

# Ten-Year Temporal Trends in Medical Complications After Acute Intracerebral Hemorrhage in the United States

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**Background and Purpose**—Data on medical complications after intracerebral hemorrhage (ICH) are sparse. We assessed trends in the prevalence of urinary tract infection, pneumonia, sepsis, deep venous thrombosis (DVT), pulmonary embolism, acute renal failure (ARF), and acute myocardial infarction after ICH in the United States.

**Methods**—A total of 575 211 adult ICH cases were identified from the 2004 to 2013 Nationwide Inpatient Sample. Weighted complication risks were computed by sex and mechanical ventilation status. Multivariate models were used to evaluate trends in complications and assess their association with in-hospital mortality, cost, and length of stay.

**Results**—Overall risks of urinary tract infection, pneumonia, sepsis, DVT, pulmonary embolism, ARF, and acute myocardial infarction after ICH were 14.8%, 7.8%, 4.1%, 2.7%, 0.7%, 8.2%, and 2.0%, respectively, but risk differed by sex and mechanical ventilation status. From 2004 to 2013, odds of DVT and ARF increased, whereas odds of pneumonia, sepsis, and mortality declined over time. All complications were associated with >2.5-day increase in length of stay and >\$8000 increase in cost. ARF and acute myocardial infarction were associated with increased mortality in all patients; sepsis and pneumonia were associated with increased mortality only in nonmechanical ventilation patients, whereas urinary tract infection and DVT were associated with reduced mortality in all patients.

**Conclusions**—Despite significant mortality reduction, ARF and DVT risk after ICH have increased, whereas odds of sepsis and pneumonia have declined over the last decade. All complications were associated with increased cost and length of stay, but their associations with mortality were variable, likely due in part to survival bias. Innovative strategies are needed to prevent ICH-associated medical complications. (*Stroke*. 2017;48:596-603. DOI: 10.1161/STROKEAHA.116.015746.)

**Key Words:** cerebral hemorrhage ■ hospital mortality ■ myocardial infarction ■ pneumonia ■ stroke

Intracerebral hemorrhage (ICH) is the most deadly form of stroke<sup>1,2</sup> and accounts for 10% of all strokes in the United States.<sup>3</sup> Up to 50% of stroke-related mortality is attributable to medical complications.<sup>4</sup> Over the last decade, ICH-related mortality in the United States has decreased,<sup>5</sup> but data on the current rates of medical complications after ICH outside of clinical trials are sparse.<sup>4</sup> The aging population and an increase in persons with multiple chronic diseases may have resulted in greater medical complication during hospitalization; however, many of these are potentially preventable, and advances in medical practice and clinical management guidelines<sup>6,7</sup> may have led to decreased frequency. Therefore, the current magnitude and direction of ICH-associated complications are unknown.

The primary aim of this study is to describe current trends in the prevalence of pneumonia, urinary tract infection (UTI), sepsis, deep vein thrombosis (DVT), pulmonary embolism (PE), acute renal failure (ARF), and acute myocardial infarction (AMI) in hospitalized acute ICH patients in the United States from 2004 to 2013. We secondarily evaluated the

current association of each complication with other clinical factors, in-hospital mortality, length of stay, and cost.

## Methods

Data for this study were obtained from the 2004 to 2013 Nationwide Inpatient Sample (NIS). The NIS is the largest all-payer inpatient care database in the United States and comprises a 20% stratified random sample of all US hospital discharges. Sampling weights provided in the NIS allow for calculation of national estimates. Each individual hospital discharge in the NIS is deidentified so all discharges were considered to be independent. Further details on the NIS design are available at <http://www.hcup-us.ahrq.gov>.

## Study Population

We identified all patients with a primary diagnosis of ICH (n=116 706) by querying the NIS using the International Classification of Disease-Clinical Modification, 9th Revision code 431 (Methods in the [online-only Data Supplement](#)).

## Definition of Outcomes

All complications were defined using secondary International Classification of Disease, 9th Revision codes or Healthcare Cost and

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Utilization Project (HCUP) constellation of codes corresponding to these diagnoses (Methods in the [online-only Data Supplement](#)). In-hospital mortality, home disposition, and length of stay were studied using HCUP variables named DIED, DISPUNIFORM and LOS, respectively.

### Covariate Assessment

Comorbidities associated with ICH hospitalization were used to calculate the modified Charlson comorbidity index for all patients. We defined craniotomy/craniectomy, hydrocephalus requiring external ventricular drain or ventriculoperitoneal shunt, and mechanical ventilation (MV) status using International Classification of Disease, 9th Revision or HCUP procedural codes (Methods in the [online-only Data Supplement](#)).

### Statistical Analysis

Baseline characteristics of participants were summarized using descriptive statistics. We computed the unadjusted national weighted prevalence of each complication and in subgroups categorized by sex. We further stratified some complications by preexisting conditions or interventions expected to influence their occurrence: pneumonia, DVT, and PE risk by MV status and ARF and MI risk by chronic kidney disease (CKD) and coronary artery disease, respectively. We evaluated trends in prevalence of each complication over time by constructing logistic regression model with each complication as the dependent variable and year of discharge as the independent variable, evaluated continuously, with significance of differences in trend over time assessed using the Wald test.

We used a series of nested logistic regression models to evaluate the association of each complication with hospitalization variables and to assess factors that may account for any observed trends in complication risks and control for confounding (Methods in the [online-only Data Supplement](#)).

## Results

The 116706 admissions identified in the NIS represent 575211 ICH hospitalizations in the United States from 2004 to 2013 (Table II in the [online-only Data Supplement](#)). About 49.7% of patients were females, and mean age at admission was 68.9 years. The proportion of patients with comorbid hypertension, diabetes mellitus, CKD, and baseline coagulopathy increased over time (Table II in the [online-only Data Supplement](#);  $P$  trend  $<0.001$ , not displayed). Most patients had low Charlson comorbidity index scores, but the proportion of patients with Charlson comorbidity index score  $\geq 4$  increased from 13.3% to 24.7% over time. MV was administered to 26.0% to 29.6%, of patients of which 16.8% to 25.3% occurred in the first 48 hours of admission (Table II in the [online-only Data Supplement](#)). Mean length of stay did not change over time, but the proportion of patients transferred to skilled nursing facilities increased from 42.3% in 2004 to 46.9% in 2013 ( $P < 0.001$ ; Table III in the [online-only Data Supplement](#)).

### Total Medical Complication Risks

Over the study period, 29.3% of all patients and 37.1% of MV patients had at least 1 medical complication during hospitalization (Table 1). The most common complications were UTI (14.8%), ARF (8.2%), and pneumonia (7.8%), but significant disparity existed by sex and prespecified clinical factors: UTI was the most common complication in females (19.8% versus 9.9% in males), whereas ARF was the most common

complication in males (10.6% in males versus 5.9% in females). Overall weighted risks of most other complications, including pneumonia (9.1% versus 6.4), sepsis (4.8% versus 3.2%), DVT (3.2% versus 2.1%), and PE (0.9% versus 0.5%), were  $\approx 30\%$  greater in males compared with females ( $P$  value for comparison  $<0.001$ ), but AMI risks did not differ by sex. In analysis stratified by specific clinical factors, we identified  $>2$ -fold higher risks of pneumonia and DVT in ventilated compared with nonventilated patients. Moreover, ARF and AMI risks were greater in patients with CKD and coronary artery disease compared with patients with no coronary artery disease and no-CKD, respectively. Among those with DVT, 10.4% had a PE diagnosis, whereas 39.4% of patients with PE had coexisting DVT.

Overall in-hospital mortality was 23.8%, but death risk in MV patients was 59.5%. Notably, 61.6% of in-hospital deaths occurred in the first 3 days of admission, and 82.4% of all deaths occurred within the first week of hospitalization (Table IV in the [online-only Data Supplement](#)). Among those that died within the first week of hospitalization, only 16.4% had at least 1 complication compared with the 59.7% complication risk in those that died after 7 days of hospitalization.

### Trend Analysis

In-hospital mortality decreased from 27.8% in 2004 to 21.0% in 2013 (relative decline 24.4%; Figure 1), but the proportion of patients with at least 1 complication increased from 26.0% to 31.2% over the same period (relative increase 19.7%; Table 1). The increase in total complication risk was driven mainly by a nearly 3-fold increase in ARF risk (4.4% to 12.2%) over the 10-year period (Figure 2; Table 1). DVT risks also increased by 53.4% (2.0% to 3.2%) but mainly in MV patients, and UTI risks increased over time but only in females (Figures 1 and 2; Table 1). The unadjusted weighted prevalence of pneumonia, sepsis, and PE did not change over time, although PE risks in MV patients increased marginally over time (Figures 1 and 2; Table 1).

### Multivariate Association of Each Complication With Clinical Factors

After multivariate analyses including adjusting for MV, odds of pneumonia declined by 4% (odds ratio, 0.96; 95% confidence interval, 0.95–0.97) and sepsis by 3% (odds ratio, 0.97%; 95% confidence interval, 0.96–0.98) for each year (Table 2), whereas odds of ARF increased by 9% (odds ratio, 1.09; 95% confidence interval, 1.08–1.10) per year (Table 2).

Some clinical factors were associated with multiple complications. Compared with whites, blacks had higher odds of UTI, pneumonia, and ARF but lower odds of AMI. Atrial fibrillation, dysphagia, high Charlson comorbidity index score, and Medicaid as opposed to Medicare insurance increased the odds of having  $\geq 4$  complications. Surprisingly, MV was associated with decreased odds of UTI but increased odds of all other complications, whereas smoking was associated with reduced odds of all complications except AMI (Table 2). Although odds of sepsis and ARF were greater in teaching hospitals compared with rural hospitals, no consistent significant patterns in multivariate-adjusted odds of complications existed by hospital region or yearly stroke volume (Table 2).

**Table 1. Prevalence of Medical Complications After Acute Intracerebral Hemorrhage Hospitalization in the United States From 2004 to 2013**

Overall	Overall	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	P Value
<b>Any complication</b>												
Total	29.3	26.0	25.1	27.3	28.9	30.9	30.4	31.2	30.9	31.5	31.2	<0.001
Males	28.1	24.1	23.7	26.1	27.6	29.4	29.7	29.9	29.8	30.0	30.1	<0.001
Females	30.6	27.9	26.5	28.5	30.1	32.3	31.1	32.6	32.0	33.2	32.3	<0.001
No MV	27.3	25.2	24.1	25.7	27.1	29.1	28.4	28.5	28.8	28.5	27.8	<0.001
MV	37.1	29.6	30.3	34.1	36.5	37.8	37.6	39.6	37.9	40.4	41.7	<0.001
<b>In-hospital mortality</b>												
Total	23.8	27.8	26.9	24.8	23.6	23.8	23.5	22.8	21.5	22.1	21.0	<0.001
Males	23.4	27.5	26.9	24.9	23.3	22.9	23.4	22.3	22.2	21.4	20.2	<0.001
Females	24.0	28.1	26.9	24.6	24.0	24.7	23.6	23.3	20.7	22.8	21.9	<0.001
No MV	14.3	19.7	18.6	16.0	15.2	14.6	13.9	12.5	10.7	11.0	9.7	<0.001
MV	59.5	66.4	68.0	64.4	60.7	60.1	59.8	56.6	56.6	54.8	54.5	<0.001
<b>Urinary tract infection</b>												
Total	14.8	13.7	13.3	13.9	14.9	15.7	15.0	16.3	15.4	15.4	14.2	<0.001
Males	9.9	9.0	9.5	9.4	10.0	10.5	10.4	10.8	10.4	10.0	8.9	0.193
Females	19.8	18.2	17.1	18.4	19.7	21.1	19.7	22.0	20.3	21.1	20.1	<0.001
<b>Pneumonia</b>												
Total	7.8	7.2	7.5	7.8	8.5	8.5	7.6	7.9	7.6	7.7	7.2	0.573
Males	9.1	8.6	8.3	9.3	9.8	10.3	9.0	9.4	9.0	9.0	8.3	0.763
Females	6.4	5.8	6.7	6.5	7.3	6.7	6.4	6.4	6.2	6.2	5.9	0.325
No MV	5.7	4.2	4.2	4.2	4.5	4.5	3.8	3.6	3.7	3.5	3.2	<0.001
MV	15.7	12.9	13.8	15.5	17.5	16.9	15.6	16.9	15.6	16.4	15.4	0.060
<b>Sepsis</b>												
Total	4.1	3.8	3.7	4.1	4.3	4.8	4.3	4.3	3.9	4.0	4.0	0.631
Males	4.8	4.6	4.3	4.7	5.1	5.4	5.3	4.9	4.8	4.7	4.6	0.792
Females	3.4	3.1	3.0	3.6	3.5	4.1	3.3	3.6	3.1	3.2	3.3	0.833
<b>Deep vein thrombosis</b>												
Total	2.7	2.0	2.2	2.4	2.7	2.8	3.2	2.7	2.6	2.8	3.2	<0.001
Males	3.2	2.4	2.2	3.2	3.3	3.3	3.7	3.2	3.1	3.4	3.8	<0.001
Females	2.1	1.7	2.0	1.7	2.1	2.2	2.6	2.2	2.1	2.3	2.3	0.010
No MV	2.2	2.0	2.0	2.3	2.4	2.5	2.8	2.1	2.1	2.1	2.1	0.977
MV	4.2	2.1	2.6	3.3	4.1	3.7	4.4	4.6	4.4	5.1	6.1	<0.001
<b>Pulmonary embolism</b>												
Total	0.7	0.6	0.5	0.8	0.7	0.7	0.8	0.7	0.7	0.7	0.8	0.054
Males	0.9	0.6	0.5	1.1	1.0	0.9	0.9	0.9	1.1	0.7	0.9	0.145
Females	0.5	0.5	0.5	0.5	0.5	0.5	0.6	0.6	0.4	0.6	0.7	0.239
No MV	0.7	0.6	0.5	0.9	0.6	0.7	0.7	0.6	0.7	0.6	0.7	0.492
MV	0.8	0.4	0.5	0.5	1.3	0.7	1.2	1.0	0.9	0.9	1.0	0.0129
<b>Acute renal failure</b>												
Total	8.2	4.4	4.8	5.8	7.1	8.6	8.9	9.5	10.2	11.5	12.2	<0.001
Males	10.6	5.4	6.1	7.6	9.5	10.6	11.4	12.2	13.1	14.6	15.2	<0.001
Females	5.9	3.3	3.5	3.9	4.8	6.4	6.4	6.6	7.3	8.2	8.9	<0.001

(Continued)

Table 1. Continued

Overall	Overall	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	P Value
No chronic renal disease	5.7	3.3	3.6	3.8	4.9	5.7	6.1	6.7	6.9	7.8	8.7	<0.001
Chronic renal disease	30.1	24.5	23.2	24.1	25.2	32.0	30.5	30.5	31.4	35.9	34.9	<0.001
Acute myocardial infarction												
Total	2.0	2.0	1.6	1.9	1.8	1.8	2.4	2.4	1.8	2.0	2.3	0.007
Males	2.0	1.8	1.5	2.1	2.0	1.8	2.5	2.6	1.4	2.0	2.4	0.024
Females	2.0	2.2	1.7	1.7	1.6	1.9	2.3	2.2	2.2	2.0	2.2	0.090
No coronary artery disease	1.6	1.8	1.4	1.5	1.6	1.6	1.8	1.9	1.4	1.5	1.7	0.902
Coronary artery disease	3.5	3.0	2.2	3.5	2.8	3.0	4.6	4.4	3.4	4.0	4.5	<0.001

MV indicates mechanical ventilation.

### Multivariate Association of Complications With Length of Stay, Cost, Home Disposition, and In-Hospital Mortality

All complications were associated with increased length of stay and increased cost (Table V in the [online-only Data Supplement](#), multivariate model 1). Sepsis and DVT were associated with the highest mean increase in length of stay

(12.9 and 10.5 days, respectively) and cost (\$35 755 and \$32 336, respectively; Table V in the [online-only Data Supplement](#), multivariate model 1). After mutually adjusting for other medical complications, the associations of each complication with cost and length of stay were attenuated (Table V in the [online-only Data Supplement](#), multivariate model 2). This suggests that some of the increase in cost and length of

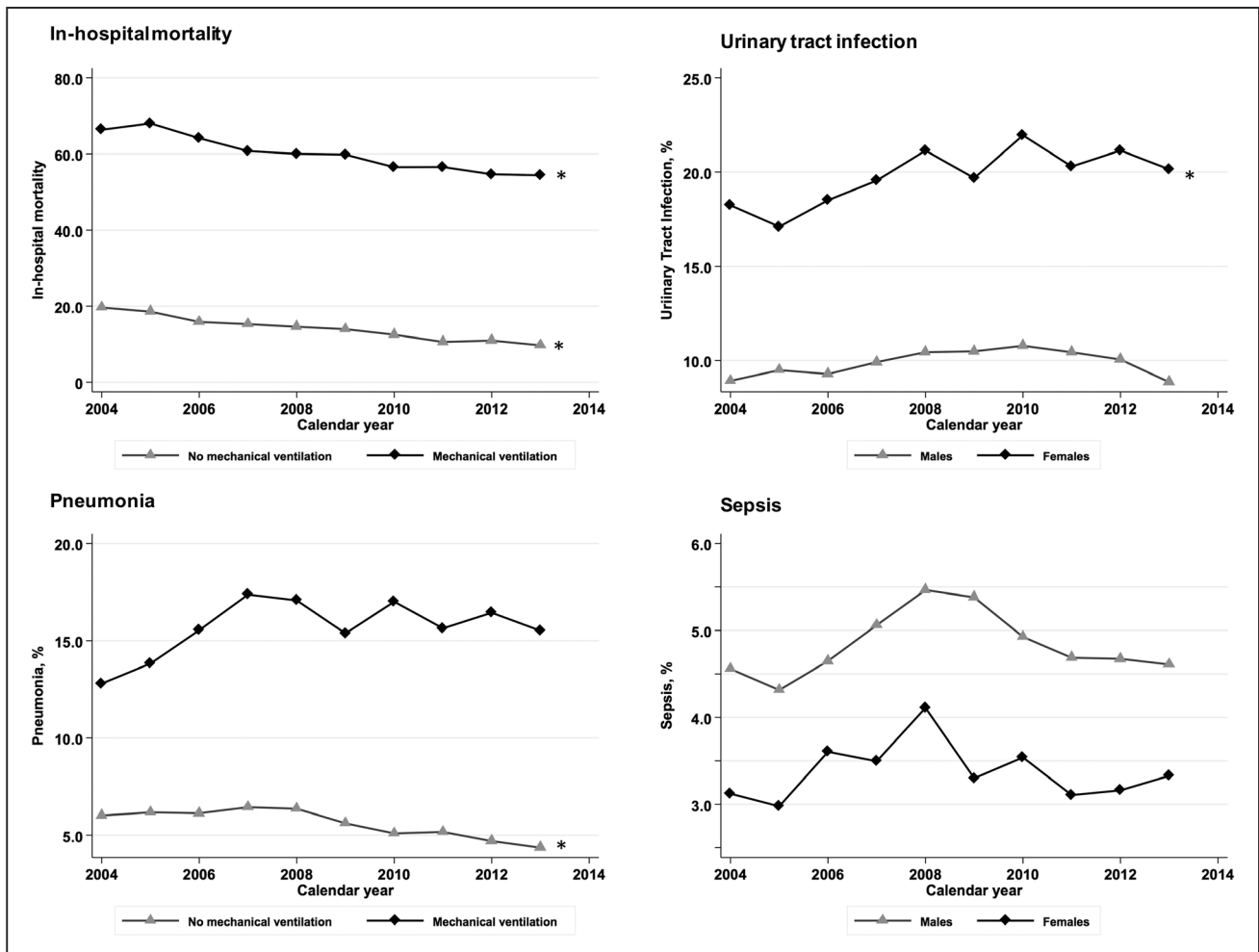
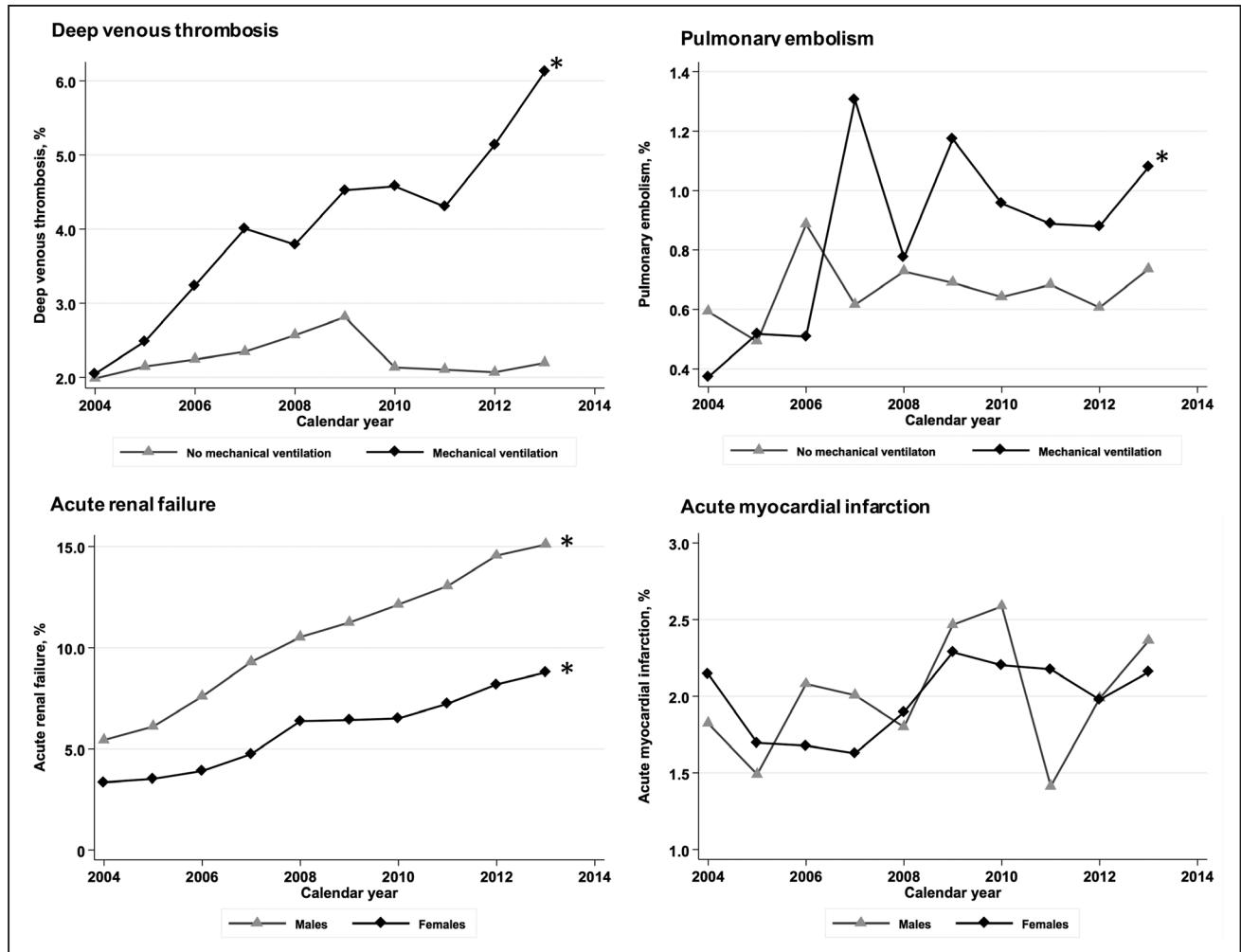


Figure 1. Weighted risk of in-hospital mortality, urinary tract infection, pneumonia, and sepsis after acute intracerebral hemorrhage in the United States according to sex or mechanical ventilation status. \*P value for trend <0.05.

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**Figure 2.** Weighted risk of deep venous thrombosis, pulmonary embolism, acute renal failure, and acute myocardial infarction after acute intracerebral hemorrhage in the United States according to sex or mechanical ventilation status. \**P* value for trend <0.05.

stay associated with these complications is mediated by their association with other complications.

Similarly, all complications were associated with reduced odds of home disposition, but their associations with in-hospital death were variable. Whereas ARF and AMI were associated with increased odds of mortality, concomitant UTI diagnosis during ICH admission was associated with decreased odds of death.

When evaluating the associations of pneumonia, sepsis, and PE with mortality, we found significant effect modification of their association with mortality by MV, so mortality associations of these complications were stratified by MV status. Pneumonia and sepsis were associated with increased odds of mortality in nonventilated patients but were associated with decreased odds of mortality in ventilated patients (Table V in the [online-only Data Supplement](#)).

## Discussion

In this contemporary analysis of the NIS, we found that 29% of all ICH admissions in the United States have at least 1 medical complication, and any complication risk increased by  $\approx 20\%$  from 2004 to 2013. This increase was driven mainly by a >2-fold relative increase in proportion of ARF, a >50% increase

in unadjusted DVT risk, and marginal increase in UTI prevalence. Whereas AMI risk increased only in patients with coronary artery disease and PE risk increased only in MV patients, pneumonia and sepsis risks declined over time. Overall in-hospital mortality after ICH declined by  $\approx 25\%$  from 27% in 2004 to 21% in 2013, but death risk in MV patients remained >50%. Over 60% of all ICH-associated deaths occurred within the first 3 days of hospitalization and over 80% within 7 days.

The high frequency of MV, high mortality in MV patients, and huge percentage of all deaths that occur within the first few days after ICH are consistent with reports of previous studies.<sup>8–10</sup> These reflect the high proportion of ICH patients who still present with severe or devastating hemorrhage and emphasize the need for innovative severe ICH prevention and management strategies. However, as more patients survive their ICH hospitalization, emphasis is slowly shifting from survival to improving ICH-related morbidity and optimization of functional recovery. Quantification of disparities and trends in complication burden is a crucial step in ameliorating ICH outcome because it highlights aspects of ICH care where marginal progress has been made and accentuates other areas where additional efforts are needed. Complications such as DVT are potential quality measures for ICH hospitalization,



**Table 2. Association of Medical Complications During Acute Intracerebral Hemorrhage Hospitalization in the United States From 2004 to 2013 With Clinical and Hospital Factors**

Variable	UTI	Pneumonia*	Sepsis*	DVT	PE	ARF†	Acute MI‡
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Y, per unit increase in y	1.00 (1.00–1.01)	0.96 (0.95–0.97)‡	0.97 (0.96–0.98)‡	1.01 (0.99–1.03)	1.01 (0.98–1.04)	1.09 (1.08–1.10)‡	1.01 (0.99–1.02)
<b>Age (y)</b>							
40–59 vs 18–39	1.29 (1.15–1.46)‡	1.13 (1.00–1.29)	1.05 (0.90–1.23)	0.94 (0.78–1.14)	1.08 (0.75–1.54)	1.05 (0.92–1.19)	1.48 (1.06–2.06)§
60–79 vs 18–39	1.47 (1.32–1.67)‡	1.09 (0.95–1.26)	0.85 (0.72–1.00)§	1.05 (0.85–1.28)	1.06 (0.73–1.53)	0.95 (0.84–1.09)	1.56 (1.10–2.21)§
≥80 vs 18–39	1.83 (1.61–2.07)‡	1.11 (0.95–1.31)	0.66 (0.55–0.79)‡	0.64 (0.51–0.81)‡	0.59 (0.39–0.90)§	0.91 (0.79–1.05)	1.47 (1.03–2.10)§
Sex, females vs males	2.25 (2.17–2.34)‡	0.75 (0.71–0.79)‡	0.79 (0.74–0.84)‡	0.77 (0.72–0.84)‡	0.73 (0.63–0.84)‡	0.62 (0.59–0.66)‡	1.06 (0.97–1.16)
<b>Race</b>							
Blacks vs whites	1.07 (1.01–1.14)§	1.07 (0.99–1.15)	1.40 (1.26–1.55)‡	1.23 (1.08–1.40)‡	1.17 (0.97–1.42)	1.66 (1.55–1.78)‡	0.83 (0.71–0.97)§
Hispanics vs whites	1.10 (1.02–1.18)§	1.17 (1.07–1.28)‡	1.24 (1.10–1.41)‡	0.80 (0.68–0.96)§	0.72 (0.53–0.99)§	1.09 (1.00–1.20)	1.04 (0.88–1.22)
Others vs whites	1.04 (0.97–1.12)	1.15 (1.03–1.27)‡	1.16 (1.04–1.30)‡	0.71 (0.60–0.85)‡	0.75 (0.55–1.02)	1.17 (1.07–1.29)‡	1.02 (0.87–1.21)
<b>Income</b>							
\$39 000–\$47 999 vs <\$39 000	1.04 (0.99–1.09)	0.96 (0.90–1.02)	1.01 (0.93–1.10)	1.07 (0.96–1.19)	1.03 (0.85–1.27)	1.00 (0.94–1.07)	0.99 (0.87–1.11)
\$48 000–\$62 999 vs <\$39 000	1.00 (0.94–1.05)	0.88 (0.82–0.95)‡	0.92 (0.83–1.01)	1.11 (0.99–1.26)	0.93 (0.75–1.16)	1.00 (0.93–1.08)	0.93 (0.81–1.07)
≥\$63 000 vs <\$39 000	0.97 (0.92–1.03)	0.91 (0.83–0.99)§	0.93 (0.84–1.03)	1.16 (1.02–1.33)§	1.02 (0.78–1.24)	0.94 (0.86–1.02)	0.95 (0.83–1.09)
<b>Insurance</b>							
Medicaid vs Medicare	1.26 (1.17–1.36)‡	1.37 (1.26–1.50)‡	1.43 (1.28–1.60)‡	1.34 (1.15–1.56)‡	1.53 (1.17–2.00)‡	1.62 (1.49–1.76)‡	1.13 (0.94–1.36)
Private vs Medicare	0.84 (0.79–0.88)‡	1.02 (0.95–1.09)	0.88 (0.81–0.97)§	1.30 (1.17–1.44)‡	1.25 (1.03–1.54)§	1.11 (1.04–1.19)‡	0.92 (0.81–1.05)
Self-pay vs Medicare	0.85 (0.78–0.93)‡	0.88 (0.78–0.99)§	0.93 (0.81–1.08)	0.91 (0.74–1.11)	1.25 (0.91–1.71)	1.63 (1.47–1.79)‡	1.13 (0.91–1.39)
Other vs Medicare	0.86 (0.76–0.97)§	1.03 (0.89–1.19)	0.94 (0.79–1.11)	1.29 (1.04–1.60)§	1.14 (0.75–1.72)	1.35 (1.18–1.54)‡	1.13 (0.87–1.47)
<b>Hospital region</b>							
Midwest vs Northeast	0.93 (0.86–1.00)	1.11 (0.99–1.24)	0.80 (0.69–0.92)‡	0.94 (0.79–1.13)	0.78 (0.62–0.98)§	0.95 (0.86–1.05)	0.99 (0.83–1.17)
South vs Northeast	1.11 (1.04–1.19)‡	1.08 (0.97–1.20)	0.96 (0.85–1.10)	0.81 (0.68–0.96)	0.77 (0.62–0.96)§	1.09 (0.99–1.19)	0.94 (0.79–1.09)
West vs Northeast	1.05 (0.98–1.12)	1.00 (0.89–1.13)	0.83 (0.72–0.96)§	0.87 (0.72–1.05)	0.91 (0.70–1.17)	0.99 (0.88–1.11)	0.94 (0.79–1.13)
<b>Hospital location/teaching status</b>							
Urban nonteaching vs rural	1.09 (0.99–1.21)	1.11 (0.98–1.26)	1.63 (1.31–2.04)‡	1.27 (0.80–2.00)	0.95 (0.60–1.51)	1.67 (1.42–1.95)‡	1.19 (0.94–1.49)
Urban teaching vs rural	1.25 (1.12–1.39)‡	1.17 (1.02–1.42)§	1.99 (1.58–2.51)‡	1.55 (0.95–2.56)	1.20 (0.74–1.91)	1.92 (1.63–2.27)‡	1.33 (1.05–1.69)
<b>Stroke volume per y</b>							
Middle tertile vs lowest tertile	1.06 (1.00–1.11)	0.93 (0.85–1.00)	0.87 (0.78–0.97)§	1.16 (1.03–1.38)§	1.02 (0.83–1.27)	0.98 (0.90–1.06)	0.81 (0.72–0.93)§
Upper tertile vs lower tertile	1.17 (1.09–1.25)‡	1.00 (0.90–1.11)	0.83 (0.72–0.95)‡	1.44 (1.20–1.73)‡	1.12 (0.87–1.45)	0.90 (0.81–0.99)§	1.02 (0.86–1.20)
<b>Hospital bed size</b>							
Medium vs small	1.02 (0.93–1.11)	0.94 (0.86–1.06)	1.34(1.11–1.62)‡	1.32 (0.97–1.80)	0.79 (0.56–1.11)	1.03 (0.89–1.19)	1.12 (0.90–1.39)
Large vs small	1.05 (0.96–1.14)	0.98 (0.87–1.10)	1.30 (1.08–1.55)‡	1.42 (1.04–1.94)§	1.01 (0.73–1.41)	1.11 (0.97–1.28)	1.15 (0.93–1.42)
Weekend admission	1.00 (0.96–1.04)	1.02 (0.97–1.07)	0.96 (0.90–1.03)	1.00 (0.92–1.09)	0.93 (0.80–1.10)	1.00 (0.95–1.05)	1.04 (0.95–1.14)
Baseline coagulopathy	1.28 (1.20–1.37)‡	1.52 (1.40–1.65)‡	2.18(1.98–2.40)‡	1.90(1.68–2.13)‡	1.58 (1.24–2.00)‡	1.66 (1.53–1.80)‡	1.44 (1.23–1.69)‡
Atrial fibrillation	1.17 (1.12–1.23)‡	1.29 (1.22–1.37)‡	1.19 (1.10–1.29)‡	1.07 (0.96–1.19)	1.15 (0.94–1.40)	1.28 (1.20–1.36)‡	1.04 (0.90–1.14)
Dysphagia	2.17 (2.06–2.28)‡	1.99 (1.86–2.13)‡	1.49 (1.36–1.64)‡	1.73 (1.57–1.91)‡	1.33 (1.09–1.62)‡	1.37 (1.28–1.47)‡	0.94 (0.82–1.09)

(Continued)

Table 2. Continued

Variable	UTI	Pneumonia*	Sepsis*	DVT	PE	ARF†	Acute MI
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Mechanical ventilation	0.74 (0.70–0.78)‡	3.88 (3.19–4.71)‡	1.78 (1.64–1.93)‡	1.31 (1.19–1.44)‡	0.90 (0.75–1.02)	1.51 (1.41–1.61)‡	1.67 (1.50–1.86)‡
Coma	0.75 (0.70–0.80)‡	1.06 (0.98–1.15)	1.05 (0.95–1.17)	0.75 (0.65–0.88)‡	0.76 (0.57–1.01)	1.00 (0.92–1.09)	1.07 (0.92–1.24)
AVM or aneurysm	1.05 (0.93–1.19)	1.36 (1.18–1.57)‡	1.14 (0.94–1.39)	1.57 (1.30–1.90)‡	1.40 (0.96–2.04)	0.74 (0.63–0.88)‡	0.95 (0.70–1.29)
Craniotomy	1.20 (1.01–1.43)§	1.84 (1.58–2.15)‡	1.49 (1.23–1.81)‡	2.16 (1.74–2.69)‡	1.67 (1.09–2.54)§	1.04 (0.84–1.28)	1.21 (0.86–1.71)
EVD/VPS	1.67 (1.55–1.80)‡	2.72 (2.51–2.95)‡	2.22 (2.03–2.43)‡	2.33 (2.09–2.60)‡	2.06 (1.65–2.56)‡	1.49 (1.38–1.61)‡	1.42 (1.22–1.65)‡
Smoking	0.78 (0.73–0.84)‡	0.79 (0.73–0.86)‡	0.58 (0.51–0.65)‡	0.51 (0.44–0.60)‡	0.43 (0.32–0.58)‡	0.83 (0.77–0.90)‡	0.98 (0.84–1.14)
Modified CCI							
CCI=2 vs CCI=1	1.19 (1.13–1.24)‡	1.19 (1.11–1.27)‡	1.16 (1.07–1.28)‡	1.00 (0.88–1.12)	0.93 (0.73–1.17)	1.33 (1.25–1.43)‡	1.03 (0.91–1.17)
CCI=3 vs CCI=1	1.32 (1.25–1.39)‡	1.61 (1.50–1.73)‡	1.54 (1.41–1.69)‡	1.73 (1.55–1.93)‡	1.60 (1.32–1.95)‡	1.50 (1.39–1.62)‡	1.11 (0.97–1.27)
CCI≥4 vs CCI=1	1.33 (1.26–1.40)‡	1.86 (1.73–1.99)‡	1.74 (1.59–1.90)‡	1.90 (1.71–2.11)‡	1.99 (1.62–2.45)‡	1.51 (1.39–1.63)‡	1.13 (0.98–1.31)

Multivariate logistic models adjusted for all factors above with estimates. ARF indicates acute renal failure; AVM, arteriovenous malformation; CCI, Charlson comorbidity index; CI, confidence interval; DVT, deep venous thrombosis; EVD/VPS, hydrocephalus requiring external ventricular drain/ventriculoperitoneal shunt placement; MI, myocardial infarction; OR, odds ratio; PE, pulmonary embolism; and UTI, urinary tract infection.

\*Models for pneumonia and sepsis also include interaction term between age and mechanical ventilator use.

†Model for ARF also includes further adjustment for chronic renal failure (OR, 5.32; 95% CI, 4.96–5.72;  $P < 0.001$ ) and for acute myocardial infarction further adjusted for coronary artery disease (OR, 1.86; 95% CI, 1.68–2.06), congestive heart failure (OR, 2.63; 95% CI, 2.33–2.96), valvular heart disease (OR, 1.38; 95% CI, 1.18–1.61), all  $P$  values  $< 0.001$ .

‡ $P$  value  $< 0.001$ .

§ $P$  value  $< 0.05$  but  $\leq 0.01$ .

‖ $P$  value  $< 0.01$  but  $\leq 0.001$ .

but national reference data have hitherto been lacking. This study provides a robust assessment of the current national patterns of important medical complications after ICH with additional information on relevant population subgroups.

A major finding in this study is the exponential increase in ARF. Whereas the proportion of patients with hypertension, diabetes mellitus, and CKD increased over time and may have contributed to some of the observed increase, risks remained significantly high after adjusting for these conditions, suggesting that the additional factors are responsible. Potential explanations include more aggressive lowering of blood pressure in the acute period of ICH to prevent hematoma expansion<sup>4,11</sup> or nephropathy associated with increased use of contrast imaging, but no definite conclusions can be drawn using our retrospective analysis. That aggressive blood pressure control can increase ARF risk was evidenced in the ATACH II trial (Antihypertensive Treatment of Acute Cerebral Hemorrhage II), where adverse renal events occurred in 9.0% of patients in the intensive blood pressure-lowering arm versus 4.0% of patients in the standard-treatment arm.<sup>12</sup> Other prospective studies are needed to assess these and other possible etiologic factors.

ICH patients are at particularly high risk for DVT because of their immobility and altered mental status.<sup>13</sup> Although DVT and PE risks reported in this study are consistent with those in previous studies,<sup>14</sup> rising risks imply that current measures to prevent DVT in ICH patients are far from adequate. Innovative DVT preventive measures are needed particularly in ventilated patients who accounted for all of the observed increase in risks. Current guidelines recommending deferral of subcutaneous anticoagulation for the initial few days may require reappraisal. The observed increase in DVT risk seen

in our study may be partly because of increased DVT detection as a result of advancement in imaging technology and improvement in clinical practices, but low frequency of DVT prophylaxis in ICH patients in the United States may also be partly responsible.<sup>15</sup> Ventilated patients represent a subgroup of ICH patients with potentially greater morbidity and disability from their ICH, and there may possibly be a growing reluctance to use DVT prophylaxis in this group of patients.<sup>16</sup> These factors also need to be evaluated prospectively.

The inverse association of DVT and UTI with mortality may reflect early pickup of nonfatal cases of these conditions. Similarly, MV patients are usually monitored closely in an intensive care unit, thus the negative association of sepsis and pneumonia with mortality in ventilated patients may partly be secondary to early diagnosis and aggressive treatment of mild cases. There could also be some survival bias. MV patients are likely to have the most severe ICH and consequently more likely to die quickly from ICH before they develop complications such as DVT, pneumonia, or sepsis. Moreover, the sickest ICH patients on MV are more likely to have withdrawal of clinical care. In such cases where care is withdrawn, mortality is likely greater, and there could be decreased detection and diagnosis of complications.

Disparities in odds of various complications with respect to race and insurance status may be related to differences in timing of withdrawal of care. Compared with whites, black patients in the United States are more likely to have care withdrawn late and therefore more prone to higher detection of complications.<sup>17</sup> Black patients with ICH also have lower white blood cell counts compared with whites and consequently more predisposed to increased risk for infectious complications.<sup>18</sup> These factors also need further evaluation.

This study has limitations. Although we relied on previously validated codes for ICH and for complications, we cannot exclude potential inaccuracies because of coding errors. There is great variability in the accuracy of International Classification of Disease, 9th Revision codes for medical complications and in how clinicians actually diagnose pneumonia,<sup>19</sup> sepsis, and other complications. Our study of trends in complications is based on the implicit assumption that coding practices remained unchanged over time. However, numerous coding guidelines may have led to the improvement in coding over time. We were unable to provide information on the clinical and radiological severity of ICH by virtue of inherent limitations in our database. However, we used ventilator status, hydrocephalus, dysphagia, and coma as surrogate measures of ICH severity and adjusted for comorbid disease status in all multivariate analyses. A significant proportion of medical complications occur subacutely after ICH admission and still contribute to morbidity and mortality, so true prevalence estimates of complications and mortality are likely higher than reported in this analysis. Thirty-day and 90-day outcome measures may provide more accurate information on complication burden. Our finding of excess cost and length of stay associated with all complications should be interpreted with caution because we were unable to show temporal correlation between complications and these outcomes. Reverse causation is also possible. For example, patients surviving and staying longer in the hospital for other reasons not related to a medical complication may be predisposed to a DVT as opposed to a DVT leading to prolonged hospital stay. We were unable to evaluate the impact of withdrawal of care on medical complication burden because this information is unavailable in the NIS.

Despite these limitations, this study represents the most comprehensive assessment to date of medical complications after ICH. Important strengths of our study include better ICH case ascertainment by use of clinically diagnosed hospitalized ICH. The large sample size of our study with national representation and generalizability to all ICH patients in the United States provides a comprehensive evaluation of the risks, associated determinants, outcomes, and importance of medical complications in ICH patients. Medical complications are frequent and pose significant threats to morbidity and mortality for ICH patients, and our findings should trigger increased efforts to prevent them and to lessen their burden.

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Dr Otite had full access to all of the study data and takes responsibility for the integrity and accuracy of the data analysis. Drs Otite and Romano provided study concept and design. All authors involved in acquisition, analysis, and interpretation of data and revised the article critically for important intellectual content. Dr Otite drafted the article. Dr Otite performed statistical analysis. Drs Malik, Chaturvedi, Sacco, and Romano provided administrative, technical, or material support. Dr Romano supervised the study.

### Disclosures

None.

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## Ten-Year Temporal Trends in Medical Complications After Acute Intracerebral Hemorrhage in the United States

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## SUPPLEMENTAL MATERIALS

### Supplementary Methods

Data for this study was obtained from the 2004-2013 Nationwide Inpatient Sample (NIS). The NIS is maintained as part of the Health Care Utilization Project (HCUP) of the Agency for Healthcare Research and Quality (AHRQ). It is the largest all-payer inpatient care database in the US and comprises a 20% stratified random sample of all US hospital discharges. Each discharge in the NIS is de-identified so all discharges were considered to be independent. The unit for this analysis was each discharge rather than each individual. Further details on the NIS design are available at <http://www.hcup-us.ahrq.gov>.

### Study Population

From n=78,327,564 hospitalizations contained in the NIS from 2004-2013, we identified all patients with a primary diagnosis of ICH (n=131,730) by querying the database using the International Classification of Disease-Clinical Modification, 9th revision (ICD-9 CM) code 431.<sup>1</sup> This code has a positive predictive value of 79%-97% and a sensitivity of 81%-85% for ICH (supplementary table 1).<sup>2</sup> To ensure only acute ICH cases were captured, we excluded n=6,359 hospitalizations designated as elective admissions. We further excluded n=6,482 hospitalizations with length-of-stay of <24 hours, n=17 patients with missing length-of-stay, n=741 patients with co-existing brain tumor diagnosis, n=781 patients with secondary head trauma diagnosis and n=644 patients <18 years of age leading to a final study population of n=116,706 patients.

### Definition of Outcomes

Most complications were identified by searching all secondary diagnoses fields using the HCUP-defined constellation of ICD-9 codes corresponding to these diagnoses and contained in the HCUP Clinical Classification Software (CCS). UTI was identified using CCS code 159, while pneumonia, septicemia, ARF and AMI were identified using codes 122, 2, 157 and 100 respectively. DVT was identified by searching for ICD-9 codes 453.4X, 453.8x, 451.11 451.19, 451.2, 451.9 while PE was identified using codes 415.1X excluding 415.12 for septic pulmonary embolism.

In-hospital mortality, home disposition and length-of-stay were studied using HCUP variables named “DIED”, “DISPUNIFORM” and “LOS” respectively, and cost was calculated by multiplying total hospital charge in the NIS by cost-to-charge ratios provided as an additional file in the NIS. Calculated cost of each hospitalization was adjusted for inflation and expressed in terms of 2015 US dollars using coefficients obtained from the Bureau of Labor and Statistics website:

[http://www.bls.gov/data/inflation\\_calculator.htm](http://www.bls.gov/data/inflation_calculator.htm).

### Covariate assessment

Comorbidities associated with ICH hospitalization were identified by AHRQ comorbidity measures available in the NIS. AHRQ comorbidity measures identify different comorbidities using ICD-9-CM diagnoses and the Diagnosis Related Group (DRG) that are likely to have been present prior to hospitalization.<sup>3</sup> The modified Charlson

Comorbidity Index (CCI),<sup>4</sup> a validated weighted comorbid disease severity score composed of 17 comorbid conditions was calculated for all participants and patients were categorized into quartiles according to their CCI scores.

We identified mechanically ventilated patients using ICD-9 procedural codes 967, 967.1 and 967.2. In order to capture patients that were mechanically ventilated before they developed a complication as opposed to those that were intubated secondary to a complication, we defined mechanical ventilation (MV) status as positive only if patients were intubated within 48 hours of admission and as negative otherwise.

Patients with arteriovenous malformations and aneurysms were identified by searching all secondary diagnosis fields for ICD-9 codes 747.81 for intracranial arteriovenous malformation, searching all ICD-9 procedural codes 39.51, 39.52, 39.72, 39.76, 39.79 for clipping, coiling or embolization of aneurysm or arteriovenous malformation and ICD-9 codes 01.59 for open resection of arteriovenous malformation. Craniotomy/craniectomy was identified using ICD-9 codes 01.23 or 01.24 and hydrocephalus requiring external ventricular drain or ventriculoperitoneal shunt defined using ICD-9 procedural codes 02.2, 02.21 or HCUP CCS procedural code 2 for insertion, replacement or removal of extracranial ventricular shunt.

Information on hospital characteristics including region, teaching status and bed-size were extracted. Total annual AIS admissions of hospitals were counted and hospitals were grouped annually into tertiles based on their yearly stroke volumes.

### **Statistical analysis**

Baseline characteristics of participants were summarized using descriptive statistics. We used weights<sup>5</sup> provided in the NIS to compute the overall unadjusted weighted prevalence of each complication and in subgroups categorized by sex. We further stratified some complications by pre-existing conditions or interventions expected to influence the occurrence of the complications: pneumonia, DVT and PE rates by MV status, ARF rate by chronic renal failure, and myocardial infarction rate by coronary artery disease. We evaluated trends in prevalence of each complication over time by constructing logistic regression model with each complication as the dependent variable and year of discharge as the independent variable, evaluated continuously, with significance of differences in trend over time assessed using the Wald test.

We used a series of nested logistic regression models adjusted for demographic, clinical, and hospital variables to evaluate the association of each complication with hospitalization variables, and to assess factors that may account for any observed trends in complication rates and control for confounding. We used the CCI as a measure of the overall condition of patients in these models including baseline risk of developing in-hospital complications and used MV status, craniotomy/craniectomy and hydrocephalus-requiring EVD placement as surrogate measures for ICH severity.

Similarly, multivariate logistic regression models adjusted for demographic, comorbid conditions, and hospitalization factors were used to evaluate the association of each

complication with mortality and odds of home disposition at discharge (in surviving patients only). We checked for possible effect modification by MV in all models by including interaction terms for MV status and where applicable reported effect estimates stratified by MV status. We assessed the associations of each complication with cost and length-of-stay by fitting generalized linear models with a gamma variance distribution.

Since this was an exploratory analysis with no specific hypothesis, adjustment for multiple testing was not considered necessary.<sup>6,7</sup> A two-tailed alpha of <0.05 was required for statistical significance. All analyses were performed using Stata 13 (StataCorp, LP, College Station, Texas). We took into account the weighting, clustering and stratification needed in the complex NIS survey design in all analysis by use of Stata's SVY suite of commands with use of the hospital as the primary sampling unit and applying relevant probability sampling weights for robust variance estimation to all models. We assessed all models for collinearity by assessing variation inflation factor diagnostics using Stata's "Collin" command.

### **Missing variables**

Most variables had missing values in <1% of participants except for race and cost data that were missing in 19.1% and 2.7% of participants, respectively. Missing data were imputed to the dominant category for categorical variables and the median for continuous variables.<sup>8</sup> Missing insurance status for those aged  $\geq 65$  years was imputed to Medicare. Missing race data was handled using multiple imputation. Missing cost data were handled using re-weighting technique recommended by HCUP<sup>9</sup> and missing hospital variables such as teaching status (0.8%) and number of beds (0.8%) were excluded. Main effect estimates were similar when Stata's MI suite of commands was used to account for all missing variables using multiple imputation.

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**Supplementary table 1: Reported range of sensitivities and positive predictive values of International Classification of Disease 9 CM codes for intracerebral hemorrhage and complications in published systematic reviews.**

Variable	Sensitivity, %	Positive predictive value
Intracerebral hemorrhage <sup>1</sup>	82-85	79-97
Acute myocardial infarction <sup>2</sup>	49-94	49-99
Acute renal failure <sup>3</sup>	15-81	15-96
Sepsis <sup>4</sup>	17-82	6-100
Pneumonia <sup>5</sup>	54-98	57-96
Urinary tract infection <sup>6</sup>	22.2	92.3
Deep venous thrombosis <sup>7</sup>	61-100	31-97
Pulmonary embolism <sup>7</sup>	24-100	24-92

\* Single center study, Used only two ICD-9 codes 599.0 and 996.64 to identify UTI patients.

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Dyslipidemia	28.3	16.0	19.3	22.4	25.2	27.9	30.9	32.1	35.2	36.8	37.3
Diabetes uncomplicated	22.2	19.1	19.4	20.0	21.8	22.9	23.8	23.0	23.9	23.6	24.6
Complicated diabetes	3.4	2.6	2.8	2.9	3.5	3.4	3.5	3.5	4.2	4.0	3.7
Hypertension	79.5	72.8	74.6	76.2	78.5	79.5	81.2	81.5	82.8	83.8	84.5
Chronic Renal failure	10.5	5.1	6.4	9.6	10.9	10.7	11.5	11.5	13.3	13.2	13.1
Atrial fibrillation	18.1	16.1	17.8	17.5	18.7	17.6	18.9	18.0	18.7	18.7	18.8
Congestive heart failure	10.4	10.2	10.8	10.9	10.7	10.2	10.6	10.3	10.4	10.3	10.0
Valvular disease	5.5	5.1	5.3	5.7	5.7	5.4	5.3	5.5	5.5	5.6	5.9
Coronary artery disease	19.2	17.2	18.4	18.6	18.5	19.4	20.3	18.9	20.4	20.3	20.4
Peripheral vascular disease	4.8	3.8	4.0	4.1	4.8	4.9	5.3	4.3	5.8	5.0	5.8
Drug abuse	3.6	2.8	3.5	3.6	4.0	3.2	3.1	3.9	4.1	3.9	4.3
Tobacco smoking	10.3	7.3	8.4	8.7	8.9	10.0	10.8	11.7	12.2	12.8	12.8
Alcohol abuse	6.2	5.4	5.8	6.0	6.0	6.0	6.2	5.9	6.9	7.1	6.9
Chronic lung disease	12.4	11.9	11.3	12.2	12.9	12.3	12.4	12.3	12.2	13.2	13.1
AIDS	0.2	0.3	0.3	0.2	0.2	0.3	0.2	0.3	0.3	0.2	0.2
Liver disease	2.4	1.9	2.1	2.1	2.2	2.3	2.5	2.1	3.0	3.1	2.9
Coagulopathy	6.3	5.4	5.6	5.1	5.6	5.6	6.3	6.3	7.3	7.7	8.2
<b>Modified Charlson's Comorbidity index, CCI</b>											
CCI=1	39.6	45.5	44.5	43.3	40.6	39.4	38.6	38.6	36.0	35.3	33.9
CCI=2	23.7	25.9	25.2	23.7	23.6	23.6	23.1	22.6	23.1	22.8	23.4
CCI=3	17.2	15.3	16.0	16.8	16.9	17.6	18.3	17.9	17.9	17.6	18.0
CCI≥4	19.5	13.3	14.2	16.3	18.9	19.3	20.1	20.9	23.0	24.3	24.7
Dysphagia	11.5	7.6	8.4	8.3	9.8	11.1	13.0	13.1	14.1	14.6	15.1
Coma	8.6	7.4	7.6	7.2	6.8	7.8	8.6	8.2	9.4	11.3	11.5
Mechanical ventilation	27.7	27.3	26.3	26.0	26.5	27.1	27.9	28.7	28.4	29.6	29.2
Mechanical ventilation within 48hrs	20.9	17.5	16.8	18.0	18.6	20.2	20.8	23.4	23.5	25.3	25.3
AVM/aneurysm†	2.0	1.8	1.7	2.0	2.0	2.0	1.8	2.1	2.3	2.3	2.4
Craniotomy/craniectomy	1.1	1.2	0.8	1.1	1.5	1.0	1.2	1.2	1.1	1.2	1.2
EVD or VP shunt	8.3	7.6	7.1	7.8	8.1	8.4	8.6	9.5	8.4	8.7	8.5

\* Number of short-term acute beds in a hospital. See full bed categorization detailed at [www.hcup-us.ahrq.gov/db/vars/hosp\\_bedsizes/nisnote.jsp](http://www.hcup-us.ahrq.gov/db/vars/hosp_bedsizes/nisnote.jsp).

† AVM represents arteriovenous malformation

**Supplementary table 3: Disposition of adult intracerebral hemorrhage patients after hospitalization from 2004-2013**

	<b>2004</b>	<b>2005</b>	<b>2006</b>	<b>2007</b>	<b>2008</b>	<b>2009</b>	<b>2010</b>	<b>2011</b>	<b>2012</b>	<b>2013</b>	<b>P-trend</b>
Length of stay, days (SE)	8.4 (0.2)	7.9 (0.2)	8.5 (0.2)	8.5 (0.2)	8.6 (0.2)	8.3 (0.2)	8.5 (0.2)	8.0 (0.2)	8.3 (0.1)	8.0 (0.1)	0.233
Home	19.6	18.9	21.0	20.1	19.1	20.0	20.0	18.9	19.8	19.9	0.943
Home health care	6.3	7.0	7.2	7.6	7.6	6.7	7.5	8.4	8.3	8.3	<0.001
Skilled facility	42.3	43.8	42.8	43.6	44.6	45.7	45.8	47.2	45.9	46.9	<0.001
In-hospital death*	27.8	26.9	24.8	23.6	23.8	23.5	22.8	21.5	22.1	21.0	<0.001
Other†	4.0	3.6	4.3	5.1	5.0	4.1	4.0	4.0	4.0	4.0	0.597

\*Includes discharge to hospice, long term care hospital, skilled nursing facility and intermediate care facility

† includes transfer to short term hospital, discharge against medical advice, discharged alive but destination unknown, missing

**Supplementary table 4. Proportion of medical complications among all patients that died during ICH hospitalization in the United States from 2004-2013 according to their hospital length-of-stay**

	Length of stay <3 days	Length-of-stay <7days*	Length-of-stay >=7days
Died, %	61.6	82.4	17.6
Any complication, %	12.1	16.4	59.7
Urinary tract infection, %	2.8	4.2	W0.1
Pneumonia, %	2.1	3.7	26.8
Sepsis, %	1.3	2.2	18.8
Deep venous thrombosis, %	0.4	0.6	5.7
Pulmonary embolism, %	0.2	0.3	1.8
Acute renal failure, %	5.2	6.8	22.2
Acute myocardial infarction, %	2.2	2.5	5.1

\*Includes all patients with length-of-stay <3 days plus patients that died between days 3 and 6 of admission.



**Supplementary table 5: Association of medical complications during intracerebral hemorrhage hospitalization with length-of-stay, hospitalization cost, home disposition and in-hospital mortality**

Variable	Unadjusted model			Multivariate model 1			Multivariate model 2		
	Estimate	95% CI	P-value	Estimate	95% CI	P-value	Estimate	95% CI	P-value
<b>Length-of-stay, days</b>									
Urinary tract infection	7.22	6.78-7.66	<0.001	4.98	4.71-5.24	<0.001	3.84	3.63-4.06	<0.001
Pneumonia	13.36	12.68-14.03	<0.001	9.65	9.14-10.16	<0.001	7.25	6.87-7.63	<0.001
Sepsis	16.92	15.78-18.06	<0.001	12.85	11.94-13.76	<0.001	9.32	8.52-10.12	<0.001
Deep venous thrombosis	14.52	13.60-15.44	<0.001	10.49	9.65-11.33	<0.001	6.91	6.27-7.55	<0.001
Pulmonary embolism	12.62	10.94-14.29	<0.001	8.75	7.37-10.12	<0.001	3.76	2.81-4.71	<0.001
Acute renal failure	7.86	7.39-8.32	<0.001	4.91	4.58-5.24	<0.001	2.54	2.32-2.76	<0.001
Acute myocardial infarction	4.28	3.50-5.06	<0.001	2.75	2.26-3.23	<0.001	1.13	0.79-1.46	<0.001
<b>Hospitalization cost, \$</b>									
Urinary tract infection	16007	14,527-17,487	<0.001	8,629	7998-9,130	<0.001	6,052	5,644-6,460	<0.001
Pneumonia	45,457	43,128-47,786	<0.001	29,103	27,456-30,750	<0.001	22,123	20,743-23,504	<0.001
Sepsis	51,344	48,210-54,478	<0.001	35,755	33,392-38,118	<0.001	25,844	23,857-27,831	<0.001
Deep venous thrombosis	50,518	46,648-54,388	<0.001	32,336	29,570-35,102	<0.001	21,850	19,559-24,141	<0.001
Pulmonary embolism	46,392	39,998-52,787	<0.001	30,095	25,441-34,749	<0.001	14,819	11,112-18,526	<0.001
Acute renal failure	24,662	22,978-26,346	<0.001	13,387	12,387-14,386	<0.001	6,730	6,110-7,350	<0.001
Acute myocardial infarction	15,050	12,271-17,829	<0.001	8,860	7,202-10,519	<0.001	4,065	3,119-5,011	<0.001
<b>Home disposition</b>									
Urinary tract infection	0.41	0.38-0.45	<0.001	0.50	0.47-0.54	<0.001	0.55	0.51-0.59	<0.001
Pneumonia	0.28	0.24-0.32	<0.001	0.45	0.39-0.52	<0.001	0.55	0.48-0.63	<0.001
Sepsis	0.26	(0.23-0.31)	<0.001	0.33	0.28-0.39	<0.001	0.46	0.40-0.53	<0.001
Deep venous thrombosis	0.40	0.34-0.47	<0.001	0.47	0.40-0.56	<0.001	0.60	0.52-0.71	<0.001
PE	0.45	0.35-0.57	<0.001	0.46	0.36-0.60	<0.001	0.66	0.51-0.87	<0.001
Acute renal failure	0.58	0.54-0.63	<0.001	0.67	0.62-0.72	<0.001	0.79	0.74-0.86	<0.001

Acute myocardial infarction	0.40	0.35-0.46	<0.001	0.52	0.44-0.61	<0.001	0.60	0.51-0.71	<0.001
<b>In-hospital mortality</b>									
Urinary tract infection	0.36	0.34-0.38	<0.001	0.35	0.32-0.37	<0.001	0.35	0.33-0.37	<0.001
Pneumonia in no-MV	1.52	1.41-1.65	<0.001	1.26	1.15-1.38	<0.001	1.21	1.11-1.33	<0.001
Pneumonia in MV	0.22	0.20-0.24	<0.001	0.28	0.25-0.30	<0.001	0.33	0.30-0.37	<0.001
Sepsis in no MV	2.01	1.83-2.20	<0.001	1.93	1.73-2.16	<0.001	2.15	1.92-2.41	<0.001
Sepsis in MV	0.37	0.34-0.42	<0.001	0.47	0.41-0.53	<0.001	0.80	0.69-0.92	<0.001
Deep venous thrombosis	0.49	0.44-0.54	<0.001	0.35	0.31-0.41	<0.001	0.39	0.33-0.45	<0.001
Pulmonary embolism in no MV	1.21	0.98-1.52	0.083	1.21	0.94-1.55	0.138	1.36	1.04-1.79	0.024
Pulmonary embolism in MV	0.30	0.22-0.41	<0.001	0.46	0.31-0.66	<0.001	0.89	0.56-1.40	0.612
Acute renal failure	1.22	1.16-1.28	<0.001	1.09	1.02-1.17	0.008	1.23	1.15-1.31	<0.001
Acute myocardial infarction	1.76	1.61-1.91	<0.001	1.49	1.33-1.67	<0.001	1.63	1.43-1.81	<0.001

Abbreviations: MV represents mechanical ventilation

Multivariate Model 1 – adjusted for age, sex, race, year, insurance type, income, hospital region, hospital location/teaching status, hospital bedsize, yearly stroke volume, atrial fibrillation, smoking, mechanical ventilation use, craniotomy/craniectomy, hydrocephalus requiring external ventricular drain or ventriculoperitoneal shunt, arteriovenous malformation/ aneurysm, coma, dysphagia, weekend admission.

Multivariate model 2- mutually adjusted model 1 containing all variables in model 1 + inclusion of all other medical complications.