

BIBLIOGRAPHIC INFORMATION SYSTEM

JOURNAL FULL TITLE: Journal of Biomedical Research & Environmental Sciences

ABBREVIATION (NLM): J Biomed Res Environ Sci **ISSN:** 2766-2276 **WEBSITE:** <https://www.jelsciences.com>

SCOPE & COVERAGE

- ▶ **Sections Covered:** 34 specialized sections spanning 143 topics across Medicine, Biology, Environmental Sciences, and General Science
- ▶ Ensures broad interdisciplinary visibility for high-impact research.

PUBLICATION FEATURES

- ▶ **Review Process:** Double-blind peer review ensuring transparency and quality
- ▶ **Time to Publication:** Rapid 21-day review-to-publication cycle
- ▶ **Frequency:** Published monthly
- ▶ **Plagiarism Screening:** All submissions checked with iThenticate

INDEXING & RECOGNITION

- ▶ **Indexed in:** [Google Scholar](#), IndexCopernicus (ICV 2022: 88.03)
- ▶ **DOI:** Registered with CrossRef ([10.37871](#)) for long-term discoverability
- ▶ **Visibility:** Articles accessible worldwide across universities, research institutions, and libraries

OPEN ACCESS POLICY

- ▶ Fully Open Access journal under Creative Commons Attribution 4.0 License (CC BY 4.0)
- ▶ Free, unrestricted access to all articles globally

GLOBAL ENGAGEMENT

- ▶ **Research Reach:** Welcomes contributions worldwide
- ▶ **Managing Entity:** SciRes Literature LLC, USA
- ▶ **Language of Publication:** English

SUBMISSION DETAILS

- ▶ Manuscripts in Word (.doc/.docx) format accepted

SUBMISSION OPTIONS

- ▶ **Online:** <https://www.jelsciences.com/submit-your-paper.php>
- ▶ **Email:** support@jelsciences.com, support@jbresonline.com

[HOME](#)[ABOUT](#)[ARCHIVE](#)[SUBMIT MANUSCRIPT](#)[APC](#)

 **Vision:** The Journal of Biomedical Research & Environmental Sciences (JBRES) is dedicated to advancing science and technology by providing a global platform for innovation, knowledge exchange, and collaboration. Our vision is to empower researchers and scientists worldwide, offering equal opportunities to share ideas, expand careers, and contribute to discoveries that shape a healthier, sustainable future for humanity.

SYSTEMATIC REVIEW

Beyond Confusion: Recognition, Prevention and Management of Delirium in Hospitalized Adults

Devina Wadhwa*, BSC (Pharm), MD, FRCPC

Northern Ontario School of Medicine University, Thunder Bay, Ontario, Canada

Abstract

Delirium is one of the most common and clinically significant neuropsychiatric syndromes encountered in hospitalized adults, particularly among older patients, critically ill individuals, and those undergoing major surgery. Characterized by an acute disturbance in attention, awareness, and cognition, delirium is associated with increased mortality, prolonged hospitalization, functional decline, institutionalization, long-term cognitive impairment, and substantial healthcare costs. Despite its prevalence, delirium remains underrecognized, especially in patients presenting with hypoactive symptoms.

Advances in recent years have improved understanding of the complex pathophysiological mechanisms underlying delirium, highlighting the interplay between neuroinflammation, neurotransmitter imbalance, oxidative stress, blood-brain barrier dysfunction, and impaired cerebral network connectivity. Prevention through multicomponent, non-pharmacological interventions remains the most effective strategy for reducing delirium incidence, while pharmacological therapy continues to have a limited role and should be reserved for carefully selected patients with severe distress or behaviours that threaten patient or staff safety.

Emerging research has focused on artificial intelligence (AI)-based prediction models, blood-based biomarkers, electroencephalography, and precision medicine approaches that may improve early identification of high-risk patients and facilitate individualized prevention strategies. However, important challenges remain, including the underrecognition of hypoactive delirium, limited evidence supporting pharmacological interventions, and the need for prospective validation of emerging diagnostic technologies.

This narrative review summarizes the contemporary evidence regarding

*Corresponding author(s)

Devina Wadhwa, Northern Ontario School of Medicine University, Thunder Bay, Ontario, Canada

Email: devinamaya@gmail.com

DOI: 10.37871/jbres2322

Submitted: 22 July 2026

Accepted: 12 August 2026

Published: 13 August 2026

Copyright: © 2026 Wadhwa D.

Distributed under Creative Commons CC-BY 4.0 ©¹

OPEN ACCESS

Keywords

- Delirium
- Hospitalized adults
- Prevention
- Diagnosis
- Neuroinflammation
- Artificial intelligence
- Biomarkers
- Intensive care
- Geriatrics

VOLUME: 7 ISSUE: 8 - AUGUST, 2026



How to cite this article: Wadhwa D. Beyond Confusion: Recognition, Prevention and Management of Delirium in Hospitalized Adults. J Biomed Res Environ Sci. 2026 August 13; 7(8): 14. Doi: 10.37872/jbres2322



the epidemiology, pathophysiology, risk factors, diagnosis, prevention, and management of delirium in hospitalized adults while highlighting current controversies, recent advances, and future directions that may shape clinical practice.

Introduction

It is two o'clock in the morning. A previously independent 78-year-old woman insists she must catch a train that left decades ago. She repeatedly attempts to climb out of bed, pulls at her intravenous line, and no longer recognizes her daughter. By morning she is calm, yet later that afternoon she struggles to maintain attention long enough to answer simple questions. This is more than confusion. It is delirium, one of the most common, costly, and potentially preventable complications of acute hospitalization.

Delirium is an acute neuropsychiatric syndrome characterized by disturbances in attention, awareness, and cognition that develop over a short period and fluctuate throughout the course of the day. It represents a manifestation of acute brain dysfunction precipitated by medical illness, surgery, medication effects, or other physiological stressors in vulnerable individuals. Although delirium has long been recognized as a medical emergency, it remains one of the most frequently underdiagnosed complications of hospitalization, particularly among older adults and patients presenting with hypoactive symptoms. Unlike dementia, which typically develops gradually over months or years, delirium has an abrupt onset and fluctuating course, making prompt recognition essential for timely investigation and treatment [1-3].

Delirium affects approximately 15-30% of hospitalized medical patients, with substantially higher rates reported among critically ill individuals, postoperative patients, and older adults. In intensive care units, the incidence may exceed 50%, and among mechanically ventilated patients, reported rates approach 80%. Delirium is independently associated with in-

creased mortality, prolonged hospitalization, functional decline, institutionalization, health-care expenditures, and persistent cognitive impairment that may continue long after hospital discharge. Despite these significant consequences, hypoactive delirium remains particularly underrecognized because patients often appear withdrawn, quiet, or excessively somnolent rather than overtly agitated, resulting in delayed diagnosis and missed opportunities for intervention [2-4].

The pathogenesis of delirium is complex and multifactorial, reflecting the interaction between baseline patient vulnerability and acute physiological insults. Contemporary research has expanded our understanding of the biological mechanisms involved, highlighting the roles of neuroinflammation, neurotransmitter dysregulation, oxidative stress, blood-brain barrier dysfunction, impaired cerebral metabolism, and disruption of large-scale neuronal networks. At the same time, growing evidence has demonstrated that a substantial proportion of delirium episodes are preventable through multicomponent, non-pharmacological interventions focused on early mobilization, sleep optimization, medication review, hydration, orientation, and family engagement. These advances have shifted the emphasis of delirium care from reactive management toward proactive prevention and early recognition [2-6].

Despite important progress, several challenges remain. Delirium continues to be overlooked in routine clinical practice, particularly in patients with hypoactive presentations or pre-existing dementia, and pharmacological treatment options remain limited. In recent years, emerging technologies, including artificial intelligence (AI)-based prediction models, machine learning algorithms, blood-based bi-



omarkers, electroencephalography (EEG), and digital health tools, have generated considerable interest as potential methods for improving early detection and individualized prevention. While these innovations show promise, most remain investigational and require further validation before widespread clinical implementation [6–14].

As population's age and medical complexity continues to increase, the burden of delirium is expected to rise worldwide. Improving recognition, prevention, and evidence-based management therefore remains a major priority across all areas of inpatient care. This narrative review summarizes the contemporary evidence regarding the epidemiology, pathophysiology, risk factors, diagnosis, prevention, and management of delirium in hospitalized adults. In addition, it critically examines current controversies, recent advances in delirium research, and future directions that may shape clinical practice over the coming decade.

Epidemiology

Delirium is among the most common neurological complications of acute hospitalization and represents a major source of morbidity, mortality, and healthcare utilization worldwide. Reported incidence varies according to patient population, underlying illness severity, and the diagnostic methods employed. Delirium affects approximately 15 to 30% of general medical inpatients, while substantially higher rates are observed among critically ill individuals, post-operative patients, and older adults. In intensive care units, the incidence frequently exceeds 50%, and among mechanically ventilated patients, reported rates may approach 80% [2–5].

Advanced age remains one of the strongest risk factors for delirium owing to age-related reductions in physiological reserve, increasing multimorbidity, polypharmacy, and a higher prevalence of pre-existing cognitive impair-

ment. Delirium is particularly common following major orthopaedic, cardiac, and vascular surgery, where perioperative physiological stress, anaesthetic exposure, pain, and inflammation contribute to increased susceptibility. Similarly, patients with severe infection, sepsis, malignancy, organ failure, and critical illness experience disproportionately high rates of delirium because of systemic inflammatory responses and metabolic disturbances [2–4,15].

The clinical consequences of delirium extend well beyond the acute hospital admission. Numerous studies have demonstrated independent associations between delirium and prolonged hospitalization, increased healthcare costs, functional decline, falls, institutionalization, hospital readmission, persistent cognitive impairment, and both short and long-term mortality. Delirium has also been identified as an independent risk factor for subsequent dementia, particularly among older adults with underlying cognitive vulnerability. These findings emphasize that delirium is not merely a transient manifestation of acute illness but rather an important predictor of adverse patient outcomes and long-term loss of independence [2–4].

Despite its high prevalence, delirium remains substantially underrecognized in routine clinical practice. Hypoactive delirium, characterized by reduced motor activity, lethargy, and withdrawal, is particularly likely to be missed because affected patients often appear calm rather than agitated. Consequently, delayed recognition may postpone investigation of underlying reversible causes and reduce opportunities for early intervention [2,3].

Pathophysiology

The pathophysiology of delirium is multifactorial and remains incompletely understood. Current evidence supports a multifactorial model in which delirium develops through the interaction between baseline patient vulnerability and acute physiological stressors. Rather



than resulting from a single pathological process, delirium appears to reflect the convergence of neuroinflammation, neurotransmitter dysregulation, oxidative stress, impaired cerebral metabolism, blood-brain barrier dysfunction, circadian rhythm disruption, and altered neuronal network connectivity [2,5,6].

One of the leading hypotheses involves systemic inflammation. Acute illness, infection, trauma, or surgery trigger the release of pro-inflammatory cytokines, including interleukin-1, interleukin-6, and tumour necrosis factor- α . These inflammatory mediators activate microglia and astrocytes within the central nervous system, resulting in neuronal dysfunction, altered synaptic transmission, and impaired cerebral communication. Older adults and patients with pre-existing neurodegenerative disease appear particularly susceptible because age-related neuroinflammatory changes reduce the brain's ability to maintain normal cognitive function during physiological stress [5-8].

Neurotransmitter imbalance also plays a central role in delirium development. Cholinergic deficiency remains one of the most widely accepted mechanisms because acetylcholine is essential for attention, learning, and memory. Concurrently, relative dopaminergic excess may contribute to agitation, hallucinations, and psychotic symptoms frequently observed in hyperactive delirium. Additional abnormalities involving serotonin, gamma-aminobutyric acid, glutamate, melatonin, and noradrenaline have also been implicated, highlighting the complex neurochemical disturbances associated with delirium [2,6].

Oxidative stress, impaired cerebral perfusion, mitochondrial dysfunction, and disruption of the blood-brain barrier further contribute to neuronal injury during acute illness. Sleep deprivation and disturbances of circadian rhythm, both common among hospitalized patients, may exacerbate cognitive dysfunction by

impairing normal neurophysiological recovery and melatonin regulation. Recent neuroimaging and electroencephalographic studies suggest that delirium is associated with widespread disruption of functional brain networks rather than localized structural injury, supporting the concept of delirium as a disorder of global cerebral connectivity [5,6].

Contemporary research increasingly views delirium as a syndrome resulting from impaired cerebral resilience. Individuals with multiple predisposing factors, such as advanced age, frailty, dementia, or chronic illness, possess reduced physiological reserve and therefore require only relatively minor physiological insults to precipitate acute brain dysfunction. This vulnerability model explains the considerable heterogeneity observed in delirium presentations and reinforces the importance of both identifying baseline risk factors and minimizing preventable hospital-related precipitants [2,6].

Risk Factors

Risk factors for delirium are traditionally classified as predisposing factors, which increase baseline vulnerability, and precipitating factors, which trigger delirium during acute illness. The development of delirium is best understood through the interaction of these factors. Patients with substantial baseline vulnerability may develop delirium following relatively minor physiological stressors, whereas healthier individuals generally require more severe insults before delirium occurs [2,16] (Table 1).

Patients admitted to hospital often possess multiple predisposing and precipitating risk factors simultaneously. Consequently, comprehensive risk assessment at the time of admission provides an important opportunity to identify high-risk individuals and implement early preventive interventions before delirium develops. Recognition of modifiable risk factors, particularly medication review, optimization of hydration and nutrition, treatment of pain, promotion



of normal sleep, and avoidance of unnecessary urinary catheters and physical restraints, remains a cornerstone of evidence-based delirium prevention [2,4,15].

Clinical Presentation

Delirium is characterized by the acute onset of disturbances in attention, awareness, and cognition that fluctuate throughout the course of the day. Symptoms typically develop over hours to days and represent a marked departure from the patient's baseline level of functioning. Fluctuation is a defining feature, with patients often appearing lucid during one assessment and markedly impaired only hours later. This variability contributes significantly to delayed diagnosis, particularly when cognitive assessments are performed infrequently [1-3].

Impaired attention remains the hallmark clinical feature of delirium and is often more diagnostically useful than memory impairment. Patients may struggle to maintain focus during conversation, follow simple instructions, recite the months of the year in reverse order, or perform tasks requiring sustained concentration. Additional cognitive disturbances include disorganized thinking, impaired orientation, language dysfunction, visuospatial impairment,

and deficits in short-term memory and executive functioning. Alterations in the sleep-wake cycle are common and frequently manifest as daytime somnolence with nighttime agitation [1-3]. Delirium is traditionally classified into three motor subtypes. Hyperactive delirium is characterized by agitation, restlessness, emotional lability, hallucinations, and inappropriate behaviour. These patients often attract immediate clinical attention because of disruptive behaviours or attempts to remove medical devices. Hypoactive delirium, the most frequently overlooked subtype, presents with lethargy, reduced motor activity, withdrawal, decreased responsiveness, and apathy. Because these patients are often perceived as simply tired or depressed, diagnosis is commonly delayed. Mixed delirium, in which patients alternate between hyperactive and hypoactive symptoms, represents the most common motor subtype encountered in clinical practice [2,3].

Although hallucinations and perceptual disturbances are frequently associated with delirium, they are neither universal nor required for diagnosis. Visual hallucinations are more common than auditory hallucinations and should prompt careful assessment for underlying medical causes rather than immediate attribution to

Table 1: Predisposing and Precipitating Risk Factors for Delirium.

Predisposing Factors	Precipitating Factors
Advanced age	Infection and sepsis
Dementia or mild cognitive impairment	Major surgery
Previous delirium	Polypharmacy
Frailty	High-risk medications including anticholinergics, benzodiazepines and opioids
Sensory impairment	Hypoxia
Multiple chronic illnesses	Electrolyte disturbances
Functional dependence	Dehydration
Malnutrition	Pain
Depression	Urinary retention
Alcohol use disorder	Constipation
Visual impairment	Sleep deprivation
Hearing impairment	Intensive care admission
Polypharmacy	Physical restraints
Parkinson disease	Environmental change

a primary psychiatric disorder [1,3].

Diagnosis

Delirium remains a clinical diagnosis requiring careful bedside assessment, collateral history, and systematic evaluation for underlying medical causes. Because symptoms fluctuate throughout the day, a single normal cognitive assessment does not exclude delirium. Repeated evaluations are often necessary when clinical suspicion remains high [1-3,17]. The diagnosis begins with establishing the patient's baseline cognitive and functional status. Family members, caregivers, and healthcare providers frequently provide essential information regarding the timing of symptom onset, behavioural changes, and fluctuations in cognition. Distinguishing delirium from dementia is particularly important, as patients with dementia remain at substantially increased risk of developing delirium during acute illness. While dementia generally progresses gradually over months or years, delirium develops abruptly and is characterized by impaired attention, altered consciousness, and fluctuating symptoms [18].

Several validated screening instruments facilitate delirium recognition in clinical practice. The Confusion Assessment Method (CAM) remains the most widely used bedside assessment tool and demonstrates excellent diagnostic accuracy across a variety of inpatient settings. Diagnosis using the CAM requires the presence of acute onset with a fluctuating course, inattention, and either disorganized thinking or an altered level of consciousness. For critically ill or mechanically ventilated patients who cannot communicate verbally, the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) has been extensively validated and is recommended for routine screening in intensive care settings [17]. The 4 'A's Test (4AT) has gained increasing popularity because of its rapid administration, requiring less than two minutes to complete without formal training. It evalu-

ates alertness, cognition, attention, and acute change or fluctuating course, making it particularly useful in emergency departments, acute medical wards, and geriatric practice [17].

Once delirium has been identified, clinicians should immediately investigate reversible causes. A comprehensive assessment includes medication review, physical examination, neurological evaluation, laboratory investigations, and targeted imaging when clinically indicated. Common reversible contributors include infection, hypoxia, dehydration, electrolyte abnormalities, hypoglycaemia, urinary retention, constipation, uncontrolled pain, medication adverse effects, alcohol or sedative withdrawal, and metabolic disturbances. The diagnostic workup should always be individualized according to the patient's clinical presentation rather than performed routinely [2-4].

The differential diagnosis includes dementia, depression, primary psychotic disorders, catatonia, intoxication, withdrawal syndromes, and other causes of altered mental status. Careful attention to the temporal pattern of symptom onset, fluctuating course, and impairment of attention remains fundamental to distinguishing delirium from these conditions.

Prevention

Prevention remains the most effective strategy for reducing the incidence and consequences of delirium. Unlike many complications of acute hospitalization, a substantial proportion of delirium episodes are preventable through structured, multicomponent interventions that target modifiable risk factors. Consequently, prevention should begin at the time of hospital admission with early identification of patients at increased risk [2,4,15].

Multicomponent non-pharmacological interventions consistently demonstrate the greatest benefit and remain the cornerstone of



delirium prevention. Effective strategies include regular orientation, cognitive stimulation, promotion of normal sleep, early mobilization, optimization of hydration and nutrition, effective pain management, avoidance of unnecessary urinary catheters and physical restraints, medication review, and correction of sensory impairment through the use of hearing aids and corrective lenses. Family involvement further supports orientation, reassurance, and communication, particularly among patients with pre-existing cognitive impairment [2,16].

One of the most influential prevention initiatives is the Hospital Elder Life Program (HELP), which employs standardized multidisciplinary interventions targeting cognitive orientation, mobility, hydration, nutrition, sleep hygiene, and sensory optimization. Numerous studies have demonstrated that HELP significantly reduces delirium incidence while improving functional outcomes and reducing healthcare costs. Its success highlights the importance of coordinated, team-based approaches to delirium prevention [2,16].

Medication optimization represents another essential preventive strategy. Clinicians should minimize exposure to medications associated with delirium whenever possible, particularly anticholinergic agents, benzodiazepines, sedative hypnotics, and unnecessary opioid therapy. Polypharmacy should be reviewed regularly throughout hospitalization, especially in older adults with multiple comorbidities [4,15].

Sleep disruption is increasingly recognized as an important modifiable contributor to delirium. Hospital environments frequently expose patients to excessive nighttime noise, frequent clinical interruptions, and inappropriate lighting. Simple environmental interventions, including minimizing overnight disturbances, reducing noise, maintaining normal day-night lighting patterns, and avoiding unnecessary overnight investigations, may substantially

improve sleep quality and reduce delirium risk [2,4]. Successful prevention requires collaboration among physicians, nurses, pharmacists, therapists, patients, and families. Because delirium frequently results from the interaction of multiple contributing factors, prevention is most effective when delivered through coordinated multidisciplinary care rather than isolated interventions.

Management

The management of delirium begins with the prompt identification and treatment of the underlying cause. Delirium should be considered a medical emergency until proven otherwise, as it frequently reflects acute physiological dysfunction. Effective management requires a systematic approach that combines correction of reversible precipitating factors with supportive, patient-centred care. Because delirium is often multifactorial, successful treatment usually depends on addressing several contributing factors simultaneously rather than focusing on a single diagnosis [2-4].

Identification and Treatment of Reversible Causes

The initial priority is to identify and correct reversible contributors. A careful history, medication review, physical examination, and targeted investigations should be undertaken to evaluate for common precipitating factors including infection, hypoxia, dehydration, electrolyte abnormalities, hypoglycaemia, uncontrolled pain, constipation, urinary retention, medication adverse effects, alcohol or sedative withdrawal, and metabolic disturbances. Management should be individualized according to the patient's clinical presentation rather than relying on routine diagnostic testing alone [2,4].

Medication review deserves particular attention. Drugs with anticholinergic properties, benzodiazepines, sedative hypnotics, corticosteroids,

teroids, and opioid analgesics have all been associated with delirium and should be discontinued or minimized whenever clinically feasible. Polypharmacy should be reassessed throughout hospitalization, particularly in older adults with multiple chronic conditions [2,4].

Non-pharmacological Management

Non-pharmacological interventions remain the cornerstone of delirium management and should be implemented in all patients regardless of symptom severity. These interventions aim to restore normal cognitive function by optimizing the patient's physical and environmental conditions while minimizing additional physiological stress [3,4].

Key components include regular reorientation, visible clocks and calendars, promotion of normal sleep, early mobilization, adequate hydration and nutrition, correction of sensory impairment with hearing aids or corrective lenses, effective pain management, and avoidance of unnecessary urinary catheters and physical restraints. Family members play a particularly valuable role by providing reassurance, familiar conversation, and information regarding the patient's baseline cognitive status [4,15]

The hospital environment itself may contribute to delirium through excessive noise, sleep disruption, frequent room changes, and sensory deprivation. Whenever possible, patients should be cared for in quiet, well-lit environments that support normal circadian rhythms while minimizing unnecessary overnight interruptions [2,4].

Pharmacological Management

Pharmacological therapy has a limited role in the treatment of delirium and should not be used routinely. Numerous randomized controlled trials have failed to demonstrate that antipsychotic medications reduce delirium duration,

severity, mortality, or long-term cognitive outcomes. Consequently, current clinical guidelines recommend reserving these medications for carefully selected patients experiencing severe agitation, psychotic symptoms causing significant distress, or behaviours that pose an immediate risk to the safety of the patient or others [2-4].

When pharmacological treatment becomes necessary, the lowest effective dose should be prescribed for the shortest possible duration with frequent reassessment. Clinicians should remain mindful of potential adverse effects including extrapyramidal symptoms, excessive sedation, orthostatic hypotension, QT interval prolongation, and increased fall risk, particularly among frail older adults [2,18].

Benzodiazepines should generally be avoided because they may worsen delirium and contribute to excessive sedation. Their use should be restricted to specific clinical situations such as alcohol withdrawal delirium or benzodiazepine withdrawal, where they remain first-line therapy [2,18].

Physical Restraints

Physical restraints should be avoided whenever possible because they are associated with increased agitation, prolonged delirium, immobility, pressure injuries, falls, and psychological distress. Alternative strategies including increased observation, family presence, environmental modification, and individualized behavioural approaches should always be considered before restraints are used. When restraints become unavoidable because of immediate safety concerns, they should be applied for the shortest possible duration with frequent reassessment and ongoing efforts to discontinue them promptly [15].

Multidisciplinary Care

Optimal delirium management requires col-



laboration among physicians, nurses, pharmacists, physiotherapists, occupational therapists, speech-language pathologists, dietitians, and family caregivers. Nurses often identify early behavioural changes, pharmacists contribute medication optimization, and therapists facilitate mobilization and functional recovery, while family members provide valuable collateral history and reassurance. A coordinated multidisciplinary approach consistently produces better outcomes than isolated interventions delivered by individual disciplines [2,4].

Special Populations

Although delirium may occur in patients of any age, several populations experience substantially greater risk because of increased physiological vulnerability and medical complexity [2,3].

Older Adults

Older adults account for the majority of hospitalized patients who develop delirium. Age-related reductions in physiological reserve, multimorbidity, frailty, sensory impairment, polypharmacy, and pre-existing cognitive impairment all contribute to increased susceptibility. Delirium in older adults is associated with accelerated functional decline, prolonged hospitalization, institutionalization, and increased mortality. Importantly, delirium should never be considered a normal consequence of aging and always warrants careful evaluation for reversible causes [4,17].

Delirium Superimposed on Dementia

Patients with dementia are particularly vulnerable to delirium because neurodegenerative disease reduces cerebral reserve and resilience. Delirium superimposed on dementia presents significant diagnostic challenges because baseline cognitive impairment may obscure the

acute changes characteristic of delirium. Careful collateral history from family members and caregivers is therefore essential to establish whether new symptoms represent an acute departure from the patient's usual cognitive function. Failure to recognize delirium in this population may delay diagnosis of potentially reversible medical illness and contribute to worse clinical outcomes [18].

Critically Ill Patients

Delirium affects more than half of critically ill patients and remains one of the most common neurological complications encountered in intensive care units. Mechanical ventilation, deep sedation, sepsis, metabolic disturbances, prolonged immobilization, and sleep disruption all contribute to increased risk. ICU delirium has been associated with prolonged mechanical ventilation, increased mortality, longer intensive care stays, and persistent cognitive impairment following hospital discharge. Routine delirium screening using validated tools such as the CAM-ICU should therefore be incorporated into daily intensive care practice [4].

Postoperative Delirium

Postoperative delirium commonly develops within the first several days following major surgery, particularly after orthopaedic, cardiac, and vascular procedures. Contributing factors include perioperative inflammation, anaesthetic exposure, blood loss, pain, sleep disruption, electrolyte abnormalities, and opioid use. Early mobilization, multimodal analgesia, medication optimization, and structured delirium prevention programs have demonstrated benefit in reducing postoperative delirium among high-risk surgical patients [2,3].

Long-Term Outcomes

Although delirium has traditionally been viewed as an acute and reversible complication of hospitalization, increasing evidence demon-

strates that its consequences often extend well beyond the initial illness. Delirium is independently associated with persistent cognitive decline, loss of functional independence, reduced quality of life, caregiver burden, institutionalization, and increased long-term mortality [2-4].

Several longitudinal studies suggest that delirium may accelerate cognitive decline in susceptible individuals and increase the risk of subsequent dementia. While the precise relationship remains incompletely understood, delirium may both reflect underlying neurodegenerative vulnerability and contribute directly to neuronal injury through neuroinflammatory and metabolic mechanisms. Regardless of causality, these findings emphasize the importance of prevention, early recognition, and prompt treatment [4,15].

Functional recovery following delirium is frequently incomplete. Many patients experience prolonged impairments in mobility, activities of daily living, and executive functioning that persist for months after hospital discharge. Consequently, discharge planning should include assessment of rehabilitation needs, medication review, communication with primary care providers, and education for patients and caregivers regarding the potential for ongoing cognitive recovery [4].

Recognition that delirium may have lasting consequences reinforces the need to view it not simply as a transient episode of confusion but as a serious marker of acute brain dysfunction with implications that may extend well beyond hospitalization [2,3].

Current Controversies and Limitations

Despite substantial advances in the understanding of delirium over the past two decades, important controversies remain regarding its

diagnosis, prevention, and management. Although delirium is widely recognized as a medical emergency associated with significant morbidity and mortality, considerable uncertainty persists regarding optimal screening strategies, pharmacological treatment, biomarker development, and implementation of emerging technologies into routine clinical practice.

One of the most debated areas concerns the use of antipsychotic medications. Historically, antipsychotics have been prescribed frequently to manage agitation and psychotic symptoms associated with delirium. However, contemporary evidence has demonstrated little benefit for the routine treatment of delirium itself. Randomized controlled trials have generally failed to show consistent reductions in delirium duration, severity, hospital length of stay, or mortality with antipsychotic therapy. Consequently, current international guidelines recommend that these medications should not be used routinely and should instead be reserved for carefully selected patients experiencing severe distress or behaviours that pose an immediate risk to themselves or others after non-pharmacological interventions have proven insufficient.

The diagnosis of delirium also remains challenging. Although validated screening instruments such as the Confusion Assessment Method and the 4AT have improved recognition, delirium continues to be underdiagnosed, particularly in patients with hypoactive presentations. Unlike hyperactive delirium, which often attracts attention because of agitation or disruptive behaviour, hypoactive delirium may present with lethargy, reduced interaction, and withdrawal, leading clinicians to incorrectly attribute symptoms to depression, fatigue, or progression of dementia. The fluctuating nature of delirium further complicates diagnosis, as patients may appear cognitively intact during one assessment and significantly impaired only hours later. These observations reinforce the importance of repeated clinical assessments and collateral history from caregivers [4].



Another ongoing challenge involves delirium superimposed on dementia. Distinguishing acute delirium from chronic cognitive impairment may be difficult, particularly in patients with advanced neurodegenerative disease or limited baseline cognitive information. Although attention deficits and fluctuating consciousness remain distinguishing features, accurate diagnosis frequently depends on information provided by family members or caregivers who can identify acute changes from baseline function [4].

Research into biological markers of delirium has expanded considerably in recent years. Investigators have explored inflammatory cytokines, neurofilament light chain, glial fibrillary acidic protein, tau proteins, C-reactive protein, and markers of endothelial dysfunction as potential diagnostic and prognostic biomarkers. While many studies have demonstrated promising associations between these biomarkers and delirium risk or severity, findings remain inconsistent because of differences in study populations, laboratory techniques, timing of specimen collection, and diagnostic criteria. At present, no biomarker has demonstrated sufficient accuracy, reproducibility, or clinical utility to replace careful bedside assessment, and delirium remains fundamentally a clinical diagnosis [2,3].

Artificial intelligence and machine learning have emerged as promising tools for identifying patients at increased risk of delirium before symptoms become clinically apparent. Algorithms developed using electronic health record data have demonstrated encouraging predictive performance by integrating demographic characteristics, laboratory values, medication exposure, physiological parameters, and clinical documentation. Nevertheless, most prediction models have been developed within single healthcare systems and require prospective external validation before routine implementation. Concerns regarding algorithm transparency, data quality, clinical interpretability, and

integration into existing healthcare workflows remain important barriers to widespread adoption [2,3].

Finally, considerable heterogeneity continues to limit delirium research. Studies frequently employ different diagnostic criteria, screening instruments, outcome measures, and patient populations, making direct comparison difficult. Future investigations would benefit from standardized definitions, consistent reporting standards, and multicentre collaboration to improve the quality and generalizability of evidence. Addressing these limitations will be essential for translating emerging scientific discoveries into meaningful improvements in patient care.

Future Directions

Delirium research is entering a period of rapid innovation driven by advances in neuroscience, digital health, and computational medicine. Although contemporary management continues to emphasize early recognition and multicomponent prevention strategies, emerging technologies have the potential to transform delirium care by facilitating earlier diagnosis, individualized risk prediction, and more targeted preventive interventions [2,3].

Artificial intelligence and machine learning represent some of the most promising developments in the field. By analysing large volumes of electronic health record data, these models can integrate demographic information, physiological observations, laboratory investigations, medication exposure, comorbidities, and clinical documentation to identify patients at increased risk of developing delirium. Dynamic prediction models may eventually enable clinicians to initiate preventive interventions before delirium develops, shifting care from reactive treatment toward proactive prevention. Future research should focus not only on improving predictive accuracy but also on evaluating whether these technologies improve meaningful clinical out-

comes when incorporated into routine practice [2,18].

Biomarker research continues to expand rapidly. Blood-based markers including neurofilament light chain, glial fibrillary acidic protein, inflammatory cytokines, and markers of neuronal injury are being investigated as potential tools for identifying patients at increased risk, monitoring disease progression, and predicting long-term cognitive outcomes. Although current evidence remains preliminary, advances in biomarker science may ultimately complement clinical assessment and facilitate earlier diagnosis. Standardization of laboratory methods and validation across diverse patient populations will be essential before these biomarkers can be incorporated into routine clinical care [4].

Electroencephalography and advanced neuroimaging techniques are also providing new insights into the neurobiology of delirium. Quantitative electroencephalographic analysis has demonstrated characteristic alterations in brain activity that may improve diagnostic accuracy, particularly in patients with hypoactive delirium or complex neurological presentations. Similarly, functional neuroimaging studies continue to enhance understanding of disrupted brain network connectivity during acute delirium, providing opportunities for future therapeutic investigation [15].

Digital health technologies, including wearable physiological monitors and continuous bedside monitoring systems, may further improve delirium detection by identifying subtle changes in sleep patterns, mobility, autonomic function, and cognitive performance before overt clinical deterioration becomes apparent. These innovations could prove particularly valuable in intensive care units and among high-risk hospitalized older adults, where continuous monitoring is already common.

Precision medicine represents another emerging direction in delirium research. Rather than applying identical prevention strategies to

all patients, future approaches may integrate clinical characteristics, genetic susceptibility, biomarker profiles, physiological monitoring, and artificial intelligence prediction models to develop individualized prevention and management strategies. Such approaches have the potential to improve resource allocation while reducing unnecessary interventions among lower-risk patients.

Implementation science will also play an increasingly important role. Many evidence-based delirium prevention strategies remain inconsistently applied despite strong supporting evidence. Future research should therefore examine how best to integrate validated prevention bundles into everyday clinical practice, improve clinician education, enhance multidisciplinary collaboration, and overcome organizational barriers to implementation [2-4].

Although these innovations are highly promising, bedside clinical assessment remains the foundation of delirium diagnosis and management. Emerging technologies should be viewed as tools that enhance, rather than replace, comprehensive clinical evaluation. Continued collaboration between clinicians, researchers, engineers, and healthcare systems will be essential to ensure that scientific advances translate into safer, more effective, and more patient-centred delirium care [2,3].

Clinical Pearls

- Delirium is an acute medical emergency until proven otherwise.
- Inattention is the hallmark clinical feature and is often more diagnostically useful than memory impairment [3,4].
- Symptoms fluctuate throughout the day, making repeated assessment essential [3,4].
- Hypoactive delirium is common and frequently overlooked.



- Delirium should never be considered a normal consequence of ageing.
- Prevention through multicomponent, non-pharmacological interventions remains more effective than pharmacological treatment [3,4].
- Medication review is essential, particularly in older adults receiving multiple medications [2,4,15].
- Antipsychotic medications should not be used routinely and should be reserved for carefully selected patients with severe distress or behaviours that threaten safety [3,4].
- Family members frequently recognize subtle cognitive changes before healthcare providers [2,18].

Delirium is associated with long-term cognitive decline, functional impairment, and increased mortality, emphasizing the importance of early recognition and prevention [2-4].

Conclusion

Delirium remains one of the most common, serious, and potentially preventable complications of acute hospitalization. Although considerable progress has been made in understanding its complex pathophysiology, improving diagnostic tools, and developing effective prevention strategies, delirium continues to be underrecognized and undertreated across many healthcare settings. Early identification of vulnerable patients, prompt investigation of reversible causes, and implementation of evidence-based, non-pharmacological interventions remain the foundation of optimal management [2-4].

Recent advances in artificial intelligence, biomarker discovery, digital health technologies, and precision medicine have created exciting opportunities to improve delirium prediction, diagnosis, and individualized prevention. However, these innovations remain complementary

to, rather than replacements for, careful bedside assessment and multidisciplinary clinical care. Continued research is required to validate emerging technologies, standardize diagnostic approaches, and translate scientific discoveries into meaningful improvements in patient outcomes [6-14].

As populations continue to age and medical complexity increases, delirium will remain a major challenge for clinicians across all inpatient settings. Strengthening awareness, promoting early recognition, and embedding evidence-based prevention strategies into routine clinical practice have the potential to reduce the substantial personal, societal, and economic burden of delirium. Ultimately, improving delirium care is not simply about managing an episode of acute confusion. It is about protecting brain health, preserving independence, and improving the quality of care delivered to some of the most vulnerable patients in our healthcare system.

Conflict of Interest

The author declares no conflicts of interest related to this manuscript.

Funding

No funding was received for the preparation of this manuscript.

Author Contributions

DW conceived the review, conducted the literature review, wrote the manuscript, critically revised the content, and approved the final version for submission.

Acknowledgements

None.

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-5-TR. 5th ed.,



- text rev. Washington (DC): American Psychiatric Association; 2022.
2. Inouye SK, Westendorp RGJ, Saczynski JS. Delirium in elderly people. *Lancet*. 2014;383(9920):911-22. doi:10.1016/S0140-6736(13)60688-1.
 3. Marcantonio ER. Delirium in hospitalized older adults. *N Engl J Med*. 2017;377(15):1456-66. doi:10.1056/NEJMcp1605501.
 4. Devlin JW, Skrobik Y, Gélinas C, Needham DM, Slooter AJC, Pandharipande PP, et al. Clinical practice guidelines for the prevention and management of pain, agitation, sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. *Crit Care Med*. 2018;46(9):e825-e873. doi:10.1097/CCM.0000000000003299.
 5. Liu SB, Wu HY, Duan ML, et al. Delirium in the ICU: how much do we know? A narrative review. *Ann Med*. 2024;56(1):2405072.
 6. Smith CJ, Hodge D, Harrison FE, Williams Roberson S. The pathophysiology and biomarkers of delirium. *Semin Neurol*. 2024;44(6):720-31.
 7. O'Keeffe F, Cervoni I, Ganau M, Prisco L. Serum biomarkers of delirium in critical illness: a systematic review of mechanistic and diagnostic evidence. *Intensive Care Med Exp*. 2025;13(1):90. doi:10.1186/s40635-025-00795-z.
 8. Sankel JKR, Cranø NB, Johansson PI, Andersen LPK. Blood-based biomarkers and delirium in critically ill adults in the ICU: a systematic review. *Intensive Care Med Exp*. 2026;14(1):48. doi:10.1186/s40635-026-00894-5.
 9. Shankar R, Kannan J, Tan YH, Xu Q. Natural language processing techniques to detect delirium in hospitalized patients from clinical notes: a systematic review. *NPJ Digit Med*. 2025;8:701. doi:10.1038/s41746-025-02051-w.
 10. Ara L, Ben Miled Z, Boustani M, et al. Machine learning and artificial intelligence for delirium prediction with electronic health records: a scoping review. *BMC Med Inform Decis Mak*. 2026;26:84.
 11. Young M, Kotfis K, Bellomo R. Using artificial intelligence to detect and treat delirium. *Intensive Care Med*. 2025;51:389-92. doi:10.1007/s00134-024-07774-0.
 12. Strating T, Shafiee Hanjani L, Tornvall I, Hubbard R, Scott IA. Navigating the machine learning pipeline: a scoping review of inpatient delirium prediction models. *BMJ Health Care Inform*. 2023;30:e100767.
 13. Park C, Han C, Jang SK, et al. Development and validation of a machine learning model for early prediction of delirium in intensive care units using continuous physiological data: retrospective study. *J Med Internet Res*. 2025;27:e59520.
 14. Pandian V, Rahimibashar F, Arabfard M, Alhalaiqa F, Vahedian-Azimi A. The role of AI-driven communication in delirium prevention, detection, and care for critically ill ICU patients: a systematic review with inductive thematic synthesis. *Intensive Crit Care Nurs*. 2026;93:104323.
 15. American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults. Postoperative delirium in older adults: best practice statement. *J Am Geriatr Soc*. 2015;63(1):142-50.
 16. Inouye SK, Charpentier PA. Precipitating factors for delirium in hospitalized elderly persons. *JAMA*. 1996;275(11):852-7.
 17. Bellelli G, Morandi A, Davis DHJ, Mazzola P, Turco R, Gentile S, et al. Validation of the 4AT, a new instrument for rapid delirium screening. *Age Ageing*. 2014;43(4):496-502.
 18. Fick DM, Agostini JV, Inouye SK. Delirium superimposed on dementia. *J Am Geriatr Soc*. 2002;50(10):1723-32