



# A practical program for preventing delirium in hospitalized elderly patients

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## ABSTRACT

Delirium in hospitalized elderly patients is common and often unrecognized (especially the hypoactive type), and can lead to serious complications. A systematic program can improve the rate of recognition of this problem and decrease its incidence, and is cost-effective.

## KEY POINTS

Delirium is easy to miss when it does not present classically with agitation and hallucinations. Most elderly patients with delirium are lethargic and somnolent.

Delirium can be quickly screened for by recognizing its key features: acute onset, fluctuating course, inattention, and either disorganized thinking or altered consciousness.

Patients with impaired vision, severe illness, cognitive impairment, or dehydration on hospital admission are more likely to develop delirium.

Delirium is likelier to develop in hospitalized patients who have physical restraints, weight loss, more than three medications added in a 24-hour period, an indwelling bladder catheter, or an iatrogenic event.

Unnecessary medications should be avoided in elderly patients, as should sleep medications, histamine-2 blockers, diphenhydramine, and long-acting benzodiazepines.

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A 78-YEAR-OLD WOMAN presents to the emergency department with unstable angina. She has diabetes, arthritis, and cataracts, but lives independently. She is admitted to the intensive care unit and is treated with intravenous nitroglycerine, morphine, lidocaine, lorazepam, and ranitidine. A bladder catheter is placed.

The next day, she undergoes cardiac catheterization with angioplasty. In the evening, however, she becomes very agitated, confused, disoriented, and paranoid, believing that the staff is trying to experiment on her. After trying to escape from the room, she is managed with physical restraints, additional doses of lorazepam, and haloperidol.

On hospital day 3, she develops a fever, due to a urinary tract infection. Her bladder catheter is removed, and she is found to be incontinent. A pressure area is noted on her skin in the sacral area. Her confusion increases.

By hospital day 9, she is still incontinent, has a large sacral decubitus ulcer, and is unable to walk or care for herself. Social work is consulted to seek nursing facility care after discharge.

## COMMON AND SERIOUS

Delirium is a marker of poor hospital care for older people<sup>1</sup>; it is associated with serious complications; it often goes unrecognized by physicians and nurses; and its occurrence is integrally linked with processes of hospital care, such as overuse of medications and iatrogenic events. Unfortunately, delirium is common and can lead to increased mortality, morbidity, and loss of independence.

The estimated occurrence rates of delirium range from 14% to 56% during the course

**TABLE 1****Distinguishing characteristics of delirium and dementia**

FEATURES	DELIRIUM	DEMENCIA
Onset	Abrupt (hours to days)	Insidious (months to years)
Attention	Impaired	Normal (except in terminal stages)
Level of consciousness	Fluctuates (usually reduced)	Clear (except in terminal stages)
Speech	Incoherent, disorganized, often in fragments	Ordered (may have aphasic errors)

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of hospitalization.<sup>1</sup> Estimated rates range widely because of different patient characteristics in different studies: the highest rates are seen in the oldest patients and in those in intensive care and postoperative settings.

Hospital mortality rates of patients with delirium range from about 10% to 65%,<sup>1</sup> more than twice as high as for matched controls. Thus, delirium has a case fatality rate as high as that of acute myocardial infarction or sepsis.

No studies have been done to estimate the costs of excess health care due to delirium in hospitalized older persons, but if we extrapolate from vital health statistics, conservatively assuming a delirium rate of 20%, delirium necessitates 17.5 million additional inpatient hospital days each year, with an estimated annual cost to Medicare of over \$8 billion for hospital costs alone. The real cost is even more, because post-hospital services such as institutionalization, intensive rehabilitation, and home care are also frequently needed.

**■ HYPOACTIVE DELIRIUM IS OFTEN OVERLOOKED**

Delirium, also known as acute confusional state, is defined as an acute disturbance in consciousness and cognition, with evidence of an underlying medical etiology.<sup>2</sup> The spectrum of delirium ranges from hypoactive delirium (characterized by reduced motor activity with lethargy) to hyperactive delirium (characterized by increased motor activity with agi-

tation, hallucinations, and inappropriate behavior). The hyperactive type is usually recognized easily; however, more commonly, elderly patients present with the hypoactive or mixed form, which is often missed by both doctors and nurses.<sup>3</sup>

Some studies indicate that hypoactive delirium tends to have a poorer prognosis.<sup>3–5</sup> Not only is it more often unrecognized and left untreated, but patients are also prone to aspiration pneumonia, decubitus ulcers, and pulmonary emboli as a result of the extreme somnolence.

In contrast to delirium, which comes on acutely, dementia is a chronic confusional state. Delirium and dementia are distinguishable in several important ways (TABLE 1).

**■ MANY CAUSES**

The pathophysiology of delirium remains poorly understood.

On electroencephalography, patients with delirium show a generalized slowing of background activity,<sup>6,7</sup> consistent with widespread cortical dysfunction. While the degree of slowing correlates grossly with degree of cognitive impairment, it is nonspecific in terms of underlying etiologies. The slowing pattern reverses when the clinical delirium resolves.

Some researchers believe that delirium is the final common pathway of many pathogenic mechanisms, resulting in a widespread reduction of cerebral oxidative metabolism. A

**Delirium has a fatality rate as high as acute myocardial infarction or sepsis**

number of neurotransmitter pathways have been implicated in delirium, including the cholinergic, dopaminergic, GABA-ergic, and serotonergic systems. The dominant current theory of neurotransmission involves a relative state of cholinergic deficiency and dopaminergic excess.<sup>8</sup>

In practical terms, delirium seems to involve an interaction between baseline vulnerability and precipitating factors (or noxious insults).<sup>9</sup> Even a young healthy person can become delirious if exposed to multiple noxious insults, such as major surgery, general anesthesia, multiple psychoactive medications, and prolonged sleep deprivation. Delirium is more common in the elderly because they tend to be more vulnerable at baseline. For a vulnerable elderly person who may have impaired cognition and hearing, and multiple chronic conditions, a single sleeping pill may be enough to trigger delirium.

### ■ PREDICTORS OF DELIRIUM

Almost any condition can make delirium more likely, but some factors are recognized as more significant, eg:

**Dementia** (increases the risk of delirium fourfold to fivefold during hospitalization, and about 30% to 40% of patients with delirium have underlying dementia)

**Electrolyte disturbances** (especially hyponatremia and hypercalcemia, even if the imbalance is only mild)

**Major organ system disease** (including acute myocardial infarction, which may present as delirium in the elderly)

**Occult respiratory failure** (This has become more common now that oxygen saturation meters have largely replaced arterial blood gas measurements. An elderly patient with an oxygen saturation of 89% who is put on supplemental oxygen may have an already-rising  $PCO_2$ . Older patients often do not manifest the typical signs or symptoms of respiratory failure, such as shortness of breath or a rapid respiratory rate. Lethargy and delirium may be the only signs of respiratory failure.)

**Occult infection**, such as urinary tract infection or pneumonia (which may present in the elderly solely as delirium instead of fever or an elevated white blood cell count)

### Injury or pain

**Emotional stress and unfamiliar environment**

**Metabolic problems**, especially disturbances in blood sugar, cortisol, or the thyroid.

Our group studied characteristics present on admission that helped predict which patients would develop delirium during hospitalization.<sup>10</sup> Patients were at least 70 years old and had no baseline delirium. Four risk factors were identified as significant: impaired vision, severe illness, cognitive impairment (even if mild), and dehydration (as indicated by a blood urea nitrogen-creatinine ratio of 18 or more).

Factors during hospitalization that were likely to lead to delirium were use of physical restraints (typically, vest restraints used to prevent falls and single wrist restraints to protect intravenous lines), weight loss or decline in serum albumin (indicators of malnutrition), more than three medications added in a 24-hour period (70% of which were psychoactive medications), use of an indwelling bladder catheter, and any iatrogenic event.<sup>9</sup>

### ■ MEDICATIONS: MOST COMMON CAUSE OF DELIRIUM

Medications are the most common contributors to delirium in the elderly and are the most easily reversible cause. Many elderly people are on multiple medications; approximately 50% of patients over the age of 65 take five or more chronic medications per day.<sup>11</sup>

Many medications are associated with delirium (TABLE 2). While they cannot usually be eliminated altogether, psychoactive drugs such as sleep medications, histamine-2 blockers, and diphenhydramine should be avoided if possible, especially for particularly vulnerable patients, such as those with dementia.

### Reduce medication load, titrate more slowly

The dosage for an average patient is often higher than is needed for the elderly, particularly for psychoactive medications. One way to reduce the psychoactive medication load for elderly patients is to reduce the recommended dosage and titrate medications more slowly than for younger patients.

**In a vulnerable older patient, a single sleeping pill may be enough to trigger delirium**

It is also important to assess a hospitalized patient's medication list every day or two to ensure that every medication is really indicated. One should minimize the use of psychoactive medications, choose the least risky drugs from each class, and avoid prescribing medications "as needed."

Hospitalization is the ideal time to re-evaluate a patient's long-term medications. Those without apparent indications should be considered for tapering and discontinuing. Often patients have taken a medication for many years and no longer remember the reason (nor can a reason be found in the medical records). A medication a patient has taken for years may seem an unlikely culprit for acute delirium; however, liver and kidney function may decline over the years, and the medication may no longer be cleared as effectively.

### Avoid known delirium culprits

Some medications to avoid or particularly watch out for in the elderly include:

**Long-acting benzodiazepines**, which are particularly dangerous because they have a very long half-life. Flurazepam has a half-life of more than 5 days in healthy older persons.

**Meperidine**, which has an active metabolite with an especially long half-life.

**Histamine-2 blockers**, which are a common cause of delirium because they are so often routinely prescribed in older patients for ulcer prophylaxis. They should be prescribed only when necessary, such as for active gastrointestinal bleeding. For ulcer prophylaxis, antacids or sucralfate should be used instead.

**Steroids**, which are known to cause "steroid psychosis," a type of delirium.

**Atropine/diphenoxylate**, a very commonly used combination for treating diarrhea. Psyllium plus kaolin and pectin is a safer alternative.

## ■ RECOGNIZING DELIRIUM

### Missing delirium is easy

Most physicians assess delirium on the basis of two characteristics: disorientation and inappropriate behavior. Although someone with these features probably has delirium, relying on those features alone will result in many delirium cases being missed. Studies indicate

**TABLE 2**

### Medications associated with delirium

#### Sedative-hypnotics

- Benzodiazepines
  - Flurazepam
  - Diazepam
- Barbiturates
- Sleeping medications
  - Chloral hydrate

#### Narcotics

#### Anticholinergics

- Antihistamines
  - Diphenhydramine
  - Hydroxyzine
- Antispasmodics
  - Belladonna derivatives
  - Atropine/diphenoxylate
- Tricyclic antidepressants
- Antiparkinsonian agents
  - Benzotropine
  - Trihexyphenidyl
- Antiarrhythmics
  - Quinidine
  - Disopyramide

#### Cardiac medications

- Digoxin
- Lidocaine

#### Antihypertensive medications

- Beta-blockers
- Methyldopa

#### Others

- Histamine-2 blockers
- Steroids
- Metoclopramide
- Lithium
- Anticonvulsants
- Nonsteroidal anti-inflammatory drugs

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**Half of persons over the age of 65 take five or more chronic medications per day**

that between one third and two thirds of cases of delirium are unrecognized by physicians.<sup>12-15</sup>

In our studies, we also found that nurses often missed patients with delirium. We found this particularly worrisome, not only because nurses tend to spend more time with hospital-

ized patients, but because physicians often rely on them to report changes in a patient's mental status. To address this issue, we conducted a prospective study comparing nurses with trained interviewers in recognizing delirium in nearly 800 hospitalized patients assessed daily. Nurses recognized delirium in only 31% of the delirious patients and in only 19% of the daily observations. Nearly all of the disparity was due to underrecognition, particularly in patients older than 80 or those with hypoactive delirium, dementia, or impaired vision.<sup>16</sup>

### Confusion Assessment Method

We developed the Confusion Assessment Method to quickly and accurately detect delirium in both research and clinical settings.<sup>17</sup> The key features are:

- Acute onset and fluctuating course (comes on abruptly over hours to days, then comes and goes over the course of the day)
- Inattention (reduced ability to maintain attention or shift attention)
- Disorganized thinking (disorganized or incoherent speech)
- Altered level of consciousness (usually lethargic or stuporous).

To diagnose delirium, the first two features must be present, as well as either one of the last two.

The method was assessed at two sites, using a 90-minute comprehensive psychiatric assessment performed by a geriatric psychiatrist as the reference standard. In 56 patients at two sites, the assessment had a sensitivity of 94% to 100% and a specificity of 90% to 95%. Given its imperfect sensitivity and specificity, the Confusion Assessment Method should be used for screening purposes only. Suspected delirium cases should be confirmed with further evaluation.

The test is now widely used for clinical and research purposes. It has been translated into at least eight languages and has been used in more than 150 published studies.

### Shortened Mini-Mental State Examination

At the bedside, a good tool to assess mental status and assist with scoring the Confusion Assessment Method is a shortened form of the Mini-Mental State Examination,<sup>18</sup> which

takes just a few minutes to complete and requires no writing. A patient who passes but has struggled to get correct answers should be more thoroughly evaluated.

**Orientation.** To assess orientation to time, ask for the year, season, month, and day, as many people with normal mentation do not keep track of exact dates. For further orientation pertinent to the hospital, ask what meal they just had, what time of day it is, how long they have been in the hospital, and if they know why they have been hospitalized. To assess orientation to place, ask patients if they know the state, town and the hospital floor where they are located.

**Short-term memory, registration, and recall.** Name three objects, such as an apple, table, and penny, and ask the patient to repeat the words until they are learned. Then, ask the patient to spell "world" backwards as a distraction task, and ask for the three objects again.

### Digit span test

Inattention is another key feature of delirium and can be quickly assessed with a digit span test.<sup>19</sup> A string of digits for the patient to repeat back is recited at a rate of about one per second, starting with three digits, then four, then five. This should be relatively easy for patients who do not have delirium; even patients with dementia can usually successfully perform this immediate repetition task, although they may not be able to recall the digits after a short period of time.

## THE DELIRIUM WORK-UP

**History.** It is essential to find out if the condition is, in fact, an acute deterioration. The physician should track down a family member, caregiver, nursing home staff member, or a visiting nurse to obtain that information.

Both preadmission and current medications should be reviewed, and alcohol use at home should be determined in case drug or alcohol withdrawal may be a factor.

**Physical examination.** A careful physical examination and a neurologic examination are needed.

**Laboratory.** A targeted metabolic work-

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up is recommended, which should be tailored to the individual clinical situation. Laboratory tests to consider include a complete blood count, electrolytes, serum urea nitrogen-creatinine ratio, blood glucose, liver function tests, blood calcium level, blood oxygen saturation, and electrocardiography, as needed. Occult infection is common and should always be investigated.

**Neuroimaging studies and lumbar puncture** are needed in fewer than 5% of patients, but are obtained in a much higher proportion. While evidence-based guidelines have not yet been developed, we recommend neuroimaging if there has been a recent fall or head trauma, signs of head trauma (bruises on shoulders or above), focal neurologic changes, suspicion of encephalitis in a patient with fever and acute mental status change, or if no other cause of the problem can be determined and the patient is not improving.

## ■ NONPHARMACOLOGIC APPROACHES

### Sleep protocol:

#### Nonpharmacologic alternatives to drugs

To avoid the use of sleeping medications, a leading risk factor for delirium, we have developed a nonpharmacologic sleep protocol, implemented by the nursing staff or trained volunteers, which is completely nontoxic and acceptable to patients. It involves:

- A 5-minute backrub
- A warm drink (milk or herbal tea, according to patient preference)
- Relaxing music.

After 1 hour the patient is assessed, and a sleeping pill is given at that time if still required.

In a study of 111 patients,<sup>20</sup> we found an adherence rate of 74%. The quality of sleep correlated with the number of parts of the protocol received, and the use of sleep medication was reduced from over one half to less than one third. In the study, the patients who insisted on sleep medications were those who had chronically used sleeping medications at home or had a history of drug or alcohol abuse.

To further enhance sleep at night on the ward, we try to schedule 6 hours of sleeping time without interruption for medications,

**TABLE 3**

### The Yale Delirium Prevention Program

RISK FACTOR	INTERVENTION
<b>Cognitive impairment</b>	Reality orientation Therapeutic activities protocol (eg, word games)
<b>Sleep deprivation</b>	Nonpharmacologic sleep protocol Sleep enhancement protocol
<b>Immobilization</b>	Early mobilization protocol Minimizing immobilizing equipment
<b>Vision impairment</b>	Vision aids Adaptive equipment
<b>Hearing impairment</b>	Amplifying devices Adaptive equipment and techniques
<b>Dehydration</b>	Early recognition and volume repletion

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vital signs, or procedures. Lights are dimmed and noise levels reduced, and patients are discouraged from taking naps during the day.

### Multiple practical interventions

The Yale Delirium Prevention trial<sup>21</sup> was the first trial to show that delirium can be prevented. It involved 852 matched elderly patients who received either a number of practical strategies targeted at six risk factors for delirium (TABLE 3) or usual care. Trained research staff, who were blinded to the study hypothesis and who did not participate in the interventions, performed interviews at baseline and daily throughout hospitalization, as well as at 6-month and 12-month follow-up. The incidence of delirium was significantly reduced from 15% in the usual care group to just under 10% in the intervention group (matched odds ratio, 0.60; 95% confidence interval 0.39–0.92). The total number of days with delirium and the number of episodes were also significantly reduced, although the intervention did not affect severity or the recurrence rate once delirium occurred.

The intervention in this study has been adapted as the Hospital Elder Life Program (HELP),<sup>22</sup> which is being implemented in 36 hospitals in the United States, Canada, and

**A night-time relaxation program can reduce the need for sleep medications**



Australia, on medical and surgical wards. Many of the interventions are implemented by trained volunteers, who enjoy the work and tend to be retained at a high rate.

The program has been shown to be cost-effective.<sup>23</sup> For patients at intermediate risk (72% of study patients), an average of \$831 (range \$415–\$1,689) per patient was saved, more than offsetting the cost of the intervention. The savings to the hospital occurred in every cost category we studied, including nursing care, room charges, diagnostic procedures, intensive care unit, and pharmacy. Cost-effectiveness was not demonstrated for patients in the high-risk category (28% of study patients).

### ■ HALOPERIDOL AS A LAST RESORT

It is important to avoid pharmacologic management of delirium whenever possible and encourage the use of nonpharmacologic alternatives. The drugs used to treat delirium have the potential to worsen mental status and prolong the course. They should be reserved for severely agitated patients who are in danger of interfering with their care: ie, they are likely to extubate themselves, pull out a dialysis catheter, or physically harm themselves or the staff. Loud verbal behavior is not a sufficient indication for medication.

Haloperidol is the only drug shown in randomized clinical trials to treat delirium effectively and possibly shorten its course.<sup>24</sup> Start with a low dose (0.5–1.0 mg), repeated every 30 minutes until the patient is manageable. It should be given orally or intramuscularly; the duration of action is only about 20 minutes when given intravenously. After the first 24 hours, 50% of the loading dose should be given in divided doses over the next 24 hours, then the drug should be tapered off over the next few days.

No more than 5 mg of haloperidol should be given in a 24-hour period to a patient who has not previously been exposed to this class of drugs. Studies have shown that the dopamine D-2 receptors where haloperidol binds are 90% occupied at a dose of 5 mg in 24 hours.<sup>25</sup> Increasing the dosage beyond that offers no additional therapeutic value and exposes the patient to unnecessary toxic side effects.

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