Guidelines On The Management Of Delirium In Palliative Care Settings

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Responsible Committee:	Medicines Optimisation Group		
Lead Author(s):	Dr Emma Padfield, Dr Lucy Harborow		
Supporting Author(s):	Professor Matthew Hotopf		
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This procedure applies in the following areas of St Christopher's:

All teams and departments	☒
In-Patient Unit	☒
Sydenham based teams	☒
Bromley based teams	☒

Contents

Key points

Delirium is a syndrome which is both common and under-recognised.

The prognosis is variable but it carries a high morbidity and mortality, and a significant number of patients never regain their previous level of functioning after an episode of delirium.

Prevention is therefore much better than treatment.

The treatment of delirium is to treat the underlying cause, and manage the symptoms of the syndrome using non-pharmacological methods.

There is little or no evidence that pharmacological agents reduce the length or severity of delirium – medication is used to manage specific symptoms, mostly agitation leading to risky behaviour and intractable distress.

Please contact the liaison psychiatry team if additional support or advice is needed.

I. EPIDEMIOLOGY

Prevalence

The overall prevalence of delirium among medical inpatients is estimated at 23%, with higher rates in intensive care units and for those on mechanical ventilation [1]. In the palliative care setting, the pooled point prevalence of delirium on admission to an inpatient palliative care unit is 35% [2]. Estimates for the prevalence among palliative patients in the community are 4-12%, though the prevalence in care homes may be up to 60% [3]. 45-62% of patients in palliative inpatient settings developed delirium during admission and around three quarters of these cases were of the hypoactive delirium subtype [4]. The prevalence of delirium prior to death across all settings was 42-88% [2].

Prognosis

Aside from the acute distress and suffering to the patient and their family, an episode of delirium is associated with significantly poorer outcomes. Patients who develop delirium have longer inpatient stays and have a greater risk of in-hospital death [5] as well as a 62% increased risk of mortality in 1yr and an average of 13% of a year of life lost compared with patients who do not develop delirium [6]. They are also at higher risk of functional decline and institutional placement on leaving hospital [7].

Most cases of delirium resolve within a few days or weeks but about 20% cases in the elderly are estimated to persist for six months or more [8]. Up to 60% of people have persistent cognitive impairment following an episode of delirium, and they are three times more likely to develop dementia [1,9].

The prognosis is poorer for those with hypoactive delirium [10] – the reason for this is unclear but may be related to poorer recognition and treatment. Hypoactive delirium may be perceived by carers and professionals as the patient being “calm” or “not in distress” and may therefore be significantly under-recognised and reported.

II. ASSESSMENT AND DIAGNOSIS

Clinical features

Delirium is a clinical syndrome, and only occurs as a **direct consequence of another medical condition**. It has five diagnostic features [11]:

- Disturbance in **attention** and **awareness** with reduced orientation to the environment;
- Disturbance in **cognition** (memory, disorientation, language, visuospatial skills or perception);
- The disturbance develops over a **short period** (hours to days), represents an **acute change from baseline** and tends to **fluctuate** in severity during the course of a day;
- The disturbances are not better explained by a pre-existing neurocognitive disorder;
- The disturbance is the **direct** physiological consequence of a medical condition, substance intoxication or withdrawal, medication, toxins or a combination of these.

The underlying cause(s) of delirium can include virtually any medical condition or disorder. It is beyond the scope of this guideline to list these further, but it is essential for the cause(s) to be identified and for clinicians to remember that most cases of delirium are multi-factorial.

Clinical subtypes

There are three clinical subtypes, with different clinical presentations and prognoses [10]:

- **Hyperactive**: characterised by increased motor activity with agitation, hallucinations and inappropriate behaviour.
- **Hypoactive**: characterised by reduced motor activity and lethargy; long-term outcomes are poorer for patients with this subtype.
- **Mixed**: features of both hypoactive and hyperactive subtypes.

Risk factors

Delirium is almost always multifactorial and the risk is greater as the number of risk factors increases. These risk factors can be divided into static factors and precipitating factors [1]. The lists below are not exhaustive but cover the most common or relevant factors for the palliative population.

Static factors	**Precipitating factors**

• Older age (>65)
• Pre-existing cognitive impairment or dementia
• Multiple co-morbidities
• Polypharmacy (>4 drugs)
• Frailty
• Visual or hearing impairment
• Poor nutrition
• Depression
• Alcohol or drug misuse
• History of delirium, stroke, neurological disease, falls or gait disorder
	• Any acute illness:
	  ○ Acute infection
	  ○ Dehydration
	  ○ Electrolyte imbalance
	  ○ Liver dysfunction
	  ○ Heart failure
	  ○ Seizures
	  ○ Any major surgery
	• Drug withdrawal (including alcohol)
	• Pain
	• Invasive devices
	• Any psychoactive drugs including opiates, antipsychotics and benzodiazepines.
	• Anticholinergic burden
	• Sleep deprivation

Tools for evaluation and diagnosis

The diagnosis of delirium can be made clinically, based on the standard criteria above (*see p.5*).

Various screening tools have been developed to assist diagnosis. The National Institute for Health and Clinical Excellent (NICE) recommends the **Confusion Assessment Method (CAM)** [12] as the best diagnostic tool [13]. The CAM has a sensitivity of 94% and specificity of 89% on pooled analysis [14].

The CAM assesses for four domains; the diagnosis requires domains 1 and 2 and either 3 or 4 to be present:

1. Acute onset and fluctuating course
   AND
2. Inattention
   AND EITHER
3. Disorganised thinking
   OR
4. Altered level of consciousness

A copy of the CAM is in appendix 1.

The **4 A's Test (4AT)** [15] is a shorter assessment tool designed for routine use without requiring specific training. It takes less than two minutes to complete. Compared to standard diagnostic criteria or validated tool, the 4AT had a pooled sensitivity of 88% and specificity of 88% [16]. It is a valid alternative if a shorter tool is preferred [17]. It has four questions:

1. Alertness (normal/mild sleepiness/clearly abnormal)
2. AMT4 (age, date of birth, place, current year)
3. Attention (months of year backwards)
4. Acute change or fluctuating course (yes/no)

A copy of the 4AT, including scoring instructions, is in appendix 2.

Differential diagnosis with terminal agitation

Terminal agitation is anxious, restless or distressed behaviour occurring at the end of life. It is also referred to as terminal restlessness, terminal delirium, refractory delirium, terminal anguish or confusion at the end of life; these terms have subtly different but overlapping meanings [18].

Terminal agitation is frequently caused by delirium but some patients can become agitated without a delirium, such as in emotional or spiritual distress.

Discriminating between terminal agitation and delirium is difficult as there is no standardised assessment tool and it relates to the patient's stage of illness. A diagnosis should therefore be made by experienced physicians. They may decide palliative sedation is appropriate for patients at the end of life when the cause of delirium is judged to be irreversible and it is required to control distress during the dying process [19]. Details of palliative sedation are not covered in this guideline.

III. PREVENTION OF DELIRIUM

Identification of at-risk patients

Delirium causes significant suffering for patients and family members, and is associated with significantly poorer outcomes (*see p.3*). Prevention of delirium is therefore a priority and prevention strategies should be integrated into good clinical care for patients in the community and in inpatient units.

Given that risk factors for delirium are well-known and often easy to identify, it ought to be possible to screen patients for risk factors at the time of admission and at regular points during admission, and to act quickly to reduce any modifiable risk.

There is no high-quality validated tool for assessing delirium risk. NICE recommends that all patients should be assessed for risk of delirium within 24 hours of admission, and advises that if **any of the following four features** is present they are at risk of delirium [13]:

- 65 years or older
- Cognitive impairment and/or dementia
- Current hip fracture
- Severe illness (condition that is deteriorating or at risk of deterioration).

In practice, we would expect at least one of these to apply to **all** patients within the palliative setting on the grounds that they have a severe illness at risk of deterioration.

Multicomponent interventions for delirium prevention

For patients identified as at risk of delirium, there is good evidence that a multicomponent and multidisciplinary approach to delirium prevention is effective in reducing the incidence of delirium [1]. There is **no pharmacological intervention** with high-level evidence for prevention of delirium. Prevention relies on the managing team being alert to the possibility of delirium and integrating the interventions below into daily care and treatment.

NICE recommends a multicomponent intervention tailored to the patient's needs and addressing ten domains of care. The full guideline is available online [13]; the following is a summary of the key recommendations, but in the palliative population it is expected that some of the interventions may not be appropriate. The package should be clearly tailored to the patient's needs and appropriate to their current clinical condition.

Cognitive impairment and disorientation

- Appropriate lighting, clear signage, visible clock and calendar.
- Reorienting the person – where they are, who they are, what your role is.
- Cognitively stimulating activities such as reminiscence.
- Regular visits from family and friends.

Dehydration and constipation

- Adequate fluid intake (appropriate to clinical condition).

Hypoxia

- Optimise oxygen saturation (appropriate to clinical condition).

Infection

- Looking for and treating infection.
- Avoiding unnecessary catheterisation.
- Following infection control procedures to reduce risk of healthcare-associated infections.

Mobility

- Walking or range-of-motion exercises (appropriate to clinical condition).

Pain

- Assessing for pain, including non-verbal signs, especially in those with communication difficulties.
- Starting and reviewing appropriate pain management.

Medicines optimisation

- Carry out a medication review; consider using the STOPP tool and Anticholinergic Cognitive Burden tool, which are discussed on p.10 below.
- If possible, avoid benzodiazepines and antipsychotics.

Nutrition

- Ensure appropriate nutrition and dentition.

Sensory impairment

- Resolve reversible causes such as earwax.
- Ensure hearing aids and visual aids are available and working.

Sleep

- Avoid interventions and medication rounds during sleeping hours.
- Reduce noise and light during sleeping hours.

IV. MANAGEMENT

General principles of management [10]

1. **Prevention** is far more effective than treatment.
2. Treat delirium as a **medical emergency**.
3. Treat the **underlying cause** as the first priority.
4. Management strategies should be **non-pharmacological** wherever possible.
5. Only use pharmacological management where other methods have failed and only to treat **specific symptoms**.

The following recommendations are supportive measures to manage the symptoms and reduce the duration of delirium. The most important intervention is to **TREAT THE UNDERLYING CAUSE(S),** as the delirium may never resolve if this is not done.

Non-pharmacological management of delirium

Polypharmacy and anticholinergic burden

- **Medicines optimisation** should be carried out, ideally by a pharmacist, and any medicines which are not immediately necessary should be reviewed and stopped if possible.
    - **STOPP** (Screening Tool of Older Persons' potentially inappropriate Prescriptions) is an evidence-based tool to reduce iatrogenic harm from polypharmacy and inappropriate prescribing [20]. There is evidence that using this tool reduces falls, delirium episodes and visits to primary care and emergency settings [21]. A copy is in appendix 3.
- Estimate the **anticholinergic risk burden**, taking into account the total number of drugs with anticholinergic effects and their relative potency, and consider altering prescriptions to reduce anticholinergic burden.
    - There is no high quality evidence preferring one anticholinergic risk tool over others, but the Anticholinergic Cognitive Burden [22] has been validated [23], and a score of 3 or more is associated with increased mortality [24]. There is also an electronic anticholinergic burden calculator available online at www.acbcalc.com [25].

Multidisciplinary support and environmental conditions

There is little primary research assessing the quality and effectiveness of each of the interventions below. They are recommended largely on the basis of common sense and consensus opinion. They are broadly similar to the recommendations for the prevention of delirium and therefore should be carried out throughout a patient's care pathway, rather than just after an episode of delirium has developed. Please refer to NICE guideline CG103 for further information [13].

- Optimise **hydration** and **nutrition**, ensuring the patient has access to **dentures** if needed and these are fitted correctly, and addressing **constipation** where necessary.
    - The degree of hydration and nutrition given should of course be tailored to the patient's individual needs, depending on their wishes, their physical state and the stage of illness.
- Assess for **pain**, including non-verbal signs of pain, and treat assertively when present.
- Minimise sensory deprivation:
    - **Sight** – ensure glasses are available and in good working order.
    - **Hearing** – treat reversible causes of hearing loss such as earwax; ensure hearing aids are easily accessible and in good working order.

- **Mobility** – encourage walking if appropriate, using aids if necessary; if the patient cannot walk, encourage active range-of-motion exercises.
- Prioritise **sleep/wake cycle** – avoid procedures and medication rounds during sleeping hours; reduce noise during sleeping hours; maintain light/dark times using natural light where possible and avoid artificial lighting during the night; offer eye masks and ear plugs at night; encourage the patient to get up and dressed during the day if practical.
- **Re-orientation** – provide clear signage, have a clock and calendar with the day of the week clearly visible to the patient, use consistent staff where possible, remind the patient where they are and who is caring for them.
- Regular **visits** from friends and family, or use of photographs and reminiscence where this is not possible.
- **Education** for patient and family on the nature of delirium and the key strategies for management.

Pharmacological management of delirium

There is **no good evidence** to support or refute the use of any pharmacological agent in the **treatment** of delirium. A recent Cochrane review evaluated the evidence for various drug treatments in managing delirium in the palliative population [26]. They found the quality of evidence was low, but based on the research available, there is no evidence to support the use of haloperidol, risperidone, olanzapine, lorazepam or chlorpromazine in treating delirium. Another Cochrane review found no evidence that antipsychotic treatment reduces delirium severity, resolves symptoms faster or reduces risk of death in delirium [27]. In some trials, antipsychotics appeared to worsen the symptoms of delirium [26]. Antipsychotic treatment may be less effective for the palliative population than the general population [10].

Medications therefore have a limited role in the management of delirium, and they are used not for treatment of the syndrome but for **management of symptoms** that have not responded to non-pharmacological methods. In these cases, there is still very little good quality evidence, and guidelines generally advise using medicines on the basis of expert consensus opinion [1]. The use of psychotropic medication in delirium needs to be justified on the basis of **intractable distress** of the patient, or **agitation leading to significantly risky behaviours**. This may include the patient themselves being at risk (for example from attempting to leave the ward) or placing others at risk (for example due to aggression). However, medication should never be the first response to such behaviours, and every attempt should first be made to de-escalate the situation without the use of medication or restraint.

If a medicine is used to manage distress or agitation, there is a risk that the patient will become sedated and this will simply **mask a hypoactive delirium** which is less likely to be recognised and treated. Just because a patient becomes more sedated does not mean their delirium has resolved.

Medications for intractable distress or significant agitation

The following is a summary of the current evidence regarding specific medications.

None of these medications has good quality evidence as a treatment for delirium, and they should only be used to support management of intractable distress or agitation leading to significantly risky behaviours.

The following notes and medication dosages follow the recommendations of the Maudsley Prescribing Guidelines (13th Edition) [10]. All prescribing decisions should be tailored to the individual patient and with reference to any contraindications and drug interactions.

Second generation antipsychotics

- The majority of studies have found no difference in efficacy or safety between quetiapine, olanzapine and risperidone in management of delirium symptoms [27].
- However there is some limited evidence that quetiapine may be safer than olanzapine or risperidone [28] and that olanzapine [29] and risperidone [30] may be less effective in the older age group.
- All antipsychotics are associated with increased risk of stroke in dementia.
- All antipsychotics carry the risk of extrapyramidal side-effects, which include acute dystonias, akathisia and Parkinsonian symptoms (such as tremor, bradykinesia and rigidity). Extrapyramidal effects are less likely with quetiapine and olanzapine as they have lower affinity for the dopamine D_2 receptor than risperidone or first generation antipsychotics.
- The immediate-release form of quetiapine (rather than modified-release) is recommended in this context.
- For those who cannot swallow tablets, quetiapine is available in liquid form, olanzapine is available as an orodispersible tablet of olanzapine and risperidone has both liquid and orodispersible forms.

Drug	Oral dosing	Parenteral option	Adverse effects
Quetiapine	12.5–25mg daily, then increase to twice daily, then increase dose every 12hrs if needed. Max 200mg in 24hrs (50mg in elderly).	No	Sedation Postural hypotension Increased risk of stroke in dementia
Olanzapine	2.5–5 mg initially. Max 20mg in 24hrs (10mg in elderly). Orodispersible form available.	IM available but not recommended in delirium	Sedation Postural hypotension Increased risk of stroke in dementia
Risperidone	0.25–0.5 mg initially, twice a day if needed. Max 4mg in 24hrs (2mg in elderly). Orodispersible form available.	No	Hypotension Extrapyramidal effects Increased risk of stroke in dementia

First generation antipsychotics

- No trials have demonstrated superiority of other antipsychotics over haloperidol; however the risk of adverse events is likely to be higher in the elderly and the palliative population than the general medical population.
- ECG is recommended prior to starting and regularly during treatment due to risk of QT prolongation. However ECG monitoring is not available at the hospice. Avoid first generation antipsychotics in patients with known a known history of cardiac disease or in conjunction with other medications that might prolong the QT interval.
- All antipsychotics are associated with increased risk of stroke in dementia.
- First generation antipsychotics should <u>not</u> **be used in people with Parkinson's disease or** Lewy body disease due to their strong affinity for the dopamine D_2 receptor and resulting extrapyramidal effects.
- Levomepromazine is not recommended in the Maudsley Guidelines for delirium; it is however licensed for restlessness and confusion in palliative care and has a useful advantage of subcutaneous administration. Haloperidol also has a subcutaneous form – please refer to the BNF for details.
- An oral solution of haloperidol is available for those who cannot swallow tablets.

Drug	Oral dosing	Parenteral option	Adverse effects
Haloperidol	0.5–1mg initially, then every 4hrs if needed. Max 5mg in 24hrs.	IM 0.5–1mg, peak effect 20-40 mins, repeat after 30-60 mins if needed. SC injection or infusion – see BNF.	Extrapyramidal effects, especially above 3mg Prolonged QT interval Increased risk of stroke in dementia
Levomepromazine	Not recommended in delirium.	SC 6.25mg every 2hrs as required.	Extrapyramidal effects Prolonged QT interval Postural hypotension Increased risk of stroke in dementia

Benzodiazepines

- All benzodiazepines are associated with **prolongation and worsening of delirium** and should therefore be avoided if possible.
- They do however have a key role in the treatment of **alcohol withdrawal** and are the first line treatment for this. The identification of alcohol withdrawal is therefore key in the appropriate management of delirium. A long-acting benzodiazepine (chlordiazepoxide or diazepam) should be used unless there is severe liver failure, in which case lorazepam is safer. Lorazepam is also the first line treatment for delirium tremens. The management of alcohol withdrawal is briefly discussed on p.14 below; please refer to NICE guideline CG115 for full details [31].
- Benzodiazepines may also be used in delirium if antipsychotics are contraindicated (for example in Lewy body disease, Parkinson's Disease or neuroleptic malignant syndrome).
- Lorazepam has a short half-life and is more likely to cause paradoxical excitement. Diazepam has a long half-life and should be used very cautiously outside the management for alcohol withdrawal.

Drug	Oral dosing	Parenteral option	Adverse effects
Lorazepam	0.25–1 mg every 2-4 hrs as needed. Max 4mg in 24 hours (2mg for elderly).	IM dose is the same as oral.	Respiratory depression Over-sedation Paradoxical excitement
Diazepam	5–10 mg initially (2mg elderly); consider higher doses for alcohol withdrawals.	Not recommended.	Respiratory depression Over-sedation
Chlordiazepoxide	Fixed dose regimen titrated to symptoms and severity of alcohol withdrawal (refer to BNF).	No	Respiratory depression Over-sedation

Sedating antihistamines

- Drugs such as promethazine have a high anticholinergic burden and are therefore more likely to prolong and worsen symptoms of delirium. They are therefore **not recommended** for management of delirium.

Cholinesterase inhibitors

- There is no good evidence for the use of cholinesterase inhibitors (which include donepezil and rivastigmine). In a randomised double-blind trial rivastigmine did not reduce duration of delirium and may be associated with increased mortality [32]. Research into their use in delirium prevention is ongoing but at present they are **not recommended** for use in delirium.

Management of alcohol dependence

A discussion of alcohol dependence or the detailed management of withdrawal is beyond the scope of this guideline. Clear advice is given in NICE Guideline CG115 [31] and all staff are encouraged to be familiar with this advice. A brief summary of the management of alcohol dependence is given below.

- All patients should be asked routinely about alcohol consumption. If harmful drinking is suspected, consider using a **screening tool** for alcohol dependence. NICE recommends the AUDIT tool.
- All patients with alcohol dependence should be offered care from **specialist alcohol support services**, including care co-ordination or case management as appropriate. Professionals should consider using motivational interviewing techniques and brief psychological interventions in people with harmful drinking, according to their training and experience.
- Sudden withdrawal from alcohol carries serious risks of seizures, delirium tremens and death.
- Medical detoxification from alcohol is usually carefully planned in advance and incorporated as part of a comprehensive rehabilitation programme. However in the hospice inpatient setting, alcohol withdrawal may not be expected or planned for, if the extent of the person's drinking was not known prior to admission.
- If inpatient detoxification is necessary, assess withdrawal symptoms using the **CIWA-Ar tool** (*appendix 4*) and use a fixed-dose benzodiazepine regimen, titrated to the level of drinking and/or severity of withdrawals. Seek advice from liaison psychiatry and pharmacy colleagues regarding the detox regimen, if needed. Please see p.13 above for drug choice.
- All patients with harmful or dependent drinking should be offered **thiamine** for prophylaxis of Wernicke's Encephalopathy. This can be given orally or parenterally depending on their physical condition and the degree of risk. In acute withdrawals it is usually given as intramuscular Pabrinex for three days followed by oral supplementation [33.]
- Delirium tremens is a medical emergency and has a mortality of 10-20%. It typically develops 3-4 days after the last drink and is characterised by clouding of consciousness, vivid hallucinations and marked tremor [33]. It should be treated assertively with oral or parenteral **lorazepam**. Parenteral haloperidol may also be needed, and consider transferring the patient to the acute medical setting, if appropriate.

Management of delirium in the community

There is very little research on the management of delirium in the community setting, either at home or in institutional care. Early recognition of delirium is critical, and it is recommended to screen all patients under community hospice care regularly for delirium using the CAM (*appendix 1*) or 4AT (*appendix 2*) as described on p.6 above.

Prevention is far better than treatment and community teams may have a particular role in promoting delirium prevention practices (*summarised on pp.8-9 above*), especially through reducing polypharmacy, reducing the anticholinergic burden and early identification of patients at risk, for example if they develop an acute infection or metabolic disorder.

For patients living at home, carer stress may be considerable and high-quality education should be given to carers on the causes, symptoms and treatment of delirium. Carers may be an extremely useful component of the patient's care, especially if they are skilled in the recognition and non-pharmacological management of delirium, but careful attention should be paid to the carer's own needs and a formal assessment of these needs should be offered regularly.

Medication for symptom management should be used particularly cautiously in community care because of the difficulties with regular review and reassessment. Prescribing guidelines recommend that any medicine for delirium symptoms is reviewed every 24 hours and should be discontinued within a week of symptoms resolving [10]. This may be particularly difficult when the patient is living at home, rather than in institutional care where there may be professionals who can monitor their response more closely. If medication is felt to be necessary, the prescription should not be given for more than seven days and the patient should be reviewed by a member of the multidisciplinary team as often as practicable.

Community teams have a useful role in reviewing and stopping medications after a patient is discharged from hospital, if they are prescribed an ongoing supply of an antipsychotic or benzodiazepine after resolution of symptoms of delirium. However, abrupt withdrawal of treatment may be risky, depending on the duration and dose of treatment; prescribers should seek advice from pharmacy colleagues if this is uncertain.

Legal considerations

It is essential to ascertain a patient's capacity to consent to treatment and care. Every patient should be assumed to retain capacity to consent to treatment unless it can be shown that they lack this capacity. It is unlawful to treat an adult without their consent unless legal safeguards are used, which may include the Mental Capacity Act, Mental Health Act or common law. Any healthcare professional involved in the care of patients must receive training in consent, capacity assessment and the application of appropriate legal principles.

Any assessment and decision regarding capacity should be thoroughly and clearly documented in the patient's notes, and capacity should be regularly re-assessed. There is no such thing as a blanket 'lack of capacity' – each decision is made individually and at the time the decision needs to be made. If a person's care includes aspects which may deprive them of their liberty, such as using handrails to keep them in bed or having a 1:1 nurse to prevent them leaving the ward, consider applying for Deprivation of Liberty Safeguards (DoLS) [34].

A detailed discussion of capacity and the application of the law is beyond the scope of this guideline. A useful summary of the Mental Capacity Act and DoLS can be found on the Social Care Institute for Excellence website [35] and helpful information on the application of both the Mental Health Act and Mental Capacity Act is available in the book, *'A Clinician's Brief Guide to the Mental Health Act'* [34].

SUMMARY OF MEDICATION RECOMMENDATIONS

These are not used for the direct treatment of delirium and may worsen or prolong delirium. Use of medication should be justified for management of intractable distress or agitation posing significant risk, where all other methods of treatment have failed.

IF NO PARKINSON'S DISEASE / LEWY BODY DISEASE

1st line: Quetiapine – initially 12.5–25mg orally daily, then increase to twice daily, then increase dose every 12hrs if needed. Max 200mg in 24hrs (50mg in elderly).

2nd line: Haloperidol – 0.5–1mg initially, then every 4hrs if needed. If the oral route is not possible, use IM 0.5–1mg, repeating after 30-60 mins if needed. Max 5mg in 24hrs.
OR
Olanzapine – 2.5–5 mg initially. Max 20mg in 24hrs (10mg in elderly).
OR
Risperidone – 0.25–0.5 mg initially, twice a day if needed. Max 4mg in 24hrs (2mg in elderly).

If subcutaneous route is needed, consider levomepromazine SC 6.25mg every 2hrs as required.

IF PARKINSON'S DISEASE / LEWY BODY DISEASE

1st line: Lorazepam – 0.25–1 mg oral/IM every 2-4 hrs as needed. Max 4mg in 24hrs (2mg for elderly).
OR
Diazepam – 5–10 mg oral initially (2mg in elderly).

2nd line: Quetiapine or olanzapine as above, but start low and go slow. Avoid other antipsychotics.

ACUTE ALCOHOL WITHDRAWAL

Uncomplicated:
Chlordiazepoxide or diazepam – use a fixed dose reduction regimen titrated to the severity of dependence and withdrawals (refer to BNF).
AND Pabrinex I+II three times daily for 3 days then oral thiamine in long-term.

Complicated (severe liver failure; delirium tremens):
Lorazepam – use a fixed dose reduction regimen titrated to the severity of dependence and withdrawals (refer to BNF).
AND Pabrinex I+II three times daily for 3 days then oral thiamine in long-term.

Please contact the liaison psychiatry team at the hospice if further support or advice is needed.

APPENDIX 1: Confusion Assessment Method (CAM) [12]

If both items 1 and 2 are present, and either item 3 or 4, then delirium is highly likely.

1a. **Acute onset**: Is there evidence of an acute change in mental status from the patient's baseline?

OR

1b. **Fluctuating course**: Did the (abnormal) behavior fluctuate during the day, that is tend to come and go or increase and decrease in severity?

AND

2. **Inattention**: Did the patient have difficulty focusing attention, for example being easily distractible, or having difficulty keeping track of what was being said?

AND

3. **Disorganised thinking**: Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?

OR

4. **Altered level of consciousness**: Overall, how would you rate this patient's level of consciousness? Any answer other than 'alert' indicates an abnormal level of consciousness.

APPENDIX 2: 4AT rapid clinical test for delirium [15]

[1] ALERTNESS

This includes patients who may be markedly drowsy (eg. difficult to rouse and/or obviously sleepy during assessment) or agitated/hyperactive. Observe the patient. If asleep, attempt to wake with speech or gentle touch on shoulder. Ask the patient to state their name and address to assist rating.

Normal (fully alert, but not agitated, throughout assessment)	**0**
Mild sleepiness for <10 seconds after waking, then normal	**0**
Clearly abnormal	**4**

[2] AMT4

Age, date of birth, place (name of the hospital or building), current year.

No mistakes	**0**
1 mistake	**1**
2 or more mistakes/untestable	**2**

[3] ATTENTION

Ask the patient: "Please tell me the months of the year in backwards order, starting at December."
To assist initial understanding one prompt of "what is the month before December?" is permitted.

Months of the year backwards	Achieves 7 months or more correctly	**0**
	Starts but scores <7 months / refuses to start	**1**
	Untestable (cannot start because unwell, drowsy, inattentive)	**2**

[4] ACUTE CHANGE OR FLUCTUATING COURSE

Evidence of significant change or fluctuation in: alertness, cognition, other mental function (eg. paranoia, hallucinations) arising over the last 2 weeks and still evident in last 24hrs

No	**0**
Yes	**4**

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4 or above: possible delirium +/- cognitive impairment
1-3: possible cognitive impairment
0: delirium or severe cognitive impairment unlikely (but delirium still possible if [4] information incomplete)

4AT SCORE ☐

APPENDIX 3: Screening Tool of Older Persons' Prescriptions (STOPP) version 2 [20]

Freely available online and accessed via https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4339726/#sup1 (Supplemental material)

The following prescriptions are potentially inappropriate to use in patients aged 65 years and older.

Section A: Indication of medication

1. Any drug prescribed without an evidence-based clinical indication.
2. Any drug prescribed beyond the recommended duration, where treatment duration is well defined.
3. Any duplicate drug class prescription e.g. two concurrent NSAIDs, SSRIs, loop diuretics, ACE inhibitors, anticoagulants (optimisation of monotherapy within a single drug class should be observed prior to considering a new agent).

Section B: Cardiovascular System

1. Digoxin for heart failure with normal systolic ventricular function (no clear evidence of benefit)
2. Verapamil or diltiazem with NYHA Class III or IV heart failure (may worsen heart failure).
3. Beta-blocker in combination with verapamil or diltiazem (risk of heart block).
4. Beta blocker with bradycardia (< 50/min), type II heart block or complete heart block (risk of complete heart block, asystole).
5. Amiodarone as first-line antiarrhythmic therapy in supraventricular tachyarrhythmias (higher risk of side-effects than beta-blockers, digoxin, verapamil or diltiazem)
6. Loop diuretic as first-line treatment for hypertension (safer, more effective alternatives available).
7. Loop diuretic for dependent ankle oedema without clinical, biochemical evidence or radiological evidence of heart failure, liver failure, nephrotic syndrome or renal failure (leg elevation and /or compression hosiery usually more appropriate).
8. Thiazide diuretic with current significant hypokalaemia (i.e. serum K+ < 3.0 mmol/l), hyponatraemia (i.e. serum Na+ < 130 mmol/l) hypercalcaemia (i.e. corrected serum calcium > 2.65 mmol/l) or with a history of gout (hypokalaemia, hyponatraemia, hypercalcaemia and gout can be precipitated by thiazide diuretic)
9. Loop diuretic for treatment of hypertension with concurrent urinary incontinence (may exacerbate incontinence).
10. Centrally-acting antihypertensives (e.g. methyldopa, clonidine, moxonidine, rilmenidine, guanfacine), unless clear intolerance of, or lack of efficacy with, other classes of antihypertensives (centrally-active antihypertensives are generally less well tolerated by older people than younger people)
11. ACE inhibitors or Angiotensin Receptor Blockers in patients with hyperkalaemia.
12. Aldosterone antagonists (e.g. spironolactone, eplerenone) with concurrent potassium-conserving drugs (e.g. ACEI's, ARB's, amiloride, triamterene) without monitoring of serum potassium (risk of dangerous hyperkalaemia i.e. > 6.0 mmol/l – serum K should be monitored regularly, i.e. at least every 6 months).
13. Phosphodiesterase type-5 inhibitors (e.g. sildenafil, tadalafil, vardenafil) in severe heart failure characterised by hypotension i.e. systolic BP < 90 mmHg, or concurrent nitrate therapy for angina (risk of cardiovascular collapse)

Section C: Antiplatelet/Anticoagulant Drugs

1. Long-term aspirin at doses greater than 160mg per day (increased risk of bleeding, no evidence for increased efficacy).
2. Aspirin with a past history of peptic ulcer disease without concomitant PPI (risk of recurrent peptic ulcer).
3. Aspirin, clopidogrel, dipyridamole, vitamin K antagonists, direct thrombin inhibitors or factor Xa inhibitors with concurrent significant bleeding risk, i.e. uncontrolled severe hypertension, bleeding diathesis, recent non-trivial spontaneous bleeding) (high risk of bleeding).
4. Aspirin plus clopidogrel as secondary stroke prevention, unless the patient has a coronary stent(s) inserted in the previous 12 months or concurrent acute coronary syndrome or has a high grade symptomatic carotid arterial stenosis (no evidence of added benefit over clopidogrel monotherapy)
5. Aspirin in combination with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with chronic atrial fibrillation (no added benefit from aspirin)
6. Antiplatelet agents with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with stable coronary, cerebrovascular or peripheral arterial disease (No added benefit from dual therapy).
7. Ticlopidine in any circumstances (clopidogrel and prasugrel have similar efficacy, stronger evidence and fewer side-effects).
8. Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first deep venous thrombosis without continuing provoking risk factors (e.g. thrombophilia) for > 6 months, (no proven added benefit).
9. Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first pulmonary embolus without continuing provoking risk factors (e.g. thrombophilia) for > 12 months (no proven added benefit).
10. NSAID and vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in combination (risk of major gastrointestinal bleeding).
11. NSAID with concurrent antiplatelet agent(s) without PPI prophylaxis (increased risk of peptic ulcer disease)

Section D: Central Nervous System and Psychotropic Drugs

1. TriCyclic Antidepressants (TCAs) with dementia, narrow angle glaucoma, cardiac conduction abnormalities, prostatism, or prior history of urinary retention (risk of worsening these conditions).
2. Initiation of TriCyclic Antidepressants (TCAs) as first-line antidepressant treatment (higher risk of adverse drug reactions with TCAs than with SSRIs or SNRIs).
3. Neuroleptics with moderate-marked antimuscarinic/anticholinergic effects (chlorpromazine, clozapine, flupenthixol, fluphenzine, pipothiazine, promazine, zuclopenthixol) with a history of prostatism or previous urinary retention (high risk of urinary retention).

4. Selective serotonin re-uptake inhibitors (SSRI's) with current or recent significant hyponatraemia i.e. serum Na+ < 130 mmol/l (risk of exacerbating or precipitating hyponatraemia).
5. Benzodiazepines for ≥ 4 weeks (no indication for longer treatment; risk of prolonged sedation, confusion, impaired balance, falls, road traffic accidents; all benzodiazepines should be withdrawn gradually if taken for more than 4 weeks as there is a risk of causing a benzodiazepine withdrawal syndrome if stopped abruptly).
6. Antipsychotics (i.e. other than quetiapine or clozapine) in those with parkinsonism or Lewy Body Disease (risk of severe extra-pyramidal symptoms)
7. Anticholinergics/antimuscarinics to treat extra-pyramidal side-effects of neuroleptic medications (risk of anticholinergic toxicity),
8. Anticholinergics/antimuscarinics in patients with delirium or dementia (risk of exacerbation of cognitive impairment).
9. Neuroleptic antipsychotic in patients with behavioural and psychological symptoms of dementia (BPSD) unless symptoms are severe and other non-pharmacological treatments have failed (increased risk of stroke).
10. Neuroleptics as hypnotics, unless sleep disorder is due to psychosis or dementia (risk of confusion, hypotension, extra-pyramidal side effects, falls).
11. Acetylcholinesterase inhibitors with a known history of persistent bradycardia (< 60 beats/min.), heart block or recurrent unexplained syncope or concurrent treatment with drugs that reduce heart rate such as beta-blockers, digoxin, diltiazem, verapamil (risk of cardiac conduction failure, syncope and injury).
12. Phenothiazines as first-line treatment, since safer and more efficacious alternatives exist (phenothiazines are sedative, have significant anti-muscarinic toxicity in older people, with the exception of prochlorperazine for nausea/vomiting/vertigo, chlorpromazine for relief of persistent hiccoughs and levomepromazine as an anti-emetic in palliative care).
13. Levodopa or dopamine agonists for benign essential tremor (no evidence of efficacy)
14. First-generation antihistamines (safer, less toxic antihistamines now widely available).

Section E: Renal System. The following drugs are potentially inappropriate in older people with acute or chronic kidney disease with renal function below particular levels of eGFR (refer to summary of product characteristics datasheets and local formulary guidelines)

1. Digoxin at a long-term dose greater than 125µg/day if eGFR < 30 ml/min/1.73m2 (risk of digoxin toxicity if plasma levels not measured).
2. Direct thrombin inhibitors (e.g. dabigatran) if eGFR < 30 ml/min/1.73m2 (risk of bleeding)
3. Factor Xa inhibitors (e.g. rivaroxaban, apixaban) if eGFR < 15 ml/min/1.73m2 (risk of bleeding)
4. NSAID's if eGFR < 50 ml/min/1.73m2 (risk of deterioration in renal function).
5. Colchicine if eGFR < 10 ml/min/1.73m2 (risk of colchicine toxicity)
6. Metformin if eGFR < 30 ml/min/1.73m2 (risk of lactic acidosis).

Section F: Gastrointestinal System

1. Prochlorperazine or metoclopramide with Parkinsonism (risk of exacerbating Parkinsonian symptoms).
2. PPI for uncomplicated peptic ulcer disease or erosive peptic oesophagitis at full therapeutic dosage for > 8 weeks (dose reduction or earlier discontinuation indicated).
3. Drugs likely to cause constipation (e.g. antimuscarinic/anticholinergic drugs, oral iron, opioids, verapamil, aluminium antacids) in patients with chronic constipation where non-constipating alternatives are available (risk of exacerbation of constipation).
4. Oral elemental iron doses greater than 200 mg daily (e.g. ferrous fumarate> 600 mg/day, ferrous sulphate > 600 mg/day, ferrous gluconate> 1800 mg/day; no evidence of enhanced iron absorption above these doses).

Section G: Respiratory System

1. Theophylline as monotherapy for COPD (safer, more effective alternative; risk of adverse effects due to narrow therapeutic index).
2. Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate-severe COPD (unnecessary exposure to long-term side-effects of systemic corticosteroids and effective inhaled therapies are available).
3. Anti-muscarinic bronchodilators (e.g. ipratropium, tiotropium) with a history of narrow angle glaucoma (may exacerbate glaucoma) or bladder outflow obstruction (may cause urinary retention).
4. Non-selective beta-blocker (whether oral or topical for glaucoma) with a history of asthma requiring treatment (risk of increased bronchospasm).
5. Benzodiazepines with acute or chronic respiratory failure i.e. $pO_2 < 8.0$ kPa ± $pCO_2 > 6.5$ kPa (risk of exacerbation of respiratory failure).

Section H: Musculoskeletal System

1. Non-steroidal anti-inflammatory drug (NSAID) other than COX-2 selective agents with history of peptic ulcer disease or gastrointestinal bleeding, unless with concurrent PPI or H2 antagonist (risk of peptic ulcer relapse).
2. NSAID with severe hypertension (risk of exacerbation of hypertension) or severe heart failure (risk of exacerbation of heart failure).
3. Long-term use of NSAID (>3 months) for symptom relief of osteoarthritis pain where paracetamol has not been tried (simple analgesics preferable and usually as effective for pain relief)
4. Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthrtitis (risk of systemic corticosteroid side-effects).
5. Corticosteroids (other than periodic intra-articular injections for mono-articular pain) for osteoarthritis (risk of systemic corticosteroid side-effects).
6. Long-term NSAID or colchicine (>3 months) for chronic treatment of gout where there is no contraindication to a xanthine-oxidase inhibitor (e.g. allopurinol, febuxostat) (xanthine-oxidase inhibitors are first choice prophylactic drugs in gout).
7. COX-2 selective NSAIDs with concurrent cardiovascular disease (increased risk of myocardial infarction and stroke)

8. NSAID with concurrent corticosteroids without PPI prophylaxis (increased risk of peptic ulcer disease)
9. Oral bisphosphonates in patients with a current or recent history of upper gastrointestinal disease i.e. dysphagia, oesophagitis, gastritis, duodenitis, or peptic ulcer disease, or upper gastrointestinal bleeding (risk of relapse/exacerbation of oesophagitis, oesophageal ulcer, oesophageal stricture)

Section I: Urogenital System

1. Antimuscarinic drugs with dementia, or chronic cognitive impairment (risk of increased confusion, agitation) or narrow-angle glaucoma (risk of acute exacerbation of glaucoma), or chronic prostatism (risk of urinary retention).
2. Selective alpha-1 selective alpha blockers in those with symptomatic orthostatic hypotension or micturition syncope (risk of precipitating recurrent syncope)

Section J. Endocrine System

1. Sulphonylureas with a long duration of action (e.g. glibenclamide, chlorpropamide, glimepiride) with type 2 diabetes mellitus (risk of prolonged hypoglycaemia).
2. Thiazolidenediones (e.g. rosiglitazone, pioglitazone) in patients with heart failure (risk of exacerbation of heart failure)
3. Beta-blockers in diabetes mellitus with frequent hypoglycaemic episodes (risk of suppressing hypoglycaemic symptoms).
4. Oestrogens with a history of breast cancer or venous thromboembolism (increased risk of recurrence).
5. Oral oestrogens without progestogen in patients with intact uterus (risk of endometrial cancer).
6. Androgens (male sex hormones) in the absence of primary or secondary hypogonadism (risk of androgen toxicity; no proven benefit outside of the hypogonadism indication).

Section K: Drugs that predictably increase the risk of falls in older people

1. Benzodiazepines (sedative, may cause reduced sensorium, impair balance).
2. Neuroleptic drugs (may cause gait dyspraxia, Parkinsonism).
3. Vasodilator drugs (e.g. alpha-1 receptor blockers, calcium channel blockers, long-acting nitrates, ACE inhibitors, angiotensin I receptor blockers,) with persistent postural hypotension i.e. recurrent drop in systolic blood pressure ≥ 20mmHg (risk of syncope, falls).
4. Hypnotic Z-drugs e.g. zopiclone, zolpidem, zaleplon (may cause protracted daytime sedation, ataxia).

Section L: Analgesic Drugs

1. Use of oral or transdermal strong opioids (morphine, oxycodone, fentanyl, buprenorphine, diamorphine, methadone, tramadol, pethidine, pentazocine) as first line therapy for mild pain (WHO analgesic ladder not observed).
2. Use of regular (as distinct from PRN) opioids without concomitant laxative (risk of severe constipation).
3. Long-acting opioids without short-acting opioids for break-through pain (risk of persistence of severe pain)

Section N: Antimuscarinic/Anticholinergic Drug Burden

Concomitant use of two or more drugs with antimuscarinic/anticholinergic properties (e.g. bladder antispasmodics, intestinal antispasmodics, tricyclic antidepressants, first generation antihistamines) (risk of increased antimuscarinic/anticholinergic toxicity)

APPENDIX 4: Clinical Institute Withdrawal Assessment – Alcohol Revised (CIWA-Ar)

Monitor for signs of withdrawal every 1-2 hours for 24 hours.

Date							
Time							
Nausea and vomiting **Do you feel sick to your stomach? Have you vomited?** 0 No nausea and vomiting 1 Mild nausea with no vomiting 2 3 4 Intermittent nausea with dry heaves 5 6 7 Constant nausea, frequent dry heaves & vomiting							
Tremor – Arms extended and fingers spread apart. 0 No tremor 1 Not visible but can be felt fingertip to fingertip 2 3 4 Moderate with patients arm extended 5 6 7 Severe even with arms not extended							
Paroxysmal sweats 0 No sweat visible 1 Barely perceptual sweating, palms moist 2 3 4 Beads of sweat obvious on forehead 5 6 7 Drenching sweats							
Anxiety – Ask: do you feel nervous? 0 No anxiety, at ease 1 Mild anxiety 2 3 4 Moderately anxious, or guarded, so anxiety inferred 5 6 7 Equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions							
Agitation Observation 0 Normal activity 1 Somewhat more than normal activity 2 3 4 Moderately fidgety and restless 5 6 7 Paces back and forth during most of interview or constantly thrashes about							
Tactile disturbances – Ask: Have you experienced any itching, pins and needles, burning or numbness, or do you feel bugs crawling on or under your skin? 0 None 1 Very mild itching, pins and needles, burning or numbness 2 Mild itching, pins and needles, burning or numbness 3 Moderate itching, pins and needles, burning or numbness 4 Moderately severe hallucinations 5 Severe hallucinations 6 Extremely severe hallucinations 7 Continuous hallucinations							

Auditory disturbances – Ask: Are you more aware of sounds around you? Are they harsh? Do they startle/frighten you? Are you hearing anything that is disturbing to you? Are you hearing things that you know are not there? 0 Not present 1 Very mild harshness or ability to startle/frighten 2 Mild harshness or ability to startle/frighten 3 Moderate harshness or ability to startle/frighten 4 Moderately severe hallucinations 5 Severe hallucinations 6 Extremely severe hallucinations 7 Continuous hallucinations							
Visual disturbances – Ask: Does the light appear to be too bright? Is its colour different from normal? Does it hurt your eyes? Are you seeing anything that disturbs you or that you know isn't there? 0 Not present 1 Very mild sensitivity 2 Mild sensitivity 3 Moderate sensitivity 4 Moderately severe hallucinations 5 Severe hallucinations 6 Extremely severe hallucinations 7 Continuous hallucinations							
Headache fullness in head Ask: Does your head feel different to usual? Does it feel like there is a band around your head? (Do not rate for dizziness or light headedness). Observe, rate severity. 0 Not present 1 Very mild 2 Mild 3 Moderate 4 Moderately severe 5 Severe 6 Very severe 7 Extremely severe							
Orientation and clouding of sensorium Ask: What day is it? Where are you? Who am I? 0 Oriented and can do serial additions 1 Cannot do serial additions and/or is uncertain about date 2 Disoriented to date by no more than 2 calendar days 3 Disoriented to date by more than 2 calendar days 4 Disoriented to place and/or person							
Total CIWA-Ar Score (max possible 67)							

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