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## Mortality and Cost of Pneumonia After Stroke for Different Risk Groups

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## Abstract

**Introduction**—An evidenced based approach to detecting and treating dysphagia needs to be informed by costs and risks associated with pneumonia. In this study the cost of pneumonia during hospitalization after stroke and the effect of pneumonia on mortality were estimated. The effect of pneumonia on mortality and cost for different levels of risk were also analyzed.

**Methods**—The data come from the 2005 and 2006 Nationwide Inpatient Sample. Regression models, including the propensity for pneumonia, were used to estimate the in hospital mortality associated pneumonia, and the marginal cost of pneumonia on the hospitalization. A stratified analysis based on quintile of propensity for pneumonia was also undertaken.

**Results**—There were 183, 976 hospitalizations for stroke in the sample. The adjusted relative risk of death associated with pneumonia was 2.0 (95% CI 1.9–2.1). The average marginal cost of pneumonia on the hospitalization was \$27,633 (95% CI \$27,078–\$27,988). The quintile of hospitalizations with the highest propensity for pneumonia had the highest average marginal cost associated with pneumonia and the lowest adjusted relative risk of death. There was an inverse relationship between adjusted relative risk of death and propensity for pneumonia.

**Conclusions**—Pneumonia after stroke is associated with higher mortality and hospitalization costs. Patients with the lowest risk for pneumonia have the highest risk for death associated with pneumonia. Screening is important at all levels of risk.

## Introduction

Pneumonia is a common occurrence after stroke and contributes to the morbidity and mortality experienced by stroke survivors. It is estimated that 6–22% of stroke survivors will experience pneumonia.<sup>1–4</sup> The primary risk factor for pneumonia after stroke is thought to be dysphagia that allows aspiration of ingested food, liquids, or oral secretions. There is evidence that treatment of dysphagia is associated with a reduction in the incidence of pneumonia.<sup>5</sup> Dysphagia screening is part of stroke care guidelines<sup>6–9</sup> though it is not clear which form of screening should be utilized.

There are tradeoffs between the many approaches to screening for dysphagia after stroke. Sensitive screening approaches such as the videofluoroscopic swallowing study (aka the

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modified barium swallow study) are more costly while clinical bedside evaluations, tend to be less sensitive but nearly free of cost.<sup>11,12</sup> It has been suggested that some type of risk assessment would allow practitioners to determine the ideal screening method for each patient so that only those who would benefit would undergo tests that are more costly, less convenient, or potentially harmful than other available alternatives.<sup>13</sup> At this point it is not clear which patients would benefit from different methods of swallowing evaluation.

An evidenced based approach to detecting and treating dysphagia while taking cost into consideration is limited by current estimates in the literature. There have been innovative studies that have provided estimates on the effects of pneumonia on mortality <sup>4,14,15</sup> and an estimate of the marginal cost of pneumonia on hospitalization.<sup>10</sup> These studies report differences in the mortality risk due to pneumonia (adjusted relative risk 1.9–6.0), and the cost estimate was limited to Medicare patients in a small geographic area.

The purposes of this study are twofold. The first is to determine the marginal cost of pneumonia during the acute hospitalization after stroke in a large, national sample that is more generalizable than samples used in prior studies. The second purpose is to determine the effect of pneumonia on inpatient mortality among patients of differing risk for pneumonia to test the hypothesis that the effect of pneumonia on mortality is the greatest in patients with the greatest risk for pneumonia. Identifying those stroke survivors who incur the greatest risk of death associated with pneumonia will provide an initial step in determining which patients would benefit the most from screening for dysphagia after stroke.

#### **METHODS**

This study was determined to be of exempt status by the local institutional review board of the author.

#### Data

These data come from the 2005 and 2006 Nationwide Inpatient Sample (NIS). The NIS contains data on inpatient stays from states that participate in the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality (AHRQ). The project is a stratified probability sample of acute-care hospitals in the United States. The 2005 and 2006 NIS datasets contain information on approximately eight million discharges each from nearly 1000 hospitals across the nation. The NIS contains information regarding the hospital inpatient stay, including admission diagnosis, secondary diagnoses, age, gender, disposition, as well as information regarding the hospital status, etc.). The unit of analysis in the NIS is the hospital episode that precludes longitudinal person-level analysis.

#### Subjects

Hospitalizations for stroke were identified using International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes for ischemic and hemorrhagic stroke (430.xx, 431.xx, 432.9, 433.x1, 434.xx, 436.xx, and 997.02) as the primary diagnosis for hospitalization. As has been done elsewhere, hospitalized patients who died within three days of admission were excluded to limit analyses to those patients who would benefit the most from efforts to reduce pneumonia.<sup>4</sup> Hospitalizations were also excluded for patients with age less than 18 years and who had missing values. All hospitalizations in Texas in the year 2005 were excluded because of lack of cost-to-charge ratio data.

#### Pneumonia

Occurrence of pneumonia during the hospitalization was identified using ICD-9-CM codes of secondary diagnoses (481.xx 482.xx, 485.xx, 486.xx, 507.x, and 997.3). Up to 14 secondary diagnoses could be coded within the 2005 and 2006 NIS.

#### Cost Model

A regression model was used to isolate the effect of pneumonia on the cost of hospitalization from other factors that could influence costs. Covariates within the model included nineteen comorbid illnesses, a score of the propensity for pneumonia (see below), a disease specific severity of illness measure (Disease Mortality Scale), patient age and gender, admission from the emergency department, and hospital factors of teaching status and rural/urban status. Comorbid diseases were identified using software that assigns variables in hospital discharge records using the diagnosis coding of ICD-9-CM codes based on comorbidity measures reported by Elixhauser, et al.<sup>16</sup> The Disease Mortality Scale (DMS) is a disease specific severity of illness measure that was included to isolate the effects of greater illness burden on the cost of hospitalization. The DMS is a scale of the predicted likelihood of death resulting from disease progression and is independent of the treatment process.<sup>17</sup>

#### **Mortality Model**

A regression model similar to that used for cost was also used to isolate the effect of pneumonia on mortality during the hospital stay. Covariates included twenty-three comorbid illnesses, a score for the propensity for pneumonia, patient age and gender, hospital factors of teaching status and rural/urban status, and if the patient was on mechanical ventilation during the hospitalization.

#### Propensity for pneumonia

The patients with pneumonia are likely different in ways that influence the probability of contracting pneumonia, and thus may provide a biased estimate of the effect of pneumonia on outcomes. A propensity model was used to reduce the bias that may exist between the patients with and without pneumonia. The propensity model was based on an established model and known risk factors for pneumonia.<sup>4,14,18</sup> The propensity for pneumonia was predicted using logistic regression with a diagnosis of pneumonia as an outcome, and covariates of patient age, gender, admission from skilled nursing facility, secondary diagnosis of dysphagia, paralysis, placement of a gastrostomy or nasogastric tube, any occurrence of parenteral or enteral feeding, comorbid diagnoses of acquired immune deficiency syndrome, rheumatoid arthritis/collagen vascular disorders, chronic lung disease, congestive heart failure, diabetes mellitus, liver disease, metastatic disease or solid tumor, pulmonary circulation disorders, renal failure, peptic ulcer disease, paralysis, or mechanical ventilation.

The ability of the propensity model to balance covariates between stroke survivors with and without pneumonia was evaluated by examining the balance of covariates within quintiles of the propensity score.

**Statistical Methods**—The NIS includes all discharges from sampled hospitals which are stratified by region, location/teaching status, bed size category, and ownership. All analyses and models take into account the sampling design and sample discharge weights within the SAS 9.2 software<sup>a</sup> and R 2.9.1 software<sup>b</sup>.

**<u>Cost of pneumonia</u>**: To obtain the cost for each hospitalization, total charges were multiplied by the hospital specific cost to charge ratio (CCR), when available, or group

average CCRs when the hospital specific CCR wasn't available (approximately 25% of the time). Group average CCRs are based by state, urban/rural, investor-owned/other, and number of beds for the hospitals for which CCRs were unavailable. Costs were adjusted to 2009 dollars using the Medical Component of the Consumer Price Index.

The average incremental cost of pneumonia was estimated using a generalized linear model. <sup>19</sup> To adjust for non-normality of the cost data and differences of the variances a gamma distribution with log link was applied to the model.<sup>20</sup> The model adjusted for patient covariates as outlined above. The average incremental cost was the average difference in the predicted cost for those with pneumonia and those without. A 95% confidence interval was established using a bootstrap method of 1000 iterations.

**Mortality due to pneumonia:** The adjusted relative risk of mortality due to pneumonia was examined using a generalized linear model with poisson regression and log link<sup>21,22</sup> predicting in-hospital death with pneumonia as the independent variable and with covariates of age, gender, propensity for pneumonia, medical comorbidities, and hospital characteristics of teaching status and urban/rural status.

**Risk stratified cost and mortality:** The cost and mortality models were analyzed by utilizing domain analyses by propensity quintile. Domain analyses allow computation of statistics on subpopulations while taking into account the variance of the entire sample. The mortality model was also run with acute myocardial infarction (ICD-9 code 410.xx) as the independent variable for comparison with the effects of pneumonia on mortality within each propensity quintile.

## RESULTS

There were 207,718 hospitalizations with the primary diagnosis of stroke in the 2005 and 2006 NIS. Of those, 652 were excluded for age less than 18 years, 11,071 died within the first three days of admission, 8,056 were excluded from Texas in 2005, and 3,963 were excluded for other missing information. The final sample consisted of 183,976 admissions with the primary diagnosis of stroke. A secondary diagnosis of pneumonia was established in 8.1% (95% CI 7.8%–8.3%) of hospitalizations. The in-hospital mortality rate for those with pneumonia was 20.0% (95% CI 19.4%–20.8%) compared to 3.5% (95% CI 3.4%–3.7%) in those without pneumonia (Relative Risk 5.7, 95% CI 5.4–6.0). Many differences exist in between the group with pneumonia and those without (Table 1).

## Multivariable Regression of mortality due to pneumonia

The adjusted relative risk for mortality in stroke survivors with pneumonia was 2.0 (95% CI 1.9–2.1). Stratifying by quintile of propensity for pneumonia showed that the group with the lowest risk of pneumonia (quintile 1) had the highest adjusted relative risk for death when a diagnosis of pneumonia was present (Figure 1), with a decreasing adjusted relative risk for death as the risk of pneumonia increased. This pattern is similar to the effect of a diagnosis of acute myocardial infarction on mortality; however, there was a greater risk of mortality due to pneumonia than acute myocardial infarction among the quintiles with a lower risk for pneumonia.

#### Cost of pneumonia

The average unadjusted cost per stroke hospitalization with pneumonia was \$34,706 (95% CI \$32,685–\$36,727) while the average unadjusted cost per stroke hospitalization without pneumonia was \$11,604 (95% CI \$11,154–\$12,053). The average unadjusted incremental cost in those with pneumonia was \$23,102. The average adjusted incremental cost in those

with pneumonia was \$27,633 (95% CI \$27,078–\$27,988). The average adjusted incremental cost of pneumonia in the quintile of highest risk was \$34,057 (quintile 5) compared to \$10,815 in the quintile of lowest risk (quintile 1, see Table 2). Quintiles 2–4 had the lowest average adjusted incremental costs of pneumonia of \$6,748–\$7,868.

## DISCUSSION

This study confirms that the cost of pneumonia after stroke is not trivial and that the average adjusted cost may be higher than previously estimated. Katzan, et al. estimated the cost of pneumonia to be \$21,338 (95% CI \$20,762–21,913), inflation-adjusted in 2009 US dollars, about \$6,300 less than the estimate from this study.<sup>10</sup> If this study were limited to Medicare recipients, as in Katzan's study, the average adjusted incremental cost of pneumonia would be \$23,292, within \$2,000 of the inflation-adjusted cost estimated previously.

This study also confirms that pneumonia after stroke is associated with a higher relative risk of in-hospital death.<sup>4,14,15, 23–25</sup> The unadjusted relative risk for death in the hospital due to pneumonia in this study (5.7, 95% CI 5.4–6.0) is similar to that found by Ovbiagele<sup>14</sup>(6.4, 95% CI 3.8–10.6) and to the 30-day mortality risks found by Katzan<sup>4</sup> (5.9, 95% CI 5.1–6.8) and Saposnik<sup>15</sup> (5.18, 95% CI 3.9–6.9). After adjustment the relative risk in this study (2.0, 95% CI 1.9–2.1) is similar to that of Saposnik<sup>15</sup> (1.9, 95% CI 1.23–2.95) and lower than the studies by Katzan<sup>4</sup> (3.0, 95% CI 2.4–3.7) and Ovbiagale<sup>14</sup> (6.0,95% CI 3.0–11.7). Because these differences are more pronounced after adjustment they likely arise because of differences between the samples, models, and methods used.

The finding that the adjusted relative risk for death associated with pneumonia is inversely related to propensity for pneumonia did not support the initial hypothesis. One potential reason can be seen in Table 2 where the propensity for pneumonia is associated with greater burden of illness. It is possible that the marginal risk for mortality associated with pneumonia in those with the greatest illness burden is blunted by the higher mortality risk that is shared within propensity quintile. Mortality increases as the propensity for pneumonia increases even among those who did not have a diagnosis of pneumonia. A similar phenomenon is seen with a secondary diagnosis of acute myocardial infarction. It is possible that the greater burden of illness in the highest risk group also accounts for the greater incremental cost of hospitalization associated with pneumonia. The greater proportion of hospitalizations with mechanical ventilation and enteral or parenteral nutrition in those with pneumonia in the highest risk group provides some insight into the additional burden of illness and required level of care that likely contributes to the costs.

The inverse relationship of propensity for pneumonia and the magnitude of the relative risk for death is an important finding when considering how to approach screening for dysphagia in stroke survivors. This study suggests that screening for dysphagia is important regardless of the apparent risks for pneumonia. The number of cases of pneumonia that need to be prevented to prevent one death is similar for the quintiles two through five, accounting for 80% of the hospitalizations. The idea that patient selection can offer the key to utilization of appropriate screening techniques may be more difficult to apply than previously thought, if not misguided altogether. It is possible that a better choice would be to screen all stroke survivors by the most sensitive test available. Pneumonia confers a greater monetary cost for those patients with the highest risk of pneumonia yet greater risk of mortality in those patients who appear to have the lowest risk of pneumonia.

There are several limitations to this study. First, secondary data of this sort have inherent problem of relying on physicians or coders to correctly document diagnoses. It is likely that

some diagnoses that may not seem salient to the hospitalization at hand are not recorded yet may have improved the estimates from these analyses had they been. While it would be preferable to have the ability to perform a quality-check on the diagnostic codes within the dataset it is not possible within this dataset. Second, the unit of analysis for the NIS is the hospitalization and not the individual and multiple hospitalizations by the same person could be present within the data. There is no way to estimate how often repeat admissions occur within the data. The results are still representative of hospitalizations occurring within this group and thus provide insight as to where efforts might be best spent for prevention of pneumonia. Finally, risk in this study is based on statistical methods of a limited number of after the fact diagnoses that may not accurately represent the risk that practitioners are able to estimate by clinical examination. It would have been ideal to have such information to include in this study but that was not possible with the data sources utilized for this study.

Many questions remain to be answered about pneumonia prevention after stroke. Foremost, it is not clear how well dysphagia treatments prevent pneumonia. In practice, multiple treatments and strategies are utilized in various combinations in attempt to decrease aspiration, and treatments are often tailored to the individual. One study evaluated the incidence of pneumonia in a population with stroke after implementation of a comprehensive dysphagia treatment program resulted in a 3 month incidence of pneumonia of 1.8%, considerably lower than the 8.1% prevalence found in this study.<sup>11</sup> Two studies have shown that a formal dysphagia screening program reduces aspiration pneumonia, and one completely eliminated it, though the diagnostic criteria for aspiration pneumonia are not provided. <sup>24, 26</sup> It is also not clear, if it is presumed that dysphagia treatment is effective, which screening method is best. While the videofluoroscopic swallowing study is considered the best instrument for diagnosing dysphagia and determining the best treatment the examination protocol has not been standardized and thus effectiveness is likely to vary.<sup>27</sup> It's also not clear whether using such a method for dysphagia screening in all stroke survivors would be cost-effective.

## Conclusion

This study of a large, nationally representative sample confirms that pneumonia after stroke is associated with higher mortality and hospitalization costs. The marginal cost of pneumonia is higher for those who have the highest risk of pneumonia while the risk of mortality associated with pneumonia is highest in those who are the least likely to be diagnosed with pneumonia. Preventing pneumonia after stroke should be a top priority at all levels of risk.

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#### Figure 1.

Adjusted relative risk of inhospital death by quintile of propensity for pneumonia. The error bars represent 95% confidence intervals. Q1= Quintile 1, Q2=Quintile 2, Q3= Quintile 3, Q4=Quintile 4, Q5=Quintile 5.

#### Table 1

## Demographic information and comorbid illnesses

	Pneumonia –	Pneumonia +	pval
n, unweighted	169,243	14,870	
n, weighted <sup>a</sup>	827,155	72,693	
Age (years)	70.6	73.3	p<0.0001
Died	0.035	0.200	p<0.0001
Female	0.546	0.494	p<0.0001
Admitted from			-
$\mathrm{SNF}^b$	0.008	0.014	p<0.0001
$FD^{\mathcal{C}}$	0.773	0.745	p<0.0001
Comorbid Conditions			•
AIDSd	0.002	0.002	p=0.07
Alooholism	0.036	0.054	p<0.0001
Anomia	0.030	0.034	p < 0.0001
Andina	0.000	0.139	p<0.0001
Bloodloss	0.021	0.017	p < 0.001
GUE	0.005	0.013	p<0.0001
CHF <sup>e</sup>	0.120	0.200	p<0.0001
Chronic Lung Disease	0.136	0.210	p<0.0001
Coagulopathy	0.022	0.054	p<0.0001
Depression	0.078	0.051	p<0.0001
Diabetes Mellitus	0.295	0.245	p<0.0001
Drug Abuse	0.019	0.023	p=0.0015
Hypertension	0.742	0.630	p<0.0001
Hypothyroidism	0.104	0.077	p<0.0001
Liver Disease	0.009	0.014	p<0.0001
Lymphoma	0.004	0.004	p=0.99
Metastatic Cancer	0.013	0.018	p<0.0001
Other Neurologic	0.004	0.055	0.0000
Disease	0.004	0.055	p<0.0001
Obesity	0.046	0.029	p<0.0001
Paralysis	0.246	0.296	p<0.0001
Mechanical Ventilation	0.040	0.330	p<0.0001
Peripheral Vascular	0.0-0	0.0	0.000
Disease	0.068	0.053	p<0.0001
Psychiatric Disease	0.024	0.020	p<0.001
Pulmonary Circulation			
Disease	0.013	0.014	p=0.28
Renal Failure	0.074	0.113	p<0.0001
Tumor	0.015	0.019	p<0.001
Peptic Ulcer	< 0.001	< 0.001	p=.4

	Pneumonia –	Pneumonia +	pval
Valvular Disease	0.096	0.094	p=.36
Weightloss	0.018	0.091	p<0.0001
Dysphagia <sup>f</sup>	0.115	0.429	p<0.0001
Gastrostomy Tube	0.037	0.265	p<0.0001
Nasogastric Tube	0.002	0.014	p<0.0001
Enteral/Parenteral			
Nutrition	0.024	0.154	p<0.0001
Insurance			
Medicare	0.663	0.715	p<0.0001
Medicaid	0.064	0.075	p<0.0001
Private	0.203	0.153	p<0.0001
Other	0.070	0.055	p<0.0001
Hospital			
Urban	0.856	0.879	p<0.0001
Teaching	0.411	0.462	p<0.0001

 $^{a}$ All analyses take into account the weighted sample.

<sup>b</sup>Skilled Nursing Facility

<sup>c</sup>Emergency Department

 $^{d}$ Acquired Immune Deficiency Syndrome

<sup>e</sup>Congestive Heart Failure

 $f_{\rm Dysphagia-}$  derived from ICD-9 code (438.82, 787.2) and other clinical codes associated with dysphagia

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Pneumonia	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
n, unweighted	36,117	593	35,845	936	35,451	1,465	34,346	2,431	27,367	9,425
n, weighted <sup>a</sup>	175,936	2,894	175,375	4,586	173,554	7,181	168,364	11,934	133,925	46,098
Age (years)	53.08	52.59	69.06	06.69	77.43	78.48	78.55	79.69	76.80	72.54
Female	0.656	0.638	0.570	0.627	0.554	0.626	0.420	0.467	0.516	0.459
Admitted from SNF <sup>b</sup>	0.001	0.002	0.003	0.004	0.006	0.011	0.014	0.020	0.021	0.014
AIDS	< 0.001	0.002	0.001	0.004	0.002	0.003	0.003	0.002	0.002	0.002
Arthritis	0.024	0.019	0.024	0.037	0.020	0.021	0.018	0.020	0.017	0.013
CHFd	0.002	0.009	0.009	0.016	0.029	0.039	0.228	0.279	0.405	0.331
Chronic Lung Disease	0.024	0.036	0.058	0.068	0.102	0.113	0.274	0.274	0.255	0.233
Diabetes Mellitus	0.370	0.311	0.314	0.354	0.168	0.193	0.190	0.211	0.181	0.188
Liver Disease	0.004	0.003	0.008	0.008	0.00	0.011	0.012	0.012	0.015	0.017
Metastatic Cancer	0.001	0.002	0.006	0.007	0.011	0.020	0.029	0.030	0.022	0.016
Pulmonary/Circulatory Disorders	0.012	0013	0.013	0.026	0.00	0.011	0.016	0.017	0.015	0.013
Renal Failure	0.033	0.059	0.046	0.069	0.057	0.070	0.112	0.113	0.137	0.127
Tumor	0.003	0.012	0.008	0.008	0.014	0.020	0.032	0.031	0.023	0.018
Peptic Ulcer	< 0.001	0	< 0.001	0	< 0.001	0.001	0.001	0	0.001	0.001
Paralysis	0.195	0.192	0.216	0.238	0.225	0.238	0.272	0.293	0.347	0.319
Mechanical Ventilaiton	0	0	0	0	0	0	< 0.001	0	0.246	0.520
Dysphagia <sup>e</sup>	< 0.001	0.002	0.003	0.006	0.012	0.008	0.116	0.116	0.541	0.645
Gastrostomy Tube	0	0	0	0	0	0	0.001	< 0.001	0.227	0.417
Nasogastric Tube	0	0	< 0.001	0	< 0.001	0	0.001	0.001	0.014	0.022
Enteral/Parenteral Nutrition	0	0	< 0.001	0.003	0.001	0.001	0.00	0.015	0.142	0.244
Died	0.005	0.086	0.012	0.118	0.022	0.142	0.029	0.152	0.131	0.237
Adjusted Relative Risk Death	1	12.511	1	7.1863	1	5.37102	1	4.41061	1	1.3208
Cost of Hospitalization	\$12,722	\$23,537	\$9,926	\$17,794	\$9,097	\$15,950	\$9,330	\$16,078	\$17,745	\$51,802
JUN1		13		10		6		6		10

Wilson

 $^{a}$ Quintile 1 is the lowest risk for pneumonia, Quintile 5 has the highest risk for pneumonia.

b All analyses take into account the weighted sample.

<sup>c</sup>Skilled Nursing Facility

d Acquired Immune Deficiency Syndrome

 $^{e}$ Congestive Heart Failure

 $f_{
m Dysphagia}$  - derived from ICD-9 code (438.82, 787.2) and other clinical codes associated with dysphagia

<sup>g</sup>Number of pneumonia cases that would need to be prevented to prevent one death. Calculated as the reciprocal of the absolute difference in death rounded up to the nearest whole integer.