SYSTEMATIC REVIEW

Systematic review and meta-analysis of the effect of cognitive impairment on the risk of admission to long-term care after stroke [version 1; peer review: 1 approved with reservations]

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V1 First published: 26 May 2020, 3:28
https://doi.org/10.12688/hrbopenres.13055.1
Latest published: 26 May 2020, 3:28
https://doi.org/10.12688/hrbopenres.13055.1

Abstract

Introduction: Admission to long-term care (LTC) post-stroke can be a significant source of costs. Studies evaluating the effect of cognitive impairment (CI) and dementia on risk of LTC admission post-stroke have not been systematically reviewed. The aim of this paper was to conduct a systematic review and meta-analysis of studies of the association between post-stroke CI/dementia and admission to LTC.

Patients and methods: PubMed, PsycInfo and Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases were searched for peer-review articles in English published January 2000-June 2018. Included studies were population-based or hospital-based studies assessing the relationship between CI or dementia, and admission to LTC post-stroke. Abstracts were screened, followed by full-text review of potentially relevant articles. Relevant data was extracted using a standard form and the Crowe Critical Appraisal Tool was used for quality appraisal. Results were pooled using random-effects meta-analysis and heterogeneity was assessed using the I² statistic.

Results: 18 articles were included in the review and 12 in a meta-analysis. 14/18 studies adjusted for covariates including functional impairment. Increased odds of admission to LTC was associated with post-stroke CI [Odds Ratio (CI 95%): 2.36 (1.18, 4.71), I²=77%] and post-stroke dementia [Odds Ratio (CI 95%): 2.58 (1.38 to 4.82), I²=60%].

Discussion and conclusion: Post-stroke CI and dementia increase odds of admission to LTC post-stroke, independent of functional
impairment. This indicates the potential for interventions that reduce post-stroke CI and dementia to also reduce risk of admission to LTC post-stroke, and ultimately costs.

**Keywords**
stroke, cognitive impairment, dementia, long-term care, systematic review.

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Competing interests: No competing interests were disclosed.

Grant information: Health Research Board Ireland [ICE-2015-1048] JS is supported by the Irish Aid Fellowship Training Programme. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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How to cite this article: Shumba J, McLoughlin A, Browne L et al. Systematic review and meta-analysis of the effect of cognitive impairment on the risk of admission to long-term care after stroke [version 1; peer review: 1 approved with reservations] HRB Open Research 2020, 3:28 https://doi.org/10.12688/hrbopenres.13055.1

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Introduction
Stroke is a leading cause of death and disability\(^1\). Annually, 15 million people suffer from stroke globally; 5 million die due to stroke and 5 million have permanent disability, associated with an increased care and support burden for families, communities and nations\(^2\). Admission to long-term care (LTC) can be a significant source of stroke-related costs. In Europe in 2017, an estimated 43 million days were spent in long-term residential care as a result of stroke, costing €4.7 billion (8% of total stroke costs)\(^3\). Understanding predictors of admission to LTC post-stroke, and estimating the magnitude of the association, is critical for health and social care planning, and for identifying potential targets for interventions to reduce the need for LTC.

Several studies have examined the clinical and social factors predicting post-stroke discharge destination but have not reached consensus on the key factors\(^4-7\). Systematic reviews have been conducted to synthesise the evidence of factors\(^8-9\), however, meta-analysis of results has been limited. No systematic review has specifically examined post-stroke cognitive impairment (PSCI) and discharge destination; rather PSCI has been examined as one of several predictors. It is estimated that 15 to 20% of patients have dementia within one-year post-stroke\(^10\), with almost 40% presenting with a level of cognitive impairment (CI) that does not meet dementia criteria (cognitive impairment no dementia, CIND))\(^11\).

Meta-analysis of predictors of admission to LTC can be challenging due to heterogeneity across studies\(^8\). The association between CI and admission to LTC may vary depending on the definition and measurement of CI\(^3\), and setting-specific factors, such as cost and availability of long-term care. The role of informal care, which is likely to affect LTC utilisation, may also vary across countries, depending on cultural factors and societal values\(^12\).

The primary objective of this study was to examine the association between PSCI (including dementia) and risk of admission to LTC. We hypothesised that PSCI increases risk of admission to LTC and conducted a systematic review and meta-analysis to test this hypothesis.

Method
This study used the Preferred Reporting Items for Systematic Reviews and Meta-analysis Statement (PRISMA) guidelines\(^13\).

Search strategy
Three databases were searched (PubMed, PsycInfo and CINAHL). Title, abstract and Pubmed Medical Subject Headings (MeSH) (mapped to similar topic terms in the other databases) terms for stroke, cognitive impairment, dementia, LTC, and discharge outcome were used in developing the search strategy. The Pubmed search strategy is provided as extended data (Table S1\(^14\)). Searches were limited to English peer-reviewed journals between January 2000 and June 2018 to obtain the most current research and a feasible number of articles. Search results were exported to EndNote X8 and duplicates were removed. Abstracts were screened by a team of reviewers (AMc, LB, AS), with each abstract screened independently by two reviewers, followed by full text review of potentially relevant articles (JS & ES). Any disagreements were discussed until consensus was reached.

Inclusion and exclusion criteria
Studies that used a longitudinal, cross-sectional and observational design were included. Studies with ischaemic stroke patients only or mixed stroke (ischaemic and haemorrhagic, or without transient ischaemic attack (TIA)) patients were included. Studies with haemorrhagic stroke patients or TIA patients only were excluded. Studies that assessed any definition of PSCI, including as a continuous or categorical variable, or as mild CI or dementia, were included. Studies that assessed pre-stroke cognition only were excluded. Eligible studies could be hospital-based or population-based and were included if they reported the discharge destination at any time post-stroke.

LTC was defined as a discharge setting outside home where a patient receives professional support from qualified staff for a long period of time. Terminology used for settings varies, and can include terms such as nursing home, residential care and skilled nursing facility. Destinations excluded from this broad definition were home living, home care, inpatient rehabilitation, acute care, transitional care, and delayed discharge. If discharge to LTC was examined in combination with other discharge outcomes (e.g., formal home care), the study was included but these were examined separately in stratified analysis.

Studies published in English in peer-reviewed journals were included. Qualitative studies, commentary or review articles, case reports and conference abstracts were excluded.

Data extraction
Data were extracted by JS using a standard form (Table S2 in extended data\(^14\)) and checked by ES. Data items included: study population; setting; definition of PSCI; proportion with PSCI; discharge destination; effect sizes (e.g., odds ratio) and measures of uncertainty (e.g., confidence interval) for the association between PSCI and discharge destination and covariates adjustment.

Quality assessment
The Crowe Critical Appraisal Tool (CCAT) was used for quality assessment\(^15\). Individual studies were scored on a scale of 0 to 5 on eight dimensions; introduction, design, sampling, ethical matters, results, discussion and preliminaries (abstract and title). Quality Assessment was done by (JS) and checked by (ES). With a maximum possible score of 40, three categories of study quality were created; high quality (CCAT score >30, a mean score >3.8/5 across dimensions), medium quality (CCAT score 25–30, or a mean score of 3–3.8/5 across dimensions) and low quality (CCAT score <25, or a mean score <3/5 across sections).

Analysis
The analysis included a narrative synthesis and a quantitative meta-analysis. For the narrative synthesis, study results were tabulated summarising the population, definition of PSCI, discharge destination, covariate adjustment and results.
Where feasible, study estimates were pooled in a random-effects meta-analysis. To facilitate the quantitative pooling of studies, results from studies were converted to Odds Ratios (OR) and 95% Confidence Intervals (CI), where possible, consistent with Cochrane guidelines. To convert the mean scores to ORs, two effect size conversion calculators were used. Mean cognitive functioning scores for discharge destinations in individual studies were first converted to Cohen’s d and its confidence intervals. ORs and their confidence intervals were subsequently calculated from Cohen’s d.

The meta-analysis was divided into two parts: i) analysis of association between PSCI and LTC, and ii) association between post-stroke dementia and LTC. Within the PSCI analysis, studies that defined PSCI as a continuous variable, and as a categorical variable, were pooled separately. The following sensitivity analyses were planned where feasible: how studies measured CI, study quality categories, definition of LTC and whether studies reported adjusted estimates. Heterogeneity was assessed using the I² statistic and interpreted using the Cochrane Review guidelines. Data management and analysis were done using the Cochrane Review Manager 5 (RevMan 5) software.

For studies that had more than one measure of PSCI, estimates of the measure best representing the primary focus of this study was selected for the meta-analysis, decided based on consensus discussions (JS and ES). If adjusted and unadjusted estimates were reported, the adjusted estimate was included in any analysis. If LTC was compared with more than one discharge destination (e.g., home, rehabilitation), the estimate using home as the reference group was included in the meta-analysis, as this was more similar to other studies in the review.

Results

Included articles
A total of 1,219 unique records were identified and the full texts of 59 articles were reviewed (see Figure 1). The full texts of 30 articles were further examined in detail and 18 articles were selected for qualitative synthesis. Of these, 12 provided sufficient information for inclusion in meta-analysis.

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**Figure 1.** Flow chart of included studies in systematic review and meta-analysis.

<table>
<thead>
<tr>
<th>Abstracts screened = 1219</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excluded = 1160</td>
</tr>
<tr>
<td>• Includes patients with cognitive impairment, dementia or Alzheimer’s only = 192</td>
</tr>
<tr>
<td>• Haemorrhagic stroke patients only = 12</td>
</tr>
<tr>
<td>• Non-stroke population = 357</td>
</tr>
<tr>
<td>• Not relevant = 436</td>
</tr>
<tr>
<td>• Nursing home setting = 133</td>
</tr>
<tr>
<td>• Pre-stroke cognition = 5</td>
</tr>
<tr>
<td>• Systematic review = 8</td>
</tr>
<tr>
<td>• Traumatic/acquired brain injury population = 16</td>
</tr>
<tr>
<td>• Not peer reviewed = 1</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>59 full texts screened</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excluded = 29</td>
</tr>
<tr>
<td>• Cognition not measured = 4</td>
</tr>
<tr>
<td>• Dementia/CI only patients = 4</td>
</tr>
<tr>
<td>• Discharge destination not examined = 6</td>
</tr>
<tr>
<td>• Non-stroke population = 10</td>
</tr>
<tr>
<td>• Not relevant = 3</td>
</tr>
<tr>
<td>• Pre-stroke cognition = 1</td>
</tr>
<tr>
<td>• Not peer review article = 1</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>30 full text examined in detail</th>
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<tbody>
<tr>
<td>Excluded = 12</td>
</tr>
<tr>
<td>• Relationship between cognition and nursing home admission not examined = 9</td>
</tr>
<tr>
<td>• Only memory is examined = 1</td>
</tr>
<tr>
<td>• Discharge to nursing home is not an outcome = 2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>18 articles included in qualitative synthesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excluded = 6</td>
</tr>
<tr>
<td>• 1 article had insufficient descriptive information and no multivariate analysis information</td>
</tr>
<tr>
<td>• 3 study results on cognitive impairment and institutionalization could not be statistically converted to facilitate quantitative pooling</td>
</tr>
<tr>
<td>• 2 articles categorized patients into groups and analysis was conducted for groups and not the whole sample</td>
</tr>
</tbody>
</table>

| 12 articles included in meta-analysis |

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Table 1 displays the characteristics and results of the 18 included studies, with more detail provided in Table S2 (extended data\(^\text{\textsuperscript{14}}\)). Study settings were mixed, with rehabilitation centres (k=7) and stroke units (k=7) the most common recruitment settings, and two community-based studies. In total, 15 studies examined overall PSCI, while three examined dementia and

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>Setting</th>
<th>N</th>
<th>Quality</th>
<th>Definition of PSCI</th>
<th>Comparison</th>
<th>Adjusted for</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PSCI as a categorical variable</strong></td>
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<tr>
<td><strong>Included in meta-analysis</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Nguyen 2015(^\text{31})</td>
<td>USA</td>
<td>Rehabilitation</td>
<td>2085</td>
<td>M</td>
<td>“Cognitive deficits” – not clearly defined</td>
<td>Home v Skilled Nursing Facility</td>
<td>Sociodemographics, motor function, other</td>
<td>Significant association</td>
</tr>
<tr>
<td>Pettersen 2002(^\text{34})</td>
<td>Norway</td>
<td>Rehabilitation</td>
<td>103</td>
<td>M</td>
<td>Cognitive problems assessed using standardised tests developed by authors</td>
<td>Home v Nursing Home</td>
<td>None</td>
<td>Significant association</td>
</tr>
<tr>
<td>Rundek 2000(^\text{35})</td>
<td>USA</td>
<td>Population</td>
<td>893</td>
<td>M</td>
<td>Standard neuropsychological battery</td>
<td>Home v Nursing Home</td>
<td>Sociodemographics, stroke severity other</td>
<td>Significant association</td>
</tr>
<tr>
<td>Meijer 2005(^\text{29})</td>
<td>Netherlands</td>
<td>Acute Hospital</td>
<td>338</td>
<td>M</td>
<td>MMSE</td>
<td>Favourable discharge (including, home) versus poor discharge (including, nursing home, death)</td>
<td>Sociodemographics, functional impairment, other</td>
<td>Significant association</td>
</tr>
<tr>
<td><strong>Not included in meta-analysis</strong></td>
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<tr>
<td>Stineman 2015(^\text{36})</td>
<td>USA</td>
<td>Acute Hospital</td>
<td>6515</td>
<td>H</td>
<td>Three stages: low, medium and high cognitive independence</td>
<td>Home v dependent (any setting requiring care, death)</td>
<td>None</td>
<td>Significant association</td>
</tr>
<tr>
<td>Brodaty et al., 2010(^\text{31})</td>
<td>Australia</td>
<td>Acute Hospital</td>
<td>150</td>
<td>H</td>
<td>Vascular Mild Cognitive Impairment (VaMCI)</td>
<td>Home v Nursing Home</td>
<td>None</td>
<td>No significant association</td>
</tr>
<tr>
<td>Massucci 2006(^\text{38})</td>
<td>Italy</td>
<td>Rehabilitation</td>
<td>793</td>
<td>H</td>
<td>MMSE &lt; 24</td>
<td>Home v other (including LTC and death)</td>
<td>None</td>
<td>Significant association</td>
</tr>
<tr>
<td>Horn 2005(^\text{25})</td>
<td>USA</td>
<td>Rehabilitation Severe stroke only</td>
<td>413</td>
<td>M</td>
<td>CI ascertained based on chart Also FIM (continuous)</td>
<td>Home/ community v Skilled Nursing Facility, Other</td>
<td>Sociodemographics, motor FIM, other</td>
<td>No significant association</td>
</tr>
</tbody>
</table>
### PSCI as a continuous variable

#### Included in meta-analysis

<table>
<thead>
<tr>
<th>Author, Year Country</th>
<th>Setting</th>
<th>N</th>
<th>Quality</th>
<th>Definition of PSCI</th>
<th>Comparison</th>
<th>Adjusted for</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farner et al., 2010&lt;sup&gt;23&lt;/sup&gt;</td>
<td>Rehabilitation</td>
<td>126</td>
<td>H</td>
<td>Continuous (RBANS)</td>
<td>Home v Nursing Home</td>
<td>Functional impairment, other</td>
<td>Significant association</td>
</tr>
<tr>
<td>Norway</td>
<td></td>
<td></td>
<td></td>
<td>Continuous (MMSE)</td>
<td></td>
<td>None</td>
<td>No significant association</td>
</tr>
<tr>
<td>Geubbels 2015&lt;sup&gt;24&lt;/sup&gt;</td>
<td>Acute Hospital</td>
<td>211</td>
<td>H</td>
<td>MoCA (continuous)</td>
<td>Independent v dependent (any setting requiring care, including nursing home)</td>
<td>None</td>
<td>Significant association</td>
</tr>
<tr>
<td>Netherlands</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sociodemographic, functional impairment, other</td>
<td>Not significant</td>
</tr>
<tr>
<td>Van der Zwaluw 2011&lt;sup&gt;27&lt;/sup&gt;</td>
<td>Acute Hospital</td>
<td>188</td>
<td>H</td>
<td>MMSE, CST and CDT (each continuous)</td>
<td>Independent (Home) v dependent (home with care, all other non-home destinations)</td>
<td>Sociodemographics, functional impairment, other</td>
<td>Significant association for CST, non-significant for MMSE and DCT</td>
</tr>
<tr>
<td>Mutai 2012&lt;sup&gt;30&lt;/sup&gt;</td>
<td>Rehabilitation</td>
<td>174</td>
<td>M</td>
<td>Cognitive FIM</td>
<td>Home v Nursing facility or hospital</td>
<td>Sociodemographics, functional impairment, other</td>
<td>Significant association</td>
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<tr>
<td>Italy</td>
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<tr>
<td>Denti, Agosti &amp; Franceschini 2008&lt;sup&gt;21&lt;/sup&gt;</td>
<td>Rehabilitation</td>
<td>359</td>
<td>L</td>
<td>MMSE, Cognitive FIM</td>
<td>Home discharge v Other (including LTC)</td>
<td>Sociodemographics</td>
<td>Significant association</td>
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<td></td>
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#### Not in meta-analysis

<table>
<thead>
<tr>
<th>Author, Year Country</th>
<th>Setting</th>
<th>N</th>
<th>Quality</th>
<th>Definition of PSCI</th>
<th>Comparison</th>
<th>Adjusted for</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim 2006&lt;sup&gt;26&lt;/sup&gt;</td>
<td>Nursing Home and Homecare agencies</td>
<td>99</td>
<td>M</td>
<td>Cognitive Performance Scale (continuous)</td>
<td>Home care v Nursing home</td>
<td>None</td>
<td>Significant association in opposite direction</td>
</tr>
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<td>South Korea</td>
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</tr>
<tr>
<td>Nguyen 2015&lt;sup&gt;31&lt;/sup&gt;</td>
<td>Rehabilitation</td>
<td>2085</td>
<td>M</td>
<td>Cognitive FIM</td>
<td>Home v Skilled Nursing Facility</td>
<td>None</td>
<td>Significant association</td>
</tr>
<tr>
<td>USA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sociodemographics, motor function, cognitive deficits, other</td>
<td>Not significant (effect size not reported)</td>
</tr>
<tr>
<td>Orme 2016&lt;sup&gt;33&lt;/sup&gt;</td>
<td>Acute Hospital</td>
<td>124</td>
<td>L</td>
<td>MoCA</td>
<td>Home v Placement (including nursing or residential home)</td>
<td>None</td>
<td>Significant association</td>
</tr>
</tbody>
</table>
one examined dementia and CIND separately. Of the studies examining overall PSCI, 8 examined PSCI as a categorical variable, and 7 as a continuous variable.

The most frequently used measure of cognitive function was the Mini-Mental State Examination (MMSE, k=5), with other measures used including the Repeated Battery for the Assessment of Neuropsychological Status (RBANS)²³, the (MoCA)²⁴, and the cognitive category of the Functional Independence Measure (FIM)²²,²₅,³₀,³¹. Of the three studies that examined dementia, one used DSM-IV criteria, one used ICD-9²⁷ and one used Vascular Dementia criteria²¹.

Most studies adjusted for covariates such as age or sex. Overall functional impairment was adjusted for in 14 of the 18 studies, using a measure such as the modified Rankin scale (mRS) or Barthel Index²⁶,²₅,₂₇,₂₉,₃₁–₃₃,₃₇.

Study quality
Two studies were in the low-quality category²²,²³ (score <25); nine studies²₅,₂₇,₂₉,₃₀,₃₁,₃₃–₃₅ were in the medium-quality category (25–30) and seven studies²₀,₂₁,₂₃,₂₄,₂₆,₂₈,₃₇ were in the high-quality category (>30). Low quality (score <3/5) was most frequently observed in the sections on reporting results and analysis (k=5) and reporting ethical matters and approval (k=8), with poor performance defined as a score <3/5. Full quality appraisal scores by dimension are displayed in Figure S1 (extended data³⁹).

PSCI and admission to LTC
PSCI was reported as significant predictor of LTC in 12 studies²₁,²₃,₂₆,₂₉,₃₁–₃₄,₃₇, with three studies failing to find a significant association²¹,²₄,²₅.

PSCI as categorical predictor
Eight studies reported PSCI as a categorical predictor²₁,₂₃,₂₅,₂₆,₂₉,₃₁–₃₄,₃₇, with six reporting a significant association with admission to LTC, and two reporting no significant association. One of these two examined CIND separately from dementia²¹, and the other was the only study in the review to focus on severe stroke alone²₅.

Four studies²⁶,₃₀,₃₁,₃₄,₃₅ reporting sufficient information were pooled together in a random-effects meta-analysis. PSCI significantly increased the odds of LTC [OR: 2.36 (95% CI: 1.18, 4.71, p=0.011)] and there was substantial heterogeneity (F=77%, p=0.004), see Figure 2. Two of the four studies had clear definitions of PSCI, including standard tests and cut-offs²⁶,₃₅. When these were combined in a sensitivity analysis, there was no significant heterogeneity (F=0%, p=0.75) and PSCI significantly predicted LTC, [OR: 3.11 (95% CI: 1.79, 5.43, p<0.0001)] (see Figure S2, extended data³⁴).

One study combined several outcomes in the “poor discharge” category, including death before discharge²⁶. Excluding this study in a sensitivity analysis, PSCI did not significantly
predict LTC [OR: 2.09 (95% CI: 0.98 to 4.45, p=0.06)] and heterogeneity was significant \((P=76\%, p=0.002)\), (see Figure S3, extended data\(^{14}\)). A further sensitivity analysis of three studies that reported adjusted estimates\(^{30,31,38}\) indicated that PSCI significantly predicts LTC \([OR: 2.13 (95\% CI: 1.02, 4.46, p=0.04)]; (P=76\%, p=0.006)\) (see Figure S4, extended data\(^{14}\)). All four studies were in the medium quality category, and no sensitivity analysis by quality category was carried out.

**PSCI as a continuous predictor of admission to LTC**

Seven studies reported PSCI as a continuous predictor of LTC\(^{22,23,26,30,32,37}\). Of these, four studies\(^{22,23,30,31}\) reported that lower levels of cognitive impairment (or better cognitive function) reduced odds of LTC. One study examined three PSCI measures (MMSE, CDT and CST), adjusting for all simultaneously, reporting that only one (CST) significantly predicted the discharge destination\(^{38}\). One study using the MoCA did not find PSCI to significantly predict discharge destination\(^{38}\), when adjusted for covariates, while another study found stroke patients in home care settings to have worse PSCI than stroke patients in long-term care\(^{36}\). This study was excluded from the meta-analysis as it assessed cognitive deficits (i.e., a higher score represented worse cognition), while other studies assessed cognitive function (a higher score represented better cognition), and pooling estimates was not feasible\(^{36}\). Another study did not report sufficient estimates to facilitate inclusion in a meta-analysis\(^{35}\).

Five studies\(^{22,24,30,37}\) were pooled together in a meta-analysis (Figure 3). Low levels of PSCI significantly reduced the odds of LTC \([OR: 0.89 (95\% CI: 0.84,0.95, p=0.0007)]\) and heterogeneity was not statistically significant, \((P=48\%, p=0.10)\).

Results from the four studies that reported adjusted effect sizes\(^{22,30,37}\) showed that heterogeneity reduced \((P=18\%, p=0.30)\) and lower levels of PSCI remained significantly associated with reduced odds of LTC \([OR: 0.91 (95\% CI: 0.87, 0.95, p<0.01)]\) (see Figure S5, extended data\(^{14}\)).

When estimates from the four studies\(^{22,24,30,37}\) that defined LTC as a combination of nursing home/long term care and other destinations, were pooled together, low levels of PSCI significantly reduced odds of LTC \([OR: 0.88 (95\% CI, 0.79, 0.98, p=0.02)]\) and heterogeneity was moderate to substantial \((P=61\%, p=0.05)\), see Figure S6 (extended data)\(^{16}\).

Three studies that were in the high study quality category\(^{23,24,37}\) were pooled together. Low levels of PSCI did not significantly reduce odds of LTC \([OR: 0.77 (95\% CI: 0.57,1.05, p=0.10)]\) and heterogeneity was substantial \((P=69\%, p=0.04)\) (see Figure S7, extended data\(^{14}\)). Although all 5 studies\(^{22,23,24,30,37}\) used different cognitive assessment tools, each included a clear definition of PSCI, and a sensitivity analysis by PSCI definition was not conducted.

**Dementia and admission to LTC**

Four studies examined the relationship between dementia and LTC and they all found dementia to significantly increase the odds of LTC after stroke\(^{20,21,27,33}\). Three studies\(^{20,27,33}\) were pooled in a meta-analysis and dementia statistically significantly increased odds of LTC \([OR (CI: 2.58 (95\% CI, 1.38, 4.32, p=0.003)]\) and heterogeneity was substantial though not significant \((P=60\%, p=0.80)\), see Figure 4.

When two studies that were in the medium quality category\(^{27,33}\) were pooled together in a sensitivity analysis, heterogeneity was increased \((P=68\%, p=0.08)\) and dementia did not significantly predict LTC \([OR (CI 95\%): 2.70 (0.91, 7.97, p=0.07)]\) (see Figure S8, extended data\(^{18}\)). All three studies had clear definitions of PSCI and LTC, and adjusted for key covariates, and sensitivity analyses were thus not carried out with respect to these factors.

**Discussion**

Overall, 16/18 studies identified in this review reported that PSCI or dementia significantly predicted admission to LTC post-stroke. Of the studies, 12 that identified a significant association adjusted for age or functional impairment. The main meta-analysis indicated that PSCI (categorical or continuous) and dementia significantly predict the risk of admission to LTC post-stroke, with an approximate 2-fold increase in the odds of admission to LTC.
This effect, however, was attenuated in some sensitivity analyses. Excluding studies that combined discharge to LTC with other outcomes, including death, reduced the size of the association. This led to a non-statistically significant result in sensitivity analysis of the association between categorical PSCI and admission to LTC. Excluding studies that did not adjust for key covariates also reduced the magnitude of the association. Study quality was a further factor: in the meta-analysis of the association between continuous PSCI and admission to LTC, higher quality studies reported a weaker association that was not statistically significant.

Definitions of PSCI also appeared to have an effect on results: two studies reported a significant association for one definition or measure of PSCI, and not for others. Studies with a clearer definition of PSCI appeared to report a stronger and less heterogeneous association between PSCI and LTC admission. The only study that examined CIND and dementia separately reported that only dementia had a significant effect on risk of admission to LTC. In South Korea, families preferred to look after severely impaired stroke patients. In addition, LTC settings

Previous reviews that examined a range of measures identified CI as a significant predictor of admission to LTC among stroke patients, consistent with the present study. This current review adds to this literature by including a greater number and range of studies, and conducting a meta-analysis, yielding a pooled estimate for the effect of PSCI and dementia on post-stroke admission to LTC.

Heterogeneity was moderate but not statistically significant in two of the main meta-analyses, related to continuous PSCI and post-stroke dementia. Statistically significant heterogeneity was observed in the meta-analysis of the association between categorical PSCI and LTC admission, though this heterogeneity was reduced in sensitivity analysis that only included studies with clear definitions of PSCI. Given the variation in settings and definitions, the level of heterogeneity was lower than might have been expected. This indicates that the influence of PSCI on risk of admission to LTC may not diverge widely across different health system contexts.

A notable exception of this was the study set in South Korea reporting that patients with lower levels of CI were discharged to LTC while patients with severe PSCI were using home care agencies. In South Korea, families preferred to look after severely impaired stroke patients. In addition, LTC settings
are not reimbursed adequately for severely impaired patients, and
avoid admitting such patients to reduce costs. This indicates
how setting-specific factors related to health system organisation
and financing, and cultural and societal values, can modify
determinants of admission to LTC for stroke patients.

Study quality

Studies had some consistency in the definition of CI with
studies using the same cognitive screening tool reporting the
same PSCI cut-off scores. However, some studies did not
provide clear definitions of CI and the measures used for
cognitive screening. Two studies described CI as cognitive
deficits and one study did not specify the cognitive
screening tools used.

Few studies reported how they statistically handled missing
data and some studies did not provide comprehensive
information on ethical approval which affected the quality
of the evidence. In some studies, the definition of LTC was
combined with other destinations and stroke outcomes including
death, contaminating the definition of LTC.

Strengths and limitations of the review

To our knowledge, this is the first systematic review and
meta-analysis to examine the effects of CI and dementia post-
stroke on admission to LTC. The review was conducted accord-
ing to the PRISMA guidelines for conducting systematic
reviews. Rigorous quality appraisal was undertaken using the
CCAT. Sensitivity analyses were carried out in relation to
definitions of CI and nursing home admissions, covariate
adjustment, and study quality.

The meta-analysis was limited by the number of studies that
were eligible for pooling. PSCI measured as a categorical and
continuous variable had to be analysed separately. A number of
studies with negative results did not report parameter estimates,
and could not be meta-analysed, introducing a potential bias
towards positive results in the meta-analysis. Only studies in
high-income countries were identified, limiting the global
generalizability of results.

Implications and conclusion

Previous studies have reported that LTC is resource-intensive
care for stroke patients. The findings from this review can
inform population-based planning of social care services for
stroke, and highlight the potential benefits of interventions that
aim to prevent or delay CI post-stroke, particularly dementia, in
reducing the costs associated with post-stroke LTC.

Data availability

Underlying data

All data underlying the results are available as part of the article
and no additional source data are required.

Extended data

Figshare: Extended Data.docx. https://doi.org/10.6084/m9.figshare.12291005.v1

This projection contains the following extended data:
- Extended Data.docx (File containing supplementary figures and tables)

Table S1: Sample Search Strategy for Systematic Review

Table S2: Full Details of Included Studies

Figure S1: Quality Appraisal Results

Figure S2: Sensitivity analysis using definition of PSCI (CI as categorical predictor)

Figure S3: Sensitivity analysis using the definition of long-term care (PSCI as categorical predictor)

Figure S4: Sensitivity analysis using whether studies reported adjusted estimates (PSCI as a continuous predictor).

Figure S5: Sensitivity analysis using whether studies reported adjusted estimates (PSCI as a continuous predictor).

Figure S6: Sensitivity analysis using how studies defined long-term care (PSCI as a continuous predictor).

Figure S7: Sensitivity analysis using study quality categories (PSCI as a continuous predictor).

Figure S8: Sensitivity analysis using study quality categories (dementia as a predictor of LTC).

Reporting guidelines

Figshare: PRISMA checklist for ‘Systematic review and meta-
analysis of the effect of cognitive impairment on the risk of admission to long-term care after stroke’ https://doi.org/
10.6084/m9.figshare.12291005.v1

Data are available under the terms of the Creative Commons Zero “No rights reserved” data waiver (CC0 1.0 Public domain dedication).

References

Open Peer Review

Current Peer Review Status: ?

Version 1

Reviewer Report 06 July 2020

https://doi.org/10.21956/hrbopenres.14151.r27509

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Overall, I had no major issue and thought the manuscript was well executed and clearly written. However, I do believe that a stronger rationale should be provided as to why this research was required.

Abstract:
○ Although I am aware this point is more of an editorial one, I was struck at the number of acronyms in the abstract.

Introduction:
1. The following population-based cohort study by Pendlebury et al. should be highlighted in the introduction⁴.

2. I was not convinced by the introduction provided by the authors as to why the need for a meta-analysis in this area. The introduction would benefit from a stronger rationale for why the need for this research.

Methods:
1. Can the authors clarify why EMBASE was not searched?

2. Could the authors state why studies with haemorrhagic stroke patients only were excluded? This then raises some questions: a) if studies reported results for ischaemic and haemorrhagic stroke patients separately, were the results for haemorrhagic patients included in the analysis?; b) If a study's sample, say, contained 90% haemorrhagic stroke patients, would that study be included in the review?

3. Quality assessment: Did the authors rate a study as high quality if the study had: a) CCAT score >30 AND a mean score >3.8/5 across dimensions; or b) CCAT score >30 OR a mean score >3.8/5 across dimensions.
score >3.8/5 across dimensions.

4. Cognitive impairment and Confidence Intervals share the same acronym in the study, which can at times generate confusion (e.g. The following sensitivity analyses were planned where feasible: how studies measured CI). The authors should rectify this.

5. Figure 1. I am taking that the four studies excluded as being dementia/CI only were because their patients did not have (or not reported as having) stroke.

Discussion:
- The discussion was I thought a very true reflection of the authors’ findings. However, I do not feel the conclusions in the abstract truly reflected those from the discussion. The observation in the abstract that post-stroke CI increases odds of admission to LTC post-stroke, independent of functional impairment, should be caveated.

References

Are the rationale for, and objectives of, the Systematic Review clearly stated?
Partly

Are sufficient details of the methods and analysis provided to allow replication by others?
Yes

Is the statistical analysis and its interpretation appropriate?
Yes

Are the conclusions drawn adequately supported by the results presented in the review?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Stroke, cohort studies, health economics, statistics

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.