PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A person-centered support program (RESPECT intervention) for women with breast cancer treated with endocrine therapy: A feasibility study
AUTHORS	Ahlstedt Karlsson, Susanne; Henoch, Ingela; Olofsson Bagge, Roger; Wallengren, Catarina

VERSION 1 – REVIEW

REVIEWER	Di Meglio, Antonio Gustave Roussy
REVIEW RETURNED	12-Apr-2022

GENERAL COMMENTS	This manuscript reports on a study of feasibility and acceptability of an intervention including education material and a nurse navigator vs. usual care aimed at improving management of side effects and problems due to endocrine-therapy among 41 patients receiving endocrine therapy for breast cancer. The study is interesting and the problem of suboptimal management of endocrine therapy related side effects and its impact on treatment adherence is particularly relevant. There are a number of points where the manuscript could be improved. I am listing some suggestions below. My major point was that the process of development of the intervention, as well as the study design, including population selection, power considerations, and definition of outcomes are not sufficiently detailed. My specific comments below. - FIGURE 1, 2, and 3 do not appear in the proof pdf. - TITLE: I suggest including that this is about women “with breast cancer” treated with endocrine therapy - ABSTRACT: Please specify patient population in the “participant section”. In addition, information regarding duration of the intervention and primary outcome measures should be included. Results should mirror the outcome measures announced in the methods. For example there is a mention to intervention completion in the results, however this is not well defined in the methods. In the conclusions authors state that the “intervention seems to be feasible and acceptable among patients”, however there is no mention in the methods of prespecified criteria for evaluation. MANUSCRIPT TEXT - I was not sure how the acronym was identified in the following “Person-cEntred Support Program EndoCrine Therapy (RESPECT)” - Authors refer to a previous study where rationale was identified and an intervention of person-centered support program was developed (i.e., Ahlstedt Karlsson, Henoch I, Olofsson Bagge R, et al. An intervention mapping-based support program that empowers

	patients with endocrine therapy management). However, this manuscript is not available yet (status is submitted) therefore it is not possible to fully understand the rationale and development process of the intervention. This manuscript is referenced several times throughout the present proof. - In the introduction authors mention that “a combination of information with cognitive behavioral therapy to manage the side effects of tamoxifen showed successful results for the development of management skills in patients who were unable to stay in treatment”. Although patent education and psycho-social interventions are cornerstones of management of endocrine-therapy side effects, I feel that there is a lack of focus on other important management strategies (such as physical activity interventions) that could be used to manage side effects and improve adherence - It was not completely clear to me how the sample size was calculated(“Based on the recommendations for feasibility studies and an expected attrition rate of 20%, the sample size was set to 20 participants in each group”). I think this section belongs after the definition of the main outcome, on which I suspect the calculation was performed. - In Table 1, since receipt of chemotherapy was an exclusion criteria, it is redundant to report that no patients received adjuvant chemotherapy. Is there any particular reason why patients that received chemotherapy were excluded? Many side effects of chemotherapy may be exacerbated and more persistent among patients receiving endocrine therapy. - What is the time since endoctine therapy inception in this study? Participants could enroll any time after breast cancer diagnosis? With a small sample size and a relatively short duration of the intervention (12 weeks) time since endocrine therapy initiation may play a major role, due to fluctuations in symptoms and variability among patients with varying duration of time on treatment. - In addition in Table 1, were there any differences between the two groups? This does not seem to be the case in absolute terms, but were any formal statistical comparisons made? There is a mention of doing so in the analysis section, but then results are not presented in Table 1. - The Control Group seemed to receive patient education + a nurse navigator within a “Usual Care” program. Although I understand that through the Swedish Patient Act each patient has the right to have permanent contact with health care, I am not sure about the choice of the definition of “Usual Care” for the Control Group. In many systems outside of Sweden, nurse navigators are not part of “standard” or usual care. - What is the specific role of the nurse navigator in the Usual Care group vs. that of the Intervention group? - It seemed that this was a 12-week intervention. Was this the case also for the Usual Care group? - The number of follow-up sessions and whether relatives were to be included during the 12-week intervention were agreed upon between the patient and the nurse navigator. Does this mean that the intervention is not standardized? How would this flexibility be taken into account when it comes to implementation of the intervention in the clinical care setting? I suggest this point to be discussed. - Was this a randomized study? How would participants be grouped into the Usual Care vs Interventional group? - Outcomes of interest: which is the primary outcome of the study? The first outcome that is mentioned is “recruitment”. This is defined as follows: “The criterion was determined to be successful if the percentage rates of recruitment were > 70%.” How was this number

	obtained? What is the denominator? Is that 70% of patients willing to participate over the number of patients to whom participation to the stud was proposed? - I am not sure about the “compliance” outcome. This is defined as “The criterion was determined to be successful if all three parts of the intervention were offered”. It looks like this criterion is evaluating whether the nurse navigator offered participation, but not whether the patients actually accepted to participate/whether the three parts were requested by the patients. - In the outcomes description it looks like there are three forms/parts of educational support (face-to face, telephone, and computer), but these are not described in the methodology. Please clarify. I would suggest to keep a consistent language to help the reader navigate the different sections of the manuscript. - How did you measure time spent per education session (“Length per education session”) - Line 19, page 23 of 37. “Completion rate of questionnaires was studied to determine if the patient was willing to answer the questionnaires, i.e., at baseline and 12 weeks.” There is no mention of “questionnaires” before, therefore it is not possible to understand what the authors are referring to. Questionnaires are then presented in the “Data collection” section after, however these should be presented before. - I am not sure why authors report that “One hundred percent of the patients in both groups had invasive breast cancer”. This is a study among women who received endocrine therapy therefore I assume that all included women had a diagnosis of (early-stage) invasive HR+ breast cancer. - The results section contains a number of methodological details that I fell belong to the Methods. Please consider redistributing these information in the appropriate sections. For example: “At the first measurement point, two reminder messages were sent to three patients in the intervention group before one patient was recorded as a drop out”. How many reminders should be send before recording a drop out? - Table 4 mentions “secondary outcomes”. However, I do not seem to find a definition of such outcomes.

REVIEWER	Harder, Helena University of Sussex, SHORE-C Brighton and Sussex Medical School
REVIEW RETURNED	22-Jun-2022

GENERAL COMMENTS	Adjuvant endocrine/hormone therapy in breast cancer has consistently proven to improve outcomes in those with hormone positive breast cancer, and benefits of this treatment gave been well documented. Treatment compliance, however, remains variable for multiple reasons, including debilitating side-effects. The authors of this study developed an intervention – based on person-centered care - to support patients starting with endocrine therapy for early stage breast cancer to manage treatment-related challenges. In this paper, they describe the outcomes of their feasibility study in 41 patients. Unfortunately, the descriptions of the intervention, study methods and results are quite confusing and require a major revision. Please see my (brief) comments below. Title - abstract It’s not clear from the title + abstract that this study involves patients

	with breast cancer. Please add this information. Article summary Can the authors explain the last statement further? (e.g. how did they get to this conclusion?) Background Please include information about compliance (both adherence and persistence) to endocrine therapy. Research shows that a substantial proportion of patients discontinue treatment, affecting their long-term outcomes. Include a brief description of the intervention in the background section. Please move feasibility outcomes to methods section. Methods Please explain why patients receiving adjuvant chemotherapy were excluded (+ row with chemotherapy information in Table 1 can be deleted). The description of the intervention, including Table 2, is unclear. E.g. is it for patients, or healthcare staff or both? What did they patients get? e.g. contact, educational materials or both? Feasibility outcomes: did the team look at recruitment logs? It would have been helpful to have had some qualitative feasibility data as well, for example the team could have interviewed some patients and asked them about their experiences of taking part in the trial. Results This section is 'difficult to read' (i.e. I'm not quite sure what the authors found in their study other than numbers on appointments, etc.) Please try to avoid duplicating information in the text and tables. What did the digital session consist of? (mentioned in table/text) Table 3 – difficult to read (e.g. not aligned, different font sizes, etc.) Please provide footnotes for Tables Table 5: are the data in this Table correct? (the control group seems to 'do better' than the intervention group) Discussion Please limit the discussion to the findings of the feasibility study (e.g. not sure if text about self-efficacy is applicable) Study limitations: please add that because the intervention uses nurse navigators, it can only be used in the authors' country of residence (Sweden) as healthcare provision varies worldwide. References List includes unpublished work, e.g. reference 10 Whole manuscript

	Please check English grammar and spelling.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1:
- FIGURE 1, 2, and 3 do not appear in the proof pdf.

Our respons: The figures will be submitted according to the journal standard and checked in the proof during submission.

- TITLE: I suggest including that this is about women “with breast cancer” treated with endocrine therapy

Our respons: Thank you for the suggestion, the title is edited as suggested.

- ABSTRACT: Please specify patient population in the “participant section”. In addition, information regarding duration of the intervention and primary outcome measures should be included. Results should mirror the outcome measures announced in the methods. For example there is a mention to intervention completion in the results, however this is not well defined in the methods. In the conclusions authors state that the “intervention seems to be feasible and acceptable among patients”, however there is no mention in the methods of prespecified criteria for evaluation.

Our responss: Thank you for these suggestions. It have been included that the intervention was delivered for 12 weeks, in the abstract. However, as this is a feasibility trial, feasibility outcomes were the primary outcomes as described in the abstract. When evaluating the study TIDieR checklist and the CONSORT 2010 statement was used. According to this statement the aim of the study was “to determine the recruitment rate, assess the rate of retention, explore whether the intervention was delivered according to the protocol, assess the preferred form of educational support, rate of education sessions, length per education session, and length between each education session, determine the distribution of education materials, and assess completion rates of patient-report instruments”. Using this CONSORT 2010 statement criterions of success was determined and described in the manuscript. Further evaluation will be processed in a later study. This study was conducted to evaluate the intervention to be feasible i.e., accepted among patients. This was chosen, prior a full-scale intervention study, to increase the likelihood for the complex intervention to be successful.

MANUSCRIPT TEXT
- I was not sure how the acronym was identified in the following “Person-cEntred Support Program EndoCrine Therapy (RESPECT)”

Our respons: Thank you for identifying the fault in the used acronym. The name is corrected to “peRson-cEntred Support Program EndoCrine Therapy (RESPECT).

- Authors refer to a previous study where rationale was identified and an intervention of person-centered support program was developed (i.e., Ahlstedt Karlsson, Henoch I, Olofsson Bagge R, et al. An intervention mapping-based support program that empowers patients with endocrine therapy management). However, this manuscript is not available yet (status is submitted)
therefore it is not possible to fully understand the rationale and development process of the intervention. This manuscript is referenced several times throughout the present proof.

Our respons: This reference is now available and updated in the reference list.

- In the introduction authors mention that “a combination of information with cognitive behavioral therapy to manage the side effects of tamoxifen showed successful results for the development of management skills in patients who were unable to stay in treatment”. Although patent education and psycho-social interventions are cornerstones of management of endocrine-therapy side effects, I feel that there is a lack of focus on other important management strategies (such as physical activity interventions) that could be used to manage side effects and improve adherence

Our respons: Hopefully the Background section is clearer as the intervention building article is now published.
Furthermore, text is added in the manuscript regarding training interventions: “Furthermore, training intervention with a physiotherapist or personal trainer followed by adapted training at home could be effective. However, a problem with this intervention was program adherence, as patients reported difficulty meeting the training goal in frequency and intensity due to other demands in life 14 Also, training has not been found to have effect on musculoskeletal symptoms in patients treated with AIs 15.”
However, as described in the article (ref 10) training and physical activity wasn´t suggested as targets in the intervention, therefore isn´t it further evaluated.

- It was not completely clear to me how the sample size was calculated(“Based on the recommendations for feasibility studies and an expected attrition rate of 20%, the sample size was set to 20 participants in each group”). I think this section belongs after the definition of the main outcome, on which I suspect the calculation was performed.

Our respons: In the future, a full-scale study will be carried out, so we needed to find out what can hamper the success of the newly developed intervention. Therefore, it has been chosen to conduct a feasibility study focusing on the following feasibility outcome: process, resources, scientific challenges. According to Julious, sample sizes should be related to formulated feasibility outcomes. According to Eldridge, a study that studies feasibility does not have to report how the number of participants is calculated. However, it is essential that there is a justification for why the number of participants was chosen. We decided that the intervention was the result of 18 people in each group completed participation. Therefore, we set the sample size to 20 participants with an expected attribution rate of 20%. Based on the recommendations for feasibility studies and an expected attrition rate of 20%, the sample size was set to 20 participants in each group according to Julious. This number is chosen because it can reveal whether the process, resources and scientific challenges hinder the newly developed intervention (Eldridge).

- In Table 1, since receipt of chemotherapy was an exclusion criteria, it is redundant to report that no patients received adjuvant chemotherapy. Is there any particular reason why patients that received chemotherapy were excluded? Many side effects of chemotherapy may be exacerbated and more persistent among patients receiving endocrine therapy.

Our respons: Thank you for this comment. The information about 0% of patients had received chemotherapy is now removed. Following sentence has been added to the manuscript: “Patients receiving adjuvant chemotherapy were excluded as the study aimed to investigate an intervention targeting patients treated with ET.”.

- What is the time since endoctine therapy inception in this study? Participants could enroll any time

after breast cancer diagnosis? With a small sample size and a relatively short duration of the intervention (12 weeks) time since endocrine therapy initiation may play a major role, due to fluctuations in symptoms and variability among patients with varying duration of time on treatment.

Our respons: There is added to the text that the patients were prescribed ET when they were included in the study. Hopefully this clarifies. I have added a clarifying description why the intervention was delivered for 12 weeks (with reference to the article that describes the development process).

- In addition in Table 1, were there any differences between the two groups? This does not seem to be the case in absolute terms, but were any formal statistical comparisons made? There is a mention of doing so in the analysis section, but then results are not presented in Table 1.

Our respons: Baseline characteristics were compared by the chi-squared test for characteristics and there was no significant differences between the two groups. However, as the sample size was too small and to avoid a typ two error there was no report of the results. The sentence in the Analysis section is now removed.

- The Control Group seemed to receive patient education + a nurse navigator within a “Usual Care” program. Although I understand that through the Swedish Patient Act each patient has the right to have permanent contact with health care, I am not sure about the choice of the definition of “Usual Care” for the Control Group. In many systems outside of Sweden, nurse navigators are not part of “standard” or usual care.

Our respons: Thank you for making us aware of this fact. However, as the study was conducted in Sweden and contact nurses, as we have renamed them, are part of the usual care as all patients are allocated one as this is a statuary right for patients when being diagnosed with a cancer disease. Internationally the name is Clinical Nurse Specialist, and we have added this information to increase the understanding. There is provided a description of the content in usual care to ensure readers to understand the context.

- What is the specific role of the nurse navigator in the Usual Care group vs. that of the Intervention group?
It is the same role in bort groups. The difference is that the contact nurse in the intervention have got additional education to increase patients understanding about ET.

Our respons: There have been added a paragraph in the Background to further describe the contact nurse. Furthermore, under the heading Control group, we have described the specific role of contact nurses. In order to try to clarify the differences we have renamed the nurse in the intervention to “intervention nurse”.

- It seemed that this was a 12-week intervention. Was this the case also for the Usual Care group?

Our respons: No. However, both groups were evaluated after 12 weeks as described in the manuscript.

- The number of follow-up sessions and whether relatives were to be included during the 12-week intervention were agreed upon between the patient and the nurse navigator. Does this mean that the intervention is not standardized? How would this flexibility be taken into account when it comes to implementation of the intervention in the clinical care setting? I suggest this point to be discussed.

Our respons: The intervention is not yet standardized, as the result from this feasibility is used to

identify any pitfalls in the enrollment, follow up, and in the delivering of the intervention. In paragraph three in the Discussion section this is discussed, but there is added some text to further clarify this

- Was this a randomized study? How would participants be grouped into the Usual Care vs Interventional group?

Our respons: This was a before and after cohort study design in this feasibility study.

- Outcomes of interest: which is the primary outcome of the study? The first outcome that is mentioned is “recruitment”. This is defined as follows: “The criterion was determined to be successful if the percentage rates of recruitment were > 70%.” How was this number obtained? What is the denominator? Is that 70% of patients willing to participate over the number of patients to whom participation to the stud was proposed?

Our respons: The primary feasibility outcome will be evaluated according to process, and specifically the outcomes of interest are recruitment and retention rates. We have chosen to have these primary outcomes as recruitment and retention are areas of focus that can affect the intervention's internal validity och generate high costs if participants relapse from the study. Furthermore, few participants included in the intervention may also create unclear results and blurred effects on the participants (Thoma et al., 2010). The recruitment rate examines the number of recruited participants, while the retention rate measures the number of participants who remain until after the trial. The literature suggests that the loss of participants should be less than 15% (Zelle et al., 2013). In this study we accepted 30% of lost. Our secondary feasibility outcomes are process (compliance), resources (form of educational support, number of educational sessions, length per education session, length between each education sessions, distribution of education materials and limited efficacy (Completion rate of questionnaires, The estimated treatment effect). Additional text have been added in order to clarify.

- I am not sure about the “compliance” outcome. This is defined as “The criterion was determined to be successful if all three parts of the intervention were offered”. It looks like this criterion is evaluating whether the nurse navigator offered participation, but not whether the patients actually accepted to participate/whether the three parts were requested by the patients.

Our respons: “Compliance” is referred as compliance to the trial protocol. As the intervention is flexible to the patients’ needs and wishes there is no mandatory parts to be delivered other than the learning plan. This is as the intervention is using a person-centered care approach where the parts are delivered using a partnership between the patient and the contact nurse.

- In the outcomes description it looks like there are three forms/parts of educational support (face-to face, telephone, and computer), but these are not described in the methodology. Please clarify. I would suggest to keep a consistent language to help the reader navigate the different sections of the manuscript.

Our respons: Thank you for this input, we have changed “computer” to “digital”. We have also added text to increase clarity.

- How did you measure time spent per education session (“Length per education session”)
We have added text to clarify, and the text is now: “Length per education session

Our respons: Telephone support sessions ranged between 5 and 60 minutes, and digital support sessions ranged between 30 and 45 minutes (Table 3) and was clocked by the intervention nurse.”

- Line 19, page 23 of 37. “Completion rate of questionnaires was studied to determine if the patient was willing to answer the questionnaires, i.e., at baseline and 12 weeks.” There is no mention of “questionnaires” before, therefore it is not possible to understand what the authors are referring to. Questionnaires are then presented in the “Data collection” section after, however these should be presented before.

Our respons: Thank you for this suggestion. Data collection is now presented before feasibility outcomes.

- I am not sure why authors report that “One hundred percent of the patients in both groups had invasive breast cancer”. This is a study among women who received endocrine therapy therefore I assume that all included women had a diagnosis of (early-stage) invasive HR+ breast cancer.

Our respons: God points. We have removed the sentence.

- The results section contains a number of methodological details that I fell belong to the Methods. Please consider redistributing these information in the appropriate sections. For example: “At the first measurement point, two reminder messages were sent to three patients in the intervention group before one patient was recorded as a drop out”. How many reminders should be send before recording a drop out?

Our respons: The comment is understandable. However, as this is a feasibility study this is aimed to be investigated and is for this reason presented as Results.

- Table 4 mentions “secondary outcomes”. However, I do not seem to find a definition of such outcomes.

Our respons: We have renamed the table for clarification.

Reviewer: 2
Title - abstract
It’s not clear from the title + abstract that this study involves patients with breast cancer. Please add this information.

Our respons: Thank you for this suggestion. Breast cancer is now included in the title and the abstract.

Article summary
Can the authors explain the last statement further? (e.g. how did they get to this conclusion?)

Our respons: The last statement is now removed.

Background
Please include information about compliance (both adherence and persistence) to endocrine therapy. Research shows that a substantial proportion of patients discontinue treatment, affecting their long-term outcomes.

Our respons: Thank you for this suggestion. However, we don´t agree to adding text about compliance as this is a study who test an intervention based on person-centered care (Ekman, 2011). The core of person-centered care is not to demand compliance. It is about offering the women a

partnership with the contact nurse to discuss how the individuals best can take their medication. Furthermore, the Background includes text about the difficulties women can face in relation to ET that causes its need for management.

Include a brief description of the intervention in the background section.
Our respons: The intervention is briefly mentioned in the Background in following sentence:

“To include aspects of treatment important to the individual patient, such as different side effects, health care structures, fear of side effects, and lack of management skills and for support, a person-centered support program was developed (ref 10)”

Please move feasibility outcomes to methods section.

Our respons: Unfortunately, we are not sure what the reviewer is suggesting as the feasibility outcomes are in the method section.

Methods
Please explain why patients receiving adjuvant chemotherapy were excluded (+ row with chemotherapy information in Table 1 can be deleted).

Our respons: Thank you for the suggestion. We have deleted the row in Table 1t.

Following sentence has been added to the manuscript: “Patients receiving adjuvant chemotherapy were excluded as the study aimed to investigate an intervention targeting patients treated with ET.”.

The description of the intervention, including Table 2, is unclear. E.g. is it for patients, or healthcare staff or both?
Table 2 is an overview of the education to the intervention nurse before the conducted study.
What did they patients get? e.g. contact, educational materials or both?

Our respons: The patients in the intervention group received step 1-3 in addition to usual care.

Feasibility outcomes: did the team look at recruitment logs?

Our respons: In the manuscript it is stated: “Data were collected from September 2020 – June 2021. Feasibility outcomes were collected during the whole study period by the trial leader and were documented directly after every session in a trial log to secure the data collection 47. The trial log contained a summary of the results of the feasibility criteria using Excel (Microsoft© Excel, version 16.50).”

It would have been helpful to have had some qualitative feasibility data as well, for example the team could have interviewed some patients and asked them about their experiences of taking part in the trial.

Our respons: Thank you for this suggestion, However, this is to be done in a later stage.

Results
This section is ‘difficult to read’ (i.e. I’m not quite sure what the authors found in their study other than numbers on appointments, etc.)

Our respons: As number of appointments was the aim to find in this study, as well as the other

feasibility criterions stated in CONSORT 2010 statement, we are unsure how to reply to this comment. However, in the Analysis section it is stated ” To analyze demographic variables, we used descriptive statistics (number, percent, mean, range). We calculated the percentage rates of recruitment, retention, and completion of questionnaires. We calculated the number, median and range of educational sessions, distribution of education materials, length per education session, and length between each education session.”

Please try to avoid duplicating information in the text and tables.

Our respons: The duplicated text is removed to increase the readability.

What did the digital session consist of? (mentioned in table/text)

Our respons: A short explanation is added that both the telephone sessions and the digital sessions was educational sessions, i.e., used as communication tools.

Table 3 – difficult to read (e.g. not aligned, different font sizes, etc.)

Our respons: The text is corrected.

Please provide footnotes for Tables

Our respons: Footnotes are provided as suggested.

Table 5: are the data in this Table correct? (the control group seems to ‘do better’ than the intervention group)

Our respons: The data is correct. However, as the Covid-19 pandemic was increased when recruiting the intervention group a line about this have been added in the limitation section.

Discussion
Please limit the discussion to the findings of the feasibility study (e.g. not sure if text about self-efficacy is applicable)

Our respons: Thank you for this suggestion. Text about self-efficacy is removed from the Discussion section.

Study limitations: please add that because the intervention uses nurse navigators, it can only be used in the authors’ country of residence (Sweden) as healthcare provision varies worldwide.

Our respons: This is an important point, and we have added text about Clinical Nurse Specialists to enable more countries to understand the role of the contact nurse.

References
List includes unpublished work, e.g. reference 10

Our respons: The article is now published and the reference is accurate.

Whole manuscript
Please check English grammar and spelling.

Our respons: Springer Nature Author Services is used for grammar check. The manuscript was language revised before submission, order ID: R49GZV5SH. They have also helped with the tables and figures. If the language is not found to be appropriate it is of importance that they are informed.

VERSION 2 – REVIEW

REVIEWER	Di Meglio, Antonio Gustave Roussy
REVIEW RETURNED	11-Jul-2022

GENERAL COMMENTS	The authors have addressed my comments in the revised version of the manuscript therefore I have no additional remarks.

REVIEWER	Harder, Helena University of Sussex, SHORE-C Brighton and Sussex Medical School
REVIEW RETURNED	21-Jul-2022

GENERAL COMMENTS	Thank you for revising your paper and implementing some of the suggested changes. The paper is still rather long and remains 'difficult to read' (often there is too much detail in the text or duplication). Please try to be specific and to-the-point, and perhaps look at published feasibility studies in BMJ Open or other journals (e.g. BMC's Pilot and Feasibility Studies https://pilotfeasibilitystudies.biomedcentral.com/about) Some further comments on the revised manuscript Thank you for including breast cancer in the title and abstract. Can the authors ensure that this is also done throughout the paper (e.g. article summary)? Women who are taking ET for breast cancer are taking this for a minimum of 5 years. Compliance to the medication is important for long term outcomes, and should be addressed in an intervention. This can be done in many different ways, including informing patients on what (side-effects) to expect and how to manage this. It is not so much 'demanding compliance' but more about helping patients to be prepared, what to expect, and knowing where to go for support. The feasibility outcomes on page 6 can be removed as they are already described in detail to methods section (section 'feasibility outcomes' – page number 1X?). It is sufficient to just mention the aim at the end of the background section. Can the authors clarify that they conducted this feasibility study in preparation of a randomised controlled trial? If so, please add this to the paper (text and abstract). Thank you for clarifying why patients receiving chemotherapy were excluded. I think it would be useful to add on page 6 (section

	participants) that patients eligible for study were starting ET It is still unclear how patients were assigned to either UC or the intervention. Does patient preference play a role here? Please clarify this. Some of the tables are still unclear. For example, table 4: it is not clear what MSAS often, severe, means. This is not clarified in the text or table. Please add some of the figures and/or tables to supplementary materials section. Please check English grammar and spelling again. There are still errors / typos (incl. in the title). Perhaps the authors could ask a native English speaker to check the text?

VERSION 2 – AUTHOR RESPONSE

Thank you for your consideration of this manuscript. A major revision of the manuscript has been conducted, and we believe it has further improved the manuscript. The CONSORT 2010 checklist is updated. This is the responses to the reviewers' comments.

Thank you for revising your paper and some of the suggested changes. The paper is still rather long and 'difficult to read' (often there is too much detail in the text or duplication) Please try to be specific and to-the-point and perhaps look published feasibility studies BMJ Opener other journals (e.g. Pilot and Feasibility Studies) https://pilotfeasibilitystudies.biomedcentral.com/about.

Our response: Thank you for your suggestion. However, when reporting this study, the CONSORT statement 2010 (Eldridge et al., 2016) was used to ensure the feasibility outcomes to be sufficient addressed. However, when reporting this study, the CONSORT statement 2010 (Eldridge et al., 2016) was used as they suggest that their guideline facilitate higher quality research.

This is an effectiveness trial, as it is delivered in a reality context. According to Craig (2013) a feasibility study could also provide important understandings about the context of the intervention. Furthermore, recruitment was studied to determine whether the patients were willing to participate in the study. It has been suggesting that the loss of participants should be less than 15%. The criterion was determined to be successful if the percentage rates of recruitment were > 70% (Thabane & Landcaster, 2019). According to Craig feasibility studies are suggested to estimate important parameters such as:

- Standard deviation of the outcome measures, which can be used to estimate sample size,
- Willingness of participants to be randomized,
- Willingness of clinicians to recruit participants,
- Number of eligible patients,
- Designing a suitable outcome measure,
- Follow up rates, response to questionnaires, and compliance to the protocol,
- Availability of the needed data,
- Time needed to collect and analyze data.

These bullet points are the read thread in the manuscript alongside with the CONSORT 2010

statement, which we have followed thoroughly. To ensure trustworthiness of this complex intervention, with several interacting components, we believe that all details are needed. As we also choose to use a person-centered approach it is of importance to ensure that we are true to the chosen theory (PCC) which demands a rich description of how partnership is built and maintained throughout the intervention.

However, as we see your point regarding the readability and to increase the texts readability some text from the discussion section is now removed. This could be done as some of the tables now is added to supplementary materials as you suggested.

Some further comments on the revised manuscript.

1. Thank you for including breast cancer in the title and abstract. Can the authors ensure that this is also done throughout the paper (e.g. article summary)?

Our response: Thank you for this suggestion. This have been conducted in the revised manuscript.

2. Women who are taking ET for breast cancer are taking this for a minimum of 5 years. Compliance to the medication is important for long term outcomes and should be addressed in an intervention. This can be done in many different ways, including informing patients on what (side-effects) to expect and how to manage this. It is not so much ‘demanding compliance’ but more about helping patients to be prepared, what to expect, and knowing where to go for support.

Our response: We see your point, and this is what the intervention aims to accomplish in the partnership between the patient and the contact nurse. Although, even if the intervention isn’t targeting compliance as endpoint, this could be achieved when delivering the right amount of information, or as we prefer “patients’ knowledge and understanding”, at the right time.

3. The feasibility outcomes on page 6 can be removed as they are already described in detail to methods section (section "feasibility outcomes"– page 1X?). It is sufficient to just mention the aim at the end of the background section.

Our response: Thank you for this suggestion. The feasibility outcomes on page 6 are now removed.

4. Can the authors clarify that they conducted this feasibility study in preparation of a randomized controlled trial? If so, please add this to the paper (text and abstract).

Our response: Text regarding complex interventions is added in the background section and in the abstract to clarify why a feasibility study is important before conducting a RCT.

5. Thank you for clarifying why patients receiving chemotherapy were excluded. I think it would be useful to add on page 6 (section participants) that patients eligible for study were starting ET.

Our response: This is added as suggested.

6. It is still unclear how patients were assigned to either UC or the intervention. Does patient preference play a role here? Please clarify this.

Our response: At page 6, second paragraph it is stated that this is a “controlled before- and after design”. We believe that no further text is needed.

7. Some of the tables are still unclear. For example, table 4: it is not clear what MSAS often, severe,

means. This is not clarified in the text or table.

Our response: An abbreviation is added to table 4 to clarify OFTEN, SEVERE, and DISTRESS.

8. Please add some of the figures and/or tables to supplementary materials.

Our response: Two of the tables is now supplementary materials as suggested. Also, two figures are supplementary to avoid duplications in the text, but still be available for readers to better understand the flow if needed.

9. Please check English grammar and spelling again. There are still errors / typos (incl. in the title). Perhaps the authors could ask a native English speaker to check the text?

Our response: The manuscript has already gone through language revision by a professional, and by the journal certified, medical writer. If the editor agrees that another language revision is necessary, we will happily arrange with that.

VERSION 3 – REVIEW

REVIEWER	Harder, Helena University of Sussex, SHORE-C Brighton and Sussex Medical School
REVIEW RETURNED	23-Aug-2022

GENERAL COMMENTS	Thank you for your reply and the second revision of the manuscript. The readability of the paper has improved. Please find my responses (in italic) to some of your comments below. 6. It is still unclear how patients were assigned to either UC or the intervention. Does patient preference play a role here? Please clarify this. Our response: At page 6, second paragraph it is stated that this is a "controlled before- and after design". We believe that no further text is needed. *Study participants were breast cancer patients attending an outpatient clinic at a hospital (one location). They were not randomised, which is by itself acceptable, but I believe more explanation is needed about who decided whether consented patients followed the usual care pathway or took part in the intervention.* *In this study, the authors collected information about recruitment, retention, compliance and patient acceptability. The results could have been affected (or biased) if allocation was based on patient preference. For example, choosing an intervention may enhance motivation, and study retention is most likely higher if participants can choose their own study group.*

	Reading through the text of the paper (page 9 and 10), I can see that patients in the control group were longer on study (Sept 2020 – June 2021), than those in the intervention group (Dec 2020 – June 2021). So, perhaps time factors played a role; however, this remains unclear and needs clarification. 7. Some of the tables are still unclear. For example, table 4: it is not clear what MSAS often, severe, means. This is not clarified in the text or table. Our response: An abbreviation is added to table 4 to clarify OFTEN, SEVERE, and DISTRESS. *Thank you for making the changes in the tables and figures, and 'moving' some of them to the supplementary section online.* *The MSAS figure (also quite blurry) and table are still unclear, and abbreviations are missing. For example, in the figure (3?), 'MSAS severe' is displayed twice, can you please explain why that is and what this represents?* *I assume 'MSAS no' means the 'number of symptoms' but this can not be found in the footnotes. Please explain as not all readers are familiar with this questionnaire.* 9. Please check English grammar and spelling again. There are still errors / typos (incl. in the title). Perhaps the authors could ask a native English speaker to check the text? Our response: The manuscript has already gone through language revision by a professional, and by the journal certified, medical writer. If the editor agrees that another language revision is necessary, we will happily arrange with that. *My opinion is that the paper still needs further language revision as there are errors (spelling + grammar) throughout the document, and I don't think this meets the standards of BMJ Open.* *Just a few examples: spelling errors on page 2, line 4 + page 7, line 34, and some nouns/verbs errors on page 4, line 28 '…sessions was restricted' + page 7 line 34 'Patients and health care professionals was involved …'.* *However, I leave it up to the editor to decide on this.*

VERSION 3 – AUTHOR RESPONSE

This is our response to the reviewer. As the previous comment was included in the response from the reviewer, the second response is the latest response. The response in **bold** is the latest.

"The RESPECT intervention is considerate to be complex intervention due to the context. The aim of the study was to explore the feasibility of the trial design and patient acceptability of the intervention and outcome measures and to provide data to estimate the parameters required to design the final intervention."

This text isn't written in grammatically correct English, and is quite cryptic as to what you mean. Perhaps the following would be clearer and/or express what you intend?:

"The RESPECT intervention is a complex intervention encompassing a person-centered support program for patients with breast cancer being treated with endocrine therapy. The aim of this study was to explore the feasibility of the trial design and patient acceptability of the intervention and outcome measures and to provide data to estimate the parameters required to design the final intervention".

Our Response: Thank you for this suggestion, we have changed the paragraph as accordingly.

6. It is still unclear how patients were assigned to either UC or the intervention. Does patient preference play a role here? Please clarify this.

Our response: At page 6, second paragraph it is stated that this is a “controlled before- and after design”. We believe that no further text is needed.

Reviewers Response:
Study participants were breast cancer patients attending an outpatient clinic at a hospital (one location). They were not randomized which itself is acceptable, but I believe ore explanation s needed about ho decides whether counted patients followed the usual care pathway or took art in the intervention.
In the study , authors collected formation about recruitment, retention, compliance, and patient acceptability. The results affected (or biased) if allocation was based on patient preferences.
For example , choosing an intervention may enhanced motivation, and study retention s mostly higher in f participants n choose their own study group. Reading through the text f the paper (age 9 and 10) can see that patients in the control group was longer in the study (Sep 2020 - June 2021)than those in the intervention group (Dec 2020 - June 2021). o, perhaps time factor played a role however, this mains unclear d needs clarification.

Our Response: As this is a controlled before. and after design it’s not possible for patients to choose or not choose intervention. Timing of the enrollment affects which group they are being enrolled too. This led to patients enrolled September 2020- December2020 was enrolled in the UC group, and patients enrolled from December 2020 - March 2021 was enrolled in the intervention group. This is also described in File 1 and 2 in Supplementary Materials. A clarifying text in the manuscript is also added.

8. Please add some of the figures and/or tables to supplementary materials.

Our response: Two of the tables is now supplementary materials as suggested. Also, two figures are supplementary to avoid duplications in the text, but for readers to better understand the flow if needed.

Reviewers Response: Thank you for making the changes in the tables and figures, and ‘moving’ some of them to the supplementary section online.

The MSAS figure (also quite blurry) and table are still unclear, and abbreviations are missing. For example, in the figure (3?), ‘MSAS severe’ is displayed twice, can you please explain why that is and what this represents?

Our Response: Thank you for noticing this. The figure is now corrected, and severe is only displayed once.
To ensure the MSAS figure to meet the standard it will be sent to Springer Nature Author Service for renewed formatting.

Reviewer response: I assume 'MSAS no' means the 'number of symptoms' but this can not be found in the footnotes. Please explain as not all readers are familiar with this questionnaire.

Our Response: This is now corrected.

9. Please check English grammar and spelling again. There are still errors / typos (incl. in the title). Perhaps the authors could ask a native English speaker to check the text?

Our response: The manuscript has already gone through language revision by a professional, and by the journal certified, medical writer. If the editor agrees that another language revision is necessary, we will happily arrange with that.

Reviewer response: My opinion is that the paper still needs further language revision as there are errors (spelling+ grammars) throughout the document, and I don't think this meets the standards of BMJ Open.

Just a few examples: spelling errors on page 2, line 4 + page 7, line 34, and some nouns/verbs errors on page 4, line 28 '...sessions was restricted' + page 7 line 34 'Patients and health care professionals was involved ...'.
However, I leave it up to the editor to decide on this.

Our Response: We have sent the manuscript for a renewed language revision.