Author’s response to reviews

Title: Phase-Based Treatment versus Immediate Trauma-Focused Treatment in Patients with Childhood Trauma-Related Posttraumatic Stress Disorder: Study Protocol

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Author’s response to reviews:

Dear Dr. Krieger,

We greatly appreciate the effort that was taken to review our manuscript. The manuscript has been edited taking the helpful comments of the reviewers into account. The changes in the revised manuscript are marked in yellow. Please find below a point-by-point response to the specific issues raised below. We hope that the adjustments make the manuscript suitable for publication in Trials, and we look forward to your response.

Reports Reviewer #1

The current manuscript provides an overview of a novel study looking into the effects of treating complex PTSD with (a) a phase based treatment consisting of and (b) delivery of exposure/EMDR directly. The trial is a very timely one that will with no doubt be well received in the scientific and clinical community, as such studies are so far lacking. The question of whether a phase-based treatment is more effective (or feasible) than immediate exposure in complex PTSD is extremely relevant. It is laudable that both originators of the treatment protocols agreed to supervise treatment delivery, this is methodologically very relevant. I have several critical points, however, that should be reviewed before the paper merits publication:

1. It is hypothesised that "based on the results of previous studies", the phase-based condition will be sign more effective in reducing PTSD symptoms than the immediate trauma-focused therapy. This is not fully in line with the studies reviewed above on p.5. and 6, so the authors should expand. The second hypothesis is reasonable and builds on the research reviewed in the introduction.
We thank the reviewer for his or her positive remarks and thoughtful comment. We have added information in the introduction (p.4) that formed the basis of our first hypothesis and added the following information on p.7. to explain the rationale for our hypothesis: “Our first hypotheses is based upon the current guidelines for the treatment of Complex PTSD [8], and expert consensus about the treatment of this target population [13].”

2. How are the authors planning to incorporate patients in need of potentially more/fewer sessions?

We acknowledge this concern and added the following text in the manuscript under Methods/design > Study design (p.8):

“For this study, we chose to use a fixed number of sessions. All patients in the STAIR-EMDR condition will receive eight sessions STAIR while in both conditions patients will receive a maximum of 16 sessions EMDR. In case of EMDR therapy, when all targets are processed to SUD (Subjective Unit of Distress)=0 and VoC (Validity of Cognition)=7, the patient will be assessed using the CAPS to determine whether he or she does not meet the criteria of PTSD anymore. In case of early completion, the remaining EMDR sessions are cancelled.” After STAIR, patients will always receive EMDR sessions, as STAIR is meant as a first-phase treatment before trauma-focused treatment. Early completion during STAIR is not possible.

3. Can the authors assert that numbers will be large enough to have enough power to investigate the moderator hypotheses?

Indeed, the sample size (n = 122) will be large enough to enable enough power to investigate moderator hypotheses. For your information, we added a screenshot of the g-power calculation reflecting a regression analysis with 3 independent variables (i.e., predictor, moderator and interaction predictor x moderator) rendering a sample size of n = 77.

4. How is severe use of alcohol defined as an exclusion criteria?

We clarified this by adding that we use the criteria according to the DSM-IV-TR on p.9. Before inclusion we will ask the patient if he or she does use alcohol en check for the DSM-IV-TR criteria.

5. How are STAIR-EMDR/EMDR only groups matched for therapist contact and general psychotherapy effects? Will all patients receive an equal number of sessions?

First of all, all patients will receive an equal number of EMDR sessions per condition, except for early completers. Further, all patients will be assigned to one of the therapists based on availability for which it is important to note that all therapists are trained in both interventions and all therapists deliver both treatments. We added this in the text on p.8 and 10.

6. Who conducts the intake procedure? Is the assessor blind to patients' group assignment?
We thank the reviewer for his/her question. The intake procedure is a fixed procedure at Dimence, carried out by an independent caretaker. He/she is blind to patients’ group assignment. Independent research assistants will assess whether the patients meet the inclusion and exclusion criteria of the study. They do not have any influence on the treatment assignment. Due to the nature of the trial, participants and participating therapists in the study cannot be blinded to treatment assignment. We clarified this in the text on p.11.

7. Will the authors be able to make a statement about the "ideal" length of the STAIR phase of the treatment? In the manual, transition to the NT/EMDR part is to be arranged with patients according to their progress and symptoms. How is this approached using a predefined number of sessions? What if patients are in need of further STAIR sessions? What if they are ready to move on to exposure after STAIR session 3 or so?

We thank the reviewer for his or her clarifying questions and thoughtful comments. All patients will receive sixteen sessions EMDR whether or not preceded by eight sessions STAIR. This is the minimal amount of STAIR sessions, based upon the original protocol with eight sessions. During treatment patients cannot skip or stop early STAIR sessions. We explained this more clearly now on p.8.

Reports reviewer #2:

The authors present a study protocol of a randomized controlled trial comparing Eye Movement Desensitization and Reprocessing (EMDR, 16 sessions) therapy preceded by a stabilization phase (8 sessions Skills Training in Affect and Interpersonal Regulation, STAIR) or only EMDR therapy (16 sessions) for patients suffering from complex PTSD. The study protocol is well-written and most information to make the study reproducible is provided.

However, there are some minor points that I think the authors should address in a revised version of the manuscript.

1. A limitation of the present study seems to be that if the combined STAIR/EMDR condition shows to be superior compared to the only EMDR condition it is possible that this is because of a mere dose effect. This limitation of the present study should be included. Also how the authors think to address this issue.

We thank the reviewer for this comment. We address this issue by assessing all patients after every eight therapy sessions. In this way it will be possible to determine whether a phase-based treatment approach has any added value to a direct trauma-focused approach while keeping the number of sessions equal. We have explained this issue on p. 8: “By assessing every eight sessions it will be possible to determine the added value of a stabilisation phase and to examine the results after an equal amount of sessions”.

2. Please specify whether the randomization is within or between therapists, i.e., do therapists deliver treatment in both conditions or not?
Patients will be assigned to a therapist based on availability of the therapist.

All therapists will provide treatment in both conditions and are trained in both interventions. We added this information on p. 10.

3. Please provide the information whether the follow-up assessments are from randomization or from the end of treatment. This is important since treatment ends in one group 2 months earlier than in the other group.

Follow-up assessments are from the end of treatment. This information has been added to the text of the revised manuscript (p.8).

4. Introduce abbreviation CAPS-5 when it first appears

This has been corrected in the revised manuscript.

5. The power calculation suggests that the primary endpoint for the given study is at 6-month follow-up. Please state clearly, what the primary endpoint of the study is.

The primary endpoint of the study is post-treatment. Measurements will take place pre-treatment, after every eight sessions (i.e., after stabilization in the STAIR/REMDR condition and after eight and 16 sessions of EMDR in both conditions), and at 3 and 6 months follow-up. The power, given our sample size of n = 122, to find a small effect varies between .67 and .81 depending on the analysis (3, 4, or 5 measurements) and the power to find a medium effect approaches 1 for all these analyses. We did not incorporate all these power calculations in the manuscript because as explained, we will actually perform a linear mixed model analysis but to our knowledge no power calculation are available for this model. The present calculation in the ms is thus a conservative approximation.

6. In addition, the resolution of Figure 1 seems to be rather low. Please provide a Figure with a higher resolution.

We provided the original figure.