

# Burden of Respiratory Syncytial Virus Among Adults in the United States from 1997 to 2012

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## Abstract

**Objective:** Respiratory syncytial virus (RSV) is an established cause of serious respiratory infection hospitalizations among children, but the burden in adults is less well-studied.

**Methods:** Annual hospitalization rates for RSV in adults 20 years and older were estimated using the National Inpatient Sample (NIS), a nationally representative database. Patients were classified as immunocompromised or not based on an existing AHRQ algorithm. Hospitalizations were characterized by diagnostic categories, in-patient mortality, length of stay (LOS), mechanical ventilation use, and total cost (2015\$).

**Results:** 28,237 adult RSV hospitalizations occurred, with 34% classified as immunocompromised. RSV hospitalizations were more often 60 and older (58%), female (57%), and non-Hispanic white (61%). The rate of RSV hospitalizations increased steadily from 1997-2012, dramatically so for those 60 and older. Unspecified pneumonia rates in those 60 and older decreased significantly ( $p<0.001$ ). Regarding severity, more immunocompromised patients died in hospital than non-immunocompromised patients (7.6% vs. 5.6%,  $p=0.01$ ), mean LOS was longer (7.3 days vs. 5.4 days,  $p<0.01$ ), and mean cost was higher (\$66,476 vs. \$29,316  $p<0.01$ ), but mechanical ventilation was used less frequently (15% vs. 18%,  $p=0.02$ ). Overall, influenza hospitalizations were less severe than RSV hospitalizations.

**Conclusions:** The incidence of RSV hospitalizations in adults is increasing, likely due to increasing recognition and diagnosis. The burden of RSV in adults deserves attention, as there are fewer hospitalizations but they are more severe than influenza.

## Background

- Outbreaks identified in long-term care facilities in the late 1970s and early 1980s first drew attention to RSV as a potential cause of serious respiratory disease in elderly adults.
- More recent evidence suggests that the burden of RSV-related illness among adults may approach or even exceed that of non-pandemic influenza A.
- RSV infections have been found to be more severe than influenza, with longer symptomatic time and more time away from work.
- Older adults are at higher risk for severe morbidity due to RSV.
- Immunocompromised adults are at particularly high risk for severe RSV illness

## Methods

- Data from the 1997-2012 National Inpatient Sample (NIS) databases were used.
- Hospitalizations were classified by review of available ICD-9 diagnoses.
- RSV definition:
  - ICD9 480.1 (Pneumonia due to RSV)
  - ICD9 466.11 (Bronchiolitis due to RSV)
  - ICD9 079.6 (RSV)
- Influenza definition:
  - ICD9 487.00-488.99
- Hospitalizations were classified as immunocompromised or not based on an established AHRQ algorithm. This algorithm was developed to measure health care quality using hospital administrative data. A set of ICD9 codes were compiled to define immunocompromised status.
- Stratifications by age were calculated for 3 age groups: 20-44, 45-59, 60+.
- Disease severity was examined using several indicators defined by NIS: inpatient mortality, length of stay, mechanical ventilation use, and total cost. Severity of RSV was compared to that of influenza to assess disease burden.
- Costs were adjusted to 2015
- Hospitalization rates were calculated using the weighted estimate of RSV hospitalizations annually relative to the US population estimates from US Census data.
- Unspecified pneumonia rates were also calculated to understand if changes in RSV incidence was driven by changes in RSV diagnosis frequency or true disease incidence compared to a similar respiratory disease.
- All data management and statistical analysis was carried out using SAS 9.3.

**Table 1. Hospital Characteristics of RSV Compared to Influenza by Immunocompromised (IC) Status, 1997-2012**

Characteristic	RSV n (%)			Influenza n (%)		
	IC	Not IC	Total	IC	Not IC	Total
Total Hospitalizations	9,483 (33.6%)	18,754 (66.4%)	28,237 (100%)	66,944 (10.3%)	585,874 (89.7%)	652,818 (100%)
Region						
NE	1,954 (22.7%)	4,527 (26.3%)	6,481 (25.1%)	11,382 (18.2%)	89,130 (15.9%)	100,512 (16.1%)
Midwest	2,041 (23.7%)	4,841 (28.1%)	6,882 (26.6%)	18,462 (29.5%)	174,603 (31.1%)	193,065 (30.9%)
South	2,639 (30.6%)	4,610 (26.8%)	7,249 (28.1%)	22,001 (35.2%)	215,460 (38.4%)	237,461 (38.1%)
West	1,983 (23.0%)	3,247 (18.9%)	5,231 (20.2%)	10,684 (17.1%)	82,267 (14.7%)	92,951 (14.9%)
Location						
Rural	126 (1.5%)	1,615 (9.5%)	1,741 (6.8%)	8,536 (13.7%)	154,446 (27.6%)	162,982 (26.2%)
Urban nonteaching	832 (9.7%)	4,336 (25.4%)	5,168 (20.2%)	21,901 (35.2%)	221,756 (39.6%)	243,657 (39.2%)
Urban teaching	7,612 (88.8%)	11,091 (65.1%)	18,703 (73.0%)	31,806 (51.1%)	183,351 (32.8%)	215,157 (34.6%)
Bedsize						
Small	503 (5.9%)	2,043 (12.0%)	2,546 (9.9%)	7,400 (11.9%)	105,106 (18.8%)	112,506 (18.1%)
Medium	1,171 (13.7%)	3,477 (20.4%)	4,648 (18.1%)	12,950 (20.8%)	145,675 (26.0%)	158,625 (25.5%)
Large	6,896 (80.5%)	11,523 (67.6%)	18,419 (71.9%)	41,892 (67.3%)	308,772 (55.2%)	350,664 (56.4%)

**Table 2. Severity indicators for RSV compared to Influenza by Immunocompromised (IC) Status, 1997-2012**

Characteristic	RSV n (%)			Influenza n (%)		
	IC	Not IC	Total	IC	Not IC	Total
Total Hospitalizations	9,483 (33.6%)	18,754 (66.4%)	28,237 (100%)	66,944 (10.3%)	585,874 (89.7%)	652,818 (100%)
Died during hospitalization	695 (7.3%)	1,056 (5.6%)	1,751 (6.2%)	3,833 (5.7%)	15,873 (2.7%)	19,706 (3.0%)
Age 20-44	139 (6.4%)	71 (2.4%)	210 (4.1%)	507 (4.0%)	1,519 (1.2%)	2,026 (1.5%)
Age 45-59	267 (8.3%)	156 (4.3%)	423 (6.2%)	923 (5.6%)	2,321 (2.0%)	3,244 (2.5%)
Age 60+	289 (7.0%)	828 (6.8%)	1,118 (6.9%)	2,402 (6.3%)	12,033 (3.5%)	14,436 (3.8%)
Mechanical ventilation use	1,389 (14.6%)	3,319 (17.7%)	4,708 (16.7%)	7,899 (11.8%)	38,877 (6.6%)	46,777 (7.2%)
Age 20-44	262 (12.1%)	452 (15.6%)	714 (14.1%)	1,380 (10.9%)	8,131 (6.5%)	9,510 (6.9%)
Age 45-59	469 (14.6%)	810 (22.2%)	1,279 (18.6%)	2,475 (15.0%)	10,655 (9.4%)	13,130 (10.1%)
Age 60+	657 (16.0%)	2,058 (16.9%)	2,715 (16.6%)	4,045 (10.7%)	20,092 (5.8%)	24,137 (6.3%)
Length of stay (days) <sup>1</sup>	7.3	5.4	6.0	4.8	3.5	3.6
Age 20-44	7.4	4.6	5.6	4.1	2.6	2.7
Age 45-59	7.5	5.3	6.2	4.8	3.3	3.5
Age 60+	7.1	5.6	6.0	5.1	4.0	4.1
Adjusted cost (\$)¹	66,476.1	29,316.2	38,827.6	25,198.5	13,634.9	14,519.1
Age 20-44	71,822.3	27,021.1	41,202.0	24,070.5	11,831.5	12,627.4
Age 45-59	73,896.5	33,196.5	48,431.2	29,294.9	14,761.9	16,098.0
Age 60+	58,648.8	28,785.8	34,609.1	23,958.1	13,985.2	14,742.5

<sup>1</sup> Geometric mean

## Results

### Patient Characteristics

- Influenza (n=652,818) was more commonly diagnosed than RSV (n=28,237).
- A larger proportion of RSV patients (33.6%) were immunocompromised compared to influenza patients (10.3%).
- The proportion of hospitalized patients aged 60 and older (RSV=57.8%, Influenza=58.8%), women (RSV=56.6%, Influenza=58.9%) and whites (RSV=60.8%, Influenza=57.3%) was similar for RSV and Influenza.

### Hospital Characteristics (Table 1)

- RSV cases were more often identified in urban teaching hospitals (73.0%) compared to urban non-teaching (20.2%) or rural (6.8%) hospitals.

- Influenza patients, in contrast, were more evenly distributed between rural, urban teaching and urban nonteaching hospitals.

### Severity Indicators and Hospitalization Costs (Table 2)

- All severity indicators were higher for RSV than influenza.
- Mortality was twice as high for RSV (6.2%) than for influenza (3.0%).

- RSV and influenza mortality increased with age, but other indicators (LOS, mechanical ventilation, costs) were highest in 45-59 year olds.

- RSV costs per hospitalization were higher than influenza costs regardless of immuno-status or age.

- Immunocompromised RSV patients had more severe disease than non immunocompromised for all indicators but mechanical ventilation use.

### Trends

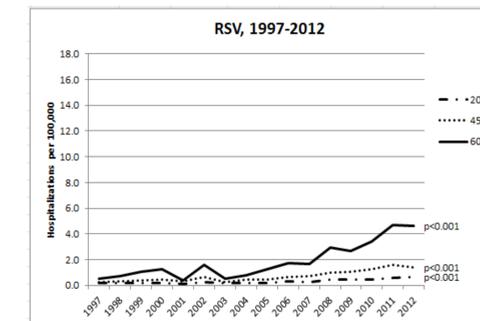
- The rate of RSV hospitalizations increased significantly for all ages between 1997 and 2012 ( $p<0.001$ ), most dramatically for patients 60 and older (Figure 1).
- Conversely, a decreasing trend was seen in unspecified pneumonia among those 60 and older ( $p<0.001$ ), but not in the younger age groups (Figure 2).

### Potential conflicts of interest

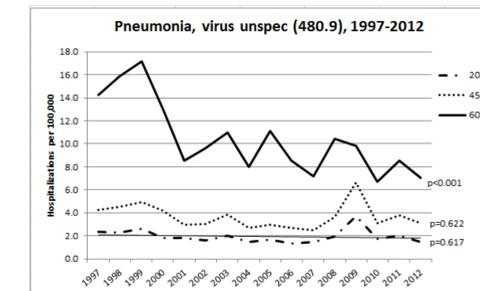
Hackett J, and Villafana T are shareholders in AstraZeneca / MedImmune.

Pastula S, Coalson J, Jiang X, and Fryzek J are consultants to AstraZeneca.

References available upon request.



**Figure 1. Trends in RSV Hospitalization Rates by Year and Age group, 1997 – 2012**



**Figure 2. Trends in non-RSV Pneumonia Hospitalization Rates by Year and Age group, 1997 – 2012**

## Conclusions

- RSV is a serious respiratory disease in children that has only recently been recognized and diagnosed as a serious cause of illness in adults.
- As clinicians become more aware of and diagnose more cases of RSV, rates may continue to climb.
- RSV hospitalizations appear to be consistently more severe than influenza hospitalizations, especially for older adults and those that are immunocompromised.
- There is more of an economic burden from an RSV hospitalization than one related to influenza; RSV inpatient stays last longer and cost more. RSV hospitalizations are also more severe in terms of mortality and mechanical ventilation use, especially in those over 60 years of age and in immunocompromised patients.
- RSV disease deserves attention as a potentially severe cause of hospitalizations due to respiratory disease in adults, and the burden likely continues to be underestimated due to under-diagnosis.