PEER REVIEW HISTORY

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ARTICLE DETAILS

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<th>TITLE (PROVISIONAL)</th>
<th>Study protocol for Virtual Leisure - a mixed methods pilot clinical trial investigating the effect of Virtual reality delivered stress reduction, entertainment, and distraction on the use of coercion and need-based medication and patient satisfaction at a closed psychiatric intensive care unit</th>
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VERSION 1 – REVIEW

<table>
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<th>Bicego, Aminata</th>
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<td>University of Liege, Sensation and Perception Research Group - GIGA Conscisouneys</td>
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<td>REVIEW RETURNED</td>
<td>03-Feb-2023</td>
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GENERAL COMMENTS

The study aims to assess the acceptability, feasibility and effectiveness of a virtual reality intervention in an in-patient psychiatric ward. While be believe studies investigating virtual reality are necessary on order to better characterize and understand the clinical value of this device, the manuscript needs substantial revision before being published.

Title:
The title should explicitly mention is it a protocol and not a "design".

Abstract:
The abstract lacks clarity. The method should be explicitly written.

Introduction:
General comment: this section significantly lacks clarity and references. Indeed, a lot of concepts are listed without any explicit explanation. We believe that since it is a protocol, authors have to thoroughly explain the background and rationale of the study.

Page 2
Line 19: “[…] where routines and rules are inconsistent meanwhile also offering safety.” Could the authors better explain what they mean.

Line 20: “[…] various mental disorders”. Could the author be more explicit.

Line 22: define "need-based medication, coercive action, and treatment".

Line 24: Could the authors better explain what they mean by entertaining interventions?

Page 3
Line 5: authors should be cautious with the use of “non-intrusive” when they refer to VR because VR might be experienced as intrusive for some patients.

Line 11: Could the authors be more explicit about “treatment settings”.

Line 11: “[...] in mental health research, and treatment [...]” Could be authors specify what they mean.

Page 4

Line 5: on what population is the study 17 about.

The authors mention a lot of different types of VR: VR alone, VR combined with relaxation, VR combined with mindfulness, and distractive VR. They should better explain what is VR in general and in what way it can be combined to other complementary approaches such as relaxation and mindfulness. They should also know that mindfulness and relaxation are two separate concepts.

Line 19: When they mention that VR leads to lesser costs, authors should say as to what they compare the costs of the VR.

Line 23 “The fun and entertaining aspects of VR may also increase engagement and thereby the probability that the patients in fact uses the scenarios.” This sentence is not clear.

Page 5

Line 6: what do the author mean by satisfactory? Based on what do they estimate it is satisfactory or not?

Aim and hypothesis

Line 8: “multiple” authors should be much more precise and prefer to use a number rather than terms that are vague.

The aims and hypothesis are quite vague and should be more specific.

Methods and materials

Ethics should be in this section

Study Design

The study design is quite vague and should be thoroughly and explicitly explained.

Page 6

Line 1: could the authors specify “regularly”. An estimated frequency of use based on previous literature or clinical experience could help the authors to determine a specific amount of VR exposure.

Line 9: what is the treatment?

Line 11: could the authors specify the affective disorders and personality disorders?

Line 14: same comment on frequency.

Line 18: a lot of exclusion criteria are missing. The authors might consider these:

• Age under 18 years old
• disabling hearing impairment
• blindness
• frequent loss of balance nausea
• seizures
• increased sensitivity to infrared and ultraviolet light
• contagious skin conditions
• head injury
• claustrophobia

Page 7
The sample size calculation, qualitative analyses and quantitative analyses should be different sections.

The sample size calculation should also consider previous literature similar as the present study to calculate the sample size.
Line 23: why do the authors except to enroll 80% ? Based on what ?

Page 8
Line2: could the authors be more explicit about the "coercions" ?
Line 5: what is a relevant reduction ? Based on what ?
Line 10: we do not understand how the interrupted time series will answer the hypothesis of the authors. Could the authors provide why they will rely on this statistical test? The statistical significance is not mentioned. This part should be thoroughly described.

The qualitative and quantitative analyses are written in a confusing way as they also contain parts of the procedure. The authors should re-write these sections and be careful to only include the analyses they will do. The procedure is another part of the manuscript. Also the procedure should be written before the analyses.

Page 9
We suggest that the authors re-write this section as it needs to be more specific and clear.
They use different types of VR, interactive and passive. Perhaps the authors could already discuss these differences in the introduction.

Could they better explain each VR intervention in detail?:
- how do the patients interact?
- the duration
- what are the differences and the similitude?

Page 10
Line 6: what will be proposed to the patients that are too much agitate ?
Line 6: “The VR entertainment could be instigated when patients experience lack of activities or are hospitalized for a longer period (weeks) and need to maintain a sense of connection with the outside society.” Could the authors re-phrase this sentence ? what do they mean?
Line 10: The study procedures needs to be re-written as it needs extensive clarification and explanations.
Line 15: If authors except to include 80% of the patients, we do not understand how 80% is an acceptability measure. Could the authors explain ?
Line 16: this needs to be thoroughly described. How will the authors do ?
Line 18: same comment

Page 11
Line 3: the questionnaire needs to be explained and described. And time of evaluation should be made explicit.
Line 6: same comment. When the authors mention questionnaires, they should describe them and explain them thoroughly.

General comments:
They are a lot of blurry parts to this study protocol.
- What is the frequency of use of the VR?
- It is not clear if the patient in the two separate ward will receive the VR and the control session or if one ward will propose nothing and the other will propose the VR. This should be better explained as the reader does not understand which patient will receive what, where and at which frequency.
- The authors use two different types of VR which are furthermore subdivided in different types. This will probably impact differently the outcomes. Have the authors addressed this issue? If so, they should explain what they will do to assess the specificity of each VR exercise.
- What will the authors do if the patients experience any side effect?
- Every section of the manuscript needs more detailed information in order for other researchers and clinicians to understand what the question is, what is being done and how, what will the authors do to answer their questions.
- Discussion needs to be reviewed according to the comments and modification of the manuscript.

Reviewer: Găină, Marcel
Grigore T Popa University of Medicine and Pharmacy Faculty of Medicine, 3rd Medical, Psychiatry

Review returned: 06-Feb-2023

General Comments:
Regarding the proposed protocol entitled: „Design of the Virtual Leisure pilot Study - Virtual reality delivered stress reduction, entertainment, and distraction at a closed psychiatric intensive care unit”

The conceptualisation of this protocol seems flawless, and embeds the state-of-the-art overview of current progress regarding virtual reality randomised control trials. Still, there are a few suggestions I would like to underline:

Page 3, line 5 "The periods will be in reversed order in the 6 wards." could be rephrased to ensure a clearer understanding for the reader.”

1) Virtual reality and control (virtual reality without sound and image) – a bold suggestion would be including a control group, to ensure an even greater quality and statistical impact of the data collected. This aspect could be managed clinically by embedding the EaseVR study protocol, a currently FDA Approved device, that managed to effectively realise the blinding process - Garcia, L.M.; Birkhead, B.J.; Krishnamurthy, P.; Sackman, J.; Mackey, I.G.; Louis, R.G.; Salmasi, V.; Maddox, T.; Darnall, B.D. An 8-Week Self-Administered At-Home Behavioral Skills-Based Virtual Reality Program for Chronic Low Back Pain: DoubleBlind, Randomized, Placebo-Controlled Trial Conducted During COVID-19. J. Med. Internet Res. 2021, 23, e26292

Although lesser exclusion criteria would ensure a greater participant population, certain determinations would be better stratified if using an even narrower patient inclusion, by aspects of somatic health and individual differences.

Page eleven, row 5 – Exploratory outcomes – the Spielberger STATE-TRAIT inventory could offer a panoramic perspective on the impact of immersive IVR experiences on perceived anxiety.
Finally, I would like to congratulate the group of authors for undertaking such a demanding task and pledge to offer my support by any means necessary for contributing to the development and implementation of immersive virtual reality in medical sciences. The development of this protocol into an interventional clinical trial will offer valuable data regarding the feasibility of implementing Immersive Virtual Reality for patients suffering from mental disorders.

**VERSION 1 – AUTHOR RESPONSE**

Reviewer: 1
Dr. Aminata Bicego, University of Liege

Comments to the Author:
The study aims to assess the acceptability, feasibility and effectiveness of a virtual reality intervention in an in-patient psychiatric ward. While we believe studies investigating virtual reality are necessary on order to better characterize and understand the clinical value of this device, the manuscript needs substantial revision before being published.

1. Title:
The title should explicitly mention it is a protocol and not a “design”.
REPLY: Thank you for pointing this out, we have changed the title to “Study protocol for Virtual Leisure - a mixed methods pilot clinical trial investigating the effect of Virtual reality delivered stress reduction, entertainment, and distraction on the use of coercion and need-based medication and patient satisfaction at a closed psychiatric intensive care unit”

2. Abstract:
The abstract lacks clarity. The method should be explicitly written.
REPLY: We have revised the method section to be more explicit. It now reads “Methods: The study is a clinical trial, employing a mixed-methods design, enrolling 124 patients hospitalized at a closed psychiatric ward in the Capital Region of Denmark. Outcomes (e.g., coercion, need-based medication, and perceived stress) from a 12-month period where patients hospitalized at a PICU are offered VR-based recreational experiences are compared to a 12-month period without the availability of VR-experiences at the PICU. Feasibility and acceptability will be explored with qualitative interviews supplemented with non-participant observations and focus groups”.

3. Introduction:
General comment: this section significantly lacks clarity and references. Indeed, a lot of concepts are listed without any explicit explanation. We believe that since it is a protocol, authors have to thoroughly explain the background and rationale of the study.
REPLY: We agree that the clarity of the background section could be enhanced and have revised accordingly, e.g., added explanations when appropriate and rephrased sentences when needed. Also, we have rewritten the first paragraph.

Page 2
4. Line 19: “[…] where routines and rules are inconsistent meanwhile also offering safety.” Could the authors better explain what they mean.
REPLY: We have deleted the sentence, as we can see it is unclear and it doesn’t contribute anything.

5. Line 20: “[…] various mental disorders”. Could the author be more explicit.
REPLY: We have added information, so it now reads: “with patients suffering from various different
disorders such as personality disorders and psychotic illness"

REPLY: Thank you for pointing this omission out. We have added explanations and it now reads: “.. which may be a cause of conflicts, use of need-based medication, (i.e. medication such as benzodiazepines, antipsychotic medication, and sedative hypnotics, that is not taken regularly, but as needed), coercive actions (i.e. comprise physical retention, mechanical restraint (belt fixation) and forced sedation (injecting the patient with sedating medication without their consent) and a low overall satisfaction with staying at the ward”

7. Line 24: Could the authors better explain what they mean by entertaining interventions?
REPLY: We have included an explanation, so it now reads: “To reduce the use of coercion, recreational and entertaining interventions (i.e more gamified and fun interventions) are generally recommended”.

8. Line 5: authors should be cautious with the use of “non-intrusive” when they refer to VR because VR might be experienced as intrusive for some patients.
REPLY: Thank you for pointing this out. This is a simple error, what was meant was non-invasive interventions. We have changed the word.

9. Line 11: Could the authors be more explicit about “treatment settings”.
REPLY: We have elaborated on this and added “such as hospital inpatient, residential or outpatient”

10. Line 11: “[…] in mental health research, and treatment […]” Could be authors specify what they mean.
REPLY: We have attempted to make it clearer and changed it to: “Research in mental health has shown great potential for the use of VR which has been found to be an effective tool for the treatment of many psychiatric diagnoses, with minimal side effects”.

11. Line 5: on what population is the study 17 about.
REPLY: Study 17 is a review covering a broad range of diagnoses. We have added that information, so it now reads “Learning mindfulness is a skill that can be transferred to many situations, and a recent review found mindfulness carried out in VR to reduce anxiety and depression and improve sleep quality, emotion regulation, and mood across a broad range of diagnoses”

12. The authors mention a lot of different types of VR: VR alone, VR combined with relaxation, VR combined with mindfulness, and distractive VR. They should better explain what is VR in general and in what way it can be combined to other complementary approaches such as relaxation and mindfulness. They should also know that mindfulness and relaxation are two separate concepts.
REPLY: Thank you for pointing out this unclarity. We do not use VR combined with relaxation etc but VR-based relaxation etc (i.e., relaxation in a VR environment). We have added the following clarification: “Over the past decade, several studies have investigated the effect of VR based relaxation (i.e relaxation conducted in VR) on stress levels in people with psychiatric problems”. We are aware that mindfulness and relaxation are two separate concepts, but both are passive activities focusing on internal events (mindfulness on acceptance of present moment internal events, while relaxation practices teach strategies to change internal events), aiming to reduce stress. To clarify the fact that these are separate concepts we have added the following: “Mindfulness is among the most commonly applied types of VR experience with a relaxation focus, aiming to reduce stress, and appears to be broadly applicable”
13. Line 19: When they mention that VR leads to lesser costs, authors should say as to what they compare the costs of the VR.
REPLY: We agree that this unclear and have changed it to: “Applying VR for recreational use in the form of stress reduction, entertainment, and distraction could provide an alternative to regular practice, that can be planned more flexibly and demand a reduced number of resources compared to in vivo”

14. Line 23: “The fun and entertaining aspects of VR may also increase engagement and thereby the probability that the patients in fact uses the scenarios.” This sentence is not clear.
REPLY: Thank you for pointing this out. What is meant is that due to the gamified nature of the VR experiences, these are expected to be perceived as entertaining and attractive increasing the commitment to use them. We have changed the sentence, so it now reads “The fun and entertaining aspects (due in part to the gamified nature) of VR may make it more attractive and increase engagement and thereby the probability that the patients use the scenarios”

15. Line 6: what do the author mean by satisfactory? Based on what do they estimate it is satisfactory or not?
REPLY: What is meant is that is has not been thoroughly explored and more studies are needed. We can, however, see that this can be misunderstood, so to make it clearer and avoid confusion we have changed it to “has not been thoroughly explored”

Aim and hypothesis
16. Line 8: “multiple” authors should be much more precise and prefer to use a number rather than terms that are vague.
REPLY: We agree that the aim could be more precise, but are uncertain if the reviewer suggests that we propose an aim regarding a specific number of VR experiences? The idea is to explore the effect of having a broad selection of diverse VR experiences available. To make this clearer we have changed the sentence to “The aim of the current study is to identify whether the availability of a broad selection of diverse VR experiences…..”

17. The aims and hypothesis are quite vague and should be more specific.
REPLY: We have attempted to make it less vague and more specific and it now reads: “The aim of the current study is to identify whether the availability of a broad selection of diverse VR experiences comprising stress reduction, entertainment, and distraction are feasible and acceptable and can reduce number of coercions, use of need-based medication, and increase patient satisfaction at closed PICUs. We hypothesize that 1) VR-based experiences will be feasible and acceptable for patients at a PICU. 2) the availability of VR-based experiences will decrease the number of coercive interventions, use of need-based medication, and increase overall patient satisfaction at the PICU in a 12-month one-year period with VR experiences available compared to a one-year period when these are not available”

Methods and materials
18. Ethics should be in this section
REPLY: We have moved Ethics to a paragraph on “Ethics and dissemination” in the section on methods and materials

Study Design
19. The study design is quite vague and should be thoroughly and explicitly explained.
REPLY: Thank you for making us aware of this. We have attempted to follow all suggestions to make it clearer
20. Page 6
Line 1: could the authors specify “regularly”. An estimated frequency of use based on previous literature or clinical experience could help the authors to determine a specific amount of VR exposure.
REPLY: Regular does not refer to a specific frequency, but only refers to the fact that it is offered repeatedly, with similar amounts of time between one time and the next. We strive for a constant availability for the patients to use VR, and the patients are approached by staff and offered use when any of the indications listed in the 3rd paragraph in the section on 2.4. Virtual Reality experiences are present, or the staff consider it relevant for any other reason. We do not wish to dictate a specific frequency, but want to leave room for individual differences. We have specified this and changed it to the following: "Quantitative measures will be used to compare outcomes for a twelve-month period where all patients are offered VR experiences at least daily (and repeatedly, with similar amounts of time between one time and the next) to outcomes for a twelve-month period with no availability of VR experiences”

21. Line 9: what is the treatment ?
REPLY: It is the treatment corresponding to what they would all have received at the PICU had the study not existed, with specific treatment depending on diagnosis. However, the treatment aspect is not the essential part here so we have changed it to the following to avoid distractions: “The study will enroll all patients referred for inpatient admission at a specified closed PICU in the capital region of Denmark”

22. Line 11: could the authors specify the affective disorders and personality disorders?
REPLY: We have specified the disorders, so it now is: “The ward treats a broad selection of patients with different psychiatric disorders such as schizophrenia spectrum disorders, affective disorders (such as depression and anxiety), and personality disorders (such as borderline personality disorder)”

23. Line 14: same comment on frequency.
REPLY: see #20

24. Line 18: a lot of exclusion criteria are missing. The authors might consider these :
• Age under 18 years old
• disabling hearing impairment
• blindness
• frequent loss of balance nausea
• seizures
• increased sensitivity to infrared and ultraviolet light
• contagious skin conditions
• head injury
• claustrophobia
REPLY: Thank you for pointing our attention to these potential criteria, which we agree are worth considering. In the current setup it is not possible to do thorough individual screening for eligibility (in addition to the one at admission), and we wish to only exclude a minimum, and have the participants be as representative of the PICU as possible. Finally, we wish to ensure as large as possible a participant population
However, we have added head injury (as VR might inflict distress) to the criteria. Also, to make our considerations clear, we have added: “We have kept the criteria at a minimum to have the participants be as representative of the PICU as possible”

Page 7
25. The sample size calculation, qualitative analyses and quantitative analyses should be different sections.
REPLY: We have divided them into different sections and put in subheadings.

26. - The sample size calculation should also consider previous literature similar as the present study to calculate the sample size.
REPLY: The study is based on convenience sampling as participants are selected based on availability and willingness to take part. The calculations are estimations of what we will have power to detect based on the expected sample size. We have tried to make this clearer in the following: “The ward is scaled to accommodate 13 in-patients and has an average hospitalization of 8 weeks per patient. Thus, the expected number of patients during the two periods are approximately 156 in total. We expect to enroll 80% (N=62) of patients in each twelve months study period, resulting in a total convenience sample of N=124”

PARTICIPATION RATE

27. - Line 23: why do the authors except to enroll 80% ? Based on what ?
REPLY: P6? The expected participation rate is set to 80% based on a previous study assessing the feasibility and tolerability of using a VR headset in a PICU that found that 81% of the patients meeting eligibility criteria took part (N=17/21)(Mark et al., 2021)
And on our experiences with previous/ongoing VR studies in our research group, and on high patient interest conveyed through conversations with both patients and staff. Added: “Based on a previous study assessing the feasibility and tolerability of using a VR headset in a PICU that found that 81% of the patients meeting eligibility criteria took part (Mark et al., 2021), on previous and ongoing VR studies in our research group, and on high patient interest conveyed through conversations with both patients and staff, we expect to enroll 80% (N=62) of patients in each 12-month study period, resulting in a total N=124”

Page 8
28. - Line2: could the authors be more explicit about the “coercions” ?
REPLY: We have elaborated on this in the section on qualitative analyses

29. - Line 5: what is a relevant reduction ? Based on what ?
REPLY: As we are sure the reviewer will acknowledge it is not possible to set general/absolute standards for such an evaluation. However, previous studies have considered such a reduction rate significant. Thus, we have added
“This corresponds to a reduction rate of 31%. This is in line with what previous studies have considered relevant. For instance, an evaluation of a Safewards trial found reduced seclusion rates by 36% which the authors considered significant and high enough to recommend implementation1. A similar study analyzing data from cluster randomized controlled trial reported an estimated 15% decrease in conflict and 26.4% decrease in ‘containment’, which the authors considered being a demonstrable impact on conflict and containment rates

30. - Line 10: we do not understand how the interrupted time series will answer the hypothesis of the authors. Could the authors provide why they will rely on this statistical test? The statistical significance is not mentioned. This part should be thoroughly described.
REPLY: We have added the following to make it clearer: “Interrupted time series are powerful tools for analyzing the effects of natural experiments. In essence, they test whether the development of coercions prior to the intervention differs from the development after the intervention, in terms of either a change in level or slope (or both).”

31. - The qualitative and quantitative analyses are written in a confusing way as they also contain parts of the procedure. The authors should re-write these sections and be careful to only include the analyses they will do. The procedure is another part of the manuscript.
Also the procedure should be written before the analyses.
REPLY: We have attempted to differentiate clearer between procedure and analysis, and moved procedure up before he analyses. See also reply to comment #25

Page 9
32. - We suggest that the authors re-write this section as it needs to be more specific and clear. They use different types of VR, interactive and passive. Perhaps the authors could already discuss these differences in the introduction.
REPLY: SEE REPLY TO #33 BELOW

33. - Could they better explain each VR intervention in detail:
- how do the patients interact?
- the duration
- what are the differences and the similitude?
REPLY: As there are a large number of VR experiences it not feasible to go through each one, but as we can see the need for more detailed information on the VR experiences, we have elaborated in in the section on VR experiences.

Page 10
34. - Line 6: what will be proposed to the patients that are too much agitate?
REPLY: We have added: "If the patients are too agitated for the VR experiences to be recommended, the staff will propose what they consider suitable according to standard practice at the ward e.g need-based medication".

35. - Line 6: “The VR entertainment could be instigated when patients experience lack of activities or are hospitalized for a longer period (weeks) and need to maintain a sense of connection with the outside society.” Could the authors re-phrase this sentence? what do they mean?
REPLY: We have rephrased the sentence so it now reads: "The VR experiences could be instigated when patients are restless and long for activities or are hospitalized for a longer period (weeks) and start feeling isolated and need to maintain a sense of connection with the outside society"

36. - Line 10: The study procedures needs to be re-written as it needs extensive clarification and explanations.
REPLY (see reply to #31)

37. - Line 15: If authors except to include 80% of the patients, we do not understand how 80% is an acceptability measure. Could the authors explain?
REPLY: There is no established threshold for defining a high response rate but a rate of 80% or higher is generally considered excellent, so such a response rate would be a strong indicator of acceptability.

38. - Line 16: this needs to be thoroughly described. How will the authors do?
REPLY: This is further elaborated in the section on qualitative analyses under method

39. - Line 18: same comment
REPLY: This is further elaborated in the section on qualitative analyses under method

Page 11
40. - Line 3: the questionnaire needs to be explained and described. And time of evaluation should be made explicit.
REPLY: We have added info on the questionnaire, and it now reads: “Patients satisfaction is assessed

41. Line 6: same comment. When the authors mention questionnaires, they should describe them and explain them thoroughly.
REPLY: We have added info on the questionnaire, and it now reads: “Global perceived level of stress over the past week is assessed at discharged from hospital with the Perceived Stress Scale, assessing the degree to which situations are appraised as stressful. It includes 10 items that are designed to tap how unpredictable, uncontrollable, and overloaded respondents find their lives.”

General comments:
42. -They are a lot of blurry parts to this study protocol.
   - What is the frequency of use of the VR?
   REPLY see reply to comment #20

43. - It is not clear if the patient in the two separate wards will receive the VR and the control session or if one ward will propose nothing and the other will propose the VR. This should be better explained as the reader does not understand which patient will receive what, where and at which frequency.
REPLY: As we have changed the number of wards to one this is no longer relevant.

44. - The authors use two different types of VR which are furthermore subdivided in different types. This will probably impact differently the outcomes. Have the authors addressed this issue? If so, they should explain what they will do to assess the specificity of each VR exercise.
REPLY: We agree that the different types of VR could have a different impact. Unfortunately, with the current design we cannot look into this. However, we have added a paragraph on future studies in the end of the discussion stating that: “Future studies may want to look into the impact of individual factors such as diagnoses as well as the potential differential impact of the different types of VR experiences”

45. - What will the authors do if the patients experience any side effect?
REPLY: as stated in the section on 5.1 Ethics approval and consent to participate: “Side effects and adverse events will be monitored and recorded throughout the study period. Any adverse events will be reported to the Committee on Health Research Ethics of the Capital Region Denmark”

46. - Every section of the manuscript needs more detailed information in order for other researchers and clinicians to understand what the question is, what is being done and how, what will the authors do to answer their questions. Discussion needs to be reviewed according to the comments and modification of the manuscript.
REPLY: We have attempted to adjust the manuscript according to your previous 45 points and have updated the discussion.

Reviewer: 2
Dr. Marcel Găină, Grigore T Popa University of Medicine and Pharmacy Faculty of Medicine

Comments to the Author:
Dear Authors,

Regarding the proposed protocol entitled: „Design of the Virtual Leisure pilot Study - Virtual reality delivered stress reduction, entertainment, and distraction at a closed psychiatric intensive care unit”
1. The conceptualization of this protocol seems flawless, and embeds the state-of-the-art overview of current progress regarding virtual reality randomized control trials. Still, there are a few suggestions I would like to underline: Page 3, line 5 “The periods will be in reversed order in the 6 wards.” could be rephrased to ensure a clearer understanding for the reader.

REPLY: thank you for the positive comments. As we have changed the number of wards from 2 to 1, the line in question is no longer relevant, and has been deleted.

2. Virtual reality and control (virtual reality without sound and image) – a bold suggestion would be including a control group, to ensure an even greater quality and statistical impact of the data collected. This aspect could be managed clinically by embedding the EaseVR study protocol, a currently FDA Approved device, that managed to effectively realise the blinding process - Garcia, L.M.; Birckhead, B.J.; Krishnamurthy, P.; Sackman, J.; Mackey, I.G.; Louis, R.G.; Salmasi, V.; Maddox, T.; Darnall, B.D. An 8-Week Self-Administered At-Home Behavioral Skills-Based Virtual Reality Program for Chronic Low Back Pain: DoubleBlind, Randomized, Placebo-Controlled Trial Conducted During COVID-19. J. Med. Internet Res. 2021, 23, e2629

REPLY: thank you for the suggestion, and for pointing our attention to this interesting protocol. Unfortunately, the study is ongoing and it is not possible to make changes in the basic design. However, we will definitely be looking into this for future studies.

3. Although lesser exclusion criteria would ensure a greater participant population, certain determinations would be better stratified if using an even narrower patient inclusion, by aspects of somatic health and individual differences.

REPLY: We agree with the reviewer that there would be certain benefits of a narrower population, but the aim of the current study is to study the effect of VR experiences at a ward level. However, in a later and larger study it would definitely be interesting to look at different more specified populations as well as the effect of the different types of VR experiences. We have therefore added a paragraph on future studies in the end of the discussion stating that: “Future studies may want to look into the impact of individual factors such as diagnoses as well as the potential differential impact of the different types of VR experiences”

4. Exploratory outcomes – the Spielberger STATE-TRAIT inventory could offer a panoramic perspective on the impact of immersive IVR experiences on perceived anxiety.

REPLY: This is an interesting idea which could be interesting to pursue. However, the current study is ongoing and it is not possible to add measures. Furthermore, outcomes are at ward level.

Finally, I would like to congratulate the group of authors for undertaking such a demanding task and pledge to offer my support by any means necessary for contributing to the development and implementation of immersive virtual reality in medical sciences. The development of this protocol into an interventional clinical trial will offer valuable data regarding the feasibility of implementing Immersive Virtual Reality for patients suffering from mental disorders.

REPLY: thank you.