BJPsych The British Journal of Psychiatry (2014)
205, 478–485. doi: 10.1192/bjp.bp.113.139865

Frequency of delirium and subsyndromal delirium in an adult acute hospital population

D. Meagher, N. O'Regan, D. Ryan, W. Connolly, E. Boland, R. O'Caoimhe, J. Clare, J. Mcfarland, S. Tighe, M. Leonard, D. Adamis, P. T. Trzepacz and S. Timmons

Background
The frequency of full syndromal and subsyndromal delirium is understudied.

Aims
We conducted a point prevalence study in a general hospital.

Method
Possible delirium identified by testing for inattention was evaluated regarding delirium status (full/subsyndromal delirium) using categorical (Confusion Assessment Method (CAM), DSM-IV) and dimensional (Delirium Rating Scale-Revised-98 (DRS-R98) scores) methods.

Results
In total 162 of 311 patients (52%) screened positive for inattention. Delirium was diagnosed in 55 patients (17.7%) using DSM-IV, 52 (16.7%) using CAM and 58 (18.6%) using DRS-R98 ⩾ 12 with concordance for 38 (12.2%) individuals. Subsyndromal delirium was identified in 24 patients (7.7%) using a DRS-R98 score of 7–11 and 41 (13.2%) using 2/4 CAM criteria. Subsyndromal delirium with inattention (*v.* without) had greater disturbance of multiple delirium symptoms.

Conclusions
The point prevalence of delirium and subsyndromal delirium was 25%. There was modest concordance between DRS-R98, DSM-IV and CAM delirium diagnoses. Inattention should be central to subsyndromal delirium definitions.

Declaration of interest
P.T.T. is a full-time employee and minor shareholder at Eli Lilly & Company. P.T.T. holds the copyright for the Delirium Rating Scale – Revised-98, but does not charge a fee for its non-for-profit use.

Delirium is a complex neuropsychiatric syndrome that is associated with a variety of adverse outcomes such as prolonged hospital admissions, reduced long-term independence and mortality that are independent of the confounding effects of age, prior cognitive function and medical morbidity.[1] In addition to full syndromal delirium, subsyndromal delirium – a milder state characterised by the presence of certain delirium symptoms but without meeting full diagnostic criteria thresholds – is also prognostically important, with intermediate outcomes between full and no delirium.[2–6] However, there is a lack of clear definition for subsyndromal delirium such that previous studies have defined it in various ways – both categorically using dichotomous presence of one or two core diagnostic features or elements of the Confusion Assessment Method (CAM) algorithm[3,6–15] and dimensionally with predefined subsyndromal delirium score ranges on the 16-item Revised Delirium Rating (DRS-R98)[16–18] or the Intensive Care Delirium Screening Checklist (ICD-SC).[4,19–21]

The recognition of subsyndromal delirium is hampered by uncertainty regarding its frequency, especially in in-patient populations where many non-delirious patients have mild non-specific symptoms that could be misattributed to subsyndromal delirium (for example mild inattention, sleep difficulties, agitation, drug-induced sedation). The reported frequency of subsyndromal delirium varies (7–50%) according to the definition applied and the clinical population studied.[4,6,12,13,22] Existing frequency estimates for both full and subsyndromal delirium are based upon studies of individual services (for example geriatric medicine, intensive care units, palliative care) such that a more definitive estimation of prevalence in a single hospital is needed. Moreover, improved understanding of how symptoms that can occur in delirium are expressed in general hospital populations can assist efforts to better understand the frequency, clinical significance and detection of subsyndromal delirium. To address these issues we: (a) identified the point prevalence of full and subsyndromal delirium defined by both categorical and dimensional methods in an acute hospital over a 36 h period, and (b) compared the clinical profile of full and subsyndromal delirium defined according to both categorical and dimensional approaches.

Method

Study population

The study was conducted over a 36 h weekend period at Cork University Hospital, a tertiary referral centre with 500 acute beds serving a 500 000 population in the South West of Ireland. All adult in-patients on the 15 May 2010 were considered for inclusion. Patients in the specialist units for psychiatry, intensive care and isolation unit were not assessed. Patients were also excluded if they were comatose, deemed too unwell for interview by nursing staff; unable to communicate because of speech or language issues; or did not consent to study participation.

Assessments

The primary focus was to identify the frequency of delirium in a general hospital.[23] Because DSM-IV criteria[24] require inattention, patients without disturbed attention do not have DSM-IV delirium. We thus optimised efficiency by applying three phases of assessment including an initial screening for inattention and other evidence of 'possible' delirium. Patients without these primary indicators of possible delirium were not included in subsequent assessments, which focused upon clarifying diagnosis and phenomenological profile by delirium experts.

Assessment for cognitive impairment/possible delirium

Formal cognitive testing. Trained junior medical staff screened all patients for inattention using (a) the Spatial Span Forwards (SSF) test,[25] and (b) the Months Backwards Test.[26] Significant

https://doi.org/10.1192/bjp.bp.113.139865 Published online by Cambridge University Press

inattention was deemed present in any patient who either (a) scored less than 5 on the SSF or (b) was unable to correctly recite at least 5 months of the year in reverse order. Previous work has identified that such cut-offs are sensitive to the presence of delirium.[27]

Patient, nursing and medical recognition of cognitive problems. All patients were questioned by junior medical staff regarding current or recent confusion ('since coming into hospital, have you been muddled in your thinking, or have you felt confused?'). The nurse in charge of the patient's care was interviewed using standardised questions probing for recent changes to and fluctuations in mental state, altered consciousness, confusion and disorganised conversation and whether they thought that the patient had delirium. Medical documentation of possible delirium was ascertained by reviewing medical notes for reports of delirium or proxy terms such as 'confusion'.

Assessment of delirium phenomenology and syndromal status

Any patient with inattention on either attention test, or who had subjective, nurse-identified, or case-note documented confusion, was then formally tested for delirium using the CAM algorithm[28] and the DRS-R98.[29]

CAM. This was administered by geriatricians who had undergone a 3-month training programme based on the original training manual, and involving a total training time of 8 h. The CAM diagnostic algorithm requires the presence of (a) acute onset or fluctuating course, (b) inattention, and either (c) disturbed consciousness or (d) disorganised thinking. Subsyndromal delirium has been defined according to presence of CAM features without meeting CAM diagnostic criteria. The presence of two CAM features (rather than a single feature) is closer to the concept of syndromal delirium and significantly more clinically relevant in respect of outcomes.[3,6,8,14] It was thus applied herein. A formal assessment of interrater reliability for CAM assessments ($n = 20$) was conducted on the day of the study and revealed 95% agreement between raters.

DRS-R98. The DRS-R98 assessments were conducted by psychiatrists with specific training based upon the DRS-R98 administration manual[30] that includes establishing high interrater reliability. The DRS-R98 is a validated diagnostic and severity assessment tool that rates symptoms over the previous 24 h. It has high interrater reliability, sensitivity and specificity for distinguishing delirium from other neuropsychiatric conditions including dementia, depression and schizophrenia.[29] It is a 16-item, clinician-rated scale with 13 severity items and 3 diagnostic items. Assessments are based upon all available sources of information, including patient assessment and discussion with nursing staff and family/carers. Item ratings are guided by text descriptions along a continuum from normal (0) to severely impaired (3) for severity items, and from 0 to either 2 or 3 for diagnostic items.

The DRS-R98 total scale score ranges from 0 to a maximum of 46. A cut-off score of $\geqslant 18$ is typically applied to delirium diagnosis, especially where high specificity is desirable, but other work suggests that such cut-offs exclude many cases of DSM-IV delirium[18,31,32] and lower cut-off scores are advocated where diagnostic sensitivity is the primary goal. For this general hospital population, in consultation with the DRS-R98 developer (P.T.T.) we applied relaxed cut-off scores to enhance diagnostic sensitivity (especially to milder delirium) to equate total scores of 0–6 with no delirium, 7–11 with subsyndromal delirium and $\geqslant 12$ for full syndromal delirium.

DSM-IV. We determined DSM-IV delirium[24] *post hoc* by consensus agreement among the psychiatry panel using all available information (case-notes, collateral sources, specific assessments). For each patient, the psychiatrist who conducted the DRS-R98 assessment did not attribute (and was thus masked to) DSM-IV status (i.e. other panel members allocated DSM-IV status).

Assessment of previous cognitive status

Medical case-notes were reviewed for documentation of prior cognitive impairment (mild cognitive impairment or dementia). If this was not evident, premorbid cognition was determined using the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) – a validated screening tool for detecting cognitive impairment.[33]

Additional data

Data was also gathered regarding demographic details. Junior medical trainees collected information relating to medical history, medication use, social history and current and previous alcohol history from the medical case-notes and laboratory results from the hospital's electronic system. Charlson comorbidity scores[34] were calculated by one of the specialist registrars (N.O.'R.).

Ethical procedures

The procedures and rationale for the study were explained to all patients and relatives but because many patients had cognitive impairment at study entry it was presumed that many were not capable of giving informed written consent. Because of the non-invasive nature of the study, ethics committee approval was given to augment patient assent with proxy consent from next of kin (where possible) or a responsible caregiver for all participants, in accordance with the Helsinki Guidelines for medical research involving human participants.[35] All patients with identified delirium were communicated to the treating teams both verbally to nursing staff and by inserting a purpose-designed form into the clinical case-notes.

Statistical analyses

Statistical analysis was conducted using the SPSS-19 package for Windows. Demographic and rating scale data were expressed as means (s.d.) or medians (and IQR). In order to detect with 95% power a 10% difference in prevalence in our hospital from the previously reported[36] prevalence in in-patients, (10–31%) a sample size of 267 would be required. Concordance between diagnostic systems was compared using kappa (κ) values. Continuous variables (such as age, total DRS-R98 scores) were compared by one-way analysis of variance (ANOVA) with independent *t*-tests used for *post hoc* comparisons. Categorical and non-normal data (for example dementia status, DRS-R98 item scores) were compared with non-parametric tests (chi-squared tests, Kruskal–Wallis tests with Mann–Whitney *U*-tests for between-group comparisons). A Bonferroni correction of $P < 0.001$ was applied to the DRS-R98 item score comparisons.

Results

Patient clinical and demographic profile

There were 358 adult in-patients in the hospital on the day of assessment, of whom 311 (87% of all in-patients) were assessed (Fig. 1). The median age of the study cohort was 69 years (range 17–95), 51.1% were male and 52% were on medical wards.

https://doi.org/10.1192/bjp.bp.113.139865 Published online by Cambridge University Press

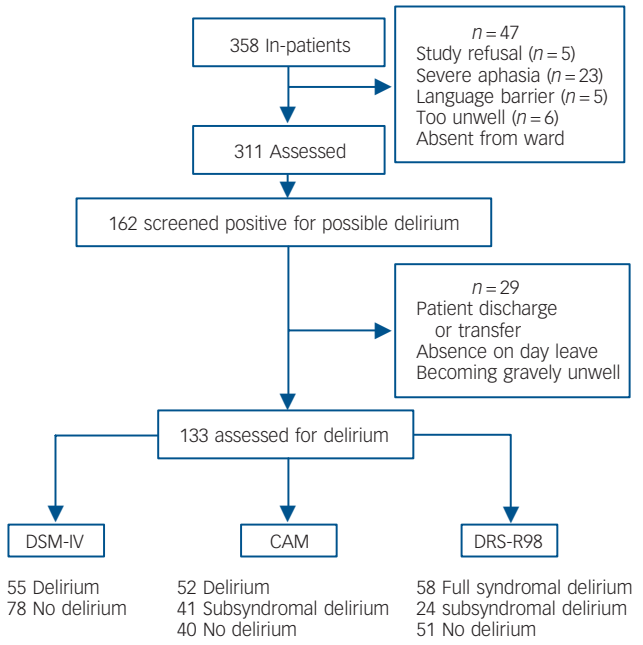

Fig. 1 Diagram of patient flow in the study.

CAM, Confusion Assessment Method; DRS-R98, 16-item Revised Delirium Rating.

Dementia status was clarified in 203/311 (65%) patients, of whom 17% had evidence of comorbid dementia. Median duration of hospital stay at the time of the assessment was 6 days (IQR 0–37). A clear reason for admission was documented in 72% ($n = 225$) and included: to undergo a procedure/surgery ($n = 39$), neurological causes ($n = 33$), respiratory causes ($n = 31$), cardiac causes ($n = 30$) and malignancy/tumours ($n = 25$).

Assessment of cognition and possible delirium

Of the 311 patients who underwent screening, 162 (52%) were positive for possible delirium by virtue of any of demonstrated inattention on either of the two screening tools ($n = 142$; 69 failed months backwards, 129 scored < 5 on SSF), self-reports of confusion ($n = 41$), possible delirium identified by nursing staff ($n = 52$), or delirium/synonym documented in medical case-notes ($n = 29$). Formal evaluation with three diagnostic tools (DRS-R98, CAM and DSM-IV) was conducted for 133 patients (82% of those with possible delirium; 43% of the total study group); omission was because of a combination of patient discharge or transfer, absence on day leave, or severe worsening of medical status during the study period (see Fig. 1).

Frequency of delirium and subsyndromal delirium

The frequencies (%) of delirium in the 133 who underwent detailed assessments were DSM-IV = 55 (17.7%, 95% CI 0.13–0.22), CAM = 52 (16.7%, C.I. 0.13–0.21), DRS-R98 = 58 (18.6%, 95% CI 0.14–0.23). In addition, a further 75 CAM-negative patients had at least one CAM feature (i.e. 127/133 (96%) of patients screening positive for possible delirium had at least one CAM feature) and 41 had at least two CAM features (13.2%, 95% CI 0.10–0.17). Only 6/133 patients had no CAM features. For patients with two CAM features, the frequency of items was acute onset or fluctuating course ($n = 19$), inattention ($n = 33$), disorganised thinking ($n = 16$) and altered consciousness ($n = 30$). A single CAM feature was present in 34 patients, 31 accounted for by disturbed consciousness and 3 by inattention. For DRS-R98 ratings, 24 patients (7.7%, 95% CI 0.05–0.11) had subsyndromal delirium (as defined by scores between 7 and 11).

Concordance between diagnostic systems

Figure 2 shows the agreement in classification between CAM, DRS-R98 and DSM-IV diagnoses for delirium. Concordance ranged from 93% (DSM-IV and DRS-R98; $\kappa = 0.86$) to 78% (CAM with either DSM-IV ($\kappa = 0.56$) or DRS-R98 ($\kappa = 0.58$)). Although 71 patients were identified as having delirium by at least one of the three methods, all three methods agreed for only 38 patients.

The degree of concordance between DRS-R98-defined and CAM-defined subsyndromal delirium is shown in Fig. 3. The frequencies for subsyndromal delirium varied from 24 DRS-R98 patients to 41 patients by the criteria requiring two CAM features. Concordance between these two methods was 50% ($\kappa = 0.21$), with the remaining 12 patients with DRS-R98-defined subsyndromal delirium having either full CAM delirium ($n = 4$) or a single CAM feature ($n = 8$). Agreement in overall attribution of delirium status (combined full or subsyndromal delirium) between DRS-R98 ($n = 82$) and the CAM ($n = 93$) was evident for 69 patients (i.e. two-thirds of all identified by either method).

Comparison of symptom profile according to delirium syndromal status

Patient demographic and clinical characteristics according to delirium syndromal status are shown in Table 1. The DRS-R98 delirium syndromal status was associated with increasing age (between-groups ANOVA, $F = 6.77$, $P = 0.02$). The frequency of comorbid dementia was also higher with greater DRS-R98 syndromal status ($\chi^2 = 15.6$, d.f. = 2, $P < 0.001$) but there was minimal relationship to other comorbidities. Similarly, the median duration of in-patient stay was longer with greater DRS-R98 delirium syndromal status (i.e. full syndromal delirium > subsyndromal delirium > no delirium, $P = 0.006$). Although this population were selected according to possible cognitive problems, and thus have high frequencies of failed SSF testing regardless of syndromal status, performance on the Months Backwards Test significantly discriminated patients according to syndromal status by all three diagnostic approaches.

Table 2 shows the DRS-R98 item and scale scores and item frequencies according to delirium syndromal status as per the DRS-R98, CAM and DSM-IV. The DRS-R98 total and severity scores were distinguishing of different syndromal status of delirium by each of the three methods. Of note, full syndromal delirium was significantly more affected than subsyndromal delirium for language and thinking, for contextual items, and for cognition in respect of attention and orientation when diagnosed by all three methods. In addition, DRS-R98-defined subsyndromal delirium differed from no delirium for disorganised thinking, inattention and both short- and long-term memory.

We did not identify significant differences in severity of individual DRS-R98 items in subsyndromal delirium defined by CAM *v.* DRS-R98 methods. We also compared DRS-R98 item scores for patients with subsyndromal delirium with ($n = 27$) and without ($n = 26$) impaired attention (on the Months Backward Test). Patients with subsyndromal delirium with inattention had significantly higher scores for DRS-R98 total and severity scales, DRS-R98 attention, thought process abnormality, language and acuity of onset (all $P < 0.001$) as well as for agitation, orientation, visuospatial function and symptom fluctuation (all $P < 0.05$).

https://doi.org/10.1192/bjp.bp.113.139865 Published online by Cambridge University Press

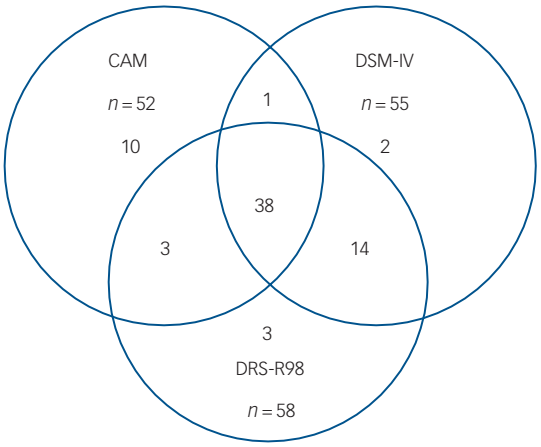

Fig. 2 Venn diagram for those with full syndrome delirium from among a consecutive sample of 133 patients to compare diagnoses according to DSM-IV criteria, Confusion Assessment Method (CAM) algorithm and 16-item Revised Delirium Rating (DRS-R98) total scale methods.

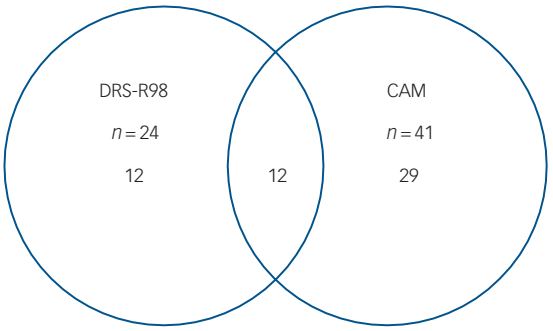

Fig. 3 Venn diagram for those with subsyndromal delirium from among a consecutive sample of 133 patients to compare diagnostic approaches. All were diagnosed according to a dichotomous Confusion Assessment Method (CAM) algorithm and 16-item Revised Delirium Rating (DRS-R98) total scale methods.

Influence of prior cognitive impairment

Among those with DSM-IV delirium ($n = 55$), pre-existing cognitive decline was detected in 28 (51%) patients, primarily through IQCODE telephone interview (only five patients had a prior diagnosis of dementia documented in the case-notes). Compared with those patients with delirium without dementia ($n = 27$), patients who were comorbid had significantly higher DRS-R98 severity ($P = 0.03$) and total ($P = 0.01$) scale scores.

Discussion

This study investigates the frequency of delirium symptoms and syndromal illness among a more complete adult general hospital population than any previous studies. A principal finding is that approximately 20% of in-patients have delirium when assessed

Table 1 Demographic and clinical characteristics of patients ($n = 133$) according to delirium syndromal status as defined by the Confusion Assessment Method (CAM), 16-item Revised Delirium Rating (DRS-R98) and DSM-IV

	Defined by DRS-R98			Defined by CAM			Defined by DSM-IV	
Characteristic	Delirium ($n = 58$)	Subsyndromal delirium ($n = 24$)	No delirium ($n = 51$)	Delirium ($n = 52$)	Subsyndromal delirium ($n = 41$)	No delirium ($n = 40$)	Delirium ($n = 55$)	No delirium ($n = 78$)
Age,[a] mean (s.d.)	76.2 (15.1)	72.5 (14.5)	64.5 (19.1)	76.0 (13.1)	69.2 (18.3)	64.5 (19.7)	76.9 (13.2)	67.0 (18.8)
Female gender, *n* (%)	30 (52)	16 (67)	20 (39)	25 (48)	20 (49)	22 (55)	27 (49)	39 (50)
Comorbid dementia,[b] *n* (%)	28/57 (49)	6/22 (27)	1/24 (4)	24/46 (52)	7/29 (24)	4/28 (14)	28 (51)	7/48 (15)
Number of active medical comorbidities, mean (s.d.)	2.5 (2.4)	2.5 (2.1)	2.2 (1.8)	2.8 (2.6)	1.8 (1.5)	2.3 (1.9)	2.5 (2.5	2.3 (1.9)
Duration of in-patient stay at assessment,[d] mean (s.d.)	22.5 (23.6)	12.3 (17.2)	12.3 (13.9)	20.7 (22.5)	16.6 (19.9)	10.7 (11.5)	20.3 (21.4)	13.8 (17.4)
Scoring 4 or less on Spatial Span Forwards test, *n* (%)	53 (92)	22 (88)	46 (90)	48 (93)	36 (88)	35 (88)	49 (89)	66 (85)
Failure of Months Backward test,[e] *n* (%)	51 (88)	10 (42)	8 (16)	38 (73)	17 (42)	10 (26)	46 (84)	22 (28)
DRS-R98 severity score,[f] mean (s.d.)	15.9 (6.3)	6.5 (1.7)	1.8 (1.2)	14.5 (7.9)	6.1 (5.3)	4.0 (4.5)	16.1 (6.4)	3.6 (3.1)
DRS-R98 total score,[f] mean (s.d.)	20.2 (6.7)	8.6 (1.3)	2.9 (1.7)	18.1 (9.2)	8.6 (6.2)	5.8 (5.6)	20.4 (6.9)	5.2 (3.6)
Number of medications, mean (s.d.)	7.4 (3.4)	6.9 (2.8)	7.8 (3.7)	7.5 (3.2)	7.3 (3.3)	7.4 (3.6)	7.5 (3.3)	7.4 (3.5)
Overall length of stay,[g] mean (s.d.)	60.5 (54.1)	30.4 (36.6)	31.3 (31.7)	50.1 (46.2)	48.8 (46.7)	31.9 (44.1)	57.1 (53.9)	34.6 (36.7)

a. DRS-R98 full syndromal delirium > no delirium at $P < 0.001$; CAM delirium > CAM subsyndromal delirium at $P < 0.05$; DSM-IV delirium > no delirium at $P < 0.001$.
b. DRS-R98 full syndromal delirium > no delirium at $P < 0.001$ and subsyndromal delirium > no delirium at $P < 0.05$; CAM delirium > CAM subsyndromal delirium at $P < 0.05$; DSM-IV delirium > no delirium at $P < 0.001$.
c. Total *n* differs because dementia status known for 103/133 (77%).
d. DRS-R98 full syndromal delirium > no delirium at $P < 0.05$; CAM delirium > CAM no delirium at $P < 0.05$.
e. DRS-R98 full syndromal delirium > no delirium at $P < 0.001$, full syndromal delirium > subsyndromal delirium at $P < 0.01$ and subsyndromal delirium > no delirium at $P < 0.05$; CAM delirium > CAM subsyndromal delirium at $P = 0.02$ and delirium > no delirium at $P < 0.001$; DSM-IV delirium > no delirium at $P < 0.001$
f. DRS-R98 full syndromal delirium > subsyndromal delirium, full syndromal delirium > no delirium and subsyndromal delirium > no delirium at $P < 0.001$; CAM delirium > subsyndromal delirium and no delirium at $P < 0.001$, CAM subsyndromal delirium > no delirium at $P < 0.05$; DSM-IV delirium > no delirium at $P < 0.001$.
g. DRS-R98 full syndromal delirium > no delirium at $P < 0.01$, full syndromal delirium > subsyndromal delirium at $P < 0.01$; CAM delirium > no delirium at $P < 0.05$; DSM-IV delirium > no delirium at $P < 0.01$.

https://doi.org/10.1192/bjp.bp.113.139865 Published online by Cambridge University Press

https://doi.org/10.1192/bjp.bp.113.139865 Published online by Cambridge University Press

Table 2 Phenotype descriptions using the DRS-R98 items to compare phenomenology across groups defined as non-delirium, subsyndromal delirium (two methods) and delirium to compare three methods for defining the groups (Confusion Assessment Method (CAM), 16-item Revised Delirium Rating (DRS-R98) and DSM-IV)[a]

	Mean (s.d.) % any severity (% moderate or great severity)[b]							
	Defined by DRS-R98, mean (s.d.)			Defined by CAM			Defined by DSM-IV	
DRS-R98 items	Delirium (*n* = 58)	Subsyndromal delirium (*n* = 24)	No delirium (*n* = 51)	Delirium (*n* = 52)	Subsyndromal delirium (*n* = 41)	CAM-defined No delirium (*n* = 40)	Delirium (*n* = 55)	No delirium (*n* = 78)
1. Sleep–wake cycle disturbance	1.5 (0.7) 91 (50)	0.9 (0.6) 75 (9)	0.7 (0.6) 64 (6)	1.3 (0.8) 85 (42)	1.0 (0.8) 76 (23)	0.8 (0.6) 70 (8)	1.5 (0.7) 89 (51)	0.8 (0.6) 70 (8)
2. Perceptual disturbances	0.3 (0.9) 17 (11)	0.2 (0.6) 8 (4)	0.0 (0.0) 0 (0)	0.3 (0.8) 17 (10)	0.0 (0.0) 0 (0)	0.2 (0.7) 8 (5)	0.4 (0.9) 18 (11)	0.1 (0.4) 3 (1)
3. Delusions	0.7 (1.1) 33 (23)	0.1 (0.3) 8 (0)	0.1 (0.3) 4 (2)	0.7 (1.2) 31 (21)	0.1 (0.5) 8 (5)	0.1 (0.4) 8 (3)	0.8 (1.2) 34 (24)	0.1 (0.3) 5 (1)
4. Lability of affect	0.7 (0.8) 47 (21)	0.3 (0.4) 25 (0)	0.1 (0.4) 8 (2)	0.6 (0.8) 46 (17)	0.2 (0.7) 18 (10)	0.1 (0.4) 14 (0)	0.7 (0.8) 51 (22)	0.1 (0.4) 12 (2)
5. Language	1.0 (0.9) 69 (24)	0.1 (0.3) 13 (0)	0.1 (0.2) 4 (0)	0.9 (0.9) 63 (25)	0.3 (0.6) 15 (3)	0.1 (0.4) 14 (0)	1.0 (0.9) 65 (26)	0.1 (0.3) 12 (0)
6. Thought process abnormalities	1.7 (0.9) 88 (64)	0.6 (0.7) 50 (13)	0.1 (0.3) 10 (0)	1.5 (1.0) 79 (54)	0.6 (0.9) 36 (18)	0.4 (0.8) 30 (11)	1.7 (0.9) 87 (66)	0.3 (0.6) 26 (5)
7. Motor agitation	0.9 (1.0) 55 (24)	0.2 (0.4) 17 (0)	0.1 (0.2) 6 (0)	0.8 (1.0) 48 (21)	0.1 (0.7) 23 (5)	0.2 (0.4) 14 (3)	0.9 (1.0) 58 (26)	0.1 (0.3) 9 (0)
8. Motor retardation	0.7 (0.8) 47 (19)	0.3 (0.4) 25 (0)	0.1 (0.1) 2 (0)	0.6 (0.8) 40 (19)	0.2 (0.4) 16 (0)	0.2 (0.4) 14 (3)	0.7 (0.8) 45 (18)	0.1 (0.4) 12 (1)
9. Orientation	1.2 (0.9) 88 (37)	0.3 (0.5) 21 (4)	0.1 (0.2) 6 (0)	1.2 (0.9) 77 (37)	0.2 (0.7) 26 (8)	0.1 (0.3) 8 (0)	1.3 (0.9) 78 (38)	0.1 (0.4) 13 (1)
10. Attention	1.8 (0.8) 95 (66)	0.8 (0.6) 67 (8)	0.1 (0.4) 8 (2)	1.7 (1.0) 85 (58)	0.3 (0.9) 46 (20)	0.3 (0.5) 30 (3)	1.9 (0.8) 98 (67)	0.3 (0.6) 27 (5)
11. Short-term memory	1.9 (1.1) 88 (64)	1.3 (1.1) 79 (33)	0.2 (0.4) 16 (2)	1.8 (1.2) 81 (60)	1.0 (1.1) 56 (26)	0.5 (0.9) 32 (14)	2.0 (1.0) 91 (64)	0.6 (1.0) 36 (14)
12. Long-term memory	1.4 (1.1) 67 (52)	0.5 (0.7) 46 (8)	0.1 (0.1) 2 (0)	1.3 (1.2) 60 (44)	0.4 (0.8) 28 (13)	0.3 (0.8) 22 (8)	1.4 (1.2) 65 (53)	0.2 (0.5) 19 (4)
13. Visuospatial ability	2.1 (1.0) 93 (62)	1.0 (0.9) 70 (29)	0.4 (0.6) 30 (6)	1.8 (1.0) 89 (62)	1.0 (1.0) 59 (31)	0.7 (1.0) 40 (19)	2.1 (1.0) 91 (73)	0.7 (0.8) 47 (16)
14. Temporal onset of symptoms	1.4 (0.8) 88 (43)	0.5 (0.7) 42 (8)	0.1 (0.3) 10 (0)	1.2 (1.0) 71 (33)	0.4 (0.8) 49 (18)	0.3 (0.6) 22 (8)	1.5 (0.8) 91 (44)	0.3 (0.5) 22 (4)
15. Fluctuation in symptom severity	1.0 (0.7) 79 (24)	0.2 (0.4) 21 (0)	0.1 (0.2) 6 (0)	0.9 (0.7) 65 (21)	0.4 (0.6) 33 (5)	0.2 (0.5) 16 (3)	1.1 (0.7) 80 (26)	0.1 (0.3) 13 (0)
16. Physical disorder	1.8 (0.4) 100 (81)	1.4 (0.6) 96 (42)	1.1 (0.7) 82 (24)	1.6 (0.6) 92 (67)	1.4 (0.6) 95 (46)	1.3 (0.6) 92 (35)	1.8 (0.4) 100 (80)	1.2 (0.6) 87 (33)

a. Comparison of scores with Bonferroni correction significance applied at $P < 0.001$: DRS-R98 comparisons: all 3 DRS-R98 groups for items 1, 4–16, DRS-R98 full syndromal delirium > no delirium for all categories, DRS-R98 full syndromal delirium > subsyndromal delirium for items 5, 6, 9, 10, 13–16, DRS-R98 subsyndromal delirium > no delirium for items 6, 10–12; CAM status comparisons: CAM positive > no delirium for all items except item 2; CAM positive > CAM subsyndromal delirium for items 5, 6, 9, 10, CAM subsyndromal delirium > CAM no delirium for items 11 and 14; DSM-IV comparisons: DSM-IV delirium > no DSM-IV delirium for all items except item 2. CAM subsyndromal delirium *v.* DRS-R98 subsyndromal delirium – non-significant for all items.
b. Mean DRS-R98 item scores are shown along with frequencies % when present at any severity followed by % when present at moderate or greater severity in parentheses for 133 patients.

cross-sectionally, regardless of diagnostic definition used. In addition, a substantial number of patients have significant delirium symptoms without full syndromal illness, so-called subsyndromal delirium, but the frequency of this phenomenon varied considerably according to whether categorical or dimensional definitions were applied. There was considerable discordance in identification of syndromal delirium according to DSM-criteria, the CAM diagnostic algorithm and DRS-R98 cut-off scores, which did not concur in a third of 'possible' cases. Although the attribution of DSM-IV by an expert assessor is considered the gold standard for delirium assessment, a clearly defined and systematic means of conducting this remains lacking. The emergence of new DSM-5 criteria[37] for delirium can provide an opportunity to establish a consensus among delirium researchers as to how best to approach identifying delirium for research efforts.

Towards a definition of subsyndromal delirium

The phenomenological comparisons between full, subsyndromal and no delirium highlighted how core diagnostic features of delirium (disturbed higher-order thinking and impaired cognition – especially inattention) were the most distinguishing regardless of whether categorical or dimensional approaches were used to attribute delirium syndromal status. Some previous work defined subsyndromal delirium according to the presence of any CAM features without full syndromal delirium (i.e. including patients with a single CAM item). This work emphasises how such a definition generates an overinclusive concept of subsyndromal delirium that is frequently based upon altered consciousness without any other core features of delirium, and therefore has limited relevance to the syndrome of delirium.

We did not identify significant differences in age, dementia status or individual DRS-R98 item scores for subsyndromal delirium defined by the CAM and DRS-R98 methods. These findings suggest that subsyndromal delirium might be usefully defined by either categorical or dimensional means. However, the disparity in patient overlap between methods raises concerns as to the optimal definition – if subsyndromal delirium is defined by the absence of a single key diagnostic criterion for delirium then subsyndromal delirium attribution may be especially prone to rater error. Moreover, the CAM is less reliable when rated by non-experts, with assessment of attention and disorganised thinking especially challenging.[38–40] A more fundamental issue relates to whether the relatively non-specific, poorly recognised, highly variable and fluctuating nature of delirium symptoms allows for reliable identification of mandatory features.

We compared subsyndromal delirium with and without inattention and found that the presence of inattention distinguished patients with subsyndromal delirium, which was more closely related to traditional phenomenological descriptions of delirium, with more prominent disturbance of higher-order thinking, more acute onset and greater impairment of multiple cognitive functions consistent with the generalised disturbance of brain function that is typical of delirium. These findings suggest that definitions of subsyndromal delirium should include inattention as a required element.

Diagnostic criteria for delirium serve various functions – to facilitate the recognition of a discrete neuropsychiatric syndrome and to identify patients with cognitive problems that are associated with poor outcomes. For the former, use of dimensional methods that include a wide range of features is preferable as this dilutes the diagnostic impact of individual symptoms that occur commonly in physically morbid patients and lack specificity for delirium. Central to this issue is whether the prevailing highly inclusive 'umbrella' concept of delirium represents the optimal approach to describing acute cognitive and neuropsychiatric disturbances in the physically unwell. The treatment implications of identifying subsyndromal delirium are key to this issue – with some work indicating that antipsychotic prophylaxis can reduce transition from subsyndromal delirium to delirium in patients post cardiac surgery.[21] Ultimately, the preferred approach to case identification may be determined by the expertise of the assessor, with the simplicity of categorical definitions of subsyndromal delirium more attractive in many settings.

The disparity in overall attribution of delirium status (combined full and subsyndromal delirium) between the DRS-R98 and the CAM for a third of cases suggests that the current boundaries of what is considered delirium require more detailed study. Overall, the literature regarding subsyndromal delirium concurs that subsyndromal delirium resembles full syndromal delirium but at a lesser severity.[16,41,42] Recently published DSM-5 criteria[37] include a description of delirium in the neurocognitive disorders section that is minimally changed from DSM-IV, albeit somewhat more restrictive. The concept of subsyndromal delirium is accounted for as 'attenuated delirium syndrome' but the available subsyndromal delirium literature was considered inadequate to support a new diagnostic description. Based upon our findings, we suggest a definition of subsyndromal delirium that can incorporate both categorical and dimensional elements as required by the assessor (see Appendix) to facilitate more systematic and readily comparable studies of subsyndromal delirium. The application of these criteria can allow for more consistent efforts to identify treatment needs and prognosis for patients with subsyndromal delirium, as well as studies to explore how it relates temporally to full syndromal illness (for example as part of an evolving or resolving illness and to what extent it is a distinct entity whereby patients can experience subsyndromal delirium without ever progressing to full syndromal delirium.

Strengths and weaknesses

To our knowledge, this is the first study to assess the point prevalence of delirium in the general wards of an entire hospital rather than extrapolating from selected cohorts or combining data from more than one study. In order to optimise diagnostic efficiency, we used an initial screening phase whereby the CAM, DRS-R98 and DSM-IV assessments were performed on patients with either impaired attention at the time of assessment or evidence of recent 'confusion'. Because delirium diagnosis requires inattention as a mandatory feature, we believe that these methods will have detected most cases of delirium in this population. Although it is possible that some cases may have been missed because of the fluctuating nature of delirium, the combination of detailed cross-sectional assessment for clinically significant inattention combined with recent evidence of confusion by any of three sources minimised the likelihood of missed cases.

We applied DRS-R98 cut-off scores that were relatively low in order to maximise diagnostic sensitivity. This may have had an impact on the relative frequencies of full *v.* subsyndromal delirium but the observed concordance (93%) between full syndromal delirium defined by the DRS-R98 and independently determined DSM-IV, along with other studies[18,31,32] suggests that this lower cut-off is justified where high sensitivity (including to milder delirium) is required.

The uncertainty as to whether inattention should be a required feature of subsyndromal delirium means that we may have underestimated its frequency in the population who did not screen positive at the initial phase of assessment. However, our findings that subsyndromal delirium with inattention was clinically more significant suggest that these screening methods can also be

https://doi.org/10.1192/bjp.bp.113.139865 Published online by Cambridge University Press

usefully applied to identification of significant subsyndromal illness. In addition, the high participation supports the applicability of these methods to everyday clinical practice. Moreover, our approach to delirium detection is an efficient means of optimising delirium detection that includes multiple sources of information and utilises both verbal and non-verbal cognitive testing.

The frequency of delirium is likely to have been high in the severely ill patients who were excluded. The true frequency of both full and subsyndromal delirium is thus likely to be somewhat higher. Ideally, all in-patients would have undergone the full battery of assessments but this was not possible because of resource and time restrictions. The differences between 'no delirium' and subsyndromal delirium may be more marked where assessments also include patients who do not screen positive for possible delirium because these patients are likely to have even lower ratings with the DRS-R98 and other measures.

The differences in delirium diagnostic frequency between CAM assessments and DRS-R98/DSM-IV criteria could relate to the relative expertise of raters, since the latter two methods were applied by highly experienced delirium researchers from consultation–liaison psychiatry backgrounds. However, the extensive CAM training and seniority of the geriatricians who conducted the CAM assessments suggests that differences in delirium detection reflect core issues of accuracy of the instruments involved.

Finally, the study relates to a single hospital, and although we believe (and selected) this to be representative of modern in-patient centres, further work replicating these findings (and applying the description of subsyndromal delirium defined herein) elsewhere can further enhance our understanding of the syndromal frequency of delirium.

Implications

Delirium is present in approximately one in five in-patients at any time. Additionally, a substantial number of patients experience subsyndromal illness that is phenomenologically and prognostically on a continuum between no delirium and full syndromal illness. There is considerable disparity in the frequency of delirium diagnosis by DSM-IV, DRS-R98 and CAM methods. Similarly, there is only modest overlap in patients with subsyndromal delirium identified by dimensional and categorical methods. These findings suggest that the prevailing syndromal concept of delirium, and the methods by which we define it, lack precision as the low concordance evident in this work may underpin inconsistencies in the literature. We describe a definition of subsyndromal delirium that can facilitate more systematic and comparable studies of subsyndromal delirium. Future definitions of delirium can be informed by further studies of the phenomenological footprint of delirium in different clinical populations.

Funding

D.M., M.L., S.T. and N.O'R. are all in receipt of funding from the Health Research Board.

Appendix

Suggested criteria for diagnosis of subsyndromal delirium

(a) Absence of full syndromal criteria;

(b) evidence of acute or subacute onset (must be a temporally discrete syndrome) disturbance of brain function that includes;

(c) evidence of disturbed attention, and

(d) either any other CAM feature or evidence of cognitive and neuropsychiatric disturbances (for example measured on the DRS-R98) that are not better accounted for by a dementia or other neuropsychiatric condition (such as depression).

D. Meagher, MD, PhD, MRCPsych, Foundation Chair of Psychiatry, Head of Teaching and Research in Psychiatry, University of Limerick Medical School, Limerick, Director of the Cognitive Impairment Research Group, Centre for Interventions in Infection, Inflammation & Immunity (4i), Graduate Entry Medical School, University of Limerick and Department of Psychiatry, University Hospital Limerick, Ireland; **N. O'Regan**, MRCPI, **D. Ryan**, MRCPI, **W. Connolly**, MB, **E. Boland**, MB, **R. O'Caoimhe**, MB, **J. Clare**, MRCP, Centre for Gerontology and Rehabilitation, St Finbarr's Hospital, Cork, Ireland; **J. Mcfarland**, MD, MRCPsych, **S. Tighe**, MRCPsych, University of Limerick Medical School, Limerick and Clare-Limerick Mental Health Services, HSE-West, Mental Health Services, Ireland; **M. Leonard**, MD, MRCPsych, University of Limerick Medical School, Limerick and Cognitive Impairment Research Group, Centre for Interventions in Infection, Inflammation & Immunity (4i), Graduate Entry Medical School, University of Limerick, Ireland; **D. Adamis**, MD, MRCPsych, University of Limerick Medical School, Limerick, Cognitive Impairment Research Group, Centre for Interventions in Infection, Inflammation & Immunity (4i), Graduate Entry Medical School, University of Limerick, Ireland, Sligo-Leitrim Mental Health Services, Sligo, Ireland, and Research and Academic Institute of Athens, Athens, Greece; **P. T. Trzepacz**, MD, Lilly Research Laboratories, Indianapolis, Indiana, University of Mississippi Medical School, Jackson, Tufts University School of Medicine, Massachusetts and Indiana University School of Medicine, Indiana, USA; **S. Timmons**, MD, MRCPI, Centre for Gerontology and Rehabilitation, St Finbarr's Hospital, Cork, Ireland.

Correspondence: David Meagher, Graduate-entry Medical School, University of Limerick, Ireland. Email: david.meagher@ul.ie

First received 3 Oct 2013, final revision 30 May 2014, accepted 6 Jun 2014

References

1 Witlox J, Eurelings LS, de Jonghe JF, Kalisvaart KJ, Eikelenboom P, van Gool WA. Delirium in elderly patients and the risk of post discharge mortality, institutionalization, and dementia: a meta-analysis. *JAMA* 2010; **304**: 443–51.

2 Marcantonio E, Ta T, Duthie E, Resnick NM. Delirium severity and psychomotor types: their relationship with outcomes after hip fracture repair. *J Am Geriatr Soc* 2002; **50**: 850–7.

3 Dosa D, Intrator O, McNicoll L, Cang Y, TenoJ. Preliminary derivation of a Nursing Home Confusion Assessment Method based on data from the minimum data set. *J Am Geriatr Soc* 2007; **55**: 1099–105.

4 Ouimet S, Riker R, Bergeron N, Cossette M, Kavanagh B, Skrobik Y. Subsyndromal delirium in the ICU: evidence for a disease spectrum. *Intensive Care Med* 2007; **33**: 1007–13.

5 Cole MG, McCusker J, Ciampi A, Belzile E. The 6- and 12-month outcomes of older medical inpatients who recover from subsyndromal delirium. *J Am Geriatr Soc* 2008; **56**: 2093–9.

6 Martinez-Velilla N, Alonso-Bouzon C, Cambra-Contin K, Ibañez-Beroiz B, Alonso-Renedo J. Outcome in complex patients with delirium and subsyndromal delirium one year after hospital discharge. *Int Psychogeriatrics* 2013; **25**: 2087–8.

7 Cole M, McCusker J, Dendukuri N, Han, L. The prognostic significance of subsyndromal delirium in elderly medical inpatients. *J Am Geriatr Soc* 2003; **51**: 754–60.

8 Cole MG, McCusker J, Voyer P, Monette J, Champoux N, Ciampi A, et al. Subsyndromal delirium in older long-term care residents: incidence, risk factors, and outcomes. *J Am Geriatr Soc* 2011; **59**: 1829–36.

9 Bourdel-Marchasson I, Vincent S, Germain C, Salles N, Jenn J, Rasoamanarivo E, et al. Delirium symptoms and low dietary intake in older inpatients are independent predictors of institutionalization: a 1-year prospective population-based study. *J Gerontol Biol Med Sci* 2004; **59**: 350–4.

10 Marcantonio ER, Kiely DK, Simon SE, John Orav E, Jones RN, Murphy KM, et al. Outcomes of older people admitted to postacute facilities with delirium. *J Am Geriatr Soc* 2005; **53**: 963–9.

11 Tan MC, Felde A, Kuskowski M, Ward H, Kelly RF, Adabag AS, et al. Incidence and predictors of post-cardiotomy delirium.*Am J Geriatric Psychiatry* 2008; **16**: 575–83.

12 Leonard M, Spiller J, Keen J, MacLullich A, Kamholtz B, Meagher D. Symptoms of depression and delirium assessed serially in palliative-care inpatients. *Psychosomatics* 2009; **50**: 506–14.

13 Bond SM, Dietrich MS, Shuster JL Jr, Murphy BA. Delirium in patients with head and neck cancer in the outpatient treatment setting. *Support Care Cancer* 2012; **20**: 1023–30.

https://doi.org/10.1192/bjp.bp.113.139865 Published online by Cambridge University Press

14 von Gunten A, Mosimann UP. Delirium upon admission to Swiss nursing homes: a cross-sectional study. *Swiss Med Wkly* 2010; **140**: 376–81.

15 Zuliani G, Bonetti F, Magon S, Prandini S, Sioulis F, D'Amato M, et al. Subsyndromal delirium and its determinants in elderly patients hospitalized for acute medical illness. *J Gerontol A Biol Sci Med Sci.* 2013; **68**: 1296–302.

16 Franco JG, Trzepacz PT, Mejía MA, Ochoa SB. Factor analysis of the Colombian translation of the Delirium Rating Scale (DRS), Revised-98. *Psychosomatics* 2009; **50**: 255–62.

17 Grover S, Mattoo S, Chakravarty K, Trzepacz PT, Meagher D, Gupta N. Symptom profile and etiology of delirium in a referral population in Northern India: factor analysis of the DRS-R98. *J Neuropsychiatry Clin Neurosci* 2012; **24**: 95–101.

18 Meagher D, Adamis D, Trzepacz P, Leonard M. Features of subsyndromal and persistent delirium. *Br J Psychiatry* 2012; **200**: 37–44.

19 Ceriana P, Fanfulla F, Mazzacane F, Santoro C, Nava S. Delirium in patients admitted to a step-down unit: analysis of incidence and risk factors. *J Crit Care* 2010; **25**: 136–43.

20 Skrobik Y, Ahern S, Leblanc M, Marquis F, Awissi DK, Kavanagh BP. Protocolized intensive care unit management of analgesia, sedation, and delirium improvesanalgesia and subsyndromal delirium rates. *Anesth Analg* 2010; **111**: 451–63.

21 Hakim SM, Othman AI, Naoum DO. Early treatment with risperidone for subsyndromal delirium after on-pump cardiac surgery in the elderly: a randomized trial. *Anesthesiology* 2012; **116**: 987–97.

22 Voyer P, Richard S, Doucet L, Carmichael PH. Detecting delirium and subsyndromal delirium using different diagnostic criteria among demented long-term care residents. *J Am Med Dir Assoc* 2009; **10**: 181–8.

23 Ryan DJ, O'Regan NA,Ó Caoimh R, Clare J, O'Connor M, Leonard M, et al. Delirium in an adult acute hospital population: predictors, prevalence and detection. *BMJ Open* 2013; **3**: e001772.

24 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorder (4th edn) (DSM-IV)*. APA, 1994.

25 Hart RP, Levenson JL, Sessler CN, Best AM, Schwartz SM, Rutherford LE. Validation of a cognitive test for delirium in medical ICU patients. *Psychosomatics* 1996; **37**: 533–46.

26 Blessed G, Tomlinson BE, Roth M. The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. *Br J Psychiatry* 1968; **114**: 797–811.

27 Meagher DJ, Leonard M, Donnelly S, Conroy M, Saunders J, Trzepacz PT. A comparison of neuropsychiatric and cognitive profiles in delirium, dementia, comorbid delirium-dementia and cognitively intact controls. *J Neurol Neurosurg Psychiatry* 2010; **81**: 876–81.

28 Inouye SK, C. H. van Dyck, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med* 1990; **113**: 941–8.

29 Trzepacz PT, Mittal D, Torres R, Kanary K, Norton J, Jimerson N. Validation of the Delirium Rating Scale-Revised-98: comparison with the delirium rating scale and the cognitive test for delirium. *J Neuropsychiatry Clin Neurosci* 2001; **13**: 229–42.

30 Trzepacz PT, Maldonado JR, Kean J, Abell M, Meagher DJ. *The Delirium Rating Scale- Revised-98 (DRS-R98) Administration Manual. A Guide to Increase Understanding of How to Solicit Delirium Symptoms to Administer the DRS-R98*. Paula Trzepacz, 2010.

31 Franco JG, Mejía MA, Ochoa SB, Ramírez LF, Bulbena A, Trzepacz PT. Delirium rating scale-revised-98 (DRS-R-98): Colombian adaptation of the Spanish version. *Actas Esp Psiquiatr* 2007; **35**: 170–5.

32 Kato M, Kishi Y, Okuyama T, Trzepacz PT, Hosaka T. Japanese version of the Delirium Rating Scale, Revised-98 (DRS-R98-J): reliability and validity. *Psychosomatics* 2010; **51**: 425–31.

33 Jorm AF. The Informant Questionnaire on cognitive decline in the elderly (IQCODE): a review. *IntPsychogeriatrics* 2004; **16**: 275–93.

34 Charlson ME, Pompei P, Ales KL, Mackenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chron Dis* 1987; **40**: 373–83.

35 World Medical Association. *Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects*. World Medical Association, 2004 (http://www.wma.net/en/30publications/10policies/b3/).

36 Siddiqi N, House AO, Holmes JD. Occurrence and outcome of delirium in medical in-patients: a systematic literature review. *Age Ageing* 2006; **35**: 350–64.

37 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorder (5th edn) (DSM-5)*. APA, 2013.

38 Inouye SK, Foreman MD, Mion LC, Katz KH, Cooney LM Jr. Nurses' recognition of delirium and its symptoms: comparison of nurse and researcher ratings. *Arch Intern Med* 2001; **161**: 2467–73.

39 Ryan K, Leonard M, Guerin S, Donnelly S, Conroy M, Meagher D. Validation of the confusion assessment method in the palliative care setting. *Palliat Med* 2009; **23**: 40–5.

40 Sands MB, Dantoc BP, Hartshorn A, Ryan CJ, Lujic S. Single Question in Delirium (SQiD): testing its efficacy against psychiatrist interview, the Confusion Assessment Method and the Memorial Delirium Assessment Scale. *Palliat Med* 2010; **24**: 561–5.

41 Meagher DJ, Leonard M, Donnelly S, Conroy M, Adamis D, Trzepacz PT. A longitudinal study of motor subtypes in delirium: relationship with other phenomenology, etiology, medication exposure and prognosis. *J Psychosom Res* 2011; **71**: 395–403.

42 Trzepacz PT, Franco JG, Meagher DJ, Lee Y, Kim JL, Kishi Y, et al. Phenotype of subsyndromal delirium using pooled multicultural Delirium Rating Scale—Revised-98 data. *J Psychosom Res* 2012; **73**: 10–7.

https://doi.org/10.1192/bjp.bp.113.139865 Published online by Cambridge University Press