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Mortality of Dialysis Patients According to Influenza and Pneumococcal Vaccination Status

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Background: Data from an immunocompromised subpopulation in which both vaccine recipients and nonrecipients have frequent opportunities for vaccination can help determine the associations between vaccination against seasonal influenza and pneumococcal disease and all-cause mortality.

Study Design: We surveyed dialysis centers and performed a retrospective analysis of health status at dialysis therapy initiation, vaccination for influenza and pneumococcal disease, laboratory results, and mortality associated with the 2005-2006 influenza season for patients in 3 End-Stage Renal Disease Networks across the United States.

Setting & Participants: Of 1,033 dialysis facilities considered, 903 centers with a total patient population of 54,734 reported vaccination data. Analysis was limited to 36,966 patients on dialysis treatment for at least 1 year as of December 31, 2005.

Predictor: Vaccination status.

Outcomes: OR for all-cause mortality (vaccinated vs unvaccinated patients).

Results: The estimated adjusted OR for mortality was significantly less than 1.0 for patient who received either vaccination and was lower for patients who had received both vaccinations than for those who had received either. Survival analysis confirmed these findings.

Limitations: Possible misclassification due to self-report of vaccination for some patients. Lack of vaccination date.

Conclusions: Vaccination against influenza and pneumococcal disease is associated with improved survival in dialysis patients. The 2 vaccinations have independent effects on mortality.
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INDEX WORDS: Seasonal influenza; pneumococcal disease; vaccine; immunization practices; end-stage renal disease (ESRD).

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Unlike most community-dwelling patient populations, most patients with end-stage renal disease (ESRD) have frequent exposure to health care providers, in the form of hemodialysis sessions approximately thrice weekly. This frequent interaction permits repeated opportunities to deliver preventive care. Because patients with ESRD have a significantly higher adjusted mortality rate than the average population, 192.8 per 1,000 patient-years for this population with a mean age of approximately 60 years,[1] they are prioritized for immunization against vaccine-preventable diseases, including hepatitis B, pneumococcal disease, and seasonal influenza.[2-4] The aim of this study was to determine for the 2005-2006 influenza season whether dialysis patients who received influenza vaccination, vaccination against pneumococcal disease, or both had lower mortality.

METHODS

The patient population for this study included hemodialysis and peritoneal dialysis patients in ESRD Networks 6 (North Carolina, South Carolina, and Georgia), 11 (Michigan, Minnesota, North Dakota, South Dakota, and Wisconsin), and 15 (Arizona, Colorado, Nevada, New Mexico, Utah, and Wyoming). These 3 Networks, which serve more than 65,000 patients in 1,033 dialysis facilities, collected the data used here as part of an ad hoc working group, the Safe and Timely Immunization Coalition (STIC). STIC, a consortium of administrators from these 3 Networks and representatives of large dialysis providers, nursing groups, quality improvement organizations, patient groups, and Emory University, was convened to coordinate efforts to increase immunization rates.

Patients were eligible for inclusion in this assessment if they had been receiving dialysis for at least 1 year as of December 31, 2005 (Fig 1). Individual patient baseline data were available through each patient's ESRD initiation form (Centers for Medicare & Medicaid Services [CMS] 2728). The annual ESRD facility survey (CMS 2744) was used to specify facility characteristics. Death and cause of death information through December 31, 2006, was

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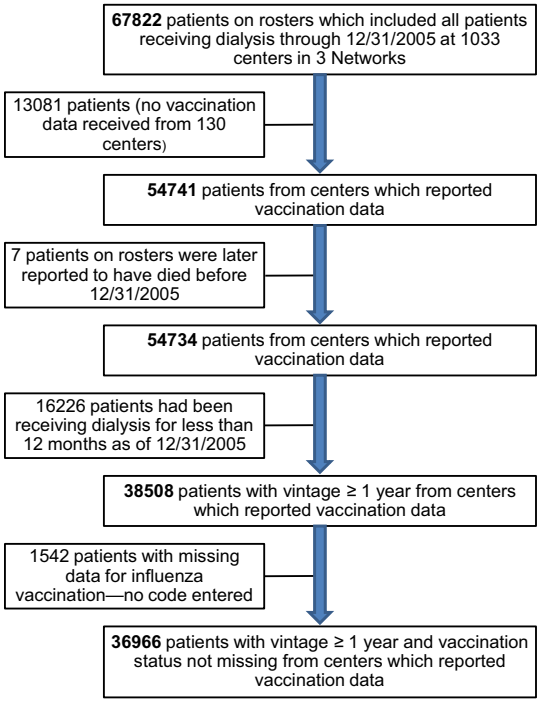

Figure 1. Study flow: patient inclusion and exclusion.

collected through the ESRD death notification form (CMS 2746). We excluded patients with missing vaccination data for the 2005-2006 influenza season from the analysis.

Monthly laboratory data for albumin, hemoglobin, and Kt/V (a urea-based measure of dialysis adequacy) for the 3-month vaccination period (October-December) came from electronic records at each center. All tests were conducted as part of routine patient care. Mean values for each test were calculated over the 3 months if at least 1 value was available for a given test. Patients' values were recorded as in or out of range based on contemporary guidelines (albumin ≥4.0 mg/dL, hemoglobin ≥10 mg/dL, and Kt/V ≥1.7). Patients with all laboratory data missing for a given month were documented as "missing" for that month; an integer (count) variable was included in each model for the number of months with missing laboratory values as a proxy for quality of dialysis care.

The participating ESRD Networks conducted a survey to collect vaccination data for each patient in each center. Both influenza vaccination (received 2005-2006 vaccination) and vaccination against pneumococcal disease (ever vaccinated) were available. Patients were considered vaccinated against influenza if they were recorded as having been vaccinated within the treatment center or reported vaccination was "received at another location." Otherwise patients were considered unvaccinated against influenza. Status of pneumococcal vaccination was provided as recorded in each patient's chart or vaccination record at their dialysis center.

Patient characteristics by vaccination status were compared by χ^2 tests (categorical variables) and analysis of variance tests (continuous variables). The likelihood of mortality was assessed by multivariable logistic regression controlling for patient age, race, sex, time on dialysis (vintage), modality (hemodialysis, continuous cyclic peritoneal dialysis, or continuous ambulatory peritoneal dialysis), diabetes as primary cause of ESRD (yes or no), comorbid conditions at dialysis therapy initiation (congestive heart failure, cerebrovascular disease, peripheral vascular disease, history of hypertension, chronic obstructive pulmonary disease, and malignant neoplasm), and mean monthly patient laboratory values for albumin, hemoglobin, and Kt/V during the 3-month influenza vaccination period. These characteristics and all possible interaction terms for patient demographics—age, race, sex, time on dialysis (vintage), modality, and diabetes as cause of ESRD—were included in the multivariable models. Models also controlled for the effect of center (to account for confounding due to unmeasured dialysis facility characteristics) by including a fixed-effect term for center in a maximum likelihood model (SAS, version 9.2, www.sas.com) for all centers with a patient population of 20 or more. (Patients from smaller centers were assigned a "missing" value for center code, but were included in the analysis.).

A survival analysis also was conducted to examine the association of mortality with vaccination over the course of the year. The survival analysis was run in PROC PHREG (SAS, version 9.2) and performed under the assumption that the benefits of influenza vaccination take effect on the last day of 2005 and no influenza cases are present before the first day of 2006. This was necessary because influenza vaccination date is not known. Some patients may have been vaccinated in early 2006.

Sensitivity analyses were conducted to explore: (1) whether excluding patients with influenza vaccination status listed as "UNKNOWN, not known by patient" affected estimate odds ratios (ORs), (2) whether herd immunity was influential, and (3) how altering the observation period influenced observed outcomes. The first sensitivity analysis was conducted because the high observed death rate for "UNKNOWN, not known by patient" suggests that it was the default category for patients who died or discontinued dialysis therapy between December 31, 2005, and the time the survey was filled out. Altering the observation period allowed exploration of healthy vaccine recipient bias.

Cause of death was investigated for patterns related to infection (vs cardiac-related death and other deaths).

This was an analysis of data only, performed for the STIC coalition under a data use agreement with Emory. Institutional review board approval was not required or sought.

RESULTS

Of patients who had been receiving dialysis since at least January 1, 2005, a total of 41.8% were vaccinated against influenza during the 2005-2006 season and also had been vaccinated against pneumococcal disease. Compared with patients who had received neither vaccine, dual recipients were significantly less likely to be black (37.9% vs 57.6%), older on average, and more likely to receive hemodialysis (rather than peritoneal dialysis; Table 1). They also had generally worse baseline health status, evidenced by differences in rates of comorbid conditions at the time of dialysis therapy initiation: congestive heart failure, cardiovascular disease, peripheral vascular disease, history of hypertension (influenza only), diabetes, chronic obstructive pulmonary disease, and malignant neoplasm. Patients who had received vaccinations had better laboratory values for 3-month mean hemoglobin and Kt/V. They also were less likely to miss blood draws for their laboratory tests.

Of 36,966 patients who met the inclusion criteria, 6,309 (17.1%) died (Table 2). Mortality rates included substantial variability within groups (vaccinated and unvaccinated). For example, patients who were docu-