High Morbidity and Mortality in Adults Hospitalized for Respiratory Syncytial Virus Infections
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Background
- important cause of lower respiratory tract infections in infants and young children, leading to hospitalizations and deaths
- impact in adults only appreciated in recent years
- RSV estimated to infect 3-10% of adults annually
- most infections mild, but severe lower respiratory tract infections can occur (older adults, underlying conditions)
- RSV may account for 5-15% of community-acquired pneumonia, 9-10% of hospital admissions for acute cardiorespiratory diseases, and excessive deaths during seasonal peaks
- disease burden can approach that of influenza
- little is known about the clinical manifestations, complications, and outcomes of severe RSV infections in adults; factors associated with severe and fatal infections are largely unknown

Aim of the study
- to describe RSV infections in adults, identify factors associated with development of pneumonia, respiratory failure, and death and to compare RSV infections with influenza infections

Methods
- Study population and case finding
  o retrospective cohort study on adults (> 18 years) hospitalized with RSV infections between January 2009 and 31 December 2011 in 3 participating hospitals in Hong Kong, with laboratory confirmed RSV infections
  o RSV and influenza infections prospectively diagnosed (reasons for admittance: potentially serious medical conditions and/or exacerbation of chronic illness not manageable at home
  o in all patients: collection of nasopharyngeal aspirates, tested for RSV and influenza antigens using an immunofluorescence assay, chest X-ray, sputum samples for bacterial culture
- Data collection and definition of variables
  o clinical data: demographics, co-morbidities, illness onset time, presenting symptoms, cardiorespiratory complications, requirement for supplemental oxygen therapy and/or ventilator support, antibiotic use, use of systemic corticosteroids, hospitalization duration, and all-cause death
  o laboratory data: routine blood tests, bacterial pathogens from respiratory and/or blood samples
  o Definitions
    ▪ pneumonia: physician diagnosed pneumonia based on symptoms and signs of acute lower respiratory tract infections together with new pulmonary infiltrate
    ▪ acute respiratory failure requiring ventilatory support: persistent respiratory failure despite supplemental oxygen therapy which necessitated noninvasive positive pressure ventilation or invasive mechanical ventilation
- Main outcome: all-cause death
- Secondary outcome: development of acute respiratory failure requiring ventilatory support and total duration of hospitalization
- **Additional analysis:** Comparison of patients with RSV infections and patients with influenza infection during the same period
- **Virological investigations:** viral antigen detection for a panel of respiratory viruses using an immunofluorescence assay
- **Radiographic assessment:** radiographic review by two independent radiologists (blinded to all clinical information and outcomes)
- **Statistical analysis:**
  - Univariate analysis with Student t, Mann-Whitney U, and Chi-square test; multivariate Cox proportional hazard model

**Results:**
- 607 RSV cases among hospitalized patients
- Patients’ baseline characteristics and clinical manifestations (Table 1)
  - Mean age 80 years
  - 87.3% with one or more coexisting medical conditions
  - Mean time of admission 2.6 days
  - Symptoms: fever (75%), cough (87.5%), sputum production (81.2%), and wheezy breathing and dyspnea (68.9%)
- Complications: lower respiratory tract complications (pneumonia, COPD exacerbation): 71.9%, bacterial superinfection 12.5%, cardiovascular complications 14.3%
- 38.9% systemic corticosteroids, 94.7% antibiotics, 67.9% supplemental oxygen therapy, 11.1% ventilatory support (NIPPV 9.1%, invasive ventilation 2.0%)
- Risk factor for acute respiratory failure requiring ventilatory support (table 2): chronic lung disease, pneumonia, elevated serum urea concentration, elevated liver enzymes
- Crude all-cause mortality within 30 days and 60 days was 9.1 and 11.9%, respectively (direct cause of death: pneumonia, COPD exacerbation, acute cardiovascular events and underlying medical conditions complicated by pneumonia/sepsis)
- Mean duration of hospitalization: 12 days
- Comparison with seasonal influenza: patients similar in age, but RSV more frequently with underlying chronic lung disease and major systemic co-morbidities; use of supplemental oxygen and assisted ventilation higher in RSV patients; no significant difference in overall outcome

**Discussion:**
- RSV can cause severe lower respiratory complications in older adults with underlying diseases
- Severe lower respiratory complications common with potentially fatal outcome
- Clinical manifestation, complications, and outcomes of RSV infections comparable to those of seasonal influenza
- No antiviral treatment or vaccination for RSV infections available, not much data on the use of Ribavirin and immunoglobulins available

**Strengths and limitations**
- Strengths: largest adult cohort of hospitalized RSV patients, multicenter design, virological confirmation of cases
- Limitations: retrospective approach; use of IFA instead of PCR (lower sensitivity -> less severe cases probably not detected)

**Conclusion:**
- Adults hospitalized for RSV infection have high morbidity and mortality