Does This Patient Have Delirium?: Value of Bedside Instruments
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CLINICAL SCENARIO
An 85-year-old man with non–small cell lung cancer was admitted yesterday to the oncology ward for treatment of pneumonia. He started antibiotics and supplemental oxygen. Prior to hospitalization, he lived independently in the community. An overnight nursing report indicates that he did not sleep and was pacing up and down the ward. During morning rounds, he was easily startled and noted to be picking at the bed sheets. The patient’s daughter says, “This is not my father. Right now, he’s in his own little world. He never behaves this way!” What instruments could the nurse and physician use to determine if these changes and observations are indicative of a delirium?

BACKGROUND
Patients with delirium have a reduced ability to focus, to sustain or shift attention with an associated change in cognition, or they develop a perceptual disturbance that occurs over a short period of time and tends to fluctuate over the course of the day. There is usually evidence of a medical cause from history, physical examination, or investigations. Many hospitalized older patients become delirious and delirium is an independent marker for increased mortality during the 12 months after hospital admission. In addition to death, developing delirium has been associated with longer length of hospital stay, increased hospital-acquired complications, persistent cognitive deficits, and increased discharge rates to long-term care.

Context Delirium occurs in many hospitalized older patients and has serious consequences including increased risk for death and admission to long-term care. Despite its importance, health care clinicians often fail to recognize delirium. Simple bedside instruments may lead to improved identification.

Objective To systematically review the evidence on the accuracy of bedside instruments in diagnosing the presence of delirium in adults.

Data Sources Search of MEDLINE (from 1950 to May 2010), EMBASE (from 1980 to May 2010), and references of retrieved articles to identify studies of delirium among inpatients.

Study Selection Prospective studies of diagnostic accuracy that compared at least 1 delirium bedside instrument to the Diagnostic and Statistical Manual of Mental Disorders–based diagnosis made by a geriatrician, psychiatrist, or neurologist.

Data Synthesis There were 6570 unique citations identified with 25 prospectively conducted studies (N = 3027 patients) meeting inclusion criteria and describing use of 11 instruments. Positive results that suggested delirium with likelihood ratios (LRs) greater than 5.0 were present for the Global Attentiveness Rating (GAR), Memorial Delirium Assessment Scale (MDAS), Confusion Assessment Method (CAM), Delirium Rating Scale Revised-98 (DRS-R-98), Clinical Assessment of Confusion (CAC), and Delirium Observation Screening Scale (DOSS). Normal results that decreased the likelihood of delirium with LRs less than 0.2 were calculated for the GAR, MDAS, CAM, DRS-R-98, Delirium Rating Scale (DRS), DOSS, Nursing Delirium Screening Scale (Nu-DESC), and Mini-Mental State Examination (MMSE). The Digit Span test and Vigilance “A” test in isolation have limited utility in diagnosing delirium. Considering the instrument’s ease of use, test performance, and clinical importance of the heterogeneity in the confidence intervals (CIs) of the LRs, the CAM has the best available supportive data as a bedside delirium instrument (summary-positive LR, 9.6; 95% CI, 5.8-16.0; summary-negative LR, 0.16; 95% CI, 0.09-0.29). Of all scales, the MMSE (score < 24) was the least useful for identifying a patient with delirium (LR, 1.6; 95% CI, 1.2-2.0).

Conclusion The choice of instrument may be dictated by the amount of time available and the discipline of the examiner; however, the best evidence supports use of the CAM, which takes 5 minutes to administer.
The symptoms of delirium may become apparent when a patient has difficulty in carrying on a normal conversation. Because visiting family members or nurses often spend more time with the patient than physicians do, they may be the first to detect delirium. Health care workers fail to recognize more than half of delirium cases. The Diagnostic and Statistical Manual of Mental Disorders (Third Edition) (DSM-III) criteria for delirium, when applied systematically to 133 consecutively admitted patients to an acute medical ward, led to a diagnosis of delirium in 20 patients, only 1 of whom was reported as delirious by the primary clinician. Delirium is often iatrogenic, resulting from a diversity of problems such as adverse drug reactions, the multiple stresses of surgery, complications of procedures, or immobilization. Given that multiple factors usually contribute to the development of delirium, randomized trials have shown multicomponent preventive strategies to be effective in preventing delirium.

How to Diagnose Delirium

The diagnosis is primarily clinical and based on careful observation of key features. Consensus from an expert panel identified several clinical features of delirium: acute onset and fluctuating course, inattention, disorganized thinking, altered level of consciousness, disorientation, memory impairment, perceptual disturbances, increased or decreased psychomotor activity, and disturbance of the sleep-wake cycle. The key diagnostic feature that helps to distinguish delirium from dementia is that delirium has an acute and rapid onset, whereas dementia is much more gradual in progression. Alternations in attention and changes in level of consciousness also favor a diagnosis of delirium. Delirium typically presents in 1 of 2 major forms—hypochotic or hyperactive. The hyperactive form is characterized by agitation, increased vigilance, and often hallucinations; this form rarely goes unnoticed by clinicians or caregivers. There is also a mixed form of delirium in which patients fluctuate between the hypoactive and hyperactive forms. The criterion standard for the diagnosis of delirium as defined by the DSM continues to evolve. A formal assessment using this reference standard, however, may involve an in-depth interview and series of cognitive tests by a clinician familiar with DSM-IV criteria. Even in the hands of experts, the reference standard for delirium is a clinical diagnosis based on the DSM-IV criteria and may be prone to some subjectivity. For example, one study noted the agreement $k$ for reliability between 2 geriatricians with each classification of delirium to be 0.74 (DSM-III), 0.74 (DSM-III-R), and 0.72 (DSM-IV). Simpler bedside instruments may better guide which patients should receive formal consultation and intervention. The objective of this review was to determine the diagnostic accuracy of bedside delirium instruments.

METHODS

Literature Search Strategy

Searches of MEDLINE (from 1950 to May 2010) and EMBASE (from 1980 to May 2010) using Ovid were completed to identify studies performed in a clinical setting. The search strategy used terms including confusion and delirium combined with validated search filters for retrieving articles on the diagnosis of health disorders (eBox available at http://www.jama.com). Additional articles were identified from searching the bibliographies of retrieved articles.

Study Selection and Data Extraction

Inclusion criteria were published prospective studies that were conducted in hospitalized patients not in the intensive care unit, described the use of an appropriate reference standard (DSM-III, DSM-III-R, or DSM-IV), had the reference standard performed by a specialist physician (geriatrician, neuropsychologist, or psychiatrist), applied the same index test to most patients (>80%), applied the same reference tests to all patients and all reference test results were available, and included participants with and without delirium. Exclusion criteria were studies involving mostly alcohol-related delirium or a pediatric population, studies in which the index and reference tests were performed by the same individual, and duplicate or non–English-language publication. The bedside index instrument must be feasible in a clinical setting, without requiring special equipment, and may be performed by a nonexpert. Furthermore, primary data or appropriate summary statistics had to be available. When necessary, additional data were obtained by contacting study authors.

Each abstract was reviewed independently by 2 reviewers to select relevant publications that met the inclusion criteria for data extraction. In cases of doubt, full-text articles were retrieved for review and discussion. Two investigators independently reviewed each full-text article to confirm that inclusion and exclusion criteria were met. Disagreements were resolved by discussion, and when necessary, with a third reviewer.

Data were extracted from the included studies independently by 2 reviewers. Disagreements were resolved by consensus with the third reviewer. Information was extracted using a specially designed form based on the principles outlined by the Standards for Reporting of Diagnostic Accuracy (STARD). Details pertaining to study quality included study size, participant recruitment method, demographic characteristics of participants, application of reference standard, application of diagnostic test(s), presence of blinding, independence of tests, and attrition rates. Study quality was summarized using a quality checklist designed for the Rational Clinical Examination series in which a threshold...
of 100 patients was used to distinguish level 1 from level 2 studies.23

Statistical Methods
For studies of test accuracy, sensitivity, specificity, and likelihood ratios (LRs) were calculated from the raw data and then rounded for display in the data tables.24 If a study contained any zeros in the 2×2 table, resulting in likelihood estimates of zero or infinity, 0.5 was added to all the counts for that study for calculating the LR and respective confidence intervals (CIs). For studies that evaluated the same instrument at different threshold levels, the data were abstracted at each level and then the optimum threshold was selected based on a balance between the diagnostic odds ratio (OR) and our confidence in the findings because the threshold was studied by multiple investigators. The diagnostic OR (positive LR divided by negative LR) is a single indicator of test performance in which higher values indicate better discriminatory test performance. Summary LRs for instruments were derived using a univariate random-effects model (Comprehensive MetaAnalysis, version 2.2046, Biostat Inc, Englewood, New Jersey) since bivariate measures were similar or failed to converge on a solution.25

Heterogeneity was explored using $I^2$, which describes the percentage of total variation across studies that is due to heterogeneity rather than chance. Heterogeneity was categorized as low, moderate, and high to $I^2$ values of 25%, 50%, and 75%.25 If there was at least moderate heterogeneity, summary statistics were recalculated by eliminating the individual studies that contributed most to heterogeneity or by selecting only certain subgroups in a sensitivity analysis. Heterogeneity was assessed using Meta-Disc, version 1.4 (Unit of Clinical Biostatistics, Ramón y Cajal Hospital, Madrid, Spain).27

RESULTS

Study Characteristics
We identified 6570 potential citations of which 79 unique studies were retrieved for full-text review. Fifty-four studies were later excluded for a variety of reasons, leaving 25 studies15,28-51 suitable for data extraction and synthesis (eFigure 1).

The included studies ranged in size from 26 to 791 participants (N=3027; eTable 1). Eleven bedside delirium instruments, with data on diagnostic accuracy, met our inclusion and exclusion criteria (Box 1).8

All studies provided details on participant recruitment, and 9 enrolled consecutive patients.30-33,36,38,41-43 Eighteen studies described the use of independent, blinded assessment of reference and diagnostic tests in a clinical setting.9 Application of the diagnostic tests was consistent and complete in all but 2 studies.39,42 Application of the reference test, a DSM-based diagnosis by a specialist physician, was identical within each study. Overall, 1, 7, 9, and 8 studies were rated levels 1, 2, 3, and 4, respectively, in terms of quality level of evidence using the Rational Clinical Examination quality scale (eTable 1).23

Prevalence of Delirium
From the 9 studies30,33-36,38,41-43 that enrolled patients consecutively, the study prevalence of delirium ranged from 9% to 63% depending on the clinical setting (eTable 1). The prevalent cases in some of these studies likely included patients admitted with delirium, but also patients who developed delirium (incident cases). The highest prevalence, 63%, was in a study of hospitalized patients in an oncology or palliative care ward presenting with mental status change.33 The prevalence of delirium among patients admitted to a geriatric unit ranged from 9% to 43%36,38,62,46 and from 12% to 27% among patients in a postcardiac surgery unit.35,41

Accuracy of Clinical Examination Findings in the Diagnosis of Delirium

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Positive LR</th>
<th>Negative LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRS-R-98</td>
<td>1.6</td>
<td>0.19</td>
</tr>
<tr>
<td>CAM</td>
<td>1.0</td>
<td>0.03</td>
</tr>
<tr>
<td>MDAS</td>
<td>5.3</td>
<td>0.14</td>
</tr>
<tr>
<td>GAR</td>
<td>1.6</td>
<td>0.19</td>
</tr>
</tbody>
</table>

*References 15, 29, 31, 38, 39, 47, 48, 52-55.
†References 15, 29-34, 36-41, 45, 47, 48, 50, 51.
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When only levels 1 and 2 evidence of heterogeneity persisted (LR, 19; 95% CI, 6.7-51), but the heterogeneity LR increased (summary-positive LR, 0.19; 95% CI, 0.13-0.27). Subanalysis by language or DSM version did not resolve heterogeneity. Interrater reliability data were available for some of the studies for the CAM, DRS, DRS-R-98, and MDAS. All had a substantial degree of agreement (eTable 2).

**COMMENT**

Limitations

The results of this review should be interpreted within the context of the study's limitations.
| Table. Summary Data for Diagnostic Accuracy of Bedside Instruments for Diagnosing Delirium* |
|---------------------------------|-------------|-----------------------------|-----------------------------|
| Source                          | Sample Size | Delirium Prevalence, %       | Examiner Specialty          |
| Pompei et al.,39 1995         | 428         | 15                          | Research assistant          |
| CAM                            | 10b,h        |                             |                             |
| Farrell and Ganzini,31, 1995   | 72          | 45                          | Osteopathic physician       |
| Leung et al.,2008              | 100         | 25                          | Family physician            |
| Pompei et al.,2006             | 428         | 15                          | Research assistant          |
| Inouye et al.,1990 (site 1)    | 30          | 33                          | Geriatricist                |
| Inouye et al.,1990 (site 2)    | 26          | 62                          | Geriatricist                |
| Lauria et al.,2002            | 81          | 40                          | Geriatricist                |
| Leung et al.,2008              | 100         | 25                          | Family physician            |
| Pompei et al.,2006             | 428         | 15                          | Research assistant          |
| Rolfson et al.,1999           | 30          | 27                          | Nurse                       |
| Ryan et al.,2007              | 52          | 33                          | Hospitalist                |
| Zhu et al.,1998               | 87          | 49                          | Nurse                       |
| DRS-R-98;41,1996              | 406         | 13                          | Research assistant          |
| Grassi et al.,2001            | 105         | 63                          | Research psychologist       |
| Rockwood et al.,1996          | 67          | 37                          | Resident physician in geriatric medicine |
| Rosen et al.,1994             | 791         | 9                           | Research clinician          |
| Trzepacz et al.,1988          | 47          | 43                          | Psychiatrist                |
| Pompei et al.,1995            | 95          | 90                          | 78 (63-96)                  |
| Pompei et al.,2006            | 428         | 15                          | Research assistant          |
| DRS (13-Item)                 | 87          | 10                          | Nurse                       |
| Schuurmans et al.,2003        | 92          | 20                          | Nurse                       |
| Pool et al.                   | 178         |                             |                             |
| DRS-R-98,2008                  | 64          | 40                          | Researcher                  |
| de Negreiros et al,2006        | 65          | 35                          | Geriatricist or psychiatrist |
| Pool et al.                   | 129         |                             |                             |
| DRS-R-98,2008                  | 64          | 40                          | Researcher                  |
| de Negreiros et al,2006        | 65          | 35                          | Geriatricist or psychiatrist |
| Pool et al.                   | 129         |                             |                             |
| DRS <10b,h                    | 87          | 21                          | Geriatricist                |
| O’Keeffe and Cosney,1997       | 87          | 21                          | Geriatricist                |
| MDAS <10b,h                   | 30          | 58                          | Psychiatrist                |
| Breitbart et al.,1997          | 33          | 52                          | Psychiatrist                |
| Matsuoka et al,2001            | 37          | 43                          | Psychiatrist                |
| Pool et al.                   | 330         |                             |                             |
| MMSE <24                      | 105         | 63                          | Trained research psychologist |
| Nu DESC 3.0                   | 100         | 25                          | Nurse                       |
| Vigilance "A" Test            | 421         | 15                          | Research assistant          |
| % (95% Confidence Interval)    |              |                             |                             |
| Sensitivity                    |              |                             |                             |
| Specificity                    |              |                             |                             |
| Positive                       |              |                             |                             |
| Negative                       |              |                             |                             |

Abbreviations: CAC, Clinical Assessment of Confusion; CAM, Confusion Assessment Method; DOSS, Delirium Observation Screening Scale; DRS, Delirium Rating Scale; DRS-R, Delirium Rating Scale-Revised; GAR, Global Attentiveness Rating; MDAS, Memorial Delirium Assessment Scale; MMSE, Mini-Mental State Examination; Nu DESC, Nursing Delirium Screening Scale.

*Reliability measures are available at eTable 2, see http://www.jama.com.

1Heterogeneity was explored using I^2, which describes the percentage of total variation across studies that is due to heterogeneity rather than chance. Heterogeneity was categorized as low, moderate, and high, respective to P values of 25%, 50%, and 75%. Positive and negative I^2 values were 65 and 65 for CAM, 65 and 0 for DOSS, 14 and 0.19 for DRS, 73 and 0 for DRS-R-98, and 65 and 69 for MDAS.

2Calculated using the more conservative results of the 2 examiners.

3Using Diagnostic and Statistical Manual of Mental Disorders Fourth Edition criteria as the reference standard.

4Study not included in the summary data because results were based only on 8 patients with delirium and only 1 patient in the entire study population received positive screening results using the CAM instrument.

5There was also a pilot study with 32 patients in the same publication.

6Univariate random effects.

7Specific threshold chosen based on summary diagnostic odds ratio and validation in multiple studies.

8Individual data not available for confidence interval calculations or inclusion in meta-analysis.

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Diagnosing Patient Delirium

Box 2. The Confusion Assessment Method (CAM) Diagnostic Algorithm

Features and Descriptions

Feature 1: Acute onset and fluctuating course

Is there an acute change in mental status from the patient’s baseline? Did this behavior fluctuate during the past day (tend to come and go or increase and decrease in severity)?

Feature 2: Inattention

Does the patient have difficulty focusing attention, for example, being easily distractible, or having difficulty keeping track of what was being said?

Feature 3: Disorganized thinking

Is the patient’s speech disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?

Feature 4: Altered level of consciousness

Overall, how would you rate this patient’s level of consciousness?

Alert (normal)
Vigilant (hyperalert)
Lethargic (drowsy, easily aroused)
Stupor (difficult to arouse)
Coma (unarousable)

The diagnosis of delirium requires a present/abnormal rating for features 1 and 2 and also for either feature 3 or 4.

The algorithm is based on the cardinal elements of the Diagnostic and Statistical Manual of Mental Disorders (Third Edition, Revised) criteria for delirium. Adapted from Inouye (1990) and Ely (2001). A space for clinicians to indicate each of the 4 features as either absent or present appears on the actual algorithm.

Some training is recommended for optimal use and an instruction manual is available online (http://hospitalelderlifeprogram.org/pdf/). The validity of the CAM for unstandardized observations is poor and performance is linked to the quality of training. Thus, the CAM was designed to be scored based on observations made during formal cognitive assessment with brief instruments like the MMSE and the Digit Span test, which were used in the original validation study. Although there are several clinical features of delirium, the CAM diagnostic algorithm is based on only 4 cardinal elements of the DSM-III-R criteria for delirium: acute onset and fluctuating course, inattention, disorganized thinking, and altered level of consciousness (Box 2; eFigure 2). The algorithm should be based on observations during any contact with the patient and need not be limited to the interview period alone, but the algorithm should be applied immediately following the interview to ensure accuracy. Although not included in this review, the CAM has also been adapted for other clinical settings such as the intensive care unit, emergency department, and nursing home.

GAR. The global assessment is based on a minimum of 2 minutes of general conversation with the patient, without necessarily any formal cognitive testing or corroborative information. The question to be answered by the clinician is, “How well did the patient keep his mind on interacting with you during the hospital admission” with a wide spectrum of pretest probabilities. The pretest probability depends on the clinical setting (e.g., whether the patient is postoperative) and underlying diagnoses. This broad spectrum of probabilities can lead to varying estimates of the probability of delirium after using the screening tests.

For most of the LRs with heterogeneity, the clinical impact can still be inferred from the CIs. While heterogeneity was still present for instruments with many studies such as the CAM, these studies also allow the instrument to be tested across multiple populations to ensure its adequate performance and generalizability across different settings. Clinicians should be less certain when interpreting LRs based on single, small studies. For instance, the extremely high, positive LR and extremely low, negative LR for certain thresholds on the MDAS and DRS have not been validated with further studies. Some studies may have been missed given we limited the search terms to confusion and delirium. Like other types of systematic reviews, systematic reviews of diagnostic tests are subject to publication bias and may exaggerate the summary estimate of test accuracy if publication is related to the positivity of results. There were insufficient studies to look for funnel plot asymmetry.

How to Learn the Method for Diagnosing Delirium

CAM. Some training is recommended for optimal use and an instruction manual is available online (http://hospitalelderlifeprogram.org/pdf/). The validity of the CAM for unstandardized observations is poor and performance is linked to the quality of training. Thus, the CAM was designed to be scored based on observations made during formal cognitive assessment with brief instruments like the MMSE and the Digit Span test, which were used in the original validation study. Although there are several clinical features of delirium, the CAM diagnostic algorithm is based on only 4 cardinal elements of the DSM-III-R criteria for delirium: acute onset and fluctuating course, inattention, disorganized thinking, and altered level of consciousness (Box 2; eFigure 2). The algorithm should be based on observations during any contact with the patient and need not be limited to the interview period alone, but the algorithm should be applied immediately following the interview to ensure accuracy. Although not included in this review, the CAM has also been adapted for other clinical settings such as the intensive care unit, emergency department, and nursing home.

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ing the interview?” The answer is rated on an uninterrupted 10-cm visual analog scale.

We systematically determined the accuracy of bedside delirium instruments in diagnosing the presence of delirium and found several sensitive, specific, rapid, and simple instruments which may be useful for assessment of delirium. Although there have been other systematic reviews of bedside delirium instruments, 59,60 to our knowledge, this is the first study to include such a breadth of instruments and which also quantifies diagnostic accuracy with summary LRs.

The prevalence of delirium is high enough that a bedside delirium instrument should be used in patients 65 years old or older, particularly if there is an impression of a change in mental status. Because of its accuracy, brevity, and ease of use by clinical and lay interviewers, the CAM has become the most widely used standardized delirium instrument for clinical and research purposes over the past 2 decades. 60 It has been translated into 10 languages for which published articles are available. 60

Since a busy physician may not have 5 minutes to spend assessing a patient’s mental status, the most time-efficient screening approach may be to simply have a 2-minute general conversation with the patient. Although the overall impression of the quality and ease with which the physician can easily keep the patient engaged throughout a minimum of 2 minutes of general conversation may be a very valuable guide to delirium (GAR), this is supported by only 1 study with geriatricians. Thus, generalizability may be limited to physicians with expertise in this patient population.

This review highlights some gaps in the literature pertaining to bedside delirium instruments. Future areas of study include testing educational interventions to improve the ability of health care professionals to identify delirium with the available instruments, correlating results of the instruments with clinical outcomes, and validating these instruments outside of the hospital setting.

SCENARIO RESOLUTION

The older hospitalized patient should be evaluated for delirium, especially if there is an impression of mental status change. The pretest probability of delirium in this patient was 63% based on the clinical setting (oncology ward patient with pneumonia). 33 After conducting a formal cognitive assessment with the MMSE, both the physician and nurse used the CAM and agreed the change in mental status was acute and fluctuating in course, the patient was inattentive, and there was an altered level of consciousness. The postest probability of a delirium was 93% and 97% (pretest odds × positive LR=posttest odds) for the nurse and physician, respectively. The causes for his delirium require prompt assessment.

Author Contributions: Dr Wong had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Wong, Holroyd-Leduc, Straus.

Acquisition of data: Wong, Straus.

Analysis and interpretation of data: Wong, Holroyd-Leduc, Simel, Straus.

Drafting of the manuscript: Wong, Straus.

Critical revision of the manuscript for important intellectual content: Wong, Holroyd-Leduc, Simel, Straus.

Statistical analysis: Wong, Simel.

Study supervision: Holroyd-Leduc, Simel, Straus.

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DIAGNOSING PATIENT DELIRIUM


