

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Rehabilitation during intensive treatment of acute leukemia including allogenic stem cell transplantation – a qualitative study of patient experiences
AUTHORS	Jepsen, Lene Østergaard; Friis, Lone Smidstrup; Hoybye, Mette Terp; Marcher, Claus Werenberg; Hansen, Dorte

VERSION 1 – REVIEW

REVIEWER	Mackenzi Pergolotti ReVital Cancer Rehabilitation, Select Medical Colorado State University USA Dr. Pergolotti receives a salary from Select Medical.
REVIEW RETURNED	01-Mar-2019

GENERAL COMMENTS	<p>Thank you for the invitation to review this paper. Overall, I think this paper brings up a great points about the state of rehabilitation in cancer care that transcends multiple contexts.</p> <p>I have a few concerns I think need to be addressed before publication. I found the introduction section to be not clearly headed towards a certain argument. Once I got to the results and conclusion I could see where the authors were going with the study and project. I think this paper adds to what we know about cancer rehabilitation- especially when it comes to perceptions about the care that is provided from survivors and the barriers they come up against-- including the lack of connection/understanding between having a PT there at the site, but not accessing this care when it could have been most helpful. Furthermore, the idea that they are "too good" for rehabilitation definitely needs to be explored.</p> <p>My point is, that I think the introduction did not set that stage and needs revision.</p> <p>Minor points: Use of "cancer patient" and "gender" are not recommended and language such as "individual with cancer" and "sex" should be used (unless describing gender as an expression, not as a biological difference).</p> <p>I think the context for cancer rehabilitation section could be cut significantly.</p> <p>I suggest in results and in discussion making clear the connections to ICF- which responses go with what parts of the model? and the transactions among the concepts of the ICF?</p>
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REVIEWER	Satoshi Iyama Department of Hematology, Sapporo Medical University School of Medicine, Japan
REVIEW RETURNED	06-Mar-2019

GENERAL COMMENTS	<p>General comment: The manuscript by Jepsen LO and colleagues reported the rehabilitation during intensive treatment of acute leukemia. The manuscript is generally well-written and the employed methods are adequately applied. Patients can have persistent muscle weakness after intensive chemotherapy for acute leukemia. This is an informative study with significance, but I have several comments as follows.</p> <ol style="list-style-type: none"> 1. The author should describe the limitation of semi-structured interview and the reason why you chose it (compare with structured interview). 2. Please describe each example of question from interviewer. 3. The vertical line is not necessary for Table.
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REVIEWER	Faith Gibson Great Ormond Street Hospital for Children NHS Foundation Trust and university of Surrey, UK
REVIEW RETURNED	23-Aug-2019

GENERAL COMMENTS	<p>Thank you for asking me to review this paper. Rehabilitation, exercise and impact on patient experience are timely areas to study. This is a qualitative study, reporting on a final interview in a larger study. It is always difficult when reporting part of, to make sure the context of the whole is as clear as it can be, without plagiarising our own work, but I do think this paper needs some additional context of that larger study. I have some other comments, that relate to content and style, that I would like the authors to consider.</p> <ol style="list-style-type: none"> 1. The abstract does need some work, as a qualitative study, approach to sampling and data analysis is important to include, at the moment that is missing. Results, normally categories, and number of, would be described here also. 2. Just a thought, in your title, and here in the abstract you describe your patient group as 'acute leukaemia' patients, but looking at the demographic some patients are described as 'chronic', do you need to re-consider how you refer to your population. 3. Strengths section, page 3, you talk here and in the body of your work about selection bias, but actually provide no detail on how your sample was identified, recruited and consented. Figure 1 is in part helpful, but not sure the reader knows about the approach to sampling that enabled you to 'assess for eligibility: as you know sampling is crucial in qualitative work. 4. Page 5, 'rehabilitation needs and offers', sorry I am not sure what offers means, does this mean offer of rehabilitation, the sentence might just need some slight re-wording. 5. I wonder if it might help readers to know what the research question was that was driving your larger study, earlier papers report on the first two rounds of interviews, why did you choose to report these interviews separately. If a longitudinal study, were you building on what was revealed early, asking different questions
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	<p>that arose out of your earlier rounds of analysis: some clarity over your research design, and where these interviews fit would be helpful.</p> <p>6. Page 6, as mentioned already, text that described clearly your approach to sampling is really important to add.</p> <p>7. Page 7, second to last paragraph is important to describe more fully, rehabilitation is offered, what does this consist of, or what might this group of patient have been offered.</p> <p>8. Page 7, last paragraph, 'this study took outset' I think there might be a word missing here.</p> <p>9. Typo, as you know data are always plural, so were not was on Page 8.</p> <p>10. You describe a Theoretical Framework, how did this assist you in your analysis, how did you use this when reporting your data?</p> <p>11. Page 9, I would somewhere at the start prepare the reader for what is to follow, so how have you chosen to present your results?</p> <p>12. I know why this is done, usually to reduce word count, but as a qualitative researcher, I don't find it helpful separating the quote from text. My suggestion would be to add quotes from Tables into the body of the work, this is a much better way of reporting your study.</p> <p>13. Page 9, line 37, 'all experienced' not sure this makes sense, sorry.</p> <p>14. Page 10, AL, again not sure what this abbreviation means, if it is an abbreviation, then I would put in full at the start of a sentence.</p> <p>15. Table 1, you report n of 1, do you need this level of detail, that could identify patients in your study.</p> <p>16. In terms of your discussion, what does this data set add to your whole study, feels like it needs to be brought together somehow, goes back I guess to what question you were asking.</p> <p>17. A final point, what does this mean for practice, what does it mean for the services you deliver. I appreciate small study, but these are important reflections from patients, and they contribute to this body of work around rehabilitation, but you need to help readers with what links can be made.</p> <p>Thank you for considering these suggestions.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer #1:

1. Thank you for the invitation to review this paper. Overall, I think this paper brings up a great points about the state of rehabilitation in cancer care that transcends multiple contexts. I have a few concerns I think need to be addressed before publication. I found the introduction section to be not clearly headed towards a certain argument. Once I got to the results and conclusion I could see where the authors were going with the study and project. I think this paper adds to what we know about cancer rehabilitation- especially when it comes to perceptions about the care that is provided from survivors and the barriers they come up against-- including the lack of connection/understanding between having a PT there at the site, but not accessing this care when it could have been most helpful. Furthermore, the idea that they are "too good" for rehabilitation definitely needs to be explored.

My point is, that I think the introduction did not set that stage and needs revision.

ANSWER:

We thank the reviewer for finding that the subject of rehabilitation in cancer care across multiple contexts is interesting. This is very encouraging for our work onwards in this field.

We further thank the reviewer for drawing relevant attention to ambiguities in the introduction. We have revised the introduction to better head toward the aim of the study. Please follow changes in red (page 5).

2. Minor points: Use of "cancer patient" and "gender" are not recommended and language such as "individual with cancer" and "sex" should be used (unless describing gender as an expression, not as a biological difference).

ANSWER: Thank you to the reviewer for this advice. We made changes accordingly (page 2-13).

3. I think the context for cancer rehabilitation section could be cut significantly.

ANSWER: We have reduced this section but not significantly as we see the description of the context as very important for the understanding of the findings of the study (page 7).

4. I suggest in results and in discussion making clear the connections to ICF- which responses go with what parts of the model? and the transactions among the concepts of the ICF?

ANSWER: We used the ICF-model to frame the concept of rehabilitation. It is a dynamic model showing the interrelation between various aspects of functioning and contextual factors. It was not the scope neither our intention to explain the model in detail. Our results and discussion point to the fact that impairment and well-being may include physical, psychosocial and existential aspects of bodily function, activity and participation. We refer to the model several times in the discussion section. We have underlined the interrelationship and dynamics of the model in the section 'theoretical framework and analysis' and 'discussion'. In addition, we have included the following wording in the beginning of the result section 'subcategories of physical activity, mental well-being and social activity were constructed and will be described separately in the following although strongly interrelated as conceptualized in the ICF-model' (page 9-10).

Reviewer #2:

The manuscript by Jepsen LO and colleagues reported the rehabilitation during intensive treatment of acute leukemia. The manuscript is generally well written and the employed methods are adequately applied. Patients can have persistent muscle weakness after intensive chemotherapy for acute leukemia. This is an informative study with significance, but I have several comments as follows.

1. The author should describe the limitation of semi-structured interview and the reason why you chose it (compare with structured interview).

ANSWER: We are very happy that reviewer 2 finds that our manuscript is well written. We agree with the reviewer that methodological clarifications are of importance and have sought to add to the methodological transparency of this study in the revised manuscript. The structured interview leaves very little space for expressing and exploring experiences, which is why we found the semi-structured approach to interviews to be more in line with our research objective. We had a relatively small group of possible participants to recruit from for the study, and as we wanted to explore the experiences of rehabilitation among patients in an outpatient setting, we chose the semi-structured interview. The semi-structure allows the interviewer to ask counter questions, if new and unexpected areas come up ensures that the interviewer did not set the mind-map of answers.

We have added a brief clarification in the revised manuscript page 6.

2. Please describe each example of question from interviewer.

ANSWER: When performing semi-structured interviews, the questions asked by the interviewer will include a combination of those from the thematic interview guide used and questions found to be

relevant for that specific interview, based on what the interviewee had explained. For this reason, an example is described in the manuscript and we have added a brief clarification in the revised manuscript page 6.

3. The vertical line is not necessary for Table.

ANSWER: We thank the reviewer for the guideline to our tables. We have removed the vertical lines (table 2-5).

Reviewer #3:

Thank you for asking me to review this paper. Rehabilitation, exercise and impact on patient experience are timely areas to study. This is a qualitative study, reporting on a final interview in a larger study. It is always difficult when reporting part of, to make sure the context of the whole is as clear as it can be, without plagiarizing our own work, but I do think this paper needs some additional context of that larger study. I have some other comments, that relate to content and style, that I would like the authors to consider.

1. The abstract does need some work, as a qualitative study, approach to sampling and data analysis is important to include, at the moment that is missing. Results, normally categories, and number of, would be described here also.

ANSWER: We thank the reviewer for stressing the need for more information on the data analysis and the reporting of results. Please see the updates in the abstract of the manuscript (page 2).

2. Just a thought, in your title, and here in the abstract you describe your patient group as 'acute leukemia' patients, but looking at the demographic some patients are described as 'chronic', do you need to re-consider how you refer to your population.

ANSWER: We thank the reviewer for being aware of the difference between acute and chronic leukemia and the discrepancy between title, text and patients under study. All the diagnoses included in this study were handled identically in the outpatient setting and received treatment equivalent to acute leukemia patients regiments. Please see the added note in table 1: The CML, CMML and RAEB diagnoses are special leukemia diagnoses, which are chronic diseases but often turn into acute leukemia after a short time. Therefore, they received the same treatment as acute leukemia patients and were handled identically to them (page 8).

3. Strengths section, page 3, you talk here and in the body of your work about selection bias, but actually provide no detail on how your sample was identified, recruited and consented. Figure 1 is in part helpful, but not sure the reader knows about the approach to sampling that enabled you to 'assess for eligibility: as you know sampling is crucial in qualitative work.

ANSWER: We agree with the reviewer that sampling is crucial in qualitative work as well as in quantitative research. To be included in the study, patients had to meet the standard requirements for outpatient management in the outpatient setting and additionally be able to understand and speak Danish. All patients meeting the inclusion criteria were asked by the interviewer herself to participate. Written, informed consent was obtained from patients wishing to participate. The process is described in detail in a previous paper, referenced in the manuscript page 6 (reference number 15). We agree with the reviewer that a few more details are required in the manuscript, and have added the following sentence to the Design section: 'Patients were consecutively invited by and gave consent to the first author, LØJ, who conducted the interviews. LØJ presented herself as a PhD student and a young medical doctor with previous experience in the department (page 6).

4. Page 5, 'rehabilitation needs and offers', sorry I am not sure what offers means, does this mean offer of rehabilitation, the sentence might just need some slight re-wording.

ANSWER: We thank the reviewer for pointing out the difficulty of understanding the sentence on page 5 and the meaning of the word offer. Regarding offer, we refer to situations where a patient is offered an intervention like for example group exercising in a rehabilitation center and in line with perceived needs, resources and prioritization may or may not accept such an offer. We have done some re-wording so please see the manuscript page 5.

5. I wonder if it might help readers to know what the research question was that was driving your larger study, earlier papers report on the first two rounds of interviews, why did you choose to report these interviews separately. If a longitudinal study, were you building on what was revealed early, asking different questions that arose out of your earlier rounds of analysis: some clarity over your research design, and where these interviews fit would be helpful.

ANSWER: We thank the reviewer for being so interested in this group of patients. To help readers with insight into the larger study, which this study is part of, we added information to the Design section of the manuscript: 'The material derives from individual interviews with 16 patients, six months after end of treatment. These interviews were the third and final interview, conducted as part of a larger qualitative study with the overall aim of exploring the outpatient setting as a context of intensive cancer treatment.' This third paper 'from the larger' study is about impairment, functioning and rehabilitation, which were mainly addressed during the third round of interviews. The interview findings were very different across time. Basically, impairment and future functioning were not addressed or experienced as important by interviewees in earlier treatment phases (page 6).

6. Page 6, as mentioned already, text that described clearly your approach to sampling is really important to add.

ANSWER: As explained above, we have added information about sampling i.e. the invitation procedure, consent form and diagnosis.

7. Page 7, second to last paragraph is important to describe more fully, rehabilitation is offered, what does this consist of, or what might this group of patient have been offered.

ANSWER: Generally, rehabilitation of these patients is not offered systematically neither at department nor municipality level, and those offered are, to some degree, individualized to address specific needs and resources. To better explain the optional offers, we rearranged/changed the section 'context of rehabilitation' to:

Rehabilitation has previously been understood as a practice related to the post-treatment life of patients, but the facilities and practices of the hospital during in and outpatient management may also be considered a context of rehabilitation of patients with AL. In addition, non-hospital settings may be part of the rehabilitation context.

The course of treatment for newly diagnosed patients with AL who are candidates for curative intended chemotherapy contains both in and outpatient periods. The latter where the patients during periods with severe hematological cytopenia, stay at home and appear at follow-up visits every second day [15].

The Outpatient Setting (OPS) was situated next to the hematological department, OUH, where all the patients could use the fitness facilities located there. A physiotherapist was present twice a week to instruct the patients. Before receiving the transplant, patients were instructed in some simple exercises by a physiotherapist. Furthermore, all patients had an exercise-bike in their bed-room at the hospital during periods of isolation.

In addition to physical exercise, patients could, at any time, ask for a referral for individual advice by a physiotherapist, a psychologist, a chaplain or a medical social worker at the department. Furthermore, psychologists from The Danish Cancer Society were available to patients and relatives in facilities at the hospital.

In Denmark, the overall responsibility of rehabilitation is located at the local municipality level (98 municipalities/5.6 million inhabitants). Due to different demographics, staff and geography of the municipalities patients encounter different offers and knowledge about their disease [17] (page 8-9).

8. Page 7, last paragraph, 'this study took outset' I think there might be a word missing here.
ANSWER: We thank the reviewer to stress a missing word. We have re-written the sentence (page 7).

9. Typo, as you know data are always plural, so were not was on Page 8.
ANSWER: Again, we thank the reviewer helping to improve the language. The mistake has been corrected on page 8.

10. You describe a Theoretical Framework, how did this assist you in your analysis, how did you use this when reporting your data?
ANSWER: As addressed above we have improved the manuscript regarding how we based our conceptual understanding and research analysis on the dynamic ICF-model.

11. Page 9, I would somewhere at the start prepare the reader for what is to follow, so how have you chosen to present your results?
ANSWER: We thank the reviewer for the tip of better preparing the reader for what is to follow. Please see the first paragraph of the Result section (page 8).

12. I know why this is done, usually to reduce word count, but as a qualitative researcher, I don't find it helpful separating the quote from text. My suggestion would be to add quotes from Tables into the body of the work, this is a much better way of reporting your study.
ANSWER: We fully agree with the reviewer that quotes in the text are preferable. The reviewer is right as to why we did it in the first place. The manuscript contains a lot of details, and we therefore keep the lay-out of the quotations.

13. Page 9, line 37, 'all experienced' not sure this makes sense, sorry.
ANSWER: Again, we thank the reviewer for helping us to improve the text. We have re-written the sentence page 9.

14. Page 10, AL, again not sure what this abbreviation means, if it is an abbreviation, then I would put in full at the start of a sentence.
ANSWER: AL is the abbreviation for acute leukemia. We did not include this abbreviation in the title or abstract and defined it where it is mentioned the first time (page 5).

15. Table 1, you report n of 1, do you need this level of detail, that could identify patients in your study.
ANSWER: Thank you to the reviewer for having focus also on the level of details of table 1 reporting the demographic and clinical characteristics of study participants. We have made some changes regarding age and treatment location for transplantation. Talking into consideration the number of patients eligible for this study, we now feel sure about the possibility of recognizing individual patients (page 7-8).

16. In terms of your discussion, what does this data set add to your whole study, feels like it needs to be brought together somehow, goes back I guess to what question you were asking.
ANSWER: In line with this comment we have rewritten the second paragraph of the 'Discussion section' to more clearly point out what this study adds to previous studies and thus how patients' motivation changed substantially over time (page15-16).

17. A final point, what does this mean for practice, what does it mean for the services you deliver. I appreciate small study, but these are important reflections from patients, and they contribute to this body of work around rehabilitation, but you need to help readers with what links can be made.

ANSWER: This study is of importance to future practice. After re-reading the paper we have agreed that the meaning to practice is clear from the 'Perspective' and 'Conclusion' sections of the main paper but could be improved by revision of the conclusion of the abstract. We changed the latter to: Future programs must pay attention to the contextual changes of treatment of this patient group and individuals' changing needs and motivation for physical exercise (page 17-18).

VERSION 2 – REVIEW

REVIEWER	Satoshi Iyama Sapporo Medical University School of Medicine, Japan
REVIEW RETURNED	10-Oct-2019

GENERAL COMMENTS	All the questions and concerns that I raised seem to be properly addressed and the manuscript has been revised well.
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REVIEWER	Faith Gibson University of Surrey UK
REVIEW RETURNED	07-Oct-2019

GENERAL COMMENTS	<p>Thank you for asking me to review this paper for a second time. I am happy with the revisions made to this paper, I just have a few comments for the authors to consider that mainly relate to the style of reporting, hope these are helpful.</p> <ol style="list-style-type: none"> 1. Abstract, line 33, should read were, not was, as data is always plural. Sorry if I missed this last time, abstract line 42 should read, 'to feel safe'. 2. Staying with the abstract, you might want to tweak the sentence.....through an inductive ongoing four-step process, with the final step, selective coding, that resulted in.....always tricky as you can use a reference in the abstract, its making it clear there was a process you followed. 3. Page 6, to be clear, I would refer to an interview not a talk, so, possible suggested change.....additional questions to cover the topic sufficiently. 4. Page 8, to be clear to the reader,With permission, all interviews were digitally recorded. 5. Page 9, line 50, you might want to refer to these as steps, seems as you have called them that, so instead of First...Secondly.....use Step 1, Step 2, etc. 6. Page 10, sorry I might not have been clear, take the quote out of the Table style, Quote 1 is redundant, you just need the quote itself, with participant number at the end. So, for each quote, its needs to flow with the body of the text. If you want to make multiple quotes, then there needs to be text between them, text that links them. 7. Staying with the quotes, some are long, you might well be able to reduce the number in the text, Table 5, will need these quotes embedded with linked text. 8. Page 17, line 14, not sure that 'hampers' works best, what about 'limits', that is the word traditionally used. <p>Thank you for considering these suggestions.</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer #3:

1. Abstract, line 33, should read were, not was, as data is always plural. Sorry if I missed this last time, abstract line 42 should read, 'to feel safe'.

ANSWER: We thank the reviewer helping to improve the language. Line 33 and 42 has been corrected.

2. Staying with the abstract, you might want to tweak the sentence.....through an inductive ongoing four-step process, with the final step, selective coding, that resulted in.....always tricky as you can use a reference in the abstract, its making it clear there was a process you followed.

ANSWER: Again, we thank the reviewer helping to improve the language and have made the suggested corrections.

3. Page 6, to be clear, I would refer to an interview not a talk, so, possible suggested change.....additional questions to cover the topic sufficiently.

ANSWER: We thank the reviewer and have changed the sentence according to the suggestion.

4. Page 8, to be clear to the reader,With permission, all interviews were digitally recorded.

ANSWER: To be clear we have changed the sentence as advised.

5. Page 9, line 50, you might want to refer to these as steps, seems as you have called them that, so instead of First...Secondly.....use Step 1, Step 2, etc.

ANSWER: We thank the reviewer and have re-written the paragraph by using Step 1-4.

6. Page 10, sorry I might not have been clear, take the quote out of the Table style, Quote 1 is redundant, you just need the quote itself, with participant number at the end. So, for each quote, its needs to flow with the body of the text. If you want to make multiple quotes, then there needs to be text between them, text that links them.

ANSWER: We thank the reviewer for stressing that the Table style should not be used. The quotes are now to be found in the text in the revised manuscript.

7. Staying with the quotes, some are long, you might well be able to reduce the number in the text, Table 5, will need these quotes embedded with linked text.

ANSWER: We have reduced and deleted some quotes. Furthermore embedded all quotes in the text in the revised manuscript.

8. Page 17, line 14, not sure that 'hampers' works best, what about 'limits', that is the word traditionally used.

ANSWER: Again, we thank the reviewer and have changed the word.

Reviewer #2:

ANSWER: We thank the reviewer for finding the questions and concerns properly addressed and that the manuscript has been revised well.