

SYSTEMATIC REVIEW

The association of delirium severity with patient and health system outcomes in hospitalised patients: a systematic review

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Abstract

Background: delirium is an acute state of confusion that affects >20% of hospitalised patients. Recent literature indicates that more severe delirium may lead to worse patient outcomes and health system outcomes, such as increased mortality, cognitive impairment and length of stay (LOS).

Methods: using systematic review methodology, we summarised associations between delirium severity and patient or health system outcomes in hospitalised adults. We searched MEDLINE, EMBASE, PsycINFO, CINAHL and Scopus databases with no restrictions, from inception to 25 October 2018. We included original observational research conducted in hospitalised adults that reported on associations between delirium severity and patient or health system outcomes. Quality of included articles was assessed using the Newcastle–Ottawa Scale. The level of evidence was quantified based on the consistency of findings and quality of studies reporting on each outcome.

Results: we included 20 articles evaluating associations that reported: mortality ($n = 11$), cognitive ability ($n = 3$), functional ability ($n = 3$), patient distress ($n = 1$), quality of life ($n = 1$), hospital LOS ($n = 4$), intensive care unit (ICU) LOS ($n = 2$) and discharge home ($n = 2$). There was strong-level evidence that delirium severity was associated with increased ICU LOS and a lower proportion of patients discharged home. There was inconclusive evidence for associations between delirium severity and mortality, hospital LOS, functional ability, cognitive ability, patient distress and quality of life.

Conclusion: delirium severity is associated with increased ICU LOS and a lower proportion of patients discharged home. Delirium severity may be a useful adjunct to existing delirium screening to determine the burden to health care system resources.

Keywords: delirium, severity, outcomes, hospital, older people

Key points

- Delirium severity is associated with health system outcomes.
- Delirium severity is associated with increased length of stay.
- Delirium severity is associated with increased institutionalisation.

Background

Delirium is a state of confusion, characterised by impairment of attention, consciousness and cognition [1]. Delirium affects >20% of all hospitalised patients [2] and 80% of mechanically ventilated intensive care unit (ICU) patients [3]. Research suggests that delirium severity is associated with worse patient outcomes, including mortality and cognitive impairment [3,4]. Evaluating relationships between delirium severity and patient outcomes may allow for more accurate prediction of health outcomes and monitoring of changes throughout inpatient stays. Delirium severity may be associated with health care system burden through increased length of stay (LOS) and staff workload [5,6]. Recognition of delirium severity in clinical practice may help inform appropriate staffing and predict patient and caregiver needs following discharge.

Evidence suggests that more severe delirium is associated with worse patient and health system outcomes; however, the reported associations are variable [3,7,8]. The strength of these associations must be evaluated to recognise the utility of delirium severity measurement in clinical practice and future research. The current review aims to summarise associations between delirium severity and patient health outcomes and health system outcomes.

Methods

Protocol and registration

This systematic review followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [9]. We drafted the study protocol [10] *a priori* and registered on the International Prospective Register of Systematic Reviews (CRD42018095048) [11].

Eligibility criteria

Included studies were original peer-reviewed research of observational study design, conducted in adult patients (≥ 18 years old) admitted to any hospital setting (defined as any inpatient facility/ward providing acute medical care), reported on delirium severity with respect to any patient outcome (e.g. mortality, cognitive or functional decline, patient distress and quality of life) occurring after the course of delirium (i.e. excluded delirium feature studies) or any health system outcome (e.g. hospital and ICU LOS, discharge home). Delirium severity was defined as a continuous/ordinal measure of delirium based on the prominence of delirium symptoms, rated by a validated

delirium assessment tool. Individual studies defined mild, moderate and severe delirium based on the delirium severity measurement tool used, and others defined ‘more severe’ delirium as higher scores on continuous delirium severity measures. Multivariable studies were defined as studies that controlled for covariates, as defined by the studies (e.g. age, sex, illness severity), whereas univariable studies did not. Studies using duplicate data were excluded.

Search

The search strategy was finalised with a medical librarian and conducted in online databases: MEDLINE, EMBASE, PsycINFO, CINAHL and Scopus, from inception to 25 October 2018 with no restrictions. The search terms included delirium, severity and outcomes and related synonyms and medical subject headings (Appendix A1). Reference lists of included full-text articles and relevant reviews were searched to identify additional studies.

Study selection

Two reviewers (B.K.R. and H.M.) independently screened titles and abstracts in duplicate using EndNote X7 (Clarivate Analytics, Philadelphia, PA). Two reviewers (B.K.R. and K.D.K.) independently reviewed full-text articles in duplicate using the standardised eligibility criteria. Both reviewers agreed on inclusion and exclusion reasons. Disagreements were resolved by a third reviewer (K.M.F.). Reviewers translated non-English manuscripts using Google Translate [12].

Data extraction and study quality

One reviewer (B.K.R.) extracted data independently from included studies using a standardised electronic data form. Data were independently checked by a second reviewer (K.D.K.). Data elements extracted included: study information, patient demographics, delirium severity measurement tool used and patient or health system outcomes reported with respect to delirium severity. Two reviewers (B.K.R. and K.D.K.) assessed methodological quality of included studies independently and in duplicate using the Newcastle–Ottawa Scale (NOS), scored based on the Agency for Healthcare Research and Quality (AHRQ) guidelines [13,14]. We used semi-quantitative methodology to quantify levels of evidence as strong (consistent findings in $\geq 75\%$ of studies, including ≥ 2 good-quality multivariable studies), moderate (consistent findings in $\geq 60\%$ of studies, including ≥ 2 fair-quality multivariable studies), inconclusive (inconsistent findings) or none (no multivariable associations, no association in

Table 1. Semi-quantitative levels of evidence for association with delirium severity

Level of evidence	Criteria
Strong	Consistent findings in $\geq 75\%$ of studies, including ≥ 2 good-quality studies that used multivariable analysis
Moderate	Consistent findings in $\geq 60\%$ of studies, including ≥ 2 fair-quality studies that used multivariable analysis
Inconclusive	Inconsistent findings regardless of study quality or only fair-quality and low-quality articles in the multivariable analysis or only univariate analysis completed
None	No associations in multivariable analyses and no association in ≥ 3 good-quality articles using multivariable analysis

≥ 3 good-quality multivariable studies) (Table 1). Because of the presence of many potential confounding variables in the included studies, the semi-quantitative framework required inclusion of ≥ 2 multivariable studies to be classified as strong, moderate or no evidence.

Data synthesis and analysis

All analyses were conducted in Stata (version 11.0). We summarised study and patient characteristics using descriptive statistics with appropriate variability estimates. A *P*-value < 0.05 was considered significant. A meta-analysis was not conducted because of the heterogeneity of study setting, follow-up duration, delirium severity category cutoff values, delirium severity measurement tool used and outcome reporting.

Results

Study characteristics

The search strategy identified 3,203 unique citations, 166 articles met inclusion for full-text review and 20 studies were included (Figure 1). All studies were prospective cohort in design. There were 6,090 patients included, and the mean (\pm standard deviation, SD) number of patients in each study was 305 (± 323) with a mean (\pm SD) age of 72.3 (± 11.9) years (Table 2).

Study quality assessment

Table 3 presents study quality, evaluated using the NOS. Quality ratings were good ($n = 11$) [15–25], fair ($n = 6$) [26–31] and poor ($n = 3$) [32–34].

Patient health outcomes

Mortality

There was inconclusive evidence that delirium severity was associated with mortality (Table 4). Five studies reported a significant association between delirium severity and mortality (studies using multivariable analyses [18,24,30], studies

using univariable analyses [33,34]), and six studies reported no significant associations (multivariable [17,22,27,28], univariable [25,31]). Results were similar when stratified into ICU and non-ICU populations.

In 518 ICU patients, severe delirium was associated with higher odds of in-hospital mortality compared to those with mild–moderate delirium (multivariable; odds ratio, OR 2.92; 95% confidence interval, CI 1.17–7.26, *P* = 0.02) [18]. In 919 medical patients, more severe delirium was associated with a higher risk ratio (RR) of mortality at 1 month (multivariable; mild delirium RR 1.9, moderate delirium RR 4.1, severe delirium RR 8.3, *C*-statistic *P* < 0.01) [30]. A study of 441 post-acute care unit patients reported that hypoactive delirium is associated with 6-month mortality, regardless of its severity [24]. Patients who had severe or mild hypoactive delirium were more likely to die by 6 months, with hazard ratios (HR) of 1.67 (95% CI 0.97–2.05) and 1.62 (95% CI 1.05–2.49), compared to patients who had mild delirium with normal psychomotor behaviour HR 1.48, 95% CI 0.91–2.39) [24]. A study of 214 geriatric patients reported that patients within the highest quintile of delirium severity had 2.8 times higher odds of mortality at 3 months compared to patients with less severe delirium (univariable; *P* < 0.05) [33]. In 140 ICU patients, those who died during their stay had higher mean (\pm SD) Delirium Rating Scale Revised 1998 (DRS-R-98) severity scores: 13.86 (± 4.34) versus 9.86 (± 3.36) (univariable; *P* < 0.001) [34].

Conversely, a study of 139 hospitalised older adults with dementia reported that death at 1-month post-hospital follow-up was not significantly correlated with incident peak delirium severity (OR 1.05, 95% CI 0.96–1.14, *P* = 0.2719) [17]. In 537 ICU patients, there were no differences between Intensive Care Delirium Screening Checklist (ICDSC) scores ≥ 4 and time to death in multivariable analyses (*P* = 0.5433) [22]. In 122 hospitalised patients admitted for acute hip fracture surgery, there was no significant difference in odds of mortality in patients with severe delirium, compared to mild delirium at 1 and 6 months (multivariable; 1-month RR 1.0, 95% CI 0.1–14.5; 6-month RR 1.6, 95% CI 0.4–6.0) [27]. In 361 medical care unit patients, higher mean delirium severity was associated with increased mortality at 1 year in univariable models (HR 1.09; 95% CI 1.03–1.15), but the association was attenuated in multivariable models (HR 1.02; 95% CI 0.95–1.09) [28]. In 234 step-down unit patients, there was no correlation between ICDSC scores and mortality in univariable analyses [25]. In 164 geriatric care patients, there was no significant association between delirium severity and mortality in-hospital or at 6-month follow-up (univariable; *P* > 0.05) [31].

Functional ability

There was inconclusive evidence for the association between delirium severity and functional ability (Table 4); one study reported a significant negative association between delirium

Table 2. Characteristics of included studies

Severity measurement tool	Author	Country	Setting	Sample size	Age, years (mean ± SD)	Delirium prevalence (%)	Delirium incidence (%)
ICDSC	Ceriana et al. [25]	Italy	Step-down unit	234	69.8 ± 11.0	—	—
ICDSC	Ouimet et al. [22]	Canada	ICU	537	65 ± 15	—	—
ICDSC	Sakuramoto et al. [20]	Japan	ICU	79	67.4 ± 14.5	63.3	—
ICDSC	Van Rompaey et al. [23]	Belgium	ICU	105	—	—	19.0
MDAS	Kelly et al. [33]	USA	Geriatric unit	214	88	28.5	—
MDAS	Marcantonio et al. [27]	USA	Medical unit	122	79 ± 8	40	—
MDAS	Yang et al. [24]	USA	Post-acute care unit	441	84.1 ± 7.2	21.5	—
CAM-S	Cavallari et al. [26]	USA	Post-operative unit	113	76 ± 5	22.0	—
CAM-S	Vasunilashorn et al. [30]*	USA	Medical unit	919	80.0 ± 6.5	—	13.0
CAM-S	Vasunilashorn et al. [21]	USA	Post-operative unit	560	76.7 ± 5.2	—	24.0
DRS	Adamis et al. [31]	UK	Geriatric unit	164	84.6 ± 6.6	28.7	3.0
DRS	Brown et al. [15]	USA	Post-operative (ICU)	66	70 ± 7	—	56.0
DRS	Brown et al. [16]	USA	Post-operative unit	89	—	40.4	—
DRS-R-98	Fick et al. [17]	USA	Medical unit	139	83 ± 7	32	—
DRS-R-98	Sharma et al. [34]	India	ICU	140	43.91 ± 17.0	53.6	24.4
DI	McCusker et al. [28]	Canada	Medical unit	361	—	67.3	—
DI	McCusker et al. [29]	Canada	Medical unit	359	83.48 ± 7.03	57.0	11.0
CAM-ICU-7	Khan et al. [18]	USA	ICU	518	60.2 ± 16.1	—	—
CAM	Qu et al. [19]	China	Neurology	261	61.3 ± 14.8	—	14.6
NEECHAM	Breitbart et al. [32]	USA	Oncology unit	101	58.3 ± 16.7	—	—

MDAS: Memorial Delirium Assessment Scale, DI: Delirium Index, *Asterisk indicates Project Recovery Cohort.

Table 3. Quality assessment of included studies using the NOS

Quality	Author	(i) Representativeness of population	(ii) Selection of population	(iii) Ascertainment of delirium status	(iv) Presence of delirium at study start	(v) Comparability of cohorts	(vi) Assessment of outcome	(vii) Adequacy of follow-up period	(viii) Adequacy of follow-up
Good	Brown et al. [15]	C	A*	B*	B	A*	B*	A*	A*
Good	Brown et al. [16]	C	A*	B*	B	A*	B*	A*	A*
Good	Ceriana et al. [25]	A*	A*	B*	A*	A*	B*	A*	A*
Good	Fick et al. [17]	C	A*	B*	A*	A*	C	A*	A*
Good	Khan et al. [18]	A*	C	B*	B	A*	B*	A*	A*
Good	Qu et al. [19]	C	A*	B*	B	A*	C	A*	A*
Good	Sakuramoto et al. [20]	A*	A*	B*	B	A*	C	A*	A*
Good	Vasunilashorn et al. [21]	C	A*	B*	A*	A*	A*	A*	A*
Good	Ouimet et al. [22]	B*	A*	B*	B	A*	B*	A*	A*
Good	Van Rompaey et al. [23]	B*	A*	B*	B	A*	C	A*	A*
Good	Yang et al. [24]	B*	A*	B*	B	A*	B*	A*	A*
Fair	Adamis et al. [31]	C	A*	B*	B	A*	B*	A*	B*
Fair	Cavallari et al. [26]	C	A*	B*	B	A*	A*	A*	B*
Fair	Marcantonio et al. [27]	C	A*	B*	B	A*	C	A*	A*
Fair	McCusker et al. [28]	C	A*	B*	B	A*	C	A*	A*
Fair	McCusker et al. [29]	C	A*	B*	B	A*	C	A*	A*
Fair	Vasunilashorn et al. [30]	C	A*	B*	B	A*	A*	A*	A*
Poor	Breitbart et al. [32]	C	C	B*	B	A*	C	A*	A*
Poor	Kelly et al. [33]	B*	A*	B*	B	C	C	A*	A*
Poor	Sharma et al. [34]	A*	A*	B*	B	C	D	A*	A*

(i) Representativeness of hospitalised adults with delirium: (a) no restrictions placed on selection*; (b) few restrictions placed on selection (e.g. age)*; (c) restricted selection (e.g. age, clinical condition) and (d) no description of selection. (ii) Selection of hospitalised adults without delirium: (a) drawn from same population as patients with delirium*; (b) drawn from different source and (C) no description. (iii) Ascertainment of delirium status: (a) secure record*; (b) structured interview*; (c) self-report and (d) no description. (iv) Demonstration that outcome was not present at start of study: (a) yes*; (b) no. (v) Comparability of cohorts: (a) controls for age*; (b) controls for any additional confounding factor* and (c) no controls or no description. (vi) Assessment of outcome: (a) independent blind assessment*; (b) record linkage*; (c) self-report and (d) no description. (vii) Adequacy of follow-up period: (a) follow-up time adequate for outcome to occur*; (b) follow-up time not adequate for outcome to occur. (viii) Adequacy of follow-up: (a) all subjects accounted for*; (b) >80% participants accounted for or description of those lost suggested no different from those followed*; (c) < 80% participants accounted for and no description of those lost and (d) no description.

Table 4. Summary of studies that reported on associations between delirium severity and patient outcomes in univariable or multivariable analyses

	Multivariable analysis		Univariable analysis		Level of evidence (stratified by ICU versus non-ICU)	Level of evidence (all settings)
	Positive association	Negative association	No association	No association		
Mortality	Non-ICU	ICU	Non-ICU	ICU	Inconclusive	Inconclusive
	Yang <i>et al.</i> [24]	Khan <i>et al.</i> [18]; Vasunilashorn <i>et al.</i> [30]	Marcantonio <i>et al.</i> [27]; McCusker <i>et al.</i> [28]; Fick <i>et al.</i> [17]; Outmet <i>et al.</i> [22]	Kelly <i>et al.</i> [33]; Sharma <i>et al.</i> [34]	Adamis <i>et al.</i> [31]; Certiana <i>et al.</i> [25]	
Functional ability	Non-ICU	ICU	ICU		Inconclusive	Inconclusive
		Fick <i>et al.</i> [17]	Marcantonio <i>et al.</i> [27]; Qu <i>et al.</i> [19]			
Cognitive ability	Non-ICU	ICU	Non-ICU		Inconclusive	Inconclusive
		Vasunilashorn <i>et al.</i> [21]; Sakuramoto <i>et al.</i> [20]	Cavallari <i>et al.</i> [26]			
Patient distress	Non-ICU	ICU			Inconclusive	Inconclusive
				Breitbart <i>et al.</i> [32]		
Quality of life	Non-ICU	ICU			Inconclusive	Inconclusive
				Van Rompaey <i>et al.</i> [23]		
Hospital LOS	Non-ICU	ICU	Non-ICU		Inconclusive	Inconclusive
	Fick <i>et al.</i> [17]		Brown <i>et al.</i> [16]; McCusker <i>et al.</i> [29]; Brown <i>et al.</i> [15]			
ICU LOS	Non-ICU	ICU			Inconclusive	Strong
	Brown <i>et al.</i> [15]; Khan <i>et al.</i> [18]					
Discharge home	Non-ICU	ICU	Non-ICU		Inconclusive	Strong
		Brown <i>et al.</i> [16]; Khan <i>et al.</i> [18]				

and functional ability using multivariable analyses [17] and two studies reported no significant association between functional ability and delirium severity using multivariable analyses [19,27]). Only studies in non-ICU settings reported functional ability, therefore associations were not stratified by setting.

In 139 hospitalised patients, Katz impaired in Activities of Daily Living (ADL) score (range, 0–6) increased by 0.05 units as incident delirium severity increased 1 unit (multivariable; $P = 0.0437$) at 1-month post-hospital follow-up [17]. Lawton IADL scores decreased by 0.003 units as incident delirium severity increased 1 unit, but the association was not significant (multivariable; $P = 0.9260$) [17]. Conversely, a study of 261 stroke patients reported that delirium severity delirium was not significantly associated with Lawton Instrumental ADL scores (range 0–8) at 3 months (multivariable; $r = 0.016$, $P = 0.928$) or 6 months (multivariable; $r = -0.04$, $P = 0.831$) [19]. Similarly, in 122 medical care unit patients, the RR of Katz ADL score decline between mild and severe delirium groups was 1.0 (95% CI 0.1–1.4) at 1 month and 1.4 (95% CI 0.7–2.6) at 6 months (multivariable) [27].

Cognitive ability

There was inconclusive evidence for the association of delirium severity with cognitive ability (Table 4); two studies reported a negative association between delirium severity and cognitive function (multivariable [20,21]), and one study reported no significant associations (multivariable [26]). Results were similar when stratified into ICU and non-ICU populations.

A study of 79 ICU patients demonstrated that average ICDSC score and ICDSC score at ICU discharge were associated with cognitive impairment at hospital discharge (multivariable; average score OR 1.6, 95% CI 1.02–2.55, $P = 0.004$; score at discharge OR 1.6, 95% CI 1.08–2.40, $P = 0.002$) [20]. In 560 post-surgical patients, there was a significant linear trend of increasing cognitive decline measured by the Global Cognitive Performance (GCP) scale with increasing delirium severity on the Confusion Assessment Method Severity (CAM-S) ($P = 0.009$) [21]. Patients with severe delirium demonstrated the greatest magnitude of cognitive decline (CAM-S 8–19: -0.82 GCP units/year, 95% CI -1.28 to -0.37) when compared to patients with mild delirium (CAM-S 0–2: -0.17 GCP units/year, 95% CI -0.35 to -0.01) and moderate delirium (CAM-S 3–7: -0.30 GCP units/year, 95% CI -0.51 to -0.09) [21]. Patients with mild and moderate delirium returned to baseline GCP scores by 2 months, but patients with severe delirium experienced progressive GCP score decline to 3 years [21]. Additionally, the study reported a linear trend of increasing Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) impairment with increasing delirium severity, but the trend was not statistically significant ($P = 0.07$) [21]. Conversely, a multivariable study of 113 post-operative patients reported

that GCP scale changes at 1-year follow-up were not associated with delirium severity [26].

Patient distress and quality of life

There was inconclusive evidence for the association of delirium severity with patient distress or quality of life (Table 4); one univariable study reported no significant association between delirium severity and patient distress [32]. One univariable study measured quality of life; it reported a significant negative association between delirium severity and quality of life [23]. One non-ICU setting reported patient distress and one ICU setting reported quality of life, therefore associations were not stratified by setting.

In 101 oncology patients, delirium severity was negatively associated with patient delirium recall and was non-significantly associated with delirium-related patient distress (univariable; chi-squared 4.7; $P = 0.09$) [32]. In 105 ICU patients, there was a significant positive correlation between less severe delirium (measured by Neelson and Champagne, NEECHAM, confusion scale) and higher Short Form-20 (SF-20) scores using univariable analyses in physical function ($r = 0.35$), role function ($r = 0.31$) and health perception ($r = 0.25$) at 3 months, and with physical function ($r = 0.27$), role function ($r = 0.34$), social function ($r = 0.30$) and mental health ($r = 0.28$) at 6 months [23]. Overall, a lower NEECHAM score (indicating more severe delirium) was significantly associated with decreased SF-20 scores [23].

Health system outcomes

Hospital LOS

The level of evidence for the association of delirium severity with hospital LOS was inconclusive (Table 4); one multivariable study reported a significant positive association between delirium and hospital LOS [17], and three multivariable studies reported no significant associations [15,16,29]. Results were similar when stratified into ICU and non-ICU populations.

In a study of 139 hospitalised patients, delirium severity was significantly correlated with increased hospital LOS (multivariable; coefficient 0.43, standard error 0.06, $P < 0.0001$) [17]. Conversely, in 66 cardiac surgery patients, there was a non-significant relationship between delirium severity and longer hospital LOS (multivariable; $P = 0.07$) [15]. A study of 89 post-spinal surgery patients reported a non-significant association between delirium severity and hospital LOS (multivariable; OR 1.09, 95% CI 0.96–1.23; $P = 0.18$) [16]. In 359 medical patients, there was no significant association between delirium severity and hospital LOS [29].

ICU LOS

The level of evidence for the association between delirium severity and ICU LOS was strong; two studies reported significant positive associations between delirium and ICU LOS (multivariable [15,18]).

A study of 66 cardiac surgery patients reported a significant correlation between delirium severity and ICU LOS (multivariable; $P = 0.012$) [15]. In 518 ICU patients, higher median and peak delirium severity scores during a patient's ICU stay were associated with longer ICU LOS (multivariable; median $r = 0.145$, $P = 0.001$; peak $r = 0.327$, $P < 0.001$) [18].

Discharge home

The level of evidence for the association between delirium severity and discharge home was strong (Table 4); two studies reported significant negative associations between delirium and discharge home using multivariable analyses [16,18]. When stratified by ICU versus non-ICU populations, only one study was reported in each strata.

In a study of 89 post-spinal surgery patients, delirium severity was associated with lower odds of being discharged home (multivariable; $P = 0.003$) and for every increased unit on the DRS-R-98, odds of discharge home decreased by 11% [16]. In 518 ICU patients, higher peak Confusion Assessment Method for the ICU-7 (CAM-ICU-7) scores were associated with lower odds of being discharged home (multivariable; OR 0.78, 95% CI 0.71–0.86) [18]. Specific discharge destinations were not reported in either study, but may include another medical facility, an assisted living facility or living with a family caregiver.

Discussion

This systematic search included 20 studies of 5,673 patients, 2,513 had delirium. There was strong evidence that delirium severity was associated with increased ICU LOS and decreased proportion of patients discharge home. There was inconclusive evidence that delirium severity was associated mortality, hospital LOS, functional ability, cognitive ability, patient distress and quality of life. When associations were stratified by ICU versus non-ICU settings, associations between delirium severity and ICU LOS and discharge home were inconclusive due of the small number of studies reported.

All patient health outcomes had inconclusive evidence of association with delirium severity, likely due to differences in delirium severity measurement tool used and clinical population. For example, nine different delirium severity tools were used with different cutoffs for delirium severity. The clinical population evaluated may have modified associations between delirium severity and outcomes due to varying delirium etiologies and clinical factors like illness severity. To reduce this clinical heterogeneity, we separated studies that reported ICU and non-ICU patients. However, after stratifying by setting, too few studies were included in each to meaningfully evaluate the level of evidence.

Quantification of delirium severity may allow health care organisations to better predict projected health care costs attributable to factors such as ICU LOS and discharge location. Though further research in ICU and non-ICU settings

is required, health care professionals and administrators may wish to document delirium severity. Many delirium screening tools routinely used in hospitals across the world can measure severity, making documentation of delirium severity feasible. This review highlights the need for future studies in both ICU and non-ICU settings. Future studies should use validated delirium measurement tools and regression analyses to report relationships between delirium severity and outcomes, controlling for potential confounding variables, such as age, illness severity and frailty. A larger body of high-quality studies is needed to understand associations between delirium severity and outcomes, which will yield valuable conclusions regardless of presence of association. If associations with patient and health system outcomes are present, further research will inform how delirium severity measurement can be used in adjunct to dichotomous delirium measurement to predict patient outcomes and inform resource utilisation. For example, measurement of delirium severity may identify patients with a higher risk of developing poor outcomes, such as cognitive impairment or death. Identifying these patients may provide better prognostic information and inform selection of interventions to mitigate long-term burdens associated with delirium. Similarly, identification of patients with a higher risk of developing poor outcomes may help identify which patients may be most appropriate for inclusion in research. In delirium management studies, identification of treatment effects may be most optimal in patients with the most severe delirium. In addition, quantification of delirium severity may allow health care organisations to better predict projected health care costs attributable to factors such as LOS and discharge location.

Several qualities strengthen the conclusions of this systematic review. We followed a rigorous, published protocol (following PRISMA guidelines) to ensure transparency and reproducibility [9]. We aimed to reduce heterogeneity by including only hospitalised patients because the pathophysiology of delirium may be different between hospital and community settings.

Several factors may have limited the strength of study conclusions. First, studies used different delirium severity measurement tools, limiting our ability to calculate pooled estimates. Second, outcomes were measured at different time points during or after hospital stay with different tools and definitions of delirium severity, contributing to variability in the data. Third, many studies did not include patient outcomes as primary endpoints and thus may not have adequate power to detect significant associations. Fourth, some included studies had suboptimal quality ratings, highlighting the need for additional high-quality studies. Lastly, many included studies reported univariable analyses, which did not adjust for confounding factors (e.g. age, illness severity, frailty). Due to unmeasured confounding, conclusions could not be drawn from the univariable analyses. For this reason, the semi-quantitative methodology used ensured that emphasis was placed on inclusion of multivariable studies when determining the level of evidence.

Conclusions

Delirium severity is associated with increased length of ICU stay and a lower proportion of patients discharged home. Despite the importance of this disorder the current body of literature is limited and variable in setting, methodology and quality, highlighting a need for new high-quality studies. The current evidence indicates that delirium severity may be a useful adjunct to existing delirium screening to determine the burden to patients, health care system resources and care teams.

Supplementary data: Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

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References

1. American Psychiatric Association. Diagnostic Statistical Manual for Mental Disorders 5th Edition. Arlington, VA: American Psychiatric Publishing, 2013.
2. Ryan DJ, Regan NA, Caoimh R *et al.* Delirium in an adult acute hospital population: predictors, prevalence and detection. *BMJ Open* 2013; 3: e001772.
3. Ely E, Shintani A, Truman B *et al.* Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *JAMA* 2004; 291: 1753–62.
4. Girard TD, Jackson JC, Pandharipande PP *et al.* Delirium as a predictor of long-term cognitive impairment in survivors of critical illness. *Crit Care Med* 2010; 38: 1513–20.
5. Adriaenssens J, De Gucht V, Van Der Doef M *et al.* Exploring the burden of emergency care: predictors of stress-health outcomes in emergency nurses. *J Adv Nurs* 2011; 67: 1317–28.
6. Schmitt EM, Gallagher J, Albuquerque A *et al.* Perspectives on the delirium experience and its burden: common themes among older patients, their family caregivers, and nurses. *Gerontologist* 2017; 59: 327–37.
7. Andrew MK, Freter SH, Rockwood K. Incomplete functional recovery after delirium in elderly people: a prospective cohort study. *BMC Geriatr* 2005; 12: 141–4.
8. Rockwood K, Cosway S, Carver D *et al.* The risk of dementia and death after delirium. *Age Ageing* 1999; 28: 551–6.
9. Liberati A, Altman DG, Tetzlaff J *et al.* The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med* 2009; 6: e1000100.
10. Rosgen B, Krewulak K, Wesley E *et al.* Delirium severity and patient health outcomes: a systematic review and meta-analysis 2018. Available from: <http://hdl.handle.net/1880/106550>. (25 April 2018, date last accessed).
11. Research NifH. International Prospective Register of Systematic Reviews (PROSPERO) York, UK: Centre for Reviews and Dissemination [online]. Available at <https://www.crd.york.ac.uk/prospere/>. (18 May 2018, date last accessed).
12. Google. Google translate. Available at <https://translate.google.ca/>. (1 February 2020, date last accessed).
13. Wells G, Shea B, O'Connell D *et al.* The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses [online]. Available at http://www.ohri.ca/programs/clinical_epidemiology/nos_manual.doc. (1 April 2020, date last accessed).
14. Newcastle-Ottawa Quality Assessment Form for Cohort Studies. Available at <https://www.ncbi.nlm.nih.gov/books/NBK115843/bin/appe-fm3.pdf>, accessed April 1, 2020.
15. Brown C, Laflam A, Max L *et al.* The impact of delirium after cardiac surgical procedures on postoperative resource use. *Ann Thorac Surg* 2016; 101: 1663–9.
16. Brown C, LaFlam A, Max L *et al.* Delirium after spine surgery in older adults: incidence, risk factors, and outcomes. *J Am Geriatr Soc* 2016; 64: 2101–8.
17. Fick DM, Steis M, Waller J *et al.* Delirium superimposed on dementia is associated with prolonged length of stay and poor outcomes in hospitalized older adults. *J Hosp Med* 2013; 8: 500–5.
18. Khan BA, Perkins A, Gao S *et al.* The Confusion Assessment Method for the ICU-7 Delirium Severity Scale: a novel delirium severity instrument for use in the ICU. *Crit Care Med* 2017; 45: 851–7.
19. Qu J, Chen Y, Luo G *et al.* Delirium in the acute phase of ischemic stroke: incidence, risk factors, and effects on functional outcome. *J Stroke Cerebrovasc Dis* 2018; 27: 2641–7.
20. Sakuramoto H, Subrina J, Unoki T *et al.* Severity of delirium in the ICU is associated with short term cognitive impairment. A prospective cohort study. *Intensive Crit Care Nurs* 2015; 31: 250–7.
21. Vasunilashorn SM, Fong TG, Albuquerque A *et al.* Delirium severity post-surgery and its relationship with long-term cognitive decline in a cohort of patients without dementia. 2018; 61: 347–58.
22. Ouimet S, Riker R, Bergeron N *et al.* Subsyndromal delirium in the ICU: evidence for a disease spectrum. *Intensive Care Med* 2007; 33: 1007–13.
23. Van Rompaey B, Schuurmans M, Shortridge-Baggett L *et al.* Long term outcome after delirium in the intensive care unit. *J Clin Nurs* 2009; 18: 3349–57.
24. Yang FM, Marcantonio E, Inouye SK *et al.* Phenomenological subtypes of delirium in older persons: patterns, prevalence, and prognosis. *Psychosomatics* 2009; 50: 238–54.
25. Ceriana P, Fanfulla F, Mazzacane F *et al.* Delirium in patients admitted to a step-down unit: analysis of incidence and risk factors. *J Crit Care* 2010; 25: 136–43.
26. Cavallari M, Dai W, Guttmann CRG *et al.* Longitudinal diffusion changes following postoperative delirium in older people without dementia. *Neurology* 2017; 89: 1020–7.

27. Marcantonio E, Ta T, Duthie E *et al.* Delirium severity and psychomotor types: their relationship with outcomes after hip fracture repair. *J Am Geriatr Soc* 2002; 50: 850–7.
28. McCusker J, Cole M, Abrahamowicz M *et al.* Delirium predicts 12-month mortality. *Arch Intern Med* 2002; 162: 457–63.
29. McCusker J, Cole M, Dendukuri N *et al.* Does delirium increase hospital stay? *J Am Geriatr Soc* 2003; 51: 1539–46.
30. Vasunilashorn SM, Marcantonio ER, Gou Y *et al.* Quantifying the severity of a delirium episode throughout hospitalization: the combined importance of intensity and duration. *J Gen Intern Med* 2016; 31: 1164–71.
31. Adamis D, Treloar A, Darwiche F *et al.* Associations of delirium with in-hospital and in 6-months mortality in elderly medical inpatients. *Age Ageing* 2007; 36: 644–9.
32. Breitbart W, Gibson C, Tremblay A. The delirium experience: delirium recall and delirium-related distress in hospitalized patients with cancer, their spouses/caregivers, and their nurses. *Psychosomatics* 2002; 43: 183–94.
33. Kelly KG, Zisselman M, Cutillo-Schmitter T *et al.* Severity and course of delirium in medically hospitalized nursing facility residents. *Am J Geriatr Psychiatry* 2001; 9: 72–7.
34. Sharma A, Malhotra S, Grover S *et al.* Incidence, prevalence, risk factor and outcome of delirium in intensive care unit: a study from India. *Gen Hosp Psychiatry* 2012; 34: 639–46.
35. Robinson TN, Eiseman B. Postoperative delirium in the elderly: diagnosis and management. *Clin Interv Aging* 2008; 3: 351–5.
36. Lorenzl S, Füsgen I, Noachtar S. Acute confusional states in the elderly—diagnosis and treatment. *Dtsch Arztebl Int* 2012; 109: 391–400.

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