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Hospitalisation and surgery: are there hidden cognitive consequences? Evidence from The Irish Longitudinal study on Ageing (TILDA)

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Abstract

Background: the dramatic shift in the global population demographic has led to increasing numbers of older people undergoing hospitalisation and surgical procedures.
Objectives: to determine whether hospitalisation or hospitalisation with surgery under general anaesthesia is associated with poorer cognitive performance in adults over the age of 50.
Methods: cognitive function in the domains of global cognition, memory and executive function was assessed in 8,023 individuals at waves 1 and 2 of The Irish Longitudinal Study on Ageing (TILDA), 2 years apart. Mixed-effects models were used to investigate the hypothesis after adjustment for risk factors for cognitive decline and potential confounders.
Results: during the 12 months preceding wave 1, 472 participants were hospitalised (mean age 67.0, 54.9% female) and a further 560 participants (mean age 64.6, 52.1% female) were hospitalised and underwent surgery with general anaesthesia; 6,938 (mean age 63.5, 54.5% female) were not hospitalised. There was a 14% higher error rate (IRR[95% CI] = 1.14[1.06, 1.22]) in the MMSE in the hospitalisation group and a 6% higher error rate (IRR[95% CI] = 1.06[0.99, 1.13]) in the surgery group compared to those with no hospitalisation. Poorer cognitive performance in the memory tasks was evident in both hospitalisation and hospitalisation with surgery groups (immediate recall: [95% CI] = −0.13 words[−0.22,−0.04] versus −0.13 words[−0.21,−0.04] and delayed recall: −0.20 words[−0.33,−0.06] versus −0.20[−0.32, −0.07]) compared to those with no hospitalisation. Increased error in the time-based prospective memory task was observed in the hospitalisation group and the surgery group (OR[95% CI] = 1.32[1.08, 1.60] versus 1.29[1.07, 1.55]).
Conclusion: hospitalisation and hospitalisation with surgery and general anaesthesia are associated with poorer global and domain specific cognitive performance.

Keywords: *surgery, cognition, cognitive impairment, hospitalisation, cognitive performance, older people*

Introduction

The dramatic shift in the global population demographic will continue to present new challenges with increasing emergency admission rates in older people [1] and progressively older patients undergoing surgery [2]. The association between cognitive decline and advancing age is well recognised [3], however, the impact of hospitalisation and of surgery in this complex patient group is less clear. Emerging evidence suggests that cognitive function declines following hospitalisation in observational studies [4, 5].

Improved survival rates from critical illness have resulted in significant long-term morbidity such as impaired function, reduced quality of life and increased neuropsychological symptoms including cognitive impairment [6–8]. However, the underlying mechanisms remain poorly understood.

It is widely recognised that patients who undergo surgery with general anaesthesia (GA) may experience cognitive changes

in the postoperative period [9, 10] and some never return to baseline cognitive function [11]. In a series of studies [12–14] up to 25% of older patients undergoing non-cardiac surgery had significant cognitive deterioration at 1 week post-op, 10% at 3 months and 1% at 1 year [15]. Two population-based case-control studies found that there was an increased risk of dementia following exposure to cardiac and non-cardiac surgery and anaesthesia, with evidence of a dose-response relationship and shorter duration to dementia diagnosis [16, 17].

The Irish Longitudinal Study on Ageing (TILDA) is a population-representative longitudinal cohort study and provides sufficient data to robustly investigate the relationship between hospitalisation and subsequent cognitive performance. Using TILDA data, the purpose of our study was to assess whether hospitalisation and hospitalisation with surgery and general anaesthesia is associated with poorer cognitive performance in patients over the age of 50 relative to those not undergoing hospitalisation.

Methods

Study design

Data from the first two waves of TILDA were analysed. TILDA is a longitudinal population-representative cohort study of community-dwelling adults aged 50 and older in Ireland. Wave 1 took place between 2009 and 2011 and wave 2 in 2012. 8,175 individuals aged 50 and older took part in wave 1, after exclusions 8,106 participants were eligible for our analysis at wave 1 and after attrition 6,938 participants were eligible for analysis at wave 2 (Figure 1). Full details of the study design and sampling procedure are available elsewhere [18–20] (Supplementary methodology, available at *Age and Ageing* online).

Hospitalisation and surgery

At each wave, participants were asked about hospitalisations and details of surgery with anaesthesia occurring in the previous 12 months (Appendix 1, available at *Age and Ageing* online). Any reported hospitalisation and any reported hospitalisation with surgery and full anaesthetic were labelled as belonging to either the 'hospitalised', 'surgery', or 'control' group (no hospitalisation), and this could vary between waves for a given individual.

Cognitive outcomes

Cognition was assessed at wave 1 and at wave 2, on average 2 years later. The measures included in both waves were a global assessment of memory using the MMSE, word recall tasks-immediate recall and delayed recall, two prospective memory tests, an executive function test- a verbal fluency test, and a subjective memory test and are described in Appendix 2, available at *Age and Ageing* online [21–30, 31–34]. The MMSE was administered at wave 1 in the health assessment and at wave 2 in the Computer Assisted Personal Interview (CAPI) (Supplementary Methodology, available at *Age and Ageing* online). Therefore, participants who did not undergo a health assessment at wave 1 are missing MMSE outcome data for wave 1 (n = 2,264) (Figure 1). All other cognitive tests were administered as part of the CAPI at both waves.

Covariates

Covariates selected for adjustment at wave 1 and 2 were recognised risk factors for cognitive impairment, or variables known to impact upon cognitive performance [35–39]. Information on age, sex, educational attainment, health behaviours including smoking status, exercise status using the short International Physical Activity Questionnaire (IPAQshort), a doctor diagnosis of chronic substance abuse including alcohol or drug abuse, doctor-diagnosed medical conditions, and medication usage was gathered at both wave 1 and wave 2. Doctor-diagnosed medical conditions included hypertension, angina, myocardial infarction, heart failure, arrhythmia, structural heart disease, hypercholesterolaemia, diabetes, stroke, transient ischaemic attack, chronic lung disease and Parkinson's disease. History of open heart surgery was also attained at both waves due to its link with postoperative cognitive dysfunction (POCD) [40]. Self-reported medication use was recorded and confirmed by cross-checking with medication labels. Medications were classified according to the Anatomical Therapeutic Classification (ATC) (http://www.whocc.no/atc_ddd_index/). Antidepressant medication ('N06A') use represents a surrogate marker for depression as this is known to impact upon cognitive performance [41], and may influence propensity for hospitalisation.

Exclusion criteria

Doctor's diagnosis of dementia, serious memory impairment or were taking an anti-dementia medication ('N06D') at wave 1 were excluded from the analysis (N = 69).

Statistical analysis

Firstly descriptive analysis was conducted to characterise the sample and to identify differences between groups (Table 1). Secondly an omnibus test was performed to assess differences in cognitive outcomes across groups in the fully adjusted mixed effects models. Thirdly mixed-effects models were fitted for which the family-wise type 1 error rate was set to 0.05 using P values adjusted by Hochberg procedure [42] for cognitive variables within the same domain.

A single adjusted mixed-effects model was fitted for each cognitive outcome. Mixed-effects poisson regression, linear regression, logistic regression and ordered logistic regression models were used depending on the cognitive outcome variable.

The variables entered as predictors in all models were hospitalisation, and surgery and general anaesthesia within the previous 12 months before wave 1 and wave 2, and adjusted for covariates at wave 1 and wave 2 as defined previously. All independent variables (including the exposure variable) were included as time-varying apart from sex and education

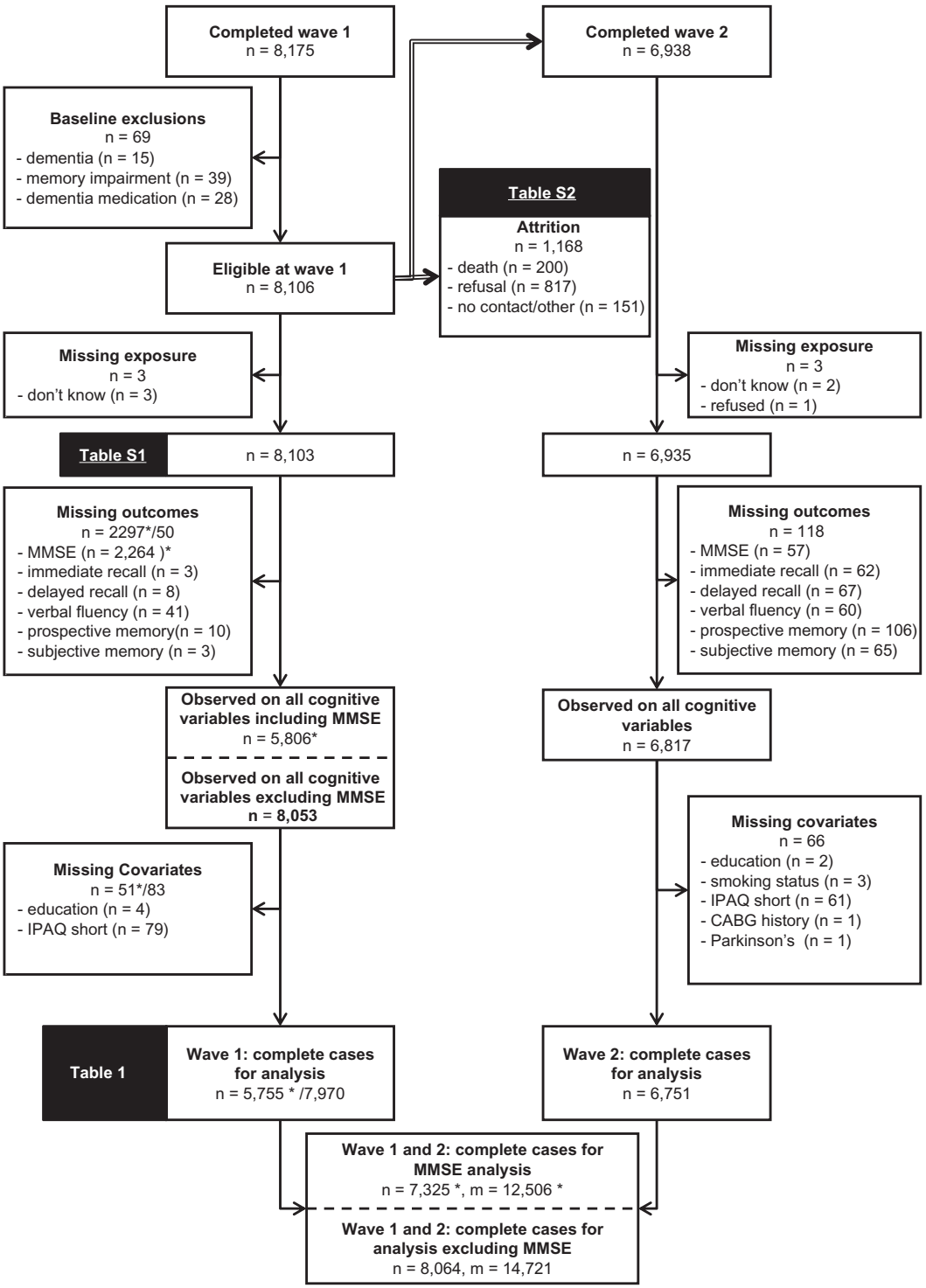

Figure 1. Flowchart.

attainment. This meant that a participant's cognitive outcomes at wave 1 were modelled as functions of their exposure in the preceding 12 months, and their covariate values at wave 1, and similarly for wave 2 outcomes and wave 2 covariates.

Statistical analysis was conducted using Stata 14.0 [43]. Further details on statistical analyses are available in Supplementary methodology, available at *Age and Ageing* online.

Results

Study sample

Figure 1 presents the numbers of individuals eligible at each stage of the study at wave 1 and wave 2 and provides reasons for non-participation or for not being analysed due to missing data. The total number of complete cases for analysis of MMSE was 5,755 at wave 1 and 6,751 at wave 2. The total

number of complete cases for analysis of other cognitive variables was 7,970 at wave 1 and 6,751 at wave 2 (Figure 1). Ignoring the MMSE variable, a total of 7,970 participants had complete data for at least one wave, and 6,657 participants had complete data for both waves. Further details in Figure 1 list the number of eligible participants with missing data on relevant variables. Characteristics of the eligible sample at wave 1 prior to exclusions for missing data (N = 8,103) are presented in Supplementary Table S1, available at *Age and Ageing* online by exposure preceding wave 1. Reasons for attrition (N = 1,168) between wave 1 and 2 are presented in supplementary Table S2, available at *Age and Ageing* online, broken-down by exposure preceding wave 1. Mortality was considerably higher in the hospitalised group compared to the surgery group and the control group (7.8% versus 3.2% versus 2.1%, respectively).

Characteristics of the sample

Characteristics of complete cases for analysis at wave 1 are presented in Table 1. Participants in the hospitalisation group were older (mean [SD] = 67.0[10.1]) than the surgery group (64.6[9.5]) and the reference group, no hospitalisation(63.5 [9.7]). Cases within the hospitalisation group had lower educational attainment levels than the surgery group, and the reference group. Individuals within the hospitalisation group had poorer health behaviours than the surgery group, and the reference group as evidenced by higher levels of former and current smokers, lower activity levels measured with the IPAQ, higher BMI's and higher levels of substance abuse. The hospitalisation group were also less healthy than the surgery group and the reference group, with higher levels of multi-morbidity. The notable exception to this was a higher percentage of cancer diagnosis in the surgery group versus the hospitalisation and reference group.

Details of hospitalisation and surgery

During the 12 months preceding wave 1, 472(5.9%) participants were hospitalised and 560(7.0%) participants underwent surgery with general anaesthesia; 6,938(87.1%) were not hospitalised. A total of 445(6.6%) participants were hospitalised, 479(7.1%) underwent surgery with general anaesthesia, and 5,827 (86.3%) were not hospitalised within the 12 months preceding wave 2. It is also important to note that there is a reasonable correlation between hospitalisation preceding wave 1 and hospitalisation preceding wave 2 (S4).

The median (interquartile range(IQR)) length of stay was 5 [2, 10] days at wave 1 and 5[2, 10] days at wave 2 for the hospitalisation group, with corresponding figures for the surgical group of 5[2, 10] days and 5[2, 12] at wave 1 and wave 2, respectively. For those in the hospitalisation group, 349 (73.9%), 72(15.3%), 51(10.8%) participants had 1, 2 or >2 hospital admissions in the 12 months preceding wave 1; the corresponding figures for wave 2 were 336(75.5%), 61 (13.7%), 48(10.8%). For those in the surgical group, 451 (80.5%), 80(14.3%), 29(5.2%) had 1, 2 or >2 surgeries performed during their hospital admissions. The corresponding figures for wave 2 were 375(78.6%), 79(16.6%), 23(4.8%).

Multivariate analyses of the association between exposure to hospitalisation and hospitalisation with surgery and general anaesthetic

The association between hospitalisation with and without surgery, and poorer cognitive performance from adjusted mixed-effects regression models using the full analytic sample is presented in Table 2.

Global cognition

There was evidence of a difference across the three groups through the omnibus test (Po/bus = 0.001); compared to the control group there was a 14% increased error rate in individuals hospitalised prior to wave 1 and wave 2 (IRR[95% CI] = 1.14[1.06, 1.22], $P < 0.001$) and an increased error rate in the surgery group (IRR [95% CI] = 1.06[0.99, 1.13], $P = 0.110$, not statistically significant).

Retrospective/episodic memory

There was evidence of difference in immediate recall scores across groups (Po/bus = 0.001) and in delayed recall scores (Po/bus = 0.001). The pattern of lower performance is similarly reflected in the hospitalisation group and surgery group when compared with the control group (immediate recall: β [95% CI] = −0.13[−0.22, −0.04], $P = 0.005$ versus −0.13 [−0.21, −0.04], $P = 0.005$, and delayed recall: −0.20[−0.33, −0.06], $P = 0.005$ versus −0.20[−0.32, −0.07]), $P = 0.005$).

Prospective memory

There was evidence of difference in prospective memory 1 scores across groups (Po/bus = 0.003) and difference in prospective memory 2 scores (Po/bus = 0.03). These differences consisted of increased error in the prospective memory 1, a time-based task, and prospective memory 2, an event-based task in the hospitalisation and surgery group compared with the control group (prospective memory 1: OR[95% CI] = 1.32[1.08, 1.60], $P = 0.02$ versus 1.29[1.07, 1.55], $P = 0.02$ and prospective memory 2: OR[95% CI] = 1.27[1.05, 1.54], $P = 0.02$ versus 1.12[0.93, 1.35], $P = 0.22$).

Executive function

A difference in verbal fluency is evident (Po/bus = 0.03) across groups, lower in both exposure groups in the fully adjusted model(hospitalisation: β coef[95% CI] = −0.46 [−0.83, −0.08], $P = 0.02$ versus surgery: ß coef[95% CI] = −0.34[−0.69, 0.01], $P = 0.06$, not statistically significant) compared to the control group.

Self-rated memory

An increase in subjective memory complaints was observed in both groups (hospitalisation: OR[95% CI] = 1.17[0.98, 1.39]

Table 1. Demographics and health covariates of the sample at wave 1.

Characteristics	No hospitalisation *n* = 6,938	Hospitalisation *n* = 472	Surgery *n* = 560	*P* value
Health assessment, *n* (%)[a]	5,022 (72.4)	330 (69.9)	412 (73.6)	0.403
Age, mean (SD)	63.5 (9.7)	67.0 (10.1)	64.6 (9.5)	0.0001
Female, *n* (%)	3,782 (54.5)	259 (54.9)	292 (52.1)	0.542
Education, *n* (%)[b]				
Some primary/none	229 (3.3)	21 (4.5)	17 (3.0)	<0.030
Primary school	1,843 (26.6)	166 (35.2)	141 (25.2)	
Intermediate/junior	1,629 (23.5)	95 (20.1)	140 (25.0)	
Leaving certificate	1,159 (16.7)	72 (15.3)	96 (17.1)	
Diploma/certificate	1,084 (15.6)	62 (13.1)	87 (15.5)	
Primary degree	589 (8.5)	33 (7.0)	51 (9.1)	
Postgraduate/higher degree	405 (5.8)	23 (4.9)	28 (5.0)	
Smoking status, *n* (%)				
Never	3,067 (44.2)	178 (37.7)	242 (43.2)	0.015
Former	2,611 (37.6)	190 (40.3)	230 (41.1)	
Current	1,260 (18.2)	104 (22.0)	88 (15.7)	
Level of Physical Activity (IPAQ), *n*(%)[b]				
Low	2,088 (30.1)	213 (45.1)	237 (42.3)	<0.001
Medium	2,415 (34.8)	149 (31.6)	182 (32.5)	
High	2,435 (35.1)	110 (23.3)	141 (25.2)	
BMI (kg/m^2), mean (SD)[b]	28.6 (5.0)	29.8 (5.8)	28.9 (4.8)	0.0001
Substance abuse, *n* (%)	97 (1.4)	17 (3.6)	14 (2.5)	<0.001
Private Health Insurance, *n* (%)	4,040 (58.3)	239 (50.6)	337 (60.2)	0.003
Mental Health				
CES-D, mean (SD)	5.6 (7.0)	7.6 (7.9)	6.7 (7.9)	0.0001
Disease prevalence, *n* (%)				
Hypertension	2,466 (35.5)	237 (50.2)	237 (42.3)	<0.001
Angina	321 (4.6)	72 (15.3)	43 (7.7)	<0.001
Myocardial infarction	266 (3.8)	61 (12.9)	41 (7.3)	<0.001
Heart failure	59 (0.9)	16 (3.4)	10 (1.8)	<0.001
Diabetes	491 (7.1)	68 (14.4)	58 (10.4)	<0.001
Stroke	83 (1.2)	22 (4.7)	12 (2.1)	<0.001
TIA	109 (1.6)	29 (6.1)	26 (4.6)	<0.001
Valvular heart disease	302 (4.4)	42 (8.9)	31 (5.5)	<0.001
Cardiac arrhythmia	419 (6.0)	83 (17.6)	69 (12.3)	<0.001
High cholesterol	2,611 (37.6)	209 (44.3)	226 (40.4)	0.009
Chronic	246 (3.6)	51 (10.8)	20 (3.6)	<0.001
lung disease				
Parkinson's disease	33 (0.5)	4 (0.9)	6 (1.1)	0.116
Cancer or malignant tumour	373 (5.4)	42 (8.9)	84 (15.0)	<0.001
None of these	2,470 (35.6)	73 (15.5)	138 (24.6)	<0.001
History of open heart surgery, *n* (%)	71 (1.0)	18 (3.8)	13 (2.3)	<0.001
Frailty (Fried)[b]				
Non-frail	3,449 (70.9)	148 (47.6)	205 (51.9)	<0.001
Pre-frail	1,325 (27.2)	128 (41.2)	162 (41.0)	
Frail	93 (1.9)	35 (11.3)	28 (7.1)	
Function ADLs, *n* (%)				
0 ADLs	6,449 (93.0)	374 (79.2)	487 (87.0)	<0.001
1 ADL	336 (4.8)	59 (12.5)	42 (7.5)	
2 ADLs	82 (1.2)	18 (3.8)	11 (2.0)	
3 or more ADLs	71 (1.0)	21 (4.5)	20 (3.6)	
Polypharmacy, *n* (%)[b]	1,216 (17.7)	235 (50.2)	173 (31.2)	<0.001
Anti-depressants, *n* (%)	439 (6.3)	53 (11.2)	44 (7.9)	<0.001
Psycholeptics, *n* (%)	418 (6.0)	71 (15.0)	35 (6.3)	<0.001
Opioids, *n* (%)	188 (2.7)	35 (7.4)	40 (7.1)	<0.001
Cognitive Scores				
MMSE score, median (IQR)	29 (28 30)	28 (27 30)	29 (27 30)	0.0001
Immediate recall, mean (SD)	6.6 (1.6)	6.0 (1.8)	6.3 (1.7)	<0.001
Delayed recall, mean (SD)	5.9 (2.4)	5.0 (2.5)	5.5 (2.6)	<0.001
Verbal fluency, mean (SD)	20.5 (7.1)	18.8 (7.0)	19.7 (6.9)	<0.001
Prospective memory 1 incorrect, *n* (%)	1,585 (22.9)	157 (33.3)	155 (27.7)	<0.001
Prospective memory 2 incorrect, *n* (%)	1,105 (15.9)	110 (23.3)	108 (19.3)	<0.001
Subjective memory (Poor), *n* (%)	156 (2.3)	27 (5.7)	18 (3.2)	<0.001

BMI, body mass index; CES-D, Centre for Epidemiologic Studies Depression; TIA, transient Ischaemic attack; ADLs, activities of daily living.
[a]Health assessment: At wave 1, health assessment included MMSE assessment. Therefore, if no health assessment, no MMSE at wave 1.
[b]Missing data: BMI *n* = 2,227 (14.8%), CES-D *n* = 117 (0.8%), Frailty *n* = 2,397 (15.9%), Polypharmacy *n* = 72 (0.5%), MMSE *n* = 2,215 (14.7%).
Analysis of variance was performed for continuous variables and chi^2 tests for categorical variables.

Table 2. Results of Cognitive outcomes by exposure type for wave 1 and 2. (i) Reference group, no hospitalisation/no surgery, (ii) Hospitalisation, no surgery group and (iii) Hospitalisation and surgery group within 12 months (all cognitive scores excluding MMSE, n = 8,064; MMSE score n = 7,325).[a]

Domain	Measure	Hospitalisation			Surgery			*P* (omnibus)
		Coefficient	95% CI	*P* value[e]	Coefficient	95% CI	*P* value[e]	
Global cognition	MMSE[b]	1.14	(1.06, 1.22)	<0.001	1.06	(0.99, 1.13)	0.110	0.001
Retrospective memory	Immediate Recall[c]	−0.13	(−0.22, −0.04)	0.005	−0.13	(−0.21, −0.04)	0.005	0.001
	Delayed Recall[c]	−0.20	(−0.33, −0.06)	0.005	−0.20	(−0.32, −0.07)	0.005	0.001
Prospective memory	Prospective Mem1[d]	1.32	(1.08, 1.60)	0.02	1.29	(1.07, 1.55)	0.02	0.003
	Prospective Mem2[d]	1.27	(1.05, 1.54)	0.02	1.12	(0.93, 1.35)	0.22	0.03
Executive function	Verbal Fluency[c]	−0.46	(−0.83, −0.08)	0.02	−0.34	(−0.69, 0.01)	0.06	0.03
Self-rated memory	Subjective Memory[d]	1.17	(0.98, 1.39)	0.16	1.03	(0.88, 1.21)	0.72	0.21

[a]Adjusted for age, sex, education, smoking status, alcohol and substance abuse, IPAQ-short, history of CABG, cardiovascular disease, diabetes, cerebrovascular disease, parkinson's disease, chronic lung disease and anti-depressants.

[b]MMSE results presented as Incidence Rate Ratio (IRR) using mixed-effects (ME) poisson regression models; values >1 indicate worse cognitive function

[c]Immediate Recall, Delayed Recall and Verbal Fluency presented as beta coefficients (β) using ME linear regression models; a decline indicates a decline in cognitive function

[d]Prospective Mem1 and 2, and Subjective Memory presented as odds ratios (OR) using ME logistic regression and ME ordered logistic models; OR > 1 indicates an error in the prospective memory task and poorer subjective memory.

[e]*P* values were adjusted by Hochberg procedure for similar hypotheses for each effect of interest, confidence intervals are unadjusted.

MMSE, Mini-Mental State Examination; Mem, Memory; IPAQ-short, International Physical Activity Questionnaire; CABG, coronary artery bypass grafting.

Note: For the MMSE, the number of errors was calculated (30–total score achieved) and modelled as a Poisson distribution.

See Statistical Analysis in Supplementary Methodology, available at *Age and Ageing* online section for further details.

versus surgery: OR[95% CI] = 1.03[0.88, 1.21]) when compared with the control group but there was no evidence of difference across the three groups (P = 0.21). Findings were not statistically significant.

Discussion

An association between hospitalisation, with and without surgery, and poorer cognitive performance in the domains of global cognition, retrospective/episodic memory and executive function was identified in a population-representative longitudinal cohort study of individuals over the age of 50. This was observed after full adjustment of all models and supports our hypothesis that hospitalisation is associated with poorer cognitive performance. Our findings add to the sparse literature to date in this important topic, the relationship between hospitalisation and cognition, and additionally look at the relationship between surgery with anaesthesia and cognitive function, in a large nationally representative sample.

Whereas other studies have demonstrated an association between hospitalisation and cognitive decline [4, 5], and surgery with general anaesthesia and cognitive decline [12, 15–17, 44], we have an additional ability to combine both interventions in the same sample, and use objective and subjective cognitive tests, physical and mental health measures, and medication use at relatively short follow up periods every 2 years to investigate this relationship.

Strengths of our study include a population-representative sample inclusive of those with and without health insurance. Previous studies were unlikely to be population-representative as they used geographically defined populations only inclusive of members of a health maintenance organisation, were reliant on health insurance data or the national social insurance program [4, 5]. Other population-based studies were unable to adjust for educational level, behavioural health status-smoking and exercise, cardiovascular disease or Parkinson's disease, important confounders for cognitive impairment [16, 17]. Our study is also a community sample rather than a clinical sample. These study design features bolster the generalisability of our findings. Furthermore, our longitudinal study consists of cognitive testing within 12 months of the individual's hospitalisation in contrast to other studies with longer periods of follow up which introduce the possibility of additional mediating factors. The neurocognitive testing methods used in TILDA are validated, objective measures that assess all cognitive domains and have a novel subjective memory component previously unexplored in the literature. The sample size in TILDA has adequate statistical power across two waves of the study.

The main limitation of the study is the lack of data pertaining to the indication for hospitalisation, and the type of surgery and anaesthesia. This is due to the absence of national unique patient identifiers in Ireland which inhibits cross-linkage of data. The CAPI questionnaire asks if the patient has been admitted to hospital within the last 12 months, therefore variability in the timing of cognitive testing from the participant's discharge date may exist between individuals. The power to detect poorer cognitive performance may have been limited due to insufficient post-hospitalisation data as only two waves 2 years apart were available for analysis, a relatively short time period compared with other studies. Analysis of future waves in TILDA is required to investigate the relationship between hospitalisation and cognitive change. It is also important to recognise that survivors of hospitalisation and surgery included in the analysis at both waves may not represent all survivors as they are likely to be healthier and

more cognitively intact. Therefore, it is possible that our results are underestimating the cognitive decline experienced by the full sample following exposure. Our results of poorer cognitive performance following hospitalisation with surgery may also be weaker than for hospitalisation alone, as it has been recently suggested that removal of the pro-inflammatory illness necessitating surgery may in fact improve cognition [45]. These findings may also be due to potential bias in the surgical group as those deemed 'unfit' for surgery may have been included in the hospitalisation group. Furthermore, it is important to acknowledge the possibility of a bidirectional causal relationship as two previous studies have demonstrated an association between cognitive impairment and increased risk of hospitalisation [46, 47].

Proposed mechanisms of cognitive decline after hospitalisation are multi-factorial, and include delirium [48, 49], hypoxaemia [50], hypotension [51], glucose dysregulation [52], systemic inflammation [53–55], sedative [56, 57] and analgesic medications [58]. The underlying pathophysiology proposed in postoperative cognitive dysfunction includes surgical stress-associated systemic or localised inflammatory reactions, compromised blood brain barrier in neurodegenerative conditions, alterations in hormonal homoeostasis such as cortisol, disruption in neurotransmitter activity and direct anaesthetic toxicity [55, 59–63]. Delirium is common in the older patient [64], affecting up to 75% of those with critical illness [65], 15–20% of older general medical inpatients by criteria [66], and is frequently under-recognised when it presents as subsyndromal delirium [65, 67, 68] and may play a role in our findings. The incidence of postoperative delirium varies widely from 10% in elective surgery to 30-65% after specific surgeries such as hip fracture surgery, cardiac and emergency surgery [69, 70]. Postoperative delirium can progress to postoperative cognitive dysfunction [10, 71] which may be reflected in our results.

It has been suggested that acute illness causes an abrupt loss of cognitive function rather than an increased rate of cognitive decline [4]. Participants may have experienced cognitive impairment due to the illness that led to their hospitalisation or as a consequence of the treatment they received [72]. In view of this, covariates selected for adjustment accounted for risk factors for cognitive impairment and the major causes of hospitalisation.

Currently, there are over 46 million people living with dementia worldwide and this is predicted to increase to 131.5 million by 2050 [73, 74]. Our study findings demonstrate the detrimental impact of hospitalisation on cognition. Better understanding of the underlying mechanisms responsible may lead to the identification of risk factors and novel research strategies in the prevention of cognitive impairment and dementia. Strategies to avoid hospitalisation with improved chronic disease management in the community, coupled with improved awareness and interventions for cognitive dysfunction may improve outcomes.

Key points

- First time a longitudinal population-representative study has demonstrated this relationship for both exposures.
- Increasing number of older people undergoing hospitalisation and surgical procedures.
- Our findings: Hospitalisation and surgery are associated with poorer global and domain specific cognitive performance.
- Hospitalisation and surgery may have cognitive consequences.

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.

Ethics Committee Approval

Trinity College Research Ethics Committee.

References

Note: The very long list of references supporting this article has meant that only the most important are listed here. The full list of references is available in the Supplementary data.

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