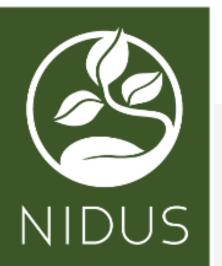
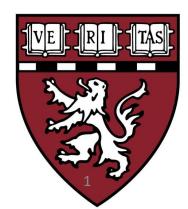
Being Truly Responsive: How to Win over Your Reviewers





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Join NIDUS to connect to Delirium Research

What is NIDUS? Network for Investigation of Delirium: Unifying Scientists!

 NIA-funded research network dedicated to advancing the study of delirium through collaborative studies, use of NIDUS research resources, career development opportunities, and dissemination of delirium science.

How to be involved:

- Apply to attend the Delirium Boot Camp 2.5-day workshop on delirium research,
 Nov. 13-15, 2022, in Chapel Hill, NC
 - Application open February 1
 - Applications due July 22
 - Join a junior faculty working group—email us!
- Participate in the American Delirium Society Meeting, June 12-14, 2022 (Indianapolis)
- Register for website <u>deliriumnetwork.org</u> to access our blog, resources and receive NIDUS newsletter and announcements, pilot and collaboration awards, webinars.

Follow NIDUS online!

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<u>Overview</u>

- So...You've done the hard work, and you've written the paper or grant
- Now, you have received back comments from reviewers with a request to resubmit.

Now....The ball is in your court!

Birth of the Kassirer Method...



The most important lesson...

- Put yourself into the mind of the harried editor—juggling so many papers and balls.
- Keep this image in your mind at all times as you respond
- Understand that your job is to make the re-evaluation of your paper as easy and painless for the editor as possible

General Principle I: Everything in one place

- Create a response letter that contains EVERYTHING the editor needs to reevaluate your paper, without needing to click open another document
 - Verbatim comments from editors and reviewers (cut and paste)—in order
 - Number the comments, so you can cross refer
 - Your thoughtful response to the comment
 - Any text changes made—cut and paste verbatim and give their Page and Line location in the revised manuscript
 - Make each of these items crystal clear
 - No page limit to a response letter (sometimes longer than the MS)—have never had a complaint from an editor

Remember: the goal is to have the response letter complete and clear, so no need to flip to any other document

Example response

CRITIQUE 1 (VERBATIM):

The authors used the DEL-IB to better understand the psychometric performance of widely used delirium identification instruments and scorings. They demonstrated its use to create new instruments. They hoped the DEL-IB might be used to create optimized delirium identification instruments and to spur the development of a unified approach to identify delirium. The challenge of this approach was that only one study site provided datasets with DSM-5 validated assessments. As a statistical approach, the authors used latent trait analysis for comparison.

RESPONSE:

We appreciate this comment from the Reviewer. We agree with the reviewer about the limitation that "only one study site provided datasets with DSM-5 validated assessments" and we have added that limitation more explicitly to our limitations section. We have added the following text to the discussion (page 11, line 289-290):

"Several limitations deserve comment. First, the Adamis dataset had a delirium prevalence that was lower than the other two studies. This is important since our simulations were based on extrapolating the Adamis results. This limitation is magnified by the fact that only the Adamis study provides reference standard DSM diagnoses."

General Principle II: Respond to everything

- Respond to every negative comment
- Make a change to the manuscript, if at all possible, to be viewed as responsive
- Don't be argumentative: Avoid pushing back, over-justifying, etc. This
 may make you feel better but wastes the time of the editor.
 - Don't defend
 - Don't apologize
- We will cover in more detail the many different types and nuances of responses

General Principle III: Adjust your mindset

- Be in the head of the editor/reviewer
- Don't see the review as a personal "attack"
- See the review as an opportunity, a collaboration, a chance to make the paper clearer
 - If something was misunderstood or missed, you have the chance to make things crystal clear
 - Remember: if the reviewer didn't get it, chances are other readers will not get it either...and it needs to be clearer

There is no such thing as great writing, only great rewriting

--Louis D. Brandeis

Specifics: Being responsive

- In general, try to make a text change if you possibly can—the only reasons for not making a change are: it will invalidate your work, or it is not feasible to do (e.g., you don't have the data, you cannot redo the study).
 - Note: these situations will be rare
- For most comments, the principle is there should be a text change somewhere in the manuscript to address the comment.
 - Revisions may require new analyses, incorporating new variables, revising tables/figures, sensitivity analyses. Do them if at all possible.
- Wording should demonstrate direct responsiveness to the editor/reviewer's comments. Use words like:
 - "To address the reviewer's concerns, the following revisions have been made (Pg, Line):..."
 - "We agree with the reviewer's comment, and thus, have edited the text as follows (Pg, Line):.."
 - "While we are unable to make this change (due to lack of data,), we agree that this is an important limitation and have addressed this in the discussion section as follows..."

Note: permission granted from all authors to share their actual response letters—to help you!!

Example 1: We agree, straightforward edit

- Reviewer comment: That you intend CAM-S to be used in addition to CAM was not clear. Specifically, it is important that readers understand that you do not think CAM-S should be used to define the presence or absence of delirium (and that CAM continues to be required for this).
 - **Response**: We agree with this important point. To clarify for the readers, we have added the following text on Pg. 6, Para 4 Lines 125-127: "<u>The CAM-S is intended to be used in addition to the original CAM algorithm; that is, the CAM-S will not yield a delirium diagnosis, only a means to quantify the intensity of delirium symptoms observed at the bedside."</u>

Example 2: We agree, more complex edit

- Reviewer comment: It is not clear if and how multiple measures within the same patient were handled in your analyses. It is not clear how the repeated CAM-S measurements within patient were handled in the analyses. This issue was especially important for the analyses of outcomes (predictive validity), as we expect a patient's CAM-S might vary quite a bit during a hospital stay.
 - **Response**: We agree that our paper was confusing in its handling of repeated measures within patients. To address this concern, we have opted to present all analyses with *one measure per patient*, the most severe CAM-S score. We tried several approaches (including mean, median, or final severity score per patient), and using the most severe score per patient was the most straightforward and logical approach. To address this comment, we have clarified in the analysis section (Pg. 8, Para 2, Lines 170-172): "For all analyses, one measure per patient (the most severe CAM-S score during hospitalization) was used; the only exception was convergent agreement where all observations were used for purposes of daily comparison."

Example 3: You disagree with reviewer

- The principle here is to be very diplomatic and try to make your case in a way that you can "win over" the reviewer.
- Reviewer comment: As mentioned on page 5 the validation cohort is @ 15 years old, though both samples used the CAM and utilized rigorous methods and training. The differences in dementia rates in the SAGES and Project Recovery samples and differences in how divergent validity was assessed should be noted as a possible limitation since SAGES did not have a dementia sample and had sig. lower co-morbidity. The authors do state the sample differences in the limitations section. Both samples use state of the art methods for delirium measurement.
 - Response: We agree with the reviewer's statements about the differences between the study cohorts—being 15 years apart and with differences in prevalence of dementia. However, these differences may also be viewed as a strength. To fully address the reviewer's concern, we have added the following to the discussion section (Pg. 13, Para 3, Lines 296-299): "While the many differences between the two study populations might be viewed as a limitation, in fact, their disparate nature lends strong support that the CAM-S will work well in different populations, under different conditions, supporting generalizability of the findings."

Example: Reviewer missed something

- This happens all the time!
- Remember reviewers are very busy people, doing things quickly, volunteer role (they're not paid to review your paper/grant)
- The burden is on you to make things clearer, to figure out why the statement was missed. Consider:
 - Moving the important missed fact to the first sentence of the section/paragraph
 - Rewording the sentence to make it clearer. *Even if you only reword it only slightly you can then underline the entire sentence in the revised manuscript*
 - Add point to the methods AND results (if applicable)

Example: You don't have data needed

- Here, you agree with the reviewer about the importance of the point (sometimes it is even your NEXT planned study).
 - You respond in a way that indicates you 100% agree with the reviewer about the importance of the point
 - Yet this point is beyond the scope of the current paper, or you don't have that data yet. You can add this would be an important area for future investigation
 - Situations where this applies:
 - Don't have needed data
 - Not feasible
 - Outside scope of present study

Example: Outside of scope of present work

- Editor's comment: We are not sure whether and what additional data you have to address the clinical and/or research utility of CAM-S. For example, are you able to assess whether a patient's course vis-à-vis delirium is associated with differences in outcomes (e.g., is a patient's outcome associated with the best, worst, or some other measure of the multiple CAM-S scores recorded during the hospitalization)? Can you tell us about the responsiveness of the CAM-S (how much variation was there in a patient's course)? Is CAM-S able to detect clinically important changes resulting from interventions aimed at alleviating delirium?
 - Response: We wish we could provide this to you, but unfortunately, this request is ahead of its time. We do not currently have the data to be able to examine the differences in outcomes associated with the many different patterns or courses patient may have throughout the course of hospitalization (that is, many possible combinations of delirium severity, duration, recurrence); or the responsiveness of the measure to intervention. We totally agree with you about the importance of this direction of work! We have acknowledged the importance of this area in the Discussion section (Pg. 15, Para 1, Lines 334-336): "Finally, examining the relative and combined contributions of delirium severity, duration, and recurrence to outcomes is essential to better define the clinical impact of delirium. While beyond the scope of the present study, these are important areas for future investigation."

Example: Reviewer didn't understand

- This is really important, and sometimes requires careful evaluation by you, your coauthors and mentor
- Sometimes the reasons for not understanding:
 - You didn't explain things well
 - You didn't set the context or framework for the study well
 - You assumed a priori knowledge of the reviewer for your prior work or recent publications
 - You used too much jargon or specific methodologic language so the reviewer could not readily follow what you did, or what you are saying
- If any of these are the case, then you need to revise
 - Set the stage, create a more <u>robust introduction</u>, more background and refs
 - Create an <u>overview section</u> (end of intro or first para of Methods)—which outlines where you are within a body of work
 - Develop a conceptual framework, and show where this work fits in

Example: Reviewer didn't understand

- Reviewer's comment: The paper appears to be an extension of the work by Gross et al. 2019 which was co-authored by some of the same authors as the present manuscript (reference 29). Gross et al. used statistical methods (item-response theory) to harmonise three delirium severity instruments: the CAM, DRS-R-98 severity scale and MDAS. The papers share clear similarities the tools, the approach, the data, and the resulting crosswalk tables. The authors acknowledge this in the Discussion, but the Gross et al. work appears to form the basis for the present study and should therefore be clearly described from the outset i.e. in the Introduction. The authors should also clarify what the added value is of their work relative to the Gross et al. study.
 - Response: Thank you for this comment, and the chance to clarify the importance and novelty of the present work. We acknowledge that the current manuscript is closely related to the Gross et al 2019 work. However, we believe there are many important new aspects and developments. In response to the reviewer's helpful comment, we have clarified the innovation in the introduction section, as follows (page 4, line 73): "Previously (14), we have described the harmonization of three delirium severity instruments (CAM, DRS, MDAS) using a single study (Better Assessment of Severe Illness, BASIL) which is also included in the work presented in this manuscript. The current manuscript expands and extends this prior work in several important ways. First, we expand the prior work by including two additional international data sources and extend the analyses with two additional instruments. Second, we expand the prior work by focusing on case identification of delirium (rather than the rating of delirium severity) and describe how each instrument relates to the DSM-based reference standard delirium diagnosis from one of the included studies. Finally, we formalize creation an item bank, which is a dataset containing each individual instrument's items and their corresponding estimated population level item response theory (IRT) parameters. This item bank is called the Delirium Item Bank (DEL-IB), which we hope will ultimately serve as a resource for the field".

Formatting the response:

- Letter format
- Table format
- Choice: Personal preference

[See examples]

Response: Letter Format

November 4, 2022

Dr. Jane Austen Executive Deputy Editor Journal of Reproducible Results

Dear Dr. Austen:

Thank you so much for communicating with us about this paper, and for inviting us to revise and resubmit. Below, please find our item-by-item response to each comment from the Editors and Reviewers, and the exact location of each revision by Page, Paragraph, and Line location in the new (revised) manuscript, attached. All text changes have been underlined. Below, we start with each comment (verbatim) by Editor or Reviewer, and then give our detailed response, with any relevant text changes provided in quotations.

Editors' Comments:

Our editorial team felt...that our readership would be less interested on such a major focus on validation itself (e.g., items such as convergent and divergent validity) but rather more interested in a paper highlighting more directly how CAM-S might be useful for research and/or patient care. We would be interested in a paper that can demonstrate the research and/or clinical utility of the CAM-S

We are not sure how to best advise you do this. Some of the potential clinical and/or research utility of CAM-S might be addressed with the results related to predictive validity showing the associations between CAM-S score and important health outcomes. But, we believe our readership would want more.

Editor's comment: We are not sure whether and what additional data you have to address the clinical and/or research utility of CAM-S. For example, are you able to assess whether a patient's course vis-à-vis delirium is associated with differences in outcomes (e.g., is a patient's outcome associated with the best, worst, or some other measure of the multiple CAM-S scores recorded during the hospitalization)? Can you tell us about the responsiveness of the CAM-S (how much variation was there in a patient's course)? Is CAM-S able to detect clinically important changes resulting from interventions aimed at alleviating delirium?

Response: We wish we could provide this to you, but unfortunately, this request is ahead of its time. We do not currently have the data to be able to examine the differences in outcomes associated with the many different patterns or courses patient may have throughout the course of hospitalization (that is, many possible combinations of delirium severity, duration, recurrence); or the responsiveness of the measure to intervention. We totally agree with you about the importance of this direction of work! We have acknowledged the importance of this area in the Discussion section (Pg. 15, Para 1, Lines 334-336): "Finally, examining the relative and combined contributions of delirium severity, duration, and recurrence to outcomes is essential to better define the clinical impact of delirium. While beyond the scope of the present study, these are important areas for future investigation."

Response: Table Format

EDITOR COMMENTS

Thank you for your interest in our journal. The editors appreciate your efforts to improve hospital care for older persons. However, we feel your paper needs substantial revision, particularly with respect to how your results are interpreted. We hope to be able to give you a better sense as to whether the paper is a good fit after assessing your revision. In addition to responding to comments of the reviewers, please address the following comments from the editors:

 We thought the novel feature of your intervention was the effort to simultaneously focus on preventing multiple complications of hospitalization simultaneously. This focus is an important contribution as there is reasonable evidence that geriatric syndromes worsened by hospitalization have common etiologies, yet most intervention studies have focused on a single syndrome, usually disability or delirium. Your introduction should highlight this novelty.

2) However, the paper seems to emphasize the single positive finding (delirium), and downplay the primary outcome, the combined outcome. We believe the paper needs to be unequivocally clear that this is a negative study with respect to the primary outcome. It is very unlikely that our journal will accept a paper that does present the findings in such a way.

Among the modifications that are necessary (a) All parts of the paper-including the key points, abstract, and discussion should incorporate this interpretation. (b) Whenever outcomes are presented or discussed, you should lead with the combined outcome. (c) You should avoid equivocating language--for example, stating that negative findings are inconclusive---you should simply state the intervention did not lead to an improvement in the outcome. (d) While you can note the positive finding with respect to delirium, it is subcomponent of the main

RESPONSES

We thank the Editors and Reviewers for their careful consideration of our paper and the helpful and constructive suggestions to improve it. We provide our point by point responses below.

We agree that the simultaneous focus on multiple syndromes is novel, and have clarified this focus more in the introduction. We now state (page 6 para 1): "These common and distressing complications share risk factors and often coexist, and people with a greater number of hospital complications have longer stays, more facility discharge and higher mortality. Previous interventions have usually focussed on preventing a single complication, particularly delirium and hospital-associated disability. There is strong evidence that multi-component interventions addressing fundamental principles of age-friendly care including mobility, cognitive and social activities, nutrition and hydration, sleep and pain management significantly reduce delirium," and may reduce falls and hospital-associated disability, suggesting the potential that systematic attention to these fundamental principles could have an additive effect on hospital complications and mediate better outcomes for older people. "

Thank you for recommending rephrasing our findings to be clearer about the negative primary outcomes through modifications in the key points, abstract and discussion.

In the key points (page 3) we have changed our wording to:

"There was no reduction in the composite primary outcome of any hospitalassociated complication of older people (46% intervention vs 52% control) or length of stay (6 days intervention vs 7 days control). Incident delirium was significantly lower in intervention wards (16% vs 31%) but other hospital complications were not reduced.

Meaning: Hospital-associated complications were very common in older inpatients. The intervention did not reduce the primary outcome of any hospital complication, although there was a significant reduction in delirium."

In the abstract we have re-ordered and amended results, and amended conclusions and relevance (page 4-5):

Formatting the response: Important principles

- Number every response (so you can cross-refer). Don't need to keep by numbering assigned by journal
- For multi-part responses by reviewers, break them up as subitems, separately numbered, and respond to each separately [See example]
- Don't repeat responses—very important.
 - Remember editors are very busy people and you don't want to add to their time (and annoy them) by repeating exact responses multiple times, just cross-refer. They appreciate this!
 - You can say: "This concern has been previously addressed in detail, see response to Reviewer 1, Comment 4 above".

DON'T

- 6. Please address the limitations of the manuscript that are threats to the internal validity of the results:
- The unit of analysis should be the wards as well as the patient
- Biased assessments by the RA cannot be excluded-please clarify
- Address the degree of inter-rater agreement by RA across the 4 hospitals
- Random allocation was determined by a flip of a coin, creating a possible allocation bias.
 Any quality checks? Was the intervention, EWE and primary outcomes, known by the individual?
- The study was negative: that needs to be better emphasized and explained in the Discussion.
- The secondary outcome of delirium could have been a chance finding resulting from patient risk factors for incident delirium or ward assignment. Ascertainment of delirium was based on the 3D-CAM but was there independent confirmation of the clinical diagnosis (for example, review of chart)?
- Mention the costs of the intervention including training of RA
- In Methods section, give description of usual care (did the intervention patients receive usual care plus EWE?) Explain why different types of wards were selected for intervention versus control groups

Thank you for these clear requests and we respond to each of these points in turn:

- Regarding unit of analysis, please see our response to question 2 above
- As a pragmatic trial where the research assistants were collecting data on two wards per hospital, they may have been aware which ward was implementing Eat Walk Engage through staff or patient comments or by seeing the EWE-SF or EWE-MPA on the intervention ward, although we did not share the study hypotheses or analysis methods with any of the research assistants. We minimised the likelihood of this influencing outcome assessments through clear outcome definitions, structured questions and pre-defined information sources; training the RAs in reliable measurement; the investigators cross checking a random sample of ten chart extractions per ward; and using a combination of outcomes, including "hard" outcomes such as length of stay, discharge destination, mortality and readmissions. We have provided additional information about these measures in the methods section (page) as follows: "Research assistants received two full days of training from investigators AM and PM including pilot testing patient interviews, watching 3D-CAM training videos and being observed performing the 3D-CAM on several patients.. Two investigators completed check data extraction on a convenience sample of ten charts for each ward to identify any areas of misinterpretation. Data collection was supported by a comprehensive data manual and weekly telephone support by the data manager and chief
- The statistician who undertook allocation was not involved in any aspect of the intervention design or delivery beyond the statistical analysis.
 Although he knew the planned outcomes from the protocol, he was only provided with ward numbers to allocate, and had no access to data about the ward type, ward practices, or patient characteristics at the time of randomisation
- We have made the negative primary outcomes clearer throughout the document as outlined in the response to the Editors (point 2)
- As outlined in the methods, delirium was assessed using the three-minute diagnostic interview for CAM-defined delirium (3D-CAM) ¹⁸

DO

Please address the limitations of the manuscript that are threats to the internal validity of the results:	Please see our response to point 2 above	
The unit of analysis should be the wards as well as the patient		
7. Biased assessments by the RA cannot	We agree with the reviewer that in a pragmatic	
be excluded-please clarify Address the	trial where the research assistants were	
degree of inter-rater agreement by RA	collecting data on two wards per hospital, they	
across the 4 hospitals	may have been away	-1
	patient comments or	الر
	EWE-MPA on the inf	S
	methods with the resemble part 165ports	,
	minimised the likelihood of biased outcome	
	assessments through clear outcome definitions.	
	structured questions and pre-defined information	
	sources; training the RAs in standardized and	
	reliable measurement; the investigators	
	conducting a blinded reliability cross-check in a random sample of ten chart extractions per	
	ward; and using a combination of outcomes.	
	including "hard" outcomes such as length of	
	stay, discharge destination, mortality and	
	readmissions.	
	We have provided additional information about these measures in the methods section (page 11	
	para 2) as follows:	
	"Research assistants received two days of	
	training from the chief investigator and program	
	manager including pilot testing patient	
	interviews, watching 3D-CAM training videos	
	and being observed performing the 3D-CAM on several patients. Two investigators conducted a	
	reliability cross-check of data extraction on a	
	convenience sample of ten charts for each ward	
	to identify any areas of misinterpretation. Data	
	collection was supported by a comprehensive data manual and weekly telephone support by	
	the data manager and chief investigator."	
	We did not formally test inter-rater agreement,	
	but implemented the quality measures outlined	
O. Dondon ellevetine was determined by	above to minimize the risk of bias	
Random allocation was determined by a flip of a coin, creating a possible allocation	The statistician who made the random allocation was blinded to the intervention and was not	
bias. Any quality checks? Was the	involved in any aspect of the intervention design	
intervention, EWE and primary outcomes,	or delivery beyond the statistical analysis.	
known by the individual?	Although he knew the planned outcomes from	
	the protocol, he was only provided with ward	
	numbers to allocate, and had no access to data about the ward type, ward practices, or patient	
	characteristics at the time of randomisation.	

Do's and Don'ts: Don't be argumentative or defensive

- Being argumentative equates with being non-responsive.
- Note: You only need 1-2 non-responsive responses for an editor's eyes to glaze over, and their finger to push the "reject" button.

Rate responsiveness: Trial 1

Reviewer Comment:

Table 1 provides very limited or specific information about the specific bedside or hands-on intervention strategies. Please provide much more specific information. Is there an appendix or supplemental table to enhance the description of these strategies? The concept of overcoming barriers is less relevant to readers who might wish to implement the program in their hospital.

Response:

Reporting of complex interventions within a single article is challenging, and more detail of specific strategies will be published in our implementation paper. In table 1 we have deliberately used the approach of matching example strategies to barriers, because the concept of overcoming barriers is central to our theoretical approach using implementation science. The i-PARIHS theory and framework underpinning the program states that successful implementation of evidence into clinical practice is an interaction between the innovation (in our case, the key principles), the recipients (older patients and ward staff caring for them) and the context (including a large range of patient, staff and organisational barriers and enablers which differ between different wards). Navigating this interaction involves a role and set of strategies called facilitation. The intervention thus comprises both the implementation ('change') strategies initiated by the (additional) facilitator as well as the clinical interventions delivered by (existing) staff, and both are 'tailored' to the local context. As mentioned in our discussion, we recognise that our approach makes it hard to manualise or precisely replicate our intervention, but are actively investigating effective scale and spread through our state-wide expansion program as well as through pilot programs nationally and internationally.

Rate responsiveness: Trial 2

Reviewer Comment:

Table 1 provides very limited or specific information about the specific bedside or hands-on intervention strategies. Please provide much more specific information. Is there an appendix or supplemental table to enhance the description of these strategies? The concept of overcoming barriers is less relevant to readers who might wish to implement the program in their hospital.

Response:

Thank you for requesting further clarification, which we have addressed through redrafting of the intervention description and substantial modification to Table 1, as outlined in our response to reviewer 2 (point 1). To address the reviewer's comment, in this table we have now removed discussion of barriers and instead aligned potential interventions with the program principles and goals, according to our program logic model (eTable 2).

Do's and Don'ts: Don't use jargon

- What is jargon? It consists language and abbreviations that are only understandable to persons within a very specialized field.
- Use instead:
 - Language that is clear, accessible, and interpretable by intelligent lay people
 - Test: see if what you have written can be understood by an intelligent person who is NOT in your field
 - My sons in college and med school (or my husband in basic science) sometimes served as my "proof-readers", especially for the introductions to papers, and significance sections of grants...if they could "get it", then I knew I had passed the bar.

Does this method work?

- For me personally, my acceptance rate following a major R&R went from <50% to nearly 100%.
- In fact, I think only 1-2 times (out of >250 resubmissions) since Dr. Kassirer taught me this method in 2000 that an R&R has been rejected after I applied the Kassirer method.
- Many testimonials from others....
- Try it out!!!!!