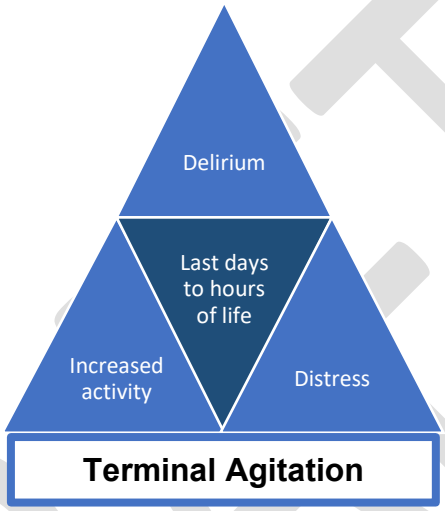
Last days of life: severe agitation, delirium or distress

Scottish Palliative Care Guidelines

Healthcare Improvement Scotland

Introduction

For the purposes of this guideline, the terms "terminal agitation" and "severe agitation, delirium or distress in the last days of life" are used interchangeably.



Definition

Terminal agitation is an umbrella term which encompasses a triad of increased psychomotor activity, distress and delirium that occurs exclusively in the last days to hours of life. It is considered one of the most distressing and difficult aspects of the normal dying process.

Presentation

Individual presentations vary as does their overall severity. Terminal agitation is common.

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People with terminal agitation may demonstrate some of the following behaviours:

Psychological	Verbal	Physical
Anxiety Distress Confusion Paranoia Anger	Groaning Calling for help Persistent need to "go somewhere" such as home, toilet (even if catheterised) Verbal aggression	Restlessness or non-purposeful movement Plucking at sheets or clothes Reaching up for something that's not there Pulling at intravenous lines or catheter Trying to get out of bed or chair Physical aggression

Causative and reversible factors

Terminal agitation should only be diagnosed **once reversible factors have been excluded** or **deemed inappropriate to further investigate or treat,** and the patient is in the last days of life. Reversible factors may include:

- urine retention/constipation
- drug toxicities or drug withdrawals
- severe hepatic or renal impairment
- infection
- hypoxia
- electrolyte imbalances (sodium and corrected calcium), and/or
- steroid use.

It can be very difficult to recognise when a person is entering their last days of life. If unsure about whether there is reversibility, please seek experienced or specialist advice.

Predisposing factors

The underlying cause of terminal agitation is unknown but is very likely multifactorial, with the following thought to increase risk:

- **physical symptoms**: difficult to manage pain or breathlessness
- **psychological factors**: previous life trauma, fear, denial, pre-existing mental health diagnoses
- **existential and spiritual factors**: spiritual distress, existential crisis, denial, previous avoidance of future care planning, younger age, and

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- **social factors**: young children, complex family dynamics, highly anxious family, substance misuse history, previous incarceration.

People experiencing the most severe cases of terminal agitation tend to have multiple predisposing factors. Early identification of these factors by ongoing holistic enquiry allows us to plan ahead, and to prepare patients, loved ones and staff.

Assessment

Effective assessment and communication of terminal agitation is key to manage expectations, reduce distress and minimise conflict among loved ones and care teams, and members of the multidisciplinary team.

Richmond Agitation Sedation Scale – Palliative Version (RASS-PAL) is a simple observational bedside scale which can be administered by any member of the multidisciplinary team in around one minute and should be used to guide the management of terminal agitation. See RASS-PAL (pdf).

RASS-PAL describes a patient's behaviour and cognitive state using a numbered scale with:

- increasing positive scores describing a patient with escalating state of agitation
- a score of zero representing a calm and alert patient, and
- decreasing negative scores describing a patient with a deepening level of sedation.

RASS-PAL is not intended to detect delirium.

Non-pharmacological management

Supportive care

Whilst there is no evidence for non-pharmacological strategies in the management of terminal agitation, supportive strategies such as those used in delirium may be helpful or comforting for patients and loved ones and represent good practice in holistic person-centred care. These techniques may be used in people with less severe symptoms, or to supplement a medication-based approach. (See Delirium Guideline)

To enhance symptom control, attentive personal and comfort care should continue, focusing on:

- bladder and bowel care
- mouth care

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- skin and pressure care
- nicotine replacement therapy for individuals who smoke, and
- active and passive methods to reduce pyrexia.

Pharmacological management

Palliative sedation

Palliative sedation is the intentional, proportionate use of medications to reduce consciousness in people experiencing severe agitation, delirium or distress in the last days of life. The following key principles apply:

- **Continuous light sedation**: use of continuous subcutaneous infusion (CSCI) to achieve a RASS-PAL goal of a score of -1 to -3.
- **Constant communication**: an ongoing dialogue around shared goals between patients, loved ones and staff can help manage expectations and reduce distress.
- **Explaining drug choices/delivery**: it takes 4–6 hours for CSCI changes to equilibrate in the body, and it is normal to need medications as required (PRN) both before and after this point. It is important to convey that use of sedating medications is a process and not an immediate “off-switch” for difficult symptoms.
- **Clear sedation goals**: sedative medications should be titrated to the minimum level required to achieve patient comfort. This does not mean that all patients should be completely unresponsive and still. An initial RASS-PAL score of -1 to -3, or “drowsy” to “moderate sedation”, is recommended provided that the patient is comfortable and not distressed.
- Opioids should **not** be used to achieve sedation. Opioids remain appropriate to manage symptoms of pain or breathlessness that may be contributing to a person’s agitation or distress.

Special patient populations

Please seek immediate specialist advice for severe agitation, delirium or distress in the last days of life in those with a history of:

- substance use disorder
- antipsychotic or atypical antidepressant medication use for underlying mental health issues
- Lewy body dementia, or
- Parkinson’s disease.

Individuals with any of these histories may need different alternative choices or doses for symptom control.

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Person centred considerations

Cultural aspects	Some faiths are uncomfortable with the use of sedation at the end of life, and some faiths have specific practices leading up to death which are culturally important.
Communication	The ability to communicate may be reduced when sedation is used, meaning the person cannot interact with loved ones or healthcare professionals. There should be an opportunity to say goodbye where possible before commencing sedation.
Comfort care	All comfort and dignity care will continue to be provided, including mouth care, personal care and repositioning.
Nutrition and hydration	The ability to manage oral food or fluid intake is likely to be lost as part of the normal dying phase of illness, this may be reduced further by sedation. Artificial hydration and nutrition requests may be evaluated on an individual basis, considering patients' and loved ones' wishes, local practices and national guidance. No robust evidence exists yet to weigh up potential risks and benefits of these interventions in the last days of life.

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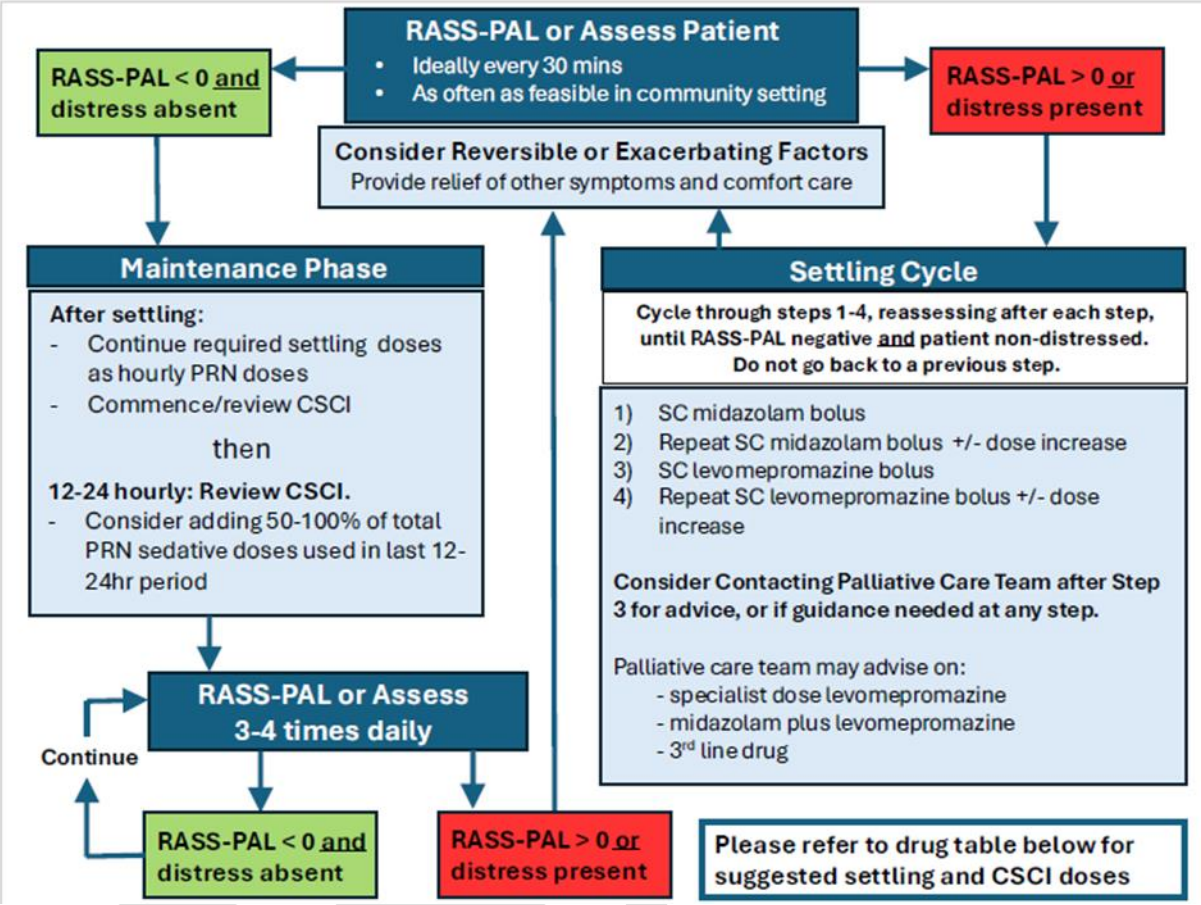
Terminal agitation



If unable to use RASS-PAL, regularly assess the patient's condition and comfort level with the same suggested frequency. It is recognised that this may be challenging to achieve in some settings, such as in the community.

(See section below Doses: First- and second-line sedative medication for dosing information)

Settling cycle

If the RASS-PAL score is >0, begin a settling cycle which is a repeating process:

- Administer a subcutaneous (SC) bolus dose of sedative medication.
- Reassess its effect on person after 30 minutes.
- If the person's RASS-PAL score
    - remains positive (>0) or they appear distressed escalate to next medication step, but if it
    - is negative (<0) and they are not distressed move to the maintenance phase.

Suggested bolus medication steps in the settling cycle are:

1. midazolam SC bolus
2. repeat midazolam SC bolus, or consider giving increased dose
3. levomepromazine SC bolus, and
4. repeat levomepromazine SC bolus or consider giving increased dose.

Consider seeking specialist palliative care support after step 3, or if advice is needed at any step.

Doses: First- and second-line sedative medication

The following contains recommendations for first- and second-line sedative dose ranges.

Doses should be titrated with the aim of using the lowest doses possible to relieve agitation or distress and optimise patient comfort.

Settling doses can be administered at 30-minute intervals, moving back to standard 1-hourly PRN doses once sedation goal is achieved.

First-line: midazolam.

SC bolus dose: 2 mg as required.

Note that younger people or those with prior benzodiazepine tolerance may require SC Bolus dose 2–5 mg.

If further titration is required specialist palliative care advice should be sought.

Note: some centres use low dose **haloperidol** as an adjunct to midazolam as a first-line strategy, particularly if delirium is evident.

Second-line: levomepromazine.

SC bolus dose: 2 mg as required.

- Continue midazolam but discontinue any haloperidol before adding levomepromazine.
- Note that younger people or people in severe agitation (+3 or more) a higher starting dose of 5–10 mg SC as required second line for agitation, maximum once hourly, maximum six total doses in 24 hours.
- It is good practice to review the patient once three or more doses have been used in 24 hours. Do not exceed six doses without medical review.
- Use 5 mg in elderly patients, those with organ failures and those who are benzodiazepine naïve.

Important: It takes 3 hours for levomepromazine to reach peak effect from a SC bolus dose, and 3 days to a steady state from initiation of a syringe driver. It is helpful to observe the settling total dose needed in the first 24 hours before commencing a syringe driver with 100% of the prior 24-hour dose requirement, aiming to maintain the same level of comfort.

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Please seek urgent specialist palliative care advice if:

- Person is experiencing severe distress or is RASS-PAL +4 as higher initial settling doses may be necessary for safety.
- Bolus or CSCI doses reach upper limits shown above.
- Person has a history of substance use disorder, antipsychotic use, atypical antidepressant use, Parkinson's disease or Lewy body dementia.

Specialist advice may include increased bolus doses as SC/intramuscular bolus doses of 25 mg, use of combination midazolam and levomepromazine bolus doses, or escalation to a third-line sedative medication.

QT prolongation is **not** a concern in the last short days of life.

Maintenance phase

- Use doses of SC bolus medications established during the settling phase. Repeat hourly as required, with a maximum of six doses in 24 hours. If this maximum is reached the patient should be reviewed and the dose may need to be altered.
- Review CSCI: consider adding 50–100% of total established PRN doses of midazolam and/or 100% levomepromazine required in last 24 hours to existing CSCI doses.
- Assess RASS-PAL score 3–4 times daily.
- If the patient's RASS-PAL is negative (<0) and they are not distressed, continue current management.
- If the patient's RASS-PAL score remains positive (>0) or they appear distressed move back to settling cycle.

For CSCI drug compatibilities please see Syringe Pump/Driver Compatibles.

Managing goals and expectations

Differences in expectations are a potential source of conflict for anyone who may be present when a person is actively dying, and this is particularly true when sedative medications are being used to manage agitation or distress.

Managing expectations involves:

- **Constant communication**: an ongoing dialogue around shared goals between patients, loved ones and staff can help manage expectations and reduce distress.
- **Explaining drug choices/delivery:** it takes 4-6 hours for CSCI changes to equilibrate in the body, and it is normal to need PRN doses of medications both before and after this point. It is important to convey that use of sedating medications is a process and not an immediate "off-switch" for difficult symptoms.
- **Clear sedation goals:** sedative medications should be titrated, in line with symptomatic need, to the minimum level required to achieve patient comfort. This does not mean that all patients should be completely unresponsive and still. An initial RASS-PAL score of -1 to -3, or "drowsy" to "moderate sedation", is recommended provided that the patient is comfortable and non-distressed.

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Assessment and monitoring

Recording RASS-PAL scores allows us to objectively demonstrate both

- **proportionality**: whether the medications and doses we use are appropriate in each individual scenario, and
- **efficacy**: whether we are achieving our aim to relieve suffering by means of deliberate reduction of consciousness.

Collaboration

The decision to manage difficult symptoms in the last hours to days of life with sedative medications should be made collectively between the patient, their loved ones and the care team. Some clinicians include this discussion much earlier in a person's illness as part of future care planning. Ongoing and open conversation is needed at every stage of the process, from refractory symptom onset until after death has occurred.

Documentation

Clear documentation and discussion around each step in the decision-making process is essential

Evidence base

There is no high-quality evidence for any of the medications used in palliative care for the specific indication of terminal agitation, because conducting randomised-controlled trials with distressed participants in their last hours to days of life would be unethical. Medication guidance in this clinical guideline therefore reflects expert opinion on current best practice.

Debrief and support

Witnessing a difficult death can bring high levels of psychological distress for families and care teams alike.

Care of the bereaved

- **Risk of complex grief**: terminal agitation prevents formation of peaceful memories, leading to inability to find meaning in death. Families should be given the chance to discuss the death with the care team, and to ask questions, to help them achieve closure.
- **Future expectations:** experiencing the terminal agitation of a loved one may result in individuals fearing their own death, thus developing risk factors for terminal agitation themselves.
- **Bereavement support**: independent hospices often offer bereavement support as standard for family members. Outwith hospice care, loved ones can be directed to their own GP, local bereavement services and online support such as Good Life, Good Death, Good Grief.

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Care of colleagues and teams

- **Moral injury:** witnessing intense suffering leads to moral injury in staff. This can be compounded by feelings of helplessness or failure around resistant symptoms, any interpersonal or team conflicts, and lead to difficulty "switching off" at the end of a shift. Staff experiencing prolonged moral injury are at risk of developing burnout.
- **Debrief:** formal debrief can be helpful for clinical teams by facilitating learning and diffusing tension after challenging cases. Informal debrief may also involve peer support and opportunities to reminisce about the deceased person which can be comforting for staff.
- **Wellbeing resources:** some hospices offer integrated staff support for team members who are struggling. NHS staff can reach out to their occupational health team or to the National Wellbeing Hub, a confidential service for NHS health and social care staff in Scotland.

Key points

- Terminal agitation can often be part of the dying phase. It is important to prepare families and staff if a person is at higher risk of experiencing this, as well as to support families and staff during the period of agitation, and after death.
- Effective and timely management is key to prevent complex grief in bereaved loved ones, and reduce distress, conflict and moral injury within care teams.
- RASS-PAL is a recommended objective, observational tool used to assess the patient, aid communication around the clinical presentation of the patient as well as assessing the efficacy of administered medicines in reducing agitation. RASS-PAL strongly correlates with patient comfort.
- Proportionate palliative sedation is standard intervention to relieve patient distress (an intentional act). The goal of care is to deliver the least amount of sedating medication necessary to achieve acceptable symptom control and comfort in the quickest time possible.
- There is no high-quality evidence for medications used in palliative care for terminal agitation. There is a wide variation in specialist practice based on clinicians' experience, care setting and geographical location. This guideline is a suggested approach based on expert opinion and current good practice.
- Opioid medications should not be used to achieve sedation.

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