

5-9-2015

A Ten Year Retrospective Study of Pediatric Pneumonia Cases in Haiti

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Recommended Citation

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A Ten Year Retrospective Study of Pediatric Pneumonia Cases in Haiti

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Colby College, 2009

A Thesis

Submitted in Partial Fulfillment of the

Requirements for the Degree of

Master of Public Health

At the

University of Connecticut

2015

APPROVAL PAGE

Masters of Public Health Thesis

A Ten Year Retrospective Study of Pediatric Pneumonia Cases in Haiti

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2015

Acknowledgements

I would like to acknowledge my major advisor during this and previous public health projects, Professor Judy Lewis. Professor Lewis' expertise, guidance, and encouragement have greatly helped me accomplish this work. Her passion and experience in global health has also inspired me to pursue global health in my studies at the University of Connecticut and in my future endeavors as a pediatrician.

I am also full of appreciation to the other members of my thesis advisory committee, Dr. David Gregorio and Dr. Jane Ungemack, for guiding me through this work and my entire public health degree. Thank you also to Dr. Bette Gebrian for her assistance and advice during this thesis project and to Deborah Paturzo and Holly Samociuk who assisted with data manipulation and analysis.

I would also like to acknowledge my fiancé, Peter Hitt, my sister, Marisa Savic, and my parents, Anna and Michael Savic. I could not have succeeded in my pursuit of a dual MD/MPH degree without their unrelenting support throughout this process. Lastly, I have special thanks to all my friends who have helped me de-stress and kept me sane, especially at times when I needed their friendship the most.

Introduction

Childhood pneumonia is the top cause of childhood mortality in children under five years of age, and the incidence of childhood pneumonia is much greater in developing countries than developed countries (Fischer Walker et al., 2013; Rudan et al., 2008). In 1990, the World Health Organization (WHO)/United Nations (UN) formed eight Millennium Development Goals (MDGs) to establish concrete targets to improve worldwide disease and hunger. One of those, MDG Goal 4, was to reduce the under-five mortality rate by two-thirds by 2015 (WHO, 2013). The focus of those efforts has been pneumonia prevention through vaccinations, reduction of risk factors, early diagnosis, and treatment.

The experiences of a community oriented primary care (COPC) program of a small non-governmental organization (NGO) located in southern Haiti illustrates the approaches and successes of pneumonia prevention for children in a developing country. Haiti provides an excellent case study due to its extreme poverty and economic and governmental fragility, especially following the 2010 7.0 earthquake. The under-five mortality in Haiti was 75.6 per 1,000 live births in 2012, much higher than the average for Caribbean and Latin American countries of 19 per 1,000 live births (WHO, 2012; UNDP, 2014). Contributing to the high rates of childhood mortality in Haiti is a lack of access to care: approximately 40% of the population of Haiti did not have access to health services in 2006 (Ivers, 2011).

In 1993, the NGO affiliated with this study established an organized acute respiratory infection (ARI) program with community case management (CCM) by

community health workers (CHWs) to cover their catchment population of 200,000 people (Lewis & Gebrian, 2009). Previous research of the ARI program showed a decline in childhood pneumonia mortality from 6.3/1000 to 3.1/1000 in this program from 1993-1997 (Dowell & Heffelfinger, 1997). This current study evaluates more recent evidence of the ARI program's effectiveness through analysis of all reported cases of pediatric pneumonia from 2004-2013. This study also examined geographical and seasonal factors that may be associated with increased risk for pneumonia. This study is intended to contribute to a better understanding of the potential of community case management programs to adequately identify and treat childhood pneumonia cases and reduce overall childhood mortality in developing countries.

ABBREVIATIONS

1. **ALRI** =Acute lower respiratory infection
2. **ARI** =Acute respiratory infection
3. **CCM** =Community case management
4. **CHWs** =Community Health Workers
5. **COPC** =Community oriented primary care
6. **GAPP** =Global Action Plan for Prevention and Control of Pneumonia
7. **Hib** =*Haemophilus influenzae* type b
8. **IMCI** =Integrated Management of Childhood Illnesses
9. **MDGs** =Millennium Development Goals
10. **NGO** =Non-governmental organization
11. **PCM** =Protein-calorie malnutrition
12. **PCV7 or PCV13** =7-valent or 13-valent pneumococcal conjugate vaccine
13. **RSV** =Respiratory Syncytial Virus
14. **UN** =United Nations
15. **WHO** =World Health Organization

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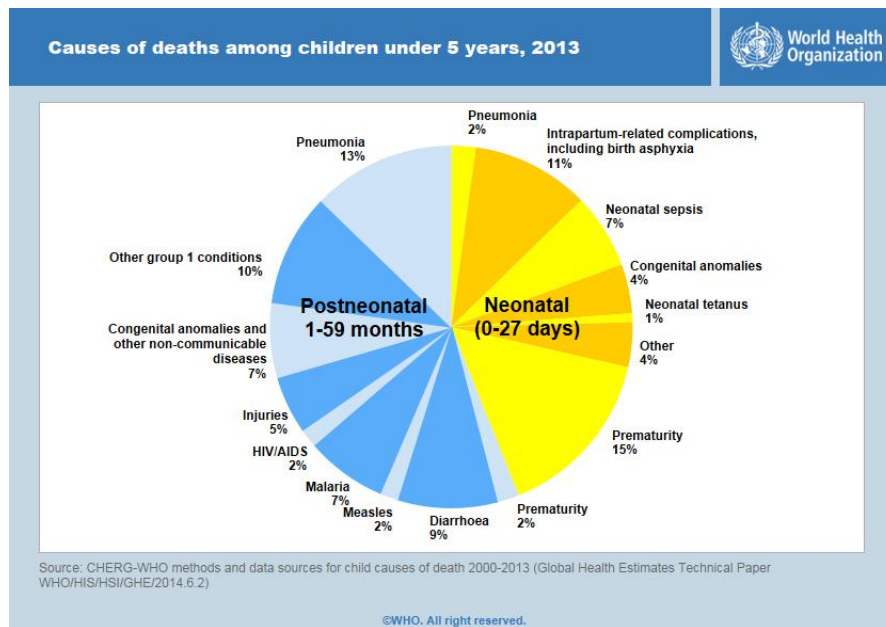
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Background

Scope of the Problem

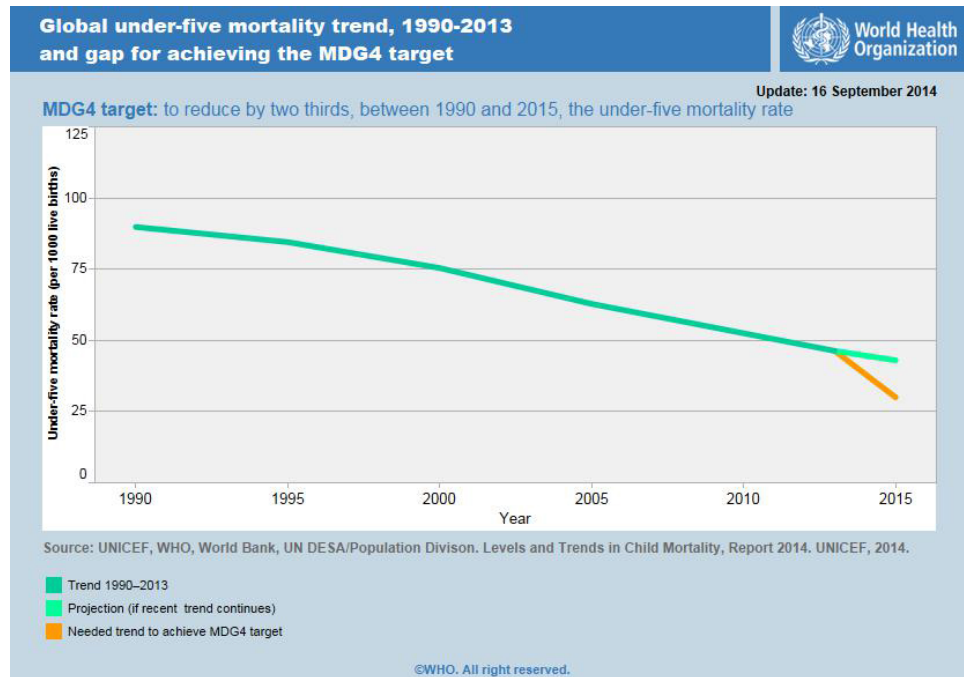
In 2013, 6.3 million children under five years old died worldwide, nearly 17,000 every day (WHO, 2013). Almost 75% of all child deaths are attributed to only six conditions: neonatal causes, pneumonia, diarrhea, malaria, measles, and HIV/AIDS (see Figure 1). Pneumonia is the leading cause of death in children under five, with 1.3 million deaths out of a total 120 million episodes of pneumonia in 2011 (Fischer Walker et al., 2013). Approximately 11-20 million cases (7-13%) of pneumonia are severe enough to require hospitalization (Rudan et al., 2008; Singh & Aneja, 2011). Although pediatric pneumonia affects children worldwide, the majority of cases occur in developing countries. In 2000, the estimated incidence of pneumonia in children under 5 years old in developing countries was 0.29 episodes per child-year compared to 0.05 episodes per child-year in developed countries (Rudan et al., 2008).

Figure 1. Global causes of under-five mortality (WHO, 2013)



Goal 4 of the WHO MDGs was to reduce the under-five mortality rate in 1990 by two-thirds by 2015 (WHO, 2013). Significant progress has been made – under-five deaths declined from 12.7 million in 1990 to 6.3 million in 2013. WHO estimated that there were 17,000 fewer children dying every day in 2013 compared to 1990. However, as shown in Figure 2, the WHO projected that the MDG of 4 million deaths by 2015 would not be reached. Pneumonia will continue to be a focus of ending preventable child deaths for the foreseeable future. Many more deaths can be prevented with a focus on pneumonia causes, management, and prevention in developing countries.

Figure 2. WHO global under-five mortality trend, 1990-2013 (WHO, 2014)



Etiology of Pediatric Pneumonia

The majority of pediatric pneumonia cases in developing countries are due to bacterial causes. In particular, the most common organism is *Streptococcus pneumoniae*, which has been identified in 30-50% of pneumonia cases (Singh & Aneja, 2011). The second most common bacteria causing pneumonia is *Haemophilis influenzae* type b (Hib), followed by *Staphylococcus aureus* and *Klebsiella pneumoniae*. Viral pathogens such as RSV, influenza A & B, parainfluenza, human metapneumovirus, and adenovirus can also lead to acute respiratory infections.

Streptococcus pneumoniae

S. pneumoniae is the leading cause of community-acquired pneumonia worldwide (van der Poll & Opal, 2009). There are currently 91 recognized serotypes of *S.*

pneumoniae. It is a bacterium that is a common resident in the upper respiratory tract of humans causing many individuals to be carriers. It is estimated that 10% of adults and 20-40% of healthy children are carriers, allowing the organism to be maintained in human populations. It is transmitted through direct contact with respiratory secretions, most commonly of those in the same household. Although pneumococci are not considered highly contagious, large community-wide outbreaks can still occur, especially in urban settings or areas with high population density. It commonly affects patients with AIDS and other immunocompromised states and the elderly as well as children under 5. One report found 13.8 million cases of pneumococcal pneumonia in 2000, accounting for 41% of all pneumonia deaths in children (Izadnegahdar et al., 2013). In addition, at least 1-2 million infant deaths yearly can be attributed to *S. pneumoniae* (van der Poll & Opal, 2009).

Pneumococcal pneumonia usually begins as a mild upper airway infection similar to a viral respiratory infection. If the pneumococcal bacteria enter the lower airways despite responses to prevent its descent such as coughing, mucous clearance, and local immune defenses, pneumonia will develop abruptly (van der Poll & Opal, 2009). The initial symptoms of pneumococcal pneumonia include fever, chills, fatigue, cough, and shortness of breath. The cough associated with pneumococcal pneumonia will then become purulent with blood-tinged sputum and will be associated with chest pain. If left untreated, this disease can progress to acute respiratory failure, septic shock or death within days of onset. *S. pneumoniae* can also have clinical manifestations of meningitis, sepsis, pericarditis, and endocarditis. The more severe manifestations often occur in those

with immunocompromised states including the elderly, neonates, HIV positive individuals, and asplenic individuals.

Haemophilus pneumoniae

Haemophilus pneumoniae type b (Hib) is the second most common bacteria-causing pneumonia worldwide. Hib pneumonia caused about 7.9 million cases worldwide in 2000 and accounted for 16% of total pneumonia deaths in children (Izadnegahdar et al., 2013). Hib's total mortality in children age 1-59 months is high at 371,000 deaths yearly (Watt et al., 2009). Combined with *S. pneumoniae*, these two pathogens are directly responsible for as many deaths worldwide as HIV/AIDs, malaria, and tuberculosis combined (Rudan & Campbell, 2009). In addition to causing pneumonia, Hib has other severe and life-threatening manifestations of meningitis and epiglottitis (Watt et al., 2009). Similarly to *S. pneumoniae*, Hib also resides in the nose and throat mucosa and can be spread through respiratory droplets (Hall, 2010). Hib pneumonia and pneumococcal pneumonia are both forms of lobar community-acquired pneumonias and present clinically in the same way.

Respiratory Syncytial Virus

The most common viral cause of pneumonia is Respiratory Syncytial Virus (RSV), which caused 33.8 million cases of acute lower respiratory infections (ALRI) in children under five in 2005 (Hall, 2010). This estimate corresponds to 22% of all ALRI and 3-9% of ALRI-related deaths. RSV occurs worldwide, yet has the greatest burden of disease in developing countries; 96% of ALRI caused by RSV and 99% of fatal cases of RSV were in developing countries in 2005. RSV has been attributed to 15-40% of

children hospitalized for pneumonia or bronchiolitis in developing countries (Singh & Aneja, 2011). The age group primarily affected by RSV pneumonia is between 2 and 12 months of age (Weber et al., 1998). Specifically, the infants most at risk are those with underlying conditions including prematurity, lung disease, malnutrition, or congenital heart disease. RSV is a seasonal virus and occurs in cold seasons or wet seasons in temperate and Mediterranean climates, respectively. In islands in which there is perennial high rainfall, RSV seasonality can be difficult to predict (Weber et al., 1998).

RSV bronchiolitis begins as an upper respiratory tract infection with rhinitis, cough, and fever. These signs precede involvement of the lower respiratory tract in which patients begin to have shortness of breath, difficulty feeding, and respiratory distress (Simoes, 1999). In RSV bronchiolitis, unlike typical bacterial pneumonias, patients often also have a wheeze, prolonged expiratory phase, and air trapping, similar to asthmatics. RSV can also cause a pneumonia-like syndrome in one-third of cases, which requires longer respiratory support than bronchiolitis, and most often occurs in infants with underlying diseases. Viral and bacterial pneumonia often coincide. In one study in Pakistan, greater than 25% of patients with RSV also had a co-infection with *S. pneumoniae* or Hib (Singh & Aneja, 2011). Co-infection with bacteria is predicted to account for a large part of the mortality caused by RSV (Simoes, 1999).

Treatment in RSV bronchiolitis and pneumonia is mostly supportive with oxygen therapy and mechanical ventilation as needed (Simoes, 1999). In addition, since airway inflammation is a major factor in mortality due to RSV, the use of a long-acting beta adrenergic inhaler or inhaled racemic epinephrine are possible treatment options, although they have had mixed results in clinical studies. In developing countries, anti-

viral treatment with ribavirin is rarely used due to its high cost and lack of consensus on its efficacy in RSV.

Influenza

Another viral cause of pneumonia that is recently considered to be a bigger contributor to pediatric pneumonia cases in developing countries than originally thought is influenza. In the United States and other temperate regions, influenza plays a big role in respiratory disease in children. In a 25-year prospective study by Neuzil et al. (2002) at Vanderbilt University, the rate of influenza-associated complications among children <2 years old was approximately 3-4 per 1000 children (Brooks et al., 2010). However, there was much uncertainty about influenza's contribution to pediatric pneumonia in tropical and sub-tropical climates. Recent studies in tropical developing countries have shown that influenza was associated with 10-17% of all pneumonia cases in under-five children (Brooks et al., 2010; Rudan et al., 2013). In one study in Bangladesh, influenza was present year-round with peaks in wet seasons (Brooks et al., 2010). Of the influenza subtypes, influenza A (H3N2) was associated with 47% of all influenza-related pneumonia, approximately 3 times more strongly associated with pneumonia than the other influenza viruses, influenza A (H1N1) and influenza B. In addition, influenza has been shown to interact with other pathogens, most notably pneumococcal pneumonia, to exacerbate pneumonia severity.

Diagnosis and Treatment of Childhood Pneumonia in Low Resource Settings

Since pneumonia continues to be a leading cause of mortality in children under 5 in developing countries and a major barrier to achievement of the WHO MDG 4, the

WHO developed guidelines to assist in diagnosis and treatment of childhood pneumonia in low-resource settings in 1991. The diagnosis guidelines were based on clinical signs of pneumonia (see Table 1.). The WHO criteria used for diagnosis of pneumonia requires cough or difficulty breathing as well as age-specific tachypnea (Wingerter et al., 2012). Age-specific tachypnea is defined as greater than 60 breaths/minute for children less than 2 months old, greater than 50 breaths/minute for children 2-11 months of age, and greater than 40 breaths/minute for children 1-5 years of age. WHO identifies three categories of pneumonia: very severe, severe, or not severe. These categories are determined following the WHO algorithm as follows: “very severe” pneumonia contains one of the following signs or symptoms: central cyanosis, inability to breastfeed or drink, severe respiratory distress, or convulsions, lethargy, or unconsciousness. “Severe” pneumonia is defined as not meeting criteria for “very severe” pneumonia and having one of the following: retractions, nasal flaring, or grunting. Lastly, “not severe” pneumonia is defined by the WHO as meeting the general criteria for pneumonia, but not meeting the criteria for “very severe” or “severe” pneumonia (Wingerter et al., 2012).

Table 1. WHO Diagnosis of Pneumonia Guidelines (Wingerter et al., 2012)

WHO Diagnosis of Pneumonia requires:		
1) Age-Specific Tachypnea: For <2 months old defined as >60 breaths/min; For 2-11 months old defined as >50 breaths/min; For 1-5 years old defined as >40 breaths/min		
AND 2) Cough or Difficulty Breathing		
Very Severe if signs of: 1) Central cyanosis 2) Inability to breastfeed or drink 3) Severe respiratory distress 4) Convulsions 5) Lethargy 6) Unconsciousness	Severe if DO NOT meet criteria for very severe and if signs of: 1) Retractions 2) Nasal flaring 3) Grunting	Not Severe: If meet criteria for diagnosis of pneumonia but DO NOT meet criteria of very severe or severe pneumonia

While the WHO diagnosis algorithm is clear and easy to follow, studies comparing it to diagnosis of pneumonia by radiographs in the United States indicate that these guidelines are neither sensitive nor specific in diagnosing pneumonia in children (Wingerter et al., 2012). Radiographs are not ideal for diagnosis either, though, since there is much disagreement on their findings which often leads to over-diagnosis (Izadnegahdar et al., 2013). Other diagnostic approaches include blood culture to assess for bacteria, which would only be available 24-48 hours after presentation, and blood PCR assays, which can be used for viruses as well as bacteria. Yet, use of blood tests often has low yields and they are best for diagnosing pneumonia after it becomes severe. Nasopharyngeal samples are more sensitive, but can also be complicated by difficulty

distinguishing between pathogenic and carrier bacteria. There is therefore a need for improved diagnostic methods in developing countries to guide treatment.

In 1992, WHO created recommendations for treatment, the Integrated Management of Childhood Illnesses (IMCI) guidelines, based on the recommendations for diagnosis of pediatric pneumonia (Izadnegahdar et al., 2013). These treatment guidelines were originally separated into “not severe”, “severe”, and “very severe” pneumonia and were revised in the 2013 update of the IMCI guidelines (see Table 2), with the categories re-named: “not severe” pneumonia was changed to “fast breathing” pneumonia, “severe” pneumonia was changed to “chest indrawing” pneumonia, and the “very severe” pneumonia category, which includes pneumonia with any danger signs, was changed to “severe” pneumonia category. The treatment recommendations are as follows. For “severe” pneumonia, the guidelines advise treatment with parenteral antibiotics of ampicillin, penicillin or gentamicin and if treatment fails, to use ceftriaxone. In “chest indrawing” pneumonia, it is recommended to treat with oral amoxicillin for 5 days. The “fast breathing” pneumonia category is divided based on the presence of wheeze. If the child does not have a wheeze, they should be treated with oral amoxicillin for which duration would be 3 days or 5 days for low-prevalence areas and high-prevalence areas, respectively. In children with a wheeze, which would point to contribution of asthma or RSV bronchiolitis to the patient’s illness, a bronchodilator challenge is recommended prior to administration of oral amoxicillin (Izadnegahdar et al., 2013).

Table 2. Updated Integrated Management of Childhood Illnesses (IMCI) guidelines

(Izadnegahdar et al., 2013)

Severe Pneumonia (previously "very severe")	Chest Indrawing Pneumonia (previously "severe")	Fast Breathing Pneumonia (previously "not severe")
<ul style="list-style-type: none"> • Parenteral antibiotics of ampicillin, penicillin, or gentamicin • If treatment fails, use ceftriaxone 	<ul style="list-style-type: none"> • Oral amoxicillin for 5 days 	<ul style="list-style-type: none"> • If no wheeze: <ul style="list-style-type: none"> • Oral amoxicillin • 3 days if low-prevalence area • 5 days if high-prevalence area • If wheeze: <ul style="list-style-type: none"> • Bronchodilator challenge recommended prior to use of oral amoxicillin

Earlier versions of the IMCI guidelines used the antibiotic co-trimoxazole rather than oral amoxicillin, but this was changed due to increasing treatment failure, attributed to increasing bacterial resistance to co-trimoxazole (Izadnegahdar et al., 2013). However, amoxicillin is a more expensive antibiotic and more difficult to obtain in developing countries. Also, since studies have also shown that hypoxia during a pneumonia event is a high predictor for mortality, the most recent IMCI guidelines have also added recommendations for frequent monitoring of oxygen saturation with pulse oximetry (a low cost and mobile device) and oxygen therapy when needed. This addition of oxygen therapy to the IMCI guidelines has resulted in a 35-50% reduction in pneumonia mortality. As intended by the WHO, these guidelines allow for simple training of first-level health care providers, such as community health workers (CHWs) in low-resource

locations, to diagnose and quickly treat mild to moderate pneumonia cases in home-based settings, eliminating the need to refer to hospital-based care for non-complicated cases (Izadnegahdar et al., 2013).

Continued Obstacles to Pneumonia Management in Developing Countries

Despite the WHO's efforts to create clear guidelines for diagnosis and treatment of pneumonia in children, challenges remain. In particular, due to increasingly drug resistant bacterial pathogens, antibiotics alone are not an adequate strategy to fight pediatric pneumonia in developing countries. In addition, *S. pneumoniae*, the most prevalent pathogen, has 91 total serotypes that are constantly shifting (Izadnegahdar et al., 2013). Also, although the antibiotics in these guidelines address non-resistant pneumococcal and Hib pneumonia, they do not address the increased recognition of viral pathogens to development of severe pneumonia, most commonly RSV and influenza A. Therefore, regardless of the advances in pediatric pneumonia treatment once patients are ill, larger reductions in mortality can be made by focusing on prevention of pneumonia through vaccination programs and reduction of risk factors.

Vaccination Programs

In the effort to reduce pediatric pneumonia worldwide, much research over the past several decades has focused on the creation of vaccines against the most common etiologic agents of pediatric pneumonia. Historically, pertussis and measles were significant causes of childhood pneumonia (Madhi et al., 2008). The pertussis vaccination, which has been available since the 1950s and is included in most immunization programs worldwide, is estimated to have prevented 38.3 million cases and

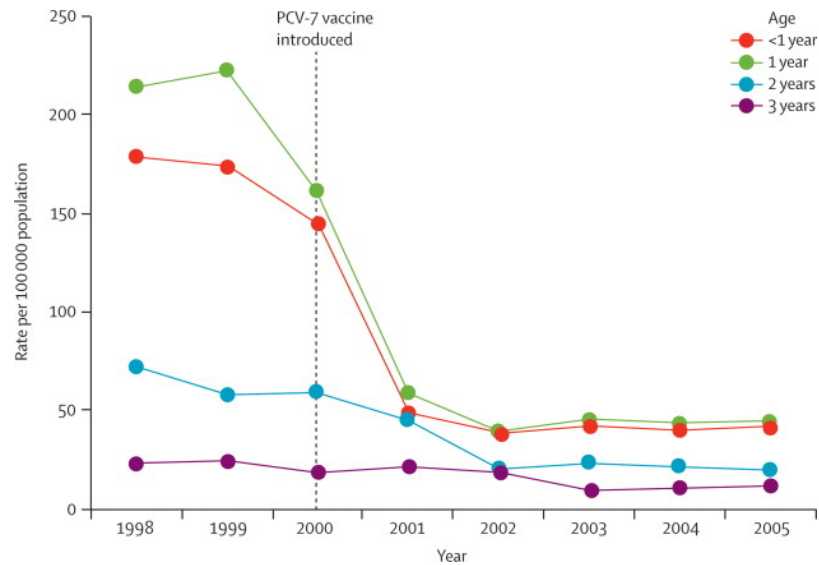
607,000 deaths. The measles vaccination has also had a significant effect; measles deaths declined from 2.5 million to 873,000 from 1980 to 1999. More recently, vaccines have been developed for *S. pneumoniae*, *H. influenzae* type b, and influenza.

Many recent advances in pneumococcal vaccination have occurred over the past two decades. There are two different types of pneumococcal vaccination, a pneumococcal polysaccharide vaccine that is composed of purified preparations of the pneumococcal capsular polysaccharide, and a pneumococcal conjugate vaccine that includes purified pneumococcal capsular polysaccharide conjugated to a non-toxic variant of diphtheria toxin (CDC, 2012). The first pneumococcal vaccine was a polysaccharide vaccine which was licensed in the U.S. in 1977 and contained 14 types of pneumococcal bacteria. This vaccine was improved upon and in 1983 a 23-valent polysaccharide vaccine replaced the 14-valent one. Although this pneumococcal polysaccharide vaccine has been in use since the early 1980s, it is not recommended in pediatric populations due to studies showing that the ability to mount adequate immune responses to polysaccharide vaccines is absent in neonates and children below 2 years of age (Balloch et al., 2010). Instead, vaccine developers focused on production of a pneumococcal conjugate vaccine, which was first introduced in 2000 with 7 serotypes of *S. pneumoniae* (PCV7), including serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F (CDC, 2012). Since then, a 13-valent pneumococcal conjugate vaccine (PCV13) was introduced in 2010.

The 7-valent pneumococcal conjugate vaccine, although only containing 7 of the total 91 serotypes of *S. pneumoniae*, originally targeted 80% of pneumococcal infections in children living in developing countries (van der Poll & Opal, 2009). It was approved for use in children younger than 2 years of age and in children younger than 5 years of

age with high-risk conditions. This vaccine had significant effects when first introduced: it reduced the incidence of invasive pneumococcal disease in infants under 1 year of age in the U.S. by 82% (see Figure 3). In addition, it eliminated carrier states in children, producing a high degree of herd immunity which benefitted adults that were not vaccinated and infants too young to be vaccinated. Within 3 years of the vaccine's introduction, as many as 2 adult cases were prevented for every vaccinated child (Paradiso, 2011). The vaccine was expanded to include 13 serotypes in 2010 (adding serotypes 1, 3, 5, 6A, 7F, and 19A) because PCV7 covered the majority of pneumococcal disease in the world, but it only covered 50% of strains in some countries, mostly in developing countries in Africa, South America, and Asia. In addition, there has been a marked increase in invasive disease attributable to non-PCV7 vaccine serotypes of *S. pneumoniae* (van der Poll & Opal, 2009). Since the PCV13 was only recently introduced in the U.S. and with slow implementation globally, its effects in developing countries have yet to be adequately evaluated.

Figure 3. Incidence of pneumococcal disease in children in the USA before and after introduction of PCV7 Vaccine (van der Poll & Opal, 2009)



In contrast, the *H. influenzae* type b conjugate vaccine has been in routine use in the U.S. since 1987 (Morris et al., 2008). Similar to the development of the pneumococcal vaccine, the Hib vaccine started as a polysaccharide vaccine that was not immunogenic in children under 2 years old. The conjugate vaccine was subsequently created using diphtheria toxoid. There was much success in the U.S. after its initial introduction: invasive Hib disease decreased by 85-99% from 1983 to 1995. As of December 2007, 119 countries had programs for routine administration of Hib vaccine in infants. In particular, 97% of countries in the Americas and its surrounding islands had Hib vaccine programs. Despite high implementation of vaccination programs, the success of these programs varied greatly. In 2003, the WHO estimated that in developing countries, only 42% of the eligible population was vaccinated against Hib, compared to 92% in the developed world. Estimates show that, in 2006, almost 20 years after its initial introduction in the U.S., only 26% of the world's children received the Hib conjugate

vaccine (Morris et al., 2008). The WHO recommends inclusion of both the Hib and PCV13 vaccines in routine immunization programs with the prediction that, if applied worldwide, these two vaccines are expected to prevent at least 1,075,000 child deaths each year (Madhi et al., 2008).

The increasing contribution of viral causes of pneumonia to pediatric mortality worldwide requires that they also be addressed. Thus far, vaccinations are not available for most viral causes of pneumonia including RSV, the most prevalent viral pneumonia in children. Due to the growing recognition of influenza as a viral cause of pneumonia in developing countries, influenza vaccination programs have been encouraged worldwide by the WHO, which delivered the first set of recommendations in 2000. The influenza vaccine contains protection against the influenza subtypes A (H3N2), A (H1N1), and B and is available in both a killed intramuscular version as well as a live attenuated intranasal version (Madhi et al., 2008; CDC, 2014). Despite common use in developed countries, the influenza virus is more challenging than most vaccines to create due to the virus' frequent mutations (Verma et al., 2012). In particular, there are minor antigenic drifts in the influenza virus every year requiring new vaccine production yearly. The new vaccine each year is selected based on research conducted to determine which influenza virus strains are circulating and spreading (CDC, 2014). Due to their complicated production mechanism, these vaccines are created in developed countries. There are logistical hurdles to providing this vaccine in developing countries with lack of adequate distribution to developing countries, difficulty cold-storing the live attenuated vaccine, and the need for yearly re-vaccination (Madhi et al., 2008; van Essen et al., 2003). Despite the challenges, there is an encouraging trend in increasing influenza

vaccine use. In 2000, approximately 34% of the influenza vaccine doses used worldwide were in countries outside western Europe, North America, Australia, and New Zealand (van Essen et al., 2003).

Although these vaccines have much potential to reduce childhood mortality in developing countries, one of the biggest challenges for developing countries to provide vaccines for all children is financing. In order to address this issue, the GAVI Alliance, an international organization, was created in 2000 with the goal of providing support for the purchase and development of immunization programs in developing countries (Madhi et al., 2008). The GAVI Alliance originally provided countries with up to 5 years of guaranteed financing directed towards vaccine procurement and supporting systems. This guaranteed financing specifically was used to expand the vaccinations of pertussis, measles, and the Hib conjugate vaccine. In 2005, the funding by GAVI Alliance was extended for 10 more years. Over this time, its total funding commitments are over \$6 billion, including more than \$500 million towards strengthening health systems and \$1.5 billion for the purchase and distribution of PCV vaccinations. Other health organizations, such as the WHO and the CDC, provide additional support as well.

Despite providing vaccinations to developing countries, the GAVI Alliance has discovered challenges in accelerating introduction of these vaccines into clinical practice due to the lack of evidence-based decision making and policy support in most developing countries (Madhi et al., 2008). GAVI Alliance has responded by creating the Pneumococcal Vaccines Accelerated Development and Introduction Project in 2003 and the Hib Initiative in 2005. These teams are designed to support efforts for surveillance,

research, and cost-effectiveness analyses, which in turn, act to encourage better decision making and policy development by national governments and international agencies.

Epidemiologic Risk Factors for Childhood Pneumonia

In addition to vaccination programs, another key factor in prevention of pediatric pneumonia cases involves identifying and addressing the major risk factors that contribute to the development of pediatric pneumonia. In 2008, Rudan et al. performed a meta-analysis to determine the causal factors for development of pediatric pneumonia at the community level and separated them into three categories: definite, likely, and possible. The definite category contained risk factors with the most consistent evidence. The likely category has risk factors with strong evidence, but some contradictory findings or inconsistent evidence. Lastly, the possible category contains risk factors that have sporadic or inconsistent evidence. These risk factors are shown in Table 3. In 2010, Rudan et al. did further meta-analysis and determined odds ratios for the 5 most important risk factors contributing to pediatric pneumonia to be as follows: 1.8 for malnutrition, 1.4 for low birth weight, 1.3 for non-exclusive breastfeeding, 1.8 for household use of solid fuels, and 2.0 for crowding (Rudan et al., 2013). Malnutrition was defined as weight-for-age with a z-score less than 2, low birth weight was defined as less than or equal to 2500g at birth, and crowding was defined as 7 or more persons sharing the same household.

Table 3. Risk factors related to pediatric pneumonia in developing countries (Rudan et al., 2008)

Definite Risk Factors	Likely Risk Factors	Possible Risk Factors
Malnutrition	Parental smoking	Mother's education
Low birth weight	Zinc deficiency	Day-care attendance
Non-exclusive breastfeeding	Mother's experience as a caregiver	Rainfall (humidity)
Indoor air pollution	Concomitant diseases (e.g. diarrhea, heart disease, asthma)	High altitude (cold air)
Crowding		Vitamin A deficiency
Lack of measles immunization within first 12 months of life		Birth order
		Outdoor air pollution

Of the important risk factors that contribute to pediatric pneumonia as defined by Rudan et al. (2008), many cause reduced host defenses against pneumonia pathogens. First, malnutrition in children can greatly affect the body's response to serious illnesses (Rodriguez et al., 2011). Protein-calorie malnutrition (PCM), in particular, is a strong risk factor for higher morbidity and mortality rates in infectious diseases overall. This phenomenon is likely affiliated with immune system deficiencies. PCM individuals have been found to have multiple immune system abnormalities including T-cell deficiency, altered ratios of T-cell subsets, decreased natural killer cell activity, and decreased cytokine production causing inappropriate lymphocyte response (Rodriguez et al., 2011). Indoor air pollution can also affect the airway immune system in numerous ways; most commonly, smoke can inhibit the muco-ciliary apparatus of the airways which function to filter and remove pathogens as well as causing chronic airway inflammation which leads to dysfunctional cellular killing of pathogens (Smith et al., 2000). Exclusive

breastfeeding is a protective factor since it also provides numerous host defenses properties. In particular, breast milk contains factors that aid and develop an infant's immune systems (Heinig, 2001). Low birth weight, the fourth risk factor, is linked to pediatric pneumonia mostly due to neonatal causes (Barton et al., 1999). The majority of neonatal deaths are congenital pneumonia cases due to amniotic fluid infections. Lastly, the risk factor with the highest odds ratio according to Rudan et al. (2013), household crowding, most likely contributes to the development of pneumonia through cross-infection and ease of spread of respiratory infections through air droplets (Cardoso et al., 2004).

In addition to the 5 major risk factors contributing to childhood pneumonia, others have been identified. One is the age of the child. In a birth cohort study in Cape Town, South Africa, it was shown that the majority of the pneumonia burden among children is within the first 2 years of life (Campbell & Nair, 2015). The results of this study indicated that severe pneumonia accounts for the most pneumonia deaths in the first 6 months of life. This relationship of increased pneumonia cases in younger ages has also been demonstrated in other studies (Monto, 1994; Selwyn, 1990). This study also evaluated the effect of gender and revealed a male: female incidence ratio of 2:1, hypothesizing a “biological frailty” in males compared to females or differences in care-seeking by gender (Campbell & Nair, 2015). A longitudinal cohort study in Pakistan by Khan et al. (2009) noted similar increased incidences of childhood pneumonia in younger children and males. In addition, Khan et al.'s (2009) study conducted in the Himalayas showed that high altitude is significantly associated with increased pneumonia cases. High altitude is likely to contribute to pneumonia due to lung physiologic compensatory

mechanisms such as increased ventilation, increased cardiac output, and a shift in the oxygen-hemoglobin affinity curve. These compensations are delayed in infants who take 3-4 years to adapt fully. Seasonality is another possible risk factor identified by Rudan et al. (2008), likely related to seasonal viruses including RSV and influenza. Lastly, socioeconomic factors contribute to high childhood pneumonia rates. In particular, poverty and other factors that inhibit access of care including migrant status, residence in rural areas, and low parental education levels have been shown to be associated with increased incidence of childhood pneumonia (Feng et al., 2012; Konseiga et al., 2006).

The reduction of worldwide childhood pneumonia from 1990 to present can be attributed partly to the minimization of these risk factors. Rudan et al. (2013) found that 4 of the 5 main risk factors declined significantly in all low- and middle-income countries between 2000 to 2010. In particular, malnutrition declined from 26.9% to 21.9%, low birth weight from 15.9% to 8.8%, non-exclusive breastfeeding from 64.4% to 52.6%, and solid fuel use (indoor air pollution) from 65.5% to 52.2%. Crowding was unable to be assessed due to change in definitions over the 10 year span. The Global Action Plan for Prevention and Control of Pneumonia (GAPP) predicted that exclusive breastfeeding for the first 6 months of life could cause a 15-23% reduction in pneumonia incidence and a 13% reduction in all child deaths (WHO/UNICEF, 2009). GAPP also predicted that improved nutrition through the first 5 years of life including adequate micro-nutrient intake would result in a 6% reduction of all child deaths. Therefore, not only do efforts to increase diagnosis and treatment of childhood pneumonia and increased immunization programs contribute to worldwide reduction of childhood pneumonia, the minimization of risk factors can also play a significant role.

Programs for Community Settings

Comprehensive community-based programs are necessary in developing countries to address the reduction of morbidity and mortality from pediatric pneumonia in an integrative manner. The GAPP initiative provided a framework for community-based programs in 2007 (Izadnegahdar et al., 2013). GAPP separated recommendations to prevent pneumonia into three areas: protecting children, preventing children becoming ill, and treating children who become ill. The first focuses on the provision of good nutrition and a healthy environment to reduce risk factors such as malnutrition, indoor air pollution, and non-exclusive breastfeeding. The second emphasizes the prevention of childhood pneumonia through immunizations. The third discusses the early recognition, treatment, and referral of cases, referred to as case management.

GAPP's 2008 report demonstrated the need for better integration across these three types of interventions since prior service delivery had been uneven and uncoordinated (WHO/UNICEF, 2009). For example, exclusive breastfeeding was only practiced by 34.8% of mothers worldwide in 2008 and only 82% of children had been vaccinated against measles. While 61/72 GAVI-eligible countries had introduced the Hib vaccination, very few had included PCV vaccine in national programs. In addition, case management was also falling behind in 2008; only 54% of children with pneumonia were taken to a qualified health care provider in developing countries and only 19% of under-five children with clinical pneumonia received antibiotics.

Community-based programs in developing countries and underserved areas need to overcome numerous challenges, including lack of human resources and lack of funding

(Izadnegahdar et al., 2013). These programs also require governmental policy frameworks that provide appropriate infrastructure. In order to tackle these obstacles, GAPP made recommendations to help developing countries strengthen their prevention systems to address childhood pneumonia. The first recommendation was to develop a national action group for pneumonia control that can take responsibility of forming and coordinating the implementation of an integrative action plan (WHO/UNICEF, 2009). This group would be responsible for advocating for increased resources and monitoring progress. Second, GAPP emphasized the importance of advocacy with policy- and decision-makers in order to ensure national resources will be dedicated to pneumonia interventions. GAPP's third recommendation was to conduct a situation analysis for pneumonia using data on the prevalence of risk factors, vaccination coverage, and appropriate case management. This situation analysis can show country-specific estimates that can help stimulate discussion about the appropriate mix of interventions that are needed. Next, GAPP recommended involving both health programs that are already involved in pneumonia prevention and control and non-health programs that address risk factors. The fifth recommendation was to identify areas for collaboration among these various programs in order to ensure a harmonized integrative implementation for pneumonia prevention and care. GAPP's sixth recommendation was to utilize a three-pronged approach: increasing vaccination coverage, increasing access to case management, and promotion of exclusive breast-feeding. The seventh recommendation by GAPP was to identify locally-appropriate goals, targets and indicators and to track progress in order to modify the action plan and resource mobilization as needed. Lastly, GAPP endorses engaging support from international

agencies and possible donors in order to obtain more resources as well as guidelines for implementation (WHO/UNICEF, 2009).

One major aspect of GAPP's recommendations, in addition to increased vaccination coverage and reduction of risk factors, is the improvement of community case management. In order to improve access to care, especially for the most underserved, community health workers (CHWs) trained to perform case management are critical to the success of pneumonia prevention efforts (WHO/UNICEF, 2009). CHWs are especially important in rural areas with scattered populations to complement facility-based care in urban areas since these rural populations have reduced adequate health care access (Greenwood, 2008). A 2005 recommendation from WHO and UNICEF stated that CHWs could diagnose pneumonia in children and subsequently treat with antibiotics and, if necessary, refer those with danger signs to health facilities (Marsh et al., 2008). WHO/UNICEF also recommended these CHWs be "well-trained and supervised". This training can be achieved using international guidelines such as WHO and IMCI guidelines for pneumonia diagnosis and treatment (WHO/UNICEF, 2009). In addition, training and franchising shop keepers in rural areas can also ensure increased access to antibiotics (Greenwood, 2008).

A 2003 meta-analysis of nine studies showed that community case management reduced overall mortality in children 0-4 years by 24% and pneumonia-specific mortality in children 0-4 years by 36% (Sazawal & Black, 2003). In a survey of 57 African and Asian countries by Marsh et al.(2008), half of the countries reported some implementation of community case management for pneumonia, but few countries had a large-scale sustainable program. These countries had wide variation of programs and

roles of CHWs. In addition, only one-third of the countries reported policies supporting community case management for pneumonia. Therefore, despite the emphasis on community case management by WHO/UNICEF and GAPP, more system-wide support is needed to increase community case management in developing countries.

Since the GAPP recommendations were first published, many countries have begun to implement the recommended interventions. The most striking example is in Rwanda, which was the first developing country to create a national immunization program for the PCV vaccine with support from the GAVI Alliance (Frist & Sezibera, 2009). In 2006, Concern Worldwide, with the International Rescue Committee and World Relief, and with support from USAID, created an Expanded Impact Child Survival Program in partnership with the Rwanda's Ministry of Health entitled Kabeho Mwana (meaning "Life for a Child") in an effort to increase the implementation of community case management for childhood malaria, diarrhea, and pneumonia as well as promote prevention at the household level (Concern Worldwide, 2010). To address community case management, Rwanda implemented an extensive training plan for 6,177 CHWs from 88 health sectors and provided these CHWs with tools including lock boxes to store drugs and supplies, amoxicillin, and a respiratory rate timer. To ensure accurate training of the CHWs, Care Groups of 10-15 CHWs met on a monthly basis under the supervision of community health supervisors for supplemental trainings. Overall, 660 Care Groups were established. In addition, to encourage quality assurance, Kabeho Mwana created dedicated positions at health centers to document the number of children referred or seeking care, availability of drugs, and number of cases correctly treated by CHWs. Due to this system, care-seeking for pneumonia treatment increased from 13% to 63% in the

first five years. As a result, CHWs became the first-line providers for treatment of children with fever, respiratory symptoms or diarrhea; by 2011, 69% of mothers of children up to 23 months old had consulted a CHW at least once (Concern Worldwide, 2010).

In order to address the risk factors for childhood mortality, Kabeho Mwana also integrated a program for malnutrition in their case management program by training CHWs to screen for malnutrition using mid-upper arm circumference, to provide nutrition counseling, and to refer severe malnutrition to health-facility based outpatient programs (Concern Worldwide, 2010). As a result, more than 8,000 children were successfully treated for malnutrition at the facility level. Also, CHWs were trained to carry out various health promotion activities to households using visual aids. Rwanda's Kabeho Mwana program is an excellent example of successful implementation of GAPP's recommendations.

Another successful example of a developing country's efforts to prevent and treat childhood pneumonia is Pakistan's Lady Health Worker Program (WHO/Global Health Workforce Alliance, 2008). This program was implemented in order to improve case management due to an insufficient number of health managers, nurses, paramedics, and skilled birth attendants in Pakistan. Female CHWs were trained and deployed throughout the country. By 2006, there were 96,000 Lady Health Workers of an estimated 150,000 needed to cover the entire country, each responsible for an average of 1000 people. The Lady Health Workers receive training from a government health facility for 15 months; 3 months of classroom and 12 months of clinical training. Lady Health Workers receive a small allowance and medical supplies from their affiliated facility. After training, they

continue to be monitored and supervised by provincial and district coordinators. The impact of this program was impressive. By 2007, more than half of Pakistan's population had access to primary health care through this program. Also, there was a reduction in infant mortality rate from 250 to 79 per 100,000 live births and increased immunization rates from 57% in 2000 to 68% in 2008 (WHO/Global Health Workforce Alliance, 2008; Zhu et al., 2014). During the first 8 years of the program, Pakistan's government spent \$155 million, of which only 11% came from external donors (WHO/Global Health Workforce Alliance, 2008).

The Haitian Experience

Overview of Haiti

This study was conducted in Haiti, formally known as the Republic of Haiti, which gained independence from France in 1804 in the first successful slave revolt (BBC, 2012). Haiti, with a total area of 27,750 km², is located on the Western portion of the island of Hispaniola, which it shares with the Dominican Republic. Hispaniola is part of the Greater Antillean archipelago in the Caribbean, which also includes Cuba, the Cayman Islands, Puerto Rico, and Jamaica. By 2011, the UN estimated that Haiti's population had grown to 10.1 million, an increase from 3.1 million in 1950, making it the 2nd most populous Caribbean nation. The population is concentrated most heavily in urban areas, coastal plains, and valleys.

According to the UN Development Program (UNDP), Haiti is the poorest country in the Western hemisphere, ranking near countries in sub-Saharan Africa on the Human Development Index (UNDP, 2014). Almost half (44.9%) of workers in Haiti live on less

than USD \$1.25 per day. The proportion of Haiti's population living below the national poverty line was 59% in 2012. The extreme poverty rate in Haiti has fallen from 27.5% in 1995 to 11.4% in 2012, nearly a 60% reduction; however, it still remains far above the average of 3% estimated for Latin America and the Caribbean. Poverty is higher in rural areas, 75.2%, compared to urban areas, 40.8%. There is also much vulnerability in Haiti due to natural disasters; the WHO estimates that approximately a million Haitians have the possibility of falling into poverty with a natural disaster, economic shocks, or cholera epidemics (UNDP, 2014). The Fragile State Index, an annual report created by The Fund for Peace, a U.S. think tank, that ranks countries of the world based on several indicators, can be used to compare Haiti to other countries world-wide (Fund for Peace, 2014). The ranking is based on the degree of fragility with the most fragile states receiving the highest scores. The indicators used include demographic indicators (food scarcity, mortality, population growth), refugees or internationally displaced persons, group grievance (tensions among groups within the state), uneven economic development (disparities amongst various groups), poverty and economic decline, state legitimacy or level of corruption, provision of public services, and the level of external intervention. Haiti had reached its best rank on this scale in 2008 at #14, but the fragility ranking increased after the 2010 earthquake to #5 in 2011. By 2014, Haiti was ranked #9 behind other "fragile" countries including South Sudan, Somalia, Democratic Republic of the Congo, and Afghanistan (see Figure 4) (Fund for Peace, 2014).

Figure 4. Haiti's Scores on the Fragile State Index, 2006-2013 (Fund for Peace, 2014)



Most Haitians are descendants of African slaves. Mulattoes, who are of mixed African and European descent, comprise much of the nation's social elite, holding many government positions (BBC, 2012). French and Haitian Creole are the national languages, but education and government are conducted in French. Creole is the language of most of the population living in rural and poor urban areas. The adult literacy rate is low at 48.7% (UNICEF, 2013). Haiti has had significant political instability and violence throughout its history. From 1957 to 1986, Haiti was ruled by the brutal dictatorships of Francois "Papa Doc" Duvalier and his son, Jean-Claude. Tens of thousands of people were killed during their reign (Raphael, 2013; BBC, 2012). Following their rule, there were a series of military coups and elections. In 1990, Jean-Bertrand Aristide, a former priest, was elected president and was overthrown in 1991. US-led military intervention in 1994 forced a return to constitutional government with President Aristide. Aristide served as president from 1995-1996 and was re-elected in 2000, during which political dissent

grew. After a bloody rebellion in 2004, President Aristide was forced out of the country. A UN stabilization force was sent following Aristide's departure and remains in country. Democratic elections followed, but unrest continued with rival gangs, political groups and violent demonstrations (Raphael, 2013; BBC, 2012). Michel Martelly was elected president in 2011 with a goal of re-building the country following the devastating 2010 earthquake. His government has also faced protests due to claims of corruption and failure to alleviate poverty (BBC, 2012).

In addition to political instability, Haiti has faced many natural disasters throughout history, contributing to high levels of poverty and instability (see Table 4). Haiti is in a vulnerable location since it is prone to tropical storms and flooding exacerbated by severe deforestation (BBC, 2012). While it had been 150 years since a major earthquake, Haiti is located along the boundary of two tectonic plates, which may result in future earthquakes. On January 12, 2010, a magnitude 7.0 earthquake had its epicenter just outside of Haiti's capital, Port-au-Prince, in Leogane. While the actual number of fatalities will never be known, there have been variable estimates. A survey of 1800 households in Port-au-Prince before and after the earthquake conducted by Kolbe et al. (2010) estimated a total of 158,679 deaths during the earthquake or in the 6-week period immediately after. This study found that children under age 12 accounted for 65.9% of all deaths; children were twice as likely to die of an illness after the earthquake than adults. In addition, Kolbe et al. found that 18.6% of households surveyed faced severe food insecurity after the earthquake and 24.4% of households were completely destroyed. The Haitian government's official estimate of mortality from the earthquake was 316,000 deaths (O'Connor, 2012). However, there has been much dispute about the

accuracy of this estimate and numerous sources including USAID have calculated estimates as low as 46,000 deaths.

After the earthquake, Haiti's government called on the international community for assistance. Many nations, multi-national agencies, and NGOs responded. The U.S committed resources from the CDC and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) (Tappero & Tauxe, 2011). Further compounding the effects of the earthquake was a cholera epidemic beginning in October 2010 which was attributed to UN troops from Nepal. This resulted in more deaths and disruption. By July 2011, a total of 419,511 cases and 5,968 deaths had been reported. Approximately \$2.5 billion of international aid had been received by Haiti by 2013 (Beaubien, 2013). In spite of these funds, uncoordinated relief efforts have prevented Haiti from fully recovering and as of January 2015, approximately 79,000 individuals were still living in relief camps (Charles, 2015).

Table 4. Summary of Haiti Natural Disasters (BBC, 2012)

<u>Year</u>	<u>Natural Disaster</u>	<u>Effect</u>
1770	Earthquake	Destruction of Port-au-Prince
1842	Earthquake	Destroys Cap-Haitien and other cities
1935	Tropical Storm	Kills 2,000 people
1946	Tsunami	Kills 1,790 people
1954	Hurricane Hazel	Kills hundreds of people
1963	Hurricane Flora	Kills 6,000 in Haiti and Cuba
1994	Hurricane Gordon	Kills hundreds of people
1998	Hurricane Georges	Destroys 80% of crops
2004	Floods	Kill 2,600 people
2004	Tropical Storm Jeanne	Kills 1,900 people
2007	Tropical Storm Noel	Triggers mudslides & floods
2008	Three hurricanes & tropical storms	Kills 800 people
2010	Earthquake in Port-au-Prince	Kills tens of thousands of people
2010	Cholera outbreak	Kills nearly 6,000 people

Pediatric Health in Haiti

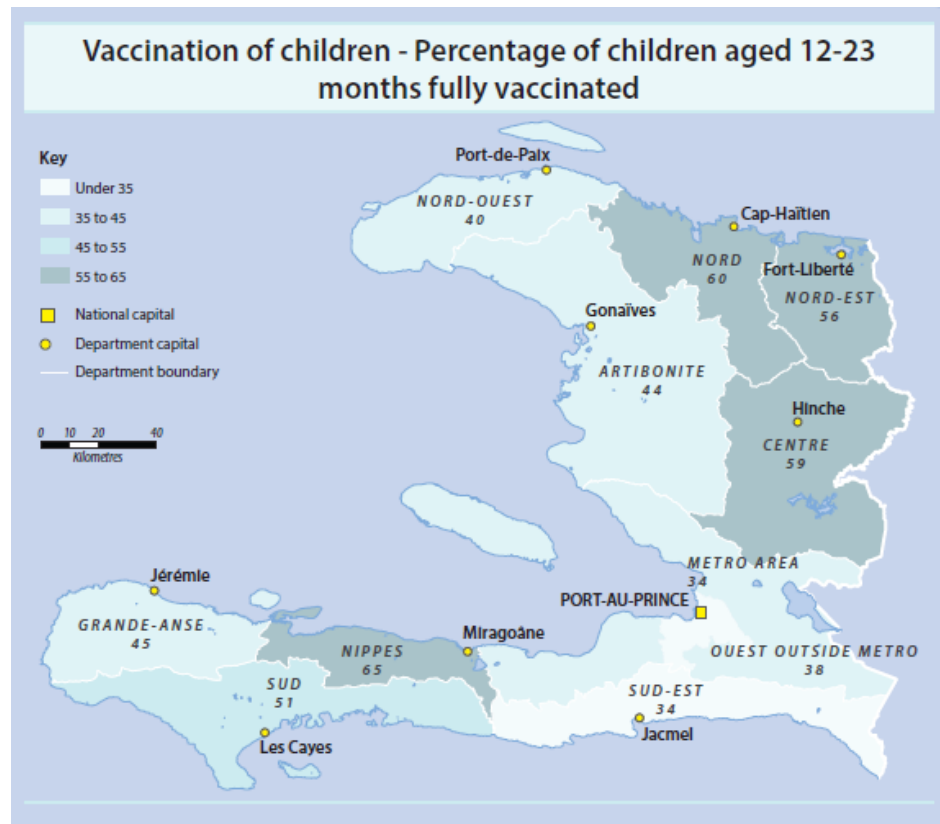
In 2012, the mortality rate for children under age five was 75.6 per 1000 live births, of which 66% of under-five mortality occurred between 1-59 months of life (WHO, 2012). Haiti has made progress with MDG 4. The proportion of children dying before age five dropped 44% between 1990 and 2012, a rate faster than the worldwide trend (UNDP, 2014). Despite this strong reduction, Haiti's under five mortality rate remains higher than the average for Latin America and the Caribbean of 19 per 1000 live births. The infant mortality rate in Haiti declined from 109 to 59 deaths per 1000 live births from 1990-2012. Neonatal mortality (under 28 days of age) decreased slightly from 26 per 1000 live births in 2010 to 25 in 2013 (World Bank, 2015).

There have been few studies looking at under five mortality from pneumonia in Haiti. One study at Albert Schweitzer Hospital in Deschapelles, Haiti in 2005 found that 45% of all under-five deaths were attributable to acute lower respiratory infections (ALRI) (Perry et al., 2005). In 1994, the Pan American Health Organization estimated that one of every four deaths in children under five in Haiti was due to ARI (acute respiratory infection) (PAHO, 1995). In 1997, another study conducted by CDC physicians using records from the NGO affiliated with this study found that pneumonia-specific mortality for children under age 5 was 3.1/1000 (Dowell & Heffelfinger, 1997; Lewis & Gebrian, 2009). Rudan et al. (2008) found that Haiti has 0.31-0.40 pneumonia episodes per child-year, compared to <0.10 episodes per child-year in the neighboring Dominican Republic. The pneumococcal mortality rate in Haiti in children 1-59 months old is approximately 100-300 deaths per 100,000 children under five years old, excluding HIV-positive deaths (O'Brien et al., 2009). Also, Hib pneumonia is responsible for 100-200 deaths per 100,000 children aged 1-59 months in Haiti (Watt et al., 2009).

In order to combat the high under-five mortality, Haiti has focused on increasing its vaccination rates. Many geographic disparities remain in immunization coverage in Haiti (see Figure 5). Only 45% of children aged 12-23 months were fully vaccinated in 2012 in the entire nation (UNDP, 2014). The GAVI Alliance, as previously mentioned, is an international organization that was created in 2000 with the goal of providing support for the purchase and development of immunization programs in developing countries (Madhi et al., 2008). Haiti has received help from the GAVI Alliance in delivering vaccinations to the population. In particular, the GAVI Alliance has been providing funding to Haiti since 2001 with a total disbursement of \$9,129,342, of which 64% was

dedicated to vaccine support (GAVI, 2015). \$3,275,842 was directed towards non-vaccine support including health system strengthening, immunization support services, injection safety support, and a vaccine introduction grant. Since 2012, \$4,198,500 of the money dedicated to vaccine support was used for the pentavalent vaccine. The pentavalent vaccine protects against diphtheria-tetanus-pertussis (DTP), hepatitis B, and Hib. The pentavalent vaccine is administered in a 3 dose schedule at 6 weeks, 10 weeks, and 14 weeks of age (PAHO/WHO, 2014). Official country estimates put the pentavalent immunization coverage in Haiti to be 85% in 2013 while WHO/UNICEF estimated it at 68% in 2013 (GAVI, 2015). \$5,037,500 was just recently committed to Haiti for the PCV vaccination by the GAVI Alliance in 2015 in addition to the previous disbursement of \$9,129,342. There was no GAVI support for pneumonia-specific vaccines prior to 2012 with the pentavalent vaccine program and no dedicated funding for PCV vaccines prior to 2015.

Figure 5. Percentage of Children Aged 12-23 months with Completed Recommended Vaccinations in Haiti in 2012 (UNDP, 2014).



Health Systems in Haiti

Haiti has four health systems: the public sector, the semi-public sector, non-governmental organizations (NGOs), and the private sector (Kuo, 2006). Prior to 2010, 35.7% of the country's 633 health institutions were government-owned, yet the Haitian government had limited capacity to provide funds for even this small percentage of health services, thus the public sector received subsidies from international health agencies in addition to government funding. The semi-public sector, managed by the private sector and supported by NGOs, was staffed by the public sector. Thousands of NGOs and the private sector provided the majority of health services in Haiti prior to the earthquake, yet

only 60% of the population had access to health services in 2006 (Ivers, 2011). Physicians are mainly concentrated in Port-au-Prince and other large cities. Physician density per 1000 population was 0.25 in 1998 and nursing density was 0.107 in 1998 (WHO, 1998). Contributing to this shortage is the migration of skilled professionals primarily to the U.S. or Canada; this rate was 30% between 2005 and 2008 (Ivers, 2011).

Even when health services are available, many Haitians still use traditional healers first when they have illnesses, including for pediatric pneumonia cases. One form of traditional healers in Haiti are voodoo priests (female –*mambo*, male –*hougan*), who serve as spiritual healers (Colin, 2003). Voodoo is an important religious component in Haiti and believers seek healing services from these priests, especially for illnesses related to spiritual causation. Treatment often consists of dancing, incantations, herbal preparations, and prayer (Salisbury, 2003). The most common traditional healers used are herbalists (*doktè fèy*), who are often sought for common illnesses including colds and diarrhea. These herbalists are also skilled in treating a supernatural illness called the evil eye (*Maldyok*). It is estimated that up to 40% of the population in rural areas use traditional medicine (Coreil, 1980; Kuo, 2006).

Prior to the 2010 earthquake, the public sector and semi-public sector had limited resources and human resources shortages. They were further reduced when the earthquake hit, causing the collapse of the Ministry of Health's building and killing more than 200 staff-members (WHO, 2010). Many Haitian doctors and nurses were killed, diminishing Haiti's ability to restore its health system. Since the earthquake, external support has included both financial assistance and health system experts, including 300 technical experts from the CDC (Dowell et al., 2011). WHO/PAHO worked with UN

agencies and NGOs in Haiti to coordinate the international response, creating a Health Cluster in February 2010, with which 396 national and international organizations had been registered. The Haitian Ministry of Health has been strengthened and a National Health Commission was created to coordinate local and international aid supporting mobile health centers, fixed health centers, and hospitals (WHO, 2010). Also, the Haitian Ministry of Public Health and Population has made progress since the earthquake with the implementation of several public health programs addressing long-term public health goals with the help of the CDC and other organizations as shown in Figure 6 (Vertefeville et al., 2013).

Figure 6. Improvement in Haiti Public Health Indicators, 2009-2012 (Vertefeville et al., 2013)

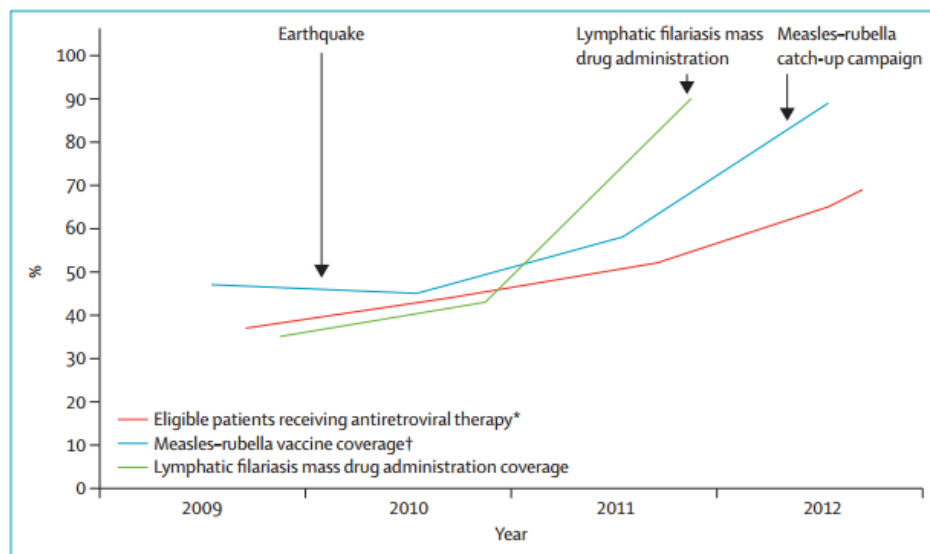


Figure: Public health progress in Haiti, 2009-12

*Calculated by using UNAIDS estimate of the number of people needing antiretroviral therapy in 2009, based on WHO treatment guidelines issued in 2010.⁸ †In 2009, children aged 12-23 months;³ in 2010 and 2011, children aged <12 months;⁹ in 2012, children aged 1-4 years (Tohme RA, Centers for Disease Control and Prevention, personal communication).

Acute Respiratory Infection (ARI) Program in the Context of COPC in southern Haiti

This study was conducted in association with a small NGO which has been working in Haiti's southern peninsula for the past 30 years. The region's economy is primarily subsistence level agriculture and fishing, and the geographic area served by the public health program is primarily mountainous with limited road access. The most distant areas are 14 hours walking time from the departmental capital. At the time of the study, this NGO served a registered population (persons in its assigned service area) of 128,217 and several thousand more who live outside the area but come for services. Among the registered population, which includes all household members, the NGO collects specific tracking information about all maternal and child health interventions (Pepin et al., 2012). The NGO's programs are funded mostly by grants (30% from USAID), private foundations, and donors (Kuo, 2006). The staff consists of 175 employees who are primarily Haitian (Lewis & Gebrian, 2009). The foundation of the public health program is COPC working through CHWs, who are called "Health Agents" or "*Agents de Santé*" in French. The health agents provide primary health care and conduct health education each for a population of 3,000-4,000. These health agents are selected by their communities and trained in a rigorous government 12-month curriculum paid for by this NGO. These CHWs are residents in their villages and available 24/7, with the ability to contact the NGO to obtain help with emergency services, including an ambulance for emergency obstetrical and newborn care, when needed. Preventive health care provided by CHWs includes growth monitoring, immunizations, vitamin distribution, and prenatal care. The educational sessions they conduct for their mainly non-literate communities regarding practical disease interventions consist of songs, skits,

and stories. They also treat numerous diseases including childhood pneumonia as advised by the WHO and IMCI guidelines using a timer to diagnose elevated respiratory rates. A study by the CDC showed the success of the ARI program with a reduction in pneumonia-specific mortality by half from 6.2/1000 in 1993 to 3.1/1000 in 1997 (Dowell & Heffelfinger, 1997). This thesis examines the ongoing impact of the program.

Methods

This study was conducted as a secondary data analysis of all reported pneumonia episodes treated by the NGO. The data were comprised of all pneumonia episodes that were treated by the health agents. For episodes resulting in mortality, the cause of death was confirmed by the medical director of the NGO. The final dataset used for analysis contained 20,024 episodes of pneumonia in 11,054 children under 5 years of age from 2004-2013. For each episode of pneumonia, the data included date of episode, age of child, locality, and outcome. Migrant status was also included in the data-set; however, since only 305 (2.8%) children in the data-set were migrants, migrant status was not used for analysis. In addition, this data-set included 493 pneumonia-associated deaths at presentation of first episode and for each case included date of death and age of child at time of the episode. For 293 episodes, information was available on the gender of the child. Data was analyzed using SPSS V.22 to calculate frequencies and analyze relationships. P values ≤ 0.5 were accepted as statistically significant for independent t-tests, chi-square tests and logistic regression.

Results

Pneumonia Episodes

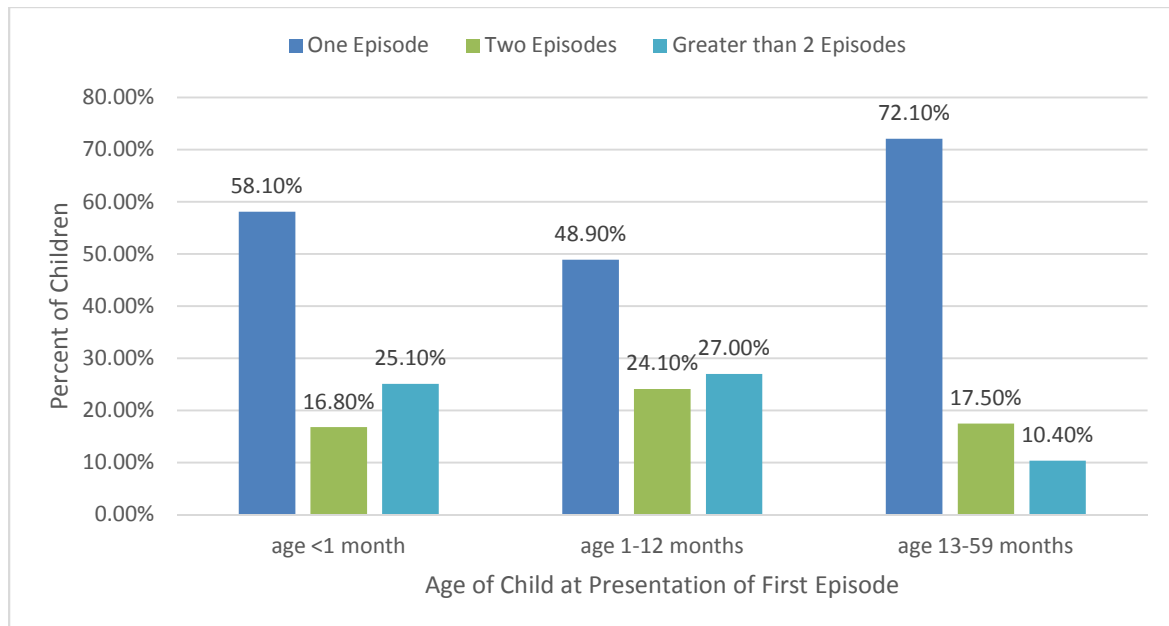
The data-set contained a total of 11,054 children under 5 years of age who presented with 20,024 episodes of pneumonia from 2004-2013. The number of pneumonia episodes per child ranged from 1 to 23 during the 9-year period. The majority of children who presented to the NGO (60.1%, 6646 children) had only one episode of pneumonia; 20.9% (2305 children) had two episodes of pneumonia, 9.4% (1041 children) had three episodes, and 4.4% (485 children) had four episodes. In addition, 14 children had 11 episodes, but only one child had >15 episodes of pneumonia (this child had a total of 23 episodes). The mean # of episodes per child was 1.81 episodes (SD =1.441). The average time-span between 1st and 2nd episodes of pneumonia was 10.42 months (SD =10.13); median was 7.03 months. The average time-span between the 2nd and 3rd episodes of pneumonia was 8.76 months (SD =8.57); median was 5.98 months. The average time-span between the 3rd and 4th episodes of pneumonia was 7.47 months (SD =7.23); median was 5.03 months.

Age of First Episode

Since previous studies have shown higher pneumonia burden and severity at younger ages, the age of first episode with pneumonia episodes was evaluated. The mean age of the children presenting with their first episode of pneumonia was 16.33 months (SD =13.84), with 1.5% (167 children) under 1 month of age, 50.7% (5604 children) 1-12 months of age and 47.8% (5283 children) 13-59 months of age. Children with a first episode at younger age were more likely to have subsequent episodes of pneumonia (Chi-

Square =702.76, $p= 0.00$) (see Figure 7). This association held when controlling for elevation and distance to referral sites. Specifically, 25% of the children under 1 month of age had more than 2 episodes of pneumonia, 27% of the children from 1-12 months of age had more than 2 episodes of pneumonia, and 10% of children from 13-59 months of age had more than 2 episodes of pneumonia. Older children at first presentation of pneumonia also had longer intervals between 1st and 2nd episodes, but this was not a meaningful difference.

Figure 7. Episodes of Pneumonia by Age at First Episode



Pneumonia over Time

Because pneumonia incidence is affected by seasonal and environmental factors, pneumonia incidence over time was examined. The highest number of pneumonia episodes from 2004-2013 was in 2012 with 13.6% of the total episodes followed by 2013

with 12.6% of the episodes and 2010 with 12.2% of the episodes. The years with the lowest episodes were 2004 (6.8%), 2005 (7.4%), and 2006 (8.1%) (see Figures 8 and 9).

Figure 8. Frequency of pneumonia episodes by year, 2004-2013

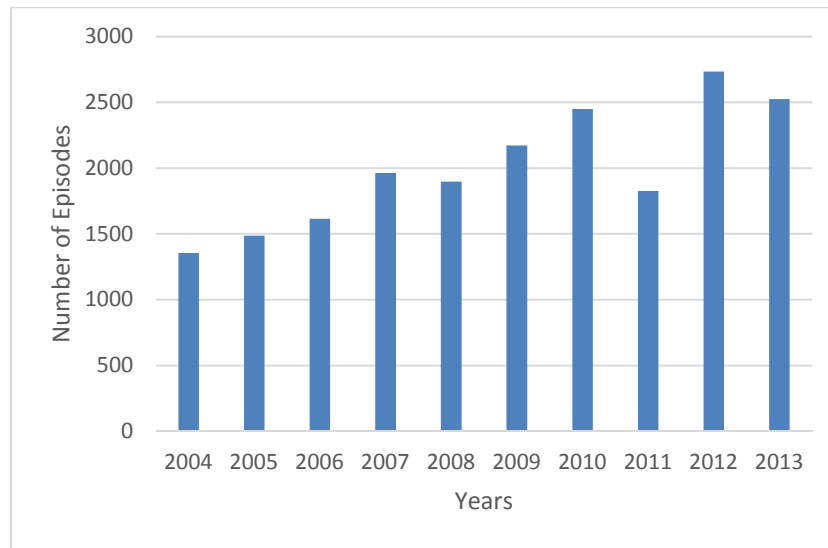
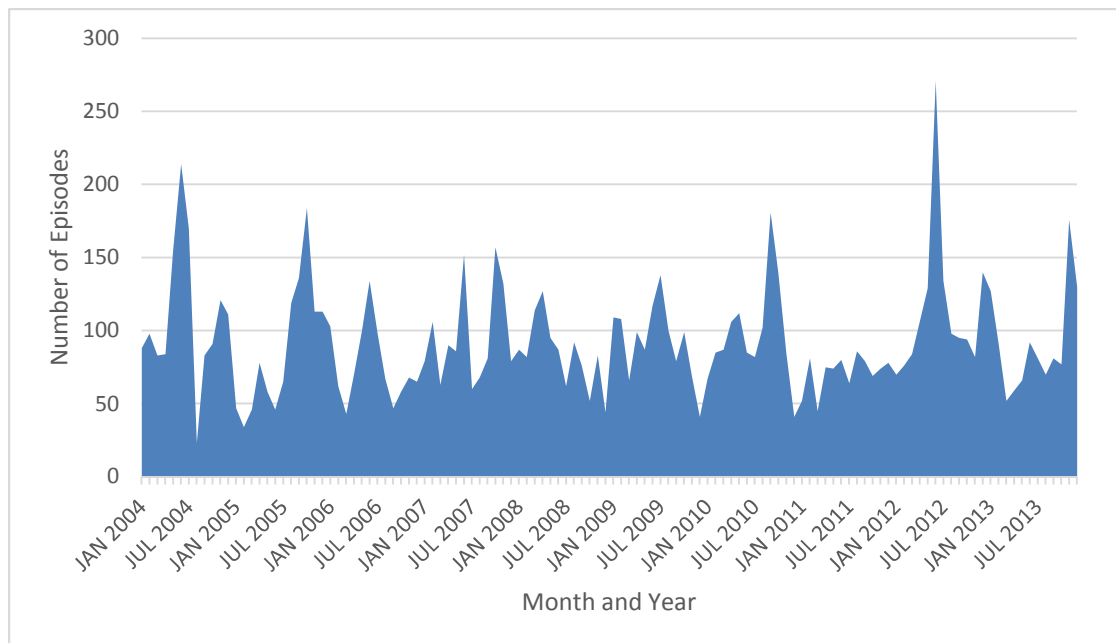


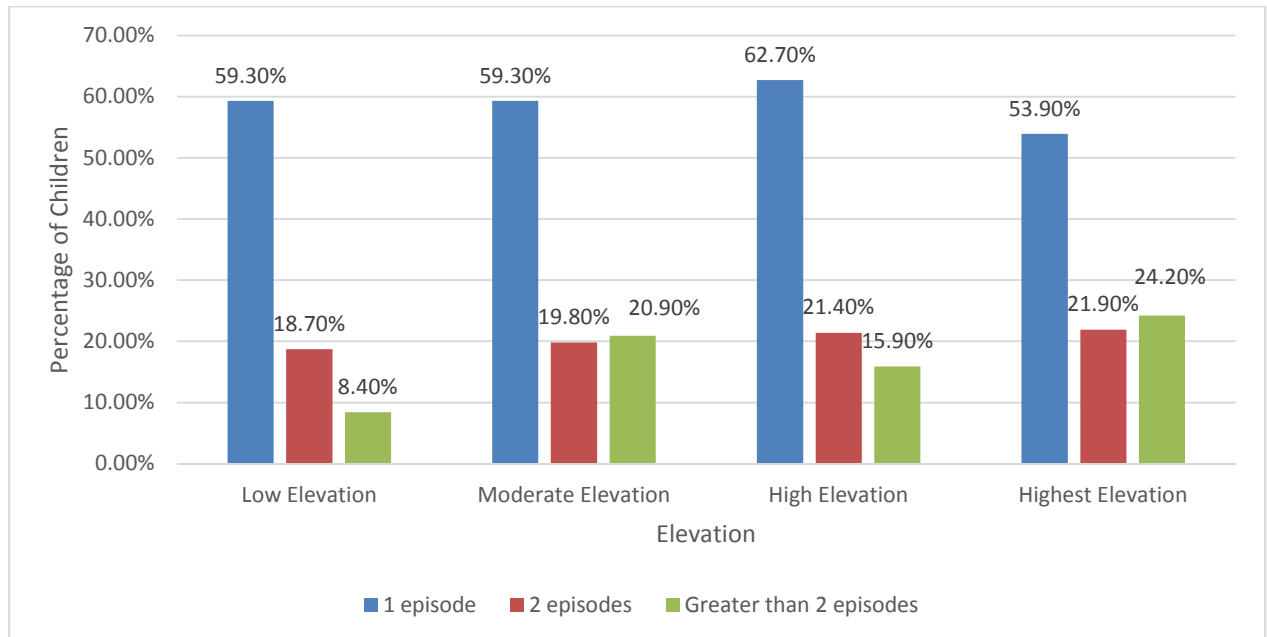
Figure 9. Frequency of pneumonia episodes by month, 2004-2013



Altitude/Elevation

The areas served by the NGO public health program is geographically varied ranging from plains to high mountains. To examine the relationship between altitude of residence and pneumonia, villages were grouped into four elevations: low (sea level to 250 meters), moderate (251-500 meters), mid-high (501-650 meters), and highest elevation (650+ meters). Twelve percent of the children presenting with pneumonia episodes lived in low elevation, 23.5% lived in moderate elevation, 27.1% lived in mid-high elevation, and 37.4% lived in highest elevations. The likelihood of multiple pneumonia episodes increased with altitude/elevation, even when controlling for age or distance from the referral sites. The data showed that 8.4% of children in low elevations had more than two episodes of pneumonia, 21% in moderate elevations had more than two episodes of pneumonia, 16% in mid-high elevations had more than two episodes of pneumonia, and 24% of the residents of the highest elevations had more than two episodes of pneumonia (see Figure 10).

Figure 10. Pneumonia Episodes by Elevation



Distance to Referral Care

Referral care was available at the departmental hospital and clinics in the provincial capital. Distance to referral care was determined in hours of walking time, which is the primary mode of transport and the way villagers think about distance. The mean distance by foot to referral care was 9.05 hours (SD =3.501) with a median of 10 hours and a range of 1-15 hours. The number of episodes of pneumonia that children had was not significantly different for children living at further distances when controlling for elevation. When comparing children whose first episode of pneumonia presented as an infant (0-12 months of age) to those aged >12 months, the children with first episodes at a younger age lived at further distances from referral sites, although it was not a meaningful difference. The association was not substantively changed when controlling for elevation.

Pneumonia-Associated Mortality

There were 493 total cases of pneumonia-associated mortality. Therefore, the overall episode-specific mortality rate was 2.46%. The pneumonia-specific deaths were 49.8% female and 50.2% male. Younger children had significantly higher mortality than older children ($t=6.20$, $p=0.00$). The average age for children who lived was 16.49 months compared to the average age of children who died of 12.91 months. In addition, mortality was significantly higher in children with only one episode of pneumonia compared to children with repeated episodes (Chi-Square =134.41, $p=0.00$). Of children who had only one episode, 93.7% survived. In comparison, of the children with 2 episodes of pneumonia, 97.7% survived, and of children with >2 episodes of pneumonia, 98.9% survived. Mortality was not significantly related to altitude or distance by foot to referral sites.

The peak of mortality occurred in 2007 (18.3%), followed by 2008 (15.8%) and 2009 (15.8%), with a decline to 2013 with 4.5% (see Figure 11). The episode-specific fatality rate peaked in 2005 with 4.91% fatality, and fell steadily to 0.87% in 2013 (see Figure 12). The estimated population of children under-five in this NGO's catchment area was calculated as 15,771 children; therefore, the pneumonia-specific deaths averaged at 3.85/1000 over the decade under study (Cayemittes et al., 2012). Specifically, the peak of pneumonia-specific deaths was in 2004 with 4.6/1000 and fell to 1.4/1000 in 2013.

Figure 11. Pneumonia mortality, 2004-2013

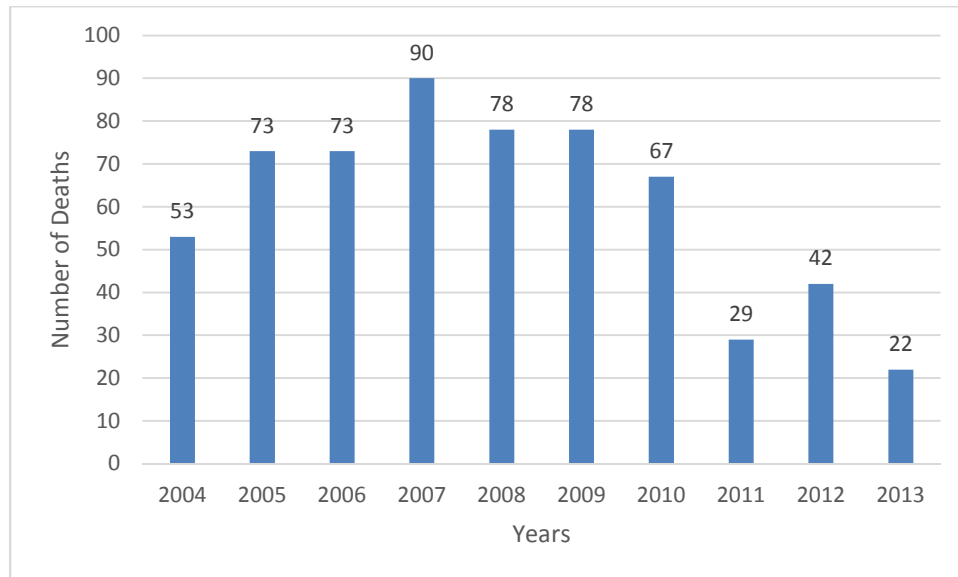
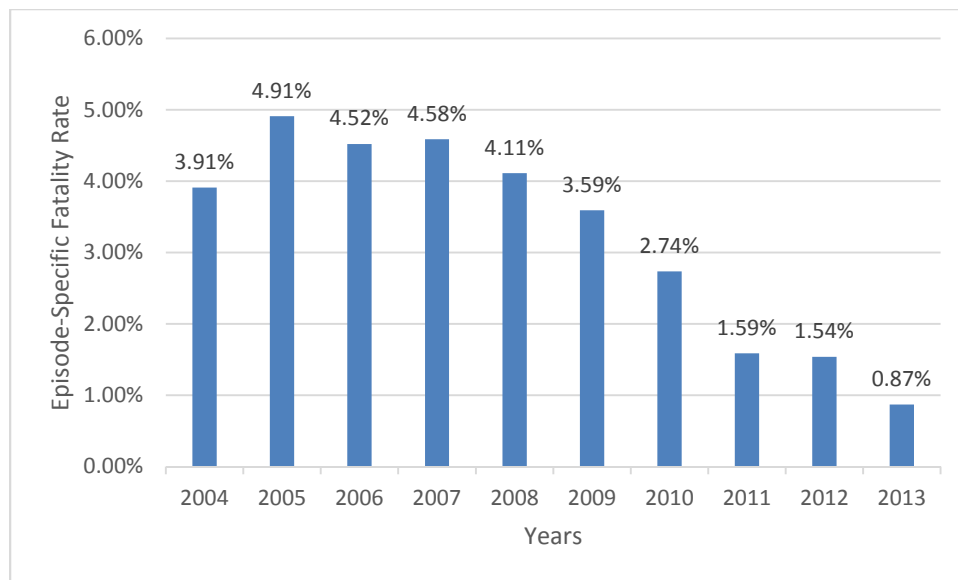


Figure 12. Pneumonia episode-specific mortality rate, 2004-2013



Seasons

From 2004-2013, the month with highest number of episodes was June with 11.0% of the pneumonia episodes. Other months with high numbers of episodes were

November (9.1%), October (9.1%), and September (8.6%). The months with lowest number of total pneumonia episodes were March (6.4%), February (7.1%), April (7.8%), and January (7.8%). The months with the highest number of pneumonia deaths were June (15.4%) and October (14.0%). The months with the lowest number of pneumonia deaths were January (7.3%), March (7.7%), April (8.1%), and July (9.1%) (see Figures 13 and 14).

Figure 13. Pneumonia Episode Pattern by Month, 2004-2013

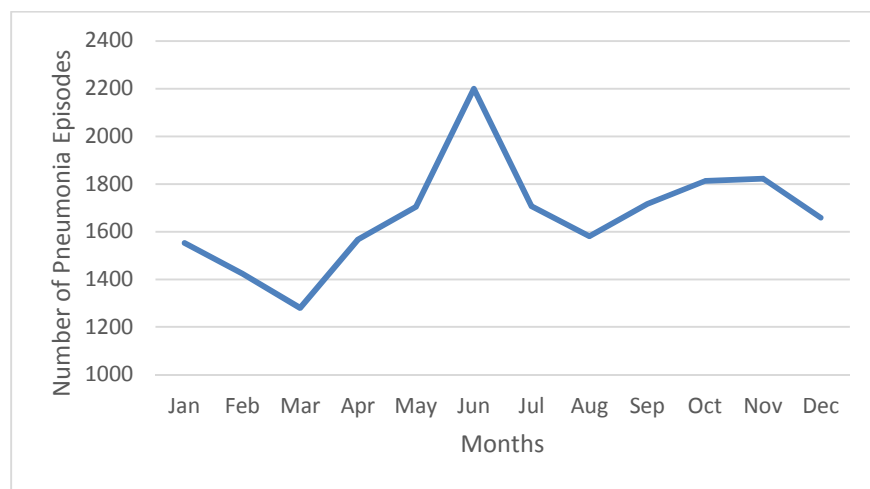
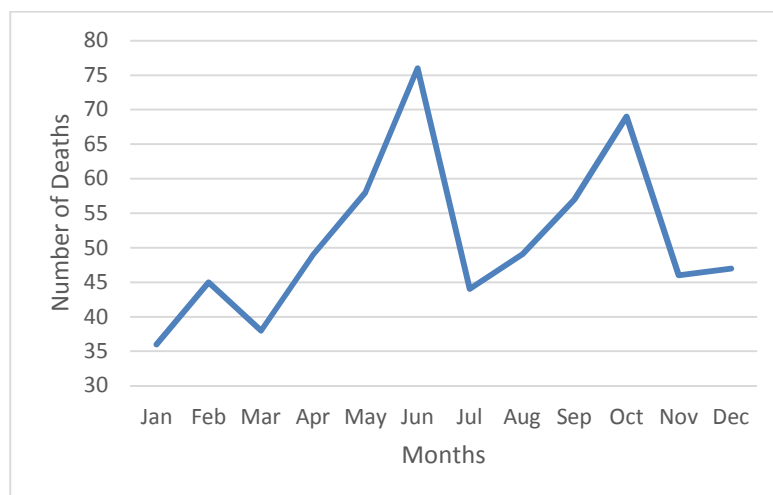


Figure 14. Pneumonia Mortality by Month, 2004-2013



Discussion

Pneumonia Episode Trends

This study showed an increasing trend of treated pneumonia episodes seen by the NGO from 2004-2013 with a peak occurring in 2012 with 2,733 episodes, an increase from the 1,356 episodes seen in 2004. Although there were fewer episodes in 2013, 2,525 episodes were still seen. The year of the 7.0 magnitude earthquake in Haiti, 2010, also had a high number of episodes with 2,449 episodes. Yet, 2011 had a decline to 1,826 episodes. Numerous factors could have contributed to these findings. One possible explanation is an increased care seeking, early identification and treatment of pneumonia episodes by the health agents from 2004-2013. Additional health agents were selected and trained in 2005 and 2007, contributing to increased access to care. Also, in January 2012, CHWs made home visits to provide the newly available pentavalent immunizations to children under-two, and this may have contributed to increased pneumonia case identification and treatment. An increase in number of ARI trained health agents likely also led to increased awareness of pneumonia and the work of health agents in the communities which may have increased care seeking.

The decline in pneumonia episodes in 2011 occurred during the cholera epidemic in southern Haiti. In the southern region of Haiti in which this NGO operates, cholera was not seen until November 2, 2010 and then peaked in November-December 2010, when 50% of all cholera cases died (Lewis, 2011). The Cholera Treatment Center at the local hospital did not open until December 2010; yet in rural areas that the CHWs service, cholera cases continued steadily and increased to 600 cases in May 2011, at the

start of the rainy season (Lewis, 2011). During this time period, pneumonia care seeking was possibly reduced due to fear, most people stayed home to avoid exposure to cholera. Although it is difficult to draw causal relationships from retrospective data, this was compounded in this study because of the profound unrelated secular trends that occurred from 2004-2014, including the earthquake and cholera epidemic. However, it is important to note the public health program area's increase in pneumonia care seeking, case identification and treatment over the decade under study.

Pneumonia Mortality Trends

Despite the rise in pneumonia episodes from 2004-2013, deaths from pneumonia did not follow the same pattern. The pneumonia deaths per year peaked in 2007 with 90 deaths and slowly declined to 2013 with 22 deaths (Figure 14). The episode-specific fatality rate saw a major reduction, falling 82% from a peak of 4.91% in 2005 to 0.87% in 2013 (Figure 15). Also, the pneumonia-specific deaths dropped from 4.6/1000 in 2005 to 1.4/1000 in 2013. This aligns with the previous finding by Dowell & Heffelfinger (1997) of a 50% fall in under-five pneumonia-specific mortality from 6.2/1000 to 3.1/1000 from 1993-1997 in this NGO's catchment population. Although there was a slight increase from 3.1/1000 to 4.6/1000 from 1997-2004, the pneumonia-specific deaths continued to decline to 2013.

These results show significant reductions in pneumonia mortality in children less than 5 years of age in this NGO's catchment area. This success can be attributed to the ARI-specific program that they developed which trained and supervised health agents (CHWs) to diagnose and treat childhood pneumonia using the WHO and IMCI

guidelines. This program has also grown during the decade under study with new CHWs trained in 2005 and 2007. This corresponds with GAPP recommendations and studies that have shown that coordinated community case management using well-trained CHWs can significantly reduce pneumonia-specific mortality in children less than 5 years of age (Marsh et al., 2008; WHO/UNICEF, 2009).

Repeated Pneumonia Episodes

In this study, 60.1% of children had only one episode of pneumonia, so almost 40% had repeated episodes of pneumonia, including one child with 23 repeated episodes of pneumonia. The children with 1-3 episodes of pneumonia constituted 90.4% of the children who presented with pneumonia and the mean number of episodes per child was 1.81 episodes. Less than one out of ten (9.6%) of children had more than 3 episodes of pneumonia. The average time-span between 1st and 2nd episodes was 10.42 months (SD =10.13; median =7.03), which showed that these repeated episodes often occur within a year from the first episode. One explanation could be that children who have repeated episodes of pneumonia have risk factors, such as malnutrition, or other vulnerabilities that put them at risk for repeated episodes of pneumonia. Another explanation is that children who have already had pneumonia may continue to be exposed to a member (or members) of their household who is a healthy carrier of *S. pneumoniae* or *H. influenza* bacterium leading to re-infection through respiratory droplet spread (van der Poll & Opal, 2009).

Also, the interval between episodes appeared to decrease as the number of episodes increased, from a mean of 10.42 months (SD =10.13) between 1st and 2nd

episodes to a mean of 8.76 months (SD =8.57) between 2nd and 3rd episodes and a mean of 7.47 months (SD =7.23) between 3rd and 4th episodes. There is not a clear reason for this but it could be due to repeated episodes causing increased airway inflammation and leading to dysfunction in muco-ciliary clearance of airways as well as the cellular killing of pathogens, similar to the effects of indoor air pollution, an airway irritant (Smith et al., 2000).

Children were more likely to die in the first episode, which may be due to improved immunity among children with repeated episodes. However, this finding may also have been skewed by the collection method of the data since the data-set only has information on children with pneumonia when they have interacted with the CHWs. There may have been children who were only brought to the attention of the CHW for a severe episode that resulted in death; these children may have had prior episodes that resolved without the assistance of the CHW. In addition, parents who sought help from a CHW for a previous episode may have been more likely to seek out the CHW for the next episode, leading to increased case identification and treatment of episodes and improved survival.

Risk Factors for Pneumonia

Since risk factor identification and reduction is an important aspect of pneumonia prevention, several risk factors were analyzed in this study. The age of a child has been shown to be a significant risk factor to pneumonia development and mortality in this study, corresponding with previous studies (Campbell & Nair, 2015; Monto, 1994; Selwyn, 1990). In particular, children who had their first episode of pneumonia at earlier

ages had higher mortality than older children. The most likely explanation for this finding is that children's immune systems are still developing over the first two years of life. The GAVI Alliance support to increase administration of the pentavalent and PCV vaccinations to children under age one in Haiti will hopefully help reduce the greater risk among very young children. Also, analysis showed that children younger at first episode had significantly more episodes. However, the method of entry and exit into and out of this data-set may have skewed this finding. This data-set relies on the first reported episode as being the first episode, which may not have always been the case as prior episodes may have gone unidentified and untreated. Therefore, there may have been an under-reporting of children having pneumonia episodes at younger ages.

The relationship between elevation and pneumonia incidence and mortality has been noted by others (Khan et al.). This study showed the majority of the children presenting with pneumonia cases lived at the highest elevation (37.4%). Also, the number of multiple episodes among children living at higher elevations was greater than children living at lower elevations. This result aligns with previous studies that have shown increased pneumonia cases in higher altitudes, possibly related to decreased lung compensatory mechanisms at greater altitude in children (Khan et al., 2009). More importantly, due to cold at higher altitudes, households have indoor air pollution while heating their homes, which has been shown in many studies as a definite risk factor for pneumonia development (Rudan et al., 2008). In Haiti, this exposure occurs around cooking fires which are located outside the sleeping area. Despite the difficulties that higher altitudes pose to community health workers, population distributions in higher altitudes in Haiti are more dispersed and higher altitudes are more difficult to traverse by

foot, this study showed that altitude was not significantly related to pneumonia mortality. Another risk factor that was considered in this study was distance from referral sites. Children living further from referral sites presented at younger ages with their first episode of pneumonia, even when controlling for elevation. This may be related to increased awareness of health agents and care seeking in further distances from referral sites. Also, health agents in these rural communities likely sought out younger children for pentavalent vaccination administration after 2012 leading to increased case identification and treatment. Longer distances to referral sites was not shown to be related to repeated pneumonia episodes, when controlling for elevation, or to be related to increased pneumonia mortality.

The last risk factor analyzed in this study was the effect of seasonality on pneumonia episodes and mortality which has been demonstrated in previous studies (Rudan et al., 2008). According to the National Oceanic and Atmospheric Association (NOAA), Haiti's two rainy seasons are April-June and August-mid-November, and June-November has increased susceptibility for tropical storms (NOAA, 2010). For both pneumonia episode frequencies, the highest incidence of cases for the period 2004-2013 were observed in June, November, October, and September. When looking at the 1st episode by month and year, pneumonia episodes in June and September-November were consistently elevated. There were especially high peaks as in June 2012, June 2004, October 2007 and September 2010, and November 2012. Pneumonia mortality had similar peaks, especially in June and October months. Since this study shows that pneumonia episodes and mortality are elevated during the rainy seasons, there is likely to be a component of seasonal respiratory viruses including RSV and influenza. These

viruses lead to co-infection with bacterial causes of pneumonia to produce to further mortality. Whereas global recommendations to address viral forms of pneumonia are to consider seasonal vaccination of influenza and use of a bronchodilator in treatment, these are not feasible options in Haiti at this time.

Limitations and Strengths

The data-set used in this study has some limitations. Since children are only included in the data-set at times of pneumonia case identification and treatment by the CHWs, the actual number of pneumonia episodes among children under-five in this NGO's catchment area may be under-counted. Children could be missed by this approach including those who did not seek care, went to the hospital, or traditional healers. However, this is unlikely to be a significant limitation since many traditional healers in this area of Haiti have been included in community pneumonia education and refer pneumonia cases to health agent care and hospitalized cases require health agent follow-up after discharge so would be included in the data. Secondly, there are incomplete cohorts for some percentage of these children who may have been in the early years of this cohort period who were part of the NGO's service population prior to 2004.

The strength of the data-set is that it provides longitudinal community data for all children treated for pneumonia over a 10-year period, a very large cohort study, and the opportunity to make comparisons with previous work done by the CDC in the same area. This allows for examination of incidence and mortality over a long period of time. Being able to monitor continuity over time and community treatment is often missing in other studies.

Future Recommendations

This study demonstrates the need for comprehensive analysis in the future. The shortcomings in this study are informative and helpful in structuring future research. Future studies should include additional risk factors such as measures of household crowding, exclusive breast-feeding, indoor air pollution, parent education levels, and malnutrition to determine their effects on pneumonia development and mortality. Further research could also focus more specifically on the risk factors that were identified in this study to contribute to pneumonia development and mortality, age and elevation. Future research should examine the effect of new prevention efforts such as vaccination rates for pentavalent and PCV vaccines.

Conclusion

In addition to documenting increases in pneumonia case identification and treatment over most of the decade under study, this study revealed a decrease in pneumonia mortality in the target population. The decrease in pneumonia mortality is encouraging and consistent with previous studies with this NGO's catchment population. It also demonstrates that community case management of pneumonia continued to be effective as the catchment population increased four-fold. The findings of this work are important as a benchmark for future work. Since this study has revealed a continued decline in pneumonia-specific mortality in this NGO's catchment population, it is likely the ARI-program for CHWs is successful in case identification and treatment.

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