



## Effective Health Care

### Delirium: Diagnosis, Prevention, and Treatment

#### Results of Topic Selection Process & Next Steps

The nominator, the American Geriatrics Society (AGS), is interested in using a new systematic review to focus on harms of antipsychotics for delirium prevention and treatment; and the comparison of antipsychotics to nonpharmacologic interventions. A new review would support the next version of the Beers Criteria. A separate nomination, from the American Psychiatric Association (APA), covers screening, prevention, diagnosis and treatment of delirium. APA intend to use a new review to inform a guideline.

The nomination from the AGS focused on antipsychotics for prevention and treatment of delirium (KQ 2 and 4), including comparisons of antipsychotics to non-pharmacologic interventions, will go forward for refinement as a systematic review. The scope of this topic, including populations, interventions, comparators, and outcomes, will be further developed in the systematic review.

Due to limited program resources, the program is unable to develop a review on the scope of the APA nomination.

#### Topic Brief

**Topic Name:** Delirium Diagnosis, Prevention and Treatment, #717, 721

**Nomination Date:** 10/28/2016

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**Conflict of Interest:** None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

**Summary of Key Findings:**

- This topic meets all selection criteria
- In our assessment of feasibility, we found many studies overlapped conceptually with both prevention and treatment.
- We found many reviews related to the nomination scope, though they did not examine all subgroups of interest
- This nomination has high value potential, given that both nominators plan to use a review to inform guidelines for practice.

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## Introduction

Delirium is a common, complex and costly condition in older adults. Every year, over 7 million hospitalized Americans suffer from delirium.<sup>1</sup> A recent systematic review found that 31% of critical care patients have delirium, and delirium is associated with higher mortality during admission (risk ratio 2.19) as well as longer duration of mechanical ventilation.<sup>2</sup> Delirium is also common in medical and surgical inpatients.

Delirium is often under-recognized, especially when sub-syndromal or when hypoactive delirium is present.<sup>3</sup> Up to half of ICU patients with delirium are not detected, even when using a screening tool.<sup>4</sup> Identification of delirium can also be important in recognizing other treatable and clinically urgent conditions such as alcohol withdrawal, medication related toxicities, or infection.

Delirium is a high priority in federal research. In 2014, the National Institute on Aging (NIA) and American Geriatrics Society (AGS) held a conference about delirium in older adults that has led to several recent research request for applications.<sup>5</sup> Notable recent grants related to delirium include the CMS innovation grant “Delirium detection and prevention across the continuum” (\$11,785,095, Houston area, 2012) and the Network for Investigation of Delirium across the U.S. (\$3.7 million, National Institute on Aging).

This assessment covers two separate nominations from the American Psychiatric Association (APA) and the American Geriatric Society (AGS). Topic nomination #0717 was nominated by the APA on October 28, 2016, and covers screening, prevention, diagnosis and treatment of delirium. They intend to use a new review to inform a guideline. The AGS nomination is focused on harms of antipsychotics for delirium prevention and treatment; and the comparison of antipsychotics to nonpharmacologic interventions. A new review would support the next version of the Beers Criteria.

### **Nominator and Stakeholder Engagement:**

This topic brief was initially developed by the Scientific Resource Center in March 2017. Because of continued interest by the nominator, APA, AHRQ consulted with them about the nomination's scope and updated the topic brief for consideration in FY18. The nominator indicated that reviews on prevention and screening identified in the previous workup would not meet their needs; and their priority was on delirium treatment. This updated assessment is therefore limited to KQ 4 and 5, focusing on pharmacologic and nonpharmacologic treatments for delirium.

The AGS affirmed that antipsychotics for delirium prevention and treatment continue to be the focus of concern for them.

### **Key Questions:**

- 1) What is the effectiveness of screening for delirium in adult inpatients?
  - a) Do these results vary by medical unit, age, gender or comorbid conditions?
  - b) Does screening for delirium improve clinical outcomes?
- 2) What are the effectiveness and harms of delirium prevention strategies in adult inpatients at risk of delirium?
  - a) Do these results vary by medical unit, age, gender or comorbid conditions?
- 3) What is the comparative diagnostic accuracy of tools used to detect delirium?
- 4) What are the benefits and harms of interventions to treat delirium in adults?

- a) Pharmacologic
  - b) Non-pharmacologic
- 5) What subgroup/patient characteristics affect the benefits and harms of pharmacologic and non-pharmacologic treatments in adults with delirium?
- a) Demographic factors (age, sex, race, ethnicity, SES, etc.)
  - b) Comorbid conditions (including SUD, dementia and other psychiatric disorders)
  - c) Concomitant medications

To define the inclusion criteria for the key questions we specify the population, interventions, comparators, and outcomes (PICO) of interest in Table 1.

**Table 1. Key Questions and PICOs**

<b>Key Questions</b>	<p>1. What is the effectiveness of screening for delirium in adult inpatients?</p> <p>a) Do these results vary by medical unit, age, gender or comorbid conditions?</p> <p>b) Does screening for delirium improve clinical outcomes?</p>	<p>2. What are the effectiveness and harms of delirium prevention interventions and strategies in adult inpatients at risk of delirium?</p> <p>a) Do these results vary by medical unit, age, gender or comorbid conditions?</p>	<p>3. What is the comparative diagnostic accuracy of tools used to detect delirium?</p>	<p>4. What are the benefits and harms of interventions and strategies to treat delirium in adults?</p> <p>a) Pharmacologic</p> <p>b) Non-pharmacologic</p>	<p>5. What subgroup/patient characteristics affect the benefits and harms of pharmacologic and non-pharmacologic treatments in adults with delirium?</p> <p>a) Demographic factors (age, sex, race, ethnicity, SES, etc.)</p> <p>b) Comorbid conditions (including SUD, dementia and other psychiatric disorders)</p> <p>c) Concomitant medications</p>
<b>Population</b>	Adult inpatients at risk of delirium*	Adult inpatients at risk of delirium*	Adult inpatients	Adult inpatients with delirium	Adult inpatients with delirium
<b>Interventions</b>	Risk prediction models, screening tools, assessment tools	Delirium prevention strategies, excluding intra-operative strategies	Diagnostic tools	Pharmacologic and non-pharmacologic interventions	Pharmacologic and non-pharmacologic interventions
<b>Comparators</b>	Clinical judgment alone	Placebo, no prevention or other prevention strategy	Other diagnostic tools	Placebo, no intervention, other intervention	Placebo, no intervention, other intervention
<b>Outcomes</b>	Sensitivity, specificity, positive and negative predictive values, clinical outcomes	Delirium free days, delirium severity, length of time on mechanical ventilation, length of stay in critical care and in hospital, time in restraints, time on continuous observation, need for post-hospital rehabilitation or long-term care, significant in-hospital complications (e.g. falls, mortality), and post-hospital complications (e.g., readmissions, cognitive impairment, falls, mortality, PTSD).	Sensitivity, specificity	Delirium free days, delirium severity, length of time on mechanical ventilation, length of stay in critical care and in hospital, time in restraints, time on continuous observation, need for post-hospital rehabilitation or long-term care, significant in-hospital complications (e.g. falls, mortality), and post-hospital complications (e.g., readmissions, cognitive impairment, falls, mortality, PTSD).	Delirium free days, delirium severity, length of time on mechanical ventilation, length of stay in critical care and in hospital, time in restraints, time on continuous observation, need for post-hospital rehabilitation or long-term care, significant in-hospital complications (e.g. falls, mortality), and post-hospital complications (e.g., readmissions, cognitive impairment, falls, mortality, PTSD).

\*Risk factors include but are not limited to old age, medical frailty, comorbid conditions, and use of certain medications.  
Abbreviations: ICU=Intensive Care Unit; PTSD=Post-traumatic Stress Disorder; SES=Socioeconomic Status

## Methods

To assess topic nomination Delirium: Diagnosis, Prevention, and Treatment for priority for a systematic review or other AHRQ EHC report, we used a hierarchical process based on established criteria, with each assessment determining the need for further evaluation. Details related to our assessment are provided in Appendix A.

1. Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. Establish the overall *importance* of a potential topic as representing a health or healthcare issue in the United States.
3. Determine the *desirability of new evidence review* by examining whether a new systematic review or other AHRQ product would be duplicative.
4. Assess the *potential impact* a new systematic review or other AHRQ product.
5. Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. Determine the *potential value* of a new systematic review or other AHRQ product.

### Appropriateness and Importance

We assessed the nomination for appropriateness and importance (see Appendix A).

### Desirability of New Review/Duplication

We searched for high-quality, completed or in-process evidence reviews pertaining to the key questions of the nomination. Appendix B includes the list of the sources searched and potentially relevant titles identified.

### Impact of a New Evidence Review

The impact of a new evidence review was assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was hypothetically possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

### Feasibility of New Evidence Review

We conducted a literature search in PubMed for the past 5 years, up to 10/14/2017 focused on KQ 4 and 5. In addition, for all topics, we searched ClinicalTrials.gov for in-process or recently completed unpublished studies. See Appendix C for the PubMed search strategy and links to the ClinicalTrials.gov search. See Appendix D for methods for March 2017 assessment.

We identified and reviewed 220 abstracts and titles for inclusion and classified included studies by study design, to assess the size and scope of a potential systematic review.

### Value

We assessed the nomination for value (see Appendix A). We considered whether or not the topic would inform clinical policy in community and/or clinical settings, and if there was a partner organization that would use this evidence review to do disseminate this policy.

### Compilation of Findings

We constructed a table outlining the selection criteria as they pertain to this nomination (see Appendix A).

## Results

### Appropriateness and Importance

This is an appropriate and important topic.

## **Desirability of New Review/Duplication**

For the APA nomination, a new systematic review would partly duplicate existing systematic reviews on the prevention (KQ2) and treatment (KQ4 and KQ5) of delirium

- The most relevant reviews include: two in-process reviews of non-pharmacologic interventions to treat delirium; and an in-process review on pharmacologic treatment focused on ICU patients.
- While these reviews will likely cover the breadth of pharmacologic and non-pharmacologic interventions, they do not address the patient groups and subgroups of interest, and do not compare pharmacologic to non-pharmacologic interventions.

For the AGS nomination, a new systematic review would partly duplicate existing systematic review

- Kishi et al reviewed antipsychotics for the treatment of delirium (KQ 4). While it included harms, the patient population included non-elderly adults.
- Neufeld et al reviewed antipsychotics for prevention and treatment of delirium (KQ 2 and 4). The search end-date however is from 2013.

See Table 2 for details.

## **Impact of a New Evidence Review**

A new AHRQ systematic review on the treatment of delirium has high impact potential because the standard of care is unclear and resulting practice variation. Existing guidance is out of date, and the standard of care is unclear. Guidelines by the American Geriatrics Society (AGS) for adult postoperative patients don't address screening and diagnosis,<sup>34</sup> and the APA's practice guidelines on screening and diagnosis of delirium are old (published in 1999 with a new literature search in 2004).<sup>35</sup>

## **Feasibility of a New Evidence Review**

A new AHRQ systematic review on the treatment of delirium is feasible.

- We found 24 completed treatment studies, and 19 additional studies in clinicaltrials.gov. Ten completed treatment studies studied antipsychotics; two additional studies were identified in clinicaltrials.gov.
- There are few studies comparing one delirium treatment to another and particularly a lack of studies comparing pharmacological treatment to non-pharmacological treatment.
- We found many studies overlapped conceptually with both prevention and treatment.
- Without preventive therapy, this is likely a small review, and with preventive therapy, it is likely a medium size review.

See Table 2, Feasibility column for the citations that addressed the key questions.



**Table 2. Key Questions, Results of Duplication Search, and Results of Feasibility Search**

Key Question	Selected Duplication Findings* (Completed or In-Process Evidence Reviews; 9/2014-9/2017)	Feasibility Findings (Published and Ongoing Research; 10/2012-10/2017)
KQ 2: Effectiveness of prevention strategies-pharmacologic	<b>Total number of identified systematic reviews: 14</b>  Completed SR-11 <ul style="list-style-type: none"> <li>• General-4<sup>37-40</sup></li> <li>• Postoperative-4<sup>41-44</sup></li> <li>• Intensive Care Unit-3<sup>45-47</sup></li> </ul> In-process SR-3 <sup>48-50</sup>	NA
KQ 2: Effectiveness of prevention strategies-non pharmacologic	<b>Total number of identified systematic reviews: 19</b>  Completed SR-14 <ul style="list-style-type: none"> <li>• General-7<sup>37,51-56</sup></li> <li>• Age, postoperative-2<sup>57-58</sup></li> <li>• Intensive Care Unit-3<sup>59-61</sup></li> <li>• Postoperative-2<sup>62-63</sup></li> </ul> In-process SR-5 <ul style="list-style-type: none"> <li>• General-1<sup>64</sup></li> <li>• ICU-3<sup>48,65-66</sup></li> <li>• Postoperative-1<sup>67</sup></li> </ul>	NA
KQ 4 and 5: Benefits and harms of treatments for delirium-pharmacologic  Benefits and harms of treatments by patient characteristics	<b>Total number of identified systematic reviews: 9</b>  Completed SR-6 <sup>68-73</sup>  In-process SR-3 <ul style="list-style-type: none"> <li>• ICU-3<sup>74-76</sup></li> </ul>	<u>Size/scope of review</u> Relevant Studies Identified:19 <ul style="list-style-type: none"> <li>• RCT- g<sup>84,86,92,95,97,100,102,104,106</sup></li> <li>• Observational-3<sup>89,94,103</sup></li> <li>• Controlled Trial-3<sup>90, 91,105</sup></li> <li>• Ancillary Study-1<sup>93</sup></li> <li>• Prospective cohort-3<sup>98,99,101</sup></li> </ul> <u>ClinicalTrials.gov</u> Relevant Trials:12 <ul style="list-style-type: none"> <li>• Recruiting: #8<sup>111-115,117-119</sup></li> <li>• Active: #1<sup>121</sup></li> <li>• Complete: #3<sup>110,116,123</sup></li> </ul>
KQ 4 and 5: Benefits and harms of treatments for delirium-nonpharmacologic  Benefits and harms of treatments by patient characteristics	<b>Total number of identified systematic reviews: 12</b>  Completed SR-8 <sup>46,52-53,77-81</sup>  In-process SR-4 <sup>64-65,82-83</sup>	<u>Size/scope of review</u> Relevant Studies Identified: 5 <ul style="list-style-type: none"> <li>• RCT-3<sup>85,87,100</sup></li> <li>• Prospective cohort-1<sup>88</sup></li> <li>• Observational-1<sup>96</sup></li> </ul> <u>ClinicalTrials.gov</u> Relevant Trials: 7 <ul style="list-style-type: none"> <li>• Recruiting: #5<sup>107-109,118,120</sup></li> <li>• Active: #0</li> <li>• Complete: #2<sup>116,122</sup></li> </ul>

*Abbreviations:* KQ=Key Question; ICU=Intensive Care Unit; NA=not applicable; SR=Systematic Review  
**Table 2.** Key questions with the identified corresponding evidence reviews and original research

## Value

This nomination has high value potential. Delirium is managed by multiple provider groups, including psychiatrists, geriatricians, hospitalists, intensivists, and neurologists. A review would be more valuable if there was commitment by multiple specialty groups to implement findings into clinical practice.

- APA will use a new AHRQ systematic review to update their 1999 guidelines.
- AGS has indicated they would also use the review if it were developed. For FY17, they had submitted a nomination focused on antipsychotics for delirium prevention and treatment. This nomination was not funded.
- Correspondence indicates that other groups including ACP and AMDA might also be interested if a review goes forward.

## Summary of Findings

- Appropriateness and Importance: The topic is both appropriate and important.
- Duplication: Existing systematic reviews partly duplicate both nomination scopes.
  - For the APA nomination
    - While three reviews will likely cover the breadth of pharmacologic and non-pharmacologic interventions, they do not address the patient groups and subgroups of interest, and do not compare pharmacologic to non-pharmacologic interventions.
  - For the AGS nomination
    - While we found two reviews, one included a broader patient population than of interest to AGS, and the other was not sufficient current.
- Impact: A new AHRQ systematic review on the treatment of delirium has high impact potential because the standard of care is unclear and resulting practice variation. Existing guidance is out of date, and the standard of care is unclear.
- Feasibility: A new AHRQ systematic review on the treatment of delirium is feasible.
  - We found 24 completed treatment studies, and 19 additional studies in [clinicaltrials.gov](http://clinicaltrials.gov).
  - Ten completed treatment studies studied antipsychotics; two additional studies were identified in [clinicaltrials.gov](http://clinicaltrials.gov).
- Value: This nomination has high value potential, given the APA will use a new AHRQ systematic review to update their 1999 guidelines. AGS has indicated they would also use the review if it were developed to inform an update of the Beers Criteria.

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## Appendix A. Selection Criteria Summary

Selection Criteria	Supporting Data
<b>1 Appropriateness</b>	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes, this topic represents health care drugs and interventions available in the U.S.
1b. Is the nomination a request for a systematic review?	Yes, this topic is a request for a systematic review.
1c. Is the focus on effectiveness or comparative effectiveness?	The focus of this review is on both effectiveness and comparative effectiveness.
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes, it is biologically plausible. Yes, it is consistent with what is known about the topic.
<b>2 Importance</b>	
2a. Represents a significant disease burden; large proportion of the population	Yes, this topic represents a significant burden. Every year, over 7 million hospitalized Americans suffer from delirium. <sup>1</sup> A recent systematic review found that 31% of critical care patients have delirium, and delirium is associated with higher mortality during admission (risk ratio 2.19) as well as longer duration of mechanical ventilation. <sup>2</sup> Delirium is also common in medical and surgical inpatients.
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes, this topic affects health care decisions for a large, vulnerable population.
2c. Represents important uncertainty for decision makers	Yes, this topic represents important uncertainty for decision makers.
2d. Incorporates issues around both clinical benefits and potential clinical	Yes, this nomination addresses both benefits and potential harms of preventative strategies, non-pharmacologic treatments, and pharmacologic treatments for delirium.
2e. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes this topic represents high costs due to the association of delirium with worse outcomes among inpatients, which leads to increased need for and intensity of medical interventions.
<b>3 Desirability of a New Evidence Review/Duplication</b>	

<p>3. Would not be redundant (i.e., the proposed topic is not already covered by available or soon-to-be available high-quality systematic review by AHRQ or others)</p>	<p><b>October 2017 assessment:</b> A new AHRQ systematic review would largely duplicate existing systematic reviews on the prevention (KQ2); and partly duplicate those on treatment (KQ4 and KQ5) of delirium. There are over 50 systematic reviews pertinent to the questions in the nomination.</p> <p>Pharmacologic prevention (KQ2). Collectively these reviews cover the breadth of interventions but not all subgroups of interest.</p> <p>Nonpharmacologic prevention (KQ 2). Collectively these reviews cover the breadth of interventions, and many subgroups of interest.</p> <p>Pharmacologic treatment (KQ 4 and 5). These reviews cover the breadth of interventions for ICU patients but not hospitalized patients, as well as many subgroups of interest.</p> <p>Non-pharmacologic treatment (KQ 4 and 5). The reviews will examine both ICU and hospitalized patients, but few subgroups.</p> <p>No reviews compared pharmacologic to nonpharmacologic interventions.</p> <p>Two reviews were focused on antipsychotics (Kishi et al and Neufeld et al), and most relevant to the focus of the AGS nomination. One focused on treatment, and the other on prevention and treatment. These however included adults 18 years and older, which includes adults outside of the target population for the Beers criteria; and one review, though published in 2016, had a search end-date of 2013 and was not considered sufficiently current to be useful to the nominator.</p> <p><b>March 2017 assessment:</b> A new AHRQ systematic review would duplicate existing systematic reviews on the prevention (KQ2) and treatment (KQ4 and KQ5) of delirium but not on screening (KQ1) and diagnosis (KQ3).</p> <p>There are over 50 systematic reviews pertinent to the questions in the nomination. There are up-to-date reviews of multicomponent interventions to prevent delirium, including the 2015 overview of reviews “Efficacy of Non-Pharmacological Interventions to Prevent and Treat Delirium in Older Patients: A Systematic Overview” (KQ2, KQ4, KQ5).<sup>6</sup> This overview is part of a major European Union initiative, Optimal Evidence-Based Non-drug Therapies in Older People (ONTOP).<sup>7</sup> Similarly, a 2016 systematic review “Interventions for Preventing Delirium in Hospitalised Non-ICU Patients”</p>
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Selection Criteria	Supporting Data
	<p>found strong evidence supporting multi-component interventions to prevent delirium (KQ2).<sup>8</sup> A 2016 systematic review of 12 studies (4 on prevention and 8 on treatment) found Haldol effective for pre-surgical prevention and comparable to other antipsychotics for treatment (KQ2, KQ4, KQ5).<sup>9</sup></p> <p>A 2011 review entitled “Delirium: Screening, Prevention, and Diagnosis” conducted by the VA Evidence-based Synthesis Program is the most recent, comprehensive examination of screening and diagnosis of delirium (KQ1, KQ3).<sup>10</sup> Updating this review would cover the parts of the nomination that are not addressed in recent reviews.</p>
4 Impact of a New Evidence Review	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	<p>Yes, the standard of care is unclear due to a lack of current guidance. In 2013, the Society for Critical Care Medicine (SCCM) published guidelines on the management of delirium in adult ICU patients which included screening and diagnosis; however the literature search only extended to 2010.<sup>33</sup> Guidelines by the American Geriatrics Society (AGS) for adult postoperative patients don’t address screening and diagnosis,<sup>34</sup> and the APA’s practice guidelines on screening and diagnosis of delirium are old (published in 1999 with a new literature search in 2004).<sup>35</sup></p>
4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	<p>Yes, there is practice variation because of the unclear standard of care.</p>
5 Primary Research	

Selection Criteria	Supporting Data
<p>5. Effectively utilizes existing research and knowledge by considering:</p> <ul style="list-style-type: none"> <li>- Adequacy (type and volume) of research for conducting a systematic review</li> <li>- Newly available evidence (particularly for updates or new technologies)</li> </ul>	<p><b>October 2017 assessment:</b> A new AHRQ review on delirium is feasible. We found 24 completed treatment studies, and 19 additional studies in clinicaltrials.gov. Ten completed treatment studies studied antipsychotics; two additional studies were identified in clinicaltrials.gov. that were relevant solely to antipsychotics. However there are few studies comparing one delirium treatment to another and particularly a lack of studies comparing pharmacological treatment to non-pharmacological treatment.</p> <p>The majority of studies are labeled as prevention therapy rather than treatment which is challenging to distinguish between in the studies. Often the intervention (pharmacologic or non-pharmacologic) is evaluated with daily assessments of delirium, which can wax and wane on a continuum, so it is unclear when preventive therapy becomes treatment. Most studies are for a defined population such as patients with cancer, in the post-operative period, or in the intensive care unit.</p> <p>There would be additional studies if preventive therapy was included in the evidence review. Without preventive therapy, this is likely a small study and with preventive therapy, it is likely a medium size study.</p> <p><b>March 2017 assessment:</b> A new AHRQ review on delirium is feasible.</p> <p><i>Size/scope of review:</i> A new evidence review examining screening and diagnostic tools for delirium is feasible. We identified 18 total studies: 11 observational studies<sup>11-21</sup> on screening tools for delirium (KQ1) and 8 observational studies<sup>11,22-28</sup> on diagnostic tools for delirium (KQ3). We project there may be 32 studies relevant to these key questions.</p> <p><i>Clinicaltrials.gov:</i> Our search in Clinicaltrials.gov identified 4 recently completed or ongoing studies: 2 studies<sup>29,30</sup> relevant to screening tools (KQ1) and 2 studies<sup>31,32</sup> relevant to diagnostic tools.</p>
6 Value	
6a. The proposed topic exists within a clinical, consumer, or policy-making context that is amenable to evidence-based change	Yes this topic exists within a clinical context that is amenable to evidence-based change.

Selection Criteria	Supporting Data
6b. Identified partner who will use the systematic review to influence practice (such as a guideline or recommendation)	This nomination has high value potential, given the APA will use a new AHRQ systematic review to update their 1999 guidelines. Other groups may also develop guidance using the review. Groups include AGS, ACP and AMDA. Of note: because patients with delirium are diagnosed and managed by multiple provider groups, including psychiatrists, geriatricians, hospitalists, intensivists, and neurologists, a review would be more valuable if there was commitment by multiple specialty groups to implement findings into clinical practice.

*Abbreviations:* APA=American Psychiatric Association; AHRQ=Agency for Healthcare Research and Quality; ICU=Intensive Care Unit; KQ=Key Question; VA ESP=Veteran Affairs Evidence-based Synthesis Program

## Appendix B. Sources searched for Duplication

AHRQ: Evidence reports and technology assessments, USPSTF recommendations
VA Products: PBM, and HSR&D (ESP) publications, and VA/DoD EBCPG Program
Cochrane Systematic Reviews and Protocols <a href="http://www.cochranelibrary.com/">http://www.cochranelibrary.com/</a>
PubMed <a href="https://www.ncbi.nlm.nih.gov/pubmed/">https://www.ncbi.nlm.nih.gov/pubmed/</a>
PROSPERO Database (international prospective register of systematic reviews and protocols) <a href="http://www.crd.york.ac.uk/prospéro/">http://www.crd.york.ac.uk/prospéro/</a>

## Appendix C. Search Strategy & Results (Feasibility)

### March 2017 assessment

Ovid MEDLINE(R) and Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

Date Searched: March 21, 2017

Searched by: Robin Paynter, MLIS

1	delirium/ or deliri*.tw,kf.	14184
2	confusion/ or confus*.tw,kf.	55130
3	(NEECHAM or "Neelon and Champagne Confusion Scale").tw,kf.	54
4	(MMSE or mini-mental stat\$ exam\$).tw,kf.	16098
5	or/1-4	82826
6	sensitiv*.tw,kf.	1285664
7	"predictive value*".tw,kf.	93689
8	accurac*.tw,kf.	330119
9	or/6-8	1574196
10	and/5,9	5727
11	exp mass screening/ or screen*.tw,kf.	692154
12	exp diagnosis/ or diagnos*.tw,kf.	9231263
13	or/11-12	9554872
14	and/10,13	3955
15	exp Postoperative Complications/ or (postoperat* or post-operat* or postsurg* or post-surg*).tw,kf.	886782
16	14 not 15	3819
17	randomized controlled trial.pt.	507428
18	controlled clinical trial.pt.	98142
19	randomized controlled trials as topic/	125106
20	random allocation/	98331
21	double-blind method/	158051
22	single-blind method/	26567
23	clinical trial.pt.	547426
24	exp clinical trial as topic/	338136



25	(clin* adj25 trial*).ti,ab.	408535
26	((single* or doubl* or trebl* or tripl*) adj25 (blind* or mask*)).ti,ab.	172072
27	placebos/	37079
28	placebo*.ti,ab.	208253
29	random*.ti,ab.	997244
30	research design/	105468
31	comparative study/	1959172
32	exp evaluation studies/	247782
33	follow up studies/	628489
34	prospective studies/	492217
35	(control* or prospective* or volunteer*).ti,ab.	4062703
36	or/17-35	7095402
37	animals/ not humans/	4816437
38	36 not 37	5786092
39	and/16,38	1916
40	limit 39 to english language	1801
41	limit 40 to yr="2012 -Current"	515
42	limit 41 to ("middle age (45 to 64 years)" or "middle aged (45 plus years)" or "all aged (65 and over)" or "aged (80 and over)")	354

Clinicaltrials.gov

[https://clinicaltrials.gov/ct2/results?term=screening+diagnosis&type=&rslt=&recr=&age\\_v=&age=1&age=2&gndr=&cond=Delirium&intr=&titles=&out=&spons=&lead=&id=&state1=&cntry1=&state2=&cntry2=&state3=&cntry3=&locn=&rcv\\_s=01%2F01%2F2012&rcv\\_e=&lup\\_s=&lup\\_e=](https://clinicaltrials.gov/ct2/results?term=screening+diagnosis&type=&rslt=&recr=&age_v=&age=1&age=2&gndr=&cond=Delirium&intr=&titles=&out=&spons=&lead=&id=&state1=&cntry1=&state2=&cntry2=&state3=&cntry3=&locn=&rcv_s=01%2F01%2F2012&rcv_e=&lup_s=&lup_e=)

14 studies found for: screening diagnosis | Delirium | Adult, Senior | Studies received on or after 01/01/2012

#### October 2017 assessment

Topic: Delirium Treatment Date: October 15, 2017 Database Searched: PubMed	
<b>Concept</b>	<b>Search String</b>
Delirium	(((((delirium[Title/Abstract])

Not Editorials, etc.	NOT "letter"[Publication Type]) NOT "news"[Publication Type]) NOT "patient education handout"[Publication Type]) NOT "comment"[Publication Type]) NOT "editorial"[Publication Type]) NOT "newspaper article"[Publication Type]
Limit to Study-type, last 5 years, Human, English, Adult	Randomized Controlled Trial, Observational Study, Multicenter Study, Clinical Trial, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Controlled Clinical Trial, Clinical Study, published in the last 5 years, Humans, English, Adult: 19+ years
<b>N=220</b>	

Clinicaltrials.gov

[https://clinicaltrials.gov/ct2/results?cond=Delirium&term=treatment+&cntry1=&state1=&sfpd\\_s=01%2F01%2F2012&sfpd\\_e=&Search=Search&recrs=a&recrs=d&recrs=e&age=1&age=2#tableTop](https://clinicaltrials.gov/ct2/results?cond=Delirium&term=treatment+&cntry1=&state1=&sfpd_s=01%2F01%2F2012&sfpd_e=&Search=Search&recrs=a&recrs=d&recrs=e&age=1&age=2#tableTop)

108 Studies found for:

treatment | Recruiting, Active, not recruiting, Completed Studies | Delirium | Adult, Senior | First posted on or after 01/01/2012

## Appendix D: Duplication and Feasibility from March 2017 assessment

### Methods

We conducted a literature search on screening and diagnostic tools for delirium in PubMed from March 2012 to March 2017. We also searched Clinicaltrials.gov for recently completed or in-process unpublished studies. See Appendix B for the PubMed search strategy and links to the ClinicalTrials.gov search.

Because a large number of articles (n=354) were identified, we reviewed a random sample of 200 titles and abstracts for inclusion and classified identified studies by study design, to assess the size and scope of a potential evidence review. We then calculated the projected total number of included studies based on the proportion of studies included from the random sample. See Table D-1, Feasibility Column, Size/Scope of Review Section for the citations of included studies.

Table D-1: KQ, Duplication results, and Feasibility results for March 2017 assessment

Key Question	Selected Duplication Findings* (Completed or In-Process Evidence Reviews; 1/2012-1/2017)	Feasibility Findings (Published and Ongoing Research; 3/2012-3/2017; Yield=354)
KQ 1: Effectiveness of screening for delirium	Total number of completed and in-process systematic reviews - 1 <ul style="list-style-type: none"> <li>VA ESP: 1<sup>10</sup></li> </ul>	Size/scope of review Relevant Studies Identified: 11 <ul style="list-style-type: none"> <li>Prospective cohort: 10<sup>11-20</sup></li> <li>Cross-sectional: 1<sup>21</sup></li> </ul> Projected total: 19  <a href="#">Clinicaltrials.gov</a> <ul style="list-style-type: none"> <li>Completed: 1<sup>29</sup></li> <li>Recruiting: 1<sup>30</sup></li> </ul>
KQ 2: Effectiveness of prevention strategies	Total number of completed and in-process systematic reviews - 4 <ul style="list-style-type: none"> <li>Cochrane: 1<sup>8</sup></li> <li>VA ESP: 1<sup>10</sup></li> <li>Other - 1<sup>6,9</sup></li> </ul>	NA
KQ 3: Comparative diagnostic accuracy of the tools used to detect delirium	Total number of completed and in-process evidence reviews – 1 <ul style="list-style-type: none"> <li>VA ESP: 1<sup>10</sup></li> </ul>	Size/scope of review Relevant Studies Identified: 8 <ul style="list-style-type: none"> <li>Prospective cohort: 2<sup>11,22</sup></li> <li>Cross-sectional: 4<sup>23-26</sup></li> <li>Prospective observational: 2<sup>27,28</sup></li> </ul> Projected total: 14  <a href="#">Clinicaltrials.gov</a> <ul style="list-style-type: none"> <li>Completed: 1<sup>31</sup></li> <li>Recruiting: 1<sup>32</sup></li> </ul>
KQ 4: Benefits and harms of treatments for delirium	Total number of completed evidence reviews – 2 <ul style="list-style-type: none"> <li>Other: 2<sup>6,9</sup></li> </ul>	NA
KQ 5: Benefits and harms of treatments by patient characteristics	Total number of completed systematic reviews - 2 <ul style="list-style-type: none"> <li>Other: 2<sup>6,9</sup></li> </ul>	NA