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Functional Disability, Cognitive Impairment, and Depression Following Hospitalization for Pneumonia

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Abstract

Purpose—To examine if hospitalization for pneumonia is associated with functional decline, cognitive impairment, and depression, and to compare this impairment to that seen following known disabling conditions such as myocardial infarction or stroke.

Methods—We used data from a prospective cohort of 1,434 adults over age 50 who survived 1,711 hospitalizations for pneumonia, myocardial infarction, or stroke drawn from the Health and Retirement Study (1998–2010). Main outcome measures included the number of Activities and Instrumental Activities of Daily Living requiring assistance and the presence of cognitive impairment and substantial depressive symptoms.

Results—Hospitalization for pneumonia was associated with 1.01 new impairments in Activities and Instrumental Activities of Daily Living (95% Confidence Interval [CI]: 0.71, 1.32) among patients without baseline functional impairment and 0.99 new impairments in Activities and Instrumental Activities of Daily Living (95% CI: 0.57, 1.41) among those with mild-to-moderate baseline limitations, as well as moderate-to-severe cognitive impairment (odds ratio [OR], 2.46, 95% CI: 1.60, 3.79) and substantial depressive symptoms (OR, 1.63, 95% CI: 1.06, 2.51). Patients without baseline functional impairment who survived pneumonia hospitalization had more subsequent impairments in Activities and Instrumental Activities of Daily Living than those who

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survived myocardial infarction hospitalization. There were no significant differences in subsequent moderate-to-severe cognitive impairment or substantial depressive symptoms between patients who survived myocardial infarction or stroke and those who survived pneumonia.

Conclusions—Hospitalization for pneumonia in older adults is associated with subsequent functional and cognitive impairment. Improved pneumonia prevention and interventions to ameliorate adverse sequelae during and following hospitalization may improve outcomes.

Keywords

pneumonia; hospitalization; functional impairment; cognitive impairment; depression

INTRODUCTION

Pneumonia accounts for an estimated 390,000 hospitalizations among older adults annually, costing Medicare over \$7.3 billion.¹ Pneumonia hospitalizations are projected to nearly double by 2040.² As pneumonia-related in-hospital mortality decreases,³ the number of older pneumonia survivors will increase dramatically. While nearly half of older pneumonia hospitalization survivors die within one year,⁴ little is known about how else survivors are impacted.

Older adults hospitalized or receiving outpatient treatment for pneumonia have reported diminished quality of life,^{5,6} though reasons why are unclear. Survivors of critical illnesses are at risk for incident cognitive and functional impairment,⁷ and have high rates of depression.⁸ However, the rates of these adverse outcomes following hospitalization for specific non-critical acute illnesses such as pneumonia are unknown. Determining pneumonia survivors' long-term risks of functional disability, cognitive impairment and depression is crucial given the consequences of these outcomes,^{9–11} and their potential to create substantial chronic care needs.^{12–14}

The present study utilizes an ongoing longitudinal investigation of older Americans to determine whether hospitalization for pneumonia is independently associated with functional disability, cognitive impairment, and depression. We also examined how the risks of these outcomes compare to those seen following hospitalizations for myocardial infarction or stroke, two acute conditions recognized as associated with subsequent functional decline, cognitive impairment and depression.^{15–20}

METHODS

Population

Our study is a secondary analysis of data from the Health and Retirement Study (HRS), a prospective longitudinal investigation of U.S. adults over age 50. HRS details have been described previously.^{7,8} The HRS protocol was approved by the University of Michigan Institutional Review Board.

We studied all HRS respondents with at least 1 interview from 1998–2006 and for whom there were Medicare claims-based data for a subsequent hospitalization for pneumonia, myocardial infarction, or stroke from 1998–2007. All patients were followed through death or the 2010 interview. Our analyses focus on hospitalizations survived long enough to complete at least 1 follow-up interview.

Demographic and Clinical Characteristics

Data on demographics (*e.g.*, age, race/ethnicity, sex, education, and marital/partnered status) and health-risk behaviors (*e.g.*, alcohol use and smoking) came from HRS interviews.

Baseline Charlson Comorbidity score²¹ and hospitalization-related characteristics (length of stay, intensive care unit or coronary care unit admission, and requirements for mechanical ventilation, major surgery, and dialysis) came from Medicare claims.

Definitions of Conditions

We used International Classification of Disease, Ninth Revision, Clinical Modification diagnostic codes to identify hospitalizations for pneumonia, myocardial infarction, and stroke based on validated algorithms.^{22–24} Hospitalizations were included if the principal discharge diagnosis was for one of the three conditions of interest and were longer than 1 day.

Functional Impairment

To examine functional disability, respondents (or their proxies) were asked if they required assistance with any of 6 activities of daily living: walking, dressing, bathing, eating, getting into/out of bed, and toileting, or 5 instrumental activities of daily living: preparing a hot meal, grocery shopping, making telephone calls, taking medicines, and managing money. We defined baseline mild-to-moderate disability as 1 to 3 impairments in Activities and Instrumental Activities of Daily Living, and baseline moderate-to-severe disability as 4 impairments.⁷

Cognitive Impairment

Cognitive impairment was assessed using versions of the modified Telephone Interview for Cognitive Status.^{25,26} Proxies completed cognitive impairment assessments for patients unable to be interviewed themselves. We defined thresholds for mild-to-moderate and moderate-to-severe cognitive impairment based on previous HRS studies and the methods used for the Aging, Demographics, and Memory Study.^{7,8,27,28}

Depression

Depression was assessed at each HRS interview using the 8-item version of the Center for Epidemiologic Studies Depression Scale (CES-D)²⁹ from patients (not proxies).³⁰ We used a cutoff score of 4 to define substantial depressive symptoms because this threshold is comparable to the cutoff score of 16 on the full CES-D,³⁰ and has been used in prior studies.^{8,12,31}

Analysis

Hospitalization was the unit of analysis for all analyses. For analyses of post-hospitalization functional status, our outcome was the total number of impairments in Activities and Instrumental Activities of Daily Living. For unadjusted analyses, we grouped patients by the number of HRS interviews they completed since hospitalization. For multivariable models, we used fixed-effects regression models which use the longitudinal nature of the data to control for all stable patient characteristics.^{7,8} These models used only within-person variation over time to estimate the effect of hospitalization for pneumonia—that is, patients serve as their own controls. We also adjusted for post-pneumonia cognitive impairment to examine the association with impairments in Activities and Instrumental Activities of Daily Living beyond that which can be explained by cognitive impairment. Fixed-effects models were estimated using *xtreg, fe* in STATA 11.2 (Stata Corporation, College Station, TX). We repeated analyses of impairments in Activities and Instrumental Activities of Daily Living

after pneumonia hospitalization restricted to subjects with only one pneumonia hospitalization. Further details are provided in the online appendix on statistical methods.

For analyses of cognition and depression following pneumonia hospitalization, our outcomes were the level of cognitive impairment and the presence of substantial depressive symptoms, respectively. Unadjusted analyses were conducted similarly to those for functional disability. We used conditional logistic regression for multivariable analyses to examine the impact of pneumonia hospitalization on development of moderate-to-severe cognitive impairment or substantial depressive symptoms, respectively. These were estimated using *clogit* in STATA 11.2. In our final depression models, we adjusted for post-pneumonia cognitive impairment and functional impairments. We used similar models to examine the effect of pneumonia on these outcomes among subjects with only one hospitalization.

To compare the effect of pneumonia hospitalization to myocardial infarction or stroke hospitalizations on our primary outcomes, we created cohorts combining pneumonia and myocardial infarction or stroke survivors. For each cohort, interaction terms between time and pneumonia hospitalization were estimated to measure the marginal effect of pneumonia hospitalization compared to the other condition.

To examine if our outcomes of interest differed among patients with non-critical pneumonia hospitalizations or among those who were older, we conducted *a priori* analyses in three sub-groups: those not requiring mechanical ventilation or intensive care unit/coronary care unit admission, and patients ≥ 65 years old.

To ascertain if any associations that we found between pneumonia hospitalization and our outcomes of interest were explained by degree of chronic medical burden, we conducted a sensitivity analysis in which we stratified our fixed-effects models by Charlson Comorbidity Score quartiles.

To confirm that our results were not driven by intercurrent illnesses, we reanalyzed data for the smaller subset of 423 patients without hospitalizations between their baseline HRS interview and their first pneumonia hospitalization.

A challenge for our analyses of post-hospitalization depression was that 23% of pneumonia survivors were missing post-hospitalization depression measurements, typically because the primary respondent required a proxy. The HRS protocol did not ask proxies to report on depression.³⁰ Therefore, we used non-response propensity score adjustment in our final depression model to quantify how much our results might be biased.³²

We used two-sided significance tests with statistical significance at $P = 0.05$. Analyses were performed with the IBM SPSS Statistics 18 (SPSS Inc., Chicago, IL) and STATA 11.2 statistical software programs.

RESULTS

From 1998–2007, there were 1,434 individuals who survived 1,711 hospitalizations for pneumonia, myocardial infarction, or stroke and completed at least one follow-up interview (Figure 1). Table 1 describes baseline and clinical characteristics of survivors, whose median age was 77 (interquartile range: 70, 83). Patients were followed for up to 5 surveys (range: 7.7–9.8 years) before hospitalization and up to 6 surveys (range: 9.9–12.7 years) afterward.

Functional Impairment Following Pneumonia

Survivors of hospitalizations for pneumonia were at greater risk for impairments in Activities and Instrumental Activities of Daily Living in unadjusted analyses, particularly those with better baseline functioning (Figure 2). The independent effects of hospitalizations for pneumonia on impairments in Activities and Instrumental Activities of Daily Living among patients with better baseline functioning persisted in multivariable analyses (no impairment: 1.01 new functional impairments, 95% Confidence Interval [CI]: 0.71, 1.32; mild-to-moderate impairments: 0.99 new functional impairments, 95%CI: 0.57, 1.41) (Table 2). These associations remained among those with only one pneumonia hospitalization (no impairment: 0.95 new functional impairments, 95%CI: 0.65, 1.24; mild-to-moderate impairments: 1.02 new functional impairments, 95%CI: 0.52, 1.52), and after adjusting for post-hospitalization cognitive impairment (no baseline deficits: 0.86 new functional impairments, 95%CI: 0.58, 1.13; mild-to-moderate deficits: 0.82 new functional impairments, 95%CI: 0.41, 1.22). In contrast, patients with pre-pneumonia moderate-to-severe functional impairment did not have a statistically significant increase in subsequent functional impairments.

Cognitive Impairment Following Pneumonia

Surviving one or more pneumonia hospitalizations was associated with a significant increase in moderate-to-severe cognitive impairment (Figure 3). For instance, 14.9% (95%CI: 12.4%, 17.3%) of survivors had moderate-to-severe cognitive impairment at the last HRS interview before pneumonia, which increased to 25.2% (95%CI: 22.2%, 28.1%) at the first interview after ($P < 0.001$ by χ^2 test). In fixed-effects regression, surviving one or more pneumonia hospitalizations remained associated with progression to moderate-to-severe cognitive impairment (Odds Ratio [OR]: 2.46, 95%CI: 1.60, 3.79) (Table 3). This association persisted among patients with only one pneumonia hospitalization (OR: 2.27, 95%CI: 1.32, 3.90). There was no association between surviving pneumonia hospitalizations and net prevalence of mild-to-moderate cognitive impairment in unadjusted (Figure 3) or adjusted analyses, reflecting a balance between the numbers of patients progressing into this state from normal cognition and those developing worsened cognition after pneumonia.

Depression Following Pneumonia

In unadjusted analyses, the prevalence of substantial depressive symptoms increased from 25.4% (95%CI: 22.2%, 28.7%) at the last pre-pneumonia HRS interview to 29.5% (95%CI: 26.0%, 33.1%) ($P = 0.37$ by χ^2 test) at the first interview after. In a simple multivariable model, surviving one or more pneumonia hospitalizations was associated with 1.57-times the odds (95%CI: 1.05, 2.35) of substantial depressive symptoms. This association remained significant after adjusting for post-pneumonia cognitive and functional impairment as well as non-response propensity scores (Table 3). The point estimates suggested a similar magnitude of association among patients with only one pneumonia hospitalization, but were less precise (OR: 1.41, 95%CI: 0.88, 2.27).

Comparisons to MI or Stroke

Among survivors without baseline functional impairment, pneumonia hospitalization survivors had 0.61 *more* new impairments in Activities and Instrumental Activities of Daily Living (95%CI: 0.23, 0.99) than myocardial infarction hospitalization survivors. Respondents hospitalized for pneumonia versus myocardial infarction with baseline mild-to-moderate or moderate-to-severe functional impairment did not significantly differ in post-hospitalization impairments in Activities and Instrumental Activities of Daily Living (mild-to-moderate: 0.34 more new functional impairments for pneumonia patients than myocardial infarction patients, 95%CI: -0.38, 1.05; moderate-to-severe: -0.09 new functional

impairments for pneumonia patients than myocardial infarction patients, 95%CI: -1.15, 0.97) (Table 4). In contrast, pneumonia survivors without baseline functional impairment or with mild-to-moderate baseline functional impairment had significantly fewer functional impairments than stroke hospitalization survivors (-1.05 new functional impairments, 95%CI: -1.69, -0.42; -1.66 new functional impairments, 95%CI: -2.55, -0.77, respectively) (Table 4). The odds of moderate-to-severe cognitive impairment or substantial depressive symptoms were similar between pneumonia, myocardial infarction and stroke survivors (Table 5).

Subgroup and Sensitivity Analyses

Pneumonia hospitalization was independently associated with subsequent increased functional impairments, moderate-to-severe cognitive impairment, and substantial depressive symptoms among patients who did not require mechanical ventilation or intensive care unit/coronary care unit admission, and in adults 65 or older (eTables 1 and 2). For example, pneumonia not requiring critical care was associated with 0.78 new functional impairments (95% CI: 0.67, 1.28) for patients without pre-hospitalization functional impairments, and 0.87 (95% CI: 0.45, 1.29) for patients with mild-to-moderate pre-hospitalization functional impairments, and 2.77-times (95% CI: 1.77, 4.33) greater odds of moderate-to-severe cognitive impairment.

When we stratified our analyses by Charlson Comorbidity Score quartiles, pneumonia hospitalization was independently associated with subsequent increased functional impairments regardless of degree of comorbidity, and moderate-to-severe cognitive impairment among those with one or fewer comorbid conditions (eTables 3 and 4). Even among patients without any comorbid conditions, hospitalization for pneumonia was associated with 0.47 new functional impairments (95%CI: 0.09, 0.85) and 3.32-times (95%CI: 1.15, 9.58) greater odds of moderate-to-severe cognitive impairment.

In the sub-group of patients without a hospitalization between their baseline HRS interview and their first pneumonia hospitalization, pneumonia hospitalization remained significantly associated with development of moderate-to-severe cognitive impairment (OR: 2.47, 95%CI: 1.42, 4.32) and increased functional impairments (0.66 new functional impairments, 95%CI: 0.38, 0.93) among those without baseline functional impairment. Pneumonia hospitalization was associated with increased functional disability among those with baseline mild-to-moderate functional impairment, although this association did not reach statistical significance in this subgroup (0.48 new functional impairments, 95%CI: -0.07, 1.02) (eTables 5 and 6). Pneumonia hospitalization was not significantly associated with increased functional impairments in those with moderate-to-severe baseline functional impairment or substantial depressive symptoms in this sub-group, although these analyses may be limited by insufficient statistical power.

DISCUSSION

In this nationwide cohort of older Americans, we have demonstrated that hospitalization for pneumonia is independently associated with subsequent functional decline, nearly 2.5-times the odds of subsequent moderate-to-severe cognitive impairment, and 1.6-times the odds of subsequent substantial depressive symptoms. Importantly, these associations were present among those who were hospitalized only once over a 9 year period and those without substantial medical comorbidity, and are not limited to older adults whose pneumonia required critical care. In sum, our results show that even a non-critical pneumonia hospitalization can lead to long-term adverse outcomes.

Furthermore, we found that older adults without baseline functional impairment were at greater risk of acquiring functional impairments following hospitalization for pneumonia than hospitalization for myocardial infarction. Those hospitalized for myocardial infarction or strokes were at similar risk of developing moderate-to-severe cognitive impairment or substantial depressive symptoms with those hospitalized for pneumonia. The magnitude of these effects for pneumonia is greater than previously published estimates for general medical admissions, but less than severe sepsis for functional and moderate-to-severe cognitive impairment.⁷ In total, these findings suggest that investing resources into pneumonia prevention and treatment comparable to those for cardiovascular disease prevention in older adults may be warranted, given the comparable rates of hospitalization, long-term disability and cognitive sequelae.

While we cannot prove causation, plausible causal pathways do exist. Immobility and lack of physical therapy in patients hospitalized for pneumonia could exacerbate age-related muscle atrophy,³³ and may worsen direct inflammatory, apoptotic, and hypoperfusion-mediated muscle fiber and neuronal degradation.^{7,34,35} Pneumonia-related hypoxia may contribute to subsequent cognitive impairment.^{36,37} Also, pro-inflammatory cytokines are elevated in patients with pneumonia and in depressed patients,^{38,39} and have been hypothesized to lead to late-life neurodegenerative changes.⁴⁰ Additional research is needed to elucidate the pathophysiologic mechanisms underlying how pneumonia may lead to these adverse outcomes.

Reframing pneumonia from not only being an acute life-threatening event but also a profoundly life-altering event changes the cost-benefit calculus when considering potential prevention and therapeutic strategies. There are several plausible interventions to prevent or ameliorate long-term disability, cognitive impairment, and depression after pneumonia, such as: (1) improving community management of pneumonia, particularly timeliness and appropriateness of antibiotics; (2) vaccination against influenza; (3) anti-pneumococcal vaccinations to prevent sequelae of pneumonia such as sepsis; and (4) screening older adults following pneumonia hospitalizations for depression. Further, there is some suggestion that extending early physical rehabilitation, which improves outcomes for mechanically ventilated patients,³⁵ beyond the intensive care unit for patients hospitalized for pneumonia, could potentially prevent or ameliorate subsequent physical dysfunction.^{41,42} Clearly, rigorous evaluation of these interventions is necessary before they can be suggested, but such evaluation seems warranted.

Our study has several limitations. We primarily demonstrate long-term functional and cognitive effects; important short-term deficits (e.g., less than 6 months) could be greater, and transient deficits, such as those due to delirium, may improve before follow-up. Although the neuropsychological battery assessed global cognitive function and was not designed to test individual cognitive domains or diagnose clinical mild cognitive impairment or dementia, we used categories and cutoff scores that have shown strong correlation with clinical dementia as assessed by neuropsychiatric interview.⁴² Since we assessed depression with a questionnaire, we could not diagnose major depression. Also, our results may include asymmetric censoring due to patients with worse cognition and functioning after pneumonia dying before follow-up. If such bias is present, the effect of pneumonia hospitalization seen here is underestimated. Additionally, our inability to detect a significant association between pneumonia hospitalization and increased functional impairment among participants with moderate-to-severe baseline impairment is most likely due to ceiling effects in our measurements of functioning.

Further, we cannot definitively rule out that the effects seen here are due to hospitalization itself or other simultaneous events rather than pneumonia. Medicare claims lack the depth of

information necessary to separate whether specific acute interventions are associated with differing long-term outcomes. However, we did find that unimpaired older adults hospitalized for pneumonia may have worse functional outcomes than those hospitalized for myocardial infarction despite briefer average length of stay, which along with credible pathophysiologic mechanisms linking pneumonia to adverse outcomes suggests that post-hospitalization functional and cognitive decline in older adults may have different trajectories based on the nature of the acute insult. Finally, the possibility of residual confounding remains as in any observational study.

In conclusion, we found that hospitalization for pneumonia is independently associated with subsequent new functional impairments and moderate-to-severe cognitive impairment, and may be associated with subsequent substantial depressive symptoms. Future research identifying the mechanisms that link pneumonia with functional disability, cognitive impairment and depression—along with improved interventions that prevent pneumonia and/or these negative sequelae—are imperative in light of the aging of the population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Health and Retirement Study (1998–2010) patient cohorts for analyses of post-hospitalization outcomes

Figure 2. Trajectories of Activities and Instrumental Activities of Daily Living in patients with one or more hospitalization for pneumonia without functional impairments or with mild-to-moderate functional impairments at baseline

Abbreviations: CI = Confidence Interval; IQR = interquartile range.

The unadjusted mean number of impairments in Activities and Instrumental Activities of Daily Living in surviving cohort members is shown. Error bars represent 95% confidence intervals.

Interpretive Example: Patients without limitations prior to their hospitalization for pneumonia developed approximately 1.3 (95%CI: 1.0, 1.5) new functional impairments after pneumonia.

Figure 3. Cumulative proportion of mild-to-moderate and moderate-to-severe cognitive impairment in participants with one or more hospitalizations for pneumonia

Abbreviation: IQR = interquartile range.

The proportion of patients with mild-to-moderate and moderate-to-severe cognitive impairment in surviving cohort members is shown.

Interpretive Example: The proportion of patients with moderate-to-severe cognitive impairment prior to their hospitalization for pneumonia increased from 15% at the last HRS interview before pneumonia to 25% at the first HRS interview after pneumonia.

Table 1

Baseline demographics and hospitalization characteristics of survivors by diagnosis (n = 1,711 hospitalizations)

Variables	Pneumonia Hospitalization (n = 827)	Myocardial Infarction Hospitalization (n = 450)	Stroke Hospitalization (n = 434)
Panel A: Demographic & Social Characteristics			
Age (years)	77.1(9.4)	75.8 (8.2)	77.0 (8.4)
Female	455 (55%)	203 (45%)	240 (55%)
Race			
White	714(86%)	398 (88%)	344 (80%)
Black	97(12%)	49(11%)	82 (19%)
Other	16 (2%)	3 (1%)	8 (1%)
Education			
0–11 years	345 (42%)	163 (36%)	165 (38%)
12 years	279 (34%)	157 (35%)	127 (29%)
13 or more years	199 (24%)	130 (29%)	139 (32%)
Living Arrangement			
Married/partnered	364 (44%)	279 (62%)	215 (50%)
Unmarried but living with others	168 (20%)	51(11%)	59 (14%)
Unmarried and living alone	295 (36%)	120 (27%)	160 (36%)
Alcohol use			
Drinks less than once per week	665 (80%)	4 (76%)	363 (84%)
Drinks once per week	43 (5%)	24 (5%)	16 (4%)
Drinks twice per week	27 (3%)	21 (5%)	12 (3%)
Drinks more than twice per week	92(11%)	60 (13%)	41 (9%)
Smoking Status			
Never smoked	259(31%)	159 (35%)	197 (45%)
Former smoker	438 (53%)	240 (53%)	186(43%)
Current smoker	122 (15%)	49(11%)	48(11%)
Charlson Comorbidity Score	1.6(1.4)	2.2(1.2)	2.4(1.3)
Pre-hospitalization functional impairment	385 (47%)	277 (62%)	218 (50%)
No limitations	260(31%)	124 (27%)	136(31%)
Mild-Moderate limitations	182(22%)	49(11%)	80 (18%)
Severe limitations			
Pre-hospitalization cognition			
No cognitive impairment	460 (56%)	291 (65%)	225 (52%)
Mild-moderate cognitive impairment	244 (30%)	116(26%)	138 (32%)
Moderate-severe cognitive impairment	123 (15%)	43(11%)	71 (16%)

Variables	Pneumonia Hospitalization (n = 827)	Myocardial Infarction Hospitalization (n = 450)	Stroke Hospitalization (n = 434)
Pre-hospitalization substantial depressive symptoms	181 (22%)	68 (15%)	130 (30%)
Required proxy at baseline	116 (14%)	36 (8%)	49 (11%)
Panel B: Characteristics of the Hospitalization			
Hospital length of stay (days)	5.1 (3.5)	6.0 (5.1)	6.2 (6.6)
Admitted to an intensive care unit or coronary care unit	95 (11%)	275 (61%)	100 (23%)
Required mechanical ventilation	14 (2%)	10 (2%)	13 (3%)
Required major surgery	16 (2%)	95 (21%)	32 (7%)
Required dialysis	19 (2%)	1 (0.2%)	3 (0.7%)
Required proxy at first HRS wave post-hospitalization	190 (23%)	36 (8%)	122 (28%)

All values are mean $\pm$ SD or *n* (%) unless otherwise indicated.

Table 2

Acquisition of impairments in Activities and Instrumental Activities of Daily Living before and after hospitalization for pneumonia, by functional class at baseline^a

One or More Pneumonia Hospitalizations	No Impairment (n=385)	Mild-Moderate Impairment (n=260)	Moderate-to-Severe Impairment (n=182)
Trajectory Before Pneumonia, per year	0.003	0.20	0.69
(95%CI)	(-0.03, 0.03)	(0.14,0.26)	(0.53,0.84)
P value	0.85	< 0.001	< 0.001
Effect of Pneumonia	1.01	0.99	-0.10
(95%CI)	(0.71,1.32)	(0.57, 1.41)	(-1.01,0.08)
P value	< 0.001	< 0.001	0.09
Trajectory After Pneumonia, per year	0.20	0.31	0.04
(95% CI)	(0.13,0.27)	(0.19,0.43)	(-0.67, 0.48)
P value	< 0.001	< 0.001	0.74

Abbreviation: CI = confidence interval.

Interpretive Example: As shown in the third column, 260 patients who were hospitalized for pneumonia had mild-to-moderate pre-hospitalization impairment. The patients in this group had been acquiring new impairments in Activities and Instrumental Activities of Daily Living at an average rate of 0.20 per year *prior* to being hospitalized for pneumonia. However, with the onset of pneumonia they suddenly developed an average of 0.99 new further impairments in Activities and Instrumental Activities of Daily Living, which persisted throughout follow-up.

^aResults of latent growth curve regression with individual-level fixed effects, controlling for all time invariant characteristics of the patient. The absence of an association would be signified by acquiring 0 new impairments in Activities and Instrumental Activities of Daily Living. The within-patient R^2 for patients with one or more pneumonia hospitalization were 0.23 for the no limitation group, 0.31 for the group with mild-to-moderate baseline limitations, and 0.34 for the group with moderate-to-severe limitations.

Table 3

Moderate-to-severe cognitive impairment and substantial depressive symptoms following hospitalization for pneumonia^a

One or More Pneumonia Hospitalizations		
Moderate-to-Severe Cognitive Impairment	OR (95% CI)	P Value
Trajectory Before Pneumonia, per year	1.33(1.17,1.51)	< 0.001
Effect of Pneumonia	2.46(1.60,3.79)	< 0.001
Trajectory After Pneumonia, per year	1.12(1.01, 1.24)	0.03

Substantial Depressive Symptoms	OR (95% CI)	P Value
Trajectory Before Pneumonia, per year	0.96(0.88, 1.04)	0.34
Effect of Pneumonia	1.63 (1.06,2.51)	0.03
Trajectory After Pneumonia, per year	0.93 (0.83, 1.03)	0.17
Time-Varying Control Variables:		
Mild-Mod Cognitive Impairment	0.91 (0.58, 1.42)	0.67
Mod-Severe Cognitive Impairment	0.61 (0.26, 1.47)	0.28
Post-Pneumonia Functional Impairments	1.27(1.14, 1.41)	< 0.001

Abbreviation: CI = confidence interval; OR = Odds Ratio.

Interpretive Example: With each passing year, older adults who survive one or more hospitalization for pneumonia are more likely to develop moderate-to-severe cognitive impairment. After pneumonia, patients had a 2.5-times greater odds of developing moderate-to-severe cognitive impairment than before pneumonia.

^aResults of latent growth curve regression with individual level fixed effects, controlling for all time-invariant characteristics of the patient. The absence of association would be signified by an odds ratio of 1. The analyses for substantial depressive symptoms post-pneumonia are also adjusted for post-pneumonia cognitive impairment, functional impairments and non-response propensity scores.

Table 4

Comparison of the association of hospitalization for pneumonia versus hospitalization for myocardial infarction or stroke and acquisition of new impairments in Activities and Instrumental Activities of Daily Living by baseline functioning^a

Functional Class at Baseline by Limitations in Activities and Instrumental Activities of Daily Living			
Comparison of Effects	No Impairment	Mild-Moderate Impairment	Moderate-to-Severe Impairment
Pneumonia vs. Myocardial Infarction	0.61	0.34	−0.09
(95% CI)	(0.23, 0.99)	(−0.38, 1.05)	(−1.15, 0.97)
<i>P</i> value	0.002	0.35	0.86
Pneumonia vs. Stroke	−1.05	−1.66	−0.61
(95% CI)	(−1.69, −0.42)	(−2.55, −0.77)	(−1.68, 0.46)
<i>P</i> value	< 0.001	< 0.001	0.26

Abbreviation: CI = Confidence Interval.

Interpretive Example: For patients with no impairments prior to hospitalization, and controlling for their pre-hospitalization trajectory, a hospitalization for pneumonia was associated 0.61 *more* new functional impairments than was a hospitalization for a myocardial infarction. In contrast, hospitalizations for pneumonia were associated with *fewer* new functional impairments than were hospitalizations for stroke.

^aAs in Table 2, a within-patient regression was estimated, but in this case in two synthetic cohorts; the first combined pneumonia survivors with survivors of myocardial infarction hospitalizations, while the second combined pneumonia survivors with survivors of stroke. The continuous outcome variable was the number of impairments in Activities and Instrumental Activities of Daily Living. For each synthetic cohort, interaction terms between time and pneumonia hospitalization were estimated to measure the marginal effect of hospitalization for pneumonia compared to myocardial infarction hospitalization in the first cohort and the marginal effect of pneumonia hospitalization versus stroke hospitalization in the second cohort. Please note that the main effects of these synthetic cohorts may not generalize to any population of interest. The marginal effects, or differences, are meant to answer the question: “how different is the association with pneumonia hospitalization than the association with myocardial infarction/stroke hospitalization?” 95% confidence intervals are in parentheses. The absence of an association is signified by the acquisition of 0 new functional impairments.

Table 5

Comparison of the association of hospitalization for pneumonia versus hospitalization for myocardial infarction or stroke and subsequent moderate-to-severe cognitive impairment and substantial depressive symptoms^a

Comparison of Effects	Outcome	
	Moderate-Severe Cognitive Impairment	Substantial Depressive Symptoms
Pneumonia vs. Myocardial Infarction	1.46	1.16
(95% CI)	(0.69, 3.09)	(0.59, 2.26)
P-value	0.32	0.67
Pneumonia vs. Stroke	0.64	0.82
(95% CI)	(0.30, 1.34)	(0.40, 1.70)
P-value	0.24	0.60

Abbreviation: CI = Confidence Interval.

^aAs in Table 3, within-person regressions were estimated but in this case in two synthetic cohorts; the first combined pneumonia survivors with survivors of myocardial infarction hospitalizations, while the second combined pneumonia survivors with survivors of stroke. The dichotomous outcome in the first set of regressions was the presence or absence of moderate-to-severe cognitive impairment at that HRS interview, while the dichotomous outcomes in the second set of regressions was the presence or absence of subsequent depressive symptoms. For each synthetic cohort, interaction terms between time and pneumonia hospitalization were estimated to measure the marginal effect of hospitalization for pneumonia compared to myocardial infarction hospitalization in the first cohort and the marginal effect of pneumonia hospitalization versus stroke hospitalization in the second cohort. Please note that the main effects of these synthetic cohorts may not generalize to any population of interest. The marginal effects, or differences, are meant to answer the question: “how different is the association with pneumonia hospitalization than the association with myocardial infarction/stroke hospitalization?” 95% confidence intervals are in parentheses. The absence of an association is signified by an odds ratio of 1 for the development of moderate-to-severe cognitive impairment or substantial depressive symptoms.