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**Financial Disclosures:** Dr Friberg reported receiving speaker and consultant honoraria from EUSA Pharma and Innocoll and speaker honoraria from Swedish Orphan. Dr Söderquist reported being a consultant for Pfizer and Janssen-Cilag. Dr Svedjeholm reported no disclosures.

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**In Reply:** Our study and a companion study in colorectal surgery[1] are 2 large phase 3 trials targeting separate common surgical procedures; both clearly failed to demonstrate efficacy of use of the gentamicin-collagen sponge. These are not the first trials to fail to show efficacy. Dr Corn cites 2 positive European trials.[2,3] However, the study by Eklund et al was negative as indicated by its authors who wrote that their " . . . prospective, randomized study showed no significant difference between infection rates in the two groups."[2]

To Corn's main point, it is unlikely that wetting of the sponge for 1 to 2 seconds had any effect on its efficacy. Serum gentamicin levels obtained in our study patients (Figure 3 in the article) were similar and even slightly higher compared with those obtained at the same points in patients from the positive study by Friberg et al.[3,4] This argues against there being significant loss of gentamicin when the sponge is wet immediately prior to implantation and, in our opinion, is unlikely to be an explanation for our trial's negative result.

We agree with Dr Friberg and colleagues that their trial and ours show a high incidence of sternal wound infections despite routine care; therefore, there is an unmet need for new effective strategies. Although the use of this drug appears to be straightforward, a learning curve may be involved. Our study, however, was not designed to address this particular question. In clinical practice, the sponge is intended for use by a wide variety of surgeons, most of whom will do a limited number of cases per year.

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## Diagnosing Delirium

**To the Editor:** One of the main problems that physicians encounter when a patient with delirium is admitted to a hospital is to assess the degree of cognitive impairment present before the acute clinical event that caused hospitalization. This is important because dementia is both a risk factor for delirium and a strong prognostic modulator of the patient's global health status and survival.[1,2]

As highlighted in the Rational Clinical Examination article by Dr Wong and colleagues,[3] physicians often fail to recognize delirium and therefore they may underdiagnose it. However, the risk of underdiagnosing delirium when it is superimposed on dementia is also relevant.[4]

Wong et al stated that the key diagnostic feature distinguishing delirium from dementia is that delirium has an acute and rapid onset whereas dementia is much more gradual in progression, and that alternations in attention and changes in level of consciousness also favor a diagnosis of delirium. However, in clinical practice it is often not easy or feasible to make such a distinction. Furthermore, the tools used to diagnose delirium are frequently inappropriate in people with dementia.

For example, there are a number of reasons that the Confusion Assessment Method (CAM) cannot always be used for the diagnosis of delirium superimposed on dementia. First, it might be problematic to establish with an acceptable level of accuracy an acute change and fluctuating course of the patient's mental status because caregivers may not live with the patient. Second, the patient's ability to focus, sustain, or shift attention may not be easily detected in patients with delirium superimposed on dementia because impairment of attentive functions and difficulties understanding the task are often present even before delirium appears. For example, a common method to detect inattention is to ask the patient to tell the days of the week backward, starting with Saturday. However, patients with dementia may not be able to do this. Third, disorganized thinking and irrelevant conversation may be also a preexisting disorder before the occurrence of delirium.

Therefore, the tools proposed for the diagnosis of delirium are not useful for diagnosing delirium superimposed on dementia, despite this condition being prevalent among community-dwelling and hospitalized elderly patients.[4] The accuracy of physicians to distinguish dementia from delirium and to make the diagnosis of delirium superimposed on dementia should be improved.

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**To the Editor:** Dr Wong and colleagues[1] provided a systematic review that included discussion of easy-to-use bedside instruments to detect delirium; such tools are paramount in early diagnosis and treatment. However, there are 2 important additional aspects that we would like to address.

*Delirium* as a term for acute cerebral dysfunction falls short when perceived as a binary phenomenon with the only options of present or completely absent. This approach will arbitrarily generate a cutoff on a continuous or ordinal range of dysfunction. For either conservative or interventional measures, early detection of delirium—even at predelirium or subsyndromal levels—is of great importance. Similar to pain, delirium presents in degrees better represented on an ordinal scale (eg, 0-10) than represented simply as yes or no. As with pain, evolving delirium should alert physicians to look for underlying possible causes and opens the possibility of treatment before reaching a critical value. With respect to outcomes, the severity as well as the length of delirium symptoms matters.[2] Additionally, patients with subsyndromal delirium are at an increased risk of adverse outcomes.[3]

The review by Wong et al did not determine the diagnostic accuracy for bedside delirium but rather the accuracy of delirium detection according to current *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) (*DSM-IV*) criteria. The results would certainly be different if criteria from *International Statistical Classification of Diseases, 10th Revision* (*ICD-10*); the *DSM-IV* predecessors *DSM-III* or *DSM-III-R*; or the upcoming *DSM-5* were used.[4] Therefore, a question not answered by this review is whether the goal should be to determine if a patient fulfills the criteria for delirium according to *DSM-IV* or to screen for an acute cerebral dysfunction requiring immediate attention.

A key to any delirium intervention is early detection. From the clinical perspective, any instrument that cannot be easily integrated into daily routine because of time and complexity is of limited use as a screening instrument. The Nursing Delirium Screening Scale (Nu-DESC), which can be integrated into daily nurse or physician rounds, was developed with these characteristics in mind. In a study of 88 patients, 17 of whom developed delirium, it took a mean of 1.27 minutes to complete and did not need a require a complex algorithm or instruction, yet provided excellent test characteristics.[5] This needs to be considered when delirium instruments are compared and recommended for use in clinical routine.

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**Financial Disclosures:** Dr Spies reported receiving honoraria or speaking fees from Akzo Nobel, Fresenius, BBraun, Baxter, Abbott, Essex Pharma, and GlaxoSmithKline and grants from Abbott, Akzo Nobel, Aspect, Baxter, BBraun, Deltex Medical, Edwards, Fresenius, GlaxoSmithKline, Köhler Chemie, Lilly, Merck Sharp and Dohme, Novalung, Orion Pharma, Pfizer, Pfrimmer Nutricia, and Wyeth. No other disclosures were reported.

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**To the Editor:** In their systematic review, Dr Wong and colleagues[1] supported the use of the CAM because of its brevity and ease of use. The article indicated that the CAM takes 5 minutes to administer; however, this does not include the time required to perform the formal cognitive assessments on which the validity of the CAM relies.[2]

Although the extra 10 minutes required to perform a formal cognitive assessment (such as the Mini-Mental State Examination [MMSE]) is unlikely to be burdensome when diagnosing a sporadic case of delirium, evidence indicates that the CAM is not reliable for bedside nursing surveillance in a real-world clinical setting.[3] The good CAM test characteristics presented in the article by Wong et al reflect the ability of highly trained, specialized research nurses to perform the CAM accurately. When the CAM is used as part of a bedside nursing delirium surveillance system for at-risk patients, the amount of time and training required to replicate a valid CAM assessment is likely to be onerous for bedside nursing. In a study in which the CAM was used by bedside nurses for surveillance, the sensitivity rate was only 66%.[4] Moreover, 15 or more minutes multiplied by the number of patients a nurse is monitoring can result in an unacceptable burden for nurses with other patient care responsibilities during a typical shift. The time pressures of clinical care compromise the ability of a clinician to correctly assess a sophisticated psychometric test like the MMSE and to apply its results to the scoring of the CAM algorithm.

For the systematic surveillance of delirium in at-risk patients, a coordinated effort between nurses and physicians is needed. We believe that a short, highly sensitive screening instrument to detect altered patient consciousness and cognition (ie, sustained attention and likely executive function) needs to be developed for bedside use by nurses.[5] Ideally, if such a test yielded a positive result, a physician could then be summoned to evaluate the patient and make an accurate diagnosis of delirium with a valid CAM assessment. An adaptation of the CAM instrument to improve objective testing on sustained attention and executive function (reciting days or months backward) may increase the tool's effectiveness at the bedside.

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**In Reply:** We concur with Drs Bellelli and Trabucchi that delirium superimposed on dementia may present diagnostic challenges, particularly in the absence of caregivers to provide collateral information. Information about a fluctuating course of confusion should be easily obtained in hospitalized patients where there is 24-hour nursing care with careful documentation. We agree that inattention and disorganized thinking may be present due to preexisting conditions, particularly with severe dementia, but the CAM algorithm requires several cardinal features beyond inattention and disorganized thinking. In the original CAM study, Inouye et al[1] deliberately challenged the CAM with a broad range of participants, including those with underlying dementia. The CAM has been shown to be valid in patients with and without dementia, in the original study and subsequent validation studies.[2]

Dr Radtke and colleagues highlight the clinical importance of subsyndromal delirium. The objective of our review was to determine the diagnostic accuracy of various bedside delirium instruments, and the validity of detecting subsyndromal delirium was beyond the scope of this review. However, the CAM has been used as an ordinal instrument, in which patients who have 1 or more CAM features but do not meet full criteria are categorized as subsyndromal delirium; these patients had poorer outcomes than patients who had no features of delirium.[3] We concur that the fundamental objective is to determine which patients require immediate attention, including implementation of evidence-based delirium prevention strategies. One of the studies included in our review (reference 36 in our article) compared the CAM against different versions of the *DSM* and the *ICD-10*. We chose to use the *DSM* as the gold standard because its definition of delirium is more inclusive than the *ICD-10*.

Radtke et al and Drs Young and Arseven state that proper administration of the CAM may be difficult to integrate widely because it requires rigorous training and it may be onerous for busy clinicians. The CAM instruction manual[4] outlines the suggested training process, but perhaps it is only through such rigor that validity is achieved. The updated instructions now recommend a more brief assessment (the Modified Mini-Cog Test[5] with the Digit Span) in lieu of the MMSE. The Nu-DESC[6] holds promise as a screening tool with its low negative likelihood ratio; however, only 1 diagnostic study met our inclusion and exclusion criteria, whereas the CAM has been studied by multiple investigators, resulting in narrower confidence intervals. We look forward to more validation studies on instruments such as the Nu-DESC.

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## Diagnosing Influenza

**To the Editor:** A comprehensive discussion of the diagnosis of influenza, as in the Clinical Crossroads review of the clinical features of influenza by Dr Barry,[1] seems incomplete without consideration of radiographic features. Although chest imaging is not required in all cases of suspected or confirmed influenza, it is often performed in the workup of acute respiratory illness, especially when pneumonia is considered.[2]

In patients with influenza, plain chest radiography most commonly either is normal or shows unifocal or multifocal airspace opacities. As in other causes of community-acquired pneumonia, computed tomography (CT) of the chest is more sensitive than plain radiography for detecting imaging abnormalities in patients with influenza.[3,4] CT findings may be normal or may include features of both airways and airspace disease such as bronchial wall thickening, nodular opacities (which may have a tree-in-bud appearance), ground glass opacities, and consolidations; these infiltrates are most often multifocal and bilateral.[3,4] Pleural effusions are seen in a small minority of patients with either imaging modality. These features are recognized as nonspecific and reaffirm the maxim that radiographic findings cannot be used to discern the (microbiologic) etiology of acute respiratory tract infections.

Multiple studies have also shown a positive correlation between the presence and extent of radiographic infiltrates and severity of disease in patients with influenza, thereby also providing prognostic information.[3,4] In addition, chest imaging may reveal evidence of influenza-related pulmonary complications, including acute respiratory distress syndrome, secondary bacterial pneumonia, acute exacerbation of chronic obstructive pulmonary disease, and decompensation of preexisting cardiac disease.[5]

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**Financial Disclosures:** None reported.

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**In Reply:** Dr Pierce raises an interesting question on the role of radiologic studies in the diagnosis of influenza. In persons with uncomplicated influenza, involvement is confined to the larynx, trachea, and/or bronchi, and chest imaging is generally not necessary.[1] Most information on the frequency of influenza-related pneumonia is based on data from hospitalized patients, a group skewed toward those with more severe illness.[2-4] Outpatients whose clinical history or physical examination suggests pneumonia or another respiratory complication of influenza should have chest imaging performed because abnormal findings may result in changes in clinical management such as the initiation of antibiotic therapy.

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## Importance of Blinding in Randomized Trials

**To the Editor:** In their Commentary, Drs Psaty and Prentice[1] added to the available evidence that lack of blinding in randomized trials favors the intervention, even with studies that have what are considered hard end points. We agree about the importance of investigator blinding and would add a few observations and some cautions to their statements.