

The Burden of Respiratory Syncytial Virus (RSV) Disease in Adult Patients with Underlying Lung Disease: Interim Analysis from a Retrospective Patient Chart Review

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Background

- Although it has long been established that respiratory syncytial virus (RSV) is an important cause of respiratory tract infections in children, the burden of RSV is under-recognised in adults¹
 - There are limited data demonstrating the burden of RSV disease in adults²
 - Computer modelling of UK data from seasons between 1995 and 2009 has estimated that in adults aged 18 years or older, a mean of 487247 general practitioner episodes (first consultation ≥28 days following previous consultation for same diagnosis), 17799 hospitalisations, and 8482 deaths per season are attributable to RSV³
 - A surveillance study of adults hospitalised for respiratory illnesses in New York, USA, showed that the rate of RSV infections was 7%⁴
 - Adult groups at risk of severe disease that were identified are the elderly (≥65 years old), patients with underlying cardiopulmonary disease and immunocompromised patients.⁵
- It is important to understand the current burden of disease and patient pathway in order to optimise the standard of care for patients.
- This patient chart review intends to quantify the impact of diagnostics and treatments in these at-risk adult populations hospitalised with RSV. Here, we present an interim analysis that describes the burden of RSV on healthcare services, as well as the potential impact of diagnosis on RSV burden, specifically in patients with underlying lung disease (such as chronic obstructive pulmonary disease [COPD] or asthma).
- In these analyses of patients with RSV we describe:
 - Symptoms present at hospital admission
 - Sampling method used for diagnostic testing
 - Diagnosis method and timing in patient pathway
 - Treatment selection during hospital stay
 - Prevalence of bacterial coinfection and use of antibiotics
 - Intensive care unit (ICU) admission and reasons for admission
 - Length of stay (LOS) in hospital and time to clinical stability
 - The need for post-hospitalisation care, such as readmission and skilled nursing.

Methods

Study Design

- A retrospective review of patient charts (October 2014–2016) was conducted in the USA. Physicians were selected based on the criterion that they had been the primary treating physician for at least three confirmed hospitalised RSV cases in adult patients (≥18 years) over the past two RSV seasons, and spent at least 50% of their professional time working in a hospital setting.
- Each physician was asked to submit details from up to three randomly-selected patient cases from their electronic medical records to an online survey
 - Survey questions were either multiple choice with pre-selected topics, or physicians were asked to provide a numerical answer
 - In order to avoid choosing memorable cases, random selection was ensured through a program which assigned a random letter in the alphabet to each respondent, and instructed respondents to begin searching for patients whose last name begins with that letter.
- Patients for the following target sub-populations were identified: elderly (≥65 years), immunocompromised patients, other adult patients and patients with underlying lung disease; for the latter, the interim analyses are presented here.
- Of responding physicians, 10 were randomly selected to participate in follow-up anonymous telephone interviews (physicians were able to opt in to follow-up interviews when submitting case details). Physicians were asked to confirm cases within the timeframe of the quantitative analysis period, and were also asked specific questions about their submitted cases, such as patient type, presentation symptoms, diagnosis, treatment, and LOS.

Patient Inclusion Criteria

- Patients were explicitly classified as having an underlying lung disease if they had any of the following conditions, and were not classified as immunocompromised:
 - COPD (including chronic bronchitis or emphysema)
 - Treated tuberculosis
 - Interstitial lung disease
 - Cystic fibrosis
 - Asthma*
 - Bronchiectasis
 - Other lung comorbid condition.

*Asthma was alternatively an option under the 'allergies' category, therefore patients with asthma which had been described as an allergy were not categorised as having underlying lung disease.

Results

Physician Demographics

- Data for adult patients (≥18 years) with a confirmed diagnosis of RSV were collected from 132 physicians (hospitalists, infectious disease specialists, intensivists, oncologists, pulmonologists or geriatricians) distributed across 32 states, working in a hospital setting
 - Sixty-one percent of patient cases were submitted by physicians from an Integrated Delivery Network.

Patient Demographics

- Charts from 379 adult patients with confirmed RSV infection were reviewed, of which 119 were classified as having underlying lung disease. Patient demographics are shown in Table 1.

Table 1. Demographics of Patients with RSV Infection and Underlying Lung Disease

	Patients with underlying lung disease (N=119)
Male sex, n (%)	66 (56)
Median age, years (Interquartile range)	59 (54–72)
Race, n (%)	
Caucasian	68 (57)
African-American	31 (26)
Asian	3 (3)
Native American/Alaskan Native	2 (2)
Hispanic/Latino ethnicity, n (%)	12 (10)
Smoking history, n (%)	
Current smoker	46 (39)
Previous smoker	55 (46)
Never smoked	15 (13)
Don't know	3 (3)

Comorbidities

- The majority of patients had COPD (Table 2a), which was mostly mild or moderate in severity (stage I–II; Global Initiative for Chronic Obstructive Lung Disease classification) (Table 2b).
- Other common underlying comorbidities among patients were coronary artery disease and hypertension (Table 2a).

Table 2a. Comorbidities of Patients with RSV Infection and Underlying Lung Disease, Presented by Most Frequent to Least Frequent

Comorbidities, n (%)	Patients with underlying lung disease (N=119)
COPD	93 (78)
Hypertension	32 (27)
Coronary artery disease	27 (23)
Asthma	25 (21)
Congestive heart failure	19 (16)
Interstitial lung disease	10 (8)
Bronchiectasis	7 (6)
Cystic fibrosis	6 (5)
Cerebrovascular disease or prior stroke	3 (2)
Non-ischemic cardiomyopathy	2 (2)
Treated tuberculosis	1 (1)
Valvular heart disease or prior heart valve replacement	1 (1)

Some patients had more than one underlying comorbidity

Presenting Symptoms

- Cough, dyspnea, wheezing and fever are the symptoms most frequently reported by patients upon admission to the hospital (Table 3).

Table 2b. COPD Severity of Patients with RSV Infection and Underlying Lung Disease

Comorbidities, n (%)	Patients with underlying lung disease (N=119)
COPD, n (%)	93 (78)
Mild	22/93 (24)
Moderate	48/93 (52)
Severe	17/93 (18)
Very severe	2/93 (2)
Severity unknown	4/93 (4)

Table 3. Common Symptoms (≥20% of Patients) of Respiratory Infection in RSV Infected Patients with Underlying Lung Disease Observed at Hospital Admission

Symptom reported, n (%)	Patients with underlying lung disease (N=119)
Cough	94 (79)
Dyspnoea	84 (71)
Wheezing	82 (69)
Fever	65 (55)
Fatigue/weakness	53 (45)
Sputum production	50 (42)
Body aches/myalgia	49 (41)
Nasal congestion	47 (39)
Rhinorrhoea	38 (32)
Hoarseness	31 (26)
Sore throat	29 (24)
Headache	24 (20)

Hospital Sampling and Diagnosis

- Seventy-seven per cent (92/119) of patients were admitted to hospital via the emergency department, while 23% (27/119) were admitted directly to hospital.
- While many patients were diagnosed in the emergency department (ED), nearly 60% of patients were actually diagnosed later in the patient pathway, in the hospital or in the ICU (Figure 1).

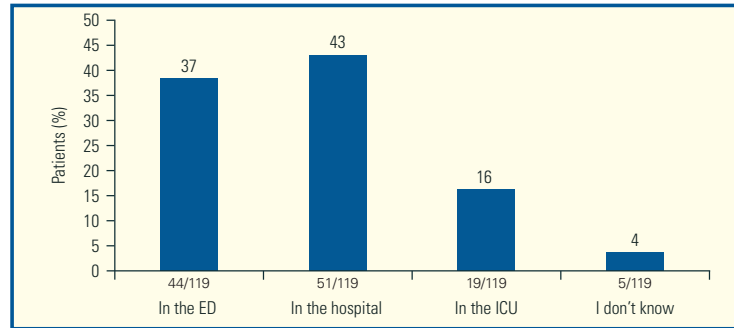


Figure 1. Hospital Department Where RSV Infection Was Diagnosed (N=119)

- There was a mean of 2.7 hours (range: 1–6) delay between initial admission of a patient to the ED and the attending physician ordering an RSV diagnostic test, while the mean delay for patients admitted to the hospital was 10.9 hours (range: 1–72)
 - Overall, patients waited for a mean of 11.6 hours (range: 1–48) between their physician ordering an RSV diagnostic test and receiving positive results.

- The most commonly used sampling methods were nasopharyngeal swab (59%; Table 4) and nasal swab (29%; Table 4), and the vast majority of patients were diagnosed with RSV via a PCR-based assay (92%; Table 4).
- Of those diagnosed via rapid antigen testing (10%; Table 4), the majority (8/12; 67%) were also tested by a PCR-based diagnostic, likely as a confirmatory test.

Therapies Used During Hospitalisation

- The most common therapies during hospitalisation were supplemental oxygen and bronchodilators, followed by corticosteroids, antibiotics and ribavirin (Figure 2).
- A high proportion of patients were given treatments to support respiratory function, such as supplemental oxygen, bronchodilators, and corticosteroids (Figure 2).

Table 4. Sampling and RSV Diagnostic Methods Used in Patients with Underlying Lung Disease

Sampling method (N=119), n (%)	Diagnostic method (N=119), n (%)
Nasopharyngeal swab	Viral Respiratory Panel including RSV (PCR based)
Nasal swab	Rapid RT-PCR RSV assay
Sputum sample	Rapid antigen detection RSV assay
Throat swab	Central laboratory RT-PCR RSV assay
Bronchoalveolar lavage	Cell culture detection RSV assay
Nasal wash	Immunofluorescent RSV assay
Middle turbinate swab	I don't know
I don't know	

Patients may have been diagnosed using more than one method

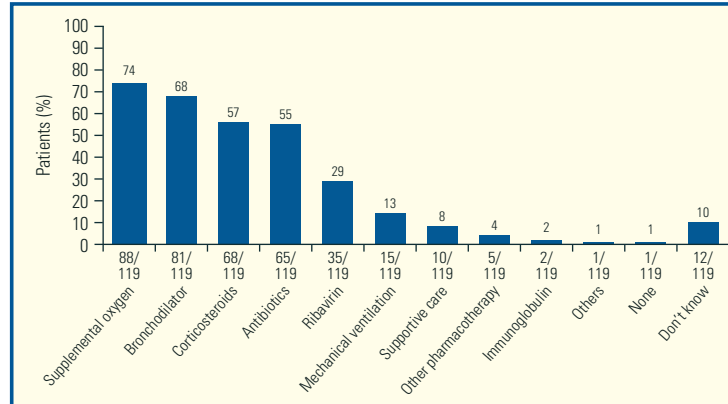


Figure 2. Treatment Regimen of RSV Infected Lung Comorbid Patients in Hospital (N=119)

Occurrence of Bacterial Coinfections

- Twenty-four percent of patients had bacterial coinfection confirmed by diagnostic testing, which was physician selected (based on current clinical practice)
 - A further 35% suspected as having bacterial coinfection but not confirmed (Figure 3a). 'Not confirmed' included patients who were not tested and those who received a negative test result.
- Sixty percent of patients were treated with antibiotics either prior to hospitalisation or during their hospital stay (Figure 3b).

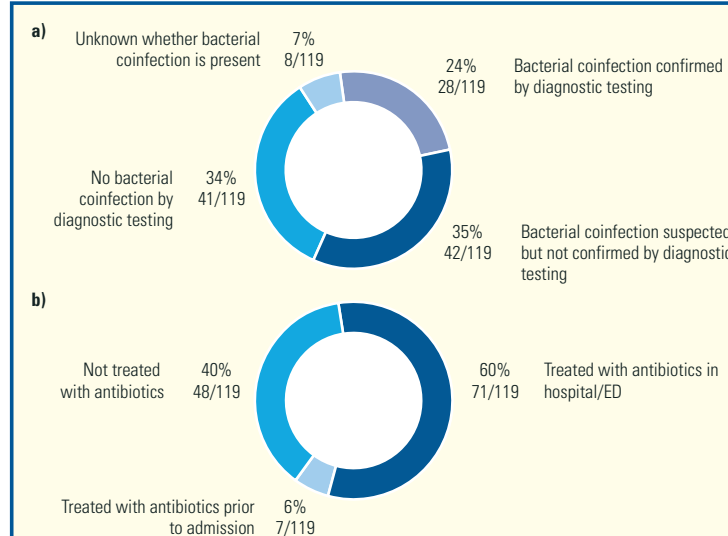


Figure 3. Proportion of Patients with Bacterial Coinfection (a), and Reported Antibiotic Usage (b) in Patients with RSV and Underlying Lung Disease (N=119)

- Of patients treated with antibiotics, 85% were on continued antibiotic treatment for at least 1 day after RSV diagnosis was confirmed.

ICU Admission

- Twenty-nine percent of patients with underlying lung disease were admitted to the ICU. The most common reason for admission was respiratory difficulty or other respiratory support (Figure 4).

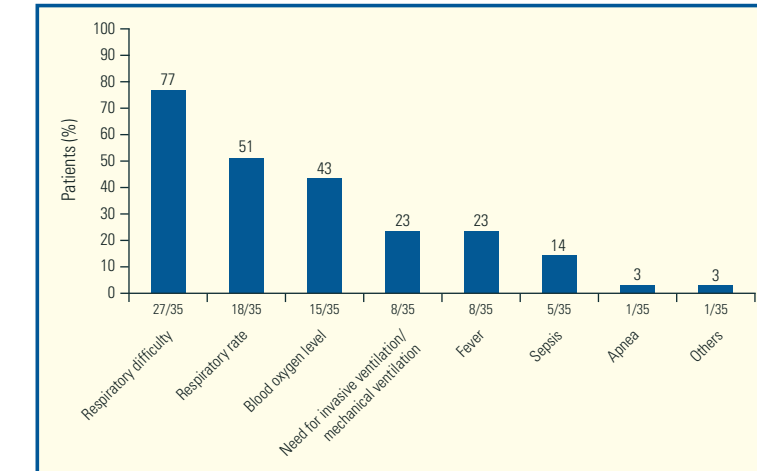


Figure 4. Reasons for RSV Patients with Underlying Lung Disease to be Admitted to the Hospital's ICU Department (N=35)

- Among those for whom data was available, the median length of ICU stay for patients was 4–6 days (Figure 5).

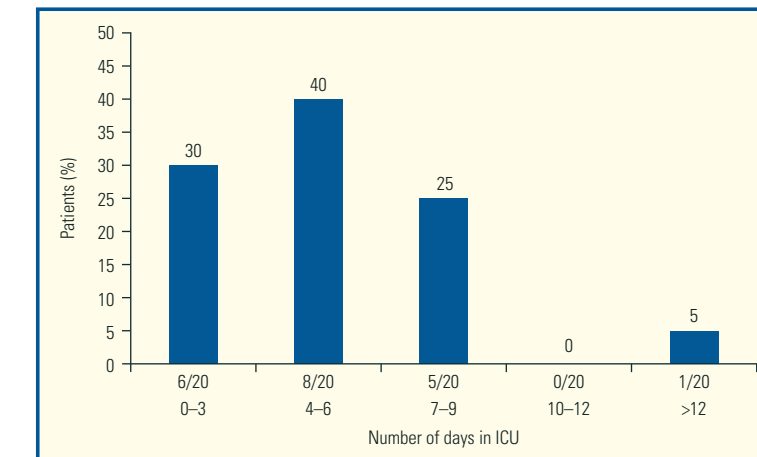


Figure 5. LOS in ICU (N=20) of RSV Infected Patients with Underlying Lung Disease

Length of Hospitalisation and Recovery

- The mean hospital LOS for the patients in this analysis was 7.5 days (range: 2–34) (N=118), and it took patients a mean of 6.1 (1–60) days to return to clinical stability, defined as the mean number of days after hospital admission to normalise.
- Of 72 patients with collected data post-hospitalisation, the vast majority of patients required some follow-up care, as per general standard of care for hospitalised patients
 - Ten percent of patients required skilled nursing post-hospitalisation, 6% of which was in a long-term care facility (Figure 6).
- The proportion of patients receiving antibiotics after discharge from the hospital was 28%.
- Within 60 days of initial hospitalisation, 3% (2/69) of patients died.

Limitations of Study

- Physicians may have had limited visibility of patient outcomes beyond in-patient care, including mortality.
- Follow-up data was only available for 72 patients, which may over- or underestimate burden of follow-up care

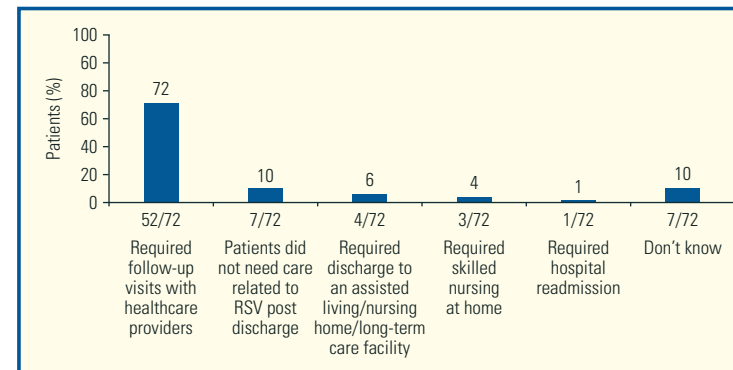


Figure 6. Percentage of RSV Infected Patients with Underlying Lung Disease Requiring Different Types of Follow-up Care Post-hospitalisation (N=72)

Conclusions

- Results from this study show that the healthcare burden of RSV complications in adults is high, due to many factors including long hospital stays, antibiotic usage, ICU admission and respiratory support treatments (e.g. mechanical ventilation).
- The majority of patients in this study were diagnosed with RSV by PCR-based diagnostics, which suggests physicians believe the improved accuracy of PCR over rapid antigen tests is important to optimise patient care⁶
 - This aligns with the current situation in influenza, where rapid antigen tests have been reclassified from Class I to Class II by the FDA due to poor performance resulting in many misdiagnosed cases⁷
 - However, more than half of patients in our study were diagnosed late in the patient pathway, i.e., in the hospital or the ICU
 - Patients experienced a substantial mean waiting time between their physician ordering an RSV diagnostic test and receiving positive results
 - Recent studies have suggested that earlier diagnosis of respiratory viruses is beneficial to patients, even in the absence of effective therapeutics, which may indicate educational and resource needs for increased diagnosis at the ED or even earlier.⁸
- Fever was present at hospital admission in 55% of patients
 - Diagnostic testing for influenza-like illness is often indicated when fever is present, this may play a role in under-recognising the RSV burden.⁹
- These data identified a need for continued care after discharge
 - Ten percent of patients required skilled nursing either at home or in a long-term care facility.
- This study demonstrates that hospitalised adult patients with RSV and underlying lung disease, predominantly COPD, place a substantial burden on healthcare resources, both during and following hospitalisation
 - Studies of burden in other at-risk adult populations are ongoing, including the elderly and immunocompromised populations, as well as adults not considered to be at risk of severe RSV.

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