Risk Factors for Infection-Related Hospitalization in In-Center Hemodialysis

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Abstract

Background and objectives Infection-related hospitalizations have increased dramatically over the last 10 years in patients receiving in-center hemodialysis. Patient and dialysis facility characteristics associated with the rate of infection-related hospitalization were examined, with consideration of the region of care, rural-urban residence, and socioeconomic status.

Design, setting, participants, & measurements The US Renal Data System linked to the American Community Survey and Rural-Urban Commuting Area codes was used to examine factors associated with hospitalization for infection among Medicare beneficiaries starting in-center hemodialysis between 2005 and 2008. A Poisson mixed effects model was used to examine the associations among patient and dialysis facility characteristics and the rate of infection-related hospitalization.

Results Among 135,545 Medicare beneficiaries, 38,475 (28%) had at least one infection-related hospitalization. The overall rate of infection-related hospitalization was 40.2 per 100 person-years. Age ≥85 years old, cancer, chronic obstructive pulmonary disease, inability to ambulate or transfer, drug dependence, residence in a care facility, serum albumin <3.5 g/dl at dialysis initiation, and dialysis initiation with an access other than a fistula were associated with a ≥20% increase in the rate of infection-related hospitalization. Patients residing in isolated small rural compared with urban areas had lower rates of hospitalization for infection (rate ratio, 0.91; 95% confidence interval, 0.86 to 0.97), and rates of hospitalization for infection varied across the ESRD networks. Measures of socioeconomic status (at the zip code level), total facility staffing, and the composition of staff (percentage of nurses) were not associated with the rate of hospitalization for infection.

Conclusions Patient and facility factors associated with higher rates of infection-related hospitalization were identified. The findings from this study can be used to identify patients at higher risk for infection and inform the design of infection prevention strategies.

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Introduction

As of 2012, >400,000 adults were receiving hemodialysis for ESRD in the United States (1). Infection is a well recognized complication (2,3) and the second leading cause of hospitalization and death in adults receiving hemodialysis. Hospitalizations primarily for infection have increased 34% between 1993 and 2012 (1) and are associated with high rates of 30-day readmission and death (4). In recognition of these important clinical consequences, policy changes to the ESRD Quality Incentive Program (5) designed to lower infection rates were implemented, including reporting to the Centers for Disease Control and Prevention's (CDC's) National Healthcare Safety Network (NHSN) starting in payment year 2014 and the addition of NHSN bloodstream infections as a clinical measure starting in payment year 2016 (6). To develop the most effective and efficient infection prevention strategies, it is important to better understand patient– and facility–level risk factors for infection-related hospitalization. The primary objective of our study was to identify patient characteristics and dialysis facility characteristics associated with the risk of infection-related hospitalization among Medicare beneficiaries starting in-center hemodialysis, with consideration of the region of care, rural-urban residence, and socioeconomic status (SES) indicators. We examined both modifiable and nonmodifiable characteristics, because modifiable characteristics (*e.g.*, vascular access type and staffing) could be actionable, and nonmodifiable factors may be useful for risk stratification.

Materials and Methods

Study Cohort and Data Collection

We used the US Renal Data System (USRDS) linked to the US Census Data from the American Community Survey (ACS) and Rural-Urban Commuting Area (RUCA) codes to retrospectively assemble a cohort of adults starting dialysis between January of 2005

and June of 2008. We limited the cohort to adults 18–100 years of age who survived the first 90 days of dialysis, had Medicare Parts A and B (and one or more institutional claims, which include dialysis-related claims, in the 180 days after study start), had an initial Medical Evidence Form (Centers for Medicare & Medicaid Services Form 2728) version 2005, and were receiving dialysis in a free–standing dialysis facility with known profit status on day 91 of dialysis. We have previously characterized this cohort in detail (7); for this study, we limited our examination to patients on in-center hemodialysis and further excluded patients with missing data on SES indicators (n=1941) or RUCA codes (n=454), who were receiving care in dialysis centers with missing dialysis facility volume (n=519), implausible facility data (*i.e.*, reported data inconsistent with subsequent years of data) (n=9), or zero or missing nursing staff data reported the year of study entry (n=2105); or who were hospitalized throughout the entire duration of his/her follow-up (n=92) (Supplemental Figure 1).

We incorporated SES data collected from the 2007–2011 ACS 5-year estimates for the zip code–tabulated area (ZCTA) (8). We linked the ZCTA-level data to patient–level zip codes at the start of dialysis using the Dartmouth Atlas 2009 zip code to ZCTA cross–walk file (9). To assign residence to a rural or urban area, we used the zip code approximation of the RUCA codes using the zip code–level RUCA version 2.0 files available through the Washington, Wyoming, Alaska, Montana, Idaho Rural Health Research Center at the University of Washington (10).

We collected the following patient characteristics from the Medical Evidence Form: demographics, coexisting illnesses, inability to ambulate or transfer, residence in a care facility, tobacco use, alcohol dependence, drug dependence, serum albumin concentration, height and weight (used to calculate Quételet [body mass] index [BMI]), eGFR calculated from the abbreviated Modification of Diet in Renal Disease equation (11), vascular access type used at the first outpatient dialysis session, and nephrology care before dialysis initiation (classified as unknown, none, or $<$6, 6–12, or $>$12 months). We ascertained the ESRD network, and we classified patient rural-urban location as follows: urban, large rural town (micropolitan), small rural town, and isolated small rural town (12). We determined zip code–level SES indicators: percentage of persons under poverty in the last 12 months and percentage of adults ages 25 years old or older with a high school degree or higher education. We collected facility-level data: profit status (for profit or nonprofit), volume (defined as the number of patients receiving hemodialysis at the end of the annual survey period), presence and size of a home dialysis program, and staffing. The presence and size of a home dialysis program were ascertained to account for differences in staffing between clinics with and without home programs, because dialysis facilities do not report staff separately for home and in-center dialysis. For staffing, we focused on registered nurses, licensed practical/visiting nurses, and patient care technicians. To determine the total staffing level, we used a previously outlined approach (13) to calculate the number of full–time equivalent positions, considering each reported part-time employee as a 0.5 full-time employee. To derive a composite index of the number of nurses, we added the number of licensed practical/visiting nurses and registered nurses. For facility-level metrics, we assigned each patient the facility reported data on the basis of day 91 of dialysis.

Infection-Related Hospitalization

We examined the rate of hospitalizations for infection during follow-up. We excluded hospitalizations for which the date of admission was the same as the date of discharge, and we combined overlapping hospitalizations, selecting discharge diagnoses from the first or longest hospital record (7% of all hospital records were combined). We classified a hospitalization as infection related if the principal discharge diagnosis included International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) codes of interest (Supplemental Table 1) (14,15). Types of infection examined included dialysis access or central venous catheter (CVC) related; bloodstream infection or sepsis; pulmonary; gastrointestinal, peritoneal, or hepatobiliary; genitourinary; device, procedure, or surgery related (excluding dialysis access); skin and soft tissue; bone and joint; central nervous system; and cardiac.

We followed our cohort for all infection–related hospitalization(s) starting on day 91 of dialysis until the time of death (n=34,778), transplant (n=2338), recovery of kidney function (n=1913), change in dialysis modality (n=5200), change in facility (n=59,537), change in facility profit status (n=522), or study end on December 31, 2009 (n=31,257).

Statistical Analyses

To examine the associations among patient– and facility–level factors and the rate of infection-related hospitalization, we used a Poisson mixed effects model with facility identification as a random intercept using SAS procedure PROC GLIMMIX with Laplace as the approximation method. The total follow-up time for each person (days at risk) excluded periods of hospitalization. In the primary multivariable model, we included patient characteristics (age, sex, race, ethnicity, BMI, coexisting illnesses, vascular access type, nephrology care before dialysis initiation, residence in a care facility, tobacco use, alcohol and/or drug dependence, eGFR, serum albumin, ESRD network, zip code–level SES indicators, and RUCA codes) and facility characteristics (volume, number and composition of staff, and presence and size of a home dialysis program). Volume was classified into quartiles, because we did not have *a priori* cutpoints. The presence and size of a home dialysis program were classified as none/0, 1–10, 11–25, or $\geq$26 patients. Two variables were included to account for staffing: (*1*) total staffing (total number of nurses + patient care technicians) and (*2*) proportion of staff composed of nurses (nurses/[nurses + patient care technicians]). We examined the rate of all infection hospitalizations, and then, we applied the same Poisson mixed effects model to examine the rates of four specific types of infection-related hospitalization: (*1*) bloodstream infections or sepsis, (*2*) dialysis access, (*3*) pulmonary, or (*4*) other types of infection. We express rate ratios (risk) derived from the Poisson model comparing rates across patient and facility characteristics. We used multiple imputation to create 10 datasets and imputed the following when missing: albumin (23%),

eGFR (0.4%), BMI (1.3%), and dialysis access type (0.4%). We also conducted sensitivity analyses, excluding patients with extreme outlier values for volume or staffing defined as values ≤1st or ≥99th percentile. In secondary models, we added an additional facility characteristic—profit status. All statistical analyses were conducted using SAS version 9.4. Our study was not considered human subjects research by the University of California, Davis Institutional Review Board.

Results

We examined 135,545 Medicare beneficiaries (Table 1). During a median follow-up of 313 days (89–664), 38,475 (28%) patients had at least one infection-related hospitalization: 18% had one, 6% had two, 2% had three, and 2% had four or more hospitalizations. The median time to infection-related hospitalization was 161 days (55–379).

The overall rate of infection-related hospitalization was 40.2 per 100 person-years. The rates of hospitalization were highest for dialysis access or CVC-related infections, bloodstream infections or sepsis, and pulmonary infections, with rates (per 100 person-years) of 11.9, 10.2, and 8.4, respectively.

All–Cause Infection–Related Hospitalization

In the primary multivariable model, patient characteristics associated with a higher rate of infection-related hospitalization included age <45 years old or 75 years old and older, women, white race, non-Hispanic ethnicity, BMI<20 kg/m^2, coexisting illnesses, inability to ambulate or transfer, drug dependence, residence in a care facility, higher eGFR, lower serum albumin concentrations at dialysis initiation, dialysis initiation with an access other than an arteriovenous fistula, and limited nephrology care before dialysis (Table 2). Patient residence in an urban area was associated with a higher rate of infection-related hospitalization, whereas measures of neighborhood SES were not, and ESRD networks were strongly associated with the rate of hospitalization for infection (Table 2).

In the multivariable model, higher facility volume was associated with a higher rate, but only a facility volume of 64–91 patients was statistically significantly higher compared with facilities with <42 patients (P value =0.05). The total number and composition of staff were not associated with overall infection–related hospitalization rates (Table 2). In sensitivity analyses, when we removed outliers, we did not find substantive differences in the associations among patient, geographic, and facility characteristics and all–cause infection–related hospitalization, although nephrology care <6 months became significantly associated with a higher rate.

In secondary analyses, in which profit status was included as an additional facility characteristic, care in a for-profit facility was associated with an 11% higher rate of infection-related hospitalization (Supplemental Table 2). The addition of profit status to the model did not substantively change the interpretation of the other characteristics under consideration. However, select ESRD networks were no longer statistically significantly associated with the rate of infection (Table 2, Supplemental Table 2).

Cause–Specific Infection–Related Hospitalization

The association between patient characteristics and the rate of infection-related hospitalization differed by type of infection. For example, chronic obstructive pulmonary disease was associated with a nearly 80% higher rate of hospitalization for pulmonary infections, whereas dialysis catheters at dialysis initiation were associated with a 3-fold higher rate of hospitalization for dialysis access infection (Table 3).

Rates of hospitalization for dialysis access–related infection varied substantially across ESRD networks. Rural-urban residence was significantly associated with hospitalization for dialysis access and other types of infection. SES, as measured by poverty and educational attainment at the zip code level, did not have consistent associations with the rate of cause–specific infection–related hospitalization (Table 3).

Interestingly, dialysis facility volume was associated with hospitalization for pulmonary infections. A higher percentage of nurses was associated with a lower rate of hospitalization for dialysis access infections, whereas a higher total number of staff was associated with a lower rate of hospitalization for pulmonary infections. In sensitivity analyses, when we removed outliers, we did not find substantive differences in the effect size of associations between patient, geographic, and facility characteristics and the rate of cause–specific infection–related hospitalization. However, some marginally nonsignificant P values became significant, whereas some marginally significant P values became nonsignificant. When profit status was added to the primary model, for-profit status was only associated with a higher rate of hospitalization for dialysis access or CVC-related infection (Supplemental Table 2). The addition of profit status to the models examining cause-specific infection did not substantively change the interpretation of the vast majority of other characteristics under consideration. However, some P values became significant, whereas others became nonsignificant (Table 3, Supplemental Table 2).

Discussion

We systematically examined the associations among patient, geographic, and facility characteristics, including indicators of SES, and the rates of overall and cause–specific infection–related hospitalizations among Medicare beneficiaries starting in-center hemodialysis. We undertook this study to improve our understanding of the relative association of each of these factors with the rate of infection-related hospitalization and inform our understanding of where preventive efforts and intervention may yield the greatest benefit.

Patient characteristics most strongly associated with a higher rate of all–cause infection–related hospitalization included initiation of dialysis with a catheter, albumin concentrations <2.5 g/dl, inability to ambulate or transfer, and residence in a care facility at initiation of dialysis. Although these findings are not surprising, they remind us that we can risk stratify our patients to identify those who are at highest risk. Lack of nephrology care before dialysis initiation was associated with higher rates of bloodstream infections or sepsis and dialysis access–related infections.

Table 1. Baseline characteristics of Medicare beneficiaries receiving in-center hemodialysis

Patient and Facility Characteristics	*n*=135,545
Patient characteristics	
Age, yrs	
18–44	13,567 (10)
45–64	41,782 (31)
65–74	37,402 (28)
75–84	33,854 (25)
≥85	8940 (7)
Men	73,466 (54)
Race	
White	88,115 (65)
Black	41,346 (31)
Asian	3436 (3)
Native American	1505 (1)
Pacific Islander	765 (1)
Multiracial, other, unknown	378 (0.3)
Hispanic	16,011 (12)
Body mass index, kg/m^2	
<20	11,061 (8)
20 to <25	37,735 (28)
25 to <30	38,419 (28)
30 to <35	23,265 (17)
≥35	23,352 (17)
Missing	1713 (1)
Diabetes mellitus	80,818 (60)
Atherosclerotic heart disease	32,055 (24)
Cerebrovascular disease	14,847 (11)
Peripheral vascular disease	21,435 (16)
Congestive heart failure	49,910 (37)
History of amputation	4580 (3)
Hypertension	119,756 (88)
Cancer	10,062 (7)
COPD	13,606 (10)
Inability to ambulate or transfer	9827 (7)
Etiology of renal disease	
Diabetes	64,106 (47)
Hypertension	42,079 (31)
GN	7350 (5)
Cystic kidney	1927 (1)
Other or unknown	20,083 (15)
Access type	
AV fistula	18,710 (14)
AV graft	6349 (5)
Catheter	108,262 (80)
Other	1659 (1)
Missing	565 (0.4)
Hemoglobin, g/dl	10.0±1.7
eGFR, ml/min per 1.73 m^2	11.1±5.7
Albumin, g/dl	
<2.5	18,508 (14)
2.5–2.9	22,572 (17)
3.0–3.4	28,706 (21)
3.5–3.9	23,188 (17)
≥4	10,949 (8)
Missing	31,622 (23)
Tobacco use, current smoker	8841 (7)
Alcohol dependence	1939 (1)
Drug dependence	1772 (1)
Institutionalization	
Assisted living	1000 (1)
Nursing home	9321 (7)
Other	581 (0.4)
Prior nephrologist care, mo	
None	41,366 (31)
<6	14,088 (10)
6–12	32,560 (24)
>12	31,388 (23)
Unknown	16,143 (12)
Geographic characteristics	
RUCA	
Isolated small rural	5796 (4)
Small rural	8825 (7)
Large rural	15,698 (12)
Urban	105,226 (78)
ESRD network (patient)	
1	4815 (4)
2	5703 (4)
3	3671 (3)
4	5733 (4)
5	8181 (6)
6	14,687 (11)
7	9034 (7)
8	9084 (7)
9	11,577 (9)
10	5383 (4)
11	8321 (6)
12	5537 (4)
13	7102 (5)
14	14,060 (10)
15	5482 (4)
16	3580 (3)
17	4973 (4)
18	8622 (6)
Socioeconomic status	
Adults ≥25 yrs old with high school education or higher, %	
<50	1782 (1)
50–75	27,058 (20)
>75	106,705 (79)
Below poverty in past 12 mo, %	
<5	9397 (7)
5–9.9	25,303 (19)
10–14.9	27,746 (20)
15–19.9	25,215 (19)
20–24.9	18,623 (14)
≥25	29,261 (22)
Facility characteristics	
Volume, no. of facility patients	
≤41	18,409 (14)
42–63	28,549 (21)
64–91	37,254 (27)
≥92	51,333 (38)
Volume of home program	
0/None	74,735 (55)
1–10	27,796 (21)
11–25	20,135 (15)
≥26	12,879 (10)
Total staffing, nurses, and PCTs	13 [9, 18]
Staffing composition, % nurses[a]	41 [33, 50]
For profit	123,697 (91)

Data are presented as *n* (%), mean±SD, or median [25th, 75th percentiles]. COPD, chronic obstructive pulmonary disease; AV, arteriovenous; RUCA, rural-urban commuting area; PCT, patient care technician.

[a](Nurses/[nurses + PCTs]) × 100.

Table 2. Multivariable model examining characteristics associated with all–cause infection–related hospitalization

Variable	Rate Ratio (95% Confidence Interval)	*P* Value
Age, yrs		
18–44	1.12 (1.07 to 1.17)	<0.001
45–64	Reference	
65–74	1.03 (1.00 to 1.06)	0.08
75–84	1.14 (1.10 to 1.17)	<0.001
≥85	1.30 (1.23 to 1.37)	<0.001
Men	0.86 (0.84 to 0.88)	<0.001
Race		
White	Reference	
Black	0.82 (0.79 to 0.85)	<0.001
Other	0.85 (0.80 to 0.90)	<0.001
Hispanic	0.89 (0.85 to 0.93)	<0.001
Body mass index, kg/m^2		
<20	1.10 (1.06 to 1.15)	<0.001
20 to <25	Reference	
25 to <30	0.95 (0.92 to 0.98)	<0.001
30 to <35	0.95 (0.91 to 0.98)	0.002
≥35	1.00 (0.97 to 1.04)	0.94
Congestive heart failure	1.09 (1.06 to 1.11)	<0.001
Atherosclerotic heart disease	1.01 (0.98 to 1.04)	0.70
Cerebrovascular disease	1.12 (1.08 to 1.16)	<0.001
Peripheral vascular disease	1.10 (1.07 to 1.14)	<0.001
Hypertension	0.84 (0.81 to 0.87)	<0.001
History of amputation	1.19 (1.11 to 1.26)	<0.001
Diabetes mellitus	1.16 (1.13 to 1.19)	<0.001
Cancer	1.20 (1.15 to 1.25)	<0.001
COPD	1.25 (1.21 to 1.30)	<0.001
Inability to ambulate or transfer	1.33 (1.27 to 1.39)	<0.001
Vascular access type		
AV fistula	Reference	
Catheter	1.59 (1.53 to 1.65)	<0.001
AV graft	1.37 (1.28 to 1.45)	<0.001
Other	1.46 (1.30 to 1.64)	<0.001
eGFR per 5 ml/min per 1.73 m^2	1.11 (1.10 to 1.12)	<0.001
Albumin concentration, g/dl		
<2.5	1.44 (1.35 to 1.53)	<0.001
2.5 to <3.0	1.31 (1.24 to 1.39)	<0.001
3.0 to <3.5	1.21 (1.14 to 1.29)	<0.001
3.5 to <4.0	1.11 (1.05 to 1.18)	<0.001
≥4	Reference	
Tobacco use, current smoker	0.98 (0.94 to 1.03)	0.51
Alcohol dependence	1.05 (0.95 to 1.15)	0.35
Drug dependence	1.26 (1.14 to 1.40)	<0.001
Residence in care facility	1.51 (1.44 to 1.58)	<0.001
Nephrology care before dialysis initiation, mo		
<6	1.04 (1.00 to 1.09)	0.07
6–12	1.04 (1.01 to 1.07)	0.02
≥12	Reference	
None	1.13 (1.09 to 1.17)	<0.001
Unknown	1.19 (1.14 to 1.25)	<0.001
RUCA		
Urban	Reference	
Large rural	0.96 (0.91 to 1.00)	0.04
Small rural	0.95 (0.90 to 1.00)	0.04
Isolated small rural	0.91 (0.86 to 0.97)	0.003
ESRD network		
1	1.16 (1.03 to 1.30)	0.01
2	1.14 (1.01 to 1.29)	0.04
3	1.28 (1.11 to 1.48)	<0.001
4	1.13 (1.01 to 1.27)	0.04
5	1.28 (1.15 to 1.42)	<0.001
6	1.25 (1.14 to 1.38)	<0.001

Table 2. (Continued)

Variable	Rate Ratio (95% Confidence Interval)	*P* Value
7	1.36 (1.23 to 1.51)	<0.001
8	1.20 (1.08 to 1.33)	<0.001
9	1.22 (1.10 to 1.35)	<0.001
10	1.20 (1.08 to 1.35)	0.001
11	1.15 (1.04 to 1.28)	<0.01
12	1.13 (1.01 to 1.26)	0.04
13	1.29 (1.16 to 1.44)	<0.001
14	1.15 (1.04 to 1.27)	<0.01
15	1.10 (0.99 to 1.23)	0.08
16	Reference	
17	1.10 (0.99 to 1.23)	0.09
18	1.18 (1.06 to 1.32)	0.002
Adults ≥25 yrs old who are high school graduates or higher, %		
<50	Reference	
50–75	1.03 (0.92 to 1.16)	0.60
>75	1.01 (0.89 to 1.15)	0.85
All people below poverty in the past 12 mo, %		
<5	Reference	
5–9.9	0.98 (0.93 to 1.04)	0.59
10–14.9	0.99 (0.93 to 1.05)	0.69
15–19.9	1.00 (0.94 to 1.06)	0.92
20–24.9	1.02 (0.96 to 1.08)	0.54
≥25	1.04 (0.97 to 1.10)	0.27
Volume, no. of facility patients		
≤41	Reference	
42–63	1.04 (0.99 to 1.09)	0.12
64–91	1.05 (1.00 to 1.11)	0.05
>91	1.04 (0.97 to 1.11)	0.29
Total no. of nurses and PCTs per five staff increase	0.99 (0.98 to 1.01)	0.29
Staff composition per 10% nurse increase	0.99 (0.98 to 1.00)	0.10
Home program volume		
None or 0	Reference	
1–10	1.07 (1.03 to 1.11)	<0.001
11–25	1.02 (0.97 to 1.07)	0.47
≥26	1.00 (0.94 to 1.06)	0.98

COPD, chronic obstructive pulmonary disease; AV, arteriovenous; RUCA, rural-urban commuting area; PCT, patient care technician.

Despite limiting our examination of hospitalizations to those occurring after the first 90 days, we found an association between nephrology care before dialysis initiation and infection, raising important questions about when nephrologists, dialysis facilities, and others should become accountable for the outcomes of patients who may be relatively newly under their care.

We noted significant variation in the rate of dialysis access infection–related hospitalization by ESRD network, raising the possibility that patients in these regions differ in ways that we have not measured (*e.g.*, access to transplantation and/or other clinical risk factors), facilities themselves have adopted practices that differ region by region, and/or some local network–driven quality initiatives have been effective at lowering the risk of infection. ESRD networks are nonprofit organizations that contract with the Centers for Medicare & Medicaid Services to oversee the quality of care within dialysis facilities (16), and the structure of these networks allows for unique opportunities to provide guidance on preventing infection-related hospitalizations and monitor individual facility performance. Residence in an urban area was associated with higher rates of specific types of infection-related hospitalizations (*e.g.*, dialysis access). Whether this finding reflects access to hospitals, differences in management of infection in urban versus rural outpatient dialysis facilities, or other factors is unknown and may warrant additional exploration.

We did not find consistent associations between measures of poverty or education at the patient zip code level and the risk of hospitalization for infection. The lack of association may have been related to our cohort being restricted to Medicare Parts A and B beneficiaries. Interestingly, another and perhaps better potential measure of access to care—nephrology care before dialysis—was associated with the rate of infection-related hospitalization.

We examined modifiable and nonmodifiable facility–level factors, including volume, staffing, and profit status. Higher volume facilities had higher and graded relative rates of pulmonary infection; higher total staffing was associated with a lower rate of hospitalization for pulmonary infections, whereas a higher percentage of nurses

Table 3. Multivariable model examining characteristics associated with cause–specific infection–related hospitalization

Variable	Bloodstream Infection or Sepsis		Dialysis Access Infection		Pulmonary Infection		Other Infection	
	RR (95% CI)	*P* Value	RR (95% CI)	*P* Value	RR (95% CI)	*P* Value	RR (95% CI)	*P* Value
Age, yrs								
18–44	0.86 (0.79 to 0.94)	<0.001	1.34 (1.26 to 1.42)	<0.001	0.98 (0.90 to 1.07)	0.62	1.07 (0.99 to 1.15)	0.08
45–64	Reference		Reference		Reference		Reference	
65–74	1.19 (1.13 to 1.26)	<0.001	0.84 (0.80 to 0.88)	<0.001	1.17 (1.10 to 1.23)	<0.001	1.00 (0.95 to 1.06)	0.97
75–84	1.39 (1.31 to 1.47)	<0.001	0.82 (0.78 to 0.87)	<0.001	1.36 (1.28 to 1.45)	<0.001	1.11 (1.05 to 1.18)	<0.001
≥85	1.57 (1.44 to 1.71)	<0.001	0.93 (0.85 to 1.01)	0.08	1.61 (1.48 to 1.75)	<0.001	1.26 (1.16 to 1.38)	<0.001
Men	0.91 (0.87 to 0.95)	<0.001	0.90 (0.87 to 0.93)	<0.001	0.90 (0.86 to 0.94)	<0.001	0.72 (0.69 to 0.75)	<0.001
Race								
White	Reference		Reference		Reference		Reference	
Black	0.92 (0.87 to 0.98)	<0.01	0.95 (0.90 to 1.00)	0.05	0.68 (0.64 to 0.72)	<0.001	0.66 (0.63 to 0.70)	<0.001
Other	0.89 (0.79 to 1.00)	0.05	0.98 (0.89 to 1.09)	0.74	0.86 (0.77 to 0.95)	0.004	0.68 (0.61 to 0.76)	<0.001
Hispanic	0.86 (0.79 to 0.93)	<0.001	0.92 (0.85 to 0.99)	0.03	0.89 (0.82 to 0.97)	<0.01	0.87 (0.81 to 0.94)	<0.001
Body mass index, kg/m^2								
<20	1.14 (1.06 to 1.24)	<0.001	1.02 (0.95 to 1.10)	0.53	1.20 (1.12 to 1.29)	<0.001	1.02 (0.94 to 1.11)	0.57
20–24	Reference		Reference		Reference		Reference	
25–29	0.97 (0.92 to 1.02)	0.24	0.95 (0.91 to 1.00)	0.07	0.88 (0.83 to 0.92)	<0.001	0.98 (0.93 to 1.03)	0.44
30–34	0.95 (0.89 to 1.01)	0.10	0.95 (0.90 to 1.01)	0.08	0.81 (0.76 to 0.86)	<0.001	1.06 (1.00 to 1.13)	0.05
≥35	1.00 (0.94 to 1.06)	>0.99	1.05 (1.00 to 1.11)	0.07	0.75 (0.70 to 0.80)	<0.001	1.16 (1.10 to 1.23)	<0.001
Congestive heart failure	1.13 (1.09 to 1.18)	<0.001	1.02 (0.98 to 1.06)	0.36	1.15 (1.10 to 1.21)	<0.001	1.07 (1.03 to 1.12)	0.001
Atherosclerotic heart disease	0.99 (0.94 to 1.04)	0.71	0.97 (0.93 to 1.02)	0.29	0.99 (0.94 to 1.05)	0.81	1.04 (0.99 to 1.09)	0.16
Cerebrovascular disease	1.19 (1.12 to 1.26)	<0.001	1.11 (1.05 to 1.17)	<0.001	1.07 (1.01 to 1.14)	0.03	1.10 (1.03 to 1.16)	0.003
Peripheral vascular disease	1.12 (1.06 to 1.19)	<0.001	1.13 (1.07 to 1.19)	<0.001	1.01 (0.95 to 1.07)	0.70	1.11 (1.05 to 1.17)	<0.001
Hypertension	0.75 (0.71 to 0.80)	<0.001	0.87 (0.82 to 0.92)	<0.001	0.91 (0.85 to 0.97)	0.003	0.84 (0.79 to 0.90)	<0.001
History of amputation	1.31 (1.18 to 1.45)	<0.001	1.15 (1.05 to 1.26)	0.004	1.04 (0.92 to 1.18)	0.53	1.21 (1.09 to 1.34)	<0.001
Diabetes mellitus	1.24 (1.18 to 1.30)	<0.001	1.11 (1.06 to 1.16)	<0.001	1.03 (0.99 to 1.08)	0.15	1.28 (1.22 to 1.34)	<0.001
COPD	1.20 (1.13 to 1.29)	<0.001	1.10 (1.03 to 1.18)	0.003	1.78 (1.68 to 1.89)	<0.001	1.05 (0.98 to 1.12)	0.17
Cancer	1.28 (1.19 to 1.38)	<0.001	1.11 (1.03 to 1.20)	<0.01	1.19 (1.10 to 1.28)	<0.001	1.18 (1.09 to 1.28)	<0.001
Inability to ambulate or transfer	1.57 (1.46 to 1.69)	<0.001	1.21 (1.12 to 1.31)	<0.001	1.11 (1.02 to 1.22)	0.02	1.32 (1.22 to 1.42)	<0.001
Vascular access type								
AV fistula	Reference		Reference		Reference		Reference	
Catheter	1.54 (1.44 to 1.65)	<0.001	3.07 (2.82 to 3.36)	<0.001	1.14 (1.07 to 1.22)	<0.001	1.32 (1.24 to 1.40)	<0.001
AV graft	1.41 (1.28 to 1.57)	<0.001	2.36 (2.09 to 2.68)	<0.001	1.06 (0.95 to 1.18)	0.30	1.15 (1.04 to 1.28)	<0.01
Other	1.43 (1.18 to 1.73)	<0.001	2.93 (2.39 to 3.60)	<0.001	1.04 (0.85 to 1.26)	0.71	1.17 (0.95 to 1.45)	0.15
eGFR per 5 ml/min per 1.73 m^2	1.15 (1.13 to 1.17)	<0.001	1.08 (1.07 to 1.10)	<0.001	1.09 (1.07 to 1.11)	<0.001	1.10 (1.09 to 1.12)	<0.001
Albumin concentration, g/dl								
<2.5	1.54 (1.38 to 1.72)	<0.001	1.36 (1.25 to 1.49)	<0.001	1.48 (1.33 to 1.65)	<0.001	1.38 (1.25 to 1.51)	<0.001
2.5 to < 3.0	1.36 (1.23 to 1.50)	<0.001	1.28 (1.18 to 1.40)	<0.001	1.32 (1.18 to 1.46)	<0.001	1.28 (1.17 to 1.41)	<0.001
3.0 to < 3.5	1.27 (1.14 to 1.41)	<0.001	1.15 (1.05 to 1.25)	0.002	1.28 (1.17 to 1.40)	<0.001	1.17 (1.08 to 1.28)	<0.001

Table 3. (Continued)

Variable	Bloodstream Infection or Sepsis		Dialysis Access Infection		Pulmonary Infection		Other Infection	
	RR (95% CI)	*P* Value	RR (95% CI)	*P* Value	RR (95% CI)	*P* Value	RR (95% CI)	*P* Value
3.5 to < 4.0	1.08 (0.98 to 1.20)	0.13	1.11 (1.02 to 1.21)	0.02	1.21 (1.10 to 1.33)	<0.001	1.05 (0.96 to 1.16)	0.27
≥4	Reference		Reference		Reference		Reference	
Tobacco use, current smoker	0.91 (0.83 to 0.99)	0.02	0.96 (0.89 to 1.04)	0.28	1.15 (1.06 to 1.25)	<0.001	0.91 (0.84 to 0.99)	0.03
Alcohol dependence	1.02 (0.85 to 1.21)	0.86	1.05 (0.90 to 1.22)	0.54	0.84 (0.70 to 1.01)	0.06	1.24 (1.04 to 1.48)	0.02
Drug dependence	1.14 (0.93 to 1.40)	0.21	1.20 (1.03 to 1.40)	0.02	1.45 (1.20 to 1.75)	<0.001	1.30 (1.08 to 1.57)	<0.01
Residence in care facility	1.76 (1.64 to 1.89)	<0.001	1.65 (1.54 to 1.76)	<0.001	1.15 (1.06 to 1.25)	<0.001	1.43 (1.32 to 1.53)	<0.001
Nephrology care before dialysis initiation, mo								
<6	1.08 (1.00 to 1.17)	0.06	1.07 (1.00 to 1.16)	0.06	1.04 (0.96 to 1.12)	0.35	1.02 (0.95 to 1.10)	0.55
6–12	1.09 (1.02 to 1.16)	<0.01	1.07 (1.01 to 1.13)	0.03	1.05 (0.99 to 1.11)	0.13	1.00 (0.95 to 1.06)	0.92
≥12	Reference		Reference		Reference		Reference	
None	1.24 (1.17 to 1.33)	<0.001	1.21 (1.14 to 1.28)	<0.001	1.03 (0.97 to 1.10)	0.30	1.04 (0.98 to 1.10)	0.18
Unknown	1.30 (1.20 to 1.40)	<0.001	1.25 (1.16 to 1.34)	<0.001	1.07 (0.99 to 1.16)	0.09	1.21 (1.12 to 1.31)	<0.001
RUCA								
Urban	Reference		Reference		Reference		Reference	
Large rural	1.01 (0.94 to 1.09)	0.76	0.89 (0.83 to 0.95)	<0.001	1.02 (0.95 to 1.09)	0.62	0.91 (0.85 to 0.97)	<0.01
Small rural	0.95 (0.86 to 1.04)	0.24	0.91 (0.83 to 1.00)	0.04	1.06 (0.97 to 1.16)	0.18	0.87 (0.79 to 0.95)	0.003
Isolated small rural	0.93 (0.83 to 1.03)	0.15	0.92 (0.83 to 1.02)	0.10	1.01 (0.91 to 1.12)	0.88	0.81 (0.73 to 0.90)	<0.001
ESRD network								
1	0.78 (0.64 to 0.95)	0.01	1.13 (0.93 to 1.38)	0.21	1.36 (1.11 to 1.65)	0.002	1.46 (1.22 to 1.76)	<0.001
2	1.16 (0.94 to 1.43)	0.16	1.22 (1.01 to 1.47)	0.04	1.00 (0.82 to 1.23)	0.97	1.17 (0.97 to 1.41)	0.10
3	1.10 (0.88 to 1.39)	0.40	1.37 (1.11 to 1.68)	0.003	1.13 (0.89 to 1.42)	0.32	1.44 (1.19 to 1.76)	<0.001
4	1.05 (0.87 to 1.28)	0.60	1.26 (1.04 to 1.53)	0.02	1.11 (0.91 to 1.35)	0.30	1.15 (0.97 to 1.37)	0.12
5	1.19 (0.99 to 1.43)	0.06	1.35 (1.13 to 1.60)	<0.001	1.34 (1.11 to 1.61)	0.002	1.27 (1.07 to 1.51)	<0.01
6	1.07 (0.90 to 1.28)	0.41	1.47 (1.25 to 1.73)	<0.001	1.30 (1.09 to 1.55)	0.004	1.18 (1.00 to 1.38)	0.05
7	1.15 (0.97 to 1.37)	0.11	1.85 (1.56 to 2.19)	<0.001	1.01 (0.84 to 1.22)	0.91	1.39 (1.18 to 1.64)	<0.001
8	1.02 (0.85 to 1.22)	0.83	1.30 (1.09 to 1.54)	0.003	1.29 (1.07 to 1.56)	<0.01	1.23 (1.04 to 1.46)	0.02
9	1.05 (0.88 to 1.25)	0.58	1.26 (1.06 to 1.50)	<0.01	1.33 (1.11 to 1.59)	0.002	1.22 (1.04 to 1.44)	0.02
10	1.08 (0.89 to 1.30)	0.45	1.13 (0.93 to 1.36)	0.22	1.39 (1.15 to 1.69)	<0.001	1.32 (1.10 to 1.58)	0.003
11	1.06 (0.89 to 1.27)	0.52	1.36 (1.14 to 1.62)	<0.001	1.07 (0.89 to 1.30)	0.47	1.10 (0.93 to 1.31)	0.27
12	0.86 (0.70 to 1.04)	0.12	1.19 (0.99 to 1.43)	0.07	1.32 (1.09 to 1.62)	<0.01	1.23 (1.03 to 1.47)	0.02
13	1.18 (0.98 to 1.42)	0.08	1.49 (1.25 to 1.77)	<0.001	1.33 (1.10 to 1.62)	0.003	1.18 (0.99 to 1.41)	0.06
14	0.96 (0.81 to 1.15)	0.67	1.24 (1.06 to 1.47)	<0.01	1.16 (0.97 to 1.39)	0.11	1.19 (1.01 to 1.39)	0.04
15	0.87 (0.71 to 1.05)	0.15	1.24 (1.03 to 1.50)	0.02	1.21 (1.00 to 1.47)	0.05	1.11 (0.92 to 1.34)	0.26
16	Reference		Reference		Reference		Reference	
17	1.09 (0.90 to 1.31)	0.39	1.01 (0.83 to 1.22)	0.93	1.24 (1.02 to 1.50)	0.03	1.09 (0.90 to 1.31)	0.38
18	1.37 (1.14 to 1.64)	<0.001	1.13 (0.95 to 1.34)	0.18	1.07 (0.88 to 1.30)	0.50	1.10 (0.92 to 1.31)	0.28

Table 3. (Continued)

Variable	Bloodstream Infection or Sepsis		Dialysis Access Infection		Pulmonary Infection		Other Infection	
	RR (95% CI)	*P* Value	RR (95% CI)	*P* Value	RR (95% CI)	*P* Value	RR (95% CI)	*P* Value
Adults ≥25 yrs old who are high school graduates or higher, %								
<50	Reference		Reference		Reference		Reference	
50–75	0.95 (0.79 to 1.13)	0.55	1.17 (0.98 to 1.41)	0.09	0.93 (0.77 to 1.13)	0.48	1.04 (0.88 to 1.23)	0.66
>75	0.89 (0.74 to 1.08)	0.24	1.17 (0.97 to 1.41)	0.11	0.90 (0.74 to 1.10)	0.30	1.04 (0.87 to 1.24)	0.69
All people below poverty in the past 12 mo, %								
<5	Reference		Reference		Reference		Reference	
5–9.9	0.97 (0.88 to 1.07)	0.51	0.98 (0.90 to 1.08)	0.70	1.03 (0.94 to 1.13)	0.55	0.97 (0.89 to 1.06)	0.53
10–14.9	0.96 (0.87 to 1.06)	0.47	0.99 (0.90 to 1.08)	0.76	1.03 (0.94 to 1.13)	0.55	0.98 (0.89 to 1.06)	0.58
15–19.9	0.97 (0.88 to 1.07)	0.54	0.99 (0.90 to 1.09)	0.84	1.05 (0.95 to 1.15)	0.36	1.02 (0.93 to 1.12)	0.70
20–24.9	0.99 (0.89 to 1.10)	0.90	0.99 (0.90 to 1.09)	0.86	1.12 (1.01 to 1.25)	0.03	1.01 (0.91 to 1.11)	0.85
≥25	0.98 (0.88 to 1.10)	0.77	1.06 (0.96 to 1.18)	0.23	1.10 (0.99 to 1.22)	0.09	1.02 (0.93 to 1.13)	0.65
Volume, no. of facility patients								
≤41	Reference		Reference		Reference		Reference	
42–63	1.03 (0.95 to 1.13)	0.47	1.02 (0.94 to 1.10)	0.65	1.03 (0.95 to 1.11)	0.48	1.09 (1.01 to 1.17)	0.03
64–91	1.02 (0.93 to 1.12)	0.68	1.05 (0.97 to 1.14)	0.23	1.12 (1.03 to 1.22)	<0.01	1.07 (0.99 to 1.16)	0.07
>91	0.96 (0.86 to 1.08)	0.50	1.06 (0.96 to 1.18)	0.22	1.16 (1.05 to 1.28)	0.003	1.08 (0.99 to 1.19)	0.10
Total no. of nurses and PCTs per five staff higher	1.00 (0.98 to 1.03)	0.83	0.98 (0.96 to 1.01)	0.20	0.97 (0.95 to 0.99)	0.01	0.98 (0.96 to 1.00)	0.12
Staff composition per 10% higher nurse composition	1.00 (0.98 to 1.01)	0.72	0.98 (0.96 to 0.99)	0.004	1.00 (0.98 to 1.02)	0.97	1.00 (0.98 to 1.02)	0.98
Home program volume								
0/None	Reference		Reference		Reference		Reference	
1–10	1.04 (0.98 to 1.11)	0.18	1.06 (1.00 to 1.13)	0.04	1.07 (1.01 to 1.13)	0.03	1.07 (1.01 to 1.14)	0.02
11–25	0.99 (0.92 to 1.07)	0.84	1.03 (0.95 to 1.11)	0.48	1.03 (0.96 to 1.10)	0.45	1.04 (0.98 to 1.11)	0.20
≥26	0.98 (0.88 to 1.08)	0.66	1.00 (0.91 to 1.10)	0.95	0.93 (0.84 to 1.01)	0.10	1.01 (0.92 to 1.10)	0.82

RR, rate ratio; 95% CI, 95% confidence interval; COPD, chronic obstructive pulmonary disease; AV, arteriovenous; RUCA, rural-urban commuting area; HS, high school; PCT, patient care technician.

was associated with a lower relative rate of hospitalization for dialysis access–related infections. Secondary models that further included profit status found for-profit status to be associated with a higher rate of overall infections and in analyses of cause-specific hospitalizations, infection related to the dialysis access. These findings highlight our need to better understand how organizational structure, facility characteristics, and staffing influence the risk of infection-related hospitalization. For example, higher facility volume may heighten the risk of infection because of a greater likelihood of exposure to ill patients at the dialysis facility (*e.g.*, viral pulmonary infections) or less attention to infection prevention because of demands on efficiency. The association between higher staffing and lower rate of pulmonary infection may reflect the greater availability of resources needed to counsel patients about vaccination and ensure implementation of infection prevention and control guidelines, whereas a higher percentage of nurses may allow for effective vascular access management. We note that, in the years after our cohort began dialysis therapy, numerous initiatives have been undertaken by dialysis organizations to lower the prevalence of dialysis catheters (17) and the incidence of bloodstream infections (18). Future studies should examine whether and to what extent these initiatives have altered the trajectory of infection-related hospitalizations.

Our study has a number of strengths, including our examination of a broad range of factors that contribute to infection risk, and provides targets for interventions. We examined all–cause and cause–specific infection to better identify and conceptualize risk and opportunities for targeted prevention. We also examined this question within existing frameworks for quality improvement, namely with respect to ESRD networks. Lastly, we examined a problem of great importance—infection—that has received relatively little study.

Our study also has limitations. Our findings are limited to Medicare beneficiaries receiving care in free-standing facilities and those who survive the first 90 days. Our reliance on ICD-9-CM codes is a limitation, and we acknowledge the potential for misclassification of the type of infection. However, the principal inpatient diagnosis is clearly and consistently defined as the diagnosis established as having been principally responsible for the admission of the patient to the hospital. The available staffing data may not accurately reflect true full–time equivalents and presumably, do not include per diem employees; also, the data do not account for skill or training, which may be more important than the absolute number of staff. The SES data were at the zip code level, which may have resulted in misclassification.

Reliance on the Medical Evidence Form to collect data was another limitation of our study. First, our conclusions are limited to patient characteristics at the time of dialysis initiation. Second, we cannot exclude residual confounding. A study conducted between 1995 and 1998 examined the sensitivity and specificity of a prior version of the Medical Evidence Form for comorbidity ascertainment of 17 conditions and found the overall sensitivity to be 0.59 and the specificity to be ≥0.91 (19). In addition, Kim *et al.* (20) examined the concordance between nephrology care reported on the Medical Evidence Form and the first outpatient Medicare claim for nephrology consultation and found an overall accuracy of 0.70 (the accuracy differed by patient characteristics). Thus, we cannot make definitive conclusions about the association between pre–ESRD nephrology care and the risk of infection-related hospitalization. However, our findings suggest that there may be an important link that warrants additional study.

The findings from our study and the most recent statistics from the 2014 USRDS Annual Data Report (1) remain sobering and a reminder of the burden of serious infections in the dialysis population. Increasing attention has been focused on infection prevention and control as exemplified by a number of initiatives and changes in policy, including the CDC's NHSN dialysis event reporting system, the CDC's Dialysis Bloodstream Infection Collaborative (21), select ESRD network initiatives, large dialysis organization quality initiatives targeting reduction of dialysis catheters or bloodstream infections (17,18), and the expanded and defined role of dialysis facility medical directors in infection prevention and control (22,23). The CDC has developed core interventions for dialysis facilities to prevent bloodstream infections among patients on dialysis (24).

In conclusion, our findings can be used to identify patients at higher risk for infection and inform the design of strategies aimed to decrease risk. Age, select comorbidities, inability to ambulate or transfer, and residence in a care facility at dialysis initiation can be used to risk-stratify patients, whereas ongoing facility and physician efforts to reduce tunneled dialysis catheter use are imperative to lowering the risk of infection. Finally, variation across ESRD networks should motivate us to explore whether ESRD networks with the lowest rates of infection-related hospitalization have instituted region–wide infection control initiatives that have proved successful.

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