Comparative Effectiveness Review Disposition of Comments Report

Research Review Title: *Strategies to De-escalate Aggressive Behavior in Psychiatric Patients*

Draft review available for public comment from January 28, 2016, to February 23, 2016 (and for peer review until February 25, 2016).

Research Review Citation: Gaynes BN, Brown C, Lux LJ, Brownley K, Van Dorn R, Edlund M, Coker-Schwimmer E, Zarzar T, Sheitman B, Palmieri Weber R, Viswanathan M, Lohr KN. Strategies to De-escalate Aggressive Behavior in Psychiatric Patients. Comparative Effectiveness Review No. 180. (Prepared by the RTI-UNC Evidence-based Practice Center under Contract No. 290-2015-00011-I) AHRQ Publication No. 16-EHC032EF. Rockville, MD: Agency for Healthcare Research and Quality. July 2016. www.effectivehealthcare.ahrq.gov/reports/final.cfm.

Comments to Research Review

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The tables below include the responses by the authors of the review to each comment that was submitted for this draft review. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the Agency for Healthcare Research and Quality.

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Section	Commentator and Affiliation	Comment	Response
Executive Summary	TEP #5	In Table of Tables (pgs. 7-8), superscript letters accompanying titles were misleading for me in this section, I was looking for a footnote or something at the end of this section.	Thank you for catching these typos. We have now corrected them.
Executive Summary	TEP #5	Executive Summary pg. 10 ln. 50: "…involve both nonpharmacologic and pharmacologic..": This language emphasizes pharmacologic and seems to de-emphasize behavioral, cognitive, emotional, social, organization, and environmental aspects of intervening at any point "along this continuum." Perhaps consider rewording to reflect more broad and inclusive perspectives.	We have modified this phrase in the Executive Summary and in the Introduction section of the report to be more inclusive. It now reads, "they can involve a wide variety of strategies that can have educational, behavioral, emotional, organizational, environmental, and/or pharmacologic components."
Executive Summary	TEP #5	Executive Summary pg. 10 ln. 55: wording change "It can involves unit.."	We corrected. Thank you.
Executive Summary	TEP #5	Executive Summary pg. 15 ln. 44: it may be helpful to have a bit of descriptive info about KQs rather than saying "KQ 1a, three CRTs; KQ2, three RCTs…" hard cognitively to remember all KQs as a reader	We have reworded these in the Executive Summary and in the Results section of the report to read: "KQ 1a (benefits of prevention), three CRTs; KQ 2b (harms of de-escalating aggression), three RCTs; KQ 1c (harms of reducing seclusion/restraint use), one RCT and one retrospective cohort study."
Executive Summary	TEP #5	Perhaps clarification on "multimodal" interventions in particular may be helpful to most readers. Perhaps just a brief statement similar the one used in Discussion "which include multiple commponents that may be part of other strategies"?	We agree and have added text as you suggested. Thank you.

Section	Commentator and Affiliation	Comment	Response
Executive Summary	TEP #5	Executive Summary pg. 24, section "Implications for Clinical and Policy Decisionmaking" – authors mention the implementation decisions may need to be delayed without further evidence. I agree with this comment, and it may be worthwhile to again discuss how quality measures and our current performance monitoring strategy may exert some level of tension along these lines. Eg, what impact, if any, does delaying implementing strategies to improve performance have, when performance is actively being monitored, and improvement heavily incentivized? Quality measures that are not actually actionable based on evidence-based practices present a problem for decision makers. (Not the authors job to answer this question, obviously, but perhaps this is an opportunity to point out this potentially difficult reality for decision making).	We agree, and have added the following sentence to a list of important questions in the Executive Summary and in the Discussion section of the report: "What is the role of quality measures, designed to incentivize higher quality care, when the evidence base for those measures is unclear?"

Section	Commentator and Affiliation	Comment	Response
Executive Summary	Phyllis Foxworth (Depression and Bipolar Support Alliance)	**Structured Abstract:** DBSA applauds the project's objective on page ii: "To compare the effectiveness of strategies to prevent and de-escalate aggressive behaviors in psychiatric patients in acute care settings, including interventions aimed specifically at reducing use of seclusion and restraints." However we are disappointed that language in the Conclusion on that same page stigmatizes patients by not recognizing behaviors as symptoms of underlying medical issues of the brain by stating: "Given the ethical imperative, clinical mandate, and legal liability associated with failure to assess and manage violence risk…" DBSA believes language is important. Words can be used to lift up or tear down. Language can be used to either fuel or extinguish the flames of discrimination and stigma surrounding mental health. Patient-centered and wellness-focused language that is built on respect for all is of utmost importance if we are to build up, rather than tear down, and succeed in changing the way the world views mental health conditions and the people who live with them. Language sets the tone for the research project and those who read the report. DBSA believes that respecting the dignity of the patient and the mental health condition that precipitates the patient's arrival at the acute care setting will better serve the identified project aims of comparing effectiveness of strategies that decrease (1) aggressive behaviors, and (2) use of seclusion and restraints.	We have modified this wording in the abstract, the Executive Summary, and the Discussion section of the report to avoid any suggestion of stigma. It now reads: "Given the ethical imperative for treating all patients with dignity, the clinical mandate of finding evidence-based solutions to these mental health challenges, and the legal liability associated with failure to assess and manage violence risk across the treatment continuum, the need for evidence to guide clinical and policy decisionmaking for de-escalating aggressive behavior is critical."
Introduction	Peer Reviewer #1	Appropriate.	Thank you.
Introduction	Peer Reviewer #2	Fine	Thank you.
Introduction	Peer Reviewer #3	The analytic framework is well designed on p. 6.	Thank you.

Section	Commentator and Affiliation	Comment	Response
Introduction	TEP #1	The introduction is clear and addresses the broad scope of the problem. The introduction also identifies the focus of the review, populations of interest and the focus of the study. The model helps a great deal and one can follow how the questions were derived.	Thank you.
Introduction	TEP #2	Introduction is clear and concise.	Thank you.
Introduction	TEP #3	Relevant	Thank you.
Introduction	TEP #4	See above [General comments].	We have addressed all of TEP# 4's comments in the General Comments section, where they were listed in the submitted review.
Introduction	TEP #5	Pg. 32, lines 49-57: Perhaps mention the implied assumption of using such quality measures, that lower is better. Not only closely-followed but desirable performance can be tied to incentives, meaning that we really should have confidence that such measures are appropriate tests of "quality"- based on good evidence base, etc.	We agree. We have modified the text beginning at line 49 as follows: "Finally, using seclusion and restraints is closely monitored as a quality-of-care measure, particularly for psychiatric patients in hospital settings. Various organizations have defined quality care as the lowest possible use of seclusion and restraint, making it important to understand what evidence base exists behind this definition."
Introduction	TEP #5	This section is well detailed and provides a high-quality introduction to the topic area. I think the intro makes a strong argument about why this review is important to conduct. I have no negative or concerning notes to raise about the introduction. The above point is my only suggestion.	Thank you.

Section	Commentator and Affiliation	Comment	Response
Introduction	Phyllis Foxworth (Depression and Bipolar Support Alliance)	**Key Questions:** DBSA agrees with the overview of the Key Questions (ES-2) that interventions involve both pharmacologic and nonpharamcologic strategies and that the strategies target a reduction in either aggressive behavior or use of seclusion and restraints.	Thank you.
Methods	Peer Reviewer #1	For the most part, I found the inclusion and exclusion criteria justifiable, but I do question the inclusion of delirium as a 'psychiatric illness' (even though the diagnosis does appear in DSM-V). The profound confusion and altered level of consciousness typically present in delirium likely makes non-pharmacologic approaches, such as de-escalation techniques, of limited value, especially compared to agitation in more traditional psychiatric states such as those due to psychosis, paranoia or mania, where a patient may still have a level of coherent thought and understanding. I did very much appreciate, however, the addition of consideration of quality of life and longer-term issues for patients around their treatment during an agitated or aggressive phase, in addition to side effects. Too many studies of agitation/aggression have focused solely on reduction of level of agitation response to pharmacologic agents, and would consider an outcome where a patient's agitation was quelled but the patient was also rendered unconscious for 24 hours, or had severe dystonia or other side effects, or long-lasting dysphoria, or future reluctance to seek psychiatric care, as fully positive and equal to an approach that calmed a patient without side effects, oversedation or lasting psychologic impact. Clearly such studies do not present clinicians with a full understanding necessary for an informed choice in treatment approaches -- the fact the authors recognized this in their discussion is to be commended.	We acknowledge and thank the reviewer for the appreciation of our consideration of quality of life and long-term issues. Regarding the inclusion of delirium: we agree that delirium is a psychiatric diagnosis distinct from what many consider a “traditional” psychiatric diagnosis, but inclusion of delirium was specifically requested by supporters for this topic, and is a key question for clinicians working in acute care medical, surgical, and emergency settings, so we believe it is important to keep this information in the report.
Methods	Peer Reviewer #1	Statistical methods used were appropriate.	Thank you.

Section	Commentator and Affiliation	Comment	Response
Methods	Peer Reviewer #2	It fine for this work. I personally do not think that it was the appropriate study or correct population to study in the first place. For one, the public state hospitals have been doing this work for many more years than the majority of private hospitals. Second, most of the EU research reports are better compared to the US public mental health hospitals; the EU and others are all mostly government run.	We appreciate the reviewer's comments. We report on the eligible and relevant data that our search identifies, and we note any limitations to the evidence review process in the Discussion section.
Methods	Peer Reviewer #3	Inclusion and exclusion criteria are reasonable. There were no outcomes measures identified. Search criteria are fairly well developed. Statistics were not used--paper was basically a re-review of the literature which did not prove to be fruitful the last time.	Thank you.
Methods	TEP #1	The inclusion and exclusion criteria for the review and the articles reviewed are justified and logical. The search strategies are well defined and the overarching model helps to define the strategies for the questions. The definitions and diagnostic criteria for the outcomes are well defined but do point out the lack of standardization that limits the SOE of the studies currently reported. The inclusion of the literature from other countries adds significant breadth and depth to the work. The attempts to cover all of the information including the CRT, RCT's and other types of pre post test studies gives a clear understanding of the breadth of the review. The statistical methods and criteria are appropriate and well described in those studies with some SOE.	Thank you.
Methods	TEP #2	All are fine.	Thank you.
Methods	TEP #3	yes	Thank you.

Section	Commentator and Affiliation	Comment	Response
Methods	TEP #5	Are the inclusion and exclusion criteria justifiable? Yes, I find the inclusion exclusion criteria are fully described and reproducible, as well as scientifically justified and sound.	Thank you.
Methods	TEP #5	Are the search strategies explicitly stated and logical? Yes, given the author's presentation of methodology, I believe one could precisely replicate this study.	Thank you.
Methods	TEP #5	Are the definitions or diagnostic criteria for the outcome measures appropriate? Yes, first, I found the author's search for appropriate outcomes rather comprehensive given the scope of this review. It is an impressive search for relevant outcomes to the topic. I agree with their grouping of outcomes, approach to relating them through a conceptual framework, and tie to their Key Questions. The study strikes me as a cogent and reasonable systematic assessment of the topic.	Thank you.
Methods	TEP #5	Are the statistical methods used appropriate? Yes, the authors appear to have taken great care in applying AHRQ's and other validated methods for assessing risk of bias and strength of evidence. They have made what I consider the appropriate decision not to pursue meta-analyses with the results obtained. This is a particular strength of the report, that the gaps in research are so clearly identified.	Thank you.

Section	Commentator and Affiliation	Comment	Response
Results	Peer Reviewer #1	The detail in the results section is appropriate, the characteristics of the studies are clearly described, and the key messages are explicit and applicable Figures, tables and appendices are adequate and descriptive. I found no studies that the investigators overlooked. Once again, however, I do question the decision to include agitation due to delirium alongside agitation due to more traditional psychiatric diagnoses.	We appreciate the reviewer's comments. Regarding delirium: we agree that delirium is a psychiatric diagnosis distinct from what many consider a "traditional" psychiatric diagnosis, but inclusion of delirium was specifically requested by supporters for this topic, and is a key question for clinicians working in acute care medical, surgical, and emergency settings, so we believe it is important to keep this information in the report.
Results	Peer Reviewer #3	Detail is appropriate to the type of study. Figures, tables, and appendices were only minimally required for the display of data.	Thank you.
Results	TEP #1	The amount of detail presented in the results section is very appropriate and quite detailed. Impressively so actually. The studies included are well described and well written. At no point was I lost. There were some times when they noted that the SOE was insufficient and I had to refer back to the earlier sections to recall the criteria. The figures, and tables follow each section and are well described. There was no exclusion of studies that I am aware of and I thought the reviews, including the European content was beneficial.	Thank you.
Results	TEP #2	Clear	Thank you.
Results	TEP #3	yes	Thank you.

Section	Commentator and Affiliation	Comment	Response
Results	TEP #4	See above [General comments].	We have addressed all of TEP# 4's comments in the General Comments section, where they were listed in the submitted review.
Results	TEP #5	Pg. 51, ln. 54: wording to correct – "…of articles. , #209Patient characteristics…"	We have deleted the citation, which was a copy/paste error.
Results	TEP #5	Is the amount of detail presented in the results section appropriate? Yes, the amount of detail is appropriate, and I appreciated the author's presentation of results in multiple formats, providing a comprehensive level of detail.	Thank you.
Results	TEP #5	Are the characteristics of the studies clearly described? Yes, I found the pertinent information sufficiently described. The particular importance in this review is lack of data points across studies rather than a problem of adequately capturing ample or overwhelmingly large amounts of data points. The authors sufficiently described those studies that were included, and were clear in highlighting gaps throughout as well.	Thank you.
Results	TEP #5	Are the key messages explicit and applicable? Yes.	Thank you.
Results	TEP #5	Are figures, tables and appendices adequate and descriptive? I believe so. I commend the author's display of information.	Thank you.
Results	TEP #5	Did the investigators overlook any studies that ought to have been included or conversely did they include studies that ought to have been excluded? I found their inclusion and exclusion decisions acceptable.	Thank you.

Section	Commentator and Affiliation	Comment	Response
Results	Phyllis Foxworth (Depression and Bipolar Support Alliance)	**Key Questions [continued]**: However DBSA believes the study categories: interventions, staff training, risk assessment, multimodal, environmental, and medication protocols are limiting with a noticeable lack of categories around patient-centered care. We don't know if this is because no eligible studies exist or if these categories were intentionally left out. We strongly encourage AHRQ to address this missing focus area.	Patient-centered categories were not intentionally left out. The categorizations identified here did not limit our search; rather, they reflect what interventions in eligible studies are described in the literature. These include patient-centered ones (e.g., environmental interventions, strategies to decrease use of seclusion and restraints) as well as outcomes that reflect patient-centered measures.
Results	Phyllis Foxworth (Depression and Bipolar Support Alliance)	**Recommendations:** We agree with the findings of the report that insufficient research exists to provide guidance and direction on how best to prevent and de-escalate aggressive behavior in acute care settings and that more research is required.	Thank you.
Results	Karen Kanefield (American Psychiatric Association)	The systematic review includes one study (Michaud et al., 2014) of restraint use that is quite different from the other included articles. Although delirium is a psychiatric condition, the patient population in the study of Michaud and colleagues involved intubated patients in an intensive care unit. Such individuals have very different medical and psychiatric issues than individuals who are evaluated and treated on psychiatric units or in emergency settings. At many places in the document, the unique aspects of this study are not highlighted, which could lead a reader to draw incorrect conclusions. For example, on pp. 17, 22, 24, 58, 72, 88 and 90, it would be helpful to include the fact that these were intubated ICU patients when making reference to the study and its findings. Alternatively, the authors may wish to exclude this citation from the report.	We agree that delirium is a psychiatric diagnosis distinct from what many consider a "traditional" psychiatric diagnosis, but inclusion of delirium was specifically requested by supporters for this topic, and is a key question for clinicians working in acute care medical, surgical, and emergency settings, so we believe it is important to keep this information in the report. We agree that clarification that these patients were intubated is informative, and we have added these clarifications in the Results section.

Section	Commentator and Affiliation	Comment	Response
Results	Karen Kanefield (American Psychiatric Association)	Also, on p. 24 and on p. 90, the citation numbering for the Michaud et al., paper is incorrect and exchanged with the citation number for the Currier et al., 2004 article.	We have moved both citations to their correct locations in the text.
Results	Karen Kanefield (American Psychiatric Association)	In the discussion of the study by Putkonen and colleagues (2013), the text describes on p. 66 gives an excellent description of the intensity and duration of training and implementation support that was used in applying the Six Core Strategies during the clinical trial. This significant investment in training and support may be worth including in discussing the clinical and policy decision-making implications of this trial (on p. 24 and on p. 90).	We appreciate your comment. Unfortunately, the Putkonen article has now been excluded from the review due to determining that it does not meet the review's definition of acute care setting.
Discussion/Conclusion	Peer Reviewer #1	The implications of the major findings are clearly stated. Are The limitations of the review/studies described adequately, especially the recognition that the present literature base is definitely insufficient on this topic. The future research section clear and easily translated into new research, and indeed calls for more such work to be done.	Thank you.
Discussion/Conclusion	Peer Reviewer #2	Discussion and Conclusion did the best it could with the limited available results. Again, violence in mental health inpatient settings is a very complex issue and cannot be addressed by a list of interventions alone.	Thank you.
Discussion/Conclusion	Peer Reviewer #3	The key message, that based on the paucity of evidence, implications are for future research rather than clinical or policy judgments was well stated. Advice to researchers was clear as per ES-17. We know the answers are not in traditional published literature. Much of the basis is in practice-based experience that needs to be quantified.	Thank you.

Section	Commentator and Affiliation	Comment	Response
Discussion/Conclusion	TEP #1	The implications of the major findings are clearly stated and do a nice job of summarizing the evidence to date. The cmparison of methods from assessment to medication comparators to the interventions and the research on each are clearly stated.	Thank you.
Discussion/Conclusion	TEP #1	The limitations are nicely reviewed and consistent with the systematic reviews. there is no literature that is missing and not covered under the umbrella searches that I am aware of.	Thank you.
Discussion/Conclusion	TEP #1	The future research section is clear and translatable but I found it to be pretty standard. I would suggest some part be put in on 1. Difficulties of doing RTC's and other studies in this area. Sort of like saying we wiill give someone schizophrenia in order to get a pure control group. This is not going to happen. However, the discussion did point out some things that I think recommendations can be made for... 1. Based on the reviews, what are the minimum descriptors of interventions that should be included in studies and reports, 2. What is the minimum data set that should be included in these reports, 3. What are the minimum instruments and measures that should be included in studies and reports, and 4. What are the meaningful clinical outcomes that should be included in studies and reports. Based on the lack of sufficient evidence and the review, this was like comparing apples to grapes to lemons. One of the report recommendations that would be helpful to future change in the field would be a set of recommendations for future studies and reports.... This would give the report some solid teeth and not just explain that the evidence is not sufficient but provide a rallying point for future solutions.	We appreciate the reviewer's prompt to try to make our future recommendations more informative. We have made recommendations about we believe need to be next steps for the field, but given the largely limited evidence available, the specifics of recommendations (e.g., this specific outcome should be tested) are necessarily constricted. We had already made some specific recommendations that we think are necessary next steps: Describe components clearly, assess the comparative accuracy of risk assessment protocols, and use consistent and clinically meaningful measures that are more patient-centered. To these points, we now added in the Discussion and Executive Summary, "Selection of these outcomes needs to be informed by key stakeholders, including patients."

Section	Commentator and Affiliation	Comment	Response
Discussion/Conclusion	TEP #2	My main issue is how to best use what is known. The odds of large well conducted studies addressing these questions is very low. I understand the purpose of the review, but it would be good if the studies weren't just reduced to a categorical. I know this is difficult and perhaps is something better done by an expert panel, but we need better guidance on what to do to reduce risk. Another issue is that increasingly specific hospitals are getting a higher concentration of at risk patients.	We agree with the clinical importance of using what is known and yet, it would be beyond the scope of a systematic review to make recommendations where there is no evidence. The one place where we could make a recommendation would be to say that there is low quality evidence, but still evidence, for the use of risk assessment and thus, more research is needed in this area. In other words, this review simply clarifies and makes upfront to the public that the majority of existing policies are primarily informed by ethical beliefs (i.e., that reduced seclusion and restraint is preferable from a human rights standpoint) rather than evidence of effectiveness or safety.
Discussion/Conclusion	TEP #3	yes	Thank you.
Discussion/Conclusion	TEP #4	Although the review was technically executed satisfactorily, the clinical considerations outlined above can be considered as discussion points. Readers can be directed elsewhere for additional information regarding these issues.	The reviewer makes an excellent and very clinically relevant point. We have no addressed these clinical considerations by referring to the evidence base for agitation by citing the Krakowski paper and a paper by Bosanac.
Discussion/Conclusion	TEP #5	I would again encourage highlighting the tension that a lack of evidence might create for monitoring quality. Not encouraging authors to comment or speculate on actual impact of issue, other than to point out that additional research may help us understand the impact of evidence on performance monitoring and decision making.	We agree and have added this point in the Implications sub-section in the Discussion.

Section	Commentator and Affiliation	Comment	Response
General	Peer Reviewer #1	Yes, the report is clinically meaningful, the target population and audience are explicitly defined, and key questions are appropriate and explicitly stated.	Thank you.
General	Peer Reviewer #1	Clarity and Usability: The report is well structured and organized. The main points are clearly presented. And while the main conclusions are centered around the determination that the present literature base is insufficient, this is an important contribution to present understanding, and underscores the need for more quality and data-driven research in this area in the future.	Thank you.

Section	Commentator and Affiliation	Comment	Response
General	Peer Reviewer #2	This report in clinically meaningful in a moderate way. Since no interventions were found to be of clinical significance this writer is not sure what the take away is other than "need more research". Of course, since the issue of violence in inpatient settings is very complicated and has not been studied much, if at all, one question is to why the focus on RCT when that evidence base is not there. Why not more of a focus on qualitative research to help build some basic information?	We clarify that two interventions—risk assessment protocol, and multimodal interventions—were found to have supporting evidence, even if low strength of evidence, so there is data to guide decisions. The question about focusing on qualitative research is thoughtful and important one. We note that systematic reviews always start with a focus on potential or actual "best evidence" -- that is, evidence that can show a causal link between the interventions and the outcomes. That perspective dictates starting with randomized controlled trials or certain other study designs (e.g., nonrandomized controlled studies) that come close to RCTs (all other things equal, such as levels of risk of bias). Many observational studies (i.e., "qualitative research") might have a fairly high probability of being high risk of bias for such purposes -- that is, they would not be able to contribute to answering the key questions. Our charge was to be able to address these key questions in a systematic review, and these questions and the methods to address them were informed by our Technical Expert Panel and approved by AHRQ (after public review). That said, the qualitative research piece is very important—but it would be the focus of a different kind of review.

Section	Commentator and Affiliation	Comment	Response
General	Peer Reviewer #2	Clarity and Usability: Yes to all these questions as a written report. Not sure any new information or understanding was contributed other than we have a long way to go.	Thank you.
General	Peer Reviewer #3	Questions are fairly well stated. It became clear very early in the document that the empirical data was not available and that more research had to be done. It seemed a bit of a paperwork exercise to go through the entire process with much repetition of the same concerns about the lack of rigorous study and the inability to draw conclusions. That leads me to rate clinical meaningfulness as low. It is important to learn that we don't know and the recommendation for development of a stronger evidence base is helpful if it is acted upon. The charge to the field to do research is the most helpful part of the paper.	We appreciate the reviewer's observation. We think that the findings of low SOE for two interventions indicates that there is some evidence that two interventions—risk assessment protocols, and multimodal interventions, do have some evidence support. We agree that the research recommendations can be informative.
General	Peer Reviewer #3	Clarity and Usability: I think the study restates the results of former reviews. It adds the finding that application of risk assessment and management to ALL patients (not just those who are actively aggressive) MAY decrease aggression. I do not rate that as highly significant new information or understanding.	This review is the first one to compare the effectiveness of these strategies in aggressive populations (not just agitated ones), so the violence bar is higher. It clarifies the current body of evidence.
General	TEP #1	From an evidence based perspective, this is an excellent report demonstrating the state of the science. The audience and populations of interest are accurately described	Thank you.

Section	Commentator and Affiliation	Comment	Response
General	TEP #1	Clarity and Usability: The report well structured and organized and the authors are to be commended for tackling an important task in the care and management of the acutely ill. The main points are presented but unfortunately there is not enough good evidence to provide direction, which limits policy or practice decisions. This is where the suggestions for data based on 1. Based on the reviews, what are the minimum descriptors of interventions that should be included in studies and reports, 2. What is the minimum data set that should be included in these reports, 3. What are the minimum instruments and measures that should be included in studies and reports, and 4. What are the meaningful clinical outcomes that should be included in studies and reports. would be a seminal starting points.	We appreciate the reviewers prompt to try to make our future recommendations more informative. We have made recommendations about we believe need to be next steps for the field, but given the largely limited evidence available, the specifics of recommendations (e.g., this specific outcome should be tested) are necessarily constricted. We had already made some specific recommendations that we think are necessary next steps: Describe components clearly, assess the comparative accuracy of risk assessment protocols, use consistent and clinically meaningful measures that are more patient-centered. To these points, we now added in the Discussion and Executive Summary, "Selection of these outcomes needs to be informed by key stakeholders, including patients."
General	TEP #2	Yes. The report is very clear and outlines strengths and weaknesses of this approach.	Thank you.
General	TEP #2	Clarity and Usability: I thought it was well written and logical.	Thank you.
General	TEP #3	yes. yes It would be helpful to know about the sex ratios to see if sex differences change to findings. Also the IQ of patients, specifically intellectual disability might indicate different interventions for that population.	We agree that this information would be informative, but the limited evidence did not allow us to address the role of moderators (e.g., age, sex, intellectual disability).

Section	Commentator and Affiliation	Comment	Response
General	TEP #3	There is no mention of comfort rooms as an alternative to seclusion and this intervention has been helpful in some settings to reduce the use of seclusion. The Open door seclusion room study is not the same as a comfort room .Also the patient in the open door study who tried to commit suicide should not have been in a seclusion .	We agree that such an intervention may be in use and described in the literature, but no such intervention study met our eligibility criteria.
General	TEP #3	There are no studies about using virtual reality strategies to reduce seclusion or restraint, but they are effective in treating distress in psychiatric conditions like PTSD and should be used.	We agree that such an intervention may be in use and described in the literature, but no such intervention study met our eligibility criteria.
General	TEP #3	I could not find a summary of harms related to restraint particularly suffocation and yet the joint commission reports about 15 deaths a year due to this. I think Pulse Oximetry if widely used might help identify patients at risk for suffocation and halt restraint when oxygen saturation dropped, The Report does not mention PTSD reactions as a cause of seclusion and restraint or a focus of staff training, but this is potentially an issue. Generic Staff training may fail to help these patients. So I think the report should indicate that staff training needs to be specific to the population being treated otherwise it might not target the symptoms that lead to aggression.	We appreciate your thoughtful clinical recommendations. We did not find any studies meeting inclusion criteria for this review that provided data on the use of pulse oximetry to reduce harm from, or the moderating effect of specific diagnoses (such as PTSD) on the use of, seclusion and restraint.
General	TEP #3	IT is not clear in the report if patient attacks on staff have different triggers and interventions that patient on patient violence and this is important because at least some studies show that the 6 core strategies are much more effective in reducing patient on staff violence but not patient on patient violence.	We agree that such a distinction may be relevant and described in the literature, but no such intervention study with this information met our eligibility criteria.

Section	Commentator and Affiliation	Comment	Response
General	TEP #3	Finally the study reports on interventions that have been used in the past. Novel interventions are not addressed and I think the report should note that possibly new approaches in addition to comparing know ones is a way forward to dealing with aggression.	We agree that such interventions may be in use and described in the literature, but no such intervention study met our eligibility criteria. However, we have now made reference to this limitation in our Discussion section in the Limitations of the Systematic Review process section.
General	TEP #3	Clarity and Usability: yes	Thank you.
General	TEP #4	Although the stated objective was to "To compare the effectiveness of strategies to prevent and de-escalate aggressive behaviors in psychiatric patients in acute care settings, including interventions aimed specifically at reducing use of seclusion and restraint," the search and resultant work product may have been unduly narrow and may have omitted aspects of care that are considered routine in public psychiatry.	We agree that the search was focused. However, due to budgetary constraints, the current scope was prioritized with input from the topic nominator and Key Informants. We have discussed this point in our “Limitations of the Systematic Review Process” section. We do not believe that this narrowed scope affects the validity of our findings-- they do apply to the identified population. However, we agree that a broader scope might make the findings more usable by, for example, addressing the effectiveness of the six core strategies. We have discussed this point in our “Limitations of the Systematic Review Process” section.

Section	Commentator and Affiliation	Comment	Response
General	TEP #4	Clinically, strategies for the management of persons who are aggressive fall under two broad categories: 1 - Management of acute episodes of agitation/aggression and 2 - The reduction of intensity and frequency of future episodes of agitation/aggression. A caveat is that agitated behavior does not always escalate into aggressive behavior and aggressive behavior is not always preceded by agitation. Discussing this would help place the report into clinical context, and provide an expanded opportunity to discuss additional RCTs and meta-analyses that have examined interventions for agitation, with the understanding that intervening early in managing agitation is key in reducing potential aggression and physical harm to self and others. It would also make available the opportunity to discuss strategies to decrease aggression over time that have been tested in RCTs and missed in this report (e.g., Krakowski et al. Arch Gen Psychiatry. 2006 Jun;63(6):622-9), and the general strategy of decreasing hostility over time, which although 'hostility' was searched for, was not elaborated upon in the longer-term context (see also Volavka et al. Eur Psychiatry. 2016 Jan;31:13-9).	The reviewer makes an excellent and very clinically relevant point. We had noted this limitation previously in our limitations section, but now have referred to evidence base for agitation by citing the Krakowski paper and a paper by Bosanac.
General	TEP #4	Clarity and Usability: See above [General comments].	We have addressed all of TEP# 4's comments in the General Comments section, where they were listed in the submitted review
General	TEP #5	Clarity and Usability: Yes, this is a very important research effort, in my opinion. Yes, it contributes significantly to our base of knowledge, especially given the strong "charismatic" outcomes that incentivize clinical and policy decision making surrounding seclusion and restraints.	Thank you.
General	TEP #5	Clarity and Usability: The authors presented an accessible and clear message about the low strength of evidence that does exist, and a clear lack of evidence in this area of research.	Thank you.

Section	Commentator and Affiliation	Comment	Response
General	TEP #5	Clarity and Usability: There recommendations for future endeavors in aggression reduction will undoubtedly improve care for what are generally vulnerable patient populations. Thank you for this important work.	Thank you, we are grateful for the opportunity to conduct this systematic review.
General	Phyllis Foxworth (Depression and Bipolar Support Alliance)	**Recommendations [continued]:** While comparative research on the clinical interventions is important, DBSA notes lack of inclusion of the patient perspective on those clinical interventions. One criteria of patient-centered care is to engage patients in their own treatment. There are several reasons this is good practice, especially for an individual experiencing agitation symptoms. To quote the report on ES-3 "We also look at longer term or final health outcomes. These include quality of life, functioning or patient experience; improved therapeutic relationship; and decreased subsequent aggressive behavior." A therapeutic alliance not only helps achieve these outcomes, but lessens the trauma that can be produced by physically restraining a patient through force or medication. Research that can shed light on whether or not a positive first experience can create a desire and motivation for the patient to pursue long-term treatment once discharged from the acute care setting is critical.	Thank you. We will pass this information on to AHRQ through this disposition report.

Section	Commentator and Affiliation	Comment	Response
General	Phyllis Foxworth (Depression and Bipolar Support Alliance)	**Recommendations [continued]:** Just as critical is comparative research that identifies best-practices for engaging the patient in their own care. Recommended areas of study include the following: • Does engaging patients in their own treatment decision lead to a therapeutic alliance that decreases the risk of returning to the acute care setting for treatment of aggressive behavior? • Can utilizing peer support specialists as part of the acute care treatment team increase patient engagement with medical staff and support self-determined care when treating aggressive behavior? • What cost benefit does the acute care setting derive from investing in appropriate staff and staff-training to better support patient-centered care and outcomes in treating aggressive behavior? • Does improving measurement tools to include wellness outcomes as defined by people experiencing acute aggressive behavior improve the outcome benefits identified in this report?	Thank you. We will pass this information on to AHRQ through this disposition report.
General	Phyllis Foxworth (Depression and Bipolar Support Alliance)	**Conclusion:** Not only does DBSA applaud AHRQ for engagement on this topic we also want to help. We believe that DBSA is uniquely positioned to assist AHQR in systematic efforts to gather, analyze, understand, and act upon individuals' perspectives about their lived experiences of agitation treatment in the acute care setting. DBSA would welcome the opportunity to collaborate actively with AHRQ, in particular by helping to identify and engage commenters with mood disorder diagnoses and research projects.	Thank you.

Section	Commentator and Affiliation	Comment	Response
General	Karen Kanefield (American Psychiatric Association)	The tables in the document are very informative. For the summary of findings tables, it may be useful to include the author and date for the relevant citation rather than simply including a footnoted citation in the far right table column.	Thank you for the suggestion. We now provide first author's last names and publication years in the summary of findings tables, in addition to their footnoted citations.