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RESEARCH ARTICLE

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Hospitalisation and surgery: Is exposure associated with increased subsequent depressive symptoms? Evidence from The Irish Longitudinal Study on Ageing (TILDA)

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Background: The dramatic shift in the global population demographic has led to increasing numbers of older people undergoing hospitalisation and surgical procedures. While necessary, these exposures may lead to an increase in depressive symptoms.

Objectives: To determine whether hospitalisation or hospitalisation with surgery under general anaesthesia is associated with an increase in depressive symptoms in adults over the age of 50.

Methods: Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale in 8036 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 depression and potential confounders.

Results: During the 12 months preceding wave 1, a total of 459 participants were hospitalised (mean age, 67.0; 55.3% female), and a further 548 participants (mean age, 64.6; 51.8% female) were hospitalised and underwent surgery with general anaesthesia; 6891 (mean age, 63.5; 54.3% female) were not hospitalised. Analysis of waves 1 and 2 data using mixed-effects models demonstrated that there was a 7% increased adjusted incidence rate of depressive symptoms (IRR [95% CI] = 1.07 [1.02-1.11]) in the Center for Epidemiologic Studies Depression Scale in the hospitalisation group and a 4% increased adjusted incidence rate of depressive symptoms (IRR [95% CI] = 1.04 [1.00-1.08]) in the surgery group compared with those with no hospitalisation.

Conclusion: Hospitalisation and hospitalisation with surgery and general anaesthesia are associated with increased depressive symptoms. This is the first time a longitudinal population-representative study has demonstrated this relationship for both exposures simultaneously.

KEYWORDS

depression, depressive symptoms, hospitalisation, low mood, surgery

1 | INTRODUCTION

The ageing population will continue to present new challenges with increasing hospitalisations among older people with multi-morbidity[1-3] and progressively older patients undergoing surgery.[4] Recent literature has reported that hospitalisation for a range of different medical conditions may increase the risk of depression[5,6] and cognitive decline.[7-9] We recently demonstrated poorer cognitive performance in adults over the

age of 50 exposed to hospitalisation or surgery in the previous year compared with those with no hospitalisation.[10] Depressive symptoms and cognitive impairment are associated with an increase in health care utilisation, hospitalisation, and premature mortality.[11-13] The World Health Organisation predicts[14] that depression will become the second leading cause of disability by 2030, which further emphasises the importance of early identification and management to preserve functional independence.[15]

Older patients suffering from chronic illness have a higher prevalence of major depressive illness,[16] with conditions including arthritis, dermatological conditions, circulatory conditions, and speech disorders previously implicated.[17] However, this association between depression and chronic illness may be a secondary psychological reaction to the development of the illness mediated by disability. Cross-sectional studies have demonstrated a linear relationship between physical disability from illness and depression with an increase in disability leading to an increase in depressive symptoms.[18-20]

Depression is frequently underdiagnosed in patients with chronic obstructive pulmonary disease and is known to be associated with poorer prognosis as it predisposes to chronic obstructive pulmonary disease exacerbations, thus increasing mortality.[21] Heart failure patients also commonly experience depressive symptoms, which have been shown to independently predict adverse clinical outcomes in this cohort.[22] Furthermore, depressive symptoms after hospitalisation for acute myocardial infarction are a predictor of 1-year cardiac mortality.[23] The surgical literature has also demonstrated that lung transplant patients with greater post-operative depressive symptoms have a higher mortality rate.[24] Alternatively, metastatic breast cancer patients with improving depressive symptoms have been shown to have improved survival rates[25] at 1 year, further highlighting the importance of early recognition and treatment.

Hospitalisation due to medical illness or surgical intervention can be viewed as a stressful life event. The association between the number of stressful life events a person experiences and depressive symptoms is well documented[26-28] and is similar across all age groups, including later life.[29] Using data from The Irish Longitudinal Study on Ageing (TILDA), the purpose of our study was to assess whether hospitalisation and hospitalisation with surgery and general anaesthesia are associated with an increase in depressive symptoms in patients over the age of 50 relative to those not undergoing hospitalisation.

Key points

- Hospitalisation and surgery are associated with increased subsequent depressive symptoms.
- Increasing numbers of older people are experiencing hospitalisation and undergoing surgical procedures.
- Depression may be a prodromal feature of dementia.
- Early recognition of depressive symptoms and raising patient, carer, and physician awareness may improve outcomes.

2 | METHODS

2.1 | Study design

Data from the first 2 waves of TILDA were analysed. The Irish Longitudinal Study on Ageing is a longitudinal population-representative cohort study of community-dwelling adults aged 50 and older in Ireland. Full details of the study design and sampling procedure are available elsewhere.[30-32] Wave 1 took place between 2009 and 2011 and wave 2 in 2012. Eight thousand one hundred seventy-five individuals aged 50 and older took part in wave 1; after exclusions, 7976 participants were eligible for our analysis at wave 1, and after attrition, 6707 participants were eligible for analysis at wave 2 (Figure 1). Data collected include a computer-assisted personal interview (CAPI) performed in the participant's own home, a self-completion questionnaire, and a health assessment performed by trained nurses in a dedicated health centre or in the participant's own home. Ethical approval for the study was obtained from the Trinity College Dublin Research Ethics Committee, and all participants were asked to provide written informed consent.

2.2 | Hospitalisation and surgery (exposure definition)

In the CAPI at each wave, participants were asked about hospitalisations and details of surgery with anaesthesia occurring in the previous 12 months (Appendix S1). Any reported hospitalisation and any reported hospitalisation with surgery and full anaesthetic were each coded with an indicator variable, and groups were mutually exclusive. Thus, those with a given exposure in the preceding 12 months were labelled as belonging to either the "hospitalised," "surgery," or "control" group, and this could vary between waves for a given individual.

2.3 | Depression outcome

Symptoms of depression were assessed in the CAPI using the Center for Epidemiologic Studies Depression Scale (CES-D),[33] a short self-report scale that is designed to measure the current level of depressive symptoms in the general population.[33] It was validated in the general population and primary care settings and has been shown to have acceptable screening accuracy in these populations.[34] The CES-D has been used in general population epidemiological studies and in clinical settings as a measure of depressive symptoms in patients with chronic conditions such as heart failure and cancer[22,25] and also as a diagnostic measure of depression.[35,36]

The scale contains 20 items about symptoms that occurred in the previous week with response options from 0 to 3 that refer to frequency of symptoms. The scale ranges from 0 (best) to 60 (worst) with a higher number indicative of increasing depressive symptoms. Depressive symptoms were assessed using the CES-D as a continuous outcome variable with a range from 0 to 60.

2.4 | Covariates

Covariates selected for adjustment were recognised risk factors for late-onset depression, or variables known to impact upon depressive

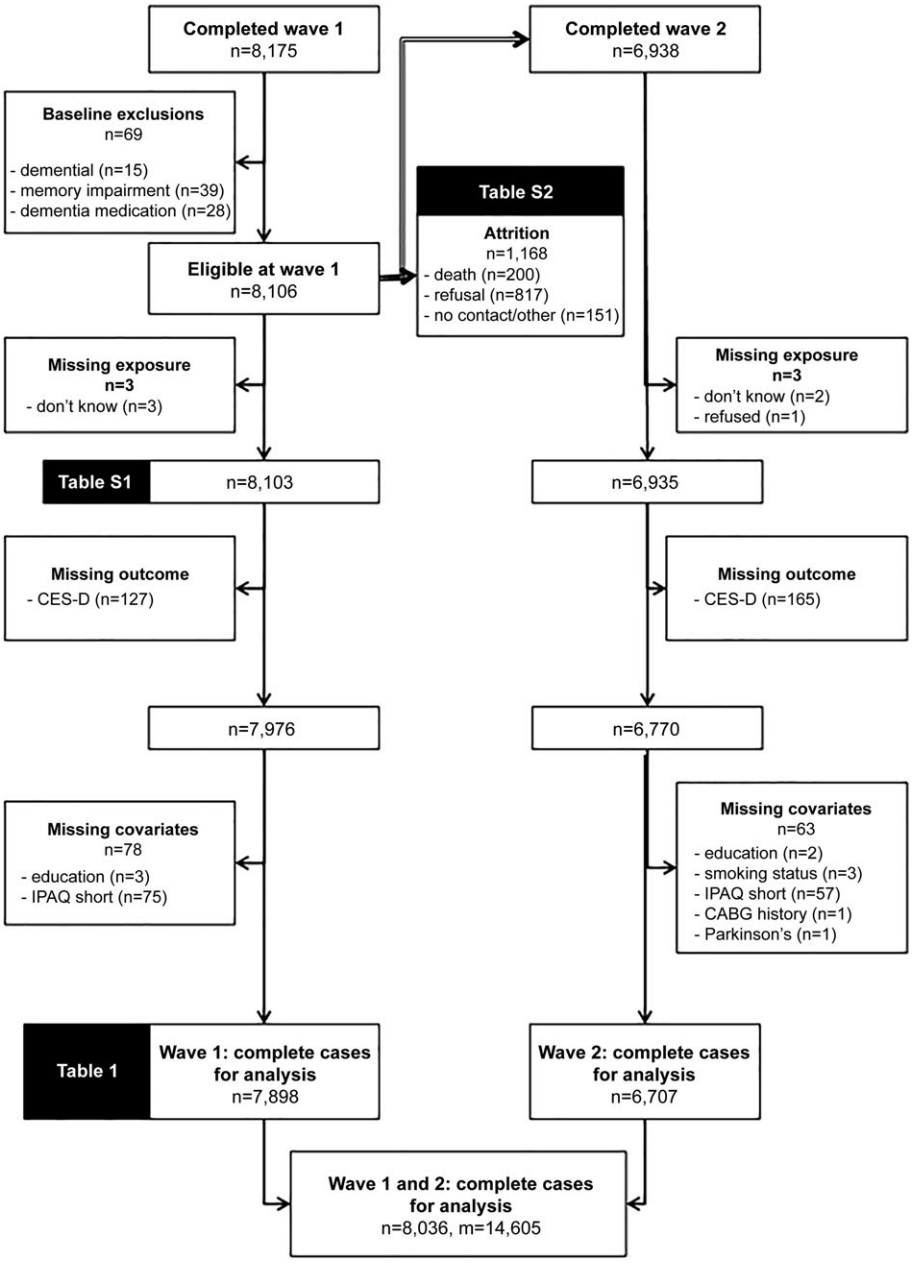

FIGURE 1 Flowchart: sample for analyses

symptoms.[37-45] Information on age, sex, educational attainment (some primary/none, primary, intermediate/junior certificate, leaving certificate, diploma/certificate, primary degree, and postgraduate/higher level), health behaviours including smoking status, exercise status using the short International Physical Activity Questionnaire, a doctor diagnosis of chronic substance abuse including alcohol or drug abuse, doctor-diagnosed medical conditions, and medication usage was gathered at both waves 1 and 2. At both waves, all participants were asked whether they had received a doctor's diagnosis of any of the following conditions: high blood pressure, angina, heart attack, heart failure, arrhythmia, heart murmur, high cholesterol, diabetes, stroke, transient ischaemic attack, chronic lung disease, and Parkinson's disease. Information on whether the participant had a history of open heart surgery was also attained at both waves due to the link between depression and cardiovascular disease.[42] Self-reported medication use was recorded during the CAPI, confirmed by cross-checking with medication labels, and classified according to the Anatomical Therapeutic Classification (http://www.whocc.no/atc_ddd_index/). A dichotomous variable was generated to indicate usage of antidepressant medications ("N06A") and represent participants with a pre-existing diagnosis of depression on treatment.

2.5 | Exclusion criteria

Any participants who reported a doctor's diagnosis of dementia and serious memory impairment or were taking an antidementia medication ("N06D") at wave 1 were excluded from the analysis (N = 69). This is based on our hypothesis that hospitalisation for acute illness or surgery can result in an increase in depressive symptoms that are not associated with co-morbid dementia or cognitive impairment.[37]

2.6 | Statistical analysis

Analysis of the association between hospitalisation or hospitalisation with surgery and increased depressive symptoms at waves 1 and 2 was performed using a mixed-effects model. The CES-D was modelled as a Poisson distribution. From this, an incidence rate ratio (IRR) greater than 1 for an exposure would indicate an increase in depressive symptoms.

The variables entered as predictors in all models were hospitalisation and hospitalisation with surgery and general anaesthesia within the previous 12 months before waves 1 and 2 and adjusted for covariates at waves 1 and 2 as defined previously: age, age-squared, sex, education, smoking status, exercise status, doctor diagnosis of chronic substance abuse including alcohol or drug abuse, cardiovascular conditions, cerebrovascular conditions, Parkinson disease, chronic lung disease, and antidepressant medication use. All independent variables (including the exposure variable) were included as time-varying apart from sex and education attainment. This means that a participant's depression outcome at wave 1 was modelled as a function of their exposure in the preceding 12 months and their covariate values at wave 1 and similarly for the wave 2 outcome and wave 2 covariates.

The model had 3 levels, including random intercepts to account for the clustering of longitudinal observations within participant and the clustering of participants within households. The random effect within the model was used to account for repeat observations. Therefore, the fixed predictor terms (hospitalisation and surgery) in the model were our primary focus, and results presented are representative of this.

Statistical analysis was conducted using Stata 14.0,[46] and the family-wise type-1 error rate *P* values were set to .05. An omnibus test was performed initially to assess the evidence for differences across the 3 exposure groups, followed by post hoc pairwise comparisons between the 3 exposure groups (*hospitalised vs nonhospitalised and hospitalised with surgery vs nonhospitalised*).

2.7 | Missing data

Only observations with complete data at a given wave were analysed, thus missing data were assumed to be missing completely at random. The plausibility of this assumption in our analysis is strengthened by the inclusion of relevant covariates and the use of wave 1 data for participants who did not complete wave 2 (reducing attrition bias).

2.8 | Sensitivity analysis

To ensure that covariates adjusted for in the mixed-effects model did not include possible intermediate variables, we performed a sensitivity analysis of depressive symptoms only at wave 2 including as independent variable, the exposure variable preceding wave 2, age, sex and education at wave 2, and all other covariates at wave 1 (rather than at wave 2).

An additional sensitivity analysis with further adjustment for medications including opioids and psycholeptics was performed as it is unclear whether initial prescription of these was before or after exposure.

3 | RESULTS

3.1 | Study sample

Figure 1 presents the numbers of individuals eligible at each stage of the study at waves 1 and 2 and provides reasons for nonparticipation or for not being analysed due to missing data. The total number of complete cases for analysis of CES-D was 7898 at wave 1 and 6707 at wave 2 (Figure 1). A total of 7898 participants had complete data for at least one wave, and 6707 participants had complete data for both waves. Figure 1 also lists the number of eligible participants with missing data on relevant variables and those missing at wave 2 due to attrition. Characteristics of the eligible sample at wave 1 prior to exclusions for missing data (N = 8103) are presented in Table S1 by exposure preceding wave 1. Reasons for attrition (N = 1168) between waves 1 and 2 are presented in Table S2, broken down by exposure preceding wave 1. Mortality was considerably higher in the hospitalised group compared with the control group and surgery group (7.8% vs 2.1% vs 3.2%, respectively).

3.2 | Characteristics of the sample

Characteristics of complete cases for analysis at wave 1 are presented in Table 1 (T1). Participants in the hospitalisation group were older (mean [SD] = 67.0 [10.1]) than the surgery group (64.6 [9.4]) 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 International Physical Activity Questionnaire, higher body mass index, and higher levels of substance abuse (T1). The hospitalisation group was also less healthy than the surgery group and the reference group, with higher levels of multi-morbidity (T1). The notable exception to this was a higher percentage of cancer diagnosis in the surgery group versus the hospitalisation and reference group.

3.3 | Details of hospitalisation and surgery (exposure)

During the 12 months preceding wave 1, a total of 459 (5.8%) participants were hospitalised and 548 (6.9%) participants underwent surgery with general anaesthesia; 6891 (87.3%) were not hospitalised. A total of 448 (6.7%) participants were hospitalised, 479 (7.1%) underwent surgery with general anaesthesia, and 5780 (86.2%) 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 and surgery preceding wave 1 and surgery preceding wave 2 (Table S3 [ST3]).

For both waves 1 and 2, the median (interquartile range) length of stay was 5 (2-10) days at wave 1 and 5 (2-10) days for the hospitalisation group, with corresponding figures for the surgical group of 5 (2-10) days and 5 (2-12) at waves 1 and 2, respectively.

TABLE 1 Demographics and health covariates of the sample at wave 1

Characteristics	No Hospitalisation n = 6891	Hospitalisation n = 459	Surgery n = 548	*P* Value
Age, mean (SD)	63.5 (9.7)	67.0 (10.1)	64.6 (9.4)	.0001
Female, n (%)	3744 (54.3)	254 (55.3)	284 (51.8)	.465
Education, n (%)[a]				.045
Some primary/none	227 (3.3)	20 (4.4)	17 (3.1)	
Primary school	1833 (26.6)	160 (34.9)	134 (24.5)	
Intermediate/junior	1620 (23.5)	92 (20.0)	139 (25.4)	
Leaving certificate	1152 (16.7)	72 (15.7)	94 (17.2)	
Diploma/certificate	1074 (15.6)	60 (13.1)	86 (15.7)	
Primary degree	586 (8.5)	32 (7.0)	50 (9.1)	
Postgraduate/higher degree	399 (5.8)	23 (5.0)	28 (5.1)	
Smoking status, n (%)				.027
Never	3043 (44.2)	175 (38.1)	240 (43.8)	
Former	2599 (37.7)	187 (40.7)	225 (41.1)	
Current	1249 (18.1)	97 (21.1)	83 (15.2)	
Level of physical activity (IPAQ), n (%)[a]				<.001
Low	2068 (30.0)	209 (45.5)	230 (42.0)	
Medium	2409 (35.0)	142 (30.9)	178 (32.5)	
High	2414 (35.0)	108 (23.5)	140 (25.6)	
BMI (kg/m^2), mean (SD)[a]	28.6 (5.0)	29.8 (5.8)	28.9 (4.8)	.0001
Substance abuse, n (%)	97 (1.4)	17 (3.7)	14 (2.6)	<.001
Private health insurance, n (%)	4014 (58.3)	235 (51.2)	330 (60.2)	.007
Disease prevalence, n (%)				
Hypertension	2456 (35.6)	230 (50.1)	232 (42.3)	<.001
Angina	317 (4.6)	68 (14.8)	42 (7.7)	<.001
Myocardial infarction	264 (3.8)	59 (12.6)	41 (7.5)	<.001
Heart failure	59 (0.9)	16 (3.5)	10 (1.8)	<.001
Diabetes	486 (7.1)	66 (14.4)	58 (10.6)	<.001
Stroke	81 (1.2)	19 (4.1)	12 (2.2)	<.001
TIA	109 (1.6)	29 (6.3)	24 (4.4)	<.001
Valvular heart disease	303 (4.4)	41 (8.9)	31 (5.7)	<.001
Cardiac arrhythmia	413 (6.0)	82 (17.9)	68 (12.4)	<.001
High cholesterol	2592 (37.6)	199 (43.4)	220 (40.2)	.030
Chronic lung disease	248 (3.6)	49 (10.7)	20 (3.7)	<.001
Parkinson disease	32 (0.5)	4 (0.9)	6 (1.1)	.087
Cancer or malignant tumour	375 (5.4)	40 (8.7)	82 (15.0)	<.001
None of these	2453 (35.6)	72 (15.7)	136 (24.8)	<.001
History of open heart surgery, n (%)	71 (1.0)	18 (3.9)	13 (2.4)	<.001
Frailty[a,b]				<.001
Nonfrail	3443 (71.1)	148 (48.8)	203 (52.2)	
Prefrail	1308 (27.0)	122 (40.3)	160 (41.1)	
Frail	89 (1.8)	33 (10.9)	26 (6.7)	
Function ADLs, n (%)				<.001
0 ADLs	6411 (93.0)	367 (80.0)	476 (86.9)	
1 ADL	332 (4.8)	57 (12.4)	41 (7.5)	
2 ADLs	80 (1.2)	17 (3.7)	11 (2.0)	
3 or more ADLs	68 (1.0)	18 (3.9)	20 (3.7)	
Polypharmacy, n (%)[a]	1198 (17.6)	227 (49.9)	170 (31.3)	<.001
Antidepressants, n (%)	430 (6.2)	49 (10.7)	43 (7.9)	.001
Psycholeptics, n (%)	410 (6.0)	66 (14.4)	34 (6.2)	<.001
Opioids, n (%)	184 (2.7)	35 (7.6)	38 (6.9)	<.001

(Continues)

TABLE 1 (Continued)

Characteristics	No Hospitalisation n = 6891	Hospitalisation n = 459	Surgery n = 548	*P* Value
Cognitive scores: MMSE score, median (IQR)	29 (28 30)	28 (27 30)	29 (27 30)	.0001
Mental health				
CES-D, mean (SD)	5.6 (7.0)	7.6 (7.9)	6.7 (7.9)	.0001
CES-D ≥ 16 depression diagnosis, n (%)	605 (8.8)	71 (15.5)	70 (12.8)	<.001

Abbreviations: ADLs, activities of daily living; BMI, body mass index; CES-D, Centre for Epidemiologic Studies Depression; IQR, interquartile range; MMSE, Mini-Mental State Examination; TIA, transient ischaemic attack.

[a]Missing data: BMI, n = 2199 (14.6%); frailty, n = 2366 (15.7%); polypharmacy, n = 71 (0.5%); MMSE, n = 2190 (14.6%).

[b]Frailty: Frailty phenotype as described by Fried 2001.[47]

For those in the hospitalisation group, 341 (74.3%), 70 (15.3%), and 48 (10.4%) participants had 1, 2, or >2 hospital admissions at wave 1, respectively; the corresponding figures for wave 2 were 339 (75.7%), 61 (13.6%), and 48 (10.7%). For those in the surgical group at wave 1, a total of 440 (80.3%), 79 (14.4%), and 29 (5.3%) had 1, 2, or >2 surgeries performed during their hospital admissions, respectively. The corresponding figures for wave 2 were 375 (78.5%), 81 (17.0%), and 22 (4.6%).

3.4 | Cognitive scores at wave 1

Cognitive scores were on average high across all groups as would be expected in this generally healthy population. There were minor differences in unadjusted Mini-Mental State Examination (MMSE)[48] scores between the hospitalisation group, the hospitalisation with surgery group, and the reference group at wave 1 (median [interquartile range] = 28 [27-30] versus 29 [27-30] and 29 [28-30]). There were appreciable unadjusted differences between the groups in other cognitive variables, typically becoming worse from control to surgery to hospitalisation groups.

3.5 | CES-D scores at wave 1

There were minor differences in unadjusted CES-D scores between the hospitalisation group, the hospitalisation with surgery group, and the reference group at wave 1 (mean [SD] = 7.6 [7.9] versus 6.7 [7.9] and 5.6 [7.0]). There were appreciable unadjusted differences in the unadjusted CES-D cut-off scores for depression diagnosis between the hospitalisation group, the hospitalisation with surgery group, and the reference group at wave 1 (15.5% versus 12.8% and 8.8%).

3.6 | 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 increasing depressive symptoms from fully adjusted mixed-effects regression models using the full analytic sample is presented in Table 2 (T2). Models were compared before and after adjustment for covariates; associations with the explanatory variables was robust to covariate adjustment. Therefore, results are reported from the fully adjusted models, which provide the most conservative estimates of association when compared with univariate analysis.

3.7 | Depressive symptoms

There was evidence of a difference across groups (P = 0.001); compared with the control group, there was a 7% increase in depressive symptoms using the CES-D in individuals hospitalised prior to waves 1 and 2 (IRR [95% CI] = 1.07 [1.02-1.11], P = .001) and a 4% increase in depressive symptoms in the surgery group (IRR [95% CI] = 1.04 [1.00-1.08], P = .038).

There are 2 estimates of the variance in the coefficients, one for households about the central intercept estimate for the sample and the other for individuals within households about the central estimate for their given household. The estimates from the fully adjusted mixed-effects Poisson regression model show that 58% [(0.86/0.86 + 0.62) * 100] of the explained variance in the coefficients occurs within households, while the remainder occurs among households.

TABLE 2 Results of CES-D depression outcome by exposure type for waves 1 and 2: (1) reference group, no hospitalisation/no surgery; (2) hospitalisation, no surgery group; and (3) hospitalisation and surgery group within 12 months

Depression Measure	Hospitalisation			Surgery			*P* (Omnibus)
	Coefficient	95% CI	*P* Value	Coefficient	95% CI	*P* Value	
CES-D[a,b] continuous outcome	1.07	(1.02, 1.11)	.001	1.04	(1.00-1.08)	.038	.0014

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; IPAQ-short, short International Physical Activity Questionnaire.

[a]Adjusted for age, sex, education, smoking status, alcohol and substance abuse, IPAQ-short, history of open heart surgery, cardiovascular disease, diabetes, cerebrovascular disease, Parkinson's disease, chronic lung disease, and antidepressants.

[b]CES-D continuous outcome scores presented as incidence rate ratio; values greater than 1 indicate an increased incidence of depressive symptoms.

3.8 | Sensitivity analysis

In the sensitivity analysis, the hospitalisation group exhibited a similar but stronger pattern to the original analysis of depressive symptoms (Table S3 [ST3]). In the surgery group, there was also a similar and stronger pattern of increasing depressive symptoms when compared with the original analysis (ST3).

The additional sensitivity analysis with further adjustment for medications including opioids and psycholeptics reported a similar pattern of increasing depressive symptoms following exposure (Table S4 [ST4]).

Further sensitivity analysis adjusting for only the most prevalent co-morbidities (hypertension, hypercholesterolaemia, arrhythmia, angina, diabetes, myocardial infarction, and chronic lung disease) was also performed. Results were in line with the main analysis. There was evidence of a difference across groups ($P = .0001$); compared with the control group, there was an 8% increase in depressive symptoms using the CES-D in individuals hospitalised prior to waves 1 and 2 (IRR [95% CI] = 1.08 [1.04-1.12], $P < .001$) and a 5% increase in depressive symptoms in the surgery group (IRR [95% CI] = 1.05 [1.01-1.09], $P = .016$).

4 | DISCUSSION

In this population-representative longitudinal cohort study, we have identified an association between hospitalisation, with and without surgery, and an increase in subsequent depressive symptoms in individuals over the age of 50. This was observed after full adjustment of all models and supports our hypothesis that hospitalisation is a stressful life event associated with increased depressive symptoms. In addition to assessing the impact of hospitalisation on mood, our study also has a unique ability to examine the impact of surgery with anaesthesia on depressive symptoms using an objective validated tool—the CES-D, in the same large nationally representative sample.

Further strengths of TILDA include a population-representative sample inclusive of those with and without health insurance over the age of 50, unlike other studies reliant on data from beneficiaries aged 65 and older with health insurance through a national social insurance programme.[6] Our findings, while in line with previous work in older adults,[6] additionally demonstrate this relationship using cross-sectional and longitudinal analysis among middle-aged and older individuals, adding to the sparse literature to date. One cross-sectional study of 7197 community-dwelling adults over 65 years from the National Health and Aging Trends Study demonstrated that hospitalisation in the previous year was independently associated with substantial depressive symptoms.[6] Another substudy of 1434 adults, mean age of 77.1 years, from the Health and Retirement Study reported an association between hospitalisation for pneumonia and increased depressive symptoms.[5] However, neither study had the ability to examine the relationship between surgery and depressive symptoms. Other strengths include a community sample rather than a clinical sample and a large sample size with adequate statistical power across 2 waves of the study. These study design features bolster the generalisability of our results.

The main limitation of the study is the lack of data pertaining to the indication for hospitalisation, the type of surgery and anaesthesia, and the course of admission. This should serve as a motivation to increase the capability of population-representative studies to avail of hospital admission data, to better understand what may be driving our findings. The CAPI questionnaire asks if participants have been admitted to hospital within the last 12 months; therefore, variability in the timing of CES-D from the participant's discharge date may exist between individuals. Moreover, survivors of hospitalisation and surgery included in the analysis at both waves may not represent *all* survivors as they are likely to be healthier, more cognitively intact, and have fewer depressive symptoms accounting for their willingness to participate. Therefore, it is possible that our results underestimate the impact of exposure on mood experienced by the full sample.

Although findings are weaker in the surgery group, an increase in depressive symptoms following surgery is evident. This may be due post-operative cognitive dysfunction (POCD), a syndrome characterised by impairments in global cognitive function, memory, and executive function in the weeks to months following surgery.[48] While causes of POCD are multifactorial, there is overlap between vascular risk factors for both POCD and depression[49,50] suggesting a common pathway. 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 previous studies have demonstrated that increased depressive symptoms may be a risk factor for subsequent hospitalisation.[51,52] This may be due to the adverse effect of depression on health habits such as smoking, diet, overeating and sedentary lifestyle, poor medication compliance, and adverse physiological effects such as decreased heart rate variability, increased platelet aggregation, and higher levels of inflammatory risk markers.[16] However, our fully adjusted models accounted for this by adjustment for confounders including the use of antidepressants as a surrogate for depression diagnosis. Nonetheless, we acknowledge that our findings may include individuals with a predisposition to depressive symptoms due to previous depression diagnosis or those noncompliant with treatment. Our sensitivity analysis shows an even stronger effect when depressive symptoms at wave 2 are adjusted for wave 1 covariates including use of antidepressants at wave 1, which suggests that our original analysis may underestimate the impact of hospitalisation and surgery on mood due to the inclusion of intermediate variables.

Hospitalisation for a wide range of medical conditions or surgery may lead to an increase in depressive symptoms through several mechanisms. Depression has recently been recognised as a possible prodromal feature for dementia; therefore, our findings may represent individuals with undiagnosed cognitive impairment.[37] Moreover, approximately 32% of patients with mild cognitive impairment experience depression, which may be reflected in our results.[53] Therefore, causes of increased depressive symptoms after hospitalisation and surgery may be linked to cognitive impairment and are multifactorial; systemic inflammation,[54-56] hypoxaemia,[57] and hypotension,[58] all potentially mediated by the development of delirium.[59,60] In recent years, research has focussed on structural changes within the brain and has proposed vascular risk factors such as cerebrovascular

disease[38] and hypotension[61] as possible attributing factors to depression. An association between late-onset depression and white matter hyperintensities and leukoencephalopathy on neuro-imaging has also been reported.[39] Furthermore, hospitalised patients with a prior history of depression are more vulnerable to recurrent depressive episodes.[62] Hospitalisation for medical illness and surgery may result in prolonged immobility, which can lead to muscle atrophy, neuronal degradation,[63,64] and subsequent physical disability associated with depression.[5,62,65] As outlined, a number of possible mechanisms may be responsible for our findings, and further research is required to delineate these complex pathways.

Our study has demonstrated an association between hospitalisation and surgery in the previous 12 months and a subsequent increase in depressive symptoms. Depressive symptoms and cognitive impairment are associated with an increase in health care utilisation, hospitalisation, rehospitalisation, and premature mortality.[6,11-13,51,52] Increased depressive symptoms following hospitalisation may lead to a decline in cognition and health, resulting in repeat hospitalisation. If this bidirectional relationship can be interrupted through early recognition of depressive symptoms and raising patient, carer, and physician awareness, there is the potential for a reduction in health care utilisation and thus improvements in the overall health and well-being of individuals at a personal and population level.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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