Delirium

Annmarie Hosie, Ingrid Amgarth-Duff, and Meera Agar

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A. Hosie · I. Amgarth-Duff
Faculty of Health, University of Technology Sydney,
Ultimo, NSW, Australia
e-mail: annmarie.hosie@uts.edu.au; Ingrid.Amgarth-
Duff@uts.edu.au

M. Agar (✉)
Faculty of Health, University of Technology Sydney,
Ultimo, NSW, Australia
South Western Sydney Clinical School, University of New
South Wales, Sydney, NSW, Australia
Ingham Institute for Applied Medical Research, Liverpool,
NSW, Australia
Palliative Care Service, South Western Sydney Local
Health District, Sydney, NSW, Australia
e-mail: Meera.Agar@uts.edu.au

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1 Introduction

Delirium is a great source of suffering and perplexity for people receiving palliative care and the health professionals who care for them. The opportunities to appropriately respond to the needs of people with palliative diagnoses mirror other populations at risk of delirium; and there are similar challenges to delivering this care. Additional considerations relate to the burden, benefit, and goals of care in the context of living and dying with advanced illness.

Having optimal cognition, safety, and a sense of self and relationship with others at the end of life are highly valued by seriously ill people (Delgado-Guy et al. 2016; Spichiger 2008; Steinhauser et al. 2000). Equally, when a loved one has delirium, family carers want clinicians to give more information about what is happening and show respect and sensitivity for the person and their subjective experience (Namba et al. 2007; Brajtman 2003). Family feel supported when clinicians demonstrate respect and understanding of the person’s needs and preferences and address suffering in ways which support them to communicate with each other (Bolton et al. 2016; Finucane et al. 2017).

This chapter outlines how health professionals can work to optimize care to achieve these important goals for people with palliative diagnoses and their families. Best evidence for delirium prevention, recognition, assessment, management, and support for people with advanced illness is presented. Where evidence is lacking for this population, we present evidence, guidelines, and standards for optimal delirium care of older hospitalized patients. We advocate for nuanced approaches to delirium care that are based on the individual needs and wishes of the person and informed by the intent of palliative care to prevent, recognize, and impeccably assess distressing symptoms and to relieve suffering. Ethical dilemmas, complexities, and uncertainties that clinicians and teams may encounter when caring for delirious people and their families in the last months, weeks, and days of life are discussed. Lastly, we propose how delirium outcomes for people receiving palliative care may be improved through research and clinical practice development.

2 Phenomenology

Delirium is an acute neurocognitive disorder, medical emergency, and serious healthcare complication. Delirium arises from physiological disturbances related to a medical condition, substance intoxication or withdrawal, and/or a toxin and manifests as acute disturbances to attention, awareness, and cognition (American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) 2013). Disturbances present variously in each patient,
each delirium, and even during the course of one episode (Meagher et al. 2012a). Cognitive changes include memory deficit; disorientation to time, place, and/or person; language and visuospatial disabilities; and perceptual disturbances, such as illusions, hallucinations, or delusions. Perceptual disturbances are almost always frightening for the person experiencing them, and this fear may cause him or her to become withdrawn, suspicious, and/or aggressive toward others, including family and clinicians (Breitbart and Alici 2008). Labile mood and altered sleep-wake cycle frequently occur but are not required for a diagnosis (Meagher et al. 2011). The intensity of delirium symptoms may range from mild to severe; and episodes may be brief (i.e., last for hours to days) or sometimes continue for weeks, even months (American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) 2013).

2.1 Diagnostic Criteria

Delirium was first included within the American Psychiatric Association Diagnostic and Statistical Manual (APA-DSM) in 1980. There have since been five iterations of delirium diagnostic criteria, reflecting evolving understanding of core features. Current criteria are:

1. Disturbed attention (i.e., reduced ability to focus, sustain, or shift attention) and awareness (reduced orientation to the environment).
2. Disturbance developed over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of the day.
3. An additional disturbance in cognition, e.g., memory deficit, disorientation, language, visuospatial ability, or perception.
4. The disturbances in criteria A and C are not better explained by another pre-existing, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.
5. Evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication, or withdrawal (i.e., due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies (American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) 2013).

While classified as one disorder, delirium is further categorized as three subtypes according to the level of psychomotor activity:

(i) Hyperactive delirium: increased motor activity, agitation, and heightened states of arousal
(ii) Hypoactive delirium: decreased motor activity, delayed response, and drowsiness

Whereas in a study of patients receiving palliative care, a small proportion (6%) experienced no particular subtype, and around 40% experienced a varied subtype, across the course of a delirium episode (Meagher et al. 2011).

3 Pathophysiology

The understanding of the pathophysiology of delirium is evolving. Hypotheses include those that primarily are theoretical and others that are being empirically investigated. The main theoretical models are as follows:

Neuronal Ageing: This model proposes that, with aging, central nervous system (CNS) immune cells undergo excessive production of pro-inflammatory cytokines in response to peripheral stimulation, providing a possible pathway for CNS dysfunction and consequent delirium. According to this model, elderly patients are
more at risk of developing delirium, because of age-related cerebral changes in stress-regulating pathways (Maldonado 2008, 2013).

**Oxidative stress:** In which physiologic insults, such as tissue damage, trauma, hypoxia, severe illness, and infections, cause decreased oxidative metabolism, leading to cerebral dysfunction with associated cognitive decline and behavioral symptoms seen in people with delirium (Berr 2000).

**Neurotransmitter:** Relates to deficits in central cholinergic functioning. This hypothesis suggests that excess release of dopamine, glutamate, and acetylcholine (Ach), as well as altered levels of serotonergic and gamma-aminobutyric acid (GABA) activity, may underlie clinical presentations of delirium (Maldonado 2008, 2013). It has further been proposed that decreased tryptophan and increased melatonin may result in decreased serotonin in people with delirium (Van Der Mast et al. 1991; Karlidag et al. 2006).

**Circadian cycle:** Disruptions to the 24-h circadian cycle and usual sleep-wake cycle have long been linked to development of delirium. This hypothesis suggests that alterations in the metabolism of melatonin (a hormone involved in the regulation of the sleep-wake cycle) may also play a role in the development of delirium (Maldonado 2008, 2013).

**Neuroendocrine model:** Suggests that sustained high levels of glucocorticoid levels occurring with acute stress can impair neurons in the brain and in turn may trigger and/or sustain delirium (Maldonado 2013; Olsson 1999).

The models with developing empirical evidence are

**Neuroinflammatory:** Altered neurotransmitter levels are commonly implicated in delirium. Higher serum levels of interleukin (IL)-6 and IL-8 (Van Munster et al. 2008) and raised S100 calcium-binding protein B (S100B) (van Munster et al. 2010) have been reported in people with delirium. Low levels of anti-inflammatory markers, such as insulin-like growth factor 1, are also reported (Adamis et al. 2009). As these studies report no correlation with clinical outcomes, with the exception of cognitive changes during delirium, it is therefore difficult to ascertain whether the altered levels are etiological or simply an epiphenomena (Caplan et al. 2010).

**Glucose metabolism hypotheses:** Lower cerebrospinal fluid (CSF) neuron-specific enolase (NSE) and higher CSF lactate are reported in people with delirium, suggesting the following hypotheses: (1) disrupted glycolysis, with switching from aerobic to anaerobic glucose metabolism by neuronal cells; (2) suppression of the glycolytic pathway in neurons; or (3) disrupted lactate uptake by neuronal cells (Caplan et al. 2010). Recent research further revealed widespread reduction in glucose metabolism in older inpatients with delirium and levels returning to baseline following delirium resolution (Haggstrom et al. 2017).

Most of these hypotheses are complementary and intersecting (Maldonado 2013). Ideally, further research into the complex neurochemical cascades leading to delirium will inform future development and testing of novel therapeutic approaches.

### 4 Epidemiology

#### 4.1 Risk Factors

Epidemiological data indicates that people most at risk of developing delirium are those who are older, have advanced illness, and/or prior cognitive impairment (National Clinical Guideline Centre for Acute and Chronic Conditions 2010). Other predisposing factors are visual or hearing impairment, poor functional status, current hip fracture, and impaired nutrition. Yet any person – adult or child – can experience delirium when physiological insults are sufficiently great. Precipitants associated with illness, injury, and medical treatment are many and include (but are not limited to) polypharmacy, metabolic disturbance, presence of an indwelling catheter, dehydration, infection, and use of physical restraints. Additional precipitants related to advanced cancer are psychoactive medication (benzodiazepines, antipsychotics, and corticosteroids) and bone, liver, and brain metastases (Caraceni 2013) (Table 1). People receiving inpatient palliative care are
likely to have multiple causes, up to as many as six (Meagher et al. 2011); a multimodal model of delirium risk proposes that predisposing and precipitating factors for delirium are cumulative (Inouye and Charpentier 1996).

### 4.2 Prevalence and Incidence

Delirium occurs frequently in palliative care contexts, where people are highly vulnerable through often having several predisposing and precipitating factors. Prevalence in studies conducted in adult palliative care units and hospices ranged from 13.3 to 42.3% at admission, 26% to 62% during admission, 58.8% in the weeks prior to death, and for almost all participants (88%) within six hours of death (Hosie et al. 2013; Rainsford et al. 2014). In the studies that screened participants at least once daily, incidence was 33–45%, compared to studies where daily screening did not take place (3–7%) (Hosie et al. 2013).

Hypoactive delirium is the most prevalent subtype, occurring in 68–86% of delirious inpatients in one study (Hosie et al. 2013) and in 58% in another of inpatients with advanced cancer (Uchida et al. 2015). Meagher et al. (2012b) reported a lower proportion of patients in a palliative care unit with hypoactive delirium (35%), likely because the study applied a different subtype categorization of motor behavior than that of the current APA-DSM 5 (American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) 2013) and these other studies.

There are no data on delirium prevalence or incidence in children receiving palliative care. A retrospective chart review of pediatric oncology admissions reported a 1-year incidence of 10%, which was likely an underestimate, as no prospective structured screening or diagnosis methods were used to detect cases (Combs et al. 2014). There are also minimal data on delirium prevalence or incidence in people having palliative care in their home or a residential aged care facility. One study reported an estimate of confusion occurring in 50% of US hospice patients in the previous week, measured by nurses’ retrospective clinical report rather than a standardized tool (Nowels et al. 2002). Another reported delirium

### Table 1 Delirium risk factors

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<tr>
<th>Predisposing factors</th>
<th>Precipitating factors</th>
<th>Additional risk factors in patients with cancer</th>
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<tr>
<td>Potentially modifiable</td>
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<tr>
<td>• Sensory impairment (vision and hearing)</td>
<td>• Polypharmacy</td>
<td>• Benzodiazepines</td>
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<td>• Diminished function/performance status</td>
<td>• Anticholinergic load</td>
<td>• Opioids</td>
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<td>• Malnutrition</td>
<td>• Indwelling catheter</td>
<td>• Corticosteroids</td>
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<tr>
<td>Non-modifiable</td>
<td>• Use of physical restraints</td>
<td>• Other psychoactive medications</td>
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<td>• ≥65 years</td>
<td>• Drug intoxication</td>
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<tr>
<td>• Advanced illness</td>
<td>• Dehydration</td>
<td>Non-modifiable</td>
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<tr>
<td>• Prior cognitive impairment</td>
<td>• Infection</td>
<td>• Prior delirium</td>
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<td>• Multiple comorbidities</td>
<td>• Hypoxia</td>
<td>• Bone metastases</td>
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<td>• Current hip fracture</td>
<td>• Pain</td>
<td>• Liver metastases</td>
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<td></td>
<td>• Anemia</td>
<td>• Hematological malignancies</td>
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<td>• Emotional stress</td>
<td>• Metastases to brain or meninges</td>
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<td>• Prolonged hospital stay</td>
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<td>• Metabolic disturbance</td>
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<td>• Drug or alcohol withdrawal</td>
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prevalence of one in three people with pre-existing moderate to severe cognitive impairment in seven long-term care facilities in Canada (McCusker et al. 2011). Delirium is elsewhere reported to be present in almost one in five older people on arrival to the emergency department and almost half of people who reside in a nursing home (Inouye et al. 2014). The acute onset of delirium in an older person may be a key reason why emergency hospital care is sought.

4.3 Adverse Outcomes

Delirium adversely impacts on the individual, their family, clinicians, and the healthcare system.

During delirium, acute decline in attention and cognitive function reduces the person’s capacity to make decisions and communicate with others, which suddenly and often unexpectedly compounds the other physical and functional losses of advanced illness. A delirious person may be reluctant or unable to verbally communicate his or her disturbed thinking, and feelings of fear, confusion, and isolation are common (O’Malley et al. 2008). While not always unpleasant, altered perception most often has a nightmarish, hellish quality, including visions of snakes, spiders, and ants crawling on walls and bedclothes, and beliefs that doctors and nurses plan to murder, experiment on, and sexually assault themselves and/or other patients (Boodman 2015). Being delirious also makes it harder for the person to verbally communicate other distressing symptoms, such pain or breathlessness, which may lead to inadequate management of those symptoms and greater discomfort and distress (Gagliese et al. 2016). In studies of people with advanced cancer who had experienced delirium in hospital, the majority remembered the experience (Breitbart et al. 2002; Bruera et al. 2009). Memories generated feelings of distress, embarrassment, humiliation, and ongoing fear, including that the delirium will return (Breitbart et al. 2002; Bruera et al. 2009; Teodorczuk et al. 2011).

Adverse effects of delirium are increased risk of falls, pressure areas, longer-term cognitive and functional decline, longer hospital stay, and mortality (National Clinical Guideline Centre for Acute and Chronic Conditions 2010; Australian Commission on Safety and Quality in Health Care 2013). An episode of delirium more than doubles the cost of an older patient’s healthcare in the following year, due to spending a greater number of days in hospital or a nursing home (Leslie et al. 2008).

During delirium, family members experience high levels of distress (Breitbart et al. 2002). A review of 33 studies of family caregivers of patients with delirium in palliative care contexts found that they experienced anxiety, fear, helplessness, embarrassment, anger, disappointment, sadness, and guilt (Finucane et al. 2017). Delirium adversely impacted on relationships with the person, other family members, and health professionals. Caregivers wanted the person’s suffering to be relieved, but did not want the possibility of communication to be thwarted because of sedation (Finucane et al. 2017).

Health professionals, particularly nurses, find identifying and appropriately responding to delirium challenging and experience uncertainty, strain, and distress (O’Malley et al. 2008; Leventhal et al. 2013). Nurses working in palliative care reported feeling compassion, distress, surprise, puzzlement, and frustration when delirium occurred (Agar et al. 2012; Hosie et al. 2014a). In one study, delirium severity and presence of perceptual disturbances were most significant predictors of nurse distress (Breitbart et al. 2002). In another of palliative care team members’ experiences of caring for family of people dying with agitated secondary to delirium, participants felt the suffering of patients and family, tried to maintain control of the situation (usually through use of medication), felt ambivalent about the use of sedation, and valued communication to inform the family about the rationale of interventions and to reduce conflict (Brajtman 2005).

5 Prevention

There is growing evidence that the most effective way to improve delirium outcomes for people in hospital is to prevent it from occurring. Meeting
basic human needs, such as for physical and cognitive activity, sleep, hearing, vision, and hydration, significantly reduced delirium incidence in older hospitalized patients by up to 50% (Hshieh et al. 2015; Siddiqi et al. 2016). In contrast, a delirium prevention intervention for people with advanced cancer in seven Canadian specialist palliative care inpatient units reported a negative result (Gagnon et al. 2012), possibly because this intervention was not sufficiently targeted at these fundamental physical and cognitive needs. Instead, physicians were notified about delirium risk factors for each patient and asked to consider medication changes in response; while nurses oriented patients to time and place and gave patients and family information about early delirium symptoms. Despite almost 90% adherence to the study protocol, the intervention made no difference to delirium incidence, severity or duration, or dosage of psychotropic medication received by patients (Gagnon et al. 2012).

Psychoactive medications (Table 1) are commonly prescribed in palliative care to manage symptoms, such as pain, breathlessness, nausea, and fatigue, and may contribute to the increase risk of delirium (Gaudreau et al. 2005a; Clegg and Young 2011). It is important to discuss the potential risks with the person prior to commencing new psychoactive medication, so that they may make informed decisions about which means of symptom control are best for them. For example, some people would prefer to forgo some degree of pain relief to maintain optimal cognition. Choice of psychoactive medication should consider the side effect profile, pharmacokinetics and pharmacodynamics for the individual, and possible non-psychoactive alternative therapies and also pay close attention to drug-drug interactions. It is important to use the lowest effective dose and ensure ongoing regular review of the dose, necessity for ongoing treatment, and possible adverse effects.

Whether multicomponent delirium prevention interventions specifically targeted to risk factors and proven elsewhere are feasible and effective during receipt of palliative care is yet to be established. That the strategies address fundamental human needs does warrant that they are valued for all people in every care setting. Yet a potential barrier to routine implementation in palliative care is that people with advanced illness are frequently frail and fatigued and may be unable to fully participate in activities such as exercise. To make informed decisions about participating in these interventions, people first need to also understand the risks associated with delirium. They need accurate, timely, and sensitively delivered information about delirium and preventative strategies from clinicians at key points in the illness trajectory, such as on admission to a service and when deterioration occurs. Integrating delirium prevention into palliative care requires health professionals to view delirium as serious and potentially preventable in advanced illness, value this care, and offer and deliver preventative interventions in a safe, supportive, and informed way that is tailored to the individual.

6 Recognition

Early recognition of delirium risk and symptoms by all who are caring for the affected person, whether in primary care, the emergency department, or specialist palliative care settings, is essential so that his or her needs and those of their family can be assessed, a diagnosis or differential diagnosis made, and appropriate interdisciplinary care planned and implemented.

Historically, delirium is under-recognized and misdiagnosed across settings, including palliative care (National Clinical Guideline Centre for Acute and Chronic Conditions 2010; Barnes et al. 2010). Hypoactive delirium, which can easily be mistaken for depression or fatigue, is the least well-recognized subtype. One study in a palliative care unit reported a one-in-five detection rate of patients with hypoactive delirium by any member of the multidisciplinary team, significantly lower than detection of those with hyperactive and mixed delirium (Fang et al. 2008; Spiller and Keen 2006).

Poor recognition of delirium is due in part to it being a complex and fluctuating condition that manifests in various ways, even within one episode. Other reasons are health professionals’ inadequate knowledge of delirium, particularly its
diagnostic criteria (Jenkin et al. 2016); attitudes that poor cognition is normal in older age and serious and advanced illness (McCarthy 2003); and lack of routine use of delirium screening, assessment, and diagnostic tools (“tools”) and organizational direction (Hosie et al. 2014b). There are additional challenges to recognizing delirium in people with limited ability to speak, such as young children (Smith et al. 2013), those with an existing cognitive impairment (Morandi et al. 2016), and during intubation and sedation (Girard et al. 2008) and dying (Bush et al. 2014).

Timely recognition is supported by evidence-based knowledge of delirium as an abnormal condition, its seriousness, and who is most at risk (together denoting “awareness”) and routine screening of those at risk using brief, validated tools and/or diagnostic criteria to confirm the diagnosis (National Clinical Guideline Centre for Acute and Chronic Conditions 2010; Australian Commission on Quality and Safety of Healthcare 2017).

Awareness requires evidence-based understanding of delirium that aligns with accepted diagnostic criteria, as in the APA-DSM-5, provided earlier. Across settings and time, numerous misnomers for delirium have been used in different areas of clinical practice and research, with examples being ICU psychosis, sundowning, and confusion. Increasingly these terms are being discouraged in the literature (Girard et al. 2008; Morandi et al. 2009) because they are imprecise, downplay the significance and severity of delirium, and contribute to under-recognition. Likewise, terminal agitation and terminal restlessness are widely used by palliative care practitioners to describe what may be delirium or other unspecified sources of distress (Hosie et al. 2014a; Brajtman 2005; Heyse-Moore 2003). Use of these terms has similarly contributed to under-recognition of delirium and delayed assessment and intervention for delirious patients in palliative care units (Hosie et al. 2014a), likely because the prefix “terminal” implies that a delirious person is in the last days of life and communicates a presumption that interventions aimed at reversal are no longer the priority. Nurse participants in this study reported clinical incidents when they challenged their nurse colleagues’ use of these terms, whereupon a more comprehensive assessment found that their delirious patients had reversible causes such as urinary retention and infection, which were successfully treated and these patients’ delirium and distress resolved (Hosie et al. 2014a). To ensure an evidence-based approach to assessment and intervention when delirium symptoms occur, whatever the person’s stage of illness trajectory or likelihood of reversal, it is recommended that use of terminal agitation and terminal restlessness be discontinued in palliative care practice and literature in preference for the more diagnostically precise “delirium.”

Awareness also incorporates knowing the general risk of delirium to people with advanced illness, older age, and/or cognitive impairment (including the seriousness of its outcomes) and assessing the specific risk for an individual. General awareness is knowing that delirium is moderately to highly prevalent in people receiving palliative care, having “a high index of suspicion” that delirium is the cause of acute attentional and cognitive changes (LeGrand 2012), and understanding that all subtypes of delirium are a medical emergency that require urgent intervention (see chapter “Delirium as a Palliative Care Emergency”). While there is no tool to assess specific risk for people receiving palliative care, a simple and pragmatic approach outlined in evidence-based guidance is for any person with one or more risk factors (i.e., “age ≥ 65 years, known cognitive impairment/dementia, severe medical illness and current hip fracture” or any others) be asked, along with their family, on admission to hospital about any recent changes to behavior or thinking, undergo cognitive screening, and have preventative measures put in place (National Clinical Guideline Centre for Acute and Chronic Conditions 2010; Australian Commission on Quality and Safety of Healthcare 2017). Because by definition each person receiving palliative care has life-limiting illness, it is prudent to consider all to be at risk of delirium, with risk heightened for people who are older than 65 years, have an existing cognitive impairment, and one or more precipitants present (Table 1).

Screening patients for delirium requires routine and ongoing use of a structured tool by trained
clinicians. Delirium screening tools that are brief and low burden and/or include family observations include the:

- 4AT (McLullich 2015)
- Nursing Delirium Screening Scale (Nu-DESC) (Gaudreau et al. 2005b)
- Brief versions of the Confusion Assessment Method (CAM), such as the CAM-ICU (Ely et al. 2001) and short-, 3D-, or bCAM (Han et al. 2013; Hospital Elder Life Program 2015; Marcantonio et al. 2014)
- Single Question in Delirium (SQiD) (Sands et al. 2010)
- Recognizing Acute Delirium As part of your Routine tool (RADAR) (Voyer et al. 2015)

These tools were developed for various settings and users, and none have been tested or are routinely used in palliative care (Barnes et al. 2010; Irwin et al. 2008). Testing delirium tools and integrating them into current systems for symptom and problem screening (Palliative Care Outcomes Collaborative 2014; Cicely Saunders Institute 2012) is therefore an important area for palliative care practice development.

Confirmation (diagnosis) of delirium is best achieved by applying a validated confirmation tool, such as brief version of the CAM (as above) and/or diagnostic criteria (American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) 2013). Confirmation of delirium is not solely the responsibility of physicians; the process can be shared with other clinicians in the team who are trained in the use of the tool and have knowledge of the criteria (Australian Commission on Quality and Safety of Healthcare 2017). Potential differential and concurrent diagnoses, such as dementia or depression, need to be considered during the diagnostic process.

7 Comprehensive Assessment

Comprehensive assessment of a delirious patient is structured, multifaceted and interdisciplinary, and broader than a diagnostic assessment (Canadian Coalition for Seniors’ Mental Health 2010; Australian Commission on Quality and Safety of Healthcare 2015). Given that delirium is a medical emergency, when symptoms are present and a diagnosis suspected, it is essential to determine likely causes through history taking, physical examination, and various investigations, aligned with the patient’s goals of care. Understanding the experience from the patient’s perspective, his or her level of distress, and need for information and reassurance are key components that are valued by patients and family (Day and Higgins 2015; O’Malley et al. 2008). Communicating the implications of delirium and the possible options for investigation and management and relative success rates expected helps people to make informed choices about the level of investigation. Understanding also informs any decisions for admission to hospital or a palliative care unit if the person is at home.

Elements of assessment of a person with suspected or confirmed delirium are several and include:

- History, including reported symptoms of delirium and precipitating medical conditions, baseline cognition, and previous episodes of delirium (some which may be from collateral history)
- Physical examination
- Likely causes and potential for reversibility
- Predicted prognosis
- Immediate, intermediate, and longer-term goals of care
- Decision-making capacity
- Level and cause of distress
- Safety: risk of falls, wandering, pressure areas, and injury to self or others
- Preference for location of care
- Social, psychological, cultural, or spiritual needs
- Family information and support needs
- The need for referral to appropriate psychiatric or geriatric specialists or specialist services if delirium is severe and/or persisting

Comprehensive assessment also involves the person and his or her family, and results in a plan of care that addresses identified needs, priorities,
wishes, and short- and longer-term goals (National Clinical Guideline Centre for Acute and Chronic Conditions 2010; Canadian Coalition for Seniors’ Mental Health 2010; Australian Commission on Quality and Safety of Healthcare 2015).

8 Management

The goals of palliative care of a delirious person are to reduce distress, maintain function and physical and emotional safety, and resolve the delirium, wherever possible. These goals are best achieved through targeting the causes, effective communication, and practical strategies to meet patients and families’ immediate needs.

While clinical decision-making about intervention to resolve delirium often contains elements of uncertainty about effectiveness, treating the identified causes is the most logical medical route to relieving distress. Potential for reversal of delirium remains even in far-advanced illness when modifiable precipitants, such as infection, dehydration, and psychoactive medication, are treated (Lawlor et al. 2000). Some people will have less modifiable causes of delirium, such as metabolic disturbances related to organ failure (Lawlor et al. 2000; Leonard et al. 2008). Ethical decision-making with the patient and family about treatment therefore requires consideration of and discussion about the likely success of the treatment (both for the precipitant and the delirium), where it would need to occur (e.g., hospital, home or palliative care unit), and the degree of invasiveness (e.g., oral versus intravenous antibiotics). As there are usually several precipitants for each episode of delirium (Meagher et al. 2011), treatment is often multifaceted.

Further details of the investigative and intervention approach to treat delirium are outlined in chapter ▶ “Delirium as a Palliative Care Emergency”.

8.1 Pharmacological Treatment

There are no approved or proven pharmacological interventions that directly prevent or treat delirium. Rational pharmacological treatments for delirium are those which target the identified cause and any associated discomfort, for example, antibiotics to treat infection, rectifying polypharmacy, discontinuing or reducing the dose of suspected medication precipitants, paracetamol to relieve fever, and ensuring adequate analgesia for pain (Canadian Coalition for Seniors’ Mental Health 2010).

Antipsychotics have for many years been recommended in clinical guidelines and commonly prescribed to relieve delirium symptoms within both palliative care and other settings, yet there is growing evidence that this medication is not effective. A recent systematic review and meta-analysis of 19 randomized controlled trials and cohort studies of antipsychotics to prevent or treat delirium found no association with reduction of delirium severity or duration (Neufeld et al. 2016). Clinical trials conducted in intensive care settings report that use of antipsychotics did not increase participants’ number of days without delirium (Page et al. 2013; Girard et al. 2010). Most recently, the first adequately powered trial of antipsychotics (risperidone vs haloperidol vs placebo) in patients receiving palliative care found that, at three days, participants in the risperidone and haloperidol arms had delirium symptom scores significantly higher than those in the placebo arm. Participants in the active arms had significantly more extrapyramidal effects, while participants in the placebo arm received significantly lower doses of rescue midazolam and had the best overall survival (Agar et al. 2016).

Benzodiazepines, such as midazolam and lorazepam, are recommended and used as a second-line pharmacological palliative intervention for delirium when the patient is highly distressed (Palliative Care Expert Group 2016), with an absence of robust trials to evaluate efficacy and toxicity, and are also a class of medication which can contribute to or worsen delirium. A 2009 Cochrane review found no evidence that benzodiazepines improved delirium outcomes (Lonergan et al. 2009). The review authors highlighted that participants in the lorazepam arms had unacceptable side effects in two included studies, including severe sedation,
which caused one randomized controlled trial to be prematurely discontinued (Breitbart et al. 1996).

A recent Cochrane review investigating the benefit of palliative sedation on quality of life, survival, and refractory symptoms in terminally ill adults in the last days of life examined 14 studies (12 in hospice and palliative care units and primarily of midazolam) and reported insufficient evidence that palliative sedation improved quality of life or symptom control (Beller et al. 2015). Of the eight included studies measuring sedation for delirium, none reported improved delirium symptom control, and four reported worsening of delirium symptoms; the one study measuring unintended adverse effects reported 6% of participants experienced drug-induced delirium (Beller et al. 2015).

Based on current evidence, antipsychotic and/or benzodiazepine medication should therefore be viewed as an emergency, last resort, and short-term intervention for a severely distressed or agitated delirious person, after all other therapeutic strategies to relieve distress and maintain safety have been trialled and when the immediate risks to the patient are assessed as greater than these pharmacological interventions. Whenever possible, the principle of informed consent requires that the affected person or their surrogate decision-maker be fully advised of the intent, potential for benefit, possible adverse effects, and plan for use of these medications, before they are prescribed and administered.

### 8.2 Communication

People with delirium value verbal and nonverbal language that communicates respect for them as a person and understanding of what they are experiencing, while family members feel supported when they are consulted and given timely information by health professionals (Finucane et al. 2017; O’ Malley et al. 2008).

Delirium is usually frightening and alienating, and many people struggle to communicate its symptoms, even more so for those who speak a language other than English or have other pre-existing barriers to communication. Being alert to the person’s fears and difficulties; using simple, concise, and slow-paced ways of speaking; sensitively asking about the experience; respectfully promoting orientation (e.g., using the person’s name, introducing self, referring to the day and place in conversations) without directly contradicting the person’s altered reality; and obtaining the help of interpreters where required are the recommended ways of communicating with a delirious person (Canadian Coalition for Seniors’ Mental Health 2010).

People affected by delirium also appreciate knowing that it is common during medical illness, usually short in duration and often treatable. Highlighting that the causes are physiological clarifies that symptoms do not mean that the person is suddenly developing dementia or a mental illness, which is a common misunderstanding (Breitbart and Alici 2008). Naming symptoms as ‘delirium’ is therefore important. However, explaining that delirium is common should not be intended to communicate that it is normal, because delirium is always an abnormality for the person (Hosie et al. 2016). Communication instead seeks to understand the experience of delirium from the person’s and family’s perspective, identify the level of distress, and acknowledge the real impact. Informing family about delirium, including with written information, and involving them in practical and emotional care of the person are desired and acceptable to them and potentially beneficial for both (Finucane et al. 2017). As outlined above, communication with the person and family members includes discussion about treatment options and likely outcomes.

An episode of delirium, particularly subsequent episodes, may also signal that the person’s prognosis is grave and death is near. At this time, interdisciplinary reassessment of the person’s circumstances and needs, and honest, sensitive communication with the patient and family about the possible significance of delirium, enables a clear and agreed upon plan of care.

Effective team collaboration, communication and functioning improve processes and outcomes for people receiving palliative care (Tieman 2007; Abernethy et al. 2013). However, communication between team members, especially between
nurses and physicians, can be a barrier to optimal delirium care in palliative care contexts. Nurses do not always clearly report observed symptoms as delirium, and then perceive a lack of respect or listening from physicians and nursing managers (Hosie et al. 2014a). When delirium occurs, interdisciplinary communication is best enabled by shared use of diagnostic language, understanding of delirium and the rationale for a plan of care, established roles for each discipline, and more frequent and focused discussion at the bedside; in other words, informed, explicit, structured, and whole team consideration of delirium symptoms, with the person and family placed at the center of assessment, decision-making, and care (Vasilevskis et al. 2010).

8.3 Practical Strategies

There are numerous practical strategies recommended in clinical practice guidelines for care of a delirious person. Examples include:

- Continuation of care that helps the person maintain optimal movement, vision, hearing, cognition, hydration, and sleep.
- Optimizing the environment:
  - Natural day and night lighting, noise levels, and activity.
  - Avoid transfers and maintain familiar surroundings and belongings.
  - Orientating equipment such as clocks, calendars, and wall schedules.
- Assess and minimize risk of falls and injury while avoiding restraints and allowing the person to move as freely as possible.
- Supporting those who are familiar to and trusted by the person to remain with him or her, including family members, friends, and professional carers.

The reader is referred to relevant guidelines for more comprehensive details of these strategies (Canadian Coalition for Seniors’ Mental Health 2010; Australian Commission on Safety and Quality in Health Care 2014).

8.4 Delirium in the Last Days of Life

Delirium is very common when someone is dying, although not inevitable. When delirium occurs in the last days and hours of life, there remains the need for a prompt and individualized response to the meticulously assessed needs of the person and his or her family.

Numerous studies have consistently reported what is most important to patients and family at the end of life. In the hospital setting, patients and family highly valued expert, respectful, and compassionate care, effective communication and shared decision-making, an adequate environment, involvement of family, support with financial affairs, and trust and confidence in clinicians (Virdun et al. 2015, 2016). Patients also wanted to maintain a sense of self and not be a burden to others; and family further valued preparation for death, the patient to be safe and enabled to make choices, and family care continuing past the death of the person (Virdun et al. 2016). A study of the end of life wishes of people with advanced cancer, conducted in the United States, reported the ten most important as being, in this order: to be at peace with God, pray, have family present, free of pain, not be a burden to family, trust in the doctor, maintain a sense of humor, say goodbye to those who were important to them, have family prepared for death, and be able to help others (Delgado-Guay et al. 2016). Studies in Japan with bereaved family members of people who had delirium when they were dying from cancer reported that family experienced high levels of distress; more than half believed clinicians should have shown more respect for the person, explained what was happening on a daily basis, helped to relieve the physical and psychological burden on family, and better prepared them for death (Namba et al. 2007; Morita et al. 2007).

Given the consistency of the descriptive data over time and setting, and the growing evidence for ineffectiveness of pharmacological interventions to reduce delirium duration, severity, or distress, it is clear that physical, emotional, and spiritual care to help people who are delirious in the last days of life to be seen as a person; connect
and communicate with family, health professionals, and God; and prepare for death ought to be the focus of both clinical practice and future interventional research.

Palliative care for a person who is delirious in the last days of life, and their family, therefore continues all appropriate strategies to relieve suffering, as outlined above. If agitation is present for a dying person, all potential contributors, such as pain, urinary retention, fecal impaction, and psychological and spiritual distress, should be assessed and managed accordingly. If any level of sedation is considered for a person who is suffering from refractory agitated delirium in the last days of life, or other symptoms, health professionals should be guided by the European Association for Palliative Care (EAPC) framework for palliative sedation (Bush et al. 2014; Cherny and Radbruch 2009). Briefly, this framework includes that the person is comprehensively assessed by experienced palliative care physicians and teams, and any other appropriate specialist; that patients and family members are fully informed and provide consent; that sedation is proportional to the person’s needs and wishes, that the person’s physical, hydration, nutrition, and concomitant medication needs are considered and met; that supportive care of the family continues; and that the views and well-being of team members with respect to decision-making and intervention are also considered (Cherny and Radbruch 2009). Care must also be taken that any sedating intervention is given primarily for the wellbeing of the person, and not for that of family or team members.

9 Future Approaches to Improving Palliative Care of People at Risk of Delirium

Improving delirium outcomes for people receiving palliative care requires greater empirical evidence in every domain: prevention, recognition, assessment, treatment, and support, including for family in bereavement (Lawlor et al. 2014). Numerous descriptive data exist, but proven interventions are lacking. Next steps to improving palliative care of people at risk of delirium are therefore to develop interventions that are based on the aspects of care that have consistently been reported as the most important to people at the end of life and test them in well-designed studies (Finucane et al. 2017). Interventions proven to be effective for other patient groups and settings, such as delirium prevention through meeting fundamental human needs, can also be tailored and tested in palliative care (Hshieh et al. 2015; Siddiqi et al. 2016). Novel therapeutic targets based on pathophysiological evidence of pathways to delirium ideally will guide future trials of pharmacological prevention and treatment therapies. Theories of grief and bereavement could be developed and tested as interventions to support family of people with delirium in advanced, life-limiting illness. For example, the theory of ambiguous loss acknowledges and addresses the loss experienced by family when a living person is physically present yet psychologically absent – as can occur during delirium – to find greater meaning, mastery, connection, hope, and resilience in the difficulty of the situation (Boss 2010; Day and Higgins 2016).

At the health system level, patients receiving palliative care require equitable access to organizational initiatives to improve delirium systems and practice. For example, in Australia, a new delirium clinical care standard will include people receiving palliative care in its remit (Australian Commission on Quality and Safety of Healthcare 2017).

Delirium education for health professionals should be based on those known to be most effective in changing attitudes, knowledge, and practice. Examples include interprofessional education (Sockalingam et al. 2014) and spaced education (Phillips et al. 2014).

10 Conclusion and Summary

This chapter has outlined how health professionals may best prevent, recognize, assess, manage, and support people with palliative diagnoses who are at risk of delirium, and their families, according to best evidence and the circumstances, needs, and
wishes of the person. The chapter also presented evidence-practice gaps in delirium care in palliative contexts and briefly outlined directions for future research and clinical practice development.

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