Diagnosis, prevention and management of delirium: spot it, stop it, treat it

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ARTICLE

SUMMARY

Delirium frequently occurs among hospital in-patients, with significant attributable healthcare costs. It is associated with long-term adverse outcomes, including an eightfold increased risk of subsequent dementia. The purpose of this article is to inform clinicians of the best practices for spotting, stopping and treating delirium and provide guidance on common challenging clinical dilemmas. For spotting delirium, suggested screening tools are the 4 'A's Test (in general medical settings) and the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). Prevention is best achieved with multicomponent interventions and targeted strategies focusing on: (a) avoiding iatrogenic causes; (b) brain optimisation by ensuring smooth bodily functioning; (c) maintaining social interactions and normality. Non-pharmacological approaches are the first line for treatment; they largely mirror prevention strategies, but the focus of empirical evidence is on prevention. Although sufficient evidence is lacking for most pharmacological approaches, an antipsychotic at low doses for short durations may be of utility for highly distressing or high-risk situations, particularly in hyperactive delirium, but only as a last resort.

LEARNING OBJECTIVES

After reading this article you will be able to:

- apply best practice guidelines on how to spot, stop and treat delirium in hospital in-patients, including those in the ICU
- describe management strategies for specific diagnostic challenges with delirium, including hypoactive delirium versus depression, catatonia, Lewy body dementia and delirium tremens.
- recognise the importance of appropriate management and treatment for each individual patient.

KEYWORDS

Delirium; practice guidelines; antipsychotic agents; physical restraint; confusion.

Delirium is commonly experienced by older adult hospital in-patients, with an estimated overall prevalence of 23% in general medical settings (Gibb 2020) and even higher, at 31.8%, among patients in the intensive care unit (ICU) (Krewulak 2018). It is often missed despite being one of the most common hospital complications. Several potential reasons for this oversight have been suggested, including healthcare staff's lack of education about the condition, insufficient attention given to patients with hypoactive delirium (as these patients do not pose immediate challenges for the medical staff), therapeutic nihilism and diagnostic overshadowing by other conditions, such as dementia.

Long-term sequelae: personal and financial burden

Although delirium might traditionally be considered a temporary condition, the prognosis of those who experience it is poor. Epidemiological studies are exposing the long-term cognitive trajectories of patients who have suffered an episode of delirium. One meta-analysis found greater post-discharge institutionalisation, morbidity and mortality (Witlox 2010) and recent cohort studies, such as Delirium and Cognitive Impact in Dementia (DECIDE), have shown that delirium accelerates cognitive decline and increases the risk of dementia in a dose-dependent fashion, irrespective of comorbidity and baseline level of cognitive decline (Richardson 2021). Compared with control groups without delirium, the odds of mortality among older persons with delirium in the emergency department setting are increased 5.5-fold (Anand 2022) and in the ICU they are increased 7-fold (Aung Thein 2020). Unlike other conditions, there has been no improvement in mortality outcomes for patients with delirium, despite advancements in research into the condition (Aung Thein 2020). Especially vulnerable are those with delirium superimposed on dementia. The long-term cognitive sequelae of episodes of delirium include cognitive deficits that are similar to those seen with moderate traumatic brain injury (Pandharipande 2013). Moreover, delirium in older persons has been

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shown to be associated with an eightfold increase in the risk of subsequent dementia (Davis 2012).

The financial toll is also considerable, as the healthcare costs attributable to post-operative delirium have been estimated at £25.9 billion ($32.9 billion) per year in the USA alone (Gou 2021). The costs continue to grow as the population ages.

Aetiological theories

The pathophysiology of delirium is still relatively unknown, although it is thought there may be a final common pathway leading to the delirium syndrome. Evidence for specific metabolic and pharmacological precipitants of delirium have been demonstrated in human studies of hypoxia, hypoglycaemia and cholinergic antagonism (Wilson 2020). The recently proposed systems integration failure hypothesis theorises that acute brain failure results from 'a combination of neurotransmitter function and availability, variability in the integration and processing of sensory information, motor responses to both external and internal cues, and the degree of breakdown in neuronal network connectivity' (Maldonado 2018). A competing theory of inflammation is also prominent, although the precise mechanism of how it disturbs brain function is only partially understood. Some of the suspected mechanisms include neuronal dysfunction, injury or cell death resulting from microglial-derived inflammatory mediators such as interleukin 1-beta (IL-1β) and tumour necrosis factor (TNF) that can directly affect neuronal function (Feng 2017). As a result, such indicators are currently being investigated as potential plasma biomarkers for delirium.

The landmark study by Inouye and colleagues detailed the stress vulnerability hypothesis, which is key to understanding how to manage delirium (Inouye et al 1999). Based on this, the Hospital Elder Life Program (HELP) in the USA demonstrated that good general practice targeted at the risk factors can prevent delirium in a third of cases (Inouye 2006).

Best practice

The purpose of this article is to inform readers of the best delirium practices relating to spotting, stopping and treating delirium in hospital in-patients. In addition, we consider three special diagnostic dilemmas that clinicians might encounter and provide clues to help guide practice.

Spot it: diagnosis/identification

Clinical features

Delirium presents in a phenotypically diverse manner ranging from a hypoactive subtype (65% of cases) with a withdrawn patient with decreased motor activity, to an agitated and overexcited patient described as the hyperactive subtype (25%), or a mix of both symptoms (10%) – although the incidence of each can vary with different durations of observation (Meagher 2000). Extreme cases can include a catatonic variant, which is not to be confused with pure catatonia (Meagher 2000). 'Subsyndromal' delirium is used to describe patients who have begun to fluctuate in awareness and cognition but do not meet all criteria for delirium (van Velthuijsen 2018) and evidence shows existence of 'persistent' delirium where many patients are discharged with ongoing delirium (Whitby 2022).

The starting point of delirium may be a prodrome in which increasing symptoms of restlessness, anxiety, irritability and sleep disturbances develop. As delirium progresses, impaired attention, cognition and consciousness, as well as perceptual disturbances and behavioural changes, characterise the syndrome. Of note, hallucinations that can occur in delirium are usually non-auditory and are often misinterpretations of environmental or interpersonal cues, especially in visual and tactile cases (Oldham 2018).

The clinical presentation of delirium (Box 1) may overlap with other diagnoses, such as those reviewed in the final section of this article. Diagnostic testing may help distinguish between diagnoses that cannot easily be differentiated by history and presentation alone.

Diagnosis

The first step in the evaluation of delirium is the history obtained from an informed observer (e.g. family member or staff), followed by a cognitive assessment to screen and confirm delirium. The Single Question in Delirium (SQiD) asks the patient's family/carers whether they feel that the patient has been more confused lately, which may be a feasible screening tool when limited time is available for interview (Sands 2021). It is crucial to define a baseline level of cognition, consciousness and attention – ideally, in at-risk or prodromal patients, but if necessary also in those who are already in the throes of an acute episode. In addition, given the fluctuating nature of this syndrome, being oriented during one evaluation does not necessarily rule out the diagnosis.

The current standard diagnostic criteria for delirium are outlined in DSM-5-TR (American Psychiatric Association 2022) and ICD-11 (World Health Organization 2022). In terms of preferred screening tools, variability is commonplace. In review of studies to date, work by MacLullich and colleagues (MacLullich 2019) suggests that the 4 'A's Test (4AT) (Table 1) may be the screening tool of choice in the general medical setting. Based

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BOX 1 Clinical features of delirium

Prodromal features

Anxiety, restlessness, irritability, disorientation, sleep disturbances

Cognitive disturbance

Impaired attention, awareness, arousal, orientation, concentration, organisation of thought process, immediate recall and recent memory, visuospatial function, language, speech

Perceptual disturbance and delusions

Hallucinations (usually visual or tactile), illusions

Psychomotor disturbance

Hypoactive, hyperactive, mixed (unpredictable, fluctuating features of both)

Sleep–wake cycle disturbance

Insomnia, nightmares, reversal of sleep–wake cycles, excessive daytime somnolence

Emotional disturbance

Anxiety, fear, irritability, emotional lability, euphoria, depression, apathy, withdrawal

Neurological abnormality

Asterixis, tremor, myoclonus, frontal release signs, anomic aphasia (dysnomia), dysgraphia, constructional apraxia

Timeline

Rapid development over hours to a few days. Fluctuation of severity over a 24-hour period. Lasting around 1 week in most hospital in-patients with reversible precipitating factors, although may persist for longer

(Adapted from Bush 2018)

on a well-conducted head-to-head trial comparing it with the Confusion Assessment Method (CAM), 4AT showed higher sensitivity and similar specificity (Shenkin 2019). A key benefit of the 4AT is that it is quick and simple to administer and a range of health and social care practitioners can carry out the screen without specialised training. Therefore, it is recommended that staff members who have frequent scheduled contact with the patient (e.g. nursing staff) perform the screening and that patients with positive screens are brought to the attention of the healthcare provider for further diagnostic evaluation. Modified versions of the CAM have been identified as effective tools in different settings, such as the ICU (CAM-ICU) with sedated patients or the time-constrained emergency department (Brief CAM) (Box 2).

Workup

Delirium can be the initial signal of a medical emergency. Consequently, the next steps in evaluating delirium must include the timely evaluation of potential causes and precipitating factors. Table 2 summarises the potential routine investigations and additional methods of workup for specific indications. Of note, the selection of the appropriate workup needs to be context specific and may be varied according to local service provision and practice. Moreover, it is important to note that, according to one study, no attributable cause of delirium may be identified in up to 30% of cases in clinical settings (van Velthuijsen 2018).

Stop it: prevention

Managing risk factors

Risk factors for delirium among ICU patients have been well studied (Box 3) and several risk factors can apply universally to populations in any clinical setting, such as older age, frailty, functional disabilities and high burden of coexisting conditions (including baseline cognitive impairment). Although many of these risk factors are non-modifiable, identifying high-risk patients can help improve the proactive implementation of preventive strategies such as closer monitoring, identifying the target areas for intervention, and prognostic decision-making.

Non-pharmacological prevention strategies

Multicomponent approaches have the strongest evidence for the prevention of delirium, compared with any single-component interventions (Kim 2022). The ‘ABCDEF bundle’ (Box 4) is an example of a multicomponent approach that has been recommended for reduction of delirium risk in the ICU (Devlin 2018). The above-mentioned Hospital Elder Life Program is another widely disseminated and evidence-based multicomponent intervention that is less specific to the ICU setting and can be applied in the general medical setting (Inouye 2006). The protocol uses non-pharmacological approaches to systematically target visual and hearing impairment, immobility, disorientation, sleep deprivation and dehydration.

Individual approaches that have shown efficacy in prevention can be grouped into the following categories: (a) avoiding iatrogenic causes; (b) ensuring smooth bodily functioning, which in turn optimises brain function; (c) regular monitoring and social interactions.

Avoiding iatrogenic causes includes medication reviews and avoidance of medications with high deliriogenic potential (e.g. benzodiazepines, meperidine) or anticholinergic load. This includes avoiding GABAergic agents (e.g. propofol, midazolam) for agitation, particularly in older persons. Table 3 summarises the medications to be reviewed for potential removal or titration based on each patient’s clinical circumstances by weighing the

TABLE 1 Outline of the 4 'A's Test (4AT) delirium assessment tool[a]

	Score
1. Alertness[b]	
Normal	0
Mild sleepiness for <10 s after waking, then normal	0
Clearly abnormal	4
2. Abbreviated Mental Test – 4 (AMT4): ask the patient their age, date of birth, name of hospital/building, current year)	
No mistakes	0
One mistake	1
Two or more mistakes or untestable	2
3. Attention: ask the patient to list the months of the year backwards[c]	
≥7 months correct	0
Starts but scores <7 months, or refuses to start	1
Untestable (cannot start because unwell, drowsy)	2
4. Acute change or fluctuating course: evidence of significant change or fluctuation in alertness, cognition, other mental function (e.g. paranoia, hallucinations) arising over the past 2 weeks and still evident in past 24 h	
No	0
Yes	4
Scoring: ≥4: possible delirium with or without cognitive impairment; 1–3: possible cognitive impairment; 0: delirium or severe cognitive impairment unlikely (but delirium still possible if information at item (4) is incomplete)	

a. The full assessment tool and additional information on use are freely accessible on the website developed by the test's author, Alasdair MacLullich (www.the4at.com).
b. If patient is asleep attempt to wake with speech or gentle touch on shoulder. Ask patient to state their name and address to assist rating.
c. To assist initial understanding one prompt of 'what is the month before December?' is permitted.

benefits and risks associated with the medication and the condition it is treating. Consultations with a clinical pharmacist are helpful in making the relevant clinical decisions to cautiously titrate down any medications that may be contributing to delirium. Medicines reconciliation together with a pharmacist before discharge is also essential to reduce the contributory effects of these agents.

Infection prevention during hospital admission is another important step, which can be achieved by avoiding unnecessary urinary catheterisation and implementing appropriate infection control protocols.

Although physical restraints are often employed in clinical settings for hyperactive delirium, these should be avoided as much as possible, as they actually increase the risk of delirium (Wilson 2020). Physical restraint in ICUs (as opposed to other hospital areas) may be justified by the perceived requirement to prevent the removal of life-sustaining devices such as endotracheal tubes and vascular access catheters; however, there is little evidence that restraint alone effectively achieves this goal (Smithard 2022).

BOX 2 Screening tools of choice for different medical settings

- General medical setting (patient able to speak): 4AT
- ICU or post-anaesthesia care unit (patient conscious): Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)
- Emergency department (with time constraints): Brief CAM (bCAM)

(National Institute for Health and Care Excellence 2010; Han 2013).

The second category – ensuring brain optimisation – is achieved by ensuring smooth bodily functioning (Box 5). Regular monitoring of at-risk patients can be achieved through the routine use of delirium screening scales (e.g. by each shift up to post-operative day 5) and diagnostic interviews by properly trained staff. Staff education focused on recognition, screening, risk factors, prevention and management has also been shown to be effective, as it allows for a concerted effort by all members of the treatment team (Rudolph 2011). Assessing for pain, including non-verbal signs in patients with communication difficulties (e.g. people with intellectual disability or dementia, or those unable to speak owing to the presence of an endotracheal or tracheostomy tube) is also crucial to ensure adequate pain management, which is associated with a reduction in delirium risk (Peden 2021).

Social interactions are also integral to reducing delirium risk and can be facilitated by family and visitors as well as the hospital staff. Some specific examples include daily awakening protocols for ICU patients (i.e. 'sedation holidays'), cognitive stimulation (e.g. books, puzzles, games) and reorientation (e.g. introducing self, role and location at every patient encounter; using an orientation board).

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TABLE 2 Workup for delirium

Potential contributors	Routine investigations
Hypoxaemia	Pulse oximetry
Hypoglycaemia	Blood glucose level
Infection	Complete blood count, urinalysis, chest X-ray, blood/urine cultures
Electrolyte imbalance	Urea and electrolytes
Hepatic failure	Liver function tests
Cardiac dysfunction	Electrocardiogram (ECG)
Indications for additional investigations	**Relevant investigations**
Hypercapnia/acidosis	Blood gas analysis (arterial/venous), lactate level
Suspected intoxication	Urine toxicology tests
Head trauma or new focal neurological deficit	Cerebral imaging
Suspected seizure	Electroencephalogram (EEG)[a]
Nuchal rigidity, fever	Lumbar puncture

a. Delirium can result in a characteristic pattern of 'a diffuse slowing with increased theta and delta activity and poor organization of background rhythm' on the EEG that reflects its severity (Jenssen 2005).
Sources: Marcantonio (2017); Oh (2017).

Pharmacological prevention strategies

In terms of preventing delirium in critical care patients, use of anaesthetics such as dexmedetomidine (an alpha-2 agonist) as adjuncts to GABAergic agents (e.g. propofol, midazolam) has been supported by evidence (Burry 2019). For pain management, multimodal analgesia should be utilised while seeking to avoid or at least minimise use of opioids (Aldecoa 2017).

Acetylcholinesterase inhibitors (e.g. rivastigmine or donepezil) should be continued for patients with dementia who are already on the medication at home (Maldonado 2017). They should not be newly prescribed peri-operatively for delirium prevention or treatment, however, as clinical trials have shown that agents such as rivastigmine resulted in higher delirium duration and mortality compared with placebo (van Eijk 2010).

Melatonin may reduce the incidence of post-operative delirium by allowing for improved sleep (Maneeton 2022). Ramelteon (a melatonin receptor agonist) has not shown efficacy in preventing delirium, however, and neither melatonin nor ramelteon individually have shown efficacy in preventing delirium in older persons (Maneeton 2022). Additional studies are needed for a stronger recommendation and to determine the optimal dosage, duration and formulation of melatonin.

BOX 3 Risk factors for delirium among intensive care unit (ICU) patients

- Older age (>65 years):
  - frailty[a]
  - functional disabilities[a]
  - high burden of coexisting conditions[a]
- Dementia or baseline cognitive impairment
- Pre-ICU emergency surgery
- Trauma (e.g. hip fracture)
- Higher score on the Acute Physiology and Chronic Health Evaluation II (APACHE II)
- Mechanical ventilation
- Metabolic acidosis
- Prior episode of delirium

a. Predisposing factors for delirium that are associated with advanced age.

(Maldonado 2017)

Treat it: management

Non-pharmacological management

When encountering a patient experiencing delirium, the first step to take is verbal and non-verbal

BOX 4 The ABCDEF bundle

The Awakening and Breathing Coordination, Delirium monitoring/management, and Early exercise/mobility strategy (ABCDEF) focuses on:

- Assessing, preventing and managing pain
- Breathing – both spontaneous awakening trials and spontaneous breathing trials
- Choice of analgesia and sedation
- Delirium: assessment, prevention and management
- Early mobility and exercise
- Family engagement and empowerment[a]

a. Included in the revised version of the ABCDE bundle.

(Balas 2014)

TABLE 3 Medications to review for delirium prevention

Class of medication	Examples
Anti-emetics[a]	Prochlorperazine, promethazine
Antimuscarinics (urinary incontinence)[a]	Oxybutynin, darifenacin, fesoterodine, flavoxate, solifenacin, tolterodine, trospium
Tricyclic antidepressants[a]	Amitriptyline, amoxapine, clomipramine, desipramine, doxepin (>6 mg), imipramine, nortriptyline, protriptyline, trimipramine
Other antidepressants	Paroxetine[b]
Antihistamines (first generation)[a]	Diphenhydramine (oral), hydroxyzine, brompheniramine, doxylamine, meclizine, carbinoxamine, chlorpheniramine
Skeletal muscle relaxants[a]	Cyclobenzaprine, orphenadrine
Antispasmodics[a]	Hyoscyamine, scopolamine, methscopolamine, propantheline, clidinium–chlordiazepoxide combination, dicyclomine, homatropine (excludes ophthalmic)
Benzodiazepines	Midazolam, alprazolam, lorazepam, triazolam, clonazepam, clorazepate, diazepam, chlordiazepoxide
Non-benzodiazepine benzodiazepine receptor agonist hypnotics[c]	Zolpidem, eszopiclone, zaleplon
Pain medications	Meperidine[b]
Corticosteroids (oral and parenteral)[d]	Prednisone, prednisolone, methylprednisolone, dexamethasone
H_2-receptor antagonists	Cimetidine, famotidine, nizatidine, ranitidine

a. Collectively identified as anticholinergics.
b. Individual agents identified as having particularly high anticholinergic and deliriogenic potentials.
c. Formally classified as 'sedative hypnotics' in the previous version of the AGS Beers Criteria.
d. Although these may be required for conditions such as chronic obstructive pulmonary disease exacerbation, should be prescribed in the lowest effective dose for shortest possible duration.
Source: This list was created based on the findings of our literature review for this article and the American Geriatrics Society 2019 AGS Beers Criteria (American Geriatrics Society Beers Criteria® Update Expert Panel 2019).

de-escalation, such as adopting a respectful, non-confrontational and empathetic tone and posture while talking calmly and slowly to the patient (Box 6). It is important to understand how distressing the experience of delirium may be to a patient: one individual describes feeling that they experienced '7 years worth of torture' during 3 weeks with delirium in an ICU (Hudson 2022).

Another immediate step after the identification of delirium should be medical evaluation, appropriate diagnostic tests and clinical consultations to look

BOX 5 Specific components of brain optimisation

- Adequate oxygenation, hydration and nutrition
- Prevention of constipation and urinary retention
- Improvement in sleep and restoration of circadian rhythm (e.g. ensure natural lighting during the day, noise and light reduction with earplugs and eye covers at night, relaxation techniques to promote sleep, avoid medical/nursing procedures and unnecessary scheduled medications at night)
- Early post-operative mobilisation (i.e. physical therapy at least once or twice daily, at least daily passive range of motion in bedbound patients)
- Adaptations for visual and hearing impairment

(Maldonado 2017; Oh 2017; Devlin 2018)

BOX 6 How to implement non-pharmacological management of delirium

- Engage in verbal and non-verbal de-escalation
- Correct malnutrition, dehydration and electrolyte abnormalities as quickly and safely as possible
- Review the inventory of all prescribed and over-the-counter pharmacological agents, discontinuing any, if feasible, known to cause delirium (e.g. GABAergic agents, opioids) or that have high anticholinergic potential
- Promptly restore circadian rhythms and reduce noise and light affecting sleep
- Remove unnecessary immobilising lines and devices (e.g. chest tubes, intravenous lines, urinary catheters) and physical restraints as early as possible
- Correct sensory deficits (e.g. glasses, hearing aids)
- Minimise environmental isolation by providing reorientation and cognitive stimulation at the level adjusted to the individual patient (i.e. provide more stimulation for hypoactive delirium but reduce stimulation for hyperactive delirium)
- Empower family members and loved ones to assist in the process
- Increase mobility and physical activity (including physical and occupational therapy)

(National Institute for Health and Care Excellence 2010; American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults 2015; Australian Commission on Safety and Quality in Health Care 2021)

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for identifiable causes. A caveat to note is that in clinical settings, causes of delirium are often multifactorial. In fact, numerous causes of smaller effect can sometimes cumulatively lead to an episode of delirium, which makes it more challenging to identify the causes in vulnerable patients.

As family members can also be distressed when encountering a relative in a state of delirium, family education about the condition and their role in providing interpersonal stimulation and therapeutic presence is vital.

It is also important to note that the management of delirium does not necessarily end on discharge – arranging follow-up services for patients who experienced delirium while in hospital can help manage any complications and ensure rehabilitation to minimise any prolonged negative consequences of delirium.

Pharmacological management

Antipsychotics

Although non-pharmacological approaches remain first line, an antipsychotic at the lowest effective dose for the shortest possible duration may be used as a last resort in cases of severe agitation that pose a risk of substantial harm to the patient or others if behavioural interventions have failed or are not possible. A single dose can be sufficient in managing severe agitation in hyperactive delirium, and ongoing use needs to be evaluated daily with an in-person examination (American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults 2015).

It is important to highlight the limitations of the recommendation for use of antipsychotics in the management of severe agitation in delirium, as evidence does not support their routine use in treating delirium. For example, a Cochrane review found no reported data on improvements in the duration of delirium, length of hospital stays, discharge disposition or health-related quality of life with antipsychotic treatment (Burry 2018). Moreover, older patients (>75 years) were found to be less likely to respond to antipsychotics, particularly to olanzapine (Yoon 2013). Low-dose haloperidol, risperidone and several second-generation antipsychotics are used in clinical practice without any particular agent shown to be universally more effective (Nikooie 2019). As a result, the side-effects profile must be considered when selecting the right agent for the individual patient when required. For example, owing to its antihistamine effect quetiapine is a particularly sedating option among the atypical antipsychotics, so it is indicated for patients with predominantly hyperactive delirium. Moreover, antipsychotics are not indicated for hypoactive delirium.

Before and during the use of antipsychotics, ideally a 12-lead electrocardiogram (ECG) should be obtained for evaluation of the QTc interval, and electrolyte abnormalities should be screened and corrected, particularly potassium and magnesium (Maldonado 2017). Of note, guidelines recommend discontinuing antipsychotic use if the QTc increases by more than 25% of baseline or more than 500 ms, to avoid the rare but potentially fatal arrhythmia of torsade de pointes (Maldonado 2017). Moreover, the patient's family must be involved in the decisions to prescribe.

If antipsychotics are prescribed during an admission, providers must be cautious to prevent patients from inadvertently continuing the medication post-discharge without a clear indication.

Dexmedetomidine

Dexmedetomidine has been suggested for the management of delirium in the ICU, in addition to prevention (Lewis 2022). As it has been shown to decrease the duration of mechanical ventilation, dexmedetomidine is recommended for delirium in mechanically ventilated adults with severe agitation that precludes weaning or extubation (Reade 2016). Although dexmedetomidine is licensed for continued use following extubation in a critical care environment because of the unique nature of its sedative effects in preserving airway reflexes and respiratory drive, the evidence for the safety and effectiveness of dexmedetomidine as a delirium treatment for ward patients is not yet sufficient, as only a small effect in shortening delirium duration was found in a single study (Reade 2016).

Special cases in liaison psychiatry: challenging clinical dilemmas

In clinical practice, it is sometimes challenging to distinguish depression from hypoactive delirium, given their overlap in clinical presentation. For example, one might mistake hypoactivity for psychomotor retardation or misdiagnose features of depressive agitation as hyperactive delirium. Table 4 describes the key distinguishing factors between delirium and depression on clinical presentation.

It is important to note that early delirium may sometimes present initially with mood lability in the absence of other sentinel symptoms. Therefore, we recommend providers perform a delirium screen for all patients presenting with symptoms of depression in the hospital setting. Accurate diagnosis and appropriate management are crucial to reduce symptom duration and severity, as well as to decrease the risk of exacerbating the delirium with inappropriate pharmacological agents such as antidepressants. For example, initiating

TABLE 4 Key factors distinguishing hypoactive delirium from depression

	Hypoactive delirium	Depression
Course	Rapid, definable	Insidious, difficult to pinpoint exact onset and offset. Worse in the morning
Orientation	Fluctuates throughout day	Generally fully oriented
Consciousness	Altered level of consciousness	Usually not altered
Thought content	Confusion but not persistent hopelessness or helplessness	Hopelessness, helplessness that persists throughout the day
Cognitive functioning	Overall lower scores than depression but higher effort level	Overall better scores than delirium but low effort level

Sources: Milisen (2006); O'Sullivan (2014).

antidepressants with high anticholinergic potential, such as tricyclics and paroxetine, should be avoided in patients with delirium. First-line treatment for major depressive disorder in any setting includes psychotherapy and antidepressant therapy tailored to patient comorbidities, typically beginning with a selective serotonin reuptake inhibitor.

Similarly, clinical entities such as catatonia, delirium tremens secondary to alcohol withdrawal, and Lewy body dementia may pose diagnostic challenges because of features that overlap with delirium (Table 5).

Lewy body dementia stands out from other common types of dementia, such as Alzheimer's disease, as the cognitive deterioration typically manifests in fluctuating levels of alertness and attention rather than as gradual and progressive change. Delirium may also be superimposed onto pre-existing dementia, which poses a further challenge in diagnosis.

As regards delirium tremens, it is important to note that the patient may not be able to give an accurate drinking history – or may be disinclined to do. Delirium tremens may also appear in a mixed state such as with hepatic encephalopathy. It is also important to note that even in mixed states treatment should start with benzodiazepines at least until withdrawal symptoms have lessened.

Important commonality among these conditions is that their management differs from the typical pharmacological approaches for managing delirium (Table 5). Misdiagnosis can potentially exacerbate the corresponding condition owing to inappropriate management. It is also important to highlight that other medical teams can consult psychiatry and other relevant experts to provide a second opinion when facing such challenging clinical scenarios.

Conclusion

As we reviewed how to best to spot, stop and treat delirium we hope this three-stage approach filters into clinical practice, given the limited accurate knowledge about the condition held within textbooks. This is especially important as some argue that incidence of delirium during hospitalisation provides 'a window to hospital care', affording a wider glimpse of how hospitals are managing their patients and the possibility of change (Inouye 1999). Patients with delirium are vulnerable and often fall through the cracks in hospital systems.

In terms of implications for clinicians, issues that hinder the implementation of best practice recommendations must be considered. For example, multicomponent approaches for prevention can be labour-intensive and may not be feasible with the available medical and nursing staff in certain settings. Consistently implementing non-pharmacological approaches may also be difficult owing to contextual variations in busy ward environments. Educating families and carers to assist with care is critical. Furthermore, complex clinical situations often force clinicians to balance competing and conflicting demands, posing a challenge to following the outlined strategies. For example, opioid medications should be avoided but insufficiently managed pain is itself a risk factor for delirium. Therefore, we must weigh the pros and cons of each intervention for the individual patient, factoring in their comorbidities and current required treatment needs, in order to maximise benefit and minimise harm.

A final but important consideration is that treatment approaches call on us as practitioners to draw on the humanity that we have in our care processes. Compassion, kindness and the understanding that education is at the core of good delirium practice are central to effective approaches. All too often, in the busyness of clinical practice, humane approaches in medicine have gone adrift; perhaps a refocus on improving delirium management can help inject a much-needed dose of humanity into an increasingly technical and super-specialised medical world. As Wes Ely claimed, what is important is to unlearn the depersonalising aspects of care and think about magnifying dignity (Ely 2022).

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TABLE 5 **Challenges in liaison psychiatry: conditions with features that overlap with delirium**

Condition	Features similar to delirium	Features distinct from delirium	Management
Catatonia	Can occur in critically ill patients Similar risk factors (cognitive impairment, cardiovascular/renal disease, visual/hearing impairment) Presence of hypoactive and hyperactive subtypes Alterations in attention and awareness Language deficit/mutism	Catalepsy Waxy flexibility Posturing Grimacing Echolalia Echopraxia Usually able to recall details of previous episodes (awareness retained) Normal EEG	Diagnosis: Bush–Francis Catatonia Rating Scale Management: benzodiazepines (e.g. lorazepam challenge); ECT for refractory symptoms
Delirium tremens	Shared risk factors such as medical comorbidities and nutritional/electrolyte derangements, which can result from chronic alcohol misuse	Typically manifests 3–5 days after sudden cessation or significant curtailing of alcohol consumption Preceding symptoms: minor alcohol withdrawal symptoms (tachycardia, hypertension, insomnia, anxiety, restlessness, tremor, GI disturbances, headache and diaphoresis); hallucinosis with clear sensorium (12–48 h after last drink); seizures (12–48 h after last drink)	Symptoms tracked using revised CIWA-Ar scale (Sullivan 1989) First line: long-acting benzodiazepines (e.g. diazepam or chlordiazepoxide) Supportive strategies: IV fluids to dehydrated patients, vitamin repletion (i.e., thiamine) Significant liver dysfunction: lorazepam Refractory cases: phenobarbital (either in lieu of or in combination with benzodiazepines), propofol In suspected mixed picture benzodiazepines still employed, at least initially (Mart 2021)
Lewy body dementia	Cognitive fluctuations (changes in arousal level, excessive daytime drowsiness) Visual hallucinations	REM sleep behaviour disorder Parkinsonism Antipsychotic sensitivity	Diagnostic criteria: International DLB Consortium (McKeith 2017) Management: multidisciplinary approach (OT, PT, SLP) for mobility and communication difficulties; cholinesterase inhibitor (donepezil, rivastigmine) for symptomatic treatment of cognitive fluctuations, psychotic symptoms; levodopa for Parkinsonism (slow, careful titration to minimise psychotic symptoms); melatonin or clonazepam may be used for symptoms of REM sleep disorders; avoid typical antipsychotics

CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol; ECT, electrocardiogram; EEG, electroencephalogram; GI, gastrointestinal; IV, intravenous; OT, occupational therapy; PT, physical therapy; REM, rapid eye movement; SLP, speech/language therapy.
Sources: Sullivan (1989); McKeith (2017); Wilson (2017); Mart (2021).

MCQ answers
1 c 2 b 3 b 4 c 5 d

Data availability

Data availability is not applicable to this article as no new data were created or analysed in this study.

Author contributions

I.A.Y.: write-up and revision of manuscript, data acquisition and synthesis, edits to sections from co-authors; D.G.: critical review and revision of manuscript; M.W.: write-up of subsections (clinical features, workup, hypoactive delirium vs depression, catatonia); J.P.: write-up of delirium tremens section, assistance with data synthesis; A.X.M.: write-up of Lewy body dementia section, assistance with data synthesis; M.C.R.: critical review of manuscript, expert opinion on delirium management in ICU; A.T.: conception, write-up of subsections (introduction, discussion, conclusion), critical review of manuscript.

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Declaration of interest

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References

Aldecoa C, Bettelli G, Bilotta F, et al (2017) European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium. *European Journal of Anaesthesiology*, **34**: 192–214.

American Geriatrics Society Beers Criteria® Update Expert Panel (2019) American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society*, **67**: 674–94.

American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults (2015) American Geriatrics Society abstracted clinical practice guideline for postoperative delirium in older adults. *Journal of American Geriatric Society*, **63**: 142–50.

American Psychiatric Association (2022) *Diagnostic and Statistical Manual of Mental Disorders* (5th edn, text revision) (DSM-5-TR). APA.

Anand A, Cheng M, Ibitoye T, et al (2022) Positive scores on the 4AT delirium assessment tool at hospital admission are linked to mortality, length of stay and home time: two-centre study of 82,770 emergency admissions. *Age and Ageing*, **51**(3): afac051.

Aung Thein MZ, Pereira JV, Nitchingham A, et al (2020) A call to action for delirium research: meta-analysis and regression of delirium associated mortality. *BMC Geriatrics*, **20**: 325.

Australian Commission on Safety and Quality in Health Care (2021) *Delirium Clinical Care Standard*. Australian Commission on Safety and Quality in Health Care.

Balas MC, Vasilevskis EE, Olsen KM, et al (2014) Effectiveness and safety of the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle. *Critical Care Medicine*, **42**: 1024–36.

Burry L, Mehta S, Perreault MM, et al (2018) Antipsychotics for treatment of delirium in hospitalised non-ICU patients. *Cochrane Database of Systematic Reviews*, **6**: CD005594.

Burry L, Hutton B, Williamson DR, et al (2019) Pharmacological interventions for the treatment of delirium in critically ill adults. *Cochrane Database of Systematic Reviews*, **9**: CD011749.

Bush SH, Lawlor PG, Ryan K, et al (2018) Delirium in adult cancer patients: eSMO Clinical Practice Guidelines. *Annals of Oncology*, **29**(suppl 4): iv143–65.

Davis DH, Muniz Terrera G, Keage H, et al (2012) Delirium is a strong risk factor for dementia in the oldest-old: a population-based cohort study. *Brain*, **135**: 2809–16.

Devlin JW, Skrobik Y, Gélinas C, et al (2018) Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. *Critical Care Medicine*, **46**: e825–e873.

Ely W (2022) *Every Deep-Drawn Breath: A Critical Care Doctor on Healing, Recovery, and Transforming Medicine in the ICU*. Simon & Schuster.

Feng X, Valdearcos M, Uchida Y, et al (2017) Microglia mediate postoperative hippocampal inflammation and cognitive decline in mice. *JCI Insight*, **2**: e91229.

Gibb K, Seeley A, Quinn T, et al (2020) The consistent burden in published estimates of delirium occurrence in medical inpatients over four decades: a systematic review and meta-analysis study. *Age Ageing*, **49**: 352–60.

Gou RY, Hshieh TT, Marcantonio ER, et al (2021) One-year Medicare costs associated with delirium in older patients undergoing major elective surgery. *JAMA Surgery*, **156**: 462–70.

Han JH, Wilson A, Vasilevskis EE, et al (2013) Diagnosing delirium in older emergency department patients: validity and reliability of the delirium triage screen and the brief confusion assessment method. *Annals of Emergency Medicine*, **62**: 457–65.

Hudson M (2022) *The Lived Experience (Mark Hudson on the Patient Experience of Delirium #WDAD2022)*. YouTube (https://youtu.be/nOmwZMa2ayg).

Inouye SK, Schlesinger M, Lydon TJ (1999) Delirium: a symptom of how hospital care is failing older persons and a window to improve quality of hospital care. *Am J Med*, **106**: 565–73.

Inouye SK, Bogardus ST, Jr, Charpentier PA, et al (1999) A multicomponent intervention to prevent delirium in hospitalized older patients. *New England Journal of Medicine*, **340**: 669–76.

Inouye S, Baker D, Fugal P, et al (2006) Dissemination of the Hospital Elder Life Program: implementation, adaptation, and successes. *Journal of American Geriatric Society*, **54**: 1492–9.

Jenssen S (2005) Electroencephalogram in the dementia workup. *Am J Alzheimers Dis Other Demen*, **20**: 159–66.

Kim YH, Kim NY, Ryu S (2022) Effects of non-pharmacological interventions for preventing delirium in general ward inpatients: a systematic review & meta-analysis of randomized controlled trials. *PLoS One*, **17**: e0268024.

Krewulak KD, Stelfox HT, Leigh JP, et al (2018) Incidence and prevalence of delirium subtypes in an adult ICU: a systematic review and meta-analysis. *Critical Care Medicine*, **46**: 2029–35.

Lewis K, Alshamsi F, Carayannopoulos KL, et al (2022) Dexmedetomidine vs other sedatives in critically ill mechanically ventilated adults: a systematic review and meta-analysis of randomized trials. *Intensive Care Medicine*, **48**: 811–40.

MacLullich AM, Shenkin SD, Goodacre S, et al (2019) The 4 'A's test for detecting delirium in acute medical patients: a diagnostic accuracy study. *Health technology assessment*, **23**(40): 1–194.

Maldonado JR (2017) Acute brain failure: pathophysiology, diagnosis, management, and sequelae of delirium. *Critical Care Clinics*, **33**: 461–519.

Maldonado JR (2018) Delirium pathophysiology: an updated hypothesis of the etiology of acute brain failure. *International Journal of Geriatric Psychiatry*, **33**: 1428–57.

Maneeton B, Kongsaengdao S, Maneeton N, et al (2022) Melatonin receptor agonists for the prevention of delirium: an updated systematic review and meta-analysis of randomized controlled trials. *Current Neuropharmacology*, **20**: 1956–68.

Marcantonio ER (2017) Delirium in hospitalized older adults. *New England Journal of Medicine*, **377**: 1456–66.

Mart MF, Williams Roberson S, Salas B, et al (2021) Prevention and management of delirium in the intensive care unit. *Seminars in Respiratory and Critical Care Medicine*, **42**: 112–26.

McKeith IG, Boeve BF, Dickson DW, et al (2017) Diagnosis and management of dementia with Lewy bodies: fourth consensus report of the DLB Consortium. *Neurology*, **89**: 88–100.

Meagher DJ, Trzepacz PT (2000) Motoric subtypes of delirium. *Seminars in Clinical Neuropsychiatry*, **5**: 75–85.

Milisen K, Braes T, Fick DM, et al (2006) Cognitive assessment and differentiating the 3 Ds (dementia, depression, delirium). *Nursing Clinics of North America*, **41**: 1–22.

National Institute for Health and Care Excellence (2010) *Delirium: Prevention, Diagnosis and Management in Hospital and Long-Term Care (Clinical Guideline CG103)*. NICE.

Nikooie R, Neufeld KJ, Oh ES, et al (2019) Antipsychotics for treating delirium in hospitalized adults: a systematic review. *Annals of Internal Medicine*, **171**: 485–95.

Oh ES, Fong TG, Hshieh TT, et al (2017) Delirium in older persons: advances in diagnosis and treatment. *JAMA*, **318**: 1161–74.

Oldham MA, Flanagan NM, Khan A, et al (2018) Responding to ten common delirium misconceptions with best evidence: an educational review for clinicians. *Journal of Neuropsychiatry and Clinical Neurosciences*, **30**: 51–7.

O'Sullivan R, Inouye SK, Meagher D (2014) Delirium and depression: inter-relationship and clinical overlap in elderly people. *Lancet Psychiatry*, **1**: 303–11.

Pandharipande PP, Girard TD, Jackson JC, et al (2013) Long-term cognitive impairment after critical illness. *New England Journal of Medicine*, **369**: 1306–16.

Peden CJ, Miller TR, Deiner SG, et al (2021) Improving perioperative brain health: an expert consensus review of key actions for the perioperative care team. *British Journal of Anaesthesia*, **126**: 423–32.

Reade MC, Eastwood GM, Bellomo R, et al (2016) Effect of dexmedetomidine added to standard care on ventilator-free time in patients with agitated delirium: a randomized clinical trial. *JAMA*, **315**: 1460–8.

Richardson SJ, Davis DHJ, Stephan BCM, et al (2021) Recurrent delirium over 12 months predicts dementia: results of the Delirium and Cognitive Impact in Dementia (DECIDE) study. *Age and Ageing*, **50**: 914–20.

Rudolph JL, Boustani M, Kamholz B, et al (2011) Delirium: a strategic plan to bring an ancient disease into the 21st century. *Journal of American Geriatric Society*, **59**: S237–40.

Sands MB, Sharma S, Carpenter L, et al (2021) "SQiD, the single question in delirium; can a single question help clinicians to detect delirium in hospitalised cancer patients?" running heading single question in delirium" (bcan-D-20-01665). *BMC Cancer*, **21**: 75.

Shenkin SD, Fox C, Godfrey M, et al (2019) Delirium detection in older acute medical inpatients: a multicentre prospective comparative diagnostic test accuracy study of the 4AT and the confusion assessment method. *BMC Medicine*, **17**: 138.

Smithard D, Randhawa R (2022) Physical restraint in the critical care unit: a narrative review. *New Bioethics*, **28**: 68–82.

Sullivan JT, Sykora K, Schneiderman J, et al (1989) Assessment of Alcohol Withdrawal: the revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar). *British Journal of Addiction*, **84**: 1353–7.

van Eijk MM, Roes KC, Honing ML, et al (2010) Effect of rivastigmine as an adjunct to usual care with haloperidol on duration of delirium and mortality in critically ill patients: a multicentre, double-blind, placebo-controlled randomised trial. *Lancet*, **376**: 1829–37.

van Velthuijsen EL, Zwakhalen SMG, Mulder WJ, et al (2018) Detection and management of hyperactive and hypoactive delirium in older patients during hospitalization: a retrospective cohort study evaluating daily practice. *International Journal of Geriatric Psychiatry*, **33**: 1521–9.

Whitby J, Nitchingham A, Caplan G, et al (2022) Persistent delirium in older hospital patients: an updated systematic review and meta-analysis. *Delirium*, **1**: 36822.

Wilson JE, Carlson R, Duggan MC, et al (2017) Delirium and catatonia in critically ill patients: the delirium and catatonia prospective cohort investigation. *Critical Care Medicine*, **45**: 1837–44.

Wilson JE, Mart MF, Cunningham C, et al (2020) Delirium. *Nature Reviews Disease Primers*, **6**: 90.

Witlox J, Eurelings LS, De Jonghe JF, et al (2010) Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: a meta-analysis. *JAMA*, **304**: 443–51.

World Health Organization (2022) *International Classification of Diseases, Eleventh Revision (ICD-11)*. WHO.

Yoon H-J, Park K-M, Choi W-J, et al (2013) Efficacy and safety of haloperidol versus atypical antipsychotic medications in the treatment of delirium. *BMC Psychiatry*, **13**: 1–11.

MCQs

Select the single best option for each question stem

1 Which of the following is **not** correct regarding clinical features of delirium?

a Prodromal features can include anxiety, restlessness, irritability and sleep disturbance.
b Emotional disturbance such as fear, lability, depression and apathy can occur.
c Hallucinations and delusions are rare in delirium.
d Symptoms are not better explained by another preexisting, established, or evolving neurocognitive disorder.
e The disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal, or exposure to a toxin, or has multiple aetiologies.

2 Which medication class should generally be avoided in the treatment of delirium, owing to their potential to worsen confusion?

a Antidepressants
b Anticholinergics
c Antihypertensives
d Anticonvulsants
e None of the above.

3 Which of the following strategies is **not** recommended for preventing delirium in hospital in-patients?

a Early mobilisation and physical therapy
b Regular use of benzodiazepines for sleep
c Adequate hydration and nutrition
d Minimising use of physical restraints
e Appropriate family involvement in education.

4 Which the following statements about the 4AT screening tool is **not** correct?

a The tool assesses for alertness, rating mild sleepiness for <10 s after waking as normal.
b Attention is assessed by asking the person to list the months of the year backwards.
c Assessment should be deferred if the person appears to be asleep.
d The timeline of acute change or fluctuating course of alertness, cognition or other mental function is determined as being within the past 2 weeks, with changes still evident in the past 24 h.
e It includes orientation items asking the person to give their age, date of birth, current location and the current year.

5 Which of the following factors is **not** an established risk factor for delirium?

a High APACHE-II score
b Advanced age
c Use of sedatives
d Family history of delirium
e Morphine use.

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