PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Therapist-guided and self-guided Internet-delivered behavioural activation for adolescents with depression: a randomised feasibility trial
AUTHORS	Grudin, Rebecca; Ahlen, Johan; Mataix-Cols, David; Lenhard, Fabian; Henje, Eva; Månsson, Cecilia; Sahlin, Hanna; Beckman, Maria; Serlachius, Eva; Vigerland, Sarah

VERSION 1 – REVIEW

REVIEWER	Martell, Christopher University of Massachusetts Amherst, Psychological and Brain Sciences
REVIEW RETURNED	04-Aug-2022

GENERAL COMMENTS	This was a well-designed feasibility trial. The authors' have taken note of the "heterogeneity" of the TAU condition, and acknowledged that most participants may have desired to be in one of the iCBT conditions. I believe a limitation is also that the experimental treatments were available, due to how they were designed to be delivered, on-line while TAU was through referrals to local clinics. I have some concern that differences may be as much to dissatisfaction with the treatment accessibility as it was to any difference in the type of treatment. The authors are to be commended for having feedback provided by three patient representatives who had previously suffered from depression and who provided feedback on language and inclusivity of content.

REVIEWER	Schmitt , Julia C. Universidad Nacional de Educación a Distancia, Departamento de Personalidad, Evaluación y Tratamientos Psicológicos
REVIEW RETURNED	11-Oct-2022

GENERAL COMMENTS	Language - Authors should decide whether they want to use British or American English. Right now, the text contains a mix of both (e.g., behavioral vs. behavioural, randomization/randomized vs. randomisation/randomised). - If authors opt for the use of the oxford coma, it should be used consistently. - There are still some typos throughout the manuscript. - Concerning the general style, sentences rather stand on their own than being connected to another.

	- A careful language revision of the whole manuscript seems appropriate. Abstract - Participants: Indicate how many participants were in each condition. - Interventions: Provide more information on the nature of the three conditions. - Outcomes: Many variables are assessed in this study and should be mentioned here. Mention that the three-month follow-up is the “primary endpoint”. - Results: Reasons for drop out and groups of which the participants dropped out should be indicated. Specify which statistical tests were used. - Article summary: Strengths and limitations of this study: It should be stated more clearly that the third bullet point refers to a limitation. Introduction - Reference 1. and 2.: More recent data should be cited (the articles are from 2011 and 2005). - Line 21: “Behavioural activation (BA) is a common type of CBT for depression.” A reference for this affirmation should be included. In general, the authors should argue more strongly in this paragraph why only BA and not a complete CBT should be used to tackle depression in adolescents. - Reference 16.: It seems more appropriate to include another reference, e.g. a guideline or meta-analysis. - iCBT: Titov is an important author in the field of iCBT and could be included among the references. - Line 42: Reference 20. appears twice which seems to be a mistake. - Some relevant iCBT studies haven’t been taken into consideration: Schmitt, J. C., Valiente, R. M., García-Escalera, J., Arnáez, S., Espinosa, V., Sandín, B., & Chorot, P. (2022). Prevention of depression and anxiety in subclinical adolescents: Effects of a transdiagnostic internet-delivered CBT program. International Journal of Environmental Research and Public Health, 19(9), 5365. https://doi.org/10.3390/ijerph19095365 Sandín, B.; García-Escalera, J.; Valiente, R.M.; Espinosa, V.; Chorot, P. Clinical utility of an internet-delivered version of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Adolescents (iUP-A): A 2 pilot open trial. Int. J. Environ. Res.Public Health 2020, 17, 8306. https://doi.org/10.3390/ijerph17228306 Pasarelu, C.R.; Dobrean, A.; Andersson, G.; Zaharie, G.C. Feasibility and

	clinical utility of a transdiagnostic internet-delivered rational emotive and behavioral intervention for adolescents with anxiety and depressive disorders. Internet Interv. 2021, 26, 100479. https://doi.org/10.1016/j.invent.2021.100479 - Line 15: Specify which “important feasibility questions” should be addressed. Methods Study design - Line 33: “single-masked”: Specify who was masked, the participants or the raters. - Line 38: “Child and Adolescent Psychiatry Research Center”: As this is first mentioned here, include the abbreviation. - The context of the Child and Adolescent Psychiatry Research Center and how and to whom the treatment was offered should be described in more detail. Participants - In the appendix it seems that part of the program could/should be done via a smartphone. This should be specified in the inclusion criteria. Sample size - Reference 29.: The article is only a study protocol, not a study that was run. - Line 22: Specify which attrition rate was assumed. - How were the power calculations conducted (e.g., using G*Power)? - Explain why the goal of 45 participants couldn’t be met in the end. Recruitment and procedures - Line 31: “CAMHS”: The abbreviation should be explained earlier in the manuscript. Interventions - Line 19: “The I-BA treatment protocol was inspired by previously published literature on BA”: State more clearly that a new, non-validated protocol was used. - Specify how long it takes to complete a chapter of the program. - Apart from BA, the protocol includes psychoeducation and sleep hygiene and on page 8 of the manuscript we see that it even includes parental traps, communication skills, conflict management, shifting focus, take care of yourself, problem solving and relapse prevention. It should be pointed out that we are not talking about pure BA but rather about a more complete CBT program. This should be made clearer in the title, abstract and introduction and should be justified in these sections. This is the first time that this is mentioned. - How did the asynchronous contact with the therapist take place (e.g., e-mail, chat…)? Was there a time limit/limit of number of contacts per family concerning

	therapist contact? Later on, the reader casually learns that there were phone calls as well. This should be explained in this section. - Line 46: When the word "treament as usual" is used for the first time in the manuscript, mention the abbreviation in brackets and henceforward only use the abbreviation. - In the appendix it seems that part of the program could/should be done via a smartphone. This should be explained in this section. - It should be clearer if there are home assignments, how many etc. - The following information that can be found in the appendix should be mentioned in this section: “4. Encrypted messaging function which is included in guided I-BA. 3 The psychologist responds within 1-2 days on weekdays to messages from the participant.” Measures - Give more detailed and structured about each instrument. Make subparagraphs for each instrument. Indicate the scale of each instrument (e.g., Likert) and its levels. - Baseline assessment: □ Did the authors use a special instrument to assess suicide risk (e.g., the corresponding part of the MINI-KID)? □ The authors should consider describing the kind of demographic data that was collected. - Acceptability of I-BA: □ The authors should specify the four qualitative questions that were used to assess treatment credibility. □ That's the first time the phone calls with the therapist are mentioned. This should be explained in more detail in the intervention section. - Clinical outcomes: □ Did the authors use translations into Swedish of the instruments? Were these validated? □ Lines 26-27: “Adolescent- and parent-rated questionnaires were administered online at pre- and posttreatment and at three-month follow-up”: This should me mentioned when the procedure is discussed, not in the “Measures” section. □ Line 27: “SMFQ”: Authors should indicate the full name of the instrument. □ Line 34: The assessment of anxiety symptoms should be justified in the introduction. □ Line1 43-35: The assessment of sleep difficulties and irritability should be justified in the introduction.

	Analytical methods - Line 29: Authors should describe how exactly missing data is handled within the model. - Lines 39-41: Authors should explain why the proportion of treatment responders was not computed at post-treatment but at three-month follow-up and which were the pre-specified criteria. - Justify why comparisons are done between baseline and three-month follow-up and not post-treatment. Results - Participant retention and study flow: □ Lines 7-8: “Table 2 shows the demographic and clinical characteristics of the sample at baseline”: Authors should perform statistical analysis to rule out that there were any baseline differences between the groups. □ Line 10: Reasons for drop-out should be specified if available (see flow chart) - Table 2: The high comorbidity should be commented somewhere as it is the norm, not the exception. - Treatment content in TAU: Give more detail (i.e., percentages) in the text about which form of treatment (medication, psychological, supportive, combinations) the participants received. - Acceptability of I-BA: □ Adverse events and negative effects: If the authors consider that there is a difference between these two constructs they should define them better in the instruments section. - Therapist time (therapist-guided I-BA): The therapist attention should be explained more clearly in the intervention section. How were the messages on the 4 platform registered in minutes? Did the therapist talk to the parents, to the participants or to both? - Secondary outcome measures □ Effects for CGAS, CGI-S, RCADS-S-A/P, KIDSCREEN-10-A/P, ISI, ARI and WSAS-P should be commented in the text, not only in the supplementary material. - Non-significant results should be stated. Discussion - Authors should initiate a new paragraph after the first sentence. Like this the first sentence summarizes the study design and research questions and the second paragraph starts with the feasibility. - The low attrition should be mentioned as part of the feasibility of the study. - Non-significant results should be stated and explained.

	- The benefits of BA compared to TAU seem convincing, but the authors should discuss why BA instead of a more complete CBT intervention could be beneficial. - The authors should mention again that the protocol is new and not validated. - The authors should consider if they want to mention the following additional limitations of the study: 1) It was not possible to compare groups due to insufficient power; 2) after treatment the authors did not assess if participants still had a MDD diagnosis (or comorbid diagnoses). - Line 60: The authors claim that the two measures of TAU content (medical records and interviewing parents) were in good agreement with each other. This should be mentioned before in the results section. How are the authors able to conclude this? - A section on future studies is missing (e.g., full CBT comparison group instead of TAU). Author statements - Contributors: There are 10 co-authors but in this section only the contributions of 7 authors are mentioned. The contributions of the 3 missing authors should be detailed. - Acknowledgements: Authors should detail the services that were used from the eHealth Core Facility at Karolinska Institutet. References - The titles of the different articles should be written without capitalizing every word. Figure 1 - The authors should check the abbreviations: The ones explained do not come up in the figure and there are some abbreviations in the figure which are not explained in the note. Figure 2 - The text refers to error bars which are not depicted in the graph. Table S2. - "^Observed means. †Coefficients at post-treatment and at the 3-month follow-up compared with baseline. §Primary endpoint": This information does not come up in the table.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Christopher Martell, University of Massachusetts Amherst

Comments to the authors:

This was a well-designed feasibility trial. The authors have taken note of the "heterogeneity" of the TAU condition and acknowledged that most participants may have desired to be in one of the iCBT conditions. I believe a limitation is also that the experimental treatments were available, due to how they were designed to be delivered, on-line while TAU was through referrals to local clinics. I have some concern that differences may be as much to dissatisfaction with the treatment accessibility as it was to any difference in the type of treatment.

The authors are to be commended for having feedback provided by three patient representatives who had previously suffered from depression and who provided feedback on language and inclusivity of content.

Response:

Thank you for your feedback! We agree that differences in accessibility to ICBT vs TAU might have impacted (apparent) differences in outcome between groups. In the Discussion we have added this as a limitation.

See Discussion, page 21, lines 507–511:

> Furthermore, both ICBT treatments started immediately after randomisation, while some participants in TAU had to wait to start treatments at their local clinics. This inherent difference between the interventions and potential dissatisfaction with treatment availability in TAU may have influenced clinical outcomes.

Reviewer: 2
Dr. Julia C. Schmitt, Universidad Nacional de Educación a Distancia

Comments to the author:
It has been a pleasure to review your manuscript which I consider of high interest to the research community. Below, I will outline some minor issues that should be resolved before publishing the paper.

Response:

We would like to start by thanking the reviewer for the thorough reading of the manuscript and the detailed and specific comments. This is very helpful and we are grateful for the time and attention that you have given us.

Language

#1. Authors should decide whether they want to use British or American English. Right

now, the text contains a mix of both (e.g., behavioral vs. behavioural, randomization/randomized vs. randomisation/randomised).
We have reviewed the whole manuscript and supplementary materials to assure British English is used consistently throughout the manuscript.

#2. If authors opt for the use of the oxford coma, it should be used consistently.
We have revised the whole manuscript according to the use of Oxford comma.

#3. There are still some typos throughout the manuscript.
We have had the whole manuscript reviewed with an English language editing service and hope that the manuscript has improved.

#4. Concerning the general style, sentences rather stand on their own than being connected to another.
We have read through the entire manuscript several times and worked on having clear connections between sentences in the same paragraph and transitions between paragraphs.

#5. A careful language revision of the whole manuscript seems appropriate.
Please see our response to comment #3.

Abstract
#6. Participants: Indicate how many participants were in each condition.
See page 2, lines 17-18:

> 154 adolescents were screened and 32 were randomised to therapist-guided I-BA (n = 11), self-guided I-BA (n = 10), or TAU (n = 11).

#7. Interventions: Provide more information on the nature of the three conditions.
See page 2, lines 10-12:

> Ten weeks of therapist-guided I-BA or self-guided I-BA, or treatment as usual (TAU). Both versions of I-BA included parental support. TAU included referral to usual care within child and youth psychiatry or primary care.

#8. Many variables are assessed in this study and should be mentioned here.
We added study-take up to the list of feasibility measures.

See page 2, lines 13-15:

> Feasibility measures included study take-up, participant retention, acceptability, safety, and satisfaction. The primary outcome measure was the masked assessor-rated Children's Depression Rating Scale, Revised.

Due to the limited word count (300 words for abstract), we chose to provide information on secondary efficacy measures first in methods, and not in abstracts. However, we would be happy to add this information to the abstract if the editor requests it.

#9. Mention that the three-month follow-up is the "primary endpoint".
See page 2, lines 15-16:

> The primary endpoint was the three-month follow-up.

#10. Reasons for drop out and groups of which the participants dropped out should be indicated
See page 2, line 18-19:

> Participant retention was acceptable, with two drop-outs in TAU.

Reasons for drop-out are specified under Results.

#11. Specify which statistical tests were used.
See page 2, line 22-23:

> Following an intent-to-treat approach, the linear mixed effects model revealed that…

Article summary

#12. Strengths and limitations of this study: It should be stated more clearly that the third bullet point refers to a limitation.
See page 3, line 38-39:

> Limitations include the heterogenous condition of TAU and masked assessors correctly guessing group allocation more often than by chance.

Introduction

#13. Reference 1. and 2.: More recent data should be cited (the articles are from 2011 and 2005).

Thanks for bringing this to our attention. We have updated these references to these more recent articles:

1. Depression and other common mental disorders: global health estimates: World Health Organization, 2017.
2. Merikangas K, He J, Brody D, et al. Prevalence and treatment of mental disorders among US children in the 2001-2004 NHANES. *Pediatrics* 2010;125(1):75-81. doi: 10.1542/peds.2008-2598
3. Daly M. Prevalence of depression among adolescents in the US from 2009 to 2019: analysis of trends by sex, race/ethnicity, and income. *J Adolesc Health* 2022;70(3):496-99. doi: 10.1016/j.jadohealth.2021.08.026

#14. Line 21: "Behavioural activation (BA) is a common type of CBT for depression." A reference for this affirmation should be included.

We have adjusted this sentence slightly and added a reference that supports it.

See page 4, lines 56-57:

> Behavioural activation (BA) is an important component of CBT for depression, but can also be delivered as a stand-alone therapy (ref 15).

Reference:

15. Jacobson NS, Martell CR, Dimidjian S. Behavioral activation treatment for depression: returning to contextual roots. *Clinical Psychology (New York, NY)* 2006;8(3):255-70. doi: 10.1093/clipsy.8.3.255

#15. In general, the authors should argue more strongly in this paragraph why only BA and not a complete CBT should be used to tackle depression in adolescents.

Thank you for this helpful suggestion. We have added arguments to why BA might be a viable option for adolescents with depression.

See page 4, lines 63-72:

> BA, unlike traditional CBT for depression, does not include cognitive restructuring (ref 22), although seems to be equally effective (ref 23). Furthermore, dismantling studies have proposed that BA might be a sufficient treatment component on its own (ref 24-25). In line with this suggestion, a meta-analysis of adolescent depression treatments found that psychological interventions with a cognitive component were not more effective than those without cognitive work (ref 26). Because BA is brief and readily understood, it might suit adolescents particularly well. Another potential benefit is that, given its focus on reducing avoidance behaviours, BA

may also be effective for reducing anxiety (ref 27), which is important because anxiety is often co-morbid with depression in this age-group (ref 5).

References:

22. Dimidjian S, Barrera M, Martell C, et al. The Origins and Current Status of Behavioral Activation Treatments for Depression. *Annu Rev Clin Psychol* 2011;7(1):1-38. doi: 10.1146/annurev-clinpsy-032210-104535
23. Cuijpers P, Van Straten A, Andersson G, et al. Psychotherapy for Depression in Adults: A Meta-Analysis of Comparative Outcome Studies. *J Consult Clin Psychol* 2008;76(6):909-22. doi: 10.1037/a0013075
24. Jacobson NS, et al. A Component Analysis of Cognitive-Behavioral Treatment for Depression. *J Consult Clin Psychol* 1996;64(2):295-304. doi: 10.1037/0022-006X.64.2.295
25. Dimidjian S, Hollon SD, Dobson KS, et al. Randomized Trial of Behavioral Activation, Cognitive Therapy, and Antidepressant Medication in the Acute Treatment of Adults with Major Depression. *J Consult Clin Psychol* 2006;74(4):658-70. doi: 10.1037/0022-006X.74.4.658
26. Weisz JR, McCarty CA, Valeri SM. Effects of psychotherapy for depression in children and adolescents: A meta-analysis. *Psychol Bull* 2006;132(1):132-49. doi: 10.1037/0033-2909.132.1.132
27. Tindall L, Mikocka-Walus A, McMillan D, et al. Is behavioural activation effective in the treatment of depression in young people? A systematic review and meta-analysis. *Psychol Psychother* 2017;90(4):770-96. doi: 10.1111/papt.12121
5. Orchard F, Pass L, Marshall T, et al. Clinical characteristics of adolescents referred for treatment of depressive disorders. *Child and Adolescent Mental Health* 2017;22(2):61-68. doi: 10.1111/camh.12178

#16. Reference 16: It seems more appropriate to include another reference, e.g. a guideline or meta-analysis.

We have added references to two guidelines (APA and NICE).

See page 4, lines 59-60:

BA is considered an evidence-based treatment for adults with depression (ref 20-21) …

References:

20. American Psychological Association (APA). Clinical practice guideline for the treatment of depression across three age cohorts 2019 [Available from: https://www.apa.org/depression-guideline accessed May 3, 2022.
21. National Institute for Health and Care Excellence (NICE). Depression in adults: treatment and management: National Institute for Health and Care Excellence; 2022 [NICE Guideline [NG222]:[Available from: https://www.nice.org.uk/guidance/ng222 accessed May 1, 2022.

#17. iCBT: Titov is an important author in the field of iCBT and could be included among the references.

Thanks for this suggestion. We agree that Titov is an important author in this field and have considered adding Titov as a reference. However, we have chosen to limit our literature review to

studies mainly done with children and young people. Nevertheless, to give a brief review of current knowledge of the relative efficacy of guided and unguided ICBT for *adult* depression, we have added another reference to a recent meta-analysis on this topic in the introduction

See page 5, 91-94:

> According to a recent meta-analysis of ICBT for adults, therapist-guided ICBT was associated with greater improvement compared to self-guided treatment (ref 40). However, self-guided ICBT was as effective as guided ICBT among adults with mild or sub-threshold depression.

Reference:

40. Karyotaki E, Efthimiou O, Miguel C, et al. Internet-based cognitive behavioral therapy for depression: a systematic review and individual patient data network meta-analysis. *JAMA Psychiatry* 2021 doi: 10.1001/jamapsychiatry.2020.4364

#18. Line 42: Reference 20 appears twice which seems to be a mistake.

Thanks for pointing out this mistake. It has now been corrected.

#19. Some relevant iCBT studies haven't been taken into consideration:

Thank you for this suggestion. We have added references to additional ICBT studies in our literature review in the Introduction.

See page 5, lines 81-89:

> To date, three trials on ICBT with clinically depressed adolescents have been published. Two of them (both N = 70), included therapist-chat communication and showed significant reductions in depressive symptoms for adolescents compared to attention control (ref 33-34). The third, an open trial (N = 15) investigating the feasibility of a transdiagnostic Internet-delivered intervention based on rational emotive behaviour therapy for adolescents diagnosed with anxiety and depressive disorders, found a reduction in self-reported anxiety and depressive symptoms (ref 35). A number of studies on ICBT have also been conducted in subclinical samples with promising results (ref 36-39).

References

33. Topooco N, Berg M, Johansson S, et al. Chat- and internet-based cognitive-behavioural therapy in treatment of adolescent depression: randomised controlled trial. *Bjpsych Open* 2018;4(4):199-207. doi: 10.1192/bjo.2018.18
34. Topooco N, Byléhn S, Dahlström Nysäter E, et al. Evaluating the efficacy of Internet-delivered cognitive behavioral therapy blended with synchronous chat sessions to treat adolescent depression: randomized controlled trial. *J Med Internet Res* 2019;21(11):e13393-e93. doi: 10.2196/13393
35. Păsărelu C-R, Dobrean A, Andersson G, et al. Feasibility and clinical utility of a transdiagnostic Internet-delivered rational emotive and behavioral intervention for adolescents with anxiety

and depressive disorders. *Internet interventions* 2021;26:100479-79. doi: 10.1016/j.invent.2021.100479
36. Makarushka MM. Efficacy of an Internet-based intervention targeted to adolescents with subthreshold depression. University of Oregon, 2011.
37. Sethi S, Campbell AJ, Ellis LA. The use of computerized self-help packages to treat adolescent depression and anxiety. *Journal of Technology in Human Services* 2010;28(3):144-60. doi: 10.1080/15228835.2010.508317
38. Sandín B, García-Escalera J, Valiente RM, et al. Clinical utility of an Internet-delivered version of the unified protocol for transdiagnostic treatment of emotional disorders in adolescents (iUP-A): a pilot open trial. *Int J Environ Res Public Health* 2020;17(22) doi: 10.3390/ijerph17228306 [published Online First: 2020/11/14]
39. Schmitt JC, Valiente RM, García-Escalera J, et al. Prevention of depression and anxiety in subclinical adolescents: effects of a transdiagnostic Internet-delivered CBT program. *Int J Environ Res Public Health* 2022;19(9):5365. doi: 10.3390/ijerph19095365

#20. Line 15: Specify which "important feasibility questions" should be addressed.
This has been specified.

See *pages 5, lines 98-107:*

> However, important questions regarding feasibility of study design, acceptability of interventions, and preliminary efficacy should be addressed before conducting large trials. Therefore, we designed a randomised feasibility trial of therapist-guided and self-guided Internet-delivered BA (I-BA), to compare to treatment as usual (TAU). The primary objective of the study was to evaluate the feasibility of the study design, e.g., study take-up, participant retention, and feasibility of using TAU as a control group. Secondary objectives were to explore the acceptability of the I-BA interventions, e.g., treatment adherence, credibility, satisfaction, and adverse events, and to provide preliminary clinical efficacy data to assist with power calculations for a fully powered trial.

Methods

Study design

#21. Line 33: "single-masked": Specify who was masked, the participants or the raters.
This has been clarified.

See page 6, lines 113-114:

> Group allocation was masked for outcome assessors, but not for participants or therapists.

#22. Line 38: "Child and Adolescent Psychiatry Research Center": As this is first mentioned here, include the abbreviation.
Child and Adolescent Psychiatry Research Center is only mentioned once in the manuscript; thus, we haven't used an abbreviation. Please also see response to #29.

#23. The context of the Child and Adolescent Psychiatry Research Center and how and to whom the treatment was offered should be described in more detail.
To clarify, we have changed this in the manuscript:

See page 6, lines 114-116:

> The study was conducted at a clinical research unit within Child and Adolescent Mental Health Services (CAMHS) in Stockholm, Sweden.

Please see sections Participants and Recruitment and procedures for details who was eligible in this study, and how interested families applied to this study.

Participants

#24. In the appendix it seems that part of the program could/should be done via a smartphone. This should be specified in the inclusion criteria.
This has been adjusted accordingly.

See page 6, line 129:

> …access to the internet via a smartphone and a computer.

Sample size

#25. Reference 29: The article is only a study protocol, not a study that was run.
Thanks for pointing out this mistake. We have now replaced this reference:

Arjadi R, Nauta MH, Scholte WF, et al. Guided Act and Feel Indonesia (GAF-ID) - Internet-based behavioral activation intervention for depression in Indonesia: study protocol for a randomized controlled trial.(Report). *Trials* 2016;17(1) doi: 10.1186/s13063-016-1577-9

With this:

46. Arjadi R, Nauta MH, Bockting CLH. Acceptability of internet-based interventions for depression in Indonesia. *Internet interventions* 2018;13:8-15. doi: 10.1016/j.invent.2018.04.004 [published Online First: 2018/09/13]

#26. Line 22: Specify which attrition rate was assumed.
This has been added.

See pages 6-7, lines 141-144:

> Based on previous results, we aimed to recruit a total of 45 participants to be able to detect a within-group effect of *d*=1.2 (alpha value of 0.05 and 90% power), taking a potentially high attrition of 25% into account.

#27. How were the power calculations conducted (e.g., using G*Power)?
Thanks for this comment. We used the free website Statulator which has been added to the manuscript including a reference.

See page 7, line 144:

> Power calculation was performed using Statulator (ref 47).

Reference:

47. Dhand N, Khatkar M. Statulator 2014 [Available from: www.statulator.com accessed October 15, 2022.

#28. Explain why the goal of 45 participants couldn't be met in the end.
We have added an explanation to this.

See page 15, lines 365-368:

> Although we had not reached the goal of including 45 participants after the planned six-month recruitment period, we decided to end recruitment because we had fewer drop-outs than expected and thus enough participants to answer our feasibility questions.

#29. Line 31: "CAMHS": The abbreviation should be explained earlier in the manuscript.
Thanks for bringing this to our attention. This has been adjusted.

Interventions

#30. Line 19: "The I-BA treatment protocol was inspired by previously published literature on BA": State more clearly that a new, non-validated protocol was used.
We agree with the reviewer's comment and have clarified this.

See page 8, lines 176-186:

> The specific I-BA protocol was developed and adapted to an online format for this study, and although it otherwise evaluated in its current form, it was inspired by previous BA protocols (ref 18, 48). BA commonly provides treatment rationale and psychoeducation, activity monitoring,

activity scheduling, contingency management, values and goal assessments, skills training in problem solving and communication skills, relaxation techniques, and relapse prevention. BA also targets verbal and avoidance behaviours (ref 49). While various BA protocols include and emphasize different components, activity monitoring and scheduling are always present (ref 50). In our protocol, we included all of the aforementioned BA components apart from relaxation. Verbal behaviours were targeted through shifting focus. Sleep hygiene was added to the BA protocol because sleep problems are a common comorbidity of depression (ref 5) that are often addressed in face-to BA (ref 51).

References:

18. McCauley E, Gudmundsen G, Schloredt K, et al. The Adolescent Behavioral Activation Program: Adapting Behavioral Activation as a Treatment for Depression in Adolescence. *Journal of Clinical Child & Adolescent Psychology* 2016;45(3):1-14. doi: 10.1080/15374416.2014.979933
48. Pass L, Hodgson E, Whitney H, et al. Brief Behavioral Activation Treatment for Depressed Adolescents Delivered by Nonspecialist Clinicians: A Case Illustration. *Cognitive and Behavioral Practice* 2018;25(2):208-24. doi: 10.1016/j.cbpra.2017.05.003
49. Kanter JW, Manos RC, Bowe WM, et al. What is behavioral activation? A review of the empirical literature. *Clinical psychology review* 2010;30(6):608-20. doi: 10.1016/j.cpr.2010.04.001
50. Martin F, Oliver T. Behavioral activation for children and adolescents: a systematic review of progress and promise. *Eur Child Adolesc Psychiatry* 2019;28(4):427-41. doi: 10.1007/s00787-018-1126-z
5. Orchard F, Pass L, Marshall T, et al. Clinical characteristics of adolescents referred for treatment of depressive disorders. *Child and Adolescent Mental Health* 2017;22(2):61-68. doi: 10.1111/camh.12178
51. Barlow DH. Clinical Handbook of Psychological Disorders: A Step-By-Step Treatment Manual. 6 ed. New York: Guilford Publications 2021.

#31. Specify how long it takes to complete a chapter of the program.

This information has been added.

See page 8, line 190:

Each chapter took approximately 30 to 60 minutes to complete.

#32. Apart from BA, the protocol includes psychoeducation and sleep hygiene and on page 8 of the manuscript we see that it even includes parental traps, communication skills, conflict management, shifting focus, take care of yourself, problem solving and relapse prevention. It should be pointed out that we are not talking about pure BA but rather about a more complete CBT program. This should be made clearer in the title, abstract and introduction and should be justified in these sections. This is the first time that this is mentioned.

We have provided a more through description of our intervention in the methods section, and clarified that the treatment protocol used in the trial was developed by the research team and has not been previously evaluated in its current form. We have not added this information to the abstract, as we believe it would be an unnecessary detail there. However, if the editor requests it

we would of course be happy to add this

Additionally, we have expanded the description of the parent course.

See page 9, lines 213-216:

> This parental course was based on CBT-strategies commonly used in parent training programs (ref 52) such as praise and other forms of positive parental attention aiming at strengthening the relationship between caregivers and their children.

Please see more in response to #30.

Reference:

52. Webster-Stratton C, Herman KC. The Impact of Parent Behavior-Management Training on Child Depressive Symptoms. *J Couns Psychol* 2008;55(4):473-84. doi: 10.1037/a0013664

#33. How did the asynchronous contact with the therapist take place (e.g., e-mail, chat…)? Was there a time limit/limit of number of contacts per family concerning therapist contact? Later on, the reader casually learns that there were phone calls as well. This should be explained in this section.
Thanks for pointing this out. This has now been clarified.

See page 8, lines 202-207:

> In the therapist-guided I-BA arm, the participants had weekly asynchronous contact with a clinical psychologist via written messages within the platform. The psychologists logged in at least every other day during workdays to provide feedback, answer questions, and, if needed, prompt the participants to complete the next chapter. The therapists were recommended to spend around 20 to 30 minutes per family per week. Occasional phone calls were added when deemed necessary.

#34. Line 46: When the word "treatment as usual" is used for the first time in the manuscript, mention the abbreviation in brackets and henceforward only use the abbreviation.
This has been corrected.

See page 9, line 216:

> The control condition was treatment as usual (TAU).

#35. In the appendix it seems that part of the program could/should be done via a smartphone. This should be explained in this section.

A section with a description of the mobile application included in the I-BA interventions has been added to the manuscript.

See page 8, lines 197-201:

> To assist the adolescents with these assignments, a mobile application was developed to provide summaries of each chapter, instructions for homework assignments, and an activity diary to help with planning and evaluation of scheduled activities. The application included automatic prompts to login in case of inactivity and an easily-accessible individualized emergency plan.

#36. It should be clearer if there are home assignments, how many etc.
This has been added.

See page 8, lines 196-197:

> Between each chapter, both adolescents and parents were assigned homework (see **Table 1** for details).

#37. The following information that can be found in the appendix should be mentioned in this section: "4. Encrypted messaging function which is included in guided I-BA: The psychologist responds within 1-2 days on weekdays to messages from the participant."
Please see response to review comment #33.

#38. Give more detailed and structured about each instrument. Make subparagraphs for each instrument. Indicate the scale of each instrument (e.g., Likert) and its levels.
Due to the limited word count, we chose to provide this information in the supplemental material (Data supplement 1). Given that the other proposed changes will increase the length of the manuscripts, we are reluctant to add this information to the main text. However, we would be happy to add this if the editor requests it.

#39. Did the authors use a special instruments to assess suicide risk (e.g., corresponding part of the MINI-KID)?
This information has been added.

See page 11, lines 231-233:

> Suicide risk assessment was based on all available information, including the sections about suicidality in MINI-KID and CDRS-R collected at the inclusion assessment visit.

#40. The authors should consider describing the kind of demographic data that was

collected.
This has been specified in Methods, section Measures.

See *page 11, lines 234-237:*

> Demographic data of adolescents (e.g., age, gender, current and previous psychotropic medication, and previous psychological treatment) were collected at the initial assessment, and data about the parents were collected through an online questionnaire.

#41. Acceptability of I-BA:
The authors should specify the four qualitative questions that were used to assess treatment credibility.

This info has been added to *Methods, section Measures.*

See page 11-12, lines 252-256:

> To measure treatment credibility, four questions were administered to all adolescents and their parents at week three: 1) How much did they believe the treatment suited adolescents with depression? 2) How much did they believe the treatment would help them? 3) If and to what extent would they recommend this treatment to a friend with depression? and 4) How much improvement did they expect from the treatment?

#42. That's the first time the phone calls with the therapist are mentioned. This should be explained in more detail in the intervention section.
Please see response to reviewer comment #33.

#43. Did the authors use translations into Swedish of the instruments? Were they validated?
In this study we used Swedish translations of all measures. We added information on whether translations to Swedish have been evaluated to the Data supplement 1.

#44. Lines 26-27: "Adolescent- and parent-rated questionnaires were administered online at pre- and posttreatment and at three-month follow-up": This should be mentioned when the procedure is discussed, not in the "Measures" section.
This sentence has been moved to Recruitment and procedures.

See page 7, lines 171-173:

> Follow-up assessments were conducted at post-treatment and after three months by assessors masked to treatment allocation. Self- and parent-reported measures were completed online at all assessment points.

#45. Line 27: "SMFQ": Authors should indicate the full name of the instrument.
This has been adjusted accordingly.

See page 13, line 300-302:

> Depressive symptoms were assessed with the Short Mood and Feelings Questionnaire (SMFQ, adolescent and parent versions, total range 0–26 with higher values representing more symptoms) (ref 61-62).

References:

61. Angold A, Costello, E. J., Messer, S. C., & Pickles, A. . The development of a short questionnaire for use in epidemiological studies of depression in children and adolescents. *Int J Methods Psychiatr Res* 1995; 5:237 - 49.
62. Jarbin H, Ivarsson T, Andersson M, et al. Screening efficiency of the Mood and Feelings Questionnaire (MFQ) and Short Mood and Feelings Questionnaire (SMFQ) in Swedish help seeking outpatients. *PLoS One* 2020;15(3):e0230623-e23. doi: 10.1371/journal.pone.0230623

#46. Line 32: The assessment of anxiety symptoms should be justified in the introduction.
This has been added to the introduction.

See page 4, lines 46-48:

> Comorbidity with other mental disorders is prevalent among adolescents with depression (ref 4), with sleep disorders and anxiety being among the most common (ref 5).

References:

4. Avenevoli S, Swendsen J, He JP, et al. Major depression in the national comorbidity survey-adolescent supplement: prevalence, correlates, and treatment. *Journal of the American Academy of Child and Adolescent Psychiatry* 2015;54(1):37-44. doi: 10.1016/j.jaac.2014.10.010
5. Orchard F, Pass L, Marshall T, et al. Clinical characteristics of adolescents referred for treatment of depressive disorders. *Child and Adolescent Mental Health* 2017;22(2):61-68. doi: 10.1111/camh.12178

See page 4, lines 69-72:

> Another potential benefit is that, given its focus on reducing avoidance behaviours (ref 27), BA may also be effective for reducing anxiety, which is important because anxiety is often co-morbid with depression in this age group (ref 5).

Reference:

27. Tindall L, Mikocka-Walus A, McMillan D, et al. Is behavioural activation effective in the treatment of depression in young people? A systematic review and meta-analysis. *Psychol Psychother* 2017;90(4):770-96. doi: 10.1111/papt.12121
5. Orchard F, Pass L, Marshall T, et al. Clinical characteristics of adolescents referred for treatment of depressive disorders. *Child and Adolescent Mental Health* 2017;22(2):61-68. doi: 10.1111/camh.12178

#47. Line 43-45: The assessment of sleep difficulties and irritability should be justified in the introduction.

Please see response to #46.

Analytical methods

#48. Line 29: Authors should describe how exactly missing data is handled within the model.

We have added information on how missing data is handled.

See page 14, lines 345-348 for the revised version:

> In contrast to standard modeling of repeated data, where listwise deletion is used for all cases with missing data at any time point (ref 70), the linear mixed model estimates effects using all available observations at all time-points. The linear mixed model has been shown to yield reliable estimates in various types of missing data patterns (ref 71).

Reference:

70. Muth C, Bales KL, Hinde K, et al. Alternative models for small samples in psychological research: applying linear mixed effects models and generalized estimating equations to repeated measures data. *Educ Psychol Meas* 2015;76(1):64-87. doi: 10.1177/0013164415580432
71. Lane P. Handling drop-out in longitudinal clinical trials: a comparison of the LOCF and MMRM approaches. *Pharmaceutical Statistics* 2008;7(2):93-106. doi: https://doi.org/10.1002/pst.267

#49. Lines 39-41: Authors should explain why the proportion of treatment responders was not computed at post-treatment but at three-month follow-up and which were the pre-specified criteria. Justify why comparisons are done between baseline and three-month follow-up and not post-treatment.

We agree that this needs to be clarified and have added an explanation.

See page 6, lines 118-121:

> There were two reasons for setting the three-month-follow up as the primary end point: first, this increased the likelihood that participants assigned to TAU would have received treatment; second, previous ICBT trials have shown a continued improvement from post-treatment to three-month follow-up (ref 43-44).

References:

43. Jolstedt M, Wahlund T, Lenhard F, Ljótsson B, Mataix-Cols D, Nord M, Öst LG, Högström J, Serlachius E, Vigerland S. Efficacy and cost-effectiveness of therapist-guided internet cognitive behavioural therapy for paediatric anxiety disorders: a single-centre, single-blind, randomised controlled trial. Lancet Child Adolesc Health. 2018 Nov;2(11):792-801. doi: 10.1016/S2352-4642(18)30275-X.
44. Vigerland S, Ljótsson B, Thulin U, et al. Internet-delivered cognitive behavioural therapy for children with anxiety disorders: A randomised controlled trial. *Behaviour Research and Therapy* 2016;76:47-56. doi: 10.1016/j.brat.2015.11.006

Results

#50. Participant retention and study flow:
Lines 7-8: "Table 2 shows the demographic and clinical characteristics of the sample at baseline": Authors should perform statistical analysis to rule out that there were any baseline differences between the groups.

In line with CONSORT 2010 statement, we did not perform significance testing of baseline differences between groups. The reasons are several, as outlined by, for example de Boer et al 2015. They write: "The methods section of a paper should inform the reader whether randomization was performed properly and no statistical test will add any information about the correctness of this very procedure. Altman expressed this as "performing a significance test to compare baseline variables is to assess the probability of something having occurred by chance when we know that it did occur by chance" (Altman, 1985).

Reference:

de Boer MR, Waterlander WE, Kuijper LDJ, et al. Testing for baseline differences in randomized controlled trials: an unhealthy research behavior that is hard to eradicate. *Int J Behav Nutr Phys Act* 2015;12(1):4-4. doi: 10.1186/s12966-015-0162-z
Altman, D. G. (1985). Comparability of randomised groups. Journal of the Royal Statistical Society: Series D (The Statistician), 34(1), 125-136.

#51. Line 10: Reasons for drop-out should be specified if available (see flow chart).
This information has been added.

See page 15, lines 375-377:

> Both drop-outs were dissatisfied that they had been allocated to TAU and did not want to attend their appointments within regular healthcare or continue as study participants.

#52. Table 2: The high comorbidity should be commented somewhere as it is the norm, not the exception.
This information has been added under *Discussion*.

See page 21, lines 491-492:

> Most participants screened positive for two or more diagnoses according to MINI-KID, indicating that comorbidity was common in this sample.

#53. Treatment content in TAU: Give more detail (i.e., percentages) in the text about which form of treatment (medication, psychological, supportive, combinations) the participants received.
This information has been added to Results.

See page 17, lines 394-398:

> According to interviews with families and medical records at the three-month follow-up, patients in TAU received pharmacological (n = 1), psychological (n = 1), supportive (n = 1), or a combination of these interventions (n = 4) as well as psychiatric (n = 1) or neuropsychiatric assessment and medications (n = 1) during the study. Details on TAU content are presented in supplementary **Table S1a-b.**

#54. Acceptability of I-BA:
Adverse events and negative effects: If the authors consider that there is a difference between these two constructs, they should define them better in the instruments section.

We added an explanation to why we included two measures on adverse events:

See page 12, lines 269-273:

> Because we did not systematically ask about adverse events, the administration of NEQ at predefined time points increased the likelihood of identifying adverse events. Furthermore, NEQ includes treatment-related questions like lacking confidence in one's treatment or having unpleasant memories resurface (these factors are often not reported spontaneously).

#55. Therapist time (therapist-guided I-BA): The therapist attention should be explained more clearly in the intervention section. How were the messages on th platform registered in minutes? Did the therapist talk to the parents, to the participants or to both?
We have added more information on how time was registered.

See page 12, lines 275-282:

> Therapist time was logged automatically in the treatment platform. The platform registered how many minutes the therapist spends on each participant (including reading their responses and providing feedback). The entire time a therapist had a certain participant "open" was included, e.g., navigating between worksheets, answering messages, etc. If therapists were interrupted while working, they could edit the amount of time registered to a more accurate sum. Time

spent on phone calls with adolescents and their parents was logged manually by the therapist. These two indicators, i.e., therapist time in the platform and time spent on phone calls, were combined as a measure of therapist time per family and chapter.

#56. Effects for CGAS, CGI-S, RCADS-S-A/P, KIDSCREEN-10-A/P, ISI, ARI and WSAS-P should be commented in the text, not only in the supplementary material.

Non-significant results should be stated.

A brief comment on these results has been added to the results section.

See page 20, lines 468-472:

Of the secondary measures, CGAS, ISI, KIDSCREEN-10 (adolescent- and parent-rated) showed significant improvements in all three groups. Remaining secondary measures (CGI-S, RCADS-S-A/P, WSAS-P, ARI) showed significant improvements in some, but not all groups. Means and within-group effects for CGAS, CGI-S, RCADS-S-A/P, KIDSCREEN-10-A/P, ISI, ARI, and WSAS-P are presented in supplementary **Table S3.**

#57. Authors should initiate a new paragraph after the first sentence. Like this the first sentence summarizes the study design and research questions and the second paragraph starts with the feasibility.
This has been adjusted accordingly.

#58. The low attrition should be mentioned as part of the feasibility of the study.
Thanks for this comment. We added a brief sentence on this.

See page 21, line 493-494:

Drop-out of participants was low and data loss acceptable.

#59. Non-significant results should be stated and explained.
Since this was a pilot study, we believe that adding information on non-significant results to the Discussion would be too much emphasis on meaning of significance, and does not add anything essential to the paper itself. However, we would be happy to add this if the editor requests it.

#60. The benefits of BA compared to TAU seem convincing, but the authors should discuss why BA instead of a more complete CBT intervention could be beneficial.
We have added a more thorough rationale for choosing BA rather than a more complete CBT intervention to the Introduction, see page 4. Please see response to #15.

#61. The authors should mention again that the protocol is new and not validated.
We considered adding this information in the first paragraph in the Discussion, however since it is already explained in the methods, we do not see value of adding this in the Discussion. If the editor requests it, we would be happy to add this.

#62. The authors should consider if they want to mention the following additional limitations of the study: 1) It was not possible to compare groups due to insufficient power; 2) after treatment the authors did not assess if participants still had a MDD diagnosis (or comorbid diagnoses).
Thank you for this feedback. We have discussed this and as comparing groups was never an aim in this study, we do not consider it to be a limitation.

As for diagnostic status, we did assess if participants still had a MDD diagnosis at primary endpoint and have added this information to the result section. Since we did not assess comorbid diagnoses in any systematic way at follow-ups, we have not added information on this.

See page 20, lines 477-478:

> At the three-month follow-up, 78%, 67%, and 56% no longer fulfilled criteria for MDD in therapist-guided I-BA, self-guided I-BA, and TAU respectively.

#63. Line 60: The authors claim that the two measures of TAU content (medical records and interviewing parents) were in good agreement with each other. This should be mentioned before in the results section. How are the authors able to conclude this?
No statistical comparison of agreement between medical records and parent report was conducted. However, at closer inspection of reported interventions from medical records and parents respectively (in terms of treatment type, number of sessions, type of medication etc.), agreement was quite good. Please see Data supplement 3. This question arose during the study as we noticed that it was cumbersome and difficult to collect medical records from several different care providers in many different regions. We realized that it would not be feasible to rely on medical records in a future larger trial and thus the comparison with parent-report became important from a feasibility perspective.

#64. A section on future studies is missing (e.g., full CBT comparison group instead of TAU).
Although it would be interesting to discuss other potential research questions and study designs, we believe it would be beyond the scope of this study. As our aim was to assess the feasibility of conducting a future definitive RCT, we believe that the parts of our discussion on conducting a fully powered RCT correspond to a section on future studies.

In the Discussion, we have also commented on potential improvements in the future definitive RCT (concerning masking procedures and recruitment strategies).

See page 21, lines 498-501:

Implications for a future large-scale RCT include the importance of broad recruitment strategies, such as nationwide participant inclusion, and close collaboration with clinical services to ensure that participants randomised to TAU have access to treatment as soon as possible.

See page 22, lines 549-552:

Fourth, despite our best efforts, masked assessors correctly guessed group allocation more often than they would have by chance. Additional measures, such as employing external masked assessors who are fully unaware of study aims and hypotheses (ref 76) might be needed to improve masking.

References:

76. Mataix-Cols D, Andersson E. Ten practical recommendations for improving blinding integrity and reporting in psychotherapy trials. *JAMA Psychiatry* 2021;78(9):943-44. doi: 10.1001/jamapsychiatry.2021.1419

#65. Contributors: There are 10 co-authors but, in this section, only the contributions of 7 authors are mentioned. The contributions of the 3 missing authors should be detailed.

This information has been added.

See page 24, lines 559-560:

All authors (RG, JA, DMC, FL, EH, CM, HS, MB, ES, and SV) contributed to and have approved the final manuscript.

#66. Acknowledgements: Authors should detail the services that were used from the eHealth Core Facility at Karolinska Institutet.

We have detailed this accordingly.

See page 25, lines 594-596:

This work used the BASS platform for data collection from the eHealth Core Facility at Karolinska Institutet, which is supported by the Strategic Research Area Healthcare Science (SFO-V).

#67. The titles of the different articles should be written without capitalizing every word.

This has been adjusted accordingly.

#68. Figure 1: The authors should check the abbreviations: The ones explained do not

come up in the figure and there are some abbreviations in the figure which are not explained in the note.
Thanks for this observation. This has been adjusted.

Previous footnote:

Figure 1 Consolidated Standards of Reporting Trials flow diagram.

Abbreviations: I-BA = Internet-delivered behavioural activation; CDRS-R = Children's Depression Rating Scale, revised; SMFQ = Short Mood and Feelings Questionnaire.

Revised footnote:

Figure 1 Consolidated Standards of Reporting Trials flow diagram.

Abbreviations: I-BA = Internet-delivered behavioural activation; CBT = Cognitive Behavioural Therapy; CAMHS = Children and Adolescent Mental Healthcare Services

#69. Figure 2: The text refers to error bars which are not depicted in the graph.
We have now removed this sentence: "Error bars indicate 95% CIs.", which had been left there by mistake from a previous version of the figure. We decided not to depict error bars in this graph as it made it less visible.

#70. Table S2: "^Observed means. †Coefficients at post-treatment and at the 3-month follow-up compared with baseline. §Primary endpoint": This information does not come up in the table
Thanks for this comment. We removed ^Observed means and †Coefficients at post-treatment and at the 3-month follow-up compared with baseline this as it was unnecessary information, while we added the symbol § (primary endpoint) to the table.