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# Review on Pneumonia

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## I. Introduction

Pneumonia is an infection that inflames the air sacs in one or both lungs. The air sacs may fill with fluid or pus (purulent material), causing cough with phlegm or pus, fever, chills, and difficulty breathing. A variety of organisms, including bacteria, viruses and fungi, can cause pneumonia.

Pneumonia can range in seriousness from mild to life-threatening. It is most serious for infants and young children, people older than age 65, and people with health problems or weakened immune systems

The lung is constantly exposed to microorganisms. A complex system of host defenses is required to prevent these organisms from gaining access to the lung and for removing them from the lung. This process, however, may be breached and pathogenic microorganisms may reach the alveoli. The combined effects of microorganism multiplication and host response determine the clinical condition known as pneumonia.

The most useful classification of pneumonia is based on the origin of the infection because this factor implies a different etiology, prognosis and treatment. The term 'community-acquired pneumonia' (CAP) refers to the appearance of infection in a nonhospitalized population with no risk factors for multi-drug-resistant pathogens whereas the term 'hospital acquired pneumonia' (HAP) or 'nosocomial pneumonia' is used when there is no evidence that the infection was present or incubating at the time of hospital admission. The latter type of pneumonia is most frequently found in patients receiving mechanical ventilation, hence the term 'ventilator-associated pneumonia.'

Pneumonia is the single leading cause of mortality in children under five and is a major cause of child mortality in every region of the world, with most deaths occurring in subSaharan Africa and South Asia. Pneumonia kills more children under five than AIDS, malaria, and measles combined, yet increased attention in recent years have been on the latter diseases.3 Pneumonia is a form of acute respiratory tract infection (ARTI) that affects the lungs. When an individual has pneumonia, the alveoli in the lungs are filled with pus and fluid, which makes breathing painful and limits oxygen intake. Pneumonia has many possible causes, but the most common are bacteria and viruses. The most common pathogens are Streptococcus pneumoniae, Haemophilus influenzae type b (Hib), and respiratory syncytial virus (RSV). S. pneumoniae is the most common cause of bacterial pneumonia in children under five years in the developing world.4 The second most common cause of bacterial pneumonia in children is Hib, followed by RSV - the most common cause of viral pneumonia in children under two years. The populations most at risk for pneumonia are children under five years, people aged 65 or over, and people with pre-existing health problems. Streptococcus pneumoniae frequently colonizes the upper respiratory tract. The human nasopharynx is the only natural reservoir for S. pneumoniae and these bacteria along with viruses are commonly found in a child's nose or throat; these pathogens are then aspirated into the lungs, causing disease. Pneumonia can be spread in a number of ways. The pathogen is transmitted through direct contact with respiratory secretions, colonizes the nasopharynx and may then cause blood-borne diseases.5 S. pneumoniae can cause both noninvasive and invasive disease in all age groups, particularly in children younger than five years and adults 65 years or older. 2,3 In addition, people with certain medical conditions, such as chronic heart, lung, or liver diseases, or sickle cell anemia are also at increased risk for pneumococcal diseases. People living with HIV/AIDS or people who have had organ transplants and are taking medications that decrease their immunity to infection are also at high risk of getting this disease. 5 A healthy child has many natural defenses that protect its lungs from pneumonia. Undernourished children, especially those who are not exclusively breastfed or with inadequate zinc intake, are at a higher risk of developing pneumonia. 4 Immunosuppression due to other coinfections are important risk factors in pneumonia-related mortality; infants, children, or the elderly suffering from illnesses, such as AIDS, measles, or malaria are also more likely to develop pneumonia. Additionally, environmental factors, such as crowded living conditions and exposure to indoor air pollution may contribute to increasing children's susceptibility to pneumonia. The Lancet Global Burden of Disease (GBD) Study 2010 has a category for lower respiratory tract infections (LRTI), which includes influenza, Streptococcus pneumoniae (pneumococcal pneumonia), Haemophilus influenzae type b (Hib), respiratory syncytial virus (RSV), and "other lower respiratory infections".

Symptoms

The signs and symptoms of pneumonia vary from mild to severe, depending on factors such as the type of germ causing the infection, and your age and overall health. Mild signs and symptoms often are similar to those of a cold or flu, but they last longer.

Signs and symptoms of pneumonia may include:

- Chest pain when you breathe or cough
- Confusion or changes in mental awareness (in adults age 65 and older)
- Cough, which may produce phlegm
- Fatigue
- Fever, sweating and shaking chills
- Lower than normal body temperature (in adults older than age 65 and people with weak immune systems)
- Nausea, vomiting or diarrhea
- Shortness of breath

Causes

Many germs can cause pneumonia. The most common are bacteria and viruses in the air we breathe. Your body usually prevents these germs from infecting your lungs. But sometimes these germs can overpower your immune system, even if your health is generally good.

Pneumonia is classified according to the types of germs that cause it and where you got the infection.

***Community-acquired pneumonia***

Community-acquired pneumonia is the most common type of pneumonia. It occurs outside of hospitals or other health care facilities. It may be caused by:

- **Bacteria.** The most common cause of bacterial pneumonia in the U.S. is Streptococcus pneumoniae. This type of pneumonia can occur on its own or after you've had a cold or the flu. It may affect one part (lobe) of the lung, a condition called lobar pneumonia.
- **Bacteria-like organisms.** Mycoplasma pneumoniae also can cause pneumonia. It typically produces milder symptoms than do other types of pneumonia. Walking pneumonia is an informal name given to this type of pneumonia, which typically isn't severe enough to require bed rest.
- **Fungi.** This type of pneumonia is most common in people with chronic health problems or weakened immune systems, and in people who have inhaled large doses of the organisms. The fungi that cause it can be found in soil or bird droppings and vary depending upon geographic location.
- **Viruses, including COVID-19.** Some of the viruses that cause colds and the flu can cause pneumonia. Viruses are the most common cause of pneumonia in children younger than 5 years. Viral pneumonia is usually mild. But in some cases it can become very serious. Coronavirus 2019 (COVID-19) may cause pneumonia, which can become severe.

***Hospital-acquired pneumonia***

Some people catch pneumonia during a hospital stay for another illness. Hospital-acquired pneumonia can be serious because the bacteria causing it may be more resistant to antibiotics and because the people who get it are already sick. People who are on breathing machines (ventilators), often used in intensive care units, are at higher risk of this type of pneumonia.

***Health care-acquired pneumonia***

Health care-acquired pneumonia is a bacterial infection that occurs in people who live in long-term care facilities or who receive care in outpatient clinics, including kidney dialysis centers. Like hospital-acquired pneumonia, health care-acquired pneumonia can be caused by bacteria that are more resistant to antibiotics.

***Aspiration pneumonia***

Aspiration pneumonia occurs when you inhale food, drink, vomit or saliva into your lungs. Aspiration is more likely if something disturbs your normal gag reflex, such as a brain injury or swallowing problem, or excessive use of alcohol or drugs.

Risk factors

Pneumonia can affect anyone. But the two age groups at highest risk are:

- Children who are 2 years old or younger
- People who are age 65 or older

Other risk factors include:

- **Being hospitalized.** You're at greater risk of pneumonia if you're in a hospital intensive care unit, especially if you're on a machine that helps you breathe (a ventilator).
- **Chronic disease.** You're more likely to get pneumonia if you have asthma, chronic obstructive pulmonary disease (COPD) or heart disease.

- **Smoking.** Smoking damages your body's natural defenses against the bacteria and viruses that cause pneumonia.
- **Weakened or suppressed immune system.** People who have HIV/AIDS, who've had an organ transplant, or who receive chemotherapy or long-term steroids are at risk.

Complications

Even with treatment, some people with pneumonia, especially those in high-risk groups, may experience complications, including:

- **Bacteria in the bloodstream (bacteremia).** Bacteria that enter the bloodstream from your lungs can spread the infection to other organs, potentially causing organ failure.
- **Difficulty breathing.** If your pneumonia is severe or you have chronic underlying lung diseases, you may have trouble breathing in enough oxygen. You may need to be hospitalized and use a breathing machine (ventilator) while your lung heals.
- **Fluid accumulation around the lungs (pleural effusion).** Pneumonia may cause fluid to build up in the thin space between layers of tissue that line the lungs and chest cavity (pleura). If the fluid becomes infected, you may need to have it drained through a chest tube or removed with surgery.
- **Lung abscess.** An abscess occurs if pus forms in a cavity in the lung. An abscess is usually treated with antibiotics. Sometimes, surgery or drainage with a long needle or tube placed into the abscess is needed to remove the pus.

Prevention

To help prevent pneumonia:

- **Get vaccinated.** Vaccines are available to prevent some types of pneumonia and the flu. Talk with your doctor about getting these shots. The vaccination guidelines have changed over time so make sure to review your vaccination status with your doctor even if you recall previously receiving a pneumonia vaccine.
- **Make sure children get vaccinated.** Doctors recommend a different pneumonia vaccine for children younger than age 2 and for children ages 2 to 5 years who are at particular risk of pneumococcal disease. Children who attend a group child care center should also get the vaccine. Doctors also recommend flu shots for children older than 6 months.
- **Practice good hygiene.** To protect yourself against respiratory infections that sometimes lead to pneumonia, wash your hands regularly or use an alcohol-based hand sanitizer.
- **Don't smoke.** Smoking damages your lungs' natural defenses against respiratory infections.
- **Keep your immune system strong.** Get enough sleep, exercise regularly and eat a healthy diet.

Diagnosis

- **Blood tests.** Blood tests are used to confirm an infection and to try to identify the type of organism causing the infection. However, precise identification isn't always possible.
- **Chest X-ray.** This helps your doctor diagnose pneumonia and determine the extent and location of the infection. However, it can't tell your doctor what kind of germ is causing the pneumonia.
- **Pulse oximetry.** This measures the oxygen level in your blood. Pneumonia can prevent your lungs from moving enough oxygen into your bloodstream.
- **Sputum test.** A sample of fluid from your lungs (sputum) is taken after a deep cough and analyzed to help pinpoint the cause of the infection.
- **CT scan.** If your pneumonia isn't clearing as quickly as expected, your doctor may recommend a chest CT scan to obtain a more detailed image of your lungs.
- **Pleural fluid culture.** A fluid sample is taken by putting a needle between your ribs from the pleural area and analyzed to help determine the type of infection.

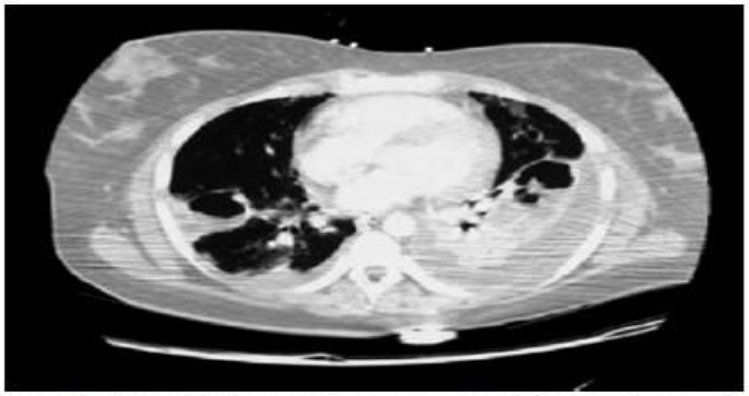

**Figure 2** Necrotizing pneumonia on chest CT showing multiple bilateral nodules and cavitation, lower left lobe consolidation, and pleural effusion in a patient with methicillin-resistant *Staphylococcus aureus*.

Treatment

Treatment for pneumonia involves curing the infection and preventing complications. People who have community-acquired pneumonia usually can be treated at home with medication. Although most symptoms ease in a few days or weeks, the feeling of tiredness can persist for a month or more.

Specific treatments depend on the type and severity of your pneumonia, your age and your overall health. The options include:

- **Antibiotics.** These medicines are used to treat bacterial pneumonia. It may take time to identify the type of bacteria causing your pneumonia and to choose the best antibiotic to treat it. If your symptoms don't improve, your doctor may recommend a different antibiotic.
- **Cough medicine.** This medicine may be used to calm your cough so that you can rest. Because coughing helps loosen and move fluid from your lungs, it's a good idea not to eliminate your cough completely. In addition, you should know that very few studies have looked at whether over-the-counter cough medicines lessen coughing caused by pneumonia. If you want to try a cough suppressant, use the lowest dose that helps you rest.
- **Fever reducers/pain relievers.** You may take these as needed for fever and discomfort. These include drugs such as aspirin, ibuprofen (Advil, Motrin IB, others) and acetaminophen (Tylenol, others).

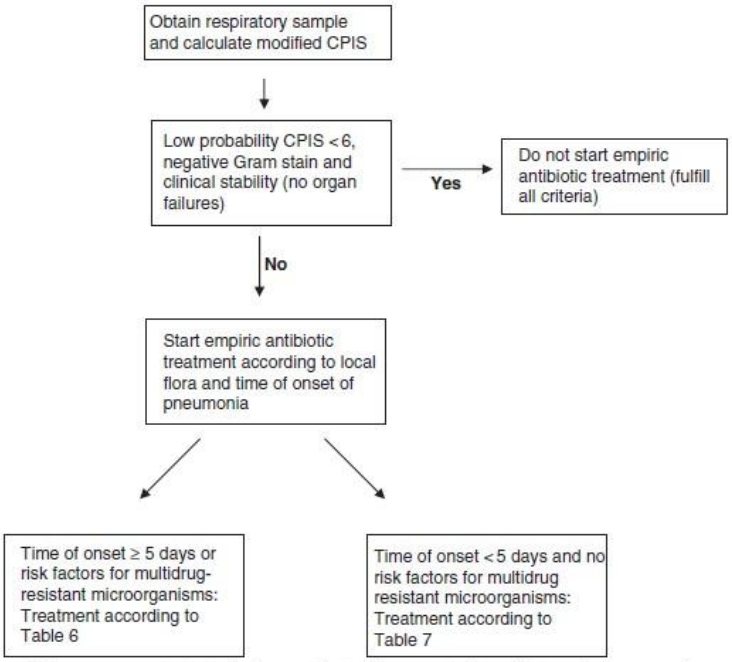


**Figure 3** Summary of the management strategies for a patient with suspected hospital-acquired pneumonia.

**Vaccination**

Vaccination is a safe, effective, and cost-effective tool for preventing pneumonia. There are vaccines against major infectious diseases that can cause pneumonia –the flu (influenza virus), measles, pertussis, Hib, and pneumococcus. The WHO recommends that all routine childhood immunization programs include vaccines that protect against these diseases.24 New vaccines against Hib and pneumococcus are available; many low-income countries have already introduced the Hib vaccine, and pneumococcal conjugate vaccines (PCVs) are increasingly becoming available in developing countries as well. The 7- and 13-valent conjugate vaccines (PCV7, PCV13) have demonstrated effectiveness in reducing incidence and severity of pneumonia and other lower respiratory infections in children. Immunizations help reduce childhood pneumonia in two ways. First, vaccinations help prevent children from developing infections that directly cause pneumonia, such as Hib and S. pneumoniae. Second, immunizations may prevent infections that can lead to pneumonia as a complication, such as influenza, measles, and pertussis. 3 Pneumococcal conjugate vaccines are highly effective in preventing pneumococcal disease. 4 Currently, there are three vaccines on the children's routine immunization schedule that have the potential to significantly reduce childhood mortality from and related to pneumonia: measles, Hib, and pneumococcal conjugate vaccines. In 2007, the WHO recommended introducing pneumococcal conjugate vaccine (PCV) into all national immunization programs, particularly in countries with high mortality. Since that time, progress has been made in introducing PCV globally with increasing usage in low-income countries.

## II. LITERATURE REVIEW

Etiology Research for Child Health (PERCH) study is the largest multisite study of childhood pneumonia since the Board of Science and Technology for International Development (BOSTID) studies were done in the 1980s [2]. The goal of PERCH to identify the expected etiologies of pneumonia in 2015, a time when the burden of the major causes of bacterial pneumonia in the developing world, *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib), will likely be significantly reduced by widespread introduction and use of conjugate vaccines. Moreover, PERCH capitalizes upon new molecular diagnostic techniques that were not available 2 decades ago when the BOSTID studies were carried out. Another salient difference between PERCH and the BOSTID studies is that the 7 sites participating in PERCH will follow a highly standardized protocol, which includes standardization of enrollment criteria, specimen collection, and laboratory testing.

Although PERCH is the largest multicountry, childhood pneumonia etiology study in developing countries that has been conducted in the past 2 decades, it is not the only contemporary pneumonia etiology study, and cannot capture the entire complexity of all epidemiologic settings. In recent years, many developed and developing country sites have initiated pneumonia studies that provide etiology data. These studies will provide useful complementary data to the PERCH study that will more fully define and characterize the causes of childhood pneumonia throughout the world. Yet, because the clinical, laboratory and statistical analysis approaches of these studies vary significantly, collating the results of multiple etiology studies will likely prove challenging. Differences in observed etiology can arise not only from epidemiologic differences in the sites and populations studied, which are biologic and epidemiologic attributes relevant to public health decision making, but also from variability in study design. Consideration of how study design can affect the results of etiologic studies is crucial to interpreting such studies in the context of PERCH.

In this paper, we describe the global landscape of sites that are currently studying pneumonia etiology or have recently studied it in the developed and developing world as ascertained by a literature review of studies with data since the year 2000 and a survey of pneumonia researchers. We did not aim to conduct a systematic review of the literature or a meta-analysis of study results. Furthermore, we did not undertake a critical evaluation of the methods or results from the studies we identified. The purpose of this project is limited to a landscape analysis to better describe the breadth of available data on child pneumonia etiology.

The time of onset of pneumonia is an important epidemiologic variable and risk factor for specific pathogens and outcomes in patients with HAP and VAP. Early-onset pneumonia is defined as that occurring within the first 4 days of hospitalization. It usually carries the best prognosis and is more likely to be caused by microorganisms that are already carried by the host ('community flora'): S. pneumoniae, Haemophilus influenzae, S. aureus, and anaerobes. 'Late-onset' pneumonia (5 days or more) is more likely to be caused by multi-drug-resistant pathogens and is associated with a poor prognosis: Pseudomona aeruginosa (30%), S. aureus including methicillin-resistant (25%), Gramnegative enteric bacilli (25%), L. pneumophila (5%), S. pneumoniae (5%), H. influenzae (5%), Aspergillus and Candida species (5%), and polymicrobial (30%)The clinical features that point to nosocomial pneumonia include the presence of new and persistent pulmonary infiltrates, temperature greater than 38.3 C or less than 36 C, white blood cell count greater than 12 000/mm3 or less than 4000/mm3, and purulent secretions. Unfortunately, many hospitalized patients present such findings for other reasons, especially intubated patients, thus making diagnosis difficult. The diagnostic criteria of a radiographic infiltrate and at least one of the additional criteria previously mentioned have a high sensitivity but low specificity (especially in VAP), while the presence of a pulmonary infiltrate plus two additional clinical

findings result in a sensitivity of 69% and a specificity of 75% (Fabregas et al., 1999). Given the poor accuracy of an isolated clinical finding, a score of clinical findings (a 'modified clinical pulmonary infection score' – CPIS) can be used for initial decision making. This score is based on previously mentioned findings and an oxygenation index (Table 5). If the sum is 6 or greater than 6, a respiratory sample is justified and empirical antibiotic treatment is begun (Torres et al., 2006). The most important challenges in the management of suspected HAP are to avoid inappropriate or delayed antibiotic treatment with the higher mortality that this entails, and, on the other hand, to prevent the emergence of multi-drug-resistant microorganisms by avoiding indiscriminate antibiotic prescription. To achieve this double purpose it is imperative to obtain a lower respiratory tract sample for Gram stain and culture (to confirm the diagnosis) and antibiogram (adjusting the antibiotic to the sensitivity pattern when available) (Bonten et al., 2005).

In patients breathing spontaneously, respiratory secretions can be obtained by expectoration (with the same considerations as CAP for 'valid' sputum). The diagnostic accuracy of sputum in HAP has yet to be established. In intubated patients, lower respiratory tract cultures can be obtained bronchoscopically or nonbronchoscopically, and can be cultured semiquantitatively or quantitatively with different cut-off points for discriminating 'colonization' from 'infection' according to the method. Quantitative cultures and more invasive methods increase the specificity of the diagnosis without deleterious consequences. However, each institution should choose the technique based on local expertise, experience, and availability, because, when the diagnostic and therapeutic approaches are protocol driven and the initial treatment is adequate, the clinically relevant outcomes and use of antibiotics are the same with both the invasive and noninvasive (and quantitative and semiquantitative) methods. In order to facilitate the diagnostic approach, a tracheobronchial aspirate with Gram stain and semiquantitative or quantitative culture (cut-off point to differentiate colonization from infection: 105 colony forming units/mL for the quantitative method) (Canadian Critical Care Trials Group, 2007) should be obtained. Figure 3 presents a summary of the management of these patients

## III. DISCUSSION AND CONCLUSION

Discussion

The results of the literature review and survey reveal that many child pneumonia etiology studies have been and are taking place throughout the world since the year 2000, which enable an understanding of PERCH data in the context of a global landscape of ongoing pneumonia research. The large quantity and great depth of the available data highlight the challenges in interpreting various pneumonia etiology studies, particularly when comparing or combining results. Different studies employ different case definitions, levels of clinician involvement, facility types, specimens collected and laboratory tests. The use of a common protocol in a multisite study with broad geographic and epidemiologic representation will enable inferences to be drawn about the similarities and differences from other studies.

Our landscape analysis identified several gaps in the availability of data regarding childhood pneumonia etiology. First, there were few studies identified in Latin America (outside of Brazil, Chile and Argentina), in west and particularly central Africa, and in the Middle East. No studies were identified from Russia or China. This gap may be due in part to our English language inclusion criterion. It is important to have data from places where child pneumonia mortality is the highest. South Asia and parts of Africa, which are regions of the world with the greatest burden of childhood pneumonia deaths, are well-represented in pneumonia etiology studies. Nonetheless, the 5 countries with the highest burden of child pneumonia deaths—India, Nigeria, Pakistan, the Democratic Republic of Congo (DRC) and Afghanistan —are not proportionally represented in our literature review. Our literature review identified only 7 studies conducted in India, 3 in Nigeria, 2 in Pakistan and none in the DRC or Afghanistan. Second, there needs to be more pneumonia etiology studies in countries that have or are currently introducing both the Hib and pneumococcal conjugate vaccines. Such studies will help define the new distribution of pneumonia-causing etiologies in these settings, which will likely have important implications for diagnosis and empiric treatment algorithms. Third, there are few studies that report postmortem results. It is important to understand the spectrum of etiologies for the most severe cases of pneumonia, which will be critical in reducing the still high burden of childhood pneumonia mortality in the world. Although technically and culturally challenging, postmortem studies reveal a different and complementary picture of etiology that is otherwise underestimated or forgotten. This applies particularly to tuberculosis, HIV-associated conditions (eg, lymphocytic interstitial pneumonia, *Pneumocystis jiroveci (carinii)* pneumonia and cytomegalovirus disease), and to other pathogenic processes that produce a clinical syndrome that mimics pneumonia (eg, severe anemia with heart failure or interstitial lung disease).

Variation in the methods employed by different pneumonia etiology studies can lead to differences in the identified etiologies. For example, the case definition used can influence the distribution of microbial etiologies. Case definitions based on radiologic (eg, alveolar consolidation) and laboratory definitions (eg, left-shift of polymorphonuclear neutrophils) are likely to identify more bacterial than viral pneumonia cases. Alternatively, a simple clinical case definition based on tachypnea (eg, nonsevere pneumonia defined by the Integrated Management of Childhood Illness) or a definition that included wheeze might lead to the

identification of relatively more viral infections. Given the association between clinical severity and etiology, the target population and facility type can also determine the spectrum of etiologies. Thus, studies in community-based settings, health centers or outpatient wards may find different ranges of etiologies than studies in referral hospitals. Age is an influential variable and studies that exclude older children and focus on infants are likely to identify more RSV infection, which predominates in infancy. Neonates, in particular, have a distinct set of pneumonia pathogens.

Other factors that varied across studies were the type of body fluid specimens collected and the type of laboratory testing done. Detection of bacterial pneumonia is dependent to a large extent on blood culture. While a majority of studies performed blood culture, it is likely that there was considerable variation in the sensitivity of the tests, particularly for *Streptococcus pneumoniae*, which is a fastidious organism requiring optimal collection and laboratory conditions. There are other factors that may result in an over-representation of viral causes of pneumonia. It was notable that the use of PCR as a diagnostic tool was higher in the studies reported on the survey (68%) than in those already published in the literature (46%). As molecular diagnostics become more widely used, it will be important to disaggregate temporal trends in the epidemiology of viral pneumonia from trends in laboratory practice. The findings of PCR testing of nasopharyngeal and oropharyngeal swabs will need to be interpreted judiciously. The presence of viral nucleic acids in the pharynx does not necessarily mean that the virus is acutely causing pneumonia in the lungs. As PCR use increases, strategies must be used to help interpret these findings. One such strategy is to include control children (ie, those without pneumonia) in whom similar body fluids are collected and tested, which will allow for improved ability to interpret the PCR results .

Our landscape analysis had several limitations. In spite of employing multiple search strategies, we likely missed identifying some studies. Of note, we only searched the English language literature and only utilized one literature database (PubMed). This likely biased our findings by excluding studies from certain geographic regions such as China, Spanish-speaking Latin America, Russia and the Middle East where there may be a substantial body of evidence in local language publications. We did not search Embase and thus did not include conference abstracts unless researchers directed us to specific abstracts. Second, some published studies lacked sufficient detail to provide information on particular aspects of the study design that were of interest. Notable missing data were case definitions, facility types, and eligibility determination. Our survey likely suffered from similar limitations as far as incompleteness of data that was provided for some studies. Similarly, we only reached out to researchers who were already identified in the field, which might have led to gaps in those contacted. Third, not all identified studies were intended to be pneumonia etiology studies. Several had other primary objectives, such as to study invasive pneumococcal disease or influenzalike illness, and in that process identified children with pneumonia. As such, these studies are by design not comparable to studies that identify multiple pneumonia pathogens in that their case definitions and patient mix would likely differ. Finally, we were unable to verify survey responses.

In conclusion, the review of the literature and the survey of studies illustrate the context within which the PERCH study will be interpreted. Pneumonia etiologies are likely to continue to evolve as more countries introduce Hib and pneumococcal conjugate vaccines. Vaccines for other major causes of childhood pneumonia such as influenza will likely become more widely used across the globe or may be successfully developed (eg, RSV) over the next decade, and therefore, will further influence the pneumonia burden and remaining etiologies. Improvement in global socioeconomic conditions will also influence the pneumonia etiologic spectrum in the future. One of the goals of PERCH is to create a reference standard for the design, conduct and analysis of pneumonia etiology studies. This will provide a framework within which valid between-site comparisons can be drawn and integrated models can be extended geographically. PERCH will also contribute to a refinement of the case definition of pneumonia and provide evidence for the utility of certain body fluid specimens and laboratory tests. We hope that the definition of a standard, and the publication of the validation processes that were undertaken to create that standard, will encourage investigators to analyze existing studies and design future studies with reference to this standard in order to optimize the epidemiological value of the results.

**Conclusion**

Over one million children will die before their fifth birthday, nearly all of which are preventable. The attainment of the Millenium Development Goal 4 (MDG4) is possible only if life-saving newborn and child health interventions for pneumonia are rapidly scaled up in high-burden regions and countries, as well as in special population groups in the next few years. Prevention by means of vaccination would be most crucial for reducing pneumonia mortality in children under five, while effective (uptake of) antibiotic therapy for the elderly would serve to decrease mortality due to pneumonia in Europe. Community-based management of severe disease could be an important complementary strategy to reduce pneumonia mortality in children under five as well as in the elderly. Pneumonia has a great burden of morbidity and mortality in developing countries, which results in economic and social pressures on families and the country as a whole. Therefore, pneumonia prevention is not only about saving the lives of children, but it is also about preventing illness, hospitalization,

and related economic costs. An integrated care management system has proven to be effective in reducing pneumonia mortality by 17% with the available vaccines against Hib and S. pneumoniae; in addition to breastfeeding promotion and zinc supplementation, overall childhood mortality could be further reduced.

The high global burden of pneumonia warrants further investigation in technology innovation in the field of rapid diagnostic tests and in novel vaccines for viral pneumonia. Improved rapid diagnostics at point-of-care along with effective antibiotic treatments would aid in the reduction of pneumonia mortality, while wide-scale implementation of pneumococcal vaccines would help prevent incidences of pneumonia worldwide. Moving forward, research institutions, pharmaceuticals, and smalle and medium enterrpises must work alongside government and funders to create initiatives for the development of novel medical devices and biologics. The constant and unpredictable nature of pneumococcal pathogens can outpace technological and drug development, thus it is crucial for researchers and innovators to continue to make progress in research and development of pharmaceuticals and non-pharmaceuticals interventions.

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