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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 76305

Title: Application of an Internet-Delivered Transdiagnostic Treatment for Emotional Disorders during COVID-19: A Randomized Controlled Trial

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06265249

Position: Peer Reviewer

SPECIFIC COMMENTS TO AUTHORS

I would like to congratulate the authors for their good work: a very relevant topic and a well-written article. Nevertheless, I consider that some additions should be made, which I send in the attached document. Thank you and I hope my suggestions are helpful!

Authors' response: Thank you for comments. We have now addressed all of these.

1. The title must include the term "Unified Protocol" somewhere

Authors' response: Thank you for comments. We have now changed the title:

Application of Unified Protocol as a Transdiagnostic Treatment for Emotional Disorders during COVID-19: An Internet-Delivered Randomized Controlled Trial

2. In the Abstract I consider that the following should be added: 1) the average age of the participants; 2) that the participants have an emotional disorder;

Authors' response: Thank you for comments. We have now added the mentioned information. In the internet-delivered randomized controlled trial, 102 students with an emotional disorder (mean age = 28.20 years, SD = 8.89) were randomly allocated to receive UP (n=51) or treatment as the usual intervention.

3. The introduction looks very good to me but there are two aspects that I think should be reformulated:

- a) It is not only the issue of comorbidity that supports the application of UP, but the fact that different trans-diagnostic mechanisms underlying emotional disorders (namely neuroticism) have been found, which emphasize that these emotional disorders may be part of the same spectrum, at that it makes sense to be understood in a more transdiagnostic and not so categorical way. I think that this aspect should therefore be clarified in the introduction.

Authors' response:

Thank you for comments. We have now added the

Emotional disorders (e.g., depression, anxiety, trauma-related, and somatic symptom disorders) are characterized by intense and unpleasant negative emotions and aversive reactions to these affective experiences themselves, which are triggered by a reduced sense of emotion regulation [7].

- b) At the end of the introduction, the authors discuss in a very organized way the importance of the UP, followed by the importance of the UP in times of a pandemic and followed by the need and advantages of internet-based interventions. However, I think that I should finish with the studies that already exist on UP in online format and I believe that there are already some studies (I think with teenagers and I think with adults in Spain as well - check this please).

Authors' response: Thank you for comments. We have now added the studies.

47 Osma J, Peris-Baquero O, Suso-Ribera C, Farchione TJ, Barlow DH. Effectiveness of the Unified Protocol for transdiagnostic treatment of emotional disorders in group format in Spain: Results from a randomized controlled trial with 6-months follow-up. *Psychother Res* 2022; **32**: 329-342 [PMID: 34132170 DOI: 10.1080/10503307.2021.1939190]



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48 **Caiado B**, Góis A, Pereira B, Canavarro MC, Moreira H. The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Children (UP-C) in Portugal: Feasibility Study Results. *Int J Environ Res Public Health* 2022; **19** [PMID: 35162806 DOI: 10.3390/ijerph19031782.]

4. In the participants' section, I consider that the reasons for excluding the participants and the known reasons that led the participants to decline to participate in the study should be added.

Authors' response: We have now added more information to clarification.

Of these, thirty-eight students declined or uninterested (without a specific reason) to participate in the study.

5. In the exclusion criteria, I am wondering about why do you exclude patients with eating disorders (in comorbidity)? I also think that the term "unstable medication regimens" needs to be better defined.

Authors' response: we deleted the eating disorders. Also, we added brief description for unstable medication regimens. Unstable medication regimens (e.g., complex medication regimens to manage their health).

6. In the description of the UP intervention, it is not clear to me whether the internet-based program was entirely built by you or not; if it is self-guided or includes online sessions with therapists... In case of including therapists, it is necessary to describe how many therapists per group, if the therapists were from the research team or not, if they were the same ones who did the baseline interviews or not, what training do they have.... how many participants per group.... In this aspect, I consider that important information is clearly missing that needs to be added!

Authors' response:

The study (e.g., all assessments and treatments) was administered via the Internet.

7. Likewise, in the definition of TAU, it is not clear that the program is also done online (video calls? self-guided?). Moreover, I need additional information at this point on how this program was created, if the authors created it and on what basis. Is it applied individually or in a group? Who applies? The same research team that applies the UP or others? I'm also

wondering why this psychoeducation group is considered a TAU and not an active control group.

Authors' response: in page 8 we stated that:

The control group received TAU as provided by the general practitioner. TAU has been considered non-treatment and/or practical advice by the GP administered in normal care, focused on reducing unpleasant feelings and negative emotional symptomatology. TAU was delivered in 12 weekly two-hour sessions through the Internet. The participants who received the introductory modules of UP included four sessions of psychoeducation. Specifically, the TAU comprises three parts: (a) four sessions of psychoeducation, (b) four sessions of COVID-19 consideration, and (c) four sessions of sharing experiences

8. In the results section - treatment results - only the results of the experimental group are presented, without comparison with the control group. Although these results appear in the tables, with the main objective of an RCT being the evaluation of efficacy compared to a control group, it seems to me essential that this information is written in this section.

Authors' response: thank you. We revised the result section, as following.

Table 4 shows the results of the parametric test of ANCOVA to compare the effectiveness of the unified protocol intervention with TAU at post-treatment (Time 2). At the end of the study, the results of the ANCOVA revealed that students who received the UP intervention demonstrated statistically significant reduction in the ODSIS score, compared with who received TAU, Cohens' $d = -1.50$ with 95% CI [-1.90, -1.06]; Mean diff = 4.08, SE= 0.52, $P < .001$, with 95% CI [3.05, 5.11]. The results of ANCOVA also revealed that students who received the UP intervention demonstrated statistically significant reduction in the OASIS score, compared with who received TAU, Cohens' $d = -1.06$ with 95% CI [-1.48, -0.65]; Mean diff = 2.47, SE= 0.56, $P < .001$, with 95% CI [1.39, 3.56].

9. In the results section it seems important to add information on whether or not there were significant differences between the variables of the experimental group and the control group at baseline.

Authors' response: SEE TABLE 3

10. In table 5, I see that the TAU participants worsened from pre- to post-treatment in practically all variables... this result is ignored in this article... how do you explain this? I think this



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information has to be added.

Authors' response:

There were no significant changes in the dependent variables in the control group at posttreatment relative to baseline. The stressful pandemic situations may have been a confounding factor that may have elevated mental health problems and higher than usual daily psychological life distress among the control group participants



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SPECIFIC COMMENTS TO AUTHORS

The manuscript "Application of an Internet-Delivered Transdiagnostic Treatment for Emotional Disorders during COVID-19: A Randomized Controlled Trial" investigated the differential effects of the Unified Protocol and a psychoeducational intervention on symptoms of depression, anxiety, affectivity, emotion dysregulation, and healthy emotionality in university population. The findings suggest that the online Unified Protocol improves the symptoms of emotional disorders, compared to the psychoeducational intervention. One of the strengths of the study is the transdiagnostic approach to emotional symptoms and its online implementation. However, I consider that there are several aspects that must be overcome before the manuscript is published:

1. The recruitment process should be better specified Did all subjects who wanted to participate have emotional symptoms? Figure 1 does not indicate participants who did not meet the diagnoses of anxiety or depression. However, the text indicates that "only consented subjects diagnosed with depression or anxiety disorders in SCID and obtained a high self-report score on the Beck Anxiety Inventory > 15 were selected for randomization". In addition, it is indicated that 38 subjects declined to participate. This



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should be clearly explained, since according to what is understood from the manuscript, the participants were recruited through advertisements and signed up voluntarily. 2. Explain why an effect size of $f = 0.35$ is assumed to calculate the required sample size. Also, why is a 20% dropout rate expected? These two issues must be clearly explained in the text. 3. I am not sure that psychoeducational intervention can be considered TAU. Is it usual to intervene with this population with a 12-week psychoeducational protocol? 4. The data should be analyzed following both intention-to-treat (ITT) and per protocol approaches. 5. In the ITT analysis, incomplete or missing data should be considered using the maximum likelihood estimation method. 6. The dropout rate was much higher than the expected rate assumed to calculate the sample size. This should be discussed in the manuscript or at least recognized as a limitation of the work. 7. The intragroup (pre-post) and between-group (differences between standardized mean changes [pre-post] of the respective groups) effect size should appear in the tables. 8. Minor issue: On page 6 the following sentence appears "Of these, thirty-eight clients declined to participate in the study". I do not think that the word "clients" is the most appropriate in this context.

Reviewer 1

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Review Date:2022-03-17 15:39

Specific Comments To Authors: The manuscript "Application of an Internet-Delivered Transdiagnostic Treatment for Emotional Disorders during COVID-19: A Randomized Controlled Trial" investigated the differential effects of the Unified Protocol and a psychoeducational intervention on symptoms of depression, anxiety, affectivity, emotion dysregulation, and healthy emotionality in university population. The findings suggest that the online Unified Protocol improves the symptoms of emotional disorders, compared to the psychoeducational intervention. One of the strengths of the study is the transdiagnostic approach to emotional symptoms and its online implementation. However, I consider that there are several aspects that must be overcome before the manuscript is published:



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Authors' response: Thank you for the summary of our study Thank you for the positive feedback. Thank you for comments. We have now addressed all of these.

1. The recruitment process should be better specified
Did all subjects who wanted to participate have emotional symptoms?
2. Figure 1 does not indicate participants who did not meet the diagnoses of anxiety or depression. However, the text indicates that “only consented subjects diagnosed with depression or anxiety disorders in SCID and obtained a high self-report score on the Beck Anxiety Inventory > 15 were selected for randomization”. In addition, it is indicated that 38 subjects declined to participate.

Authors' response: we added text to clarification

3. This should be clearly explained, since according to what is understood from the manuscript, the participants were recruited through advertisements and signed up voluntarily.

Authors' response:

Over three months, the participants were recruited through online announcements, flyers, and referrals. Additionally, the link for the study was distributed and posted on online community platforms such as university forums. Potentially eligible individuals who applied to participate in the RCT were informed of the study's objectives, advantages, and hazards, as well as session numbers, confidentiality, assurances of anonymity, and the possibility of group assignment, *via* e-mail or telephone. Participants were informed that they could withdraw consent or stop participating at any point in the study. Additionally, they were free to skip specific questions and continue to participate.

Individuals who initially obtained a high score (greater than 15) on the Beck Anxiety Inventory [59] were requested to obtain informed consent. The consented participants underwent an interview to ensure that eligibility criteria were fulfilled. Two clinical psychologists evaluated the



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participants' personal history, mental status, personal resources, and suicide risk through clinical interviews through 45 minutes of online video communication. Individuals who met the SCID-I-IV criteria for depression or anxiety disorders were requested to rate primary and secondary outcomes.

The participants rated the primary and secondary outcomes at two time points: Time 1: pretreatment to allocation, including baseline; and Time 2: immediately after intervention, including posttreatment assessment. Intervention schedule is presented in table 1.

4. Explain why an effect size of $f = 0.35$ is assumed to calculate the required sample size. Also, why is a 20% dropout rate expected? These two issues must be clearly explained in the text.

Authors' response: thank you. We added systematic review references for effect size and dropout rate.

5. I am not sure that psychoeducational intervention can be considered TAU. Is it usual to intervene with this population with a 12-week psychoeducational protocol?

Authors' response:

we conducted such protocol in previous studies.

6. In the ITT analysis, incomplete or missing data should be considered using the maximum likelihood estimation method.

Authors' response:

Based on the intent-to-treat (ITT) procedure, the data for all randomized participants were considered in the final analysis. To handle missing data, the last observation-carried-forward method (LOCF) was considered as a next point for dropping data

7. The dropout rate was much higher than the expected rate assumed to calculate the sample size. This should be discussed in the manuscript or at least recognized as a limitation of the work.



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Authors 'response: thank you. We recognized the issue as limitation. Also, we added text in conclusion.

8. The intragroup (pre-post) and between-group (differences between standardized mean changes [pre-post] of the respective groups) effect size should appear in the tables.

Authors 'response:

Cohen effect size added in text. Within group Cohen effect size added in table 6.

9. Minor issue: On page 6 the following sentence appears “Of these, thirty-eight clients declined to participate in the study”. I do not think that the word "clients" is the most appropriate in this context.

Authors 'response: **Thirty-eight students declined to participate in the study**

4 LANGUAGE POLISHING REQUIREMENTS FOR REVISED MANUSCRIPTS SUBMITTED BY AUTHORS WHO ARE NON-NATIVE SPEAKERS OF ENGLISH

As the revision process results in changes to the content of the manuscript, language problems may exist in the revised manuscript. Thus, it is necessary to perform further language polishing that will ensure all grammatical, syntactical, formatting and other related errors be resolved, so that the revised manuscript will meet the publication requirement (Grade A).

Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further. When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript.

Authors 'response:



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We added new certificate. Also, we added the language quality assessment score by Research square digital editing platform , after digital editing by the AJE.

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Application of Unified Protocol as a Transdiagnostic Treatment for Emotional Disorders during COVID-19: An Internet-Delivered Randomized Controlled Trial

> Nabi Nazari

Abstract

Background: Coronavirus disease 2019 (COVID-19) is an emotionally challenging time, especially for young adults, associated with a substantial increase in the prevalence of mental health problems, negative symptoms, and stressful experiences that compromise well-being. However, little support exists. The study was designed to determine the application of an internet-delivered unified protocol (UP) for adults with emotional disorders during the COVID-19 pandemic.

Method: In this internet-delivered randomized controlled trial,