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# Rates of respiratory virus-associated hospitalization in children aged < 5 years in rural northern India

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Human metapneumovirus

**Summary** *Objectives:* Though respiratory viruses are thought to cause substantial morbidity globally in children aged <5 years, the incidence of severe respiratory virus infections in children is unknown in India where 20% of the world's children live.
*Methods:* During August 2009–July 2011, prospective population-based surveillance was conducted for hospitalizations of children aged <5 years in a rural community in Haryana State. Clinical data and respiratory specimens were collected. Swabs were tested by RT-PCR for influenza and parainfluenza viruses, respiratory syncytial virus (RSV), human metapneumovirus, coronaviruses, and adenovirus. Average annual hospitalization incidence was calculated using census data and adjusted for hospitalizations reported to occur at non-study hospitals according to a comunity healthcare utilization survey.
*Results:* Of 245 hospitalized children, respiratory viruses were detected among 98 (40%), of whom 92 (94%) had fever or respiratory symptoms. RSV accounted for the highest virus-associated hospitalization incidence (34.6/10,000, 95% CI 26.3–44.7) and 20% of hospitalizations. There were 11.8/10,000 (95% CI 7.9–18.4) influenza-associated hospitalizations (7% of hospitalizations). RSV and influenza virus detection peaked in winter (November–February) and rainy seasons (July), respectively.
*Conclusion:* Respiratory viruses were associated with a substantial proportion of

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hospitalizations among young children in a rural Indian community. Public health research and prevention in India should consider targeting RSV and influenza in young children.
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## Introduction

Acute respiratory infections are recognized as an important cause of mortality, hospitalization, and healthcare utilization in young children globally.[1–3] Respiratory virus infections are increasingly recognized as major contributors to the burden of severe acute respiratory illness in many countries due to expanding global surveillance and the advent of improved molecular diagnostic testing for respiratory viruses.[4–8] In studies of respiratory virus detection among children hospitalized with respiratory illness from different parts of the world, RSV and influenza are frequently associated with a substantial proportion of hospitalizations.[9–14] These findings are of public health importance because effective and safe influenza vaccines are available but not widely used in many countries, and development of respiratory syncytial virus (RSV) vaccines continues to be an area of intense study although no licensed RSV vaccine is available.[12,15,16] Understanding the incidence of respiratory virus-associated severe illness and the timing of respiratory virus circulation is critical to inform research priorities and policy decisions about introduction of available respiratory virus vaccines for children.

India is the second most populous country in the world with 20% of the world's population of children aged <5 years, and almost a third of global pneumonia cases among children aged <5 years are thought to occur in India.[3] Public health policies that effectively address causes of severe respiratory illness among children in India would have a substantial impact on global child morbidity and mortality. However, the burden of respiratory virus-associated severe illness among young children in India is unknown. In addition, the few studies that evaluated respiratory viral etiologies of severe illness among children in India were conducted before the advent of newer and more sensitive diagnostic tests, including tests to detect more recently discovered viruses.[17–20] Using data from population-based surveillance of approximately 9500 children for hospitalizations for acute medical illness in rural northern India and concomitant testing for respiratory viruses by real-time reverse transcription polymerase chain reaction (rRT-PCR), we estimate the incidence of respiratory virus-associated hospitalizations among children aged <5 years. We also describe the timing of virus circulation and clinical presentation of children hospitalized with predominant viruses.

## Patients and methods

### Study setting

The Comprehensive Rural Health Services Project (CRHSP), Ballabgarh study site includes a 323 square kilometer area in Haryana State, about 40 km south of New Delhi. The climate is temperate with a defined colder winter season during November–March and rainy season during July–September. As part of the CRHSP, a Health and Demographic Surveillance System (HDSS) was maintained under which all residents of the CRHSP study site were enrolled in a computerized database with unique identification numbers. The HDSS tracked major events such as births, deaths, marriages and migrations. During the study period, the CRHSP study site included a population of approximately 88,000 persons including approximately 9500 children aged <5 years in 28 villages.

The main providers of inpatient care to the CRHSP population are a government-funded secondary level facility with 60 beds that provides outpatient and inpatient care and serves 15–20% of the CRHSP population, two other government-funded secondary level facilities, and a large number of private health facilities (ranging in size from 5 to 35 beds) that provide inpatient and outpatient health services. Health facilities are largely situated outside CRHSP villages within a range of 3–20 km and largely accessible by two/three wheelers. Most facilities have the resources to care for patients requiring supplemental oxygen but transfer patients requiring mechanical ventilation and intensive level to tertiary care facilities outside the district.

### Hospitalized patient enrollment

Hospitalized patients were enrolled from the three secondary level facilities and 18 private facilities in Ballabgarh and Faridabad towns where patients from the CRHSP area were likely to seek inpatient care corroborated by health utilization survey. Patients were eligible for enrollment if they were residents of the CRHSP area and were being hospitalized overnight with any acute medical illness, excluding hospitalizations for the following conditions assumed to be unlikely to be related to respiratory infection: trauma, diarrhea without fever, elective surgery, accidental poisonings, elective blood transfusions, or orthopedic or ophthalmologic conditions. During August 2009–July 2011, patients were prospectively enrolled in the study as previously described.[21] Data on demographic characteristics, medical history, and clinical symptoms were obtained by interview of patients' caregivers. Data on clinical signs were abstracted from the medical record using a standardized data collection form. Respiratory specimen samples were collected by study doctors from enrolled patients within 24 h of admission using polyester swabs.

### Healthcare utilization survey

During August–December 2010, study investigators visited all houses in the 28 villages of the CRHSP area to conduct a healthcare utilization survey using a standardized questionnaire that was field testing in previous years; 90% of households in the area completed the survey. The survey asked whether any member of the household had been admitted to a hospital for an overnight stay during the