PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A Perioperative Mental Health Intervention Bundle for Older Surgical Patients: Protocol for an Intervention Development and Feasibility Study
AUTHORS	Abraham, Joanna; Holzer, Katherine; Lenard, Emily; Freedland, Kenneth E; Tellor Pennington, Bethany; Wolfe, Rachel; Cordner, Theresa; Baumann, Ana; Politi, Mary; Avidan, Michael; Lenze, Eric

VERSION 1 – REVIEW

REVIEWER	Laferton, Johannes Psychologische Hochschule Berlin, Clinical Psycology and Psychotherapy
REVIEW RETURNED	25-Mar-2022

GENERAL COMMENTS	The authors present a study protocol for a feasibility and intervention development study regarding a multi-component (behavioral activiation and medication optimization) perioperative intervention for elderly particcipatns undergoing major surgical procedures. Study rational, design andmethods are presented in a detailed and clear mannor. I have only minor comments. Point 1: It took me quite a while to understand that this trails main goal is to a) assess feasibilty of a specific intervention for elderly patients undergoing surgery and b) to furhter optimize the intervention during the study. I think the titel and the abstract could be more direct about this. "Designing mental health interventions..." sounds like general methodological advice How about soemthing like "A Perioperative behaviroarl activation and medication optimization intervention for elderly patients undergoing major surgery: An intervention development and feasibility study" Point 2: Methods section/study desing. Not everyone is familiar with this kind of study desing. It would be helpful (at least to me) if study design would be the first part of the methods section and if study design could be displayed in more detail. What is a "parallel convergent study design". So far I assume all recruited patients will be included in an intervention arm. Are there other study arms etc. plase elaborate patient flow throughout the study. Point 3: Assessment: Please detail all Assessment time points in the method section. One could deduce this from table 3 yet stating the overall assessment schedule once might help the reader ...

	Point 4: Primary Outcome: The authors define axiety and depression as Primary outcome. A) this should be more specific. Is it change in anxiety and depression? b) having quantitative primary outcomes is quite unusual for a feasibility trail given the small sample size (the authors refer to this themselves). This is similar for secondary outcomes. Isn't the primary outcome a feasibility study wether the study is feasible and acceptable to patients (i.e. what the authors refer to as reach and implementation potential and process in table 3). Point 5: Check references 39 and 40. They do not seem to uniquely identifiable the way they are presented.

REVIEWER	Van Tiem, Jennifer VA Iowa City Healthcare System
REVIEW RETURNED	03-Apr-2022

GENERAL COMMENTS	Thank you for sharing this well-described and clear protocol. It was a pleasure to read. My only thought was that you might generate some interesting data if you do CFIR Interviews during the study, as well as at the end of the study. Often barriers and facilitators change or disappear, and it could be helpful to be able to describe how that happens.

REVIEWER	Hegland, Pål André Western Norway University of Applied Sciences - Forde Campus
REVIEW RETURNED	04-Apr-2022

GENERAL COMMENTS	Thank you for the opportunity to review this protocol. The authors are planning an important study to improve the outcomes of elderly patients undergoing surgery, focusing on improving anxiety and depression and reviewing the patients´ medications associated to these conditions. The authors have made a good job in presenting the feasibility study, however I have a few comments to the manuscript. Introduction The authors state that elderly patients are at higher risk of postoperative morbidity and mortality than younger people. It will strengthen the rationale if the authors show how preoperative anxiety and depression is affecting this risk. Designing the intervention bundle I would like to see some more information on the intervention. For example – how are the patients taught the behavioral intervention, how often do they consult the Perioperative Wellness Partner and for how long each time. I find this information important so the reader can make an assessment if this intervention can realistically be implemented into routine practice. If find this information in Appendix B, however some of this information should be provided in text. The authors describe user involvement by patients and caregivers in an advisory board. It would strengthen the protocol if the authors could elaborate on how the patients and caregivers affected the final intervention bundle to show if there has been real user involvement and not just including them to “approve” a finished bundle. Initial adaptations to intervention bundle The authors have two subheadings. Under the subheading Medication optimization, the text from line 46 does not seem to

	belong under this headline? Could the authors create a new headline for this content? Study objective 1 is about to make the intervention patient-centered, and on page 11 the authors state that this information will be gathered through qualitative surveys. I would appreciate if the authors could explain in more details how this survey is performed and how these data are used to make the intervention more patient-centered. The quantitative part of the study is explained fairly detailed. In Table 3 the authors list all the primary and secondary outcomes, and in the abstract the authors list clinical outcomes as depression, anxiety, quality of life, delirium, falls, length of stay, hospitalization and pain to be collected. On page 11 the authors list the assessment measures, demographics, medical history, pain, SBT and UB-CAM. It is somewhat confusing to me how QOL, falls, length of stay and hospitalization is used. Are these outcome measures for the planned RCT, or are they used in any way in the feasibility study? On page 15 the authors state that they will report pre-post change and effect size. How will this information be used in this feasibility study? I also miss information on how the questionnaires are distributed – are they sent home to patients, or are they filled out when the patient meets for an consultation? Digital or paper questionnaires? What about those patients not being able to complete the questionnaires, will they receive any assistance? In table 3 there is information on the timepoints where the different outcome measures are collected. I miss some more of this information in the text. The authors state that they will perform a mixed-methods study, however there is sparse information about the qualitative part. I would like more information on how the qualitative study is performed. In-depth interviews or focus groups? On phone or face to face? The authors have described how to recruit patients and clinicians – will the caregivers be recruited through the patients? Tables should as a general rule could be able to read without reading the text. There are several abbreviations not explained in the tables.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1 Dr. Johannes Laferton, Psychologische Hochschule Berlin	**Author Response**
The authors present a study protocol for a feasibility and intervention development study regarding a multi-component (behavioral activation and medication optimization) perioperative intervention for elderly participants undergoing major surgical procedures. Study rational, design and methods are presented in a detailed and clear manner. I have only minor comments.	Thank you for your comments. We have addressed all of the concerns that were raised.

Point 1: It took me quite a while to understand that this trails main goal is to a) assess feasibility of a specific intervention for elderly patients undergoing surgery and b) to further optimize the intervention during the study. I think the title and the abstract could be more direct about this. "Designing mental health interventions..." sounds like general methodological advice How about something like "A Perioperative behavioral activation and medication optimization intervention for elderly patients undergoing major surgery: An intervention development and feasibility study"	We agree that our title could more appropriately represent the study objectives and, as such, have changed it to "**A Perioperative Mental Health Intervention Bundle for Older Surgical Patients: Protocol for an Intervention Development and Feasibility Study"** We have also revised the abstract and the protocol manuscript to state the main goals of this study.
Point 2: Methods section/study design. Not everyone is familiar with this kind of study design. It would be helpful (at least to me) if study design would be the first part of the methods section and if study design could be displayed in more detail. What is a "parallel convergent study design". So far I assume all recruited patients will be included in an intervention arm. Are there other study arms etc. Please elaborate patient flow throughout the study.	Thank you for pointing this out. We agree more details about this approach are necessary. We have revised the Methods section to first introduce the study design and approach. We have described the approach in more detail. Briefly, the convergent-parallel approach is one in which qualitative and quantitative data are collected simultaneously. They are then combined and compared for the subsequent interpretation of both types of data (Creswell & Clark, 2017). The reviewer is correct in their interpretation that all enrolled patients will be getting the intervention bundle. There are no study arms in this study as it is a feasibility study. **Reference** Creswell, J. W., & Clark, V. L. P. (2017). Designing and conducting mixed methods research. Sage publications.
Point 3: Assessment: Please detail all Assessment time points in the method section. One could deduce this from table 3 yet stating the overall assessment schedule once might help the reader ...	We apologize for the limited clarity. To address this comment, we have clarified in the revised Methods section, the assessments that will be collected at baseline and have indicated which measures are collected more than once. We have also further divided these sections to: "baseline assessment measures" and "outcome measures and timeline," rather than combining them into one section as was done in the original manuscript.

Point 4: Primary Outcome: The authors define anxiety and depression as Primary outcome. A) this should be more specific. Is it change in anxiety and depression? b) having quantitative primary outcomes is quite unusual for a feasibility trail given the small sample size (the authors refer to this themselves). This is similar for secondary outcomes. Isn't the primary outcome a feasibility study whether the study is feasible and acceptable to patients (i.e. what the authors refer to as reach and implementation potential and process in table 3).	Thank you for pointing this out. We agree with the reviewer that this is a feasibility study and our focus in this study should be on the feasibility of the study, and implementation-potential of the intervention bundle. As the reviewer correctly points out, our outcomes (primary and secondary) listed in this protocol will not yield any meaningful conclusions given the small sample size and the lack of a usual (control) arm. In this feasibility trial, we are only able to ascertain whether the study is feasible; whether we are able to collect the outcomes that are planned for a future RCT; whether the intervention bundle is acceptable and appropriate for this population; and the adaptations that need to be made in order to be effective for reducing anxiety and depression for older surgical patients. In other words, insights gained from this feasibility study will allow us to refine our study procedures, outcomes and also allow us to adapt the intervention bundle to make it more patient-centered. To address this comment, we have revised the outcomes in the paper to reflect the feasibility of collecting such outcomes and implementation-potential outcomes.
Point 5: Check references 39 and 40. They do not seem to uniquely identifiable the way they are presented.	Thank you for pointing this out. We have replaced these two citations with publications that describe the two approaches that are referenced.
Reviewer 2 Dr. Jennifer Van Tiem, VA Iowa City Healthcare System	**Author Response**
Thank you for sharing this well-described and clear protocol. It was a pleasure to read. My only thought was that you might generate some interesting data if you do CFIR Interviews during the study, as well as at the end of the study. Often barriers and facilitators change or disappear, and it could be helpful to be able to describe how that happens.	Thank you for your review and positive feedback. This is a great suggestion – we agree with the reviewer that barriers and facilitators may manifest in different ways at different times of the study/intervention bundle (mid-study vs. end-study). To address this, we will include CFIR interviews during and at the end of our planned RCT study.
Reviewer 3	**Author Response**

Dr. Pål André Hegland, Western Norway University of Applied Sciences - Forde Campus	
Thank you for the opportunity to review this protocol. The authors are planning an important study to improve the outcomes of elderly patients undergoing surgery, focusing on improving anxiety and depression and reviewing the patients´ medications associated to these conditions. The authors have made a good job in presenting the feasibility study, however I have a few comments to the manuscript.	We appreciate your input and comments. We have addressed the concerns and believe that our paper is strengthened as a result of these changes.
Introduction The authors state that elderly patients are at higher risk of postoperative morbidity and mortality than younger people. It will strengthen the rationale if the authors show how preoperative anxiety and depression is affecting this risk.	We agree this information strengthens our rationale. We have revised the introduction and expanded our discussion of the existing literature demonstrating how perioperative anxiety and depression significantly increase the risk of postoperative complications and mortality.
Designing the intervention bundle I would like to see some more information on the intervention. For example – how are the patients taught the behavioral intervention, how often do they consult the Perioperative Wellness Partner and for how long each time. I find this information important so the reader can make an assessment if this intervention can realistically be implemented into routine practice. If find this information in Appendix B, however some of this information should be provided in text.	We have added a clearer and more detailed description of the behavioral activation model, including the timing, format, and frequency of sessions as well as the reference to the manual that guided our practice.
The authors describe user involvement by patients and caregivers in an advisory board. It would strengthen the protocol if the authors could elaborate on how the patients and caregivers affected the final intervention bundle to show if there has been real user involvement and not just including them to “approve” a finished bundle.	Our Internal Advisory Board members are integral to this study and are members of our research team. We agree it is important to demonstrate their meaningful engagement and the value they have brought to this study. In the revised manuscript, section “Designing the Intervention Bundle: Adaptation Process” we now fully describe the 3 meetings held with IAB members, including the focus of each meeting which ultimately led to meaningful changes in the intervention bundle. Key examples of IAB input that informed our intervention bundle include: (a) focus on supporting two phases: patient preparedness (pre-operative phase) and enhancing recovery (post-operative phase); (b) choice of term to refer to study interventionists

	(partners instead of interventionists); (c) revised term of our medication optimization and deprescription (MOD) component to medication optimization. In addition, our IAB members provided several suggestions for patient recruitment and enrollment strategies.
Initial adaptations to intervention bundle The authors have two subheadings. Under the subheading Medication optimization, the text from line 46 does not seem to belong under this headline? Could the authors create a new headline for this content?	We have revised the structure of this section to describe first the components of the intervention bundle in its own subsection followed by the "Initial adaptations" subsection.
Study objective 1 is about to make the intervention patient-centered, and on page 11 the authors state that this information will be gathered through qualitative surveys. I would appreciate if the authors could explain in more details how this survey is performed and how these data are used to make the intervention more patient-centered.	We apologize for the limited clarity about the qualitative methods (interviews and surveys). Patients and caregivers will be interviewed at the end of the study to gather their perspectives on the study, their experiences with the intervention bundle components (behavioral activation and medication optimization), their interactions with the perioperative wellness partners, with specific focus on any barriers and facilitators affecting their use of our intervention bundle. We also administer the Modified-Consumer Assessment of Healthcare Providers and Systems (CAHPS), the Collaborate Survey, Acceptability of Intervention Measure, Intervention Appropriateness Measure, and Feasibility of Intervention Measure to gather their overall surgical experience and implementation measures of acceptability, feasibility and appropriateness. These interviews and surveys will be administered by a qualitative expert (first author, JA) and a research assistant with qualitative training over phone or zoom (based on patient preference). Our intervention bundle has two types of components – core components (that will not be subject to any modifications) and flexible components (that will be tailored based on patient preferences and needs). The qualitative analysis will help us identify the components that are acceptable and feasible for our patient population – which will then be used to tailor the bundle and make it more patient-centered as opposed to a one-size-fits-all intervention.

	To address this comment, we have elaborated on this in our analysis section. Thank you for bringing this up.
The quantitative part of the study is explained fairly detailed. In Table 3 the authors list all the primary and secondary outcomes, and in the abstract the authors list clinical outcomes as depression, anxiety, quality of life, delirium, falls, length of stay, hospitalization and pain to be collected. On page 11 the authors list the assessment measures, demographics, medical history, pain, SBT and UB-CAM. It is somewhat confusing to me how QOL, falls, length of stay and hospitalization is used. Are these outcome measures for the planned RCT, or are they used in any way in the feasibility study? On page 15, the authors state that they will report pre-post change and effect size. How will this information be used in this feasibility study?	This is a valid concern that other reviewers also have raised. The primary and secondary outcomes in Table 3 are of interest and potential outcomes for our planned RCT pilot study. We apologize for the confusion. Given that this is a feasibility study, we have revised our outcomes Table 3 to reflect the feasibility outcomes instead of the actual clinical outcomes. We will be assessing the reach of our study and our intervention bundle (i.e., primary outcome), the feasibility of collecting depression and anxiety outcome planned for our randomized control trial (i.e., secondary outcome) and implementation-potential of intervention bundle and other outcomes such as quality of life, readmissions (i.e., exploratory outcomes). The Behavioral Activation for Depression Scale, or BADS, is our primary measure of target engagement. We have revised the paper to reflect this.
I also miss information on how the questionnaires are distributed – are they sent home to patients, or are they filled out when the patient meets for an consultation? Digital or paper questionnaires? What about those patients not being able to complete the questionnaires, will they receive any assistance?	Patients have the option to receive the questionnaires via email if they consent to it. In all other instances, the research coordinators administer the questionnaires over the telephone. We have added this detail to our revised protocol.
In table 3 there is information on the timepoints where the different outcome measures are collected. I miss some more of this information in the text.	The revised “Outcome measures and timeline” section includes a more detailed description in the text of the outcome measures presented in Table 3. This is limited due to word count, but we have expanded on this in the revised protocol.
The authors state that they will perform a mixed-methods study, however there is sparse information about the qualitative part. I would like more information on how the qualitative study is	We appreciate the opportunity to expand on this important component of our protocol. Briefly, we will conduct semi-structured interviews along with the Modified-Consumer Assessment of Healthcare Providers and Systems (CAHPS), the Collaborate Survey, Acceptability of Intervention

performed. In-depth interviews or focus groups? On phone or face to face?	Measure, Intervention Appropriateness Measure, and Feasibility of Intervention Measure with patients and their caregivers. The qualitative analysis will help us identify the components that are acceptable and feasible for our patient population – which will then be used to tailor the bundle and make it more patient-centered as opposed to a one-size-fits-all intervention. Interviews will be conducted via Zoom or telephone and will be digitally recorded and transcribed verbatim. We have added this to the revised manuscript.
The authors have described how to recruit patients and clinicians – will the caregivers be recruited through the patients?	***We apologize for excluding this description. We have updated the study participants and recruitment procedure section to include a description of caregiver recruitment. It is also described below.*** **Patients may refer their caregivers (e.g., spouse, partner, children, friend) to contact the study team if interested, or if they prefer to share the caregiver's phone number, the study team will contact them by phone and invite them. With the patients' consent, patients' caregivers are also invited to participate by phone, or mail.**
Tables should as a general rule could be able to read without reading the text. There are several abbreviations not explained in the tables.	We apologize for the lack of clarity. All abbreviations in Tables have been either explained or removed as appropriate.

VERSION 2 – REVIEW

REVIEWER	Laferton, Johannes Psychologische Hochschule Berlin, Clinical Psycology and Psychotherapy
REVIEW RETURNED	16-Jun-2022

GENERAL COMMENTS	The authors have adequatley responded to all my comments. I do not have any further points to raise. Good luck with conducting the study

REVIEWER	Van Tiem, Jennifer VA Iowa City Healthcare System
REVIEW RETURNED	15-Jul-2022

GENERAL COMMENTS	This is exciting work. Thank you for the good work that you do.

	I only have a few thoughts, and they are only thoughts, not intended to slow or impede your work: 1) There is a methodology - "periodic reflections" - that may be particularly suitable for your efforts to iteratively adapt the intervention bundle and collect the perspectives of multiple stakeholders. It may be a useful data collection method. Edit: Oh I see you use that phrase on page 12, "periodic reflection" - are you referring to this method? The citation is: Finley, E.P., et al. Periodic reflections: a method of guided discussions for documenting implementation phenomena. BMC Med Res Methodol 18, 153 (2018). https://doi.org/10.1186/s12874-018-0610-y 2) It may be worthwhile to re-consider acute suicidality as an exclusion criteria. People who fall into that category may be some of the most in need of an intervention like yours, and knowing how to shape your intervention to help those folks seems like important new knowledge. 3) Is there any potential overlap in the populations that meet your inclusion criteria? For example, could someone receive both oncologic and orthopedic surgery? Does this matter? 4) I am familiar with a study by Dr. Katie Hadlandsmyth that does work with pain and perioperative care. It seems potentially adjacent to your study and I wonder if there are any interesting intersections that you all notice? Here is the citation: Katherine Hadlandsmyth, et al, The Perioperative Pain Self-Management (PePS) randomized controlled trial protocol: Preventing chronic post-surgical pain and prolonged opioid use, Contemporary Clinical Trials, Volume 118,2022, https://doi.org/10.1016/j.cct.2022.106810. Again, many thanks for the good work that you. Good luck.

REVIEWER	Hegland, Pål André Western Norway University of Applied Sciences - Forde Campus
REVIEW RETURNED	02-Aug-2022

GENERAL COMMENTS	The authors have made a good job in revising the manuscript, and now present a detailed and clearly written protocol. In my opinion, the protocol is ready to be published.

VERSION 2 – AUTHOR RESPONSE

Reviewer 1 Dr. Johannes Laferton, Psychologische Hochschule Berlin	**Author Response**
- The authors have adequately responded to all my comments. I do not have any further points to raise. Good luck with conducting the study	We thank the reviewer for their comment.

Reviewer 2 Dr. Jennifer Van Tiem, VA Iowa City Healthcare System	Author Response
- This is exciting work. Thank you for the good work that you do.	We thank the reviewer for the wonderful suggestions and the positive feedback.
- I only have a few thoughts, and they are only thoughts, not intended to slow or impede your work: -There is a methodology - "periodic reflections" - that may be particularly suitable for your efforts to iteratively adapt the intervention bundle and collect the perspectives of multiple stakeholders. It may be a useful data collection method. Edit: Oh I see you use that phrase on page 12, "periodic reflection" - are you referring to this method? The citation is: Finley, E.P., et al. Periodic reflections: a method of guided discussions for documenting implementation phenomena. BMC Med Res Methodol 18, 153 (2018).	The reviewer is correct in that we are referring to periodic reflections by Finley et al. to record events during the adaptation process and lifecycle of our intervention bundle and its implementation process. We have added the citation to the revised version. We thank the reviewer for bringing this up.
- It may be worthwhile to re-consider acute suicidality as an exclusion criteria. People who fall into that category may be some of the most in need of an intervention like yours, and knowing how to shape your intervention to help those folks seems like important new knowledge.	This is a valid point. We agree whole-heartedly with the reviewer. Our exclusion is only the most actively suicidal people (i.e., someone who would need emergency psychiatric care, as our care is an outpatient/telemedicine model). This does not exclude people with suicidal ideation.
-Is there any potential overlap in the populations that meet your inclusion criteria? For example, could someone receive both oncologic and orthopedic surgery? Does this matter?	Great observation. At the time of enrollment, we will include patients who belong to only one cohort. The surgery identified at the time of enrollment will represent the index surgery for the patient to avoid overlapping populations. If some patients end up with more than one surgery after enrollment, we plan to still retain the index surgery as the main surgery and account for any overlap and confounding in our analysis.
- I am familiar with a study by Dr. Katie Hadlandsmyth that does work with pain and perioperative care. It seems potentially adjacent to your study and I wonder if there are any interesting intersections that you all notice? Here is the citation: Katherine Hadlandsmyth, et al, The Perioperative Pain Self-Management (PePS) randomized controlled trial protocol: Preventing chronic post-surgical pain and prolonged opioid use, Contemporary Clinical Trials, Volume 118,2022,	We thank the reviewer for sharing this citation. The PePS study uses similar behavioral strategies to address perioperative pain – We will follow this study and its results as we plan for our trial. Chronic pain is one of the many negative outcomes associated with pre-operative psychological distress and supports the need for interventions like ours. For this reason, pain is an exploratory outcome.

- Again, many thanks for the good work that you.	
Reviewer 3 Dr. Pål André Hegland, Western Norway University of Applied Sciences - Forde Campus	**Author Response**
- The authors have made a good job in revising the manuscript, and now present a detailed and clearly written protocol. In my opinion, the protocol is ready to be published.	We appreciate the reviewer's encouraging comments.

VERSION 3 – REVIEW

REVIEWER	Van Tiem, Jennifer VA Iowa City Healthcare System
REVIEW RETURNED	04-Aug-2022

GENERAL COMMENTS	Such exciting work :) Good luck!