Published in final edited form as:

Ann Surg. 2017 April ; 265(4): 647–653. doi:10.1097/SLA.0000000000001952.

Trajectory of Functional Recovery after Postoperative Delirium in Elective Surgery

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Conflicts of Interest

None of the authors report any conflicts of interest. All co-authors fully disclose they have no financial interests, activities, relationships and affiliations.

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Abstract

Objective—To describe functional recovery following elective surgery and to determine whether improvements differ among individuals who develop delirium.

Summary Background Data—No large studies of older adults have investigated whether delirium influences the trajectory of functional recovery following elective surgery. This prospective observational study assessed this association among 566 individuals age 70 years and older.

Methods—Patients undergoing major elective surgery were assessed daily while in-hospital for presence and severity of delirium using the confusion assessment method (CAM), and their functional recovery was followed for 18 months thereafter. The Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) Scales and the Physical Component Summary of the SF-12 were obtained pre-surgery and at 1, 2, 6, 12 and 18 months. A composite index [standard deviation 10, minimally clinically significant difference (MCID) 2] derived from these scales was then analyzed using mixed effects regression.

Results—Mean age was 77 years; 58% of participants were women and 24% developed post-operative delirium. Participants with delirium demonstrated lesser functional recovery than their counterparts without delirium; at one month the covariate-adjusted mean difference on the functional composite was -1.5 (95% confidence interval, CI: -3.3 , -0.2). From two to 18 months the corresponding difference was -1.8 (-3.2 , -0.3), an effect comparable to the MCID.

Conclusions—Delirium was associated with persistent and clinically meaningful impairment of functional recovery, to 18 months. Use of multifactorial preventive interventions for patients at high risk for delirium and tailored transitional care planning may help to maximize the functional benefits of elective surgery.

Graphical abstract

In a cohort of 566 older patients undergoing elective surgery, delirium was associated with impaired functional recovery, which persisted for 18 months post-surgery. Use of multifactorial preventive interventions for patients at high risk for delirium and tailored transitional care planning may help to maximize the functional benefits of elective surgery.

Keywords

Delirium; functional status; aging; elective surgery; post-operative delirium

INTRODUCTION

Delirium is defined as an acute confusional state marked by global impairments in cognition and attention,¹ which occurs frequently in the context of surgery, acute illness and hospitalization. Post-operative delirium occurs in 11-53% of hospitalized older patients yet is frequently under-diagnosed.¹ It conveys significant mortality and morbidity, increasing risk of institutionalization, caregiver burden, cognitive impairment and death.² The pathogenesis of delirium and the mechanisms underlying its complications and sequelae remain incompletely understood.

Although most delirium is short-lived, longer-term effects of an episode of delirium may impact a patient's ability to recover from surgery and hospitalization. For example, in the shorter-term, delirium is associated with increased postoperative complications and longer-hospital stays. The long-term effects of delirium include increased risk of institutionalization, more frequent re-hospitalizations and prolonged physical and cognitive impairment. Several recent studies have shown that delirium is associated with impaired cognitive function for up to a year after the episode.^{3, 4} However, the long-term consequences for physical functioning of delirium have not been well-established, with much of the work in this area focusing on one to three months after an episode of delirium.^{5, 6} These studies have generally concluded that delirium is associated with poor functional recovery in the first few months following surgery, but over longer periods of follow-up (e.g., 12 months) functional status has been considered to be comparable in patients who did and did not develop delirium.⁷

Previous studies have typically limited their assessment of physical function to broad measures such as the Activities of Daily Living (ADL)⁸ and the Instrumental Activities of Daily Living (IADL),⁹ which may not adequately capture differences in domains of functioning, such as moderate activities, including climbing stairs and regular volunteer work. Improvement in the ability to perform such activities is often the goal of elective surgeries, particularly orthopedic and vascular surgeries, necessitating a better understanding of the association between delirium and these functional outcomes. Thus, use of an assessment of physical functioning that includes global measures of function such as ADLs and IADLs as well as more specific activities associated with quality of life, such as stair climbing and volunteer work, would provide a more complete view of physical functioning following surgery. The frequency of elective surgeries is increasing among older patients,^{10, 11} Understanding how delirium may change the trajectory of functional recovery after surgery may have important clinical implications, such as planning the content, timing and duration of pre-habilitation, acute hospital, and rehabilitation services.

The current study describes how delirium modifies the trajectory of functional performance, assessed using a variety of tools that include IADL and ADL measures as well and more fine-grained assessments of moderate activities in the 18 month period after elective surgery in a cohort of older patients. Since the goal of most of our surgeries is to improve functioning, we hypothesized that functional performance would, overall, improve in the 18 months following surgery but that patients who developed delirium would have less improvement compared to those who did not develop delirium.

METHODS

Study Design and Cohort Assembly

Our study population is from the Successful Aging after Elective Surgery (SAGES) study, an ongoing prospective cohort study of older adults undergoing major elective surgery. The study design and methods have been described in detail previously.¹² In brief, eligible participants were age 70 years and older, English speaking and able to communicate verbally, scheduled to undergo elective surgery at two Harvard-affiliated academic medical centers with an anticipated length of stay of at least 3 days, and available for in-person follow-up interviews. Eligible surgical procedures were: total hip or knee replacement, lumbar, cervical, or sacral laminectomy, lower extremity arterial bypass surgery, open abdominal aortic aneurysm repair, and open or laparoscopic colectomy. Exclusion criteria included evidence of dementia, delirium, prior hospitalization within 3 months, legal blindness, severe deafness, terminal condition, history of schizophrenia or psychosis, and history of alcohol abuse or withdrawal. A total of 566 patients met all eligibility criteria and were enrolled between June 18, 2010 and August 8, 2013.

Written informed consent for study participation was obtained from all participants according to procedures approved by the institutional review boards of Beth Israel Deaconess Medical Center and Brigham and Women's Hospital, the two study hospitals, and Hebrew SeniorLife, the study coordinating center, all located in Boston, Massachusetts.

Main Study Variables

Delirium—The main predictor variable for this study is incident delirium occurring post-operatively. Trained interviewers assessed patients daily throughout hospitalization for the development of delirium using the Confusion Assessment Method, CAM,¹³ a standardized method for delirium identification that has high sensitivity, specificity and inter-rater reliability.¹⁴ The CAM diagnostic algorithm requires the presence of acute change or fluctuating course, inattention, and either disorganized thinking or an altered level of consciousness to fulfill criteria for delirium. A standardized chart review method^{15, 16} supplemented the CAM to increase sensitivity.

Outcome measures—The main outcomes were measures of physical functioning, including the Activities of Daily Living Scale (ADLs),⁸ Instrumental Activities of Daily Living Scale (IADLs)⁹ and physical function items from the Medical Outcomes Study Short Form 12. These were assessed at baseline and 1 month, 2 months, 6 months, 12 months and 18 months after surgery. The ADL scale evaluates ability to perform basic care skills of feeding, bathing, dressing, grooming, toileting, transferring and walking. The IADL scale evaluates the ability to perform more complex skills of using the telephone, grocery shopping, using transportation, cooking, housekeeping, taking medications and managing finances. SF-12 Physical Function Summary score evaluates moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf; climbing several flights of stairs; and regular work or volunteer activities. The ADL, IADL and SF-12 Physical Function variables were combined into a Physical Function Composite score that was standardized to the nationally representative Patient Reported Outcomes Measurement

Information System (PROMIS) normative sample, such that in the normative sample the score would have a mean of 50 and a standard deviation of 10 points.¹⁷ The majority of SAGES participants had composite scores at baseline between 30 and 50 points; that is, between values at the normative mean and two standard deviations below that mean. Because of the known ceiling effects of ADL and IADL we chose to focus on the Physical Function Composite as the primary outcome measure for these analyses.

Other Study Variables

All the study participants completed a baseline interview approximately two weeks before surgery. The interview included age, gender, ethnicity, years of education, height, weight (for body mass index), living situation, Minnesota Leisure Time Assessment (MLTA),¹⁸ Geriatric Depression Scale (GDS),¹⁹ and the modified Mini-Mental State (3MS).²⁰ Medical records were reviewed to determine the type of surgery planned (orthopedic, vascular, colectomy) and score the Charlson co-morbidity index.²¹

Statistical Analysis

STATA 13 and SAS version 9.3 (SAS Inc., Cary, NC) and R version 2.3.2 (R Foundation for Statistical Computing, Vienna, AU) were used to conduct statistical analyses. Summary characteristics were derived for the overall sample as well as those with and without delirium in hospital. Linear and logistic mixed effects regression modeling was used to assess the association between delirium status and physical function variables (ADL's, IADL's SF-12 and the physical function composite). Models were adjusted for age, sex, Charlson Co-morbidity Index, education, surgery type, body mass index (BMI), depressive symptoms and 3MS scores. The estimated mean differences between participants were derived from comparisons of the delirium and non-delirium groups at one month, two months and thereafter. All point estimates were accompanied by robust (sandwich) 95% confidence intervals, and null hypotheses tested using Wald statistics. A likelihood ratio test was used to assess the composite influence of delirium on functional recovery at all time points simultaneously. As a check of convergent validity of the functional composite, we examined its association with four-meter gait speed, which is considered to be a cardinal indicator of physical functioning.²²

RESULTS

Baseline Characteristics

Demographic and baseline clinical characteristics of the 566 subjects included in this study are summarized in Table 1. The mean (standard deviation; **SD**) age of the patients was 77 years (5.2). More than half (58%) were women and most were white or non-Hispanic (92%). Post-operative delirium developed in 135 (24%) of patients. Compared with patients who did not develop delirium, those who developed delirium were older on average, with greater Charlson co-morbidity scores, higher depressive symptoms, and lower 3MS scores.

Physical Function Composite, PROMIS-scaled

Exploratory assessments revealed that baseline functional status was poorer among participants who developed delirium, but that these differences appeared to increase rather

than decrease post-surgery (Figure 1). To formally estimate the magnitude of these differences, we obtained model-based estimates of function recovery as quantified by our PROMIS-scaled composite score from baseline to 18 months after surgery in our elective surgery population (Table 2). The mean baseline (preoperative) composite score for patients who developed delirium was 36.7 points (95% confidence interval, CI: 35.0, 38.4) while the composite score for patients who did not develop delirium was 39.2 points (95% CI: 38.3, 40.2); the baseline mean (95% CI) difference between groups was therefore -2.5 points (95% CI: -4.5 , -0.6). Both groups' physical function composite (overall) score had declined at one month following surgery, but participants who developed delirium declined significantly more, to an average score of 33.9 compared with 37.9 in the non-delirious group [such that at 1 month the mean difference had increased in magnitude by 1.5 points, to -4.0 points (95% CI: -5.9 , -2.1)]. Both groups experienced improved physical function between 1 and 2 months post-surgery, but the delirium group demonstrated less recovery compared with those who did not develop delirium [mean difference -4.3 points (95% CI: -6.1 , -2.5) points].

Using multivariable modeling, we examined the overall physical function trajectory from baseline to 18 months post-surgery (Table 3). We adjusted for age, sex, Charlson Comorbidity Index, education, surgery type, body mass index, GDS score and 3MS score. At one month, the difference between participants who exhibited delirium in-hospital and those who did not was -1.5 points (95% CI: -3.3 , -0.2) above and beyond the difference exhibited at baseline, consistent with the unadjusted differences in excess of baseline described above and in table 2. At two months and thereafter, the corresponding quantity was -1.8 points (95% CI: -3.2 , -0.3). These effects were comparable to the minimum clinically important difference demonstrated for the PROMIS-scaled measure (2.0 points) in prior work, which was the within-person mean change consistent with having reported feeling "a little better" or "a little worse" over 12 months in a prior large cohort.²³ In addition to time-specific effects, the evidence for an overall effect of delirium on the trajectory of functional recovery was statistically significant ($p = 0.04$ by the likelihood ratio test).

Although the initial decline in overall physical function was greater among patients with delirium at one month post-operatively, the rate of recovery among these patients was similar between the first and second months post-operatively (Table 3, Figure 1). However, participants with delirium did not ever achieve recovery comparable to those without delirium, such that the negative effect of delirium was persistent at all post-surgery time points.

The functional composite was strongly associated with 4-meter gait speed (Pearson correlation -0.48) at baseline, such that a one-unit difference in the composite measure was associated with a -0.12 m/s difference in gait speed, a robust and clinically meaningful difference.²² Thus, convergent validity of the composite measure is demonstrated with a widely-accepted performance based measure of physical functioning.

IADL Recovery

We examined the trajectory of IADL recovery from baseline to 18 months after surgery in this elective surgery population (Figure 1, Table 2). At baseline, patients who developed

delirium had a mean IADL score of 13.2 points (95% CI: 12.9, 13.4) (on a 14-point scale) while patients who did not develop delirium had a mean IADL score of 13.5 points (95% CI: 13.4, 13.6) [mean difference attributable to delirium: -0.3 points (95% CI: $-0.6, -0.1$), $p < .05$]. Both groups' IADL scores declined in the month following surgery but the patients who developed delirium declined significantly more to a mean score of 11.8 compared to 12.6 in the non-delirious group [mean difference -0.8 points (95% CI: $-1.2, -0.4$), $p < 0.05$]. Both groups experienced IADL recovery between 1 and 2 months post-surgery, but the difference remained significant between those who developed delirium and those who did not [mean difference -0.5 points (95% CI: $-0.8, -0.2$)] in months 2 to 18. Thus the difference apparently attributable to delirium was statistically significant at 1 month difference -0.5 points (95% CI: $-0.8, -0.05$)] but not thereafter [-0.2 points (95% CI: $-0.4, 0.05$)]]; see Table 3.

SF-12 Physical Functioning Items and ADLs Dependency Score

We examined the trajectory of other physical function items, SF-12 Physical items and ADL dependency scores, from baseline to 18 months after surgery in this elective surgery population (Appendix Tables 1 and 2). Group differences by delirium status in the sum of the SF-12 physical component summary were similar to those observed for IADL scores, with significantly less functional improvement over the 18-month post-operative period in the group who developed delirium compared to those who did not (Appendix Table 1). Trajectories by delirium status on SF-12 physical function was similar to those observed for the composite score with significantly less functional improvement from two to 18 months (Appendix Table 2).

There was little change, irrespective of delirium status, in ADL dependency scores or trajectory over the 18-month follow-up period; there was limited evidence of a significant adverse effects of delirium at one month, but this effect did not persist (Appendix Table 2).

Sensitivity Analysis – Orthopedic Subgroup

We conducted a sensitivity analysis where we restricted the sample to those undergoing orthopedic surgery (N=460) since these surgeries might be most likely to improve physical function (Appendix Table 3). In this subsample, effects apparently attributable to delirium were consistent with those observed in the overall sample, but of slightly lesser magnitude and statistical significance.

DISCUSSION

We found that the trajectory of physical function after elective surgery was characterized by an initial decline in function in the month after surgery followed by improvements in function over months 2-18. Although all patients experienced improvements in function above their preoperative level in the 18-months after surgery, those who developed post-operative delirium during the index hospitalization had less relative improvement in function compared to those who did not develop delirium, with effect sizes that correspond to clinically. Moreover, this difference attributed to delirium persisted through the 18 month follow-up period of our study. Our findings suggest that the development of post-operative

delirium, which has sometimes been characterized as a transient disorder, may prevent patients from gaining full functional recovery, and thus, from experiencing the maximum long-term functional benefits from surgery. Results were consistent though less definitive when we restricted the sample to patients undergoing orthopedic surgery.

With the aging of the patient population undergoing elective surgery, patients, their families and clinicians are increasingly concerned with quality of life outcomes after surgery, including functional capacity beyond activities of daily living. Previous studies have reported that delirium is associated with short-term functional impairment, but only a few have examined long-term functional capacity and delirium.^{5-7, 24, 25} Our findings extend the previous work in important ways. First, the follow-up period was longer, up to 18 months following surgery, allowing us to span the duration of the initial postoperative recovery period and rehabilitation. In addition, our measures allowed us to capture a wider variety of functional activities that might improve following elective surgery. Previous studies have been limited in their assessment of physical function which typically included only global measures of more basic abilities such as the ADL and IADL scales. Since the goal of many elective surgeries is to improve function in a broader set of activities including moderately demanding household chores and leisure-time activities, extending measurement of physical function to include these factors is important and informative. Moreover, these broader measures of function, such as the SF-12 physical components, may also have more variability in an older surgical population and are not as limited by ceiling effects as the ADL and IADL scales. Our main outcome was a composite measure that included the physical function items from the SF-12 in addition to the more global measures of functional ability (ADL and IADL) and thus provides the more complete view of physical function that is important to patients and their families.

A major strength of our study is the large, well-characterized cohort with multiple measures of physical function, state-of-the art delirium assessment and rich clinical and patient-interview data. We had follow-up that extended 18 months post-operatively to capture longer-term functional outcomes of post-operative delirium than have been previously reported. Several limitations of the study are also important to note. Our sample was highly educated, primarily white and was recruited from two hospitals in a single geographical area. Thus, the generalizability of our findings will need to be confirmed in other studies. While the inclusion of multiple surgery types is a relative strength, improved functional capacity is the main goal of orthopedic and vascular surgery more so than colectomy. However, in a sensitivity analysis restricted to the orthopedic surgery group, we found results similar to the findings in the overall cohort. It is possible that more recovery would have occurred beyond 18 months in the delirious group, and extended follow-up may be helpful in future studies. Patients with delirium had a lower functional baseline prior to the surgery. Our study cannot rule out the possibility that these patients had other pre-existing factors besides delirium that contributed to their less favorable postoperative functional recovery. Finally, while our functional composite measure (based on 3 widely used self-report measures) correlated well with one important performance-based measure (gait speed), future work to replicate our findings with other performance-based measures would help to extend the work.

Conclusion

This large prospective study of patients undergoing elective surgery showed development of postoperative delirium was associated with impaired functional recovery in the 18-months after surgery. These findings are of clinical relevance since the risk of delirium can be assessed pre-operatively using established risk-prediction tools^{26, 27} and preventive interventions targeted to the risk factors may help to reduce the rate of delirium, such as the Hospital Elder Life Program.²⁸ An implication of our findings is that use of multifactorial preventive interventions for patients at high risk for delirium, increased surveillance for delirium in the postoperative period, and consideration of tailored transitional care planning and extended rehabilitation may be needed to maximize the functional benefits of elective surgery in our increasing older population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The authors gratefully acknowledge the contributions of the patients, family members, nurses, physicians, staff members, and members of the Executive Committee who participated in the Successful Aging after Elective Surgery (SAGES) Study. This work is dedicated to the memory of Joshua Bryan Inouye Helfand.

Sources of Funding:

This manuscript was supported in part by Grants No. P01AG031720 (SKI), K07AG041835 (SKI), T32AG000158(TH), from the National Institute on Aging from the National Institutes of Health. Dr. Hshieh is supported by a NIH funded T32 Training Grant (T32AG000158). Dr. Saczynski is supported by U01HL105268 from the National Heart Lung and Blood Institute and K01AG33643 from the National Institute on Aging. Dr. Marcantonio is supported by grant number K24AG035075 from the National Institute on Aging. Dr. Inouye holds the Milton and Shirley F. Levy Family Chair. The funding sources had no role in the design, conduct, or reporting of this study.

Abbreviations

BIDMC	Beth Israel Deaconess Medical Center
BWH	Brigham and Women's Hospital
HMS	Harvard Medical School
HSL	Hebrew SeniorLife
MGH	Massachusetts General Hospital
PI	principal investigator
UCONN	University of Connecticut Health Center

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Figure 1.

Sample mean changes in physical function by delirium status, as quantified by SAGES functional composite, IADL score, and SF-12 physical component summary, to 18 months post-surgery. 95% confidence interval estimates are also shown.

Table 1
Participant Characteristics at Baseline, mean (standard deviation) or N (percent)

	Overall (N = 566)	Delirium (N = 135)	No Delirium (N = 431)
Age, years	76.7 (5.2)	77.5 (5.0)	76.5 (5.3)
Female	330 (58)	82 (61)	248 (58)
Non-White	43 (8)	13 (10)	30 (7)
Years of Education	15.0 (2.9)	14.7 (3.0)	15.0 (2.9)
Body Mass Index, kg/m ²	29.1 (5.5)	29.7 (5.4)	28.9 (5.6)
Living Alone	169 (30)	40 (30)	129 (30)
Minnesota Leisure Time Activities, Kilocalories expended per week	471 (734)	418 (871)	485 (693)
^a Geriatric Depression Scale (GDS)	2.5 (2.5)	3.0 (2.8)	2.3 (2.4)
GDS 6 or greater	69 (12)	26 (19)	43 (10)
^b Charlson Comorbidity Index (CCI)	1.0 (1.3)	1.3 (1.4)	1.0 (1.2)
CCI 2 or greater	166 (29)	58 (43)	108 (25)
Modified Mini-Mental (3MS), mean (SD)	93.4 (5.4)	91.6 (5.9)	94.0 (5.1)
3MS less than 85	39 (7)	17 (13)	22 (5)
Surgery Type			
Orthopedic	460 (81)	106 (79)	354 (82)
Vascular	35 (6)	11 (8)	24 (6)
General	71 (13)	18 (13)	53 (12)
^c SAGES Functional Composite	38.6 (10.3)	36.7 (10.1)	39.2 (10.3)
^d IADL Dependency Score	0.6 (1.2)	0.8 (1.5)	0.5 (1.1)
^e SF-12 Physical Component Summary	31.6 (7.4)	30.5 (7.2)	31.9 (7.5)

^aFifteen point scale. Score 5 suggestive of clinical depression. Score 10 highly predictive of clinical depression.

^bComorbidities assigned a point value of 1-6, based on severity. Lower score suggests higher 1- or 2-year survival rate.

^cScaled to Patient Reported Outcomes Measurement Information System; nationally representative average score is 50, standard deviation 10.

^dIADL = Instrumental Activities of Daily Living; 14 point scale, measuring independence in telephone use, shopping, meal preparation, housekeeping, laundry, transportation, medication management, finance management (full independence yields a score of 14).

^eSF-12 = Short Form 12; 56 point scale. Score is the mean of the following SF-12 variables (items 2-5 on the interview form): moderate activities, climbing stairs, regular daily activities and work or other activities.

Table 2
Model-based Estimates of Mean Functional Recovery by Delirium Status, to 18 Months Post-Surgery

Point estimates and 95% confidence intervals provided.

SAGES Functional Composite			
Months Post-Surgery	Delirium (N = 135)	No Delirium (N = 431)	Mean Difference
0	36.7 (35.0, 38.4)	39.2 (38.3, 40.2)	-2.5 (-4.5, -0.6)
1	33.9 (32.2, 35.5)	37.9 (37.0, 38.8)	-4.0 (-5.9, -2.1)
2	39.7 (38.0, 41.3)	44.0 (43.1, 44.9)	-4.3 (-6.1, -2.5)
6	40.2 (38.6, 41.8)	44.5 (43.6, 45.3)	-4.3 (-6.1, -2.5)
12	40.9 (39.3, 42.6)	45.2 (44.4, 46.1)	-4.3 (-6.1, -2.5)
18	41.7 (40.0, 43.4)	46.0 (45.1, 46.9)	-4.3 (-6.1, -2.5)

Instrumental Activities of Daily Living Independence Score			
Months Post-Surgery	Delirium (N = 135)	No Delirium (N = 431)	Mean Difference
0	13.2 (12.9, 13.4)	13.5 (13.4, 13.6)	-0.3 (-0.6, -0.1)
1	11.8 (11.5, 12.2)	12.6 (12.4, 12.8)	-0.8 (-1.2, -0.4)
2	13.0 (12.7, 13.2)	13.5 (13.4, 13.6)	-0.5 (-0.8, -0.2)
6	13.0 (12.8, 13.3)	13.5 (13.4, 13.6)	-0.5 (-0.8, -0.2)
12	13.1 (12.8, 13.3)	13.6 (13.5, 13.7)	-0.5 (-0.8, -0.2)
18	13.1 (12.9, 13.4)	13.6 (13.5, 13.8)	-0.5 (-0.8, -0.2)

Table 3
Model-Based Estimates of Influence of Delirium on Functional Recovery to 18 Months
Post-Surgery

Point estimates and 95% Confidence Intervals Provided

SAGES Functional Composite	Unadjusted		^a Adjusted	
	Mean Effect	p-value	Mean Effect	p-value
Mean delirium effect at 1 month	-1.5 (-3.2, 0.3)	0.10	-1.5 (-3.3, 0.2)	0.09
Mean delirium effect, 2-18 months	-1.8 (-3.3, -0.2)	0.02	-1.8 (-3.3, -0.3)	0.02
^b Composite effect on recovery		0.04		0.04

Instrumental Activities of Daily Living Dependency Score	Unadjusted		^a Adjusted	
	Mean Effect	p-value	Mean Effect	p-value
Mean delirium effect at 1 month	-0.5 (-0.8, -0.05)	0.03	-0.4 (-0.8, -0.05)	0.03
Mean delirium effect, 2-18 months	-0.2 (-0.4, 0.05)	0.12	-0.2 (-0.4, 0.05)	0.12
^b Composite effect on recovery		0.003		0.004

^aModels adjusted for participants' age, sex, Charlson Comorbidity Index, education, surgery type, body mass index, Geriatric Depression Screen score and Modified Mini-Mental Status Exam score (3MS)

^bLikelihood ratio test comparing model without any interactions of the delirium term and time factors to model including interactions of the delirium term with all time factors