

# The association between cognitive impairment and functional outcome in hospitalised older patients: a systematic review and meta-analysis

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## Abstract

**Background:** in hospitalised older adults, cognitive impairments are common and may be associated with functional outcomes. Our aim was to systematically review this association.

**Method:** we systematically searched MEDLINE, CINAHL, AMED and PsycINFO from inception to April 2016. Non-English language studies were filtered out at search stage. All types of studies were considered for inclusion except reviews, conference abstracts, dissertations and case studies. Population: community-dwelling or institutionalised older adults aged 65 years or more, who are acutely hospitalised and have information on history of dementia and/or cognitive scores on admission. Setting: acute hospital (excluding critical care and subacute or intermediate care). Outcome of interest: change in a measure of physical function or disability between pre-admission or admission, and discharge or post-discharge. This review was registered on PROSPERO (CRD42016035978).

**Results:** the search returned 5,988 unique articles, of which 34 met inclusion criteria. All studies were observational, with 30 prospective and 4 retrospective from 14 countries, recruiting from general medicine ( $n = 11$ ), geriatric medicine ( $n = 11$ ) and mixed ( $n = 12$ ) wards. Twenty-six studies (54,637 participants) were suitable for the quantitative synthesis. The meta-analysis suggested that cognitive impairment was associated with functional decline in hospitalised older adults (risk ratio (RR): 1.64; 95% confidence interval (CI): 1.45–1.86;  $P < 0.01$ ). Results were similar in subanalyses focusing on diagnosis of dementia (RR: 1.36; 95% CI: 1.05–1.76;  $P = 0.02$ ;  $n = 2,248$ ) or delirium (RR: 1.55; 95% CI: 1.31–1.83;  $P < 0.01$ ;  $n = 1,677$ ).

**Conclusion:** cognitive impairments seem associated with functional decline in hospitalised older people. Causality cannot be inferred, and limitations include low quality of studies and possible confounding.

**Keywords:** cognitive impairments, functional decline, hospital, frail older adults, systematic review

## Background

In the UK, people over the age of 65 account for almost two-thirds of acute hospital beds [1]. With an ever increasing population of older people, that proportion is expected to grow, and with it the prevalence of cognitive impairments

associated with ageing [2]. The prevalence of dementia in acute hospitals has been estimated to be between 13 and 63% [3, 4], and the prevalence of delirium between 20% and 27% [5, 6]. Delirium is commonly superimposed on dementia in older inpatients [4].

Following a stressor such as an illness or fall precipitating a hospital admission, many older people experience loss of physical function, and this may be one of the reasons for an increased length of hospital stay [7]. Cognitive impairments in older people have been associated with adverse outcomes following hospitalisation including increased mortality, impaired functional recovery, acquisition of new geriatric syndromes and institutionalisation [8–11]. Cognitive impairment may make older hospitalised people more vulnerable to loss of function or may impact on their ability to regain function once lost, meaning that by discharge they may not be at their pre-admission level of function [12].

A prominent hypothesis in cognitive ageing is the existence of a ‘common factor’ responsible for age-related deterioration in cognitive and non-cognitive (e.g. motor) processes [13], and in healthy older adults, there is evidence of a positive association between performance on mobility measures and cognitive assessments [14]. Despite cognitive impairments being common in hospitalised older adults, their association with the risk of functional decline had been less studied. Our aim was to conduct a systematic review of the association between cognitive impairment and functional outcome in acutely hospitalised older people. We focused on non-specific cognitive impairment, dementia or delirium, and their association with functional outcome.

## Methods

### Search strategy

A protocol of this review was registered on PROSPERO in 2016: CRD42016035978 [15]. The following databases were searched electronically: MEDLINE, CINAHL, AMED and PsycINFO. Non-English language studies were filtered out at search stage. All types of studies were considered for inclusion except reviews, conference abstracts, dissertations and case studies. The search was performed from inception to April 2016 to identify any new studies.

Key terms and MeSH headings used to search electronic databases were synonyms of: ‘elderly’ and ‘function’ and ‘hospital’ and ‘impaired cognition’. The search strategy for the MEDLINE electronic database is in the [Supplementary data, Appendix 1, available in \*Age and Ageing\* online](#).

The reference lists of included studies, identified reviews and our own personal literature databases were searched to identify any potential studies additional to those identified through the electronic searching. This did not include a forward citation search on included studies. In addition, we searched electronic databases using the names of authors of identified conference abstracts and dissertations to check for any related published articles.

### Selection criteria

#### Population

Community-dwelling or institutionalised older adults aged 65 years or more, who are acutely hospitalised and have cognitive information on admission. Definitions of

cognitive impairment included a known diagnosis of dementia (e.g. present in the patients’ medical records), and/or low scores on validated cognitive tests or delirium screening tools.

Studies that focused on specific populations of people who had suffered an acute stroke, an acquired brain injury or a fractured neck of femur as reason for admission were excluded. This was because previous systematic reviews suggested poor association between cognitive impairment and functional recovery in those patient groups [16, 17]. If the study included a mixed population and the results could not be differentiated, the authors were contacted for further data; if no response was received, or if they were unable to provide the data the study was excluded.

#### Setting

Acute hospital ward (i.e. excluding subacute or intermediate care such as inpatient rehabilitation). Acute hospital wards include surgical wards, but not critical care settings.

#### Outcomes of interest

Any measure of physical function or disability at pre-admission or admission, and discharge or post-discharge. All studies reporting the number of patients with and without a cognitive impairment that changed in function either from pre-admission or admission to discharge or post-discharge were included. Decline in function was defined as a functional score at follow-up worse than at baseline. For studies without a measure of pre-admission function we also accepted a definition of functional decline based on the numbers of patients with and without a cognitive impairment that failed to regain independence or whose discharge or post-discharge level of function was worse than at admission.

#### Study selection

Two reviewers worked independently using the pre-set inclusion criteria to identify relevant studies. The reviewers screened the articles’ titles and abstracts and classified each as relevant, not relevant or unsure. All articles screened by both reviewers as being not relevant were excluded. The reviewers then independently reviewed all other papers in full, but only using classifications of relevant or not relevant. Any discrepancy or uncertainty regarding the eligibility of a study was discussed between the two reviewers (who read the full paper together) or with a third author until consensus was reached. If variables of interest were measured but not reported, attempts were made to contact the authors before classifying a study as not relevant. Following this, all articles classified as not relevant were excluded from the review and the reasons were documented. The Newcastle–Ottawa Scale [18] was used for assessing the quality of included nonrandomised studies.

### Statistical analyses

The meta-analyses were performed using Review Manager (RevMan5.3). The risk ratio (RR) and 95% confidence intervals (CI) were calculated. A fixed effect Mantel–Haenszel

meta-analysis was undertaken when the inconsistency value ( $I^2$ ) was 50% or less and  $\text{Chi}^2$  had  $P \geq 0.10$ . A random-effect Mantel–Haenszel meta-analysis was undertaken when  $I^2$  was  $>50\%$  and  $\text{Chi}^2$  had  $P < 0.10$ .

In addition to the main meta-analysis, subgroup meta-subanalyses were planned for three different cognitive categories:

- (1) Diagnosis of dementia.
- (2) Diagnosis of delirium.
- (3) Studies reporting a non-specific cognitive impairment as measured by a validated cognitive scale (e.g. Folstein’s Mini-Mental Status Exam (MMSE) or Pfeiffer’s Short Portable Mental Status Questionnaire).

In order to explore if the functional outcome of cognitively impaired patients was different on discharge compared to post-discharge from hospital, we conducted a subanalysis of studies that reported functional outcome after at least 1 month post-discharge.

For each cognitive impairment category, the pooled effect estimate was calculated as a weighted average and 95% CI of the individual studies.

**Results**

Our search returned 5,988 unique articles. In addition, we emailed 47 authors, of whom 27 did not reply, 12 replied with

quantitative data and 8 with qualitative data. Thirty-four articles met inclusion criteria. All studies were observational, with 30 prospective and 4 retrospective from 14 countries, recruiting from general medicine ( $n = 11$ ), geriatric medicine ( $n = 11$ ), general and geriatric medicine ( $n = 3$ ), cardiology ( $n = 2$ ), medical and surgical ( $n = 1$ ) and other mixed ( $n = 6$ ) wards. Twenty-six studies (54,637 participants) were suitable for the quantitative synthesis, and eight studies for the qualitative synthesis. Figure 1 shows the flow diagram of selected studies as per PRISMA guidelines [19]. As regards the type of cognitive impairment, 8 studies included information on dementia, 11 on delirium and 21 on non-specific cognitive impairment, but there was overlap within some studies (Table 1). As regards the timing of the functional measurements, 18 studies included information on admission and discharge, and 13 at pre-admission and post-discharge (at variable time points), with some overlap within studies as well (Table 1). Further details of the included studies, including the results of the risk of bias assessment, are summarised in Table 1. In addition, information regarding the inclusion and exclusion criteria of individual studies, definitions of functional decline and cognitive impairment, and other patient characteristics (e.g. mean age, length of hospital stay and proportion of patients with cognitive impairment) can be found in the [Supplementary data, Appendix 2, available in Age and Ageing online](#). The overall quality of evidence using the Grading of

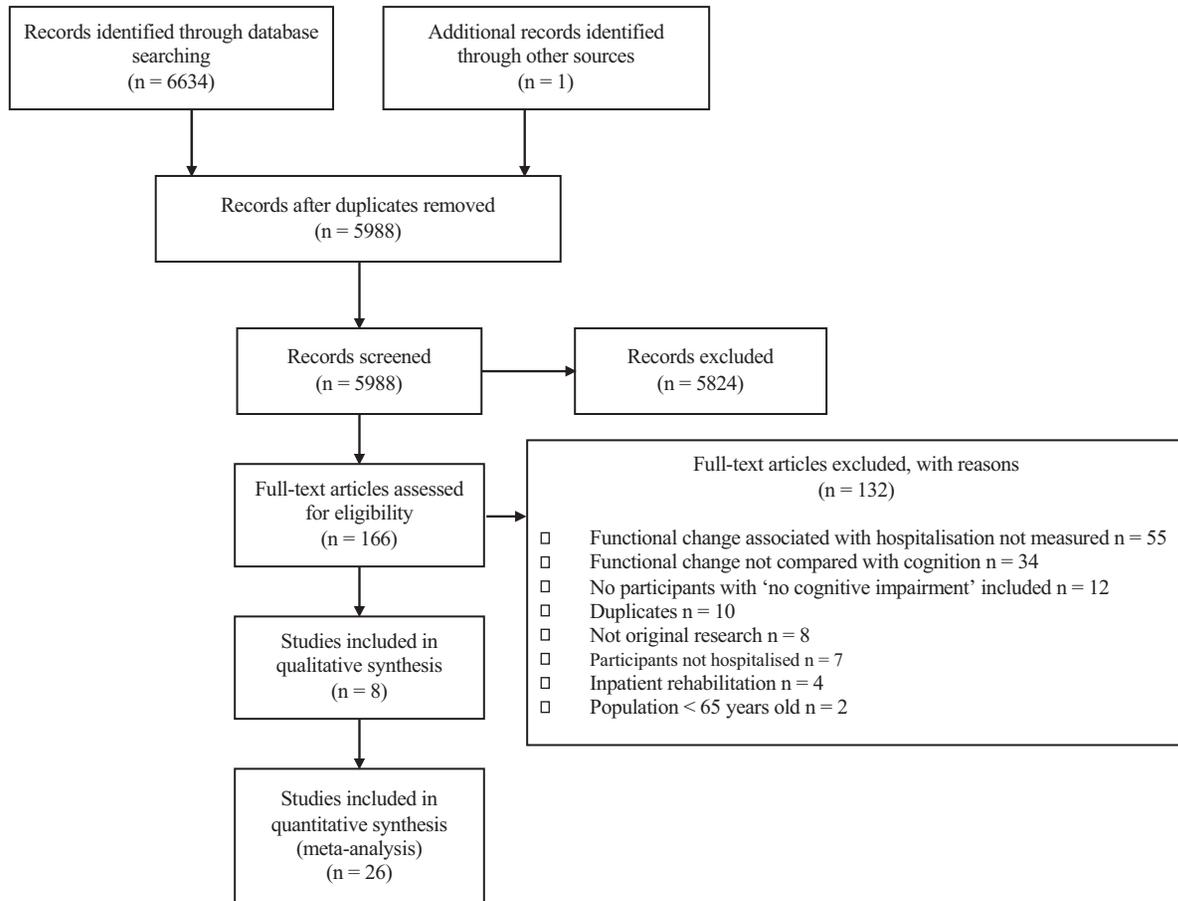


Figure 1. PRISMA flow diagram of selected studies.

Table 1. Characteristics of included studies

Author and year	Country	Participants	Numbers included in study	Cognitive impairment	Function	Time for baseline function	Time for follow-up function	Included in meta-analysis	Newcastle–Ottawa Scale
Adamis <i>et al.</i> 2011 [24]	Greece	Medical inpatients	150	Delirium NSCI	BI	Admission	Discharge	N	S *** C * O ***
Barnes <i>et al.</i> 2013 [36]	USA	Medical inpatients	449	<i>Dementia</i>	ADL IADL Mobility	Pre-admission Admission	Discharge 1 year	Y Published data	S **** C O **
Bo <i>et al.</i> 2016 [45]	Italy	Geriatric and medical inpatients	1568	NSCI	ADL	Admission	Discharge	Y Unpublished data	S *** C O ***
Chaudhry <i>et al.</i> 2004 [46]	USA	Medical inpatients	862	NSCI	ADL	Pre-admission	6 months	Y Published data	S **** C ** O ***
Chen <i>et al.</i> 2010 [47]	Taiwan	Geriatric inpatient	117	Delirium	BI TUG IADL	Admission	Discharge	Y Published data	S *** C O ***
Cornette <i>et al.</i> 2006 [48]	Belgium	Emergency admissions	625	NSCI	ADL IADL	Pre-admission	Discharge 1 month 3 months	Y Published data only	S **** C O ***
Feldman <i>et al.</i> 1999 [23]	Israel	Geriatric inpatients	61	Delirium	ADL	Admission	Discharge	N	S **** C O ***
Francis <i>et al.</i> 1992 [49]	USA	Medical inpatients	205	Delirium	ADL	Pre-admission	2 years	Y Published data	S **** C ** I ***
Friedman <i>et al.</i> 2008 [50]	USA	Geriatric inpatients	212	Delirium	ADL	Admission	Discharge	Y Unpublished data	S **** C ** O ***
Hansen <i>et al.</i> 1999 [51]	USA	Inpatients	73	Delirium NSCI	ADL IADL Mobility	Pre-admission	Discharge 1 month	Y Published data only	S **** C O ***
Hartley <i>et al.</i> 2016 [37]	UK	Geriatric inpatients	663	<i>Dementia</i>	mRS	Pre-admission Admission	Discharge	Y Unpublished data	S **** C ** O **
Inouye <i>et al.</i> 1993 [52]	USA	Medical inpatients	330	NSCI	ADL	Pre-admission	Discharge	Y Published data	S **** C ** O ***
Kruse <i>et al.</i> 2013 [35]	USA	Medical inpatients	33820 <sup>a</sup>	NSCI	ADL	Pre-admission	Within 6 months of discharge	Y Unpublished data	S **** C O ***
McCusker <i>et al.</i> 2001 [53]	Canada	Medical inpatients	315	<i>Dementia</i> <i>Delirium</i>	BI IADL	Pre-admission Admission	2 months 6 months 12 months	Y Unpublished data	S *** C * O **
Mehta <i>et al.</i> 2011 [54]	USA	Medical inpatients	885 <sup>a</sup>	NSCI	ADL IADL	Pre-admission Admission	Discharge	Y Published data	S **** C ** O ***
Mercante <i>et al.</i> 2014 [28]	Italy	Hospital inpatients	1192	NSCI	BI Rankin	Admission	Discharge	N	S *** C O ***
Mudge <i>et al.</i> 2010 [55]	Australia	Medical inpatients	615	<i>Dementia</i>	ADL	Pre-admission Admission	Discharge	Y Published data only	S **** C ** O ***
Murray <i>et al.</i> 1993 [38]	USA	Medical and surgical inpatients	291	<i>Dementia</i> <i>Delirium</i>	ADL	Pre-admission	3 months 6 months	Y Published data	S *** C * O ***
Naruishi <i>et al.</i> 2014 [56]	Japan	Hospital inpatients	1079	<i>Dementia</i>	FIM	Admission	Discharge	Y Unpublished data	S *** C O ***

Continued

Table I. Continued

Author and year	Country	Participants	Numbers included in study	Cognitive impairment	Function	Time for baseline function	Time for follow-up function	Included in meta-analysis	Newcastle–Ottawa Scale
Noriega <i>et al.</i> 2015 [57]	Spain	Cardiology inpatients	203	<i>Delirium</i>	<i>ADL</i>	<i>Pre-admission</i>	<i>Discharge</i> 1 months 12 months	Y Published data	S *** C ** O ***
O’Keeffe <i>et al.</i> 1997 [58]	Ireland	Geriatric inpatients	225	<i>Delirium</i>	<i>ADL</i>	<i>Admission</i>	<i>Discharge</i>	Y Published data	S *** C ** O ***
Pedone <i>et al.</i> 2005 [59]	Italy	Geriatric and medical inpatients	9061	<i>NSCI</i>	<i>ADL</i>	<i>Admission</i>	<i>Discharge</i>	Y Published data	S **** C O ***
Sager, Franke <i>et al.</i> 1996 [25]	USA	Medical inpatients	1279	<i>NSCI</i>	<i>ADL</i> <i>IADL</i>	<i>Pre-admission</i>	<i>Discharge</i> 3 months	N	S *** C ** O ***
Sager, Rudberg <i>et al.</i> 1996 [26]	USA	Medical inpatients	827	<i>NSCI</i>	<i>ADL</i> <i>IADL</i>	<i>Pre-admission</i>	<i>Discharge</i> 3 months	N	S **** C ** O ***
Sanchez <i>et al.</i> 2011 [60]	Spain	Cardiology inpatients	211	<i>NSCI</i>	<i>ADL</i>	<i>Pre-admission</i>	<i>12 months</i>	Y Unpublished data	S **** C O ***
Sands <i>et al.</i> 2003 [61]	USA	Medical inpatients	2557	<i>NSCI</i>	<i>ADL</i> <i>IADL</i> Mobility	<i>Pre-admission</i>	<i>3 months</i>	Y Published	S *** C ** O ***
Sleiman <i>et al.</i> 2009 [27]	Italy	Geriatric inpatients	1119	<i>NSCI</i>	<i>BI</i>	<i>Pre-admission</i> <i>Admission</i>	<i>Discharge</i>	N	S **** C O ***
Socorro Garcia <i>et al.</i> 2015 [62]	Spain	Geriatric inpatients	1023	<i>NSCI</i>	<i>BI</i>	<i>Pre-admission</i> <i>Admission</i>	<i>Discharge</i>	Y Unpublished data	S *** C O ***
Velilla <i>et al.</i> 2012 [63]	Spain	Geriatric inpatients	85	<i>Delirium</i> <i>Subsyndromal delirium</i>	<i>BI</i>	<i>Admission</i>	<i>1 month</i>	Y Unpublished data	S *** C ** O ***
Volpato <i>et al.</i> 2007 [64]	Italy	Geriatric and medical inpatients	1686	<i>NSCI</i>	<i>ADL</i> <i>IADL</i>	<i>Pre-admission</i>	<i>Discharge</i>	Y Published data	S **** C ** O ***
von Renteln-Kruse <i>et al.</i> 2015 [65]	Germany	Geriatric inpatients	237	<i>NSCI</i>	<i>BI</i>	<i>Admission</i>	<i>Discharge</i>	Y Unpublished data	S *** C O***
Wanich <i>et al.</i> 1992 [22]	USA	Medical inpatients	235	<i>Dementia</i> <i>Delirium</i>	<i>ADL</i>	<i>Admission</i>	<i>Discharge</i>	N	S *** C ** O***
Wu <i>et al.</i> 2000 [21]	USA	Hospital inpatients	804	<i>NSCI</i>	<i>ADL</i>	<i>Pre-admission</i>	<i>2 months</i> <i>12 months</i>	N	S *** C O ***
Zekry <i>et al.</i> 2011 [66]	Switzerland	Geriatric inpatients	444	<i>Dementia</i> <i>NSCI</i>	<i>FIM</i> <i>IADL</i>	<i>Admission</i>	<i>Discharge</i>	Y Unpublished data	S *** C O **

Italic font in ‘Function’, ‘Time for baseline function’ and ‘Time for follow-up function’ columns denotes the variable used in meta-analyses. NOS, Newcastle–Ottawa Scale (S, selection; C, comparability; O, outcome); ADL, Measure of dependence with activities of daily living; IADL, measure of dependence with instrumental activities of daily living; Mobility, Measure of functional mobility capabilities and required assistance; FIM, functional independence measure; mRS, modified rankin scale; Rankin, Rankin Scale; NSCI, non-specific cognitive impairment; MCI, mild cognitive impairment.

<sup>a</sup>Not including those with a new stroke or fractured hip.

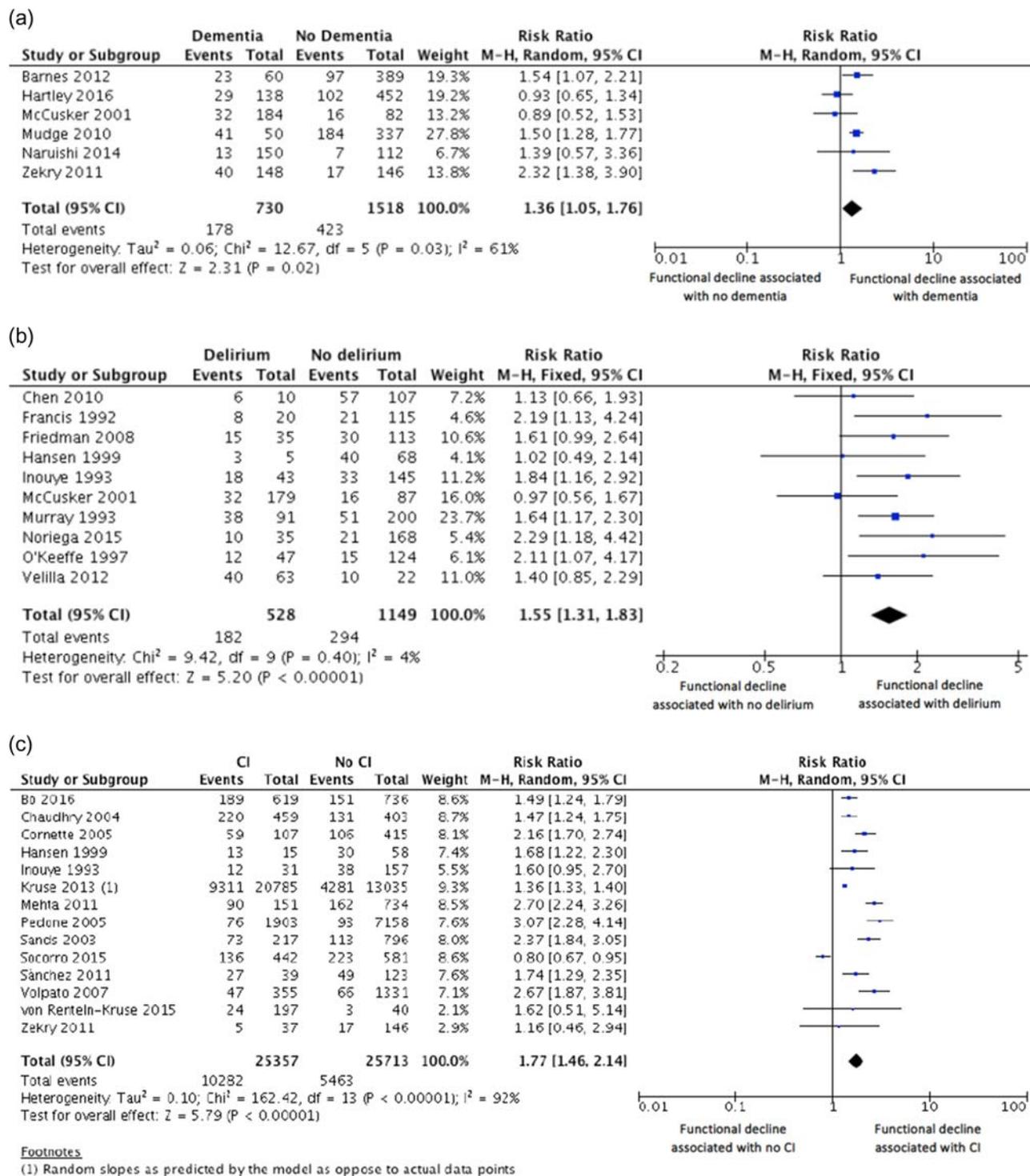
Recommendations Assessment, Development and Evaluation (GRADE) guidelines [20] was considered as ‘low’.

**Cognitive impairment versus no cognitive impairment (all studies)**

Results are presented in the [Supplementary data, Appendix 3a, available in Age and Ageing online](#). The meta-analysis of

the 26 studies suggested that cognitive impairment was associated with a statistically significant higher risk of hospitalisation-related functional decline: RR: 1.64; 95% CI: 1.45–1.86;  $P < 0.01$ ;  $n = 54,637$ .

[Supplementary data, Appendix 3b, available in Age and Ageing online](#) shows a subanalysis of the 11 studies that included at least 1 month of follow-up after discharge from hospital. Results were essentially



**Figure 2** Meta-analysis comparing the relative risk of functional decline between subgroups with and without cognitive impairments.

unchanged (RR: 1.69; 95% CI: 1.44–1.98;  $P < 0.01$ ;  $n = 37,808$ ).

**Dementia versus no dementia**

Results are presented in Figure 2a. The meta-analysis of the six studies included suggested a statistically significant higher risk of functional decline during hospitalisation

associated with a diagnosis of dementia: RR: 1.36; 95% CI: 1.05–1.76;  $P = 0.02$ ;  $n = 2,248$ .

In a study included in the qualitative synthesis, the presence of dementia was an independent predictor of poorer functional status at 2 months after hospitalisation, together with factors such as worse baseline functional status and quality of life, depth of coma (if any), lower serum albumin, depression, incontinence, being bedridden, medical record

documentation of need for nursing home and older age [21]. In contrast, a second study found dementia not to be a significant predictor of functional decline, but this was in the context of a nursing intervention targeted at factors that influence acute confusion or delirium [22].

### Delirium versus no delirium

Results are presented in Figure 2b. The meta-analysis of the 10 studies included showed a statistically significant increased risk of adverse functional outcome associated with a diagnosis of delirium: RR: 1.55; 95% CI: 1.31–1.83;  $P < 0.01$ ;  $n = 1,677$ .

A study in the qualitative synthesis also showed that delirious patients in hospital experienced functional decline, together with longer stays, more complications, higher mortality rate and cognitive decline [23]. However, another study suggested that delirium in acutely admitted patients is associated with functional decline only in those in whom the delirium does not resolve (i.e. 37% of those with prevalent delirium in this series) [24]. Finally, another study found delirium not to be a significant predictor of functional improvement [22].

### Non-specific cognitive impairment versus no cognitive impairment

Results are presented in Figure 2 c. The meta-analysis of the 14 studies included suggested that a non-specific cognitive impairment was associated with a statistically significant increased risk of adverse functional outcome: RR: 1.77; 95% CI: 1.46–2.14;  $P < 0.01$ ;  $n = 51,070$ .

The results of the meta-analysis were echoed in the qualitative synthesis. A study showed that patients at greatest risk of adverse functional outcomes at follow-up were older, had pre-admission instrumental activities of daily living (IADL) disabilities and lower mental status scores on admission, and had been re-hospitalised [25]. In another study, logistic regression analysis identified three patient characteristics that were independent predictors of functional decline: increasing age, lower admission MMSE scores and lower pre-admission IADL function [26]. In Sleiman *et al.* [27], results were suggestive of an association between higher MMSE score and functional recovery. Finally, one study found that a medium–high score of the Rankin Scale, a deficit in the items of the MMSE and a low Barthel Index (BI) score on admission were associated with an increased risk of loss of autonomy [28].

## Discussion

### Summary of key findings

Our results suggest that cognitive impairments in older patients admitted to the acute hospital may increase the risk of functional decline on discharge and after hospitalisation. Our findings contrast with previous reviews inpatients with

hip fractures [16] and patients after stroke [17], which suggested that there was little or no evidence that cognitive impairment is associated with functional recovery.

Our meta-analysis of observational studies cannot infer causality on the association between cognitive impairment and functional decline in hospitalised older patients. Mechanisms are likely to be multifactorial and may be explained in multiple non-competing ways. First, the severity of the acute illness that cognitively impaired patients present with may cause functional loss via direct inflammatory damage to the musculoskeletal system [29, 30], and it has also been suggested that central nervous system inflammation may induce muscle atrophy via activation of the hypothalamic-pituitary-adrenal axis [31]. Second, a pre-existing neurological impairment may reduce the ability to recover from an initial illness-related functional loss [32], and it has been suggested that the primary trigger of sarcopenia may be neurogenic in origin based on the intimate relationship between the nervous and muscular system [33]; third, cognitive impairment may be a marker of underlying frailty and general vulnerability [7]; lastly, it is also possible that some of the functional decline may be related to the hospital structure, organisational factors and the processes of care, including timely access to specialist care and therapies [34].

### Limitations of included studies

The exclusion of non-English articles in the search strategy is a potential selection bias. In addition, some of the studies included were purely retrospective in their design, while others excluded patients with severe cognitive impairment or dementia. However, the large study by Kruse *et al.* [35] focused on the functional outcomes of nursing home residents undergoing acute hospitalisation; this study showed that for many long-stay nursing home residents, substantial and sustained functional worsening was associated with acute hospitalisation. Therefore, we are reasonably confident that our systematic review did not exclude the most vulnerable sector of older adults.

Another limitation was the considerable heterogeneity across studies in the methods used to assess function and diagnose cognitive impairment (for the details of individual studies, see [Supplementary data, Appendix 2, available in Age and Ageing online](#)). For example, some studies [36–38] rely on a diagnosis of dementia based on the past medical history recorded in the case notes. There is evidence that only 35–50% of patients with dementia have a diagnosis on admission to hospital [4, 39], and key assessments with regard to cognitive functioning are often missing in hospitals [40]. As regards delirium, most studies did not differentiate between those who recovered and those who did not, in terms of their functional outcomes. However, a previous study showed that the risk of poor functional recovery can be as high as 70% in complex delirious patients in hospital [9, 41]. Not uncommonly, delirium is neither benign nor reversible, with a significant proportion of patients not experiencing restoration

*ad integrum* of cognition and function [42]. The subanalysis of cognitive impairment categories (e.g. dementia versus delirium) is unlikely to be a ‘clean’ one, because delirium is commonly superimposed on dementia in older inpatients [4], and this natural overlap may also be present in research studies.

A further limitation is that we investigated cognition as a dichotomous variable, so we cannot make any assumptions about the impact of severity of cognitive impairment on the risk of functional decline. The same applies to the functional outcome definition. In addition, likely confounders such as comorbidity, frailty, acute illness severity, availability of therapy and social care factors may also be substantial contributors to functional decline, and the meta-analysis could not control for these issues. A notable exception was the large study in nursing home residents by Kruse *et al.* [35], the data of which were extracted from an ‘activities of daily living (ADL) slope’ model that calculated a predicted value for patients, after adjusting by age, gender, Charlson comorbidity index, baseline cognition, baseline ADL, primary diagnosis and length of hospital stay. Otherwise, the data included in the meta-analysis was unadjusted.

In addition, we looked at cognition at a single time point (i.e. admission), in association with physical function change (i.e. at two time points) without necessarily taking account of prior (i.e. premorbid) ability. The heterogeneity in the observation time points for the collection of functional information is also a limitation, but the subanalysis of studies that included at least 1 month of follow-up after discharge did not significantly change the results (see [Supplementary data, Appendix 3b, available in \*Age and Ageing\* online](#)). Finally, exclusion of studies in intermediate care environments could mean that those that may have improved functionally by discharge (from therapy interventions) were excluded from the review.

### Limitations of the review

A major limitation of this meta-analysis is the potential confounding introduced through low quality observational studies. Causality cannot be inferred. In addition, the review is limited by the fact that we only included studies published in English language.

Prospective research is needed to clarify the causal role and relative contributions of biological, physiological and extrinsic factors towards hospital-associated loss of function in older adults; however, important questions also need to be answered as regards the role of in-hospital Comprehensive Geriatric Assessment (CGA) and interventions. There is evidence that frail patients undergoing CGA in the hospital are more likely to be alive and at home after hospital discharge [43]; and it has been suggested that gerontologically attuned hospital environments can minimise incident disability and maximise recovery of compromised activities along and after the acute event [28]. For example, in one study, a nursing intervention employed strategies to educate staff, mobilise patients, monitor medication and make environmental and sensory modifications; and subjects who received the

intervention were more likely to improve in functional status from admission to discharge than subjects who did not receive the intervention [22].

### Conclusion

This systematic review suggested that cognitive impairment is associated with functional decline in acutely hospitalised older people. However, the association seen in observational studies does not imply causation. While some of the factors driving this association may be biological and related to acute illness severity and impaired ability to recover from stressors, some may be amenable to intervention, including physical interventions [44]. A limitation is that the overall quality of evidence according to the GRADE guidelines was low. Research is needed to elucidate causal mechanisms, including the relative contributions of intrinsic versus extrinsic factors. For example, future prospective interventional studies of extra physical and/or cognitive stimulation in hospitalised patients with cognitive impairment may be able to elucidate if the functional decline can be minimised by interventions after accounting for confounders such as comorbidity, frailty, acute illness severity and social care factors.

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### Key points

- We reviewed the association between cognitive impairment and functional outcome in hospitalised older adults.
  - Twenty-six studies (54,637 participants) were suitable for the quantitative synthesis.
  - Cognitive impairment was associated with a higher risk of functional decline (risk ratio (RR): 1.64; 95% confidence interval (CI): 1.45–1.86;  $P < 0.01$ ).
  - Research is needed to elucidate the causal mechanisms independently of confounders.
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### Supplementary data

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

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### Conflicts of interest

None declared.

## Declaration of sources of funding

Our study did not require funding.

## References

Note: the very long list of references supporting this review has meant that only the first 30 are listed here. The full list of references is available on the journal website <http://www.ageing.oxfordjournals.org/> as Appendix 4.

1. DoH. National Service Framework: Older People. Available online: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/198033/National\\_Service\\_Framework\\_for\\_Older\\_People.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/198033/National_Service_Framework_for_Older_People.pdf) (31 July 2016, date last accessed). 2001.
2. Soong J, Poots AJ, Scott S *et al.* Quantifying the prevalence of frailty in English hospitals. *BMJ Open* 2015; 5: e008456.
3. Mukadam N, Sampson EL. A systematic review of the prevalence, associations and outcomes of dementia in older general hospital inpatients. *Int Psychogeriatr* 2011; 23: 344–55.
4. Timmons S, Manning E, Barrett A *et al.* Dementia in older people admitted to hospital: a regional multi-hospital observational study of prevalence, associations and case recognition. *Age Ageing* 2015; 44: 993–9.
5. Ryan DJ, O'Regan NA, Caoimh RO *et al.* Delirium in an adult acute hospital population: predictors, prevalence and detection. *BMJ Open* 2013; 3(1).
6. Whittamore KH, Goldberg SE, Gladman JR, Bradshaw LE, Jones RG, Harwood RH. The diagnosis, prevalence and outcome of delirium in a cohort of older people with mental health problems on general hospital wards. *Int J Geriatr Psychiatry* 2014; 29: 32–40.
7. Hartley P, Adamson J, Cunningham C, Embleton G, Romero-Ortuno R. Clinical frailty and functional trajectories in hospitalized older adults: a retrospective observational study. *Geriatr Gerontol Int* 2016 [Epub ahead of print].
8. Andrew MK, Freter SH, Rockwood K. Incomplete functional recovery after delirium in elderly people: a prospective cohort study. *BMC Geriatr* 2005; 5: 5.
9. Dasgupta M, Brymer C. Prognosis of delirium in hospitalized elderly: worse than we thought. *Int J Geriatr Psychiatry* 2014; 29: 497–505.
10. Mecocci P, von Strauss E, Cherubini A *et al.* Cognitive impairment is the major risk factor for development of geriatric syndromes during hospitalization: results from the GIFA study. *Dement Geriatr Cogn Disord* 2005; 20: 262–9.
11. Morrison RS, Siu AL. Survival in end-stage dementia following acute illness. *JAMA* 2000; 284: 47–52.
12. McCusker J, Kakuma R, Abrahamowicz M. Predictors of functional decline in hospitalized elderly patients: a systematic review. *J Gerontol A Biol Sci Med Sci* 2002; 57: M569–77.
13. Christensen H, Mackinnon AJ, Korten A, Jorm AF. The “common cause hypothesis” of cognitive aging: evidence for not only a common factor but also specific associations of age with vision and grip strength in a cross-sectional analysis. *Psychol Aging* 2001; 16: 588–99.
14. Demnitz N, Esser P, Dawes H *et al.* A systematic review and meta-analysis of cross-sectional studies examining the relationship between mobility and cognition in healthy older adults. *Gait Posture* 2016; 50: 164–74.
15. Hartley P, Romero-Ortuno R, Saunders A, *et al.* The Effect of Cognition on Functional Outcomes of Older Patients Admitted with Medical Illness: A Systematic Review and Meta-analysis. PROSPERO 2016:CRD42016035978. Available from [http://www.crd.york.ac.uk/PROSPERO/display\\_record.asp?ID=CRD42016035978](http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016035978). 2016.
16. Muir SW, Yohannes AM. The impact of cognitive impairment on rehabilitation outcomes in elderly patients admitted with a femoral neck fracture: a systematic review. *J Geriatr Phys Ther* 2009; 32: 24–32.
17. Veerbeek JM, Kwakkel G, van Wegen EE, Ket JC, Heymans MW. Early prediction of outcome of activities of daily living after stroke: a systematic review. *Stroke* 2011; 42: 1482–8.
18. Wells GA, Shea B, O'Connell D, *et al.* The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available from: [http://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp) (31 July 2016, date last accessed).
19. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol* 2009; 62: 1006–12.
20. Balshem H, Helfand M, Schunemann HJ *et al.* GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol* 2011; 64: 401–6.
21. Wu AW, Yasui Y, Alzola C *et al.* Predicting functional status outcomes in hospitalized patients aged 80 years and older. *J Am Geriatr Soc* 2000; 48(Suppl. 5):S6–15.
22. Wanich CK, Sullivan-Marx EM, Gottlieb GL, Johnson JC. Functional status outcomes of a nursing intervention in hospitalized elderly. *Image J Nurs Sch* 1992; 24: 201–7.
23. Feldman J, Yaretsky A, Kaizimov N, Alterman P, Vigder C. Delirium in an acute geriatric unit: clinical aspects. *Arch Gerontol Geriatr* 1999; 28: 37–44.
24. Adamis D, Treloar A, Gregson N, Macdonald AJ, Martin FC. Delirium and the functional recovery of older medical inpatients after acute illness: the significance of biological factors. *Arch Gerontol Geriatr* 2011; 52: 276–80.
25. Sager MA, Franke T, Inouye SK *et al.* Functional outcomes of acute medical illness and hospitalization in older persons. *Arch Intern Med* 1996; 156: 645–52.
26. Sager MA, Rudberg MA, Jalaluddin M *et al.* Hospital admission risk profile (HARP): identifying older patients at risk for functional decline following acute medical illness and hospitalization. *J Am Geriatr Soc* 1996; 44: 251–7.
27. Sleiman I, Rozzini R, Barbisoni P *et al.* Functional trajectories during hospitalization: a prognostic sign for elderly patients. *J Gerontol A Biol Sci Med Sci* 2009; 64: 659–63.
28. Mercante O, Gagliardi C, Spazzafumo L *et al.* Loss of autonomy of hospitalized elderly patients: does hospitalization increase disability? *Eur J Phys Rehabil Med* 2014; 50: 703–8.
29. Bartley JM, Pan SJ, Keilich SR *et al.* Aging augments the impact of influenza respiratory tract infection on mobility impairments, muscle-localized inflammation, and muscle atrophy. *Aging (Albany NY)* 2016; 8: 620–35.
30. Baylis D, Bartlett DB, Patel HP, Roberts HC. Understanding how we age: insights into inflammaging. *Longev Healthspan* 2013; 2: 8.

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