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**SYSTEMATIC REVIEW**

# 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 Chi$^2$ had $P \geq 0.10$. A random-effect Mantel–Haenszel meta-analysis was undertaken when $I^2$ was >50% and Chi2 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

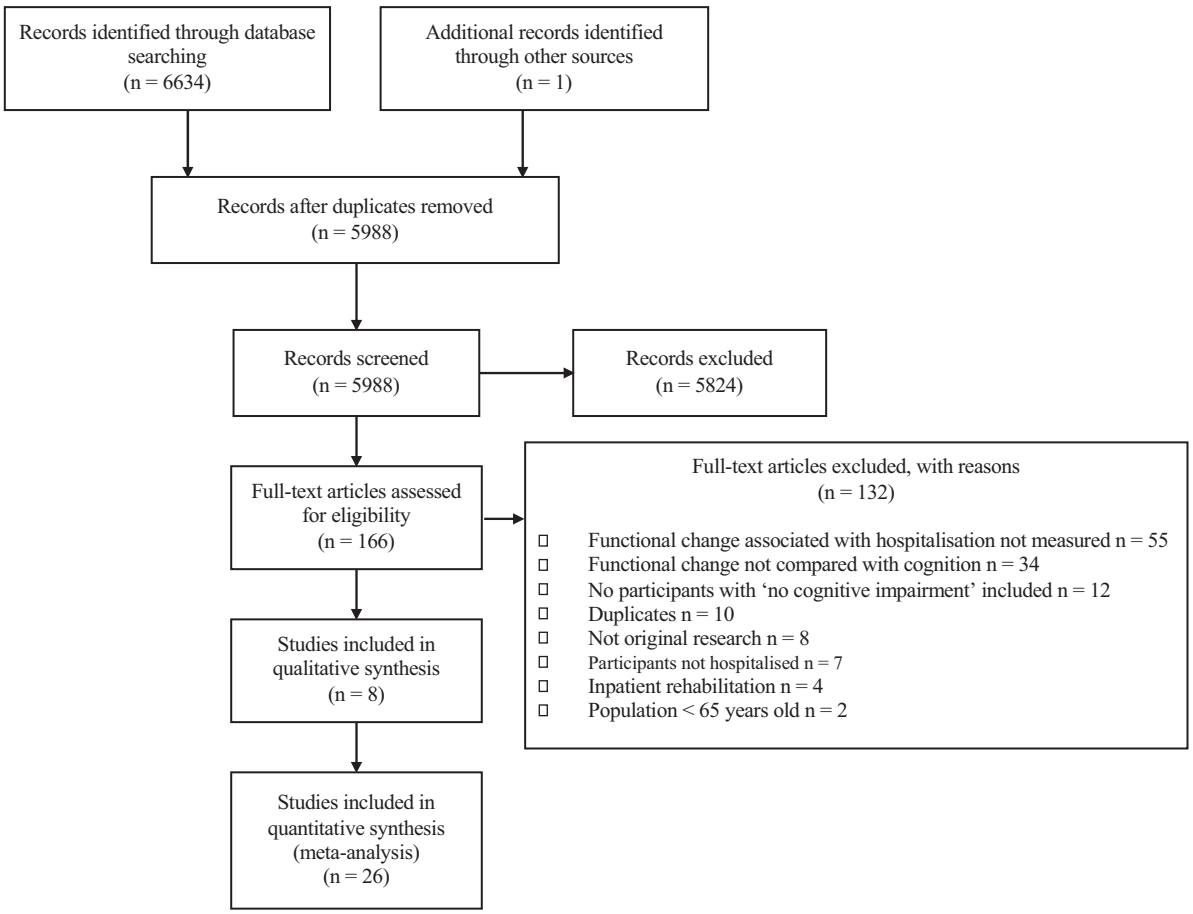


**Figure 1.** PRISMA flow diagram of selected studies.

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*et al.* 2016 [45] | Italy | Geriatric and medical inpatients | 1568 | *NSCI* | *ADL* | *Admission* | *Discharge* | Y Unpublished data | S *** C O *** |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| Friedman *et al.* 2008 [50] | USA | Geriatric inpatients | 212 | *Delirium* | *ADL* | *Admission* | *Discharge* | Y Unpublished data | S **** C ** O *** |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*et al.* 2016 [37] | UK | Geriatric inpatients | 663 | *Dementia* | *mRS* | *Pre-admission* Admission | *Discharge* | Y Unpublished data | S **** C ** O ** |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

*Continued*

Table 1. 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 *et al.* 2015 [57] | Spain | Cardiology inpatients | 203 | *Delirium* | *ADL* | *Pre-admission* | *Discharge*<br>1 months<br>12 months | Y Published data | S ***<br>C **<br>O *** |
| O'Keeffe *et al.* 1997 [58] | Ireland | Geriatric inpatients | 225 | *Delirium* | *ADL* | *Admission* | *Discharge* | Y Published data | S ***<br>C **<br>O *** |
| Pedone *et al.* 2005 [59] | Italy | Geriatric and medical inpatients | 9061 | *NSCI* | *ADL* | *Admission* | *Discharge* | Y Published data | S ****<br>C<br>O *** |
| Sager, Franke *et al.* 1996 [25] | USA | Medical inpatients | 1279 | NSCI | ADL<br>IADL | Pre-admission | Discharge<br>3 months | N | S ***<br>C **<br>O *** |
| Sager, Rudberg *et al.* 1996 [26] | USA | Medical inpatients | 827 | NSCI | ADL<br>IADL | Pre-admission | Discharge<br>3 months | N | S ****<br>C **<br>O *** |
| Sanchez *et al.* 2011 [60] | Spain | Cardiology inpatients | 211 | NSCI | ADL | *Pre-admission* | *12 months* | Y Unpublished data | S ****<br>C<br>O *** |
| Sands *et al.* 2003 [61] | USA | Medical inpatients | 2557 | *NSCI* | *ADL*<br>IADL<br>Mobility | *Pre-admission* | *3 months* | Y Published | S ***<br>C **<br>O *** |
| Sleiman *et al.* 2009 [27] | Italy | Geriatric inpatients | 1119 | NSCI | BI | Pre-admission<br>Admission | Discharge | N | S ****<br>C<br>O *** |
| Socorro Garcia *et al.* 2015 [62] | Spain | Geriatric inpatients | 1023 | *NSCI* | *BI* | *Pre-admission*<br>Admission | *Discharge* | Y Unpublished data | S ***<br>C<br>O *** |
| Velilla *et al.* 2012 [63] | Spain | Geriatric inpatients | 85 | *Delirium*<br>*Subsyndromal delirium* | *BI* | *Admission* | *1 month* | Y Unpublished data | S ***<br>C **<br>O *** |
| Volpato *et al.* 2007 [64] | Italy | Geriatric and medical inpatients | 1686 | *NSCI* | *ADL*<br>IADL | *Pre-admission* | *Discharge* | Y Published data | S ****<br>C **<br>O *** |
| von Renteln-Kruse *et al.* 2015 [65] | Germany | Geriatric inpatients | 237 | *NSCI* | *BI* | *Admission* | *Discharge* | Y Unpublished data | S ***<br>C<br>O*** |
| Wanich *et al.* 1992 [22] | USA | Medical inpatients | 235 | Dementia<br>Delirium | ADL | Admission | Discharge | N | S ***<br>C **<br>O*** |
| Wu *et al.* 2000 [21] | USA | Hospital inpatients | 804 | NSCI | ADL | Pre-admission | 2 months<br>12 months | N | S ***<br>C<br>O *** |
| Zekry *et al.* 2011 [66] | Switzerland | Geriatric inpatients | 444 | *Dementia*<br>*NSCI* | *FIM*<br>IADL | *Admission* | *Discharge* | Y Unpublished data | S ***<br>C<br>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.
[a]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

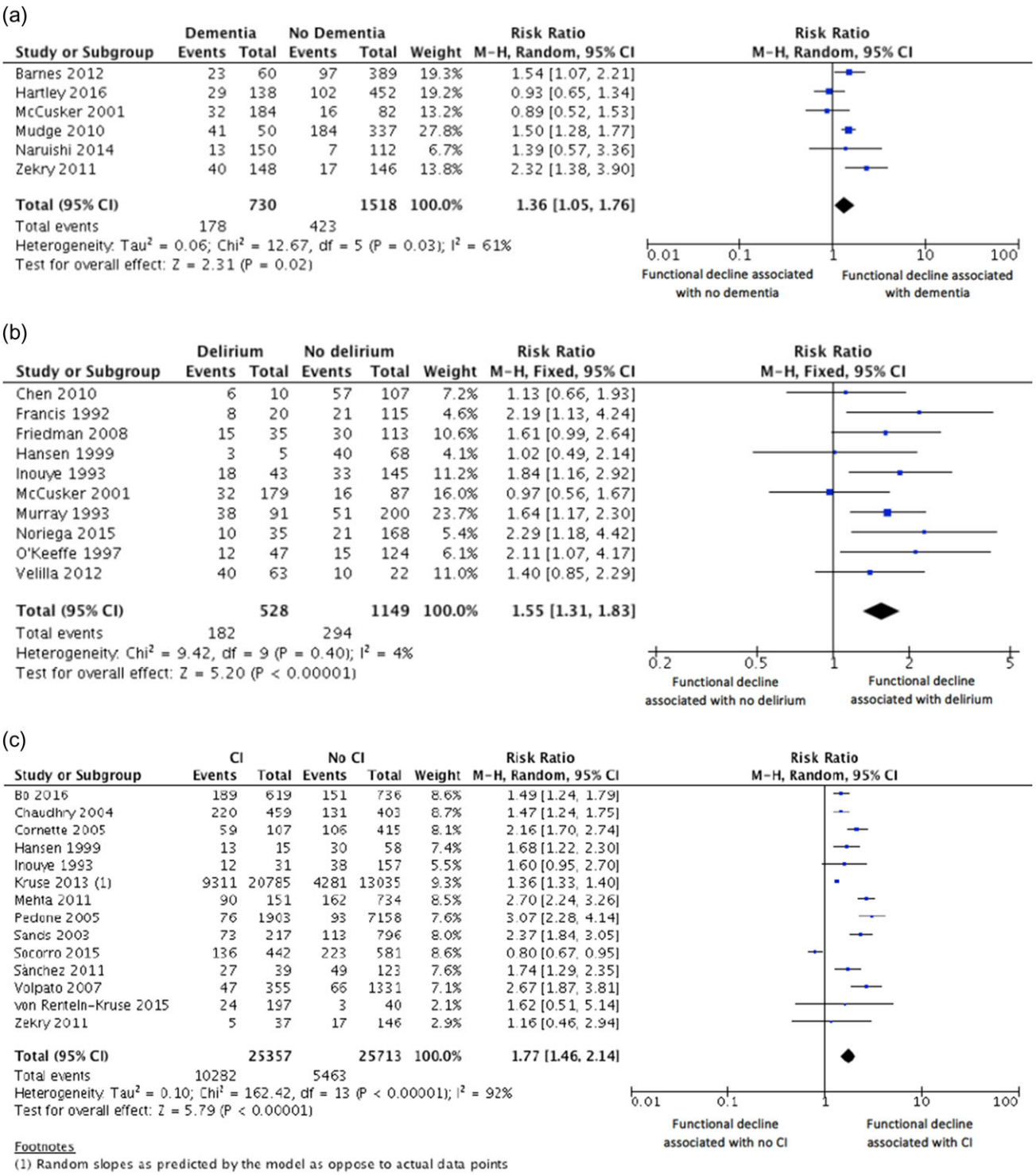


**Figure 2** Meta-analysis comparing the relative risk of functional decline between subgroups with and without cognitive impairments.

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.

## 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.

## 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.

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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.

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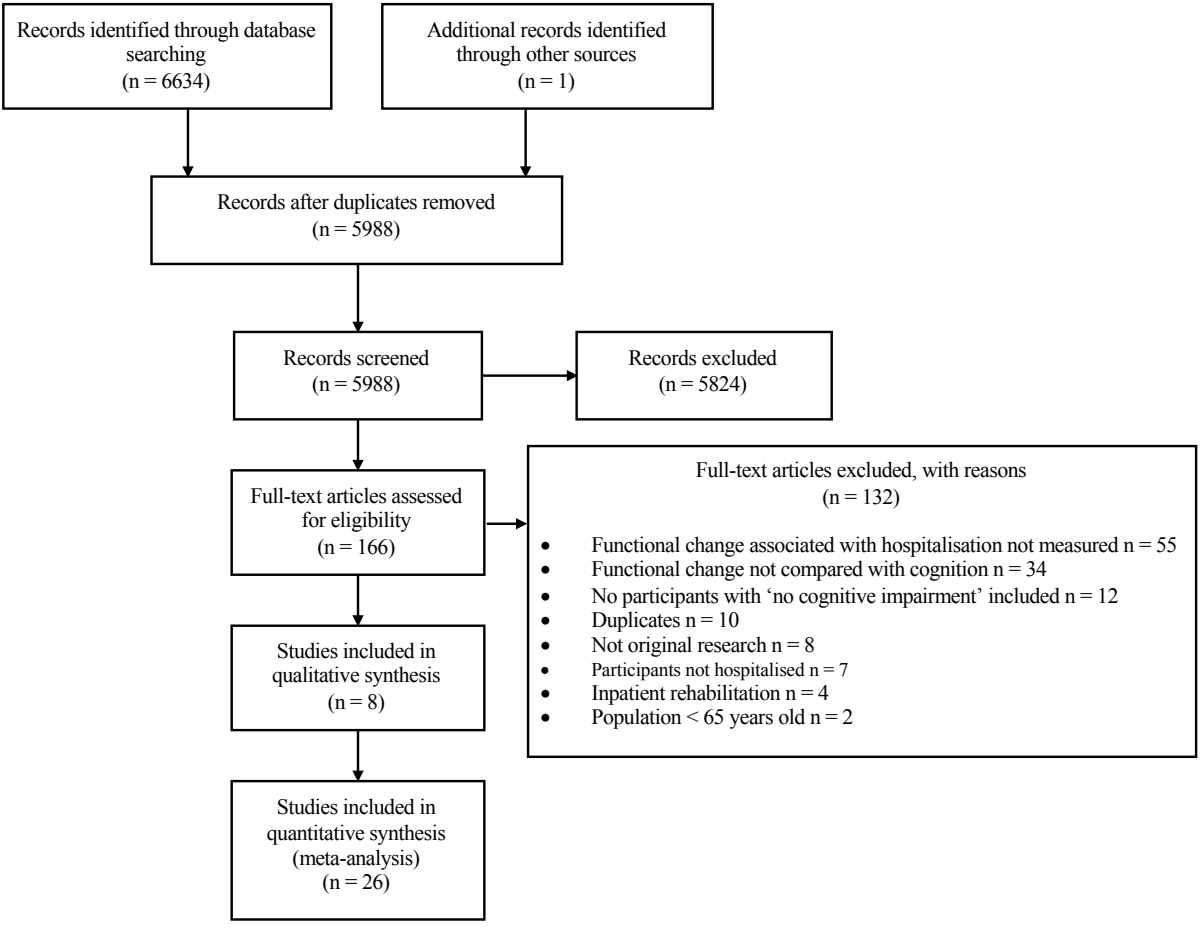
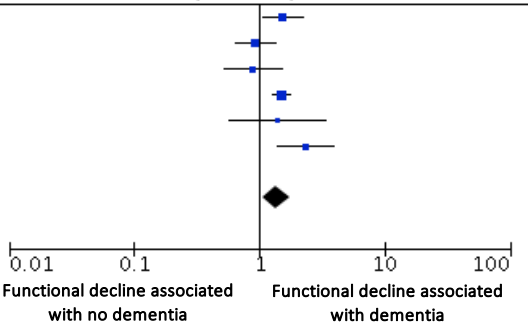

Records identified through database searching (n = 6634)
Additional records identified through other sources (n = 1)
Records after duplicates removed (n = 5988)
Records screened (n = 5988)
Records excluded (n = 5824)
Full-text articles assessed for eligibility (n = 166)
Full-text articles excluded, with reasons (n = 132)
Functional change associated with hospitalisation not measured n = 55
Functional change not compared with cognition n = 34
No participants with 'no cognitive impairment' included n = 12
Duplicates n = 10
Not original research n = 8
Participants not hospitalised n = 7
Inpatient rehabilitation n = 4
Population < 65 years old n = 2
Studies included in qualitative synthesis (n = 8)
Studies included in quantitative synthesis (meta-analysis) (n = 26)

# Figure 2a

| Study or Subgroup | Dementia Events | Dementia Total | No Dementia Events | No Dementia Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Barnes 2012 | 23 | 60 | 97 | 389 | 19.3% | 1.54 [1.07, 2.21] |
| Hartley 2016 | 29 | 138 | 102 | 452 | 19.2% | 0.93 [0.65, 1.34] |
| McCusker 2001 | 32 | 184 | 16 | 82 | 13.2% | 0.89 [0.52, 1.53] |
| Mudge 2010 | 41 | 50 | 184 | 337 | 27.8% | 1.50 [1.28, 1.77] |
| Naruishi 2014 | 13 | 150 | 7 | 112 | 6.7% | 1.39 [0.57, 3.36] |
| Zekry 2011 | 40 | 148 | 17 | 146 | 13.8% | 2.32 [1.38, 3.90] |
| **Total (95% CI)** | | **730** | | **1518** | **100.0%** | **1.36 [1.05, 1.76]** |
| Total events | 178 | | 423 | | | |

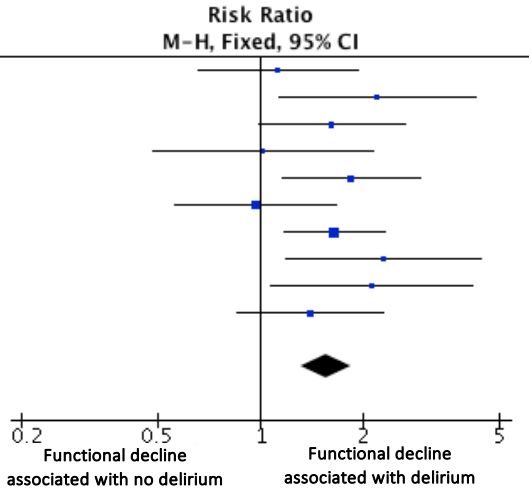
Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 12.67$, df = 5 (P = 0.03); $I^2 = 61\%$
Test for overall effect: Z = 2.31 (P = 0.02)




# Figure 2b

| Study or Subgroup | Delirium Events | Delirium Total | No delirium Events | No delirium Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Chen 2010 | 6 | 10 | 57 | 107 | 7.2% | 1.13 [0.66, 1.93] |
| Francis 1992 | 8 | 20 | 21 | 115 | 4.6% | 2.19 [1.13, 4.24] |
| Friedman 2008 | 15 | 35 | 30 | 113 | 10.6% | 1.61 [0.99, 2.64] |
| Hansen 1999 | 3 | 5 | 40 | 68 | 4.1% | 1.02 [0.49, 2.14] |
| Inouye 1993 | 18 | 43 | 33 | 145 | 11.2% | 1.84 [1.16, 2.92] |
| McCusker 2001 | 32 | 179 | 16 | 87 | 16.0% | 0.97 [0.56, 1.67] |
| Murray 1993 | 38 | 91 | 51 | 200 | 23.7% | 1.64 [1.17, 2.30] |
| Noriega 2015 | 10 | 35 | 21 | 168 | 5.4% | 2.29 [1.18, 4.42] |
| O'Keeffe 1997 | 12 | 47 | 15 | 124 | 6.1% | 2.11 [1.07, 4.17] |
| Velilla 2012 | 40 | 63 | 10 | 22 | 11.0% | 1.40 [0.85, 2.29] |
| **Total (95% CI)** | | **528** | | **1149** | **100.0%** | **1.55 [1.31, 1.83]** |
| Total events | 182 | | 294 | | | |

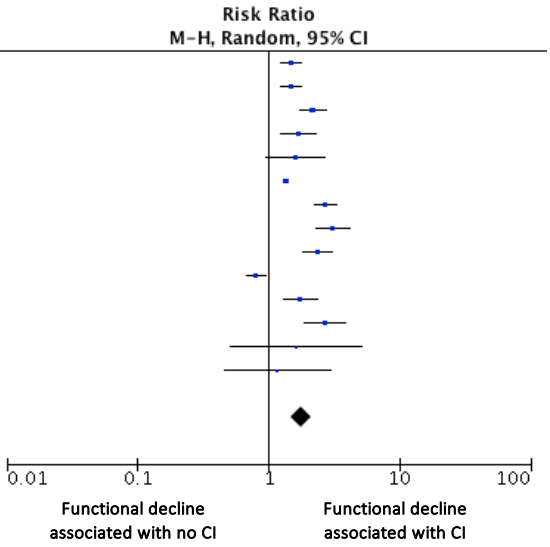
Heterogeneity: $Chi^2 = 9.42$, df = 9 (P = 0.40); $I^2 = 4\%$
Test for overall effect: Z = 5.20 (P < 0.00001)




# Figure 2c

| Study or Subgroup | CI Events | CI Total | No CI Events | No CI Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Bo 2016 | 189 | 619 | 151 | 736 | 8.6% | 1.49 [1.24, 1.79] |
| Chaudhry 2004 | 220 | 459 | 131 | 403 | 8.7% | 1.47 [1.24, 1.75] |
| Cornette 2005 | 59 | 107 | 106 | 415 | 8.1% | 2.16 [1.70, 2.74] |
| Hansen 1999 | 13 | 15 | 30 | 58 | 7.4% | 1.68 [1.22, 2.30] |
| Inouye 1993 | 12 | 31 | 38 | 157 | 5.5% | 1.60 [0.95, 2.70] |
| Kruse 2013 (1) | 9311 | 20785 | 4281 | 13035 | 9.3% | 1.36 [1.33, 1.40] |
| Mehta 2011 | 90 | 151 | 162 | 734 | 8.5% | 2.70 [2.24, 3.26] |
| Pedone 2005 | 76 | 1903 | 93 | 7158 | 7.6% | 3.07 [2.28, 4.14] |
| Sands 2003 | 73 | 217 | 113 | 796 | 8.0% | 2.37 [1.84, 3.05] |
| Socorro 2015 | 136 | 442 | 223 | 581 | 8.6% | 0.80 [0.67, 0.95] |
| Sánchez 2011 | 27 | 39 | 49 | 123 | 7.6% | 1.74 [1.29, 2.35] |
| Volpato 2007 | 47 | 355 | 66 | 1331 | 7.1% | 2.67 [1.87, 3.81] |
| von Renteln-Kruse 2015 | 24 | 197 | 3 | 40 | 2.1% | 1.62 [0.51, 5.14] |
| Zekry 2011 | 5 | 37 | 17 | 146 | 2.9% | 1.16 [0.46, 2.94] |
| **Total (95% CI)** | | **25357** | | **25713** | **100.0%** | **1.77 [1.46, 2.14]** |
| Total events | 10282 | | 5463 | | | |

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 162.42$, df = 13 (P < 0.00001); $I^2 = 92\%$
Test for overall effect: Z = 5.79 (P < 0.00001)




Footnotes
(1) Random slopes as predicted by the model as oppose to actual data points

**Appendix 1. Medline search strategy.**

1. (Dement* or deliri* or confus* or cogniti* or Alzheimer* or "mental status")
2. (MH "Memory Disorders+")
3. (MH "Delirium, Dementia, Amnestic, Cognitive Disorders+")
4. #1 or #2 or #3
5. "older person*" or "older adult*" or "older people*" or Frail* or elderly or geriatric*
6. (MH "Frail Elderly") OR (MH "Aged+")
7. #5 or #6
8. AB (MRMI "rivermead index" or EMS or "elderly mobility scale" or BI or "Barthel Index" or mRS or Rankin or FIM or "functional independence measure" or FAC "functional ambulatory category" or IADL or ADL or "activit* of daily living" or Katz) ) OR TI ( function* or mobil* or or dependen* or independen* or Disab* or ADL or IADL or activit*))) )
9. (MH "Rehabilitation+") or (MH "Recovery of Function") or (MH "Mobility Limitation") or (MH "Independent Living") or (MH "Activities of Daily Living")
10. #8 or #9
11. TI (hospital* or inpatient* or in-patient* or acute or subacute or sub-acute or "secondary care")
12. (MH "Secondary Care") or (MH "Hospitalization+") or (MH "Inpatients")
13. #11 or #12
14. #4 and #7 and #10 and #13
15. Limit to English language

**Appendix 2. Further data of included studies.**

| Author and year | Study design | Setting | Inclusion criteria | Exclusion criteria | Sampling | Definition of deterioration in function | Definition of cognitive impairment | Patient characteristics |
|---|---|---|---|---|---|---|---|---|
| Adamis *et al.* 2011 [24] | Prospective Cohort Study | Elderly Medical Unit | Age 70 or older; admitted to the elderly medical Unit within 3 days of admission | Thought to be terminally ill; included in the study on an earlier admission | Not specified | Deterioration definition not specifically defined, study reported on change in BI from admission to discharge | Delirium diagnosed per CAM criteria<br><br>NSCI diagnosed with MMSE, cut-off not specified | Mean age: 84.6<br><br>Percentage with cognitive impairment: 26%<br><br>Mean length of hospital stay: 19 days |
| Barnes *et al.* 2013 [36] | Retrospective Cohort Study | General Medical Service of University Hospitals | Age 70 or older; admitted to general medical service of 1 of 2 hospitals; fully independent in ADLs 2 weeks before admission and dependent in 1 or more ADLs at discharge | Elective admissions; admissions to Intensive Care Unit or subspecialty units; and those with a length of stay less than 2 days | A subset from 2 randomised control trials | Patients categorised into those who had recovered independence in ADLs, or remained dependent in 1 or more ADLs in the year following hospitalisation | NSCI defined as more than 5 errors on the SPMSQ | Mean age: not reported (age 70–79: n=198, age 80–89: n=191, age ≥90: n=60)<br><br>Percentage with cognitive impairment: 13%<br><br>Average length of hospital stay: not reported |
| Bo *et al.* 2016 [45] | Prospective Cohort Study | 8 acute Geriatric and Medical Wards of 2 University Hospitals | Age 65 years or older; admitted from the Emergency Department | Patients from Intensive Care Units, other hospitals, or other departments, and those who died or were discharged within 24 hours of admission | Consecutive admissions | A lower ADL score (1 or more) (increase in dependence) at discharge compared to admission, excluding those completely dependent on admission | Mild NSCI defined as 3-4 errors on the SPMSQ<br><br>Moderate to severe NSCI defined as more than 5 errors on the | Mean age: 81.3<br><br>Percentage with cognitive impairment: 46%<br><br>Median length of hospital stay: 11 days |

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|---|---|---|---|---|---|---|---|---|
| | | | | | | | SPMSQ | |
| Chaudhry *et al.* 2004 [46] | Prospective Cohort Study | General Medical Service of Teaching Hospital | Age 70 or older; willing and able to participate in interviews; had 1 of the following risk factors for delirium: visual impairment, severe illness, cognitive impairment, high blood urea nitrogen to creatinine ratio | Length of stay less than 48 hours, terminal illness, died during hospital admission or missing data on level of education or functional status at 6 months | Consecutive admissions | A lower ADL score (1 or more) (increase in dependence) at follow up than at pre-admission baseline | MMSE categorised into: 5-9, 10-15, 15-19, 20-24, more than or equal to 25.<br><br>For meta-analysis NSCI defined as MMSE less than 25 | Mean age: not reported (age: 70-79 n=37, age: 80-89 n=43, age: 90-99 n=52)<br><br>Percentage with cognitive impairment: 53%<br><br>Average length of hospital stay: not reported |
| Chen *et al.* 2010 [47] | Prospective Cohort Study | Geriatric Unit of a General Hospital | Age over 65; admitted to Geriatric Unit due to geriatric syndromes, or development of ADL dependence within 2 weeks before admission because of acute illness, as well as those referred from other wards for rehabilitation after stabilisation of an acute illness | Completely physically dependent before admission; had cancer with metastasis, had a known severe dementia before admission; with expected survival of less than 6 months; experiencing rapid recovery of physical dependence | Not specified | Functional recovery determined by improvement in the BI after discharge intervention of more than 10% | NSCI defined as MMSE less than 24 for literate and less than 14 for illiterate patients | Mean age: 80<br><br>Percentage with cognitive impairment: 9%<br><br>Mean length of hospital stay: 16 days |
| Cornette *et al.* 2006 [48] | Prospective Cohort Study | 2 General Academic Hospitals | Age 70 or older; admitted via the Emergency Department | Length of stay less than 48 hours; terminal illness; admission to the Intensive Care Unit; admission for a stroke; dependence in all ADLs | Not specified | Loss of at least 1 point on the ADL scale (increase in dependence) between premorbid evaluation on admission and 3-month post-discharge evaluation | NSCI defined as shortened version of MMSE less than15 (max score of 21) | Mean age: 80<br><br>Percentage with cognitive impairment: 21%<br><br>Average length of hospital stay: |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | not reported |
| Feldman *et al.* 1999 [23] | Prospective Cohort Study | Acute Geriatric Unit of a University Hospital | Age 70 or older; first admission to Geriatric Unit during study period | Not admitted to the Geriatric Unit on the day of admission to the hospital; admitted electively for investigations or rehabilitation; aphasia or deafness; expected to remain in the hospital for less than 48 hours; moribund conditions; not assessed by a study doctor within 48 hours of admission | Consecutive admissions | Increase in ADL score (increase in dependence) between admission and discharge | Delirium diagnosed per CAM and DRS criteria | Mean age: 81<br><br>Percentage with cognitive impairment: 18%<br><br>Mean length of hospital stay: 9 |
| Francis *et al.* 1992 [49] | Prospective Cohort Study | General Medical Service from University Hospital | Age 70 or older; living in the community and admitted to General Medical Service | Transferred from other hospitals, or Nursing Homes; terminal illness; severe dementia requiring continual assistance in ADLs; admitted for less than 48 hours; aphasia, deafness, blindness; inability to speak English | Consecutive admissions | Institutionalised or needing assistance with ADLs at follow-up (2 years), having been independent with all ADLs at pre-admission baseline | Delirium diagnosed per DSM-III-R criteria | Mean age: 78<br><br>Percentage with cognitive impairment: 22%<br><br>Mean length of hospital stay: not stated |
| Friedman *et al.* 2008 [50] | Prospective Cohort Study | Acute Elderly Care Unit in a Community Hospital | Admitted to Elderly Care Unit | n/a | Consecutive admissions | Increase in ADL score (increase in dependence) between admission and discharge (excluding those with full dependency on admission) | Delirium diagnosed per CAM criteria | Mean age: 79<br><br>Percentage with cognitive impairment: 19%<br><br>Mean length of hospital stay: 5 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Hansen *et al.* 1999 [51] | Prospective Cohort Study | Hospital | Age 65 or older, admitted for a medical (non-surgical, non-psychiatric illness) | Enrolment in hospice; diagnosis of metastatic cancer; new CVA or MI within the last 2 months; diagnosis of dementia if no caregiver in the home; more than 4 days between hospital discharge and home health enrolment; non-ambulatory status; miscellaneous, including "inability to speak English, anticipated move from the community in the next week, etc." | Not specified | Sub-group analysis of patients who were completely independent in ADLs at pre-admission baseline but dependent in 1 or more ADL by discharge. Patients were categorised as having regained independence or remaining dependent at 1 month after discharge. | Delirium diagnosed per CAM criteria<br><br>NSCI defined as MMSE score of less than 24 | Mean age: 80<br><br>Percentage with cognitive impairment: 21%<br><br>Mean length of hospital stay: 8 days |
| Hartley *et al.* 2016 [37] | Retrospective Cohort Study | Geriatric Wards of University Hospital | First admission episodes to the Geriatric Wards from within county borders | Patients who died during admission | Consecutive admissions | Increase in modified Rankin Scale (increase in dependence) of at least 1 point from pre-admission baseline to discharge (excluding those with full dependence on admission) | Dementia based on medical chart review | Mean age: 86<br><br>Percentage with cognitive impairment: 45%<br><br>Mean length of hospital stay: 15 days |
| Inouye *et al.* 1993 [52] | 2 Prospective Cohort Studies (development cohort and validation cohort) running in tandem | General Medical Wards of a University Hospital | Age 70 or older, admitted to General Medical Wards | Unable to be interviewed (e.g. intubation, coma, severe aphasia); terminal condition; discharged within 48 hours; completely dependent in all ADLs at baseline; had been enrolled in the study on a previous | Pragmatic convenience sampling (i.e. 234 patients not evaluated for logistical reasons such as weekend enrolments and unavailability of research staff) | A change from being independent to requiring partial or total assistance with an ADL, or a change from requiring partial assistance to total assistance by discharge | NSCI defined as MMSE score less than 20<br><br>Delirium diagnosed per CAM criteria | Mean age: 78<br><br>Percentage with cognitive impairment: 30%<br><br>Median length of hospital stay: 7 days |

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|---|---|---|---|---|---|---|---|---|
| | | | | admission | | | | |
| Kruse *et al.* 2013 [35] | Longitudinal Cohort Study | Hospitals and Nursing Homes | Age 67 or older; Nursing Home resident with an episode of acute hospitalisation of 30 or fewer days, and having at least 2 preceding assessments with ADL data, 1 of which was within the 30 days preceding hospitalization | Various reasons based on lacking data; residents with date discrepancies (e.g., multiple dates of death); and residents with more than 15 acute hospitalisations in 2006 and 2007; residents who died in hospital; residents who did not reside in 1 facility for all included assessments | All patients within a national database | Worsening ADL function defined as gain of 3 or more points (increase in dependence) in the 6 months post discharge | NSCI defined as a CPS score of 3-6 | Mean age: not stated (52% were age 85 years or older)<br><br>Percentage with cognitive impairment: 62%<br><br>Mean length of hospital stay: not stated |
| McCusker *et al.* 2001 [53] | Prospective Cohort Study | Medical Services of University Hospital | Age 65 or older, admitted from the Emergency Department. | A primary diagnosis of stroke; admitted to an Oncology Unit, Intensive Care Unit, Cardiac Monitoring Unit (unless they were transferred to a Medical Ward within 48 hours of admission); those who didn't speak English or French | Not specified | 1 point loss in BI (increase in dependence) from admission to discharge | Delirium diagnosed per CAM criteria<br><br>Dementia using the IQCODE with a cut-off of 3.5 for diagnosing dementia. | Mean age: not reported<br><br>Percentage with cognitive impairment: 87%<br><br>Mean length of hospital stay: not stated |
| Mehta *et al.* 2011 [54] | Secondary data analyses of 2 Prospective Studies | Medical Services of 2 Teaching Hospitals | 70 or older who had emergency admissions to the General Medical Services; independent with ADLs 2 weeks before admission | Admission to an Intensive Care Unit or Oncology Ward; elective admission or length of stay less than 2 days | Consecutive sampling | New-onset disability, defined as a new need for personal assistance in 1 or more ADLs at discharge in participants who were independent 2 weeks before hospital admission | NSCI defined as more than 5 errors on the SPMSQ | Mean age: 78<br><br>Percentage with cognitive impairment: 17%<br><br>Mean length of hospital stay: not stated |
| Mercante *et al.* 2014 [28] | Prospective Cohort Study | Hospital | Age 65 or older | Admitted for less than 24 hours; admitted to day hospital or to day surgery | Not specified | Decrease of at least 5 counts (increase in dependence) between modified | NSCI diagnosed using 4 items derived from | Mean age: 82<br><br>Percentage with |

| | | | | | | | | |
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| | | | | | | BI at discharge compared to admission | MMSE | cognitive impairment: 12.7%<br><br>Mean length of hospital stay: 10 |
| Mudge *et al.* 2010 [55] | Secondary data analysis of a Prospective Control Study | Internal Medicine Service of a Teaching Hospital | Age over 65 | Died in hospital; fully dependent in ADLs at pre-admission baseline; length of stay less than 2 days | Consecutive admissions | Increase in ADL score of 1 or more point (increase in dependence) between pre-admission baseline and admission which failed to return to (or lower than) pre-admission baseline level by discharge | Dementia based on medical chart review | Mean age: 80<br><br>Percentage with cognitive impairment: 10%<br><br>Median length of hospital stay: 7 days |
| Murray *et al.* 1993 [38] | Prospective Cohort Study | Medical and Surgical Units of Teaching Hospital | Age over 65, from 2 populations: a geographically defined community or from a Nursing Home | Direct admissions from an Intensive Care Unit or Psychiatric Unit; severe language or hearing problems; actively contagious tuberculosis; lacked an available proxy; delirium upon admission evaluation | Consecutive admissions | Increase in ADL score of 1 point or more (increase in dependence) from pre-admission baseline to 3 months post discharge | Delirium diagnosed as per DSM-III criteria<br><br>Dementia based on medical chart review | Mean age: 81<br><br>Percentage with cognitive impairment: 31<br><br>Average length of hospital stay: not stated |
| Naruishi *et al.* 2014 [56] | Retrospective Cohort Study | Hospital | Age over 70 | Not specified | Not specified | Decrease in FIM of 1 or more points (increase in dependence) from admission to discharge | NSCI diagnosed as per CDR criteria | Mean age: 83<br><br>Percentage with cognitive impairment: 57%<br><br>Mean length of hospital stay: 33 |
| Noriega *et al.* 2015 [57] | Prospective Cohort Study | Cardiology Department of a University | Age 75 or older; direct urgent admission to the Cardiology | Scheduled hospitalisations; terminal status in the first 24 hours after | Consecutive admissions | Loss of at least 1 point in the ADL scale (increase in dependence) at | Delirium diagnosed per CAM criteria | Mean age: 82<br><br>Percentage with cognitive |

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|---|---|---|---|---|---|---|---|---|
| | | Hospital | Department | admission; delirium at admission making patients unable to participate in the study | | discharge compared to pre-admission baseline | | impairment: 17%<br><br>Mean length of hospital stay: 7 |
| O'Keeffe *et al.* 1997 [58] | Prospective Cohort Study | Acute Geriatric Unit of Hospital | First admission to acute Geriatric Unit during study period | Not admitted to the Geriatric Unit on the day of admission; admitted electively for investigations, rehabilitation, or respite care; severe aphasia or deafness; expected to remain in hospital less than 48 hours; not assessed by a study doctor within 48 hours of admission | Consecutive admissions | Loss of at least 1 point in the ADL scale (increase in dependence) at discharge compared to admission. | Delirium diagnosed per DAS and DSM-III criteria | Mean age: 82<br><br>Percentage with cognitive impairment: 42%<br><br>Mean length of hospital stay: 15 |
| Pedone *et al.* 2005 [59] | Prospective Cohort Study | Geriatric and Internal Medicine Wards of 83 centres | Age over 65 | Death during hospitalisation; admission ADL score equal to 0 (full dependence); missing functional data; length of stay more than 90 days; "mental retardation" | Consecutive admissions | Loss of at least 1 point in the ADL scale (increase in dependence) at discharge compared to admission | NSCI defined as a score of less than 6 on the HAMT | Mean age: 77<br><br>Percentage with cognitive impairment: 21%<br><br>Mean length of hospital stay: 15 |
| Sager, Franke *et al.* 1996 [25] | Prospective Cohort Study | 3 University Hospitals, 2 Private Acute Care Hospitals | Age 70 or older; hospitalised for acute medical illness | Terminal illness; severe cognitive impairment with inability to give informed consent; admission to an Intensive Care Unit; living in Nursing Home before admission; admitted for surgical diagnoses; died in hospital | Not specified other than a "subgroup of patients" | Loss of at least 1 point in the ADL scale (increase in dependence) at 3 months post discharge compared to pre-admission baseline | NSCI measured with shortened MMSE (range 0-21), cut off point not used | Mean age: 79<br><br>Percentage with cognitive impairment: not reported<br><br>Mean length of hospital stay: 9 days |
| Sager, | 2 Prospective | 4 University | Age 70 or older; | Terminal illness; | Not specified | Loss of at least 1 | NSCI | Mean age: 79 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Rudberg *et al.* 1996 [26] | Cohort studies (development cohort and validation cohort) | hospitals and 2 Private Acute Care Hospitals | hospitalised for acute medical illness | severe cognitive impairment with inability to give informed consent; admission to an Intensive Care Unit; living in Nursing Home before admission; died in hospital or died 3 months post discharge | other than patients enrolled in 2 clinical trials of the "Hospital Outcomes Project for the Elderly" | point in the ADL scale (increase in dependence) at discharge and at 3 months post discharge compared to pre-admission baseline | measured with shortened MMSE (range 0-21), cut of point of less than 15 | Percentage with cognitive impairment: not reported<br><br>Mean length of hospital stay: 8 days |
| Sanchez *et al.* 2011 [60] | Prospective Cohort Study | Cardiology Department of University Hospital | Age 75 or older; admitted with acute cardiac condition; direct admission to cardiology department | Terminal status in the first 24 hours after admission; elective admission | Consecutive admissions | Loss of 1 point in the ADL scale (increase in dependence) at 12 months post discharge compared to pre-admission baseline | NSCI defined with Spanish version of MMSE (range 0-35), cut off point of less than 22 | Mean age: 82<br><br>Percentage with cognitive impairment: 24%<br><br>Mean length of hospital stay: 7 days |
| Sands *et al.* 2003 [61] | Secondary data analysis of 2 Control Studies | 2 Teaching Hospitals | Age 70 or older; enrolled in 2 trials of an intervention to improve functional outcomes after hospitalisation | Patients with a length of stay shorter than 2 days; postoperative; admitted to subspecialty Medical Teams or Intensive Care Units | Taken from both control and intervention arm of 2 previous control trials | Loss of 1 point or more in the ADL scale (increase in dependence) from admission compared to discharge, in those that were completely independent in ADLs at pre-admission baseline | Mild NSCI: 3-4 errors on the SPMSQ<br><br>Moderate to severe NSCI defined as more than 5 errors on the SPMSQ | Mean age: 80<br><br>Percentage with cognitive impairment: 42%<br><br>Average length of hospital stay: not reported |
| Sleiman *et al.* 2009 [27] | Retrospective Cohort Study | Acute Geriatric Ward of Hospital | Patients admitted to an Acute Geriatric Ward | No change in function during hospitalisation; premorbid BI less than or equal to 10; diagnosed with a stroke; died in hospital | Consecutive sampling | Functional trajectory was assessed by evaluating functional decline at admission (difference between ADLs 15 days before and at admission) and | NSCI defined as MMSE of less than 18 | Mean age: 81<br><br>Percentage with cognitive impairment: 27%<br><br>Mean length of hospital stay: 7 days |

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|---|---|---|---|---|---|---|---|---|
| | | | | | | ability or inability to regain function (difference between ADLs at admission and at discharge) | | |
| Socorro Garcia *et al.* 2015 [62] | Prospective Cohort Study | Acute Geriatric Unit of Hospital | Age 90 and over | Not specified | Not specified | Loss of 1 or more points in BI (increased dependence) at discharge compared to 2 weeks before admission | NSCI defined as CRM more than or equal to 2 | Mean age: 94<br><br>Percentage with cognitive impairment: 50%<br><br>Mean length of hospital stay: 11 days |
| Velilla *et al.* 2012 [63] | Prospective Cohort Study | Acute Geriatric Wards of 3 Hospitals | Age over 74; emergency admission to Acute Geriatric Wards | Impossibility to obtain informed consent within 2 working days; admission for palliative care; comatose; life expectancy less than 3 months; impossibility to get a family member or caregiver able to give truthful information and those suspected of alcohol withdrawal delirium | Consecutive sampling during a 48-hour observation period | Definition of decline in function not specified, but reported on change in BI at 30 days after discharge compared to admission | Delirium diagnosed as per CAM and DSM-III criteria | Mean age: 87<br><br>Percentage with cognitive impairment: 75%<br><br>Mean length of hospital stay: not reported |
| Volpato *et al.* 2007 [64] | Longitudinal Observational Study | Geriatric and Internal Medicine Units of 81 centres | Age 65 or older; independent in ADLs 2 weeks before hospital admission | Missing functional data; died during hospital stay | Consecutive sampling | New ADL dependence by time of discharge from hospital | NSCI defined as AMT of more than 4 errors | Mean age: 77<br><br>Percentage with cognitive impairment: 21%<br><br>Mean length of hospital stay: 11 days |
| von | Prospective | Department | Hospitalised and | Not specified | Consecutive | Loss of 1 or more | NSCI defined | Mean age: 82 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Renteln-Kruse *et al.* 2015 [65] | Cohort Study | of Geriatric Medicine of Teaching Hospital | admitted to Geriatric Ward; first admission during study period | | sampling | points in BI (increased dependence) at discharge compared to admission | as MMSE of less than 24 | Percentage with cognitive impairment: 83%<br><br>Mean length of hospital stay: 18 days |
| Wanich *et al.* 1992 [22] | Prospective Control study | Medical Units of Teaching Hospital | Age 70 or older; first admission during study period | Transferred from another Unit within the Hospital; admitted for a short stay procedure such as chemotherapy, transfusion, a diagnostic study or dialysis; admitted for terminal care; private physicians requested exclusion | Consecutive admissions between Sunday noon and Friday noon | Increase of 2 or more points in ADL score (increased dependence) from admission to discharge | Dementia method of diagnosis or identification not specified<br><br>Delirium diagnosed as per DSM-III criteria | Mean age: 77<br><br>Percentage with cognitive impairment: 21%<br><br>Mean length of hospital stay: 9 days |
| Wu *et al.* 2000 [21] | Prospective Cohort Study | 4 Teaching Hospitals | Age 80 or older; an acute illness | Non-English language speakers; foreign national admitted specifically for a medical procedure; diagnosis of AIDS; sustained multiple trauma; admitted for hospice care; admitted to the psychiatric service; admitted for elective surgery; transferred from another hospital; died during the admission; discharged within 48 hours; scheduled to be discharged within 72 hours | "Hospitals with an abundance of available patients employed random enrolment at a suitable ratio in order to equalise enrolment at each of the study hospitals." | Poor functional status at 2 and 12 months (as measured by ADL scale) post discharge examined by logistic regression analysis after controlling for pre-admission baseline function (as measured by ADL scale) | Dementia method of diagnosis or identification not specified | Median age: 85<br><br>Percentage with cognitive impairment: 23%<br><br>Average length of hospital stay: not reported |
| Zekry *et al.* 2011 | Prospective Cohort Study | Geriatric Hospital | Age over 75 | Disorders interfering with psychometric | Randomised sample of all | Decrease of 1 or more points | Mild NSCI diagnosed by | Mean age: 85 |

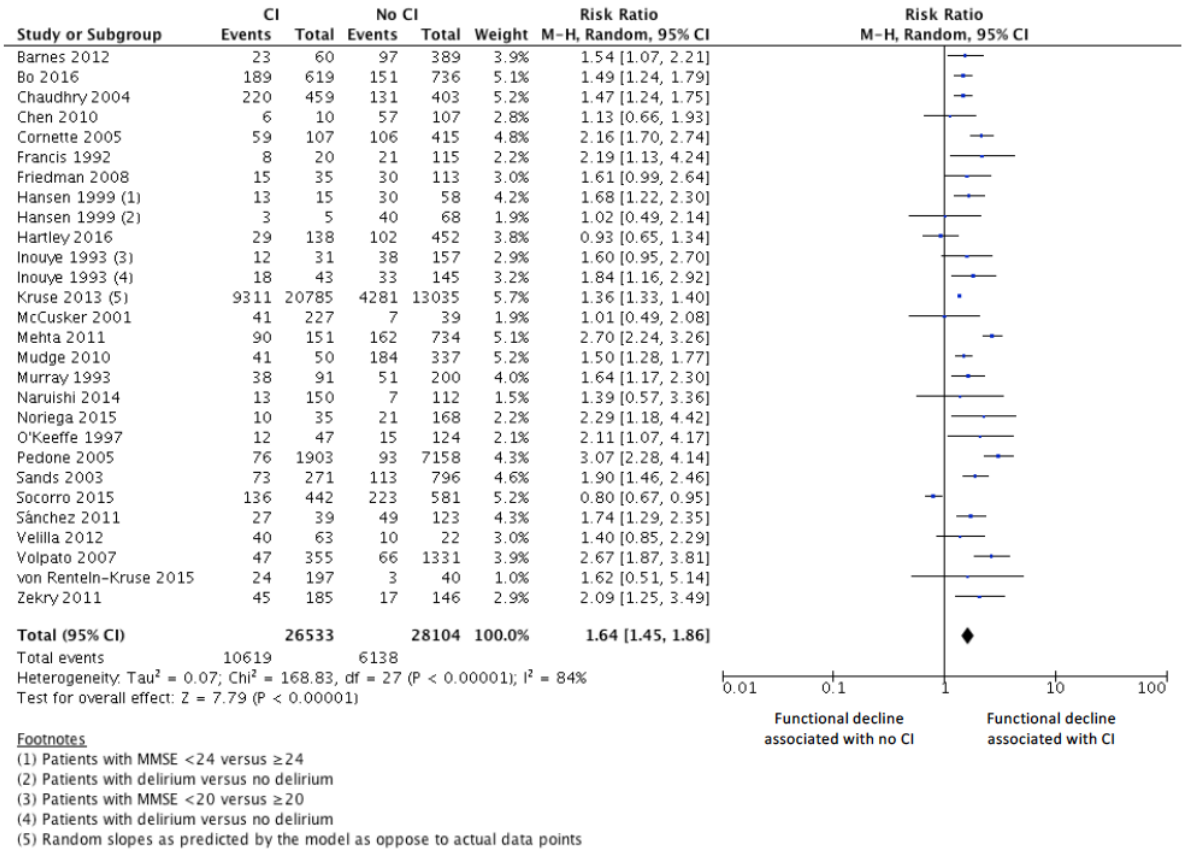
| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| [66] | | | | assessment (severe deafness or blindness, or major behavioural problems); terminal illness | admissions | (increase dependence) on FIM between admission and discharge | CDR score of 0.5, dementia diagnosed by CDR score of 1 or more | Percentage with cognitive impairment: 54%<br><br>Mean length of hospital stay: 7 days |

Abbreviations:
ADL: Activities of daily living
NSCI: Non-specific cognitive impairment

Abbreviations of Functional Assessment Tools:
ADL: Activities of Daily Living – (Various tools used, all similar to the Katz ADL scale)
BI: Barthel Index
mRS: modified Rankin Scale
FIM: Functional Independence Measure

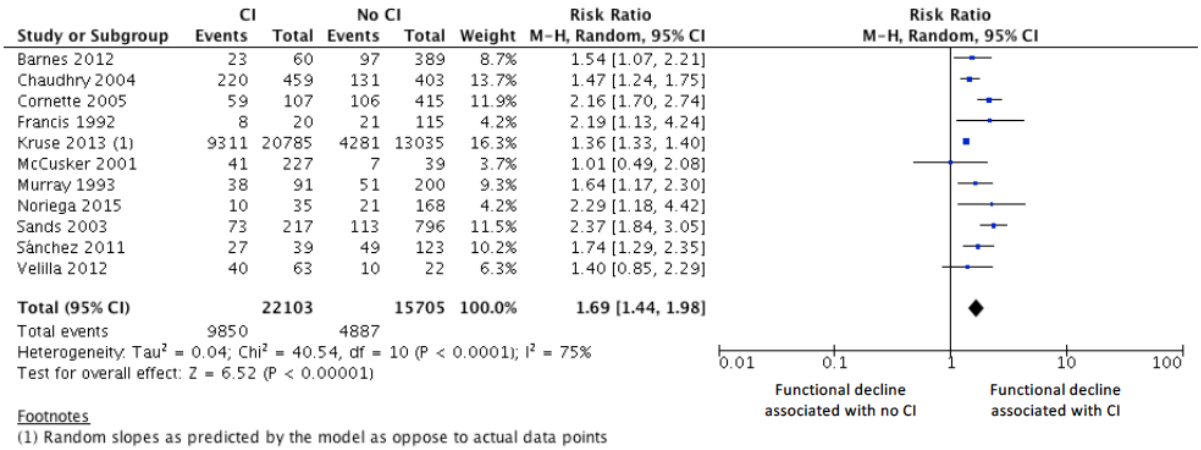
Abbreviations of Cognitive Screening Tools:
AMT: Abbreviated Mental Test
CAM: Confusion Assessment Method
CDR: Clinical Dementia Rating scale
CPS: Cognitive Performance Scale
CRM: Mental Scale of the Red Cross
DRS: Delirium Rating Scale
DSM-III/DSM-III-R/DSM-IV: Diagnostic and Statistical Manual of Mental Disorders
IQCODE: Informant Questionnaire on Cognitive Decline in the Elderly
HAMT: Hodkinson Abbreviated Mental Test
MMSE: Mini mental state examination
SCEB: Short Cognitive Evaluation Battery
SPMSQ: Short portable Mental Status Questionnaire

**Appendix 3a. Meta-analysis comparing the relative risk of functional decline between groups with and without cognitive impairment (all studies).**




Footnotes
(1) Patients with MMSE <24 versus ≥24
(2) Patients with delirium versus no delirium
(3) Patients with MMSE <20 versus ≥20
(4) Patients with delirium versus no delirium
(5) Random slopes as predicted by the model as oppose to actual data points

## Appendix 3b. Subanalysis of the studies that included at least 1 month follow up.



| Study or Subgroup | CI Events | CI Total | No CI Events | No CI Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Barnes 2012 | 23 | 60 | 97 | 389 | 8.7% | 1.54 [1.07, 2.21] |
| Chaudhry 2004 | 220 | 459 | 131 | 403 | 13.7% | 1.47 [1.24, 1.75] |
| Cornette 2005 | 59 | 107 | 106 | 415 | 11.9% | 2.16 [1.70, 2.74] |
| Francis 1992 | 8 | 20 | 21 | 115 | 4.2% | 2.19 [1.13, 4.24] |
| Kruse 2013 (1) | 9311 | 20785 | 4281 | 13035 | 16.3% | 1.36 [1.33, 1.40] |
| McCusker 2001 | 41 | 227 | 7 | 39 | 3.7% | 1.01 [0.49, 2.08] |
| Murray 1993 | 38 | 91 | 51 | 200 | 9.3% | 1.64 [1.17, 2.30] |
| Noriega 2015 | 10 | 35 | 21 | 168 | 4.2% | 2.29 [1.18, 4.42] |
| Sands 2003 | 73 | 217 | 113 | 796 | 11.5% | 2.37 [1.84, 3.05] |
| Sánchez 2011 | 27 | 39 | 49 | 123 | 10.2% | 1.74 [1.29, 2.35] |
| Velilla 2012 | 40 | 63 | 10 | 22 | 6.3% | 1.40 [0.85, 2.29] |
| **Total (95% CI)** | | **22103** | | **15705** | **100.0%** | **1.69 [1.44, 1.98]** |
| Total events | 9850 | | 4887 | | | |

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 40.54$, df = 10 ($P < 0.0001$); $I^2 = 75\%$

Test for overall effect: $Z = 6.52$ ($P < 0.00001$)



Footnotes

(1) Random slopes as predicted by the model as oppose to actual data points

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