



Delirium: Screening, Prevention, and Diagnosis – A Systematic Review of the Evidence

EXECUTIVE SUMMARY

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PREFACE

Health Services Research & Development Service's (HSR&D's) Evidence-based Synthesis Program (ESP) was established to provide timely and accurate syntheses of targeted healthcare topics of particular importance to Veterans Affairs (VA) managers and policymakers, as they work to improve the health and healthcare of Veterans. The ESP disseminates these reports throughout VA.

HSR&D provides funding for four ESP Centers and each Center has an active VA affiliation. The ESP Centers generate evidence syntheses on important clinical practice topics, and these reports help:

- develop clinical policies informed by evidence,
- guide the implementation of effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures, and
- set the direction for future research to address gaps in clinical knowledge.

In 2009, the ESP Coordinating Center was created to expand the capacity of HSR&D Central Office and the four ESP sites by developing and maintaining program processes. In addition, the Center established a Steering Committee comprised of HSR&D field-based investigators, VA Patient Care Services, Office of Quality and Performance, and Veterans Integrated Service Networks (VISN) Clinical Management Officers. The Steering Committee provides program oversight, guides strategic planning, coordinates dissemination activities, and develops collaborations with VA leadership to identify new ESP topics of importance to Veterans and the VA healthcare system.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP Coordinating Center Program Manager, at nicole.floyd@va.gov.

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BACKGROUND

Delirium is a common syndrome in hospitalized or institutionalized adults. It is characterized by the acute onset of altered mental status, hallmark by difficulty sustaining attention and a fluctuating course. Delirium frequently causes patients, families, and health care providers considerable distress. The incidence varies widely based on patient population, setting, and intensity of diagnostic ascertainment with reported values of 10% to over 80%. Delirium is associated with multiple serious outcomes including increased morbidity, length of hospital stay, healthcare costs, institutionalization, and mortality.^{1,2,3} In surgical settings, older adults and those with multiple medical conditions are at increased risk for postoperative delirium.⁴ Delirium may be under-recognized by healthcare providers and it can be difficult to resolve.^{5,6} Several brief “bedside” questionnaires and checklists exist that can help detect delirium earlier and among those with milder symptoms. Additionally, efforts to prevent the development of delirium in those at risk have been advocated.^{3,6} Medications (including sedatives, narcotics, and anticholinergic drugs), diseases and intercurrent illnesses (e.g., stroke, infection, shock, anemia), surgical procedures (especially orthopedic and cardiac surgery), and environmental factors (e.g., use of a bladder catheter, pain, and emotional stress) are all associated with delirium.^{3,7} Therefore, identifying and implementing effective strategies to prevent and detect delirium could improve clinical outcomes and resource utilization. Suggested strategies to prevent delirium include avoidance of psychoactive medications, pharmacologic interventions to decrease risk, and single- or multi-component non-pharmacologic interventions (including use of music, mobilization, fluid and nutrition management, and orientation and cognitive stimulation).^{4,6,7}

This review was undertaken to evaluate the effectiveness of screening for delirium, the effectiveness and harms of strategies to prevent delirium, and the comparative diagnostic accuracy of tools used to detect delirium. Specifically, we addressed the following 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 acute elderly inpatients?
 - a. Do these results vary by medical unit, age, gender or comorbid conditions?
3. What is the comparative *diagnostic accuracy* of the tools used to detect delirium:
 - a. In elderly medical and surgical inpatients?
 - b. In elderly medical or surgical intensive care unit (ICU) inpatients?

METHODS

We searched MEDLINE, CINAHL, and PsycINFO from 1950 to November 2010 using standard search terms (Appendix A). We limited the search to peer-reviewed articles involving human subjects and published in the English language. Additional citations were identified from reference lists and Technical Expert Panel members. Titles and abstracts were reviewed by physicians, nurses, and research assistants trained in the critical analysis of literature. Full text versions of potentially relevant articles were similarly reviewed. Study characteristics, patient characteristics, and outcomes were extracted and evidence and outcomes tables, organized by key question, were created under the supervision of the Principal Investigator, a geriatric psychiatrist.

We assessed study quality of randomized trials of prevention strategies (Key Question 2) according to the following criteria: 1) adequate allocation concealment, 2) blinding of key study personnel, 3) analysis by intention-to-treat, and 4) reporting of number of withdrawals/dropouts by group assignment. Study quality of studies reported for Key Question 3 (studies of diagnostic accuracy) was assessed using the method described in the Rationale Clinical Examination series.⁸

DATA SYNTHESIS

We constructed evidence tables showing the study characteristics and results for all included studies. We critically analyzed studies to compare their characteristics, methods, and findings. Pooled analyses were performed, where feasible, for studies of prevention strategies. All other data were narratively summarized.

PEER REVIEW

A draft version of this report was reviewed by technical experts, as well as VA clinical leadership. Reviewer comments were addressed and our responses incorporated in the final report.

RESULTS

For the screening question, we identified 1,889 abstracts and excluded 1,778. We reviewed the full text of 111 references and none met inclusion criteria. For prevention, we identified 1,175 abstracts and excluded 947. Of 228 full text articles reviewed, 31 met eligibility criteria. We added 8 references from hand-searching for a total of 39 included references. For diagnostic accuracy in intensive care units, we identified 76 abstracts and excluded 40 of those. Of 36 full text articles reviewed, 15 met inclusion criteria.

KEY QUESTION #1. What is the effectiveness of screening for delirium in adult inpatients?

- 1a. Do these results vary by medical unit, age, gender or comorbid conditions?**
- 1b. Does screening for delirium improve clinical outcomes?**

We identified no randomized controlled trials of screening for delirium in hospitalized patients. There is no direct evidence that screening for delirium is beneficial or harmful. However, while

potentially beneficial, universal screening may also pose harms, such as misclassification, subsequent treatment of non-delirious patients, or failure to accurately identify or intervene on delirious patients. Additionally, we found no evidence from recent systematic reviews that pharmacologic and non-pharmacologic treatments improve outcomes for patients with screen-detected delirium. Therefore, we conclude that the evidence is insufficient about the net benefit of delirium screening among all hospitalized patients or subgroups of patients as defined by age, gender, comorbidities or admission to intensive care units.

KEY QUESTION #2. What are the effectiveness and harms of delirium prevention strategies in acute elderly inpatients?

2a. Do these results vary by medical unit, age, gender or comorbid conditions?

We identified randomized and non-randomized trials of pharmacologic and non-pharmacologic strategies for prevention of delirium. Studies using pharmacologic interventions to prevent delirium were few in number, small in size, and examined different categories of prevention medications often in unique patient populations and settings. Moderate level evidence from two studies of atypical antipsychotics and low level evidence from one study each of analgesia via fascia iliaca compartmental block (pre- and post-operative), lighter anesthesia, or post-operative sedation with dexmedetomidine suggests that these pharmacological approaches may reduce the incidence of delirium following orthopedic or cardiac surgery. There was no difference in delirium incidence associated with the use of cholinesterase inhibitors, statins, a benzodiazepine/opioid protocol, or regional versus general anesthesia and the evidence for using typical antipsychotics is mixed. Multi-component strategies varied greatly but often included staff education plus additional components such as geriatric consultation, individual care planning, focused prevention of infection, improving mobility, frequent orientation, bowel and bladder care regimens, insomnia protocols, adequate pain management, minimizing psychoactive or sedating medications, and maintaining adequate hydration and nutrition. Strategies were generally successful in preventing delirium but intervention variability and lack of assessment of individual intervention components made it difficult to determine which components may be effective. Limited evidence suggests that staff education alone or music therapy may be effective strategies. In one small study, bright light therapy was found to be not effective for delirium prevention. Harms were infrequent and mild.

None of the included studies were stratified by medical unit, age, gender, or comorbid conditions although two studies enrolled only men. There is insufficient evidence to determine whether the effects of different preventive strategies vary by medical unit, age, gender, or comorbid conditions.

KEY QUESTION #3. What is the comparative diagnostic accuracy of the tools used to detect delirium:

- 3a. In elderly medical and surgical inpatients?**
- 3b. In elderly ICU inpatients?**

A systematic review of the comparative effectiveness of bedside instruments concluded that the Confusion Assessment Method (CAM) was a suitable tool for medical and surgical inpatients, many of whom were evaluated in geriatric units. Using Diagnostic and Statistical Manual of

Mental Disorders (DSM) criteria performed by a specialist physician as a reference standard, the pooled sensitivity and specificity of the CAM were 86% and 93%, respectively. The pooled likelihood ratio for a positive test was 9.6 (95%CI 5.8 to 16.0). The pooled likelihood ratio for a negative test was 0.16 (95%CI 0.09 to 0.29). However, there was considerable heterogeneity in the 12 studies. The ease of administration (completion in less than 5 minutes) was also considered although it was noted that administrators should be trained for optimal use and that the CAM was originally developed for use in conjunction with a formal cognitive assessment. The accuracy of bedside instruments delivered by individuals without training as stand-alone tools for delirium screening is not known.

Fewer studies have evaluated the diagnostic accuracy of tools to detect delirium for elderly intensive care unit (ICU) inpatients. The CAM-ICU, a version of the CAM adapted for use in the ICU, appears to have high specificity but the sensitivity is less consistent (ranging from 64 to 100%) indicating that some patients with delirium will not be identified using the CAM-ICU alone. Other tools have been evaluated in only one or two studies.

FUTURE RESEARCH

The highest future research need is to conduct a large multicenter pragmatic randomized trial to evaluate the clinical effectiveness and harms of screening for delirium in a broad spectrum of patients admitted to hospitals. More research is needed to verify the findings that pharmacologic and non-pharmacologic strategies can prevent delirium, particularly in larger and more diverse populations, and with reports stratified by age, medical unit, and comorbid conditions. Additionally, more research is needed to identify which components of the multi-component non-pharmacologic strategies may be most successful in delirium prevention. Finally, continued evaluation of diagnostic tools (especially bed side tools in stand-alone settings administered by clinical personnel) is warranted especially across a wide range of populations and settings.