

INTRODUCTION

- Nearly 80% of patients with kidney failure initiate hemodialysis (HD) with a central venous catheter (CVC-HD).¹
- However, CVCs have an inherent risk of catheter-related bloodstream infections (CRBSIs).
- CRBSI, defined as bacteremia caused by an intravenous catheter, is one of the most prevalent, fatal, and expensive complications of CVC-HD.²
- The Incidence of CRBSI with CVC-HD is reported to be 2.5-5.5 cases per 1,000 catheter days, or 0.9-2 episodes per patient-year.^{3,4}
- However, there are no conclusive estimates of the incidence and associated mortality of CRBSI, particularly in the long-term, among CVC-HD patients in the U.S.

OBJECTIVE

- To investigate the incidence and associated mortality of CRBSI among kidney failure patients with CVC-HD in the U.S. using real-world data.

METHODS

Study Design and Data Source: Retrospective, propensity score-matched case-control analysis using United States Renal Data System (USRDS), CROWNWeb (Consolidated Renal Operations in a Web-enabled Network), and Medicare claims spanning the period from 2013-2017

Study Population: The study population was identified in three steps (Figure 1):

- Step 1:** All Medicare ESKD patients were identified from 2014-2016 and patients initiating CVC-HD were selected.
- Step 2:** Post CVC-insertion date, occurrence/ no-occurrence of CRBSI (i.e., CRBSI /non-CRBSI) were identified on index date or assigned index date, respectively:
 - Index Date, CRBSI group:** First ICD-9/10-CM diagnostic claims of 999.32, T80211x; 999.31, or T80219x, T80218x and sepsis/bacteremia diagnosis within ±3 days of hospitalization, or sepsis/bacteremia diagnosis without occurrence for pneumonia, gangrene, or urinary tract infections within ±3 days of hospitalization.
 - Assigned Index Date, Non-CRBSI group:** Date of CVC insertion + reported median days to CRBSI in the CRBSI group.
- Step 3:** Case (CRBSI) and control (non-CRBSI) groups were 1:1 propensity score matched at CRBSI index/assigned index date on age, gender, race, comorbidities, Elixhauser Comorbidity Index, dialysis setting, and diabetes medications and were followed for 1 year from CRBSI index date/assigned index date, or until database cut-off or death.

Exclusion Criteria: Patients with ICD-9/10 codes for pneumonia, gangrene, or urinary tract infection (UTI) >3 days from sepsis/bacteremia; Patients with ≥1 CVC or HD claim or <6 months of continuous enrollment in the pre-index period.

- Study Outcomes:**
- Incidence of CRBSI following CVC insertion date until CRBSI, death, or end of database.
 - Mortality within one year of CRBSI index/assigned-index date in matched patients.

Statistical Analysis:

- Descriptive statistics were reported as frequency [n] and percentages [%] or mean or median for categorical variables for continuous variables, respectively (Table 1).
- Comparisons of baseline characteristics were carried out using Cramer's V and Wilcoxon tests.
- Associations between baseline characteristics and risk of CRBSI and mortality were assessed using Cox proportional hazards models.
- Statistical analyses were performed using R and analyzed using Rapid Analyzer™.

RESULTS

Figure 1. Patient Selection

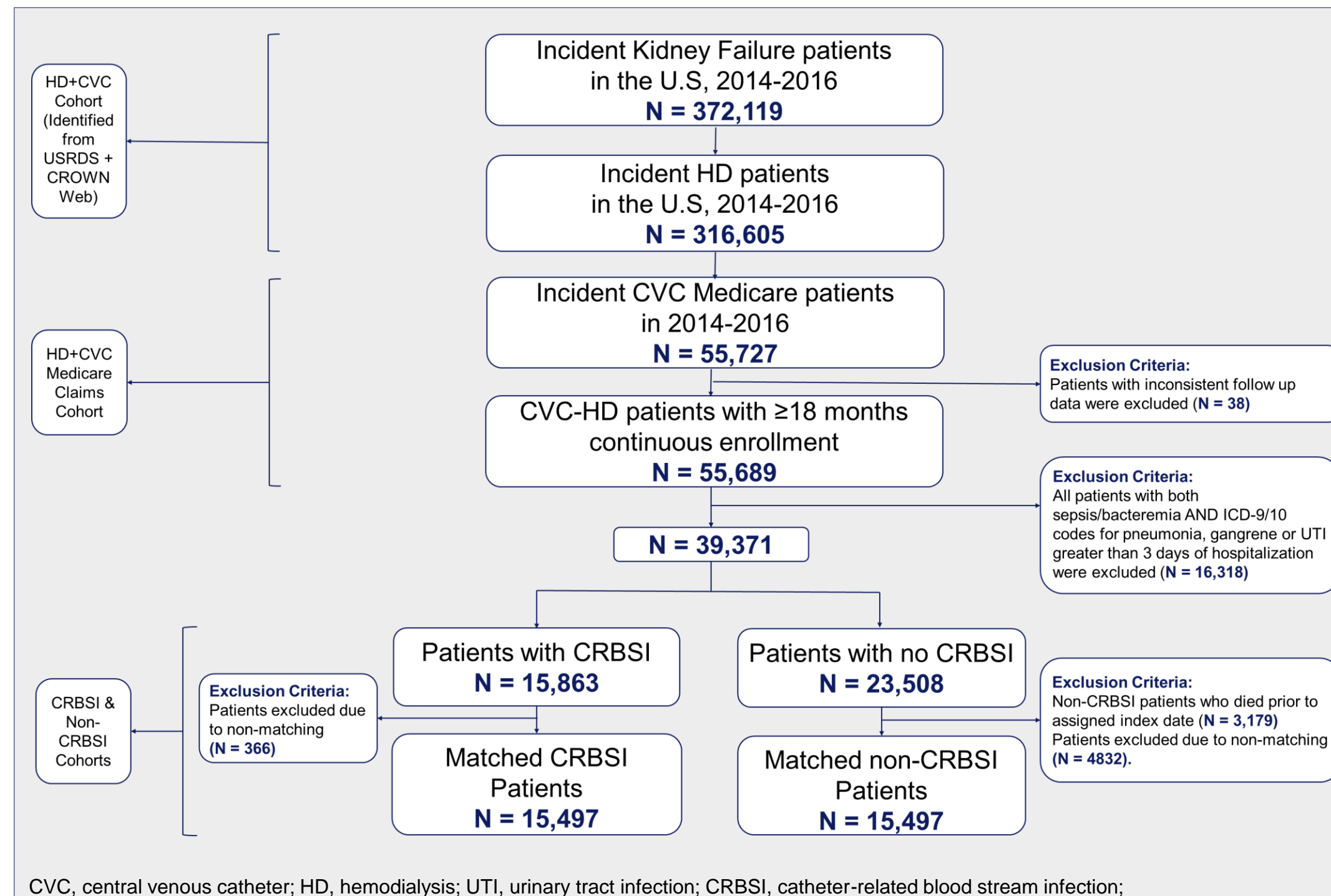


Table 1. Patient Demographics

Characteristics	CRBSI (n = 15,497)	Non-CRBSI (n = 15,497)	SMD	Cramer's V
Age	66.73	67.14	0.038	0.019
Gender (Female)	7,169 (46.3)	7,126 (46.0)	0.006	0.003
Race			0.035	0.017
African American	4,447 (28.7)	4,213 (27.2)		
Other / Unknown	677 (4.4)	664 (4.3)		
White	10,373 (66.9)	10,620 (68.5)		
Body Mass Index			0.030	0.015
Underweight	503 (3.3)	324 (2.8)		
Normal	4,247 (27.6)	3,179 (27.4)		
Overweight	3,973 (25.8)	2,982 (25.7)		
Obese	6,674 (43.3)	5,123 (44.1)		
Elixhauser Comorbidity Index			0.071	0.036
< 0	11,578 (74.7)	12,021 (77.6)		
0	26 (0.2)	27 (0.2)		
1 - 5	1,072 (6.9)	947 (6.1)		
6 - 13	2,421 (15.6)	2,194 (14.2)		
> 14	400 (2.6)	308 (2.0)		
Comorbidities				
AIDS / HIV	181 (1.2)	125 (0.8)	0.037	0.018
CHF	8,469 (54.6)	8,204 (52.9)	0.034	0.017
COPD	1,981 (12.8)	1,832 (11.8)	0.029	0.015
CVA / TIA	1,683 (10.9)	1,575 (10.2)	0.023	0.011
Diabetes	8,926 (57.6)	8,865 (57.2)	0.008	0.004
GFR MDRD	12,805 (82.6)	13,121 (84.7)	0.055	0.028
Hypertension	5,063 (32.7)	4,982 (32.1)	0.011	0.006
Metastatic Cancer	290 (1.9)	242 (1.6)	0.024	0.012
Polycystic Disease	37 (0.2)	33 (0.2)	0.005	0.003
Diabetes On Insulin	6,935 (44.8)	6,816 (44.0)	0.015	0.008
Diabetes On Oral Medications	1,725 (11.1)	1,751 (11.3)	0.005	0.003
Other Causes of ESKD	7,353 (47.4)	6,942 (44.8)	0.053	0.027
AVF Maturing			0.014	0.007
Yes	2,675 (17.3)	2,752 (17.8)		
No	12,033 (77.6)	11,944 (77.1)		
NA	789 (5.1)	801 (5.2)		
AVG Maturing			0.011	0.005
Yes	410 (2.6)	384 (2.5)		
No	14,049 (90.7)	14,064 (90.8)		
NA	1,038 (6.7)	1,049 (6.8)		

ESKD, end-stage kidney disease; BMI, body mass index; CHF, congestive heart failure; CVA/TIA, cerebrovascular accident/transient ischemic attack; GFR MDRD, glomerular filtration rate at Stage 5 (i.e., ESKD) using modification of diet in renal disease equation; AIDS/HIV, acquired immunodeficiency syndrome / human immunodeficiency virus; HD, hemodialysis; COPD, chronic obstructive pulmonary disorder; AVF, arteriovenous fistula; AVG, arteriovenous graft, NA, not available.

RESULTS (Cont.)

Figure 2: Kaplan Meier Survival Estimates, Time to CRBSI

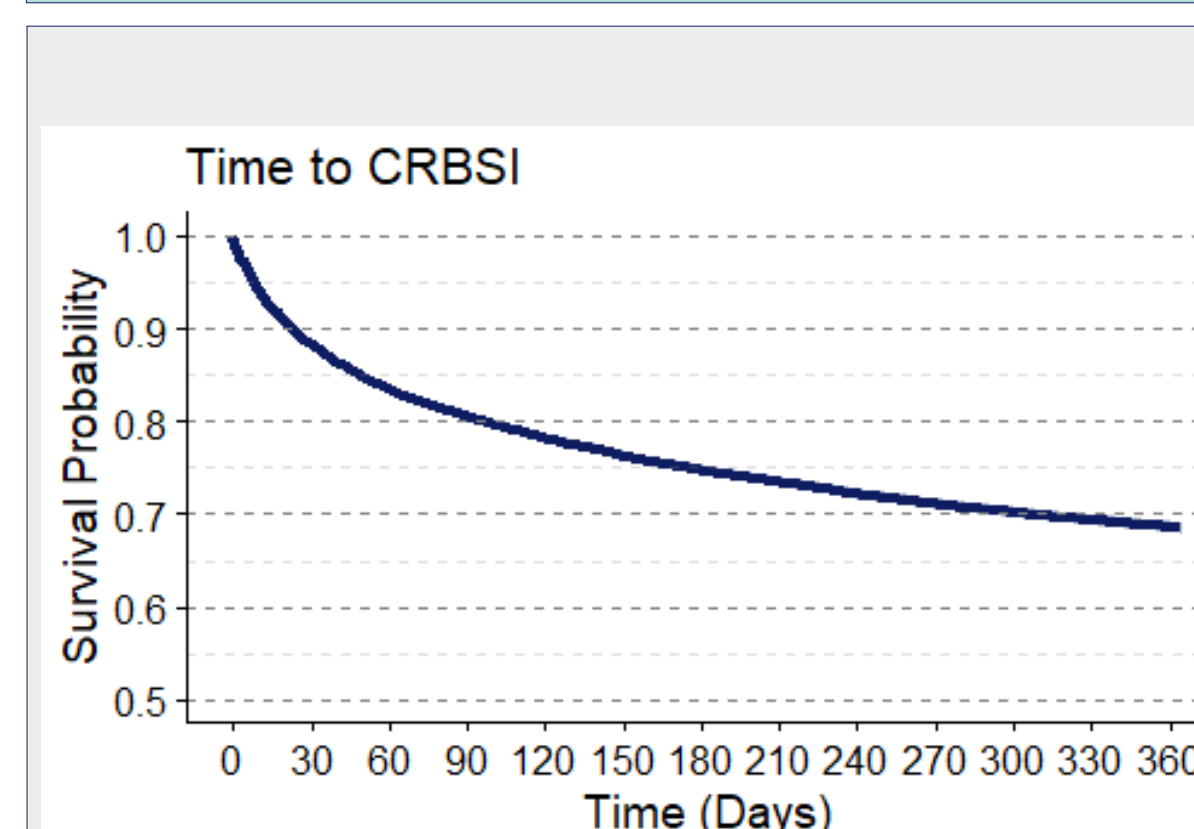
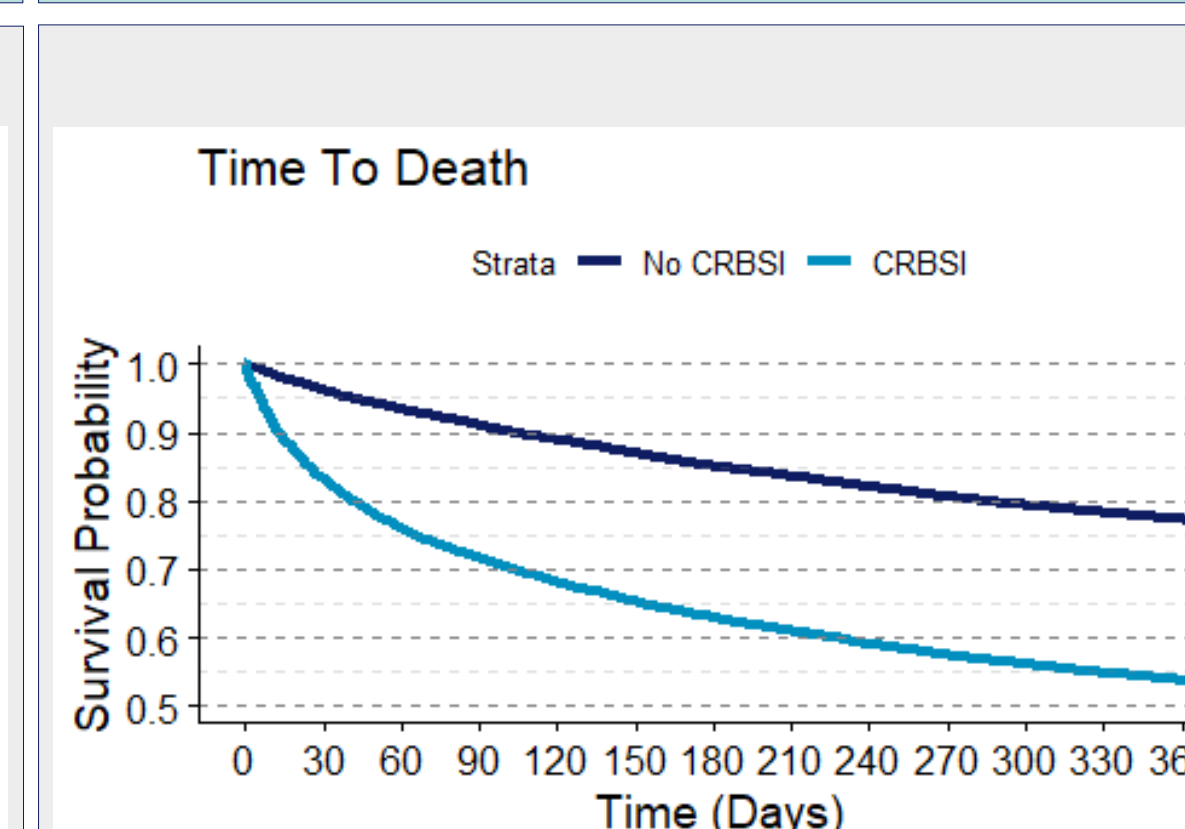


Figure 3: Kaplan Meier Survival Estimates: Time to Death from CRBSI Index/Assigned Index Date



CRBSI Incidence

- Of the 55,727 CVC-HD patients, 28.4% (n=15,863) developed CRBSI (median time, 69 days) (Figure 2).
- CRBSI developed in 54% (n=8,618), 67% (n=10,598), and 80% (n=12,736) of cases within 90, 180, and 365 days of CVC insertion, respectively, in unmatched patients.
- In the unmatched groups, CRBSI patients had shorter median survival (25.1 vs. 37.3 months) than non-CRBSI patients, with three times higher relative risk of mortality [HR: 2.68, 95% CI: 2.57, 2.80] at data cut-off beyond 1-year.

CRBSI Mortality

- After matching, mortality was 28.4% (n = 4,400), 37.1% (n = 5,754), and 46.5% (n = 7,199) in CRBSI patients and 8.9% (n=1,387), 14.9% (n=2,315), and 22.9% (n=3,552) in non-CRBSI patients at 90 days, 180 days, and 365 days from CRBSI incidence date/assigned index date, respectively (Figure 3).
- Of all deaths occurring within 1 year following CRBSI, 16.9% of patients died within 30 days of the initial event compared to 3.8% of non-CRBSI patients (Figure 4).
- As per the Cox proportional hazard model, CHF, CVA, TIA, metastatic cancer, GFR MDRD, COPD, and other causes of ESKD were significantly associated with increased risk of mortality due to CRBSI. Hypertension was significantly associated with decreased risk of mortality due to CRBSI (Table 2).

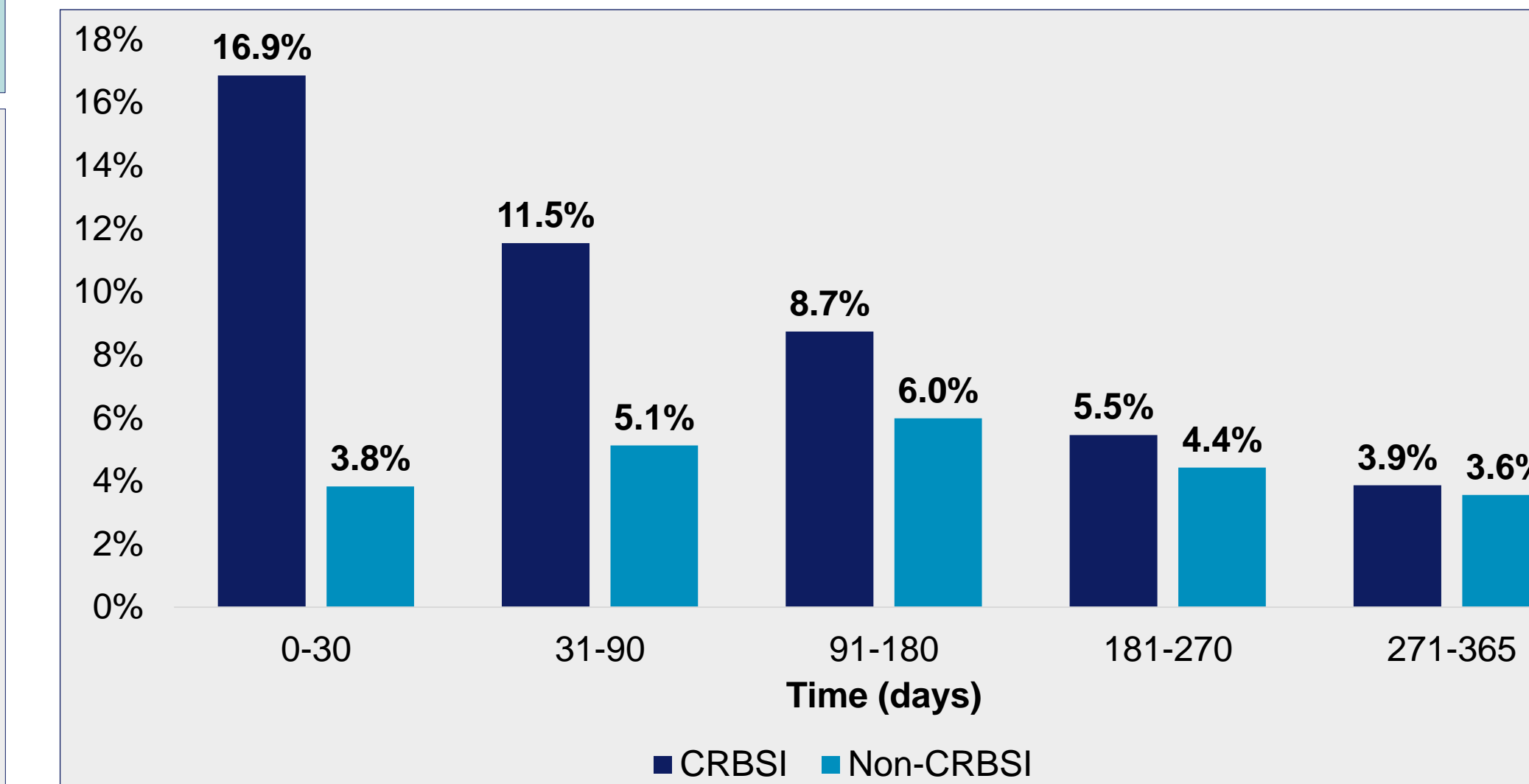
Table 2: Cox Proportional Hazards Model: Time to Death

	HR	95% CI	p-value
CRBSI	2.62	2.5, 2.74	< 0.01
Age	1.03	1.03, 1.03	< 0.01
Female	0.92	0.89, 0.96	< 0.01
Race			
White	1.23	1.18, 1.3	< 0.01
Other / Unknown	0.89	0.8, 1	0.057
BMI	0.99	0.99, 0.99	< 0.01
Elixhauser Comorbidity Index			
0	2.30	1.56, 3.38	< 0.01
1 - 5	1.31	1.22, 1.41	< 0.01
6 - 13	1.18	1.12, 1.25	< 0.01
>14	1.64	1.47, 1.82	< 0.01
CHF	1.30	1.24, 1.36	< 0.01
COPD	1.26	1.2, 1.34	< 0.01
CVA / TIA	1.09	1.03, 1.16	< 0.01
GFR MDRD	1.03	1.03, 1.04	< 0.01
Hypertension	0.89	0.85, 0.92	< 0.01
Metastatic Cancer	2.37	2.11, 2.66	< 0.01
Other Causes of ESKD	1.20	1.15, 1.25	< 0.01
Polycystic disease	0.66	0.38, 1.17	0.154

CI, confidence interval; COPD, chronic obstructive pulmonary disease; CRBSI, catheter-related bloodstream infection; CVA/TIA, cerebrovascular accident/transient ischemic attack; ESKD, end-stage kidney disease; GFR MDRD, glomerular filtration rate at Stage 5 (i.e., ESKD) using modification of diet in renal disease equation; HR, hazard ratio.

RESULTS (Cont.)

Figure 4: Mortality after CRBSI Index/Assigned Index Date (Post-matched)



LIMITATIONS

- The identification algorithm for CRBSI, which uses proxy determinates of disease, has the potential to misclassify the cause of bacteremia in patients.
- Due to the methodology, we were unable to determine whether patients had CVC still inserted at the time of the CRBSI occurrence; however, the majority of CRBSI events occurred within 6 months following CVC insertion.

CONCLUSIONS

- This is the first study of its kind to investigate the incidence and associated mortality of CRBSI among kidney failure patients with CVC-HD in the U.S.
- Almost 30% of CVC-HD patients developed CRBSI, with over 50% of infections developing within 90 days of CVC initiation.
- Nearly 30% of patients died within the first 90 days of CRBSI event.
- Patients with CRBSI had 23.6% higher 1-year mortality rates compared to patients without CRBSI (46.5% vs. 22.9%) with incremental mortality continuing to increase in CRBSI patients even after 30 days from the initial infection.
- CRBSI continues to be a common, burdensome, and highly fatal complication in the near and long-term among CVC-HD patients; hence, preventative measures are crucial in reducing the associated morbidity and mortality.

REFERENCES

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