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Relationships Between Community Virus Activity and Cardiorespiratory Rehospitalizations From Post-Acute Care

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Abstract

Objectives: Quantify the relationship between increasing influenza and respiratory syncytial virus (RSV) community viral activity and cardiorespiratory rehospitalizations among older adults discharged to skilled nursing facilities (SNFs).

Design: Retrospective cohort.

Setting and Participants: Adults aged ≥ 65 years who were hospitalized and then discharged to a US SNF between 2012 and 2015.

Methods: We linked Medicare Provider Analysis and Review claims to Minimum Data Set version 3.0 assessments, PRISM Climate Group data, and the Centers for Disease Control and Prevention viral testing data. All data were aggregated to US Department of Health and Human Services regions. Negative binomial regression models quantified the relationship between increasing viral activity for RSV and 3 influenza strains (H1N1pdm09, H3N2, and B) and cardiorespiratory rehospitalizations from SNFs. Incidence rate ratios described the relationship

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between a 5% increase in circulating virus and the rates of rehospitalization for cardiorespiratory outcomes. Analyses were repeated using the same model, but influenza and RSV were considered “in season” or “out of season” based on a 10% positive testing threshold.

Results: Cardiorespiratory rehospitalization rates increased by approximately 1% for every 5% increase in circulating influenza A(H3N2), influenza B, and RSV, but decreased by 1% for every 5% increase in circulating influenza A(H1N1pdm09). When respiratory viruses were in season (vs out of season), cardiorespiratory rehospitalization rates increased by approximately 6% for influenza A(H3N2), 3% for influenza B, and 5% for RSV, but decreased by 6% for influenza A(H1N1pdm09).

Conclusions and Implications: The respiratory season is a particularly important period to implement interventions that reduce cardiorespiratory hospitalizations among SNF residents. Decreasing viral transmission in SNFs through practices such as influenza vaccination for residents and staff, use of personal protective equipment, improved environmental cleaning measures, screening and testing of residents and staff, surveillance of viral activity, and quarantining infected individuals may be potential strategies to limit viral infections and associated cardiorespiratory rehospitalizations.

Keywords

Hospitalization; influenza A virus; influenza B virus; respiratory syncytial virus

Influenza and respiratory syncytial virus (RSV) are responsible for substantial morbidity and mortality in older adults and can lead to cardiorespiratory sequelae. These sequelae include incident adverse cardiovascular events and exacerbations of underlying chronic illnesses like heart failure (HF), chronic obstructive pulmonary disease (COPD), and asthma.¹⁻³ Older adults hospitalized and then discharged to skilled nursing facilities (SNFs) may be particularly susceptible to adverse cardiorespiratory outcomes for at least 2 reasons: (1) those requiring SNF care are more physiologically vulnerable, multimorbid, and functionally impaired than those discharged elsewhere,⁴ which collectively contribute to the most severe consequences of viral infections, and (2) the SNF environment presents a higher risk for influenza and RSV infection because these are institutional settings with spaces shared with more people, including other residents and staff. Although hospital readmissions during the post-acute period are already common among older adults in SNFs,⁵ there may be added risk of cardiorespiratory rehospitalizations when community levels of circulating influenza and RSV are highest because staff, visitors, and new SNF admissions are more likely to introduce viruses into the SNF setting, which may subsequently precipitate cardiorespiratory events. However, little is known about these relationships.

Therefore, we sought to examine the association between circulating influenza and RSV and cardiorespiratory rehospitalizations among older adults discharged to SNFs. We hypothesized that the rate of cardiorespiratory rehospitalizations would increase with greater levels of circulating influenza and RSV.

Methods

Data Sources

This study linked data from multiple national data sets. Medicare Provider Analysis and Review claims supplied information on inpatient admissions and readmission diagnoses, whereas Minimum Data Set version 3.0 assessments identified and SNF claims verified that participants were receiving post-acute care under the SNF benefit following the index hospitalization. The Medicare Master Beneficiary Summary File provided demographic information. We ascertained mean weekly temperatures through PRISM Climate Group data⁶ and used Centers for Disease Control and Prevention testing data to identify the weekly percentage of specimens testing positive for influenza A(H1N1) pandemic 2009 (pdm09), influenza A(H3N2), influenza B, and RSV. All data were aggregated to US Department of Health and Human Services (HHS) regions (Supplementary Table 1). The study protocol received institutional review board approval. Because of the use of deidentified administrative data, informed consent was not required.

Study Design

We derived our retrospective cohort from more than 10 million US SNF stays across 3 respiratory seasons between 2012 and 2015. Each year started on *Morbidity and Mortality Weekly Report (MMWR)* week 27 and ended on week 26.⁷ Eligible participants had 12 months of continuous enrollment in Medicare Part A immediately before the index date, were 65 years at the index date, and entered an SNF within 5 days of discharge from the index hospitalization with any principal diagnosis. Index dates were assigned as the date of hospital discharge. We excluded beneficiaries with an index hospitalization from a psychiatric or long-term care hospital, cancer diagnosis based on primary discharge diagnosis (defined by Clinical Classifications Software single-level diagnosis categories 11–47),⁸ discharge to an SNF located in Puerto Rico or the Virgin Islands, or missing data on any covariate used in analyses. Follow-up occurred from index date until rehospitalization, SNF discharge, Medicare Part A disenrollment, death, day 100 of follow-up (the maximum post-acute length of stay), or the study period end, whichever occurred first. The residents' first rehospitalization within 99 days of follow-up was identified. Participants could have multiple index hospitalizations per season, where rehospitalizations could also serve as index hospitalizations, and could reenter in subsequent seasons if eligibility criteria were met.

We examined rehospitalizations for cardiorespiratory causes, acute myocardial infarction (AMI), HF, COPD, and asthma. Hospital readmission diagnoses were identified by the presence of an *International Classification of Diseases, Ninth Revision*, diagnosis code in the principal position on the inpatient claim (Supplementary Table 2).

Statistical Methods

We quantified the relationships between increasing influenza and RSV viral activity and cardiorespiratory rehospitalizations by fitting negative binomial regression models. Candidate models were fit and compared, and the final model was selected based on the Akaike Information Criteria (AIC) (Supplementary Material). Our final model contained

polynomial terms for time trends; annual sine and cosine harmonic terms; proportion of residents age ≥ 75 years, proportion of White residents, and proportion of male residents in each HHS region; HHS region fixed effects; average weekly temperature in each HHS region; and 2-week lagged viral terms for percentage weekly influenza (H1N1pdm09, H3N2, and B) and RSV specimens testing positive in each HHS region (Supplementary Figure 1). Time in the SNF was aggregated into *MMWR*-defined person-weeks and included as an offset term of the natural log-transformed number of person-weeks at risk in a specific HHS region.

The model's outcome consisted of the frequency of specific readmission outcomes during a given week. Coefficient estimates were incidence rate ratios (IRRs) representing the relative change in rehospitalization rates. We reported IRRs with 95% CIs to describe the relationship between community RSV and influenza (H1N1pdm09, H3N2, B) viral activity and the rates of rehospitalization for 5 cardiorespiratory outcomes (cardiorespiratory causes, AMI, HF, COPD, and asthma). Analyses were conducted using 2 viral activity definitions: (1) as a continuous measure for percentage weekly influenza and RSV specimens testing positive in each HHS region (scaled to a 5% increase in viral activity to be more easily interpretable) and (2) as a binary measure classifying influenza and RSV as "in season" vs "out of season" based on a 10% positive testing threshold. We chose to include the proportion of specimens testing positive for each viral strain and a 10% positive testing threshold (ie, "in season" if $>10\%$ of specimens collected tested positive for the viral strain) as these measures have traditionally been used by the Centers for Disease Control and Prevention to define respiratory seasons.^{9,10} Data were analyzed using SAS, version 9.4 (SAS Institute, Inc), and R version 3.5.1 (R Foundation for Statistical Computing) using the package *flumodelr*.¹¹

Results

Study Cohort

Our study cohort included 5,053,231 SNF stays (Supplementary Figure 2). Overall, 3,773,410 (74.7%) stays included participants ≥ 75 years, 1,857,982 (36.8%) included male residents, and 4,394,151 (87.0%) included White, non-Hispanic residents (Table 1). Participant demographics and person-time contributions differed slightly by HHS region. Overall, there were 621,739 readmissions for cardiorespiratory causes, 25,673 for AMI, 138,472 for HF, 40,722 for COPD, and 6178 for asthma (Supplementary Table 3).

Influenza and RSV Association With Rehospitalization

Nationally, influenza A(H3N2) was the predominant influenza strain in the 2012–2013 and 2014–2015 seasons, whereas influenza A(H1N1pdm09) was predominant in the 2013–2014 season (Supplementary Figure 3). During the study period, cardiorespiratory rehospitalizations displayed well-defined seasonality (Supplementary Figure 4). Seasonal trends in rehospitalization rates were more apparent for HF and COPD compared to AMI or asthma (Supplementary Figures 5–8). Cardiorespiratory readmission rates increased by approximately 1% for every 5% increase in circulating influenza A(H3N2) (IRR 1.012, 95% CI 1.008–1.016), influenza B (IRR 1.014, 95% CI 1.008–1.020), and RSV (IRR

1.013, 95% CI 1.009–1.018), but decreased by 1% for every 5% increase in circulating influenza A(H1N1pdm09) (IRR 0.990, 95% CI 0.984–0.996) (Figure 1). When respiratory viruses were in season (vs out of season), cardiorespiratory rehospitalization rates increased by approximately 6% for influenza A(H3N2) (IRR 1.057, 95% CI 1.041–1.074), 3% for influenza B (IRR 1.030, 95% CI 1.013–1.047), and 5% for RSV (IRR 1.050, 95% CI 1.036–1.063) but decreased by 6% for influenza A(H1N1pdm09) (IRR 0.941, 95% CI 0.915–0.968) (Figure 2). For both viral activity definitions, influenza A(H3N2) viral activity was associated with increased rehospitalization rates for asthma and COPD; RSV was associated with increased rehospitalization rates for HF and COPD; and we found no association between influenza or RSV viral activity and readmissions rates for AMI. Associations between viral activity and rehospitalization rates differed slightly for influenza B based on the viral activity definition.

Discussion

In this retrospective cohort study, increased community viral activity for RSV and certain influenza strains was associated with greater rates of cardiorespiratory rehospitalizations from SNFs. Prior literature suggests that influenza or RSV infection may lead to cardiorespiratory sequelae,^{1–3} and some studies have investigated the association between circulating respiratory viruses and adverse cardiorespiratory outcomes in community-dwelling adults.^{12–14} However, to our knowledge, this was the first study that investigated the relationship between circulating influenza or RSV and cardiorespiratory readmissions from SNFs. Our results suggest that the respiratory season is a particularly important time period to implement interventions that reduce cardiorespiratory rehospitalizations for SNF residents. Surveilling community viral activity and employing infection control and prevention measures with proportional intensity to reduce viral transmission in SNFs may be effective strategies.

Unlike influenza A(H3N2) and B, we found that increased influenza A(H1N1pdm09) viral activity was associated with decreased cardiorespiratory rehospitalization rates. In general, older adults are at high risk of serious complications from seasonal influenza, but influenza A(H1N1pdm09) affects younger age groups more severely.¹⁵ Vaccine effectiveness against predominant circulating influenza strains also varies across respiratory seasons.¹⁶ During seasons with high vaccine effectiveness, influenza vaccination may confer the greatest protection against serious influenza complications, including cardiorespiratory sequelae. During our study period, among adults ≥ 65 years, adjusted “vaccine effectiveness” estimates were 11%–15% for influenza A(H3N2) and 59% for influenza A(H1N1pdm09) in predominant years.^{17–19} Interestingly, very few older adults in these studies received the high-dose influenza vaccine, although some literature suggest the high-dose vaccine is more effective than standard dose vaccine irrespective of circulating influenza strain or antigenic match.²⁰ Vaccination of SNF staff may also reduce influenza transmission and confer additional protection to SNF residents.²¹ Surveilling trends in predominant viral strains, seasonal vaccine match, and vaccine uptake and effectiveness by vaccine formulation in SNFs may inform when hospitals and SNFs should increase resources to prevent and treat cardiorespiratory conditions.

The ongoing Coronavirus Disease 2019 pandemic has highlighted the importance of infection control measures to reduce respiratory virus transmission and control outbreaks in SNFs, many of which are likely applicable to other respiratory viruses that may lead to outbreaks, morbidity, and mortality. Using personal protective equipment (eg, masks), handwashing, decontaminating surfaces, vaccinating residents and staff, daily symptom screening, nursing staff-initiated testing for symptomatic residents, facility-wide testing during outbreaks, cohorting residents who test positive, contact tracing, visitation restrictions during periods of high community viral spread, reducing staff presenteeism (working while ill), planning staff assignments to limit transmission between units/facilities, and routinely assessing SNFs' unmet needs may be effective strategies.^{22–28} For such measures to be successful, SNFs must overcome challenges such as maintaining adequate supplies and personnel resources, ensuring that test result turnaround and resident cohorting are efficient, and balancing the intensity of infection control practices with cost-effectiveness.²⁹ In the case of respiratory virus testing, multivirus respiratory pathogen panels may be an efficient method to guide diagnosis and treatment³⁰ and may provide useful information on the burden of other respiratory viruses (eg, human metapneumovirus, parainfluenza, rhinovirus) in SNFs, for which literature is scarce.³¹ However, future research should first compare various testing strategies specifically in the SNF setting to examine cost-effectiveness, sustainability, and clinical outcomes.³²

Our study has several limitations. Because viral activity data were only available at the HHS-region level, we were unable to report how many participants were infected with influenza or RSV and we could not account for viral outbreaks or perform other facility-level analyses. Also, we did not adjust for vaccination against influenza, person-level comorbidities, or other infectious pathogens that may cocirculate with influenza or RSV. If more granular viral testing data become available, future research should examine how increased community respiratory viral activity may operate to impact rehospitalizations at the SNF level (eg, through staffing shortages, changes in clinician behavior, sequelae due to infection) and if racial and ethnic disparities in cardiorespiratory rehospitalizations exist.

Conclusions and Implications

Our results demonstrated that increases in circulating influenza A(H3N2), influenza B, and RSV were associated with increased cardiorespiratory rehospitalization rates among older adults who were hospitalized and subsequently discharged to SNFs. Hospital readmissions during the post-acute period are already common among older adults discharged to SNFs, and our results suggest that there is added risk of cardiorespiratory rehospitalizations when community levels of circulating RSV and certain influenza strains are highest. Therefore, the respiratory season is a particularly important time period to implement interventions that reduce cardiorespiratory hospitalizations among SNF residents. Decreasing viral transmission in SNFs through practices such as influenza vaccination for SNF residents and staff, using personal protective equipment, improved environmental cleaning measures, screening and testing of residents and staff, surveilling viral activity, and quarantining infected individuals may be potential strategies to limit viral infections and associated cardiorespiratory rehospitalizations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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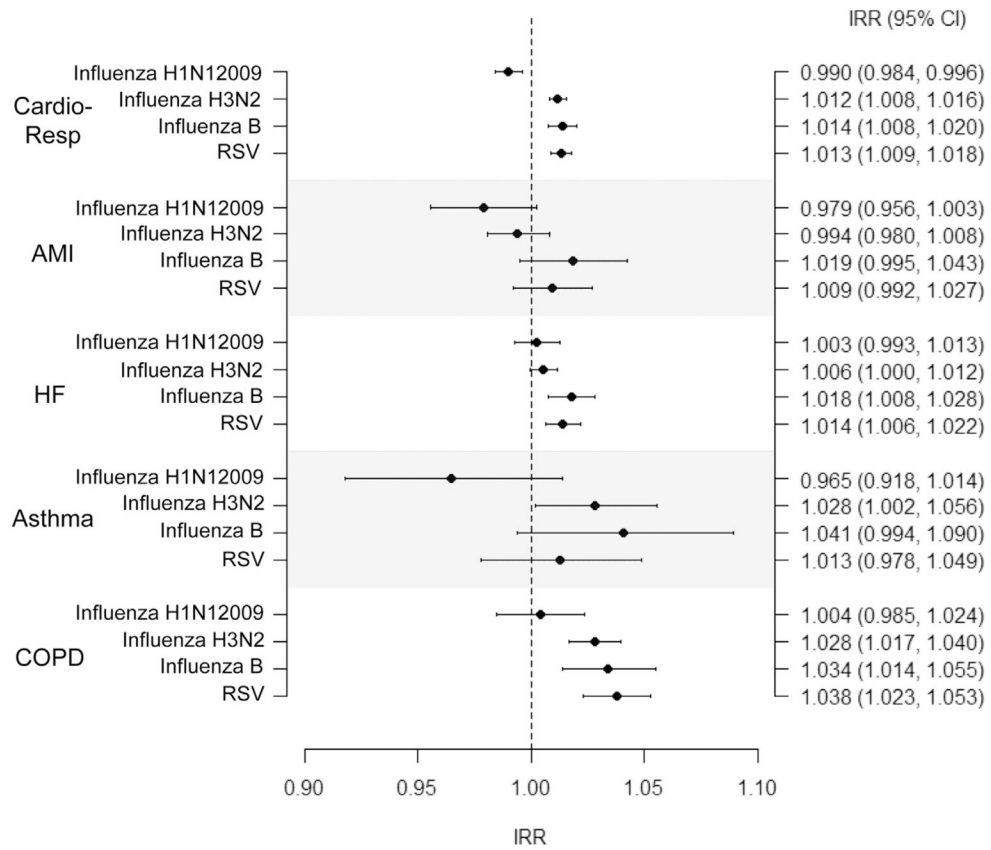


Fig. 1. Association between circulating influenza and RSV and rates of cardiorespiratory rehospitalization, per 5% increase in viral activity. IRRs for the association between 3 influenza strains [influenza A(H1N1pdm09), influenza A(H3N2), influenza B] and RSV and 5 cardiorespiratory rehospitalization outcomes, per 5% increase in viral activity. Cardio-Resp, cardiorespiratory.

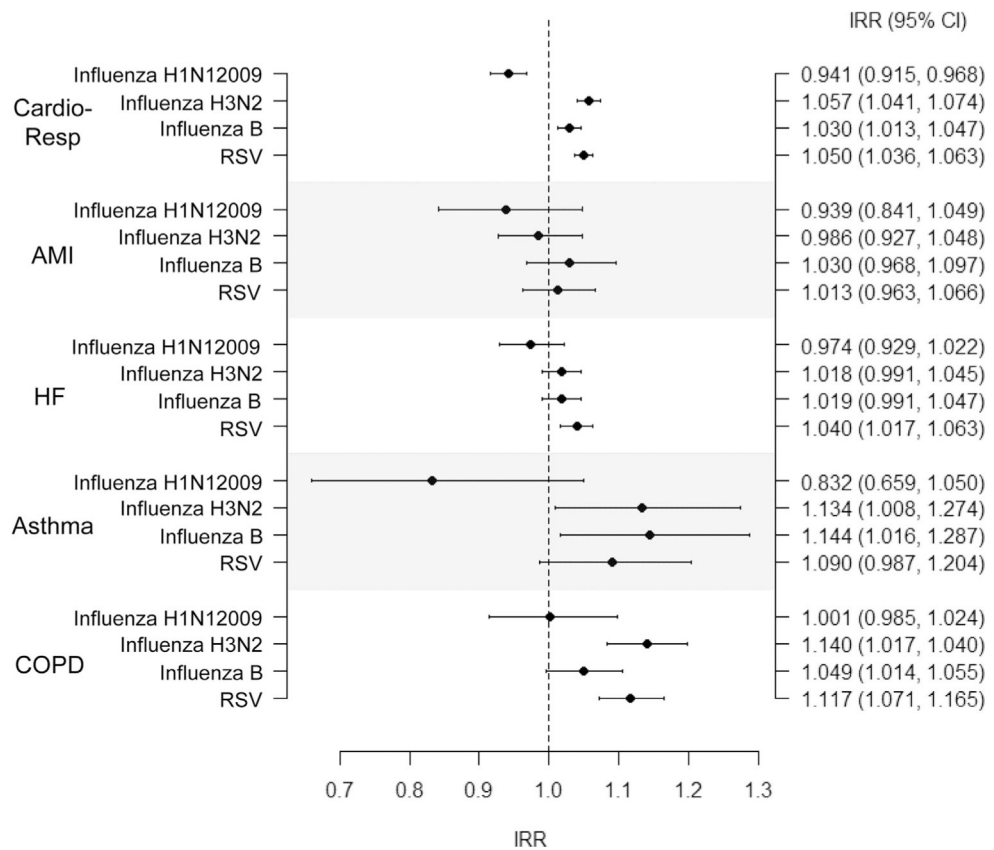


Fig. 2. Association between circulating influenza and RSV and rates of cardiorespiratory rehospitalization, in season vs out of season. IRRs for the association between 3 influenza strains [influenza A(H1N1pdm09), influenza A(H3N2), and influenza B] and RSV and 5 cardiorespiratory rehospitalization outcomes, when the respiratory viruses were in season vs out of season, based on a 10% positive testing threshold (eg, 10% of all tests for influenza were positive for influenza B). This threshold was defined separately in each HHS region, so one region could be in season whereas others were not. Cardio-Resp, cardiorespiratory.

Table 1
Participant Demographics Overall and by HHS Region, 2012–2015 (N = 5,053,231 SNF Stays)

HHS Region *	SNF Stays, n (%)	Person-Years	Age 75 [†] , n (%)	White, Non-Hispanic ^{‡,§} , n (%)	Male [‡] , n (%)
Overall	5,053,231 (100.0)	929,498	3,773,410 (74.7)	4,394,151 (87.0)	1,857,982 (36.8)
Region 1: Boston	362,707 (7.2)	68,225	280,050 (77.2)	342,802 (94.5)	133,468 (36.8)
Region 2: New York	538,757 (10.7)	98,246	418,029 (77.6)	453,757 (84.2)	198,730 (36.9)
Region 3: Philadelphia	579,293 (11.5)	105,575	437,116 (75.5)	485,851 (83.9)	210,462 (36.3)
Region 4: Atlanta	1,093,231 (21.6)	199,688	802,097 (73.4)	935,848 (85.6)	391,929 (35.9)
Region 5: Chicago	1,028,229 (20.3)	190,457	765,131 (74.4)	925,426 (90.0)	376,876 (36.7)
Region 6: Dallas	439,439 (8.7)	78,203	323,208 (73.6)	369,733 (84.1)	159,410 (36.3)
Region 7: Kansas City	237,272 (4.7)	44,163	181,722 (76.6)	223,673 (94.3)	85,001 (35.8)
Region 8: Denver	129,276 (2.6)	25,350	95,065 (73.5)	122,860 (95.0)	47,121 (36.4)
Region 9: San Francisco	496,498 (9.8)	91,045	361,870 (72.9)	394,908 (95.0)	198,359 (40.0)
Region 10: Seattle	148,529 (2.9)	28,545	109,122 (73.5)	139,293 (93.8)	56,626 (38.1)

* Participants discharged to an SNF located in Puerto Rico or the Virgin Islands were excluded from the study population, as well as those with missing region.

[†] Denominator for each cell is the SNF Stays column for the given HHS Region.

[‡] Overall, 4,394,151 (87.0%) were White, non-Hispanic participants; 454,516 (9.0%) were Black, non-Hispanic participants; 72,067 (1.4%) were Hispanic participants; and 132,497 (2.6%) participants were other races.