

# Long-term Cognitive Decline in Older Subjects Was Not Attributable to Noncardiac Surgery or Major Illness

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**Background:** Persistent postoperative cognitive decline is thought to be a public health problem, but its severity may have been overestimated because of limitations in statistical methodology. This study assessed whether long-term cognitive decline occurred after surgery or illness by using an innovative approach and including participants with early Alzheimer disease to overcome some limitations.

**Methods:** In this retrospective cohort study, three groups were identified from participants tested annually at the Washington University Alzheimer's Disease Research Center in St. Louis, Missouri: those with noncardiac surgery, illness, or neither. This enabled long-term tracking of cognitive function before and after surgery and illness. The effect of surgery and illness on longitudinal cognitive course was analyzed using a general linear mixed effects model. For participants without initial dementia, time to dementia onset was analyzed using sequential Cox proportional hazards regression.

**Results:** Of the 575 participants, 214 were nondemented and 361 had very mild or mild dementia at enrollment. Cognitive trajectories did not differ among the three groups (surgery, illness, control), although demented participants declined more markedly than nondemented participants. Of the initially nondemented participants, 23% progressed to a clinical demen-

tia rating greater than zero, but this was not more common after surgery or illness.

**Conclusions:** The study did not detect long-term cognitive decline independently attributable to surgery or illness, nor were these events associated with accelerated progression to dementia. The decision to proceed with surgery in elderly people, including those with early Alzheimer disease, may be made without factoring in the specter of persistent cognitive deterioration.

THERE is a strong public perception supported by a body of scientific research suggesting that cognitive decline with lasting and noticeable impact on daily function is common in elderly patients after surgery.<sup>1-5</sup> Recent *in vitro* and animal *in vivo* research provides biologic plausibility for the pathogenesis and evolution of postoperative cognitive decline (POCD) and even suggests that general anesthetic agents have the potential to precipitate or exacerbate Alzheimer disease.<sup>6-9</sup> The prospect of POCD may increase anxiety among older surgical patients and their families and may impact the decision to proceed with surgery. However, there are several important logistic and methodologic challenges that have made it difficult to study POCD in the clinical context, and studies have yielded conflicting results. First, it is generally impossible to determine whether participants were already on a trajectory of cognitive decline before surgery because multiple assessments of cognitive function in the period preceding surgery are difficult to obtain.<sup>1,2,10</sup> Second, previous studies have often not addressed the effects of surgery on cognitive function in participants with preexisting cognitive dysfunction or Alzheimer disease.<sup>1,2,10</sup> Finally, it is difficult to include appropriate control groups, which would consist of people who are well matched to the surgical group for all major confounders, because the relevant confounders are not well characterized.<sup>1,2,10-12</sup> We sought to conduct a study that would overcome some of these challenges.

Postoperative cognitive decline is an ambiguously defined clinical condition that has no universally accepted diagnostic criteria.<sup>3,11,13,14</sup> The natural history of POCD is unclear; the patient population exhibiting POCD at 1 week postoperatively only moderately overlaps the patient population exhibiting POCD 3 months later.<sup>1-3,10,14</sup> Strikingly, cognitive decline has not been consistently demonstrated to persist beyond 3 months after surgery.<sup>3,13,14</sup> Lasting cognitive decline has been found in more than 40% of patients up to 5 yr after cardiac surgery,<sup>15</sup> but the use of cardiopulmonary bypass may independently contribute to

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this cognitive decline.<sup>16,17</sup> The possible lack of lasting cognitive decline after noncardiac surgery has fueled a controversy surrounding the clinical significance and even the existence of POCD as a distinct phenomenon.<sup>14,18</sup> Interestingly, cognitive decline has also been described with both acute and chronic illness. For example, patients with cardiovascular disease perform worse than healthy controls on tests of cognitive function.<sup>19</sup>

When patients present for surgery or have acute exacerbation of illness, they may already have preexisting cognitive decline. Knowledge of a person's trajectory before surgery or illness is extremely important; an apparent decline in psychometric performance after surgery or illness compared with baseline performance could merely reflect a preexisting trend. Previous studies of POCD have tried to address this concern by excluding people on the basis of low scores on cognitive screening assessments such as a score less than 24 on the Mini-Mental State Examination.<sup>2,10</sup> However, this strategy cannot discriminate trends in cognitive function and could only exclude people who are already clearly demented. Existing studies of POCD have, at most, a single cognitive assessment before surgery. Because illness is not usually a predictable event, pre-event cognitive trends have also not been assessed in previous studies of post-illness cognitive decline.

Another problem with current methodologies is the assumption that the learning effect in individual surgical patients can be estimated from the average learning effect observed in a cohort of nonsurgical control patients.<sup>1,2,10</sup> This correction could severely compromise the research if the learning effect in the surgical group were more variable or had a different magnitude than in the control group. Another important advantage of obtaining multiple assessments before the event is that the learning effect is essentially decoupled from any potential effect of surgery or illness.

The Alzheimer's Disease Research Center (ADRC) at Washington University in St. Louis, Missouri, is a multidisciplinary undertaking that includes the participation of neurologists, psychiatrists, geriatricians, psychologists, clinical nurse specialists, educational specialists, social workers, and biostatisticians. It provides expert assessments of cognitive functioning in normal aging and dementia. The ADRC continually enrolls research participants, not patients, without regard to their baseline cognitive function; volunteers in the database have an average age of approximately 75 yr, and some have been assessed longitudinally for up to 21 yr. There is variable cognitive impairment among those included in the database. Both intercurrent illness and surgery are tracked. One of the unique features of the ADRC database is that it allows the estimation of trends of cognitive function before surgery or illness.

We sought to use this resource to test the hypothesis that there is measurable and lasting cognitive decline after ei-

ther noncardiac surgery or major illness in older adults. We further wanted to determine whether people with preexisting mild cognitive impairment or early Alzheimer disease are particularly vulnerable and have more substantial cognitive decline after surgery or illness. This innovative investigative approach to postoperative cognitive decline incorporates substantial pre-event data and includes people with known preexisting cognitive impairment.

## Materials and Methods

### *The Sample*

Approval for this retrospective study was obtained from the Human Research Protection Office at Washington University in St. Louis and from the Executive Committee of the ADRC. We extracted three groups from the ADRC database: (1) those who did not undergo surgery and had no major illness, (2) those who underwent surgery, and (3) those who were admitted to a hospital for a major illness not requiring surgery. Those eligible included nondemented participants and those with dementia of the Alzheimer type at the Clinical Dementia Rating (CDR) 0.5 or 1 level at the time of enrollment. All initially selected participants had at least three psychometric assessments. Those undergoing cardiac surgery, carotid surgery, and neurosurgery were excluded, as were those who had a stroke or cardiac arrest. They were excluded because these events are thought to be associated with cognitive decline and could be potential confounders. Participants were also excluded if they experienced both surgery and an unrelated major illness, if there were incomplete psychometric assessments, or if their initial CDR was determined as 0.5, whereas they were assessed at the CDR 0 level at subsequent evaluations.

### *Clinical Assessment*

Research participants provided detailed medical histories at the time of enrollment in the ADRC and at subsequent evaluations that occurred approximately annually. At all assessments, semistructured interviews with the participant and a collateral source (usually the spouse or an adult descendant) were performed by one of a group of experienced clinicians; for each assessment, the clinician performing the evaluation was randomly chosen from the group of clinicians. In addition, general physical and neurologic examinations of the participant were completed. The Washington University Human Research Protection Office approved all procedures used at the ADRC; both the participant and the collateral source gave written informed consent.

Information from both the collateral source and participant portions of the protocol was used by the clinician to determine the Washington University CDR,<sup>20</sup> by which a CDR of 0 indicates no detectable dementia, and CDRs of 0.5, 1, 2, and 3 indicate very mild, mild, mod-

**Table 1. Sample Characteristics**

	n	Initial Age, yr		Age at Event, yr		Men		Education, yr	
		Mean	SD	Mean	SD	No.	%	Mean	SD
CDR 0									
Control	108	73.7	9.4	—	—	31	29	14.5	2.9
Surgery	72	74.1	10.0	77.3	9.6	27	38	14.8	2.8
Illness	34	77.9	10.4	81.6	10.4	10	29	14.7	3.1
CDR 0.5									
Control	86	73.9	8.0	—	—	43	50	13.9	2.9
Surgery	81	74.9	9.3	77.7	8.8	38	47	13.6	3.3
Illness	58	76.5	8.2	79.5	8.4	24	41	13.8	3.4
CDR 1									
Control	82	73.6	7.8	—	—	32	39	12.1	3.5
Surgery	27	76.2	10.9	78.3	10.9	14	52	13.2	4.0
Illness	27	75.9	10.9	78.1	10.2	10	37	12.5	3.6

The control group did not have surgery or a major illness over the course of the study.

CDR = Clinical Dementia Rating.

erate, and severe dementia, respectively. The CDR is a global measure of dementia severity and is based solely on clinical information without reference to psychometric performance (table 1). Excellent interrater reliability for the CDR has been established (weighted  $\kappa$  of 0.87).<sup>21</sup> Only individuals with CDRs of 0, 0.5, or 1 before the event they experienced (or initially for those experiencing no event) were included. Those with more severe dementia were excluded because they are often unable to complete the measures included in the psychometric assessment.

### Psychometric Assessment

The 1.5-h psychometric battery, which has been described in greater detail previously,<sup>22</sup> was administered to all participants by trained psychometricians, usually a week or two after the annual clinical assessment. The mean time between the first and second psychometric assessments, for example, was 1.09 yr (SD, 0.19 yr; median, 1.05 yr). The psychometrician was unaware of the individual's diagnosis or dementia severity rating. Episodic memory was assessed with the Logical Memory and Associate Learning subtests of the Wechsler Memory Scale<sup>23</sup> and the Visual Retention Test (Form C, 10-s exposure).<sup>24</sup> Semantic memory was assessed with the Information subtest from the Wechsler Adult Intelligence Scale<sup>25</sup> and the Boston Naming Test.<sup>26</sup> Speeded psychomotor and visuospatial ability was evaluated using the Wechsler Adult Intelligence Scale<sup>25</sup> Block Design and Digit Symbol subtests, Trailmaking Test Part A,<sup>27</sup> and Crossing-Off.<sup>28</sup> An untimed measure of visuospatial ability was Form D of the Visual Retention Test.<sup>24</sup> The final set of measures in the battery assessed attention and executive ability using the Wechsler Memory Scale<sup>23</sup> Mental Control and Digit Span (forward and backward) subtests and word fluency for S and P.<sup>29</sup> A composite factor z score based on the empirically derived weights from the general factor from a principal components

analysis of scores from nondemented people reported previously served as a general summary measure.<sup>22</sup>

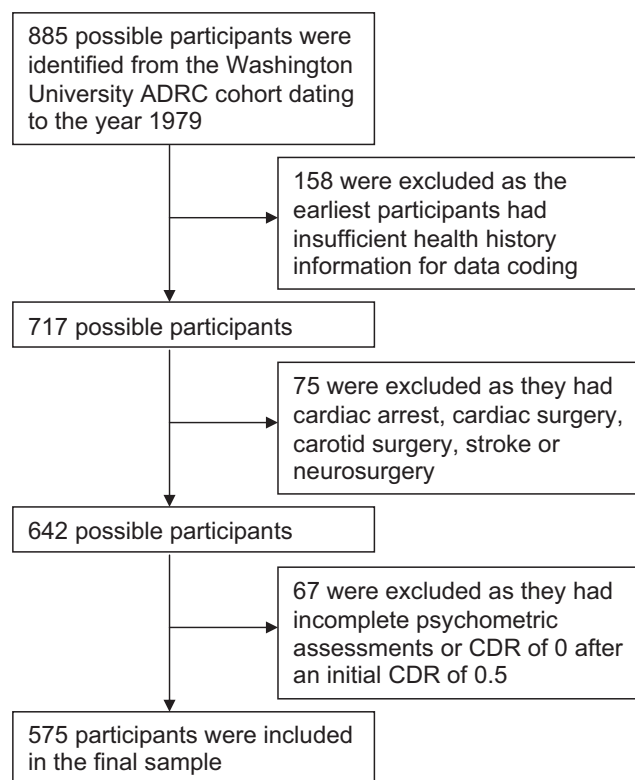
### Statistical Analyses

The groups were compared with analysis of variance for the quantitative variables, such as initial age and education, and chi-square tests of association for qualitative variables, such as sex and progression to a CDR greater than 0. Groups were compared on number of assessments after the event using the Kolmogorov-Smirnov nonparametric test. Significance levels for analyses were set at 0.05, and inference testing was with two-tailed tests.

For participants without dementia, the duration of time from initial assessment to the time participants progressed to a nonzero CDR was analyzed using Cox proportional hazards regression (SPSS version 15.0; SPSS, Chicago, IL) with initial age, group membership (surgery, illness, control [no event]), and their interaction in the model.

The effect of surgery and major illness on longitudinal course of the psychometric score in the nondemented cohort before progression to a nonzero CDR was analyzed using a general linear mixed effects model implemented in the R statistical environment (Vienna, Austria) using the lme4 package. A piecewise linear growth curve over time with a single breakpoint at the time of surgery or illness was assumed for each person, and the variation among individuals was modeled by assuming random coefficients (intercept, slope before the event, and the slope after the event) that follow a multivariate normal distribution nested within groups. The fixed effects included in the model were current age and years of education. A similar mixed model piecewise analysis using all available longitudinal psychometric data were conducted for the demented people in which the variation among individuals was modeled by assuming random coefficients (intercept, slope before the event, and





**Fig. 1. Inclusion of participants in the study.** ADRC = Alzheimer's Disease Research Center; CDR = Clinical Dementia Rating.

slope after the event) that follow a multivariate normal distribution nested within group and dementia severity (very mild *vs.* mild).

The outcomes of interest were the slopes before and after the event and the difference between these slopes. To ensure comparability of the control group with the surgical and illness groups, a simulated event was modeled for the control group. The model was fitted 5,000 times with event times for control patients randomly drawn with replacement from the empirical distribution of event times stratified by CDR. Only participants with at least two assessments after the event were included in the analyses. For each outcome, the mean slope was estimated as the mean from the 5,000 models with variance estimated by combining the variance of the means from the 5,000 models with the mean variance obtained from the models. Outcomes in the surgery and illness groups were compared against the control group using the normal Z test, which is anticonservative.

## Results

### Sample Characteristics

A total of 575 participants in the Washington University ADRC were included in this study (fig. 1) and stratified by initial CDR (table 1): 214 had a CDR of 0 (no dementia), 225 had a CDR of 0.5 (very mild dementia),

**Table 2. Surgery**

Description	No.
Major thoracic (e.g., lobectomy, esophagectomy)	2
Major gastrointestinal surgery (e.g., open cholecystectomy, colectomy, hiatal hernia, incisional hernia, gastrectomy)	27
Major vascular (e.g., open abdominal aortic aneurysm, femoral popliteal bypass)	3
Major gynecologic surgery (e.g., hysterectomy, pelvic surgery for cancer)	15
Hand surgery (e.g., nerve repair, carpal tunnel, Dupuytren)	6
Ear, nose, and throat (e.g., thyroidectomy, neck dissection)	3
Major orthopedic (e.g., hip replacement, knee replacement, back surgery, open reduction and internal fixation)	63
Urologic surgery (e.g., open and transurethral prostatectomy, nephrostomy, cystectomy)	26
Minor gastrointestinal surgery (e.g., inguinal hernia, hemorrhoid surgery, laparoscopic cholecystectomy)	13
Breast surgery (e.g., mastectomy, lumpectomy for cancer)	6
Other (e.g., major eye surgery, foot surgery, minor orthopedic surgery)	16
Total	180

and 136 had a CDR of 1 (mild dementia). Within each CDR stratum, the three event groups (surgery, illness, control [no event]) were similar with respect to sex, education, and initial age (*P* values all  $>0.05$ ), although the three event groups differed marginally ( $P = 0.09$ ) in initial age in the nondemented (CDR 0) cohort. The types and frequencies of surgeries and illness experienced in the sample are shown in tables 2 and 3. In the nondemented cohort, the median (interquartile range) years of annual assessment before surgery was 2.0 (0.8–4.9) yr; for illness, it was 3.3 (1.8–5.1) yr. The median (interquartile range) years of annual follow-up after sur-

**Table 3. Major Illness**

Description	No.
Pneumonia	18
Major gastrointestinal bleed, bowel obstruction, diverticulosis, peptic ulcer disease, cholecystitis	9
Myocardial infarction	16
Major infection/sepsis (e.g., osteomyelitis, sinusitis, cellulitis, diverticulitis, urinary tract infection)	19
Heart failure	5
Major arrhythmia (e.g., supraventricular tachycardia, acute atrial fibrillation, symptomatic complete heart block)	11
Dehydration and electrolyte derangements	12
Psychiatric and neurologic (e.g., seizures, Guillain-Barré syndrome)	5
Hematology and oncology (e.g., anemia, cancer, deep venous thrombosis, thrombophlebitis, pulmonary embolus, idiopathic thrombotic thrombocytopenia)	6
Rheumatologic (e.g., gout, pseudogout)	2
Emergencies and medically managed trauma (e.g., burns, fractures, allergic reactions, carbon monoxide poisoning)	6
Other (e.g., asthma, chronic obstructive pulmonary disease exacerbation)	10
Total	119

ger was 3.1 (1.6–5.5); for illness, it was 1.4 (0.4–4.2) yr. Nondemented individuals with major illness were significantly older at the time of hospital admission ( $P = 0.04$ ) compared with those who underwent major surgery. In the demented participants, the median (interquartile range) years of annual assessment before surgery was 2.0 (0.8–3.9) yr; it was 1.8 (1.0–4.0) yr before illness. The median (interquartile range) follow-up time after surgery was 2.1 (0.8–4.1) yr; for illness, it was 1.2 (0.3–3.3) yr. Ages at time of event were similar for the surgery and illness groups ( $P$  values  $>0.05$ ) in the two demented samples. Mini-Mental State Examination scores were not collected until 1997; scores at entry for those enrolled subsequently were 24 or greater for 80% of the very mild and 30% of the mild dementia cohorts.

The number of assessments after the event was highly skewed (a few people had many), but the surgery and illness groups at each CDR level were not significantly different ( $P$  values ranged from 0.30 to 0.98). Similarly, there were no significant differences between men and women in each CDR group in the number of assessments after the event. Age was negatively correlated with the number of assessments after the event. The correlations were the largest in the CDR 0 group ( $-0.39$  in the surgery group,  $-0.49$  in the illness group). They tended to be smaller in the two demented groups, where the progressive nature of the disease overwhelms the age effect.

#### Nondemented Sample

Almost a fourth of those who were initially nondemented progressed to a CDR greater than 0 during the course of the study, but at equal rates across the three event groups ( $P = 0.98$ ): 22% of those in the surgery group, 24% of those who experienced major illness, and 23% of those in the control group. The Cox regression analysis showed that those who were older were more likely to progress ( $P < 0.0001$ ), but, contrary to what might be expected if medical illness or surgery had a negative effect on cognition, those without an event progressed marginally ( $P = 0.07$ ) more rapidly than those experiencing either surgical or medical events. There was no interaction of age with group ( $P = 0.89$ ).

The results for all the event groups at all CDRs are similar whether individual cognitive domains or a general composite psychometric score are analyzed. We therefore report only the results of the general psychometric composite score. Annual rate of change (slopes and SEs) on the general psychometric composite in z-score form is shown in table 4. The slight upward trend ( $P = 0.02$ ) in pre-event slopes in the nondemented sample was more prominent in younger people ( $P = 0.05$ ). This upward trend did not vary with group ( $P = 0.52$  for surgery,  $P = 0.31$  for illness) but tended to be more prominent in participants who had surgery. After adjusting for initial age, the average pre-simulated event slope for participants in the control group was 0.07,

Table 4. Z-score Slopes

	Before Event	After Event	Difference
CDR 0			
Control	0.073 (0.015)	0.042 (0.009)	-0.032 (0.017)
Surgery	0.084 (0.011)	0.026 (0.008)	-0.057 (0.011)
Illness	0.049 (0.017)	0.029 (0.013)	-0.020 (0.016)
CDR 0.5			
Control	-0.190 (0.056)	-0.455 (0.079)	-0.265 (0.068)
Surgery	-0.161 (0.027)	-0.332 (0.046)	-0.171 (0.037)
Illness	-0.222 (0.045)	-0.428 (0.070)	-0.206 (0.054)
CDR 1			
Control	-0.285 (0.070)	-0.730 (0.095)	-0.446 (0.081)
Surgery	-0.457 (0.103)	-0.881 (0.140)	-0.424 (0.117)
Illness	-0.471 (0.170)	-1.021 (0.224)	-0.550 (0.169)

Annual rate of change on the general psychometric composite in z-score form is shown. The table presents estimates of slope before and after surgery, illness, or a simulated event in the control (no event) group, and the difference between these slopes, stratified by Clinical Dementia Rating (CDR). Estimates are presented as mean (SE).

compared with a slope of 0.08 before surgery and 0.05 before major illness. Postevent slopes for the three groups also did not differ ( $P = 0.18$  for surgery,  $P = 0.41$  for illness); the averages were 0.04, 0.03, and 0.03 for the control, surgical, and major illness groups, respectively. Furthermore, changes in slope from before and after the events were not significantly different from changes in slope after a simulated event in the control group ( $P = 0.22$  for surgery,  $P = 0.61$  for illness).

#### Demented Sample

Table 4 shows the slopes before and subsequent to the event of the general psychometric composite from the piecewise regression analysis for the two demented samples. Unlike the nondemented sample, the pre-event slopes were negative for the demented participants ( $P < 0.001$ ) and steeper in the mildly demented sample than in the very mildly demented sample ( $P < 0.001$ ). It was anticipated that in demented individuals, POCD might manifest as an increase in the rate of cognitive decline; however, neither slopes subsequent to the event (CDR 0.5:  $P = 0.18$  for surgery,  $P = 0.80$  for illness; CDR 1:  $P = 0.37$  for surgery,  $P = 0.23$  for illness) nor changes in slope (CDR 0.5:  $P = 0.23$  for surgery,  $P = 0.50$  for illness; CDR 1:  $P = 0.88$  for surgery,  $P = 0.58$  for illness) varied by event group.

#### Discussion

In this study, there was no evidence of a long-term effect on cognitive function independently attributable to surgery or major illness. Although almost a quarter of nondemented participants progressed to a CDR greater than zero during the course of the study, the risk of progression was not greater in the surgery or illness groups. This study also included people with mild dementia. As expected, there was an accelerating long-

term downward course for the demented people; however, the rate of that decline was not affected by the occurrence of a surgical or medical event.

This study is different in several respects from other studies focusing on postoperative cognitive decline, most notably in its collection of pre-event data and the use of modern techniques of longitudinal data analysis, similar to those used by Selnes *et al.*<sup>19</sup> Without good evidence, it has been proposed that psychometric scores of surgical patients should be adjusted based on an average learning effect among a healthy, nonsurgical control group, and further that POCD may be diagnosed based on a statistically defined threshold for this corrected psychometric score.<sup>1,2,10</sup> This approach implies that the learning effect is similar in magnitude and variability in both surgical and nonsurgical groups, that a smaller learning effect is evidence for cognitive decline, and that POCD is a binary outcome. Our method using participants in the ADRC avoided the pitfalls of defining POCD using arbitrary thresholds, of adjusting for a learning effect using untested assumptions, and of not assessing cognitive trends before the event. Remarkably, even the nondemented participants who did not have surgery or a major illness had a downward change in tests of cognitive function after a simulated event, emphasizing the danger of untested statistical assumptions.

The inclusion of demented individuals, especially those in the very mild stage of dementia, provides one potential explanation for why our conclusions differ from those of previous studies. Our results clearly demonstrate a downward longitudinal course in very mildly demented people before surgery or major illness comparable to that of very mildly demented people who do not experience such events. Two thirds of these people would have been included in other studies as nondemented given that their Mini-Mental State Examination scores were not below a commonly used threshold. Because longitudinal assessments were not available for these people in other studies, their downward course could have been inappropriately attributed to surgery rather than to the existing dementia. Screening tests more sensitive than the Mini-Mental State Examination, such as the AD-8<sup>30,31</sup> or the recently described score for detecting subtle neurologic abnormalities,<sup>32</sup> would be more likely to detect patients with early dementia or other neurologic abnormalities. Interestingly, other retrospective clinical studies that have specifically examined the impact of surgery on Alzheimer disease have also not demonstrated an association between surgery or anesthesia and the risk of Alzheimer disease exacerbation or the onset of dementia.<sup>33-35</sup> Further, a retrospective, population-based, Dutch, cross-sectional study also found no support for the notion that a history of an operation is a determinant or independent risk factor for accelerated age-related subtle cognitive decline.<sup>36</sup>

This study has several important limitations: (1) A limitation common to all studies of POCD is the difficulty in matching people undergoing surgery with appropriate controls.<sup>14</sup> One of the strengths of our study is that participants in the surgery and illness groups were included in the study substantially before these events. Nonetheless, we cannot conclude that they were well matched with the control participants, who did not have a surgery or major illness. Further, hospital admission may be a poor surrogate for determining major illness. (2) Patients with early POCD might be more likely to die in the year after surgery,<sup>2</sup> and this could mask the detection of long-term POCD in any study. Participants who died before a first postevent (surgery or illness) assessment and those who did not present for follow-up owing to ill health would not have been included in our sample. Therefore, we cannot comment on the possible confounding effect of early death or poor health on the detection of long-term POCD. Nonetheless, it is unlikely that the majority of people with cognitive decline die within the first year of surgery<sup>2,5</sup> or illness, so it is improbable that exclusion of people who died early would completely mask the detection of long-term cognitive decline. (3) Cognitive decline has been found to persist for up to 3 months after noncardiac surgery.<sup>1,2</sup> Although this study did not demonstrate long-term cognitive decline attributable to surgery or illness, early cognitive decline with subsequent recovery could not be assessed because participants were only assessed at annual intervals and the timing of cognitive tests in relation to surgery and illness was variable. It is important to emphasize that this study could not determine how short-term changes in cognition may have impacted the general well-being of older subjects. (4) The heterogeneity of surgeries and illnesses in our study presents another possible limitation; cognitive decline may only occur after certain surgeries and illnesses, thus diluting the observed effect size.<sup>13</sup> Nevertheless, because of the inclusion of surgeries and illnesses typically experienced by a cohort of elderly people, the results of this study can be readily generalized. Moreover, the results of the study were not altered when the 41 participants who had less invasive surgeries (hand surgery, minor gastrointestinal surgery, breast surgery, and others; table 2) were excluded from the general linear mixed effects model. (5) The relatively higher education of participants in the ADRC and their presumed greater motivation level, as reflected by participation in a voluntary, longitudinal research endeavor, represents another potential limitation.

Although our study did not address cognitive decline after cardiac surgery, it is notable that a recent study with long-term follow-up after open heart surgery, using a similar statistical approach and appropriate controls, was also unable to demonstrate persistent cognitive decline independently attributable to the surgery or the use



of cardiopulmonary bypass.<sup>19</sup> Although it is not known whether the patients received general or regional anesthesia, the type of anesthesia has not been shown in previous studies to influence the likelihood of postoperative cognitive decline.<sup>4,13,18</sup>

If cognitive decline after noncardiac surgery were both common and debilitating, this would have major public health implications. It would imply that alternatives to surgery should be pursued for elderly people and that stringent efforts should be pursued to determine who is vulnerable to this complication and how it may be prevented. If cognitive decline were not common, long lasting, or severe, this would suggest that elderly people could be reassured and that surgery could proceed, based on the need for surgery and the patients' general health. In this study of subjects having a mixture of surgical procedures, long-term cognitive decline attributable to noncardiac surgery was not evident. With mounting animal evidence implicating POCD as a real phenomenon,<sup>6-9</sup> coupled with long-term outcome studies associating POCD with increased mortality,<sup>2,5</sup> it is now imperative to conduct properly designed and appropriately powered studies with meaningful clinical endpoints to determine whether any specific surgery, anesthetic technique, or patient characteristic might be independently associated with long-term postoperative cognitive decline.

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