PEER REVIEW HISTORY

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

ARTICLE DETAILS

TITLE (PROVISIONAL)	Telehealth in motor neuron disease to increase access to specialist multidisciplinary care: a UK-based pilot, feasibility study
AUTHORS	Hobson, Esther; Baird, Wendy; Bradburn, Mike; Cooper, Cindy; Mawson, Susan; Quinn, Ann; Shaw, Pamela; Walsh, Theresa; McDermott, Christopher

VERSION 1 - REVIEW

REVIEWER	David Blanco Universitat Politècnica de Catalunya-Barcelona Tech
REVIEW RETURNED	22-Jan-2019

GENERAL COMMENTS	This report shows the results of an evaluation of the consistency between the CONSORT checklist you submitted and the information that was reported in the manuscript. In case of doubts, please consult the CONSORT extension for pilot and feasibility trials (https://www.bmj.com/content/bmj/355/bmj.i5239.full.pdf). Please, make the following revisions: • For CONSORT Item 6a (''Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed''), please include a subsection called “Outcomes” in the Methods section clearly describing all the information about the feasibility outcomes that are mentioned in “Aims of the study” and “Data collection”. Please, specify how and when each of these outcomes was assessed and explain whether data collection rates are also one of the feasibility outcomes of the study – this is mentioned in the abstract but not clearly stated in the Methods. • For CONSORT Item 9a (“Mechanism used to implement the random allocation sequence, describing any steps taken to conceal the sequence until interventions were assigned”), please explain how the allocation system was set up so that the person enrolling participants did not know in advance which treatment the next person was going to get. • For CONSORT Item 13a (“For each group, the numbers of participants who were randomly assigned, received intended treatment and were analysed for the primary outcome”), specify in the CONSORT flow diagram that the n in the top 3 boxes refer to patients and not to carers. Please consider changing these boxes to “Patients assessed for eligibility using ARC database (n=306)”, “Patients invited (n=95)” and “Patients randomised (n=40)”. In the

	Telehealth and Control boxes, refrain from using the letter n to describe the number of carers since it might be confusing to readers. A new possible formulation would be: Patients allocated to telehealth (n=20) [18 carers]

REVIEWER	Anne Hogden University of Tasmania, Australia
REVIEW RETURNED	22-Jan-2019

GENERAL COMMENTS	Dr Hobson and team have conducted a well-documented and interesting study that highlights the need for flexible service delivery for people living with MND. The study provides a good example of co-design with people with MND and their carers. It was good to see how the story of the trial unfolded, and what had to be changed to accommodate accommodate participants. I note that this feasibility of an RCT manuscript is a parallel paper with a process evaluation, submitted as a separate manuscript. While there are some overlaps, I believe both manuscripts work well as stand-alone papers. The feasibility manuscript is well structured and generally well presented. Even so, several typos remain, so please edit very carefully. Background: TiM needs to be written in full for it's first use in the main text (para 2) Aims: A supplementary data table of the feasibility questions is mentioned (ADePT framework. Is this table in your supplementary section, or in that of Bugge et al? As there is so much supplementary data, it would help the reader if the main text contains a reference to the appropriate table, eg in the Study design section, two tables are mentioned, but no table numbers are given. Role of funding sources: This is the first mention of Abbott Pharmaceuticals and Mylan before the Funding and acknowledgements section. A brief explanation of the functions of these groups would be helpful here. Results: Again, helpful if the main text was directly linked to the tables in the Supplementary data. Qualitative data is well expressed, and gives the reader good understanding of what is important to patients and carers in trial participation. Discussion: A good discussion of the benefits and disadvantages of RCTs for this population, and why they are not always the most useful approach. The barriers to completion of the telehealth nurse diaries spoke volumes about the limitations of RCTs alone to

	account for the intricacies of delivering and evaluating interventions in MND care.

REVIEWER	Ileana Howard, MD University of Washington, U.S.A.
REVIEW RETURNED	05-Feb-2019

GENERAL COMMENTS	This is a very interesting topic, and I appreciate the novel approach to telehealth described by the authors. The paper was well-written and does an excellent job describing the pragmatic considerations and challenges of studies in this patient population. I appreciated the thoughtful comments in the discussion about ways these challenges could be addressed.

REVIEWER	Palmira Bernocchi, PhD ICS Maugeri, Italy
REVIEW RETURNED	27-Feb-2019

GENERAL COMMENTS	This research is very important to ensure universal access to care for patients affected by motor neuron disease. The authors gathered a huge and interesting amount of data to demonstrate the feasibility of this TiM model. Although this research is very interesting the risk, however, is that too much information makes the work difficult to read, also because there is a mixture of quantitative and qualitative information. In my opinion you have to simplify as possible, to make the reading as simple as possible. I would avoid referring to a that is not described here, such in the aims the third objective. Methods In the methods you cite the usual care group but do not describe what is meant by "usual care " in the data collection it would be useful to refer to tables 1 and 2 shown in the supplements. Results In the results there is a minimal description of the numerous quantitative data reported, which in any case would be interesting In table 1 I did not understand what use do the controls of the TiM app. What is the difference between the two groups in the use of telehealth Results I realize that this work analyzes both quantitative and above all qualitative information. Regarding the second one, as to provide an understanding of the resources required to conduct a defenitive trial, I have not quite understood why it has not been calculated. We should be more schematic. The costs of personnel, of telemedicine, ... data must be reported in the results, while comments and reflections in the discussion. Discussion In the discussion, the limitations of the study should be better highlighted

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name

David Blanco

Institution and Country

Universitat Politècnica de Catalunya-Barcelona Tech

Please state any competing interests or state 'None declared':

None declared

Please leave your comments for the authors below

This report shows the results of an evaluation of the consistency between the CONSORT checklist you submitted and the information that was reported in the manuscript. In case of doubts, please consult the CONSORT extension for pilot and feasibility trials (https://www.bmj.com/content/bmj/355/bmj.i5239.full.pdf).

Please, make the following revisions:

• For CONSORT Item 6a ("Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed"), please include a subsection called "Outcomes" in the Methods section clearly describing all the information about the feasibility outcomes that are mentioned in "Aims of the study" and "Data collection". Please, specify how and when each of these outcomes was assessed and explain whether data collection rates are also one of the feasibility outcomes of the study – this is mentioned in the abstract but not clearly stated in the Methods.

We have added a section in Outcomes and added tables (Tables 1 and 2) from the Appendix to detail all the patient/carer reported outcomes.

• For CONSORT Item 9a ("Mechanism used to implement the random allocation sequence, describing any steps taken to conceal the sequence until interventions were assigned"), please explain how the allocation system was set up so that the person enrolling participants did not know in advance which treatment the next person was going to get.

This statement has been amended to:

Patients were randomised 1:1 after recruitment to receive usual care or TiM using www.sealedenvelope.com which employs permuted block randomisation with a mixture of block sizes (block size concealed). Stratification was not employed.

• For CONSORT Item 13a ("For each group, the numbers of participants who were randomly assigned, received intended treatment and were analysed for the primary outcome"), specify in the CONSORT flow diagram that the n in the top 3 boxes refer to patients and not to carers. Please consider changing these boxes to "Patients assessed for eligibility using ARC database (n=306)", "Patients invited (n=95)" and "Patients randomised (n=40)". In the Telehealth and Control boxes, refrain from using the letter n to describe the number of carers since it might be confusing to readers. A new possible formulation would be:

Patients allocated to telehealth (n=20)

[18 carers]

Amended as recommended.

Reviewer: 2

Reviewer Name

Anne Hogden

Institution and Country

University of Tasmania, Australia

Please state any competing interests or state 'None declared':

None declared

Please leave your comments for the authors below

Dr Hobson and team have conducted a well-documented and interesting study that highlights the need for flexible service delivery for people living with MND. The study provides a good example of co-design with people with MND and their carers. It was good to see how the story of the trial unfolded, and what had to be changed to accommodate accommodate participants. I note that this

feasibility of an RCT manuscript is a parallel paper with a process evaluation, submitted as a separate manuscript. While there are some overlaps, I believe both manuscripts work well as stand-alone papers.

We thank the reviewer for their positive comments.

The feasibility manuscript is well structured and generally well presented. Even so, several typos remain, so please edit very carefully.

This has been done and changes highlighted in yellow.

Background:

TiM needs to be written in full for it's first use in the main text (para 2)

We have added this.

Aims:

A supplementary data table of the feasibility questions is mentioned (ADePT framework. Is this table in your supplementary section, or in that of Bugge et al?

We have added a link directly to the ADePT online supplementary file (in square brackets).

As there is so much supplementary data, it would help the reader if the main text contains a reference to the appropriate table, eg in the Study design section, two tables are mentioned, but no table numbers are given.

We have renamed the two supplementary files “methods” and “results” and now refer to them directly including page numbers where relevant several times in the paper.

Role of funding sources:

This is the first mention of Abbott Pharmaceuticals and Mylan before the Funding and acknowledgements section. A brief explanation of the functions of these groups would be helpful here.

We have elaborated on this.

“The TiM was developed through a collaboration between the University of Sheffield (UoS), Sheffield Teaching Hospitals NHS Trust, Mylan Ltd and Abbott Healthcare. This trial was funded the National Institute for Health Research and the Motor Neurone Disease Association. Mylan Ltd supplied software, hardware and some technical expertise. The Telehealth Nurse took on the additional duties as part of her current role. The study design, conduct, analysis, and interpretation of data, writing of the report, and the decision to submit the paper for publication were conducted by the authors independently of the funders with the exception of a requirement to report adverse events the investigator deemed to be related to Abbott Pharmaceuticals’ drugs.”

Results:

Again, helpful if the main text was directly linked to the tables in the Supplementary data.

We have renamed the two supplementary files “methods” and “results” and now refer to them directly including page numbers where relevant.

Qualitative data is well expressed, and gives the reader good understanding of what is important to patients and carers in trial participation.

Discussion:

A good discussion of the benefits and disadvantages of RCTs for this population, and why they are not always the most useful approach. The barriers to completion of the telehealth nurse diaries spoke volumes about the limitations of RCTs alone to account for the intricacies of delivering and evaluating interventions in MND care.

Reviewer: 3

Reviewer Name

Ileana Howard, MD

Institution and Country

University of Washington, U.S.A.

Please state any competing interests or state ‘None declared’:

None declared

Please leave your comments for the authors below

This is a very interesting topic, and I appreciate the novel approach to telehealth described by the authors.

The paper was well-written and does an excellent job describing the pragmatic considerations and challenges of studies in this patient population. I appreciated the thoughtful comments in the discussion about ways these challenges could be addressed.

We thank the reviewer for their positive comments.

Reviewer: 4

Reviewer Name

Palmira Bernocchi, PhD

Institution and Country

ICS Maugeri, Italy

Please state any competing interests or state ‘None declared’:

none declared

Please leave your comments for the authors below

This research is very important to ensure universal access to care for patients affected by motor neuron disease. The authors gathered a huge and interesting amount of data to demonstrate the feasibility of this TiM model.

We thank the reviewer for their positive comments.

Although this research is very interesting the risk, however, is that too much information makes the work difficult to read, also because there is a mixture of quantitative and qualitative information.

In my opinion you have to simplify as possible, to make the reading as simple as possible.

I would avoid referring to a that is not described here, such in the aims the third objective.

We appreciated that there is a large amount of evidence in this trial hence why we have attempted to split the results into two parallel papers which refer to each other. We have tried to avoid overlap whilst also including sufficient information for each paper to be read independently. With this in mind we have revised both papers to try to ensure they can be read independently whilst complementing each other. We also refer to supplementary data more clearly throughout the paper to enable the reader to see all the methods and data in detail.

Methods

In the methods you cite the usual care group but do not describe what is meant by "usual care " in the data collection.

We have included this statement in Study Design section.

It would be useful to refer to tables 1 and 2 shown in the supplements.

We have moved Table 1 and 2 into the main body of the paper

Results

In the results there is a minimal description of the numerous quantitative data reported, which in any case would be interesting

We have tried gain a balance between reporting all the quantitative data and that needed to answer the feasibility questions. The supplementary data provided extensive additional information.

In table 1 I did not understand what use do the controls of the TiM app. What is the difference between the two groups in the use of telehealth

We clarified this in the Intervention section.

Results

I realize that this work analyzes both quantitative and above all qualitative information.

Regarding the second one, as to provide an understanding of the resources required to conduct a defenitive trial, I have not quite understood why it has not been calculated. We should be more schematic. The costs of personnel, of telemedicine, ... data must be reported in the results, while comments and reflections in the discussion.

We accept the cost estimates are a limitation of this trial and reflect the difficulty estimating costs of new services, particularly digital services. We have elaborated on this in the results, discussion and in the Strengths and Limitations. We have also amended the “role of funders” to better describe the costs of the intervention.

Discussion

In the discussion, the limitations of the study should be better highlighted

We have amended this in paragraph 2 and 3 and in the Strengths and limitations section.