

Supplemental Online Content

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31 This supplemental material has been provided by the authors to give readers additional
32 information about their work.

33

34

35 **eTable 1. Participant flow and follow-up through 72-month follow-up.**

36

Time point	Number in sample at assessment time point	Dropout in interval	Died in interval	In sample at end of interval	Number assessed at time point
<i>Overall</i>					
Baseline	560	0	0	560	560
1 month	560	7	1	552	548
2 months	552	6	2	544	536
6 months	544	2	4	538	528
12 months	538	8	3	527	511
18 months	527	7	6	514	499
24 months	514	12	9	493	474
30 months	493	6	11	476	325
36 months	476	4	3	469	456
48 months	469	32	24	413	385
60 months	413	13	21	379	354
72 months	379	18	26	335	313
<i>Delirium</i>					
Baseline	134	0	0	134	134
1 month	134	2	0	132	129
2 months	132	2	0	13	126
6 months	130	0	1	129	124
12 months	129	2	1	126	120
18 months	126	2	1	123	117
24 months	123	4	3	116	106
30 months	116	1	4	111	83
36 months	111	0	0	111	110
48 months	111	4	9	98	90
60 months	98	4	9	85	79
72 months	85	3	11	71	65
<i>No Delirium</i>					
Baseline	426	0	0	426	426
1 month	426	5	1	420	419
2 months	420	4	1	415	410
6 months	415	2	4	409	404
12 months	409	6	2	401	391
18 months	401	5	5	391	382
24 months	391	8	6	377	368
30 months	377	5	7	365	242
36 months	365	4	3	358	346
48 months	358	28	15	315	295
60 months	315	9	12	294	275
72 months	294	15	15	264	248

37

38 **eAppendix 1 - Statistical modeling**

39 **Overview:** This appendix describes the modeling steps we pursued that culminated in our estimation of a
40 random effects piecewise linear trajectory model (our components of change model). We describe the multiple
41 models we examined and contrast with the components of change model.

42 **Procedures:** Our analysis proceeded by first identifying a reasonable trajectory for the repeated cognitive
43 measures (GCP) from preoperative baseline to 72-month follow-up, followed by testing our hypothesis that
44 change differed according to post-operative delirium status. In our initial exploratory step, we used multiple
45 methods: mixed effect regression models, random effects models, and random changepoint models.

46 **1.0 Random changepoint model**

47 We initiated our longitudinal data analysis approach to the SAGES repeated cognitive data (GCP, general
48 cognitive performance) using a random changepoint model. Because of the observed acute decline and
49 immediate recovery effects in the SAGES sample,¹ we used data from month 6 to month 72 in the random
50 change point model. This decision was made so the estimated change point did not capture either the
51 punctuation or recovery effect, but rather change in the trajectory observed after 6 months in previous studies.¹
52 We prepended a latent difference score model² onto the latent difference score model to capture the change
53 from baseline to month 1, and month 1 to month 2, before the estimating the random change point model from
54 months 6 to 72. Covariances between the latent difference score and random change point models were
55 estimated so each time point was taken into account in both models. We also regressed delirium and the other
56 demographic covariables from the components of change model onto each latent variable.

57 **Results:** The results of the random changepoint model are shown in **Table e2**. The random change point
58 occurred 1.6 years after surgery for the non-delirium group and 1.7 years after surgery for the delirium group.
59 The mean of the slope in the no delirium group prior to the change point implied continuing improvement in
60 GCP scores (+0.3 GCP points/month), while the mean of the slope prior to the change point implied net
61 cognitive decline in the delirium group (-0.2 GCP points/month).

62 **Conclusion:** Because of the qualitative mean difference in pre change-point slopes, the meaning of the
63 changepoint is ambiguous and possibly different in the delirious and non-delirious samples. In the non-delirious,
64 the change point could signify when cognitive recovery ends. In the delirious, the change point could signify an

65 estimate of a point when cognitive change accelerates. We felt that this ambiguity warranted exploring the data
66 with additional models.

67

68 **eTable 2. Random change point model results.**

Coefficient	No Delirium	Delirium	Difference
Intercept	57.6	57.6	0.0
Punctuation	-0.7	-1.7	-1.0
Recovery	0.8	1.8	1.0
6-Month intercept	57.9	58.0	0.1
Pre-change slope	0.3	-0.2	-0.4
Post-change slope	-1.0	-1.5	-0.5
Random change point (in years from baseline)	1.6	1.7	0.1

69 Note: Table entries are parameter estimates from random changepoint model

70

71 **2.0 Random coefficient models with linear splines**

72 We followed on our random changepoint models with random coefficient models, building upon a modeling
 73 approach we have used in our report of cognitive trajectories following elective surgery and delirium through 36
 74 months in the same cohort.¹ We build a model that includes multiple piecewise linear splines with knots at
 75 months 1, and 2 to model the observed acute decline, recovery, and long-term trajectory. We also constructed
 76 alternative functional forms, including linear, quadratic (also with knots at months 1 and 2) and piecewise linear
 77 with a knots at: months 1, 2, and 12; months 1, 2, and 18; and months 1, 2, 6, and 18. We also estimated
 78 models with random change points.³ Akaike information criteria (AIC) and Bayesian information criteria (BIC) for
 79 each model was compared, and the model with the lowest AIC and BIC was considered the best fitting model.
 80 AICs and BICs for each model are shown in **Table e3**.

81

82 **eTable 3. Model fit summaries for alternative functional form models**

Models	Free Parameters	Loglikelihood	AIC	BIC
Linear	17	-14342	28717	28791
Linear segmented 1.2	19	-14219	28476	28558
Quadratic	21	-14196	28435	28526
Linear segmented 1.2.12	23	-14159	28365	28464
Linear segmented 1.2.18	23	-14150	28346	28445
Linear segmented 1.2.6.18	28	-14120	28296	28417
Random changepoint	42	-14089	28262	28444
Components of change	25	-14145	28309	28403

83 Notes: 1.2, knots at months 1 and 2; 1.2.12, knots at months 1, 2, and 12; 1.2.18, knots at months 1, 2, and 18,
 84 1.2.6.18, knots at months 1, 2, 6, and 18.

85
 86 The best fitting model included fixed effects at months 1 and 2 and knots at both month 6 and 18. Examination
 87 of the model trajectory suggested there was a positive slope (Est. = 0.33, p = .01) between months 6 and 18.
 88 This implied there was continued recovery up to 1.5 years post-surgery. We sought to better explore this longer-
 89 term recovery, and the impact delirium may have on longer-term recovery, which led to the components of
 90 change model.

91 **3.0 Components of change model**

92 The components of change model, is a random effects model comprised of five latent variables. The design
 93 matrix for the components of change model was:

94
$$X = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 \\ 1 & t_1 & 1 & 0 & 0 \\ 1 & t_2 & 1 & 1 & 0 \\ 1 & t_6 & 1 & 1 & * \\ 1 & t_{12} & 1 & 1 & * \\ 1 & t_{18} & 1 & 1 & * \\ 1 & t_{24} & 1 & 1 & * \\ 1 & t_{30} & 1 & 1 & 1 \\ 1 & t_{36} & 1 & 1 & 1 \\ 1 & t_{48} & 1 & 1 & 1 \\ 1 & t_{60} & 1 & 1 & 1 \\ 1 & t_{72} & 1 & 1 & 1 \end{bmatrix}$$

95 Where the first column represented the intercept, the second the linear slope (i.e., “long-term period”), the third
 96 the fixed effect (i.e., “acute period”) at month 1, the fourth the fixed effect (i.e., “post-acute period”) at month 2,

97 and the final column represent the second slope modeling the intermediate-period. The * for the long-term
 98 recovery slope indicate the loading was freely estimated. The estimated loadings followed a Gompertz function,
 99 which indicates slower growth at the start of a time period and faster growth near the end of the time period. We
 100 used the estimated Gompertz function based on the freely estimated time steps to generate fixed time steps,
 101 which we used for analysis. The design matrix including the fixed time steps, estimated from the Gompertz
 102 function, was:

103

$$X = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 \\ 1 & t_1 & 1 & 0 & 0 \\ 1 & t_2 & 1 & 1 & 0 \\ 1 & t_6 & 1 & 1 & .20 \\ 1 & t_{12} & 1 & 1 & .51 \\ 1 & t_{18} & 1 & 1 & .79 \\ 1 & t_{24} & 1 & 1 & .96 \\ 1 & t_{30} & 1 & 1 & 1 \\ 1 & t_{36} & 1 & 1 & 1 \\ 1 & t_{48} & 1 & 1 & 1 \\ 1 & t_{60} & 1 & 1 & 1 \\ 1 & t_{72} & 1 & 1 & 1 \end{bmatrix}$$

104 In **Table e4** below, we provide detailed models results which expand upon Table 3 in the main manuscript.
 105 These results show the effect of the included model covariables (age, gender, non-White race, education,
 106 Charlson score, GDS score, IQCODE, impairment in instrumental activities, and surgery type) on each of the
 107 latent variables in the components of change model.

108

eTable 4. Effect of covariables on component of change model

Model term	Estimate	SE	p-value
<i>Intercept regressed on</i>			
Age at surgery	-0.42	0.05	<.001
Non-White or Hispanic	-7.85	1.06	<.001
Female sex	0.98	0.54	.07
IQCODE	-0.38	1.23	.76
Any IADL impairment	-1.84	0.7	.01
Geriatric Depression Scale score	-0.41	0.12	<.001
Charlson score	-1.06	0.31	<.001
Vascular surgery	-1.59	1.06	.13
Gastrointestinal surgery	0.94	0.74	.21
<i>Acute period regressed on</i>			
Delirium	-1.18	0.34	<.001
Age at surgery	-0.01	0.03	.79
Non-White or Hispanic	0.20	0.52	.70
Female sex	0.56	0.28	.04
IQCODE	-0.21	0.58	.71
Any IADL impairment	-0.75	0.34	.03
Geriatric Depression Scale score	0.00	0.06	.94
Charlson score	-0.04	0.17	.80
Vascular surgery	-1.15	0.62	.07
Gastrointestinal surgery	0.66	0.36	.07
<i>Post-acute period regressed on</i>			
Delirium	1.12	0.32	<.001
Age at surgery	0.01	0.03	.82
Non-White or Hispanic	-0.47	0.49	.33
Female sex	-0.3	0.26	.25
IQCODE	-0.65	0.55	.24
Any IADL impairment	0.56	0.31	.07
Geriatric Depression Scale score	0.03	0.05	.62
Charlson score	-0.12	0.15	.43
Vascular surgery	0.13	0.57	.81
Gastrointestinal surgery	-1.05	0.36	.004
<i>Intermediate period regressed on</i>			
Delirium	0.10	0.47	.82
Age at surgery	0.10	0.04	.03
Non-White or Hispanic	-0.25	0.68	.71
Female sex	0.53	0.38	.16
IQCODE	-0.14	0.77	.85
Any IADL impairment	-0.65	0.55	.24
Geriatric Depression Scale score	-0.16	0.09	.05
Charlson score	0.38	0.25	.13
Vascular surgery	0.80	1.00	.42
Gastrointestinal surgery	-0.26	0.54	.63

Model term	Estimate	SE	p-value
<i>Long-term period regressed on</i>			
Delirium	-0.39	0.16	.01
Age at surgery	-0.07	0.01	< .001
Non-White or Hispanic	0.36	0.18	.05
Female sex	-0.14	0.12	.24
IQCODE	-0.23	0.29	.41
Any IADL Impairment	0.04	0.16	.80
Geriatric Depression Scale score	0.04	0.02	.09
Charlson score	-0.17	0.07	.02
Vascular surgery	-0.05	0.28	.85
Gastrointestinal surgery	0.05	0.18	.77
<i>Delirium† regressed on</i>			
Age at surgery (per year)	-0.004	0.02	.86
Non-White or Hispanic	-0.19	0.40	.64
Female sex	0.15	0.22	.50
IQCODE	1.23	0.42	.003
Any IADL impairment	0.12	0.24	.60
Geriatric Depression Scale score	0.02	0.04	.57
Charlson score	0.27	0.13	.04
Baseline GCP (<i>Intercept</i> , per GCP point)	-0.06	0.02	<.001
Vascular surgery	0.05	0.41	.90
Gastrointestinal surgery	0.19	0.32	.56
Model term	Estimate	SE	p-value

Latent variable intercepts

<i>Intercept</i> (baseline)	57.60	0.26	.003
<i>Acute period</i>	-0.46	0.16	< .001
<i>Post-acute period</i>	1.10	0.14	< .001
<i>Intermediate period</i>	1.89	0.22	< .001
<i>Long-term period</i>	-1.01	0.07	< .001

Latent variable residual variances

<i>Intercept</i> (baseline)	37.78	2.57	< .001
<i>Acute period</i>	-		
<i>Post-acute period</i>	-		
<i>Intermediate period</i>	4.00	1.39	.004
<i>Long-term period</i>	0.80	0.19	< .001

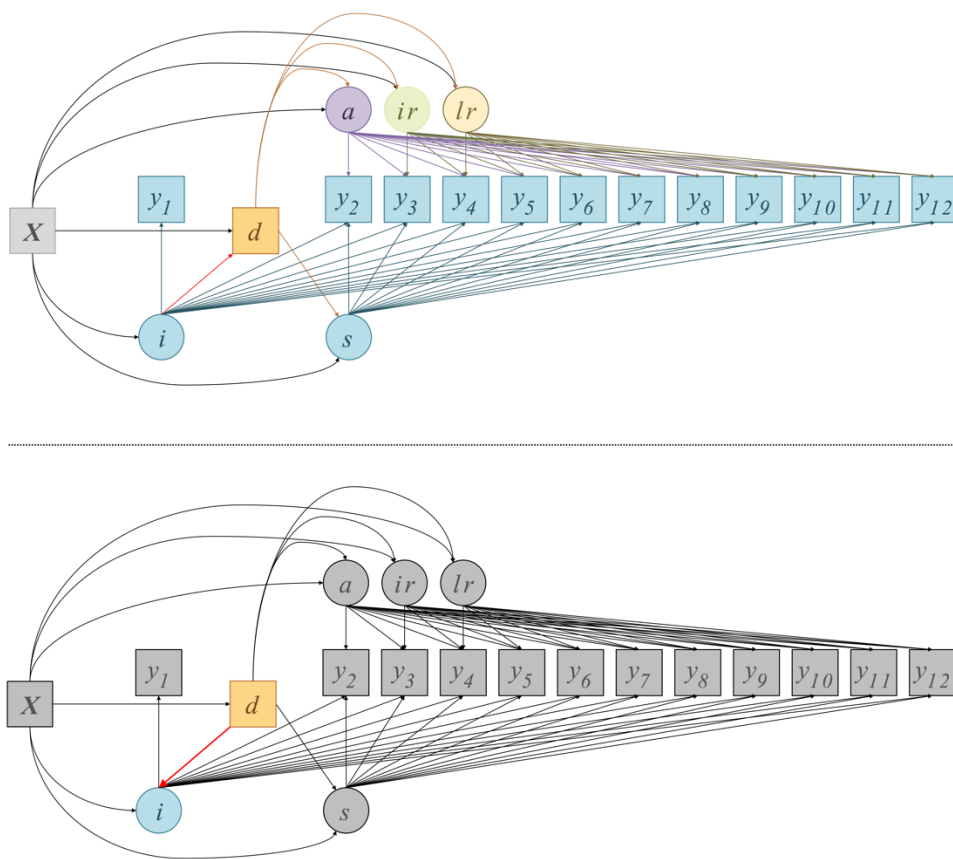
Latent variable covariances

<i>Intercept</i> (baseline) with <i>Long-term period</i>	0.92	0.28	.001
Intermediate period with <i>Long-term period</i>	-0.88	0.39	.02

112 Notes: IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; IADL, Instrumental Activities of
113 Daily Living, SE, standard error. † Parameter estimates for the regression of delirium on covariables are logistic
114 regression coefficients. All other table entries labeled regression parameters are linear regression coefficients
115

116 **3.1 Components of change model, delirium as covariable**

117 We also estimate a form of the components of change model where delirium is included as a covariable. Our
118 main model, appropriately specified with respect to the temporal ordering of baseline GCP and delirium risk,
119 regresses delirium on baseline GCP. The delirium as covariable model regresses baseline GCP on delirium
120 group. This analogous to using a two-sample t test to evaluate the mean difference in baseline GCP score
121 according to whether or not delirium occurred in the hospital stay. We use this model as a convenience tool to
122 easily obtain delirium group baseline mean differences in GCP. When results pertain to the delirium as a
123 covariable model, those are clearly identified in this appendix and the main text. The figure below (**Figure e1**)
124 illustrates the difference between the delirium as an intermediate outcome (top panel) and delirium as a
125 covariable (bottom panel) models.



126

127 **eFigure. Delirium as an intermediate outcome and delirium as a covariable components of change**
128 **model.** The top panel corresponds to our main model. The bottom panel highlights the difference in the delirium
129 as a covariable model. These path diagrams illustrate how repeatedly observed GCP scores from baseline

130 through month 72 (y_1 - y_{12} , corresponding to observations at post-surgical month 0, 1, 2, 6, 12, 18, 24, 30, 36,
131 48, 60, 72) and observed post-operative delirium (d) are related to intercept (i) and slope (s) growth functions,
132 and acute decline, immediate recovery, and longer-term recovery (a , ir , lr) effects. X denote the multiple
133 covariables (age, sex, race/ethnicity, IQCODE score, IADL impairment, Charlson comorbidity, depression, and
134 surgery type). For the sake of clarity, residual variances for all y 's, latent variables (i , s , a , ir , lr) are omitted, as
135 are covariances among the latent variables.

136

137 **eAppendix 2 – Exploring the effects of non-normality in GCP scores in the estimation of long-term cognitive**
 138 **aging slopes**

139 **Objective:** The goal of this analysis was to consider if non-normality in the distribution of GCP scores could be
 140 influencing the estimated slopes in aging-related cognitive decline (the slope parameter in the components of
 141 change model). This was motivated by our finding that the long-term slope estimates in the current analysis of
 142 cognitive change over 72-months was considerably larger than our estimate of the long-term slope in our
 143 analysis of data from this cohort followed over 36 months and published previously.¹

144 **Procedure:** We repeated our components of change model using a transformation of the GCP score. The
 145 transformation was a rank-based normalization transformation, known as the Blom transformation.⁴ Essentially,
 146 the Blom transformation involves converting the scores to ranks, and then converting the ranks to percentile
 147 ranks, and applying an inverse normal transformation to the percentile values. To increase the comparability of
 148 Blom-transformed GCP to our original metric GCP, we linearly scale the Blom-transformed values using the
 149 original metric GCP mean and standard deviation.

150 **Results:** After the Blom transformation, we fit the components of change model with covariable adjustment for
 151 age, race/ethnicity, sex, IQCODE, IADLS, GDS, and surgery type to the data. We display the results of the
 152 original components of change model and Blom-transformed components of change model in **Table e5**. The
 153 results suggest there are minor differences, at the tenth or hundredth decimal place, between the original and
 154 Blom-transformed data. These minor differences are seen in both the estimates of the intercept, acute period,
 155 post-acute period, intermediate period, and Long-term period effects as well as the estimates of delirium on
 156 each of these five variables. Based on these results, sensitivity to departures from normality do not impact the
 157 results of the components of change model in the presence or absence of delirium.

158 **eTable 5. Parameter estimates from components of change model using original GCP scaling and Blom-**
 159 **transformed GCP**

Coefficient	Original GCP scaling				Blom-transformed GCP			
	No Delirium	Delirium	Difference	SE	No Delirium	Delirium	Difference	SE
Intercept	58.2	55.8	-2.4	0.6	58.2	55.7	-2.5	0.6
Acute period	-0.5	-1.7	-1.2	0.3	-0.4	-1.5	-1.1	0.3

Post-acute period	1.1	2.2	1.1	0.3	1.1	2.2	1.0	0.3
Intermediate period	1.9	2.0	0.1	0.5	1.9	1.8	-0.1	0.4
Long-term cognitive decline	-1.0	-1.4	-0.4	0.1	-0.9	-1.2	-0.3	0.1

160 Note: The table entries are estimated from a purposefully time-order mis-specified model (with respect to the
 161 effect of baseline GCP in delirium risk), to more easily evaluate the baseline differences in GCP score
 162 according to delirium group.

163

164 **eAppendix 3 – Exploring the effect of different missing data handling strategies on main results**

165 **Objective:** The goal of the sensitivity analyses described in this appendix was to explore the impact of different
166 procedures for handling missing data, and the extent to which missing data may have on the substantive
167 conclusions from our models. We compare our preferred approach (maximum likelihood estimation) to multiple
168 imputation, extreme value imputation, and complete case analysis.

169 ***Study 1: Maximum Likelihood vs Multiple Imputation***

170 **Procedure:** In our first missing data sensitivity analysis, we used multiple imputation (MI) with age,
171 race/ethnicity, sex, IQCODE, IADLS, GDS, and surgery type as auxiliary variables in the imputation routine. We
172 display the results of the original components of change model and multiple imputation model in **Table e6**.

173

174 **eTable 6. Parameter estimates from components of change model using maximum likelihood estimation**
 175 **and multiple imputation**

Coefficient	Maximum Likelihood Estimates				Multiple Imputation Estimates			
	No Delirium	Delirium	Difference	SE	No Delirium	Delirium	Difference	SE
Intercept	58.2	55.8	-2.4	0.6	58.2	55.8	-2.5	0.6
Acute period	-0.5	-1.7	-1.2	0.3	-0.5	-1.7	-1.2	0.3
Post-acute period	1.1	2.2	1.1	0.3	1.2	2.2	1.0	0.3
Intermediate period	1.9	2.0	0.1	0.5	1.8	1.7	-0.1	0.4
Long-term cognitive decline	-1.0	-1.4	-0.4	0.1	-1.0	-1.3	-0.3	0.1

176 Note: The table entries are estimated from a purposefully time-order mis-specified model (with respect to the
 177 effect of baseline GCP in delirium risk), to more easily evaluate the baseline differences in GCP score
 178 according to delirium group.

179 **Results:** The results of **Table e6** suggest there are minor differences, at the tenth decimal place, between the
 180 ML and MI imputed data results. These minor differences are seen only in the recovery and longer-term
 181 recovery terms, and in the effect of delirium on recovery, longer-term recovery, and rate of cognitive decline
 182 (i.e., slope).

183 **Study 2: Maximum Likelihood vs Extreme Value Imputation**

184 **Procedure:** The second missing data sensitivity analysis involved imputing extreme values for participants with
 185 missing follow-up data. Extreme values were defined as the 97.5th percentile of the expected GCP value by
 186 time point for participants who experienced postoperative delirium, and the 2.5th percentile of the expected
 187 GCP value by time point for participants who did not experience postoperative delirium. In other words, we
 188 imputed the best-case scenario GCP values for participants who experienced delirium, and the worst-case
 189 scenario values for participants who did not experience delirium. These best-case and worse-case descriptions
 190 are in reference to our hypothesis that delirium is associated with a faster pace of cognitive aging.

191 **Results:** The results of the extreme value imputation, shown in **Table e7**, suggest the slope for the no delirium
 192 group was less steep for extreme value imputation compared to maximum likelihood imputation (-0.5 vs -1.0,
 193 respectively). The effect of delirium was also lessened (-0.3 vs -0.4 for extreme value vs maximum likelihood,

194 respectively). However, we still observed the same pattern of results as shown in the maximum likelihood
195 imputation approach.

196

197 **eTable 7. Parameter estimates from components of change model using maximum likelihood estimation**
 198 **and extreme value imputation**

Coefficient	Maximum Likelihood Estimates				Extreme Value Imputation Estimates			
	No Delirium	Delirium	Differ-ence	SE	No Delirium	Delirium	Differ-ence	SE
Intercept	58.2	55.8	-2.4	0.6	58.2	55.7	-2.5	0.6
Acute period	-0.5	-1.7	-1.2	0.3	-0.4	-1.5	-1.1	0.4
Post-acute period	1.1	2.2	1.1	0.3	1.1	2.2	1.1	0.3
Intermediate period	1.9	2.0	0.1	0.5	1.0	0.9	0.0	0.4
Long-term cognitive decline	-1.0	-1.4	-0.4	0.1	-0.5	-0.8	-0.3	0.1

199 Note: The table entries are estimated from the delirium as a covariable model (with respect to the effect of
 200 baseline GCP in delirium risk), to more easily evaluate the baseline differences in GCP score according to
 201 delirium group.
 202

203 **Study 3: Maximum likelihood vs Complete Case Analysis**

204 **Procedure:** The third missing data sensitivity analysis only retained participants with complete data at each
205 follow-up time point (N = 241). This is a form of complete case analysis, which is no longer a recommended
206 technique for statistical analysis.⁵ Imputation techniques, such as maximum likelihood estimate or multiple
207 imputation, should be used instead.⁵ **eTable 1** contains a description of the flow of persons, including deaths
208 and drop-out, at each study time point.

209

210 **eTable 8. Parameter estimates from components of change model using maximum likelihood estimation**
 211 **and complete cases**

Coefficient	Maximum Likelihood Estimates				Complete Case Estimates			
	No Delirium	Delirium	Difference	SE	No Delirium	Delirium	Difference	SE
Intercept	58.2	55.8	-2.4	0.6	60.0	58.2	-1.8	1.0
Acute period	-0.5	-1.7	-1.2	0.3	-0.3	-1.2	-0.9	0.5
Post-acute period	1.1	2.2	1.1	0.3	1.4	2.2	0.8	0.5
Intermediate period	1.9	2.0	0.1	0.5	1.0	1.6	0.6	0.7
Long-term cognitive decline	-1.0	-1.4	-0.4	0.1	-0.7	-0.9	-0.2	0.2

212 Note: The table entries are estimated from a the delirium as a covariable model (with respect to the effect of
 213 baseline GCP in delirium risk), to more easily evaluate the baseline differences in GCP score according to
 214 delirium group.

215 **Results:** These results are shown in **Table e8**, where the slope for the no delirium group was less steep than in
 216 the maximum likelihood imputation (-0.7 vs -1.0). The effect of delirium was also lower (-0.2 vs -0.4). However,
 217 the same general pattern of results held as shown in the maximum likelihood imputation approach.

218 **Summary:** Based on these three sensitivity analyses, our results are robust to the way missing data were
 219 handled. When using maximum likelihood imputation or multiple imputation, two modern and recommended
 220 imputation approaches, our results are nearly identical. When using extreme value imputation and complete
 221 case analysis, our estimates for cognitive decline and effect of delirium on cognitive decline lessened, but still
 222 held the same pattern of decline and delirium increasing said decline. Based on these findings, we can be
 223 confident that missing data does not impact the findings of this study.

224 **eAppendix 4 - Comparing change in non-delirium group to that of the non-surgical comparison group**

225 **Objective:** Our third sensitivity analysis explored the rate of cognitive decline in the non-surgical comparison
226 group. Because we saw increased rates of decline in this analysis compared to previous findings in the SAGES
227 sample,¹ we wanted to test if similar rates of decline were seen in non-delirium surgical group and the non-
228 surgical comparison group. We did not include the delirium surgical group in this analysis because we knew
229 there was a faster rate of cognitive decline in the delirium group based on the results reported in the main
230 manuscript.

231 **Procedure:** For this analysis, we did not use the retest-adjusted GCP score, since the retest adjustment was
232 made based on the non-surgical comparison group. Instead, we used the raw GCP scores. We also fit an
233 adjusted form of the components of change model, based on the available data for the non-surgical comparison
234 group. The adjusted design matrix for this analysis was:

235
$$X = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 \\ 1 & t_1 & 1 & 0 & 0 \\ 1 & t_2 & 1 & 1 & 0 \\ 1 & t_6 & 1 & 1 & * \\ 1 & t_{12} & 1 & 1 & * \\ 1 & t_{18} & 1 & 1 & 1 \\ 1 & t_{24} & 1 & 1 & 1 \\ 1 & t_{30} & 1 & 1 & 1 \\ 1 & t_{36} & 1 & 1 & 1 \end{bmatrix}$$

236 The adjusted design matrix still contained five latent variables: intercept, longer-term cognitive decline (slope),
237 acute period and retest, post-acute period, and intermediate period. This model was estimated as a multiple
238 group latent growth curve model, estimated simultaneously in both the surgical and non-surgical groups. The
239 intermediate period only had estimated loadings at months 6 and 12 since data were only available out to 36
240 months in the non-surgical comparison group. The acute period is referred to as acute period and retest in this
241 model, since only the surgical group experiences acute period . Moreover, post-acute and intermediate periods
242 are only estimated in the surgical group because only the surgical group experiences either of those effects.

243 **Results:** The results shown in eTable 9 suggest the only major difference between the surgical non-delirium
244 and non-surgical comparison group is in the acute period and retest effect, -1.03, SE = 0.27, p < .001. However,
245 this result is expected as the difference is showing the acute period effect observed in the surgical group which
246 is not seen in the non-surgical comparison group since they did not have surgery. There was no significant

247 difference in the longer-term cognitive decline effect between the two groups, 0.03, SE = 0.19, $p = 0.89$. Based
248 on these results, there is no evidence for a difference in the rate of longer-term cognitive decline in the non-
249 surgical comparison group and surgical non-delirium groups.

250

251 **eTable 9. Change in cognition from baseline through 36 months in the non-surgical comparison group**
 252 **and surgical non-delirium results.**

Coefficient	Non-surgical comparison group		Surgical non-delirium group	
	Estimate	SE	Estimate	SE
Intercept	58.0	0.9	58.5	0.4
Retest & acute period	2.2	0.2	1.1	0.2
Post-acute period	-	-	1.4	0.2
Intermediate period	-	-	1.2	0.3
Long-term period	-0.7	0.1	-0.7	0.1

253 Notes: SE, standard error. Table entries are parameter estimates from a multiple group growth curve model.
 254 Immediate recovery and longer-term recovery effects were estimated in the surgical sample only.

255

256 **eAppendix 5 – Rates of long-term cognitive decline in SAGES**

257 In the main text, the reported long-term cognitive decline results were in units of GCP per year and
258 standard deviation units per year. These were -1.0 GCP units per year for the non-delirium group (0.14
259 standard deviation units), and -1.4 GCP units (0.19 standard deviation units) in the delirium group.

260 The results of 0.14 and 0.19 are calculated by dividing the long-term cognitive decline effect by the
261 SAGES sample standard deviation of the GCP, which is 7.3 ($-1.0 / 7.3 = -0.14$; $-1.4 / 7.3 = -0.19$). Using the
262 sample standard deviation to calculate rates of cognitive decline is consistent with previous research on the
263 SAGES sample,¹ which found rates of -0.03 in the non-delirium group and -0.08 in the delirium group when the
264 SAGES cohort was followed out to 36 months.

265 However, when the GCP was developed, it was scaled to have a population mean of 50 and
266 population standard deviation of 10.⁶ Therefore, if the population standard deviation was used to calculate
267 decline in standard deviation units, the results would be declines of 0.10 per year in the non-delirium group and
268 0.14 per year in the delirium group in the current study, and declines of 0.02 and 0.06 in the previous study
269 following the SAGES sample to 36 months.

270 Regardless of whether the sample or population standard deviation is used to calculate decline in
271 SD/year, the non-delirium group in the current study (0.10 SD/year using population SD, 0.14 SD/year using
272 sample SD) is close to an estimate of cognitive decline in persons with mild cognitive impairment, which is
273 about 0.10 SD/year.⁷ The results for the delirium group (0.14 SD/year using population SD, 0.19 SD/year using
274 sample SD) are above the estimate of MCI and approach an estimate for preclinical Alzheimer's disease, which
275 is 0.21 SD/year.⁸

276

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