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## Review

### Delirium: A key challenge for perioperative care

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#### ABSTRACT

Delirium is highly prevalent, occurring in 20% of acute hospital inpatients and up to 62% of surgical patients. It is a significant predictor of poor outcomes including mortality and institutionalisation, however it is often viewed as simply a marker of underlying illness and is frequently overlooked in older adults. Although delirium is commonly comorbid with dementia, it represents a more urgent diagnosis, requiring prompt intervention. Delirium presents most commonly with hypoactive features (e.g. withdrawal and reduced spontaneous movement and speech). The common stereotype of hyperactive delirium tremens (e.g. agitation, hallucinations), although more visible, is less common. All presentations share acute disimprovement of cognitive function. Delirium is a highly predictable and preventable occurrence, however a major barrier to improving delirium care and impacting upon outcomes is that it remains poorly detected, particularly in surgical populations and especially in patients with hypoactive presentations. Routine ward-based screening for delirium, particularly in high-risk populations, and improved staff awareness of the significance of the problem can improve detection rates. Preventative strategies, particularly multicomponent approaches, have been most efficacious in improving patient outcomes. Optimising perioperative risk factors can lead to reduced incidence. Appropriate treatment of delirium requires thorough investigation, management of the underlying illness, avoidance of complications and simplification of the care environment. Studies suggest a role for pharmacological prophylaxis, particularly in relation to anaesthetic and sedative agents used intra- and post-operatively. Furthermore, gathering evidence suggests that judicious use of antipsychotic medications may be helpful in delirium prevention and treatment.

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### 1. Delirium: a common and complex neuropsychiatric syndrome

Delirium is a complex neuropsychiatric syndrome characterised by acutely declined cognitive function secondary to physical precipitants. It is extremely common across all healthcare settings, occurring in up to 62%<sup>1</sup> of surgical patients, particularly those older or with pre-existing cognitive impairment. Delirium is often viewed as simply a marker of underlying pathology and is commonly overlooked, especially in the older ill. However, this acute syndrome is independently associated with serious adverse outcomes such as increased mortality, functional and cognitive decline.<sup>2</sup> Although multiple studies show that these poor outcomes

can be significantly attenuated with prompt intervention, delirium remains underdetected, particularly in surgical cohorts.<sup>3–5</sup>

### 2. Incidence

Delirium is ubiquitous with a point prevalence of approximately 20% across the acute hospital.<sup>6</sup> It occurs in 11–42% of medical inpatients<sup>7</sup> and in up to 80–90% of palliative care and intensive care patients.<sup>8,9</sup> Delirium is a major preventable post-operative complication in older surgical patients,<sup>10</sup> with a reported incidence of 2%–60%,<sup>11</sup> reflective of differences between study populations and diagnostic criteria. Hip fracture and cardiac surgery patients have reported rates of up to 62%<sup>1</sup> and 52%<sup>12</sup> respectively. Lower rates have been observed in those undergoing less invasive procedures.<sup>13</sup>

Delirium typically develops early post-operatively,<sup>14</sup> often during the immediate recovery period. It is considered distinct from emergence agitation, excessive motor activity occurring

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during emergence from anaesthesia. However, this phenomenon can herald delirium onset, particularly in high risk groups.<sup>15</sup> Hence symptoms lasting over an hour, or which fluctuate, should be regarded as probable delirium.

**3. Significance**

Over the past decade, it has been well established that delirium predicts adverse outcomes independent of underlying pathology (see Fig. 1).<sup>16–20</sup> Poor outcomes are closely linked to the challenges posed by delirium symptoms,<sup>21</sup> particularly falls and self harm in hyperactive presentations and hypostasis, infections and pressure ulcers in hypoactive patients. Many patients with successful immediate surgical outcomes subsequently succumb to delirium-related complications and pose considerable management challenges in busy clinical settings.<sup>22,23</sup>

**4. Pathophysiology**

Delirium is the clinical presentation of acute generalised disturbance of brain function. The favoured neurochemical hypothesis suggests disruptions in several neurotransmitter pathways in the brain, culminating in a final common pathway of reduced cholinergic and GABAergic activity and increased dopamine, glutamate and noradrenaline release.<sup>17</sup>

Recent studies of biomarkers and genetic polymorphisms have indicated links with increased delirium incidence, severity and course<sup>24–31</sup> however studies of (anti)cholinergic parameters in delirium have been inconsistent. Other work indicates that melatonin metabolism is affected, particularly in hypoactive presentations, suggesting key alterations in circadian function.<sup>32</sup> Delirium is also associated with white matter changes on neuroimaging<sup>33</sup> and generalised slowing on EEG,<sup>34</sup> however both tests are poorly specific and often impractical for use in delirious patients.

Other studies have investigated postoperative cognitive dysfunction (POCD) and long-term cognitive impairment (LTCI),<sup>35–37</sup> less well-defined concepts characterised by cognitive decline

occurring after physical illness or interventions (such as surgery). Although, POCD/LTCI is viewed as distinct to delirium, recent work suggests a link between the two, and that patients who develop delirium post-operatively are at higher risk of subsequent LTCI.<sup>38</sup>

**5. Who is at risk?**

Delirium is a highly predictable occurrence with a range of patient, illness, and treatment factors that have considerable predictive accuracy. The most consistent predictors across patient groups are age extremes, prior cognitive impairment, severe co-morbid illness, and psychoactive medications (anticholinergic agents, opioids and benzodiazepines).<sup>39</sup> Delirium involves a dynamic interplay between pre-existing vulnerabilities and precipitating insults, with baseline predisposition especially important.<sup>40</sup> Although some risk factors (e.g. age) are unmodifiable, many can be minimised, such as uncontrolled pain, anaemia and infection (see Fig. 2).

Certain surgical subgroups, for example, hip fracture patients are at higher risk, due partly to the physiological stress and pain of the injury, as well the often emergency nature of surgery, and subsequent reduced mobility.<sup>41</sup> However, the high rates of delirium in this group may be an epiphenomenon reflecting the inherent frailty of this population.<sup>42</sup>

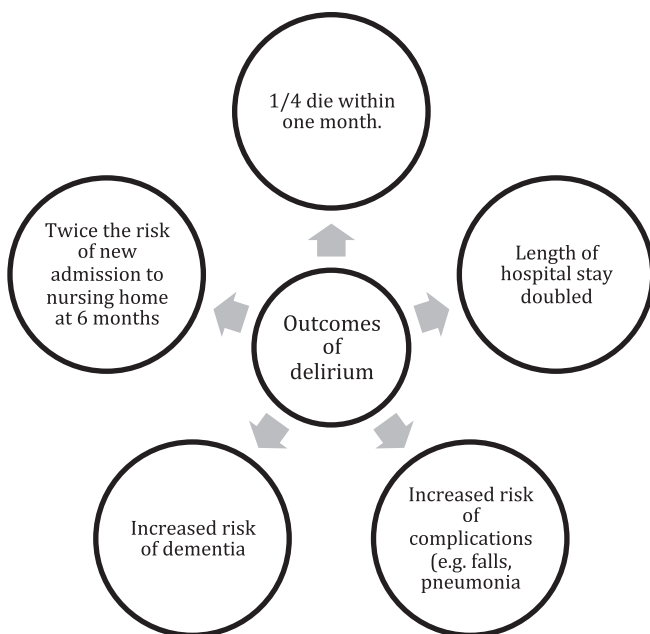
The high delirium prevalence in surgical populations has stimulated efforts to identify prediction rules for risk stratification<sup>43–45</sup> (see Table 1). Importantly, delirium risk increases exponentially with each additional risk factor. These tools facilitate surgical 'prehabilitation' programmes aimed at pre-operative optimisation of delirium risk status (see below).

**6. Assessment**

A major challenge in delirium care is to improve detection in everyday practice. Sixty-five percent of delirium cases are missed in the emergency department<sup>46</sup> and up to 72% of medical cases of delirium are missed.<sup>47</sup> Surgical patients have consistently been shown to be the cohort with lowest detection rates.<sup>3–5,48</sup>

The factors that complicate delirium recognition are manifold. Circadian disintegrity leads to nocturnal worsening of symptoms, often with relative lucidity come the morning ward round that is easily missed, particularly in the absence of routine neurocognitive assessment. Additionally, 'confusion' in ill older adults is often normalised, leading to under-appreciation of delirium as a clinically important syndrome independent of its aetiology. Some features, such as disorganised thinking, affective lability and fluctuating symptom pattern are more readily recognised by family members and nurses, who spend longer periods with the patient. Furthermore, the prevailing stereotype is of hyperactive delirium while less obvious hypoactive presentations are more common. Reduced activity is readily overlooked or misattributed to fatigue, senility and sedation with the 'good' and 'quiet' patient often presumed to have intact cognition. The prognosis for hypoactive cases is generally worse than for hyperactive patients.<sup>49</sup>

Formal delirium diagnosis is based upon careful assessment by an experienced clinician. Hence, a generalised approach to detection is best achieved in two stages; firstly, using a simple, brief and sensitive screening tool to assess for key indicators of possible delirium (inattention, disorganised thinking, behavioural changes); and secondly, more detailed assessment in those who screen positive, as per the recent NICE guidelines<sup>50</sup> (see Table 2). Ideally, given its prevalence and seriousness, all hospitalised patients should undergo daily routine delirium screening while all high-risk patients should be targeted for closer monitoring. The choice of screening instrument is guided by (a) time available for screening, (b) population being assessed, and (c) skillset of assessor, including



**Fig. 1.** Outcomes of delirium: Fast facts (independent of comorbidities and other confounders).

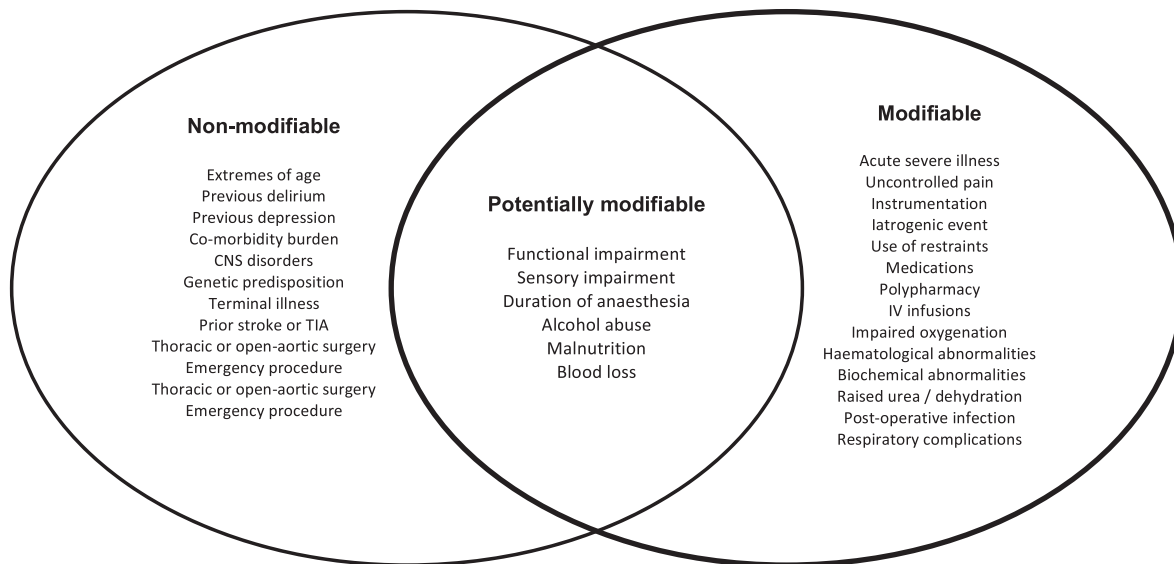


Fig. 2. Risk factors for delirium, modifiable and unmodifiable.

the availability of expert delirium assessment by consultation. The frequency and dangers of missed cases mandate that screening methods emphasise sensitivity over specificity. Table 3 outlines the most commonly used tests.<sup>51–61</sup>

The Confusion Assessment Method (CAM)<sup>58</sup> remains the most widely used screening test<sup>62</sup> and has been validated in several languages and settings, e.g. the CAM-ICU.<sup>63</sup> Its accuracy relates closely to the training level of raters such that sensitivities are as low as 50% in the minimally trained.<sup>64</sup> Collateral informants who are familiar with patients' baseline abilities can provide vital information regarding the context of symptoms. The 'SQiD' or 'Single Question in Delirium' is a useful screening question for carers/family, shown in one study to have greater sensitivity than the CAM,<sup>61</sup> emphasising the contribution of collateral sources of information in detection (see Table 3). It is crucial to interview nursing staff, as they have more consistent contact with patients and relatives over the 24-h cycle. Suitable prompts for features of

delirium are illustrated in Fig. 4. Nurses are well-placed to screen for delirium, particularly using tools based upon observation of patient behaviours, such as the NEECHAM scale<sup>60</sup> and the NuDESC<sup>59</sup> (see Table 3).

In addition to these delirium-specific screening tools, simple bedside tests of cognition can assist with delirium screening, particularly tests of inattention – the cardinal cognitive feature of delirium. Examples are outlined in Table 3. Although the Mini-Mental State Examination (MMSE)<sup>57</sup> is a commonly used tool for assessing global cognition, it lacks specificity for delirium detection,<sup>52</sup> and is not recommended.

More detailed tools are required for full diagnostic assessment, such as the Delirium Rating Scale-Revised-98 (DRS-R98)<sup>65</sup> and the Memorial Delirium Assessment Scale (MDAS).<sup>66</sup> These scales are designed for use by delirium specialists rather than for routine screening.

A principal message of the 2010 NICE guidelines is to encourage acute hospital staff to 'THINK DELIRIUM'. Approaches to delirium monitoring may vary depending on the clinical setting and patient

Table 1

Comparison of delirium prediction rules in surgical patients (MMSE: Mini Mental State Examination, GDS: Geriatric Depression Scale, TIA: Transient Ischaemic Attack).

Cardiac surgery <sup>43</sup>	Non-cardiac surgery <sup>44</sup>	Hip surgery <sup>45</sup>
<b>2 points:</b>	<b>1 point:</b>	<b>1 point:</b>
<ul style="list-style-type: none"> <li>MMSE ≤23</li> </ul>	<ul style="list-style-type: none"> <li>Age ≥70 years</li> <li>Alcohol abuse (self-reported)</li> </ul>	<ul style="list-style-type: none"> <li>MMSE &lt;24</li> <li>APACHE II score &gt;16</li> </ul>
<b>1 point each:</b>	<ul style="list-style-type: none"> <li>Poor cognitive status</li> <li>Poor functional status</li> <li>Abnormal pre-operative biochemistry</li> <li>Non-cardiac thoracic surgery</li> <li>Aortic aneurysm surgery</li> </ul>	<ul style="list-style-type: none"> <li>Poor visual acuity (&gt;20/70)</li> <li>BUN/creatinine ratio ≥18</li> </ul>
<ul style="list-style-type: none"> <li>MMSE 24–27</li> <li>GDS &gt;4</li> <li>Prior stroke/TIA</li> <li>Abnormal albumin</li> </ul>		
<b>Incidence of delirium:</b>	<b>Incidence of delirium:</b>	<b>Relative risk of delirium:</b>
18–19% if total = 0	2% if total = 0	1.0 if low risk
43–47% if total = 1	8% if total = 1	(total = 0, reference)
60–63% if total = 2	13% if total = 2	3.0 if intermediate risk
86–87% if total = 3	50% if total ≥3	(total = 1–2)
		9.8 if high risk
		(total = 3–4)

Table 2

NICE recommendations for delirium screening.<sup>50</sup>

Risk stratification (assessed on admission)	If any of these risk factors is present, the person is at risk of delirium. <ul style="list-style-type: none"> <li>Age 65 years or older.</li> <li>Cognitive impairment (past or present) and/or dementia.</li> <li>Current hip fracture.</li> <li>Severe illness (a clinical condition that is deteriorating or is at risk of deterioration)</li> </ul>
Indicators of delirium (assessed on admission and daily in those at risk)	Changes or fluctuations in: <ul style="list-style-type: none"> <li><b>Cognitive function:</b> for example, worsened concentration,<sup>a</sup> slow responses,<sup>a</sup> confusion.</li> <li><b>Perception:</b> for example, visual or auditory hallucinations.</li> <li><b>Physical function:</b> for example, reduced mobility,<sup>a</sup> reduced movement,<sup>a</sup> restlessness, agitation, changes in appetite,<sup>a</sup> sleep disturbance.</li> <li><b>Social behaviour:</b> for example, lack of cooperation with reasonable requests, withdrawal,<sup>a</sup> or alterations in communication, mood and/or attitude.</li> </ul>

<sup>a</sup> Be particularly vigilant for behaviour indicating hypoactive delirium.

**Table 3**  
Summary of commonly used delirium screening approaches.<sup>51–61</sup>

Cognitive tests	Assesses for	Time to complete	Training required	Description
Digit span forwards (DSF)/backwards (DSB)	Attention	1–2 min	Minimal	Patient must repeat a sequence of digits read out by assessor (same order for DSF, reverse order for DSB) Abnormal: DSF <5 or DSB <3 on 2 trials.
Spatial span forwards (SSF)/backwards (SSB)	Attention	1–2 min	Minimal	A visual version of the digit span, using a card with 8 coloured squares. Sequences are tapped out for the patient to repeat. Useful particularly in patients with communication difficulties. SSF is more sensitive to delirium than SSB. Abnormal: SSF <5 or SSB <3 on 2 trials.
Months of the year backwards	Attention	1 min	No	Recite the months of the year in reverse order beginning with December. Failure to reach July without error is abnormal
20 to 1	Attention	<1 min	No	Count backwards from 20 to 1. Any error is abnormal
Clock drawing test	Constructional praxis Visuospatial ability Executive function Verbal and semantic memory	1–2 min	Minimal	Various different scoring methods. Useful to screen generally for cognitive impairment but lacks specificity for delirium.
MMSE (Mini mental state examination)	Orientation Registration & short-term recall Attention and calculation Language Praxis	5 min	Minimal	Widely used (overused in delirium, high sensitivity but very poor specificity). Original form is restricted by copyright but standardised form is readily available (with guidelines for scoring). Maximum score of 30, with scores of 25 or less indicating a degree of cognitive impairment.
Delirium-specific screening tests	Psychometric properties	Time to complete	Training required	Description
Confusion assessment method (CAM)	Sensitivity 13–98% Specificity 77–100%	5–15 min	Yes	Involves interview with the patient and collateral history from staff/relative Formal cognitive testing is advised to improve sensitivity but lengthens duration of the test. Examines for the presence/absence of: 1a. Acute onset 1b. Fluctuations 2. Inattention (mandatory feature) 3. Disorganised thinking 4. Altered level of consciousness  To be graded as CAM positive, a patient must have (1A and/or 1B) and 2 and (3 and/or 4)
Nursing delirium screening scale (NuDESC)	Sensitivity 96% Specificity 69%	1 min	Minimal	Designed to assist nursing detection of delirium Measures: Orientation Behaviour Communication Perceptual abnormalities Psychomotor retardation
NEECHAM confusion scale	Sensitivity 30–95% Specificity 78–92%	10 min	Minimal	Developed as a nurse administered bedside assessment Scored 0–30, >26 is normal Incorporates physiological markers
Single question in delirium (SQiD)	Sensitivity 80% Specificity 71% (in one study)	<1 min	No	Ask one question of the patient's friend or relative: 'Do you think X has been more confused lately?' A positive response should trigger further assessment

population. On a surgical ward with a varied casemix, an appropriate screening routine may include a baseline assessment of global cognition (e.g. MMSE) in all older patients, including reports from family members, followed by daily attention tests supplemented by collateral information from nursing staff. Worsening cognitive performance and/or neuropsychiatric symptoms suggest delirium and should prompt more detailed assessment by a geriatrician or psychiatrist (see Fig. 3).

**7. Prevention**

Delirium is a highly predictable and preventable condition. It is estimated that one-third of cases can be avoided by prevention strategies.<sup>67</sup> Delirium prevention studies have identified a variety of primary preventions for medical and surgical populations, ranging from multicomponent strategies<sup>67,68</sup> concentrating on modifiable risk factor reduction, to more specific pharmacological prophylaxis strategies.

Not surprisingly, given the complex nature of delirium causation, multifaceted interventions, such as the Hospital Elder Life Program (HELP),<sup>67</sup> appear most efficacious. These programs include many shared elements such as regular re-orientation, cognitive and physical activation, feeding and fluid assistance, addressing sensory deficits, minimising pain, and using non-pharmacological sleep aids<sup>39,69</sup> and can significantly reduce the incidence and duration of delirium when implemented systematically. Early geriatric specialist medical or nursing intervention leads to reduced incidence and severity in hip fracture patients,<sup>70,71</sup> as does 'prehabilitation', where delirium risk pre-operatively is optimised, targeting hydration, oxygenation, analgesia, polypharmacy and care environment routines.<sup>72</sup> Substitution for less invasive surgical techniques, for example endovascular versus open aortic aneurysm repair, has been shown to halve delirium incidence and reduce hospital stay.<sup>73</sup>

Recent studies investigating antipsychotic prophylaxis<sup>74–78</sup> indicate that relatively small doses in the immediate perioperative period can reduce delirium incidence and severity. In contrast,

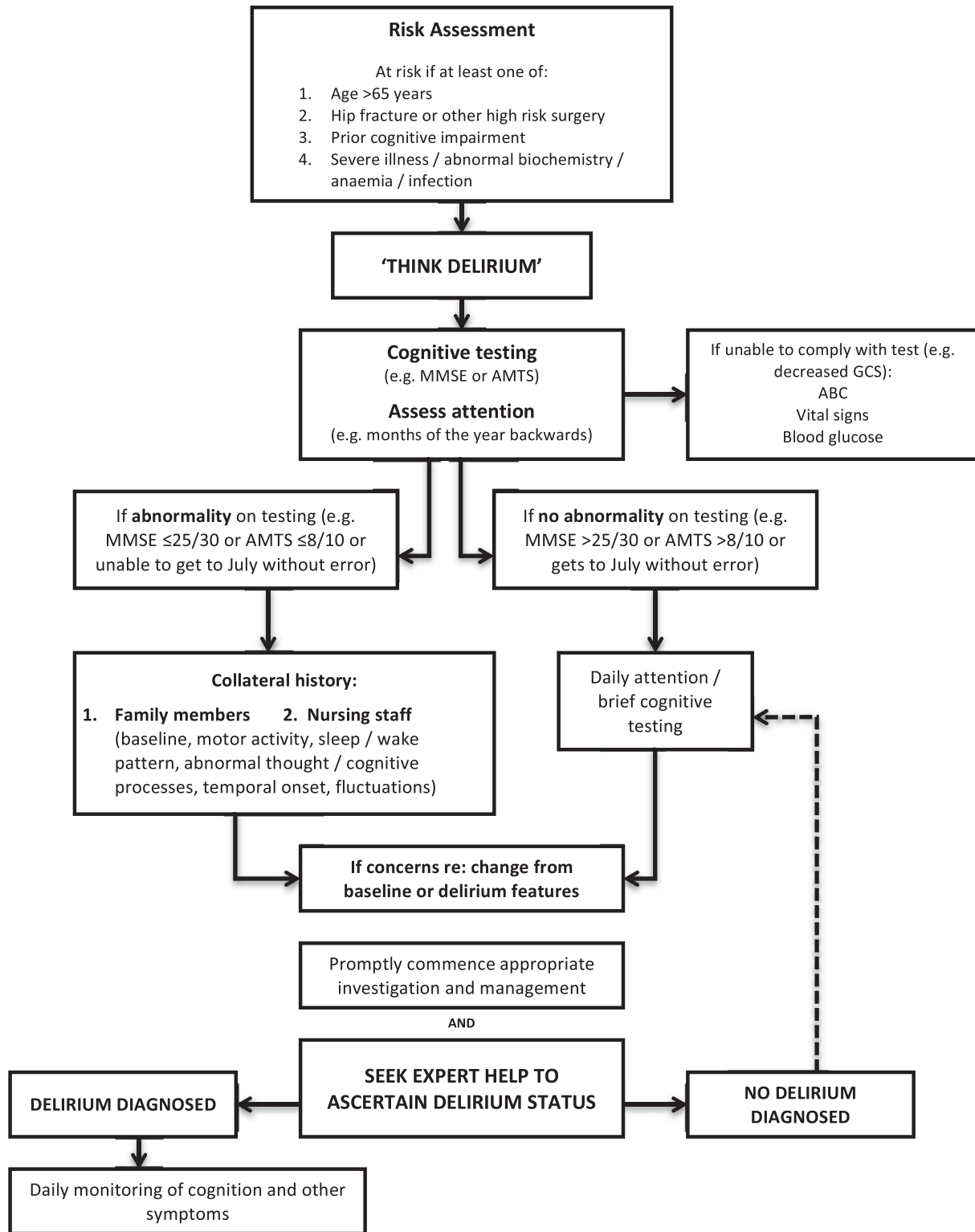


Fig. 3. Suggested approach to delirium detection on a surgical ward. AMTS: Abbreviated Mental Test Score.

studies of procholinergic agents have not demonstrated positive effects.<sup>39</sup> Other interventions are supported by preliminary evidence; ketamine use at induction<sup>79</sup> and dexmedetomidine, the alpha-2 agonist used for post-operative sedation<sup>80,81</sup> reduced delirium in cardiac surgery patients, whereas lorazepam in ICU patients has been linked to increased delirium incidence.<sup>82</sup> Nocturnal

melatonin administration decreased delirium incidence in older medical inpatients<sup>83</sup> however further investigation is required.

Attentive medical and nursing care addressing common issues such as insomnia and pain can impact significantly on delirium incidence. Although opioids can cause delirium, careful and efficient titration of analgesia has been shown to reduce delirium

1. How many days approximately have you been caring for XX?
2. Does he/ she seem delirious or acutely confused at times?
3. Has there been a sudden change in his / her mental state since admission? If so, when did you notice this change?
4. Do you think he/she is able to focus well when you're talking to him/her or does he/she tend to ramble off the point?
5. Does he/ she seem better at any period in the day compared to other times?
6. Has XX's level of consciousness been altered at all- for example, has he/ she been drowsy or not interacting, or perhaps hyperalert at times?

Fig. 4. Standard questions for nursing staff regarding possible delirium.

incidence nine-fold.<sup>84</sup> In ICU settings, a protocolised approach targeting multiple factors such as pain, sedation and medication use reduces duration of mechanical ventilation, improves pain management and attenuates delirium symptoms,<sup>85</sup> further supporting multicomponent preventative strategies.

8. Treatment of delirium

8.1. General principles

Optimal delirium management requires collaboration between primary physicians, nursing staff and delirium specialists. The underlying causes and the symptoms require simultaneous assessment and treatment. The principles of management include ensuring patient and staff safety, simplifying the care environment, and minimising sensory impediments. Communication with delirious patients should include simple language expressed in a clearly audible, slow-paced voice. Orienting techniques (e.g. calendars) and familiarising the environment (e.g. family photographs) are helpful, and engaging family members in care can be reassuring. Multidisciplinary team involvement can prevent complications such as falls, self-injury and hypostasis.

8.2. Investigating for underlying causes

A fundamental aspect of management is to identify and treat underlying causes. Delirium is typically multifactorial in aetiology and hence, comprehensive assessment is required, beginning with thorough history and examination, including collateral history from relatives and nursing staff and medication review. A suggested approach to investigating delirium is outlined in Table 4. Second-line investigations are guided by clinical assessment and preliminary test results. No identifiable cause is identified in 10% of cases.<sup>86</sup> In these cases, addressing risk factors and symptom control become even more crucial aspects of care.

8.3. Non-pharmacological measures

Evidence for non-pharmacological interventions in treating established delirium is less convincing than that for primary prevention. However, environments that are not optimally stimulating and/or

unsafe can aggravate illness course, and hence the multifaceted principles of prevention continue to apply in the actively delirious patient.

8.4. Pharmacological measures

Antipsychotics have long been the gold standard pharmacological treatment based upon their theoretical value, empirical knowledge of their use, and results from over twenty open-label prospective studies.<sup>87,88</sup> The tendency to withhold antipsychotics except in severe agitation is understandable, due to the risk of side effects (prolongation of the QT interval, sedation, hypotension and

Table 4  
Suggested approach to investigating delirium.

1.	Careful history and physical examination	
2.	Collateral history	<ul style="list-style-type: none"> <li>• Baseline cognition</li> <li>• Presence of sensory impairments</li> <li>• Exposure to risk factors</li> <li>• Review of medications, clinical notes, intraoperative data, recent test results</li> </ul>
3.	First-line investigations	<ul style="list-style-type: none"> <li>• Full blood count</li> <li>• Septic screen (Mid-stream urine, Sputum culture &amp; sensitivity, Wound swab, Blood cultures)</li> <li>• Inflammatory markers (C-Reactive Protein, Erythrocyte Sedimentation Ratio)</li> <li>• Chest X-ray</li> <li>• Renal indices and electrolytes</li> <li>• Liver function tests</li> <li>• Serum glucose</li> <li>• Serum albumin</li> <li>• Electrocardiogram</li> </ul>
4.	Second-line investigations	<ul style="list-style-type: none"> <li>• Blood gases</li> <li>• Cardiac enzymes</li> <li>• CT brain</li> <li>• Electroencephalogram</li> <li>• Lumbar puncture</li> <li>• Vitamin B12 and folate</li> <li>• Toxicology screen</li> <li>• MRI Brain</li> <li>• HIV serology</li> <li>• Porphyria screen</li> <li>• Syphilis screen</li> </ul>

extrapyramidal features) as well as the increased risk of stroke in patients with dementia. However, gathering evidence suggests that proactive antipsychotic use can reduce duration and severity of delirium in older medical and ICU patients.<sup>89,90</sup> Recent NICE guidelines recommend cautious use of olanzapine or haloperidol for the rapid control of severe agitation.<sup>50</sup> As with all dosing in the elderly, best practice is to 'start low and go slow', e.g. a starting dose of Haloperidol 0.5 mg tid orally, titrated to response, reviewed regularly and discontinued soon after symptoms improve (typically 3–5 days).

Benzodiazepines have a limited role in delirium management – they are first line treatment in withdrawal states or seizures but are otherwise best avoided as they can perpetuate delirium, cloud ongoing cognitive assessment and are linked to falls and over-sedation. Procholinergic treatments do not appear to be effective in the management of acute delirium episodes.<sup>39</sup>

### 9. Conclusions

Delirium is a highly prevalent, under-recognised and underestimated condition that occurs across healthcare settings, including hospitalised surgical patients where the perioperative period presents particular risks. It is especially common in older patients, and thus a key healthcare target for our increasingly aged society where the mean age of patients undergoing surgery is increasing.<sup>22</sup> Delirium has a profound independent negative impact upon a variety of outcomes – with regard to healthcare utilisation, patient socio-adaptive function, ongoing cognition and mortality risk.

Barriers to improved delirium care include the absence of routine risk assessment and screening in everyday practice, as well as poor awareness as to how it should be diagnosed and managed. To date, multicomponent interventions employed with a hospital-wide, systematic approach have shown most efficacy in preventing incident delirium and improving outcomes. Gathering evidence supports other preventative strategies such as optimising physiological status pre-operatively and perioperative low-dose anti-psychotic prophylaxis.

Earlier detection is achievable with simple screening using, for example, a short test of attention or a nursing observation scale. Engaging with family members is key to characterising the context of symptoms and can help re-orientation efforts. Identification of delirium should prompt the use of care pathways that include thorough investigation and treatment of underlying causes, environmental modification, symptom control and prevention of complications. Antipsychotics used cautiously can reduce severity and duration of symptoms, and timely consultation with Geriatricians or Geriatric psychiatrists<sup>91,92</sup> can improve outcomes.

Delirium is a serious, pervasive problem, presenting a huge challenge to all acute hospital staff, and imposing significant burden on those affected. It can, however, be prevented, detected and treated. Therefore, all healthcare professionals, together with hospital management, have a responsibility to 'THINK DELIRIUM', recognise those at risk and initiate appropriate screening, preventative and management strategies.

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Not applicable.

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#### Author contribution

Niamh O'Regan, James Fitzgerald, Suzanne Timmons, Henry O'Connell, David Meagher: All substantially contributed to

background research, drafting of the initial manuscript, subsequent critical revision of the manuscript and final approval.

#### Conflict of interest

None declared.

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