PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A mixed methods evaluation of a self-management group programme for patients with neuromuscular disease and chronic fatigue
AUTHORS	Veenhuizen, Yvonne; Satink, Ton; Graff, Maud; Geurts, Alexander; Groothuis, Jan T.; van Engelen, Baziel G.M.; Nijhuis-van der Sanden, Ria; Edith, H.C.

VERSION 1 – REVIEW

REVIEWER	Rosemary Twomey University of Calgary, Cumming School of Medicine
REVIEW RETURNED	21-Apr-2021

GENERAL COMMENTS	Thank you for the opportunity to review this manuscript. This manuscript describes the collection and analysis of data from questionnaires, interviews and focus groups regarding the experiences of patients who were allocated to the experimental arm of a multicenter RCT. The experiences of a support persons and healthcare professionals involved in the intervention were also considered. The RCT protocol, intervention and main findings are reported elsewhere: DOI: 10.1186/s12883-015-0314-4 and DOI: 10.1212/WNL.0000000000008393. The RCT recruited people with neuromuscular disease and chronic fatigue, and the intervention included aerobic exercise and several educational/self-management components. This data provides interesting insight based on participant feedback to guide implementation of the intervention following the RCT results. Additional comments are provided below. Title: Is “alongside an RCT” necessary in the title? The present manuscript does not report on the RCT itself. Consider reworking to e.g. “A mixed methods evaluation of experiences with a self-management programme for patients with neuromuscular disease and chronic fatigue” or similar. Introduction: Points made in discussion from your preceding RCT (results paper) provide a rationale for the present manuscript that is not captured in the current introduction. This may have been due to limits on the word count. However, I think it would be relevant to come back to the point that further insight can be gained (from your qualitative data) to optimize Energetic based on e.g., patient selection, the timing of the intervention and relapse prevention. This relates to “problem formation” as described in the COREQ. The framing of the research question only as identifying barrier and facilitators regarding the content and delivery Energetic programme needs consideration. I am not sure what a barrier/facilitator to the content would be, does this mean barriers/facilitators to the Implementation of the content? Many of the topics covered in the qualitative data collection do not fall under barriers and facilitators or content and delivery. Perhaps this should be barriers and facilitators

	to the content, delivery and effectiveness of the Energetic programme? Satisfaction is also a slightly different concept not covered by the current research question. Methods: Although most of the items are already transparently reported, it was not clear whether the authors used the relevant reporting guidelines for qualitative research i.e. the Consolidated criteria for reporting qualitative research (COREQ: https://www.equator-network.org/reporting-guidelines/coreq/) and the Standards for reporting qualitative research (SRQR: https://www.equator-network.org/reporting-guidelines/srqr/). Please can the authors add a statement in the methods and additional detail where needed. For example, one missing item is the research paradigm/theoretical framework (currently this is not included in the data analysis section). Page 8, Line 14: please include 2-4 of the NMD diagnoses of the patients included in the present study here. Page 10, Line 6-12: the abbreviations here are only useful to interpret Table 3 (please move to above/below Table 3). Results: Line 51: Are the two participants who took part in interviews but dropped out of the intervention the same two that experienced too high a burden? Did they provide specific insight that can be summarized e.g. in the discussion? Did these patients have higher fatigue at baseline? Table 1: Please note that I believe the location of healthcare professionals is provided and previously it was stated that this would be removed to ensure anonymity. Themes: Quotes provided in Table 3 are repeated within the text. Assuming these quotes provided are not the only quotes used to generate the theme/subtheme, it would be much more insightful to present additional (i.e., different) quotes in Table 3, rather than repeating the same quotes twice. For example, I am left wanting more information (example quotes) about theme 2 in particular, considering the intervention did not improve fatigue relative to usual care. Page 17, line 48: “intensity” is confusing in this context because it is referring to the overall demands of the programme rather than the exercise intensity. Please edit here and elsewhere (the discussion) to e.g. intervention demands or burden or similar. Discussion: In the interviews, were there suggestions provided to improve aspects of the intervention where patient satisfaction was lower (e.g., the length of fatigue management sessions, content of nutrition and work sessions)? The recommendations are all reasonable and useful for future implementation. However, I am interested in the authors consideration of if/how this qualitative data provides insight on patient selection (e.g. nearly half to patients who were ineligible for the RCT were excluded due to “insufficient motivation or readiness to change”) and relapse prevention (considering even highly motivated patients found the intervention demanding or even “exhausting”). How do the results compare with other interventions in people with NMD or chronic fatigue more broadly?

REVIEWER	Katie Hackett Northumbria University
REVIEW RETURNED	04-May-2021

GENERAL COMMENTS	This is an important study which goes alongside a RCT of a fatigue

	self-management intervention, as it gains insights from the patients who have participated in the intervention arm of the study, partners/next of kin of patients, the therapists and professionals involved in the delivery of the programme and gains further insights regarding satisfaction about the content and delivery of the programme which can be used to inform the implementation of the programme in the future. Some minor issues to address in the manuscript: 1) The view points of partners/NOK of participants were included in the qualitative interviews. The abstract does not include this information. 2) On page 8 and p 11 in the results more clarity is needed about sampling. It is not clear how the participants were chosen for the 1:1 interviews and for the focus groups. Was there a sampling framework? There are also some issues about the language being a little confusing when it comes to discussing focus group interviews and 1:1 semi-structured interviews. This needs to be made more clear in the text and be consistent. (e.g. see P 7 lines 20-21 - "the interviews" seem to refer to 1:1 qualitative interviews, but reading further on p 12 lines 4-5 - it seems that "interviews" does refer to both focus groups and 1:1 interviews). Please make this more clear in the text. 3) It is not immediately clear in the abstract that the satisfaction questionnaire was only completed by participants who finished the programme. 4) Typos noticed: P8 line 19 "de intervention group" should be "the intervention group". Check the grammar on p 11 line 6-7 ("emailed to all participants and" .... the word "they" is missing).

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Rosemary Twomey, University of Calgary
Comments to the Author:
Thank you for the opportunity to review this manuscript. This manuscript describes the collection and analysis of data from questionnaires, interviews and focus groups regarding the experiences of patients who were allocated to the experimental arm of a multicenter RCT. The experiences of a support persons and healthcare professionals involved in the intervention were also considered. The RCT protocol, intervention and main findings are reported elsewhere: DOI: 10.1186/s12883-015-0314-4 and DOI: 10.1212/WNL.0000000000008393. The RCT recruited people with neuromuscular disease and chronic fatigue, and the intervention included aerobic exercise and several educational/self-management components. This data provides interesting insight based on participant feedback to guide implementation of the intervention following the RCT results. Additional comments are provided below.

Title: Is “alongside an RCT” necessary in the title? The present manuscript does not report on the RCT itself. Consider reworking to e.g. “A mixed methods evaluation of experiences with a self-management programme for patients with neuromuscular disease and chronic fatigue” or similar.

Response:
We agree with the reviewer and changed the title into: “A mixed methods evaluation of a self-management group programme for patients with neuromuscular disease and chronic fatigue”

Introduction:
Points made in discussion from your preceding RCT (results paper) provide a rationale for the present

manuscript that is not captured in the current introduction. This may have been due to limits on the word count. However, I think it would be relevant to come back to the point that further insight can be gained (from your qualitative data) to optimize Energetic based on e.g., patient selection, the timing of the intervention and relapse prevention. This relates to “problem formation” as described in the COREQ.

Response:
To provide more information about the rationale we changed the following section:
Page 5 line21-25, page 6 line 1-3
“This study, therefore, presents a mixed method approach to the evaluation of the Energetic programme to gain insight in the perceived satisfaction of patients and healthcare professionals with the programme and the factors influencing the intervention. This evaluation was performed in order to provide suggestions for improvement of the content and the delivery of the intervention, the perceived impact, patient selection, timing of the intervention, and for further improvement and implementation of the Energetic programme in different clinical settings.”

The framing of the research question only as identifying barrier and facilitators regarding the content and delivery Energetic programme needs consideration. I am not sure what a barrier/facilitator to the content would be, does this mean barriers/facilitators to the Implementation of the content? Many of the topics covered in the qualitative data collection do not fall under barriers and facilitators or content and delivery. Perhaps this should be barriers and facilitators to the content, delivery and effectiveness of the Energetic programme? Satisfaction is also a slightly different concept not covered by the current research question.

Response:
We agree with the reviewer that the research question is too narrowly formulated. The perceived impact and satisfaction is missing in the research question, but is addressed in the results.
With barriers and facilitators to the content, we intend to address which elements of the content are experienced as valuable and facilitators to fatigue management and which elements of the content are not contributing to fatigue management or even are experienced as burdensome to implement.
We changed the research question:
Page 6 line 4-5
“The research questions were: what is the perceived satisfaction with the Energetic programme and what are the facilitators and barriers regarding the impact, content and delivery of the Energetic programme?”

Methods:
Although most of the items are already transparently reported, it was not clear whether the authors used the relevant reporting guidelines for qualitative research i.e. the Consolidated criteria for reporting qualitative research (COREQ: https://www.equator-network.org/reporting-guidelines/coreq/) and the Standards for reporting qualitative research (SRQR: https://www.equator-network.org/reporting-guidelines/srqr/). Please can the authors add a statement in the methods and additional detail where needed. For example, one missing item is the research paradigm/theoretical framework (currently this is not included in the data analysis section).

Response:
We checked the manuscripts regarding the COREQ guidelines and added the following points to the main text. The COREQ checklist is submitted them as supplementary file.

Sampling
Page 8 line 13-17
“For this evaluation, all patients in the intervention group were asked to fill in the satisfaction questionnaire. Ten consecutive patients and seven partners or next of kin from the first two Energetic groups were asked by email to participate in an individual semi-structured interview. Additionally, 19 patients were asked face-to-face during the intervention to participate in focus groups following the last session of the Energetic programme.”

Methodological orientation
Page 10 line 19

"The aim of the constant comparative analysis was to identify overarching themes regarding the satisfaction, impact, facilitators and barriers related to the content and delivery of the Energetic programme."

Number of codes and derivation of categories
Page 11 line 4-5
"In total 706 codes were found in the open coding process; 5) the first (YV) and last author (EC) identified potential 14 categories among the initial codes;"

Page 10 line 10
"The COREQ checklist was used for reporting the qualitative data."

Page 8, Line 14: please include 2-4 of the NMD diagnoses of the patients included in the present study here.

Response:
We added the diagnoses in the methods section
Page 8 line 11.
"The group who received the Energetic programme consisted of 8 men and 21 women (mean age 52 years, range 20-74 years) with a variety of NMD diagnoses (e.g. facioscapulohumeral dystrophy, inclusion body myositis, mitochondrial myopathy)."

Page 10, Line 6-12: the abbreviations here are only useful to interpret Table 3 (please move to above/below Table 3).

Response:
We added the abbreviations below table 3. Because the abbreviations are also used in the results section, we left the abbreviations also in the methods section.

Results:
Line 51: Are the two participants who took part in interviews but dropped out of the intervention the same two that experienced too high a burden? Did they provide specific insight that can be summarized e.g. in the discussion? Did these patients have higher fatigue at baseline?

Response:
The two dropouts had different reasons to stop with the Energetic intervention. One woman stopped because of complaints with her foot, and because she experienced a high load in her schedule while participating twice a week in the programme with a large travel distance in combination with her other weekly activities. Her score on the CIS-Fatigue at baseline was 34, which is just below the cut-off score of severe fatigue.
The other participant dropped out because the start of treatment occurred together with an acute psychological disorder. He experienced no high burden from the intervention. His CIS-fatigue score was 46.
Because there were limited similarities between the reasons for dropout, we combined the positive and negative experiences with the other participants.

Table 1: Please note that I believe the location of healthcare professionals is provided and previously it was stated that this would be removed to ensure anonymity.

Response:
We thank the reviewer for her accurateness. We deleted the sentence: "For healthcare professionals no indication of the setting was provided to ensure anonymity."

Themes: Quotes provided in Table 3 are repeated within the text. Assuming these quotes provided are not the only quotes used to generate the theme/subtheme, it would be much more insightful to present additional (i.e., different) quotes in Table 3, rather than repeating the same quotes twice. For example, I am left wanting more information (example quotes) about theme 2 in particular, considering the intervention did not improve fatigue relative to usual care.

Response:

In the manuscript, we deliberately chose to present a selection of the quotes in the results section and in the table to keep the results concise. Following the reviewer's feedback, we did add quotes in the text and table regarding theme 2.

Page 21 line 6-13
"Regarding the content of the programme, some patients mentioned that the ECM sessions were long and contained repetitions of theories.
""The afternoon hours with the occupational therapist were often a bit tedious""
For some patients, the session on the topic of work was not applicable as they were no longer working (after retirement or cessation of work due to the consequences of NMD). The session on nutrition was perceived by some patients as too short and, therefore, lacking depth.
""The session on nutrition could have been more""

Page 17, line 48: "intensity" is confusing in this context because it is referring to the overall demands of the programme rather than the exercise intensity. Please edit here and elsewhere (the discussion) to e.g. intervention demands or burden or similar.

Response:
We changed the word "intensity" to "intervention burden" in the results and discussion sections.

Discussion:
In the interviews, were there suggestions provided to improve aspects of the intervention where patient satisfaction was lower (e.g., the length of fatigue management sessions, content of nutrition and work sessions)?

Response
No concrete suggestions were given by the participants to improve the ECM, work or nutrition sessions because participants were generally very satisfied. Only a few remarks were made. On the question which parts could be left out, participants said that no elements could be deleted.
Only one hour was allocated to work. The participants that had additional work-related questions were offered individual coaching on work if needed after or alongside the Energetic programme. However, for some patients, the session on the topic of work was not applicable as they were no longer working because they were retired or stopped working due to the consequences of NMD.

Page 21 line 6-13
"Regarding the content of the programme, some patients mentioned that the ECM sessions were long and contained repetitions of theories.
""The afternoon hours with the occupational therapist were often a bit tedious""
For some patients, the session on the topic of work was not applicable as they were no longer working (after retirement or cessation of work due to the consequences of NMD). The session on nutrition was perceived by some patients as too short and, therefore, lacking depth.
""The session on nutrition could have been more""

The recommendations are all reasonable and useful for future implementation. However, I am interested in the authors consideration of if/how this qualitative data provides insight on patient selection (e.g. nearly half to patients who were ineligible for the RCT were excluded due to "insufficient motivation or readiness to change") and relapse prevention (considering even highly motivated patients found the intervention demanding or even "exhausting"). How do the results compare with other interventions in people with NMD or chronic fatigue more broadly?

Response:
Regarding the patient selection we added the following text in the discussion:
Page 24 line 18-25, page 25 line 1-3.
"During the interviews, patients reported a high willingness to change before the start of the programme, which was probably related to the motivational screening by occupational therapists before participation. The screening for (in)eligibility before the start of the RCT regarded the individual motivation to change behaviour and the expected individual intervention burden, which resulted in an exclusion of 43 patients.[6] Nevertheless, in the interviews, the Energetic programme was reported to be physically and mentally intensive and sometimes difficult to schedule within the weekly agenda, which also depended on travel distance. This perceived intervention burden is an important factor for

patients' willingness to participate in Energetic and should be clear during the screening for patients at the start of the programme. However, in the interviews, patients reported that no elements should be taken out of the programme. A way to reduce the intervention burden would be the use of blended care, for instance combining e-health and face-to-face sessions.[26 27] The recent developments during the COVID-19 pandemic, for instance the increase in video calls for regular healthcare, show that e-health can be used in combination with traditional forms of care in outpatient rehabilitation.[28]"

With respect to relapse prevention, we expect that the booster sessions (page 25 line 15-17) can be helpful in continuing to apply the AET and ECM principles in practice. This is also reported in a other study regarding an exercise programme in NMD. We added the following text.

Page 25 line 8-10
"However, in this evaluation, some patients reported that, despite this guidance, they found it difficult to implement exercising at home and maintain the acquired skills in the long term. This is in line with a study of Wallace where patients mentioned a high motivation to maintain exercising after a training programme, but experienced barriers to gym membership and implementation[24]."

Reviewer: 2
Dr. Katie Hackett, Northumbria University
Comments to the Author:
This is an important study which goes alongside a RCT of a fatigue self-management intervention, as it gains insights from the patients who have participated in the intervention arm of the study, partners/next of kin of patients, the therapists and professionals involved in the delivery of the programme and gains further insights regarding satisfaction about the content and delivery of the programme which can be used to inform the implementation of the programme in the future.
Some minor issues to address in the manuscript:
1) The view points of partners/NOK of participants were included in the qualitative interviews. The abstract does not include this information.

Response:
We changed the abstract to include the participation of the next of kin.
Page 2, line 20
"Qualitative data was collected by individual and focus group interviews to gain insight in the experiences of patients (n=18), next of kin (n=2), and healthcare professionals (n=13) with facilitators and barriers to programme implementation."

2) On page 8 and p 11 in the results more clarity is needed about sampling. It is not clear how the participants were chosen for the 1:1 interviews and for the focus groups. Was there a sampling framework?

There are also some issues about the language being a little confusing when it comes to discussing focus group interviews and 1:1 semi-structured interviews. This needs to be made more clear in the text and be consistent. (e.g. see P 7 lines 20-21 - "the interviews" seem to refer to 1:1 qualitative interviews, but reading further on p 12 lines 4-5 - it seems that "interviews" does refer to both focus groups and 1:1 interviews). Please make this more clear in the text.

Response:
To be more clear in the methods section, we deleted the part: to participate in the interviews. And we added the next paragraph in the method section

Page 8 line 11-16
"For this evaluation, all patients in the intervention group were asked ~~to participate in the interviews and~~ to fill in the satisfaction questionnaire. Ten consecutive patients and seven partners or next of kin from the first two Energetic groups were asked by email to participate in an individual semi-structured interview. Additionally, 19 patients were asked face-to-face during the intervention to participate in focus groups following the last session of the Energetic programme. All healthcare professionals involved in the organisation (secretary), recruitment (physicians), and delivery of the Energetic programme (occupational therapists and physical therapists) (n=13) were asked by email to participate in individual semi-structured interviews"

3) It is not immediately clear in the abstract that the satisfaction questionnaire was only completed by participants who finished the programme.

We added in the abstract that the questionnaire was completed by the patients who completed the programme.
Page 2 line 16
"Quantitative data was collected by a questionnaire measuring patients' (n=25; all completed the programme) satisfaction with the perceived results, content, and delivery of the programme."
4) Typos noticed:
P8 line 19 "de intervention group" should be "the intervention group".
Check the grammar on p 11 line 6-7 ("emailed to all participants and" .... the word "they" is missing).

Response:
We thank the reviewer for her accuracy and changed 'de' into 'the' and added 'they'.

VERSION 2 – REVIEW

REVIEWER	Rosemary Twomey University of Calgary, Cumming School of Medicine
REVIEW RETURNED	03-Aug-2021

GENERAL COMMENTS	Thank you for your point-by-point response to my comments which have been considered and resolved in the revised manuscript. I have no further suggestions.