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Peer Review Information

Journal: Nature Human Behaviour
Manuscript Title: Single-Session Interventions for Adolescent Depression in the Context of COVID-19: A Nationwide Randomized-Controlled Trial
Corresponding author name(s): Jessica L. Schleider

Editorial Notes:

Reviewer Comments & Decisions:

Decision Letter, initial version:

5th July 2021

Dear Dr Schleider,

Thank you once again for your manuscript, entitled "Single-Session Interventions for Adolescent Depression in the Context of COVID-19: A Nationwide Randomized-Controlled Trial." I apologize again for the delat during the peer review process.

Your manuscript has now been evaluated by 2 reviewers, whose comments are included at the end of this letter. Although the reviewers find your work to be of interest, they also raise some important concerns. We are very interested in the possibility of publishing your study in Nature Human Behaviour, but would like to consider your response to these concerns in the form of a revised manuscript before we make a decision on publication.

You will see that both Reviewer #1 and #2 raise concerns over aspects of the data analysis, regarding missing data handling and the use of a linear regression, respectively. We believe that in both of these cases it will be necessary to carry out additional analyses, as suggested by the reviewers, to resolve these important concerns.

Secondly, in order to ensure that your manuscript meets our editorial standards for clinical trials, we ask you to do the following:
1) Ensure that all secondary measures that were collected are analyzed and mentioned in the manuscript; currently, there are some measures which appear in the protocol but not in the paper
2) Report adverse events, or if no adverse event data was collected, you should state this.

Finally, your revised manuscript must comply fully with our editorial policies and formatting requirements. Failure to do so will result in your manuscript being returned to you, which will delay its

consideration. To assist you in this process, I have attached a checklist that lists all of our requirements. If you have any questions about any of our policies or formatting, please don't hesitate to contact me.

In sum, we invite you to revise your manuscript taking into account all reviewer and editor comments. We are committed to providing a fair and constructive peer-review process. Do not hesitate to contact us if there are specific requests from the reviewers that you believe are technically impossible or unlikely to yield a meaningful outcome.

We hope to receive your revised manuscript within four to eight weeks. We understand that the COVID-19 pandemic is causing significant disruption for many of our authors and reviewers. If you cannot send your revised manuscript within this time, please let us know - we will be happy to extend the submission date to enable you to complete your work on the revision.

With your revision, please:

• Include a “Response to the editors and reviewers” document detailing, point-by-point, how you addressed each editor and referee comment. If no action was taken to address a point, you must provide a compelling argument. This response will be used by the editors to evaluate your revision and sent back to the reviewers along with the revised manuscript.

• Highlight all changes made to your manuscript or provide us with a version that tracks changes.

Please use the link below to submit your revised manuscript and related files:

[REDACTED]

Note: This URL links to your confidential home page and associated information about manuscripts you may have submitted, or that you are reviewing for us. If you wish to forward this email to co-authors, please delete the link to your homepage.

We look forward to seeing the revised manuscript and thank you for the opportunity to review your work. Please do not hesitate to contact me if you have any questions or would like to discuss these revisions further.

Sincerely,
Jamie

Dr Jamie Horder
Senior Editor
Nature Human Behaviour

REVIEWER COMMENTS:

Reviewer #1:
Remarks to the Author:

The authors conducted a large randomized controlled trial of two unguided online single-session interventions for adolescent depression. They should be commended on several aspects of their design, including: (a) recruiting a large and diverse sample, (b) evaluating two active interventions, (c) evaluating interventions that are brief, scalable, and freely available, and (d) pre-registering their analyses and providing access to their analytic code.

In the following I describe one major concern, as well as some points that would benefit from clarification. If these are addressed, this piece could have a major impact on the study of brief digital mental health interventions for adolescents.

Major Concern: Handling of Missing Data

• As is common in research in this area, there was a high percentage of missing data. This makes the choices about how to address this problem especially important. The authors applied only one technique and therefore could not provide sensitivity analyses that would, in my view, provide a more robust understanding of the data. The claims they make about the effectiveness of their SSI are strong and bold, which puts more pressure on them to show that their effects are robust (or not) when applying different techniques to handle their missing data.

• The approach they chose—multiple imputation of all participants who were randomized—may artificially inflate the power of their tests. Of the 2452 participants who were randomized, 398 did not complete their condition, and 686 did not complete the follow-up measure. (It is unclear to me if this 686 figure includes the 398 who did not finish their condition, or if it means that 686 of those who finished their condition did not complete the follow-up measure). Regardless, it appears that about 25-45% of the sample either a) did not complete their intervention, b) did not fill out their follow-up measure, or c) both.

• When rates of missing data are this high, the technique(s) used to address missing data can meaningfully change a study's findings and the way that those findings are interpreted. The authors implemented the Amelia II algorithm in R to impute missing data. Although they state that this approach is more conservative than other approaches, such as listwise deletion and last-observation-carried-forward analyses, this is true only under certain conditions. Those conditions may have obtained in this dataset, but there is no way to know this from what they report.

Many multiple imputation approaches take the pattern that is observed in the available data and essentially apply that pattern of findings to the missing data. This is partially why these approaches are only considered valid if there is reason to believe – or evidence in support of – a claim that the data are Missing at Random. Missingness in the present dataset are extremely unlikely to have resulted from random processes. In particular, rates of dropout across the conditions differed substantially (from 10% in ABC to 20% in Personality) and significantly (per a chi square test). The authors should address this limitation. Possibilities include implementing at least two alternative approaches to missing outcome data, such as:

• Completers-only analyses (in which people who did not complete the intervention are excluded) with imputation for those who did not complete follow-up measures.

• Completers-only analyses with last-observation-carried-forward for those who did not complete follow-up measures.

• Completers-only analyses with listwise deletion for those who did not complete follow-up measures. If the results of additional analyses are consistent with those they included in this paper, it would inspire greater confidence in their interpretations and conclusions. If not, then the authors would need to adjust their interpretations in light of what the sensitivity analyses show. Given the tight word limits, it might be suitable for this additional content to be presented in supplemental files.

This kind of caution is especially important at this stage in research on brief digital interventions as there is reasonable skepticism about such interventions.

Additional comments follow:

Title
• It is not clear what "nationwide" means here. Did the participants represent a broad spectrum (for example, in regard to the regions of the U.S.) of the population? If not, or if it is not known, it would make sense to remove "nationwide" from the title.

Abstract
• The authors should comment on the size of their effects. Given the standardized mean differences reported in the results section, it seems that the interventions yielded "small" standardized mean differences (generally ranging from 0.1 to 0.3). Given the brevity of the interventions, this is still impressive, but the sizes of the effects should be made clearer in the abstract.

Introduction
• P.3—The relevance of the statements regarding potency and depression's heterogeneity are unclear.

• P.4—"Risk for youth depression may reach an historic high in upcoming years." This is a prediction that may or may not bear out. Can the authors cite evidence in support of this?

• P.3 & P.4—Is there any evidence to suggest that rates of adolescent depression have been on the rise during the pandemic (or before the pandemic)? Many of the points about COVID's impact on depression and its risk factors seem somewhat speculative. They also seem unnecessary for motivating the study.

• P.4—The authors should note that the behavioral activation SSIs were delivered by trained providers/doctoral students. This makes them substantially different from the unguided self-help format used in this study for the GM SSI and the BA SSI.

• P.4 & P.5—The authors should temper the claim that GM-SSIs appear to effect change by reducing maladaptive cognitions, as the evidence presented does not seem to allow one to infer that changes in cognitions are driving intervention effects. The language can be edited to say that GM-SSIs are designed to target cognitions, while BA-SSIs are designed to target behaviors.

• Relatedly, the authors may wish to acknowledge that interventions designed to target cognitions may also produce changes in behaviors, and vice-versa. For instance, it is quite plausible that a GM-SSI produces behavioral changes (e.g., approaching challenges, engaging in opportunities to learn and improve) while a BA-SSI produces cognitive changes (e.g., more positive views about the self and the world). As a result, I suggest de-emphasizing the dichotomy between "cognitive" and "behavioral" presented in the article (e.g., on page 5).

• P.5—Why did the authors choose the GM-SSI and the BA-SSI for this study? The case for the GM-SSI seems clearer, as there are already evidence from multiple RCTs. Has this unguided self-help BA-SSI been tested before? Did the authors think BA would be especially helpful during the COVID-19 pandemic, relative to other plausible candidates? (e.g., cognitive restructuring, problem solving, positive psychology interventions).

o The authors may wish to cite the relevant literature on digital behavioral activation interventions, such as: Huguet, A., Rao, S., McGrath, P. J., Wozney, L., Wheaton, M., Conrod, J., & Rozario, S. (2016). A systematic review of cognitive behavioral therapy and behavioral activation apps for depression. PloS one, 11(5), e0154248.

• P.5—Aim 2 is unclear. Did the authors mean that they intended to compare the effectiveness of the two SSIs on overall depressive symptoms? Or did the authors separate cognitive symptoms and behavioral symptoms? (i.e., examining if the GM-SSI showed a stronger effect on cognitive symptoms than the BA-SSI, and if the BA-SSI showed a stronger effective on behavioral symptoms than the GM-SSI). Unless the latter was done, I again suggest removing the language that implies that the GM-SSI is a "cognitive" intervention while the BA-SSI is a "behavioral" intervention.

• P.6—Minor point: the authors state that they tested the intervention across 3 months, but they indicate that it was tested from November-December 2020 (a two-month window). Please clarify.

• General comment— Study recruitment took place in November and December of 2020, approximately 8-9 months after major lifestyle changes in the US took place (e.g., social distancing, school closures). The authors may wish to highlight this in their introduction, making it clear that these interventions were tested in a time period when many adolescents had already "adjusted" to new norms.

General comment—The authors may wish to highlight some unique benefits of SSIs (relative to other kinds of brief interventions. As an example, it is known that engagement is a large challenge for many digital mental health interventions. One important advantage of SSIs is that participants only need to stay engaged for one session, potentially giving them an advantage over interventions that require sustained use. A relevant citation: Baumel, A., Muench, F., Edan, S., & Kane, J. M. (2019). Objective user engagement with mental health apps: systematic search and panel-based usage analysis. Journal of medical Internet research, 21(9), e14567.

Methods & Results

• P.7—The authors claim that the SSIs took 20-30 minutes; how was this determined? Are there data available to determine the mean/median duration of each SSI?

• Were there differences between those who dropped out and those who did not?

• Differential dropout as a function of condition, as noted above, needs to be described and addressed, in the Methods section and in the Discussion.

• The authors present within-group standardized mean difference for each SSI condition. It is rare for RCTs to compute within-group effect sizes; readers may (incorrectly) assume that the effect sizes

presented are between-group effect sizes. Additionally, within-group standardized mean differences are affected greatly by the standard deviation of each group. Unstandardized (raw) mean differences are not subject to this confound. As such, the authors could consider reporting raw (unstandardized) mean differences in addition to the standardized mean differences.

Discussion

• P.14—The authors note that "the SSIs in this trial might help reverse this trend, if disseminated broadly." It is unclear how this would work. If anything, it seems like these SSIs would decrease the average effect size of youth depression trials—the primary benefit of these interventions being their scalability and the potential population-level effects rather than their "per-person" effect.

• The authors should devote more space to discussing the magnitude of the interventions' (seemingly small) effect sizes. How do these effect sizes compare to those from other SSI studies? Additionally, how could these (or other) SSIs produce larger effects in future studies?

• P.16—How generalizable are these findings? The authors noted that participants were recruited via Instagram. Do the authors believe that this sample generalizes to community samples of adolescents, or might there be differences between those recruited via social media and those recruited via other means?

• As an example, the authors note that 80% of the sample identified as sexual minorities. I commend the authors for recruiting such a diverse and traditionally understudied group. At the same time, what is the nationwide percentage of US teens who identify as sexual minorities? I am not an expert on this subject, but some survey data seem to suggest that the rate is around 10% (https://williamsinstitute.law.ucla.edu/wp-content/uploads/LGBT-Youth-US-Pop-Sep-2020.pdf). Even if this an underestimate, it seems that the adolescents in this study identified as sexual minorities at a substantially higher rate than the national average. This, as well as other potential ways in which the recruitment method may have recruited a sample that differs from the US population, should be discussed further in the limitations section.

Reviewer #2:
Remarks to the Author:
This pre-registered trial provides important insights relative to youth experiencing mood-related symptoms, and provision of brief digital interventions. Links to the resources that were presented to participants are provided, enabling clear understanding of the 3 SSI conditions and how they differed from each other. Data and code are available. The paper is very well written.

Effect sizes were small (or in fact very small) for the depression outcomes comparing SSI conditions to control. For the within-group effects, effect sizes approached medium effects, but the actual difference in effect sizes between the control and the other SSI conditions seemed small/negligible. I would suggest including mention of effect sizes in the abstract.

The small magnitude of effects are clearly noted in the discussion. That said, the fact that even small effects were demonstrated after a 30-mins single session self-directed intervention is of importance.

The discussion could be clearer that even the control condition improved, and was rated similarly in terms of program feedback. Does this suggest there is room for improvement for content presented in the two active SSI conditions? Relatedly, the abstract states “Results confirm the effectiveness of two free-of-charge, online SSIs for adolescents with elevated depression, even in the high-stress context of COVID-19”. But the control condition also improved (line 227), which suggests a rewording.

It did not appear that service use between end of intervention and 3-month follow-up was assessed, and this should be clearly noted. It would seem that the sample recruited via social media were very interested in accessing mental health information/intervention, and it may be the case that a large proportion of participants in all 3 conditions were accessing other avenues of formal or informal care adjunctive to the 30 min intervention provided. If that is indeed the case (which is unknown) then effects may be attributable to other formal or informal care provided by things like hotlines or other digital interventions. Given this data was not captured (and I appreciate it is not easy to do so), this caveat should be provided on the results.

The analytic approach seems unusual given the trial design. Linear regression was used to identify if SSI group predicted improvement/symptom reduction. It appeared that just 2 time points were used in the analysis. Was a linear mixed model considered, examining the 3 time points available for some measures presented in Table 2? This could then be presented as a figure, enabling a clear presentation of where differences were observed.

88% percent female and 80% identified as a sexual minority. While this is acknowledged as a highly diverse sample, it also limits generalisation to the wider population, and this could be more clearly acknowledged. Importantly, with around just 15% male participants at baseline, the claim regarding diversity should be tempered. Relatedly, can some suggestions be offered as to how future digital SSI trials may be better able to engage/recruit/retain populations of young males?
There was a large dropout rate between intervention and 3-month follow-up. As indicated in the paper, large dropout has significant scope to effect results/interpretation. Can the authors comment on strategies for SSI to address this in future studies?

Minor – suggest presenting the scale descriptions in the method in a consistent manner (e.g., the response options).

Can the text used for Instagram recruitment (and the accompanying image) be provided, even if as supplementary? It would be helpful to know more about the recruitment process. Presumably paid advertisements were used?

Line 308 - compared “to” a supportive

Author Rebuttal to Initial comments

July 26, 2021

Dear Dr. Horder:

Many thanks to you and the reviewers for your careful review of our manuscript and recommendations for improving it. My co-authors and I are grateful for the care, time, and effort that went into the review process. Below, I outline our responses to each of the reviewer comments. If any additional changes or revisions are needed, or if we have missed anything, we will be happy to make additional changes in a future revision.

Editor's Comments

1. You will see that both Reviewer #1 and #2 raise concerns over aspects of the data analysis, regarding missing data handling and the use of a linear regression, respectively. We believe that in both of these cases it will be necessary to carry out additional analyses, as suggested by the reviewers, to resolve these important concerns.

RESPONSE: We greatly appreciate your and the reviewers' recommendations for improving our analytic approach. Per Reviewer 1's recommendations, we have now re-analyzed our data using two alternative approaches to addressing missing data. First, we re-ran pre-registered analyses on primary and secondary outcomes (3-month depressive symptoms [primary]; post-intervention and 3-month hopelessness [secondary]; post-intervention and 3-month perceived agency [secondary]; 3-month generalized anxiety symptoms [secondary]; 3-month trauma symptoms [secondary]) using two alternative missing data approaches recommended by Reviewer 1. Specifically, we conducted:

(1) Completers-only analyses with listwise deletion for those who did not complete follow-up measures;
(2) Completers-only analyses (in which people who did not complete the intervention were excluded), with imputation for those who did not complete follow-up measures

Compared to the placebo control, overall effects of Project Personality and the ABC Project on the trial's primary outcome (3-month depressive symptoms) and several secondary outcomes (post-intervention and 3-month hopelessness; post-intervention and 3-month perceived agency) were *unchanged* using these alternative missing data approaches. Only a few minor differences emerged from pre-registered imputation analyses, exclusively with respect to secondary outcomes. Compared to the placebo control and to each other, overall effects of Project Personality and the ABC Project on the trial's primary outcome (3-month depressive symptoms) and several secondary outcomes (post-intervention and 3-month hopelessness; post-intervention and 3-month perceived agency) were unchanged using these alternative missing data approaches. Only a few minor differences emerged from pre-registered imputation analyses, exclusively with respect to secondary outcomes. In our completers-only analyses with listwise deletion, the effect of the GM-SSI on COVID-related trauma symptoms at 3-month follow-up was non-significant, versus the control (d=0.12, 95% CI [-0.01, 0.12], t(987)=1.81, p=0.07); second, the GM-SSI showed a significantly stronger (more positive) effect on generalized anxiety symptoms at 3-month follow-up than did the BA-SSI (d=0.13, 95% CI [0.002, 0.25], t(994)=2.00,

p=.045). In our completers-only analyses with imputation for follow-up non-completers, the BA-SSI significantly reduced COVID-related trauma symptoms at 3-month follow-up, versus the control (d=0.12, 95% CI [0.03, 0.22], t(1637)=2.51, p=0.01), and the GM-SSI had a significantly greater, positive effect on generalized anxiety symptoms, versus the BA-SSI (d=0.11, 95% CI [0.01, 0.21], t(1632)=2.20, p=0.02). Thus, overall results patterns were similar—showing only minor differences with respect to secondary outcomes—regardless of our approach to handling missing data.

Because use of multiple imputation remains the most rigorous approach to analyzing data involving a large percentage of missingness, and to remain consistent with our pre-registered approach, we report the original results in the manuscript, noting our new sensitivity tests on page 9-10 of our revision, and directing readers to our openly-available, reproducible analytic code and full results on Open Science Framework.

Second, we appreciate and carefully considered Reviewer 2's suggestion to utilize mixed-effects modeling rather than linear regression. However, we determined that such an approach would be inappropriate in this trial, because all of our clinical and symptom-related outcomes—depression symptoms (primary outcome), anxiety symptoms, and COVID-related trauma symptoms—were measured *only* at pre-intervention and 3-month follow-up (2 time points total). As such, exploratory mixed-effects models would be impossible to conduct for both our primary outcome and for any symptom-related outcomes. The only outcomes examined at 3 time points were those that we expected to change from baseline to immediate post-intervention (hopelessness, perceived agency) — and our pre-registered predictions *only* involved pre-to-post-intervention change in those outcomes, *not* the trajectory of change in hopelessness or agency across all assessment points. Although we considered running exploratory mixed-effects models for the small subset of outcomes assessed at more than 2 time points, these tests would extend well beyond our hypothesized intervention effects. Further, the 3 assessment points for the measures administered more than twice were unevenly-spaced across time, creating interpretive challenges to these potential mixed-effects models.

Accordingly, we consulted directly with the Editor (Dr. Horder) via email on July 5, 2021 to inquire whether exploratory mixed-effects models would be appropriate. We were advised that they would not be, given the points outlined above. Thus, we have not included mixed-effects models in our submitted revision.

2. Secondly, in order to ensure that your manuscript meets our editorial standards for clinical trials, we ask you to do the following:
    a. Ensure that all secondary measures that were collected are analyzed and mentioned in the manuscript; currently, there are some measures which appear in the protocol but not in the paper

RESPONSE: We appreciate the Editor's attention to this important point. Indeed, we collected data on a handful of exploratory "other outcomes," (differentiated from "secondary outcomes" in our ClinicalTrials.gov registration), about which we did not hypothesize intervention effects. These measures were included for exploratory purposes only. To balance manuscript space limitations with the need for inclusiveness, we have tested intervention effects on these measures and added measure descriptions and results to our Supplemental Materials. These additions are referenced and described for readers on page 18 of the revised manuscript, in the Method section. We also include one set of these post-hoc analyses in our main manuscript, which revealed unexpected benefits of the online single-session interventions for restrictive eating at 3-month follow-up. These results seemed sufficiently meaningful to feature in the main text, although we have been careful to qualify that these were non-pre-registered, post-hoc, and exploratory analyses focused on an "other" (rather than primary or secondary) study outcome (see page 9 for a description of the active SSIs' significant, positive effects on restrictive eating at 3-month follow-up, relative to the control condition, and page 13 for a brief comment of the implications of these exploratory results, in our Discussion).

The additional analyses include the following outcomes, both of which were assessed at baseline and 3-month follow-up: presence of past-month restrictive eating and past-month frequency of suicidal ideation; and approach-based (versus disengagement-based) coping. One additional measure, the Implicit Theory of Personality Scale, was collected at pre- and post-intervention only. All other measures noted in the pre-registration were measured at pre-intervention only.

b. Report adverse events, or if no adverse event data was collected, you should state this.

RESPONSE: Because this study was deemed minimal-risk, and because no adverse events anticipated as a result of the surveys administered, we did not collect formal adverse events data. No unanticipated adverse events were identified in surveys or incidentally reported during the study period. This is now noted on page 16 of the revised manuscript:

> **"As a minimal-risk study (per the IRB's determination), we did not expect any adverse events to occur during the study period; as such, we included no explicit assessments of adverse events. No incidental adverse events of any kind were reported by participants or identified by the researchers during the study period."**

3. Finally, your revised manuscript must comply fully with our editorial policies and formatting requirements. Failure to do so will result in your manuscript being returned to you, which will delay its consideration. To assist you in this process, I have attached a checklist that lists all of our requirements. If you have any questions about any of our policies or formatting, please don't hesitate to contact me.

RESPONSE: We have carefully revised our manuscript in compliance with *Nature Human Behavior*'s editorial formatting requirements.

Reviewer #1 Comments

1. The authors conducted a large randomized controlled trial of two unguided online single-session interventions for adolescent depression. They should be commended on several aspects of their design, including: (a) recruiting a large and diverse sample, (b) evaluating two active interventions, (c) evaluating interventions that are brief, scalable, and freely available, and (d) pre-registering their analyses and providing access to their analytic code.

RESPONSE: We appreciate the Reviewer's positive comments!

2. In the following I describe one major concern, as well as some points that would benefit from clarification. If these are addressed, this piece could have a major impact on the study of brief digital mental health interventions for adolescents.

RESPONSE: Again, we thank the reviewer for their positive comments and suggestions for improving our manuscript, which we believe have been addressed, as described below.

3. Major Concern: Handling of Missing Data. As is common in research in this area, there was a high percentage of missing data. This makes the choices about how to address this problem especially important. The authors applied only one technique and therefore could not provide sensitivity analyses that would, in my view, provide a more robust understanding of the data. The claims they make about the effectiveness of their SSI are strong and bold, which puts more pressure on them to show that their effects are robust (or not) when applying different techniques to handle their missing data. The approach they chose—multiple imputation of all participants who were randomized—may artificially inflate the power of their tests. Of the 2452 participants who were randomized, 398 did not complete their condition, and 686 did not complete the follow-up measure. (It is unclear to me if this 686 figure includes the 398 who did not finish their condition, or if it means that 686 of those who finished their condition did not complete the follow-up measure). Regardless, it appears that about 25-45% of the sample either a) did not complete their intervention, b) did not fill out their follow-up measure, or c) both. When rates of missing data are this high, the technique(s) used to address missing data can meaningfully change a study's findings and the way that those findings are interpreted. The authors implemented the Amelia II algorithm in R to impute missing data. Although they state that this approach is more conservative than other approaches, such as listwise deletion and last-observation-carried-forward analyses, this is true only under certain conditions. Those conditions may have obtained in this dataset, but there is no way to know this from what they report. Many multiple imputation

approaches take the pattern that is observed in the available data and essentially apply that pattern of findings to the missing data. This is partially why these approaches are only considered valid if there is reason to believe – or evidence in support of – a claim that the data are Missing at Random. Missingness in the present dataset are extremely unlikely to have resulted from random processes. In particular, rates of dropout across the conditions differed substantially (from 10% in ABC to 20% in Personality) and significantly (per a chi square test). The authors should address this limitation. Possibilities include implementing at least two alternative approaches to missing outcome data, such as:

• Completers-only analyses (in which people who did not complete the intervention are excluded) with imputation for those who did not complete follow-up measures.
• Completers-only analyses with last-observation-carried-forward for those who did not complete follow-up measures.
• Completers-only analyses with listwise deletion for those who did not complete follow-up measures.

If the results of additional analyses are consistent with those they included in this paper, it would inspire greater confidence in their interpretations and conclusions. If not, then the authors would need to adjust their interpretations in light of what the sensitivity analyses show. Given the tight word limits, it might be suitable for this additional content to be presented in supplemental files. This kind of caution is especially important at this stage in research on brief digital interventions as there is reasonable skepticism about such interventions.

RESPONSE: As detailed in our response to the Editor's comments, above, we have now re-analyzed our data using two alternative approaches to addressing missing data, per Reviewer 1's recommendations. First, we re-ran pre-registered analyses on primary and secondary outcomes (3-month depressive symptoms [primary]; post-intervention and 3-month hopelessness [secondary]; post-intervention and 3-month perceived agency [secondary]; 3-month generalized anxiety symptoms [secondary]; 3-month trauma symptoms [secondary]) using two alternative missing data approaches recommended by Reviewer 1. Specifically, we conducted:

- Completers-only analyses with listwise deletion for those who did not complete follow-up measures;
- Completers-only analyses (in which people who did not complete the intervention were excluded), with imputation for those who did not complete follow-up measures

Compared to the placebo control *and* to each other, overall effects of Project Personality and the ABC Project on the trial's primary outcome (3-month depressive symptoms) and several secondary outcomes (post-intervention and 3-month hopelessness; post-intervention and 3-month perceived

agency) were *unchanged* using these alternative missing data approaches. Only a few minor differences emerged from pre-registered imputation analyses, exclusively with respect to secondary outcomes. In our completers-only analyses with listwise deletion, the effect of the GM-SSI on COVID-related trauma symptoms at 3-month follow-up was non-significant, versus the control (d=0.12, 95% CI [-0.01, 0.12], t(987)=1.81, p=0.07); second, the GM-SSI showed a significantly stronger (more positive) effect on generalized anxiety symptoms at 3-month follow-up than did the BA-SSI (d=0.13, 95% CI [0.002, 0.25], t(994)=2.00, p=.045). In our completers-only analyses with imputation for follow-up non-completers, the BA-SSI significantly reduced COVID-related trauma symptoms at 3-month follow-up, versus the control (d=0.12, 95% CI [0.03, 0.22], t(1637)=2.51, p=0.01), and the GM-SSI had a significantly greater, positive effect on generalized anxiety symptoms, versus the BA-SSI (d=0.11, 95% CI [0.01, 0.21], t(1632)=2.20, p=0.02). Thus, overall results patterns were similar—showing only minor differences with respect to secondary outcomes—regardless of our approach to handling missing data.

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4. It is not clear what "nationwide" means here. Did the participants represent a broad spectrum (for example, in regard to the regions of the U.S.) of the population? If not, or if it is not known, it would make sense to remove "nationwide" from the title.

RESPONSE: We agree that defining "nationwide" is important in the case of this manuscript. As such, we specify that adolescents were from all 50 U.S. states both in our abstract and in the Method section of the manuscript. We also include an additional Figure illustrating the geographic distribution of all study participants across the United States.

5. Abstract. The authors should comment on the size of their effects. Given the standardized mean differences reported in the results section, it seems that the interventions yielded "small" standardized mean differences (generally ranging from 0.1 to 0.3). Given the brevity of the interventions, this is still impressive, but the sizes of the effects should be made clearer in the abstract.

RESPONSE: We now include effect size ranges in our abstract.

6. P.3—The relevance of the statements regarding potency and depression's heterogeneity are unclear.

RESPONSE: We have aimed to clarify the relevance of these statements with the following revisions on pages 3-4 of the manuscript (additions are bolded):

> "**Well-powered trials of brief, focused, and rapidly-scalable interventions may overcome longstanding challenges to reducing adolescent depression—namely, the challenges of *limited potency* of existing treatments, and of *low accessibility* in predominant modes of care.** Difficulties underlying limited treatment *potency* are thought to reflect depression's heterogeneity.[7-8] Diagnostic criteria for depression place youths with 5 of 9 diverse symptoms (such as activity withdrawal, fatigue, and hopelessness) into a single category including >1,400 possible symptom combinations.[7] This heterogeneity has spurred the creation of interventions that target widely-ranging difficulties, some of which may be unrelated to an individual's needs—suggesting the utility of highly-focused, targeted interventions, rather than those characterized by "extreme comprehensiveness" (e.g., cognitive behavioral therapy).[19-20] **Large-scale trials can rigorously and definitively gauge the promise of treatments that are designed for brevity, containing just one or two treatment elements rather than 10+ separate modules.**
>
> **Separately, large trials of brief interventions may reveal solutions to the low *accessibility* of many depression interventions.** This low accessibility stems from the formats of predominant treatments, which span many weeks and are intended for delivery in brick-and-mortar clinics by highly-trained clinicians, creating major dissemination barriers.[21] Further, up to 59% of youths who do access mental health treatment drop out prematurely, compounding challenges posed by provider scarcity.[22-23] **Testing brief treatments deliverable by flexible means is a key component of solving this access-to-care crisis**."

7. P.4—"Risk for youth depression may reach an historic high in upcoming years." This is a prediction that may or may not bear out. Can the authors cite evidence in support of this?

RESPONSE: We have now removed this statement from the manuscript, as it was speculative in nature.

8. P.3 & P.4—Is there any evidence to suggest that rates of adolescent depression have been on the rise during the pandemic (or before the pandemic)? Many of the points about COVID's impact on depression and its risk factors seem somewhat speculative. They also seem unnecessary for motivating the study.

RESPONSE: We appreciate the reviewer's point in this domain. Indeed, it is impossible to know for certain how the pandemic may (or may not) affect youth depressive symptoms in the long-term. As such, we now specify that *there is a possibility* that the COVID-19 pandemic may exacerbate risk for

depression, given extant research on the impacts of environmental instability, financial strain, and social isolation on depressive symptoms. Given this possibility, we believe these points are worth including—even if they are necessarily speculative in nature—as they well-characterize the authorship team's original motivation for conducting the study, as described in our NIH grant proposal that made the trial possible. We have aimed to contextualize and temper our claims in this regard in the revised version of our manuscript.

9. P.4—The authors should note that the behavioral activation SSIs were delivered by trained providers/doctoral students. This makes them substantially different from the unguided self-help format used in this study for the GM SSI and the BA SSI.

RESPONSE: We appreciate the Reviewer's comment on this front, as it provides an opportunity for us to clarify. Some past BA SSIs have been provider delivered, but others have been self-guided by young people. Indeed, the intervention tested in this study (Project ABC) was evaluated previously in an open trial by our research team (Schleider et al., 2020). In that trial, the program demonstrated acceptability and short-term utility among high-symptom adolescents. We now specify which trials tested therapist-guided versus self-guided BA-SSIs on pages 4-5 of our revised manuscript.

10. P.4 & P.5—The authors should temper the claim that GM-SSIs appear to effect change by reducing maladaptive cognitions, as the evidence presented does not seem to allow one to infer that changes in cognitions are driving intervention effects. The language can be edited to say that GM-SSIs are designed to target cognitions, while BA-SSIs are designed to target behaviors.

RESPONSE: We removed this claim from the manuscript and restructured this section considerably to address the Reviewer's valid concern (see pages 5-6 of the revised manuscript).

11. Relatedly, the authors may wish to acknowledge that interventions designed to target cognitions may also produce changes in behaviors, and vice-versa. For instance, it is quite plausible that a GM-SSI produces behavioral changes (e.g., approaching challenges, engaging in opportunities to learn and improve) while a BA-SSI produces cognitive changes (e.g., more positive views about the self and the world). As a result, I suggest de-emphasizing the dichotomy between "cognitive" and "behavioral" presented in the article (e.g., on page 5).

RESPONSE: We have removed distinctions between the SSIs' "cognitive" and "behavioral" targets in the revised manuscript.

12. P.5—Why did the authors choose the GM-SSI and the BA-SSI for this study? The case for the GM-SSI seems clearer, as there are already evidence from multiple RCTs. Has this unguided self-help BA-SSI been tested before? Did the authors think BA would be especially helpful during the

COVID-19 pandemic, relative to other plausible candidates? (e.g., cognitive restructuring, problem solving, positive psychology interventions).

RESPONSE: We selected the only 2 existing self-guided SSIs that have shown acceptability and short (and in the case of the GM-SSI, longer-term) utility for adolescents experiencing elevated depressive symptoms, as identified in Schleider and Weisz' 2017 meta-analysis and Schleider and colleagues' 2020 manuscript on single-session interventions for youth mental health problems. These two SSIs are also quite similar in format and dosage (length), making them particularly useful for direct comparison to one another.

13. The authors may wish to cite the relevant literature on digital behavioral activation interventions, such as: Huguet, A., Rao, S., McGrath, P. J., Wozney, L., Wheaton, M., Conrod, J., & Rozario, S. (2016). A systematic review of cognitive behavioral therapy and behavioral activation apps for depression. PloS one, 11(5), e0154248.

RESPONSE: We now cite this helpful paper on page 5 of the revised manuscript.

14. P.5—Aim 2 is unclear. Did the authors mean that they intended to compare the effectiveness of the two SSIs on overall depressive symptoms? Or did the authors separate cognitive symptoms and behavioral symptoms? (i.e., examining if the GM-SSI showed a stronger effect on cognitive symptoms than the BA-SSI, and if the BA-SSI showed a stronger effect on behavioral symptoms than the GM-SSI). Unless the latter was done, I again suggest removing the language that implies that the GM-SSI is a "cognitive" intervention while the BA-SSI is a "behavioral" intervention.

RESPONSE: We have now clarified Aim 2 to more accurately express our intention: To compare the effectiveness of the two SSIs on overall depressive symptoms in adolescents during the pandemic. We did not separate cognitive and behavioral symptoms in our analysis. The revised description of this Aim is on page 6 of the revised manuscript: "Aim 2 was to test whether the GM-SSI versus the BA-SSI—currently, the only two self-guided, digital SSIs that have shown high acceptability in youths experiencing depressive symptoms—proved more impactful in this context."

15. P.6—Minor point: the authors state that they tested the intervention across 3 months, but they indicate that it was tested from November-December 2020 (a two-month window). Please clarify.

RESPONSE: We have now clarified that the *length between each individual participant's baseline and follow-up assessment* was 3 months. In contrast, we recruited our study sample during a 3-week period from November to December 2020. We have also corrected the statement on page 6 of the manuscript to read "November 2020-March 2021 to reflect the three-month study period, rather than the recruitment period.

16. General comment— Study recruitment took place in November and December of 2020, approximately 8-9 months after major lifestyle changes in the US took place (e.g., social distancing, school closures). The authors may wish to highlight this in their introduction, making it clear that these interventions were tested in a time period when many adolescents had already "adjusted" to new norms.

RESPONSE: We appreciate the reviewer's point; the context of the pandemic might indeed have impacted study results. As such, we now include the following on page 6 of the revised manuscript:

> "**Notably, the trial took place approximately 8 months after school closures and social distancing mandates were first imposed in the United States, but before the COVID-19 vaccine was publicly available. Thus, the trial took place at a time when pandemic-related conditions were still evolving and unpredictable in many U.S. regions, and also when some adolescents might have begun to adjust to lifestyle changes and norms**."

17. General comment—The authors may wish to highlight some unique benefits of SSIs (relative to other kinds of brief interventions. As an example, it is known that engagement is a large challenge for many digital mental health interventions. One important advantage of SSIs is that participants only need to stay engaged for one session, potentially giving them an advantage over interventions that require sustained use. A relevant citation: Baumel, A., Muench, F., Edan, S., & Kane, J. M. (2019). Objective user engagement with mental health apps: systematic search and panel-based usage analysis. Journal of medical Internet research, 21(9), e14567.

RESPONSE: We thank the reviewer for this helpful point and have included a statement regarding the unique benefits of SSIs on page 5 of the revised manuscript, including a reference to this article:

> **"SSIs circumvent many common treatment access barriers: they require no therapist, are completable from any location, and are < 30 minutes in length, eliminating premature drop-out concerns. Moreover, online SSIs hold advantages even over other digital interventions, which tend to require sustained effort and repeated use, leading to low engagement and rapid dropout.[27] Thus, online SSIs offer a unique opportunity for rapid-large scale tests of accessible depression interventions while the pandemic remains underway."**

18. P.7—The authors claim that the SSIs took 20-30 minutes; how was this determined? Are there data available to determine the mean/median duration of each SSI?

RESPONSE: We now note on page 9 that, "Per prior open and randomized trials including the ABC Project, Project Personality, and the Supportive Therapy SSI, each of these interventions take approximately 20-30 minutes for adolescents experiencing depressive symptoms to complete" (Schleider et al., 2020; Schleider et al., 2018).

19. Were there differences between those who dropped out and those who did not?

RESPONSE: We now include the following information on page 7 of the revised manuscript:

> "**Participants in Project ABC dropped out significantly less ($\chi 2(2) = 41.47$, $p<.001$, 11.08%) during the intervention than participants from Project Personality (19.68%) or the Sharing Feelings Placebo (22.86%). There were no significant differences in who initiated the 3-month follow up across conditions ($\chi 2(2) = 2.14$, $p=0.34$, Project ABC: 37.39%; Project Personality: 38.02%; Sharing Feelings Placebo: 40.71%). Logistic regressions using baseline depression symptom and demographic data were unable to predict whether participants would drop out during the intervention (AUC: 0.51) or at 3-month follow up (AUC: 0.56) better than chance (see analyses on the Open Science Framework for further detail: https://osf.io/8mk6x/)."**

20. Differential dropout as a function of condition, as noted above, needs to be described and addressed, in the Methods section and in the Discussion.

RESPONSE: We now include the following section on page 7 of the revised manuscript:

> **"Participants in Project ABC dropped out significantly less ($p < .001$, 11.08%) during the intervention than participants from Project Personality (19.68%) or the Sharing Feelings Placebo (22.86%). There were no significant differences in who initiated the 3 month follow up across conditions ($p = 0.34$, Project ABC: 37.39%; Project Personality: 38.02%; Sharing Feelings Placebo: 40.71%). Logistic regressions using baseline depression symptom and demographic data were unable to predict whether participants would drop out during the intervention (AUC: 0.51) or at 3-month follow up (AUC: 0.56) better than chance (see analyses on the Open Science Framework for further detail: https://osf.io/8mk6x/)."**

We also note the following on page 19 of the Discussion section:

> **"Fifth, although SSI did not predict attrition at 3-month follow-up, youths randomized to the BA-SSI were more likely than those in the GM-SSI and Control conditions to complete their assigned intervention (although completion rates were**

high, >80%, across conditions). It is possible that the greater interactivity of the BA-SSI (e.g., creation of an action plan) contributed to this higher completion rate, but tests of engagement-enhancing components of online SSIs remains a key direction for future work."

21. The authors present within-group standardized mean difference for each SSI condition. It is rare for RCTs to compute within-group effect sizes; readers may (incorrectly) assume that the effect sizes presented are between-group effect sizes. Additionally, within-group standardized mean differences are affected greatly by the standard deviation of each group. Unstandardized (raw) mean differences are not subject to this confound. As such, the authors could consider reporting raw (unstandardized) mean differences in addition to the standardized mean differences.

RESPONSE: To minimize odds of readers mis-interpreting the within-group effects reported in our paper, we have added a clarifying statement on page 7 of the manuscript noting that within-group effects are "**presented here to contextualize within-group symptom changes across conditions, not as indicators of efficacy**." Within-group comparisons are included only to contextualize the fact that *all three* interventions were associated with some degree of reduction in depressive symptoms. To avoid risk of over-emphasizing our exploratory within-group effects calculations, we have not included additional metrics of within-group effects. However, if the Editor and Reviewers believe that they are necessary to include, we will be happy to do so in a revision.

22. P.14—The authors note that "the SSIs in this trial might help reverse this trend, if disseminated broadly." It is unclear how this would work. If anything, it seems like these SSIs would decrease the average effect size of youth depression trials—the primary benefit of these interventions being their scalability and the potential population-level effects rather than their "per-person" effect.

RESPONSE: We have revised this statement to emphasize potential population-wide, rather than individual-level benefits of disseminating these SSIs broadly: "**The SSIs in this trial might help improve population-level youth depression symptoms and outcomes, if disseminated broadly.**"

23. The authors should devote more space to discussing the magnitude of the interventions' (seemingly small) effect sizes. How do these effect sizes compare to those from other SSI studies? Additionally, how could these (or other) SSIs produce larger effects in future studies?

RESPONSE: We now comment in the Discussion on page 10 how these effect sizes compare to previously-reported effects in SSI trials:

> **"effect sizes observed for the BA-SSI and the GM-SSI in this study were *identical* to meta-analytic estimates of single-session interventions' effects on youth depressive symptoms (e.g., Schleider and colleagues (2017) identified a meta-analytic effect on depressive symptoms of *d*=0.18)."**

We also note that the goal for future SSI research might not be to *increase* the overall effects of any one SSI, but rather to identify subsets of adolescents who respond best to the SSIs that already exist, to guide targeted dissemination efforts based on individual characteristics. On page 10, we make this point explicitly:

> **"Moving forward, research might focus less on how to strengthen the *average* magnitude of these SSIs' impacts and more on identifying subsets of 'best-responder' adolescents, guiding tailored dissemination based on individual odds of benefit."**

24. P.16—How generalizable are these findings? The authors noted that participants were recruited via Instagram. Do the authors believe that this sample generalizes to community samples of adolescents, or might there be differences between those recruited via social media and those recruited via other means? As an example, the authors note that 80% of the sample identified as sexual minorities. I commend the authors for recruiting such a diverse and traditionally understudied group. At the same time, what is the nationwide percentage of US teens who identify as sexual minorities? I am not an expert on this subject, but some survey data seem to suggest that the rate is around 10% (https://williamsinstitute.law.ucla.edu/wp-content/uploads/LGBT-Youth-US-Pop-Sep-2020.pdf). Even if this an underestimate, it seems that the adolescents in this study identified as sexual minorities at a substantially higher rate than the national average. This, as well as other potential ways in which the recruitment method may have recruited a sample that differs from the US population, should be discussed further in the limitations section.

RESPONSE: The question of generalizability is an important one to consider. The fact that 72% of U.S. adolescents use Instagram regularly suggests some degree of generalizability for our study's findings, but the Reviewer's comment regarding overrepresentation of certain groups remains valid. We now address this point on page 14 of the revised manuscript:

> "**Fourth, some groups of youth were potentially over-represented in our sample (e.g., sexual minority youth), whereas others were underrepresented (e.g., male-identifying youth). These sample characteristics are unlikely to reflect our Instagram-based recruitment approach, as 72% of teens ages 13-17 actively use Instagram, nearly half of whom are boys.[48] Thus, our sample may reflect youths most readily drawn to taking part in online self-help activities. Focus group-based and mixed-methods research,**

geared toward gathering youth feedback and guidance, may forward efforts to engage adolescent boys in digital, mental health-focused SSIs."

Also regarding our study's over-representation of SGM youth, we include the following comment on page 11:

"Although sexual minority youths were arguably *over-represented* in this study, most youth psychotherapy trials routinely include samples that are >90% White and seldom assess sexual orientation.[21] Thus, this sample's diversity extends the youth mental health knowledge-base, filling gaps in our knowledge of the youth intervention literature that have long remained unaddressed."

Reviewer #2 Comments

1. This pre-registered trial provides important insights relative to youth experiencing mood-related symptoms, and provision of brief digital interventions. Links to the resources that were presented to participants are provided, enabling clear understanding of the 3 SSI conditions and how they differed from each other. Data and code are available. The paper is very well written.

RESPONSE: We appreciate the reviewer's positive feedback!

2. Effect sizes were small (or in fact very small) for the depression outcomes comparing SSI conditions to control. For the within-group effects, effect sizes approached medium effects, but the actual difference in effect sizes between the control and the other SSI conditions seemed small/negligible. I would suggest including mention of effect sizes in the abstract.

RESPONSE: Between-group (i.e. pre-registered) effect size ranges are now reported in the abstract.

3. The small magnitude of effects are clearly noted in the discussion. That said, the fact that even small effects were demonstrated after a 30-mins single session self-directed intervention is of importance.

RESPONSE: We agree with the Reviewer's assessment and appreciate their kind comments!

4. The discussion could be clearer that even the control condition improved, and was rated similarly in terms of program feedback. Does this suggest there is room for improvement for content

presented in the two active SSI conditions? Relatedly, the abstract states "Results confirm the effectiveness of two free-of-charge, online SSIs for adolescents with elevated depression, even in the high-stress context of COVID-19". But the control condition also improved (line 227), which suggests a rewording.

RESPONSE: We have revised the abstract to state "results confirm the effectiveness of free-of-charge, online SSIs for adolescents with elevated depression, even in the high-stress context of COVID-19." Given word limitations, we are not able to specify further in the abstract, but we have aimed to describe the nature of observed effects as thoroughly as possible in the main text and supplement.

Regarding room for improvement in the interventions themselves: As noted in our response to Comment #23 from Reviewer #1, we also note that the goal for future SSI research might not be to *increase* the overall effects of any one SSI, but rather to identify subsets of adolescents who respond best to the SSIs that already exist, to guide targeted dissemination efforts based on individual characteristics. On page 10, we make this point explicitly:

> **"Moving forward, research might focus less on how to strengthen the *average* magnitude of these SSIs' impacts and more on identifying subsets of 'best-responder' adolescents, guiding tailored dissemination based on individual odds of benefit."**

5. It did not appear that service use between end of intervention and 3-month follow-up was assessed, and this should be clearly noted. It would seem that the sample recruited via social media were very interested in accessing mental health information/intervention, and it may be the case that a large proportion of participants in all 3 conditions were accessing other avenues of formal or informal care adjunctive to the 30 min intervention provided. If that is indeed the case (which is unknown) then effects may be attributable to other formal or informal care provided by things like hotlines or other digital interventions. Given this data was not captured (and I appreciate it is not easy to do so), this caveat should be provided on the results.

RESPONSE: We appreciate this point comment and now include the following statement in the discussion section:

> **"Second, we did not formally assess adolescents' use of other mental health supports (e.g., hotlines or textlines; formal treatment) during the study period. Notably, SSIs may function most practically as complements to (rather than replacements for) other forms of care, and we had no reason to suspect that receipt of additional support would differ by intervention condition. Indeed, results of a recent trial demonstrated that receipt of additional mental health treatments did not predict response to the GM-SSI, compared to a placebo control, across a 9-month follow-up period.[13]**

Nonetheless, future studies might collect data to explicitly capture and comment on the role of SSIs in the context of youths' full range of formal and informal mental health supports."

6. The analytic approach seems unusual given the trial design. Linear regression was used to identify if SSI group predicted improvement/symptom reduction. It appeared that just 2 time points were used in the analysis. Was a linear mixed model considered, examining the 3 time points available for some measures presented in Table 2? This could then be presented as a figure, enabling a clear presentation of where differences were observed.

RESPONSE: As noted in our response to the Editor, we appreciate and carefully considered Reviewer 2's suggestion to utilize mixed-effects modeling rather than linear regression. However, we determined that such an approach would be inappropriate in this trial, because all of our clinical and symptom-related outcomes—depression symptoms (primary outcome), anxiety symptoms, and COVID-related trauma symptoms—were measured *only* at pre-intervention and 3-month follow-up (2 time points total). As such, exploratory mixed-effects models would be impossible to conduct for both our primary outcome and for any symptom-related outcomes. The only outcomes examined at 3 time points were those that we expected to change from baseline to immediate post-intervention (hopelessness, perceived agency) — and our pre-registered predictions *only* involved pre-to-post-intervention change in those outcomes, *not* the trajectory of change in hopelessness or agency across all assessment points. Although we considered running exploratory mixed-effects models for the small subset of outcomes assessed at more than 2 time points, these tests would extend well beyond our hypothesized intervention effects. Further, the 3 assessment points for the measures administered more than twice were unevenly-spaced across time, creating interpretive challenges to these potential mixed-effects models.

Accordingly, we consulted directly with the Editor (Dr. Horder) via email on July 5, 2021 to inquire whether exploratory mixed-effects models would be appropriate. We were advised that they would not be, given the points outlined above. Thus, we have not included mixed-effects models in our submitted revision.

7. 88% percent female and 80% identified as a sexual minority. While this is acknowledged as a highly diverse sample, it also limits generalisation to the wider population, and this could be more clearly acknowledged. Importantly, with around just 15% male participants at baseline, the claim regarding diversity should be tempered. Relatedly, can some suggestions be offered as to how future digital SSI trials may be better able to engage/recruit/retain populations of young males?

RESPONSE: We agree that these features of our study are both strengths and limitation to the generalizability of results. As for engaging more male-identifying youths in SSIs, we agree with the

reviewer that work in this area is sorely needed and recommend it as a future direction in our Discussion (page 11):

> "**Fourth, some groups of youth were potentially over-represented in our sample (e.g., sexual minority youth), whereas others were underrepresented (e.g., boys). These sample characteristics are unlikely to reflect our Instagram-based recruitment approach, as 72% of teens ages 13-17 actively use Instagram, nearly half of whom are boys.[48] Thus, our sample may reflect youths most readily drawn to taking part in online self-help activities. Focus group-based and mixed-methods research, geared toward gathering youth feedback and guidance, may forward efforts to engage adolescent boys in digital, mental health-focused SSIs.**"

8. There was a large dropout rate between intervention and 3-month follow-up. As indicated in the paper, large dropout has significant scope to effect results/interpretation. Can the authors comment on strategies for SSI to address this in future studies?

RESPONSE: Indeed, attrition during randomized clinical trials is a very common issue, and not one that is specific to SSI research. We now note that future investigations might "formally test methods for increasing participant retention across longer-term study periods" (p. 11) and that our attrition rates were comparable to those observed in other depression RCTs for youth.

9. Minor – suggest presenting the scale descriptions in the method in a consistent manner (e.g., the response options).

RESPONSE: Where feasible, and within word limits, we have aimed to revise our descriptions for consistency.

10. Can the text used for Instagram recruitment (and the accompanying image) be provided, even if as supplementary? It would be helpful to know more about the recruitment process. Presumably paid advertisements were used?

RESPONSE: We now include our best-performing Instagram study advertisement in our Supplement.

11. Line 308 - compared "to" a supportive

RESPONSE: This typo has been corrected in our revision.

Decision Letter, first revision:

nature research

Our ref: NATHUMBEHAV-210414868A

16th September 2021

Dear Dr. Schleider,

Thank you for submitting your revised manuscript "A Nationwide RCT of Single Session Interventions for Adolescent Depression during COVID-19" (NATHUMBEHAV-210414868A). It has now been seen again by the original referees and their comments are below.

As you can see, the reviewers find that the paper has improved in revision. We will therefore be happy in principle to publish it in Nature Human Behaviour, pending minor revisions to satisfy the referees' final requests and to comply with our editorial and formatting guidelines.

We are now performing detailed checks on your paper and will send you a checklist detailing our editorial and formatting requirements within two weeks. Please do not upload the final materials and make any revisions until you receive this additional information from us.

However, you may wish to make a start on revising the manuscript now. There are a few issues relating to the clinical trial registration that must be addressed:
- We noticed that the ClincalTrials.gov protocol was changed in May reclassifying some of the outcomes. Please ensure that the manuscript reports all of the originally specified secondary outcomes, and states that they were the original secondary outcomes.
- Somewhere in the manuscript there should be a table clearing listing all outcome measures and their original status (Primary, Secondary, Other)
- There is an outcome (SRET task) which is mentioned in the registration, but I couldn't find any mention of it anywhere in the manuscript. This outcome needs to be reported in the manuscript. Even if no SRET data was collected for some reason, the reason for the absence of these data should be mentioned in the manuscript.

Please let me know if you have any questions about these changes.

Sincerely,
Jamie

Dr Jamie Horder
Senior Editor
Nature Human Behaviour

Reviewer #1 (Remarks to the Author):

The authors dealt very well with all the questions I raised in my review, so I would recommend publication.

Reviewer #2 (Remarks to the Author):

The revised paper and response letter are thorough and detailed. I am satisfied with the changes made (or responses offered) to my comments, and am appreciative of the efforts from the authors.

I have just one further point of feedback. At present, the title reads as “Nationwide Randomized Trial of Single-Session Interventions for Adolescent Depression amid COVID-19”. There is no mention of this being a digital intervention, and it is likely that many readers will infer that that was a face-to-face intervention from the current title (even in the pandemic). I suggest the authors consider adding a reference to “digital”, “online” or similar in the title.

Simon Rice - Reviewer

Decision letter, final requests:

** Please ensure you delete the link to your author homepage in this e-mail if you wish to forward it to your co-authors. **

Our ref: NATHUMBEHAV-210414868A

22nd September 2021

Dear Dr. Schleider,

Thank you for your patience as we’ve prepared the guidelines for final submission of your Nature Human Behaviour manuscript, "A Nationwide RCT of Single Session Interventions for Adolescent Depression during COVID-19" (NATHUMBEHAV-210414868A). Please carefully follow the step-by-step instructions provided in the attached file, and add a response in each row of the table to indicate the changes that you have made. Ensuring that each point is addressed will help to ensure that your revised manuscript can be swiftly handed over to our production team.

We would hope to receive your revised paper, with all of the requested files and forms within two-three weeks. Please get in contact with us if you anticipate delays.

When you upload your final materials, please include a point-by-point response to any remaining reviewer comments.

If you have not done so already, please alert us to any related manuscripts from your group that are under consideration or in press at other journals, or are being written up for submission to other journals (see: https://www.nature.com/nature-research/editorial-policies/plagiarism#policy-on-duplicate-publication for details).

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accepting your manuscript for publication.

In recognition of the time and expertise our reviewers provide to Nature Human Behaviour's editorial process, we would like to formally acknowledge their contribution to the external peer review of your manuscript entitled "A Nationwide RCT of Single Session Interventions for Adolescent Depression during COVID-19". For those reviewers who give their assent, we will be publishing their names alongside the published article.

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If you have any further questions, please feel free to contact me.

Best regards,
Chloe Knight
Editorial Assistant
Nature Human Behaviour

On behalf of

Jamie

Dr Jamie Horder
Senior Editor
Nature Human Behaviour

Reviewer #1:
Remarks to the Author:
The authors dealt very well with all the questions I raised in my review, so I would recommend publication.

Reviewer #2:
Remarks to the Author:

The revised paper and response letter are thorough and detailed. I am satisfied with the changes made (or responses offered) to my comments, and am appreciative of the efforts from the authors.

I have just one further point of feedback. At present, the title reads as “Nationwide Randomized Trial of Single-Session Interventions for Adolescent Depression amid COVID-19”. There is no mention of this being a digital intervention, and it is likely that many readers will infer that that was a face-to-face intervention from the current title (even in the pandemic). I suggest the authors consider adding a reference to “digital”, “online” or similar in the title.

Simon Rice - Reviewer

Final Decision Letter:

Dear Dr Schleider,

We are pleased to inform you that your Article "A Randomized Trial of Online Single Session Interventions for Adolescent Depression during COVID-19", has now been accepted for publication in Nature Human Behaviour.

Please note that Nature Human Behaviour is a Transformative Journal (TJ). Authors whose manuscript was submitted on or after January 1st, 2021, may publish their research with us through the traditional subscription access route or make their paper immediately open access through payment of an article-processing charge (APC). Authors will not be required to make a final decision about access to their article until it has been accepted. IMPORTANT NOTE: Articles submitted before January 1st, 2021, are not eligible for Open Access publication. Find out more about Transformative Journals

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We look forward to publishing your paper.

With best regards,

Jamie

Dr Jamie Horder
Senior Editor
Nature Human Behaviour

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