PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Telemedicine for the management of neuropsychiatric symptoms in long term care facilities: The DETECT Study. Methods of a cluster randomized controlled trial to assess feasibility
AUTHORS	Piau, Antoine; Nourhashemi, Fati; De Mauléon, Adélaïde; Tchalla, Achille; Vautier, Claude; Vellas, Bruno; Duboue, Maryline; Costa, Nadège; Rumeau, Pierre; Lepage, Benoit; Soto, Maria E.

VERSION 1 – REVIEW

REVIEWER	Ladislav Volicer University of South Florida, FL, USA
REVIEW RETURNED	02-Jan-2018

GENERAL COMMENTS	Interesting study but is should be published after the results are available

REVIEWER	Anne-Sophie rigaud Assistance Publique Hôpitaux de Paris & Université Paris Descartes, Paris, France
REVIEW RETURNED	02-Jan-2018

GENERAL COMMENTS	Review bmjopen-2017-020982 There are few papers that evaluate the benefit of the management of dementia with neuropsychiatric symptoms with telemedecine. This is an interesting paper dealing with an important issue in which we still have scarce knowledge. The paper provides valuable information that deserves publication after minor revisions. Abstract It provides a clear overview of the paper. Introduction In the introduction, the authors have nicely presented the field of research and the state of the art. Method and analysis The methods are accurate and clearly described. I would like to make some suggestions. Since the telemedecine consultation is useful for patients and staff because of its content (diagnosis and therapeutic pieces of advice), I suggest that the authors give more details about the intervention. Indeed in the paper, they write that they establish a “tailored plan with therapeutic priorities, overall strategy and follow-up plan”. I think that

	it would be useful for readers if authors could explain their procedure and give some examples of the tailored plans they propose to patients, families and nursing home staffs. Since the acceptability of telemedicine by professionals is examined, it seems quite relevant to evaluate both quantitative and qualitative indicators. As regards the qualitative evaluation, it would be useful to have more details about the procedure: 1) The authors plan to carry out interviews: Do the authors plan to carry out individual interviews with each staff member of the nursing homes? Do they only plan two questions: satisfaction and willingness to adopt telemedicine or do they plan other questions in other fields? How will they gather and analyze the content of the interviews? 2) The authors also plan to do two meetings. It is not clear whether the meetings are planned or already completed? Would it be possible to clarify this issue? I would also suggest that the authors give more details about the procedure to gather the material during the meetings? Will they record the meeting and analyze the content? Discussion The discussion is quite relevant. References The references are appropriate.

REVIEWER	Ruth Schneider University of Rochester Medical Center, USA
REVIEW RETURNED	22-Jan-2018

GENERAL COMMENTS	ABSTRACT 1) Please clarify in abstract that that was a cluster randomized trial. The phrase “randomized in clusters” implies something different (i.e. that multiple LTCFs were randomized in groups). 2) The authors specify in the abstract that 200 participants will be included. There is no reference to this in the body of the manuscript and no rationale is provided for this decision in the manuscript. INTRODUCTION 1) Please define or describe neuropsychiatric symptoms. 2) It is unclear what is meant by an “increase of formal caregiver burden and mistreatments.” Does the latter refer to inappropriate treatment? METHODS 1) I recommend that the authors follow the CONSORT guidelines for reporting a cluster randomized trial. Many of my recommendations seek to help the authors better align their manuscript with these guidelines. 2) Please provide greater detail regarding the LTCFs that were potentially eligible for participation and how they were enrolled. How many were potentially eligible? Were only LTCFs with telemedicine systems eligible for participation? Were all potentially eligible LTCFs individually approached regarding participation? If not, how were LTCFs made aware of the trial? As all of the LTCFs have already been enrolled and randomized, consider providing further detail here (e.g. the number excluded for < 60 beds, etc). 3) The process for randomization is not clear. Were LTCFs

	randomized as they were consented? Or were 20 LTCFs consented and then all randomized at once? How many features were used for stratification? Regarding participant eligibility criteria: 4) Please provide rationale for age cut-off. 5) Define disruptive NPS in the text (rather than linking to another document). Regarding the intervention and outcome assessment: 6) Please provide more detail on the equipment used (video-conferencing software, bandwidth, etc). 7) A strength of the design is the inclusion of qualitative and quantitative outcome measures for the assessment of acceptability. However, the primary outcome measure for assessing acceptability is never clearly specified. Therefore, it is not clear what criteria the authors would use in deciding to move forward (or not) with a more definitive trial. More detail is needed on how some of the measures will be assessed (e.g is staff willingness to adopt telemedicine assessed by Likert scale?). 8) More detail on how and when secondary outcomes will be assessed is needed. Moreover, it should be explicitly stated when the outcome measures relate to the cluster level and when they related to the individual level. 9) If the participant is not necessarily included in the telemedicine visits when and by whom are outcome measures assessed? 10) As participants are consented after cluster randomization the potential for selection bias is high. How are you addressing this concern? Is the person identifying potential participants and obtaining consent blinded to LTCF randomization? Sample Size: 11) A sample size is not calculated yet the authors state that 20 clusters will be "sufficient to qualitatively evaluate differences." Based on what? 12) There is no discussion as to why 200 was selected as the targeted number of participants (as stated in abstract). Moreover, it is not clear based on the numbers provided how the authors arrived at an estimate that 282 people would potentially meet eligibility criteria. Regarding control: 13) Usual care is not adequately described. What is the normal process for obtaining consultation for disruptive NPS? Statistical Analysis: 14) How will you "control for comparability of the two arms according to patient characteristics at inclusion"? 15) The authors state that the main analysis of acceptability will be intention to treat and all "subjects randomized will be analyzed in their allocated arm." The problem with this statement is two-fold: 1) Subjects are not randomized (LTCFs are) and 2) it further muddles the distinction between participant level and cluster level outcomes. 16) In determining the proportion of TM consults, what will be the denominator? Is it individuals with disruptive NPS? Or incidents of disruptive NPS (in which case the same individual might be counted more than once over a 24-month period)? 17) How will within cluster correlation be handled for the secondary analyses?

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

They write that they establish a “tailored plan with therapeutic priorities, overall strategy and follow-up plan”. I think that it would be useful for readers if authors could explain their procedure and give some examples of the tailored plans they propose to patients, families and nursing home staffs.
You are right, an example has been included in the manuscript.

1) The authors plan to carry out interviews: Do the authors plan to carry out individual interviews with each staff member of the nursing homes? Do they only plan two questions: satisfaction and willingness to adopt telemedicine or do they plan other questions in other fields? How will they gather and analyze the content of the interviews?
2) The authors also plan to do two meetings. It is not clear whether the meetings are planned or already completed? I would also suggest that the authors give more details about the procedure to gather the material during the meetings? Will they record the meeting and analyze the content?
The « first meeting at the study kick-off » is completed, the « second restitution meeting at the end of the study” is planned. There are no individual interviews but collective meetings lead by a sociologist. The contents of the interviews will be analyzed by sociologic research approach. We made the choice not to use Likert scales or quantitative scores but to call on social sciences methods.

Reviewer 2

1) Please clarify in abstract that that was a cluster randomized trial. The phrase “randomized in clusters” implies something different (i.e. that multiple LTCFs were randomized in groups).
You are right; it has been done in the new manuscript.

2) The authors specify in the abstract that 200 participants will be included. There is no reference to this in the body of the manuscript and no rationale is provided for this decision in the manuscript.
We assumed a mean of 80 residents by LTCF, among them we assumed that between 40% and 50% would have dementia ; we assumed that 82% of residents with dementia would have neuropsychiatric symptoms (Selbaek et al. J am med dir assoc 2013). If one third of these residents present a disruptive NPS during the inclusion period, it was estimated that around 200 patients could potentially meet the inclusion criteria. This was detailed and corrected in the abstract and sample size paragraph.

Intro

1) Please define or describe neuropsychiatric symptoms.
You are right; it has been done in the new manuscript.

2) It is unclear what is meant by an “increase of formal caregiver burden and mistreatments.” Does the latter refer to inappropriate treatment?
It was a mistake; it has been changed in the new manuscript.

Methods

1) I recommend that the authors follow the CONSORT guidelines for reporting a cluster randomized trial. Many of my recommendations seek to help the authors better align their manuscript with these guidelines.
We followed the CONSORT guidelines but as you say, we had to improve coherence with the guidelines on several points.

2) Please provide greater detail regarding the LTCFs that were potentially eligible for participation and how they were enrolled. How many were potentially eligible?
You are right; it has been done in the new manuscript.
Were only LTCFs with telemedicine systems eligible for participation?
No, “Intervention: (…) after randomization, 10 LTCF were equipped with TM in the intervention group”
Were all potentially eligible LTCFs individually approached regarding participation? If not, how were LTCFs made aware of the trial?
See the modifications in the new manuscript.
As all of the LTCFs have already been enrolled and randomized, consider providing further detail here (e.g. the number excluded for < 60 beds, etc).
You are right, but we consider this as a result and we do not address results in this paper.

3) The process for randomization is not clear. Were LTCFs randomized as they were consented? Or were 20 LTCFs consented and then all randomized at once? How many features were used for stratification?
The LTCFs were randomized immediately after their consent. Two features were used for stratification: Randomization was stratified on the region (Toulouse or Limoges region) and the presence of an Alzheimer Unit in the facility.
Regarding participant eligibility criteria:

4) Please provide rationale for age cut-off.
65 or older is commonly used as a “permissive criterion” (mean age in French LTCF is about 85 years old).

5) Define disruptive NPS in the text (rather than linking to another document).
You are right; it has been done in the new manuscript.

Regarding the intervention and outcome assessment:

6) Please provide more detail on the equipment used (video-conferencing software, bandwidth, etc).
We understand your comment, but we chose not to provide detail on the equipment as videoconferencing is not a new technique, and the technology in itself is not central to the project. We all use videoconferencing softwares in everyday life (e.g. Skype) and it doesn’t explain the gap with real life medical practice. We want to focus on acceptability process and not on technology or quantitative health indicators. The study is much more about “changes in care practices” than technology.

7) A strength of the design is the inclusion of qualitative and quantitative outcome measures for the assessment of acceptability. However, the primary outcome measure for assessing acceptability is never clearly specified.
You are right; it has been done in the new manuscript.
Therefore, it is not clear what criteria the authors would use in deciding to move forward (or not) with a more definitive trial.
We will move forward with a more definitive trial. The question is how. “results from this study will be used to develop the study design for a subsequent larger trial”; “The secondary outcome measures will provide the necessary information to design a future nationwide effectiveness and cost efficacy study”.

More detail is needed on how some of the measures will be assessed (e.g is staff willingness to adopt telemedicine assessed by Likert scale?).

There are no individual interviews but collective meetings lead by a sociologist. The content of the interviews will be analyzed by sociologic research approach. We made the choice not to use likert scales or quantitative scores but to call on social sciences methods.

8) More detail on how and when secondary outcomes will be assessed is needed.
See table 1.
Moreover, it should be explicitly stated when the outcome measures relate to the cluster level and when they related to the individual level.
You are right; it has been done in the new manuscript. Quantitative primary outcomes and secondary outcomes are measured at the individual level.

9) If the participant is not necessarily included in the telemedicine visits when and by whom are outcome measures assessed?
The only outcome that supposes patient participation is QoL-AD which is assessed a T0 and T2 if possible as exposed in Table 1.

10) As participants are consented after cluster randomization the potential for selection bias is high. How are you addressing this concern? Is the person identifying potential participants and obtaining consent blinded to LTCF randomization?
The person identifying potential participants and obtaining consent is not blinded to LTCF randomization. As the included patients will present, for most of them, moderate to severe dementia, and as the intervention is not invasive, we could reasonably expect a limited bias.

Sample Size:

11) A sample size is not calculated yet the authors state that 20 clusters will be “sufficient to qualitatively evaluate differences.” Based on what?
20 facilities should be enough to observe inter-facility variability and get information on the outcomes in the 2 interventions arms, as well as an estimation of inter- and intra-facility variances (for the estimation of design effects). It would be much less informative to carry out a feasibility study including only 2 ou 3 facilities by arm. Some authors (eg. Maas et al. Sufficient sample sizes for multilevel modeling. Methodology 2005;1(3):86) indicate that at least 30 clusters are necessary to get good estimates (regression coefficients, variances) at the group level. This high number of clusters might be recommended in confirmatory analyses but is probably too high and costly in a feasibility study. Our choice of 10 facilities per arm seemed a reasonable compromise.

12) There is no discussion as to why 200 was selected as the targeted number of participants (as stated in abstract). Moreover, it is not clear based on the numbers provided how the authors arrived at an estimate that 282 people would potentially meet eligibility criteria.
200 is the estimated number of patients we expect to recruit based on the figures detailed above. In this cluster randomized study, it is not possible to give a very precise estimate of the number of patients who will be included, as it is based on the product of several proportions. The figures are detailed in the sample size paragraph.

Regarding control:

13) Usual care is not adequately described. What is the normal process for obtaining consultation for disruptive NPS?
You are right; it has been done in the new manuscript: “NPS usual care refers to inappropriate care (use of emergency facilities) or appropriate care (memory consultations and specialized inpatient units) that also face their own limits and face important delays” (Already addressed in the introduction).

Statistical Analysis:
14) How will you “control for comparability of the two arms according to patient characteristics at inclusion”?
A simple description of baseline characteristics of the facilities and of patients included will be done for each group. We do not plan to make statistical comparisons of baseline characteristics. We replaced "we will control for comparability of the two arms according to patient characteristics at inclusion" by "we will describe baseline characteristics of the facilities and of the included patients for each group."
15) The authors state that the main analysis of acceptability will be intention to treat and all “subjects randomized will be analyzed in their allocated arm.” The problem with this statement is two-fold: 1) Subjects are not randomized (LTCFs are) and 2) it further muddles the distinction between participant level and cluster level outcomes.
We cut this sentence, and replaced it by: "The main analysis will be carried out among the included patients in the intervention group”.

16) In determining the proportion of TM consults, what will be the denominator? Is it individuals with disruptive NPS? Or incidents of disruptive NPS (in which case the same individual might be counted more than once over a 24-month period)?
This proportion will be defined as: the proportion of residents who will benefit from a TM consultation for their management after the occurrence of a disruptive NPS, among the included residents (residents who will present a disruptive NPS). So the denominator will be individuals with disruptive NPS rather than the number of disruptive NPS (events which can occur several times after the first one at inclusion). A same individual will be counted only once in this study.
17) How will within cluster correlation be handled for the secondary analyses?
Mixed models with a random intercept (corresponding to the cluster units) will be applied to handle within cluster correlation. This information was added to the statistical analysis paragraph.

VERSION 2 – REVIEW

REVIEWER	Ruth Schneider University of Rochester Medical Center, USA
REVIEW RETURNED	21-Feb-2018

GENERAL COMMENTS	1) Discrepancies within the text and with the figure regarding eligibility criteria and stratification parameters remain. Please make sure all text is consistent. 2) Although I recognize that the primary aim of this study is to determine acceptability of the telemedicine intervention, I remain concerned that the potential for bias has not been adequately addressed in the manuscript. Differential selection of participants may occur as an un-blinded study team member is responsible for ascertaining the numbers of patients with a disruptive NPS (a designation which is inherently subjective) from un-blinded LTCF staff. Moreover, un-blinded investigators at each individual LTCF are responsible for enrolling and consenting participants after cluster randomization has already occurred. Thus, the potential for unbalanced groups appears high and the limitations of this study design should be addressed. 3) Table 1: It appears that NPI-C is not being performed at any visit.

VERSION 2 – AUTHOR RESPONSE

Reviewer requirements

1) Discrepancies within the text and with the figure regarding eligibility criteria and stratification parameters remain. Please make sure all text is consistent.
You are right, the manuscript and the figure have been modified.

2) Although I recognize that the primary aim of this study is to determine acceptability of the telemedicine intervention, I remain concerned that the potential for bias has not been adequately addressed in the manuscript. Differential selection of participants may occur as an un-blinded study team member is responsible for ascertaining the numbers of patients with a disruptive NPS (a designation which is inherently subjective) from unblended LTCF staff. Moreover, un-blinded investigators at each individual LTCF are responsible for enrolling and consenting participants after cluster randomization has already occurred. Thus, the potential for unbalanced groups appears high and the limitations of this study design should be addressed.
You are right; we modified the discussion in the new manuscript. Blinded recruitment is extremely difficult and we think that this is an acceptable bias as the primary aim of this study is to determine acceptability of the TM intervention. Nevertheless, this bias should be addressed more closely in a larger scale efficacy study. Thus, even if a potential for unbalanced groups does exist, it will be partially discernible since the baseline characteristics of the facilities and patients enrolled in each group will be described.

3) Table 1: It appears that NPI-C is not being performed at any visit.
It was a mistake; it has been changed in the new manuscript.

Editor requirements

We previously queried why the study was not described as a feasibility study in the CT.gov registry. Unfortunately, we have been unable to locate your response to this point.
We confirm that our study is a feasibility study and we have modified the study description in the CT.gov registry.
Our study is done before a main study. The question is: can we confirm that TM is acceptable and thus, can we confirm that a larger implementation is possible in real life setting? This is a key issue to make sure that the main study will have a better chance of success.

Please provide an English patient consent form, as per the requirements of the SPIRIT checklist.
Done