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Hospitalization and Skilled Nursing Care are Predictors of Influenza Vaccination Among Patients on Hemodialysis:

Evidence of Confounding by Frailty

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Abstract

Background—Observational studies of preventive medications, such as vaccinations, can suffer from the healthy-user bias because vaccinated patients may be healthier than unvaccinated patients. Indicators of health status and frailty suitable for attenuating this bias could be identified in administrative data.

Objective—To examine the association of baseline variables and time-dependent hospitalization and skilled nursing care with the receipt of influenza vaccination in patients with end-stage renal disease.

Research Design—Observational cohort study using United States Renal Data System files each year from 1999 to 2005.

Subjects—Population-based cohorts that included >115,000 adult, hemodialysis patients each year.

Measures—We estimated hazard ratios for the association of baseline variables and time-dependent hospitalization days and skilled nursing days with influenza vaccination, controlling for demographic and baseline health status variables.

Results—Vaccination coverage increased from 47% in 1999 to 60% in 2005. Patients with any length of hospitalization were less likely to be vaccinated, however, the association was stronger in

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patients with longer stays [15–25 d: hazard ratio = 0.64 (95% confidence interval, 0.62–0.65); 26–30 d: 0.40 (0.38–0.42)]. Patients with any length of skilled nursing care of >1 day had similar estimates; these patients were also less likely to be vaccinated [26–30 d: 0.66 (0.64–0.69)].

Conclusions—Patients with long hospitalizations or skilled nursing stays were less likely to be vaccinated suggesting evidence of the healthy-user effect. These variables could be used to account for bias in studies of preventive services in patients on dialysis.

Keywords

influenza vaccines; bias (epidemiology); confounding factors (epidemiology); renal dialysis; cohort studies

Patients who receive prevention health care, such as preventive medications, screening tests, and vaccinations, have been shown to be in overall better health and more likely to engage in other healthy behaviors.[1,2] This situation has the potential to exaggerate the benefits of the intervention under study, resulting in what is called the healthy-user bias.[3] The healthy-user bias has been suspected in studies of preventive medications such as hormone replacement therapy and cardiovascular disease,[4] and with statin therapy and several disease outcomes.[5–7] Alternatively, it has been suggested in influenza vaccine effectiveness studies where patients who are not vaccinated had a lower functional status.[8] It appears to be difficult to adequately control for this bias using typical health care (eg, claims) data.

Yearly, inactivated influenza vaccination is recommended for patients with end-stage renal disease (ESRD) by the Advisory Committee on Immunization Practices; however, few studies have described who gets the vaccine each year, or if the vaccinated population has underlying characteristics that predispose them to have better health outcomes. ESRD patients are at a particularly high risk of hospitalization, due to an increased risk of infection and cardiovascular disease, as well as a high prevalence of comorbidities (eg, diabetes). It has been shown that preventive medications and vaccinations are less likely to be administered to patients near death,[9,10] and thus hospitalization and skilled nursing care are of particular interest as both can be identified easily in health care claims data. Understanding who is vaccinated can better elucidate characteristics that differ between the vaccinated and unvaccinated populations that must be taken into account in studies of vaccine effectiveness (ie, confounding variables).

This study aimed to describe the vaccinated population of patients on hemodialysis to identify variables implicated in the healthy-user effect. We assessed demographic and health status variables and investigated how hospitalization and skilled nursing care were related to vaccination. We hypothesized that people with many hospital days or skilled nursing days each month would be less likely to be vaccinated, suggesting that time-varying measures of hospitalization and skilled nursing care may be a way of accounting for the healthy-user bias in administrative claims data.

METHODS

Study Population

We used Medicare claims obtained from the United States Renal Data System. The United States Renal Data System is a population-based, national system that collects information on all patients with ESRD in the United States. Detailed health claims are captured for all patients with Medicare as a primary payer status (ie, we excluded patients covered by a health maintenance organization or Medicare as a secondary payer). Information collected includes physician services, International Classification of Diseases, 9th rev., Clinical Modification (ICD-9-CM) codes assigned to hospitalizations and outpatient care, information on routine dialysis care, and immunization use.

Yearly cohorts were created for each influenza season from 1999 to 2005. To limit outcome misclassification, we used those years in which influenza vaccine was not easily obtained in the community, such as grocery stores and pharmacies. Our cohorts consisted of all adult, ESRD patients with Medicare as a primary payer and continuous hemodialysis use when follow-up began on September 1 of each year. Each yearly cohort consisted of patients who had initiated dialysis before October 1 of the preceding year. An 8-month window from January 1 to August 31 before the start of follow-up of each year was used to identify insurance status and comorbidities for the patients in that cohort. Patients were required to be on continuous hemodialysis for 3 months before the start of follow-up (see online figure, Supplemental Digital Content 1, http://links.lww.com/MLR/A545). For example, the cohort identified for the 1999 season would have initiated dialysis before October 1, 1998 and would have had Medicare as a primary payer from January 1 to August 31, 1999 and used continuous hemodialysis from June 1 to August 31. Hospital days, skilled nursing days, and vaccination status were assessed beginning on September 1 of each year. We performed an analysis of time to vaccination where cohort members were followed each year until they experienced a vaccination event, death, kidney transplant, loss-to-follow-up, or administrative censoring on December 31 of that year, whichever came first.

Hospitalization, Skilled Nursing Care, and Vaccination Status

Hospitalization and skilled nursing facility admission and discharge dates were assessed using the Part A—Hospitalization Medicare claims.

To identify influenza vaccinations, Medicare Part A hospital/outpatient files and Part B physician/supplier files were searched for Current Procedural Terminology codes 90724, 90656, 90658-60, the HCFA Common Procedure Coding System codes G0008 and G8482, and the ICD-9-CM procedure code 99.52.

Time-fixed Covariates

Time-fixed covariates were assessed to determine their effect on vaccination. The Centers for Medicare and Medicaid Services form 2827, the Medical Evidence Form, was used to ascertain age, race, sex, first service date with ESRD, and cause of kidney failure. The first service date was used to calculate vintage—the length of time with ESRD as of September 1 of each year. The 8-month window from January 1 to August 31 was searched for the

following co-morbidities in both Part A and Part B claims as identified in Liu et al[11]: ischemic heart disease, congestive heart failure, cerebrovascular accident/transient ischemic attack, peripheral vascular disease, other cardiac disease, chronic obstructive pulmonary disease, gastrointestinal bleeding, liver disease, dysrhythmia, cancer, and diabetes. Comorbidities were modeled as individual dichotomous variables in the final models. Adherence to dialysis was calculated using the sum of the number of dialysis sessions over the 8-month baseline period: patients were considered adherent if they had ≥ 95 sessions, which is approximately 3 sessions a week (the standard dialysis regimen) over 8 months. Patients with no recorded dialysis sessions over the 8-month period were dropped from the analysis. We also included the number of hospital days over the baseline period and controlled for an ad-hoc selection of potential frailty markers including oxygen use and use of mobility aids. Use of mobility aids were ascertained by searching Part A and Part B claims for HCFA Common Procedure Coding System equipment codes for wheelchairs, walkers, canes, and assisted bathroom equipment during the baseline period (see online table, Supplemental Digital Content 2, http://links.lww.com/MLR/A546).

Statistical Analysis

For time-fixed covariates, we used 1 Cox proportional hazards model to estimate hazard ratios (HRs)[12] comparing baseline characteristics with vaccination status. Proportional hazards were assessed by interacting each covariate with time.

For time-dependent covariates, we used 2, separate pooled logistic models with days as a time scale, which estimate discrete-time approximations[13] of cause-specific HRs[12] by comparing patients with hospital and skilled nursing days to patients without these exposures. For each exposure, we counted the number of hospital or skilled nursing days the patient had in the prior 30 days and we fit the models by categorizing the exposures into temporary (1 d), short (2–3 d), medium (4–14 d), medium-long (15–25 d), and long stays (26–30 d). We controlled for age at the start of follow-up, race, sex, cause of ESRD, vintage, adherence to dialysis, number of mobility aids, ESRD network, baseline oxygen use, total baseline hospital days, and comorbidities in all analyses. Continuous variables entered models assuming a log-linear association with vaccination.

To evaluate the impact of these time-dependent variables, we performed a sensitivity analysis to estimate vaccine effectiveness on mortality after adjusting for hospitalization and skilled nursing care. We made the following assumptions for this analysis: (1) the hypothetical cohort consisted of 100,000 people; (2) the crude vaccine effectiveness was 25%[14,15]; (3) 50% of patients were vaccinated; (4) patients who were hospitalized or had skilled nursing care were more likely to die; and (5) there was odds ratio heterogeneity between strata of confounders (ie, the association between confounder and death would vary by the number of days). We included 3 scenarios, where we varied the strength of the association between the confounders and death (denoted Odds $\text{Ratio}_{\text{Confounder}}$) from 1.1 to 10.0, stratified by the number of days. Bias adjustment was carried out using the method outlined in Rothman et al[16] (p. 350). Briefly, for each strata of hospitalization or skilled nursing care, we calculated the adjusted cell counts using the naive person counts, Odds $\text{Ratio}_{\text{Confounder}}$, and stratum-specific vaccination prevalence estimated from the study data.

Next, we calculated the stratum-specific odds ratios for the association between vaccination and death. Finally, we combined the bias-adjusted, stratum-specific odd ratios using the Mantel-Haenszel method to produce the overall, adjusted effect estimate (denoted Odds $Ratio_{Vaccination}$). Analyses were conducted using SAS 9.2 (Cary, NC), using Efron's method for tied event times.[17] This study was determined to be exempt from full review by the Institutional Review Board at the University of North Carolina at Chapel Hill.

RESULTS

There were >100,000 patients in the cohort for each year. Vaccination coverage increased from 47% to 60% over the study years. Whites had higher coverage than blacks and this difference increased throughout the study period (Table 1). In years when there was no vaccine shortage, ~75% of vaccine doses were administered by the end of October. In the 2000, 2001, and 2004 seasons most doses were not given until November; however, on average 99% of doses were given by the end of December (Fig. 1).

In the multivariable Cox proportional hazard models adjusting for time-fixed covariates, blacks and other races were less likely to be vaccinated, as well as patients with >5-day hospital stay during the baseline period. Patients on dialysis for ≥ 10 years were generally less likely to be vaccinated, although this was a small group and thus the estimates were imprecise. Older patients and patients with a high level of dialysis adherence were more likely to be vaccinated (Table 2). Most comorbidities did not strongly predict vaccination status (Table 3). These differences persisted throughout the study period.

The pooled crude vaccination rate was lowest for patients with 26–30 hospital days (2.6/1000 person-days) and for patients with 4–14 skilled nursing days (4.4/1000 person-days) (Table 4). Patients with any length of hospital stay were less likely to be vaccinated, however, the association was stronger in patients with longer stays [15–25 d: HR = 0.64 (95% CI, 0.62–0.65); 26–30 d: 0.40 (0.38, −0.42)], suggesting that recently hospitalized patients were much less likely to be vaccinated than those not in the hospital (Table 5). The estimates were similar for patients with any length of skilled nursing care stay of >1 day; these patients were also less likely to be vaccinated [26–30 d: 0.66 (0.64–0.69)]. However, we found only a weak effect for patients with 1 day of skilled nursing care [0.95 (0.86–1.04)] (Table 5). Estimates from the bias analysis implemented within a hypothetical cohort suggest that adjusting for hospitalization or skilled nursing care would weaken the vaccine effect on mortality (Table 6). For example, when adjusting for hospitalization using the more conservative confounder-disease associations from scenario 1, the odds ratio between vaccination and death moved from 0.75 to 0.83. When using more extreme confounder-disease associations in scenarios 2 and 3 the adjusted estimates moved closer to the null. The same trend was observed when adjusting for skilled nursing care.

DISCUSSION

In this population-based study of high-risk patients with ESRD, we found that patients with a recent, long-term hospital or skilled nursing facility stay were much less likely to receive an influenza vaccination. The strength of the association for long-term stays for both

variables was similar each influenza season during the 7-year study period. Elective hospitalizations were most likely represented by short stays. Patients with stays of 2–3 hospital days were most similar to those with no hospitalizations, indicating that perhaps physicians were less likely to have time to provide vaccination for those with a stay of only 1 day, and less likely to vaccinate if the patient was sick enough to require a longer stay. Patients with only 1 day of skilled nursing care were similarly likely to be vaccinated compared with patients with no skilled nursing care. The reasons for requiring skilled nursing care for only 1 day are unclear, but it may indicate an additional encounter with the health care system or that these patients were not very ill.

In a study based on medical record review, Jackson et al[8] also found that patients with poor functional status are less likely to be vaccinated. They found that adjusting for variables such as dementia, assistance bathing, assistance ambulating, and living in a nonhome setting reduced the amount of bias present in estimates of vaccine effectiveness. These variables, however, are generally not present in administrative claims data and therefore vaccine effectiveness studies that adjust for frailty have been limited to small studies using chart review. In fact, we attempted to include variables that could be proxies for functional status —use of mobility aids and home oxygen use; however, people with these conditions were slightly more likely to be vaccinated. Although the effect was not strong, it is likely that functional status may be quantified differently in patients on dialysis, as they are being seen 3 times per week regardless of their mobility or oxygen status. However, we did find similar strength of associations for vaccination status as Jackson's functional status variables, by using recent hospitalization or skilled nursing care in a time-varying manner, which may be more applicable in characterizing health status in this population. In addition, our bias analysis suggests that the estimate of vaccine effectiveness on mortality would move toward the null upon adjustment for hospitalization and skilled nursing care, similar to what Jackson found when adjusting for functional status.

It is possible that patients got vaccinated during their hospital stay without the hospital billing Medicare for the influenza vaccine, which provides an alternative explanation for the monotonic decline in vaccination rates with increasing number of hospital days above 1 day. However, data from the hospital discharge summaries from Healthcare Cost and Utilization Project indicate that hospitals rarely gave influenza vaccinations until 2004, when vaccinations began to increase.[18] This failure to offer influenza vaccine to hospitalized patients has recently been resolved—as of January 2012, the Centers for Medicare and Medicaid Services requires that all persons over the age of 6 months who are hospitalized be offered the influenza vaccine if discharged during the influenza season. Although studies using recent data would need to take this into account, we do not think that the vaccination rate in the hospital was high enough during our study period to fully explain the results observed.

Often in studies using administrative claims, the presence of comorbidities are used to characterize the health status of each patient. Although we used algorithms for co-morbidities that were developed within the population with ESRD, we found most comorbidities were not strongly associated with vaccination status, indicating that using these variables may not adequately capture the healthy-user effect. In fact, adjustment for

comorbidities in a study estimating influenza vaccine effectiveness resulted in a more biased estimate in the presence of strong unmeasured confounding.[8] Although different definitions that attempt to include disease severity may perform slightly better in controlling the healthy-user bias in the elderly population,[8] we found little difference in the associations with vaccination in the renal population. In addition, most comorbidities are assessed over a period at baseline (8 mo in our study). Therefore, having a claim for an illness at baseline would not capture acute illness, which may be a better proxy of severe frailty. Finally, it has been suggested that using ICD-9-CM comorbidity codes from administrative data may lack the sensitivity for identifying these illnesses, which can result in substantial residual confounding.[19,20]

We found persistent demographic disparities in those who received the vaccine each year. African Americans and other races consistently were less likely to be vaccinated. This disparity has been documented in the dialysis population,[14] adults with high-risk conditions,[21] and the general Medicare population.[22] Explanations for this difference include varying rates of provider recommendations and fear of getting sick/side effects from the vaccine.[23]

There were 2 additional time-fixed variables that could potentially be variables to adjust for healthy-user bias in vaccine effectiveness studies. Patients who were more adherent to their dialysis regimens were more likely to be vaccinated, whereas patients with a long vintage, and who are presumably sicker were less likely to be vaccinated. If these variables were left unadjusted, both would make the vaccine look more protective in studies of vaccine effectiveness. In comparison, age is an indicator of confounding by indication. During the years of our study, the indications for administering influenza vaccine were partially age based—the elderly were recommended to receive the vaccine. Our results paralleled this age-based recommendation where the oldest age group was more likely to be vaccinated.

Our study may have been subjected to some outcome misclassification. As with any study on influenza vaccination, it is possible that patients could have obtained the vaccine from a nonmedical establishment and paid out-of-pocket. In this case, there would not be a Medicare claim for vaccination and we could not have determined that they were vaccinated. There have been few studies that have estimated vaccination rates using data other than Medicare billing claims. Two studies have surveyed dialysis networks and estimated influenza vaccination coverage to be 74% and 76% in 1998 and 2005, respectively.[24,25] However, self-reported influenza vaccination that was administered outside of the dialysis clinics was not validated. In addition, the studies did not report the percentage of patients who were vaccinated outside the dialysis clinic; therefore, it is difficult to use these estimates as a gold standard. To limit outcome misclassification, we chose to examine years before the popularization of obtaining vaccine in groceries and pharmacies, although the later years in our study may have been affected by this trend. In addition, because influenza vaccine is covered by Medicare for our study population and patients on dialysis usually have health care encounters 2–3 times per week, we expect that the number of people who paid out-of-pocket would be low.

In summary, this analysis suggests that patients with a recent, long-term hospitalization or skilled nursing facility stay were much less likely to undergo the preventive health measure of influenza vaccination. Further work on understanding how these variables could be used to control the healthy-user bias in effectiveness studies of preventive medications is needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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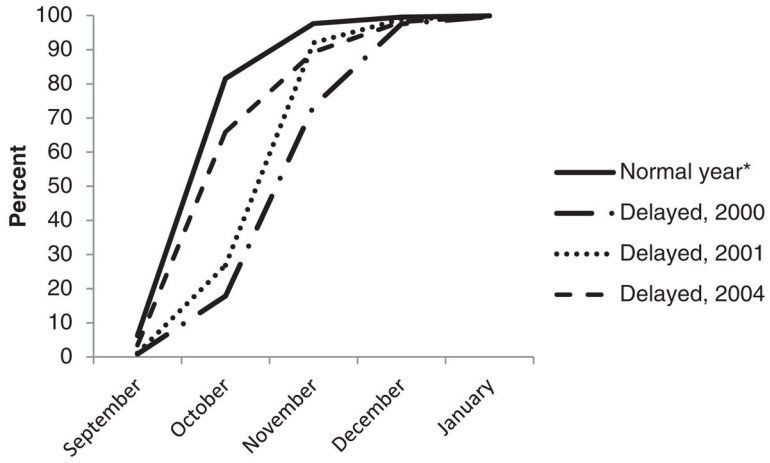

FIGURE 1.

Cumulative, administered influenza vaccine doses by month and year. *Normal year is defined as the average of 1999, 2002, 2003, and 2005.

TABLE 1

Description of Yearly Cohorts

	Percent						
Years	**1999 N = 118,659**	**2000 N = 123,241**	**2001 N = 127,954**	**2002 N = 131,179**	**2003 N = 133,154**	**2004 N = 128,847**	**2005 N = 122,671**
Mean age (SD)	62.0 (14.6)	62.3 (14.5)	62.7 (14.5)	63.0 (14.4)	63.5 (14.4)	63.8 (14.3)	64.1 (14.3)
Male sex	51.9	52.2	52.4	52.8	52.9	53.0	53.2
Race							
White	51.6	52.0	52.8	53.3	53.9	54.0	54.4
Black	43.3	42.8	41.9	41.3	40.6	40.4	39.9
Other	5.1	5.2	5.3	5.4	5.5	5.6	5.7
Cause of ESRD							
Diabetes	40.3	41.2	42.3	43.6	44.3	45.4	46.3
Hypertension	30.9	30.5	30.2	29.9	29.9	29.9	29.8
Glomerulonephritis	12.8	12.4	11.9	11.3	10.7	10.1	9.7
Cystic kidney	2.9	2.8	2.7	2.5	2.4	2.3	2.1
Other	13.2	13.0	12.9	12.7	12.7	12.3	12.1
Vintage							
0 y	2.1	2.0	2.0	1.9	1.9	2.0	1.9
1–2 y	40.8	40.5	40.1	39.7	39.2	38.6	38.0
3–4 y	25.2	25.2	25.6	26.0	25.9	26.0	26.0
5–9 y	23.1	23.4	23.4	23.4	24.0	24.3	24.6
10+	8.8	8.9	9.0	9.0	9.1	9.2	9.5
Mean hospital days (SD)	9.9 (17.3)	9.8 (17.3)	10.3 (17.9)	10.7 (18.3)	10.8 (18.4)	11.3 (18.8)	12.0 (19.4)

ESRD indicates end-stage renal disease.

TABLE 2

Adjusted* Hazard Ratios for Time-fixed Variables and Vaccination Status by Year

	HR (95% CI)							
Years	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**Pooled**
Vaccinated (%)	47.6	46.9	48.1	56.8	58.3	58.3	61.0	
Age								
18–44	1.00	1.00	1.00	1.00	1.00	1.00	1.00	
45–64	1.13 (1.10–1.16)	1.16 (1.13–1.19)	1.18 (1.15–1.22)	1.16 (1.13–1.19)	1.17 (1.14–1.20)	1.12 (1.10–1.16)	1.10 (1.07–1.13)	1.15 (1.13–1.16)
65–74	1.25 (1.22–1.29)	1.28 (1.24–1.32)	1.29 (1.25–1.33)	1.24 (1.21–1.28)	1.23 (1.19–1.26)	1.17 (1.14–1.20)	1.16 (1.13–1.20)	1.23 (1.19–1.27)
75+	1.25 (1.21–1.29)	1.31 (1.27–1.35)	1.34 (1.30–1.39)	1.26 (1.22–1.29)	1.24 (1.20–1.27)	1.22 (1.19–1.26)	1.18 (1.15–1.22)	1.25 (1.24–1.28)
Male sex	1.08 (1.06–1.10)	1.06 (1.04–1.08)	1.06 (1.04–1.08)	1.05 (1.04–1.07)	1.06 (1.04–1.07)	1.04 (1.02–1.05)	1.04 (1.02–1.05)	1.05 (1.05–1.06)
Race								
White	1.00	1.00	1.00	1.00	1.00	1.00	1.00	
Black	0.75 (0.74–0.77)	0.72 (0.71–0.74)	0.73 (0.72–0.74)	0.77 (0.76–0.79)	0.79 (0.78–0.80)	0.78 (0.77–0.79)	0.80 (0.79–0.82)	0.77 (0.76–0.77)
Other	0.88 (0.84–0.91)	0.80 (0.77–0.83)	0.83 (0.80–0.87)	0.87 (0.84–0.90)	0.93 (0.90–0.97)	0.81 (0.78–0.84)	0.87 (0.84–0.90)	0.86 (0.82–0.89)
Cause								
Diabetes	1.00	1.00	1.00	1.00	1.00	1.00	1.00	
Hypertension	0.97 (0.94–0.99)	1.00 (0.98–1.03)	1.01 (0.98–1.03)	0.99 (0.97–1.01)	0.98 (0.96–1.00)	0.99 (0.97–1.01)	0.98 (0.96–1.00)	0.99 (0.98–1.00)
Glomerulonephritis	1.00 (0.97–1.03)	1.00 (0.97–1.04)	1.03 (1.00–1.07)	1.01 (0.98–1.04)	0.99 (0.97–1.02)	0.99 (0.96–1.02)	0.98 (0.95–1.01)	1.00 (0.99–1.01)
Cystic kidney	1.05 (1.00–1.10)	1.07 (1.02–1.13)	1.04 (0.99–1.10)	1.01 (0.97–1.06)	0.99 (0.95–1.04)	1.01 (0.96–1.06)	0.99 (0.94–1.05)	1.02 (1.00–1.04)
Other	0.98 (0.95–1.01)	1.00 (0.97–1.03)	1.01 (0.98–1.04)	0.97 (0.95–1.00)	0.96 (0.94–0.99)	0.97 (0.95–1.00)	0.97 (0.94–0.99)	0.98 (0.97–0.99)
Mobility aids								
None	1.00	1.00	1.00	1.00	1.00	1.00	1.00	
1 aid	1.06 (1.02–1.10)	1.05 (1.02–1.09)	1.04 (1.00–1.07)	1.06 (1.03–1.09)	1.06 (1.03–1.09)	1.04 (1.02–1.07)	1.02 (0.99–1.05)	1.05 (1.04–1.06)
2+ aids	1.33 (1.13–1.55)	1.01 (0.84–1.21)	1.27 (1.10–1.47)	1.13 (0.98–1.29)	1.14 (1.03–1.26)	1.03 (0.94–1.12)	1.02 (0.94–1.10)	1.09 (1.05–1.14)
Vintage (y)†								
0	1.00	1.00	1.00	1.00	1.00	1.00	1.00	
1–2	0.97 (0.92–1.03)	1.03 (0.97–1.09)	0.99 (0.93–1.05)	0.98 (0.93–1.03)	1.01 (0.96–1.06)	1.07 (1.01–1.12)	0.97 (0.92–1.02)	1.00 (0.98–1.02)
3–4	0.99 (0.93–1.05)	1.03 (0.97–1.10)	0.99 (0.94–1.05)	0.98 (0.93–1.03)	0.94 (0.90–1.00)	1.09 (1.03–1.15)	1.02 (0.97–1.08)	1.00 (0.98–1.02)
5–9	0.97 (0.91–1.03)	0.99 (0.93–1.05)	0.96 (0.90–1.02)	0.97 (0.92–1.02)	1.02 (0.97–1.07)	0.95 (0.90–1.01)	0.97 (0.91–1.02)	0.98 (0.96–1.00)
10+	0.80 (0.75–0.86)	0.93 (0.87–1.00)	0.94 (0.87–1.01)	0.90 (0.84–0.96)	0.93 (0.87–0.99)	0.94 (0.88–1.00)	0.90 (0.85–0.96)	0.91 (0.88–0.93)

	HR (95% CI)							
Years	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**Pooled**
Adherence	1.42 (1.38–1.46)	1.29 (1.25–1.32)	1.47 (1.43–1.51)	1.57 (1.53–1.61)	1.51 (1.47–1.55)	1.56 (1.52–1.60)	1.58 (1.54–1.63)	1.48 (1.47–1.50)
Oxygen use	1.02 (0.99–1.06)	1.05 (1.01–1.09)	0.98 (0.94–1.03)	1.01 (0.98–1.05)	1.06 (1.02–1.09)	1.11 (1.08–1.15)	1.05 (1.02–1.08)	1.05 (1.03–1.06)
No. hospital days (d)								
None	1.00	1.00	1.00	1.00	1.00	1.00	1.00	
1–5	0.99 (0.96–1.01)	0.97 (0.94–0.99)	0.99 (0.96–1.01)	0.98 (0.96–1.00)	0.95 (0.93–0.97)	1.00 (0.98–1.02)	0.98 (0.96–1.00)	0.98 (0.97–0.99)
6–30	0.90 (0.88–0.92)	0.89 (0.87–0.91)	0.90 (0.88–0.92)	0.89 (0.87–0.90)	0.90 (0.88–0.91)	0.93 (0.91–0.94)	0.91 (0.89–0.93)	0.90 (0.90–0.91)
31+	0.77 (0.75–0.80)	0.76 (0.74–0.79)	0.78 (0.76–0.81)	0.74 (0.72–0.77)	0.78 (0.76–0.81)	0.81 (0.79–0.83)	0.80 (0.78–0.82)	0.78 (0.77–0.79)

*Adjusted for all other variables in the table, End-Stage Renal Disease Network, and baseline comorbidities.

†Vintage is defined as the length of time with end-stage renal disease as of September 1 of each year.

CI indicates confidence interval; HR, hazard ratio.

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TABLE 3

Adjusted* Association Between Comorbidities and Vaccination Status by Year

	HR (95% CI)							
Years	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**Pooled**
IHD	1.04 (1.02–1.06)	1.06 (1.04–1.08)	1.04 (1.02–1.06)	1.04 (1.02–1.06)	1.05 (1.03–1.07)	1.03 (1.02–1.05)	1.04 (1.03–1.06)	1.04 (1.03–1.05)
CHF	0.96 (0.94–0.98)	0.98 (0.96–1.00)	0.96 (0.94–0.98)	0.94 (0.92–0.96)	0.96 (0.94–0.97)	0.95 (0.94–0.97)	0.96 (0.94–0.97)	0.96 (0.95–0.97)
TIA	0.95 (0.92–0.97)	0.94 (0.91–0.96)	0.94 (0.92–0.96)	0.94 (0.92–0.96)	0.93 (0.91–0.95)	0.95 (0.93–0.97)	0.92 (0.90–0.94)	0.94 (0.93–0.95)
PVD	1.00 (0.98–1.02)	0.99 (0.97–1.01)	0.99 (0.97–1.01)	0.97 (0.96–0.99)	0.97 (0.96–0.99)	0.97 (0.96–0.99)	0.96 (0.94–0.97)	0.98 (0.97–0.98)
Other CD	1.02 (0.99–1.04)	1.00 (0.98–1.02)	1.01 (0.99–1.03)	0.99 (0.97–1.00)	1.02 (1.01–1.04)	1.02 (1.00–1.04)	1.00 (0.98–1.01)	1.01 (1.00–1.01)
Liver disease	0.88 (0.85–0.91)	0.95 (0.91–0.99)	0.93 (0.89–0.97)	0.95 (0.92–0.98)	1.00 (0.97–1.03)	1.04 (1.00–1.07)	1.03 (1.00–1.06)	0.97 (0.96–0.99)
COPD	1.00 (0.97–1.02)	1.00 (0.98–1.03)	1.00 (0.98–1.02)	1.01 (0.99–1.03)	1.00 (0.98–1.02)	1.00 (0.98–1.02)	0.99 (0.97–1.01)	1.00 (0.99–1.01)
GI bleed	0.99 (0.96–1.02)	1.03 (1.00–1.06)	0.98 (0.95–1.01)	0.98 (0.95–1.00)	0.94 (0.91–0.96)	1.00 (0.97–1.02)	0.95 (0.93–0.98)	0.98 (0.97–0.99)
Dysrhythmia	0.99 (0.97–1.02)	1.00 (0.98–1.03)	1.00 (0.98–1.02)	1.00 (0.98–1.02)	0.98 (0.96–1.00)	1.01 (0.99–1.03)	0.99 (0.97–1.01)	1.00 (0.99–1.00)
Cancer	1.03 (0.99–1.06)	1.04 (1.00–1.07)	1.05 (1.02–1.08)	1.02 (0.99–1.05)	1.02 (0.99–1.05)	1.02 (0.99–1.05)	1.02 (1.00–1.05)	1.03 (1.02–1.04)
Diabetes	1.02 (1.00–1.05)	1.04 (1.01–1.06)	1.04 (1.02–1.07)	1.02 (1.00–1.04)	1.01 (0.99–1.03)	0.99 (0.97–1.03)	0.98 (0.96–1.00)	1.01 (1.00–1.02)

*Adjusted for all other comorbidities in the table, End-Stage Renal Disease Network, and all other time-fixed covariates.

CD indicates cardiac disease; CHF, congestive heart failure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; GI, gastrointestinal; HR, hazard ratio; IHD, ischemic heart disease; PVD, peripheral vascular disease; TIA, transient ischemic attack/cerebrovascular accident.

TABLE 4

Pooled, Crude Vaccination Rate by Categories of Hospital and Skilled Nursing Days

	Rate Per 1000 Person-Days
Hospital days	
None	7.2
1	3.9
2–3	6.5
4–14	6.1
15–25	4.5
26+	2.6
Skilled nursing days	
None	7.0
1	10.9
2–3	6.6
4–14	4.4
15–25	5.0
26+	6.2

TABLE 5

Adjusted* Assessment of Hospitalization and Skilled Nursing Care as Time-varying Predictors of Vaccination

	HR (95% CI)							
Years	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**Pooled**
Hospital days (d)								
None	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
1	0.91 (0.83–1.01)	0.80 (0.73–0.87)	0.83 (0.76–0.91)	0.82 (0.75–0.89)	0.84 (0.77–0.91)	0.79 (0.72–0.86)	0.85 (0.79–0.93)	0.83 (0.81–0.86)
2–3	0.95 (0.91–1.00)	0.96 (0.92–1.00)	0.95 (0.91–0.99)	0.93 (0.89–0.97)	0.91 (0.88–0.95)	0.90 (0.87–0.94)	0.95 (0.91–0.98)	0.93 (0.92–0.95)
4–14	0.84 (0.81–0.87)	0.84 (0.81–0.87)	0.79 (0.77–0.82)	0.87 (0.84–0.89)	0.86 (0.84–0.88)	0.85 (0.83–0.88)	0.83 (0.81–0.85)	0.84 (0.83–0.85)
15–25	0.59 (0.54–0.64)	0.61 (0.56–0.66)	0.62 (0.58–0.67)	0.68 (0.64–0.73)	0.64 (0.60–0.68)	0.66 (0.62–0.70)	0.62 (0.58–0.66)	0.64 (0.62–0.65)
26–30	0.35 (0.30–0.41)	0.31 (0.26–0.37)	0.30 (0.26–0.35)	0.41 (0.36–0.46)	0.42 (0.37–0.47)	0.47 (0.42–0.53)	0.42 (0.38–0.47)	0.40 (0.38–0.42)
SNF days (d)								
None	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
1	0.62 (0.40–0.96)	0.87 (0.67–1.13)	0.52 (0.38–0.72)	0.96 (0.78–1.19)	1.07 (0.83–1.38)	1.23 (1.00–1.52)	0.98 (0.80–1.19)	0.95 (0.86–1.04)
2–3	0.58 (0.42–0.80)	0.67 (0.53–0.83)	0.67 (0.55–0.82)	0.58 (0.48–0.70)	0.62 (0.52–0.73)	0.72 (0.59–0.88)	0.67 (0.56–0.80)	0.65 (0.60–0.70)
4–14	0.64 (0.58–0.71)	0.61 (0.55–0.67)	0.64 (0.58–0.70)	0.66 (0.60–0.71)	0.67 (0.62–0.72)	0.71 (0.66–0.76)	0.65 (0.61–0.70)	0.66 (0.64–0.68)
15–25	0.63 (0.56–0.72)	0.55 (0.48–0.62)	0.61 (0.54–0.67)	0.66 (0.60–0.72)	0.63 (0.58–0.69)	0.68 (0.63–0.74)	0.65 (0.60–0.70)	0.64 (0.62–0.66)
26–30	0.68 (0.59–0.78)	0.59 (0.52–0.67)	0.55 (0.49–0.62)	0.67 (0.61–0.74)	0.61 (0.56–0.67)	0.72 (0.66–0.78)	0.72 (0.67–0.78)	0.66 (0.64–0.69)

*Adjusted for age, race, sex, cause of end-stage renal disease, vintage, adherence, mobility aids, End-Stage Renal Disease Network, oxygen use, baseline hospital days, and comorbidities.

CI indicates confidence interval; HR, hazards ratio; SNF, skilled nursing facility.

TABLE 6

Hypothetical Scenarios of the Effect of Vaccination on Death, Adjusting for Hospitalization and Skilled Nursing Care

	Odds Ratio$_{Confounder}$*					Odds Ratio$_{Vaccination}$†
	1 d	2–3 d	4–14 d	15–25 d	26+ d	
Hospitalization						
Crude						0.75
Scenario 1	1.3	1.4	1.8	2.0	3.0	0.83
Scenario 2	1.2	1.5	2.4	2.7	3.5	0.85
Scenario 3	1.1	1.6	3.0	3.5	4.0	0.86
Skilled nursing care						
Crude						0.75
Scenario 1	1.3	1.4	2.0	4.0	6.0	0.79
Scenario 2	1.2	1.5	4.0	6.0	8.0	0.81
Scenario 3	1.1	1.6	6.0	8.0	10.0	0.83

*Odds ratio for the association between the confounder and death.

†Odds ratio for the association between vaccination and death.