Clinical Policy: Critical Issues in the Diagnosis and Management of the Adult Psychiatric Patient in the Emergency Department

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From the American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on the Adult Psychiatric Patient

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ABSTRACT

This clinical policy from the American College of Emergency Physicians addresses key issues for the diagnosis and management of adult psychiatric patients in the emergency department. A writing subcommittee conducted a systematic review of the literature to derive evidence-based recommendations to answer the following clinical questions: (1) In the alert adult patient presenting to the emergency department with acute psychiatric symptoms, should routine laboratory tests be used to identify contributory medical conditions (nonpsychiatric disorders)? (2) In the adult patient with new-onset psychosis without focal neurologic deficit, should brain imaging be obtained acutely? (3) In the adult patient presenting to the emergency department with suicidal ideation, can risk-assessment tools in the emergency department identify those who are safe for discharge? (4) In the adult patient presenting to the emergency department with acute agitation, can ketamine be used safely and effectively? Evidence was graded and recommendations were made based on the strength of the available data.

INTRODUCTION

Emergency department (ED) use by psychiatric patients has been steadily increasing. In 2000, 5.4% of adult ED visits were mental health-related compared with 12.5% in 2007.[1] Additionally, the number of inpatient psychiatric beds per capita has declined 62% from 1970 to 2003.[2] Nationwide, there is a shortage of inpatient psychiatric beds.[3-6] With "deinstitutionalization," sufficient resources have not been put into place to care for mental health patients with more severe and urgent needs.[7] Substantial declines in mental health resources have additionally burdened EDs with increasing numbers of patients with mental health issues.[3,8]

Patients waiting for inpatient psychiatric beds remain in the ED 3.2 times longer than nonpsychiatric patients.[9] The "boarding" process for psychiatric patients in EDs nationwide averages 7 to 11 hours, and often takes more than 24 hours when patients require transfer to an outside facility.[10,11]

A 2015 poll by the Emergency Medicine Practice Research Network found that 70% of the emergency physicians surveyed reported psychiatric patients being boarded on their last shift.[12] An American College of Emergency Physicians (ACEP) survey reported that approximately 80% of emergency physicians state that psychiatric patients are boarded with extended stays in their EDs. Ninety percent of physicians noted an increased association of psychiatric patient boarding, with violent behavior in distressed psychiatric patients, distraction of ED staff, and ED bed shortages.[10,13] Psychiatric boarding consumes scarce ED resources, worsens ED crowding, and results in increased wait times and delayed treatment in undifferentiated medical patients with potentially life-threatening conditions.[14]

New systems and resources need to be made available to better serve psychiatric patients. Some proposed solutions to the current boarding problem include telemedicine psychiatric evaluations, holding units for

intoxicated or psychiatric patients, psychiatric observation units, and evidence-based decision tools for treatment and safe discharge.

As part of their focused medical assessment, emergency physicians are often expected to perform routine laboratory and neuroimaging testing before psychiatric evaluation and treatment. The first 2 critical questions address the use of routine diagnostic laboratory and neuroimaging testing for psychiatric patients in the ED, as opposed to their focused application.

Emergency physicians regularly care for patients with suicidal ideation and the safe disposition of these patients is paramount. The third critical question evaluates available risk-assessment tools and whether they can be safely applied in the ED.

Emergency physicians also care for acutely agitated patients in the ED and are well versed in rapid sedation of these patients with benzodiazepines, antipsychotics, or a combination of both. The 2006 version of this clinical policy[15] reviewed the most effective pharmacologic treatment for acutely agitated patients in the ED. The 2006 Level B recommendations on this topic were as follows: (1) Use a benzodiazepine (lorazepam or midazolam) or a conventional antipsychotic (droperidol or haloperidol) as effective monotherapy for the initial drug treatment of the acutely agitated undifferentiated patient in the ED. (2) If rapid sedation is required, consider droperidol instead of haloperidol. (3) Use an antipsychotic (typical or atypical) as effective monotherapy for both management of agitation and initial drug therapy for the patient with known psychiatric illness for which antipsychotics are indicated. (4) Use a combination of an oral benzodiazepine (lorazepam) and an oral antipsychotic (risperidone) for agitated but cooperative patients. The Level C recommendation was as follows: The combination of a parenteral benzodiazepine and haloperidol may produce more rapid sedation than monotherapy in the acutely agitated psychiatric patient in the ED.

Ketamine has been proposed as a novel treatment for acutely agitated patients, so the fourth critical question in this updated policy explores the safety and efficacy of ketamine for sedation of the acutely agitated patient in the ED.

METHODOLOGY

This clinical policy was created after careful review and critical analysis of the medical literature and was based on a systematic review of the literature. Searches of MEDLINE, MEDLINE InProcess, Scopus, Web of Science, and the Cochrane Database were performed. All searches were limited to English-language sources, adults, and human studies. Specific key words/phrases, years used in the searches, dates of searches, and study selection are identified under each critical question. In addition, relevant articles from the bibliographies of included studies and more recent articles identified by committee members and reviewers were included.

This policy is a product of the ACEP clinical policy development process, including expert review, and is based on the existing literature; when literature was not available, consensus of emergency physicians was used. Expert review comments were received from emergency physicians, psychiatrists, members of the American Association for Emergency Psychiatry and the American Association of Community Psychiatrists, and ACEP's Medical Legal Committee. Comments were received during a 60-day open-comment period, with notices of the comment period sent in an e-mail to ACEP members, published in *EM Today*, and posted on the ACEP Web site. The responses were used to further refine and enhance this policy; however, they do not imply endorsement of this clinical policy. Clinical policies are scheduled for review and considered for revision every 3 years; however, interim reviews are conducted when technology, methodology, or the practice environment changes significantly. ACEP was the funding source for this clinical policy.

Assessment of Classes of Evidence

All articles used in the formulation of this clinical policy were graded by at least 2 methodologists and assigned a Class of Evidence. Each article was assigned a design class with design 1 representing the strongest study design and subsequent design classes (ie, design 2 and design 3) representing respectively weaker study designs for therapeutic, diagnostic, or prognostic clinical reports, or meta-analyses (Appendix A). Articles were then graded on dimensions related to the study's methodological features, such as randomization processes, blinding, allocation concealment, methods of data collection, outcome measures and their assessment, selection and misclassification biases, sample size, and generalizability. Using a predetermined process related to the study's design, methodological quality, and applicability to the critical question, articles received a final Class of Evidence grade (ie, Class I, Class II, Class III, or Class X) (Appendix B). Articles identified with fatal flaws or

that were ultimately not applicable to the critical question received a Class of Evidence grade "X" and were not used in formulating recommendations for this policy. Grading was done with respect to the specific critical questions; thus, the level of evidence for any one study may vary according to the question for which it is being considered. As such, it was possible for a single article to receive different Classes of Evidence as different critical questions were answered from the same study. Question-specific Classes of Evidence grading may be found in the Evidentiary Table included at the end of this policy.

Translation of Classes of Evidence to Recommendation Levels

Strength of recommendations regarding each critical question were made by subcommittee members using results from strength of evidence grading, expert opinion, and consensus among subcommittee members according to the following guidelines:

Level A recommendations. Generally accepted principles for patient care that reflect a high degree of clinical certainty (eg, based on evidence from one or more Class of Evidence I or multiple Class of Evidence II studies).

Level B recommendations. Recommendations for patient care that may identify a particular strategy or range of strategies that reflect moderate clinical certainty (eg, based on evidence from one or more Class of Evidence II studies or strong consensus of Class of Evidence III studies).

Level C recommendations. Recommendations for patient care that are based on evidence from Class of Evidence III studies or, in the absence of any adequate published literature, based on expert consensus. In instances where consensus recommendations are made, "consensus" is placed in parentheses at the end of the recommendation.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, and publication bias, among others, might lead to such a downgrading of recommendations.

When possible, clinically oriented statistics (eg, likelihood ratios, number needed to treat) are presented to help the reader better understand how the results may be applied to the individual patient. For a definition of these statistical concepts, see Appendix C.

This policy is not intended to be a complete manual on the diagnosis and management of adult psychiatric patients in the ED but rather a focused examination of critical issues that have particular relevance to the current practice of emergency medicine.

It is the goal of the Clinical Policies Committee to provide an evidence-based recommendation when the medical literature provides enough quality information to answer a critical question. When the medical literature does not contain adequate empirical data to answer a critical question, the members of the Clinical Policies Committee believe that it is equally important to alert emergency physicians to this fact.

This clinical policy is not intended to represent a legal standard of care for emergency physicians. Recommendations offered in this policy are not intended to represent the only diagnostic or management options available to the emergency physician. ACEP recognizes the importance of the individual physician's judgment and patient preferences. This guideline defines for the physician those strategies for which medical literature exists to provide support for answers to the critical questions addressed in this policy.

Scope of Application. This guideline is intended for physicians working in EDs.

Inclusion Criteria. This guideline applies to adult patients presenting to the ED with psychiatric symptoms. Critical question 4 includes patients with delirium.

Exclusion Criteria. This guideline is not intended to be used for pediatric patients. It is also not intended for patients with delirium in regard to critical questions 1, 2, and 3.

For potential benefits and harms of implementing the recommendations, see Appendix D.

CRITICAL QUESTIONS

1. In the alert adult patient presenting to the ED with acute psychiatric symptoms, should routine laboratory tests be used to identify contributory medical conditions (nonpsychiatric disorders)?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. Do not routinely order laboratory testing on patients with acute psychiatric symptoms. Use medical history, previous psychiatric diagnoses, and physician examination to guide testing.

Key words/phrases for literature searches: emergency services, hospital, psychiatric, mental disorders, physical examination, diagnostic tests, routine, and variations and combinations of the key words/phrases. Searches included January 1, 2005 to search date of September 3, 2015.

Study Selection: Ninety-five articles were identified in the searches. Nine articles were selected from the search results for further review, with 2 Class III studies included for this critical question.

In patients with acute behavioral emergencies, physicians are often asked to obtain routine laboratory testing in addition to obtaining a history and performing a physical examination. The previous clinical policy on this topic, published in 2006,[15] made a Level B recommendation: "In adult ED patients with primary psychiatric complaints, diagnostic evaluation should be directed by the history and physical examination. Routine laboratory testing of all patients is of very low yield and need not be performed as part of the ED assessment"; and Level C recommendations: "Routine urine toxicologic screens for drugs of abuse in alert, awake, cooperative patients do not affect ED management and need not be performed as part of the ED assessment; urine toxicologic screens for drugs of abuse obtained in the ED for the use of the receiving psychiatric facility or service should not delay patient evaluation or transfer." However, the articles supporting this 2006 recommendation were regraded by the methodologists using the committee's current criteria and were determined to be either Class X or Class III.[16-18]

For this revision, the authors of 2 Class III studies[19,20] reached similar conclusions that laboratory testing after medical screening by an emergency physician rarely if ever changes ED management or disposition. Janiak and Atteberry[19] performed a chart review on 502 consecutive admissions at a large academic center. In this center, routine laboratory tests were obtained for all patients admitted to the psychiatric service, regardless of whether directed testing was performed by the emergency physician. The authors reviewed each of these laboratory test results and noted that, with only one exception (0.19%), laboratory tests obtained by the psychiatric service would not have changed management.

In a similar study, Parmar et al[20] obtained a convenience sample of 598 patients presenting to an ED. After medical screening by an emergency physician, which included laboratory tests in 155 patients, 44% of patients had additional laboratory tests obtained by the psychiatric service. With only one exception (0.5%), no patient had a laboratory value that led to a change in disposition.

According to these 2 studies,[19,20] it would appear that laboratory studies ordered by the psychiatric service rarely change patient disposition from an ED point of view. However, because both studies investigated only patients admitted to an inpatient unit, it is unknown whether laboratory test results influence disposition for patients sent to other locations (for instance, a crisis residence or rehabilitation facility). It is also unknown what harms the patients might have experienced had a medical illness been undetected. Finally, none of the studies reviewed included all patients presenting to the ED with acute psychotic symptoms, meaning that it is unknown whether there are patients who are missed by current ED screening methods.

In summary, existing literature indicates that routine or ancillary laboratory testing for psychiatric patients has little or no use in the ED. It is likely that subsets of patients with higher rates of disease (eg, elderly, immunosuppressed, new-onset psychosis, substance abuse) may benefit from routine laboratory testing. In addition, although urine toxicologic screening has no benefit for the management or disposition of the patient in the ED, it may be helpful to obtain an objective understanding of the patient's potential substance abuse on transfer to a psychiatric facility. When transfer to a psychiatric facility may be delayed for hours, it may be helpful to obtain a urine toxicologic screen in the ED, when feasible. To expedite the care of patients, agreement between the ED and local psychiatric facilities regarding minimal laboratory testing for psychiatric clearance should be mutually determined.

Future Research

Future research should evaluate the use of routine laboratory testing for patients with acute psychiatric symptoms by prospectively enrolling patients in the ED on presentation, prior to final diagnosis and disposition.

2. In the adult patient with new-onset psychosis without focal neurologic deficit, should brain imaging be obtained acutely?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. Use individual assessment of risk factors to guide brain imaging in the ED for patients with new-onset psychosis without focal neurologic deficit. (Consensus recommendation)

Key words/phrases for literature searches: emergency services, mental disorders, physical examination, diagnostic tests, routine, and variations and combinations of the key words/phrases. Searches included January 1, 2005 to search date of September 4, 2015.

Study Selection: Ninety-three articles were identified in the searches, and 13 articles were selected from the search results for further review. None of the 13 articles were classified as Class I, II, or III; therefore, zero studies were included for this critical question.

Historically, computed tomography (CT) of the brain has often been recommended in the evaluation of patients with new-onset psychosis without focal neurologic deficits to exclude medical pathology such as mass lesion as a cause for symptoms. Because psychosis, delirium, dementia, and encephalopathy may share similar presenting features, CT of the brain has been seen as a potentially important part of the diagnostic algorithm for new-onset psychosis.

The rate of reported neuroimaging abnormalities in the Class X studies reviewed varied widely, from 3% to 66.1%.[21-27] In many studies, the reported abnormalities were either not described or were characterized as incidental or unrelated to the patient's psychiatric condition. A study comparing neuroimaging in patients presenting with psychosis versus a control group found no difference in the frequency of clinically relevant findings (11.1% versus 11.8%).[28] In the Class X studies that did categorize imaging abnormalities, the percentage of imaging findings described as clinically relevant, influencing clinical management, or altering diagnosis ranged from 0% to approximately 5%.[21-23,25-27] Definitions of "altering treatment" or "altering diagnosis" were not strictly described and may be difficult to apply to a retrospective chart review or lack external validity. Interpretation of the effect of imaging on diagnosis and treatment also may depend on blinding, which was not applied in all studies. In addition, as described below, poor study methodology may result in underreporting of abnormalities by systematic exclusion of patients with abnormal findings. Consequently, the results of these Class X studies should be applied with caution and attention given to patient-specific risk factors for central nervous system disease.

It is difficult to ascertain an accurate estimation of significant abnormal neuroimaging findings based on the current studies in the literature.There are a number of ways in which the rate of abnormal neuroimaging study results in patients with new-onset psychosis in the ED can be underestimated. Poorly described methods may mask biases such as low-quality chart abstraction, lack of blinding, or absence of strictly defined variables. Studies that retrospectively identified patients based on final diagnostic codes for "new psychosis" may not have

included all patients who presented initially with altered mental status, such as those who later received alternative diagnoses such as encephalopathy, central nervous system mass, hydrocephalus, or stroke. In some studies, inpatient psychiatric patients were included; these patients are typically more homogeneous than patients in the ED and have fewer acute comorbidities, placing them at a lower risk than the undifferentiated patient in the ED.

Conversely, there are factors that may falsely elevate the rate of abnormal neuroimaging study results that were reported. To identify patients as having no focal neurologic deficits, a comprehensive structural examination would be required. None of these studies provided a detailed description of neurologic examination performed; it is not clear whether patients underwent a thorough examination to exclude deficits or if patients were included when there were no deficits documented in the medical record. Given that many acutely psychotic patients may not be able to cooperate with a comprehensive neurologic examination, emergency physicians may have a lower threshold to obtain neuroimaging in these patients.

The timeframe for imaging and the definition of abnormal were also not clearly defined among these studies, making their application to patients in the ED unclear.

Future Research

Future research should prospectively enroll patients in the ED using strict definitions of psychosis, new onset, and acute time frame for imaging, a well-defined neurologic examination, and definitions of clinically relevant imaging abnormalities, using a uniformly applied reference standard (ie, CT, magnetic resonance imaging [MRI], or clinical follow-up).

3. In the adult patient presenting to the ED with suicidal ideation, can risk-assessment tools in the ED identify those who are safe for discharge?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. In patients presenting to the ED with suicidal ideation, physicians should not use currently available risk-assessment tools in isolation to identify low-risk patients who are safe for discharge. The best approach to determine risk is an appropriate psychiatric assessment and good clinical judgment, taking patient, family, and community factors into account.

Key words/phrases for literature searches: suicidal ideation, ED, emergency services, hospital, risk assessment, patient discharge, and variations and combinations of the key words/phrases. Searches included January 1, 1990 to search dates of September 4, 2015, and November 5, 2015.

Study Selection: Eighty-five articles were identified in the searches. Nineteen articles were selected from the search results for further review, with 4 Class III studies included for this critical question.

Emergency physicians, as well as mental health professionals, are frequently called on to determine the suicide risk in a patient who presents with depression or suicidal ideation. There are many tools to screen for suicidal ideation, although few that determine the level of risk for the patient. There is a need to determine whether a patient has high, moderate, or low risk of suicide to help decide whether a patient should be hospitalized or discharged. An objective tool for patients' risk determination, such as the Pulmonary Embolism Rule-out Criteria (PERC) rule for pulmonary embolism, National Emergency X-radiography Utilization Study (NEXUS) criteria for cervical spine radiographs, or Thrombolysis in Myocardial Infarction (TIMI) scores for coronary artery disease, would be helpful but has eluded current investigations. For example, if a good tool existed for psychiatric patients, it might classify patients as high risk (patient needs inpatient psychiatric care), moderate risk (patient needs further evaluation and treatment from a mental health professional), and low risk (patient may only need outpatient follow-up).

That the discovery of a tool to determine the level of risk for suicidal patients has eluded medical science is not surprising because suicide is a complex disease process with many persons who present with suicidal ideation, fewer patients with suicide attempts, and lesser number who complete a suicide. This determination process is made more challenging by the waxing and waning of suicidal thoughts over time, changes in psychiatric condition, social circumstances, and contribution from substance use and stressors.

A number of studies were reviewed for inclusion in this clinical policy. However, few studies examined tools used in the ED setting that would predict suicide within a short time period. The studies varied by technique, subject enrollment, end point, and length of follow-up. Four Class III studies[29-32] were identified that investigated whether risk assessment can identify patients who are at risk for future self-harm.

Posner et al[29] used a tool developed by Columbia University, the University of Pennsylvania, and the University of Pittsburgh, the Columbia–Suicide Severity Rating Scale (C-SSRS). The tool was used to distinguish suicidal ideation from suicidal behavior. The 4 constructs measured in this tool were severity, intensity of

ideation, suicidal behavior subscale, and a lethality subscale. In adult patients with psychiatric problems, the C-SSRS had 100% sensitivity (95% confidence interval 98% to 100%) and 100% specificity (95% confidence interval 94% to 100%) for identifying lifetime actual attempts that were recorded on the Columbia Suicide Form. The study was limited by low prevalence and convenient outcome measurement, and the incremental predictive validity of C-SSRS could not be estimated. Unfortunately, the risk of lifetime suicide attempts does not help the emergency physician in the disposition of a patient presenting to the ED with suicidal ideation.

Tran et al[30] examined a large retrospective electronic medical record database of patients with at least one suicide risk assessment to develop a prediction model; the investigators then compared performance of the electronic medical record–based model with an 18-item checklist used by clinicians to estimate suicide risk. The goal was to differentiate low-, moderate-, and high-risk suicidal behaviors. Although the predictive performance of the electronic medical record–based model was inadequate as a decision support tool (sensitivity=28% for high risk), the model did perform better than clinician assessment using the 18-item checklist (sensitivity=8% for high risk) based on 90-day outcomes.

Bilen et al[31] examined a list of factors that could predict repeated deliberate self-harm or suicide. Risk factors associated with deliberate self-harm were female sex, self-injury and whether the self-injury required a surgical procedure, current psychiatric or antidepressant treatment, substance use disorder, personality disorder, and not having children younger than 6 years. Using these factors, patients could be stratified into low-, moderate-, and high-risk categories. Although deliberate self-harm has a close association to suicide, this study focused on deliberate self-harm rather than suicide.

Randall et al[32] used a number of psychiatric scales and found modest performance according to receiver operating characteristic curve analysis and predictive values. They used several questionnaires such as the Beck Hopelessness Scale, the Barrett Impulsiveness Scan, the Brief Symptom Inventory, the Drug Abuse Screening Test, and the Cut down, Annoyed, Guilt, Eye-opener (CAGE) assessment to determine which of these scales were valuable in differentiating individuals at risk for self-harm within 3 months. This study was limited by selection bias and attrition. Clinicians' predictive power was poor for high risk, as was the electronic medical record model. None of the tools were considered strong enough and the diagnostic usefulness is limited.

Although these studies were rated as Class III, the study designs were problematic. The studies need to be able to separate the tools that best predict suicide completion in an at-risk population with a low prevalence rate. The ideal tool would be useful in all age groups and have a greater than 90% sensitivity and specificity for high-risk in the next 30 days with co-occurring mental illness and substance use disorder.

This clinical policy review demonstrates that there is no tool currently available that can be solely used to predict the risk of suicide among patients in the ED who have suicidal ideation.

Future Research

Future research needs to focus on developing ED tools that can identify patients at low risk for immediate or short-term suicide attempt, who would be safe for discharge with outpatient mental health follow-up.

4. In the adult patient presenting to the ED with acute agitation, can ketamine be used safely and effectively?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. Ketamine is one option for immediate sedation of the severely agitated patient who may be violent or aggressive. (Consensus recommendation)

Key words/phrases for literature searches: ketamine sedation for agitation in ED, acute agitation, agitation, psychomotor agitation, ketamine, emergency service, hospital, emergency department, and variations and combinations of the key words/phrases. Searches included January 1, 2005 to search dates of September 4, 2015, and November 5, 2015.

Study Selection: One hundred thirty-three articles were identified in the searches, and 11 articles were selected from the search results for further review. None of the 11 articles were classified as Class I, II, or III studies; therefore, zero studies were included for this critical question.

At this time, there is a lack of Class I, II, or III studies establishing the safety and efficacy of ketamine to control acute agitation in the ED. However, there are a number of studies in the out-of-hospital literature describing its use for this indication, and there are 2 studies (Class X) addressing its use in the ED under the immediate direction of a physician.[33,34]

Management of acutely agitated patients in the ED remains a critical issue. Most of these patients can be safely sedated with antipsychotics and/or benzodiazepines, but there remains a subset of extremely agitated patients for whom this approach will not be effective. Although small in number, these patients have a significant effect on the ED staff in terms of time and dedicated resources in order to maintain a safe environment for the patient and others in the ED.[33] Multiple agents, including ketamine, have been suggested as rescue agents in instances when antipsychotics and/or benzodiazepines fail.

Ketamine has been used as a drug for sedation, anesthesia, and induction for many years. It functions through antagonism of the glutamate *N*-methyl-D-aspartate receptors, resulting in a dissociated state with analgesia and amnesia.[34] Its rapid onset of action, achieving the dissociated state within 1 to 2 minutes by the intravenous route and within approximately 3 minutes by the intramuscular route, and short half-life make it useful for procedural sedation and pretreatment of intubation in the ED. Other benefits include few effects on vital signs, with typically protected respiratory drive and rare negative effects on systolic blood pressure.

Ketamine also has several potentially serious adverse effects, most notably tachycardia and hypertension in already agitated patients. Ketamine is associated with emergence phenomenon, laryngospasm, hypersalivation, and vomiting.[34,35] Its duration of action is short; thus, patients may require readministration of medications. There are also concerns that it may worsen symptoms in psychiatric patients who are acutely psychotic.

Although no high-level studies currently describe its use in the ED, 2 Class X studies recently addressed its use for patients with acute agitation in the ED.[33,34] In a retrospective review of 27 patients who received ketamine for acute agitation in the ED, none became hypoxic.[34] Sixty-two percent of patients required additional sedating medications. The dosing range was wide in this group of patients, from 40 to 400 mg of intravenous or intramuscular ketamine. The median dose was 200 mg.[34] A 2016 study described administration of ketamine as a rescue drug in ED patients after droperidol or droperidol and benzodiazepines failed.[33] Forty-nine patients received intramuscular ketamine, with dosing of 4 to 6 mg/kg. Of these patients, 90% were adequately sedated within 1 hour; only one had hypoxia less than 90% responding immediately to oxygen administration.[33] There is also a description of its use for aeromedical retrieval of patients with acute psychiatric complaints who required critical care monitoring and transport by physicians during a prolonged period. In these instances, no patients required intubation after ketamine administration.[33,34,36] It was also thought that ketamine administration did not

result in worsening agitation or psychosis in the group of patients who required aeromedical transport.[36] Both groups of patients required additional sedating medications, and the group receiving aeromedical retrieval continued to receive ketamine throughout their transport time.[34,36] This is to be expected, given the duration of action of ketamine and the fact that it did not treat the underlying disorder that resulted in agitation. A common dosing strategy is intramuscular 4 to 6 mg/kg, and in cases in which additional sedation is required after ketamine, low dosing is a likely culprit.[33]

There are multiple studies describing the use of ketamine for the agitated patient in the out-of-hospital literature. These describe the known adverse effects of laryngospasm, hypersalivation, vomiting, and emergence reaction.[37,38] In out-of-hospital situations in which a physician was not administering the drug, respiratory depression was not uncommon and required escalation of care ranging from airway positioning to intubation in as many as 29% of patients.[39] It is unclear whether this was a result of improper dosing or concomitant sedatives either ingested by the patient or given by emergency medical services personnel; however, the authors pointed out that there was a significant difference in the dose of ketamine for patients who were intubated versus those who were not (6.16 mg/kg [SD 1.62] versus 4.90 mg/kg [SD 1.54]; *P*=.02). In most cases, emergence reaction can be easily treated with benzodiazepines.

Although there is limited literature for guidance, the skill set of emergency physicians and their familiarity with the use of ketamine make it a reasonable choice when immediate control of an acutely agitated patient is required for patient and/or staff safety.

Future Research

Given the paucity of quality literature on this topic, future high-quality research is needed to establish the safety and efficacy of ketamine compared with other agents for control of the acutely agitated patient in the ED.

Relevant industry relationships: There were no relevant industry relationships disclosed by the subcommittee members for this topic.

Relevant industry relationships are those relationships with companies associated with products or services that significantly impact the specific aspect of disease addressed in the critical question.

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Appendix A. Literature classification schema.*

Design/ Class	Therapy†	Diagnosis‡	Prognosis§
1	Randomized, controlled trial or meta-analysis of randomized trials	Prospective cohort using a criterion standard or meta-analysis of prospective studies	Population prospective cohort or meta-analysis of prospective studies
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series	Case series	Case series

*Some designs (eg, surveys) will not fit this schema and should be assessed individually.
†Objective is to measure therapeutic efficacy comparing interventions.
‡Objective is to determine the sensitivity and specificity of diagnostic tests.
§Objective is to predict outcome, including mortality and morbidity.

Appendix B. Approach to downgrading strength of evidence.

	Design/Class		
Downgrading	**1**	**2**	**3**
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

Appendix C. Likelihood ratios and number needed to treat.*

LR (+)	LR (–)	
1.0	1.0	Does not change pretest probability
1–5	0.5–1	Minimally changes pretest probability
10	0.1	May be diagnostic if the result is concordant with pretest probability
20	0.05	Usually diagnostic
100	0.01	Almost always diagnostic even in the setting of low or high pretest probability

LR, likelihood ratio.
*Number needed to treat (NNT): number of patients who need to be treated to achieve 1 additional good outcome; NNT=1/absolute risk reduction×100, where absolute risk reduction is the risk difference between 2 event rates (ie, experimental and control groups).

Appendix D. Potential benefits and harms of implementing the recommendations.

1. In the alert adult patient presenting to the ED with acute psychiatric symptoms, should routine laboratory tests be used to identify contributory medical conditions (nonpsychiatric disorders)?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. Do not routinely order laboratory testing on patients with acute psychiatric symptoms. Use medical history, previous psychiatric diagnoses, and physician examination to guide testing.

Potential Benefit of Implementing the Recommendations: The potential benefits of implementing the proposed recommendations are economic and affect length of stay. If testing is reduced, this would likely reduce the total cost and lengths of stay for mental health patients.

Potential Harm of Implementing the Recommendations: The potential harms for reducing routine testing is that there are certain subsets of patients who likely benefit from more laboratory testing (eg, elderly, immunosuppressed, new-onset psychosis, substance use). Although not well studied, reducing testing in these cohorts of patients has the potential for missing diseases in this population.

2. In the adult patient with new-onset psychosis without focal neurologic deficit, should brain imaging be obtained acutely?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. Use individual assessment of risk factors to guide brain imaging in the ED for patients with new-onset psychosis without focal neurologic deficit. (Consensus recommendation)

Potential Benefit of Implementing the Recommendations: Reducing use of diagnostic neuroimaging for patients with acute psychosis has potential benefits. The commonly used imaging tests, CT and MRI, are expensive. With CT, patients are exposed to ionizing radiation, with possible carcinogenic effect. Both tests require large equipment not readily available in many care settings outside of the ED, meaning that the perceived need for imaging may be a driver of patient referral to the ED. Reducing use of these tests in the evaluation of acute psychosis may enable psychiatric evaluation in more appropriate care settings such as psychiatric clinics or hospitals. Patient compliance is required for CT and MRI; agitated patients may require sedation, increasing patient risks.

Potential Harm of Implementing the Recommendations: Studies on this topic are biased and may under- or overestimate the diagnostic yield/incidence of important abnormal findings on neuroimaging. As a consequence, restricting use of diagnostic neuroimaging in new-onset acute psychosis without focal neurologic abnormalities may result in missed diagnosis of important brain abnormalities requiring acute intervention, such as mass lesions, central nervous system infections, or lesions resulting in increased intracranial pressure.

3. In the adult patient presenting to the ED with suicidal ideation, can risk-assessment tools in the ED identify those who are safe for discharge?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. In patients presenting to the ED with suicidal ideation, physicians should not use currently available risk-assessment tools in isolation to identify low-risk patients who are safe for discharge. The best approach to determine risk is an appropriate psychiatric assessment and good clinical judgment, taking patient, family, and community factors into account.

Potential Benefit of Implementing the Recommendations: The potential benefit of implementing the recommendation is a reduced rate of missing patients at risk for future suicide attempt in patients erroneously found to be at low risk by risk-assessment tools alone. Application of a highly sensitive tool would expedite safe disposition of low-suicide-risk cases, thereby decreasing costs, length of stay, and ED crowding.

Potential Harm of Implementing the Recommendations: A potential harm could be increased length of stay and unnecessary behavioral health consultations in a subset of patients who are safe for discharge.

4. In the adult patient presenting to the ED with acute agitation, can ketamine be used safely and effectively?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. Ketamine is one option for immediate sedation of the severely agitated patient who may be violent or aggressive. (Consensus recommendation)

Potential Benefit of Implementing the Recommendations: Potential benefits of the use of ketamine in the acutely agitated patient in the ED include rapid de-escalation of the agitated patient when staff and patient safety are at risk.

Potential Harm of Implementing the Recommendations: Given the known adverse-effect profile of ketamine, potential harms include vomiting, laryngospasm, emergence reaction, and hypersalivation. The use of ketamine in these patients may result in a decrease in respiratory drive that requires intubation and the complications associated with ventilation support.

Evidentiary Table.

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Question 1					
Janiak and Atteberry[19] (2012)	III	Inner-city, academic medical center; chart review	Consecutive adult patients admitted to the psychiatric hospital; outcome: whether an abnormal laboratory result would have changed management	N=502; positive urine drug screen result (n=221), anemia (n=136), hyperglycemia (n=139), but there was only one case (0.19%) that identified an abnormal laboratory result that would have changed management	No description of chart review, no inter-rater reliability, abstractors not blinded to the study hypothesis
Parmar et al[20] (2012)	III	2 academic centers; prospective convenience sample	Convenience sample of adults presenting to an ED who are cleared for psychiatric admission at 2 academic institutions; outcome: change in disposition from an abnormal laboratory result	N=598; primary outcome: emergency physicians ordered screening laboratory tests on 155 patients, whereas psychiatry service ordered tests on an additional 191 patients (44%); 246 subjects had no laboratory tests drawn; only 1/191 patients (0.5%) had an abnormal laboratory result (acetaminophen that warranted *N*-acetylcysteine treatment) that led to change in disposition	Convenience sample at academic institution, inclusion criteria are not well defined, and for all of the patients who did not get laboratory tests and the psychiatrist did not request further testing, it is unknown whether there could have been an abnormal laboratory result

Evidentiary Table (continued).

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Question 2					
Albon et al[22] (2008)*	X	Systematic review of 25 studies reporting additional diagnostic benefit of MRI or CT	Outcome was whether there was change in management; used a modified QUADAS to assess quality of studies, and 2 investigators conducted the search	In the 4 MRI-only studies, 5% would have had a change in management, whereas in the 16 CT-only studies, 0.5% would have had a change in management	Included studies with patients with neurologic symptoms and patients with refractory psychosis not responding to medicines, thus, indirectly applicable; unclear whether scans were interpreted without knowledge of diagnoses; during the course of illness it is unclear when the scans were obtained; did not combine studies because of heterogeneity

Evidentiary Table (continued).

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Question 2					
Goulet et al[23] (2009)*	X	Combines a systematic review of 5 articles and a case series of 46 patients who had brain imaging at a Canadian hospital	338 patients from 5 historical articles are combined with the 46 hospital patients	Five of 384 (1.3%) are reported to be abnormal	Does not state whether there were 2 authors involved in the systematic review; no comment about quality assessment of each of the studies in systematic review; no comment about heterogeneity; combined a case series with the systematic review
Khandanpour et al[25] (2013)*	X	Single tertiary referral hospital in England; retrospective cohort chart review	Patients with a FEP but no focal neurologic signs, referred by primary, secondary, or tertiary services; excluded dementia patients; a group of healthy volunteers who participated in research projects as normal controls were also imaged with MRI; outcome: incidence of intracranial disease responsible for FEP diagnosed using MRI between July 1999 and October 2010, and using CT between April 2007 and October 2010	MRI group: N=112; 3 (2.7%) had brain lesions potentially responsible for the FEP; 70 (62.5%) had incidental brain lesions; CT group: N=204; 3 patients (1.5%) had focal brain lesions potentially accountable for FEP; 133 patients (65.2%) had incidental findings; no significant difference between MRI and CT in detecting disease potentially responsible for FEP; prevalence of cerebral small vessels ischemic disease was significantly higher among individuals with FEP (45%) than control group of volunteers (3%)	Incongruent years; bias from newer-generation MRI and CT; unclear whether cases underwent chart review or if all data came from the radiology request forms; unclear how FEP diagnosis was confirmed; no reliability assessment or adjudication for CT and MRI findings; no description of why patients were selected for MRI vs CT; no accounting for drop outs and attrition; no sample size estimation or reporting

Evidentiary Table (continued).

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Question 2					
Strahl et al[26] (2010)*	X	Single academic medical center in Australia; retrospective cohort chart review	Consecutive patients for whom the imaging requests or reports provided a history of FEP but no focal neurologic signs within a 6-y period; outcome: findings that could explain psychosis or that would change patient management	Of 237 patients identified, 17.7% had findings on CT; all did not affect clinical management; most common incidental findings were small hypodensities considered likely to be old infarcts or small vessel ischemic change (5.1%), arachnoid cysts (1.7%), cerebral atrophy (1.7%), and mild ventricular asymmetry (1.7%)	No dates provided for enrollment; no reliability estimates or adjudication reported for classifying and reporting radiology findings; workup bias because only scanned patients were included in the sample; no follow-up or description of those not scanned; no description of case inclusion or other presenting factors other than having "normal neurologic examination findings"; no statistical analysis or power calculation provided; unclear whether patients presented to the ED or whether tests were ordered in other settings

Evidentiary Table (continued).

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Question 2					
Williams et al[27] (2014)*	X	Single academic medical center; chart review	290 patients between 12 and 30 y who were admitted to psychiatry service for FEP and had CT or MRI	Six of 115 had an abnormal imaging finding, but all findings were considered incidental because none resulted in specific treatment	Clinical relevance of imaging findings was not defined a priori; 175 patients excluded from analysis for substance abuse within previous month, recent head trauma, or any neurologic signs or symptoms; amphetamine use was the most common exclusion criterion
Sommer et al[28] (2013)*	X	Single academic medical center in the Netherlands; case control	656 patients who were admitted to psychiatry service with psychosis and underwent MRI; 722 healthy controls, MRI classified as normal, nonrelevant abnormality, or clinically relevant abnormality, defined a priori	Clinically relevant abnormality found in 11.1% of cases and 11.8% of controls	Includes only patients who were admitted to psychiatry service; not a consecutive sample because MRI was performed at the discretion of the treating psychiatrist

Evidentiary Table (continued).

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Question 3					
Posner et al[29] (2011)	III	3 EDs; prospective cohort study	Adults presenting with psychiatric reasons, including suicide attempt, nonsuicidal self-injurious behavior, or psychiatric symptoms without suicide attempt or nonsuicidal self-injurious behavior; study clinicians administered the C-SSRS, the Scale for Suicide Ideation, Beck's Lethality Scale, and the Columbia Suicide History Form; outcome: lifetime actual, interrupted, and aborted suicidal attempts	N=237; associations between the C-SSRS and the Columbia Suicide History Form and the outcomes were high (Φ 0.99, 0.92, and 0.94, respectively); the C-SSRS had 100% sensitivity (95% CI 98% to100%) and 100% specificity (95% CI 94% to100%) for lifetime actual attempts	Small prevalence of the outcome (reattempt); also, convenient outcome but generally considered poor for predicting future suicide; likely underpowered
Tran et al[30] (2014)	III	Single urban hospital in Australia; retrospective cohort study	Adolescents (10 y or older) and adults with at least 1 suicide risk assessment between 2009 and 2012; use of electronic health record data, including patient characteristics and use of data from clinicians' prediction of risk using a risk-assessment checklist; outcome: 6-mo repeated suicide attempt or completed suicide	N=7,399; 13 suicides at 6 mo; 53% attended the ED 3 mo before suicide assessment; clinicians were relatively poor in predicting patients at high risk (sensitivity 8%, 95% CI 2% to 20%; specificity 97%, 95% CI 96% to 98%; AUC 0.58, 95% CI 0.50 to 0.66); an electronic medical record model demonstrated better prediction than clinician assessment (sensitivity 28%, 95% CI 16% to 41%; specificity 97%, 95% CI 96% to 98%)	Electronic data abstraction; limited generalizability; validation of methods at the same institution for which they were derived; external validation required

Evidentiary Table (continued).

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Question 3					
Bilen et al[31] (2011)	III	Single urban hospital in Sweden; chart review	All adults presenting with deliberate self-harm from 2003 to 2005; structured protocol database, used CART and multivariable modeling to identify risk factors for repeated self-harm; outcome: repeated self-harm attempt or death by suicide (based on Sweden registry)	N=1,524; primary outcome: 484 patients (31.8%) had repeated deliberate self-harm episode between 2003 and 2006; 96/1,524 patients (6%) died, including 35 (2.3%) who died by suicide; factors associated with repeated deliberate self-harm: previous deliberate self-harm, female sex, whether self-injury required a surgical procedure, patient under current psychiatric treatment or on antidepressant, substance abuse, personality disorder, and not having a child younger than 6 y	No description of the validity or reliability assessment for the presence of a risk factor
Randall et al[32] (2012)	III	2 urban academic hospitals in Canada; prospective cohort study	Adults presenting with suicidal ideation or self-harm; trained research assistants performed standardized verbal interviews and had patients complete several written psychiatric questionnaires, including the Beck Hopelessness Scale, BSI, BIS, CAGE, and DAST-10; outcome: self-harm within 3 mo of ED presentation	N=270 eligible; 157 patients completed the questionnaires and constituted the study sample; 128 (82%) were successfully followed; subscales of the BSI and BIS, as well as the DAST-10 were significant predictors of self-harm based on multivariable modeling; ROC curves demonstrated modest predictive abilities (AUC range 0.54 to 0.66)	Selection bias; attrition without sensitivity analysis

Evidentiary Table (continued).

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Question 4					
Ibister et al[33] (2016)*	X	2 academic, urban medical centers; case series	Adults with acute agitation who received ketamine as rescue agent during DORM II study; prospective data collection; outcome: (1) number of patients who failed to achieve sedation within 120 min; (2) adverse events	N=49; 44 of 49 achieved adequate sedation; 2 patients vomited and 1 patient experienced oxygen desaturation	Most patients received 2 doses of droperidol 10 mg before receiving ketamine; variable doses of ketamine
Hopper et al[34] (2015)*	X	Multiple academic and community medical centers; case series	Adults with acute agitation who received ketamine in the ED; structured chart review; outcomes: (1) need for additional sedation; (2) vital sign changes	N=32 visits (27 patients); 62% required additional sedation; no recorded episodes of oxygen desaturation	Variable doses and routes (IM or IV) of ketamine; many patients received other medications before and after receiving ketamine; no comparison group

AUC, area under the curve; BIS, Barrett Impulsiveness Scale; *BSI*, Brief Symptom Inventory; *CAGE*, Cut down, Annoyed, Guilt, Eye-opener; *CART*, Classification And Regression Tree; *CI*, confidence interval; *C-SSRS*, Columbia–Suicide Severity Rating Scale; *CT*, computed tomography; *DAST-10*, Drug Abuse Screening Test; *DORM*, Droperidol Or Midazolam; *ED*, emergency department; *FEP*, first episode of psychosis; *IM*, intramuscular; *IV*, intravenous; *min*, minutes; *mo*, month; *MRI*, magnetic resonance imaging; *QUADAS*, Quality Assessment of Diagnostic Accuracy Studies in Systematic Reviews; *ROC*, receiver operating characteristic; *vs*, versus; *y*, year.

*Only select Class X articles were included in the Evidentiary Table.