Major illness and dementia. Precipitating factors of delirium in hospitalized patients.

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MAJOR ILLNESS AND DEMENTIA

- PNEUMONIA
- ARDS
- SEPSIS
- ICU COGNITIVE DECLINE
MAJOR ILLNESS AND DEMENTIA

PNEUMONIA
PNEUMONIA AND DEMENTIA

- Pneumonia is common among patients with advanced dementia, especially toward the end of life.

- Whether antimicrobial treatment improves survival or comfort is not well understood.

- The effect of antimicrobial treatment for suspected pneumonia on survival and comfort in patients with advanced dementia has been examined.

From 2003 to 2009, data were prospectively collected from 323 nursing home residents with advanced dementia in 22 facilities in the area of Boston, Massachusetts.

Participants were from the Choices, Attitudes, and Strategies for Care of Advanced Dementia at the End-of-Life (CASCADE) study; a prospective cohort study of NH residents with advanced dementia and their health care proxies (HCPs).

Each resident was followed up for as long as 18 months or until death.

All suspected pneumonia episodes were ascertained, and antimicrobial treatment for each episode was categorized as none, oral only, intramuscular only, or intravenous (or hospitalization.
Antimicrobial agents were commonly prescribed (91%) for pneumonia episodes in this cohort study.

Survival was prolonged among residents who received antimicrobial treatment compared with those who were untreated.

Treatment with antimicrobial agents does not improve the comfort of residents with advanced dementia who have pneumonia.

More aggressive care may be associated with greater discomfort.
PNEUMONIA AND DEMENTIA (2)


- A total of 9223 respondents had a baseline cognitive and functional assessment; 516 survived severe sepsis and 4517 survived a nonsepsis hospitalization to at least 1 follow-up survey and are included in the analysis.

Long-term Cognitive Impairment and Functional Disability Among Survivors of Severe Sepsis
Theodore J. Iwashyna, MD, PhD; E. Wesley Ely, MD, MPH; Dylan M. Smith, PhD; Kenneth M. Langa, MD, PhD
PNEUMONIA AND DEMENTIA (3)

- A high rate of new functional limitations was seen following pneumonia and sepsis.
- Pneumonia and sepsis were independently associated with substantial and persistent new cognitive impairment and functional disability.

*Long-term Cognitive Impairment and Functional Disability Among Survivors of Severe Sepsis*
Theodore J. Iwashyna, MD, PhD; E. Wesley Ely, MD, MPH; Dylan M. Smith, PhD; Kenneth M. Langa, MD, PhD
MAJOR ILLNESS AND DEMENTIA
The prevalence of moderate to severe cognitive impairment increased 10.6 percentage points among patients who survived severe sepsis.

Severe sepsis in this older population was independently associated with substantial and persistent new cognitive impairment and functional disability among survivors.

The magnitude of these new deficits was large, likely resulting in a pivotal downturn in patients’ ability to live independently.
Hospitalization-acquired weakness,
chronic illness myopathy and
polyneuropathy suggests that there is a direct inflammatory and hypoperfusion-mediated degradation of muscle fibers and neurons, which may be exacerbated by prolonged immobility and lack of physical therapy.

Similarly, frank hypotension or relative hypoperfusion may directly contribute to brain injury and subsequent cognitive impairment.
• **Inflammation**—a cardinal component of the pathophysiology of sepsis—is hypothesized to contribute to Alzheimer’s disease.

• **Delirium**, an acute form of brain dysfunction characterized by inattention, is common in sepsis and has been associated with increased cognitive decline among patients with Alzheimer disease.

3 out of 5 sepsis survivors experienced serious physical and/or mental declines in the years following the event.

Close to 60% of the hospitalizations for severe sepsis were associated with worsened mental and physical function, or both, in the years following the event.

Moderate to severe cognitive impairment almost tripled in the sepsis survivors, from 6% before sepsis to almost 17% after.

Among people with no mental or physical limitations before sepsis, around 40% could not walk without assistance in the years after.

A core part of sepsis is delirium and delirium is associated with progression of Alzheimer’s disease and cognitive decline.
MAJOR ILLNESS AND DEMENTIA

ARDS
ARDS AND DEMENTIA (1)

- ARDS patients experience several physical, mental, and psychological morbidities that significantly impair their health-related quality of life (HRQL).

- Persistent for years after hospital discharge, decrements in functional and neuropsychological outcomes result in lost savings, employment reduction, and a reduction in HRQL among survivors and their caregivers.

Survivors of acute respiratory distress syndrome (ARDS) are at risk for long-lasting cognitive decline due to:
1. hypoxemia,
2. sepsis and/or
3. psychological sequelae associated with
4. aggressive supportive care in the intensive care unit (ICU).

All ARDS survivors with cognitive deficits were disabled, whereas only 22.9% (n=8) of the cognitively not impaired patients gave evidence of disability.
ARDS AND DEMENTIA(3)

- Patients with cognitive deficits described the lowest HRQOL with major limitations in the domains role-physical and social functioning when compared to patients without cognitive impairments.
- Long-term ARDS survivors exhibit impaired health status and the presence of cognitive deficits is associated with disability and considerable impairments in HRQOL.

*The relationship between cognitive performance and employment and health status in long-term survivors of the acute respiratory distress syndrome/ Gen Hosp Psychiatry. 2001 Mar-Apr;23(2):90-6*
MAJOR ILLNESS AND DEMENTIA

ICU COGNITIVE DECLINE
ICU: Risk factors for cognitive dysfunction and psychological trauma
• Critically ill patients frequently develop cognitive and psychiatric impairments during and after the hospital stay manifesting as impaired memory and executive function, delirium, acute stress response, posttraumatic stress disorder (PTSD), anxiety, and depression.

• Both physical and psychiatric sequelae of critical illness may persist for years after discharge.
Patients often have poor recall of their illness, and periods of amnesia may be replaced with inaccurate recollections, often resulting in delusional and paranoid memories leading to:

1. anxiety,
2. depression,
3. PTSD,
4. hospital phobias and
5. panic attacks

that impair recovery and diminish quality of life as well as increase difficulty of future medical care.
DEMENTIA – ICU(3)

- Resultant problems with mental health, cognitive, and physical impairments have been termed **post intensive care syndrome** (PICS), an entity that is disturbingly common and yet still likely underrecognized.
- Up to 85% to 95% of ICU survivors struggle with persistent weakness.
- 50% to 70% have difficulties completing activities of daily living.
- 30% to 80% have cognitive impairment and
- more than 50% manifest various forms of psychiatric morbidity, which affect not only the patients but their caregivers as well.

Together, these impairments lead to an inability to return to the workforce and increased health care utilization.

MECHANISMS OF COGNITIVE IMPAIRMENT IN ICU (1)

- Pathogenesis of cognitive dysfunction and psychiatric morbidity is incompletely understood.

- Multiple risk factors such as:
  1. Preexisting disease burden (defined as Charlson Comorbidity Index score >3) was predictive of adverse psychological outcome after critical illness.
  2. Neuroimaging and neuropsychological data suggest an association of cognitive impairment with a nonspecific acquired brain injury.
3. Nearly all medical conditions requiring intensive care may have psychiatric manifestations.
4. Long-term cognitive impairment has been reported in association with hypoxia, hypotension, anemia, and dysglycemia commonly seen in the critically ill.

The similarity of cognitive impairment across the populations suggests that the critical illness itself, regardless of the etiology, may be casually linked with cognitive impairment.
Sleep disruption and deprivation, due to underlying psychological stressors, mechanical ventilation,
noise,
light,
patient care interactions and
medications
are exceedingly common in the ICU and have been associated with delirium, cognitive impairment, and worsened psychological recovery from critical illness.

Sleep deprivation may be clinically impossible to distinguish from delirium as both can manifest with inattention, variable mental status, and cognitive dysfunction; furthermore, severe sleep deprivation is similarly characterized by emergence of psychotic behavior and paranoia that tend to worsen during the night.


ICU STRESS/ EMOTIONS

- Emotions experienced in the ICU such as agitation and depression are also important predictors of future psychological problems.

- Inhospital acute stress symptoms were independently associated with increased severity of PTSD and depressive symptoms in the year after ICU discharge.
  

- Mood in the ICU (composed of symptoms such as anger, nervousness, low temperament, and confusion) and early intrusive memories of intensive care were the strongest acute psychological risk factors for PTSD and depression.

Early recognition of precipitating factors leading to delirium in dementia patients who underwent major illness.
### Predictive Model for the Risk of Delirium in Hospitalized Older Patients

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vision impairment</td>
<td>1</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>1</td>
</tr>
<tr>
<td>Severe illness (APACHE score &gt; 16, or nurse rating of severe)</td>
<td>1</td>
</tr>
<tr>
<td>Elevated blood urea nitrogen/serum creatinine ratio (&gt; 18)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total:</strong></td>
<td></td>
</tr>
</tbody>
</table>

Risk stratification using the point total: low risk = 0 points, 10 percent risk of developing delirium; intermediate risk = 1 or 2 points, 25 percent risk; high risk = 3 or 4 points, 80 percent risk.

APACHE = Acute Physiology and Chronic Health Evaluation.
SIGNS AND SYMPTOMS OF DELIRIUM

- Abrupt change in cognitive function (worsening confusion over hours or days), including problems with attention, difficulty concentrating, new memory problems, new disorientation

- Delayed awakening from anesthesia

- Difficulty in following instructions

- Disorganized thinking and speech difficult to follow

- Easy irritability, tearfulness, uncharacteristic refusals to cooperate.
SIGNS AND SYMPTOMS OF DELIRIUM

- New paranoid thoughts or delusions, illusions, hallucinations
- Motor changes such as slowed or decreased movements, purposeless fidgeting or restlessness, new difficulties in maintaining posture such as sitting or standing
- Sleep/wake cycle changes such as sleeping during the day and/or awake and active at night
- Decreased appetite
- New incontinence of urine or stool
- Fluctuating symptoms and/or level of arousal over the course of minutes to hours
NEUROTRANSMITTERS AND BIOMARKERS IN DELIRIUM

Figure 1-1. Neurotransmitters and biomarkers of delirium.
## Common causes of delirium and confusional states

### Drugs and toxins
- Prescription medications (e.g., opioids, sedative-hypnotics, antipsychotics, lithium, skeletal muscle relaxers, polypharmacy)
- Non-prescription medications (e.g., antihistamines)
- Drugs of abuse (e.g., ethanol, heroin, hallucinogens, nonmedicinal use of prescription medications)
- Withdrawal states (e.g., ethanol, benzodiazepines)
- Medication side effects (e.g., hyperammonemia from valproic acid, confusion from quinolones, serotonin syndrome)
- Poisons:
  - Atypical alcohols (ethylene glycol, methanol)
  - Inhaled toxins (carbon monoxide, cyanide, hydrogen sulfide)
  - Plant-derived (e.g., Jimson weed, Salvia)

### Infections
- Sepsis
- Systemic infections; fever-related delirium

### Metabolic derangements
- Electrolyte disturbance (elevated or depressed): sodium, calcium, magnesium, phosphate
- Endocrine disturbance (depressed or increased): thyroid, parathyroid, pancreas, pituitary, adrenal
- Hypercarbia
- Hyperglycemia and hypoglycemia
- Hyperosmolar and hypoosmolar states
- Hypoxemia
- Inborn errors of metabolism: porphyria, Wilson’s disease, etc.
- Nutritional: Wernicke’s encephalopathy, vitamin B12 deficiency, possibly folate and niacin deficiencies

### Brain disorders
- CNS infections: encephalitis, meningitis, brain or epidural abscess
- Epileptic seizures, especially nonconvulsive status epilepticus
- Head injury
- Hypertensive encephalopathy
- Psychiatric disorders

### Systemic organ failure
- Cardiac failure
- Hematologic: thrombocytosis, hypereosinophilia, leukemic blast cell crisis, polycythemia
- Liver failure: acute, chronic
- Pulmonary disease, including hypercarbia and hypoxemia
- Renal failure: acute, chronic

### Physical disorders
- Burns
- Electrocution
- Hyperthermia
- Hypothermia
- Trauma: with systemic inflammatory response syndrome, "head injury, fat embolism"

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*Disorders that, while not truly systemic or "medical", may produce the clinical picture of delirium or confusional state in all other aspects.*
## Drugs believed to cause or prolong delirium or confusional states*

<table>
<thead>
<tr>
<th>Analgesics</th>
<th>Corticosteroids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsteroidal anti-inflammatory agents</td>
<td></td>
</tr>
<tr>
<td>Opioids (especially meperidine)</td>
<td></td>
</tr>
<tr>
<td>Antibiotics and antivirals</td>
<td>Dopamine agonists</td>
</tr>
<tr>
<td>Acyclovir</td>
<td>Amanadine</td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>Bromocriptine</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>Levodopa</td>
</tr>
<tr>
<td>Antimalarials</td>
<td>Pergolide</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Pramipexole</td>
</tr>
<tr>
<td>Cycloserine</td>
<td>Ropinirole</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td></td>
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<tr>
<td>Isoniazid</td>
<td></td>
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<tr>
<td>Interferon</td>
<td></td>
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<tr>
<td>Linezolid</td>
<td></td>
</tr>
<tr>
<td>Macrolides</td>
<td>Gastrointestinal agents</td>
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<tr>
<td>Metronidazole</td>
<td>Antiemetics</td>
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<tr>
<td>Nalidixic acid</td>
<td>Antispasmodics</td>
</tr>
<tr>
<td>Penicillins</td>
<td>Histamine-2 receptor blockers</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Loperamide</td>
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<tr>
<td>Sulfonamides</td>
<td></td>
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<tr>
<td>Anticholinergics</td>
<td>Herbal preparations</td>
</tr>
<tr>
<td>Atropine</td>
<td>Atropa belladonna extract</td>
</tr>
<tr>
<td>Benztrapine</td>
<td>Henbane</td>
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<tr>
<td>Diphenhydramine</td>
<td>Mandrake</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>Jimson weed</td>
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<tr>
<td>Trihexyphenidyl</td>
<td>St. John’s Wort</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Valerian</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td></td>
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<tr>
<td>Levetiracetam</td>
<td>Hypoglycemics</td>
</tr>
<tr>
<td>Phenytoin</td>
<td></td>
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<tr>
<td>Valporate</td>
<td>Hypnotics and sedatives</td>
</tr>
<tr>
<td>Vigabatrin</td>
<td>Barbiturates</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Benzodiazepines</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>Muscle relaxants</td>
</tr>
<tr>
<td>Selective serotonin reuptake inhibitors</td>
<td>Badolene</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Cyclobenzaprine</td>
</tr>
<tr>
<td>Cardiovascular and hypertension drugs</td>
<td>Other CNS-active agents</td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>Disulfiram</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>Cholinesterase inhibitors (eg, donepezil)</td>
</tr>
<tr>
<td>Clonidine</td>
<td>Interleukin-2</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Lithium</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Phenothiazines</td>
</tr>
<tr>
<td>Methylidopa</td>
<td></td>
</tr>
</tbody>
</table>

* Not exhaustive, all medications should be considered.
FREQUENCY AND CHARACTERISTICS OF IATROGENIC HYPOGLYCEMIA REQUIRING MEDICAL ASSISTANCE. A MULTICENTER STUDY IN TERTIARY HOSPITALS.

Mylona M1, S. Kalopita2, L. Lanaras2, A. Papazafiropoulou3, S. Papas3, Aggelis N4, Karamagkiolis S4, Vazintari V5, Melidonis A5, Ntova V6, Xilomenos A6, Basagiannis Ch1, Voukali M7, Ioannidis I7, Zilos A8, Kaltsas G8, Karametos I9, Kapsalas D9, Liatis S1.

- **8 hospitals** (9 clinics) in 5 cities participated in **this 22-month, prospective survey** of documented iatrogenic hypoglycemia at the emergency departments (ED).
- **295 episodes** were recorded in 294 patients (compared to matched controls.)
- The majority of patients have T2D, they are **elderly** individuals suffering from **serious medical conditions** and in their great majority are treated with insulin or SUs.

### Cases-controls: multivariable analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (10y)</td>
<td>1.7</td>
<td>1.4-1.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Insulin (yes)</td>
<td>2.0</td>
<td>1.2-3.4</td>
<td>0.008</td>
</tr>
<tr>
<td>SU (yes)</td>
<td>4.0</td>
<td>2.5-6.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Metformin (yes)</td>
<td>0.5</td>
<td>0.3-0.8</td>
<td>0.002</td>
</tr>
<tr>
<td>e-GFR (10ml/min)</td>
<td>0.87</td>
<td>0.80-0.94</td>
<td>0.001</td>
</tr>
<tr>
<td>Dementia (yes)</td>
<td>8.0</td>
<td>2.6-24.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cancer</td>
<td>2.5</td>
<td>1.2-5.0</td>
<td>0.01</td>
</tr>
</tbody>
</table>
### Precipitating Factors of Delirium

**Table 1-1: Delirium: Predisposing Risk Factors**

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>AOR* (95% CI)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 85 years</td>
<td>2.4 (1.6–3.6)</td>
<td></td>
</tr>
<tr>
<td>≥1 activity of daily living impairment</td>
<td>3.1 (2–4.7)</td>
<td></td>
</tr>
<tr>
<td>Baseline activities of daily living independence</td>
<td>0.78 (0.69–0.89)</td>
<td></td>
</tr>
<tr>
<td>Vision impairment</td>
<td>3.6 (2.5–5.4)</td>
<td></td>
</tr>
<tr>
<td>Dementia diagnosis</td>
<td>6.3 (2.9–13.8)</td>
<td>5.1 (3.3–7.7)</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>2.9 (1.4–6.1)</td>
<td></td>
</tr>
<tr>
<td>Mini-Mental State Examination score &lt;2.4</td>
<td>4.1 (2.7–6.1)</td>
<td></td>
</tr>
<tr>
<td>Severe disease as rated by nurse or APACHE II score &gt;15</td>
<td>1.6 (1.1–2.4)</td>
<td></td>
</tr>
<tr>
<td>Blood urea nitrogen-to-creatinine ratio ≥18</td>
<td>1.7 (1.2–2.5)</td>
<td></td>
</tr>
<tr>
<td>Elevated creatinine</td>
<td>2.1 (1.1–4)</td>
<td></td>
</tr>
<tr>
<td>Elevated blood urea nitrogen</td>
<td>4.6 (1.4–15.6)</td>
<td></td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>30.9 (5.8–163.2)</td>
<td></td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>8.2 (2.5–26.4)</td>
<td></td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
<td>5.9 (1.2–28.7)</td>
<td></td>
</tr>
<tr>
<td>Elevated hepatic enzymes</td>
<td>6.3 (1.2–32.2)</td>
<td></td>
</tr>
<tr>
<td>Hyperamylasemia</td>
<td>43.3 (4.2–442)</td>
<td></td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>8.7 (2–37.7)</td>
<td></td>
</tr>
<tr>
<td>Low arterial pH</td>
<td>2.1 (1.1–3.9)</td>
<td>4.5 (1.1–17.7)</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>2.9 (1.3–6.7)</td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for confounding factors.

AOR = adjusted odds ratio; APACHE II = Acute Physiology and Chronic Health Evaluation II; ARR = adjusted relative risk; CI = confidence interval; OR = odds ratio.
# Precipitating Factors of Delirium

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>RR (95% CI)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical restraints&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>3.5 (2–6.3)</td>
<td>5.7 (3.6–8.9)</td>
</tr>
<tr>
<td>Bladder catheter&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>3.1 (1.7–5.5)</td>
<td>2.1 (1.4–3.1)</td>
</tr>
<tr>
<td>Any iatrogenic event&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 4 iatrogenic events&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New diagnosis of illness&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.2 (1.1–1.3)</td>
<td></td>
</tr>
<tr>
<td>Out of bed &lt; 1 time/day&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.3 (1.2–4.1)</td>
<td></td>
</tr>
<tr>
<td>Anticonvulsants&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3.6 (1.3–9.8)</td>
<td></td>
</tr>
<tr>
<td>Antiemetics&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.3 (1.1–5.1)</td>
<td></td>
</tr>
<tr>
<td>Benzodiazepine before admission to ICU&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3.4 (1.6–7)</td>
<td></td>
</tr>
<tr>
<td>Midazolam&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2.75 (1.4–5.3)</td>
<td></td>
</tr>
<tr>
<td>Lorazepam (no risk)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.45 (0.16–1.27)</td>
<td></td>
</tr>
<tr>
<td>Lorazepam&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.2 (1.1–1.4)</td>
<td></td>
</tr>
<tr>
<td>Morphine (negative risk factor)&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td>0.36 (0.16–0.82)</td>
</tr>
<tr>
<td>≥ 2 psychoactive agents&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4.5 (2.1–9.9)</td>
<td></td>
</tr>
<tr>
<td>&gt; 3 drugs added&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4.0 (2.1–7.3)</td>
<td></td>
</tr>
<tr>
<td>In emergency department for &gt; 12 hours&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.1 (1.1–3.7)</td>
<td></td>
</tr>
<tr>
<td>Malnutrition&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3.9 (2–7.5)</td>
<td></td>
</tr>
<tr>
<td>Respiratory insufficiency&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.7 (1.2–5.8)</td>
<td></td>
</tr>
<tr>
<td>Infection&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td>18.0 (3.5–90.6)</td>
</tr>
<tr>
<td>Sepsis&lt;sup&gt;f&lt;/sup&gt;</td>
<td></td>
<td>3.6 (1.03–12.9)</td>
</tr>
<tr>
<td>Fever&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td>14.3 (4.1–49.3)</td>
</tr>
<tr>
<td>Hypotension&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td>19.8 (5.3–74.3)</td>
</tr>
<tr>
<td>Anemia&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td>5.4 (1.6–17.8)</td>
</tr>
</tbody>
</table>


CI = confidence interval; ICU = intensive care unit; OR = odds ratio; RR = relative risk.
COMMON DRUG PRECIPITATING FACTORS

**Muscle Relaxants**
- Carisoprodol
- Chlorzoxazone
- Cyclobenzaprine
- Metaxalone
- Methocarbamol
- Orphenadrine
- Tizanidine

**Opioids**
- Fentanyl patches in opioid naïve
- Hydromorphone doses greater than 0.5 mg intravenously every 3 hours or 2 mg orally every 4 hours in opioid naïve
- Morphine in doses greater than 4 mg intravenously every 3 hours or 10 mg orally every 4 hours in opioid naïve (5 mg orally every 4 hours in frail elderly)
- Oxycodone in doses greater than 5 mg every 4 hours in opioid-naïve patients (2.5 mg orally every 4 hours in frail elderly)
- Meperidine
- Pentazocine

**Other**
- Corticosteroids
- Metoclopramide in doses > 5 mg before meals and at bedtime in patients with moderate to severe renal impairment
Box 1-1. Common Drugs Associated with Delirium

### Agents with Significant Anticholinergic Effects
- Amitriptyline
- Belladonna alkaloids
- Chlorpromazine
- Cyproheptadine
- Cyclobenzaprine
- Dicyclomine
- Diphenhydramine
- Doxepin
- Flavoxate
- Hyoscyamine
- Hydroxyzine
- Imipramine
- Meclizine
- Orphenadrine
- Prochlorperazine
- Promethazine
- Thioridazine
- Trimethobenzamide

### Benzodiazepines
- Alprazolam
- Chlordiazepoxide
- Clonazepam
- Clorazepate
- Diazepam
- Flurazepam
- Lorazepam
- Oxazepam
- Temazepam
Box 1-2. Evaluating for Drug-Related Causes of Delirium

1. Evaluate for drug withdrawal:
   (a) Compare before-admission agents with current agents. Look for drugs that might precipitate withdrawal with abrupt discontinuation (e.g., benzodiazepines, barbiturates, muscle relaxants).
   (b) Check that the patient is taking an appropriate dose (investigate actual as-needed use before admission).

2. Evaluate anticholinergic drug use:
   (a) Eliminate agent if possible.

3. Evaluate pain regimen:
   (a) Efficacy of current regimen (pain can also cause delirium)
   (b) Appropriateness of drug choice on the basis of age and kidney function
   (c) Efficacy of dose on the basis of drug history

4. Evaluate for any other agents with central nervous system effects:
   (a) Evaluate appropriateness of dose.
   (b) If recently initiated or dose changed, consider an alternative.

5. Evaluate for other drug-related causes of delirium:
   (a) Appropriateness of glucose control regimen
   (b) Whether electrolyte supplement is needed or requires adjustment
   (c) Appropriateness of antibiotic regimen
TREATMENT OPTIONS

• treatment of underlying conditions that predispose the individual to delirium

• non-pharmacological interventions

• pharmacological interventions
KEY CONCLUSIONS

- Major illness contributes to cognitive impairment by multiple mechanisms.
- Early recognition of delirium in demented patients is crucial.
- Multiple precipitating factors contribute to its arousal.
- Always respect the dignity and independence of the patient to prevent further disability.
Τι α το γήρα, ου γαρ ἐρχεται ὄνον.
Μένανδρος, 4ο αιών π.Χ., Αρχαίο Έλληνα ποιητή

THANK YOU