Dear Dr Daros,

Thank you once again for your manuscript, entitled "Improvements in emotion regulation are associated with effective treatment of anxiety and depression in youth: A systematic review and meta-regression", and for your patience during the peer review process.

Your Article has now been evaluated by 3 referees at Nature Human Behaviour. You will see from their comments copied below that, although they find your work of considerable potential interest, the referees have raised quite substantial concerns. In light of these comments, we cannot accept the manuscript for publication in its current form, but we would be interested in considering a revised version if you are willing and able to fully address reviewer and editorial concerns.

In particular, we believe it will be important to rerun the meta-regression analysis taking into account the comments of Referee #2. Regarding Referee #1 concerns, we would not expect you to include non-English language papers in the review, and we believe that this meta-analysis does make a novel contribution compared to the 2010 predecessor. However, ideally you should include RCTs on interpersonal emotion regulation in the revised manuscript (updating your protocol accordingly).

All three referees also raise the issue that the causal direction of the association of ER and clinical improvement cannot be demonstrated using the current analysis. The revised manuscript should therefore clarify what can be concluded regarding causality, with a clear discussion of limitations, e.g. if it is not possible to run mediator/moderator analyses using this dataset, this should be explained and you should avoid any language which implies that ER is a mediator.
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.

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.

If you wish to submit a suitably revised manuscript we would hope to receive it within 6 months. We understand that the COVID-19 pandemic is causing significant disruptions which may prevent you from carrying out the additional work required for resubmission of your manuscript within this timeframe. If you are unable to submit your revised manuscript within 6 months, 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]

<strong>Note:</strong> 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.

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 the required revisions further.

Sincerely,
Jamie

Dr Jamie Horder
Senior Editor
Nature Human Behaviour

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REVIEWER COMMENTS:
Reviewer #1:  
Remarks to the Author:  
The "Improvement in Emotion Regulation are Associated with Effective Treatment of Anxiety and Depression in Youth..." reports the results of a meta-analytic review. In general, the manuscript is well-written and the meta-analysis is in line with reporting guidelines of meta-analyses. The analyses are based on a sufficiently large number of studies for most of the comparisons. Despite these positive features, there are a number of limitations, some of which cannot be addressed in a revision. The limitations are outlined below:

1. The study provides little new information beyond what is already known. A number of experimental studies as well as qualitative and quantitative reviews have already shown that changes in anxiety and depression are associated with emotion regulation strategies as defined by the process model (e.g., doi: 10.1002/da.21888 and doi: 10.1016/j.cpr.2009.11.004).

2. As noted by the authors, we have no way of knowing (the much more important question) whether changes in mood and anxiety are caused by ER, or whether changes in ER are caused by changes in mood and anxiety, or whether both ER and mood/anxiety are overlapping constructs. There is a lot of evidence to support the latter option because rumination is a defining feature of depression, and avoidance is a feature of anxiety. In other words, what the authors call "emotion regulation strategies" appears to simply be features of some mood and anxiety states. Not surprisingly, these features change as treatment effectively targets mood and anxiety as a whole.

3. The studies are limited to the so-called process model of emotion regulation, which focuses on intrapersonal strategies, such as rumination, avoidance and suppression as maladaptive strategies, and reappraisal, problem solving and acceptance as adaptive strategies. There are other models, some of which acknowledge the interpersonal aspects of emotion regulation (e.g., doi: 10.1146/annurev-psych-010419-050830 and doi: 10.1007/s10608-014-9620-1), which can be measured with specific scales. The authors even acknowledged this when writing: “In daily life, we implement ER skills to change the frequency, intensity, and duration of our negative emotional experiences (e.g., seek social support after a bad day) or at least temporarily dampen them (e.g., with the use of alcohol or other substances). ER skills are also used to increase or maintain positive emotional experiences (e.g., celebration of a milestone with others).” I would agree that such interpersonal emotion regulation strategies are probably much more central than the ones derived from a simple process-model of ER. Yet, the authors chose to limit their analyses to the same restrictive process-model.

4. Even if we stayed within the confines of the process model, it is not clear whether problem-solving and avoidance should be considered emotion regulation strategies. These are behaviors that are motivated by emotions. This gets us into an awkward implicit definition of emotion regulation: A strategy that is motivated (or even caused) by an emotion to regulate the same emotion.

5. It is highly problematic to limit the selection of studies to only those written in English. There is nothing specific about ER in people speaking English.

6. A thorough readthrough would be beneficial, as some typos were found. For example, on page 5 line 115 “95% of studies with adults samples found” should be “with adult samples.”

7. It would be helpful to understand a bit more how anxiety and depression are defined. On page 7, it is noted that studies with an outcome measure of depression, social anxiety, and/or generalized anxiety are included. Was there a cutoff applied? Why not including diagnoses such as panic disorder, agoraphobia, or specific phobia?

8. On page 7, please specify DSM-5 if this is the edition you are referring to

9. The sentence on page 10 line 246 could use rephrasing "First, any study with least one "high" risk
rating or ≥4 “some concerns” ratings automatically received a “high” overall rating as we wanted to apply a conservative rating and distribute the ratings more evenly for later sensitivity analyses.” This should be consistent with capitalizations for “high” and “Low” as well.

10. On page 18 line 456, expand upon this finding and provide some theories as to why this may be and suggestions for future studies: “Alternatively, reductions in rumination and suppression, but not avoidance, were most likely to be associated with reductions in depression and/or anxiety symptoms.”

Reviewer #3:
Remarks to the Author:
The authors report on a meta-analysis meant to explore how intervention effects on depression and anxiety go hand in hand with effects on emotion regulation skills. In general, the meta-analysis was done in a systematic way, with a thorough search for studies and an accurate description and reporting of the analyses. The authors used the PRISMA guidelines for reporting systematic reviews, and put relevant information in supplementary documents.

The major remark I have is that the way the authors explored whether effects on depression and anxiety and effects on emotion regulation skills are related is statistically not correct. More specifically, the authors used meta-regression analyses in which the observed effect sizes on depression/anxiety are regressed on the observed effect sizes on emotion regulation. The problem is that whereas the uncertainty about the observed effect sizes on depression/anxiety are accounted for (by taking into account the sampling variance), this is not true for the effect sizes for emotion regulation. The latter are indeed treated as if they are known. An appropriate way to analyse the data is to use a multivariate meta-analysis, in which the effect sizes on depression, anxiety and emotion regulation are considered as three different dependent variables. See e.g.,
Gieser, L. J. & Olkin, I. (2009). Stochastically dependent effect sizes. In H.Cooper, L. V. Hedges, & J. C. Valentine (Eds.), The handbook of research synthesis and meta-analysis (pp. 357-376). New York: The Russell Sage
Kalaian, H. A. & Raudenbush, S. W. (1996). A multivariate mixed linear model for meta-analysis. Psychological methods, 1, 227-235.

I am afraid that this kind of meta-analysis cannot be performed in CMA, the software that was used by the authors. It can however be done for instance using the metafor package in R. Redoing these analyses may require some work, but I guess it may not have large consequences for the text itself.

A second remark is that from the text, the theoretical framework is not crystal clear to me. The beginning of the sentence in line 55-58 (“Here, we examined how three indices of emotion regulation (ER) skills change during psychological treatments for symptoms of depression and anxiety in youth and young adults aged 14-24, and their evidence as a moderator of treatment outcome.”) as well as the subsequent paragraph seem to suggest that ER is considered as a mediator variable (the intervention affects the ER skills which in turn improve the symptoms of depression/anxiety), whereas the end of that sentence suggests that ER skills are a moderator (the effect of the intervention depends on the ER skills). None of these interpretations seem to fit well with line 131-133 (“The present systematic review aimed to investigate whether improvements in ER skills are associated with improvements in symptoms in the psychological treatment of anxiety and depression”).

A third, smaller remark is that the authors are not clear about the number of effect sizes per study
that were used for each of the meta-analyses. If for anxiety, depression of each of the ER-skills, maximally one effect size per study was observed, there is no problem. If there were for some studies multiple effect sizes, however, this induces dependence in the data that should be accounted for. I guess that if this was the case, the authors used the default procedure in CMA, this is using an average effect size per study. This procedure would be fine, but transparency is needed.

Details:
- Line 33 (and elsewhere in the manuscript): Hedges should be written with a capital letter (Larry Hedges is the name of the person who proposed this measure)
- Line 33 (and elsewhere) Because g-values, corresponding standard errors as well as regression weights can in principle be larger than zero, APA guidelines stipulate that for instance 0.39 should be written rather than .39.
- Line 37: “Results were robust to study and publication bias.” I would consider reformulating this: results do not give clear evidence that there is bias, but this is not the same as saying that the results are robust to publication bias.
- Line 214: were all papers or only a selection screened by two authors?
- Line 274-277: the authors argue that given the number of studies is large, $I^2$ is better suited than the Q-statistic. I see what they mean, but I do not like this formulation because both statistics have a different role: $I^2$ expresses how large the variation is, whereas Q is a test statistic, for testing whether the variation is statistically significant. Because they give different kinds of information, I would report both.
- Line 397: the fact that included studies not necessarily have a primary focus on depression/anxiety can explain why no publication bias is found, but not the finding of asymmetry in the direction of an underestimation of the effect.
- Line 407-409: It is not clear to me how multi-arms studies were dealt with.

Reviewer #4:
Remarks to the Author:
This manuscript presents a systematic review and meta-regression of the association between improvements in emotion regulation and reductions in adolescent anxiety and depression symptoms as a result of treatment interventions. It is a well conducted and clearly reported systematic review and meta-regression on a topic of great global significance - youth mental health. I commend the authors on this endeavour, and in particular, for the inclusion of young people with lived experience in shaping the review and interpretation of its findings. The discussion is noticeably enriched by the inclusion of young people's voice. The review findings have the potential to inform more efficient and effective transdiagnostic interventions for youth depression and anxiety through improving emotion regulation skills.

Below I provide some general/major and specific/minor comments for the authors' consideration, which I hope will help to further strengthen the paper and its contributions:

General comments:
1) Please provide a justification for the age range 14-24.
Did the authors examine differences in findings based on the age of young people? There are important developmental differences in emotion regulation, ability to report on ER and symptoms,
engagement in treatment, etc.

2) Page 13 "intervention controls" - it is unclear why there is a comparison of intervention controls in analyses comparing RCTs and non-RCTs (i.e. trials without controls) - can the authors please explain?

3) Page 19 "Results also indicated that reducing ineffective ER skills was even more important for depression versus anxiety symptom reduction." - reads like there is an assumption of mediation, which was not tested. Please reword.

4) Page 20 "Therefore, we carefully considered potential biases based on study selection compared to the broader literature." - The meaning of this is unclear - it sounds as if selecting RCTs over non-RCTs is a study selection bias (as if it is not a good approach) - please clarify.

5) Page 23 "The present meta-analysis relied almost entirely on data from self-report measures, which can be susceptible to recall bias" - this is an important point that warrants expansion. As young people start to feel better, they may be more likely to report more positively, i.e. both reduced symptoms and improved ER (reductions in ineffective ER strategies, increases in effective ER strategies, and/or reductions in emotion dysregulation). EMA methods may help reduce this bias - did any study use these methods?

6) Page 23 "One possibility not examined here is that these constructs exhibit reciprocal relationships that change dynamically over time with other additional variables, such as the person’s environment and conditioning playing a role in how one learns to regulate their emotions." - this is a very important point, and especially relevant to adolescents. The authors may wish to consider the following review which proposed using an emotion regulation framework to understand the role of temperament and family processes in risk for adolescent depressive disorders:
https://pubmed.ncbi.nlm.nih.gov/17265137/

Specific/minor comments:

1) Page 12 "88 RCT (N=11,652) studies." - please either position "studies" before the parentheses, or rewrite as "88 RCTs (N=11,652)"

2) There are typographical and grammatical errors scattered throughout the manuscript - please check thoroughly and correct as appropriate. Some examples include:
-Page 13 "A summary of study characteristics for RCTs and non-RCTs are..." should be "A summary of study characteristics for RCTs and non-RCTs is"
-Page 18 "problems-solving" - remove 's'
-Page 19 "moreso"

3) Page 19 "An improvement in using effective ER skills may serve to store a balance between flexible use of less effective and more ineffective ER skills." - unclear, please reword

4) Page 21 "study and publication bias" - Did the authors mean 'study selection and publication bias'?

5) Page 21 "were held in all types of formats (e.g., group or individual)" - this phrase as presented in the sentence doesn't work, assuming the authors meant to say 'regardless of format'? Please clarify.

6) Page 23 "for example, mindfulness-based interventions more often assessed for analyses of improvements in effective skills (e.g., acceptance) whereas acceptance-based and cognitive training interventions more often assessed for analyses of declines in ineffective skills (e.g., rumination)." - should say 'trials of...interventions' rather than '...interventions'. It is also redundant to have 'assessed for' and 'analyses of' - please remove the latter.
Dear Dr. Horder,

We thank you and the reviewers for comments on our initial submission, NATHUMBEHAV-201113375. We believe that these comments have led to an overall improvement in the quality and clarity of the paper for the purpose of resubmission. Below you will find responses to each comment and references to the associated changes within the manuscript. After incorporating the comments, we attempted to reduce the text as much as possible before resubmission.

RESPONSES TO EDITOR COMMENTS

Your Article has now been evaluated by 3 referees at Nature Human Behaviour. You will see from their comments copied below that, although they find your work of considerable potential interest, the referees have raised quite substantial concerns. In light of these comments, we cannot accept the manuscript for publication in its current form, but we would be interested in considering a revised version if you are willing and able to fully address reviewer and editorial concerns.

In particular, we believe it will be important to rerun the meta-regression analysis taking into account the comments of Referee #2. Regarding Referee #1 concerns, we would not expect you to include non-English language papers in the review, and we believe that this meta-analysis does make a novel contribution compared to the 2010 predecessor. However, ideally you should include RCTs on interpersonal emotion regulation in the revised manuscript (updating your protocol accordingly).

We appreciate these Reviewer comments and have prepared responses to all recommendations and suggestions. In response to Reviewer #2’s comments on the statistical methodology, we have substantially revised our analytic approach, now including a multilevel, multivariate meta-analysis as suggested and removing the previously included meta-regression. All main effects were the same, with only minor differences to our sensitivity analyses. As you will see in our response below, we agree that this approach represents the best course of action given the issue of covarying dependent effects. We have also met with our institutional biostatistical consultant who similarly endorsed this methodology. In response to Reviewer #1’s comments regarding interpersonal emotional regulation, we identified all established measures of interpersonal ER and skills. We confirmed that additional databased extraction was not necessary and then examined studies previously excluded on the basis of an inappropriate ER measure. After reviewing more than 1100 articles, we did not find any RCTs that featured a validated assessment of interpersonal ER, highlighting this important gap in the literature. In the Supplementary Information, we now qualitatively extract results from 11 studies that incorporated measures of “social support” which are not established measures of interpersonal ER but share content or variance with these measures and may be of interest to some readers. However, we did not quantitively analyze these findings as they were not among those identified a priori, and given the conceptual issues associated with using coping scales given that they do not necessarily tap regulatory skills with respect to one’s emotional goals and motivations. We suggest that the quantitative synthesis be completed in future work once more...
interventions have incorporated a breadth of interpersonal ER measures. This is more extensively discussed below, but we believe these responses represent an appropriate course of action and transparent response, that lays out the conceptual issues relevant in this domain, the rationale for our response, and the evidence that exists for non-included but conceptually related behaviors.

All three referees also raise the issue that the causal direction of the association of ER and clinical improvement cannot be demonstrated using the current analysis. The revised manuscript should therefore clarify what can be concluded regarding causality, with a clear discussion of limitations, e.g. if it is not possible to run mediator/moderator analyses using this dataset, this should be explained and you should avoid any language which implies that ER is a mediator.

With our new methodology we have removed all reference to “meta-regression” and therefore have made significant revisions to the manuscript to avoid any suggestion of causality or causal direction. We clearly describe the limitations of our analyses and solely refer to our associations as such and not using the terms “mediation” (or “moderation”).

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 are grateful for the Reviewer’s detailed review and excellent suggestions. The only request made that we felt unable to address was the inclusion of empirical research not published in the English language; we appreciated the feedback that this specific revision was not critical to incorporate in our response and revision.

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.

Our revised manuscript has now been carefully checked against the editorial formatting document and we have appropriately formatted our Supplementary Information, which will hopefully expedite the consideration of our manuscript.

If you wish to submit a suitably revised manuscript, we would hope to receive it within 6 months. We understand that the COVID-19 pandemic is causing significant disruptions which may prevent you from carrying out the additional work required for resubmission of your manuscript within this timeframe. If you are unable to submit your revised manuscript within 6 months, please let us know. We will be happy to extend the submission date to enable you to complete your work on the revision.
We sincerely thank the handling editor and the reviewers for their comments. We believe that we have successfully revised the paper according to the comments of the reviewers. We have appreciated the timely and detailed feedback we received as part of this review process and believe our manuscript has been significantly strengthened as a result. Please do not hesitate to contact me if you require any further information at all.

Sincerely, on behalf of all the authors

ARD

RESPONSES TO REVIEWER COMMENTS

Reviewer #1:

Remarks to the Author:
The “Improvement in Emotion Regulation are Associated with Effective Treatment of Anxiety and Depression in Youth…” reports the results of a meta-analytic review. In general, the manuscript is well-written and the meta-analysis is in line with reporting guidelines of meta-analyses. The analyses are based on a sufficiently large number of studies for most of the comparisons. Despite these positive features, there are a number of limitations, some of which cannot be addressed in a revision. The limitations are outlined below:

1. The study provides little new information beyond what is already known. A number of experimental studies as well as qualitative and quantitative reviews have already shown that changes in anxiety and depression are associated with emotion regulation strategies as defined by the process model (e.g., doi: 10.1002/da.21888 and doi: 10.1016/j.cpr.2009.11.004).

Response: We thank the reviewer for this feedback and for highlighting these useful references, which largely related to examining how symptoms of anxiety and depression are associated with different emotion regulation strategies or skills in child, adolescent, and adult samples (Hofmann et al., 2012; Aldao et al., 2010). While the results of both reviews suggest that treatments for anxiety and depression can have impacts on emotion regulation strategies, they did not systematically or quantitatively examine this effect across key design features, highlighting the potential relationship with reference to a few individual studies in their discussions. For example, while Aldao et al. (2010; 25 studies, N=10,408 total participants) did investigate longitudinal relationships between depression or anxiety symptoms and emotion regulation strategies, they did not examine these relationships across important study features such as treatment characteristics. Similarly, while Hofmann et al. (2012) discusses the potential impact of psychological treatments on changes in emotion regulation strategies (p.413-414), they only reviewed a handful of studies and did not include a quantitative synthesis of findings.
We believe that this review extends this prior literature in several important ways. First, previous meta-analytic reviews examining the impact of treatments on emotion regulation have relied on strict categorical diagnostic criteria for depression and anxiety, focused on one or a few diagnostic conditions, and/or focused on one or a few specific emotion regulation skills. These design features resulted in the exclusion of numerous high-quality studies that would permit not only the quantification of these effects but also their variability across important study design features. Indeed, this review included 88 studies and 11,652 participants, a substantially increased number from these previous reviews. Second, few of these reviews have focused specifically on young persons or young adults, included young people with lived experience in their work. Third, we examined more specific relationships between the types of emotion regulation skills that are associated with treatment response which has been a topic of interest by researchers in this field (e.g., Radkowsky et al., 2014 [https://doi.org/10.1037/a0035828]; Sauer-Zavala et al., in press [https://doi.org/10.1016/j.beth.2021.03.001]). No previous review has included this form of nuanced analysis. The current investigation had a specific focus on youth and young adults and incorporated their voice in the design and implementation of this work. Finally, the revised manuscript also includes a multilevel multivariate meta-analysis, which we believe is unique from a statistical perspective as well.

2. As noted by the authors, we have no way of knowing (the much more important question) whether changes in mood and anxiety are caused by ER, or whether changes in ER are caused by changes in mood and anxiety, or whether both ER and mood/anxiety are overlapping constructs. There is a lot of evidence to support the latter option because rumination is a defining feature of depression, and avoidance is a feature of anxiety. In other words, what the authors call “emotion regulation strategies” appears to simply be features of some mood and anxiety states. Not surprisingly, these features change as treatment effectively targets mood and anxiety as a whole.

Response: We appreciate this concern raised by the reviewer. It is true that we could not examine whether changes in ER skills are caused by changes in depression/anxiety symptoms or vice versa. In accordance with another Reviewer’s suggestions, we made changes to the statistical approach in our revised manuscript, removing meta-regression analyses, which we believe has simplified our approach as well as avoided potential suggestions that we are able to appropriately examine mediation with the data extracted. We reviewed our Introduction and Discussion sections to ensure that our inability to make causal claims in the current investigation were highlighted. For example, we removed words such as “mediation” throughout the Introduction (p.3-6) and only suggested these techniques for future directions given limitations to the current investigation (p. 12-13, 18).

With regards to conceptual overlap, we agree with the reviewer and highlight the potential problems in the Discussion (p.18) noting how symptoms of depression and anxiety overlap with the definitions and measurement of certain ER skills. We also note how this may artificially inflate the correlations within the current findings. It is worth mentioning that our revised statistical methods (a multilevel multivariate meta-analysis) now also account for the covariance between each dependent variable (depression; anxiety; effective ER skills; ineffective ER skills; emotion dysregulation). In using this approach, we still
found that improvements in ER skills remained significantly associated with changes in depression and anxiety, though we recognize this still does not completely eliminate the issue raised by the reviewer.

3. The studies are limited to the so-called process model of emotion regulation, which focuses on intrapersonal strategies, such as rumination, avoidance and suppression as maladaptive strategies, and reappraisal, problem solving and acceptance as adaptive strategies. There are other models, some of which acknowledge the interpersonal aspects of emotion regulation (e.g., doi: 10.1146/annurev-psych-010419-050830 and doi: 10.1007/s10608-014-9620-1), which can be measured with specific scales. The authors even acknowledged this when writing: “In daily life, we implement ER skills to change the frequency, intensity, and duration of our negative emotional experiences (e.g., seek social support after a bad day) or at least temporarily dampen them (e.g., with the use of alcohol or other substances). ER skills are also used to increase or maintain positive emotional experiences (e.g., celebration of a milestone with others).” I would agree that such interpersonal emotion regulation strategies are probably much more central than the ones derived from a simple process-model of ER. Yet, the authors chose to limit their analyses to the same restrictive process-model.

Response: We thank the reviewer for this comment and share their view of the importance of interpersonal emotion regulation. Despite our original focus on intrapersonal ER, the search strategy we utilized included emotional regulation broadly construed; indeed, following consultation with the librarian, it was determined that an additional search was not required to identify records with a focus on interpersonal ER.

We first reviewed the papers cited by the reviewer and other seminal publications to identify measures of interpersonal ER. We determined that the following measures are currently recognized measures of interpersonal ER: (1) Emotion Regulation of Others and Self Scale (Niven et al., 2011); (2) Interpersonal ER Questionnaire (Hofmann et al., 2016). (3) Difficulties in Interpersonal Regulation of Emotions (Dixon-Gordon et al., 2018). (4) Interpersonal Regulation Questionnaire (Williams et al., 2018). (5) Interpersonal Emotion Management Scale (Little et al., 2012). (6) Interpersonal Regulation Interaction Scale (Swerdlow & Johnson, in press). Notably, these measures are relatively new (c. 2011 or later) compared to some of more common intrapersonal ER measures (e.g., CERQ; ERQ which were published in the early 2000s). We also identified several specific interpersonal ER skills referenced by these scales, some of which included reference to “social support” which is commonly assessed by coping measures. During our review of these measures, we also encountered a larger discussion raised by (Swerdlow & Johnson, in press; https://doi.org/10.1037/emo0000927) regarding coping measures, which were not necessarily developed with respondents’ emotion goals or emotion regulation skills in mind. One important way that interpersonal ER diverges from the more long-standing coping literature is that the interpersonal ER focuses on the goals between interactants and the motivations to regulate their own or another’s emotions. As discussed by Swerdlow and Johnson (in press), although coping measures may support the assessment of social support with a partial goal-directed manner, such measures often adopt a broader focus on adjustment to stress (e.g., encompassing both behaviors and interactions that are not
aimed at emotion regulation). We therefore did not include these measures as interpersonal ER measures but planned to identify these measures during our review to inform our discussion (e.g., regarding whether such coping measures that assess content related to interpersonal ER were amongst those excluded, and might demonstrate similar or discrepancy results).

We then conducted a review of the 1089 articles that were excluded at the full-text level based on lacking an appropriate ER measure review (see PRISMA diagram, Figure 1, full-text screening portion), to identify records included these recognized measures. These articles met almost all criteria for inclusion except our criterion related to ER measures. We further reviewed all 143 articles that were included for the same purpose. Unfortunately, there were no treatment studies identified that included any of these 6 gold-standard measures on interpersonal ER noted above. Measures identified were characterized by a focus on interpersonal problems, interpersonal conflict, and actual/perceived social support, which were distinct from the interpersonal ER construct described. We also found 2 studies that had previously been excluded yet contained social support measures that could broadly relate to interpersonal ER. Further, from the 143 articles we already included in our meta-analysis, we found 9 studies with a similar focus on social support using coping measures. Given the sparse number of studies and limited diversity of interpersonal ER skills located, we chose to report our findings qualitatively in the Supplementary Materials section of this paper to inform future research. Our hope is that future research could potentially answer these questions given additional time to conceptually define and gather evidence on additional interpersonal ER measures over treatment.

In conclusion, we significantly revised the manuscript to broaden our focus to include both intrapersonal and interpersonal ER. In the Introduction, we more clearly define and differentiate interpersonal and intrapersonal ER and refer readers to updated theoretical accounts of interpersonal ER (p.3-6). In addition, we integrated the above procedures into the systematic review with reference to the Supplementary Information regarding measures and definitions. In the Results section, we acknowledge that although we attempted to locate articles that examined this construct, there were no eligible articles including measures of interpersonal ER at this time (p.7). We later describe this as a future direction in the Discussion (p.18-19). We note that interpersonal ER is a newer topic of interest with fewer measures for its assessment. Further, we updated the Methods section to note and reference the Supplementary Information regarding interpersonal ER (p.20-21).

4. Even if we stayed within the confines of the process model, it is not clear whether problem-solving and avoidance should be considered emotion regulation strategies. These are behaviors that are motivated by emotions. This gets us into an awkward implicit definition of emotion regulation: A strategy that is motivated (or even caused) by an emotion to regulate the same emotion.

We acknowledge that there is some debate over what is considered an emotion regulation strategy (see Naragon-Gainey et al., 2017, which examined the common structure of emotion regulation strategies; http://dx.doi.org/10.1037/bul0000093). Others argue that the definition has become too broad (Berking & Wupperman, 2012). We grounded our approach in the “process model” of ER, which suggests that
strategies can be attempted at any stage of the emotion generation process (e.g., situation selection, situation modification, attentional deployment, cognitive change, and response modulation; Gross, 2015) to modulate an emotion or potential occurrence of emotion. Strategies can have both cognitive and behavioral components. In this way, avoidance can be considered an ER strategy because it can be enacted at several stages: physical avoidance can be used to avoid a situation entirely or one can use experiential avoidance to avoid attending (e.g., closing one’s eyes, distracting oneself) to a situation that cannot be physically avoided. Similarly, problem-solving is often enacted once a situation occurs and involves utilizing cognitive resources (at the cognitive change stage) to brainstorm potential solutions in addition to enacting them (see D’Zurilla, Nezu, & Maydeu-Olivares, 2004). Problem-solving involves engaging with the emotional situation (compared to suppression which would involve disengaging) and can also be enacted as a response modulation strategy (e.g., what can I do now that this emotional situation has come and gone). We acknowledge that the process model has its limitations, including that it provides a stage model for strategies to exist without explicitly defining all of the possible strategies in those stages. Nevertheless, we note that the measures that we have used to conceptualize and measure avoidance and problem-solving have been used in many previous seminal meta-analyses (e.g., Aldao et al., 2010; Compas et al., 2017; Prefit et al., 2019; Schafer et al., 2017; Sloan et al., 2017) and conceptual reviews regarding the structure of common emotion regulation strategies (Naragon-Gainey et al., 2017). We have made changes to the Introduction (p.3) to communicate the conceptualization of ER strategies (or skills) more clearly in this manuscript. Further, we noted that there are critical discussions revolving around the nature of defining ER strategies and whether definitions have become too broad (see p.18-19), citing the Naragon-Gainey et al., 2017 manuscript, which provides an excellent discussion on these issues raised by the reviewer.

5. It is highly problematic to limit the selection of studies to only those written in English. There is nothing specific about ER in people speaking English.

Response: We thank the reviewer for raising this concern. Unfortunately, it was not feasible for our team to review non-English databases and journals; indeed, access to these databases and to personnel able to screen records and extract the associated statistics was beyond the means of the current review. We note that the studies themselves were not limited to people who spoke English (i.e., 45 out of 90, or 50% of RCTs were from countries where English was not a primary language) and as a result we have a large sample of countries represented despite the restriction to publications written in English. Nevertheless, we added this information to the Results (p.7) and highlight this limitation of the current review in the Discussion (p.17-18), and the value of further cross-cultural knowledge syntheses in this area. Country of origin for each study is included in Supplementary Tables 1 (RCTs) and 2 (non-RCTs).

6. A thorough readthrough would be beneficial, as some typos were found. For example, on page 5 line 115 “95% of studies with adults samples found” should be “with adult samples.”
Response: This specific typo was corrected, and several independent readers have carefully reviewed the text to identify and resolve further typographical errors.

7. It would be helpful to understand a bit more how anxiety and depression are defined. On page 7, it is noted that studies with an outcome measure of depression, social anxiety, and/or generalized anxiety are included. Was there a cutoff applied? Why not including diagnoses such as panic disorder, agoraphobia, or specific phobia?

Response: We appreciate this opportunity to be clearer in our description of anxiety and depression. We defined depression and anxiety as dimensional constructs, rather than categorical diagnoses, that were assessed by validated self-report measures over time. This dimensional system was used because categorical diagnoses are not always re-assessed after treatment (see updated text in the Introduction, p.6 to outline more clearly our approach, with specific examples of measures). We did not incorporate a cut-off score because we wanted to be as inclusive as possible and examine a large range of intervention effects. Notably, we did not specifically exclude panic disorder, agoraphobia, or specific phobia. Our goal was to identify measures of social and/or generalized anxiety so that we could reduce the heterogeneity of measures and maximize the number of studies that included general measures of depression and anxiety but also emotion regulation measures (which was often a tertiary or supplemental outcome). We have revised our Method section on p.20-21 to expand the details of our methodology in including/excluding potential studies. We also carefully documented each anxiety and depression outcome measure in Supplementary Table 1 (RCTs) and 2 (non-RCTs) for those interested.

Though not a specific request, as a general response to these revisions, we are also providing our extracted dataset online (via OSF) including a list of studies that were considered for data extraction and their reasons for exclusion.

8. On page 7, please specify DSM-5 if this is the edition you are referring to.

Response: We did use the DSM-5, and this has now been specified in the Methods section as suggested.

9. The sentence on page 10 line 246 could use rephrasing “First, any study with least one “high” risk rating or ≥4 “some concerns” ratings automatically received a “high” overall rating as we wanted to apply a conservative rating and distribute the ratings more evenly for later sensitivity analyses.” This should be consistent with capitalizations for “high” and “Low” as well.

Response: We have significantly revised this sentence to present this statement more clearly with appropriate capitalizations (p.23). “First, any study with least one “High” risk rating or ≥4 “Some Concerns” ratings automatically received a “High” overall rating to improve the conservative nature of ROB ratings and distribute them more evenly for later sensitivity analyses. Second, low risk studies had either all “Low” risk ratings across the five domains or only one “Some Concerns” rating.”
10. On page 18 line 456, expand upon this finding and provide some theories as to why this may be and suggestions for future studies: “Alternatively, reductions in rumination and suppression, but not avoidance, were most likely to be associated with reductions in depression and/or anxiety symptoms.”

Response: Given significant revisions to the methodology in the revised manuscript, the results now slightly differ and the original statement reference has now been deleted. In our revised manuscript, we found that reductions in suppression and avoidance were not consistently associated with reductions in depression and anxiety symptoms (p.14) and have elaborated on potential reasons for this finding. Specifically, we added that the methodology in the current paper is different because it quantitatively analyses the association between symptoms and skills over treatment whereas previous reviews had not looked at skills individually or had not quantitatively examined the association. We hope that this provides suggestions for future directions.

Reviewer #2:
Remarks to the Author:
The authors report on a meta-analysis meant to explore how intervention effects on depression and anxiety go hand in hand with effects on emotion regulation skills. In general, the meta-analysis was done in a systematic way, with a thorough search for studies and an accurate description and reporting of the analyses. The authors used the PRISMA guidelines for reporting systematic reviews, and put relevant information in supplementary documents.

The major remark I have is that the way the authors explored whether effects on depression and anxiety and effects on emotion regulation skills are related is statistically not correct. More specifically, the authors used meta-regression analyses in which the observed effect sizes on depression/anxiety are regressed on the observed effect sizes on emotion regulation. The problem is that whereas the uncertainty about the observed effect sizes on depression/anxiety are accounted for (by taking into account the sampling variance), this is not true for the effect sizes for emotion regulation. The latter are indeed treated as if they are known. An appropriate way to analyse the data is to use a multivariate meta-analysis, in which the effect sizes on depression, anxiety and emotion regulation are considered as three different dependent variables. I am afraid that this kind of meta-analysis cannot be performed in CMA, the software that was used by the authors. It can however be done for instance using the metafor package in R. Redoing these analyses may require some work, but I guess it may not have large consequences for the text itself.

See e.g., Gleser, L. J. & Olkin, I. (2009). Stochastically dependent effect sizes. In H. Cooper, L. V. Hedges, & J. C. Valentine (Eds.), The handbook of research synthesis and meta-analysis (pp. 357-
Response: We sincerely appreciate this reviewer’s important feedback on how we conducted our analyses and their suggestions on how to revise this. We completely agree that our approach requires us to consider the dependent nature of our main variables and that a multivariate meta-analytic approach is more appropriate in our case. Accordingly, we used the “metafor” package in R to conduct a multilevel multivariate meta-analysis using all five outcome variables extracted from our included from our studies. It was necessary to add a multilevel approach because we needed to account for multiple treatment arms and sometimes multiple measures of an outcome variable, with one effect size per study. Using the multilevel framework allowed us to specify one effect size for each outcome (e.g., depression, anxiety, ineffective ER skill, effective ER skill, emotion dysregulation) per study. Moreover, by simultaneously entering all five outcome variables, we controlled for the shared sampling variance amongst all outcome variables. Corresponding to these changes, we removed the meta-regression from the revised paper and all references to it. The Method section was significantly revised to reflect these changes (p.24-26) along with the Results section (p.8-12). Overall results were largely consistent with our previous draft, with some changes because of how we ran the new sensitivity analyses (see revised Tables 2-4, which replace and extend the original versions).

In addition, to examine associations between changes in depression/anxiety symptoms and ER skills, we utilized the Spearman’s rho values produced by the meta-analytic output in the “metafor” package. These Spearman’s rho values can speak to the association between changes in emotion regulation (as defined in three ways) and changes in depression/anxiety over treatment.

We also decided to upload our extracted dataset online (via OSF), as there may be multiple ways to tackle the analytic approach for this work and we wish to support an open science approach.

A second remark is that from the text, the theoretical framework is not crystal clear to me. The beginning of the sentence in line 55-58 (“Here, we examined how three indices of emotion regulation (ER) skills change during psychological treatments for symptoms of depression and anxiety in youth and young adults aged 14-24, and their evidence as a moderator of treatment outcome.”) as well as the subsequent paragraph seem to suggest that ER is considered as a mediator variable (the intervention affects the ER skills which in turn improve the symptoms of depression/anxiety), whereas the end of that sentence suggests that ER skills are a moderator (the effect of the intervention depends on the ER skills). None of these interpretations seem to fit well with line 131-133 (“The present systematic review aimed to investigate whether improvements in ER skills are associated with improvements in symptoms in the psychological treatment of anxiety and depression”).

Response: We agree that the framework lacked clarity in our original draft, which was in large part related to the analytic approach that we previous used. Taking into consideration the reviewer’s previous
comments above, we have significantly revised the analyses, and references to moderation and/or mediation have now been removed. We now ensure our discussions refer to the associations between symptom reductions and changes in emotion regulation skills and we focus on the resulting matrix of correlational results produced by the meta-analysis as discussed above. As a result, Table 3 has been replaced with an updated presentation of correlational analyses, including those related to our sensitivity analyses. We believe that this addresses the reviewer’s concerns regarding our approach to analyses and how we frame and discuss the interpretations of the data presented in this synthesis.

A third, smaller remark is that the authors are not clear about the number of effect sizes per study that were used for each of the meta-analyses. If for anxiety, depression of each of the ER-skills, maximally one effect size per study was observed, there is no problem. If there were for some studies multiple effect sizes, however, this induces dependence in the data that should be accounted for. I guess that if this was the case, the authors used the default procedure in CMA, this is using an average effect size per study. This procedure would be fine, but transparency is needed.

Response: We agree that providing the number of effect sizes per study is an important issue that was not properly addressed in our first draft. In the revised draft, the use of metafor in R has allowed us to produce the number of unique studies (N) and number of effect sizes (k) used in each analysis. See updated Results section (p.8-12) and Tables 2-4, where we incorporated detailed reference to these values.

Details:
- Line 33 (and elsewhere in the manuscript): Hedges should be written with a capital letter (Larry Hedges is the name of the person who proposed this measure).

Response: We thank the reviewer for this helpful information and have adjusted this accordingly throughout.

- Line 33 (and elsewhere) Because g-values, corresponding standard errors as well as regression weights can in principle be larger than zero, APA guidelines stipulate that for instance 0.39 should be written rather than .39.

Response: We have adjusted this reporting accordingly throughout.

- Line 37: “Results were robust to study and publication bias.” I would consider reformulating this: results do not give clear evidence that there is bias, but this is not the same as saying that the results are robust to publication bias.

Response: We have adjusted the wording of this statement, which appeared a few times in the manuscript, as suggested. In the abstract, we changed the sentence to: “Sensitivity analyses were conducted wherein
study selection and publication bias were considered.” (p.2). In the Discussion section we now word a similar sentence as: “our findings remain unchanged even after considering potential study selection and publication bias.” (p.15).

- Line 214: were all papers or only a selection screened by two authors?
Response: We thank the reviewer for this observation and confirm that all papers were screened by two authors. We have updated the line to state “At the first stage, all titles and abstracts were screened for inclusion by two independent team members and conflicts were resolved by team consensus…” (p.22).

- Line 274-277: the authors argue that given the number of studies is large, I² is better suited than the Q-statistic. I see what they mean, but I do not like this formulation because both statistics have a different role: I² expresses how large the variation is, whereas Q is a test statistic, for testing whether the variation is statistically significant. Because they give different kinds of information, I would report both.
Response: We thank the reviewer for this important note on the distinction between the two measures. The revised text reports both indices. The Q and I² values for the main results are reported in text while the values for the sensitivity analyses are provided in a Supplementary Table 3. We also updated the Method section where we discuss heterogeneity (p.26) and support the inclusion of both indices.

- Line 397: the fact that included studies not necessarily have a primary focus on depression/anxiety can explain why no publication bias is found, but not the finding of asymmetry in the direction of an underestimation of the effect.
Response: We have removed this sentence in the revised manuscript.

- Line 407-409: It is not clear to me how multi-arms studies were dealt with.
Response: We now provide more detail in the Method section (p.24) regarding this specific concern. Specifically, we stated that if there were more than two arms, we used a multilevel data structure so that each study could only contribute one effect size per outcome (e.g., one for depression, one for anxiety, and so on…) to the meta-analytic findings, even if the study contained multiple treatment arms.

Reviewer #3:
Remarks to the Author:
This manuscript presents a systematic review and meta-regression of the association between improvements in emotion regulation and reductions in adolescent anxiety and depression symptoms as a result of treatment interventions. It is a well conducted and clearly reported systematic review and meta-regression on a topic of great global significance - youth mental health. I commend the authors on this endeavour, and in particular, for the inclusion of young people with lived experience in shaping the review and interpretation of its findings. The discussion is noticeably enriched by the inclusion of young people's voice. The review findings have the potential to inform more efficient and effective transdiagnostic interventions for youth depression and anxiety through improving emotion regulation skills. Below I provide some general/major and specific/minor comments for the authors' consideration, which I hope will help to further strengthen the paper and its contributions:

General comments:  
1) Please provide a justification for the age range 14-24. Did the authors examine differences in findings based on the age of young people? There are important developmental differences in emotion regulation, ability to report on ER and symptoms, engagement in treatment, etc.

Response: We thank the reviewer for this comment and suggestion. The justification for this age range came from multiple epidemiological studies indicating that depression and anxiety most commonly have their age of onset in adolescence, with more than 75% of cases having an onset before age 24. We more explicitly described our reasoning in the revised section of the Method section (p.20).

With regards to examining differences based on age, we appreciated this feedback and revised the manuscript such that we now have sensitivity analyses that incorporates age (see revised Tables 2 and 3). We assessed age in three groupings: 14-17.9, 18-21.9, and 22-24.9 which also corresponds well to developmental stages as well as education level (high school, college, and young adult samples). Briefly, we found that the findings were consistent (for the most part) when examining the first two age groups. Interestingly, treatment effects for depression and anxiety were not significant when we examined the third group (22-24.9), however effective ER skills and emotion dysregulation did have favorable, and significant, reductions. Symptom reductions were largely positively associated with improvements in ER skills across all three operationalizations of skills. These observations were incorporated into the Results (p.8-12) and Discussion section (p.12-15) where necessary.

2) Page 13 "intervention controls" - it is unclear why there is a comparison of intervention controls in analyses comparing RCTs and non-RCTs (i.e. trials without controls) - can the authors please explain?

Response: We thank the reviewer for this opportunity to clarify our rationale. We included this comparison to evaluate whether the study characteristics of the included RCTs were significantly different from the non-RCTs to support a supplementary analysis of the meta-analytic effects in non-RCT studies given the extent of differences. Although this result is not surprising (e.g., the non-RCTs had
significantly more single-arm studies [or no controls] and fewer active or inactive controls), we wanted to demonstrate the overall extent of the differences along with age, treatment length, mean age, sample size, etc. We have revised this section so that this justification is more clear (p.23).

3) Page 19 "Results also indicated that reducing ineffective ER skills was even more important for depression versus anxiety symptom reduction." - reads like there is an assumption of mediation, which was not tested. Please reword.

Response: We thank the reviewer for raising this concern. In response to another reviewer’s comments, we significantly revised our statistical approach, whereby we now present a multilevel multivariate meta-analysis with a simultaneous entry of all five outcome variables. This sentence was revised in accordance with slight differences in the new output of results (e.g., we removed all mention of mediation or moderation as we are not able to conduct such analyses with this data). This specific sentence was also removed. Moreover, we carefully reviewed our Discussion section (p.12-19) to that we did not infer effects of mediation and made sure that descriptions of effects are only made in reference to their effect size (e.g., small, medium, or large effect size). Additionally, we restated in our limitations that we were unable to consider such mediation analyses (p.18).

4) Page 20 "Therefore, we carefully considered potential biases based on study selection compared to the broader literature." - The meaning of this is unclear - it sounds as if selecting RCTs over non-RCTs is a study selection bias (as if it is not a good approach) - please clarify.

Response: This sentence was removed in the revised manuscript (p.22).

5) Page 23 "The present meta-analysis relied almost entirely on data from self-report measures, which can be susceptible to recall bias" - this is an important point that warrants expansion. As young people start to feel better, they may be more likely to report more positively, i.e. both reduced symptoms and improved ER (reductions in ineffective ER strategies, increases in effective ER strategies, and/or reductions in emotion dysregulation). EMA methods may help reduce this bias - did any study use these methods?

Response: We agree with this excellent comment. Notably, none of the treatment studies identified utilized EMA methods. In discussing limitations within the Discussion section, we discuss the potential value of more prospective and ecologically valid methods of ascertaining treatment outcome (p. 17).

6) Page 23 "One possibility not examined here is that these constructs exhibit reciprocal relationships that change dynamically over time with other additional variables, such as the person’s environment and conditioning playing a role in how one learns to regulate their emotions." - this is a very important point, and especially relevant to adolescents. The authors may wish to consider the following review which proposed using an emotion regulation framework to
understand the role of temperament and family processes in risk for adolescent depressive disorders: https://pubmed.ncbi.nlm.nih.gov/17265137/

Response: We thank the reviewer for this comment. We have extended our discussion by adding a new sentence highlighting the relevance to adolescents and young adults: “This may be particularly relevant for adolescents and young adults who rely on family members and caregivers for emotional support.” (p.17).

Specific/minor comments:
1) Page 12 "88 RCT (N=11,652) studies." - please either position "studies" before the parentheses, or rewrite as "88 RCTs (N=11,652)"

Response: We have corrected the statement as suggested. In fact, we needed to revise this as there are actually 90 RCTs (from 88 unique studies; 2 studies report one additional RCT); hence the sentence should read “90 RCTs (N=11,652)” for clarity.

2) There are typographical and grammatical errors scattered throughout the manuscript - please check thoroughly and correct as appropriate. Some examples include:
   -Page 13 "A summary of study characteristics for RCTs and non-RCTs are..." should be "A summary of study characteristics for RCTs and non-RCTs is"
   -Page 18 "problems-solving" - remove 's'
   -Page 19 "moreso"

Response: We thank the reviewer for these careful observations and have corrected these in the manuscript revision.

3) Page 19 "An improvement in using effective ER skills may serve to store a balance between flexible use of less effective and more ineffective ER skills." - unclear, please reword.

Response: We thank the reviewer for this suggestion and have revised this sentence.

4) Page 21 "study and publication bias" - Did the authors mean 'study selection and publication bias'?

Response: We have revised this sentence as suggested.

5) Page 21 "were held in all types of formats (e.g., group or individual)" - this phrase as presented in the sentence doesn't work, assuming the authors meant to say 'regardless of format'? Please clarify.
Response: We appreciate this feedback and have revised this sentence.

6) Page 23 "for example, mindfulness-based interventions more often assessed for analyses of improvements in effective skills (e.g., acceptance) whereas acceptance-based and cognitive training interventions more often assessed for analyses of declines in ineffective skills (e.g., rumination)." - should say 'trials of...interventions' rather than '...interventions'. It is also redundant to have 'assessed for' and 'analyses of' - please remove the latter.

Response: We have revised this sentence as suggested.
Please use the link below to submit your revised manuscript and related files:

[REDACTED]

<strong>Note:</strong> 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

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REVIEWER COMMENTS:

Reviewer #1:
Remarks to the Author:
The authors did a pretty good job addressing some of the reviewers' comments in the letter, but the revisions in the manuscript were minimal. I raised a number of issues and even recommended specific articles that were relevant. Although this was discussed at great length in the letter, it was not included in the revision (or only led to very minor changes). If the authors choose not to consider this in the revision, this should at least be justified.

I am (still) uncomfortable with the term "effective" and "ineffective" ER. What exactly does "effective" mean? The authors define "ineffective ER skills" as "skills involving disengagement from an emotional experience or stimulus..." and "effective ER" as "active engagement with an emotional experience or stimulus." Then why not call it that (e.g., engaging vs. disengaging ER skills")? Effective/ineffective means "to have/not have an effect." Suppression has been shown to be quite effective, for example. Chewing gum, on the other hand, is probably less effective for regulating emotions. Perhaps the authors mean "adaptive?" But this also depends on the context, as the authors correctly noted: "our two-factor grouping of ER skills has shortcomings in that it fails to consider the context in which those skills are used." I suggest that the author reconsider the terms "effective" and "ineffective."

Reviewer #3:
Remarks to the Author:
I appreciate the efforts that the authors have done, and the methods used now are definitely more appropriate.
Yet, I would like to see two more clarifications:
1. The authors remain vague about the approach used to do the multivariate analyses. They mention that they used a Spearman's correlation of .70 between depression and anxiety, but the text does not clarify why and how this correlation is used. It is also not clear to me why Spearman's correlation is used, and not Pearson's correlation. If this is because the authors do not want to make the assumption that variables are measured on an interval scale, they may also not willing to use standard meta-analytic techniques, that also assume interval-scales (and even normality). Further, it is not clear where the correlations between the other variables come from and what these values are.

2. The authors say that a multilevel approach was used because there were multiple effect sizes per study. They say "we ... utilized a multilevel data structure so that each study could only contribute one effect size per outcome to the meta-analytic findings, even if the study had multiple treatment arms". To me it is unclear what the authors did (and therefore whether it is correct): multilevel models are not used to obtain only one effect size per study (or per outcome within a study), but rather to keep the observed effect sizes as the dependent variable and to account for the dependencies between multiple effect sizes that come from the same study. I would like to see more information.

But in sum, I still have the impression that the paper is of good quality and can mean a valuable contribution to the existing literature.

Reviewer #4:
Remarks to the Author:
The authors should be commended for their extensive efforts to address substantive and detailed comments from 3 reviewers.
I appreciate their responses to my comments, which have largely addressed my comments. I have a few further comments:
1) Some findings from sensitivity analyses are worth discussing, even briefly. E.g. involving samples with mean ages between 14-17.9 and 22-24.9 (but not 18-21.9), and Acceptance/ER-based interventions.
2) Page 9 "but were opposite from expectations" and 'Opposite effects were found' - clarify that these were significant associations in the opposite direction to that anticipated - as currently written, it is ambiguous and could be read as suggesting non-significant associations.
3) Page 12 "Finally, reduced anxiety symptoms (p=0.87, N=6, p=.02), but not reduced depressive symptoms (p=0.64, N=9, p=.06), was significantly associated with reduced emotion dysregulation, but not depressive symptoms." - the last four words may have been repeated in error?

Author Rebuttal, first revision:
3 June 2021
Dear Dr. Horder,
We appreciate the timely review of our revised manuscript (ref # NATHUMBEHAV-201113375), entitled "A meta-analysis of emotional regulation outcomes in psychological interventions for youth with depression and anxiety". We have now reviewed the additional comments from each of the three reviewers and include detailed responses below. Thank you for your continued interest in our manuscript and for this opportunity to further strengthen our work.

Sincerely,

ARD

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RESPONSES TO REVIEWER COMMENTS:

Reviewer #1

1. The authors did a pretty good job addressing some of the reviewers' comments in the letter, but the revisions in the manuscript were minimal. I raised a number of issues and even recommended specific articles that were relevant. Although this was discussed at great length in the letter, it was not included in the revision (or only led to very minor changes). If the authors choose not to consider this in the revision, this should at least be justified.

Response: We thank the reviewer for this valuable direction. In our previous revision, we attempted to balance a fulsome response to all the previous comments with a consideration for the space limitations in the present outlet. For example, while we did not incorporate the full discussion included in the response letter within the main text, we did introduce interpersonal ER skills in our introduction and incorporated these skills in our review. In our current revision of the manuscript, we now incorporate all references recommended by the reviewer in the Introduction (p. 3-6), as well as several additional ones, as part of our conceptualization and framing of interpersonal ER skills as an underlying dimension within depression and anxiety and a treatment target. These issues are now expanded in the Introduction (p. 3-5) with greater discussion around specific interpersonal ER measures in the Supplementary Information section. "Indeed, many emotions happen in a social context and can be regulated through others as much as our own selves" [p.3] ... We even become willing to experience negative emotions for others in different interpersonal contexts (e.g., parenting, social relationships) to serve hedonic or prosocial benefits in the long-run" [p.3] ... Moreover, individual differences in interpersonal ER skills, such as becoming
dependent on others or social settings to regulate one’s own emotions (e.g., through excessive reassurance or advice seeking) have been shown to predict depressive and anxiety symptoms in adults. ... There is also great potential in examining changes in interpersonal ER skills during treatment, given their importance in maintaining depressive and anxiety symptoms.

In response to other comments raised by the reviewer in our first revision, we carefully reviewed our manuscript once again and have included additional sentences in the Introduction and Discussion to highlight some of the additional conceptual issues and limitations raised. In response to the limitation around content overlap we acknowledged: “More broadly, there is important discussion regarding the overlapping nature of depression and anxiety with certain ER skills (e.g., rumination and depression; avoidance and anxiety); this conceptual issue has been noted previously and may contribute to artificially inflated effects in the current synthesis. Moreover, there are critical discussions revolving around what constitutes an ER skill and whether definitions have become too broad. These issues can make it difficult to conclude whether changes in depression and anxiety are caused by changes in ER skills or the opposite, or whether they simply represent overlapping constructs.” (p.17-18).

As per our previous response letter, we have addressed and included more information in the manuscript regarding how anxiety and depression are defined, removed any suggestion of “mediation” or “moderation”, and more clearly presented how the current synthesis goes beyond previous work (e.g., Introduction, p.5-6).

2. I am (still) uncomfortable with the term "effective" and "ineffective" ER. What exactly does "effective" mean? The authors define "ineffective ER skills" as "skills involving disengagement from an emotional experience or stimulus." and "effective ER" as "active engagement with an emotional experience or stimulus." Then why not call it that (e.g., engaging vs. disengaging ER skills)? Effective/ineffective means "to have/not have an effect." Suppression has been shown to be quite effective, for example. Chewing gum, on the other hand, is probably less effective for regulating emotions. Perhaps the authors mean "adaptive?" But this also depends on the context, as the authors correctly noted: "our two-factor grouping of ER skills has shortcomings in that it fails to consider the context in which those skills are used." I suggest that the author reconsider the terms "effective" and "ineffective."

Response: We agree that the names we applied to the groupings of ER skills have shortcomings. In fact, we agree with the reviewer’s observation that the “effective” and “ineffective” labels imply an
outcome regarding effectiveness, much like the terms we were attempting to move away from (e.g., adaptive vs. maladaptive). We therefore agree that the use of “engagement” and “disengagement” ER skills may further strengthen the current study and now use the terms “engagement” and “disengagement” throughout the manuscript and Supplementary Information. This also allowed us to streamline minor aspects of the text in the Introduction and Discussion sections.

Reviewer #3

1. I appreciate the efforts that the authors have done, and the methods used now are definitely more appropriate. Yet, I would like to see two more clarifications: The authors remain vague about the approach used to do the multivariate analyses. They mention that they used a Spearman’s correlation of .70 between depression and anxiety, but the text does not clarify why and how this correlation is used. It is also not clear to me why Spearman’s correlation is used, and not Pearson’s correlation. If this is because the authors do not want to make the assumption that variables are measured on an interval scale, they may also not willing to use standard meta-analytic techniques, that also assume interval-scales (and even normality). Further, it is not clear where the correlations between the other variables come from and what these values are.

Response: We are grateful for the original suggestions by the reviewer that led to these methodological improvements. The reviewer raises another excellent point and we have now revised the manuscript to correct the ambiguity in our description of analyses and results.

With regards to the Spearman’s correlation of .70, we now clarify that this was part of the procedure in creating a covariance matrix between the outcome variables. We note that in a discussion of stochastically dependent effect sizes, Hedges (2019) argues that in the absence of prior knowledge of the covariance structure of the dependent effect sizes, a practical solution is to “estimate the standard weighted meta-analytic outcomes while using robust computations of the variances that consider the dependence of the effect-size estimates within studies”. Whenever working covariance matrices are used, Hedges (2019) argues that they be chosen based on some knowledge of the likely correlation among estimates in the population. Based on a previous study reporting across six waves of youth participants (Cole et al., 1998), the relationship between depression and anxiety symptoms was estimated at between .60 and .80, or .70 on average.
Relationships between ER skills and depressive or anxiety symptoms are lower, on average (e.g., < .56; Aldao et al., 2010), suggesting less content overlap, albeit still medium in terms of effect size. Thus, we tested chose a working correlation at the population level at Rho = .70 to acknowledge the highest degree of correlation between the outcomes to provide a better approximation to the covariance matrix than assuming independence of the outcomes altogether. To calculate the covariance matrix in the “metafor” package in R, we used a technique that utilizes the variance (i.e., not standard error) of each effect size outcome within each study that was imported into R after computation in Comprehensive Meta-Analysis 3.0 (see web resource by the author of the “metafor” package). This technique allows us to create an unstructured covariance matrix with the original variance estimates while assuming Rho = .70. We then tested different levels of Rho to ensure that the main findings would not change based on a lower or higher value of the assumed population-level relationship ( .50 and .90). This technique is also described on the web-resource. Thus, Spearman’s Rho is used largely more on a conceptual level to estimate the population-level correlation between depression and anxiety symptoms, and the smaller overlap between psychological symptoms and ER skills. We added further detail to the Methods section (p.25-26) to clarify these procedures and how this correlation was used within analyses.

With regards to the statistical output, the “metafor” package also produces Rho statistics rather than Pearson’s correlations to compute the associations between outcome variables (i.e., the relationships between depression or anxiety and ER skills). The package is intending to capture monotonic relationships between two variables more generally, and not just linear relationships (as detected by Pearson’s correlations). Thus, Spearman’s correlations are used to assess the overall degree of change in one variable as the other increases or decreases, so it can detect relationships that might otherwise be suppressed by Pearson’s correlations. Although Spearman correlations are appropriate for ordinal data, the effect size data in our analyses were continuous and were ranked-transformed by the “metafor” package before providing an output. We also added further detail regarding these associations to the Methods section (p.25-26). We hope these additions clarify the procedures more fully.

2. The authors say that a multilevel approach was used because there were multiple effect sizes per study. They say “we ... utilized a multilevel data structure so that each study could only contribute one effect size per outcome to the meta-analytic findings, even if the study had multiple treatment arms”. To me it is unclear what the authors did (and therefore whether it is correct): multilevel models are not used to obtain only one effect size per study (or per outcome within a study), but rather to keep the observed effect sizes as the dependent variable and to account for the
dependencies between multiple effect sizes that come from the same study. I would like to see more information. But in sum, I still have the impression that the paper is of good quality and can mean a valuable contribution to the existing literature.

Response: We agree that this sentence would benefit from revision to describe our statistical approach more clearly. The reviewer is correct that the multilevel framework was not chosen for the purpose of computing one effect size per dependent variable. The multilevel data structure simply refers to the way we set up our database, which we have now clarified in the text (p. 23-24). In addition, upon further reviewing the source documentation for methods used in this current synthesis, and current standards in the field, we realized that it is sufficient to refer to our approach as a multivariate meta-analysis (i.e., dropping the word "multilevel") as most meta-analyses rely on a multilevel structure (effect size within study) to pool results. Further, according to Harrer et al. (2021), multilevel meta-analysis would refer to a situation in which three-levels exist, which is not the case in the present manuscript. Therefore, we now refer to our statistical approach more simply as a "multivariate meta-analysis" throughout the manuscript to identify our approach more clearly.

Reviewer #4:

1. The authors should be commended for their extensive efforts to address substantive and detailed comments from 3 reviewers. I appreciate their responses to my comments, which have largely addressed my comments. I have a few further comments: 1) Some findings from sensitivity analyses are worth discussing, even briefly. E.g. involving samples with mean ages between 14-17.9 and 22-24.9 (but not 18-21.9), and Acceptance/ER-based interventions.

Response: We sincerely appreciate the original comments provided by the reviewer. We agree that sensitivity findings would benefit from further discussion, and we have actually briefly expanded discussion to all findings with significant relationships in the negative direction which was a previous oversight. In the Discussion section (p.14-15), we now highlight these findings and possible reasons for them. For example, we highlighted the potential impact of the considerable heterogeneity of studies that recruited college students upon the non-significant associations between symptom reduction and improvements in ER skills in the 18-21.9 group. This is supported by higher moderator (i.e., outcome) heterogeneity (see Supp. Table 3) in this age group compared to the two others. In addition, we agree that findings were somewhat underwhelming for trials that
incorporated Acceptance/ER-based interventions (we extended discussion to blended/online formats and shorter treatments for anxiety), even though we had expected these to be positive and significant with regards to the association between symptom reduction and ER skills improvement. It is possible that these relationships may require further research due to a smaller number of studies contributing to these analyses. Moreover, there appears to be a larger number of small samples and higher ROB concerns within these subgroupings of studies. These points are now incorporated into the Discussion section (p.14-15).

2. Page 9 "but were opposite from expectations" and 'Opposite effects were found' - clarify that these were significant associations in the opposite direction to that anticipated - as currently written, it is ambiguous and could be read as suggesting non-significant associations.

Response: Thank you for this suggestion! These were significant effects and opposite to the direction expected; we have clarified this in the text as recommended (p. 9).

3. Page 12 "Finally, reduced anxiety symptoms (ρ=0.87, N=6, p=.02), but not reduced depressive symptoms (ρ=0.64, N=9, p=.06), was significantly associated with reduced emotion dysregulation, but not depressive symptoms." - the last four words may have been repeated in error?

Response: This is indeed a mistake and we have deleted the last four words (p.12).

Decision Letter, second revision:
Our ref: NATHUMBEHAV-201113375B

21st June 2021

Dear Dr. Daros,

Thank you for submitting your revised manuscript "A meta-analysis of emotional regulation outcomes in psychological interventions for youth with depression and anxiety" (NATHUMBEHAV-201113375B). It has now been seen 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 in the next couple of days. 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 in response to the referee's final comments. You will need to make clarifications of the methods in response to both of the points raised. However, no new analysis is necessary.

Please do not hesitate to contact me if you have any questions.

Sincerely,
Jamie

Dr Jamie Horder
Senior Editor
Nature Human Behaviour

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Reviewer #3 (Remarks to the Author):

Thank you for the clarifications.
I am still not satisfied however.
Regarding my question on the 'multilevel' meta-analysis: indeed, although each meta-analysis can be considered as a multilevel analysis, but talking about multilevel analysis suggests that you have at least one additional level compared to a traditional random effects meta-analysis, so it is good that you dropped the word 'multilevel' at several places. I would however suggest also to drop again the sentence that you proposed to include at line 621-622 (of the document with track changes), because that sentence is inducing more confusion than clarity. Further, you should clarify how the effect sizes per (outcome x study) and the corresponding standard errors or variances are summarized (line 624-626).

Regarding the multivariate analysis:
In the multivariate meta-analyses as implemented in metafor, rho refers to Pearson’s correlation, not to Spearman’s correlation. Moreover, you also give advantages of using Spearman’s correlation compared to Pearson’s correlation, but I guess that also in the research that you mention to support your choice of a correlation of .70 Pearson’s correlation was used. It is also not clear to me what you mean by the sentence on line 656-658: “Although all effect size data were submitted as continuous variables, the “metafor” package rank-transformed these data before providing an output.” Maybe I did not completely understand what you did, but I think that this sentence can be dropped, and you can talk about correlations, rather than about Spearman’s correlations.

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** 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-201113375B
21st June 2021

Dear Dr. Daros,

Thank you for your patience as we’ve prepared the guidelines for final submission of your Nature Human Behaviour manuscript, "A meta-analysis of emotional regulation outcomes in psychological interventions for youth with depression and anxiety" (NATHUMBEHAV-201113375B). 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. Please also check and comment on any additional marked-up edits we have proposed within the text. 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 like to start working on your revised paper, with all of the requested files and forms, as soon as possible (preferably within two 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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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 meta-analysis of emotional regulation outcomes in psychological interventions for youth with depression and anxiety". 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 #3:
Remarks to the Author:
Thank you for the clarifications.
I am still not satisfied however.
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Author Rebuttal, second revision:
RESPONSE TO SECOND REVISION OF THE MANUSCRIPT

22 June 2021

Reviewer #3
1. Thank you for the clarifications. I am still not satisfied however. Regarding my question on the 'multilevel' meta-analysis: indeed, although each meta-analysis can be considered as a multilevel analysis, but talking about multilevel analysis suggests that you have at least one additional level compared to a traditional random effects meta-analysis, so it is good that you dropped the word 'multilevel' at several places. I would however suggest also to drop again the sentence that you proposed to include at line 621-622 (of the document with track changes), because that sentence is inducing more confusion than clarity. Further, you should clarify how the effect sizes per (outcome x study) and the corresponding standard errors or variances are summarized (line 624-626).

We appreciate these comments and have dropped the sentence to improve clarity as suggested. We also revised the second sentence highlighted to state that we first gathered all effect sizes per outcome when there were more than two treatment arms or more than one outcome of the same type. We then used outcome as an inner factor and study as the outer factor within the “metafor” package to produce only one outcome per study. The text now reads: “When more than one measure was used for a single outcome (e.g., for depression, anxiety, ER skills), or more than two interventions were compared (e.g., three-arm studies), we computed all effect sizes and standard errors and grouped them under each study using additional variables for treatment arm and specific measure. Later, in the meta-analysis we used outcome as the inner factor and study as the outer factor so that each study only contributed one effect size per outcome to the meta-analytic findings.”

2. Regarding the multivariate analysis: In the multivariate meta-analyses as implemented in metafor, rho refers to Pearson’s correlation, not to Spearman’s correlation. Moreover, you also give advantages of using Spearman’s correlation compared to Pearson’s correlation, but I guess that also in the research that you mention to support your choice of a correlation of .70 Pearson’s correlation was used. It is also not clear to me what you mean by the sentence on line 656-658: “Although all effect size data were submitted as continuous variables, the “metafor” package rank-transformed these data before providing an output.” Maybe I did not completely understand what you did, but I think that this sentence can be dropped, and you can talk about correlations, rather than about Spearman’s correlations.
We appreciate this additional comment. To fully clarify our understanding of these issues and the most appropriate reporting of outcomes, we consulted with the author of the metafor package, Dr. Wolfgang Viechtbauer, who is also an expert in meta-analysis. Dr. Viechtbauer clarified that the correlations produced by the package are estimated correlations between the random effects, which are assumed to follow a multivariate normal distribution. Thus, they are not Pearson correlations but are also not rank-order correlations and should not be described this way. We have now corrected our terminology and interpretation in the manuscript within the Methods section. In addition, Dr. Viechtbauer stated that estimated correlations are not evaluated using conventional Pearson or Spearman tests for significance given that they are distributed on a multivariate normal distribution; therefore, we removed the p-values and significance testing in our revised draft (Tables 3 and 4) and associated text to focus simply on the magnitude and direction of effects. Moreover, we remove the “Rho” word and define the correlation more precisely where appropriate (e.g., Table 3 and 4; in the Methods section). In the Results and Discussion section, we therefore remove reference to “significant” associations and discuss the associations between symptom reduction and improved ER skills more generally in terms of their magnitude and direction.

**Final Decision Letter:**

Dear Dr Daros,

We are pleased to inform you that your Article "A meta-analysis of emotional regulation outcomes in psychological interventions for youth with depression and anxiety", has now been accepted for publication in Nature Human Behaviour.

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With best regards,

Jamie

Dr Jamie Horder
Senior Editor
Nature Human Behaviour

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