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Depression and Risk of Hospitalization for Pneumonia in a Cohort Study of Older Americans

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Abstract

Objective—To determine if depression is independently associated with risk of hospitalization for pneumonia after adjusting for demographics, medical comorbidity, health-risk behaviors, baseline cognition and functional impairments.

Methods—This secondary analysis of prospectively collected data examined a population-based sample of 6,704 Health and Retirement Study (HRS) (1998–2008) participants > 50 years old who consented to have their interviews linked to their Medicare claims and were without a dementia diagnosis. The eight-item Center for Epidemiologic Studies Depression Scale and/or International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) depression diagnoses were used to identify baseline depression. ICD-9-CM diagnoses were used to identify

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CONFLICT OF INTEREST STATEMENT

All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf and declare that Dr. Katon has received honorariums for CME lectures from Eli Lilly, Forest, and Pfizer pharmaceutical companies. Drs. Davydow, Hough, Zivin and Langa have no relevant potential conflicts of interest to disclose.

hospitalizations for which the principal discharge diagnosis was for bacterial or viral pneumonia. The odds of hospitalization for pneumonia for participants with depression relative to those without depression were estimated using logistic regression models. Population attributable fractions were calculated to determine the extent that hospitalizations for pneumonia could be attributable to depression.

Results—After adjusting for demographic characteristics, clinical factors, and health-risk behaviors, depression was independently associated with increased odds of hospitalization for pneumonia (Odds Ratio [OR]: 1.28, 95% Confidence Interval [95%CI]: 1.08, 1.53). This association persisted after adjusting for baseline cognition and functional impairments (OR: 1.24, 95%CI: 1.03, 1.50). In this cohort, 6% (95%CI: 2%, 10%) of pneumonia hospitalizations pneumonia were potentially attributable to depression.

Conclusion—Depression is independently associated with increased odds of hospitalization for pneumonia. This study provides additional rationale for integrating mental health care into medical settings in order to improve outcomes for older adults.

Keywords

depression; pneumonia; hospitalization; outcome assessment (health care)

INTRODUCTION

Each year, nearly 400,000 Americans ages 65 and older are hospitalized for pneumonia [1].Pneumonia is the third most common cause of hospitalization among Americans 65–84 years old, and the second most common among those over age 85 [2]. Nearly 11% of older adults hospitalized for pneumonia die within 30 days of hospitalization [1], and approximately half die within one year [3]. Beyond increased mortality, hospitalization for pneumonia may raise the risk of subsequent cognitive and functional decline [4]. In addition, pneumonia-related hospitalizations are a burden to the American public healthcare system, costing Medicare an estimated $7.3 billion annually [1], in part due to early rehospitalizations [5]. Importantly, many hospitalizations for pneumonia could be prevented [6], and the Centers for Medicare and Medicaid Services (CMS) has begun actively incentivizing efforts to reduce rehospitalizations within 30 days of initial hospitalization for pneumonia [7]. While several studies have identified increased age and greater medical comorbidity as associated with development of pneumonia [8, 9], there remains a need to identify potentially modifiable risk factors in order to prevent pneumonia-related hospitalizations.

Depressive disorders are among the most common mental disorders in older adults [10]. Notably, over 20% of older adults with congestive heart failure (CHF) or chronic obstructive pulmonary disease, common chronic medical conditions associated with risk of developing pneumonia, may also have major depression [11, 12]. However, no study to date has examined the association between depression and risk of hospitalization for pneumonia. Although some studies have controlled for depression as a potential risk factor for pneumonia and pneumonia-related hospitalizations [13–18], none of these were primarily designed to examine depression as an independent risk factor.

The present study utilizes data from an ongoing longitudinal study of health outcomes in older adults to examine if depression is independently associated with increased risk of hospitalization for pneumonia after adjusting for demographic characteristics, medical comorbidity, and health-risk behaviors. We also sought to determine if any association found between depression and pneumonia hospitalization remained even after adjusting for potential mediators such as cognitive status and functional disability.

METHODS

Population

This study is a secondary analysis of prospectively collected, nationally representative data from Americans over age 50 participating in the Health and Retirement Study (HRS). The HRS began in 1992, and to date, over 31,000 individuals have participated. Subjects are interviewed every two years. The HRS follow-up rate has exceeded 90–95% (including proxies) with over 80% of eligible respondents consenting to linkage of their Medicare claims records with study data [19]. The HRS protocol was approved by the University of Michigan Institutional Review Board. Participants provided informed consent upon enrollment and again for linkage to Medicare claims.

Our sample was comprised of HRS respondents interviewed in 1998 or 2000 who consented to linkage of their Medicare claims records. We followed them through death or the 2008 interview. We excluded individuals with an International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) dementia diagnosis (codes 290.0–290.42, 291.2, 294.1, 294.8, 331.0, 331.1, 331.11, 331.19, or 331.82) at baseline from our analyses since dementia is known to raise the risk of pneumonia as well as hasten death and may have a bidirectional relationship with depression [20–23].

Primary Independent Variable

The primary independent variable in our analyses was baseline (i.e., the 1998 or 2000 HRS interview) presence of depression. Depression was defined as either a score of ≥ 4 on the eight-item Center for Epidemiologic Studies Depression Scale (CES-D-8) [24] at the baseline HRS interview (obtained from self-respondents only [24]) or a Medicare claims-based depression diagnosis in the year before baseline based on ICD-9-CM codes 296.2, 296.3, 298.0, 300.4, or 311.0. The CES-D-8 cutoff score of ≥ 4 has been found to be comparable to the cutoff score of ≥ 16 on the full CES-D [24], and has been used previously in other relevant studies [4, 25, 26].

Demographics, Clinical Characteristics and Health-Risk Behaviors

Demographic information (e.g., age, sex, race, education, marital/partnered status, and dual Medicare-Medicaid eligibility) was obtained from the HRS interviews. Elixhauser comorbidity diagnoses [27] as well as the number of hospitalizations in the year before baseline were obtained from Medicare claims. Information on alcohol use and smoking came from the HRS interviews. Prior substance abuse diagnoses (ICD-9-CM codes 303.0 – 305.0) were obtained from Medicare claims.

Cognitive and Functional Status

Cognition was assessed using the modified Telephone Interview for Cognitive Status (TICSm), a validated composite measure comprised of items testing immediate and delayed recall, working memory with serial sevens subtraction, and backwards counting testing attention and processing speed [28]. Scores range from 0 to 27, with higher scores indicating better cognitive functioning [28].

Functional status was ascertained by asking participants (or their proxies) if they required assistance with any of six activities of daily living (ADLs): walking, dressing, bathing, eating, getting into/out of bed, and toileting, or five instrumental ADLs (IADLs): preparing a hot meal, grocery shopping, making telephone calls, taking medicines, and managing money.

Outcome of Interest

Our outcome of interest was the first hospitalization for pneumonia occurring during the follow-up period. We used ICD-9-CM codes (see Online Supplement) to identify hospitalizations for which the principal discharge diagnosis was for bacterial or viral pneumonia based on validated algorithms [6, 29].

Statistical Analysis

We present descriptive data as means and standard deviations (SDs) or proportions. We examined bivariate associations between baseline demographic, clinical, health-risk behavioral and functional characteristics and depression using one-way analysis of variance for normally distributed continuous variables and Chi-squared or Fisher's exact tests for categorical variables.

To estimate odds ratios (ORs) and 95% Confidence Intervals (95%CIs) for the association of baseline depression with hospitalization for pneumonia, we used logistic regression models with robust error variances. First, we tested the association of depression with pneumonia hospitalization without adjustment. We then sequentially adjusted for potential confounders chosen *a priori* based on prior research identifying their associations with depression and/or health outcomes, including hospitalization for pneumonia, among older adults [5, 8, 9, 30]. Non-normally distributed covariates were categorized. The sequence of adjustments was: 1) demographic characteristics (e.g., age, sex, race categorized as white versus non-white, education categorized as < high school graduate versus ≥ high school graduate, marital/partnered status categorized as married/partnered versus single/separated/widowed, dual Medicare-Medicaid eligibility); 2) clinical characteristics (e.g., non-psychiatric Elixhauser comorbidities, number of hospitalizations in the year before baseline); and 3) health-risk behaviors (e.g., alcohol use categorized by the number of drinks per day, smoking status, and substance abuse diagnosis). In a final step, we adjusted for cognitive status (i.e., TICSm score) and total ADL/IADL impairments categorized by their interquartile range in order to examine the extent to which depression remained associated with pneumonia hospitalization even after considering these two potential mediators.

To determine the extent that any increase in hospitalizations for pneumonia could be attributable to depression, we calculated the population attributable fraction (PAF). The PAF for depression and its 95%CI was estimated using the following formula: P(OR – 1) / (1 + P[OR – 1]). In this formula, P represents the prevalence of depression and OR is the adjusted Odds Ratio for the association of depression with hospitalization for pneumonia [31].

In a set of sensitivity analyses, we estimated the association of baseline depression with pneumonia hospitalization using only the CES-D-8 threshold to define depression. In the first sensitivity analysis, we used a CES-D-8 cutoff score of ≥ 4; in the second, we used a cutoff score of ≥ 3, which has been found to have a sensitivity of 71% and a specificity of 79% for the diagnosis of major depression versus structured interview [32]. Since the CES-D-8 was only administered to self-respondents, this analysis only included the 6,137 self-respondents without a dementia diagnosis.

We used two-sided significance tests for all analyses with statistical significance set at $P < 0.05$. Analyses were performed with appropriate components of the STATA 12 (Stata Corporation, College Station, TX) statistical software program.

RESULTS

Of 7,031 HRS respondents interviewed in 1998 or 2000 who consented to linking their study data with their Medicare claims records, 327 with an ICD-9-CM dementia diagnosis at baseline were excluded, leaving a sample of 6,704 for analyses. Table 1 describes the baseline demographic, clinical, health-risk behavioral and functional characteristics of the total sample and grouped by baseline depression status. At baseline, 21.1% of the cohort was depressed based on either a depression diagnosis or a CES-D-8 score ≥ 4.

During the follow-up period (mean: 6.8 years, SD: 3.1 years), 875 (13.1%) participants were hospitalized at least once for pneumonia. Of these individuals, 248 (28.3%) were depressed at baseline.

In unadjusted analyses, baseline depression was associated with increased odds of hospitalization for pneumonia during follow-up (OR: 1.57, 95%CI: 1.34, 1.84). This association persisted after adjusting for participant demographic characteristics (OR: 1.46, 95%CI: 1.24, 1.73), clinical characteristics (OR: 1.31, 95%CI: 1.10, 1.56), and health-risk behaviors (OR: 1.28, 95%CI: 1.08, 1.53) (Table 2). Even after adjusting for potential mediators such as cognition assessed by the TICSm and impairments in ADLs and IADLs, depression at baseline remained independently associated with increased odds of hospitalization for pneumonia (OR: 1.24, 95%CI: 1.03, 1.50).

When we calculated the fraction of pneumonia hospitalizations potentially attributable to depression, we found that 6% (95%CI: 2%, 10%) may have been attributable to depression at baseline. After adjusting for cognitive status and functional impairments, 5% (95%CI: 1%, 9%) of pneumonia hospitalizations in our cohort may have been attributable to baseline depression.

In addition to baseline depression, increased age (OR: 1.03, 95%CI: 1.02, 1.04), dual Medicare-Medicaid status (OR: 1.56, 95%CI: 1.26, 1.94), chronic pulmonary disease (OR: 1.65, 95%CI: 1.24, 2.19), liver disease (OR: 2.64, 95%CI: 1.01, 6.93), and being a former smoker (OR: 1.44, 95%CI: 1.20, 1.73) or currently smoking (OR: 1.87, 95%CI: 1.44, 2.44) were consistently associated with increased odds of hospitalization for pneumonia. Being single, separated/divorced, or widowed was associated with increased odds of hospitalization for pneumonia after adjusting for demographics, clinical characteristics and health-risk behaviors (OR: 1.20, 95%CI: 1.01, 1.43), though this association became slightly less precise after adjusting for TICSm score and ADL/IADL impairments (OR: 1.20, 95%CI: 1.00, 1.44). Conversely, female sex (OR: 0.76, 95%CI: 0.63, 0.91) and higher TICSm score (OR: 0.98, 95%CI: 0.96, 0.99) were consistently associated with decreased odds of hospitalization for pneumonia.

In our sensitivity analysis in which we defined baseline depression by a CES-D-8 score ≥ 4 alone, baseline depression was associated with increased odds of hospitalization for pneumonia independently of demographic characteristics, clinical characteristics and health-risk behaviors (OR: 1.25, 95%CI: 1.03, 1.52) (Table 3). However, this association was somewhat attenuated after adjusting for TICSm score and ADL/IADL impairments (OR: 1.17, 95%CI: 0.96, 1.44). When we defined baseline depression by a CES-D-8 score ≥ 3 alone, baseline depression remained associated with increased odds of pneumonia hospitalization even after adjusting for TICSm score and impairments in ADLs/IADLs (OR: 1.23, 95%CI: 1.02, 1.47).

DISCUSSION

In this nationally representative cohort of older Americans, we have demonstrated that depression is associated with 1.28-times greater odds of hospitalization for pneumonia after controlling for demographics, clinical characteristics and health-risk behaviors. Interestingly, depression remained associated with 1.24-times greater odds of hospitalization for pneumonia even after adjusting for baseline cognitive and functional status. While this association was attenuated slightly when baseline depression was defined by a CES-D-8 score ≥ 4 alone, this finding was likely the result of diminished statistical power due to proxy-requiring HRS participants not completing a CES-D-8. This possibility is further bolstered by our finding that lowering the CES-D-8 threshold to ≥ 3 led to a result in keeping with our primary analyses.

Furthermore, we found that one out of every twenty hospitalizations for pneumonia in our cohort of older Americans may be attributable to depression. To our knowledge, the present study is the first to identify that a common psychiatric disorder in older adults, depression, could be an independent risk factor for being hospitalized for pneumonia. Importantly, depression has been found to be associated with increased risk of developing diabetes and CHF [33, 34], initiating smoking [35], and cognitive and functional impairment [36, 37], all of which are independently associated with greater risk of contracting pneumonia [9, 20, 38–40]. Therefore, our analyses may be overly conservative since they control for all of these variables, potentially underestimating the magnitude of the association of depression with hospitalization for pneumonia.

While depression is known to impair cognition and functioning in older adults [36, 37], and cognitive as well as ADL/IADL impairment are known to be associated with greater risk of developing pneumonia [20, 40], our findings suggest that a potential association between depression and increased risk of hospitalization for pneumonia may be mediated by additional factors. One possible mediator could be through depression's association with increased pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha and C-reactive protein [41]. Older adults with community-acquired pneumonia (CAP) have been found to have elevated levels of these cytokines [42], and elevated levels of IL-6 have been postulated to contribute to greater risk of progression from CAP to severe sepsis and elevated risk of mortality [42, 43]. Although elevated levels of pro-inflammatory cytokines could be epiphenomena rather than mediators of depression's association with greater odds of pneumonia hospitalization, our findings suggest the need for further longitudinal studies with sufficient power to examine whether pro-inflammatory cytokines mediate observed associations of depression with pneumonia and other inflammation-related diseases.

Our study warrants particular consideration in light of the growing recognition, especially since the passage of the Patient Protection and Affordable Care Act, that integration of mental health care with primary and specialty medical care is necessary to improve patient outcomes [44]. We demonstrate here that a common psychiatric disorder, depression, is associated with increased risk of one of the most common causes of hospitalization among older Americans, pneumonia. Previously in a related cohort, we demonstrated that hospitalization for pneumonia may be associated with increased risk of depression [4], suggesting the potential of a vicious cycle of hospitalization and rehospitalization for pneumonia among older adults. When taken together with the vast body of literature demonstrating that depression is associated with increased medical illness burden and worse outcomes for a wide-range of common medical illnesses [30, 45, 46], the present study adds further evidence supporting the need to accelerate integration of mental health with medical care. Importantly, collaborative care interventions for depression integrated into medical care settings have reduced depressive symptoms and improved functioning in older adults [47–50], and have also been adapted to improve chronic medical illness management [49]. Notably, these interventions have been shown to reduce hospitalization-related healthcare costs [51], a point relevant to the present study in light of CMS' policy of penalizing hospitals and health systems with excessive 30-day rehospitalizations following initial hospitalizations for pneumonia [7].

In addition to depression, increased age, chronic pulmonary disease, liver disease and being a former or current smoker, we found that dual Medicare-Medicaid eligibility and being unmarried/unpartnered were also associated with increased odds of hospitalization for pneumonia. Our finding that dual Medicare-Medicaid eligibility is independently associated with pneumonia hospitalization builds upon prior research identifying poverty as a potential risk factor for bacterial pneumonia [52, 53]. Moreover, previous studies have found that unmarried/unpartnered individuals had higher rates of hospitalization for sepsis and higher in-hospital mortality when admitted for pneumonia compared to those who were married/partnered [54, 55]. Prior work has found that socioeconomic factors may play an important role in clinician decisions to hospitalize patients for pneumonia at low risk for mortality

even though these characteristics (as well as psychiatric disorders) are not taken into account by decision tools currently used to identify which patients with pneumonia require hospitalization [54]. This evidence underscores the need to consider psychosocial factors when implementing interventions to improve health outcomes and reduce hospitalizations in older adults.

Our study has several limitations. Since we only assessed depression at baseline, and depressive symptom severity may have lessened over the course of follow-up, it is conceivable that other more proximate factors may have played a larger role in conveying risk for pneumonia hospitalization. Nonetheless, prior work has identified that depression in older adults with medical illnesses is frequently chronic [48]. In addition, we lack data on treatment for depression in our cohort to be able to infer whether appropriate therapies could modify the associations presented here. While the CES-D-8 cannot be used to make depression diagnoses, it has been used to examine the impact of depression on health outcomes in other relevant studies of older adults [25, 26], and our depression definition was supplemented by ICD-9-CM diagnoses. Furthermore, we only report on hospitalizations for pneumonia; our study was not designed to determine if depression is associated with development of pneumonia, particularly CAP, not requiring hospitalization. We also lack data on pneumonia severity such as Pneumonia Severity Index classifications.

An added limitation is that baseline alcohol use or smoking may not accurately reflect subsequent health behaviors over the follow-up period. However, prior studies have found that depressed smokers are significantly less likely to quit smoking [56, 57]. Also, adjustment for ICD-9-CM substance abuse diagnoses from administrative data likely underestimated the impact of this confounder. Although our analyses were not weighted to account for the HRS sampling design, a previous study using data from the HRS found no difference in estimates between weighted and unweighted analyses with only slight differences in standard errors [58]. Furthermore, our Medicare claims data did not include Medicare Advantage claims, and thus information on depression as well as pneumonia hospitalization for Medicare Advantage enrollees. Finally, residual confounding remains a possibility, as in any observational study.

In conclusion, using a nationally representative sample of older Americans, we have shown that depression is independently associated with increased odds of hospitalization for pneumonia. We also found that this association may be mediated by factors beyond depression's associations with cognitive dysfunction and ADL/IADL impairments. Additional research that illuminates the pathophysiology underlying the bi-directional relationship between depression and hospitalization for pneumonia as well as develops targeted, cost-effective interventions to prevent these hospitalizations is needed in light of the adverse consequences of hospitalizations for pneumonia for older adults, their loved ones and society.

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HIGHLIGHTS

- We examined if depression increased the risk of hospitalization for pneumonia.
- Depression was associated with 1.28-times% greater odds of pneumonia hospitalization.
- Depression accounted for 6% of pneumonia hospitalizations in our cohort.
- This study provides added rationale for integrating mental health and medical care.

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Table 1

Demographic, clinical, health-risk behavioral and functional characteristics at baseline of entire sample and by depression status

	Entire cohort (n = 6,704)	No depression (n = 5,285)	Depression (n = 1,419)	Test statistic[a]	*P* value
Demographics					
Age	74.8 (8.1)	74.8 (7.7)	74.5 (9.5)	F = 1.5	0.21
Sex					
Male	2,844 (42%)	2,401 (45%)	443 (31%)	χ^2 = 92.5	< 0.001
Female	3,860 (58%)	2,884 (55%)	976 (69%)		
Race					
White	5,800 (86%)	4,637 (88%)	1,163 (82%)	χ^2 = 32.2	< 0.001
Non-white	903 (14%)	647 (12%)	256 (18%)		
Education					
≥ High school graduate	4,124 (62%)	3,389 (64%)	735 (52%)	χ^2 = 72.5	< 0.001
< High school graduate	2,575 (38%)	1,891 (36%)	684 (48%)		
Marital status					
Married/partnered	3,867 (58%)	3,235 (61%)	632 (45%)	χ^2 = 126.1	< 0.001
Single/separated/widowed	2,832 (42%)	2,048 (39%)	784 (55%)		
Dual Medicare-Medicaid					
No	5,420 (81%)	4,467 (85%)	953 (67%)	χ^2 = 217.8	< 0.001
Yes	1,284 (19%)	818 (15%)	466 (33%)		
Clinical characteristics					
Non-psychiatric Elixhauser comorbidities					
Congestive heart failure	418 (6%)	258 (5%)	160 (11%)	χ^2 = 78.2	< 0.001
Valvular disease	249 (4%)	166 (3%)	83 (6%)	χ^2 = 22.9	< 0.001
Pulmonary circulation disease	81 (1%)	54 (1%)	27 (2%)	χ^2 = 7.3	0.007
Peripheral vascular disease	224 (3%)	147 (3%)	77 (5%)	χ^2 = 24.2	< 0.001
Paralysis	77 (1%)	51 (1%)	26 (2%)	χ^2 = 7.4	0.006
Other neurological disorders	123 (2%)	85 (2%)	38 (3%)	χ^2 = 7.1	0.008
Chronic pulmonary disease	498 (7%)	307 (6%)	191 (13%)	χ^2 = 95.2	< 0.001
Diabetes without chronic complications	412 (6%)	267 (5%)	145 (10%)	χ^2 = 51.8	< 0.001

	Entire cohort (n = 6,704)	No depression (n = 5,285)	Depression (n = 1,419)	Test statistic[a]	*P* value
Diabetes with chronic complications	107 (2%)	69 (1%)	38 (3%)	$\chi^2 = 13.4$	< 0.001
Hypothyroidism	201 (3%)	132 (2%)	69 (5%)	$\chi^2 = 21.5$	< 0.001
Renal Failure	69 (1%)	43 (1%)	26 (2%)	$\chi^2 = 11.4$	0.001
Liver disease	21 (0.3%)	12 (0.2%)	9 (0.6%)	$\chi^2 = 5.9$	0.01
Peptic ulcer disease	5 (0.1%)	4 (0.1%)	1 (0.1%)	-	0.71
AIDS	0 (0%)	0 (0%)	0 (0%)	-	-
Lymphoma	14 (0.2%)	11 (0.2%)	3 (0.2%)	-	0.59
Metastatic cancer	55 (0.8%)	45 (1%)	10 (1%)	$\chi^2 = 0.3$	0.59
Solid tumor without metastasis	120 (2%)	95 (2%)	25 (2%)	$\chi^2 = 0.01$	0.93
Rheumatoid arthritis	57 (1%)	37 (1%)	20 (1%)	$\chi^2 = 6.7$	0.01
Coagulopathy	65 (1%)	40 (1%)	25 (2%)	$\chi^2 = 11.8$	0.001
Obesity	86 (1%)	58 (1%)	28 (2%)	$\chi^2 = 6.8$	0.009
Weight loss	59 (1%)	39 (1%)	20 (1%)	$\chi^2 = 5.8$	0.02
Fluid and electrolyte disorders	476 (7%)	302 (6%)	174 (12%)	$\chi^2 = 72.7$	< 0.001
Chronic blood loss anemia	57 (1%)	36 (1%)	21 (1%)	$\chi^2 = 8.5$	0.004
Deficiency anemias	221 (3%)	137 (3%)	84 (6%)	$\chi^2 = 38.8$	< 0.001
Hypertension	1,108 (16%)	753 (14%)	355 (25%)	$\chi^2 = 94.0$	< 0.001
# of hospitalizations in previous year among hospitalized	1.6 (1.1)	1.6 (1.1)	1.7 (1.2)	F = 4.4	0.04
Health-risk behaviors					
Alcohol use					
Daily drinker	896 (13%)	779 (15%)	117 (8%)	$\chi^2 = 82.7$	< 0.001
# of drinks per day among daily drinkers	1.8 (1.4)	1.8 (1.4)	1.8 (1.4)	F = 0.6	0.43
Smoking status					
Never smoked	2,859 (43%)	2,249 (43%)	610 (43%)	$\chi^2 = 12.4$	0.002
Former smoker	3,054 (46%)	2,445 (47%)	609 (43%)		
Current smoker	748 (11%)	555 (10%)	193 (14%)		
Substance abuse diagnosis	77 (1%)	44 (1%)	33 (2%)	$\chi^2 = 22.0$	< 0.001
Functional characteristics					
TICSm score (range 0 – 27)	13.8 (4.9)	14.3 (4.8)	12.2 (5.0)	F = 186.6	< 0.001

	Entire cohort (n = 6,704)	No depression (n = 5,285)	Depression (n = 1,419)	Test statistic[a]	*P* value
Have ADL or IADL impairments	2,399 (36%)	1,560 (29%)	839 (59%)	$\chi^2 = 56.0$	< 0.001
# of ADL and IADL impairments among impaired	3.4 (2.7)	3.1 (2.7)	3.8 (2.7)	F = 37.9	< 0.001

All values are N(%) or mean (SD).

Abbreviations (in alphabetical order): ADL = activities of daily living; AIDS = Acquired Immunodeficiency Syndrome; IADL = instrumental ADLs; TICSm = Modified Telephone Interview for Cognitive Status.

[a]Results of bivariate comparisons between non-depressed vs. depressed at baseline using Pearson's chi-squared tests with 2 degrees of freedom, one-way analysis of variance with 1 degree of freedom, or Fisher's exact test.

Table 2

Adjusted associations of depression at baseline with odds of hospitalization for pneumonia

	Adjusted for demographics	Adjusted for demographics and clinical characteristics	Adjusted for demographics, clinical characteristics and health-risk behaviors	Adjusted for demographics, clinical characteristics health-risk behaviors, and functional status
	Odds Ratio (95% Confidence Interval)			
Depression	**1.46 (1.24, 1.73)†**	**1.31 (1.10, 1.56)†**	**1.28 (1.08, 1.53)†**	**1.24 (1.03, 1.50)***
Age	1.02 (1.01, 1.03)‡	1.02 (1.01, 1.03)‡	1.03 (1.02, 1.04)‡	1.03 (1.02, 1.04)‡
Female	0.67 (0.57, 0.78)‡	0.70 (0.60, 0.82)‡	0.77 (0.65, 0.91)†	0.76 (0.63, 0.91)†
Non-white	0.79 (0.63, 0.99)*	0.81 (0.65, 1.02)	0.82 (0.65, 1.03)	0.76 (0.59, 0.98)*
< High school graduate	1.08 (0.92, 1.27)	1.03 (0.88, 1.22)	1.00 (0.85, 1.18)	0.92 (0.77, 1.10)
Single/separated/widowed	1.27 (1.07, 1.50)†	1.23 (1.04, 1.46)*	1.20 (1.01, 1.43)*	1.20 (1.00, 1.44)
Dual Medicare-Medicaid	1.75 (1.44, 2.12)‡	1.61 (1.32, 1.96)‡	1.61 (1.32, 1.96)‡	1.56 (1.26, 1.94)‡
Congestive heart failure		1.05 (0.77, 1.44)	1.03 (0.75, 1.41)	0.88 (0.61, 1.25)
Valvular disease		1.22 (0.84, 1.78)	1.26 (0.86, 1.83)	1.35 (0.90, 2.30)
Pulmonary circulation disease		1.57 (0.94, 2.64)	1.61 (0.95, 2.73)	1.68 (0.93, 3.03)
Peripheral vascular disease		1.04 (0.72, 1.51)	0.97 (0.67, 1.42)	1.08 (0.72, 1.62)
Paralysis		1.36 (0.74, 2.51)	1.44 (0.78, 2.66)	1.73 (0.84, 3.58)
Other neurological disorders		1.06 (0.64, 1.74)	1.07 (0.65, 1.75)	0.94 (0.52, 1.70)
Chronic pulmonary disease		2.10 (1.63, 2.70)‡	1.92 (1.48, 2.48)‡	1.65 (1.24, 2.19)†
Diabetes without chronic complications		0.99 (0.73, 1.35)	1.00 (0.73, 1.36)	0.97 (0.70, 1.36)
Diabetes with chronic complications		1.96 (1.20, 3.20)†	1.87 (1.13, 3.09)*	1.62 (0.91, 2.88)
Hypothyroidism		0.97 (0.64, 1.45)	0.94 (0.63, 1.43)	0.95 (0.61, 1.47)
Renal failure		1.03 (0.54, 1.95)	1.02 (0.54, 1.95)	1.05 (0.50, 2.19)
Liver disease		2.96 (1.08, 8.10)*	2.81 (1.07, 7.36)*	2.64 (1.01, 6.93)*
Lymphoma		1.53 (0.38, 6.16)	1.65 (0.42, 6.42)	2.09 (0.49, 8.86)
Metastatic cancer		1.17 (0.56, 2.46)	1.14 (0.54, 2.42)	1.20 (0.54, 2.66)
Rheumatoid arthritis		0.95 (0.44, 2.04)	0.92 (0.43, 1.98)	1.04 (0.48, 2.25)
Coagulopathy		0.66 (0.33, 1.29)	0.67 (0.33, 1.33)	0.52 (0.22, 1.23)
Obesity		1.19 (0.67, 2.10)	1.19 (0.67, 2.12)	1.32 (0.72, 2.40)
Weight loss		1.36 (0.75, 2.46)	1.30 (0.72, 2.33)	1.35 (0.68, 2.66)
Fluid and electrolyte disorders		1.09 (0.82, 1.45)	1.06 (0.80, 1.41)	1.10 (0.80, 1.50)
Chronic blood loss		0.69 (0.33, 1.44)	0.69 (0.33, 1.45)	0.63 (0.27, 1.47)
Deficiency anemias		1.03 (0.70, 1.51)	1.05 (0.71 , 1.56)	0.91 (0.58, 1.41)
Hypertension		1.11 (0.89, 1.39)	1.11 (0.88, 1.39)	1.12 (0.88, 1.44)
# of hospitalizations in year pre-baseline		1.06 (0.96, 1.17)	1.08 (0.97, 1.19)	1.11 (0.99, 1.24)
Alcohol consumption				
1 drink/day			0.92 (0.73, 1.16)	0.94 (0.74, 1.19)
2 drinks/day			0.82 (0.59, 1.13)	0.84 (0.60, 1.18)

	Adjusted for demographics	Adjusted for demographics and clinical characteristics	Adjusted for demographics, clinical characteristics and health-risk behaviors	Adjusted for demographics, clinical characteristics health-risk behaviors, and functional status
3 drinks/day			1.12 (0.70, 1.80)	1.00 (0.58, 1.72)
≥ 4 drinks/day			0.64 (0.35, 1.17)	0.72 (0.39, 1.33)
Smoking				
Former smoker			1.41 (1.18, 1.68)‡	1.44 (1.20, 1.73)‡
Current smoker			1.85 (1.44, 2.38)‡	1.87 (1.44, 2.44)‡
Substance abuse diagnosis			1.10 (0.60, 2.01)	1.04 (0.53, 2.03)
TICSm score				0.98 (0.96, 0.99)*
ADL/IADL impairments				
1–2 ADL/IADL impairments				1.22 (0.99, 1.49)
3–4 ADL/IADL impairments				1.20 (0.90, 1.59)
≥ 5 ADL/IADL impairments				1.06 (0.77, 1.46)

Abbreviations (in alphabetical order): ADL = activities of daily living; IADL = instrumental ADLs; TICSm = Modified Telephone Interview for Cognitive Status.

*$P < 0.05$

†$P < 0.01$

‡$P < 0.001$

Table 3

Sensitivity analysis of adjusted associations of depression at baseline defined solely by the Eight-Item Center for Epidemiologic Depression Scale with odds of hospitalization for pneumonia

	Odds Ratio (95% Confidence Interval) for Depression defined solely as CES-D-8 ≥ 4)	Odds Ratio (95% Confidence Interval) for Depression defined solely as CES-D-8 ≥ 3)
Adjusted for demographics[a]	**1.40 (1.15, 1.69)**†	**1.47 (1.24, 1.74)**‡
Adjusted for demographics and clinical characteristics[b]	**1.28 (1.06, 1.56)***	**1.33 (1.12, 1.58)**†
Adjusted for demographics, clinical characteristics and health-risk behaviors[c]	**1.25 (1.03, 1.52)***	**1.30 (1.09, 1.55)**†
Adjusted for demographics, clinical characteristics health-risk behaviors, and functional status[d]	**1.17 (0.96, 1.44)**	**1.23 (1.02, 1.47)***

Abbreviation: CES-D-8 = Eight-Item Center for Epidemiologic Studies Depression Scale.

* $P < 0.05$

† $P < 0.01$

‡ $P < 0.001$

[a] Adjusted for age, sex, race, education, marital/partnered status and dual Medicare-Medicaid status.

[b] Adjusted for demographics, non-psychiatric Elixhauser diagnoses, and number of hospitalizations in the year before baseline.

[c] Adjusted for demographics, clinical characteristics, alcohol consumption, smoking status, and substance abuse diagnosis.

[d] Adjusted for demographics, clinical characteristics, health-risk behaviors, TICSm score, and categories of ADL/IADL impairments.