PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Transdiagnostic, affect-focused, psychodynamic, guided self-help for depression and anxiety through the Internet: study protocol for a randomized controlled trial
AUTHORS	Johansson, Robert ; Hesser, Hugo; Ljótsson, Brjánn; Frederick, Ronald; Andersson, Gerhard

VERSION 1 - REVIEW

REVIEWER	Nickolai Titov Associate Professor Macquarie University Australia I do not have competing interests.
REVIEW RETURNED	09-Oct-2012

GENERAL COMMENTS	This is an excellent protocol.

REVIEWER	Prof. Dr. med. Frank Leweke Clinics of Psychsomatcs and Psychotherapy University of Giessen No conflicts of interest to decalre. Frank Leweke
REVIEW RETURNED	10-Oct-2012

THE STUDY	The authors list several outcome measures. They include two self-report measures one, for depression (PHQ-9), another for anxiety. Furthermore, psychiatric diagnosis as well as the Clinical Global Impression - Improvement scale (CGI-I)will be rated at post-treatment and at follow-up. However, as the study includes both patients with depressive and anxiety disorders, measures should be tailored to the specific disorder. That is the outcome for patients with the principal diagnosis of a depressive disorders should be measured by the PHQ-9 and the outcome of the patients with the principal diagnosis of an anxiety disorder should be measured by instruments referring to symptoms of anxiety. This applied to the CGI-I as well. In an analogous way, outcome measurement by absence or presence of psychiatric diagnoses should refer to the respective principal diagnosis (depressive disorder no longer present; anxiety disorder no longer present). Furthermore, it is not clear why the authors do not plan to use self-report instruments that are specific to the different anxiety disorders, that is to social phobia, panic disorder and generalized anxiety disorder. The Generalized

	Anxiety Disorder Scale that the authors plan to use may indeed tap symptoms of other anxiety disorders as well, but specific self-report questionnaires for social phobia and panic disorder are available. Furthermore, it is not clear which of the measures listed by the authors are regarded as primary and which as secondary.
GENERAL COMMENTS	In the discussion section the authors state that the treatment as it is applied as an internet-guided self-help does not make use of transference relations. The authors are recommended to qualify this statement. Even if there is no face to face contact with a therapist, transference can occur. Therapists respond to participant´s questions via email. These responses may trigger transference reaction, e.g. of a “good” supporting object.

REVIEWER	Dr. Joel Town Assistant Professor Dalhousie University Halifax, Canada I report no competing interests,
REVIEW RETURNED	19-Oct-2012

THE STUDY	Is the research question clearly defined? 1. It would be helpful to separate the question examining the "effectiveness" of treatment versus the question examining the process-outcome relationship as primary and secondary questions respectively. 2. The third research question listed describes a mediation analysis. Please note the exact temporal relationship that will be examined within this process-outcome analysis i.e., Does the degree of in-session emotional processing and mindfulness mediate depressive symptoms and anxiety symptoms 7 days later? 3. It would assist the reader if the Research questions and hypotheses section came after the Introduction section. Is the overall study design appropriate and adequate to answer the research question? 4. Given the inclusion of diagnoses of panic disorder, social anxiety and generalized anxiety disorder, and a lack of clarity around the most appropriate measure for a transdiagnostic treatment, the use of three brief patient self-report measures sensitive to the symptoms associated to these three respective disorders may be more appropriate in order to detect treatment effects. 5. A limitation of the current design is the reliance on patient self-report measures for examining effectiveness. The use of blinded observer rated measures alongside patient self-report scales is recommended to significantly improve study quality. 6. Although the two research questions pertaining to the study of a process-outcome relationship are relatively clear, the objectives and basis for the chosen design to evaluate treatment process are less clear in the remainder of the protocol. First, given the seemingly complex task of examining treatment processes and the decision to use only two self-report measures to measure two sophisticated variables, it might be wise to pitch this as a "preliminary" process analysis. Second, the section on "processes of change" in the Introduction refers to the importance of "experiencing", "processing" and "desensitization" of emotions without definitions of what is meant. This in part reflects a general problem in the research and

	clinical literature regarding the concept of emotion processing and the lack of consensus around definitions. Given word constraints, the authors could provide a definition of the specific dimension they are measuring with the chosen scale and explain its theoretical overlap to APT theory. In truth, there is a lot of process research focused on the relationship between emotions and outcome in brief dynamic psychotherapy. Are the participants adequately described, their conditions defined, and the inclusion and exclusion criteria described? 7. Will the design include participants with substance use and suicidality? 8. Please provide additional details on the nature of the email contact during treatment. For example, it is common to clarify in what circumstance therapists will email participants (defining the common types of feedback to be given e.g., encouragement, task summary, answering questions on tasks), advised weekly limit to contact time, and the planned response rate (within 24 hours?). Are the methods adequately described? 9. The randomization method and information on concealment of randomization process are not mentioned. 10. Please provide details on who rates the M.I.N.I. and how the reliability of diagnoses will be confirmed. 11. Please provide details on who the therapists will be and their level of experience for each treatment group. 12. Please provide additional detail on how other psychiatric diagnoses are excluded. It should be made clear if other sections from the M.I.N.I. will be used for this purpose. 13. Please provide additional details on how the clinical interview will be conducted (face-to-face, telephone). 14. Please provide details on who the outcome assessors are and if/how the blind will be maintained. 15. Please comment on whether medication changes will be allowed during treatment. Is the main outcome measure clear? 16. See (1) Are the abstract/summary/key messages/limitations accurate? 17. See (6): It would be appropriate to amend the description of the process question within the section of "Key messages" to note the "preliminary" examination of the two specified process dimensions. 18. If blinded ratings of outcome are used this should be noted as a strength. 19. No limitations are reported. See (4) and (5) Are the statistical methods described? 20. The statistical methods are described although it would be helpful to provide more detail if space permitted. Are the references up to date and relevant? (If not, please provide details of significant omissions below.) 21. Reference 19 should be excluded. Although there are similarities with Brief Adaptive Psychotherapy, it is not accurate to report this as APT.
GENERAL COMMENTS	I commend the ingenuity of the authors to select the APT model as a transdiagnostic model for use as a computerised self-help treatment. On a conceptual level, I question whether it is accurate to describe an internet delivered self-help treatment as psychodynamic on the

	basis that the transference relationship is not utilised. Arguably, use of the transference relationship is the key defining feature of psychodynamic treatment. Nevertheless, this is a point for discussion rather than criticism of the current study. Incorporating process-outcome analysis within RCTs, as the authors aim to do within the present protocol, is a valuable empirical endeavour. The key objective here is to define a presumed ingredient of change that will be targeted by a treatment, then to isolate when it occurs and measure to what degree using a valid and objective coding system. This task is made so much more difficult by the fact that researchers cannot record and observe the therapeutic process during internet delivered treatment in the same way that is made possible in face-to-face psychotherapy. Specific instructions to participants asking them to complete the process measures in respect to the impact of the treatment exercises may help to ensure you are measuring a process associated to treatment. As always, a thorough discussion of the strengths and limitations of the methodology will aid interpretation of the subsequent findings.

VERSION 1 – AUTHOR RESPONSE

Reviewer: Prof. Dr. med. Frank Leweke
Clinics of Psychsomatcs and Psychotherapy University of Giessen

[However, as the study includes both patients with depressive and anxiety disorders, measures should be tailored to the specific disorder. That is the outcome for patients with the principal diagnosis of a depressive disorders should be measured by the PHQ-9 and the outcome of the patients with the principal diagnosis of an anxiety disorder should be measured by instruments referring to symptoms of anxiety.]

We acknowledge the fact that we probably would get more specific measures of symptoms of panic, social anxiety and worry by using e.g. the PDSS-SR, LSAS and the PSWQ, instead of the GAD-7. However, as we aim to understand as much as possible of the mechanisms of change during treatment, we made the decision to use weekly measures of both symptom and process measures. One consequence of this decision is that we had to set a strong restriction on the number of weekly questions. The number of questions per week sums up to 70 by using the PHQ-9, GAD-7, FFMQ and the EPS-25. If we would have included specific measures for all anxiety disorders, the number of weekly questions would have been far larger. These are our arguments for the continued use of the GAD-7 for conducting weekly measures of anxiety symptoms. We have made a clarification regarding this in the manuscript.

Furthermore, we will conduct clinical interviews at pre-treatment, post-treatment and at follow-up. This provides one opportunity to assess disorder-specific changes regarding anxiety.

[Furthermore, it is not clear which of the measures listed by the authors are regarded as primary and which as secondary.]

We have now emphasized in the text that the PHQ-9 and the GAD-7 are the primary outcome measures and that the EPS-25 and the FFMQ are the secondary outcome measures, besides being included as measures of change processes.

[In the discussion section the authors state that the treatment as it is applied as an internet-guided self-help does not make use of transference relations. The authors are recommended to qualify this statement. Even if there is no face to face contact with a therapist, transference can occur. Therapists

respond to participant´s questions via email. These responses may trigger transference reaction, e.g. of a “good” supporting object.]

We do not rule out that transference can occur. However, the treatment does not make use of such phenomena, i.e., no interventions are included that address this. This has now been stated more thoroughly in the Discussion.

Reviewer: Dr. Joel Town
Assistant Professor
Dalhousie University
Halifax, Canada

[It would be helpful to separate the question examining the "effectiveness" of treatment versus the question examining the process-outcome relationship as primary and secondary questions respectively.]

The manuscript has been updated with information on primary and secondary outcome measures. Furthermore, the manuscript contains different sections describing research questions regarding efficacy and processes of change.

[The third research question listed describes a mediation analysis. Please note the exact temporal relationship that will be examined within this process-outcome analysis i.e., Does the degree of in-session emotional processing and mindfulness mediate depressive symptoms and anxiety symptoms 7 days later?]

The reviewer is correct in stating that we plan to conduct a mediation analysis. While the proposed analysis (change in process variable causes a change in symptoms 1 week later) is a planned analysis, we have deliberately omitted further details on how to conduct the process analyses. This is due to the fact that multiple analyses will be conducted in an exploratory fashion.

[It would assist the reader if the Research questions and hypotheses section came after the Introduction section.]

We agree with the reviewer on this point and have changed the manuscript according to this suggestion.

[Given the inclusion of diagnoses of panic disorder, social anxiety and generalized anxiety disorder, and a lack of clarity around the most appropriate measure for a transdiagnostic treatment, the use of three brief patient self-report measures sensitive to the symptoms associated to these three respective disorders may be more appropriate in order to detect treatment effects.]

See above.

[A limitation of the current design is the reliance on patient self-report measures for examining effectiveness. The use of blinded observer rated measures alongside patient self-report scales is recommended to significantly improve study quality.]

In addition to the self-report measures, clinical outcome will be measured in a clinical interview. These interviews will be conducted by blind assessors, as already stated in the manuscript. We

acknowledge the fact that further observer-based ratings would improve the quality of the study. However, the use of weekly measures and the remote distance due to the Internet format makes the use of such assessments difficult.

[Although the two research questions pertaining to the study of a process-outcome relationship are relatively clear, the objectives and basis for the chosen design to evaluate treatment process are less clear in the remainder of the protocol. First, given the seemingly complex task of examining treatment processes and the decision to use only two self-report measures to measure two sophisticated variables, it might be wise to pitch this as a "preliminary" process analysis. Second, the section on "processes of change" in the Introduction refers to the importance of "experiencing", "processing" and "desensitization" of emotions without definitions of what is meant. This in part reflects a general problem in the research and clinical literature regarding the concept of emotion processing and the lack of consensus around definitions. Given word constraints, the authors could provide a definition of the specific dimension they are measuring with the chosen scale and explain its theoretical overlap to APT theory. In truth, there is a lot of process research focused on the relationship between emotions and outcome in brief dynamic psychotherapy.]

We acknowledge the methodological limitations in our study due to the fact that we use self-report measures to assess the processes of change. In traditional psychotherapy research, ratings of video material would probably give a more valid measure of the processes of e.g. emotional processing. As our study is conducted in the guided self-help format, such methodology was not possible to use. The use of a validated measure such as the EPS-25 is one way to still be able to draw conclusions on which mechanisms of change that are active. A further consequence of this decision, is that we have to rely on the definitions of emotional processing inherent in the measure we use, and its dimensions. While we acknowledge the reviewer's expertise in this area, we still believe that a further discussion on this are more appropriately placed in the RCT paper that will follow this study.

[Will the design include participants with substance use and suicidality?]

We will exclude patients with alcohol and drug abuse. An assessment of risk of suicide will also be conducted using the M.I.N.I. This has now been clarified in the manuscript.

[Please provide additional details on the nature of the email contact during treatment. For example, it is common to clarify in what circumstance therapists will email participants (defining the common types of feedback to be given e.g., encouragement, task summary, answering questions on tasks), advised weekly limit to contact time, and the planned response rate (within 24 hours?).]

This has now been clarified in the manuscript.

[The randomization method and information on concealment of randomization process are not mentioned.
Please provide details on who rates the M.I.N.I. and how the reliability of diagnoses will be confirmed.
Please provide details on who the therapists will be and their level of experience for each treatment group.
Please provide additional detail on how other psychiatric diagnoses are excluded. It should be made clear if other sections from the M.I.N.I. will be used for this purpose.
Please provide additional details on how the clinical interview will be conducted (face-to-face, telephone).
Please provide details on who the outcome assessors are and if/how the blind will be maintained.
Please comment on whether medication changes will be allowed during treatment.]

We have now changed the manuscript according to these suggestions.