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SYSTEMATIC REVIEW

Occurrence and outcome of delirium in medical in-patients: a systematic literature review

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Abstract

Background: Despite the acknowledged clinical importance of delirium, research evidence for measures to improve its management is sparse. A necessary first step to devising appropriate strategies is to understand how common it is and what its outcomes are in any particular setting.
Objective: To determine the occurrence of delirium and its outcomes in medical in-patients, through a systematic review of the literature.
Method: We searched electronic medical databases, the Consultation-Liaison Literature Database and reference lists and bibliographies for potentially relevant studies. Studies were selected, quality assessed and data extracted according to preset protocols.
Results: Results for the occurrence of delirium in medical in-patients were available for 42 cohorts. Prevalence of delirium at admission ranged from 10 to 31%, incidence of new delirium per admission ranged from 3 to 29% and occurrence rate per admission varied between 11 and 42%. Results for outcomes were available for 19 study cohorts. Delirium was associated with increased mortality at discharge and at 12 months, increased length of hospital stay (LOS) and institutionalisation. A significant proportion of patients had persistent symptoms of delirium at discharge and at 6 and 12 months.
Conclusion: Delirium is common in medical in-patients and has serious adverse effects on mortality, functional outcomes, LOS and institutionalisation. The development of appropriate strategies to improve its management should be a clinical and research priority. As delirium prevalent at hospital admission is a significant problem, research is also needed into preventative measures that could be applied in community settings.

Keywords: *delirium, systematic review, prevalence, incidence, prognosis, elderly*

Introduction

Delirium is said to be common in most hospital settings [**1**–**4**]. It is associated with significant adverse physical, cognitive and psychological outcomes [**1**, **5**, **6**] and increased costs to healthcare services [**4**, **7**]. It is often seen as a complication of hospital care and a marker of the quality of in-patient care [**8**]. Despite its clinical importance, surprisingly little is known about its epidemiology, outcomes, prevention or management.

Delirium has been recognised as a mental disorder for thousands of years, with fairly consistent clinical descriptions since the second century CE [**9**]. There is now agreement about its core features: disturbance of consciousness, disturbance of cognition, rapid onset, fluctuating course and external causation [10] (the syndrome can be attributed to an independently diagnosable cerebral or systemic disease or disorder). Diagnostic criteria for delirium have been formulated in the Diagnostic and Statistical Manual of Mental Disorders [11–13] (DSM-III, DSM-III-R and DSM-IV) and in the tenth edition of the International Classification of Diseases [14] (ICD-10). Use of such operationalised diagnostic criteria should improve comparability of studies [**15**].

Delirium is undetected and misdiagnosed in the clinical setting [**16**–**18**]. The transient and fluctuating nature of symptoms and the heterogeneity of presentations associated with several different delirium subtypes contribute [**15**, **19**]. Standardised research instruments have improved diagnostic consistency [**15**], but under-recognition remains a problem.

Evidence for effectiveness of measures to detect, prevent or manage delirium is sparse [**20**]. The wide range of potential aetiological factors suggests that to be effective, interventions will need to address not only the specifics of direct care but also service delivery issues [**8**, **21**]. There may also be setting-specific factors to be considered. Measures to improve delirium management may have benefits in terms of improving healthcare for in-patients generally [**8**].

A necessary first step to devising appropriate strategies to prevent and manage delirium is to determine its occurrence and outcomes in a particular setting; these will have implications in the planning and evaluation of any intervention. The cost per case and predictive value of screening will depend on how common it is in that setting. Outcomes of delirium, including its economic implications, will determine feasibility of screening and intervention strategies. The type of service offered will also be influenced by how common the disorder is.

Medical in-patient settings have patients with a wide range of conditions and include a large proportion of older patients—a known risk factor for delirium [**22**]. Investigating delirium in medical in-patients would, therefore, have advantages in terms of wider relevance and generalisability of findings.

Objectives

To determine the occurrence and outcomes of delirium in medical in-patients in hospital through a systematic review of the literature.

Criteria for selecting studies for this review

Types of study

For occurrence, we included prospective cohort and cross-sectional studies.

For outcomes, we included prospective cohort studies, case–control studies and controlled trials.

Studies in hospital general medical in-patient settings were included, as were studies in settings or population groups where patients were judged to be similar to those found in general medical in-patients. Studies in community or hospice settings, psychiatric, surgical, accident and emergency and intensive care units were excluded. Studies solely of patients referred to liaison psychiatry services were also excluded. Studies in mixed populations were only included if data for general medical in-patients were reported separately, and results for this subset only were included in the analyses.

We included studies using a case definition consistent with current consensus criteria for delirium and all its subtypes but excluded studies of delirium tremens.

Outcome measures

We included studies with preset, clearly defined important outcomes. A preliminary review of the literature suggested no single widely accepted primary outcome. We, therefore, examined immediate short-term and long-term outcomes as follows:

Up to discharge: reversibility of delirium, duration of delirium episode, number of episodes, persistence of delirium symptoms, complications (e.g. falls, infections), mortality, cognitive function, physical function, length of admission, cost of admission, requirement for institutional care, psychological distress, carer distress and impact on staff.

At 6, 12 and 24 months: mortality, presence of delirium symptoms, physical and cognitive function, psychological distress, institutionalisation and carer distress.

For details of the quality criteria and scoring and search strategy used in this review, please see Appendix 1 in the supplementary data on the journal website (http://ageing.oxfordjournals.org/).

Methods

Systematic data extraction and assessments of quality were carried out using a data extraction tool by one reviewer. A 10% sample of studies considered for inclusion was also examined by a second reviewer independently, and good agreement was found.

There is often confusion about the distinction between the statistical terms incidence and prevalence. Incidence rates represent new events, noted in the follow-up of a cohort. Prevalence represents existing events, noted at a single point in time for the state of the group under study [**23**]. In clinical practice, the distinction may be problematic, particularly in transient or fluctuating conditions, where the frequency of examination will have a major impact on reported rates. Feinstein [**23**] suggests the term 'occurrence rate' to avoid some of these ambiguities. We use this term wherever incidence or prevalence has not been clearly determined, and we give a description of the measure actually used.

Results

Prevalence, incidence and occurrence studies

The initial search produced 1,052 citations of potential relevance, and following examination of titles and abstracts, 116 full-text articles were retrieved for further consideration. Sixty-five were excluded; 26 included surgical, nursing home or liaison psychiatry settings [24–49]; 10 used inappropriate definitions for delirium [50–59]; 7 were retrospective studies [60–66]; 4 were reviews [**5**, **7**, 67, 68]; 3 included only male patients [69–71] and in 15, the incidence, prevalence or occurrence of delirium was not determined or reported [72–86].

Fifty papers met our inclusion criteria [**6**, **16**, **17**, 87–133], but several of these reported data from the same original study population (17 reports from 7 cohorts) [**6**, **16**, **17**, 89, 90, 98, 103, 105, 106, 108, 114, 117, 118, 121–123, 132]. In these, we took the earliest paper reporting relevant data as the index study. Additional information available in related subsequent papers was also extracted and presented alongside the index study. In two studies, distinct cohorts were examined and reported separately [109, 110]. Results for the occurrence of delirium in hospitalised general medical in-patients were, therefore, available for 42 cohorts reported in 40 studies (Table 1).

Sample

All studies were carried out in general medical or elderly care units, mainly sampling consecutive admissions. Two studies used a census of in-patients, over 1 week [96] and over 6 months [117]. Inclusion and exclusion criteria were broadly similar, with most studies excluding subjects with

Table 1. Summary of studies in delirium prevalence, incidence or occurrence review

Study	Sample	Screening and diagnosis	Age, mean years (SD)
Erkinjuntti, Finland [101]	>55 years (2000)	SPMSQ weekday after admission; further examination of patients with two or more errors or if untestable; diagnosis by one investigator, using information from several sources	Not given
Cole, Canada [100]	>65 years; excluded if stroke, in ICU or CCU > 48 h, admitted to geriatrics or oncology (1925)	SPMSQ and review of nursing notes for delirium symptoms within 24 h of admission and those without prevalent delirium re-screened within 1 week; CAM for those screening positive; DSMIII-R	82 (7)
Villapando-Berumen, Mexico [131]	>60 years; excluded if hospitalised <48 h, sedated, intubated, aphasic or delirium on admission (667)	Unstructured interview with patient, nurse and relative if available between 24 and 48 h of admission and daily to discharge, death or diagnosis of delirium; CAM	72.4
Zanocchi, Italy [133]	Admissions to geriatric unit (585)	Clinical review two or more times a day for episodes of delirium. Review of findings by study physician with information from medical records two or more times a day	77.1
Gaudet, France [107]	Admissions to geriatric unit (487)	Case finding methods not described; DSMIIIR criteria for diagnosis	84.5
Cole, Canada [99]	>75 years; excluded if stroke, in ICU or CCU > 48 h, admitted to geriatrics or oncology (484)	SPMSQ within 24 h of admission CAM administered by study nurse to those screening positive on SPMSQ (>5); DSMIII-R criteria	83.3
Bourdel-Marchasson, France [95]	>75 years, >36 h in hospital, not institutionalised (427)	Symptoms recorded by nurses using CAM within 24 h and every 3 days to discharge	84.8 (6)
Inouye, USA [**112**]	>75 years, no delirium at admission but at intermediate or high risk; excluded if unable to be interviewed or terminal illness (426)	MMSE, CAM, administered by trained researchers using standardised assessments within 48 h of admission and daily to discharge	79.8 (6.2)
Foy, Australia [104]	>60 years, normal cognitive function; excluded if urgent resuscitation, semi-comatose, day cases, terminal care, blind or aphasic (418)	MMSE every 48 h for 10 days or until discharge or death; diagnosis by research nurse using information from MMSE, ward staff and checklist using DSMIIIR criteria	70.2 (6.8)
Kolbeinsson, Iceland [115]	>70 years; excluded if unable to assess due to severity of condition or elective admission (272)	MSQ and MMSE; clinical examination by trained psychiatrist within 24 h of admission if MSQ < 22; DSMIII criteria	80.7
Johnson, USA [**17**]	>70 years; excluded if short stay e.g. for chemotherapy, transfusion or diagnostic study or if admitted for terminal care (235)	MMSE, BPRS, standard clinical examination by nurse research assistant within 24 h, repeated daily for 2 weeks and alternate days for 3 weeks, followed up to 5 weeks or discharge; DSMIII criteria	78 (6)
Laurila, Finland [117]	>70 years; excluded if coma (230)	Clinical interview once; operationalised DSMIV criteria using information from interview records, nurses and carers	Not given
Francis, USA [105]	>70 years, from community; excluded if terminal, overnight admissions, current psychiatric treatment, blind or deaf (229)	MMSE , clinical interview, chart review, family or carer interview, assessed every 48 h to discharge or death; DSMIIIR criteria using information from entire admission	78
O'Keefe, Ireland [121]	Excluded if not admitted to unit on first day of admission, or elective admission, aphasic or deaf (225)	One of two study physicians interviewed patients and nurses using DAS, MMSE within 24 h and every 48 h or sooner if cognitive change until discharge or death; modified DSMIII criteria	82 (4)

Table 1. *continued*

Study	Sample	Screening and diagnosis	Age, mean years (SD)
Inouye, USA [111]	>75 years; excluded if bedridden more than 2 weeks before admission or mental impairment (stroke/dementia) or terminally ill (205)	Trained researchers, standardised interviews at admission within 48 h of admission, MMSE, CAM	82.2 (6.0)
Rockwood, Canada [127]	>65 years; excluded if re-admissions or death in hospital (203)	MMSE, DRS at admission once; DSMIV criteria operationalised using clinical judgement	Not given
Vazquez, Argentina [130]	>65 years; excluded if unable to evaluate or discharge within 48 h, unable to consent, or delirium within 24 h (201)	Clinical examination within 48 h and then daily up to discharge CAM, DSMIII criteria	77.5 (8.7)
Lundstrom, Sweden [89]	>70 years; excluded if non-consenting (200)	OBS scale administered by three trained researchers on day 1, 3 and 7; DSMIV criteria	80.7 (6.2)
Inouye, USA [110]	>70 years; excluded if unable to be interviewed, risk factor data missing, previous enrolment; development cohort (196) validation (312)	Trained clinician researchers interviewed patients within 48 h of admission and on alternate days, for 9 days; MMSE, CAM, nurse interviews, medical record review, using standardised instruments	78.5 (5.7)
Jitapunkul, UK [113]	Admission to geriatric unit; excluded admissions for rehabilitation or respite care (184)	Abbreviated mental test score up to 6 weeks or discharge; diagnosis by case record review and consultant staff opinion based on DSMIIIR criteria	81.7 (6.6)
Rockwood, Canada [126]	Admissions to geriatric unit; excluded if refusal to complete MMSE (168)	Clinical judgement by internal medicine and geriatric medicine specialists with pre-defined criteria on admission (although timing of assessments in relation to admission not clear)	79 (8)
Bowler, UK [96]	In-patients in 1 week; excluded if severe illness or communication difficulties (153)	CAM; MMSE administered once by one of six psychiatrists	80.6 (7.2)
Cameron, USA [98]	Excluded if substance abuse or transferred from other services (133)	Daily assessment by clinicians until discharge or death (12.3 ± 13.5 days); clinical interview by researchers using DSMIII criteria if clinicians identified symptoms or signs of delirium	68.8
Tabet, UK [88]	>70 years, in hospital >24 h, consenting (128)	Clinical interview once by research old-age psychiatrist with information from Abbreviated Mental Test Score and modified Delirium Rating Scale	79.3
Korevaar [87]	Random sample from consecutive admissions; excluded if transferred to another unit (126)	Multi-disciplinary assessment once within 48 h of admission with MMSE and IQCODE; diagnosis using CAM criteria	82.1 (7.2)
Naughton, USA [120]	>75 years; excluded if >4 days in hospital, admission from nursing home or admission to ICU (110)	Evaluation by project nurse with chart review and carer interview on day 4 after admission; CAM	81 (6.2)
Ramsay, UK [123]	>75 years (110)	Questionnaires and semi-structured interview by two investigators within 7 days of admission, MMSE, GHQ BAS (brief assessment schedule) once in 1 week; DSMIII criteria	Median 83
Inouye, USA [109]	>70 years, no delirium at admission, no severe dementia; excluded if unable to be interviewed, terminal illness, violent behaviour, risk factor data missing; development cohort (107) validation (174)	Trained clinician researchers interviewed within 48 h of admission, MMSE, CAM, daily to discharge; diagnosis by two researchers using CAM ratings and nurse interviews and medical record data	79.3 (6.6)
Bergmann, UK [94]	>65 years, excluded if medical, psychiatric, geriatric care within 5 years; 17 died before assessment (100)	Semi-structured interview once at admission (unclear when), informant history, cognitive tests, by one investigator; case critically reviewed with second investigator and consensus reached	Not given

Table 1. *continued*

Study	Sample	Screening and diagnosis	Age, mean years (SD)
Anthony, USA [93]	Excluded if non-consenting; discharge before protocol completion (97)	Interview once by psychiatrist within 24 h of admission; clinical judgement, examining records and informant history, using Folstein and Mc Hugh (1976) method by two experienced psychiatrists	Not given
Adamis, UK [**178**]	>70 years (94)	Interviewed once within 3 days of admission; CAM or DRS (cut-off 10) by trained researcher	82.8 (6.5)
Laurila, Finland [**116**]	>70 years; excluded if coma (81)	CAM administered by one investigator (unclear when) and other investigator used information from nurses, carers, medical records; CAM, DSMIII, DSMIIIR and DSMIV criteria	Not given
Rockwood, Canada [125]	Elderly; excluded CCU and ICU patients (80)	Clinical assessment by investigator daily, SPMSQ daily (once per weekend) until discharge or death; mean LOS 16.6 days	76.8
Andres, Mexico [92]	>18 years; excluded if psychoactive medication in last 48 h; intubation; previous psychiatric diagnosis; cognitive impairment (75)	CAM, MMSE, daily for 7 days clinical interview	49.7 (18.6)
Seymour, Canada [128]	>70 years (68)	Detailed history, physical exam and MSQ within 4 h of admission, repeated after 1 week if recovered and at discharge; acute confusion defined as changing impairment of MSQ score	81.2
Uwakwe, Nigeria [129]	>70 years, conscious (64)	Unstructured interview, Self Reporting Questionnaire-24, Geriatric Mental State Schedule, MMSE once but not clear when; ICD 10 criteria using information from interviews	Not given
Feldman, Israel [102]	>70 years; excluded if elective admission or not admitted to geriatric unit on first day (61)	Clinical examination by geriatrician every 48 h for 14 days and then intermittently to discharge or death; diagnosis by CAM, DRS by two physicians	83.2 (6.8)
Mussi, Italy [119]	Excluded if pre-existing dementia or stroke, unreliable or incomplete histories (61)	CAM and clinical data collected once within 24 h of admission	79.2 (11.6)
Regazzoni, Argentina [124]	>70 years; excluded if confused within 24 h of admission, of psychosis or on antipsychotic medication (61)	MMSE daily to discharge; DSMIV criteria, CAM	80
Braekhus, Norway [97]	>75 years (58)	Clinical assessment, DSMIIIR criteria, every 3 days to discharge	83.1

BPRS, Brief Psychiatric Rating Scale; CAM, Confusion Assessment Method; DAS, Delirium Assessment Scale; DRS, Delirium Rating Scale; DSM, Diagnostic and Statistical Manual of Mental Disorders; ICU, intensive care unit; CCU, coronary care unit; GHQ, General Health Questionnaire; IQCODE, Instrumental Questionnaire on Cognitive Decline in the Elderly; LOS, length of stay (given as mean number of days, unless stated otherwise); MMSE, mini-mental state examination; MSQ, Mental Status Questionnaire; OBS, organic brain syndrome; SPMSQ, Short Portable Mental Status Questionnaire.
Studies arranged in the order of decreasing study size. Number in study is denoted within parentheses.

communication difficulties. Six studies [91, 92, 104, 109, 111, 119, 124] excluded subjects with dementia, either explicitly or by virtue of exclusion criteria such as pre-existing confusion, difficulty completing interviews or cognitive impairment. Thirty-five studies were carried out in older populations.

Methods to obtain consent and reporting of response rates also varied considerably. The number of exclusions was particularly high in controlled trials [99, 100, **112**], although participants in these studies were reported to be largely similar to those excluded.

Results for delirium prevalence, incidence and occurrence

Twenty-one studies reported delirium prevalent at admission; only eight of these indicated delirium assessment had been undertaken within 24 hours of admission (Table 2).

Table 2. Delirium prevalence at admission

Diagnostic criteria	Author	Year	Screening and diagnostic method	Prevalence at admission
CAM	Mussi	1999	CAM and clinical data	20% (12/61)
DSMIII	Anthony	1982	Clinical judgement examining subjects, records and informant history, using Folstein and McHugh (1976) method by two experienced psychiatrists	10% (10/97)
	Johnson	1990	MMSE, BPRS, standard clinical examination by nurse research assistant mostly within 6 h	16% (38/235)
	Kolbeinsson	1993	Clinical examination by trained psychiatrist if MSQ < 7 and MMSE < 22	11% (37/331)
	O'Keefe	1996	One of the two study physicians (experienced geriatricians) interviewed patients and nurses using DAS, MMSE (modified DSMIII)	18% (41/225)
DSMIII-R	Cole	1994	CAM administered by study nurse to those screening positive on SPMSQ (>5)	18% (88/484)
	Cole	2002	CAM for those screening positive on SPMSQ	13% (243/1925)
DSMIV	Lundstrom	2005	OBS scale administered by one of the three trained researchers	31% (62/200)

BPRS, Brief Psychiatric Rating Scale; CAM, Confusion Assessment Method; DSM, Diagnostic and Statistical Manual of Mental Disorders; MMSE, mini-mental state examination; MSQ, Mental Status Questionnaire; OBS, organic brain syndrome; SPMSQ, Short Portable Mental Status Questionnaire.

In 13 studies, the incidence of new delirium occurring at any time during admission was determined (Table 3). Four further studies described delirium incidence rates in varying time frames [**17**, 92, 104, 110].

Occurrence rates for delirium per admission were given or could be derived from presented data in 13 studies (Table 4). A further seven studies reported various other measures of delirium occurrence [88, 96, **116**, 117, 123, 129, 130].

Prevalence of delirium at admission ranged from 10 to 31% (limiting results to studies in which patients were examined within 24 hours of admission). Incidence of new delirium per admission ranged from 3 to 29%. Occurrence rate per admission varied between 11 and 42%.

Methodological differences

Delirium screening and diagnostic methodology differed, and there was marked heterogeneity in the measures used to describe delirium occurrence. Procedures to obtain consent also differed, and there was some variability in the methodological quality of studies. The presence of co-morbid conditions was not reported in most studies. The sensitivity and specificity of diagnostic instruments has been shown to vary depending on the training and professional background of the administrator [**30**, **134**, **135**]. Again, studies differed in the use of researchers and clinicians employed in case ascertainment. Distinction between delirium and dementia cases was also problematic in some studies.

In determining delirium incidence and occurrence rates, the frequency of assessments would be expected to influence results. However, we were not able to find any clear association between examination frequency and reported rates.

Many studies reported delirium in terms of incidence or occurrence rate per admission; clearly the length of admission would affect results. This information was not available in most studies and reported variously as median, mean or range of duration of stay in others. Where mean duration was given, it ranged from 8 to 30 days.

We were unable to pool results from studies due to methodological heterogeneity.

Outcomes studies

For the outcomes review, we examined 93 full-text articles. Of these, 65 reports were excluded; in 29, the settings or populations were not equivalent to general medical in-patients [25, 27, 29, 31, 34, **35**, 37, 40–42, 44, 45, 53, 70, 72, 136–150]; 5 used retrospective methods [63, 66, 151–153]; in 10, the diagnosis used did not approximate to currently accepted criteria for delirium [50, 59, 76, 154–160]; 17 did not examine outcomes [**21**, 69, 78, 86, 98, 109, 110, **112**, 132, 161–168] and 3 included less than 20 subjects [102, 169, 170].

Twenty-eight reports were included in the outcomes review [**6**, **16**, 79–82, 89, 90, 95, 99, 100, 103, 105–107, 111, 113, 115, 122, 123, 125–127, 130, 131, 133, 171, 172]. Of these, 15 reported outcomes from 6 original study cohorts, giving results at different time intervals [**1**, **6**, 79–82, 89, 90, 99, 103, 106, 122, 123, 125, 172] (Table 5).

Sample

Outcomes results were available for 19 study cohorts. Most employed a prospective cohort design except for one nested case–control study [131], two randomised controlled trials [99, 100] and one controlled trial [89]. Two studies included outcomes for incident cases only, 5 for admission prevalent cases only and 12 for both incident and prevalent delirium. Reporting of co-morbidity including the presence of dementia was variable, as was reporting of and methodological or statistical adjustments for relevant confounders (Table 5).

Table 3. Delirium incidence per admission

Diagnostic criteria	Author	Year	Screening	Diagnostic method	Frequency examined	Incidence admission
CAM	Inouye	1993d	Trained clinician researchers interviewed patients within 48 h, MMSE, CAM	CAM, nurse interviews, medical records, two researchers	Daily	25% (27/107)
	Inouye	1993v	Trained clinician researchers interviewed patients within 48 h, MMSE, CAM	CAM, nurse interviews, medical records, two researchers	Daily	17% (29/174)
	Inouye	1999	MMSE, CAM by trained researchers within 48 h	CAM	Daily	15% (64/426)
	Villapando-Berumen	2003	Unstructured interview with patient, nurse and relative between 24 and 48 h	CAM	Daily	12% (80/667)
DSMIII	Cameron	1987	Daily assessment by clinicians	Clinical interview by researchers	Only if indicated by clinicians	3% (5/118)
	O'Keefe	1996	One of the two study geriatricians interviewed patients and nurses, DAS, MMSE within 24 h	Modified DSMIII, one physician	48 hourly or sooner if cognitive change	29% (53/184)
	Rockwood	1989	Clinical assessment by investigator, SPMSQ	clinical judgement + SPMSQ	Daily (once per weekend)	11% (9/80)
DSMIII-R	Francis	1990	MMSE, clinical interview, chart review, family or carer interview	information from entire admission	48 hourly	7% (14/193)
	Gaudet	1993	Not described		Not clear	5% (24/466)
	Vazquez	2000	Clinical examination within 48 h	CAM	Daily	25% (51/201)
DSMIV	Bourdel-Marchasson	2004	Symptoms recorded by nurses—CAM within 24 h	CAM algorithm	Every 3 days	4% (15/393)
	Regazzoni	2000	MMSE	CAM	Daily	21% (13/61)
	Zanocchi	1998	Clinical review and review by study physician with information from medical records		Two or more times a day	15% (81/536)
Other (operationalised MMSE + DRS)	Rockwood	1993	Not described	Clinical judgement by medical specialists with pre-defined criteria	Unclear	7% (12/168)

CAM, Confusion Assessment Method; DRS, Delirium Rating Scale; DSM, Diagnostic and Statistical Manual of Mental Disorders; MMSE, mini-mental state examination; SPMSQ, Short Portable Mental Status Questionnaire.

Outcomes for delirium

Outcomes for delirium are summarised in Table 6.

Fifteen studies reported death rates at discharge. We found a wide range from 6.1 to 62%, which precluded pooling of results. The lowest values were obtained from one study that included only incident cases [131] and two studies that excluded large numbers of potential subjects [105, 111]. The two studies reporting the highest death rates were limited by small numbers. Excluding these five studies, death rate at discharge was reported to be 14.5–37%. In comparisons with controls, there were mixed results with some studies reporting no significant difference, but several reporting a significant increase. In studies which examined for the independent effect of delirium, adjusting for important confounders, two reported an increase in death rate at discharge, whilst three found no significant difference. The small numbers of cases or outcome events in most of these studies raise the possibility of both type I and type II errors. The study with the highest score for quality reported increased mortality at discharge [79]. This study also described a 2-fold independent increase in mortality at 12 months (please see Table 7 in Appendix 2 in the supplementary data on the journal website, http://www.ageing.oxfordjournals.org/).

The mean length of hospital stay (LOS) was reported in 11 studies and ranged from 9 to 32 days; again, the results varied with three studies [**16**, 105, 173] showing a significant increase in LOS, but seven other studies [111, 113, 115, 123, 126, 130, 131] showing no significant difference in comparison with controls. One study [79] showed an independent excess LOS of 8.05 days (95% CI 3.59–12.51), attributable to incident delirium, but no significant increase with prevalent delirium.

Four studies examined institutionalisation at discharge. Of these, two [111, 115] reported no difference in rates, one [105] showed a significant increase in adjusted institutionalisation rates and another [95] reported a significant increase only for prevalent delirium. At 6 months, one study [**6**] showed delirium independently increased institutionalisation, odds ratio 2.8 (95% CI 1.3–6.1); and two studies [105, 125]

Table 4. Delirium occurrence per admission

Diagnostic criteria	Author	Year	Screening and diagnostic methods	Occurrence
DSMIII	Cameron	1987	Clinical interview by researchers if indicated by physicians	15% (20/133)
	Johnson	1990	MMSE, BPRS, standard clinical examination by nurse research assistant within 24 h (mostly 6 h), repeated daily for 2 weeks and alternate days for 3 weeks; diagnosis one psychiatrist	20% (48/235)
	O'Keefe	1996	One of the two study physicians (experienced geriatricians) interviewed patients and nurses using DAS, MMSE within 24 h and every 48 h	42% (94/225)
	Rockwood	1989	Clinical assessment by investigator daily, SPMSQ; diagnosis by clinical judgement	25% (20/80)
DSMIII-R	Braekhus	1994	Clinical assessment every 3 days	24% (14/58)
	Francis	1990	MMSE, clinical interview, chart review, family or carer interview, assessed every 48 h to discharge or death	22% (50/229)
	Gaudet	1993	Not described	11% (52/487)
	Jitapunkul	1992	Abbreviated MTS score < 8 at admission, 1 week after admission, at discharge or 6 weeks (but not used in diagnosis); delirium diagnosis by case record review, consultant staff opinion	22% (40/184)
DSMIV	Bourdel-Marchasson	2004	Symptoms recorded by nurses using CAM within 24 h and every 3 days to discharge	12% (49/427)
	Zanocchi	1998	Clinical review two or more times a day; review of findings by study physician with information from medical records	22% (130/585)
Other (change in cognitive impairment)	Seymour	1980	Interview, physical examination, MSQ within 4 h of admission, repeated after 1 week if recovered, and at discharge; delirium diagnosis if initial MSQ score 7.5 and history of increasing confusion in 2 weeks prior to admission or gain in MSQ score of 2.5 points	16% (11/68)
Other (operationalised CAM + DRS)	Feldman	1999	Clinical examination by geriatrician every 48 h for 14 days and then intermittently to discharge or death; delirium diagnosis, CAM, DRS by two physicians	18% (11/61)
Other (operationalised MMSE + DRS)	Rockwood	1993	Clinical judgement by specialist physicians using pre-defined criteria on admission (although timing of assessments unclear)	26% (43/168)

BPRS, Brief Psychiatric Rating Scale; CAM, Confusion Assessment Method; DAS, Delirium Assessment Scale; DRS, Delirium Rating Scale; DSM, Diagnostic and Statistical Manual of Mental Disorders; MMSE, mini-mental state examination; MSQ, Mental Status Questionnaire; MTS, Mental Test Score; SPMSQ, Short Portable Mental Status Questionnaire.

reported no independent effect but did not adjust for potential confounders. At 12 months, one study [79] showed increased institutionalisation in patients with delirium and dementia.

In describing the clinical course of delirium, McCusker and colleagues [79] found 39% had transient symptoms (recovery within 24 hours), 29% recovered and 32% had persistent symptoms at discharge. Two other studies reported persistence of delirium symptoms at discharge to be high. In one [107], 23% subjects had no resolution of symptoms, with partial resolution in 17%, and in the other [126] complete resolution of symptoms occurred in only 40%. McCusker and colleagues [79] also reported persistence of delirium symptoms at 6 and 12 months in 32 and 41% patients, respectively. Clearly, a large proportion of patients with delirium are discharged from hospital with on-going delirium symptoms.

In functional outcomes, one study [109] found a significant association between delirium and decline in activities of daily living (ADL) scores at discharge. Francis and Kapoor [105] reported no difference in ADL or mini-mental state examination (MMSE) scores at 6 months, but McCusker and colleagues [79] showed delirium resulted in worse physical and cognitive status at 12 months.

Again, comparison of results across studies was problematic as study methodology, outcomes measurement and reporting varied so greatly. Surprisingly, many important outcomes such as psychological morbidity in patients, carers or staff, and economic costs to healthcare services were not reported for this population.

Discussion

It is clear from our review that delirium is common in general medical in-patients and has serious adverse outcomes, including increased mortality, LOS and institutionalisation. Even in highly selected groups, we found minimum occurrence rates per admission of 11% and more typical rates of 20–30%. Our findings are comparable with previous reviews [**7**, **174**] but provide more robust evidence of how common delirium is and how poor its outcomes are. The results are even more striking given that they are likely to be an underestimate [**175**], not least because we excluded delirium tremens.

Clinical implications

With typical non-detection rates of 33–66% [**175**], strategies to improve delirium management must include measures to improve its detection.

As at least 20–30% of admissions will be affected, we cannot rely on referral to psychiatry services but must rather

Table 5. Studies in delirium outcomes review

Author	Delirium diagnosis	Selection criteria	Cases	Controls	Age[a]	Dementia[b]	Comorbidity	Confounders examined	Follow-up (loss)
Bourdel-Marchasson [95]	CAM; prevalent (34) and incident (15)	>75 years; >36 h in hospital; not living in institutions	49	230	84.8 (all)	52% (all)		Important confounders examined but not adjusted	Every 3 days, to discharge or death (0%)
Cole [99]	DSMIII-R; prevalent	>75 years; not admitted to ITU, cardiac monitoring unit or referred to oncology or geriatric service	46	0	85.4 (SD 6.3)	Not given		Not applicable	At 1, 2, 4 and 8 weeks (0%)
Francis[c] [105]; Francis [106]	DSMIII-R; prevalent (36) and incident (14)	>70 years; excluded if severe dementia, nursing home residents, terminal care or metastatic cancer, under current psychiatric treatment, overnight admissions, communication difficulties	50	176	78 (all)	Severe excluded	Fluid or electrolyte imbalance, metabolic conditions, infection, drug toxicity, frequent but unclear how many cases affected	Age, sex, marital status, race, ADL, dementia, emergency admission, illness severity, psychoactive medication	Every 48 h until discharge and 6 months post discharge (4%); 2 years (8%)
Gaudet [107]	DSMIII-R; prevalent (28) and incident (24)	Geriatric internal medicine service in-patients	52	435	85.8	44%	Infections, metabolic and cardiovascular problems common	Age, sex	At discharge and 3 months after discharge
Inouye [111]	CAM; prevalent	>75 years, not admitted to ITU, not terminally ill	33	172	82.2 (all) (SD 6.0)	22% (all)	Not given separately for delirium cohort	Age, sex, dementia, illness severity, ADL	At discharge and 3 months after discharge (7%)
Jitapunkul [113]	DSMIII-R; prevalent and incident	Elderly; excluded rehabilitation and respite care patients	40	144	83.3 (SD 6.2)	30%	Infections 32%, stroke 15%		At discharge or 6 weeks after admission
Kolbeinsson [115]	DSMIII-R; prevalent	>70 years and not elective or overnight admission	37	185	81.7	0% (delirium group compared with dementia group)	Infections 32%, congestive heart failure 27%, stroke 22%	Age, sex, marital status	To discharge or death (0%)
Lundstrom[c] [89]; Edlund [90]	DSMIV, OBS scale; prevalent	>70 years; consenting	62	Not applicable	81.9 (SD 6.6)	6.4%	Stroke 32%, diabetes 19%, visual impairment 35%	Not applicable	To discharge or death (0%)

continued

Table 5. *continued*

Author	Delirium diagnosis	Selection criteria	Cases	Controls	Age[a]	Dementia[b]	Comorbidity	Confounders examined	Follow-up (loss)
McCusker[c] [79]; McCusker [80]; Cole [100]; McCusker [82]; McCusker [81]	DSMIV, CAM; prevalent (204) and incident (36)	>65 years; excluded if ICU or CCU stay>48 h, stroke, geriatric or oncology admission, transfer to long-term care	220; 243; 114; 193; 240	118	82 (SD 7)	75%; 75%; 56%; 70%; 68%	Cardiovascular diseases 23%, respiratory diseases 20%	Age, sex, marital status, living arrangements, education, illness burden, dementia, pre-morbid function	2, 6 and 12 months after enrolment; three times in first week, then weekly until discharge or 8 weeks and 6 and 12 months after enrolment; (16.6%); (16.6%); (2%); (20.6%); (0%)
O'Keefe[c] [**6**]; O'Keefe [122]	DSMIII; prevalent (41) and incident (53)	Elderly; excluded elective admissions, and severe aphasia, deafness	94	131	82 (SD 4)	42.5%		Age, sex, chronic cognitive impairment, illness severity, disability score	48 hourly and 6 months after discharge (0%)
Rahkonen [171]	DSMIII-R; prevalent and incident	>65 years, living at home, no serious underlying disorders, no dementia, alcoholism or major psychiatric disorder, admitted >24 h	51	0	82 (SD 5.4)	Excluded	Infections, stroke, cardiovascular disorder, drug related disorder common; multi-factorial in 49%	Not applicable	At 1 year (0%)
Ramsay[c] [123]; Finch [103]	DSMIII-R; prevalent and incident	Admissions to geriatric team under one consultant	22	88	83 (median)	68%		Age, sex, marital status, domicile, severity of physical illness	At 10 weeks (7.5%); at 12 months (3%)
Rockwood[c] [125]; Rockwood [172]	DSMIII; prevalent (13) and incident (9)	Elderly; not admitted to intensive or coronary care units	20	60	81.9	30%		Sex and previous residence; baseline differences in age not adjusted	Daily to discharge or death (0%)
Rockwood [126]	DSMIII; DSMII-R; prevalent and incident	Admissions to geriatric unit; excluded if MMSE not completed	48	120	82 (SD 8)	Not given	Congestive heart failure 21%, metabolic 19%, infections 23%	Age, sex, marital status	Daily until discharge
Rockwood [127]	DSMIV; prevalent	First admission during study period, survival to discharge	38	165	Not given	58%		Age, sex, comorbid illness, frailty, atypical disease presentation	At 3 years (12%)

Table 5. *continued*

Author	Delirium diagnosis	Selection criteria	Cases	Controls	Age[a]	Dementia[b]	Comorbidity	Confounders examined	Follow-up (loss)
Thomas [**16**]	DSMIII; prevalent and incident (15) (5)	Excluded transfers from ICU or other medical or surgical services, drug abuse	20	113	68.8 (SD 18)	Not given	Respiratory diseases 35%, nervous system disorders 15%, circulatory system disorders 10%	Age, sex, race, use of private physician	Daily until discharge or death (0%)
Vazquez [130]	DSMIII-R, CAM; incident	>65 years, no delirium at admission, consent obtainable; excluded if communication difficulties precluding 30 min interview	51	150	77.5 (SD 8.7) (all)	58%	Hypertension, ischaemic heart disease, cancer common	Age, sex, admission source, previous cognitive impairment, chronic illness	Daily until discharge (0%)
Villapando-Berumen [131]	CAM; incident	>60 years; excluded sedated, aphasic, intubated, or delirium on admission	80	240	75.8 (SD 6.7)	Not given		Age, sex, comorbidity	Daily until discharge; review of medical files at 5 years (19%)
Zanocchi [133]	DSMIV; prevalent (49) and incident (81)	Elderly	130	455	77.1	13%	Infections, meningitis, dehydration, heart failure and gastrointestinal bleed	Age, sex, comorbidity	Two or more times a day until discharge (0%)

ADL, activities of daily living; CAM, Confusion Assessment Method; CCU, coronary care unit; DSM, Diagnostic and Statistical Manual of Mental Disorders; ICU, intensive care unit; ITU, intensive treatment unit; MMSE, mini-mental state examination; OBS, organic brain syndrome; SD, standard deviation.

[a]Mean age of cases in years unless otherwise specified; 'all' indicates age given is for cases and controls together.

[b]Dementia prevalence in cases; 'all' indicates prevalence given in cases and controls.

[c]Index study.

Table 6. Delirium outcomes

Author	Time period	Outcomes	Quality[a]
Bourdel-Marchasson [95]	Up to discharge	Institutionalisation: prevalent D = 38%, OR = 3.19 (95% CI 1.33–7.64) ($P = 0.009$); incident D = 40%, OR = 2.64 (95% CI 0.83–8.45) ($P = 0.10$); C = 21%	14
Cole [99]	Up to discharge	At 8 weeks: 29% required restraint; LOS = 22.7; 7% required more care after discharge; death = 37%	10
Francis [105]	Up to discharge	LOS D =12.1, C = 7.2 ($P < 0.001$); institutionalisation D = 16.0%, C = 3.4% ($P < 0.05$)	16
	At 6 months	Death D = 14.3%, C = 10.1% ($P > 0.10$), effect of illness severity but not delirium independently significant; institutionalisation D = 12%, C = 5%; ADL or MMSE scores: no significant difference	
	At 24 months	Death D = 39%, C = 23% ($P = 0.03$), RR = 1.82 (95% CI 1.04–3.19), no independent effect when adjusted for cancer, ADL and cognitive impairment; loss of independent community living D = 40%, C = 18% ($P = 0.004$), RR D = 1.82 (95% CI 1.31–2.53)	
	Other	1-month death D = 10%, C = 3%	
Gaudet [107]	Up to discharge	LOS median D = 42.7, C = 24.7; no resolution D symptoms = 23.1%, partial resolution = 17.3%; time to resolution median 6.5 days; death D = 23.1%	9
	Other	Death at 3 months = 32.7%	
Inouye [111]	Up to discharge	Death D = 9%, C = 3%, adjusted OR = 0.9 (95% CI 0.1–7.0); institutionalisation adjusted OR = 2.7 (95% CI 0.9–7.9); death or new nursing home adjusted OR = 2.5 (95% CI 0.9–6.6); LOS median D = 6.8, C = 5.8 (difference NS after adjustment for confounders); ADL decline adjusted OR = 3.3 (95% CI 1.2–9.7)	19
	Other	Death at 3 months adjusted OR = 1.6 (95% CI 0.5–5.2)]; new nursing home adjusted OR = 3.9 (95% CI 1.1–13.3); combined death and nursing home placement adjusted OR = 2.9 (95% CI 1.0–8.4)	
Jitapunkul [113]	Up to discharge	LOS median D = 20, C = 16, NS; Death D = 35%, C = 16.0% ($P < 0.01$); long-stay care admission D = 7.7%, C = 2.5%, difference NS	12
Kolbeinssons [115]	Up to discharge	LOS D = 20.2, dementia = 16.5, all patients = 17.3; institutionalisation difference NS; death D = 32% ($P < 0.01$); long-stay care admission D = 7.7%, C = 2.5%, difference NS	9
Lundstrom [89]	Up to discharge	LOS mean (days) = 13.4 (SD 12.3); return home = 60%; death = 14.5%	15
McCusker [79]	Up to discharge	At 8 weeks: LOS = 19.1 (SD 16.8); prevalent D excess LOS 0.32 (95% CI –2.66 to 3.31,NS); incident D excess LOS 8.05 (95% CI 3.59–12.51) (adjusted for important covariates); death 19.3%; more dependent at discharge = 15.6%; transient D = 39%; recovered D = 29%; persistent D = 32%; proportion of days with D = 40%; time to cognitive improvement = 10.8 (SD 10.1); length of episode = 6.3 (SD 9.4); number of days with D = 7.0 (SD 9.1)	19
	At 6 months	Persistence of D = 32% (D + dementia = 38.5%, D only = 8.8%); IADL score declined; MMSE and BI scores improved	
	At 12 months	Worse physical and cognitive status (decline in MMSE, BI and IADL), BI decline only significant for D + dementia; long-term care admission increased but only significant for D + dementia; death D = 42%, C = 14%; mortality D = 63.3%, C = 17.4% (using Kaplan–Meier survival analysis); D associated with 2-fold significant increase in mortality ($P = 0.01$); persistence of D = 41%	
	Other	Worse physical and cognitive status (decline in MMSE, BI and IADL) at 2 months	
O'Keefe [6]	Up to discharge	Duration D = 7 (95% CI 6–8); persistence D sx = 32%; Death D = 16%, C = 5%, adjusted OR NS; complications adjusted OR = 2.3 significant difference; LOS D = 21, C = 11 ($P < 0.001$) adjusted significant difference; functional status significantly worse	16
	At 6 months	Death D = 31%, C = 15% adjusted OR = 1.4 (95% CI 0.7–2.8, NS); institutionalisation D = 36%, C = 13%, adjusted OR = 2.8 (95% CI 1.3–6.1)	
Rahkonen [171]	At 12 months	New institutionalisation 20%; death 10%	9
Ramsay [123]	Up to discharge	Death D = 62%, C = 14% ($\chi^2 = 12.27$, $P < 0.001$); survival-delirium independent effect on mortality (Cox model coefficient 1.35) ($P < 0.02$); LOS difference NS	12
	At 12 months	Death D = 77%, C = 37% ($\chi^2 = 11.4$, $P < 0.01$); institutionalisation difference NS; survival analysis Cox model delirium independently associated with survival ($P < 0.05$)	

Table 6. *continued*

Author	Time period	Outcomes	Quality[a]
Rockwood [125]	Up to discharge	Death D = 15%, C = 1.3%; LOS D = 20, C = 14 difference NS; change in residence difference NS; change in ADL difference NS	8
Rockwood [126]	Up to discharge	Duration of episode = 8 days; reversibility of all D symptoms = 40%; persistence of symptoms = 41.5 days (longest for memory impairment); LOS D = 32, C = 28; discharge to community D = 47%, C = 59%; death D = 19%, C = 12%	13
Rockwood [127]	Other	Survival 3 years D = 21%, C = 57%; survival median D = 510, C = 1122 ($P = 0.0001$) significant difference; death adjusted HR = 1.71 (95% CI 1.02–2.87); dementia 3-year annual incidence D = 18.1%, C = 5.6%; adjusted OR for dementia = 5.97 (95% CI 1.8–19)	13
Thomas [16]	Up to discharge	Death D = 65%, C = 4.4% ($P < 0.0001$)	15
Vazquez [130]	Up to discharge	LOS D = 9.9 (SD 3.5), C = 6.9 (SD 2.5) ($P < 0.05$); death related to delirium and illness severity	13
Villapando-Berumen [131]	Up to discharge	LOS D = 13.4 (SD 10.7), C = 10.2 (SD 6.6) ($P = 0.03$); death D = 6.1%, C = 2.3%, OR = 2.8 (95% CI 0.7–10.6) ($P = 0.26$)	15
	Other	5-year survival D = 55%, C = 70% (from graph)	
Zanocchi [133]	Up to discharge	Falls D = 24.6%, C = 14.9% ($P < 0.001$); LOS > 31 days, D = 16.9%, C = 10.3%, ($P < 0.05$); death D = 24.6%, C = 9.9% ($P < 0.001$)	14

ADL, activities of daily living; C, controls; CI, confidence interval; D, delirium; HR, hazard ratio; IADL, instrumental ADL; LOS, length of stay (given as mean number of days, unless stated otherwise); MMSE, mini-mental state examination; OR, odds ratio; RR, relative ratio; NS, non-significant.

[a]Please see Appendix 1 in the supplementary data on the journal website (http://www.ageing.oxfordjournals.org/) for details of how this score was derived.

skill up the whole team, and in particular nursing staff, to screen, detect and manage delirium. Liaison psychiatry services may still have a role in this by offering education, training and advice to staff, as well as consultation for more complex management problems.

We know that a range of aetiologies and maintaining factors are implicated in delirium requiring a broad multifactorial and multi-disciplinary approach [**4**, **19**, **112**]. However, given the scale of the problem, interventions also need to be simple and quick. The balance between a necessarily comprehensive and yet practicable intervention is difficult but must be achieved with particular attention to addressing issues of implementation and adherence [**165**].

We found delirium already present at admission to be more common than new delirium occurring during admission. Recent studies have shown that delirium is common in nursing homes [**176**, **177**]; moreover, admission from an institution rather than the community is a risk for delirium in hospital [**35**]. Intervening in these settings could have the potential to deliver important benefits, including reducing hospital admissions, and therefore needs evaluation.

Research implications

We found considerable heterogeneity in case-finding and ascertainment methods. Despite the consensus in diagnostic criteria, Laurila *et al.* [**116**] have shown how much variability is introduced simply by applying different DSM and ICD10 criteria to the same data set. Clearly there needs to be greater standardisation of delirium screening and diagnostic methods.

We found a range of measures used to describe delirium frequency. The denominator used to calculate rates is integral to the results obtained, but most studies gave incidence or occurrence rates 'per admission'; as length of admission will inevitably vary, this again limits comparisons between studies and generalisability of findings. A more useful measure may be to describe rates of delirium per in-patient day.

A common difficulty was the exclusion of some of the target population, because exclusion criteria often included properties of the index condition. Delirium may affect people's ability to consent, communicate or complete interviews, and selection criteria requiring these conditions will obviously differentially exclude more subjects with delirium. This raises ethical considerations, including issues of conducting research in unrepresentative study populations [**178**]. The high mortality associated with delirium means that any prognostic or intervention studies need to take account of attrition rates of around 20–30%. In other outcomes, as delirium increases LOS and the number of people discharged to nursing or residential institutions, it is important to include a robust economic analysis.

There is surprisingly little known about the psychological impact of delirium on patients, staff and carers in this population; future outcomes studies should include measures of psychological morbidity.

Limitations of the review

We excluded delirium tremens from this review; although this is an important cause of delirium, we judged it to be a sufficiently distinct condition to warrant a separate review. We used a broad search strategy and imposed no language restrictions for included studies but confined our search to English-language databases. Resource limitations also meant that we were unable to independently review all citations or abstracts identified by the original search. We did not contact authors for information additional to that published. Nevertheless, we believe the review was sufficiently comprehensive to identify most important findings in this area.

Conclusion

Delirium is a significant problem associated with considerable adverse outcomes including increased mortality in general medical inpatients. There are many methodological and ethical concerns which have impeded delirium research. However, given the scale of the problem, addressing the problem of delirium should be a priority for clinicians and researchers.

Key points

- Delirium is common in medical in-patients and has serious outcomes including increased mortality, length of hospital admission and institutionlisation.
- Given the scale of the problem, developing interventions to prevent and improve management of delirium should be priority for clinical services.
- We cannot rely on referral to psychiatry services alone, but must improve the skills of the whole team in detection and management of delirium in these settings.
- Delirium research is sparse, and has been impeded by methodological and ethical difficulties.
- Further research with greater standardisation of delirium screening and diagnostic methods is required.

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None.

Conflicts of interest

None.

References

The very long list of references supporting this review has meant that only the most important are listed here and are represented by bold type throughout the text. The full list of references is available as Appendix 3 on the journal website (http://www.ageing.oxfordjournals.org/).

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