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Respiratory Syncytial Virus–related Clinical Events Among a Medicare-insured Population in the United States

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Background

- Respiratory syncytial virus (RSV) infection has been historically recognized as a disease that affects infants and young children, but also causes considerable morbidity and mortality in older adults[1,2]
- RSV in older adults is associated with numerous potentially serious post-infection clinical events, including non-RSV lower and upper respiratory tract infections, pneumonia, hypoxia, and exacerbation of existing asthma, chronic obstructive pulmonary disease, and congestive heart failure[3,4]
- While the general clinical burden of medically attended RSV has been previously described,[5,6] little is known about the frequency and factors associated with RSV-related clinical events in older adults

Objective

- To describe the proportion of patients experiencing post-infection RSV-related clinical events and evaluate risk factors for these clinical events among Medicare beneficiaries aged ≥60 years in the United States

Methods

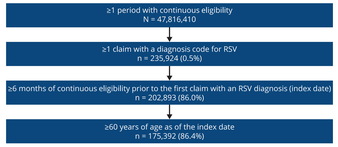
Data Source

- Data occurring January 1, 2007, through December 31, 2019, from the Centers for Medicare & Medicaid Services 100% Medicare Research Identifiable Files (RIFs) with Part D linkage were used for this study
- Fee-for-service data were available for each institutional (Part A), non-institutional (Part B), and drug event (Part D) claim type
- Since RIF data contained actual beneficiary- and physician-specific information, an institutional review board (IRB) exemption was obtained from Western Copernicus Group IRB

Study Design

- A retrospective, longitudinal cohort study design was used
- The index date was defined as the date of the first claim with a diagnosis code for RSV (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM]: 079.6, 466.11, 480.1; *International Classification of Diseases, Tenth Revision, Clinical Modification* [ICD-10-CM]: B97.4, J12.1, J20.5, J21.0)
- The baseline period was defined as the 6-month period preceding the index date
- The observation period spanned from the index date through to the earliest of 6 months later, the end of continuous health plan eligibility, or the end of data availability

Figure 1. Patient selection



RSV, respiratory syncytial virus.

Study Outcomes

- The proportion of medically attended RSV patients experiencing post-infection RSV-related clinical events, defined as the first medical claim with a diagnosis of pneumonia, acute respiratory failure, congestive heart failure, non-RSV lower and upper respiratory tract infections, chronic respiratory disease (ie, asthma or chronic obstructive respiratory disease), generalized or localized hypoxia, or dyspnea, was evaluated during the observation period
  - To be considered a clinical event, the patient was required to have no claims with a diagnosis for the corresponding event during the 6-month baseline period (ie, post-infection clinical events represented diagnoses not previously observed during the baseline period)
  - Patients with all 7 events observed during the baseline period were excluded from the at-risk population because, by definition, they would not be able to contribute a new post-infection RSV-related clinical event

Statistical Analyses

- Means, standard deviations (SDs), and medians were reported for continuous variables, while frequencies and proportions were reported for categorical variables
- Predictors (ie, demographic and baseline clinical characteristics) of having ≥1 post-infection RSV-related clinical event during the observation period were identified using multivariable Poisson regression
  - Results were reported as incidence rate ratios (IRRs) with 95% confidence intervals (CIs) and *P* values

Results

- After applying the inclusion criteria, 175,392 patients with medically attended RSV were included in the study
- The mean age was 79.0 years and 64.8% were female (**Table 1**)
- Most patients (78.4%) were White and the highest proportion of patients lived in the South (32.7%)
- In the 6 months preceding the index date (ie, the baseline period), 76.9% of patients had a prior diagnosis for ≥1 of the clinical events of interest, with the most common being dyspnea (50.5%), chronic respiratory disease (44.2%), and pneumonia (41.4%; **Table 1**)

Table 1. Baseline Demographic and Clinical Characteristics of Medicare Beneficiaries ≥60 Years Old With RSV

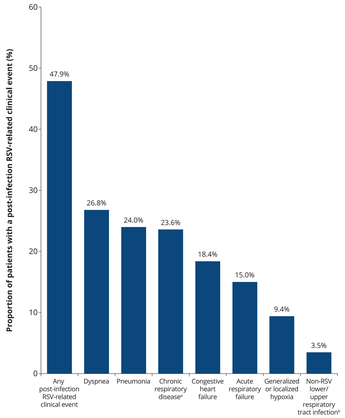
	All patients N = 175,392
Age at index date, mean ± SD [median], years	79.0 ± 9.6 [79.0]
Age category at index date, n (%), years	
60–64	9747 (5.6)
65–69	24,468 (14.0)
70–79	56,552 (32.2)
80–89	56,973 (32.5)
≥90	27,652 (15.7)
Female, n (%)	113,592 (64.8)
Race/ethnicity, n (%)	
White	137,452 (78.4)
Black/African American	14,806 (8.4)
Hispanic	13,569 (7.7)
Other/unknown	9565 (5.5)
Year of index date, n (%)	
2007–2014	113,031 (64.4)
2015–2019	62,361 (35.6)
US region, n (%)	
South	57,420 (32.7)
Northeast	50,311 (28.7)
Midwest	41,394 (23.6)
West	25,420 (14.5)
Other/unknown	847 (0.5)
Residence in long-term facility,[a] n (%)	21,251 (12.1)
Type of healthcare plan, n (%)	
Disability status	36,534 (20.8)
Dual eligibility	70,429 (40.2)
Index RSV diagnosis,[b] n (%)	
Pneumonia due to RSV	72,518 (41.3)
Acute bronchitis or acute bronchiolitis due to RSV	68,476 (39.0)
RSV or RSV as the cause of disease classified elsewhere	34,397 (19.6)
Quan–CCI, mean ± SD [median]	1.8 ± 2.1 [1.0]
Prior diagnosis of clinical events of interest, n (%)	
Acute respiratory failure	36,948 (21.1)
Chronic respiratory disease	77,546 (44.2)
Chronic obstructive pulmonary disease	67,990 (38.8)
Asthma	25,807 (14.7)
Congestive heart failure	62,398 (35.6)
Dyspnea	88,532 (50.5)
Generalized or localized hypoxia	21,833 (12.4)
Non–RSV lower and upper respiratory tract infections	5827 (3.3)
Pneumonia	72,612 (41.4)
Coronary artery disease, n (%)	64,335 (36.7)
Diabetes, n (%)	67,809 (38.7)
Immune system disorders, n (%)	18,504 (10.6)
Chemotherapy, n (%)	8897 (5.1)
Antibiotic use, n (%)	171,383 (97.7)
Influenza agent use, n (%)	30,315 (17.3)

CCI, Charlson Comorbidity Index; RSV, respiratory syncytial virus; SD, standard deviation.
[a]Residence in a long-term facility was assessed using place of service code 13 in the medical claims during the baseline period.
[b]The type of RSV diagnosis identified on the index date was assessed using the following hierarchy: (1) RSV with pneumonia, (2) RSV with acute bronchitis or acute bronchiolitis, and (3) RSV alone or RSV as the cause of diseases classified elsewhere.

Post-infection RSV-related Clinical Events

- A total of 279 patients had all 7 clinical events of interest during the baseline period and were excluded from the analysis, leaving 175,113 patients eligible to have a post-infection RSV-related clinical event during the observation period
- During the observation period, 47.9% of patients had ≥1 post-infection RSV-related clinical event, with a mean (median) time to clinical event of 1.0 (0.1) month
- The most common post-infection RSV-related clinical events were dyspnea (26.8%), pneumonia (24.0%), and chronic respiratory disease (23.6%; **Figure 2**)

Figure 2. Proportion of Medicare beneficiaries aged ≥60 years with a post-infection RSV-related clinical event



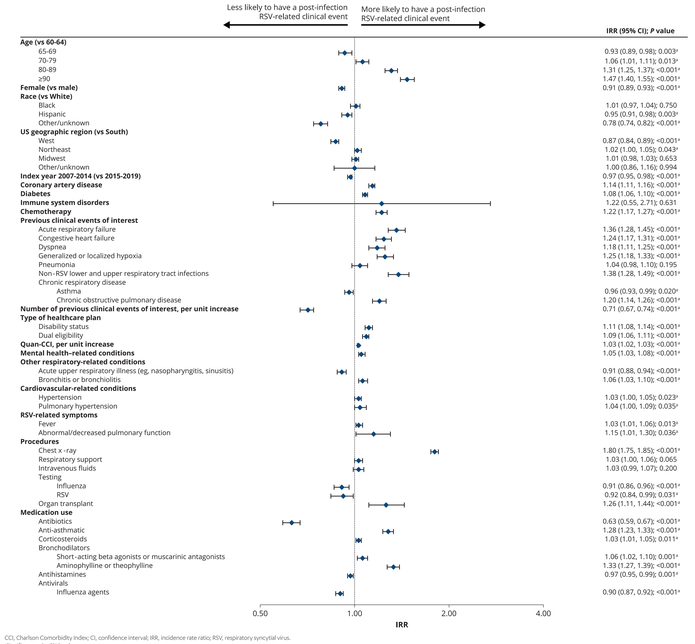
Patients at risk	175,113	86,860	102,780	97,846	112,994	138,444	153,559	169,565
Mean (median) time between RSV infection and post-infection RSV-related clinical event (months)	1.0 (0.1)	1.6 (0.9)	1.0 (0.2)	1.2 (0.3)	1.5 (0.6)	1.1 (0.2)	1.4 (0.5)	1.2 (0.4)

RSV, respiratory syncytial virus.
[a]Chronic respiratory disease includes asthma and chronic obstructive pulmonary disease.
[b]Includes the following non-RSV respiratory infections: influenza, parainfluenza, adenovirus, rhinovirus, SARS-associated coronavirus (not COVID-related given December 31, 2019 data cut-off), and human metapneumovirus.

Predictors of Having ≥1 Post-infection RSV-related Clinical Event

- Having a post-infection RSV-related clinical event during the observation period was more likely among patients with coronary artery disease, diabetes, or any of the RSV-related clinical events of interest (except pneumonia and asthma) during the baseline period (all *P* <0.001; **Figure 3**)
- Additionally, patients were more likely to have an RSV-related clinical event if they were ≥80 years old, were covered by disability Medicare, or had any of the following medical care reported during the baseline period: abnormal/decreased pulmonary function, chemotherapy treatment, a chest x-ray, an organ transplant, anti-asthmatic medication use, or aminophylline/theophylline bronchodilator use (all *P* <0.05; **Figure 3**)
- Having a post-infection RSV-related clinical event during the observation period was less likely among patients from the western US geographic region, patients who had an increasing number of baseline RSV-related clinical events, and patients who used antibiotics or influenza agents during the baseline period (all *P* <0.001; **Figure 3**)

Figure 3. Predictors of having ≥1 post-infection RSV-related clinical event



CCI, Charlson Comorbidity Index; CI, confidence interval; IRR, incidence rate ratio; RSV, respiratory syncytial virus.
*Significant at the 5% level.

Limitations

- Claims databases only contain diagnostic and procedure codes recorded for reimbursement purposes; therefore, additional information needed to fully confirm RSV diagnosis, such as diagnostic antigen and polymerase chain reaction testing results, was not available
- RSV may have been misdiagnosed as influenza given the similar etiology, epidemiology, and presence of symptoms
- The reliance on diagnosis codes to identify RSV may have led to the inclusion of patients with more severe RSV (ie, requiring medical care). As such, the proportion of patients experiencing a post-infection RSV–related clinical event may have been overestimated
- While patients were required to have no claims with a diagnosis for the clinical event of interest during the 6-month baseline period to ensure identification of newly diagnosed RSV-related clinical events, patients with pre-existing disease who did not receive medical care for that condition during the baseline period may have been included in the analysis; therefore, the event observed may not have been a new event, but rather a worsening/exacerbation of the previous condition
- This analysis did not include any comparator groups without RSV or with other similar infections, such as influenza
- Given the use of 100% Medicare data, the study findings may be generalizable to Medicare beneficiaries aged ≥60 years with medically attended RSV, but may not be representative of the overall population of patients with RSV

Conclusions

- The findings of this large, real-world study suggest that many older adults with medically attended RSV experience a significant clinical burden that impacts both the patient and the healthcare system
- Almost half of all patients experienced a post-infection RSV-related clinical event (eg, dyspnea, pneumonia) within 1 month of RSV diagnosis
- Over 75% of patients had experienced one of the clinical events of interest prior to RSV diagnosis, which predicted a higher risk of experiencing a different newly diagnosed clinical event post-RSV infection
- Patients may benefit from prophylactic strategies, such as RSV vaccination, to prevent the occurrence of post-infection clinical events or to mitigate their severity

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Disclosures

J.K. DeMartino and G. Krishnarajah are employees of Janssen Scientific Affairs, LLC, and stockholders of Johnson & Johnson. M-H. Lafeuille, B. Emond, C. Rossi, J. Wang, S. Liu, and P. Lefebvre are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to Janssen Scientific Affairs, LLC.

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