Author’s response to reviews

Title: Dynamic LED-light versus Static LED-light for depressed inpatients: results from a randomized feasibility trial Title acronym: ROOM-LIGHT feasibility

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Response to reviewers on PAFS-D-19-00124
Dynamic LED-light versus Static LED-light for depressed inpatients: results from a randomized feasibility trial Title acronym: ROOM-LIGHT feasibility

We want to thank the reviewers for very constructive, helpful and insightful comments on the paper. We have tried to answer this in detail and changed the manuscript accordingly.
Alongside this process, we came across a mistake in the CONSORT flow chart where the text in the Enrollment box was partly incorrect. This text has been deleted.

Reviewer #1: Overall, interesting and informative feasibility study on important modality to treat depression (light therapy) that requires further investigation. Major limitation includes limited power and sample size and high relative attrition rate. Authors could work to share more information about how the challenges with generating adequate power, recruitment, and attrition will inform the larger
trial. Moreover, more information and clarity is needed as to why the authors chose their primary outcome and secondary outcomes.

Answer:
Thank you for these valuable suggestions. We have added information on pages 16 in the conclusion section on how we plan to increase power, recruitment, and reduce attrition in the now running efficacy trial.

Major Comments:
1) The primary outcome for this study was the rate of discontinuation from the trial due to discomfort from the lighting conditions. Secondary outcomes were recruitment and dropout rates, visual comfort, depressive symptoms, and suicidal ideation. On page 5, lines 17-19, the authors cite evidence that light therapy has relatively few adverse events with good ocular safety. If there is good evidence to support the safety and ocular safety of light therapy (albeit with light boxes), why is important for the rate of discontinuation from the trial due to discomfort from the lighting conditions to be the primary outcome. Can you please clarify why this was selected as the primary outcome especially considering that your results also reflected that discontinuing the trial due to discomfort from the light was not an issue (as expected). Are there other important factors that have not previously been proven among light therapy trials that could deter patients from participating that have not already been proven?

Answer:
The choice of primary outcome was based on a possibility that a built-in light source with higher intensity could be uncomfortable to some patients compared to an ordinary, controllable lightbox. The concern was also focused on how patients would tolerate the luminaire built into the window jamb that could not be turned off. We though it very important to have a setup that was well tolerated, which we could build on in future studies. We have added this information into the discussion section on page 15/16. We are not aware of factors that could deter patients from participating other than the well-known problems with light sensitivity in patients with migraine. We have inserted a sentence regarding the choice of primary and secondary outcomes in the outcomes section on page 10.

2) Page 6, lines 48-60, inclusion criteria includes both bipolar and unipolar depression. Have past trials combined these populations and is there any evidence to suggest why light therapy may be more or less effective for either unipolar or bipolar depression. May consider adding a line or two regarding the decision to include both in the introduction.

Answer: We agree that this should be mentioned. Some previous studies have included mixed samples of unipolar and bipolar patients but unfortunately, they do not report results separately (Gottlieb et all, 2019 Bipolar disorders). We have inserted a sentence in the background on page 6 about this issue and added a reference) to a study showing the effect of light treatment in bipolar depression.

3) Page 9, line 24-26. Use of ceiling and reading luminaire was logged continuously by both groups. Did the participants themselves log this data? How was it logged. Could you please provide more information regarding this process.

Answer: The luminaires were logged automatically by the lighting system and not by the participants. This has been further explained on what is now page 10 at the top.

4)Page 9, line 45-47. Who were the Hamilton raters (e.g. physicians, psychometrists, were they part of the research study?)
Answer: The Hamilton rating was done by a research coordinator, educated in psychometrics and experienced in Hamilton rating, blinded to the study, and who did not have any other association with the study procedures. This information has been added to the section now on page 10 at the bottom.

5) Page 13, line 52-57 "The high dropout at endpoint made outcomes difficult to interpret. The high dropout was primarily due to early discharge which might be related to a faster improvement." I would caution against alluding that the high drop out rate due to early discharge may be related to a faster improvement rate given the sample size, attrition, and other limiting factors to conclude any statistically significant association between early discharge and faster improvement.

Answer: Thank you for pointing this out. We agree and have deleted the statement on what is now page 15.

6) Methods question. In regards to the lighting in the rooms and the setup of the trial, what were the patients told? Were they blinded in anyway to the lighting set up (A vs B vs C)? Were they informed the lighting in their room was modified and given details about specific modifications?

Answer: Patients were informed that we tested two different lighting systems to evaluate visual comfort, the system performance, and any influence on depressive symptoms. We informed participants that we did not a priori know what set-up would be best. Participants were told that in the static setup the built-in window luminaire was not active. Participants were thus not blinded to the intervention and this has been added to the end of the light intervention section on page 10.

7) Conclusions (page 14). In Figure 1 (CONSORT Flow Diagram), out of 38 individuals assessed for eligibility, 23 were excluded (17 due to meeting exclusion criteria, 1 for not meeting inclusion, 5 other, and 0 people declined). Line 17 on page 14 states a larger number of light equipped rooms would help to recruit more participants. How did you come to this conclusion? It seemed that a major barrier to recruitment was not finding enough participants meeting the inclusion/exclusion criteria.

Answer: Thank you for pointing out this error. We agree that the proportion of patients not meeting inclusion criteria will be the same regardless of the number of rooms. The point we tried to make was that an increase in the number of rooms with light equipment installed will increase the actual number of possible inclusions. We have made a note on this in the conclusion section on page 16.

8) Conclusions (page 14). What other methods will you implement to obtain endpoint assessments should patients be discharged?

Answer: In the future efficacy study, all participants are informed that an endpoint assessment is part of the study no matter if a participant is prematurely discharged or intervention is discontinued for other reason. We have addressed this important point in the last section in the conclusion section on page 15/16.

9) Conclusions (page 14). A major limitation of this study is the sample size and lower power as mentioned. Further comment is needed regarding how this feasibility study informs the larger trial in regards to improving the overall power and recruitment.

Answer: This is now explained in the last section of the conclusion; with an increased number of light
equipped rooms, a mandatory endpoint assessment, and a reduction of the study period to 3 weeks, we think that we will be able to include more participants that will complete the trial period.

10) CONSORT CHECKLIST item 7a, points to page 6 for rationale for numbers in the trial. Did not see much information regarding why the authors aimed for the numbers achieved in this trial. Please comment.

Answer: This is described in the sentence “We opted for 15 participants as we anticipated that this number would give indications of major problems with the lighting system, trial design, and adverse event.” This number was decided from the assumption that frequent side-effects would show themselves in 15 patients, of which 9 were allocated to the dynamic setup. We have now added to the text that adverse events would probably be more severe in the dynamic group, where the light was brighter and one of the luminaires could not be turned off. Therefore, we made a randomisation ratio that included more participant into the dynamic group (in a 3:2 manner) to catch these adverse events. This information is now inserted just after the cited sentence on page 6 in the methods section.

Reviewer #2: This is a feasibility randomized trial investigated the effectiveness of an LED light intervention for patients with a major depressive episode as part of a unipolar or bipolar disorder. Patients were randomized to a static vs. dynamic LED light intervention. This study is addressing an important question and easy to follow however some revisions are required. Please refer to the comments outlined below:

General comments:
1. Please review the manuscript for language and grammatical errors (e.g. page 5, line 16: Light therapy seem to have relatively few adverse effects). Also suggest revising some sentences for clarity (e.g. page 11, line 1: …diminished due to long staying of non-eligible patients admitted to one of the four light test rooms.)

Thank you for pointing this out. We have checked the paper for language and grammatical errors and simplified sentence structure where considered appropriate. A reference has also been inserted for the DSM system on page 7.

2. Please write out the full form of acronyms when they are first used (e.g. Page 6, Line 32: eCRf and CTU, Page 10, Line 9: UKU).

Answer: Thank you for finding these omissions. We have changed this and checked the paper for more oversights.

Specific comments:
Background
3. Page 6, Line 6: Suggest to state the specific study population (patients with depressive disorders) in the aim of the study rather than "inpatient psychiatric setting".

Answer: Thank you for pointing out this imprecision. We have changed the text as suggested.

Methods:
4. Page 7, Line 4: Does "coercive measures of any kind" refer to if patients are receiving mandatory psychiatric treatment? Please clarify this phrase.
Answer: Yes, that is correct – we have changed the wording to “mandatory psychiatric treatment”.

5. For the randomisation strategy, please include further information on how the treatment allocation was concealed and if the participants were blinded to the study hypothesis.

Answer: Treatment allocation was done by the OpenClinica system when entering eligibility data into the eCRF. This information has been added to the methods section on page 6/7. The procedure was thus concealed for investigators. Regarding blinding, please see the answer to reviewer 1 bullet 6.

Results:
6. Page 10, Line 38: There is a marked difference in the duration of the current depressive episode between the dynamic and static groups. Could this be due to the small sample size or error in randomisation? Perhaps it should be discussed in the Limitations section.

Answer: Thank you for pointing this out. We agree that this should be commented on and have inserted a sentence at the end of the discussion section on page 15.

Discussion:
7. Page 13, Line 55: It is difficult to make the inference that early discharge among patients may be related to faster improvement due to light therapy as they were also receiving other therapies during their stay.

Answer: We agree, and the sentence has been deleted (now on page 15).

Conclusion:
8. It is excellent that the authors will use the findings from this study to inform a larger definitive trial. In terms of recruitment, can the light fixtures be made portable so that they can be moved to rooms of eligible participants? Would this option be more feasible than to install lighting in additional patient rooms? And can the eligibility criteria be modified to include patients who are expected to stay in hospital for the duration of the study?

Answer: The efficacy trial is now running and uses the same setup with built-in luminaires. As the efficacy trial has the light system installed in 10 out of 12 rooms, we have not opted for portable light. It is in practice not possible to know a priori how long a patient will be staying in the ward. This is, among other things, dependent on the influx of new patients.