Abstract

Background: The impact of stroke associated pneumonia (SAP) on stroke complications is not well understood; we aimed to study the association between SAP and adverse outcomes including in-hospital mortality, prolonged length of stay and the risk of developing common serious complications (sepsis, respiratory failure and convulsions).

Methods: We retrospectively analysed data from a cohort of 610,668 stroke patients drawn from the Universal Coverage Health Security Scheme (a national insurance database) in Thailand which covers ~80% of the Thai population. Patients were hospitalised between October 2004 and January 2013.

Results: Pneumonia was present in 9.6 % (n=58,586) of patients. Aspiration pneumonia was present in 6.2% (n=38,060) and non-aspiration pneumonia in 3.4% (n=20,526). After adjusting for age, sex, stroke type and co-morbidities, patients with SAP had significantly higher odds of in-hospital mortality (OR 2.90: 2.83-2.96), long length of stay (OR 13.11: 12.83-13.40), sepsis (OR 8.49: 8.22-8.76), respiratory failure (OR 4.37: 4.27-4.48), and convulsions (OR 2.09: 2.00-2.17). On sub-analysis, patients with non-aspiration pneumonia were found to have higher odds of adverse outcomes compared to aspiration pneumonia; the corresponding ORs (95%CI) for above outcomes were 1.25 (1.21-1.30), 2.40 (2.32-2.49), 1.34 (1.28-1.40), 1.80 (1.73-1.88), and 1.19 (1.11-1.28), respectively.

Conclusion: SAP is associated with higher odds of inpatient mortality, long length of stay and risk of developing serious stroke complications. Non-aspiration pneumonia is associated with significantly higher likelihood of adverse outcomes compared to aspiration pneumonia in this patient population. Early identification and treatment of SAP is vital in reducing adverse outcomes in acute stroke.

Introduction

Pneumonia is the most common infectious complication of stroke. Meta-analyses have reported different incidence rates ranging between 9.0% [1] and 14.3% [2]. Stroke associated pneumonia (SAP) is thought to occur due to various mechanisms including aspiration secondary to dysphagia, impaired consciousness or impaired swallowing and immunodepression secondary to ischemic insult [3]. The association between acute pneumonia and subsequent adverse cardiovascular events, including stroke, has been well documented [4].

Regardless of the aetiology, SAP has been found to be associated with increased length of stay [5], hospital costs [6] and increased risk of mortality OR 3.62 [95% CI 2.80 – 4.68] [1]. Diagnosis of SAP can be challenging due to non-specific presentation and the inability of chest radiographs to exclude SAP [7, 8]. While previous studies have assessed many of the challenges posed by SAP, there is a paucity of data exploring the association between pneumonia and other stroke complications.

Our study therefore aimed to quantify the effect of SAP on common and severe stroke complications including sepsis, respiratory failure and convulsions. In addition, we evaluated the impact of SAP on inpatient mortality and length of hospital stay. We also stratified analyses by pneumonia sub-type (non-aspiration pneumonia vs. aspiration pneumonia) to gain deeper insight into the association between different types of SAP and the aforementioned adverse outcomes in stroke. Finally, we stratified analysis by age, sex and co-morbidity status and presented the proportion of deaths associated with SAP over time.

Methods

Study design

Data were obtained from the National Database system of the Thai population under the Universal Coverage (UC) Health Security Scheme which covers approximately 80% of the population of Thailand. Data was collected by XYZ.

All patients with a stroke, who were admitted to hospitals in Thailand between 1st October 2004 and 31st January 2013 under UC scheme were included in this study. This time period was purposely selected because stroke management in Thailand had become more in line with current international practice. Diagnosis of stroke in Thailand is made by attending clinical teams based on clinical features and investigation findings including brain computerised tomography (CT) and/or magnetic resonance imaging (MRI) and was identified from ICD coding (ICD 10-I60-I64) on reimbursement forms. In brief, all stroke patients admitted to hospitals are assessed by neurologists and diagnoses are confirmed including previous co-morbidities and complications during hospitalisation which are coded in ICD-10 codes and recorded in the Universal Health Insurance system for invoicing. We retrieved ICD-10 information for each admission episode which are also linked to admission date, discharge date and date of death.

Baseline demographic and clinical data (co-morbidities) were also obtained from reimbursement forms using ICD codes as described. Data obtained included age, sex, pneumonia status, co-morbidities (gout, hypertension, diabetes, anemia, rheumatic heart disease [RHD], chronic obstructive pulmonary disease [COPD], ischemic heart disease [IHD], chronic kidney disease [CKD], atrial fibrillation [AF], heart failure [HF], stroke type (ischemic, hemorrhagic or ischemic stroke of undetermined cause), common and serious complications of stroke occurring during the index hospital admission (defined as

pneumonia, sepsis, respiratory failure, and convulsions for this study purpose based on initial frequency checks), date of admission and discharge, and inpatient mortality. Stroke associated pneumonia (SAP) was identified using ICD codes in insurance records where the primary diagnosis of the index admission was stroke as defined above. Stroke types were categorised as hemorrhagic (I61, I62), ischemic (I63) or stroke of undetermined pathology (I64). A diagnosis of any type of pneumonia (ICD J12 – J15, J17 and J18) qualified as SAP. Aspiration pneumonia was defined as patients with ICD codes of J17 and J18. Non-aspiration pneumonia was defined as patients with ICD codes of J12 – J15. The study was approved by the Ethics Committee in Human Research, Khon Kaen University, Khon Kaen, Thailand, in accordance with the Declaration of Helsinki.

Statistical analysis

Statistical analysis was performed using Stata 11.2/SE (Texas, USA). Statistical significance was assumed where $p<0.05$. Descriptive statistics were presented separately for individuals with and without pneumonia. The Chi-squared test was used for categorical variables and the t-test for continuous variables. Stroke outcomes (inpatient mortality and long LOS) and post-stroke complications (namely sepsis, respiratory failure and convulsions) were assessed using four logistic regression models. Patients without SAP were the reference category. These models were as follows: 1. unadjusted; 2. adjusted for age and sex; 3. adjusted for age, sex and stroke sub-type; 4. adjusted for age, sex, stroke sub-type and co-morbidities.

The models were repeated after stratifying by stroke subtype (hemorrhage, ischemic and ischemic stroke of unidentified cause). Patients with non-aspiration pneumonia were the reference category in the sub-analysis comparing outcomes in aspiration vs non-aspiration pneumonia. The logistic regression models used in the sub-analysis were identical to those described above. To investigate for any change in trend for mortality rate over the study

period, the overall rate of death through time and the log odds of death in patients without pneumonia were plotted and illustrated for the period of 2004-2012 (the years for which full data was available).

Results

We included a total of 610,668 stroke patients who were hospitalized in Thailand over a 10-year period. The overall rate of stroke associated pneumonia (SAP) in the cohort was 9.6% (n = 58,586). The cohort had a mean age 63.4 (SD ± 14.7) years and males made-up 54.8% (n = 334, 490) of patients. At 50.1% (n = 306,152), just over half of the cohort had ischemic stroke, 34.6% (n = 211,378) had hemorrhagic stroke and 15.3% had undetermined types of stroke (n = 93,135). While Pneumonia was present in 9.6% (n = 58,586) of patients, 35.1% (n = 20,526) had non-aspiration pneumonia and 64.9% (n = 38,060) had aspiration pneumonia. The prevalence of other serious stroke related complications was 7.3% (n = 44,390) for respiratory failure, 3.2% (n = 19,697) for sepsis and 3.4% (n = 20,530) for convulsions. Regarding outcomes of mortality and long LOS, 13.3% (n = 81,152) of patients died in-hospital and 10.4% (n = 63,402) had a long LOS (> 14 days).

Table 1 shows the sample characteristics according to SAP status. SAP was significantly associated with higher age, male sex, hemorrhagic stroke and history of previous stroke. SAP was also associated with the presence of all of the different co-morbidities included in the analysis (IHD, HF, RHD, AF, Hypertension, Diabetes, COPD, CKD, Anemia, Gout). Anemia was particularly prevalent in those who had SAP (by three fold) compared to those without SAP. The three selected severe and common complications respiratory failure, sepsis and convulsions were significantly associated with the presence of SAP (<0.001). The other two outcomes under assessment; in patient mortality and long LOS were also strongly associated with SAP (<0.001).

Table 2 illustrates the odds of severe complications, inpatient mortality and long LOS in patients with SAP compared to those without SAP, stratified by stroke sub-type. After adjusting for potential confounders, patients with SAP had an 8.5 fold increased odds of developing sepsis, a 5 fold increased odds of respiratory failure and were twice as likely to develop convulsions post stroke. Patients with SAP also had a 3 fold increased risk of inpatient mortality and 11.5 fold increased risk long hospital stay. Patients with ischemic stroke were more likely to die in hospital and experience long LOS. Convulsions and respiratory failure were also more common in patients with infarcts.

Table 3 depicts the odds of death and prolonged LOS for SAP (reference no SAP) when the analyses were were stratified by age (<65 and >=65 years), stroke sub-type (hemorrhagic and ischemic) and the most common co-morbidities (diabetes, anemia and congestive heart failure (CHF)). Patients 65 years and over had a higher odds of death compared to their younger counterparts. However, younger patients had increased odds of developing sepsis and long LOS. The likelihood of inpatient mortality and respiratory failure was more common in patients with ischemic stroke compared to hemorrhagic stroke. In addition, patients who had diabetes and anemia had worse mortality outcomes than patients without these conditions. Finally, patients with CHF had lower odds of all outcomes assessed that their counterparts without CHF.

Supplemental Table I depicts sample characteristics and outcomes according to SAP sub-type (non-aspiration vs aspiration SAP). Aspiration SAP was associated with increasing age, female sex and ischemic stroke. Non-aspiration pneumonia was associated with various co-morbidities including hypertension, diabetes, and anaemia while aspiration pneumonia was associated with rheumatic heart disease. Finally, non-aspiration SAP was also associated with all of the outcomes under assessment; respiratory failure, sepsis, convulsions, inpatient mortality and long LOS.

Supplemental Table II depicts the odds of inpatient mortality, long LOS, sepsis, respiratory failure and convulsions by pneumonia type. Analysis was also stratified according to stroke type. After adjusting for confounders, patients with non-aspiration SAP had slightly increased odds of all outcomes assessed compared to those with aspiration SAP. After stratifying the analysis by stroke sub-type (ischemic and hemorrhagic), it was found that these relationships continued to hold relatively unchanged for both stroke types for all outcomes with the exceptions of inpatient mortality and convulsions in patients with hemorrhagic stroke, where ORs were no longer significant.

Supplementary Figure I depicts the annual mortality rates of the whole cohort, which is decreasing through time. Supplementary Figure II depicts the log-odds of ratio of death in those with SAP. Odds of death for individuals with pneumonia is increasing over time compared to individuals without pneumonia; OR for 2004 was 2.72 rising to 3.93 in 2012 (p-value for interaction = < 0.001). The association also changed over time for sepsis (OR 2004 = 8.42, OR 2012 = 8.99, p-value for interaction = 0.011), respiratory failure (OR 2004 = 4.93, OR 2012 = 6.20, p-value for interaction = < 0.001), convulsions (OR 2004 = 1.40, OR 2012 = 2.36, p-value for interaction = < 0.001) and length of stay (OR 2004 = 9.46, OR 2012 = 13.52, p-value for interaction = < 0.001). We repeated our main analysis adjusting for year of admission and the results showed slightly higher odds ratios but the overall pattern did not change. Supplementary Figure III compared the log odds of death in those with pneumonia to the log odds of death in those without SAP according to SAP sub-type. We found a decrease in overall mortality in stroke patients but a constant rate of mortality in stroke patients with SAP. Furthermore, those with non-aspiration pneumonia consistently had the higher odds of mortality compared to the aspiration related SAP.

Discussion

In this study, we found SAP was associated with increased odds of serious stroke complications, inpatient mortality and longer LOS. This was consistent across stroke types and age groups. In line with the existing literature, we also found that SAP was associated with increasing age and the presence of various co-morbid conditions including; COPD, AF and HF [9, 10, 11]. To our knowledge, this is the first study assessing the impact of SAP on serious stroke complications and the largest study to date, which has examined the association of SAP with clinically relevant stroke outcomes. Establishing and quantifying the likelihood of developing further stroke complications such as sepsis, convulsions and respiratory failure is important to patients and clinicians. Finally, by stratifying our findings by SAP sub-type we have found that outcomes are consistently worse in patients with non-aspiration pneumonia.

Various aspects of our study were consistent with the existing literature. For example, the prevalence of pneumonia in our sample population was 9.6% while an American cohort of patients with acute stroke had 6.9% [12] and a Canadian cohort of patients with ischemic stroke had 7.1% [9]. Unsurprisingly, studies conducted in an intensive care setting had a higher prevalence of pneumonia. Hannawi et al found the rate of pneumonia to be between 9.5% and 56.6% in studies examining SAP in patients admitted to neurological intensive care units (ICUs) and 17% to 50% in medical ICUs. Furthermore, the rate of pneumonia appeared to be lower in studies examining patients in standard stroke units at 3.9 – 12% [3]. This disparity may be explained by variations in the definition of SAP used, the different settings in which studies have been conducted and their variation in geographic location [13]. Furthermore, patients with more severe stroke are more likely to be admitted to ICU's and therefore may have a higher risk of complications such as SAP, thereby resulting in the observed differences in incidence. Finally, a recent systematic review and meta-analysis

found that the pooled rate of SAP in patients in all settings (ICU and non-ICU combined) was 9% [1] and this was only slightly higher than our large study based on population-based data, gathered over a 10-year period.

Our finding that SAP was associated with increased in-patient mortality was also consistent with previous studies conducted in non-ICU settings [9, 12, 13 – 18]. Conversely, studies conducted within neurological and medical ICU settings did not find an association between SAP and worse outcomes [19 – 23], with the exception of one study [23]. This could be due to the small sample sizes used and possibly selection bias. Furthermore, it may be that those with stroke admitted to ICUs are have a very poor prognosis in general and thus SAP does not further impact mortality outcomes [13].

When stratifying the analysis by age, we observed that younger patients (<65 years) had higher odds of long length of stay compared to older patients. This may be explained by the lower odds of death in younger patients, who are therefore more likely to remain in hospital for treatment and rehabilitation. We also found that younger patients have higher odds of sepsis compared to older patients. Finally, we found that patients with heart failure have lower odds of all complications compared to those without heart failure. This may be explained by selection bias or incomplete capture of outcome data on patients diagnosed with heart failure.

The current study found notable trends with regard to mortality rates; while we observed the continuous and linear decline in mortality from stroke in Thailand (Supplementary Figure I), this was accompanied by no change in rates of mortality in stroke patients with SAP, thereby resulting in an increase in the relative odds of mortality in those with SAP (Supplementary Figure II). It is possible that this reflects the lack of improvement in mortality outcome in stroke patients with SAP. Furthermore, we found that those with non-aspiration pneumonia consistently had worse outcomes than those with aspiration pneumonia

(Supplemental Figure III and Supplemental Table II). This may be because patients with non-aspiration pneumonia have higher co-morbid burden (Supplemental Table II) and increased frailty, thereby making them more likely to develop further complications and die of in-hospital as a consequence of SAP. Although we controlled for these factors in analysis, there may be residual confounding effect. It is also possible that non-aspiration pneumonia is due to nosocomial/hospital acquired infections caused by pathogens that lead to infections of greater severity and therefore have worse outcomes. It is also possible some cases of non-aspiration pneumonia contributed to the development of stroke through increased thrombotic risk due to inflammation and dehydration or embolic risk through uncontrolled AF resulting in larger stroke with higher chance of poor outcomes.

The findings in the current study and existing literature highlight the importance of accurate and rapid diagnosis of SAP in order to reduce the impact it has on mortality and other serious stroke complications. The development of standardized criteria when diagnosing pneumonia in patients with stroke is therefore of crucial. A recent systematic review assessing how pneumonia was diagnosed in clinical stroke research found that 41% of studies used unpublished ad-hoc criteria and 31% used various different types of published criteria when diagnosing SAP [24]. In order to address this issue, the Pneumonia in Stroke Consensus Group have recommended that SAP be defined as the incidence of pneumonia within the first 7 days of acute stroke, diagnosed according to a modified version of the Centre for Disease Controlled criteria [25]. A standard grading scale for the prediction of pneumonia following acute ischemic stroke has also been explored in recent studies [26 – 28]. Early prediction may reduce the impact of SAP through targeted management.

Various strategies can be used to reduce the likelihood of SAP. Stroke patients can be kept nil by mouth until a formal assessment of their swallowing function takes place. This approach has been shown to be significantly associated with a reduction in risk of developing

SAP [29, 30]. When appropriate, mobilisation of stroke patients within the first day of admission has also been shown to reduce the risk of pneumonia [17]. A more controversial method is the use of antibiotic prophylaxis. A systematic review and meta-analysis of clinical trials found that antibiotics were significantly associated with a reduction in the overall rate of pneumonia but prophylaxis was not significantly associated with a reduction in mortality and morbidity [31]. In addition, a recent clinical trial (n=1,217) has found that antibiotic prophylaxis was not associated with a significant reduction in the incidence of pneumonia OR 1.21 [95% CI 0.71 – 2.08] [32].

Our study has several strengths. As the largest study of SAP and stroke outcomes, performed using a cohort of consecutively admitted patients from a nationwide population, we were able to minimise selection bias and maximise the generalizability of our findings amongst stroke patients in Thailand. The availability of robust information on demographics and co-morbidities allowed us to adjust for many potential confounders in our analysis all of which are important determinants of stroke outcome. In addition, we were able to stratify the analysis according to SAP sub-type, stroke-subtype, age group and common associated risk factors, thereby providing deeper insight and better understanding into the association between SAP and relevant clinical outcomes.

Our study also has some limitations. We were unable to determine the exact time of pneumonia diagnosis. It is possible that some patients may have developed pneumonia shortly before their stroke, however, this is unlikely to have occurred in enough patients to substantially alter our findings. It is possible that some patients with SAP may have been deemed inappropriate for active management and this may have contributed to poorer stroke outcomes seen in patients with SAP, however this is unlikely in the context of current medical practice in Thailand where most cases were treated actively. As we used administrative data, a lack of detailed information on neurological disability from a stroke

impairment grading scale such as the National Institute of Health stroke scale (NIHSS) entailed that we were unable to adjust for this confounder.

In summary, our results confirm that SAP is significantly associated with higher mortality, longer hospitalization and greater odds of severe and common stroke complications. Early identification and treatment has the potential to reduce mortality and morbidity in patients with SAP. Future research should be aimed at developing a risk score for the prediction of SAP and interventions for preventing SAP.

Contributors: PKM conceived the idea and designed the study. ST co-ordinated the data acquisition. JHBS and ABC cleaned the data and ABC performed the statistical analysis, RSB drafted the manuscript with supervision from PKM. All authors contributed to the writing of the paper. PKM is the guarantor.

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Tables and Figures:

Table 1: Population characteristics by stroke associated pneumonia status

Table 2: Odds of inpatient mortality, long length of stay (>14 days) and selected complications in patients with stroke associated pneumonia compared to those without stroke associated pneumonia

Table 3: Odds of inpatient mortality and long length of stay in patients with stroke associated pneumonia compared to those without stroke associated pneumonia, stratified according to age, stroke type, diabetes, anemia and congestive heart failure

Supplemental Table I: Study population characteristics by type of stroke associated pneumonia

Supplemental Table II: Odds of outcome for non-aspiration pneumonia versus aspiration pneumonia

Supplementary Figure I: Log odds of death in study population

Supplementary Figure II: Log odds of death in patients with stroke associated pneumonia compared to those with stroke associated pneumonia

Supplementary Figure III: Log odds of death by pneumonia status and type

Table 1: Population characteristics by stroke associated pneumonia status

Variable	Pneumonia	No Pneumonia	P-Value
N	58,586	552,082	-
Age	67.1 +/- 14.5	63.1 +/- 14.7	<0.001
Sex			<0.001
Male	32,790 (56.0)	301,700 (54.6)	
Female	25,796 (44.0)	250,382 (45.4)	
Stroke Type			<0.001
Ischemic	27,769 (47.4)	278,383 (50.4)	
Hemorrhagic	25,660 (43.8)	185,718 (33.6)	
Other	5,157 (8.8)	87,978 (15.9)	
Previous Stroke	4,785 (8.2)	42,746 (7.7)	<0.001
Complications			
Respiratory Failure	14,576 (24.9)	29,814 (5.4)	<0.001
Sepsis	9,361 (16.0)	10,336 (1.9)	<0.001
Convulsions	3,645 (6.2)	16,885 (3.1)	<0.001
Co-Morbidities			
Chronic IHD*	2,015 (3.4)	14,329 (2.6)	<0.001
Congestive Heart Failure	2,301 (3.9)	6,699 (1.2)	<0.001
Rheumatic Heart Disease	692 (1.2)	4,799 (0.9)	<0.001
Atrial Fibrillation	6,648 (11.3)	30,535 (5.5)	<0.001
Hypertension	26,637 (45.5)	243,003 (44.0)	<0.001
Diabetes	9,969 (17.0)	90,379 (16.4)	<0.001
COPD*	2,373 (4.1)	9,221 (1.7)	<0.001
Chronic Kidney Disease	2,538 (4.3)	16,656 (3.0)	<0.001
Anemia	8,059 (13.8)	24,705 (4.5)	<0.001
Gout	1,056 (1.8)	9,214 (1.7)	<0.001
Inpatient Mortality	17,862 (30.5)	63,290 (11.5)	<0.001
Long LOS (> 14 days)	27,247 (46.5)	36,155 (6.6)	<0.001

*Ischemic Heart Disease, Chronic Obstructive Pulmonary Disease

Table 2: Odds of inpatient mortality, long length of stay (>14 days) and selected complications in patients with stroke associated pneumonia compared to those without stroke associated pneumonia

	Inpatient Mortality	Long LOS	Sepsis	Respiratory Failure	Convulsions
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Total*					
Unadjusted	3.39 (3.32 – 3.45)	12.41 (12.17 – 12.65)	9.97 (9.68 – 10.27)	5.80 (5.68 – 5.93)	2.10 (2.03 – 2.18)
Model A	3.43 (3.37 – 3.50)	13.09 (12.83 – 13.35)	9.83 (9.54 – 10.13)	5.80 (5.67 – 5.93)	2.27 (2.19 – 2.36)
Model B	3.08 (3.02 – 3.14)	12.44 (12.19 – 12.70)	9.54 (9.26 – 9.83)	5.22 (5.10 – 5.34)	2.30 (2.22 – 2.39)
Model C	2.97 (2.91 – 3.03)	11.57 (11.33 – 11.81)	8.58 (8.32 – 8.85)	4.72 (4.61 – 4.83)	2.14 (2.06 – 2.23)
Infarct †					
Unadjusted	7.76 (7.52 – 8.00)	13.05 (12.67 – 13.45)	9.90 (9.51 – 10.31)	11.05 (10.68 – 11.42)	2.46 (2.34 – 2.59)
Model A	7.50 (7.27 – 7.74)	13.19 (12.79 – 13.59)	9.57 (9.18 – 9.98)	10.65 (10.30 – 11.02)	2.69 (2.56 – 2.83)
Model B	6.84 (6.62 – 7.06)	12.00 (11.63 – 12.38)	8.48 (8.13 – 8.85)	9.29 (8.97 – 9.61)	2.48 (2.36 – 2.61)
Hemorrhage †					
Unadjusted	1.54 (1.50 – 1.59)	11.45 (11.12 – 11.78)	9.75 (9.30 – 10.22)	2.77 (2.68 – 2.86)	1.74 (1.64 – 1.85)
Model A	1.51 (1.47 – 1.55)	11.86 (11.52 – 12.21)	9.69 (9.24 – 10.16)	2.72 (2.63 – 2.81)	1.93 (1.82 – 2.06)
Model B	1.51 (1.47 – 1.56)	11.11 (10.79 – 11.45)	8.76 (8.35 – 9.20)	2.51 (2.43 – 2.60)	1.80 (1.69 – 1.91)
Other †					
Unadjusted	6.33 (5.85 – 6.85)	11.78 (10.97 – 12.66)	8.64 (7.74 – 9.65)	10.04 (9.09 – 11.08)	1.65 (1.43 – 1.90)
Model A	6.04 (5.58 – 6.55)	11.25 (10.46 – 12.10)	8.11 (7.25 – 9.07)	9.54 (8.63 – 10.55)	1.81 (1.57 – 2.08)
Model B	5.73 (5.28 – 6.22)	10.67 (9.91 – 11.49)	7.35 (6.56 – 8.24)	8.71 (7.86 – 9.65)	1.73 (1.50 – 1.99)

*Variables adjusted for are as follows: model A is age and sex; model B is model A + stroke type; model C is model B + co-morbidities
†Variables adjusted for are as follows: model A is age and sex; model B is model A + stroke type and co-morbidities

Table 3: Odds of inpatient mortality and long length of stay in patients with stroke associated pneumonia compared to those without stroke associated pneumonia, stratified according to age, stroke type, diabetes, anemia and congestive heart failure

	Death	Long LOS	Sepsis	Respiratory Failure	Convulsion
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age†					
< 65	2.31 (2.23 – 2.38)	11.98 (11.61 – 12.37)	10.20 (9.71 – 10.70)	4.61 (4.45 – 4.78)	2.05 (1.94 – 2.17)
>= 65	3.59 (3.49 – 3.69)	10.91 (10.62 – 11.21)	7.65 (7.35 – 7.95)	4.84 (4.69 – 4.98)	2.08 (1.98 – 2.20)
P-Value for Interaction‡	<0.001	<0.001	<0.001	0.269	0.89
Stroke Type†					
Hemorrhagic	1.51 (1.47 – 1.56)	11.11 (10.79 – 11.45)	8.76 (8.35 – 9.20)	2.51 (2.43 – 2.60)	1.80 (1.69 – 1.910
Ischemic	6.84 (6.62 – 7.06)	12.00 (11.63 – 12.38)	8.48 (8.13 – 8.85)	9.29 (8.97 – 9.61)	2.48 (2.36 – 2.61)
P-Value for Interaction‡	<0.001	<0.001	0.331	<0.001	<0.001
Diabetes†					
No	2.71 (2.65 – 2.77)	11.79 (11.52 – 12.06)	8.92 (8.61 – 9.23)	4.52 (4.40 – 4.63)	2.14 (2.05 – 2.23)
Yes	4.77 (4.53 – 5.02)	10.49 (9.98 – 11.02)	7.31 (6.83 – 7.83)	5.83 (5.51 – 6.17)	2.09 (1.90 – 2.30)
P-Value for Interaction‡	<0.001	0.028	<0.001	<0.001	0.04
Anemia†					
No	2.90 (2.83 – 2.96)	11.54 (11.29 – 11.80)	9.37 (9.06 – 9.68)	4.78 (4.66 – 4.90)	2.18 (2.10 – 2.28)
Yes	3.62 (3.40 – 3.85)	11.71 (11.02 – 12.45)	5.10 (4.72 – 5.51)	4.38 (4.11 – 4.67)	1.89 (1.71 – 2.09)
P-Value for Interaction‡	<0.001	0.191	<0.001	<0.001	0.013
CHF*†					
No	2.93 (2.87 – 2.99)	11.65 (11.41 – 11.90)	8.71 (8.44 – 8.99)	4.69 (4.58 – 4.80)	2.15 (2.07 – 2.23)
Yes	2.39 (2.15 – 2.66)	6.54 (5.85 – 7.32)	3.97 (3.43 – 4.60)	3.53 (3.14 – 3.96)	1.79 (1.44 – 2.22)
P-Value for Interaction‡	<0.001	<0.001	<0.001	<0.001	0.203

*CHF = Congestive Heart Failure.

†Age model adjusted for: sex, stroke type, hypertension, previous stroke, anemia, diabetes and AF. Stroke type model adjusted for: sex, age, hypertension, previous stroke, anemia, diabetes and AF. Anemia model adjusted for: sex, age, stroke type hypertension, previous stroke and AF. CHF model adjusted for: sex, age, stroke type, hypertension, previous stroke, anemia, diabetes and AF.
‡We tested for an interaction (i.e. if the effect of pneumonia was the same for both subgroups) using a logistic regression model with an interaction term between the strata (for example, age<65 vs age >=65) and pneumonia.

Supplemental Table I: Study population characteristics by type of stroke associated pneumonia

Variable	**Non-Aspiration Pneumonia**	**Aspiration Pneumonia**	**P -Value**
N (%)	20,526 (35.0)	38,060 (65.0)	-
Age	66.1 (±14.7)	67.6 (±14.4)	<0.001
Sex			<0.001
Male	11,700 (57.0)	21,090 (55.4)	
Female	8,826 (43.0)	16,970 (44.6)	
Stroke Type			<0.001
Ischemic	8,596 (41.9)	19,173 (50.4)	
Hemorrhagic	11,123 (54.2)	14,537 (38.2)	
Other	816 (4.0)	4,341 (11.4)	
Previous Stroke	2,001 (9.7)	2,784 (7.3)	<0.001
Complications			
Respiratory Failure	6,766 (32.9)	7,810 (20.5)	<0.001
Sepsis	3,920 (19.1)	5,441 (14.3)	<0.001
Convulsions	1,424 (6.9)	2,221 (5.8)	<0.001
Co-Morbidities			
Chronic IHD*	701 (3.4)	1314 (3.5)	0.802
Heart Failure	835 (4.1)	1,466 (3.9)	0.204
Rheumatic Heart Disease	192 (0.9)	500 (1.3)	<0.001
Atrial Fibrillation	2,259 (11.0)	4,389 (11.5)	0.052
Hypertension	10,473 (51.0)	16,164 (42.5)	<0.001
Diabetes	3,704 (18.0)	6,265 (16.5)	<0.001
COPD*	845 (4.1)	1528 (4.0)	0.561
Chronic Kidney Disease	926 (4.5)	1,612 (4.2)	0.122
Anemia	3,735 (18.2)	4,324 (11.4)	<0.001
Gout	344 (1.7)	712 (1.9)	0.089
Inpatient Mortality	7,107 (34.6)	10,755 (28.3)	<0.001
Long LOS > 14	12,946 (63.1)	14,301 (37.6)	<0.001

*IHD = Ischemic Heart Disease, COPD = Chronic Obstructive Pulmonary Disease

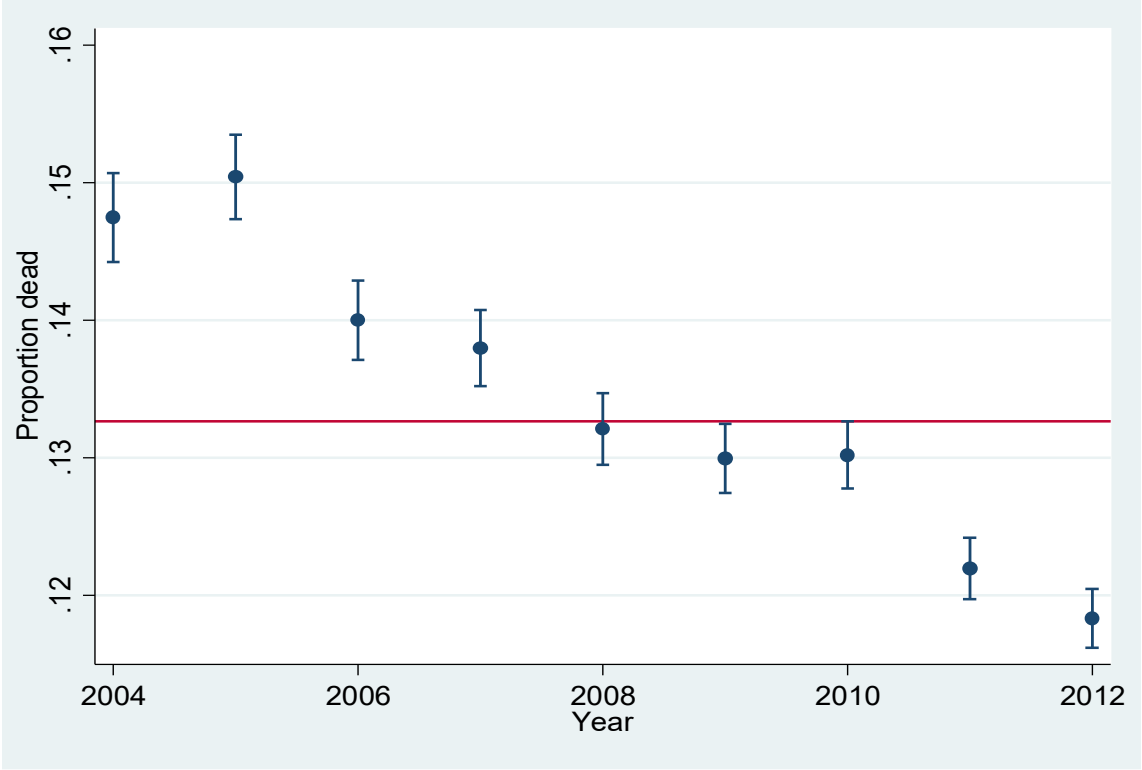
Supplemental Table II: Odds of outcome for non-aspiration pneumonia vs aspiration pneumonia

	Inpatient Mortality	Long LOS	Sepsis	Respiratory Failure	Convulsions
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Total*					
Unadjusted	1.34 (1.30 – 1.39)	2.83 (2.74 – 2.93)	1.41 (1.35 – 1.48)	1.90 (1.83 – 1.98)	1.20 (1.12 – 1.29)
Model A	1.36 (1.31 – 1.41)	2.81 (2.71 – 2.91)	1.90 (1.83 – 1.98)	1.91 (1.84 – 1.98)	1.17 (1.09 – 1.25)
Model B	1.27 (1.23 – 1.32)	2.55 (2.46 – 2.64)	1.39 (1.33 – 1.46)	1.89 (1.82 – 1.97)	1.23 (1.14 – 1.32)
Model C	1.25 (1.21 – 1.30)	2.40 (2.32 – 2.49)	1.34 (1.28 – 1.40)	1.80 (1.73 – 1.88)	1.19 (1.11 – 1.28)
Infarct†					
Unadjusted	1.60 (1.51 – 1.68)	2.78 (2.64 – 2.93)	1.67 (1.57 – 1.78)	2.03 (1.92 – 2.15)	1.37 (1.25 – 1.51)
Model A	1.60 (1.52 – 1.69)	2.78 (2.64 – 2.93)	1.68 (1.57 – 1.79)	2.03 (1.93 – 2.15)	1.37 (1.25 – 1.51)
Model B	1.57 (1.48 – 1.65)	2.60 (2.47 – 2.74)	1.60 (1.50 – 1.71)	1.93 (1.83 – 2.04)	1.34 (1.22 – 1.47)
Haemorrhage†					
Unadjusted	1.02 (0.97 – 1.08)	2.40 (2.28 – 2.53)	1.14 (1.06 – 1.22)	1.75 (1.66 – 1.86)	1.02 (0.92 – 1.14)
Model A	1.03 (0.98 – 1.09)	2.39 (2.27 – 2.52)	1.14 (1.07 – 1.22)	1.75 (1.66 – 1.86)	1.01 (0.91 – 1.13)
Model B	1.03 (0.98 – 1.09)	2.27 (2.15 – 2.39)	1.10 (1.02 – 1.17)	1.68 (1.59 – 1.78)	0.98 (0.88 – 1.10)

*Variables adjusted for are as follows: model A is age and sex; model B is model A + stroke type; model C is model B + co-morbidities

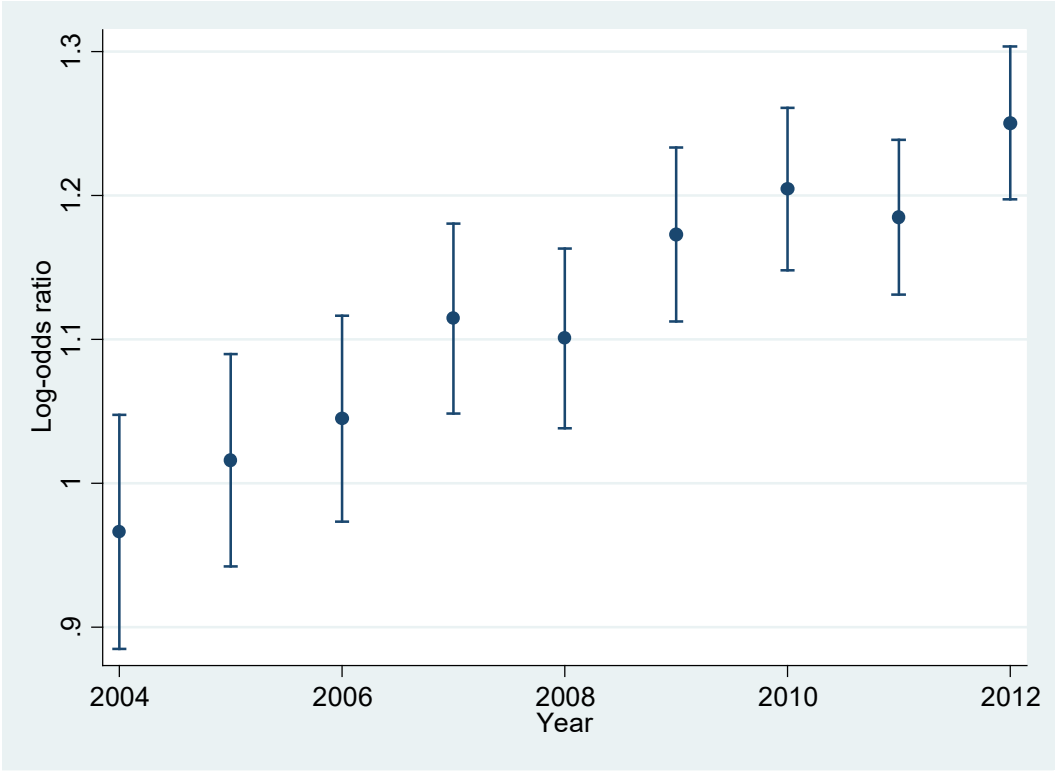
†Variables adjusted for are as follows: model A is age and sex; model B is model A + co-morbidities

Supplementary Figure 1: Log odds of death in study population



*The solid line is the overall death rate of 0.1327. The years 2003 and 2013 were excluded due to incomplete calendar years.

Supplementary Figure 2: Log odds of death in patients with stroke associated pneumonia compared to those without stroke associated pneumonia



*The years 2003 and 2013 were excluded due to incomplete calendar years.

Supplementary Figure 3: Log odds of death by pneumonia status and type