Delirium management by palliative medicine specialists: a survey from the association for palliative medicine of Great Britain and Ireland

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Abstract

Objectives Delirium is common in palliative care settings. Management includes detection, treatment of cause(s), non-pharmacological interventions and family support; strategies which are supported with varying levels of evidence. Emerging evidence suggests that antipsychotic use should be minimised in managing mild to moderate severity delirium, but the integration of this evidence into clinical practice is unknown.

Methods A 21-question online anonymous survey was emailed to Association for Palliative Medicine members in current clinical practice (n=859), asking about delirium assessment, management and research priorities.

Results Response rate was 39%; 70% of respondents were palliative medicine consultants. Delirium guidelines were used by some: 42% used local guidelines but 38% used none. On inpatient admission, 59% never use a delirium screening tool. Respondents would use non-pharmacological interventions to manage delirium, either alone (39%) or with an antipsychotic (58%). Most respondents (91%) would prescribe an antipsychotic and 6% a benzodiazepine, for distressing hallucinations unresponsive to non-pharmacological measures. Inpatient (57%) and community teams (60%) do not formally support family carers. Research priorities were delirium prevention, management and prediction of reversibility.

Conclusion This survey of UK and Irish Palliative Medicine specialists shows that delirium screening at inpatient admission is suboptimal. Most specialists continue to use antipsychotics in combination with non-pharmacological interventions to manage delirium. More support for family carers should be routinely provided by clinical teams. Further rigorously designed clinical trials are urgently needed in view of management variability, emerging evidence and perceived priorities for research.

Introduction

Delirium is an acute onset neurocognitive disorder characterised by disturbance in attention, awareness and cognition, which fluctuates during a 24-hour period. Delirium has multiple aetiologies and is common in patients receiving palliative care. It is present in 13%–42% of patients admitted to specialist palliative care inpatient units, 26%–62% during admission and 59%–88% in the last weeks of life. It is associated with falls, increased cognitive impairment after discharge and a poor prognosis.

Delirium causes high levels of distress for patients, their families and healthcare practitioners. Delirium is underdiagnosed across many clinical settings including cancer and palliative care. In one study of palliative care inpatient consults, delirium diagnosed subsequently by a palliative medicine specialist had been missed by the primary referring team in 61% of patients. Patients with missed delirium were frequently referred for pain control. In people with advanced disease, dementia or generalised central nervous system dysfunction, the diagnosis of delirium poses challenges. Furthermore, hypoactive delirium, the most underdiagnosed subtype of delirium, is...
the most prevalent subtype (68%–86% of cases) in palliative care settings.3

Detection and assessment/diagnosis is the first critical step; failure to conduct an adequate assessment commonly results in a missed diagnosis.2 11 Delirium assessment based solely on clinical judgement leads to underdetection.2 11 Validated assessment tools exist for screening, diagnosing and monitoring the severity of delirium in cancer and palliative care populations.2 11

The management of delirium is multifaceted and multidisciplinary. It includes assessment, treating the underlying causes if appropriate (50% of episodes are reversible), non-pharmacological interventions and family support.2 11 16 17 Family caregivers are important in the management of a patient with delirium.5–10 Multicomponent interventions, involving volunteers and family members, have demonstrated major reductions in delirium incidence and length of delirium cases in older (≥70 years of age) hospitalised patients compared with control groups receiving usual care.18 Pharmacological management is commonly used to specifically treat the symptoms of delirium or provide sedation for the agitated patient. Although not specifically targeting populations receiving palliative care, recent systematic reviews in heterogeneous populations do not support antipsychotic use in hospitalised patients with delirium.19 20

There are varied levels of evidence for the management of delirium and its distressing clinical components, and not all have been evaluated specifically in palliative care. As such, clinician’s opinion drives practice in this setting. Based largely on a double-blind, non-placebo-controlled trial,21 haloperidol has been the ‘practice standard’ in the symptomatic management of delirium in palliative care.22 In the largest randomised controlled trial (RCT) of palliative care patients (N=247) with mild to moderate severity delirium (assessed by the Memorial Delirium Assessment Scale (MDAS)) and with Australia-modified Karnofsky Performance Status of 30%–50%, the severity and duration of behavioural, communication and perceptual symptoms of delirium were greater in those who received either risperidone or haloperidol compared with placebo.23 In a recent single-centre RCT, hospitalised patients with advanced cancer with persistent agitated delirium, Karnofsky Performance status of 10%–40% treated with haloperidol, additional lorazepam increased the level of sedation at 8 hours compared with placebo.24 Neither lorazepam nor placebo improved the overall severity of delirium. The trial did not include a haloperidol placebo arm and does not inform the debate regarding the place of antipsychotics in the management of delirium. A Cochrane review found ‘insufficient evidence’ for drug therapy specific to delirium in terminally ill adult patients, suggesting that further research is necessary and that healthcare professionals should remain in line with up-to-date clinical guidelines.25

In view of this emerging evidence, there is a need to determine the current clinical practice of specialist palliative medicine physicians regarding their approach to delirium assessment, management and research prioritisation.

METHODS

Study design

A cross-sectional online survey design to collect quantitative and qualitative data.

Survey development

A review of the literature and previously published surveys informed the development of this online survey. The draft survey was developed and reviewed by experts in palliative medicine. After pilot testing among Marie Curie Palliative Medicine specialists in the UK (N=24), it was further modified based on their feedback (table 1).

Survey sampling

The Association for Palliative Medicine (APM) of Great Britain and Ireland is the largest organisation

| Table 1 | Outline of survey contents (see online supplementary appendix 1 for full survey) |
|---------|-----------------------------------------------------------------------------------|
| Sections | Key information |
| Section I (questions 1–5): demographic details | ▶ Current position/role  
▶ Number of years in practice  
▶ Practice settings of respondent (more than one response possible if applicable)  
▶ Delirium screening practices and tools used, if any |
| Section II (questions 6–10): cognitive and delirium screening as part of inpatient care | ▶ Delirium screening tools used, if any  
▶ Frequency of screening tool use |
| Section III (questions 11–13): delirium in the home setting and referral for inpatient admission in the last year | ▶ Number of patients seen with delirium in the community in the preceding year and the need for inpatient admission care for these patients  
▶ Factors influencing decision to recommend inpatient admission |
| Section IV (questions 14–17): specific delirium practices as part of inpatient care | ▶ Use of guidelines in symptomatic treatment of delirium  
▶ Use of non-pharmacological interventions in delirium management  
▶ Clinical scenario and respondents’ choice of pharmacological management*  
▶ Proportion of patients for which deep or palliative sedation was recommended at end of life |
| Section V (questions 18 and 19): education and support of family carers | ▶ Formal support mechanisms in respondents’ practice setting(s) for family members of patients with delirium (more than one response possible if applicable) |
| Section VI (question 20): delirium research priorities in palliative care | ▶ Respondents’ perceived research priorities to inform their clinical management of delirium |
| Survey conclusion (question 21) | ▶ Additional comments (open ended) |

*The clinical scenario posed a patient with distressing hallucinations due to delirium unresponsive to non-pharmacological measures.
of specialist Palliative Medicine physicians in the UK/Ireland, with over 1000 members (https://apmonline.org/). Eligibility criteria restricted the survey to currently practising Palliative Medicine specialists. These physicians see patients with life-limiting conditions, including cancer (any site) and non-cancer illnesses.

Survey and procedure
The survey was administered online via a secure online platform, SurveyMonkey (www.surveymonkey.com/). The final 21-question anonymous survey weblink was emailed by the APM Secretariat to preserve anonymity to all members of the APM (N=1121; 859 of which were currently practicing Palliative Medicine specialists according to APM records) on 28 February 2017. Three follow-up reminder emails were sent out to non-responders. The survey could only be completed once by each participant. Skip logic facilitated answers to specific practice setting-related questions.

Data analysis
Descriptive statistics, percentages and weighted averages were computed for the appropriate quantitative data study variables using Microsoft Excel (2010). Surveys of respondents who did not identify themselves as Palliative Medicine specialists in current practice, or who had missing data for the first five demographic questions were excluded from analysis.

RESULTS
Of 1121 APM members surveyed between 28 February 2017 and 22 July 2017, 364 responded. Out of the 364 responses, 32 were excluded due to not being in current practice, not identifying themselves as Palliative Medicine specialists or not completing the survey’s first five demographic questions. Of the 859 APM members who were known Palliative Medicine specialists in current practice, the overall survey response rate was 39% (332/859) (table 2). Not all respondents answered all questions, so the denominator is variable for subsequent questions.

Screening tool use
In the questions regarding tool and guideline use, respondents were asked to answer on behalf of the palliative care team within which they worked. Table 3 summarises screening tool use for cognitive deficits/ dementia and delirium.

Respondents who indicated that their palliative care teams use a tool to screen for cognitive deficits or dementia at inpatient assessment commonly used the Mini-Mental State Examination (MMSE) (143/231; 62%), with the 4’A’s test (4AT) and Montreal Cognitive Assessment (MoCA) each being used by 10% (24/231). The Short Orientation-Memory-Concentration Test/Blessed Orientation-Memory-Concentration (10/231; 4%) and Addenbrooke’s Cognitive Examination (2/231; 1%) were less frequently used to screen for cognitive deficits or dementia at inpatient assessment. Other tools, such as the Confusion Assessment Method (CAM), Abbreviated Mental Test (AMT), clock drawing task and six-item Cognitive Impairment Test (6CIT), were used by 12% (28/231) of teams.

Respondents who indicated that their palliative care teams use a tool to screen for delirium on the first inpatient assessment regularly used the CAM (59/127; 46%), followed by the 4AT (28/127; 22%). Other tools, such as The Delirium Observation Screening Scale (DOSS), Family Confusion Assessment Method (FAM-CAM), Single Question in Delirium, MMSE, the MoCA and AMT were used by 32% (40/127).

Delirium guideline use
Delirium guidelines were inconsistently used, with 42% (115/276) of specialist palliative care teams using local guidelines and 38% (104/276) using none. Others (57/276; 21%) stated they used other guidelines such as Palliative Medicine specialist guidelines and local guidelines.

Table 2 Demographics of the 332 palliative medicine specialist respondents (survey questions 1–5)

| Characteristics | Subcategories | N (%) |
|-----------------|---------------|-------|
| Role†           | Consultant in Palliative Medicine | 232 (70) |
|                 | Staff grade or Associate Specialist in Palliative Medicine | 50 (15) |
|                 | Specialist Trainee or Registrar in Palliative Medicine | 50 (15) |
| Experience working in palliative medicine | <1 year | 5 (2) |
|                 | 1–4 years | 44 (13) |
|                 | 5–10 years | 81 (24) |
|                 | >10 years | 202 (61) |
| Clinical practice in palliative medicine | Only inpatient care | 130 (39) |
|                 | Only community care | 9 (3) |
|                 | Both inpatient and community care | 193 (58) |
| Palliative care settings‡ | Cancer centre | 62 (19) |
|                 | Community hospital | 45 (14) |
|                 | General hospital | 146 (44) |
|                 | Hospice care | 265 (80) |
|                 | Long-term care/Nursing home | 63 (19) |
|                 | Patient’s home | 169 (51) |
|                 | Teaching hospital | 119 (36) |
|                 | Other | 9 (3) |
| Hours spent providing care in an average week | 0 | 0 (0) |
|                 | 1–10 | 12 (4) |
|                 | 11–20 | 83 (25) |
|                 | 21–30 | 111 (33) |
|                 | 30 or more | 126 (38) |

*Total N=332.
†Consultant: fully trained specialist in Palliative Medicine; Staff grade or Associate Specialist in Palliative Medicine: non-consultant grade specialist in Palliative Medicine; Specialist Trainee or Registrar in Palliative Medicine: physician undergoing Palliative Medicine specialty training.
‡If participants worked in multiple settings, they were able to select all that applied.
as The National Institute for Health and Care Excellence (NICE), Scottish Intercollegiate Guidelines Network, Palliative Adult Network Guidelines and Palliative Care Formulary.

Delirium care in the community
The majority (135/176; 77%) of Palliative Medicine specialists would recommend inpatient admission to either hospital or hospice in no more than 50% of patients seen with delirium in their own homes over the past year. Reasons for admission in the context of delirium varied but was most commonly due to inability of family caregivers to cope (figure 1).

Non-pharmacological interventions
Most respondents would routinely use non-pharmacological interventions (such as pursue optimal sound and/or lighting levels; gently reorientate; facilitate the presence of a family member) to manage delirium, either alone (106/275; 39%) or more commonly with an antipsychotic (160/275; 58%). Nine out of 275 (3%) would not routinely use non-pharmacological interventions.

Sedation
Out of 271 respondents, 130 (48%) reported rarely (<5% of cases) prescribing or recommending deep or palliative sedation for inpatients in the last days/ weeks of life with non-reversible, refractory agitated delirium. Twenty-seven per cent (73/271) reported doing so in 5%–20% of cases, with 10% (28/271) in 21%–40% of cases, 8% (23/271) in 41%–60% of cases and 6% (17/271) of respondents doing so in most (>60%) of the patients they see in this situation.

Respondents commented on their perspectives on sedation in the final open-ended question, indicating it was hard to distinguish between alleviating distress and providing palliative sedation and open to a wide range of interpretations.
Clinical scenario
Most physicians would prescribe an antipsychotic as an initial medication choice 248/273 (91%), with 190/273 (70%) using typical antipsychotics and 43/273 (16%) using atypical antipsychotics first line. Six per cent (16/273) would prescribe a benzodiazepine, 5% (15/273) would prescribe combination antipsychotic and benzodiazepine and 2% (5/273) would not use medication. In open-ended responses, respondents indicated uncertainty about using antipsychotics for the management of delirium after the publication of the Agar et al’s RCT. Respondents also indicated the importance of addressing reversible causes of delirium on a case-by-case basis and the challenges in optimising non-pharmacological interventions in busy inpatient settings.

Support of family carers
Most inpatient (153/270; 57%) and community teams (97/161; 60%) do not formally support family carers in a systematic or standardised manner. Palliative care specific information leaflets about delirium were only provided as a standard approach in 10% (27/270) of teams in inpatient settings and 7% in the community. Similarly, a generic information leaflet about delirium was not widely provided as part of inpatient (22/270; 24%) and community services (10/161; 6%). Informal verbal support was offered by 24% (64/270) in the inpatient setting and 22% (35/161) in community settings.

Delirium research priorities
Research priorities were prevention, prediction of reversibility and management (non-pharmacological and pharmacological). Respondents (n=270/335; 81%) rated the importance (0=not at all, and 4=extremely important, as anchors) of domains for future research; the three highest weighted average scores were for research on preventive strategies (2.91/4), prediction of delirium reversibility (2.96/4) and the pharmacological and non-pharmacological management of delirium (3.19/4).

DISCUSSION
This survey represents many experienced UK and Irish palliative medicine physicians. Over a third never used delirium clinical guidelines, although just under half used local guidelines. Most never used delirium screening tools. Just over half use non-pharmacological interventions to manage delirium. For distressing hallucinations unresponsive to non-pharmacological measures, most prescribe antipsychotics, but very few a benzodiazepine. Family support was informal. Delirium was reported a clinically important topic with uncertainties about best practice. Research priorities were delirium prevention, management and prediction of reversibility.

Tool and guideline use
Screening tools are used only if delirium is clinically suspected, rather than systematically on admission and during the patient’s care. This is at variance with the literature and guideline recommendations for delirium screening, which advise screening for delirium using a tool, and patient/family consultation on admission and on an ongoing basis to assess fluctuations in risk factors causing delirium and in order to detect delirium early.

Delirium guidelines were not used regularly by most of the teams, and when used, were mostly local guidelines. Although the NICE guidelines have a national UK purview, they are not specific to palliative care and excluded people at the end of life from their recommendations. This identifies a major issue with delirium guidelines; although patients with advanced illness are cared for in the settings for which these guidelines apply, there is little about how the evidence relating to caring for someone with delirium applies to patients at the end of life. There are other delirium guidelines available for national use, such as the Canadian Coalition for Seniors’ Mental Health (CCSMH) guidelines, which are specific for older people at the end of life, although these are infrequently used according to this study’s findings, suggesting a lack of geographical reach.

Our results contrast with a survey of European Delirium Association (EDA) members (only 4% were palliative care specialists), of whom 52% always or mostly use a scale to assess delirium, typically either the CAM (52%) or DOSS (30%) and 86% would review at least once a day. Most respondents (78%) reported that their institutions had specific guidelines for delirium.

Similar to cognitive screening, delirium screening tools were seldom used and rarely used consistently. When used, the CAM and 4AT were most commonly used. These results are consistent with the guidelines, NICE advises use of the short CAM or Diagnostic and Statistical Manual of Mental Disorders (DSM) IV for diagnosis and CCSMH recommends use of the CAM as a diagnostic measure in conjunction with the MMSE for assessment of cognition. A survey of Palliative Medicine specialists found the MMSE (39%), AMTs (27%) or clinical judgement alone (35%) was used to identify cognitive impairment.

In this survey, the MMSE was used by the majority of respondents to screen for cognitive deficits or dementia, whereas a few respondents used the MMSE to screen for delirium at inpatient assessment. The MMSE is neither designed nor recommended as a diagnostic tool to confirm delirium. Thus, there may be a need for improved clinical uptake of delirium screening tools as an initial screening method, although some palliative care patients find it difficult to complete, so a shorter cognitive test could be used.

Delirium care in the community
Most patients with delirium were deemed manageable at home. These findings are echoed in an Australian survey, where palliative medicine specialists would generally manage delirium in the patients’ home.
In this survey, the inability of family caregivers to cope was the most common reason for admission. As a change in environment can increase problems for older people with cognitive issues and delirium, if carer stress and coping can be supported and the patient can be managed at home, care at home might be warranted. Providing support and education for family caregivers is not only essential in the management of delirium but is also important in potentially reducing admissions and family distress.

**Non-pharmacological interventions**

Although most respondents indicated that they use non-pharmacological strategies to manage delirium either in conjunction with an antipsychotic (58%) or as a sole strategy (39%), this should be an essential part of care by all clinical teams. In an Australian survey, 85% of palliative medicine specialists would generally use non-pharmacological management. In an European Delirium Association survey, 67% initially used non-pharmacological management in hypoactive delirium and 61% initially used a combination of non-pharmacological and pharmacological interventions for hyperactive delirium.

**Sedation**

Palliative sedation has been defined as administration of sedative drugs to reduce the consciousness of a terminal patient as much as necessary to relieve refractory symptoms. ‘Deep or palliative sedation’ was used in the survey question stem and some respondents reported being unable to accurately answer the question. The overwhelming response was that sedation might be an unintended consequence of pharmacologically managing the delirium. Palliative sedation was rarely used by respondents, accepting that patients might become sedated as a result of a balanced approach to controlling symptoms and delirium, though sedation was not the primary intention of therapy. Although this is in line with UK practice, a systematic review identified refractory agitation as the main symptomatic indication for palliative sedation.

**Case scenario of management of a patient with agitated delirium**

Most respondents would prescribe an antipsychotic for a patient with distressing hallucinations, delusions and agitation unresponsive to non-pharmacological measures. The role of antipsychotics in the management of distressing delirium with severe specific symptoms in patients receiving palliative care is currently uncertain, with prior placebo-controlled data limited to patients with HIV until more recently with current available placebo-controlled data exploring specific clinical scenarios. In the two most recent trials, one included participants with mild to moderate delirium, who were experiencing specific target symptoms and the other included participants at the end of their life who remained agitated despite regular haloperidol. Both trials allowed optimal treatment of reversible precipitants and non-pharmacological measures, as clinically determined by the multidisciplinary team and asked the pragmatic question of the role of medications for shorter term symptomatic management in addition to these other established approaches of clinical care. Both had placebo arms and this provides data on impact on symptom resolution of the individualised optimal treatment of reversible precipitants and non-pharmacological measures, acknowledging this includes multifactorial measures which will vary between participants.

Benzodiazepines were indicated as being rarely used for this scenario, while a similar UK survey found that 34.5% (59/171) would prescribe benzodiazepines on an as needed basis. The aforementioned lorazepam versus placebo trial (single dose when added to regular haloperidol for a single episode of agitation or restlessness) in participants who remained agitated despite regular haloperidol, showed that while sedation was deeper for the lorazepam group at 8 hours, those in the placebo group improved to a Richmond Agitation-Sedation Scale score of around zero (alert and calm) which would appear to be the more optimal goal, especially for those who had potentially reversible delirium.

In the RCT by Agar et al (published 3 months before this survey was initially sent out), patients received treatment of the cause of delirium and supportive strategies. However, patients receiving risperidone or haloperidol had higher delirium symptom scores compared with placebo. The majority of participants had mild to moderate overall delirium severity and average doses of administered haloperidol were low. In an Australian survey, 62% of palliative medicine specialists stated antipsychotics were the pharmacological ‘agent of choice’ for symptomatic delirium management; for 38% it was benzodiazepines. In an audit of patients ≥65 years admitted to hospital with delirium, antipsychotics were used in 66% of patients with severe behavioural and or emotional disturbance associated with delirium, but in only 17% if these symptoms were not severe. In contrast, benzodiazepines were used in 38% with severe symptoms and 18% without. However, these two studies predated the Agar et al’s RCT. Some respondents reported that the study by Agar et al has made them aware of the poor evidence base for antipsychotics in this setting. Some clinicians report difficulty in applying these findings to their clinical practice and/or do not feel that current study findings fully represent their clinical practice, and, as the study’s authors state, does not inform practice for people with severe delirium, and hence many report continuing use in their clinical practice.

**Support of family carers**

As most teams do not formally support family carers of patients with delirium, this is an essential area for
improvement for both community and inpatient teams. Informal verbal support supported by information leaflets, preferably specific to palliative care, (such as the delirium information leaflet accessible from: https://www.bruyere.org/en/Delirium) may allow for improved formal support of family caregivers.

The literature indicates a need for formal support for family members, demonstrated when families of hospitalised older relatives with delirium described the experience as distressing. Studies highlight the necessity of informational skills and resources needed to mitigate family distress and provide support, including information which addresses family concerns. Although more data is needed, family caregiver education may be an important intervention to improve outcomes for both patient and caregiver.

Research priorities
All proposed areas of research were important to respondents, with preventive strategies, prediction of delirium reversibility and the pharmacological and non-pharmacological management of delirium being the most important. Further methodologically rigorous studies in palliative care populations using standardised outcome measures are needed.

Limitations
A response rate of 39% risks poor representation of the sample population. However, this response rate is higher than previously published surveys in this field and literature supports this proportion as being adequate for generalisability. However, as we were interested in the teams’ assessment and management of delirium, and several of the responding APM members might be part of the same team, this survey may not have obtained a geographically representative response. This could not be mitigated as many respondents work across settings and in order to maintain anonymity, we could neither access specific team data nor identify individual teams. We did not include questions about practices in relation to prevention of delirium.

The responses to some of the questions are subjective and provisions of numerical estimates are likely to be approximate. Free-text comments indicated a lack of clarity for ‘refractory delirium’ and ‘palliative sedation’. Open online surveys are subject to selection bias due to a volunteer effect. In this survey, an over-representation of motivated respondents with experience and interest in delirium might have skewed the results. This survey was principally answered by experienced palliative medicine physicians and the results have limited generalisability outside of this group.

Further research
The findings from this survey emphasise the need for several other research areas. These include assessing clinicians’ management of people with mild to moderate delirium and management of severe delirium in imminently dying patients, and the impact of research on clinical practice, and the implementation of existing evidence into practice. A key area is determining what would make clinicians change their practice when new evidence emerges. Further research is needed to understand physician decision-making processes when presented with delirium in a clinical context and how the care environment (community or hospice or hospital) impacts this decision-making.

CONCLUSION
This survey of UK Palliative Medicine specialists shows that delirium screening at inpatient admission is suboptimal. Systematic delirium screening should be completed using a tool and patient/family consultation on admission and on an ongoing basis. Most specialists continue to use antipsychotics in combination with non-pharmacological interventions to manage delirium. More structured support for family carers, backed up by palliative care specific information leaflets, should be routinely provided by clinical teams. Further rigorously designed clinical trials, especially to identify the standard of care for people with severe delirium, are urgently needed in view of management variability, emerging evidence and perceived priorities for research. There is also an urgent need to integrate findings from recent research into clinical practice.

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