

Peer Review Information

Journal: Nature Human Behaviour

Manuscript Title: A meta-analysis on the affect regulation function of real-time self-injurious thoughts and behaviors

Corresponding author name(s): Kevin S. Kuehn

Reviewer Comments & Decisions:

Decision Letter, initial version:

25th May 2021

Dear Mr Kuehn,

Thank you once again for your manuscript, entitled "Testing the affect regulation hypothesis of self-injurious thoughts and behaviors in daily life: A systematic review and meta-analysis", and for your patience during the peer review process.

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

We hope you will find the referees' comments useful as you decide how to proceed. If you wish to submit a substantially revised manuscript, please bear in mind that we will be reluctant to approach the referees again in the absence of major revisions. 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.

In your revision, please carefully evaluate and address all reviewer concerns. We ask you to specifically focus on the technical concerns of Reviewer 1.

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 3 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]

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

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,

Samantha Antusch
Editor
Nature Human Behaviour

Reviewer expertise:

Reviewer #1: meta-analysis; (non-suicidal) self-injurious thoughts and behaviours

Reviewer #2: (non-suicidal) self-injurious thoughts and behaviours

Reviewer #3: meta-analysis

REVIEWER COMMENTS:

Reviewer #1:

Remarks to the Author:

Thank you for inviting me to review this manuscript, which is well written and focuses on an essential mental health topic. In this systematic review and meta-analysis, the authors aim to evaluate the affect regulation hypothesis of Self-injurious Thoughts and Behaviors (i.e., SITBs, including non-suicidal self-injurious thoughts, non-suicidal self-injury, and suicidal ideation, are negatively reinforced by momentary negative affect) using 24 unique intensive longitudinal datasets (n=1,684). I commend the authors for undertaking the present study, which has substantial potential to inform the field. Consistent with the affect regulation hypothesis, results suggest increased negative affect before SITBs and decreased negative affect following SITBs. Considerable heterogeneity between studies was observed, but there was limited evidence for the moderation of a range of methodological variables (including the number of prompts per day which is remarkable because this suggests that effects are similar when measured across different time intervals). I have noted several issues/suggestions that the authors will hopefully find helpful.

- A fundamental concern with the current manuscript that needs to be addressed is that the authors did not model the relationship between negative affect and SITBs to derive effects (e.g., using multilevel modeling), but calculated difference scores that conflate within- and between-person differences. Antecedent models subtract the mean negative affect across all participants (rather than for each individual separately) for each non-SITB report from the mean negative affect before all SITB observations. Similarly, consequence models seem to ignore the multilevel structure of the data (observations are nested within individuals) by focusing on the difference in negative affect during and after a SITB for the entire sample. I would strongly encourage the authors to model the temporal relationship between negative affect and SITBs (as they have the data available to do these analyses and then pool effects) using multilevel vector autoregressive models. I believe this would make this paper considerably stronger.

- Can the authors please explain why the mean age of included data sets 24.85 (line 251) differs from the mean age reported later in the manuscript (line 340).

- Please also include figures with effect sizes in the manuscript for NSSI thoughts. In addition, publication bias and sensitivity analyses also need to be conducted for this outcome.

- The methods to assess publication bias (Mathur & VanderWeele, 2020) should be more clearly explained (11400-425).

- The statements "only those that are not affirmative are presented in Table 5", "Under these extreme scenarios", "These plots suggest that the effect sizes for non-affirmative and affirmative studies are relatively similar and that the effect sizes and standard errors are correlated, which indicates that these results may be robust to publication bias." were unclear to me. Looking at Figure 4, effect sizes on the x-axis differ substantially, no?

- Please provide more information about how to interpret Fig 4 (the footnote is not clear to me).

- Does Table 5 present a scenario where a 200-increase in publication bias is assumed in the worst-case scenario? Please clarify.

- It should be mentioned that the authors report findings that are not always in line with the results

reported in original studies (in which lagged relationships are modeled). For instance, Houben and colleagues (2017) found that the occurrence of NSSI predicted an increase of negative affect in lagged analyses. Similar findings were observed for Koenig et al. (2020), but a negative effect is reported for this dataset (Santagelo et al., 2017). Remarkably, however, a negative effect (indicating a reduction of NA) is found for both studies with the present methodology. Similarly, while Kiekens and colleagues observed a positive prospective relationship between negative affect and NSSI behavior, the authors report the opposite effect here (although non-significant). Hence, please remove the statement (line 433) that 'Kiekens et al. (2020) was the only study to report reduced negative affect prior to NSSI behavior.'

- Relatedly, the authors report that Kiekens and colleagues (2020) found that negative affect predicts NSSI thoughts but not behavior. Please note that this study observed that negative affect prospectively predicted NSSI behavior. However, this was no longer the case when accounting for the lagged effect of NSSI thoughts. This study also used the wording 'since the last beep' to assess NSSI behaviors (table 1). The issue of ideation-to-action was briefly discussed in the discussion for suicidal behaviors, but it would be good also to make this point for NSSI behaviors.

- It should be made clear that lagged/concurrent in table 1 refers to the wording of items and not the model strategy that was used in the studies.

- The section "Although some datasets queried lagged associations between current mood (t ; e.g. "Right now, I feel...") and SITBs experienced since the last assessment point ($t-1$; "Since the last assessment"), even with the inconsistent prompts, we felt that variability in affect from either $t-1$ to $t+1$ (observation prior to SITB to report post SITB), or between t and $t+1$ (timepoint at which SITB was reported to report following SITB), captured post-SITB fluctuations" is not entirely clear to me. Why are items using 'since the last assessment' considered inconsistent prompts? If the outcome is behavior, is it not appropriate to assess this retrospectively? Can the authors explain why the difference between both modeling strategies leads to such different results (Sfigure1)? For this reason, I think it is really important to model the relationship between NA and SITBs (which would allow the investigation of 1-2 lags to investigate effects over time).

- How do the authors justify analyzing studies in a similar way that assessed thoughts 'in the moment' and retrospectively? Even though I feel relationships should be modeled, would it be not more appropriate to analyze studies that used retrospective wording between t and $t-1$ and concurrent wording between t and $t+1$?

- How were outliers determined (needs to be based on substantive arguments)? I also feel these figures can go into supplementary materials (if needed to save space).

- It should be mentioned how the authors determined the occurrence of thoughts for studies that used continuous measures.

- Please exclude effect sizes in Table 3 (which are also reported in the figures) or make clear that these are derived based on the current analyses and then also include 95% CI.

- The data here may 'represent more of the long-term negative consequences on negative affect than the immediate short-term relief'. How should we understand this statement as the results indicate a

reduction (rather than increase) of negative affect.

- Please remove the statement (line 630) "The lack of other significant differences increases the confidence in the generalizability of the results to the broader literature." There still may be a non-response bias (even though you do not find differences in several study characteristics).

- I found the statement, "The attenuating roles of disengagement coping and negative urgency, two modifiable variables, should be considered so that treatments could potentially intervene and modify the risk of SITBs." a bit confusing. I would suggest excluding this statement as it is unclear why the authors focus specifically on those variables here in the conclusion of the manuscript (one can think of many other constructs that are modifiable). If you would like to keep the statement it would be good to provide a bit more justification about why specifically these variables are important.

Thank you for allowing me to review your work. I hope that some of the suggestions provided here will be found useful.

Reviewer #2:

Remarks to the Author:

This manuscript examines:

There are numerous strengths to this work, including the meta-analytic approach and comprehensive review. I only have a few minor revisions for this work.

Introduction:

- Given that the review focuses on NSSI and suicide ideation, it seems odd that the introduction to the problem (first few lines of para 1) is focused entirely on the rates/impacts of suicide death. It may be helpful to provide more comprehensive description of impact of SITBs

- Relatedly, the affect regulation model is most commonly applied to NSSI; yet, the introduction seems to conflate the terms NSSI and SITBs, and sometimes suicide, and it would be helpful if more care were taken in term use. This is particularly true because the review focuses

- It seems as though authors use the affect regulation model as applied to all SITBs; yet, early on, only those studies relating the affect model to NSSI are cited. Different literature should be highlighted and a bit more rationale for this broad use of the model needs additional support.

- Several experimental studies of lab-based pain impacting mood pre-during-post are not included in the introduction as currently written. It is also not clear why the authors chose to focus on physiological measures here.

Methods:

- I really appreciate that you provided information about sample differences between those studies you did and did not obtain data from

- Overall, description of methods is clear

Results:

- authors mention that there is large heterogeneity across methods. E.g., having read much of this literature, an area of difference is length of time after a given SITB (e.g., NSSI) before the EMA

assessment was conducted. the affect regulation model proposes immediate changes in negative mood; yet, usually, ema captures mood hour(s) after an episode. Similarly, the measures used to assess NA vary greatly. It would be helpful for descriptive statistics to describe the time course (time before SITB, on avg, from lit and time after SITB, on avg, from lit + range). Moreover, a summary of the measures used from the table could be useful.

- a data analytic section describing moderators tested would be useful here as it seems that many moderators were included; yet, it's not clear how/why they were determined or entered. For example, were all entered into one meta-regression? Or were these conducted separately? Also, what is the 'frequency of SITB' a measure of? what time course? just suicide ideation or NSSI?
- It's great that NA measures are included in the table; it would also be super helpful if measures of SI and NSSI were listed, given the very high heterogeneity in these measures. I'd also be curious if measure types moderated outcomes.
- Broadly, I found the results section a bit confusing/difficult to follow. I think that adding a data analysis section will help with this, as will thinking through organization a bit more before resubmission.

Reviewer #3:

Remarks to the Author:

The present review and meta-analysis aimed at investigating the association between negative affect and self-injurious thoughts and behaviors (SITBs) in intensive longitudinal studies (in ecological momentary assessment and daily diary studies). The aim is timely and original and I appreciate the great efforts that the authors have made in collecting the data and performing the analyses. However, the writing is not always clear, the manuscript should be consistently reduced and the methodology, extremely important in this kind of studies, is lacking of relevant details.

Authors may want to follow these suggestions to improve their manuscript.

Abstract

The results section is unbalanced because is too long. Authors may want to reduce it and add methods.

Introduction

The introduction should be focused on a better explanation of affect regulation to interpret SITBs.

Moreover, I would better explain also the automatic positive reinforcement (i.e., engaging in NSSI to feel something). An example of decreased negative affect should be reported.

The decision to focus only on NSSI thoughts, NSSI behaviors, and suicidal thoughts instead of on the entire suicidality spectrum should be better motivated.

Moreover, the introduction should be consistently shortened.

Methods

The methods lack of precision and details. Only as an example, inclusion and exclusion criteria should be re-written because are not sufficient. What about the diagnosis of the patients?

The considered definition of negative affect and suicidal outcomes should be added together with the assessment scales.

I would include only published articles, considering the paucity of unpublished ones and the possibility of bias.

Authors wrote: "Each corresponding author was contacted three times from two separate authors (first and senior authors) before excluding studies without raw data". Does this mean 6 contacts?

Lines 250-254: How was this decided and calculated?

Meta-regression, sub-group analyses and publication bias are not well-described in the methods (how you selected the variables? What about Egger test? Trim and fill?).

Results

The initial description of the included studies is not informative. Please, add some details.

Publication bias

Some parts should be added in methods and not in the results (only as an example "We used methods outlined in Mathur and VanderWeele (2020) to determine whether these effects were robust to various levels of publication bias.")

Discussion

Further limitations should be added and discussed.

Minor remarks:

Line 27: put "approximately 800,000 people" instead of "approximately 800,00 people".

Author Rebuttal to Initial comments

Title: A meta-analysis on the affect regulation function of real-time self-injurious thoughts and behaviors

Thank you for the opportunity to revise and resubmit our manuscript. We appreciate the reviewer's careful attention to our work, and feel the article is greatly improved due to their feedback. Below we address the critiques and explain our associated revisions.

Associate Editors' Critiques and Summary of the Reviews:

The associate editor highlighted the technical concerns raised by Reviewer #1. We thank Reviewer # 1, as well as the associate editor, for noting these critiques and for reading our manuscript very closely. We took Reviewer #1's concerns to heart and have completely revamped the analyses by conducting an individual participant data using the raw data. We address Reviewer #1's specific concerns below and believe these changes have greatly strengthened the paper.

Reviewer #1:

"A fundamental concern with the current manuscript that needs to be addressed is that the authors did not model the relationship between negative affect and SITBs to derive effects (e.g., using multilevel modeling), but calculated difference scores that conflate within- and between-person differences. Antecedent models subtract the mean negative affect across all participants (rather than for each individual separately) for each non-SITB report from the mean negative affect before all SITB observations. Similarly, consequence models seem to ignore the multilevel structure of the data (observations are nested within individuals) by focusing on the difference in negative affect during and after a SITB for the entire sample. I would strongly encourage the authors to model the temporal relationship between negative affect and SITBs (as they have the data available to do these analyses and then pool effects) using multilevel vector autoregressive models. I believe this would make this paper considerably stronger."

Response: We thank Reviewer #1 for pointing out this limitation of our analytic approach. We agree with R1's concern that the approach taken in the initial draft conflated within and between person variance and ignored the nested structure of the data. We now use a hierarchical linear modeling and individual participant data approach within a Bayesian framework for the revised manuscript. To do this, we constructed a three-level model (observations nested within people nested within studies) and used centering to separate within

and between person negative affect. We believe these revised analyses, which largely comes to the same conclusions as the initial manuscript (supportive of the affect regulation model), provides a more rigorous analysis. We believe this new approach addressed Reviewer #1's concern as it now accounts for the nested structure of the data and separates within from between person variance in negative affect.

We do agree that a person-centered IPD would be ideal for parsing within/between variation for these effects, we believe there are a few reasons why this approach was not possible for the present study.

The most important of which is that mIVAR requires a substantial number of observations per person (preferably at least 30 or more). Given the substantial study-to-study heterogeneity in the data structure (including within-person power and time-scale), even though we do have the raw data from a majority of studies, an individual participant data analysis using mIVAR would likely have substantial bias in the pooled estimates across studies.

Although mIVAR would be ideal for analyzing this type of data, one of the major conclusions of the paper is the necessity for researchers to consider person centered approaches, such as mIVAR, when analyzing intensive longitudinal data. This is particularly important for both substantive (i.e., individuals at high-risk for suicide are a highly heterogeneous group) and methodological (i.e., study-to-study variation in time scale, number of timepoints, frequency of SITB observations, etc.) reasons.

The following section was added which describes the revised analyses:

[Page 23, line 5 through Page 25, line 8]: Meta Analyses

We conducted six separate IPD meta-analyses⁵⁰. Antecedent models examined changes in pre SITB negative affect, while consequence models detected differences in negative affect post-SITB. Both antecedent and consequence models were run separately for NSSI thoughts, NSSI behaviors, and suicidal thoughts. As there were a small number of studies that measured NSSI urges ($k = 1$) and suicidal urges ($k = 1$), thoughts and urges were combined and labeled NSSI thoughts and suicidal thoughts. Only one study reported any instances of suicidal behavior (i.e., suicide attempts), limiting our ability to include this outcome.

We standardized negative affect in each study to account for measurement differences. We then aggregated individual studies into a combined data set prior to separating within- and between-person variance of the standardized affect variable. To tease apart variance, we used within-person and grand-mean centering⁵¹. Centering within-person reflects an individuals' deviation from their own average while grand-mean centering reveals an individuals' departure from the entire sample's average across all time points.

For each of the six analyses, we used a three level Bayesian multi-level model (observations nested within individuals nested within study). Besides accounting for the nested structure, we also nested these participant-level intercepts within studies to account for differences in SITBs across studies. We further included random slopes to account for variability in the negative affect - SITB association between participants and studies. The following R syntax was used to calculate antecedent effects:

Although somewhat counterintuitive, we chose to use within-person negative affect at $t-1$ as the dependent variable instead of SITBs. As we were concerned with the relative difference in affect between a SITB versus a non-SITB report, the coefficient from the above model provided a clean and interpretable effect size of interest. Conversely, a model with a dichotomous SITB as the dependent variable would produce a coefficient that, when exponentiated, represents a change in the odds ratio of a SITB for increasing levels of negative affect. We felt a model with negative affect as the dependent variable allowed for effect sizes to be comparable between antecedent and consequence models and produced effect sizes that were easy to interpret.

Consequence models were based on Kleiman et al.⁹ and reflect the relative difference in negative affect at time point t when a SITB was reported as compared to mean levels of within-person affect when a SITB was not reported at $t+1$. As such, here we compare a participant's reported level of negative affect together with the report of SITB to the report of negative affect at the time point following the report of SITB. The following R script was used for analyses:

Priors

To specify prior information, in line with recommendations from Gelman, Simpson, and Betancourt⁵², we chose a weakly informative prior. The purpose of these priors is to regularize parameters while taking minimal influence on the results, provided sufficient amounts of data are available. The following priors were used:

$$\text{Intercept} \sim N(0,1)$$

$$B(\text{SITB}) \sim N(0,1)$$

$$SD \sim \text{Student } t(3,0,2.5)$$

$$\sigma \sim \text{Student } t(3,0,2.5)$$

We used the "brms" package⁵³ in the R statistical environment⁵⁴ to conduct all analyses. Although this study was not preregistered, analysis scripts to calculate effects from the raw data and the resulting information to compute pooled effects were made publicly available (<https://anonymous.4open.science/r/8ae171ba-8406-4419-a76e-19b03e70f422/>).

"Can the authors please explain why the mean age of included data sets 24.85 (line 251) differs from the mean age reported later in the manuscript (line 340)."

Response: We thank Reviewer #1 for highlighting this discrepancy. These two numbers differed since the mean age reported on line 340 was a weighted mean (based on the sample size of the study), while the mean reported on line 251 did not account for differences in sample sizes across studies. We apologize for the confusion. As we now only analyze data for which we had raw data and there were no significant differences between studies that did and did not provide data, the sentence on line 251 has now been removed.

"Please also include figures with effect sizes in the manuscript for NSSI thoughts. In addition, publication bias and sensitivity analyses also need to be conducted for this outcome."

"Response: We thank Reviewer #1 for highlighting that NSSI thoughts were excluded from some analyses. We left out NSSI thought models from these analyses due to the small number of studies ($k = 8$ in initial draft; $k = 6$ in revised manuscript). As the manuscript is already lengthy and the small number of studies preclude substantive conclusions, we believe adding these analyses to the manuscript would weaken the study. We have, however, added these results to the Supplemental Materials so interested readers can have this information (Supplemental Figure 1 and Supplemental Table 2).

"The methods to assess publication bias (Mathur & VanderWeele, 2020) should be more clearly explained (ll400-425)."

Response: We agree with Reviewer #1 that the previous description was unclear. The revised manuscript reflects results from an individual participant meta-analysis using the raw data. Publication bias is less of an issue in an individual participant meta-analysis because we are relying on the raw data, not what was reported in a publication. Furthermore, we made attempts to obtain any relevant data, including from authors who collected data but had not yet published the results. We now include an analysis of publication bias in the sensitivity analysis section and abandon the previous method developed by Mathur & VanderWeele (2020).

[Page 15, line 12]: **Publication Bias**

We tested for publication bias by removing unpublished studies and reanalyzing results based exclusively on published articles. These analyses are reported in Supplementary Table 5. Results were nearly identical when excluding unpublished articles.

"The statements "only those that are not affirmative are presented in Table 5", "Under these extreme scenarios", " These plots suggest that the effect sizes for non-affirmative and affirmative studies are relatively similar and that the effect sizes and standard errors are correlated, which indicates that these results may be robust to publication bias." were unclear to me. Looking at Figure 4, effect sizes on the x-axis differ substantially, no?"

Response: We agree with Reviewer #1 that these previous statements were unclear and thank Reviewer #1 for pointing these out. We have deleted all of the statements as they are no longer relevant to the revised analyses.

"Please provide more information about how to interpret Fig 4 (the footnote is not clear to me)."

Response: We deleted Figure 4 as it is no longer relevant to the revised analyses.

"Does Table 5 present a scenario where a 200-increase in publication bias is assumed in the worst-case scenario? Please clarify."

Response: We deleted Table 5 as it is no longer relevant to the revised analyses.

"It should be mentioned that the authors report findings that are not always in line with the results reported in original studies (in which lagged relationships are modeled). For instance, Houben and colleagues (2017) found that the occurrence of NSSI predicted an increase of negative affect in lagged analyses. Similar findings were observed for Koenig et al. (2020), but a negative effect is reported for this dataset (Santagelo et al., 2017). Remarkably, however, a negative effect (indicating a reduction of NA) is found for both studies with the present methodology. Similarly, while Kiekens and colleagues observed a positive prospective relationship between negative affect and NSSI behavior, the authors report the opposite effect here (although non-significant). Hence, please remove the statement (line 433) that 'Kiekens et al. (2020) was the only study to report reduced negative affect prior to NSSI behavior.'"

Response: As we no longer include the section regarding outliers, the sentence 'Kiekens et al. (2020) was the only study to report reduced negative affect prior to NSSI behavior' has been removed from the revised manuscript.

Furthermore, we thank Reviewer #1 for their careful critique. We did note in the discussion that there were a few significant differences between what was reported in studies and the present analyses as we needed to standardize procedures across data sets. We have now added stronger language to the discussion and include a few of the points discussed below.

The revised IPD analyses continue to be discrepant from the published articles mentioned above. In our analyses, we found that within-person negative affect was reduced following NSSI in Houben and colleagues (2017) ($\beta = -0.29$; 95% CI = $-0.68 - 0.11$); Koenig et al. (2020) ($\beta = -0.42$; 95% CI = $-0.78 - -0.06$) and in Kiekens and colleagues (2020) ($\beta = -0.42$; 95% CI = $-0.76 - -0.05$). There are two main reasons for this discrepancy, one methodological and one technical. First, our analyses examine the difference in affect between t and $t+1$, but only when a SITB was not reported at $t+1$ (similar to Kleiman et al., 2017) whereas other studies used all available. Different decisions likely lead to different conclusions. We believe our approach, based on

Kleiman et al. (2017) is cleanest as it represents negative affect once someone is no longer experiencing a SITB. In contrast, an approach that uses all available data (i.e., including observations where someone experiences a SITB at both t and t+1) is problematic as affect is likely to remain artificially elevated because people are experiencing the same episode reported previously. On technical grounds, we now report random effects as estimates from individual studies. This approach produces estimates that differ from coefficients based on single studies as they are constrained by the average effect size. Studies based on small sample sizes (i.e., N = 30 in Houben et al.) are affected more than studies using a larger sample. Of course, we believe this why a meta-analysis is needed in the first place. Individual studies have used small sample sizes and have reported contradictory findings. Pooling data together produces more reliable estimates.

“Relatedly, the authors report that Kiekens and colleagues (2020) found that negative affect predicts NSSI thoughts but not behavior. Please note that this study observed that negative affect prospectively predicted NSSI behavior. However, this was no longer the case when accounting for the lagged effect of NSSI thoughts. This study also used the wording ‘since the last beep’ to assess NSSI behaviors (table 1).”

Response: We thank R1 for their careful review of our paper. The following language has been added to the paper:

[Page 8, Line 2]: “The authors reported evidence that within-person changes in negative affect prospectively predicted NSSI thoughts and behavior, however only NSSI thoughts, but not behavior, remained significant after controlling for the occurrence of NSSI thoughts at the previous timepoint.”

“The issue of ideation-to-action was briefly discussed in the discussion for suicidal behaviors, but it would be good also to make this point for NSSI behaviors.”

Response: We added a citation to a paper using an ideation-to-action framework for NSSI:

[Page 16, Line 22]: “Future research should investigate between and within person differences which might better discriminate who is most likely to engage in NSSI and suicidal forms of SITBs, and when risk is most acute. For example, individual differences in reflexive emotion regulation strategies⁴¹, or momentary improvements in self-efficacy to avoid self-injurious behavior^{26,42}, provide may discriminate between NSSI and suicidal forms of SITBs⁴³.”

"It should be made clear that lagged/concurrent in table 1 refers to the wording of items and not the model strategy that was used in the studies."

Response: The word "lagged" has been changed to "retrospective" to improve clarity.

"The section "Although some datasets queried lagged associations between current mood (t; e.g. "Right now, I feel...") and SITBs experienced since the last assessment point (t-1; "Since the last assessment"), even with the inconsistent prompts, we felt that variability in affect from either t-1 to t+1 (observation prior to SITB to report post SITB), or between t and t+1 (timepoint at which SITB was reported to report following SITB), captured post-SITB fluctuations" is not entirely clear to me. Why are items using 'since the last assessment' considered inconsistent prompts? If the outcome is behavior, is it not appropriate to assess this retrospectively? Can the authors explain why the difference between both modeling strategies leads to such different results (Sfigure1)? For this reason, I think it is really important to model the relationship between NA and SITBs (which would allow the investigation of 1-2 lags to investigate effects over time)"

Response: This paragraph was deleted due to the revised analyses and the change in how consequence models were operationalized. We now analyze the time frame of prompts (i.e., retrospective vs. in-the-moment prompts) as a moderator of the effect size. We believe this is the strongest way to test for differences. Reference point of prompts did not moderate the effect size.

"How do the authors justify analyzing studies in a similar way that assessed thoughts 'in the moment' and retrospectively? Even though I feel relationships should be modeled, would it be not more appropriate to analyze studies that used retrospective wording between t and t-1 and concurrent wording between t and t+1?"

Response: See response above

"How were outliers determined (needs to be based on substantive arguments)? I also feel these figures can go into supplementary materials (if needed to save space)."

Response: We deleted the outlier section due to the change in analyses. Based on visual inspection, there were no outliers present.

"It should be mentioned how the authors determined the occurrence of thoughts for studies that used continuous measures."

Response: Most studies used a binary yes/no indicator for the presence/absence of SITBs. A few studies measured suicidal ideation/thoughts continuously (i.e., Czyz et al., Kaurrin et al., Kiekens, et al., Evans et al., Peters et al., Salim et al., Kleiman et al., 2017 and Kleiman et al., 2018 -- see Table 2). A few of these studies also included a binary variable in which the presence or absence of a SITB was determined based on a non-zero response. This was not the case for two data sets (Kleiman et al., 2017 and Kleiman et al., 2018). As mentioned in the initial manuscript, we determined that suicidal thoughts were present when SI was greater than one standard deviation of an individuals' within-person average of SI. We made this determination because almost every observation included a non-zero response on SI in these two data sets. We include sensitivity analyses for how different decisions affect the average effect sizes and find very little differences. The heterogeneity in measurement of SITBs is certainly a limitation of this literature, and is one reason we believe why a study such as ours is greatly needed.

"Please exclude effect sizes in Table 3 (which are also reported in the figures) or make clear that these are derived based on the current analyses and then also include 95% CI."

Response: The effect sizes previously reported in Table 3 (now Table 2) have now been deleted.

"The data here may 'represent more of the long-term negative consequences on negative affect than the immediate short-term relief'. How should we understand this statement as the results indicate a reduction (rather than increase) of negative affect."

Response: This entire paragraph has been deleted in light of the new findings.

"Please remove the statement (line 630) "The lack of other significant differences increases the confidence in the generalizability of the results to the broader literature." There still may be a non-response bias (even though you do not find differences in several study characteristics)."

Response: This sentence has been deleted.

"I found the statement, "The attenuating roles of disengagement coping and negative urgency, two modifiable variables, should be considered so that treatments could potentially intervene and modify the risk of SITBs." a bit confusing. I would suggest excluding this statement as it is unclear why the authors focus specifically on those variables here in the conclusion of the manuscript (one can think of many other constructs that are modifiable). If you would like to keep the statement it would be good to provide a bit more justification about why specifically these variables are important."

Response: [Page 21, line 1]. The statement "The attenuating roles of disengagement coping and negative urgency, two modifiable variables, should be considered so that treatments could potentially intervene and modify the risk of SITBs." has been deleted.

Reviewer 2:

Introduction:

"Given that the review focuses on NSSI and suicide ideation, it seems odd that the introduction to the problem (first few lines of para 1) is focused entirely on the rates/impacts of suicide death. It may be helpful to provide more comprehensive description of impact of SITBs"

Response: We agree with R2. The following text has been added to the first paragraph: Page 3, Line 4: "While many more individuals contemplate and/or attempt suicide, approximately 800,000 people die by suicide each year¹. In the United States, 4.8% of adults 18 and older seriously considered suicide in 2018², while about 0.5% of U.S. adults reported they attempted suicide². Non-suicidal self-injury (NSSI), defined as deliberate damage to ones' body tissue without the intention to die³, is a risk factor for future suicidal behavior⁴. NSSI is suspected to increase ones' tolerance for painful stimuli and removing barriers to attempting suicide. Worldwide, an estimated 18% of adolescents engage in NSSI⁵"

"Relatedly, the affect regulation model is most commonly applied to NSSI; yet, the introduction seems to conflate the terms NSSI and SITBs, and sometimes suicide, and it would be helpful if more care were taken in term use. This is particularly true because the review focuses"

Response: We have re-written the introduction to be more precise in our distinction between NSSI and SITBs. We note early on that the affect regulation model was initially proposed to explain the maintenance of NSSI behaviors and that there is emerging work extending this model to suicidal thoughts (Kleiman et al., Mou et al.). Once we make the case that the affect regulation has been extended to suicidal cognitions, we do use the term SITBs to assist the reader.

"It seems as though authors use the affect regulation model as applied to all SITBs; yet, early on, only those studies relating the affect model to NSSI are cited. Different literature should be highlighted and a bit more rationale for this broad use of the model needs additional support."

Response: We thank Reviewer #2 for ensuring the literature review is precise and focused. The affect regulation has mostly focused on NSSI. We do note this has recently been extended to suicidal thoughts.

“Several experimental studies of lab-based pain impacting mood pre-during-post are not included in the introduction as currently written. It is also not clear why the authors chose to focus on physiological measures here.”

Response: One of the main critiques of intensive longitudinal studies is that they focus on self-reported affective states. Experimental studies, which often focus on physiological measurements, allow for a researcher to observe processes as they unfold in the lab. We primarily reference experimental studies using physiological data to strengthen our arguments and to provide additional support for the model. We believe that readers are left with a more complete understanding of the literature, and to protect against the claim that this model is entirely reliant on self-report data.

Methods:

- I really appreciate that you provided information about sample differences between those studies you did and did not obtain data from
- Overall, description of methods is clear

Response: We thank Reviewer #2 for noting clarity in our previous methods section and for appreciating how we examined differences between studies included in the meta-analysis and those in which we were unable to obtain raw data. We have retained these analyses in the revised manuscript.

Results:

“[The] authors mention that there is large heterogeneity across methods. E.g., having read much of this literature, an area of difference is length of time after a given SITB (e.g., NSSI) before the EMA assessment was conducted. The affect regulation model proposes immediate changes in negative mood; yet, usually, EMA captures mood hour(s) after an episode. Similarly, the measures used to assess NA vary greatly. It would be helpful for descriptive statistics to describe the time course (time before SITB, on avg, from lit and time after SITB, on avg, from lit + range). Moreover, a summary of the measures used from the table could be useful.”

Response: We thank Reviewer #2 for this suggestion. Although this type of information would be ideal and certainly informative, it would be nearly impossible to determine the exact timing of SITBs in relation to the rated affect. We believe this is a fundamental question but also a

limitation to the current research designs all study use. This type of granularity is often ignored by the time frame assessed in prompts (see Table 2 for differences across studies).

“A data analytic section describing moderators tested would be useful here as it seems that many moderators were included; yet, it's not clear how/why they were determined or entered. For example, were all entered into one meta-regression? Or were these conducted separately? Also, what is the 'frequency of SITB' a measure of? what time course? just suicide ideation or NSSI?”

Response: We agree with R2 that more information on moderators as well as a data analytic section would be helpful. We added the following text to the revised manuscript.

[Page 25, line 9]:

Moderation Analyses

We tested for moderation using the interaction between our hypothesized moderators and SITB variables in a three-level model. Moderation was tested in both antecedent and consequence models. We did not test for moderation with NSSI thought models due to the small number of studies. We examined sources of heterogeneity between studies and used the following variables as moderators (all moderators were tested as study-level characteristics):

Number of Prompts Per Day.

We extracted the number of intensive longitudinal prompts sent to participants per day ($M = 5.04$; $SD = 3.31$; range = 1 – 12).

Number of Hours Between Prompts.

The average amount of time (in hours) between study prompts. This was either stated in the publication or was calculated by dividing the number of prompts by the duration of the observation period used in the study ($M = 10.43$, $SD = 10.41$; range = 0.5 – 24).

Frequency of SITB.

The frequency with which each SITB variable was observed over the course of the study. This was calculated by dividing the number of observations in which a SITB was endorsed by the total number of observations (NSSI thoughts: $M = 12.44\%$, $SD = 7.37\%$; range = 3.15% – 26.60%; NSSI behaviors: $M = 3.53\%$, $SD = 2.85\%$; range = 0.05% – 8.92%; suicidal thoughts: $M = 22.82\%$; $SD = 27.28\%$; range = 3.73% – 79.01%).

Compliance Rate.

The proportion of surveys completed by participants. This was either reported in the study or calculated from the raw data ($M = 69.15\%$; $SD = 17.46\%$, range = 36% – 100%).

Percentage of Sample who Identify as Female.

We extracted the percentage of the sample that identified as female from each study ($M = 74.73\%$; $SD = 36.66\%$; range = 38.30% – 91.00%).

Percentage of Sample who Identify White.

We derived the percentage of the sample reporting a white identity from each study ($M = 80.00\%$; $SD = 11.07\%$; range = 57.00% – 100%).

Mean Age of the Sample.

We also extracted the mean age of the sample from each study ($M = 24.42$; $SD = 7.02$; range = 15.50 – 37.90).

Inclusion of Participants Diagnosed with Borderline Personality Disorder (BPD).

We created a binary variable that indicated whether studies included participants diagnosed with borderline personality disorder. Seven studies (31.82%) mentioned borderline personality disorder as an inclusion criterion and/or reported enough diagnostic information to determine if this was assessed.

Sampling Strategy (EMA versus Daily Diary).

We categorized studies as using an EMA ($n = 16$; 72.72%) or daily diary ($n = 6$; 27.27%) design.

Time Frame Assessed in Prompts (Momentary versus Retrospective).

We then examined the wording of the time frame assessed in prompts and categorized them as momentary ($n = 15$; 68.18%) or retrospective ($n = 7$; 31.82%).

"It's great that NA measures are included in the table; it would also be super helpful if measures of SI and NSSI were listed, given the very high heterogeneity in these measures. I'd also be curious if measure types moderated outcomes."

Response: We have added a column to Table 2 with more details of the measurement of SI and NSSI used in each study. We agree with Reviewer #2 that it would be interesting to know if the variance of SITB measurement affected effect sizes, however, as highlighted in Table 2, there is too much heterogeneity in how SITBs are measured to allow for this to be tested.

"Broadly, I found the results section a bit confusing/difficult to follow. I think that adding a data analysis section will help with this, as will thinking through organization a bit more before resubmission."

Response: We thank Reviewer #2 for suggesting a data analysis section. This has now been added. We have also attempted to streamline the results section to improve clarity.

Reviewer #3:

Abstract

The results section is unbalanced because is too long. Authors may want to reduce it and add methods.

Response: We trimmed the abstract to 150 words in reformatting the manuscript to comply with requirements. We believe the revised abstract is now balanced.

Introduction

The introduction should be focused on a better explanation of affect regulation to interpret SITBs. Moreover, I would better explain also the automatic positive reinforcement (i.e., engaging in NSSI to feel something). An example of decreased negative affect should be reported.

Response: We have made revisions to the introduction to increase clarity:

[Page 4, line 13]: Confirmatory factor analysis yielded a four-factor structure with automatic negative reinforcement (i.e., the affect regulation hypothesis) being the most frequently endorsed reason for NSSI (e.g., self-harming to reduce emotional distress). Other aspects identified were automatic positive reinforcement (i.e., self-harming to feel pain/a different emotion) as well as interpersonal negative and positive reinforcement. A recent meta-analysis confirmed this initial work as the affect regulation function was the most endorsed reason for NSSI across studies, with an estimated 63-78% of people reporting this function¹⁵.

The decision to focus only on NSSI thoughts, NSSI behaviors, and suicidal thoughts instead of on the entire suicidality spectrum should be better motivated.

Response: We thank Reviewer #3 for allowing us to elaborate. Only one study had data on suicidal behavior. We updated the manuscript with the following language:

[Page 23, line 9]: "As there were a small number of studies that measured NSSI urges ($k = 1$) and suicidal urges ($k = 1$), thoughts and urges were combined and labeled NSSI thoughts and suicidal thoughts. Only one study observed any instances of suicidal behavior (i.e., suicide attempts), limiting our ability to include this outcome."

"Moreover, the introduction should be consistently shortened."

Response: We have attempted to streamline the introduction. At the same time, we are trying to balance precision and specificity.

Methods

The methods lack of precision and details. Only as an example, inclusion and exclusion criteria should be re-written because are not sufficient. What about the diagnosis of the patients? The considered definition of negative affect and suicidal outcomes should be added together with the assessment scales.

Response: We did not screen articles based on specific diagnoses. We included any article that 1) was empirically based; 2) measured negative affect (continuously rather than dichotomously) in intensive longitudinal data; and 3) measured SITBs in intensive longitudinal data. We have added additional information about the measurement of negative affect and SITBs to Table 2. We limited analyses to only studies that measured affect and SITBs in intensive longitudinal data, in part, because of how we operationalized affect (brief and dynamic states, in opposition to depressive symptoms which often last weeks or more). We believe the inclusion and exclusion criteria are sufficient for replicating our results.

I would include only published articles, considering the paucity of unpublished ones and the possibility of bias.

Response: We now include a sensitivity analysis between published and unpublished data sets. As there were no differences, we believe including the studies increases our power and provides readers with a more comprehensive representation of this literature.

Authors wrote: "Each corresponding author was contacted three times from two separate authors (first and senior authors) before excluding studies without raw data". Does this mean 6 contacts?

Response: The above sentence is now changed to the following:

[Page 22, line 19]: "We made three total attempts to contact corresponding authors before excluding studies."

"Lines 250-254: How was this decided and calculated?

Meta-regression, sub-group analyses and publication bias are not well-described in the methods (how you selected the variables? What about Egger test? Trim and fill?)."

Response: These sections have all been deleted and/or revised. We have now added more information about the moderator variables (i.e., how they were selected and calculated).

"Results

The initial description of the included studies is not informative. Please, add some details.

Response: We have added additional information regarding the included studies to Tables 1 and Tables 2 (NA and SITB measures used, sampling strategy, and time-frame assessed). We believe

readers can get a better sense of the literature from the tables and are attempting to keep the information reporting in the manuscript as concise as possible.

"Publication bias

Some parts should be added in methods and not in the results (only as an example "We used methods outlined in Mathur and VanderWeele (2020) to determine whether these effects were robust to various levels of publication bias.")"

Response: We deleted the description of Mathur and Vanderweele (2020) due to the new analyses.

"Discussion

Further limitations should be added and discussed"

Response: We have strengthened the limitations section and have added additional limitations such as the time-scale assessed in intensive longitudinal studies and the inability to use a person-centered analytic approach.

Minor remarks:

Page 3, line 4: put "approximately 800,000 people" instead of "approximately 800,00 people".

Response: This has been corrected in the text.

[Page 3, line 4] "...approximately 800,000 people..."

Decision Letter, first revision:

8th December 2021

Dear Mr Kuehn,

Thank you once again for your manuscript, entitled "A meta-analysis on the affect regulation function of real-time self-injurious thoughts and behaviors," and for your patience during the peer review process.

Your manuscript has now been evaluated by 3 reviewers, whose comments are included at the end of

this letter. Although the reviewers find your work to be of interest, they also raise some important concerns. We are very interested in the possibility of publishing your study in Nature Human Behaviour, but would like to consider your response to these concerns in the form of a revised manuscript before we make a decision on publication.

To guide the scope of the revisions, the editors discuss the referee reports in detail within the team, including with the chief editor, with a view to (1) identifying key priorities that should be addressed in revision and (2) overruling referee requests that are deemed beyond the scope of the current study. We hope that you will find the prioritised set of referee points to be useful when revising your study. Please do not hesitate to get in touch if you would like to discuss these issues further.

1) Reviewer 1 has remaining concerns about the analyses and argues that modelling of lagged relationships and including auto-regressive effects would be feasible given the data. We request that you carefully evaluate these concerns and conduct the suggested analyses. Should you decide not to conduct the analyses, please provide a clear argumentation why this is not possible given the data and follow Reviewer 1's advice in acknowledging the limitations of the current analytical approach.

2) Please motivate all analytical choices and provide details about the centering used.

3) In accordance with the feedback provided by Reviewer 2, we request that you do not interpret null results.

4) We note that your literature search captures research published until September 2020. We would encourage you to consider updating your search to strengthen the corpus of evidence considered in your review and ensure your review is not out of date by the time it is published.

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

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

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

With your revision, please:

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

sent back to the reviewers along with the revised manuscript.

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

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

[REDACTED]

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

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

Sincerely,

Samantha Antusch

Samantha Antusch, PhD
Editor
Nature Human Behaviour

Reviewer expertise:

Reviewer #1: meta-analysis; (non-suicidal) self-injurious thoughts and behaviours

Reviewer #2: (non-suicidal) self-injurious thoughts and behaviours

Reviewer #3: meta-analysis

REVIEWER COMMENTS:

Reviewer #1:

Remarks to the Author:

Thank you for allowing me to review the revised version of this manuscript. Unfortunately, I still have several questions and suggestions regarding the revised version.

- While the authors have revised their analysis plan, they did not conduct the suggested analyses (i.e., modeling lagged relationships and including auto-regressive effects) based on the premise that some participants in individual studies do not have sufficient data. Although I understand that this may

indeed be the case for daily diary studies (which I would argue are not intensive longitudinal methods and do not have the necessary temporal granularity for assessing the momentary relationship between affective states and SITBs), the majority (if not all) EMA studies should have sufficiently dense sampling schedules to include most participants. The authors refer to Kleiman et al. (2017) for their analyses. However, please do note that in this paper, the following is mentioned: "This first analysis did not allow us to conclusively determine the time course of changes in affect relative to instances of suicidal thinking because suicidal thinking and affect were assessed simultaneously". In addition, Kleiman et al. also controlled for the time between responses which, if I am correct, did not happen in the analyses. Note that this may (partially) explain the larger effect of consequence models. If you want to keep the current modeling strategy, this should be explicitly acknowledged as well as the need for future studies to appropriately model lagged relationships (including auto-regressive effects and, as the authors rightfully suggested, controlling for the presence of concurrent SITBs).

- It is now mentioned that centering has been used: "To tease apart variance, we used within-person and grand-mean centering". However, please explain which type of centering was used when/at which level.

- The authors suggest that it may be that effects are non-consistent across people. However, why did the authors then not choose to include random effects for individuals? Note that emerging work indeed shows that effects of negative affect on suicidal ideation are highly individual (<https://psyarxiv.com/xj5c6/>; accepted at Behavior Research & Therapy) and that the assumption of homogeneity is not realistic (and thus may bias the results).

- I found it confusing to read in the revised intro "a quantitative synthesis has been impossible due to heterogeneity in the way intensive longitudinal studies have been designed and executed, making it impossible to compute meta-analytic estimates of effect sizes from published reports". However, this is exactly the objective of the present paper. Starting Line 167 an argument is then made for pooling effects. Please revise as it weakens the setup for the study.

- It is strange to refer to SITBs as distal antecedents of suicide mortality?

- Why is the method section included after the discussion?

- Moderation analyses were done at the study level, and I see these analyses as explorative. It is not clear why particular moderators were selected and what the hypotheses were "our hypothesized moderators". Why do the authors expect that study-level characteristics will have an effect on individual-level effects (e.g., compliance and frequency of SITB are individual characteristics)? Please comment on this in the discussion.

-Please make sure that referral to (supplementary) tables and figures is correct (e.g., supplementary table 2 should be 3, 3-4, etc). Please also reread the manuscript carefully for typos (e.g., line 225, line 358).

- Please include the more recent meta-analysis of Gillies et al. for the prevalence of NSSI: Gillies, D., Christou, M. A., Dixon, A. C., Featherston, O. J., Rapti, I., Garcia-Angueta, A., ... & Christou, P. A. (2018). Prevalence and characteristics of self-harm in adolescents: meta-analyses of community-based studies 1990–2015. *Journal of the American Academy of Child & Adolescent*

Psychiatry, 57(10), 733-741.

- "Although intensive longitudinal methods have been used to develop insights across many areas of clinical research, these methods are especially well-suited to capture the specific phenomenology of SITBs". The authors may want to refer the reader here to recent perspective papers that discussed this in detail for NSSI and STBs:

Kleiman, E. M., & Nock, M. K. (2018). Real-time assessment of suicidal thoughts and behaviors. *Current Opinion in Psychology*, 22, 33-37.

Kiekens, G., Robinson, K., Tatnell, R., Kirtley, O. J. (2021). Opening the Black Box of Daily Life in Nonsuicidal Self-injury Research: With Great Opportunity Comes Great Responsibility. *JMIR Ment Health*;8(11):e30915. doi: 10.2196/30915

- The revised discussion relies heavily on a between-person perspective: "Future research should investigate between and within person differences which might better discriminate who is most likely to engage in NSSI and suicidal forms of SITBs, and when risk is most acute: For example, individual differences in reflexive emotion regulation strategies, or momentary improvements in self-efficacy to avoid self-injurious behavior^{26,42} may discriminate between NSSI and suicidal forms of SITBs⁴³". What about investigating momentary fluctuations in these processes at the individual level to see how they relate to NSSI and STBs in daily life? I would suggest rewording this section.

-The authors found that NSSI thoughts and behaviors both reduced negative affect and indicate that this implies that relief from negative affect is an important component in the transition from thoughts to behavior. This conclusion cannot be made based on the current findings. In addition, note that a between-person explanation again follows this.

- When referring to the need of incorporating principles of open science, the authors may want to refer here to the work of Kirtley and colleagues in this area: Kirtley, O. J., Lafit, G., Achterhof, R., Hiekkaranta, A. P., & Myin-Germeys, I. (2021). Making the black box transparent: A template and tutorial for registration of studies using experience-sampling methods. *Advances in Methods and Practices in Psychological Science*, 4(1), 2515245920924686.

I hope the authors find these remaining suggestions helpful.

Reviewer #2:

Remarks to the Author:

The authors were overall very responsive to my and other reviewers' comments. The manuscript seems stronger as a result, and I believe is nearly ready for acceptance. I only have a few minor lingering concerns:

- In the introduction, there continues to be fluid use of terms across NSSI/ suicide/self-harm (e.g., "The success of intensive longitudinal methods in suicide research hinges on the ability to catalog converging evidence across diverging sampling and analytic methods. To date, three systematic reviews of intensive longitudinal studies on NSSI have been published").

Additional review may be useful in using terms consistently when possible, and clarifying within

context when other terms are incorporated. I also think there could be rationale to simply refer only to NSSI and suicidal thoughts throughout, as other SITBs (attempts, death) are not studied here, and this may help with clarity when one or both are being discussed.

Results:

- I find the framing of non-significant effects (e.g., NSSI thoughts) a bit odd, as the language used implies that, because it's in the anticipated direction, it should be interpreted cautiously (rather than not interpreted at all).

Reviewer #3:

Remarks to the Author:

The authors have properly revised the manuscript.

Author Rebuttal, first revision:

Title: A meta-analysis on the affect regulation function of real-time self-injurious thoughts and behaviors

Thank you for the opportunity to once again revise and resubmit our manuscript. We continue to appreciate the reviewers' careful attention to our work, and feel the article is greatly improved due to their feedback. Below we address the critiques and explain our associated revisions.

Response to Associate Editor's Requests:

AE.1) Reviewer 1 has remaining concerns about the analyses and argues that modelling of lagged relationships and including auto-regressive effects would be feasible given the data. We request that you carefully evaluate these concerns and conduct the suggested analyses. Should you decide not to conduct the analyses, please provide a clear argumentation why this is not possible given the data and follow Reviewer 1's advice in acknowledging the limitations of the current analytical approach.

Response: We thank R1 for their detailed and thorough review of our manuscript. In reading this comment, we realized our recent revision was not sufficiently clear as to how we tried to address this comment. Specifically, in the revised manuscript, we tested three-level hierarchical

models with lagged relationships and random subject-level slopes/intercepts. R1 is correct in noting that we did not examine autoregressive effects in the previous draft, and we didn't test iVAR models (for the reasons we articulated in the original response).

In this revision, we include sensitivity analyses that add autoregressive effects to both antecedent and consequence models. Our understanding of the reviewer's concern was whether earlier levels of the "outcome" (SITB in the antecedent models and NA in the consequence models) could account for or reduce the main effect of interest. In these models, we controlled for SITB at $t-1$ in antecedent models, and for NA at $t-1$ in consequence models. These analyses suggest that including autoregressive effects do not affect the main conclusions of the paper. The following information is included in the manuscript and the Supplementary Materials.

Page 15, line 319: "Finally, as has been done in prior studies^{30,45} we tested whether controlling for SITB at $t - 1$ influenced antecedent estimates, and if controlling for negative affect at $t - 1$ influenced consequence estimates. These results are reported in Supplementary Table 6. Controlling for dependent variables at $t - 1$ did not affect any of the main analyses."

Supplemental Table 6: Comparing average ES controlling for SITB at $t-1$

<i>Main Antecedent Models</i>				
	k	β	SE	95% CI
NSSI thoughts	6	0.06	0.06	-0.07 – 0.19
NSSI behaviors	14	0.20	0.06	0.09 – 0.31
Suicidal thoughts	13	0.11	0.04	0.03 – 0.19

Controlling for SITB at t-1

	<i>k</i>	β	SE	95% CI
NSSI thoughts	6	0.06	0.07	-0.08 – 0.19
NSSI behaviors	14	0.18	0.06	0.07 – 0.30
Suicidal thoughts	13	0.12	0.04	0.03 – 0.21

Main Consequence Models

	<i>k</i>	β	SE	95% CI
NSSI thoughts	6	-0.63	0.09	-0.79 – -0.44
NSSI behaviors	14	-0.47	0.14	-0.73 – -0.19
Suicidal thoughts	13	-0.52	0.14	-0.79 – -0.23

Controlling for NA at t-1

	<i>k</i>	β	SE	95% CI
NSSI thoughts	6	-0.65	0.11	-0.83 – -0.42
NSSI behaviors	14	-0.51	0.16	-0.82 – -0.18
Suicidal thoughts	13	-0.65	0.17	-0.98 – -0.30

Notes: None.

Finally, we appreciate the comment about controlling for time between observations. Indeed, we did not have sufficient data from all available studies to be able to control for the time between observations. We did however include the number of hours between prompts as a between study moderator. Although we recognize that this makes a strong assumption that all participants completed prompts within each study at the exact same time, our findings suggest that, at least at this crude level of analyses, time between prompts is not a strong moderator of our observed effects. (see p. 26 and Supplemental Table 2).

P.26. *Number of Hours Between Prompts.*

The average amount of time (in hours) between study prompts. This was either stated in the publication or was calculated by dividing the number of prompts by the duration of the observation period used in the study ($M = 10.43$, $SD = 10.41$; range = 0.5 – 24).

AE.2) Please motivate all analytical choices and provide details about the centering used.

Response: Thank you, we clarified our approach to centering and provided references to support our approach to centering affect within person and person-level aggregates centered from the grand mean.:

Page 23, line 505: “To tease apart within and between-person variance, we first averaged each participants’ EMA responses across the study period to create person-level averages. We then centered each observation of negative affect within-person by subtracting the participant-level mean from each EMA observation, and then grand-mean centered those participants’ averages⁶⁰. Thus, by centering level-1 variables within-person, any one observation reflects an individuals’ deviation from their own average across all time points.”

AE.3) In accordance with the feedback provided by Reviewer 2, we request that you do not interpret null results.

Response: Thanks, we agree with this comment and appreciate the suggestion. We revised our interpretation of the NSSI thoughts antecedent model and removed the language that R2 suggested.

Page 11, line 240: “The range of the 95% credible interval indicates that the data was inconclusive with regards to the degree of negative affect experienced prior to NSSI thoughts; small effects in either direction as well as a null results retain posterior plausibility”

Previously, that sentence read: “The 95 percent credible interval included zero, suggesting these results are mostly consistent with a small effect in the anticipated direction; However, a non-existing, and even a small negative, effect retain some posterior plausibility.”

AE.4) We note that your literature search captures research published until September 2020. We would encourage you to consider updating your search to strengthen the corpus of evidence considered in your review and ensure your review is not out of date by the time it is published.

Response: We updated the literature review to reflect studies published up to 1/15/22. Corresponding sections of the manuscript have all been updated.

Reviewer #1:

R1.1 While the authors have revised their analysis plan, they did not conduct the suggested analyses (i.e., modeling lagged relationships and including auto-regressive effects) based on the premise that some participants in individual studies do not have sufficient data. Although I understand that this may indeed be the case for daily diary studies (which I would argue are not intensive longitudinal methods and do not have the necessary temporal granularity for

assessing the momentary relationship between affective states and SITBs), the majority (if not all) EMA studies should have sufficiently dense sampling schedules to include most participants. The authors refer to Kleiman et al. (2017) for their analyses. However, please do note that in this paper, the following is mentioned: “This first analysis did not allow us to conclusively determine the time course of changes in affect relative to instances of suicidal thinking because suicidal thinking and affect were assessed simultaneously”. In addition, Kleiman et al. also controlled for the time between responses which, if I am correct, did not happen in the analyses. Note that this may (partially) explain the larger effect of consequence models. If you want to keep the current modeling strategy, this should be explicitly acknowledged as well as the need for future studies to appropriately model lagged relationships (including auto-regressive effects and, as the authors rightfully suggested, controlling for the presence of concurrent SITBs).

Response: We thank Reviewer #1 for their constructive feedback on our analyses, and for thinking through with us the best way to make sure that our analytic choices do not impact the results in unforeseen ways. We added sensitivity analyses along the suggestions made by Reviewer #1, which did not meaningfully alter our results (see our responses to AE.1 above).

R1.2 It is now mentioned that centering has been used: “To tease apart variance, we used within-person and grand-mean centering”. However, please explain which type of centering was used when/at which level.

Response: See our response to AE.2 above.

R1.3 The authors suggest that it may be that effects are non-consistent across people. However, why did the authors then not choose to include random effects for individuals? Note that emerging work indeed shows that effects of negative affect on suicidal ideation are highly individual (<https://psyarxiv.com/xj5c6/>; accepted at Behavior Research & Therapy) and that the assumption of homogeneity is not realistic (and thus may bias the results).

Response: We apologize for the confusion; we did include random effects in our original revision. On Page 24, we include the syntax which illustrates between person random effects. The syntax highlights that we added random intercepts nested in studies and participants as well as random slopes nested in studies and participants. Thus, we are accounting for variation at the participant and study level.

Page 24, line 518: $NA.standard.CWP.lag \sim 0 + Intercept + NSSI_thgts + (0 + Intercept | Study) + (0 + Intercept | Study:PID) + (0 + NSSI_thgts | Study) + (0 + NSSI_thgts | Study:PID)$

We definitely agree with R1 that effects of negative affect on suicidal ideation at highly variable on the individual-level (also see Kuehn, Foster, Czyz, & King; accepted at *Suicide and Life-Threatening Behavior*) and we now include a few more references in the discussion.

R1.4 I found it confusing to read in the revised intro “a quantitative synthesis has been impossible due to heterogeneity in the way intensive longitudinal studies have been designed and executed, making it impossible to compute meta-analytic estimates of effect sizes from published reports”. However, this is exactly the objective of the present paper. Starting Line 167 an argument is then made for pooling effects. Please revise as it weakens the setup for the study.

Response: We agree with R1 that the previous wording of this section weakened the rationale for our study. The argument we were making was that, *without the raw data*, it is impossible to make a quantitative synthesis of the published literature because of heterogeneity in the analytic approaches taken, and the lack of meta-analytic methods to account for such heterogeneity. We made minor revisions to argue why researchers need access to the raw data to standardize measurements and analytic decisions across studies. This section is now worded:

Page 7, line 132: “Differences in analytic strategies makes an estimation of the cumulative effect from published articles impossible from published studies alone as coefficients reported in

studies can reflect very different model assumptions (such as using a linear versus binary outcome, or a multilevel vs. a structural equation model).”

R1.5 It is strange to refer to SITBs as distal antecedents of suicide mortality?

Response: Thanks, we revised this sentence. It is now:

Page 3, line 46: “At the same time, researchers’ ability to predict self-injurious thoughts and behaviors (SITBs) is poor”

R1.6 Why is the method section included after the discussion?

Response: The method section is included after the discussion in accordance with the editorial policies of *Nature Human Behaviour*.

Page 1 of Editorial Policy and formatting checklist for Articles.docx “The manuscript file is organized in the following order:

1. Title page
2. Abstract
3. Introduction (no subheadings allowed)
4. Results (subheadings permitted)
5. Discussion (no subheadings allowed)
6. Methods (**note that they come after the results and discussion! Subheadings permitted**)
7. Protocol Registration (for Registered Reports only)

8. *Data availability statement*
9. *Code availability statement (only if you have used custom code)*
10. *References*
11. *Acknowledgements*
12. *Author contributions*
13. *Competing interests*
14. *Figure legends (no Figures!)*
15. *Tables*

R1.7 Moderation analyses were done at the study level, and I see these analyses as explorative. It is not clear why particular moderators were selected and what the hypotheses were "our hypothesized moderators". Why do the authors expect that study-level characteristics will have an effect on individual-level effects (e.g., compliance and frequency of SITB are individual characteristics)? Please comment on this in the discussion.

Response: We agree with the reviewer's critique. The use of study-level moderators is certainly a limitation of our study. We added language to explicitly state these analysis were explorative and added the following language to the discussion section:

Page 19, line 412: "Finally, our moderation analyses were exploratory and examined study-level, as opposed to individual- characteristics. We tested any variable we could operationalize from the published articles; however, it is likely that testing some of the moderators (e.g., compliance and frequency of SITB) on the individual-level would most likely lead to more precise estimates."

R1.8 Please make sure that referral to (supplementary) tables and figures is correct (e.g., supplementary table 2 should be 3, 3-4, etc). Please also reread the manuscript carefully for typos (e.g., line 225, line 358).

Response: We apologize for the typos and errors in the previous manuscript. References to the supplementary tables and figures are now correct and the specific typo mentioned above has been corrected.

R1.9 Please include the more recent meta-analysis of Gillies et al. for the prevalence of NSSI:

Gillies, D., Christou, M. A., Dixon, A. C., Featherston, O. J., Rapti, I., Garcia-Anguita, A., ... & Christou, P. A. (2018). Prevalence and characteristics of self-harm in adolescents: meta-analyses of community-based studies 1990–2015. *Journal of the American Academy of Child & Adolescent Psychiatry*, 57(10), 733-741.

Response: We now include a reference to Gillies et al. (2018) in the introduction.

Page 3, line 45: “Worldwide, an estimated 17% of adolescents engage in NSSI⁵.”

5. Gillies, D. et al. Prevalence and characteristics of self-harm in adolescents: meta-analyses of community-based studies 1990–2015. *Journal of the American Academy of Child & Adolescent Psychiatry*, 57(10), 733-741 (2018).

R1.10 “Although intensive longitudinal methods have been used to develop insights across many areas of clinical research, these methods are especially well-suited to capture the specific phenomenology of SITBs”. The authors may want to refer the reader here to recent perspective papers that discussed this in detail for NSSI and STBs:

Kleiman, E. M., & Nock, M. K. (2018). Real-time assessment of suicidal thoughts and behaviors. *Current Opinion in Psychology*, 22, 33-37.

Kiekens, G., Robinson, K., Tatnell, R., Kirtley, O. J. (2021). Opening the Black Box of Daily Life in Nonsuicidal Self-injury Research: With Great Opportunity Comes Great Responsibility. *JMIR Ment Health*;8(11):e30915. doi: 10.2196/30915

Response: We added the references mentioned above to the introduction (page 6, line 118).

R1.11 The revised discussion relies heavily on a between-person perspective: “Future research should investigate between and within person differences which might better discriminate who is most likely to engage in NSSI and suicidal forms of SITBs, and when risk is most acute: For example, individual differences in reflexive emotion regulation strategies, or momentary improvements in self-efficacy to avoid self-injurious behavior^{26,42} may discriminate between NSSI and suicidal forms of SITBs⁴³”. What about investigating momentary fluctuations in these processes at the individual level to see how they relate to NSSI and STBs in daily life? I would suggest rewording this section.

Response: We revised the paragraph above. It is now worded:

Page 17, Line 356: “Future research should investigate between and within person differences which might better discriminate who is most likely to engage in NSSI and suicidal forms of SITBs and indicate when suicide risk is most acute. For example, within-person fluctuations in reflexive emotion regulation strategies⁴⁷, or momentary improvements in self-efficacy to avoid self-injurious behavior^{26,48}, may discriminate between episodes of NSSI from suicidal forms of SITBs⁴⁹”

R1.12 The authors found that NSSI thoughts and behaviors both reduced negative affect and indicate that this implies that relief from negative affect is an important component in the transition from thoughts to behavior. This conclusion cannot be made based on the current findings. In addition, note that a between-person explanation again follows this.

Response: Thanks, that’s a good point. We deleted that paragraph.

Page 17, line 369: “It was also surprising that NSSI thoughts and NSSI behaviors were equally relieving, potentially suggesting that relief from negative affect is an important component in the transition from thinking about NSSI to engaging in the behavior. Future studies should look at habituation of distress as an explanation in this transition. Perhaps people are more likely to start self-harming when a tolerance is developed and thinking about NSSI no longer provides relief. However, substantially more data are needed to help elucidate momentary processes central in the transition from suicidal thinking to suicidal behavior as only one dataset observed any instances of suicidal behavior.”

R1.13 When referring to the need of incorporating principles of open science, the authors may want to refer here to the work of Kirtley and colleagues in this area: Kirtley, O. J., Lafit, G., Achterhof, R., Hiekkaranta, A. P., & Myin-Germeys, I. (2021). Making the black box transparent: A template and tutorial for registration of studies using experience-sampling methods. *Advances in Methods and Practices in Psychological Science*, 4(1), 2515245920924686.

Response: We thank R1 for the suggestion to highlight this excellent work. We added a reference to the discussion section.

Page 19, line 420: “By incorporating principles of open science⁵¹ (i.e., pre-registering hypotheses and making data/analysis scripts publicly available), meta-analyses could be conducted more efficiently, possibly leading to more reliable findings to assist in the prevention of SITBs.”

51. Kirtley, O. J., Lafit, G., Achterhof, R., Hiekkaranta, A. P., & Myin-Germeys, I.

Making the black box transparent: A template and tutorial for registration of studies using experience-sampling methods. *Advances in Methods and Practices in Psychological Science*, 4(1), 2515245920924686 (2021).

Reviewer #2:

The authors were overall very responsive to my and other reviewers' comments. The manuscript seems stronger as a result, and I believe is nearly ready for acceptance. I only have a few minor lingering concerns:

R2.1 In the introduction, there continues to be fluid use of terms across NSSI/ suicide/self-harm (e.g., "The success of intensive longitudinal methods in suicide research hinges on the ability to catalog converging evidence across diverging sampling and analytic methods. To date, three systematic reviews of intensive longitudinal studies on NSSI have been published").

Additional review may be useful in using terms consistently when possible, and clarifying within context when other terms are incorporated. I also think there could be rationale to simply refer only to NSSI and suicidal thoughts throughout, as other SITBs (attempts, death) are not studied here, and this may help with clarity when one or both are being discussed.

Response: We appreciate R2's thorough review of our paper and for their role in strengthening our manuscript.

The sentence highlighted above has been changed to the following:

Page 8, line 172: "The success of intensive longitudinal methods in SITB research hinges on the ability to catalog converging evidence across diverging sampling and analytic methods. To date, six systematic reviews of intensive longitudinal studies on SITBs have been published³³⁻³⁸"

We attempted to clarify throughout the introduction.

R2.2 I find the framing of non-significant effects (e.g., NSSI thoughts) a bit odd, as the language used implies that, because it's in the anticipated direction, it should be interpreted cautiously (rather than not interpreted at all)

Response: See our response to AE.3 above.

Reviewer #3:

R3.0 The authors have properly revised the manuscript.

Response: We thank R3 for their valuable input and appreciate their help in strengthening our manuscript.

Decision Letter, second revision:

22nd February 2022

Dear Dr. Kuehn,

Thank you for submitting your revised manuscript "A meta-analysis on the affect regulation function of real-time self-injurious thoughts and behaviors" (NATHUMBEHAV-210314787B). 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 within two weeks. Please do not upload the final materials and make any revisions until you receive this additional information from us.

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

Sincerely,

Samantha Antusch

Samantha Antusch, PhD
Editor
Nature Human Behaviour

Reviewer #1 (Remarks to the Author):

Thank you for allowing me to review the revised version of this manuscript. The authors have addressed all my remaining comments. This publication will be a very valuable resource for the research community, and I am happy to recommend it in its current form for publication.

Reviewer #2 (Remarks to the Author):

The authors were very responsive to reviewer concerns, and I believe the manuscript is ready for publication. Thank you.

Final Decision Letter:

Dear Mr Kuehn,

We are pleased to inform you that your Article "A meta-analysis on the affect regulation function of real-time self-injurious thoughts and behaviors", has now been accepted for publication in Nature Human Behaviour.

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

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With best regards,

Samantha Antusch

Samantha Antusch, PhD
Editor
Nature Human Behaviour