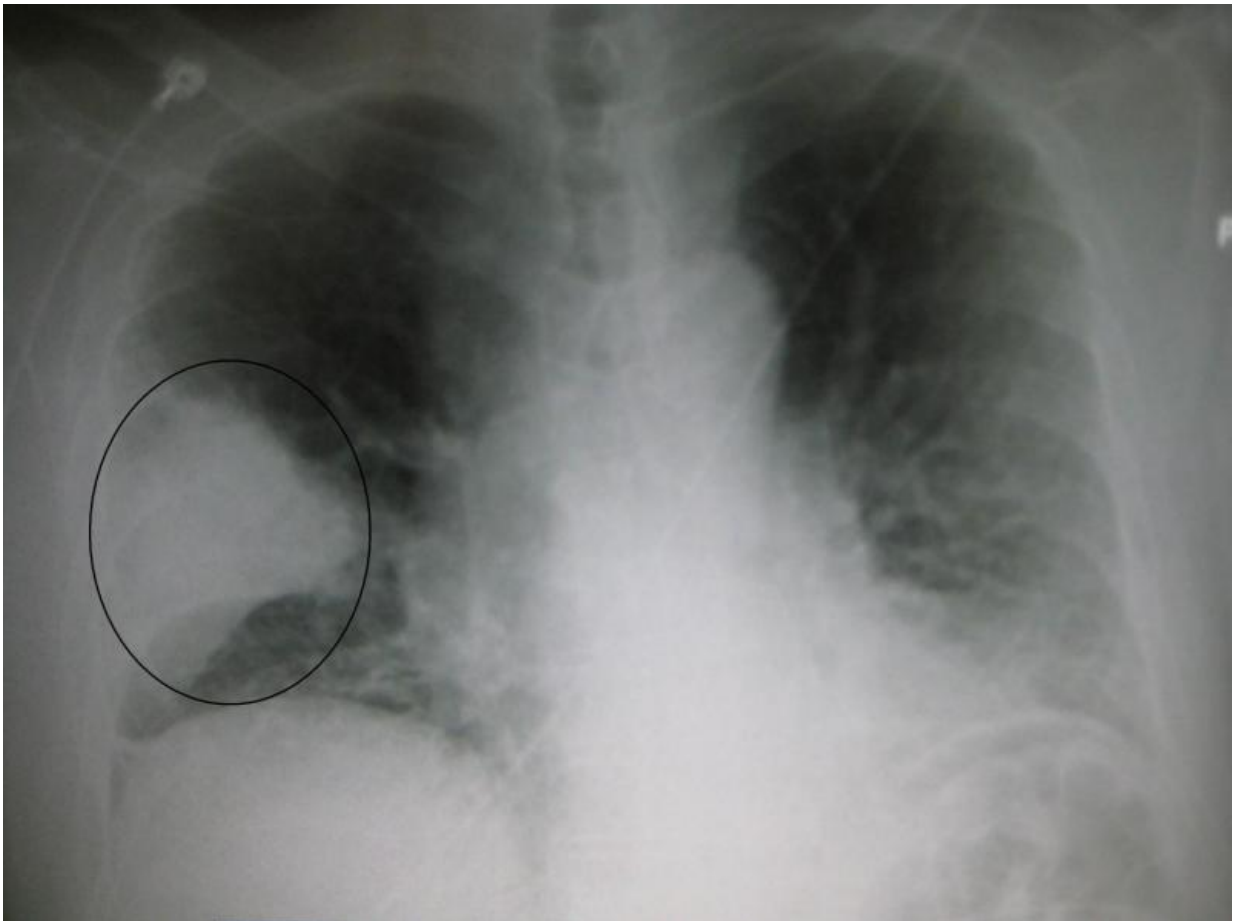


# Seven-country study reveals viruses as new leading cause of global childhood pneumonia

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A black and white X-ray picture showing a triangular white area on the left side. A circle highlights the area. Credit: James Heilman, MD./Wikipedia

Respiratory syncytial virus (RSV) and other viruses now appear to be the main causes of severe childhood pneumonia in low- and middle-income countries, highlighting the need for vaccines against these pathogens, according to a study from a consortium of scientists from around the world, led by a team at the Johns Hopkins Bloomberg School of Public Health.

Pneumonia is the leading cause of death worldwide among [children](#) under 5 years old, with about 900,000 fatalities and more than 100 million reported cases each year. This makes [pneumonia](#) a greater cause of childhood mortality than malaria, tuberculosis, HIV, Zika virus and Ebola virus combined.

The study, to be published June 27 in *The Lancet*, was the largest and most comprehensive of its kind since the 1980s. It included nearly 10,000 children in seven African and Asian countries. After testing for viruses, bacteria, and other pathogens in children with severe hospitalized pneumonia—and in community children without pneumonia—the study found that 61 percent of severe pneumonia cases were caused by viruses led by RSV, which alone accounted for 31 percent of cases.

"Prior to this study, we didn't know which specific viruses and bacteria are now causing most of the severe childhood pneumonia cases in the world, but public health organizations and vaccine manufacturers really need that information to work toward reducing the substantial childhood mortality that pneumonia still causes," says study co-principal investigator Maria Deloria Knoll, Ph.D., a senior scientist in the Bloomberg School's Department of International Health, and associate director of science at the Johns Hopkins International Vaccine Access Center (IVAC).

Identifying the germs that cause pneumonia is difficult in individual

cases and much more so on a scale of thousands of cases, especially in low- and [middle-income countries](#) where most pneumonia deaths occur. Researchers in prior pneumonia studies simply lacked the microbiological and analytical resources to produce estimates of the major pneumonia pathogens, Knoll says. And, in the past two decades, many low- and middle-income countries have introduced effective vaccines against known major bacterial causes of pneumonia—Haemophilus influenzae type b and Streptococcus pneumoniae—so the global mix of pathogens causing childhood pneumonia has changed as a result.

The new, IVAC-led study, known as the Pneumonia Etiology Research for Child Health (PERCH) study, included 4,232 cases of severe hospitalized pneumonia among children under 5 years and 5,119 community children without pneumonia during a two-year period. The study was carried out at sites in Bangladesh, The Gambia, Kenya, Mali, South Africa, Thailand, and Zambia.

For their study, researchers took nasal and throat swabs as well as blood, sputum and other fluid samples from cases and controls and tested them for pathogens using state-of-the-art laboratory techniques. Cases for the primary analysis were limited to those whose pneumonia was confirmed by chest X-ray, and children with HIV were considered in a separate analysis because the causes of their pneumonia would likely differ from those without HIV. With analytic methods unique for an etiology study, the researchers compared the pathogens found in samples from severe pneumonia cases to those from other children in the community in order to estimate the likeliest cause of each case. In this way they were able to identify the leading causes of childhood pneumonia among children in these settings.

The researchers concluded that, across all study sites combined, viruses accounted for 61.4 percent of cases, bacteria for 27.3 percent of cases,

Mycobacterium tuberculosis for 5.9 percent of cases. Fungal and unknown causes accounted for the remainder of cases.

RSV accounted for nearly a third of all cases and was the leading cause of severe pneumonia in each of the seven countries studied. Other top causes were rhinovirus, human metapneumovirus, parainfluenza viruses, and *S. pneumoniae* bacteria.

"We now have a much better idea of which new vaccines would have the most impact in terms of reducing illness and mortality from childhood pneumonia in these countries," says Katherine O'Brien, MD, who led the PERCH study as a professor at the Johns Hopkins Bloomberg School of Public Health and now serves as Director of Immunizations, Vaccines and Biologicals at the World Health Organization.

RSV has long been known as a common and potentially serious respiratory pathogen among children and the elderly. It remains the leading cause of pneumonia in children younger than 1 year in the United States, according to the Center for Disease Control and Prevention. Several RSV vaccine candidates are being developed and evaluated in clinical trials. A monoclonal antibody therapy, palivizumab, is available for the prevention of RSV disease in children with underlying medical conditions but is not suitable programmatically or financially for widespread use in routine immunization programs.

The analytical technique developed for the study to estimate the cause of individual cases of childhood pneumonia is called the Bayesian Analysis Kit for Etiology Research (BAKER), and is available online as an open-source application for use by other public health researchers.

"Estimating the etiology of pneumonia was like a complex jigsaw puzzle where the picture could only be seen clearly by assembling multiple, different pieces of information using innovative epidemiologic and

statistical methods," says Scott Zeger, Ph.D., Malone Professor of Biostatistics in the Bloomberg School's Department of Biostatistics

Provided by Johns Hopkins University Bloomberg School of Public Health

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