

# Delirium prevalence, incidence, and implications for screening in specialist palliative care inpatient settings: A systematic review

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## Abstract

**Background:** Delirium is a serious neuropsychiatric syndrome frequently experienced by palliative care inpatients. This syndrome is under-recognized by clinicians. While screening increases recognition, it is not a routine practice.

**Aim and design:** This systematic review aims to examine methods, quality, and results of delirium prevalence and incidence studies in palliative care inpatient populations and discuss implications for delirium screening.

**Data sources:** A systematic search of the literature identified prospective studies reporting on delirium prevalence and/or incidence in inpatient palliative care adult populations from 1980 to 2012. Papers not in English or those reporting the occurrence of symptoms not specifically identified as delirium were excluded.

**Results:** Of the eight included studies, the majority (98.9%) involved participants (1079) with advanced cancer. Eight different screening and assessment tools were used. Delirium incidence ranged from 3% to 45%, while delirium prevalence varied, with a range of: 13.3%–42.3% at admission, 26%–62% during admission, and increasing to 58.8%–88% in the weeks or hours preceding death. Studies that used the *Diagnostic and Statistical Manual–Fourth Edition* reported higher prevalence (42%–88%) and incidence (40.2%–45%), while incidence rates were higher in studies that screened participants at least daily (32.8%–45%). Hypoactive delirium was the most prevalent delirium subtype (68%–86% of cases).

**Conclusion:** The prevalence and incidence of delirium in palliative care inpatient settings supports the need for screening. However, there is limited consensus on assessment measures or knowledge of implications of delirium screening for inpatients and families. Further research is required to develop standardized methods of delirium screening, assessment, and management that are acceptable to inpatients and families.

## Introduction

Delirium is a serious neuropsychiatric syndrome in hospitalized patients, including those within palliative care settings,<sup>1–3</sup> and is associated with increased mortality.<sup>4,5</sup> Delirium impacts upon the patient's ability to communicate, their decision-making capacity, functional ability, and quality of life.<sup>1</sup> Patients who recover from an episode of delirium usually recall the experience<sup>6,7</sup> and report feeling frightened and humiliated.<sup>8</sup> In the last days or hours of life, hyperactive delirium symptoms—commonly referred to as “terminal agitation” or “terminal restlessness”—cause distress for family members.<sup>9–11</sup>

Core symptoms for a *Diagnostic and Statistical Manual (DSM), Fourth Edition (DSM-IV)* diagnosis of delirium include disturbed consciousness, with reduced ability to focus, sustain, or shift attention; altered cognition or a perceptual disturbance, acute onset and fluctuating symptoms, which can be mild and fleeting or severe and persistent; and evidence of an etiological cause.<sup>12</sup> Level of consciousness identifies the three delirium subtypes: hyperactive, hypoactive, or mixed.<sup>13</sup> Lethargy, mood changes, and altered sleep–wake cycle can also occur, although are not required to establish a diagnosis.<sup>12</sup>

Despite numerous interventions for delirium reversal, management and support of palliative care patients with delirium being available, evidence of their effectiveness is evolving and requires further development.<sup>14–16</sup> Identifying delirium is an important priority as approximately half of all delirium episodes are potentially reversible.<sup>4,17</sup> Iatrogenic causes, such as opioids and benzodiazepines, underscore the importance of recognition to modify palliative care interventions.<sup>18,19</sup> Optimal recognition and assessment of delirium is of clinical and ethical concern since sedation is commonly used to manage symptoms of restlessness and agitation in the terminal stage.<sup>20,21</sup> Underrecognition of delirium results in interventions being inconsistently applied in palliative care.<sup>22–24</sup>

Screening improves clinician recognition of delirium,<sup>25</sup> yet is not routinely conducted in the inpatient palliative care setting.<sup>26</sup> Previous reviews of delirium in palliative care settings have provided comprehensive examinations of the literature including delirium prevalence and assessment methods,<sup>1,3,27</sup> but to date, no reviews have examined in detail the methodological quality of delirium epidemiological studies conducted in palliative care inpatient settings, nor discussed implications of results in conjunction with other evidence required to justify implementation of routine delirium screening.<sup>28,29</sup>

## Method

### *Aims and review processes*

This systematic review aims to: (1) examine prevalence and incidence of delirium and delirium subtypes in

specialist palliative care inpatient settings, at various stages of patients' admission, (2) describe how delirium cases were identified and established in included studies, and (3) discuss results in relation to implementation of routine delirium screening in specialist palliative care inpatient units.

Although a meta-analysis of data was not undertaken, the Meta-Analysis of Observational Studies in Epidemiology (MOOSE)<sup>30</sup> guidelines were followed to facilitate systematic processes in the completion and reporting of the review, where relevant.

### *Search method*

A systematic review was undertaken between 1 December 2011 and 29 February 2012 and was limited to the studies published since 1980, when delirium was first identified within the *DSM, Third Edition (DSM-III)*,<sup>31</sup> up until early 2012. Prospective search questions guided the search strategy using the following search Medical Subject Headings (MeSH) and key words, along with their associated derivatives: “delirium” OR “confusion” OR “terminal agitation” OR “terminal restlessness” OR “psychomotor agitation” OR “cognitive failure” OR “disorientation” AND “palliative care” OR “death” OR “dying” OR “terminal care” OR “hospice care” OR “terminally ill” OR “end of life” AND “prevalence” OR “incidence” OR “epidemiology”. Search engines used were Scopus, CINAHL, and Medline. In addition, the search terms “delirium” AND “prevalence” OR “incidence” OR “epidemiology” were employed in PubMed using the palliative care filter from CareSearch.<sup>32</sup> Reference lists of included studies and relevant reviews<sup>1,3</sup> were also examined to search for other potentially eligible papers.

### *Study selection*

Criteria for inclusion of papers were prospective assessment studies reporting prevalence, incidence, or rate of occurrence of delirium, conducted within specialist palliative care inpatient settings (defined as palliative care inpatient units or hospices) with adult participants. Studies were excluded if they were not published in English, or reported the rate of occurrence of symptoms or phenomena that were not specifically categorized as delirium, such as “cognitive failure,” “confusion,” or “terminal agitation,” as the interchangeable use of such terms has previously contributed to a lack of clarity in reporting and collating of delirium occurrence in palliative care populations.<sup>3</sup> Two authors (A.H. and J.P.) examined the titles and abstracts of all papers to determine if they met the inclusion criteria, one author (A.H.) extracted the data from potentially relevant studies ( $n = 13$ ) and this guided decision making (A.H. and J.P.) about inclusion of studies.

### Assessment of methodological quality of included studies

The first author (A.H.) assessed the methodological quality of included studies with reference to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines<sup>33</sup> and criteria developed by Boyle<sup>34</sup> to evaluate prevalence studies, which were reviewed and confirmed by the other author (J.P.) as follows:

1. Sample:
  - a. Explanation of how the sample size was determined;
  - b. Study population clearly defined;
  - c. Two-phase sampling process: delirium screening followed by more comprehensive delirium assessment;
  - d. Minimum of 80% participation within eligible study population;
2. Measurement:
  - a. Standardized data collection methods for all participants of the study;
  - b. Use of valid delirium-screening and assessment tools AND/OR psychiatric assessment;
  - c. Reporting of measurement reliability processes, for example, user training in the delirium-screening and assessment tool(s), inter-rater reliability testing, supervision of clinical/research staff conducting study measurements;
3. Analysis:
  - a. Confidence intervals included for statistical analysis of frequency estimates.

### Results

The initial search generated 815 papers: Scopus ( $n = 758$ ), CINAHL ( $n = 28$ ), Medline ( $n = 8$ ), PubMed via CareSearch ( $n = 21$ ). Within Scopus, adding “AND prospective study,” further refined the search and reduced the number of results within Scopus to 84 papers, resulting in 141 papers across all search engines. Once duplicates were removed, 119 papers published between 1980 and 2011 remained (Figure 1). A further 113 papers were removed as they did not report primary research data and/or prospectively measure prevalence or incidence rates of delirium in adult specialist palliative care inpatient units, leaving six papers. Two additional papers<sup>35,36</sup> were identified from a hand search of the reference lists of the eligible papers and other reviews.<sup>1,3</sup> At the end of the search, eight studies that prospectively measured the prevalence or incidence of delirium in specialist palliative care adult inpatient settings remained (Table 1).<sup>4,5,35–37,39–41</sup> These included studies which were conducted in the northern hemisphere over a 12-year period (1996–2008).

### Setting, diagnosis, and demographics

The included studies were undertaken in patient settings described variously as hospices ( $n = 2$ ),<sup>39,41</sup> palliative care units ( $n = 3$ ),<sup>35–37</sup> acute palliative care units ( $n = 2$ ),<sup>4,40</sup> and a combined acute palliative care unit/hospice ( $n = 1$ ).<sup>5</sup> Where described, the purpose of the settings included symptom control, respite, rehabilitation, and/or terminal care for palliative care patients. The majority (98.9%) of all participants ( $n = 1079$ ) across these studies had advanced cancer, with some diagnoses not specified in one study.<sup>41</sup> Two studies included participants with other life limiting diseases: (a) immunodeficiency disorders ( $n = 11$ )<sup>36</sup> and (b) end-stage cardiac failure and cerebrovascular disease ( $n = 1$ ).<sup>41</sup>

Across the studies, there was equal representation of males and females, with a mean age of 66.24 years (range 62–68.7 years). Participation rates varied (Table 1).

### Study characteristics, design, quality, and focus

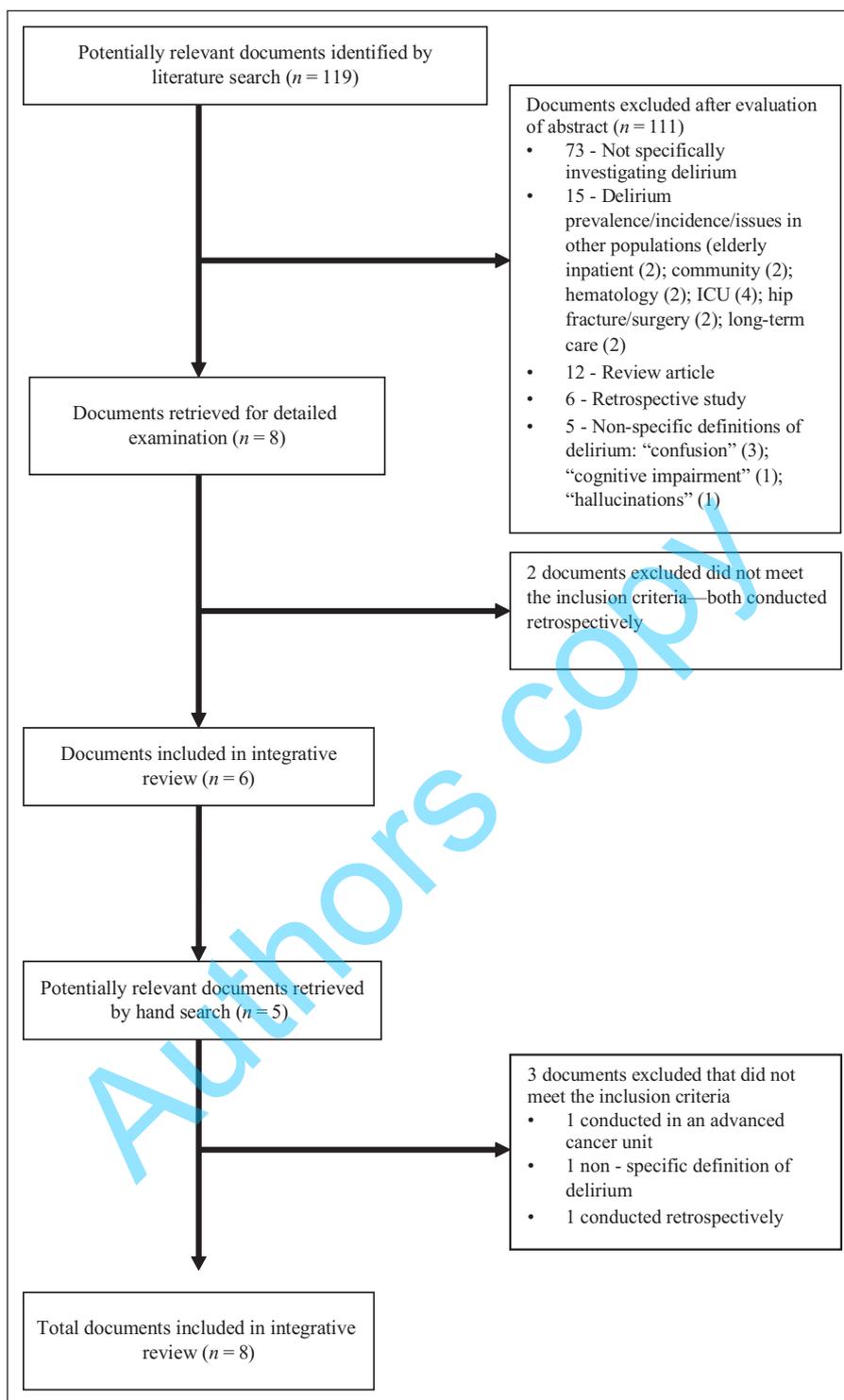
There was variability in study characteristics, design, quality, and foci, as well as participant numbers ( $X$  120, range 41<sup>40</sup>–228 people<sup>5</sup>). No studies reported statistical explanations for determination of sample size, with this appearing to be largely determined by number of patient admissions within study periods. Delirium occurrence was measured at different frequencies and points of time during the admission, while five studies measured both delirium prevalence and incidence.<sup>4,35,36,39,41</sup>

Different criteria were used to define the terminal stage, with the last weeks of life considered the “pre-terminal and terminal” stage of cancer in two studies.<sup>5,39</sup> “Terminally ill” or “terminal” cancer patients were elsewhere considered to be within the last 6 months of life.<sup>37</sup> Only one study included the data specifically collected in the 6 hours immediately prior to death, defined as “terminal delirium.”<sup>4</sup>

Methodological quality of studies varied considerably and no study met all quality criteria (Table 1).

### Definitions of delirium and diagnostic criteria used

Diagnostic criteria adopted by many of the studies, conducted at different time points, reflect the evolution of the *DSM* diagnostic criteria for delirium. The majority ( $n = 6$ ) of studies applied *DSM* criteria to diagnose delirium, with two using the research gold standard of psychiatrist assessment to confirm delirium against the *DSM* version current at the time.<sup>5,37</sup> In another four studies, diagnosis of delirium was based on the presence of the then-current *DSM* criteria, although not confirmed by psychiatric assessment.<sup>4,35,39,41</sup> The remaining two studies used an alternative criteria to establish a delirium diagnosis with one<sup>36</sup> using the International Statistical Classification of Diseases and Related Health problems (ICD-10) Diagnostic Criteria for Research,<sup>42</sup> which requires a greater range of symptoms to be present to establish a delirium diagnosis.



**Figure 1.** Flowchart of studies from search to inclusion.

### Screening and assessment tools

Eight different tools were used across the studies to assess cognition, screen for, or establish delirium (Table 1). Of the six delirium-specific screening or assessment tools, all varied in their validity, purpose (screening, diagnosis, and

severity), intended rater (psychiatrically vs nonpsychiatrically trained), ratings procedures (observation vs interview), number of items, and extent to which they correlate with different versions of *DSM* criteria for delirium.<sup>43,44</sup>

Three delirium or “confusion” screening tools included the Confusion Rating Scale (CRS) used by ward nurses<sup>39,45</sup>;

**Table 1.** Summary of included studies.

Publication	Country	Focus	Design/screening and assessment tools/DSM Criteria	Participants/ participation rate	Delirium prevalence/ incidence results	Quality considerations
Minagawa et al. <sup>37</sup>	Japan	To demonstrate a range of psychiatric disorders in a PC unit.	Prospective assessment by psychiatric investigator using MMSE, psychiatric assessment, and SCID within 1 week of admission. DSM-III-R	Terminally ill cancer inpatients (n = 93); 59% male; mean age 67.2, SD ± 11.9 years; participation rate 85%	53.7% met DSM-III-R criteria for a psychiatric disorder	Sample size: inpatients recruited over a 13-month period.  MMSE assesses cognitive function, but is not specific to delirium. SCID does not evaluate organic mental disorders—however, delirium diagnosis determined by psychiatric assessment Confidence intervals not included
Lawlor et al. <sup>4</sup>	USA	To evaluate the occurrence, precipitating factors, and reversibility of delirium in an acute PC unit	Prospective serial assessment in a consecutive cohort. DOCS (by trained ward nurses each 8-h shift), MMSE (by medical investigators on admission and twice weekly), MDAS (by medical investigators for delirious patients).  Semi-structured interview by medical investigators to operationalize DSM-IV.	Advanced cancer patients (n = 104 of 113); 51% male; mean age 62 years, SD ± 1.9 years; participation rate 100%	Prevalence: 28% (n = 26).  Delirium most common psychiatric disorder	Sample size: inpatients recruited over a 9.5-month period  DOCS had no reliability or validity testing  MMSE assesses cognitive function, but is not specific to delirium Researcher training and moderate-to-high inter-rater reliability in MDAS use was reported in a separate paper <sup>38</sup>
Gagnon et al. <sup>39</sup>	Canada	To determine delirium frequency and outcome in hospice inpatients	Prospective cohort study. CRS (by trained ward nurses 8th-hourly), BOMC to assess orientation, CAM (by two research nurses to diagnose delirium). Training and supervision of research nurses by psychiatric investigator DSM-III-R	Terminal cancer inpatients (n = 89) with a life expectancy <2 months; 48% male; mean (median) age 66 years (68 years); participation rate 95%	Prevalence: On admission, 20.2% patients (n = 18) had delirium symptoms, diagnosis confirmed in 13.3% Incidence: 52.1% of 71 patients delirium-free at admission developed delirium symptoms, diagnosis confirmed in 32.8%	Sample size: inpatients recruited over a 4-month period CRS requires further validation

(Continued)

**Table 1.** (Continued)

Publication	Country	Focus	Design/screening and assessment tools/DSM Criteria	Participants/ participation rate	Delirium prevalence/ incidence results	Quality considerations
Sarhill et al. <sup>40</sup>	USA	(a) Evaluate the use of the BCS and (b) determine prevalence, cause, precipitants, and treatment of delirium in an acute PC medicine unit	Prospective assessment by medical officer on admission using the BCS (delirium = score of $\geq 2$ ) DSM criteria for delirium not used	Consecutive patients with advanced cancer ( $n = 41/50$ ); 44% male; median age 65 years; participation rate 82%	Prevalence: 31.7% ( $n = 13$ ) on admission	Sample size: inpatients recruited over a 2-month period Multiphase sampling not used—delirium screening only BCS requires further psychometric testing Not specified who applied BCS (medical clinician, researcher, or investigator) Confidence intervals not included.
Durkin et al. <sup>41</sup>	UK	To clinically assess the prevalence of psychiatric disorder occurring in a PC unit and ascertain whether disorder had been detected and treated prior to admission	Prospective assessment of patients on admission and twice weekly by principal psychiatric investigator. Presence or absence of a psychiatric diagnosis was determined according to the ICD-10 Diagnostic Criteria for Research	Inpatients with diagnosis of AIDS or advanced cancer ( $n = 224$ ); 52% male; mean age 66 years, $SD \pm 14.2$ , range 22–90 years; participation rate 100%	62% ( $n = 139$ ) met ICD-10 diagnostic criteria for psychiatric disorder Prevalence: 19% ( $n = 43$ ) Incidence: 3% patients ( $n = 5/181$ ) delirium-free on admission developed delirium	Sample size: inpatients recruited over a 6-month period Multiphase sampling did not occur—no delirium-screening tool used Confidence intervals not included
Lam et al. <sup>42</sup>	Hong Kong	To estimate the incidence and prevalence of delirium in a PC unit and evaluate psychomotor type, etiologies, reversibility and other characteristics	Prospective daily assessment of consecutive admissions using structured evaluation, MMSE—Cantonese version, KPS. Patients assessed as delirious had further assessment by medical investigator within the same day to confirm delirium diagnosis. Experienced and trained nurse administered MDAS within 24 h of delirium diagnosis DSM-IV	Advanced cancer patients ( $n = 82/102$ ); 46% male; mean age 68 years, $SD \pm 12.5$ ; participation rate 80%.	Prevalence: 58.8% ( $n = 30/51$ ) of patients who died had delirium on average 12.4 days before death Incidence: 40.2% ( $n = 33$ ) Subtypes: 70% hypoactive Severity: 53.3% mild severity, 23.3% moderate, 20% severe	Sample size: inpatients recruited over a 4-month period MMSE assesses cognitive function, but is not specific to delirium Training and supervision of clinical staff conducting daily delirium monitoring was not reported

Table 1. (Continued)

Publication	Country	Focus	Design/screening and assessment tools/DSM Criteria	Participants/ participation rate	Delirium prevalence/ incidence results	Quality considerations
Spiller and Keen <sup>43</sup>	Scotland	To assess the prevalence of hypoactive delirium in specialist PC settings	<p>Study 1: Prospective assessments at admission and 7 days later by study investigator using MMSE, CAM, MDAS, FSS, HADS</p> <p>Study 2: 48-h point prevalence study in 8 specialist PC units using MMSE, CAM, MDAS (administered by trained clinical staff, discipline/s not specified)</p> <p>DSM-III-R</p>	<p>Study 1: Hospice inpatients (n = 100); 49% male; mean age 68.7 years, SD ± 15 years; 99/100 advanced malignancy; participation rate 88% at admission, 73% at 7 days</p> <p>Study 2: Inpatients (n = 109) of 8 PC units (6 hospices, 1 hospice ward within a general hospital, 1 PC service within a general hospital); gender not specified; mean age 68.7 years, diagnoses not specified; participation rate 87%</p>	<p>Study 1: Prevalence: 29% (n = 29) at admission—86% hypoactive, 14% mixed 26% (n = 19/73) had delirium 7 days later—68% hypoactive, 21% hyperactive, 11% mixed</p> <p>Incidence: 7% (n = 5/73) within 7 days of admission.</p> <p>Study 2: Point prevalence: 29.4% (n = 32) (range 14%–35%). 78% hypoactive, 6% hyperactive, 16% mixed</p>	<p>Determination of sample size of 100 for Study 1 was not explained. MMSE assesses cognitive function but is not specific to delirium.</p> <p>No reporting of researcher training in use of CAM, MDAS in Study 1</p> <p>Diagnoses of study population not reported in Part 2</p> <p>Confidence intervals included in Part 1, but not Part 2</p>
Fang et al. <sup>44</sup>	Taiwan	To determine the prevalence, detection, and treatment of delirium in an acute PC/hospice unit	<p>Survey and chart review, screening by trained research nurse using the DRS-CV at admission and second daily, followed by psychiatrist review for +ve DRS-CV to verify diagnosis and determine delirium subtype</p> <p>DSM-IV</p>	<p>Terminal cancer inpatients (n = 228/457); 51% male; mean age 64.57 SD ± 14.88; participation rate 49.9%</p>	<p>Prevalence: 46.9%</p> <p>Subtypes: 68.2% hypoactive, 21.5% hyperactive, 10.3% mixed</p>	<p>Sample size: inpatients recruited over a 6-month period</p> <p>Largest sample within included studies, but participation rate &lt;80%. 51% of nonparticipants were too ill to consent, indicating selection bias</p>

BOMC: Blessed Orientation Memory Concentration; BCS: Bedside Confusion Scale; CAM: Confusion Assessment Method; CRS: Confusion Rating Scale; DOCS: Delirium Observational Checklist; Scale; DRS-CV: Delirium Rating Scale—Chinese Version; DS: Delirium Scale; DSM-III-R: *DSM, Third Edition, Text Revision*; FSS: Fatigue Severity Scale; HADS: Hospital Anxiety and Depression Scale; KPS: Karnofsky Performance Scale; MDAS: Memorial Delirium Assessment Scale; MMSE: Mini-Mental State Examination; PC: palliative care; SCID: Structured Clinical Interview for DSM-III-R; ICD-10: International Statistical Classification of Diseases and Related Health problems.

the Bedside Confusion Scale (BCS) used by medical investigators<sup>40,46</sup>; and the Delirium Observational Checklist Scale (DOCS), an instrument developed by study investigators for ward nurse's use.<sup>4</sup> Although the BCS was previously validated in the palliative care setting, it requires further investigation of its psychometric properties.<sup>43</sup> The CRS requires further validation, and the DOCS is not a validated delirium-screening tool.<sup>43</sup>

Two cognition assessment tools, used to either screen for delirium or to assist in delirium assessment, were the Mini-Mental State Examination (MMSE)<sup>47</sup> used by psychiatric and medical investigators<sup>4,35,37,41</sup> or clinical staff<sup>41</sup> and the Blessed Orientation Memory Concentration (BOMC) test used by research nurses.<sup>39,48</sup>

Three delirium assessment tools were the Confusion Assessment Method (CAM)<sup>49</sup> used by research nurses<sup>39</sup> or medical investigators and trained clinical staff<sup>41</sup>; the Memorial Delirium Assessment Scale (MDAS)<sup>38,50</sup> used by medical investigators,<sup>4,41</sup> trained clinical staff,<sup>41</sup> or a research nurse<sup>35</sup>; and the Delirium Rating Scale—Chinese Version (DRS-CV)<sup>51</sup> used by a research nurse.<sup>5</sup> Only the MDAS<sup>38,50</sup> and the Delirium Rating Scale (DRS)<sup>46,52,53</sup> were validated in palliative care or advanced cancer populations prior to use in the studies under examination, with the MDAS undergoing further simultaneous validation.<sup>4,38,41</sup> The CAM<sup>49</sup> was validated in other clinical settings and languages,<sup>43</sup> and subsequently validated in the palliative care setting.<sup>54</sup>

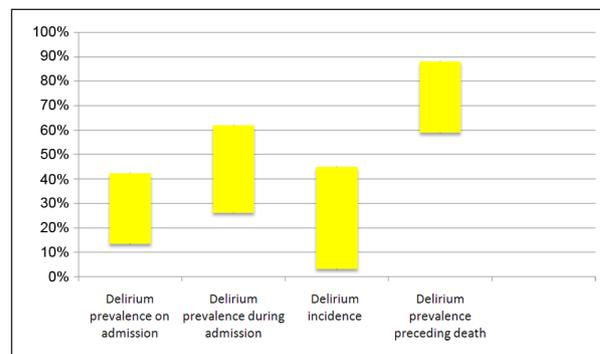
No studies reported perspectives of patients or families of the acceptability of delirium-screening and assessment processes.

### Delirium prevalence and incidence rates

The prevalence and incidence rates reported in the included studies are represented graphically in Figure 2.

**On admission.** Five studies measured delirium prevalence at admission, ranging from 13.3% to 42.3% of patients.<sup>4,36,39–41</sup> Of 104 advanced cancer admissions to an acute palliative care unit, delirium was present at admission in 42.3% of patients.<sup>4</sup> A later study, consecutively measured delirium frequency in hospice inpatients ( $n = 89$ ) and 13.3% were confirmed to have delirium.<sup>39</sup> In another, 19% of patients ( $n = 224$ ) admitted to a palliative care unit had delirium.<sup>36</sup> A third (32%) of participants ( $n = 41$ ) were classified as delirious according to presence of inattention and altered level of alertness in one acute palliative care unit,<sup>40</sup> while 29% of participating patients ( $n = 100$ ) admitted to a Scottish hospice had delirium.<sup>41</sup>

**During admission.** Delirium prevalence across the whole cohort of palliative care inpatients during each study period ranged from 26% to 62%.<sup>5,37,39,41</sup> One study measuring psychiatric morbidity at one point during the week after



**Figure 2.** Graphical representation of delirium prevalence and incidence rates in specialist palliative care inpatient units from results of included studies.

admission to a palliative care unit found that delirium was the most prevalent psychiatric disorder, occurring in 28% of all participants and representing 52% of all psychiatric diagnoses.<sup>37</sup> Another study, using delirium screening during each 8-h shift, identified that 62% of participants developed delirium at some point during hospice admission.<sup>39</sup> One study reassessed hospice patients ( $n = 73$ ) 7 days after admission and found that 26% had delirium, while across 8 hospices or inpatient palliative care services, 29.4% of patients had a delirium diagnosis during a 48-h period of assessment.<sup>41</sup> Recently, 46.9% of palliative care inpatients ( $n = 228$ ) screened second daily were found to have delirium.<sup>5</sup>

Three studies examined occurrence of delirium subtypes and all reported that the majority of delirious patients experienced hypoactive delirium (68%–86%).<sup>5,35,41</sup>

Five studies measured delirium incidence after admission and reported rates of between 3% and 45%.<sup>4,35,36,39,41</sup> Delirium developed during admission in 45% of patients ( $n = 60$ ).<sup>4</sup> In a later study involving 71 participants, 32.8% had confirmed delirium.<sup>39</sup> These two studies included screening by ward nurses each 8-h shift.<sup>4,39</sup> A study using daily screening reported, of admitted patients, 40.2% ( $n = 82$ ) developed delirium ( $n = 33/82$ ), the majority (70%) having hypoactive delirium of mild severity (53.3%).<sup>35</sup> In contrast, one study reported development of five new cases in 73 patients within a 7-day period, an incidence of 7%,<sup>41</sup> while another, using twice weekly assessment and the ICD-10 diagnostic criteria, reported an incidence of only 3%: during the 6-month study period only 5 of 181 patients delirium-free on admission subsequently developed delirium.<sup>36</sup>

**Preceding death.** Two studies measured prevalence of delirium in the weeks or hours before death, reporting rates of 58.8%–88%.<sup>4,35</sup> The most recent study reported 58% delirium prevalence in patients ( $n = 51$ ) who died during admission.<sup>35</sup> Only one study explicitly measured and reported occurrence of delirium in the last 6 h of life in an

acute palliative care unit and found that the majority (88%) had delirium.<sup>4</sup>

### *Variation in delirium prevalence and incidence according to study methods and settings*

Studies that used *DSM-IV* criteria reported higher delirium prevalence (42%–88%)<sup>4,5,35</sup> and incidence (40.2%–45%)<sup>4,35</sup>; compared to studies using earlier versions of *DSM* criteria and ICD-10 (prevalence 13.3%–29.4%)<sup>36,37,39,41</sup> and incidence 3%–32.8%).<sup>36,39,41</sup> Studies screening participants daily or more often reported higher delirium incidence (32.8%–45%)<sup>4,35,39</sup> than studies that screened or assessed delirium participants less frequently (3%–7%).<sup>36,41</sup> Delirium prevalence on admission varied slightly across settings: palliative care unit (19%), hospice (13.3%–29%), and acute palliative care units (31.7%–42%).

### *Role of clinicians in the identification and diagnosis of delirium*

In four studies, clinicians were actively involved in delirium screening and assessment study processes.<sup>4,35,39,41</sup> In two, ward nurses screened for delirium, using the DOCS<sup>4</sup> or the CRS<sup>39</sup> and received training in use of tools and features of delirium.<sup>39</sup> In another, an experienced and trained nurse assessed delirious patients using the MDAS to measure delirium severity.<sup>35</sup> In the study involving 8 separate Scottish hospices and palliative care services, clinicians received training prior to using the CAM and MDAS to identify and assess delirium over a 48-h period.<sup>41</sup>

Research nurses were also involved in delirium screening and assessment. The DRS-CV was used to screen inpatients for delirium,<sup>5</sup> delirium diagnosis was established by nurses in another using the CAM in consultation with the psychiatric investigator if there was uncertainty about the diagnosis,<sup>39</sup> and delirium severity was measured by nurses using the MDAS 24 h after delirium diagnosis by a physician.<sup>35</sup>

## **Discussion**

There were some similarities across studies, with most adopting a two-phase sampling method—delirium screening followed by assessment—and involving patients of a similar age and primary cancer diagnosis. However, there was a varying methodological quality across these studies, with heterogeneity of diagnostic criteria, sample sizes, frequency of assessment, and measurement tools adopted. Despite these differences and the variation in reported delirium occurrence, categorizing delirium prevalence at different points along the palliative care inpatient trajectory indicates that prevalence is lower at admission (range 13.3%–42.3%),<sup>4,36,39–41</sup> increases during admission (range

26%–62%),<sup>5,37,39,41</sup> with the risk of developing delirium escalating as death nears (range 58.8%–88%).<sup>4,35</sup> This review has confirmed that palliative care inpatient populations have delirium incidence and prevalence equal to or greater than other known high-risk populations, such as older people admitted to hospital,<sup>55</sup> Intensive Care Units,<sup>56–58</sup> post hip surgery,<sup>59,60</sup> and long-term care.<sup>61</sup>

The review adds to the emerging evidence that hypoactive delirium is the most prevalent subtype in palliative care populations.<sup>5,35,41,62</sup> Hypoactive delirium may appear less severe than other subtypes<sup>35</sup> and cause less difficulties in ward management,<sup>63</sup> but is associated with increased mortality.<sup>5</sup> It also has a significant impact on patients and families since cognitive changes occur as often as in the hyperactive and mixed subtypes.<sup>62,64</sup>

Clinicians were involved in patient screening and assessment in half the studies, highlighting potential for routine delirium screening outside a research context, and feasibility of increasing delirium recognition capabilities by nonpsychiatric clinicians through training and access to validated delirium-screening and assessment tools.<sup>38,50,54</sup> Delirium screening by nurses in a hospice setting has been demonstrated to be feasible and effective.<sup>14,25</sup> However, the challenges of screening for delirium in palliative care populations was also demonstrated by the small proportion of included studies measuring delirium occurrence specifically in cohorts of patients who were dying, and proportion of patients and/or families who declined to participate in the delirium assessment process, indicating delirium assessment is not always acceptable to them. Additionally, many patients were too unwell to provide consent or were excluded because they were dying, comatose, or could not speak. Similarly, a recent study<sup>14</sup> reported a low rate of CAM completion by hospice nurses (39%), highlighting the difficulty of conducting this delirium assessment in the last days of life and need for validated low-burden delirium assessment tools at this time.

Applying the *DSM-IV* criteria appears to lead to increased case finding, which has been previously reported<sup>65</sup>; and interestingly, variability in delirium prevalence and incidence noted in this review reflects results of similar reviews that included studies using less-specific delirium definitions.<sup>1,3</sup>

### *Implications for clinical practice and future research*

As daily screening increases detection of incident delirium,<sup>4,35,39</sup> the question remains: should routine screening be implemented in palliative care inpatient settings? Clinical practice guidelines for other high-risk patient populations recommend screening to improve early recognition of delirium,<sup>55,66,67</sup> although the extent to which this has been routinely adopted is unknown. However, a number of other key questions require investigation to justify routine screening<sup>28,29</sup> including: Is screening acceptable to patients and

family and cause minimal harm? Is it cost-effective? Does early recognition and treatment of delirium improve mortality and morbidity? And, what are the adverse effects of delirium treatment?<sup>28,29</sup>

Further research in delirium prevention interventions in palliative care,<sup>14</sup> and high-level evidence of the efficacy and safety of pharmacological interventions, such as antipsychotics, benzodiazepines, and methylphenidate, is needed.<sup>16,68,69</sup> Measuring impact of interventions on delirium incidence, severity, and patient mortality should continue to be a focus of research, but as improvements in morbidity and mortality are likely to be minimal in this population and the focus of care is a relief of distress and suffering, patients' and families' subjective experiences (such as perceptions of care, distress, dignity, and quality of life) related to delirium screening, recognition, and treatment are especially important outcomes to be determined.<sup>70</sup> Development of acceptable, observational delirium screening and assessment strategies for palliative care patients who are very ill, dying, or unable to communicate is also required.<sup>8,28,29</sup>

This review has highlighted the lack of consensus regarding selection of delirium screening and assessment tools in palliative care research, and this is likely to be reflected in clinical practice. Establishing the acceptability of various delirium-screening and assessment tools by patients and families would inform the sector about which are the most appropriate to use in this population, particularly in the dying stage. Establishing consensus would facilitate delirium benchmarking, quality improvement,<sup>71,72</sup> and consistency of research methodology. To further improve methodological and reporting quality of future delirium epidemiological research in palliative care populations, consideration of recently developed guidelines for observational studies in epidemiology is recommended.<sup>33,73</sup>

Health-economic analysis will also be an important inclusion in future delirium research, when high health-care costs associated with delirium occurrence in elderly inpatient populations is considered.<sup>74,75</sup>

### Study limitations and strengths

Limitations of this review include exclusion of papers not published in English, potentially contributing to selection bias and the absence of multiple independent raters in the extraction of data to assess eligibility and quality of included studies. There are limitations related to generalizability of this review due to the focus on advanced cancer diagnoses within study populations.<sup>70</sup> As the brief of palliative care shifts to nonmalignant conditions and settings where end-of-life care is routinely provided, for example, elderly medical inpatient settings or nursing homes, it is important to consider implications of this changing population.<sup>76-78</sup> In addition, although results suggest increasing delirium prevalence as death nears, this was not confirmed

within this review due to variable reporting of participants' functional status and illness staging, and variation in operational definitions of "terminal." This barrier has been previously noted with a recommendation that all future delirium occurrence studies incorporate a patient cohort classification system based on estimated prognosis.<sup>3</sup>

The strengths of this review include use of a systematic approach, with application of accepted guidelines and a structured approach to the assessment of quality of included studies.<sup>30,33</sup>

### Conclusion

This review has examined methods, quality, and results of studies prospectively measuring delirium occurrence in specialist palliative care inpatient settings and identified additional evidence needed to justify routine delirium screening in these settings. While the moderate to high rate of delirium occurrence in palliative care inpatient units supports the need for delirium screening, there is also a need to develop consensus and quality of methods for measuring delirium occurrence, and we require evidence regarding impact, acceptability, potential harms and cost-effectiveness of delirium screening and assessment, and outcomes of screening and treatments on morbidity, mortality, and patients' and families' subjective experiences.

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