Enhanced Recovery program (ERAS) after surgery? Do you usally include elderly population in the ERAS? If so, please state this in the methods section. - If not all of them are included or it will depend on different specialties/surgeons, it could be a bias when analyzing your postoperative outcomes, and so, this bias should be included in the limitations of the study.

REVIEWER	Geeta Aggarwal Royal Surrey County Hospital UK
REVIEW RETURNED	02-Jul-2019

GENERAL COMMENTS	It seems like an interesting study. I think some further clarification on the intervention, implementation group would be helpful. 65+ is quite a young age and the measurements would ideally have been more in the time between 30 and 180 days.

REVIEWER	Leila Mureebe Duke University Health System

REVIEW RETURNED	04-Jul-2019

GENERAL COMMENTS	well referenced, well thought out study

REVIEWER	Thomas O. Dalton, MD UT Southwestern Medical Center
REVIEW RETURNED	29-Jul-2019

GENERAL COMMENTS	This is a well-designed and practical feasibility study for the implementation of a complex program aimed at improving broad outcomes. The primary outcome of change in autonomous functioning (Lawton IADL scale) at 6 months is laudable and patient-relevant as are the secondary outcomes. Below are my comments: 1. The exclusion criteria are reasonable, but I question the exclusion of patients who are anticipated to require postoperative intensive care and patients with chronic use of benzodiazepines as these patients are seemingly at increased risk of POC and functional decline and perhaps therefore have the most to gain from a more intensive preoperative evaluation and management approach. 2. Regarding sample size, I think the types of surgery will be important as it regards expected functional decline rates and POCs. The exclusion criteria do a reasonable job of targetting a group of patients that are at least moderate risk, but I would try to include patients who are anticipated to have more complicated post-op courses and longer hospital stays as I think the intervention is more likely to have the largest effect size in these patients.

VERSION 1 – AUTHOR RESPONSE

PATRICIA TEJEDORS COMMENTS

I would like to congratulate the authors, as the study and the methodology are well designed and explained. The objective is clear and addresses a common concern when operating elderly population.
I have some minor comments:
- The abstract is not clear enough. You mentioned a program based on different interventions, but I am not certain what kind of interventions you mean by reading only the abstract. It would be nice to explain a bit more about the PeriAge protocol here.
Thank you for your comments and suggestions. Please see the revised abstract, page 2. I hope we could clarify the intervention and protocol to the reader's satisfaction.
- Figure 1 is not very clear as it is. I would rather delete it or modify in a way everybody can understand the risks factors you are actually mention.
We have decided to delete this figure as its information can be also found in the main text and we want to avoid confusion for the reader.
- Are the patients including in the study under an Enhanced Recovery program (ERAS) after surgery? Do you usually include elderly population in the ERAS? If so, please state this in the methods section.
- If not all of them are included or it will depend on different specialties/surgeons, it could be a bias when analyzing your postoperative outcomes, and so, this bias should be included in the limitations of the study.

Thank you for your commitment and your attentive review. Although the ERAS program is gaining popularity among many hospitals in Germany, it is still not implemented in full scale in a majority of surgical departments. While its rational and its patients are overlapping with our study procedure and aim, it is independent of the reported study. The introduction of ERAS within the University Medical Centre Hamburg-Eppendorf has not consistently happend yet for all wards but only a selection of surgical procedures are following ERAS: esophagectomy, pancreatectomy and ovarian cancer surgery. Inclusion in the ERAS programme was indeed a criterion for exclusion in our trial, so patients scheduled for these procedures were not enrolled. We have added a description of this exclusion criterion in the revised manuscript; please see page 5. Thank you for pointing this out for us. This of course also means, that we will have to and will be careful in interpreting the results, and mention it in the limitation section of the manuscripts evaluating the intervention, due to potential bias and carry over effects, especially within the control group and the interpretation of the feasibility. It will be included into the study limitations section.

GEETA AGGARWALS COMMENTS

It seems like an interesting study. I think some further clarification on the intervention, implementation group would be helpful.
65+ is quite a young age and the measurements would ideally have been more in the time between 30 and 180 days.
Thank you for your critical comment and suggestion of clarification and suggestion of time points. We have extended our description of the groups at page 6 of the revised manuscript.
While many patients aged 65+ are quite healthy and physically fit and profit less from such interventions as the one introduced here, in gerontological research such age groups are common. The patient group at 65 years and above is the one most heterogenous concerning differences between biological and chronological age. The intervention of our trial consisted of a screening of risk factors and an individualised selection of preventive measures for those at risk. Another rational for choosing this age group starting at 65+ is the comparability with other studies and interventions.
We acknowledge that more testings between the two follow up testings would be ideal. However, as our research focusses on a vulnerable patient group, we did not render it feasible to invite patients (some of which are impaired in their mobility and some having to travel quite a distance to the medical centre) for an extensive testing that in turn is demanding.
LEILA MUREEBES COMMENTS
well referenced, well thought out study
Thank you for your review.
THOMAS O. DALTONS COMMENTS
This is a well-designed and practical feasibility study for the implementation of a complex program aimed at improving broad outcomes. The primary outcome of change in autonomous functioning (Lawton IADL scale) at 6 months is laudable and patient-relevant as are the secondary outcomes. Below are my comments:
1. The exclusion criteria are reasonable, but I question the exclusion of patients who are anticipated to require postoperative intensive care and patients with chronic use of benzodiazepines as these patients are seemingly at increased risk of POC and functional decline and perhaps therefore have the most to gain from a more intensive preoperative evaluation and management approach.
Thank you for your valuable comments.
Concerning ICU: Unfortunately, organisational and methodical reasons made it impossible for us to include these patients. The patients would not have been comparable to non-ICU-patients in the first days following surgery due to different medication, frequent sedation, mobilisation and ward routine. Generally our main aim is to show that the intervention can be realised within the clinical routine care rather than show how much patients benefit from the intervention. Therefore we aimed at a broad sample, representing the typical 65+ patient at our wards.

Concerning benzodiazepines: One interventional measure was the general refrainment from administering benzodiazepines. Due to administrative, medical and ethical reasons this would not have been feasible for this patient group. Additionally, as they have a direct impact on cognitive performance, thus biasing the (neuropsychological) testing.

2. Regarding sample size, I think the types of surgery will be important as it regards expected functional decline rates and POCs. The exclusion criteria do a reasonable job of targeting a group of patients that are at least moderate risk, but I would try to include patients who are anticipated to have more complicated post-op courses and longer hospital stays as I think the intervention is more likely to have the largest effect size in these patients.
We agree with you on the importance of type of surgery. As we have a small sample only, for the exploratory analyses we plan to cluster type of surgery into clusters of invasiveness as we assume that to be a most indicative surgery parameter for potential post-operative complications.
We do not recruit patients based on anticipated complications and longer inpatient stays, but try to gather a representative patient cohort of a large hospital in a metropolitan region. However, we believe that patients who are anticipated to have more complicated post-op courses and longer hospital stays particularly benefit from our intervention. We believe that we will have some variability in our sample, including patients with more complicated post-surgery courses and longer hospitalisations.

VERSION 2 – REVIEW

REVIEWER	Patricia Tejedor Queen Alexandra Hospital, Portsmouth, UK.
REVIEW RETURNED	14-Sep-2019

GENERAL COMMENTS	The authors kindly review the paper and address all my comments and suggestions.