



# Atrial fibrillation in critically ill patients who received prolonged mechanical ventilation: a nationwide inpatient report

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**Background/Aims:** To evaluate temporal trends of atrial fibrillation (AF) prevalence in critically ill patients who received prolonged mechanical ventilation (MV) in the United States.

**Methods:** We used the 2008 to 2014 National Inpatient Sample to compute the weighted prevalence of AF among hospitalized adult patients on prolonged MV. We used multivariable-adjusted models to evaluate the association of AF with clinical factors, in-hospital mortality, hospitalization cost, and length of stay (LOS).

**Results:** We identified 2,578,165 patients who received prolonged MV (21.27% of AF patients). The prevalence of AF increased from 14.63% in 2008 to 24.43% in 2014 ( $p$  for trend < 0.0001). Amongst different phenotypes of critically ill patients, the prevalence of AF increased in patients with severe sepsis, asthma exacerbation, congestive heart failure exacerbation, acute stroke, and cardiac arrest. Older age, male sex, white race, medicare access, higher income, urban teaching hospital setting, and Western region were associated with a higher prevalence of AF. AF in critical illness was a risk factor for in-hospital death (odds ratio, 1.13; 95% confidence interval, 1.11 to 1.15), but in-hospital mortality in critically ill patients with AF decreased from 11.6% to 8.3%. AF was linked to prolonged LOS (2%,  $p$  < 0.0001) and high hospitalization cost (4%,  $p$  < 0.0001). LOS (-1%,  $p$  < 0.0001) and hospitalization cost (-4%,  $p$  < 0.0001) decreased yearly.

**Conclusions:** The prevalence of comorbid AF is increasing, particularly in older patients. AF may lead to poorer prognosis, and high-quality intensive care is imperative for this population.

**Keywords:** Respiration, artificial; Critical illness; Atrial fibrillation; Prevalence; Outcome

## INTRODUCTION

Atrial fibrillation (AF) is one of the most common cardiovascular health problems in the general population [1], and its prevalence ranges from 0.1% among people younger than 55 years to 9.1% among those older than 85

years [2]. AF is also common in critically ill patients [3], accounting for more than 61% of all kinds of arrhythmias. The incidence of AF is increasing in critically ill patients and a direct relationship between incidence and disease severity has been observed [4].

The outcomes of critically ill patients with AF are

somewhat conflicting. Some studies have suggested that AF development in critical illness is associated with increased mortality and longer hospital stay [3,5,6]. However, in a single-center prospective observational study, there was no difference in mortality rates between patients with arrhythmia and those without [7]. Although some organizations published guidelines for AF management, they did not include patients with a critical illness [8,9]; also, the risk of anticoagulation therapy during the critical illness is unclear, so the management of AF in patients with critical illness remains a great challenge [10].

AF in critically ill patients has attracted much attention in recent years. Although AF incidence and risk factors were reported by some studies, the trends and outcomes of critically ill patients with AF remain unclear. The National Inpatient Sample (NIS) offers an opportunity to retrospectively evaluate the association between critical illness and AF. Our primary aim was to describe and quantify temporal trends in the prevalence of AF in critically ill patients in the United States (US) from 2008 to 2014. Secondarily, we evaluated the association between the emergence of AF and different characteristics, such as patient demographics and hospital characteristics. Finally, we examined the impact of AF on subsequent outcomes among patients with critical illness.

## METHODS

### Data source

We used NIS data from 2008 to 2014. The NIS is the largest all-payer inpatient health care database in the US and was made available by the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality. Before 2012, data of discharges were obtained by sampling 20% of the hospitals in the US. After 2012, the NIS underwent a redesign to estimate a 20% sample of discharges from all participating hospitals, which can represent over 95% of the US population [11]. Details about the NIS are available at [www.hcup-us.ahrq.gov/nisoverview.jsp](http://www.hcup-us.ahrq.gov/nisoverview.jsp). This study was approved by the Committee on Ethics of Medical Research, Second Military Medical University (Navy Medical University), PLA (approval number: NMUMREC-2019-166). The NIS is a public and open-access database, which does not

contain identified information. Written informed consent by the patients was waived due to a retrospective nature of our study.

### Study population

We identified critically ill patients by using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure code for continuous invasive mechanical ventilation for 96 or consecutive hours (96.72), [12]. The exclusion criterion was age < 18 years. We identified a total of 2,578,165 patients (weighted) with critical illnesses.

### Covariate assessment

The NIS variables were used to identify patients' demographic characteristics including age, sex, race, income by ZIP code, and insurance type. Hospital characteristics included location/teaching status, bed size, and region [13]. We used the Elixhauser Comorbidity Index (ECI), which includes 29 comorbidities, to account for the burden of comorbidity [14]. The CHA<sub>2</sub>DS<sub>2</sub>-VASc score was used to estimate the acute ischemic stroke risk in AF [15]. We also identified the types of organ failure (Supplementary Table 1) and acute medical conditions (Supplementary Table 2) associated with critically ill status using standard ICD-9-CM codes and used them to adjust the multivariable models [16].

### Primary and secondary outcomes

The primary objective of this study was to determine the temporal trend of AF among critically ill patients from 2008 to 2014. AF was defined using ICD-9 code (427.31) in discharge diagnosis fields. The code has a specificity of 98% and sensitivity of 80% for AF [17]. The secondary objectives included in-hospital mortality, length of stay (LOS), hospitalization cost, and discharge location. The hospitalization cost was recalculated after adjustment for inflation. Discharge location was divided into home, long-term acute care hospital or skilled nursing facility (LTACH/SNF), and died.

### Statistical analysis

We derived the national estimates for the critically ill patients' measurements using the NIS survey-weighted methods. Using the strata and weights with appropriate survey commands, we can calculate the national esti-

mates from 20% of all admissions in the NIS. According to the occurrence of AF, the chi-square or *t* test was used to compare patients' baseline characteristics. The trends of the prevalence in AF were analyzed in subgroups categorized by age, sex, race, insurance type, and discharge status using the Cochran-Armitage trend test.

We constructed three models to assess the association between AF and patient-specific characteristics and hospital and clinical factors. We used a univariate logistic regression analysis (model 1) to identify the putative factors associated with AF. Hospital demographics, clinical factors, ECI score, and CHA<sub>2</sub>DS<sub>2</sub>-VASC score are included in model 2.

Several models were performed to elucidate the associations between in-hospital mortality, LOS, and hospitalization cost and AF. In model A, we used AF as the single predictor to identify the risk associated with in-hospital mortality, LOS, and hospitalization cost. To perform a sensitivity analysis, we adjusted for demographic factors, hospital factors, ECI, anticoagulants, and CHA<sub>2</sub>DS<sub>2</sub>-VASC score in model B. For binary outcomes, we used unconditional logistic regression. Since LOS and hospitalization cost were violations of normality, the log-transformation was used. In order to analyze whether stroke or bleeding was linked to the relationship between AF and in-hospital mortality, we used stroke and bleeding as mediators respectively to construct two mediation models (adjusted for demographic factors and hospital factors). The models were also used to evaluate the trends in in-hospital mortality, LOS, and hospitalization cost in critically ill patients with and without comorbid AF. Using year as a continuous predictor, we used logistic regression to analyze in-hospital mortality and linear regression to analyze LOS and hospitalization cost.

Two-sided *p* values  $\leq 0.05$  were considered significant. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

## RESULTS

### Baseline characteristics

We identified a weighted sample of 2,578,165 critically ill patients from 2008 to 2014, of whom 21.27% had a diagnosis of AF. The characteristics of patients with AF

versus those without are displayed in Table 1. Patients with AF were more likely to be older (71.48 years vs. 60.15 years,  $p < 0.0001$ ), more likely to be of white race (68.03% vs. 56.60%,  $p < 0.0001$ ), more likely to be covered by Medicare (73.28% vs. 51.81%,  $p < 0.0001$ ), and more likely to have a higher income (76th to 100th percentile: 21.14% vs. 17.47%,  $p < 0.0001$ ).

### Trends of AF prevalence in subgroups

The AF prevalence in critically ill patients increased from 14.63% in 2008 to 24.43% in 2014 ( $p$  for trend  $< 0.0001$ ). When we excluded the patients who had undergone cardiovascular operations, the trends of AF increased from 14.26% in 2008 to 23.42% in 2014 ( $p$  for trend  $< 0.0001$ ). Fig. 1 and Supplementary Table 3 show the temporal trends of AF prevalence in critically ill patients in subgroups categorized by age, sex, race, and insurance. Across all subgroups, AF prevalence steadily increased from 2008 to 2014 ( $p$  for trend  $< 0.0001$ ). The AF prevalence was higher in patients older than 75 years and higher in men than in women (25.14% vs. 23.54%, respectively). AF was more prevalent in people of white race and patients with Medicare. The temporal trends of AF in subgroups categorized by organ failure type also increased consistently over the study period ( $p$  for trend  $< 0.0001$ ). A higher prevalence of renal failure (45.80% to 65.51%), neurologic failure (21.22% to 37.31%), and metabolic failure (14.85% to 28.47%) was noted (Supplementary Table 4). Amongst different phenotypes of critically ill patients, the prevalence of AF increased in the patients with severe sepsis (38.76% to 53.14%), asthma exacerbation (1.59% to 1.83%), congestive heart failure exacerbation (7.98% to 26.42%), acute stroke (3.77% to 4.37%), and cardiac arrest (2.36% to 3.41%) (Supplementary Table 5).

### Trends in risk predictors and outcomes with or without AF

Temporal trends in risk predictor profiles among critically ill patients with AF versus without are shown in Supplementary Fig. 1. The prevalence of all risk predictor profiles increased consistently from 2008 to 2014 ( $p$  for trend  $< 0.0001$ ) and patients with AF had a higher prevalence. On the contrary, in-hospital mortality decreased consistently regardless of AF status (with AF: 35.85% to 33.20%,  $p$  for trend  $< 0.0001$ ; without AF: 30.11% to 26.90%,  $p$  for trend  $< 0.0001$ ) (Fig. 2, Supplementary

**Table 1. Baseline characteristics of critical illness patients with and without atrial fibrillation**

Variable	Atrial fibrillation		p value
	Present (n = 548,412)	Absent (n = 2,029,754)	
Age, yr	71.48 ± 0.08	60.15 ± 0.11	< 0.0001
Age group, yr			< 0.0001
18–44	12,698 (2.32)	337,033 (16.60)	
45–64	132,350 (24.13)	832,922 (41.04)	
65–74	158,293 (28.86)	437,421 (21.55)	
≥ 75	245,071 (44.69)	422,378 (20.81)	
Female sex	242,415 (44.20)	924,743 (45.56)	< 0.0001
Race			< 0.0001
White	373,079 (68.03)	1,148,796 (56.60)	
Black	60,874 (11.10)	353,268 (17.40)	
Hispanic	36,393 (6.64)	189,589 (9.34)	
Other	35,314 (6.44)	133,625 (6.58)	
Missing	42,752 (7.80)	204,476 (10.07)	
Type of insurance			< 0.0001
Medicare	401,854 (73.28)	1,051,519 (51.81)	
Medicaid	41,756 (7.61)	352,518 (17.37)	
Private	82,355 (15.02)	446,891 (22.02)	
Self-pay	11,271 (2.06)	102,862 (5.07)	
Other	11,175 (2.04)	75,965 (3.74)	
Income quartile			< 0.0001
Q1	164,735 (30.04)	712,001 (35.08)	
Q2	136,771 (24.94)	512,055 (25.23)	
Q3	130,985 (23.88)	451,192 (22.23)	
Q4	115,920 (21.14)	354,505 (17.47)	
Hospital bed size			0.0513
Small	61,954 (11.30)	217,981 (10.74)	
Medium	127,790 (23.30)	467,814 (23.05)	
Large	358,668 (65.40)	1,343,958 (66.21)	
Hospital type			< 0.0001
Rural	27,945 (5.10)	105,971 (5.22)	
Urban non-teaching	210,056 (38.30)	708,199 (34.89)	
Urban teaching	310,411 (56.60)	1,215,584 (59.89)	
Hospital region			< 0.0001
Northeast	106,250 (19.37)	412,274 (20.31)	
Midwest	124,624 (22.72)	415,599 (20.48)	
South	202,648 (36.95)	796,770 (39.25)	
West	114,889 (20.95)	405,111 (19.96)	
Elective	71,652 (13.09)	226,196 (11.18)	< 0.0001
Elixhauser Comorbidity Index			< 0.0001
0	4,076 (0.74)	59,183 (2.92)	

Table 1. Continued

Variable	Atrial fibrillation		p value
	Present (n = 548,412)	Absent (n = 2,029,754)	
1	19,952 (3.64)	167,890 (8.27)	
2	47,377 (8.64)	280,748 (13.83)	
≥ 3	477,007 (86.98)	1,521,932 (74.98)	
Major operating room procedure	133,955 (24.43)	475,624 (23.43)	< 0.0001
Tracheostomy	109,653 (19.99)	456,056 (22.47)	< 0.0001
Long-term anticoagulants	46,527 (8.48)	31,122 (1.53)	< 0.0001
Coronary artery disease	178,355 (32.52)	336,474 (16.58)	< 0.0001
Prior stroke	54,728 (9.98)	137,032 (6.75)	< 0.0001
CHA <sub>2</sub> DS <sub>2</sub> -VASC	3.10 (1.88–4.30)	1.80 (0.56–3.19)	< 0.0001
Phenotypes of critically ill			
Pneumonia	351,695 (64.13)	1,274,619 (62.80)	< 0.0001
Severe sepsis	267,766 (48.83)	1,002,057 (49.37)	0.0218
COPD exacerbation	72,951 (13.30)	209,021 (10.30)	< 0.0001
Asthma exacerbation	9,406 (1.72)	46,964 (2.31)	< 0.0001
Congestive heart failure exacerbation	103,704 (18.91)	217,379 (10.71)	< 0.0001
Acute stroke	21,655 (3.95)	109,685 (5.40)	< 0.0001
Acute coronary syndrome	70,070 (12.78)	223,085 (10.99)	< 0.0001
Cardiac arrest.	15,917 (2.90)	47,040 (2.32)	< 0.0001
Organs failure (0, 1, 2, ≥ 3)			< 0.0001
0	106,538 (19.43)	500,667 (24.67)	
1	179,079 (32.65)	655,771 (32.31)	
2	148,563 (27.09)	501,398 (24.70)	
≥ 3	114,232 (20.83)	371,918 (18.32)	
Discharge status			< 0.0001
Home	73,171 (13.34)	448,200 (22.08)	
LTACH/SNF	292,161 (53.27)	1,024,328 (50.47)	
Death	183,079 (33.38)	557,225 (27.45)	
LOS, day	16.14 (10.32–24.91)	16.33 (10.20–26.33)	< 0.0001
Adjusted cost, dollar	56,468.98 (34,457.05–94,727.91)	55,716.04 (34,577.59–91,424.39)	< 0.0001

Values are presented as mean ± SE, number (%), or median (interquartile range).

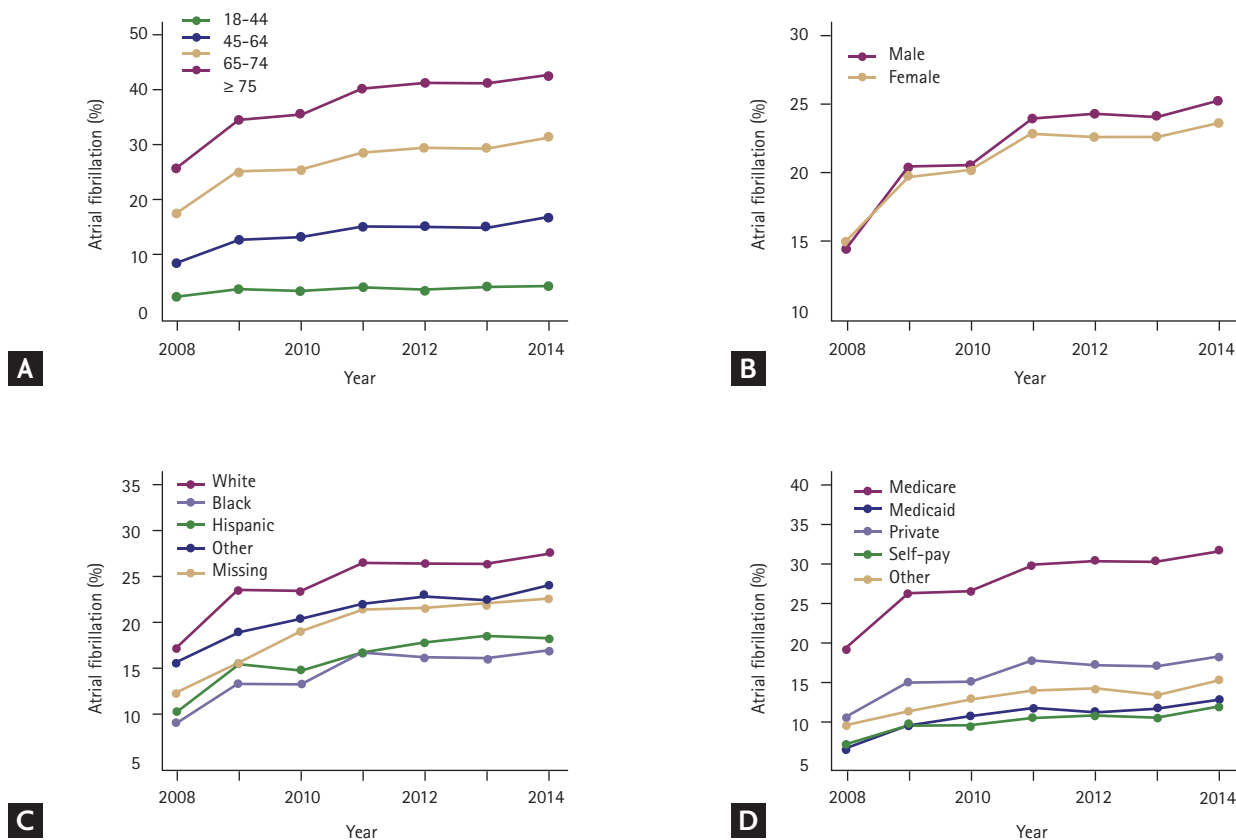
COPD, chronic obstructive pulmonary disease; IMV, invasive mechanical ventilation; LTACH/SNF, long-term acute care hospital or skilled nursing facility; LOS, length of stay.

Table 6). However, the trend of LOS increased in patients with AF (15.33 to 15.88 days, *p* for trend = 0.6211) and decreased in patients without AF (17.32 to 15.71 days, *p* for trend = 0.0015) (Fig. 3, Supplementary Table 7). Declining in-hospital mortality was accompanied by changing discharge status for critically ill patients with AF, with a significant increase to LTACH/SNF (49.27% to 53.87%, *p* for trend < 0.0001) and a decrease in discharge to home

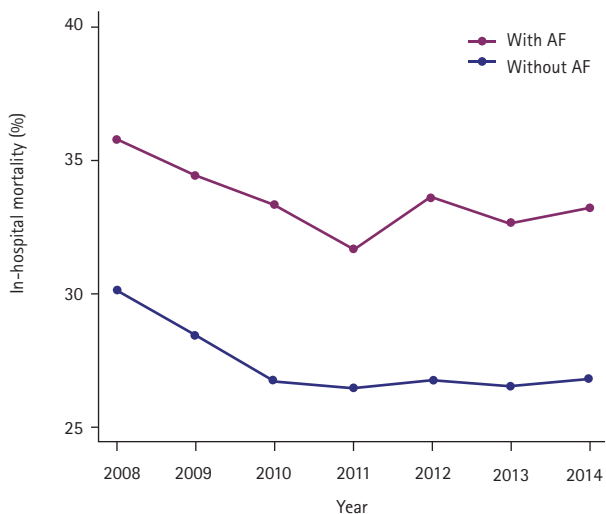
(14.91% to 12.94%, *p* for trend < 0.0001) (Fig. 4, Supplementary Table 8).

#### Association of AF with patient and hospital characteristics in critical illness

The temporally increasing trend of AF prevalence persisted over the study period after multivariable adjust-



**Figure 1.** Temporal atrial fibrillation prevalence in subgroups categorized by age (A), sex (B), race (C), and insurance (D).



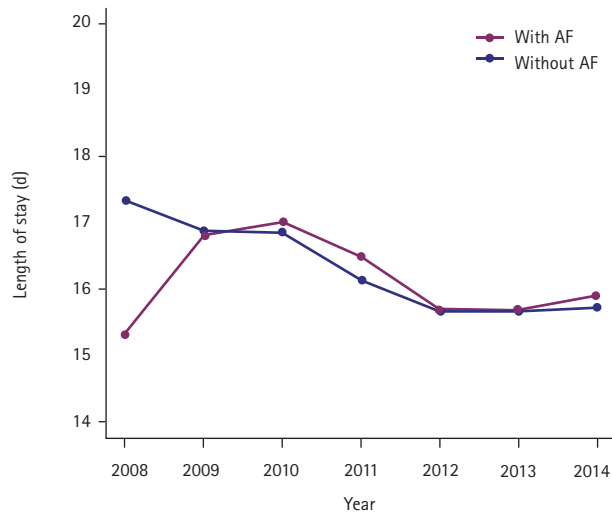
**Figure 2.** Trends in in-hospital mortality in critical illness patients. AF, atrial fibrillation.

ment. The prevalence of AF increased by 8% each year from 2008 to 2014 (odds ratio [OR], 1.08; 95% confidence

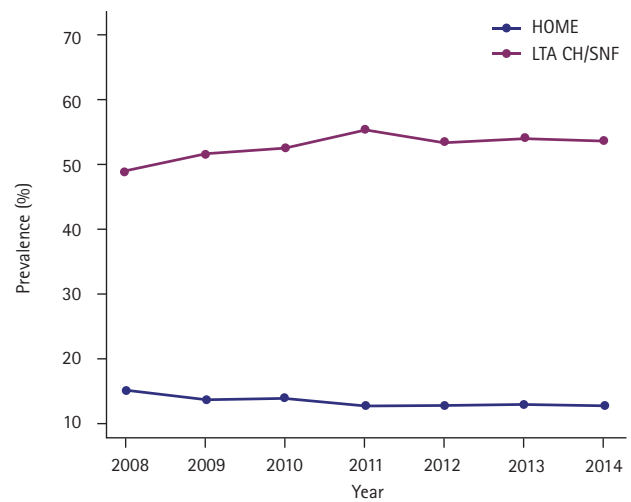
interval [CI], 1.07 to 1.09) (Table 2). Age older than 75 years, white race, Medicare insurance, male sex, higher income, urban teaching hospital, larger hospital bed size, major operating room procedure, higher ECI score, higher CHA<sub>2</sub>DS<sub>2</sub>-VASc score, prior stroke, coronary artery disease, and long-term anticoagulant use were significantly associated with the increased prevalence of AF. Among the comorbidities, deficiency anemia, coagulopathy, hypertension, hypothyroidism, fluid and electrolyte disorders, renal replacement therapy use, obesity, chronic renal failure, and valvular disease were more significantly associated with increased prevalence of AF (Table 2, Supplementary Table 9).

**Association between AF and clinical outcomes**

The unadjusted in-hospital mortality rate was significantly higher in patients with AF than in those without AF (OR, 1.32; 95% CI, 1.30 to 1.35) (Table 3). When stroke was used as a mediator, only 4.20% of the impact of AF



**Figure 3.** Trends in length of stay in critical illness patients. AF, atrial fibrillation.



**Figure 4.** Trends in discharge status (home and long-term acute care hospital or skilled nursing facility [LTACH/SNF]) for critically ill patients with atrial fibrillation.

on in-hospital mortality could be attributed to stroke. When bleeding was used as a mediator, only 0.03% of the impact of AF on in-hospital mortality could be attributed to bleeding. After multivariable adjustment, patients with AF still had a 10% higher risk than those without AF (OR, 1.12; 95% CI, 1.10 to 1.13), but the risk of death decreased each year regardless of AF diagnosis.

In the unadjusted regression model, patients with AF had a shorter LOS (−3%,  $p < 0.0001$ ) and lower hospitalization cost (2%,  $p = 0.0018$ ). However, after multivariable adjustment, an AF diagnosis was still linked to a prolonged LOS (2%,  $p < 0.0001$ ) and higher hospitalization cost (5%,  $p < 0.0001$ ). The LOS (−1%,  $p < 0.0001$ ) and hospitalization cost (−2%,  $p < 0.0001$ ) in critically ill patients with AF also decreased each year.

## DISCUSSION

Our analysis is the first to evaluate the temporal trends of AF prevalence in adult critically ill patients in the US. Many prior analyses studied the incidence of AF in critically ill patients [3,5,18] but were limited by sample size and lacked the required granularity to evaluate the AF trend. We found that the proportion of critically ill patients with comorbid AF increased from 14.63% in 2008 to 24.43% in 2014. In this analysis of over 2 million crit-

ically ill patients, close to 1 in 5 (21.27%) had a diagnosis of AF, a value that was nearly 10-fold higher than that in the general population [1]. This rate is higher than the prevalence of AF reported by previous studies, which was 4.5% to 15% in intensive care unit (ICU) patients [19–22], but is lower as per the Seguin and Launey [23] report (46%). The prevalence of AF in critically ill patients increased with age; over 70% of affected patients were over 65 years. The prevalence was also greater among patients who were white, male, and covered by Medicare, a finding that is consistent with a previous report of critically ill patients [24].

With population aging and the increasing prevalence of comorbidities, the prevalence of AF is anticipated to increase [25]. Our analysis indicated that the prevalence of AF increased significantly over the study period, which is consistent with previous studies [4]. The increased prevalence of AF in critically ill patients may be associated with several factors. First, with the development of medical treatments, improvements in survival result in more hospitalizations of critically ill patients, although in-hospital mortality rates are declining [26]. Second, the trend of increased AF prevalence may also be the result of advances in detection and surveillance, while the improved awareness of AF among physicians increased the prevalence of AF as well [27]. Third, the aging of the population and the increase in comorbidities

**Table 2. Association of comorbid atrial fibrillation with patient and hospital characteristics in critical illness**

Variable	Unadjusted model 1		Multivariable model 2 <sup>a</sup>		Multivariable model 3 <sup>b</sup>	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Year, per unit increase	1.09 (1.08–1.10)	< 0.0001	1.07 (1.07–1.08)	< 0.0001	1.08 (1.07–1.09)	< 0.0001
<b>Age, yr</b>						
Per unit increase	1.05 (1.05–1.05)	< 0.0001	1.04 (1.04–1.04)	< 0.0001	1.05 (1.05–1.05)	< 0.0001
45–64 vs. 18–44	4.22 (4.03–4.41)	< 0.0001	3.28 (3.13–3.43)	< 0.0001	3.22 (3.07–3.37)	< 0.0001
65–74 vs. 18–44	9.60 (9.17–10.1)	< 0.0001	5.56 (5.28–5.84)	< 0.0001	6.08 (5.79–6.39)	< 0.0001
≥ 75 vs. 18–44	15.39 (14.7–16.1)	< 0.0001	7.69 (7.28–8.12)	< 0.0001	9.55 (9.07–10.0)	< 0.0001
<b>Race</b>						
Black vs. white	0.53 (0.51–0.55)	< 0.0001	0.57 (0.56–0.59)	< 0.0001	0.61 (0.59–0.62)	< 0.0001
Hispanic vs. white	0.59 (0.57–0.62)	< 0.0001	0.65 (0.62–0.67)	< 0.0001	0.67 (0.65–0.70)	< 0.0001
Others vs. white	0.81 (0.78–0.85)	< 0.0001	0.79 (0.76–0.82)	< 0.0001	0.82 (0.78–0.85)	< 0.0001
Missing vs. white	0.64 (0.60–0.69)	< 0.0001	0.79 (0.74–0.83)	< 0.0001	0.81 (0.76–0.87)	< 0.0001
<b>Insurance</b>						
Medicaid vs. Medicare	0.31 (0.30–0.32)	< 0.0001	0.89 (0.86–0.92)	< 0.0001	0.92 (0.89–0.96)	< 0.0001
Private vs. Medicare	0.48 (0.47–0.49)	< 0.0001	1.02 (1.00–1.05)	0.0543	1.02 (1.00–1.05)	0.0593
Self-pay vs. Medicare	0.29 (0.27–0.31)	< 0.0001	0.88 (0.83–0.92)	< 0.0001	0.92 (0.87–0.97)	0.0020
Others vs. Medicare	0.38 (0.36–0.41)	< 0.0001	0.90 (0.86–0.95)	< 0.0001	0.92 (0.87–0.97)	0.0011
Female	0.95 (0.93–0.96)	< 0.0001	0.70 (0.69–0.72)	< 0.0001	0.82 (0.81–0.83)	< 0.0001
<b>Income quartile</b>						
Q2 vs. Q1	1.15 (1.13–1.18)	< 0.0001	1.03 (1.01–1.05)	0.0141	1.02 (1.00–1.05)	0.0801
Q3 vs. Q1	1.25 (1.22–1.29)	< 0.0001	1.08 (1.06–1.11)	< 0.0001	1.07 (1.05–1.10)	< 0.0001
Q4 vs. Q1	1.41 (1.37–1.46)	< 0.0001	1.15 (1.12–1.18)	< 0.0001	1.14 (1.11–1.17)	< 0.0001
<b>Hospital bed size</b>						
Medium vs. small	0.96 (0.91–1.01)	0.1506	1.03 (0.98–1.07)	0.2428	1.03 (0.99–1.08)	0.1793
Large vs. small	0.94 (0.89–0.99)	0.0141	1.09 (1.04–1.13)	< 0.0001	1.10 (1.05–1.15)	< 0.0001
<b>Hospital type</b>						
Urban nonteaching vs. rural	1.12 (1.05–1.21)	0.0011	1.05 (0.99–1.12)	0.0756	1.04 (0.98–1.11)	0.1580
Urban teaching vs. rural	0.97 (0.90–1.04)	0.3773	1.08 (1.02–1.15)	0.0106	1.10 (1.04–1.17)	0.0015
<b>Hospital region</b>						
Midwest vs. northeast	1.16 (1.09–1.24)	< 0.0001	1.20 (1.15–1.26)	< 0.0001	1.15 (1.10–1.21)	< 0.0001
South vs. northeast	0.99 (0.93–1.05)	0.6629	1.06 (1.01–1.11)	0.0108	1.02 (0.98–1.07)	0.3488
West vs. northeast	1.10 (1.04–1.17)	0.0013	1.10 (1.05–1.15)	< 0.0001	1.11 (1.06–1.16)	< 0.0001
Elective	1.20 (1.15–1.25)	< 0.0001	1.15 (1.11–1.19)	< 0.0001	1.14 (1.10–1.18)	< 0.0001
<b>Elixhauser Comorbidity Index</b>						
1 vs. 0	1.73 (1.58–1.89)	< 0.0001	1.48 (1.35–1.62)	< 0.0001		
2 vs. 0	2.45 (2.24–2.68)	< 0.0001	1.84 (1.68–2.03)	< 0.0001		
≥ 3 vs. 0	4.55 (4.14–5.00)	< 0.0001	2.55 (2.30–2.82)	< 0.0001		
Major operating room procedure	1.06 (1.04–1.08)	< 0.0001	1.03 (1.01–1.05)	0.0036	1.06 (1.04–1.08)	< 0.0001
Long-term anticoagulants	5.95 (5.69–6.23)	< 0.0001	4.87 (4.66–5.09)	< 0.0001	4.54 (4.35–4.74)	< 0.0001
CHA <sub>2</sub> DS <sub>2</sub> -VASC score	1.41 (1.40–1.41)	< 0.0001	1.19 (1.18–1.20)	< 0.0001		
Prior stroke	1.53 (1.49–1.57)	< 0.0001			1.13 (1.10–1.17)	< 0.0001



Table 2. Continued

Variable	Unadjusted model 1		Multivariable model 2 <sup>a</sup>		Multivariable model 3 <sup>b</sup>	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Coronary artery disease	2.43 (2.38–2.48)	< 0.0001			1.39 (1.36–1.42)	< 0.0001
AIDS	0.25 (0.21–0.31)	< 0.0001			0.64 (0.52–0.78)	< 0.0001
Alcohol abuse	0.56 (0.54–0.57)	< 0.0001			0.92 (0.89–0.95)	< 0.0001
Deficiency anemias	1.28 (1.25–1.31)	< 0.0001			1.10 (1.08–1.12)	< 0.0001
Rheumatoid arthritis	1.12 (1.07–1.17)	< 0.0001			1.04 (1.00–1.09)	0.0667
Chronic blood loss anemia	1.16 (1.09–1.22)	< 0.0001			1.09 (1.03–1.16)	0.0024
Congestive heart failure	2.40 (2.35–2.44)	< 0.0001			1.58 (1.56–1.61)	< 0.0001
Chronic pulmonary disease	1.51 (1.48–1.54)	< 0.0001			1.15 (1.13–1.17)	< 0.0001
Coagulopathy	1.19 (1.16–1.21)	< 0.0001			1.24 (1.22–1.27)	< 0.0001
Depression	0.94 (0.91–0.96)	< 0.0001			0.91 (0.89–0.94)	< 0.0001
Diabetes, uncomplicated	1.40 (1.37–1.43)	< 0.0001			1.06 (1.04–1.08)	< 0.0001
Diabetes with chronic complications	1.18 (1.15–1.22)	< 0.0001			0.93 (0.90–0.96)	< 0.0001
Drug abuse	0.34 (0.32–0.35)	< 0.0001			0.78 (0.75–0.83)	< 0.0001
Hypertension	1.78 (1.75–1.82)	< 0.0001			1.20 (1.18–1.23)	< 0.0001
Hypothyroidism	1.62 (1.58–1.66)	< 0.0001			1.16 (1.13–1.19)	< 0.0001
Liver disease	0.65 (0.63–0.67)	< 0.0001			0.90 (0.87–0.94)	< 0.0001
Lymphoma	1.06 (1.00–1.13)	0.0455			0.98 (0.91–1.04)	0.4764
Fluid and electrolyte disorders	1.12 (1.09–1.14)	< 0.0001			1.04 (1.02–1.06)	< 0.0001
Metastatic cancer	0.89 (0.86–0.93)	< 0.0001			0.94 (0.90–0.98)	0.0024
Other neurological disorders	0.81 (0.79–0.83)	< 0.0001			0.88 (0.86–0.90)	< 0.0001
Obesity	1.19 (1.17–1.22)	< 0.0001			1.20 (1.17–1.23)	< 0.0001
Paralysis	0.80 (0.78–0.82)	< 0.0001			0.92 (0.89–0.95)	< 0.0001
Peripheral vascular disorders	1.61 (1.57–1.65)	< 0.0001			1.05 (1.02–1.07)	0.0003
Psychoses	0.61 (0.58–0.63)	< 0.0001			0.80 (0.77–0.83)	< 0.0001
Pulmonary circulation disorders	1.67 (1.63–1.71)	< 0.0001			1.25 (1.22–1.28)	< 0.0001
Renal failure	1.62 (1.59–1.65)	< 0.0001			1.07 (1.04–1.09)	< 0.0001
Solid tumor without metastasis	1.20 (1.15–1.24)	< 0.0001			0.99 (0.95–1.03)	0.4994
Peptic ulcer disease	1.00 (0.74–1.34)	< 0.0001			0.97 (0.71–1.31)	0.8194
Valvular disease	2.87 (2.79–2.95)	< 0.0001			1.63 (1.58–1.68)	< 0.0001
Weight loss	1.02 (1.00–1.05)	0.0403			0.97 (0.95–0.99)	0.0068

OR, odds ratio; CI, confidence interval; AIDS, acquired immunodeficiency syndrome.

<sup>a</sup>Multivariable model 2: obtained from logistic regression model accounting for survey design and adjusting for year, age, race, insurance, sex, income, hospital region, hospital location/teaching status, hospital bed size, elective, Elixhauser Comorbidity Index, major operating room procedure, long-term anticoagulants, CHA<sub>2</sub>DS<sub>2</sub>-VASC score.

<sup>b</sup>Multivariable model 3: multivariable model 2 exclude Elixhauser Comorbidity Index and CHA<sub>2</sub>DS<sub>2</sub>-VASC scores, and added prior stroke, coronary artery disease, AIDS, alcohol abuse, deficiency anemias, rheumatoid arthritis, chronic blood loss anemia, congestive heart failure, chronic pulmonary disease, coagulopathy, depression, diabetes, uncomplicated, diabetes with chronic complications, drug abuse, hypertension, hypothyroidism, liver disease, lymphoma, fluid and electrolyte disorders, metastatic cancer, other neurological disorders, obesity, paralysis, peripheral vascular disorders, psychoses, pulmonary circulation disorders, renal failure, solid tumor without metastasis, peptic ulcer disease, valvular disease, weight loss.

**Table 3. Association of AF with clinical outcomes in critical illness**

Model	Died, OR (95% CI)		Length of stay		Adjusted cost	
	Estimate	p value	Estimate	p value	Estimate	p value
Association of AF compared to no AF with each outcome among all participants						
Model A	1.32 (1.30–1.35)	< 0.0001	–0.03	< 0.0001	–0.02	0.0018
Model B	1.12 (1.10–1.13)	< 0.0001	0.02	< 0.0001	0.05	< 0.0001
Association of each outcome with unit increase in year when restricted to participants with comorbid AF						
Model A	0.99 (0.98–0.99)	0.0007	–0.01	0.0174	–0.03	< 0.0001
Model B	0.99 (0.98–1.00)	0.0184	–0.01	0.0156	–0.02	< 0.0001
Association of each outcome with unit increase in year when restricted to participants without comorbid AF						
Model A	0.98 (0.97–0.98)	< 0.0001	–0.02	< 0.0001	–0.03	< 0.0001
Model B	0.98 (0.98–0.99)	< 0.0001	–0.02	< 0.0001	–0.03	< 0.0001

Model A: AF as the single predictor; Multivariable model B: adjusted for demographic factors, hospital factors, Elixhauser Comorbidity Index, anticoagulants, and CHA<sub>2</sub>DS<sub>2</sub>-VASC score. AF, atrial fibrillation; OR, odds ratio; CI, confidence interval.

in the general US population also increases AF risk factors [28–30]. The same results were seen in patients with end-stage renal disease and end-stage chronic obstructive pulmonary disease [31,32].

AF in critically ill patients may be new-onset or recurrent [33]. Advanced age is considered one of the most potent risk factors for independently predicting AF [34]. In our study, compared to patients younger than 45 years, those older than 75 years were nearly 10-fold more likely to develop AF. In the meantime, each additional year of age was associated with an 8% increase in the risk of developing AF. Admission to a larger urban teaching hospital was significantly associated with AF relative to small and rural hospitals. Larger urban teaching hospitals receive more critically ill patients and have advanced detection and surveillance capabilities [35]. We found that patients with an ECI > 3 were 2.5-fold more likely to develop AF than those with an ECI of 0. Several comorbidities common in critically ill patients are substrates for AF occurrence and potentially impact patient prognosis [36]. DUBY et al. [37] reported that the risk of AF in critically ill patients with congestive heart failure, hypertension, or heart disease was 4 to 7 times higher than that of patients without these comorbidities. We found that a higher CHA<sub>2</sub>DS<sub>2</sub>-VASC score was significantly associated with the increased prevalence of AF. As a scoring system for predicting cardioembolic risk, CHA<sub>2</sub>DS<sub>2</sub>-VASC scores can help clinicians make deci-

sions about antithrombotic therapy, although this has not been validated in critical illness [38].

In our study, the in-hospital mortality decreased from 35.85% to 33.20%. It is possible that treatment advances led to improved survival in critically ill patients. Compared to patients without AF, those with AF had a 10% higher risk of in-hospital mortality, which is lower than that of previous studies [5,39]. Arrigo et al. [5] demonstrated an association between AF and increased risk of in ICU and post-ICU mortality using a prospective observational multi-center cohort study. A prospective single-center study also identified AF as an independent predictor for in-hospital mortality in critical illness [24]. However, their results are limited by small sample sizes. AF can be triggered by accelerated atrial remodeling and arrhythmias, while acute loss of atrial contraction and ventricular tachycardia often result in reduced cardiac output and hemodynamic impairment [40]. Previous studies have showed an increased risk of embolic stroke and heart failure in patients with AF, which can lead to clinical deterioration and mortality [36,41]. Alternatively, AF may simply be a marker of multiple organ failure, leading to increase in-hospital mortality [42]. However, the evidence for AF as an independent risk factor for in-hospital mortality remains limited and further studies are needed. Due to database limitations, our study was limited to in-hospital mortality and was not able to study short-term or long-term post-discharge mortality.

We found that patients with AF had a 2% higher risk of prolonged LOS and 4% higher relative hospitalization costs than those without AF; that is, AF exerts a negative impact on hospitalization outcomes.

Managing AF in critically ill patients is challenging, and the strategies used in outpatients may not have the same effect [43]. Meanwhile, the efficacy of antiarrhythmic therapies may be reduced [44], though both rate and rhythm controlling agents are frequently used in the management of critically ill patients. Due to procoagulant activity and ongoing inflammation, the risk of thrombus formation and embolization is higher in critically ill patients [45]. Although guidelines and recommendations are lacking, AF in critically ill patients will trigger anticoagulation [46]. Considering the need for urgent surgery or risk for coagulopathy in the ICU, the choice of anticoagulant is a big problem for physicians, and we cannot exclude the association between mortality and anticoagulant use in critically ill patients [42].

Our study has some strengths. To our knowledge, it is the newest assessment of temporal trends of AF in critically ill patients in the US. Previous studies identified the association between AF and morbidity outcomes and in-hospital mortality, but they were insufficiently sized. To analyze sensitivity, we constructed three models to assess the association between AF and patient-specific characteristics and hospital and clinical factors as well as six models to elucidate the associations between in-hospital mortality, LOS, and hospitalization cost and AF. However, our study also has several limitations. We used the ICD-9-CM procedure code to capture the critically ill status. However, the continuous mechanical ventilation does not equal critically ill. There are critically ill patients who are not mechanically ventilated and mechanically ventilated patients who are not critically ill. It's specific but not sensitive to representative critically ill [12,47]. In addition, we couldn't evaluate the frequency of new-onset AF, history of recurrent AF or permanent AF in this setting of patients. Compared to true clinical data, the NIS contains administrative data that may be subject to coding errors [48]. Meanwhile, we are not sure that the temporal trend observed in AF prevalence is not related to coding habits. Because mechanical ventilation is a predictive risk factor for AF and the need for mechanical ventilation are significantly greater in patients with AF [49], so the AF prevalence

in our study may be higher than estimated. In addition, NIS cannot track personal records or information, including post-discharge survival status. These analyses were based on inpatient participants, so the conclusions can be generalized to inpatient settings. Long-term or post-discharge mortality is beyond the scope of our study, and future studies need to take these aspects into further consideration.

In conclusion, we found that the proportion of critically ill patients with comorbid AF steadily increased from 2008 to 2014 in a large national sample. AF was associated with higher in-hospital mortality, longer LOS, and higher hospitalization costs. More knowledge about the incidence and risk predictors of AF can benefit critical patients; thus, high-level evidence is needed to guide the management of AF in critically ill patients.

### KEY MESSAGE

1. The newest assessment of temporal trends of atrial fibrillation (AF) in critically ill patients in the United States.
2. Prevalence of comorbid AF is increasing, particularly in older patients.
3. AF in critical illness was a risk factor for in-hospital death.

### Conflict of interest

No potential conflict of interest relevant to this article was reported.

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**Supplementary Table 1. ICD-9-CM codes used for identifying the types of organ failure**

Types of organ failure	ICD-9 codes
Respiratory	518.81, 518.82, 518.85, 786.09, 799.1, 96.7
Cardiovascular	458.0, 785.5, 785.51, 785.59, 458.0, 458.8, 458.9, 796.3
Renal	584, 580, 585, 39.95
Hepatic	570, 572.2, 573.3
Hematologic	286.2, 286.6, 286.9, 287.3-5
Metabolic	276.2
Neurologic	293, 348.1, 348.3, 780.01, 780.09, 89.14

ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification.

**Supplementary Table 2. ICD-9-CM codes used for acute medical conditions associated with critically ill status**

Disease	ICD-9 codes
Pneumonia	480-487, 507.0
COPD exacerbation	491.1, 491.2
Asthma exacerbation	493.X1, 493.X2
Cardiac arrest/Ventricular fibrillation or flutter	427.41, 427.43, 427.5
Acute coronary syndrome	410.X0, 410.X1
Acute congestive heart failure	276.6, 428.21, 482.23, 428.31, 428.33, 428.41, 428.43
Stroke, intracranial hemorrhage, subarachnoid hemorrhage	433.X1, 432.9, 430
Severe sepsis	038, 020.0, 790.7, 117.9, 112.5, 112.81

ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; COPD, chronic obstructive pulmonary disease.

**Supplementary Table 3. The temporal trends of atrial fibrillation in subgroups categorized by age, gender, race, and insurance**

Variable	Total	2008	2009	2010	2011	2012	2013	2014	p for trend
<b>Age, yr</b>									
18–44	3.63	2.40	3.70	3.41	4.08	3.42	4.13	4.31	< 0.0001
45–54	13.71	8.42	12.68	13.14	15.05	15.13	14.99	16.63	< 0.0001
65–74	26.57	17.45	24.97	25.45	28.45	29.39	29.32	31.28	< 0.0001
≥ 75	36.71	25.71	34.40	35.38	40.07	41.18	41.24	42.34	< 0.0001
<b>Gender</b>									
Male	21.69	14.42	20.28	20.48	23.84	24.19	24.08	25.14	< 0.0001
Female	20.77	14.88	19.65	20.14	22.74	22.49	22.58	23.54	< 0.0001
<b>Race</b>									
White	24.51	17.18	23.56	23.51	26.64	26.38	26.38	27.59	< 0.0001
Black	14.70	9.09	13.42	13.33	16.57	16.24	16.07	17.01	< 0.0001
Hispanic	16.10	10.26	15.53	14.81	16.69	17.93	18.56	18.31	< 0.0001
Other	20.90	15.69	19.04	20.41	21.94	22.93	22.42	24.11	< 0.0001
Missing	17.29	12.30	15.61	19.04	21.47	21.59	22.06	22.74	< 0.0001
<b>Insurance</b>									
Medicare	27.65	19.12	26.19	26.55	29.81	30.48	30.41	31.72	< 0.0001
Medicaid	10.59	6.52	9.46	10.60	11.76	11.13	11.62	12.65	< 0.0001
Private	15.56	10.42	14.87	15.00	17.66	17.21	16.98	18.06	< 0.0001
Self-pay	9.88	6.89	9.58	9.30	10.45	10.65	10.55	11.82	< 0.0001
Other	12.82	9.52	11.23	12.80	13.97	14.21	13.40	15.19	< 0.0001

Values are presented as percentage.



**Supplementary Table 4. The temporal trends of atrial fibrillation in subgroups categorized by organ failure type**

Variable	Total	2008	2009	2010	2011	2012	2013	2014	<i>p</i> for trend
Type of organ failure, %									
Cardiovascular	18.25	13.01	17.15	16.81	18.37	19.86	19.61	21.07	< 0.0001
Renal	58.72	45.80	55.80	57.46	59.77	60.22	61.75	65.51	< 0.0001
Hepatic	6.88	3.85	6.29	6.08	6.85	7.60	7.48	8.89	< 0.0001
Metabolic	22.65	14.85	19.39	19.77	21.93	24.40	26.81	28.47	< 0.0001
Neurologic	31.35	21.22	27.37	30.04	31.76	32.82	35.15	37.31	< 0.0001
Hematologic	19.76	10.99	17.79	20.09	20.96	21.62	21.71	22.04	< 0.0001

**Supplementary Table 5. The temporal trends of atrial fibrillation in subgroups categorized by different phenotypes of critically ill**

Variable	Total	2008	2009	2010	2011	2012	2013	2014	p for trend
Phenotypes of critically ill, %									
Pneumonia	64.13	61.58	63.98	64.84	65.61	64.17	63.88	63.90	< 0.0001
Severe sepsis	48.83	38.76	47.48	48.41	49.36	50.15	50.91	53.14	< 0.0001
COPD exacerbation	13.30	14.18	13.84	12.50	12.66	13.28	13.64	13.36	0.0485
Asthma exacerbation	1.72	1.59	1.88	1.52	1.53	1.54	2.09	1.83	< 0.0001
Congestive heart failure exacerbation	18.91	7.98	13.04	15.73	19.62	21.59	23.71	26.42	< 0.0001
Acute stroke	3.95	3.77	3.44	3.90	3.69	4.25	4.14	4.37	< 0.0001
Acute coronary syndrome	12.78	12.57	12.85	12.74	12.79	13.01	12.47	12.94	0.4344
Cardiac arrest.	2.90	2.36	2.57	2.70	2.86	3.01	3.20	3.41	< 0.0001

COPD, chronic obstructive pulmonary disease.

**Supplementary Table 6. Trends in in-hospital mortality in critical illness patients**

Variable	Total	2008	2009	2010	2011	2012	2013	2014	<i>p</i> for trend
Patients with atrial fibrillation, %	33.38	35.83	34.42	33.28	31.71	33.60	32.68	33.18	< 0.0001
Patients without atrial fibrillation, %	27.45	30.06	28.40	26.73	26.44	26.66	26.50	26.88	< 0.0001

**Supplementary Table 7. Trends in length of stay in critical illness patients.**

Variable	Total	2008	2009	2010	2011	2012	2013	2014	p for trend
Patients with atrial fibrillation, %	16.33	15.33	16.81	17.00	16.49	15.69	15.69	15.88	0.6211
Patients without atrial fibrillation, %	16.14	17.32	16.85	16.85	16.12	15.66	15.64	15.71	0.0015

**Supplemental Table 8. Trends in discharge status (home and LTACH/SNF) for critically ill patients with AF**

Variable	Total	2008	2009	2010	2011	2012	2013	2014	p for trend
Home, %	13.34	14.91	13.65	13.89	12.86	12.77	12.97	12.94	< 0.0001
LTACH/SNF, %	53.27	49.27	51.93	52.83	55.43	53.63	54.35	53.87	< 0.0001

LTACH/SNF, long-term acute care hospital or skilled nursing facility.

**Supplementary Table 9. Association of comorbid atrial fibrillation with patient and hospital characteristics in critical illness**

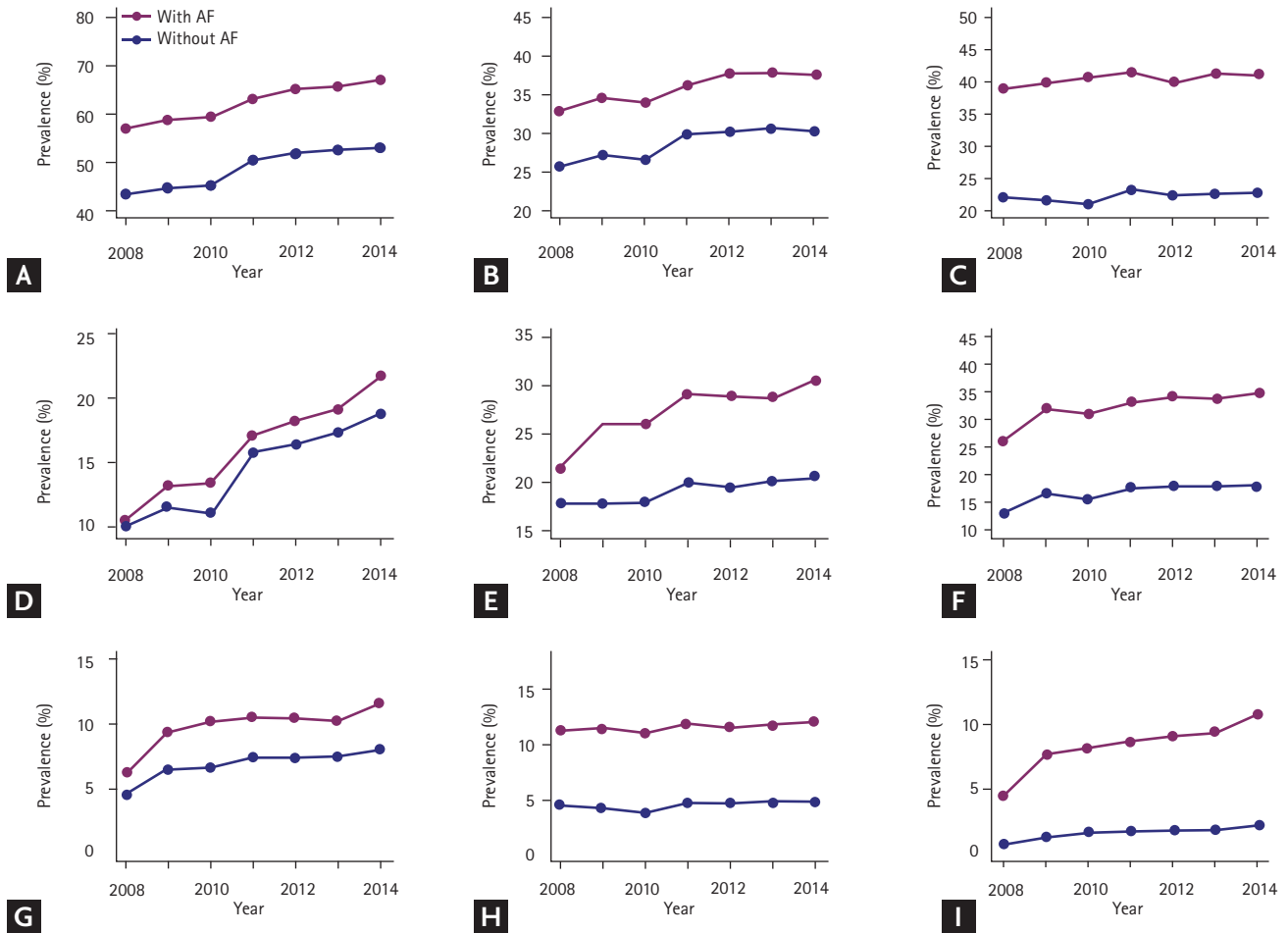
Variable	Unadjusted model 1	
	OR (95% CI)	p value
Year, per unit increase	1.08 (1.08–1.09)	< 0.0001
Age, yr		
Per unit increase	1.05 (1.05–1.05)	< 0.0001
45–64 vs. 18–44	3.22(3.08–3.37)	< 0.0001
65–74 vs. 18–44	6.11(5.81–6.41)	< 0.0001
≥ 75 vs. 18–44	9.63(9.15–10.14)	< 0.0001
Race		
Black vs. white	0.60 (0.59–0.62)	< 0.0001
Hispanic vs. white	0.67 (0.65–0.69)	< 0.0001
Others vs. white	0.81 (0.78–0.84)	< 0.0001
Missing vs. white	0.82 (0.77–0.87)	< 0.0001
Insurance		
Medicaid vs. Medicare	0.95 (0.92–0.98)	0.0016
Private vs. Medicare	1.03 (1.01–1.05)	0.0100
Self-pay vs. Medicare	0.95 (0.90–1.00)	0.0579
Others vs. Medicare	0.92 (0.88–0.97)	0.0011
Female sex	0.80 (0.79–0.82)	< 0.0001
Income quartile		
Q2 vs. Q1	1.02 (1.00–1.04)	0.1097
Q3 vs. Q1	1.07 (1.04–1.09)	< 0.0001
Q4 vs. Q1	1.13 (1.10–1.16)	< 0.0001
Hospital bed size		
Medium vs. small	1.03 (0.98–1.08)	0.1982
Large vs. small	1.10 (1.06–1.15)	< 0.0001
Hospital type		
Urban nonteaching vs. rural	1.04 (0.98–1.10)	0.2425
Urban teaching vs. rural	1.10 (1.04–1.17)	0.0013
Hospital region		
Midwest vs. northeast	1.18 (1.12–1.24)	< 0.0001
South vs. northeast	1.05 (1.00–1.10)	0.0314
West vs. northeast	1.13 (1.07–1.18)	< 0.0001
Elective	1.16 (1.12–1.20)	< 0.0001
Major operating room procedure	1.06 (1.04–1.09)	< 0.0001
Long-term anticoagulants	4.57 (4.38–4.77)	< 0.0001
Prior stroke	1.11 (1.08–1.15)	< 0.0001
Coronary artery disease	1.38 (1.36–1.41)	< 0.0001
AIDS	0.68 (0.56–0.82)	0.0001
Alcohol abuse	0.96 (0.94–0.99)	0.0192
Deficiency anemias	1.08 (1.06–1.11)	< 0.0001
Rheumatoid arthritis	1.07 (1.02–1.12)	0.0036

**Supplementary Table 9. Continued**

Variable	Unadjusted model 1	
	OR (95% CI)	p value
Chronic blood loss anemia	1.09 (1.03–1.15)	0.0047
Congestive heart failure	1.55 (1.52–1.57)	< 0.0001
Chronic pulmonary disease	1.17 (1.15–1.19)	< 0.0001
Coagulopathy	1.24 (1.21–1.27)	< 0.0001
Depression	0.93 (0.90–0.95)	< 0.0001
Diabetes, uncomplicated	1.08 (1.05–1.10)	< 0.0001
Diabetes with chronic complications	0.94 (0.91–0.97)	0.0003
Drug abuse	0.83 (0.78–0.87)	< 0.0001
Hypertension	1.19 (1.17–1.21)	< 0.0001
Hypothyroidism	1.14 (1.11–1.17)	< 0.0001
Liver disease	0.91 (0.88–0.95)	< 0.0001
Lymphoma	0.99 (0.93–1.05)	0.7154
Fluid and electrolyte disorders	1.04 (1.02–1.06)	0.0002
Metastatic cancer	0.96 (0.92–1.00)	0.0512
Other neurological disorders	0.88 (0.86–0.90)	< 0.0001
Obesity	1.25 (1.22–1.27)	< 0.0001
Paralysis	0.94 (0.92–0.97)	0.0001
Peripheral vascular disorders	1.04 (1.02–1.07)	0.0012
Psychoses	0.82 (0.79–0.85)	< 0.0001
Pulmonary circulation disorders	1.26 (1.23–1.30)	< 0.0001
Renal failure	1.01 (0.99–1.04)	0.1780
Solid tumor without metastasis	0.99 (0.95–1.04)	0.7647
Peptic ulcer disease	0.97 (0.72–1.32)	0.8534
Valvular disease	1.61 (1.56–1.66)	< 0.0001
Weight loss	0.97 (0.95–0.99)	0.0007
Renal replacement therapy	1.16 (1.13–1.19)	< 0.0001

Multivariate model: obtained from logistic regression model accounting for survey design and adjusting for year, age, race, insurance, sex, income, hospital region, hospital location/teaching status, hospital bed size, elective, Elixhauser comorbidity index, major operating room procedure, long-term anticoagulant, prior stroke, coronary artery disease, acquired immunodeficiency syndrome, alcohol abuse, deficiency anemias, rheumatoid arthritis, chronic blood loss anemia, congestive heart failure, chronic pulmonary disease, coagulopathy, depression, diabetes, uncomplicated, diabetes with chronic complications, drug abuse, hypertension, hypothyroidism, liver disease, lymphoma, fluid and electrolyte disorders, metastatic cancer, other neurological disorders, obesity, paralysis, peripheral vascular disorders, psychoses, pulmonary circulation disorders, renal failure, solid tumor without metastasis, peptic ulcer disease, valvular disease, weight loss, renal replacement therapy.

OR, odds ratio; CI, confidence interval.



**Supplementary Figure 1.** Temporal trends in risk factor profiles among critically ill patients with versus without atrial fibrillation: (A) hypertension, (B) diabetes, (C) congestive heart failure, (D) obesity, (E) chronic renal failure, (F) coronary artery disease, (G) prior stroke, (H) valvular disease, and (I) long-term anticoagulants.