Plotting Daily Incidence of Influenza Vaccine Reactions Among Patients With End-Stage Renal Disease to Inform Study Design Decisions

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DISCLOSURES

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BACKGROUND

- Evaluation of incident outcomes for analyses following initiation of a treatment or receipt of a vaccine requires excluding patients with prevalent disease.
- The appropriate length of the lookback/washout periods to identify prevalent disease may vary depending on the outcome.
  - Chronic conditions may require all available data.
  - Acute conditions or potentially recurring conditions may require shorter periods.
- Patients with end-stage renal disease (ESRD) are medically complex and may have unique patterns of health care utilization that influence when diagnoses of minor conditions are recorded in health care records.
  - These patterns may influence the appropriate length of lookback/washout periods.

OBJECTIVE

- To inform decisions about the length of prevaccination lookback/washout periods, we investigated the daily incidence of diagnoses of adverse events relative to the date of vaccination in patients with ESRD receiving in-center hemodialysis.

METHODS

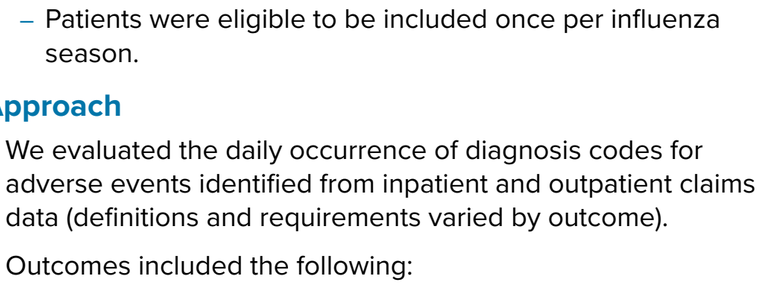
Data Source and Population

- Patients aged ≥ 65 years with ESRD receiving hemodialysis were identified in the United States Renal Data System from 2010 through 2016.[1]
- We identified individuals at their first standard-dose or high-dose influenza vaccine each influenza season (from August 1 to the end of the influenza season, as defined by the Centers for Disease Control and Prevention).
  - Patients were eligible to be included once per influenza season.

Approach

- We evaluated the daily occurrence of diagnosis codes for adverse events identified from inpatient and outpatient claims data (definitions and requirements varied by outcome).
- Outcomes included the following:
  - Serious events: anaphylaxis, angioedema, seizure, encephalopathy, Guillain-Barré syndrome
  - Milder events: urticaria/hives, rash, pain in limb, cellulitis, myalgia/myositis, any fever, any diarrhea, any nausea and vomiting, and syncope
  - Secondary events: composite gastrointestinal, composite hypersensitivity, hospitalized fever, hospitalized diarrhea, hospitalized nausea/vomiting
- We plotted daily incidence rates of recorded diagnoses relative to vaccination date:
  - Ranging from 180 days before to 180 days after vaccination
  - Multiple diagnoses per patient permitted

Figure 1. Study Design and Variable Assessment Windows Relative to Vaccination Date



[a] Defined as treatment modality as in-center hemodialysis, with institutional claims covering at least 67% of enrolled days.

[b] First occurrence of one of the following events: 180 days after vaccination, death, disenrollment from Medicare part A or B, end of the study period (December 31, 2016), switch to peritoneal dialysis, or receipt of a kidney transplant.

Note: Figure template available at http://www.repeatinitiative.org.

RESULTS

- We identified 520,876 vaccinations from 216,843 unique patients.
  - Mean age, 74.7 years (standard deviation, 7.0); 50.5% male; 63.2% white race
- Daily incidence rates of many outcomes exhibited clear periodicity relative to the day of vaccination, corresponding to regular health care interactions among patients with ESRD.
  - 2- to 3-day periods (corresponding to thrice-weekly in-center hemodialysis sessions)
    - Pain in limb (Figure 2), rash, angioedema, any diarrhea
  - Weekly periods
    - Syncope, seizure (Figure 3)
  - Monthly periods (corresponding to monthly comprehensive physician encounters)
    - Anaphylaxis, cellulitis, myalgia/myositis, any fever, and any nausea/vomiting (Figure 4)
- In contrast, no periodicity was observed in plots of outcomes requiring hospitalization (e.g., encephalopathy, secondary outcomes of hospitalized fever, hospitalized nausea/vomiting, hospitalized diarrhea) (Figure 5).

Figure 2. Two- to Three-Day Periodicity in the Daily Incidence Rate of Diagnosis Codes for Pain in Limb

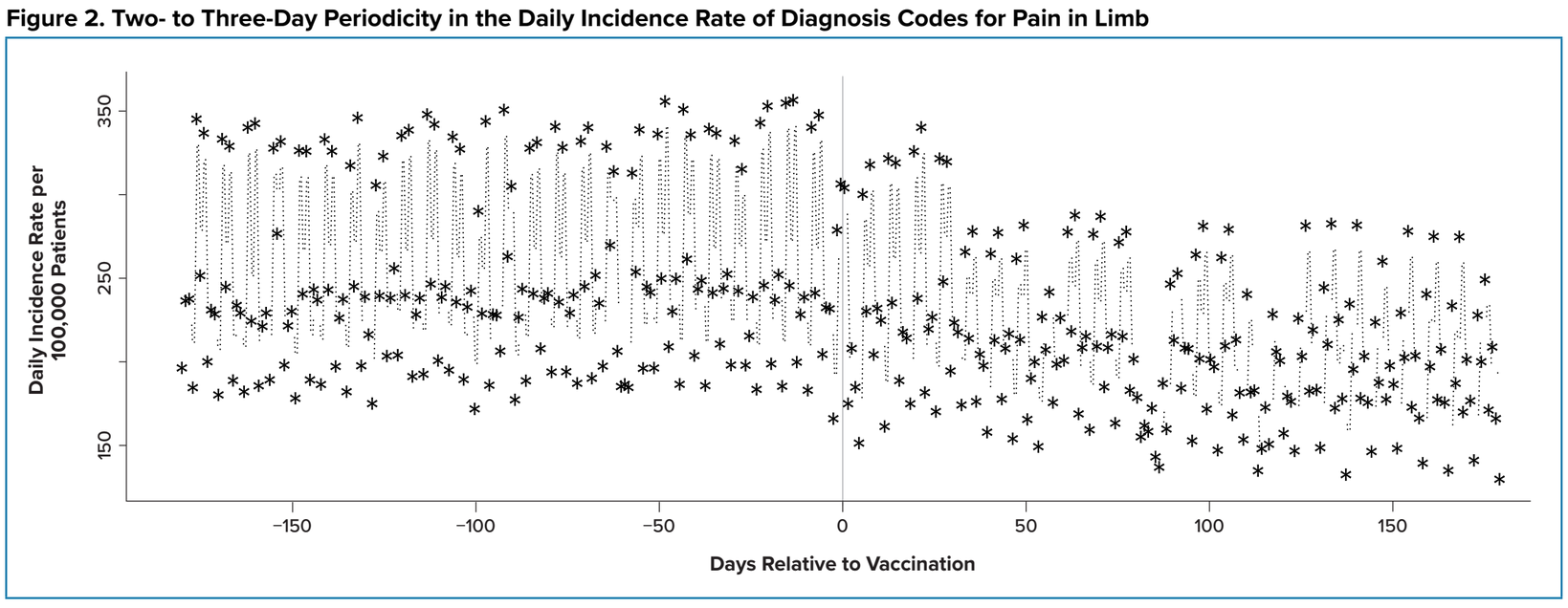


Figure 3. Weekly Periodicity in the Daily Incidence Rate of Diagnosis Codes for Seizure

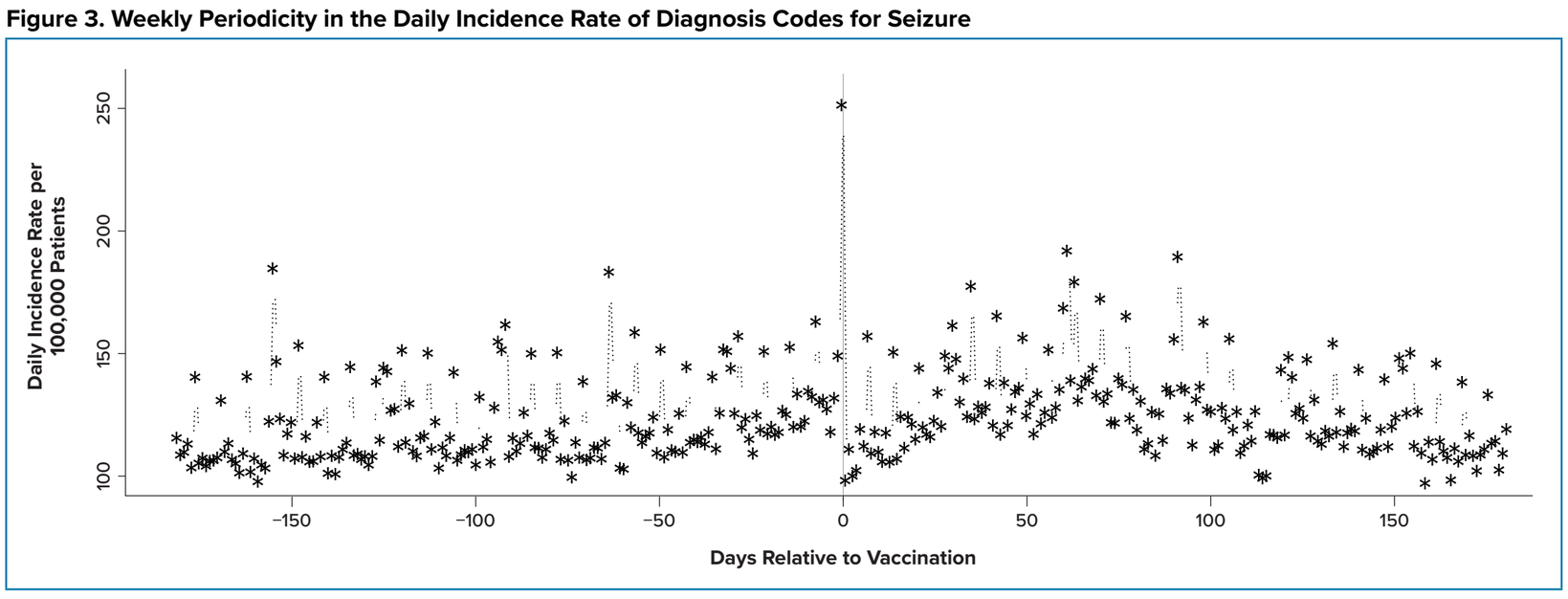


Figure 4. Monthly Periodicity in the Daily Incidence Rate of Diagnosis Codes for Nausea/Vomiting in Any Setting

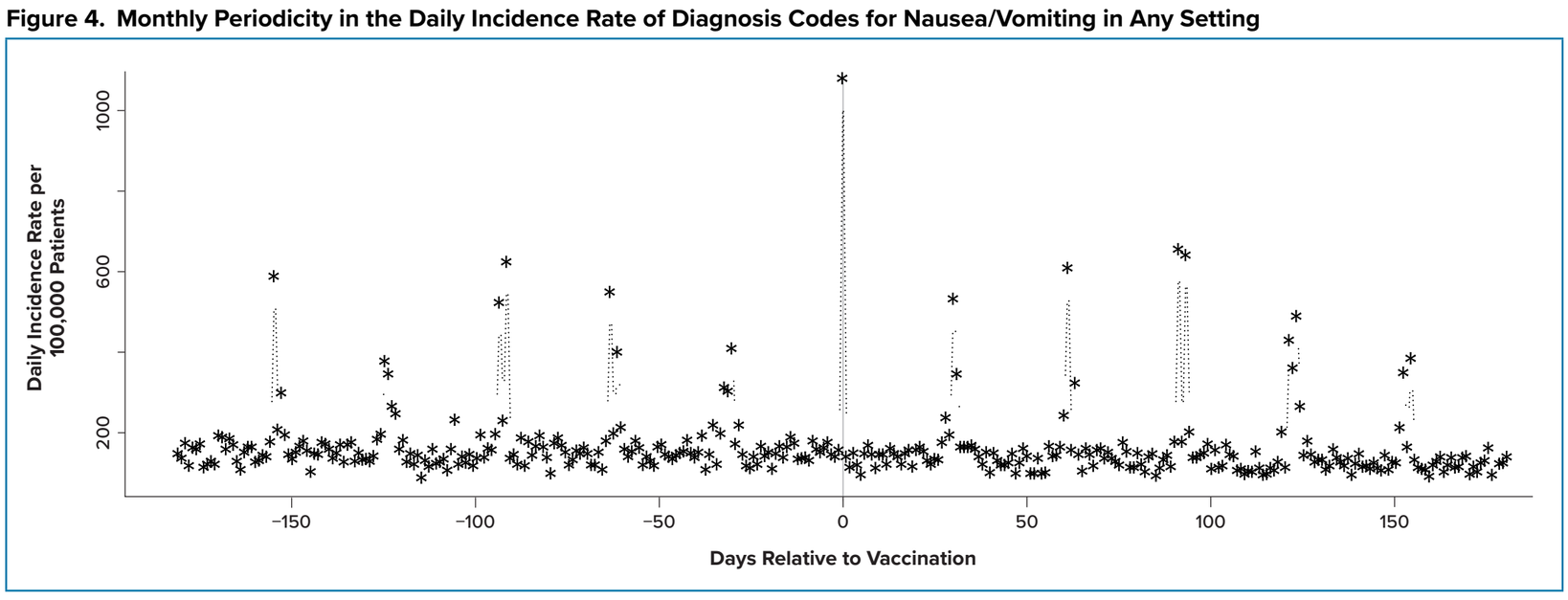
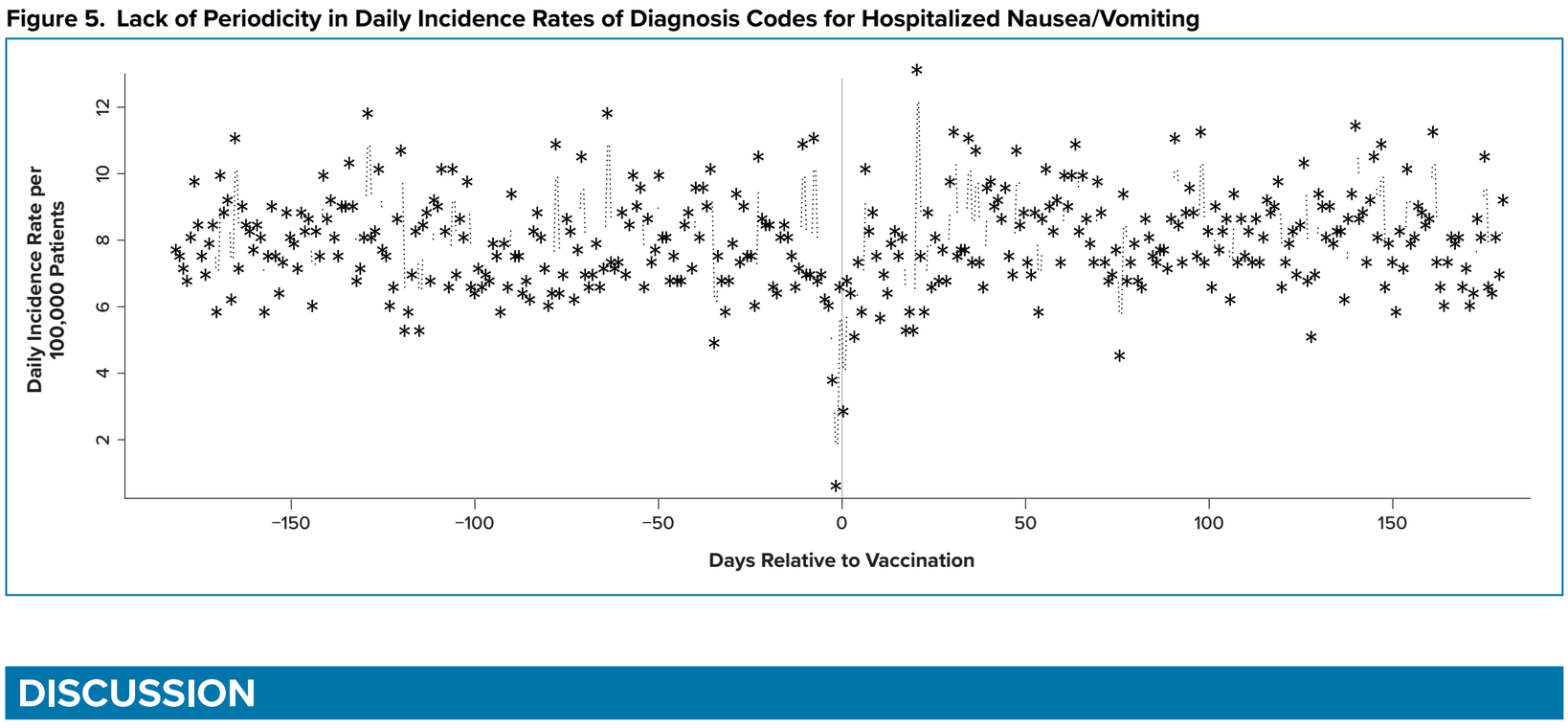


Figure 5. Lack of Periodicity in Daily Incidence Rates of Diagnosis Codes for Hospitalized Nausea/Vomiting



DISCUSSION

- Patients with ESRD had regular patterns of diagnosis codes relative to the date of influenza vaccination, suggesting that influenza vaccination was administered during a regularly occurring, routine health care encounter.
- Diagnoses for recurrent, minor, or sustained conditions may be routinely recorded at regularly occurring health care encounters, including the encounter where the vaccination was received, rather than at separate encounters.
  - Some patient populations, such as those with ESRD, may have predictable patterns of health care utilization (e.g., in-center hemodialysis sessions every 2-3 days, weekly physician encounters, and monthly comprehensive nephrologist encounters).
  - These patterns of health care utilization may result in recording of diagnoses at predictable time points.
- Hospitalized outcomes did not exhibit the same periodicity, presumably as hospitalizations do not follow regularly scheduled, recurrent patterns like hemodialysis sessions or outpatient physician encounters.
- Study design decisions should reflect the underlying patterns of health care utilization.
  - For example, in a subsequent study using these data, washout periods of 42 days before vaccination were used for acute events to ensure capture of monthly or weekly diagnoses of existing disease.

CONCLUSION

- Certain study decisions, such as the duration of baseline washout windows and outcome ascertainment windows or the inclusion of the vaccination date in the follow-up window, should account for diagnostic patterns in special populations, such as those with ESRD receiving hemodialysis, with regular patterns of health care utilization.

Reference

1. US Renal Data System. 2019 USRDS annual data report: Epidemiology of kidney disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases 2019. Available at: https://www.usrds.org/adr.aspx. Accessed 14 July 2020.

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