Decision Analysis of Novel Point-of-Care Diagnostics for Pediatric Pneumonia: Implementation in Developing Countries with Tiered Healthcare Systems

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ABSTRACT

Pediatric Pneumonia (PNA) is the single leading cause of death in children under five, accounting for 19% of all childhood deaths worldwide. Due to severe resource constraints on healthcare, the global burden of the disease in children is disproportionately shared by developing countries. In particular, India, having the highest incidence rate of PNA, accounts for more than 30% of the world’s neonatal deaths from pneumonia every year. The three-tier referral systems, shared by many other developing countries, has introduced inefficiencies into delivering appropriate healthcare to patients in need.

Point-of-care (POC) diagnostics is a type of tool used to assist physicians to make clinical decisions. Its key advantage include the quick turnaround of results, low cost and high diagnostic power could potentially improve India’s pressing situation due to pneumonia. Since the disease progresses quickly in infants and babies and transportation of patients within the healthcare system is time consuming, POC diagnostic is crucial in lowering both the mortality of children with pneumonia and the cost of treating PNA. To this effect, we investigate the potential impact of POC diagnostics when implemented in a three-tier referral system.

Using India as a case country, I construct a decision tree model that evaluates cost, mortality, and the combined cost-effectiveness in Tree-Age software as a framework which evaluates five implementation strategies of a POC diagnostic for PNA within the Indian public healthcare system. The strategies reflect various prescription decisions and referral patterns in current medical practice in India. I concluded that (1) the diagnostic will result in both higher cost and mortality in areas where the practice is to provide all patients antibiotics and thus not recommended, (2) the diagnostic is very likely to achieve lower cost and mortality when patients do not always receive antibiotics and sometimes are given only symptom-relieving drugs and thus recommended, (3) the diagnostic has great potential in generating savings by limiting patients from being transported to urban hospitals, (4) when dual diagnostic is employed combining POC diagnostics and X-ray, confirming positive cases from the diagnostic by X-ray results in lower cost and confirming
negative cases results in lower mortality and (5) the diagnostic can save resources and benefit health outcomes and should be implemented in places where X-ray is not available.

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The experience at MIT has not only made me a more intellectual person but more importantly, a spiritually strong one. As this thesis marks the end of my journey at MIT, I am prepared to embark on a quest during this new stage of my life, full of challenges and adventures. I hope this work can contribute to policies promoting a more efficient utilization of innovative technology in the realm of healthcare and can better inform health policymakers in developing countries in their efforts to save innocent lives from harmful diseases.
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1. Introduction

Pediatric pneumonia (PNA) is the single leading cause of death in children younger than five years of age, accounting for 19% of all childhood deaths worldwide (WHO Fact sheet No. 331). The disease is most prevalent in developing countries, currently the central focus of an ongoing effort to reduce burden of death associated with PNA. One of the key steps in tackling the issue is to enable physicians to diagnose the disease accurately, which has been a real challenge in resource-limited areas. Rapid, reliable and affordable point-of-care (POC) diagnostics, which have demonstrated health outcome benefits in developed countries, hold enormous promise in solving these pressing problems in developing countries. While many countries have shown willingness to introduce new POC diagnostics into their health system, not much effort has been devoted to optimizing the implementation process. Great technologies, no matter how effective or advanced, will fail to alleviate health problems if implemented at a wrong location and scale, both of which can result from a non-optimal policy decision. Therefore policies that govern how diagnostics are introduced need to be carefully analyzed and designed to realize their potential.

1.1 Pneumonia around the World and India

One of the most serious respiratory conditions, pneumonia, is a pathogen-initiated inflammatory condition of the lungs mostly caused by bacterial or viral infections. In infected lungs, microscopic air sacs known as alveoli, the primary sites of oxygen and carbon dioxide exchange, are filled up and/or clogged by pus and fluid secretion of pathogens, severely damaging oxygen uptake into the
bloodstream (Asad et al., 2013). Patients with the disease experience symptoms such as breathing difficulty, chest pain, fatigue and fever. As the disease progresses, alveoli can be permanently damaged, which eventually can lead to respiratory failure and other potentially fatal complications such as sepsis. While most bacterial infections can be treated with antibiotics, patients with viral infections do not respond to them and are often given supportive treatment. With adequate and in-time medical treatment, the disease usually stabilizes within a week and symptoms lasts for as long as 7-14 days. However, for elderly people who may have concurrent diseases, recovery can take up to a year. It has also been noted that those with pre-existing diseases such as malaria, HIV and tuberculosis, all of which are prevalent in most developing countries, have higher risks of acquiring pneumonia and faster disease progression.

Infants and young children are more susceptible to severe respiratory infections because of their immature defensive system (Smith et. al. 2000). According to estimates established by the WHO Child Health Epidemiology Reference Group, the median incidence rate of pneumonia is 0.28 episodes per child-year in developing countries, suggesting more than 150 million new cases occurring annually. While 7-13% of these new cases require long hospitalization and extensive medical resources, they still lead to a high mortality rate. Of the six countries with the highest rates of pneumonia (India, China, Pakistan, Bangladesh, Indonesia, and Nigeria), India has the highest incidence rate with 43 million new cases each year (Rudan et al., 2008). This is more than double the 21 million incident rate of China, the country with the second largest number of pneumonia
cases per year (Rudan et al., 2008). In addition, out of the 3 million deaths due to pediatric pneumonia every year, more than 30% occur in India alone. Multiple longitudinal studies in India and other developing countries have estimated the case fatality rate of the hospitalized, the proportion of death within hospitalized cases, to vary between 8.7% and 47% (Kumar et al., 2007). All lines of evidence in the published literature related to India indicate pneumonia as a serious illness for children that requires a better treatment and management system to reduce the negative impact generated.

1.2 Current Healthcare System in India: Pneumonia in the Context

While pneumonia affects children everywhere, it is most prevalent in resource-constrained countries, where a tiered healthcare system within which patients are referred often exists. This is partially because most developing countries do not have enough resources to establish sophisticated health centers that offer integrated care to all villages. Such systems place lower level facilities which are smaller and less sophisticated closer to villages so to make them more accessible to the vast rural population. Because these lower level facilities do not require significant investment and are manned with only a few health workers, more of them can be built to cover more villages. The function of the lower level facilities therefore is to make very basic healthcare accessible for a large population and filter out a narrower population more likely to have the disease and be referred to receive sophisticated care.
India has one of the world’s most established tiered public healthcare systems. It broadly consists of sub-centers, primary health centers (PHCs), secondary hospitals and tertiary hospitals. The sub-centers and primary health centers are considered lower level facilities and are located throughout the country in small villages. The secondary hospitals act as intermediates between the centers in rural areas and large specialized hospitals in the urban areas. Secondary hospitals are the first point where patients can receive an integrated treatment from a properly trained and certified physician. Tertiary hospitals are modernized, fully equipped and well-staffed hospitals in urban setting, which are not very accessible to the rural population because of the long distance. All levels of hospitals have outpatient clinics where most patients are first seen and diagnoses for various diseases are primarily made.

At the same time that this type of system solves the issue of insufficient healthcare resources to some extent, key challenges remain in India which are manifested in the high incidence of many diseases, particularly pediatric pneumonia. The disproportionate share of the disease burden is often attributed to the lack of medical infrastructure, lack of transportation and shortage of healthcare workers, which are detailed in the following sub-sections. (UNICEF, WHO, 2011).

1.2.1 Lack of Medical Infrastructure

Due to budgetary constraints, high-density populations, and a high volume of cases, many developing countries like India suffer from a significant lack of laboratory facilities, especially in
rural areas (Sharma & Singh, 2012). More than 70% of the entire Indian population live in rural areas but government has been allocating most of its health budget to urban areas (Datar et al., 2007). Currently, there is a shortage of 12% and 16% of sub-centers and PHCs compared to the recommended norm by the WHO. Of the already scarce number of facilities, 49.7% of the sub-centers and 78.0% of the PHCs are located in government buildings, making them unreachable for most of the rural population. In addition to the mere lack of quantity, the quality of service a PHC can provide is limited. National reports show that 8% of PHCs do not have a properly trained medical staff, 39% are without lab technicians and 18% do not have a pharmacist (Bhandari & Dutta, 2013). Given a referral-based system, the well-functioning of the sub-centers and PHCs is critical in controlling the patient flow and ensuring the effective use of healthcare resources.

1.2.2 Lack of Transportation in Rural Areas

A lack of personal transportation to and from health facilities is one of the main factors creating the large gap between diagnosis and actual care. In India and many highly-populated developing countries, transportation is both expensive and time-consuming, especially for population in rural areas (Mathew et al., 2011). Added to these is the scarcity of medical facilities which creates long distances between medical services and rural populations. It was highlighted in a report by the National Rural Health Mission (NHRM) of the Indian government that more than 31% of the rural population in India have to travel over 30 km to get needed medical treatment of which 70-80% is borne out-of-pocket (NHRM, 2011). Because of the long distance and lack of transportation, only 41.8% of sick newborns showing signs of pneumonia receive immediate treatment. (Mathew
et al., 2011). This causes many families to treat early symptoms of pneumonia at home or at local facilities which lack the resources and personnel to provide adequate diagnosis and treatment (Mathew et al., 2011). Many families even end up not seeking medical treatment or seeking treatment from unqualified “medicine men” whose treatments are expensive and ineffective, putting many children who would likely have been cured at a higher risk due to the delay of proper treatment.

1.2.3 Shortage of Medical Specialists

With the increasing disease complexity requiring sophisticated health technology and medical knowledge to diagnose and treat, qualified physicians and health workers have become an integral part in the delivery of satisfactory health service. However, many developing countries are facing substantial shortages in their health workforces, particularly in rural areas. With a population of nearly 1 billion people in India, including approximately 300 million poor, medical specialists are in great demand (Nath, 1998). However, it was reported that in 2005, for every 10,000 people, there are 10 qualified physicians in urban areas and only 1 in rural areas—a staggering 10 to 1 ratio (Rao et al., 2012). The reason for this is that well-trained physicians who have undergone as many as 5.5 years of training prefer urban settings due to personal and professional expectations which are incompatible with rural service. India’s government has long recognized this workforce crisis and implemented policies to expand the number of primary care givers such as community health programs which offer a bachelor of health in three years (Ahmed et al. 2011). However, these programs soon became controversial as many health leaders question the competency of
clinicians with shorter duration of medical training and criticize the quality disparity of clinicians caused by these government policies in rural areas. Other studies have also claimed the key challenge is not the shortage but the fact that most of the country’s poor are scattered throughout the country, making it very difficult for the government to send the adequate number of medical specialists to all the areas in need (Nath, 1998). In general, developing countries face enormous challenges in ensuring an adequate supply of healthcare workers, which can potentially be remedied through the employment of innovative technologies.

1.3 Current Antibiotic Use

Antibiotic misuse has been a great concern for policymakers in developing countries and is largely responsible for the rising antibiotic resistance (Kotwani et al., 2012). Current misuse of antibiotics for pneumonia treatment is attributable to both the lack of effective antibiotics and inappropriate use. Low accessibility of effective antibiotics is due to a variety of factors including resource constraints, political commitment to healthcare, and coordination between health and government agencies (Arora, 2010). The problem is especially serious in poor areas where only 12.5% of children with pneumonia symptoms receive proper antibiotics when they seek treatment (Arora, 2010). The paucity of effective antibiotics is further confirmed by Dr. Stan N. Finkelstein’s observations from visits to local clinics and other studies in India, all of which reveal that many of the health workers in rural areas carry an old type of antibiotic, cotrimoxazole — an often ineffective against the common strain of bacteria causing pneumonia (Schrag et al., 2001). In addition, it is noted that in pneumonia treatment, due to the poor diagnostic capability of rural
health centers, all patients with symptoms suggestive of pneumonia are given antibiotics (Clements et al., 2000). This behavior leads to extensive waste of important antibiotics as some proportion of the patients have viral pneumonia and don’t respond to antibiotics. The healthcare system therefore bears an indirect cost as these wasted antibiotics could have been used to treat other patients inflicted with pneumonia. Not only is it wasteful, inappropriate antibiotic prescription stimulates the development of antibiotic resistance and makes common strains of bacteria difficult to treat. With more antibiotic-resistant strains emerging, the healthcare system will experience an increase cost burden as newer and more expensive antibiotics have to be used to treat diseases which were once treatable with common antibiotics. Most of problems associated with antibiotic abuse are due to the lack of equipment necessary to medical decision-making. An innovative technology which facilitates accurate diagnoses will greatly encourage prudent antibiotic use so that the already scarce drug can be provided to those in real need.

1.4 Point of Care Diagnostics Background

POC diagnostics have gained much attention in the recent two decades owing to their rapid turnaround of test results. This type of diagnostic has been implemented in many developed countries to improve patient experience and improve the operational efficiency of the healthcare system. The diagnostics are also employed by emergency departments in various hospitals to streamline urgent care processes. In recent years, the focus of application has shifted towards developing countries where health infrastructure is weak and laboratories to aid the identification
and diagnosis of health conditions are not accessible. It has been widely believed that the ability of POC diagnostics to bypass laboratories and bring innovative technologies to improve diagnostic accuracy is a promising solution to the existing health problems in resource-poor areas. Although promising, challenges remain to introduce and scale up such devices in a country with limited resources and therefore a well-designed implementation strategy is required to make the diagnostic cost-effective.

1.4.1 POC Diagnostics in Developed Countries

A POC diagnostic is a type of medical device which facilitates clinicians to reach a diagnosis at the time of a patient visit. Its purpose is to expedite the availability of test results which can lead to an immediate decision on subsequent treatment strategy and elicit appropriate action from the patient side to prevent further disease progression. The concept was first introduced in the 50s but not widely recognized until the 80s. Starting in the 80s, a series of papers were published on the analytical capabilities of POC diagnostics in testing blood sugars, which attracted serious attention from the healthcare industry and provoked research and business development in this area. In the past three decades, persistent effort devoted to POC diagnostics R&D has expanded its menu from fewer than 10 tests to more than 100 in variety, making it a multi-billion dollar industry with sale revenues expected to double in the next 5 years (Schito et al., 2012).

As scientific knowledge advanced and engineering techniques became more sophisticated, the
analytical performance and design of POC diagnostics have improved significantly over the past decade. Current state-of-the-art POC diagnostics in many areas including HIV testing, pregnancy testing, blood sugar measurement and more complex coagulation testing offer high sensitivity and specificity comparable to laboratory testing (Luppa et al. 2011). For many acute conditions seen in the ER where a diagnosis is urgently in need or chronic conditions which require frequent testing, POC diagnostics appear to be an even more appropriate method, if not the best, rather than laboratory testing to support diagnosis and management of illness. In addition, by minimizing instrument size and simplifying procedures to carry out the test, POC diagnostics are not only becoming easier to carry, but also possible for untrained or less trained medical staff to perform them. As a result, logistics costs and cost of labor can both be reduced when POC diagnostics are employed. Since the cost of POC diagnostics is generally lower than laboratory testing and often is relatively cheap, they are also widely employed in developed countries to routinely screen a large population for a certain disease.

The unique characteristics of POC diagnostics have been thought capable of streamlining patient flow within the healthcare system to optimize care processes. In most developed countries and large cities in developing countries, conventional centralized laboratory testing is deemed a fundamental part of medical practice and integral to an accurate diagnosis. However, a patient has to be referred to a separate facility to have specimens taken which are then transported to yet another facility to be tested. After the test is performed, the patient needs to be invited back to see
the test result in person and discuss the follow-up treatment with the doctor. The lengthened waiting time, which often extends to several weeks, along with the onerous travelling between facilities, have significantly lowered the overall effectiveness of the healthcare system. The presence of a POC diagnostic at the first site of a patient’s visit saves not only patients’ travelling time and cost but also doctor’s time to chase down the result and see patients multiple times. Only if the patients’ conditions are deemed serious enough are they required to do more lab testing to confirm the disease. Therefore, having POC diagnostics can significantly lower transaction costs and unnecessary lab testing, thereby improving the overall efficiency of the healthcare system.

1.4.2 POC Diagnostics for Pneumonia in Developing Countries

Even though the cause of pneumonia has been extensively studied and understood, no diagnostic tool to date is available to make accurate diagnoses for a timely treatment (Mathew et al., 2011). An analysis from the RAND Corporation has suggested that a novel POC diagnostic for bacterial pneumonia could save 405,000 children’s lives per year (RAND Health 2007). Currently, the accepted gold standard in primary care settings is a combination of chest X-ray and clinical observations such as elevated age-specific respiration rate (Tachypnoea), chest in-drawing and other respiratory symptoms (Grossman, 2012). However, in rural area of many developing countries, most healthcare facilities are not equipped with X-ray or to provide or interpret radiological information. As a result local healthcare facilities rely on a WHO-defined guideline to predict pneumonia, which is based on a patient’s clinical symptoms including elevated respiration rates and history of coughing and breathing. In developing countries like India where
medical facilities can be very resource-limited and medical staffs are not well-trained, the guideline is often not properly carried out, further lowering the accuracy of the diagnosis (Sharma and Singh, 2012).

While the health care structure and condition in India is drastically different from that of developed countries, many characteristics of POC diagnostics can meet the special needs of India and profoundly improve its healthcare system and health outcomes. Due to the lack of medical infrastructure in India, more than two-thirds of children with pneumonia do not receive correct treatment in time. Numerous studies have shown that proper treatment can be delivered more quickly in rural India if healthcare services are located more closely to the communities (Dilip and Duggal 2003). The fact that most POC diagnostics are pocket size makes them ideal for carrying into these hard-to-reach areas, effectively reducing the distance between patients and the “laboratory”. Therefore by implementing POC diagnostics in village health centers or rural hospitals, patients will be more likely to receive accurate diagnoses following which a proper treatment can be given immediately.

Other characteristics of such an on-site diagnostic tool also benefit the patients and the healthcare system. These include minimizing the time to obtain a test result, thereby allowing clinicians to make a quicker decision, simplifying the use for non-professionals, thereby reducing inaccurate measurements and the inherently increasing in efficiency due to the diffusion of advanced
technology to poor environments (i.e. increase accessibility) (Pecoraro et al., 2014; Halpern et al., 1998). All of these advantages will be amplified in resource-constrained rural areas where prolonged transportation to urban hospitals calls for speedy diagnosis and lack of specialized health staff would benefit from simpler procedures for testing. Furthermore, due to the unique hierarchical hospital systems in India, patients are usually referred step by step through the entire system in order to reach the most appropriate treatment. By having the POC diagnostics which have the ability to measure the severity of PNA, patients can be referred to the right level of the hospital directly. Currently available ultrasound-based POC diagnostics for PNA offer a much superior diagnostic accuracy compared to existing diagnostic capability in India. Such device identifies abnormalities such as infiltration through providing visualization of the lungs in order to facilitate diagnosis. However, ultrasound-based diagnostics suffer from limitations in revealing the type of lung lesions base on which antibiotics are prescribed and identifying the extent of lung damages which is a key determinant for selecting treatment strategy. Even with limitations, new POC technologies still represent a promising way to improve clinical outcome for pneumonia patients in developing countries (Zulfiqar et al., 2007).

POC diagnostics also cost less compared to other medical equipment for similar type of diagnoses. Although miniaturized devices often produce less reliable testing results than equipment in modern hospitals, they can still offer a level of diagnostic power substantially higher than merely observing symptoms. In places such as parts of India where most of the health centers lack modern medical
equipment and doctors make medical decisions merely depending on symptoms, the diagnostics offer the potential to generate a large impact on the health outcome. The lower cost of POC diagnostics also promotes wide adoption in rural areas where adoption of traditional large-scale equipment such as X-rays is too costly to become possible in the near term. The POC diagnostics also facilitate quicker adoption during the time of fast technological advancement. As lower cost technology develops, resource-poor areas can quickly shift to the new technology by replacing the old diagnostic with the new version, which may not be feasible with more expensive equipment.

1.4.3 Novel Infrared-Based Diagnostic for Pediatric Pneumonia

A collaboration is currently underway between a group of engineers at MIT and physicians affiliated with the Massachusetts General Hospital (MGH) to develop and test a novel POC diagnostic for PNA. The device is based on a thermal imaging camera purchased from FLIR Systems, Inc. Wilsonville, OR, which can be coupled with a smartphone to generate heat distribution images of body surfaces (Figure 1.4.1). An application (app) is installed on the phone to interpret the distribution of hot spots on the image and provide treatment recommendations. The device is run on both the chest and the back of a patient with no skin contact in a non-invasive procedure which takes approximately two to three minutes. The infrared thermography captures the skin temperature which is a key indication of the underlying medical condition within the lungs.
The use of skin temperature to detect pneumonia is based on the fact that inflammation in the lungs causes the body to produce abnormal level of heat which is reflected in elevated body surface temperature (Jones, 1998). If there is an infection, there will be localized heat spots appearing in red on the thermographs. This thermal imaging diagnostic is thought to be capable of distinguishing bacterial and viral pneumonia. With bacterial pneumonia, asymmetric hot spots are expected because bacteria produce isolated areas of infiltrates which represent the accumulation of white blood cells (pus) in the lung. Such focal infiltrates will be detected by the thermal camera as discrete focal hot spots at different parts of the infected lungs, resulting in the asymmetry. On the other hand, viral pneumonia will produce symmetric hot spots as viral lung infection is a diffuse process and tends to be throughout the lungs rather than causing focal areas of increased heat. The prototype has been investigated under real clinical settings in the emergency department at the MGH. When adults/children with pneumonia present at the ER, the patient is tested using the
thermal camera in addition to the chest X-ray which is normally performed to aid diagnosis.

Preliminary results suggest the thermal camera diagnostic has the ability to identify bacterial and viral pneumonia quickly and is very promising in preventing neonatal death due to pneumonia. The intention is to scale the diagnostic to primary care facilities in resource-poor countries to promote the timely treatment of pneumonia. Since the project is still in progress and many aspects of the device are being experimented on, further details are not within the scope of this thesis and are not discussed here.

1.5 Objective of the Study

The objective of this study is to first expand the knowledge on the patient flow pattern and overall structure of India’s healthcare system which is shared by many developing countries suffering from healthcare issues with a focus on pneumonia and second, to construct decision analytic models replicating the clinical pathways to evaluate alternative policy scenarios for the implementation of a point-of-care (POC) diagnostic for childhood pneumonia. The analysis primarily focuses on outpatient clinics where most patients are first seen, whether in PHCs, secondary, tertiary hospitals or elsewhere. The outpatient setting is of great importance as it is the point where major decisions are reached. This includes not only diagnostic decisions but referral and treatment decisions. Therefore, the outpatient setting is the main focus of this study which tries to assess the influence of POC diagnostics on these critical decisions and the potential economic
and health consequences. Policy scenarios are compared in terms of their effect on cost and mortality of treating a pneumonia afflicted patient. At the end of the study, we put forward recommendations which provide guidance on the implementation of innovative POC diagnostics to address the pressing health issues and maximize their potential impact on health outcomes, especially in resource-constrained countries.

2. Model Structure and Methods

This study does not involve human subjects or any form of confidential/personal information. All of the information collected for the study is operational in nature. The proposal for this study has been reviewed by the institutional review boards (IRB) at both Harvard Medical School and Massachusetts Institute of Technology. Both committees determined that human subjects are not involved.

2.1 Data Collection in Nagpur, India

Data collection in Nagpur, India was conducted in July and November of 2014 by Dr. Stan N. Finkelstein, Corinne Carland and Sara Dolcetti. We worked with Lata Medical Research Foundation (LMRF) which hosted our team members, coordinated their site visits, translated their questions during visits and acted as a reference and guide for further information regarding the healthcare system in India.
Purpose of Site Visits:

1. Add more context to available statistics from the published literature in order to develop a model to inform how the introduction of a handheld diagnostic device could impact costs in the system and mortality rates.

2. Validate our team’s understanding of the structure of the public healthcare system in India and our model of how pneumonia patients move through the system. In doing so, we investigated the prevalence of pneumonia, barriers to treatments and pneumonia diagnostics in health care facilities in the area.

3. Determine where along the care pathway such a diagnostic would have the greatest impact.

In order to achieve the above goals and gain a deeper understanding about the prevalence rate, referral patterns, and costs associated with childhood pneumonia in Nagpur, our team members, Corinne Carland, Sara Dolcetti and Dr. Stan Finkelstein visited a variety of facilities. These included: sub-centers, primary health centers, rural hospitals, sub-district hospitals, general hospitals, private clinics, pharmacies and alternative care centers. At each level of facilities, informal interviews were conducted with physicians or health workers using the set of pre-prepared questions used to guide the conversation (refer to Appendix A).

2.2 Data Collection through Literature Search

Due to the frequently poor condition of the healthcare facilities and the lack of health registries
and databases in India, numerical values for many key parameters in the model were not identified
during our trip. Therefore, we conducted a literature search to find similar studies in which related
estimates are employed. The references of the retrieved studies were also examined to seek further
information on data needed. When searching for desired data, priority was given to regional studies
in the vicinity of Nagpur where our field work was performed and then to other provinces within
India. When no other sources of data were available, published meta-analyses from international
organizations or national survey studies were used to derive parameter estimates. A broad literature
search was also performed in an attempt to confirm there was no previous study similar to ours.

2.3 General Assumptions across all Scenarios

1. Regional prevalence for Nagpur was not available in previous literature. Therefore, the
   prevalence rate of pneumonia for children under 5 was estimated to be the national prevalence
   in India.

2. Mortality rates of infants are assumed (Based on The Million Death Study in India and Rudan
   et al., 2008).

3. Cost data are estimated according to our experience in India and interviews with local medical
   professionals and researchers in the LMRF.

4. Specificity and sensitivity are based on expert opinion from leading researchers in the
   development team of the POC diagnostic.

5. We assume adherence to treatment after leaving the healthcare facility.
6. We assume patients have access to treatment when arriving at a facility.

7. We assume patients will have no difficulty in commuting to a local healthcare facility.

8. We assume doctors make referrals strictly based on a combination of clinical judgment and results of the POC device.

9. We assume parents seek healthcare when they observe their children having symptoms indicative of pneumonia.

10. With this prevalence, sensitivity and specificity, Bayes' Theorem of Conditional Probabilities was used to calculate the probability of a positive result—(Sensitivity * Prevalence) + ((1 - Specificity) * (1 - Prevalence)—and the probability of a negative result—(Specificity * (1 - Prevalence)) + ((1 - Sensitivity) * Prevalence)—irrespective of the disease status.

2.4 Modeling Software Basics and Model Structure

The tree diagrams in this study were produced using Tree-Age Pro Suite Software Inc., Williamstown, MA. Models constructed with this software consist of decision nodes (square), chance nodes (circle) and terminal nodes (triangle). Each decision node signifies competing strategies which are defined by a set of specific events detailed in branches that follow. For each chance node, probability estimates can be assigned to indicate the occurrence of each event which is captured by branches after a chance node. The pound sign (#) signifies the complement of an event, with the event being the probability of the other branch originating from the same chance node. Sensitivity and specificity values for each test can be incorporated by treating the binary
result as a different event. At terminal nodes, payoffs, such as the cost and mortality of each approach, are allowed to be entered. The software can then analyze cost and mortality, according to the transition probabilities of each event to predict an expected outcome, also consisting of both a cost and mortality component. Finally, the software identifies the optimal strategies among competing alternatives, branching out of a decision node based on the expected outcome. The decision problem was designed from the societal perspective. The primary outcomes are the societal cost per patient and the mortality rate.

In this study, we developed a decision analysis model to estimate the economic and clinical outcomes of a new POC diagnostic in outpatient settings in both primary and secondary facilities. For scenarios 1-3, I used the methods described by de Oliveira et al., (2010) and Ricci et al., (2006) in building decision trees to evaluate screening tests. For scenarios 4 and 5, methods of evaluating dual diagnostics and calculating the posterior probability of a test described by Pooran et al. (2010) were employed. From previous experience, decision science experts have advocated the use of only two-branch chance nodes instead of three-branch nodes in decision trees to avoid difficulties in sensitivity analysis. We follow this general convention, defining two layers of two-branch nodes when a three-branch node is required. We have designed separate decision trees to allow the evaluation of 5 policy scenarios we have identified, each with a different set of assumptions corresponding to what may be happening in the real world in India. Each scenario begins with young children presenting with potential symptoms for pneumonia at a healthcare facility. At each
of the terminal nodes of a branch, the cost and the mortality of the entire branch were calculated and incorporated. All the values for cost used in the models are in US dollars. We did not consider adjustment for inflation.

All policy scenarios evaluated and compared in the model are between (1) status quo and (2) device strategy. Outlined below are the possible events for patients who are not critically ill and transferred directly to the emergency department or higher level hospitals for treatment:

**BASE CASE (STATUS QUO): Five Scenarios**

When someone arrives with a sick baby with respiratory symptoms indicative of pneumonia:

**At Primary Level:**

1. Regardless of disease status, the patient is given a course of antibiotics and sent home

2. If the case is believed to be positive for pneumonia, then antibiotics are given; if believed to be negative based solely on doctor’s judgment, then only symptom-relieving drugs are given;

3. If the case is believed to be urgent, the patient is transported directly to an urban hospital by ambulance.

**At Secondary Level:**

4. Where X-ray is available, if the case is believed to be positive then antibiotics are given, if believed to be negative then symptom-relieving drugs are given;
5. Where X-ray is not available, treat at doctor’s discretion.

DEVICE STRATEGY: Five Scenarios

Someone arrives with a sick baby who has respiratory symptoms indicative of pneumonia.

At Primary level:

1. If the case is believed to be positive, the patient is given antibiotics and send home, if negative, the patient is not given any treatment;

2. If the case is believed to be positive, then antibiotics are given, if believed to be negative based on diagnostic result, then only symptom-relieving drugs will be given;

3. If the case is believed to be very severe, depending on the result of the POC diagnostic, the patient is either transported directly to urban hospital or remain in rural hospital.

At Secondary Level:

4. Where X-ray is available, confirm positive/negative cases from the device with X-ray and if believed to be positive then antibiotics are given, if believed to be negative then symptom-relieving drugs are given

5. Where X-ray is not available, use the device; if the case is believed to be positive then antibiotics are given, if believed to be negative then symptom-relieving drugs are given

2.5 Limitations of the Study

A common limitation for all simulation studies is that the models used cannot fully capture real
world processes. The models in this study are no exception and represent a simplification of the very complex decision-making processes used by physicians to evaluate the effect of a POC diagnostic. As a result, many other possible medical options a pneumonia patient could undergo are not included in the models which may influence the effect of POC diagnostics on treatment cost and mortality.

This study only models the outpatient setting and does not evaluate effect of POC diagnostics on pneumonia treatment in emergency departments and inpatient settings. Therefore, the possible influence on the cost and mortality associated with patients being transferred from an outpatient to inpatient setting for further treatment was not captured in the models. Furthermore, according to our observation of local doctors, patients who are critically ill often do not enter the outpatient system; instead they usually present at emergency rooms directly. This phenomenon may be significant in deciding the effect of POC diagnostics on the mortality but it was not considered in the models.

With very few studies published on childhood pneumonia in India, we relied, for most of our parameter values on published data for pneumonia of all age groups in various countries with similar health system structure for resource-poor settings. Mortality values reported in these studies are subject to substantial variability. The lack of bookkeeping systems in rural clinics as well as some of the higher level healthcare facilities put barriers to our data collection on cost. Some estimates were obtained from local researchers, experts and medical practitioners. Despite
limitations in data collection, the study used the best data available in the literature.

Healthcare services in India are delivered through both public and private systems. The public division of healthcare administration offers services which are publicly funded and therefore at a lower out-of-pocket cost to the patients while private sector facilities target wealthier patients and offer more “state of the art” health care services. Although the private sector accounts for a large proportion of the Indian healthcare system, it was not extensively studied and reported on in previous research. Though members of our project team did have the opportunity to visit and conduct interviews at some private facilities, we obtained only very limited insight into their operation and therefore it was excluded from this analysis.

3. Rationale for Modeling Choice and Overall Study Design

In this study, I constructed a decision model which examines the effect of implementing a POC diagnostic in outpatient settings in primary and secondary level health centers, with more focus on the primary level in order to extract its potentials in reducing the treatment cost and mortality of PNA. Due to time constraints, our team did not visit all levels of facilities during the two weeks of stay in India. Although we did not examine in detail what level of equipment each hospital employs, from interviews with doctors and local researchers, we accrued enough insight to make the assumption that secondary hospitals in general have X-rays and more sophisticated supportive care facilities. The study did not go further into evaluating the diagnostics at tertiary hospitals. In
In this chapter, I discuss the rationale of the modeling choices made in this study.

3.1 Significance of Primary Level Decision-Making

The primary level deserves the most attention because it is the most resource-constrained part of the healthcare system and yet serves the most people. Given the extreme gap between supply and demand of resources, the diagnoses made at this level have plenty of room for improvement. However, what is much more important is that any small improvements achieved at this level could lead to a great impact because of number of people affected. Therefore, focusing on the primary level is not only necessary but will have higher marginal benefit per unit of effort devoted compared to the secondary or tertiary level.

With its unique characteristics, a POC diagnostic, if implemented at the primary level, can offer potential remedies for some of the most critical issues the Indian health system faces: the lack of transportation, medical facilities and medical specialists. Improving care in these locations increases the likelihood of an early intervention stemming from an accurate decision, making POC diagnostics more valuable clinically. In addition, the user-friendly design of modern POC diagnostics enables non-specialists to administer the test, which means that non-physician health workers or midwives can perform the test at sub-centers or in the villages when they see patients during routine visits. This potentially expands the coverage of the new technology and allows more people to benefit from it.
Given that the cost of care in secondary hospitals is three to four times that of PHCs and the volume of patients seen at primary level is much greater, the referral decisions made at PHCs are very important in terms of reducing the cost burden of the patient and saving health resources of the society. More accurate diagnosis at primary level, leading to early interventions on potential at primary level, is also of great value as it could prevent more downstream cost due to the progression of the disease. The sooner patients are informed of their conditions accurately, the more effective they can engage in self-management of the disease and keep up with the treatment, which have great implications on the chances of recovery (Coulter et al., 2008). In light of all the above considerations, models were designed to evaluate the effect of POC diagnostics in the context of different prescription and referral patterns at the primary level.

3.2 Dual Diagnostics Application at Secondary Level: POC and X-ray

Though not comparable to tertiary hospitals, secondary hospitals have many more resources than PHCs and the necessary medical equipment for the accurate diagnosis and management of PNA. Since there exist technologies that offer better sensitivity and specificity than the POC diagnostic, substituting completely the new diagnostic for the X-ray would unlikely be beneficial to clinical outcomes. However, since X-ray is an expensive test especially in resource-poor countries, its use has been limited. Applying POC diagnostics in combination with X-rays could potentially save health resources with minimal harm to mortality.
Even though secondary hospitals are equipped with X-rays, it was revealed from our interviews in India that outpatient practitioners in secondary level rarely order X-ray for diagnosing pneumonia except in a small number of teaching hospitals due to the teaching value of the film. In addition, in many facilities X-rays are often broken due to insufficient maintenance and therefore become unavailable for patients in need. If POC diagnostics are implemented, there would be an alternative to X-ray, which could improve health outcomes significantly.

Based on the above two lines of reasoning, two models were designed: the first one explores the potential possibility of applying both diagnostics one after the other (the weaker/cheaper one before stronger/expensive one) and evaluates the extent to which POC diagnostics can bring down the cost and the effect on mortality; the second one evaluates the role of POC diagnostics on PNA treatment in the absence of X-ray.

3.3 Value of Implementing at Tertiary Level Outpatient

In this study, I focused primarily on outpatient settings of primary and secondary level hospitals in accessing the effect of the diagnostic. One reason tertiary hospitals are not considered is because the level of medical facilities and doctors at these hospitals resembles that of the secondary hospitals. Therefore, by modeling the secondary level, the qualitative effects on the tertiary level will be largely the same, perhaps with a slight increase in overall cost and variation on mortality depending on assumptions. Furthermore, given the fact that tertiary hospitals cover a much smaller
population and thus have fewer patient self-refer to them, a large proportion of patients are transferred from lower levels of hospital whose condition is critical. This renders the device of less diagnostic value as most patients have undergone multiple rounds of testing before their arrival. Even when patients are self-referred, sophisticated equipment are available which offers much higher sensitivity and specificity than the POC diagnostics. The key characteristics of the POC diagnostic to help physicians make treatment and referral decisions more accurately would also be not as valuable at tertiary hospitals as at lower level hospitals. As tertiary hospitals represent the most advanced form of health care, no further transfer needs to be made and all the prior costs before arriving at tertiary hospitals, including treatment, travelling and all indirect costs, are sunken and cannot be averted. The usefulness of the device is thus not significant compared to when it can help make decision that change future treatment pathways.

4. Simulation Results of Policy Scenarios and Discussion

In this chapter, I report firstly the structure of India’s health system we learned from our field research in Nagpur and secondly the simulation results for 5 policy scenarios corresponding to outpatient settings in primary and secondary hospitals. I then discuss the impact of POC diagnostics on the cost and mortality of PNA treatment in each scenario. The observations from local health facilities together with simulation models offer insights and recommendations which can optimize policy designs to maximize the effective use of scarce health resources in developing countries.
4.1 General Structure of the Indian Health System

Figure 4.1.1: Overall structure of the Indian healthcare system and patient flow paths within the system based on referral patterns (Carland C. and Dolcetti S. 2014, based on visit to Nagpur, India)

The first step of the study is to gain a deeper understanding of the structure of and the patient flow within the Indian healthcare system. The Indian healthcare system consists of both private and public components through which healthcare is delivered. Public components receive federal and state funds and the private sector operates on its own but is said to offer both better service quality and higher cost. Patients have free choice to enter either component and the structure (levels of hospitals) within each division resemble each other. Due to time constraints, our team did not visit
enough hospitals in the private sector to collect a meaningful amount of data for analysis and therefore this section does not detail the structure of the private sector.

In the public system, there are three major tiers: primary, secondary and tertiary level (Figure 4.1.1). The primary level consists of sub-centers and primary health centers. These centers are established to serve rural populations and scattered throughout the entire nation. The sub-centers are the first level of the institutionalized health system and each of them generally cater to 6 villages, equivalent of a population around 3,000-5,000 people. The center is staffed with two auxiliary nurse midwives whose main job is delivering babies and providing basic care for pregnant women and children. There is no medical doctor who has undergone standardized training at this level. The midwives also visit villages to see sick villagers and can either treat the patient on-site with simple medications or refer the patients to the closest primary health center.

Primary health centers make up the next level above the sub-centers, serving 5-6 sub-centers and around 30,000 people. Each center is staffed with two medical officers who have completed medical school and at least one year of residency, a pharmacist and other multi-purpose workers. This is the first place where a patient from a rural village can receive proper integrated medical treatment. These PHCs are located in larger villages with a population of more than 5,000 within a distance of less than 15km from each sub-center. As opposed to sub-centers where midwives cannot make a diagnosis except by crude clinical observations, such as placing hands on children's
forehead, the medical officer at PHCs looks for a high fever, cough, increased respiration rate, and sounds in the lungs when the patient breathes. The PHCs were envisaged to provide integrated curative and preventive treatment specifically targeted to the rural population. However, with the lack of X-rays and other necessary equipment, diagnosis for many illnesses at the PHC level is done through observing clinical symptoms. If the patients have severe illness, they are referred to higher level hospitals directly.

The secondary level of the healthcare system consists of rural hospitals, sub-district hospitals and general hospitals. As hospitals move away from rural areas and more into an urban setting, the level of staff and equipment also become more sophisticated. The only type of hospitals within this level our team visited is the district hospital. There is generally one district hospital per district, which has around 100 beds, staffed with medical doctors, nurses and equipped with X-rays.

The tertiary level consists of tertiary hospitals which are fully functional specialized hospitals in urban areas. These hospitals are equipped with modern equipment and the best doctors in the nation. However, with the long distance patients have to travel from rural areas to this type of hospital, not much of the rural population can receive treatment from such hospitals. From the visit of Dr. Stan N. Finkelstein and evidences from local researchers at the LMRF, it was suggested that general hospitals and tertiary hospitals typically have outpatient clinics and patients who live in close proximity to them will tend to go there when sick, rather than to a PHC that may be farther
away. Generally speaking, these hospitals are comparable to large hospitals in the US.

4.2 Summary of Main Parameter Value Used for Scenario Analysis

This section presents common parameter values used in all the scenario analyses in the following sections. Additional parameters specific to each scenario will be introduced in its respective section.

Table 4.2.1: Transition probabilities and the mortality rate of Scenario 1.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Base Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence (pSQPos/pPos)</td>
<td>0.006</td>
<td>Kotwani and Holloway</td>
</tr>
<tr>
<td>Device Specificity (pPTNR)</td>
<td>0.7</td>
<td>Expert Opinion*</td>
</tr>
<tr>
<td>Device Sensitivity (pPTPR)</td>
<td>0.7</td>
<td>Expert Opinion</td>
</tr>
<tr>
<td>Status Quo Sensitivity (pSQTPR)</td>
<td>0.4</td>
<td>Expert Opinion</td>
</tr>
<tr>
<td>Status Quo Specificity (pSQTPR)</td>
<td>0.4</td>
<td>Expert Opinion</td>
</tr>
<tr>
<td>Doctor’s Tendency to Prescribe Antibiotics (pDrug)</td>
<td>0.6</td>
<td>Expert Opinion</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.0013</td>
<td>The Million Death Study Collaborators</td>
</tr>
</tbody>
</table>

*Expert opinions for this study were obtained from Dr. Stan N. Finkelstein, leading researchers including Dr. Linda Wang and Dr. Patricia Hibberd from the diagnostic development group at MGH, researchers led by Dr. Archana Patel at the LMRF and local health professionals in India.

Table 4.2.2: Bottom-up annual cost analysis of X-ray and POC diagnostics.

<table>
<thead>
<tr>
<th>Equipment</th>
<th>Value (U$)</th>
<th>Per-test</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>POC Diagnostic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Device cost</td>
<td>350</td>
<td>0.5</td>
<td>FLIR Website*</td>
</tr>
<tr>
<td>X-Ray</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Device cost</td>
<td>2000</td>
<td>2.7</td>
<td>Trade India Website**</td>
</tr>
<tr>
<td>Film (100 sheets)</td>
<td>30</td>
<td>0.3</td>
<td>Trade India Website</td>
</tr>
</tbody>
</table>

*For price information on the FLIR thermal camera, please refer to the official website at http://flir.com/flirone/buy-us.cfm

**For price information on X-ray equipment and film in India, please refer to http://www.tradeindia.com/TradeLeads/buy/Hospital-Medical-Supplies/X-Ray-Equipment/
Estimating the number of patients who would be using the POC diagnostics and X-ray was difficult and only crude estimates could be made. One doctor we interviewed estimated that 8-10 children 6 years and below come in per day for respiratory infection/illness. Another said that he sees 1 pneumonia case per month and yet another said he saw 4-5 per month. A researcher at LMRF suggested that at a PHC 15-20 patients will present with respiratory illness and of that, 10-15% will have pneumonia. From our observation in local hospitals, out of the hundred people coming to the hospital per day, 20 patients have respiratory/cold symptoms, and on average 6 to 8 are children. If we assume 1/3 to 1/4 of the children are given an X-ray which based on our observation is hardly ever ordered, we arrive at an estimate that there are approximately 700 to 900 patients who receive X-rays per-year. This translates into a cost of approximately $3 per X-ray procedure including the film, which is within the range of $2.81-4.61 suggested by Madsen et al. (2009). Given that the cost of the device is $350, the amortized cost to each patient over a one year period is estimated to be $0.50 dollar based on the same estimated annual patient volume. For simplicity, we assume the cost per test is the same whether in primary or secondary hospitals as we observe similar patterns of patient volume at both levels.

Table 4.2.3: Payoffs (cost and effectiveness measures) for Scenario 1.

<table>
<thead>
<tr>
<th>Cost</th>
<th>Value (U$)</th>
<th>Range</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics</td>
<td>5</td>
<td>$0.50-$10.50</td>
<td>Babu V. and Suma C.</td>
</tr>
<tr>
<td>Symptom-relieving Drugs</td>
<td>2</td>
<td>-</td>
<td>Assumed</td>
</tr>
<tr>
<td>Cost of Visit</td>
<td>10</td>
<td>-</td>
<td>Assumed</td>
</tr>
<tr>
<td>Device Cost/Visit</td>
<td>0.5</td>
<td>-</td>
<td>Assumed</td>
</tr>
<tr>
<td>Cost of the test</td>
<td>1.5</td>
<td>-</td>
<td>Assumed</td>
</tr>
<tr>
<td>Cost of Further Treatment</td>
<td>40</td>
<td>-</td>
<td>Madsen H. O. et al.</td>
</tr>
</tbody>
</table>
There is a wide range of antibiotic cost reported, depending on the type of drug and the location they are dispensed. From the range of $0.50-10.50 reported by Babu V. and Suma C. (2006), I picked the average value ($5) for the following analysis. Given that from our observation, antibiotic costs in rural areas are on the lower end of this range, sensitivity analysis on antibiotic cost was performed to determine at what cost of antibiotics the diagnostic would not be economically favored. Due to the scarcity of health workers in existing facilities, we anticipate additional workers need to be employed to run the POC test or fewer patients would be able to be served during the course of a clinic session. Therefore, the cost of performing the test using POC diagnostic includes a variable cost, the salary of the health worker, on top of the estimated fixed cost. The salary is estimated based on the mean salary among daily laborers in the population study (http://www.indiatogether2009). For simplicity and the fact that health workers’ salaries are usually above the average, I used $1.50 as the cost of the test.

4.3 Base Case: Every Patient Receives Antibiotics

Scenario 1: This scenario assumes patients, who present with respiratory symptoms suggestive of pneumonia in outpatient settings for all levels of health centers, are given antibiotics.

In this scenario (and the following ones), I will first present all the results from the model simulation including decision tree structures followed by cost calculation tables and sensitivity analysis graphs, then discuss the presented results as a whole. In this section, the decision tree starts with a patient presenting at a clinic with symptoms suggestive of pneumonia. They then face
a decision node signified by a square which branches into two strategies the Status Quo and the POC Strategy. When a patients makes a choice and enters a strategy they will face a series of chance nodes signified by circles, detailing the events within each strategy. Those who chose to enter the Status Quo will face a probability of having pneumonia or not (D+ or D-). Of those who have pneumonia, they will be either diagnosed or misdiagnosed and given antibiotic according to the sensitivity and specificity of the doctors. For each of the above two events, the antibiotic may work and the pneumonia is cured or the antibiotic may not work and the patient return for further treatment. When the patient undergoes all the events and arrive at the terminal node signified by triangles, he/she will face a cost and mortality rate associated with a particular pathway. With the structure of the decision tree laying out all the pathways a patients can travel through, the software is able to calculate an expected cost/mortality for each strategy based on the transition probabilities between each events within different pathways. Finally, by comparing the cost and mortality outputs, the software determines which strategy is dominant over the other. Due to limitation of the software, in all sensitivity analysis graphs, the mortality is designated as the effect which is shown on the y-axes.
**Figure 4.3.1:** Structure of the decision tree for the protocol of treating pneumonia in Scenario 1.
Figure 4.3.2: Structure of the decision tree for Scenario 1 with payoffs and expected outcomes. The dominant strategy is pointed by an arrow and the dominated strategy is crossed out.
Table 4.3.1: Cost savings for a primary health center according to Scenario 1 assumptions and $2 additional charge for having the test.

<table>
<thead>
<tr>
<th>Cost Saved per Patient</th>
<th>$1.41</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patient per Month</td>
<td>25 people</td>
</tr>
<tr>
<td>Cost Saved per Day</td>
<td>$35.25</td>
</tr>
<tr>
<td>Cost Saved per Year</td>
<td>$10575</td>
</tr>
</tbody>
</table>

Table 4.3.2: Cost calculation for each terminal nodes in Scenario 1.

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost (U$)</th>
<th>Calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Status Quo</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics and Recover</td>
<td>15</td>
<td>10+5</td>
</tr>
<tr>
<td>Antibiotics and Further Treatment</td>
<td>65</td>
<td>10+10+5+40</td>
</tr>
<tr>
<td><strong>POC Diagnostic at PHC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics and Recover</td>
<td>22</td>
<td>10+5+5+2</td>
</tr>
<tr>
<td>Antibiotics and Further Treatment</td>
<td>72</td>
<td>10+10+5+5+2+40</td>
</tr>
<tr>
<td>No antibiotics and Recover</td>
<td>17</td>
<td>10+5+2</td>
</tr>
<tr>
<td>No antibiotics and Further Treatment</td>
<td>67</td>
<td>10+10+5+2+40</td>
</tr>
</tbody>
</table>

Figure 4.3.3: Expected cost saving when the cost of antibiotics varies in the range of $1-5, assuming additional cost of testing is $2.
**Figure 4.3.4**: Sensitivity analysis on the sensitivity (true positive value) of the device.

**Figure 4.3.5**: Sensitivity analysis of prevalence rate of pneumonia on cost.
4.3.1 Result Analysis and Recommendation for Scenario 1

Although the assumption of providing all patients antibiotics seems unrealistic, it is a practice that still prevails in many developing countries such as India and China (Yang et al., 1993). In some rural areas, this practice has become a tradition which is passed on to new generations of doctors and patients, fostering the inappropriate use of antibiotics.

In this scenario, when antibiotics are valued at $5 per dose and the additional cost of having the device is at $2, the Status Quo always has higher cost compared to the POC strategy. However, as the price of the device is increased, the cost saving of employing the device diminishes. Net cost saving declines when the cost of the device rises. The net saving reaches 0 (breakeven point) when the additional cost for the device is approximately $3.50 per antibiotic dose. At this point, there will not be any financial benefit associated with the device. Sensitivity analyses were performed on all variables in the model. Cost is not sensitive to most of the variables except pPos which is the prevalence of pneumonia. Sensitivity for pPos was performed at a range of 0-0.2 within which the cost of the POC strategy is approaching but not reaching that of the Status Quo, leaving the POC diagnostic at a cost disadvantage.

Results also show the POC diagnostic strategy has higher mortality across all sensitivity studies. Only when the sensitivity of the diagnostic is 1, meaning the test can perfectly distinguish patients who have the disease from those who do not, can the mortality for the POC strategy be the same
as that for the Status Quo. These two observations were consistent for all variables on which a sensitivity analysis was performed.

Total potential saving for a clinic was calculated for this scenario with assumed costs (Table 4.3.1). The number of patients was calculated from data collected on site. It was observed that in 3 hours, there were 25 children who entered the center and 17 of them had symptoms of pneumonia. According to these data, we estimated that there are 50 symptom-presenting children coming to the center every day. Assuming half of the 50 patients will get pneumonia checkup and treatment, the cost saved per day by having the device is $35.25. Further, from what we learned in Nagpur, primary centers are open for 9 hours a day, 6 days a week and do not close for national holidays. Therefore, if we assume the center only closes on Sundays which means it is open 300 days a year, then the total annual saving on having the device will be $10,575. The saving seems substantial for a health center but it is subject to large variation as cost for antibiotics is different across areas.

The saving declines when the gap between the cost of antibiotic and the POC test becomes smaller. As can be seen from Figure 4.3.3, when the cost of antibiotics is set to be $3, there is only a slight saving per patient of $0.02. If we consider the antibiotic cost to be below $1, then implementing the device would incur a loss of $1.383 per patient. A sensitivity analysis was performed on the sensitivity of the device for the range from 0.7 to 1.0 with the new antibiotic cost below $1 inputted. Although the cost declines with increasing sensitivity of the device, at perfect diagnostic sensitivity
the cost of the POC strategy is still higher than the Status Quo.

Overall, when the Status Quo is to always give antibiotics, POC diagnostics can generate savings only if the cost of testing does not exceed the cost of antibiotics. Given that in most rural areas antibiotics are very cheap due to their lower quality, POC diagnostics are not recommended because of the associated financial burden. However, our assumption on the cost of the device may vary substantially depending on patient volume. Therefore, the diagnostic may still make economic sense when the volume of patients is high which reduces the cost of testing below that of the antibiotics.

4.4 Basic Case Complicated with Additional Variation of Prescription Pattern

Scenario 2: This scenario assumes that doctors give symptom-relieving drugs to patients whom they believe do not have pneumonia.
Figure 4.4.1: Structure of the decision tree for Scenario 2 with the possibility symptom-relieving drug can be prescribed in addition to antibiotics.
Figure 4.4.2: Sensitivity analysis of antibiotic prescribing rate on cost of both strategies.

Figure 4.4.3: Sensitivity analysis of antibiotic prescribing rate on mortality rate of both strategies.
Figure 4.4.4: Sensitivity analysis of True positive rate (pPTPR) of the diagnostic on the mortality rate of both strategies.

![Sensitivity Analysis](image)

Table 4.4.1: Cost calculation for each terminal nodes in Scenario 2. For returning patients, there is an additional cost for travelling ($10). For all terminal cost of the POC strategy, a cost of testing ($2) is added.

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost (U$)</th>
<th>Calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Status Quo</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics and Recover</td>
<td>15</td>
<td>10+5</td>
</tr>
<tr>
<td>Antibiotics and Further Treatment</td>
<td>65</td>
<td>10+10+5+40</td>
</tr>
<tr>
<td>Symptom-relieving and Recover</td>
<td>12</td>
<td>10+2</td>
</tr>
<tr>
<td>Symptom-relieving and Further Tx</td>
<td>62</td>
<td>10+10+40+2</td>
</tr>
<tr>
<td><strong>POCT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics and Recover</td>
<td>17</td>
<td>10+5+2</td>
</tr>
<tr>
<td>Antibiotics and Further Treatment</td>
<td>67</td>
<td>10+10+5+2+40</td>
</tr>
<tr>
<td>No antibiotics and Recover</td>
<td>12</td>
<td>10+2</td>
</tr>
<tr>
<td>No antibiotics and Further Treatment</td>
<td>62</td>
<td>10+10+2+40</td>
</tr>
</tbody>
</table>
4.4.1 Result Analysis and Recommendation for Scenario 2

Based on our observation at local hospitals, most of the time doctors prescribe antibiotics to patients believed to have pneumonia or to those who appear sicker than others. For those patients who the doctor believes do not have pneumonia, symptom-relieving drugs are provided. By adding this new prescription possibility into the model, the mortality of the Status Quo becomes higher than the previous “all-antibiotics” scenario. This result is due to the fact that now the doctors in the Status Quo can also miss cases through not providing antibiotics to those who have the disease. When the cost of testing is $2 and that of antibiotics is $5, the cost per patient for Status Quo and POC diagnostic strategy is $14.61 and $13.62 respectively. The mortality for the Status Quo is 0.04 and POC strategy is 0.05 which translates into 4 and 5 deaths per 10,000 cases. The outputs place the POC strategy in a more favorable position as it has a lower cost and only a slightly higher mortality than the Status Quo.

Sensitivity analyses were performed with all variables and two of them induced significant change of cost and mortality outputs. Doctors’ discretion on who to prescribe antibiotics and symptom-relieving drugs for is a major factor affecting both the cost and mortality. Because the cost and mortality associated with giving symptom-relieving drugs to falsely diagnosed pneumonia patients are much higher, the more inclined a doctor is to provide symptom-relieving drugs overall, the more likely a greater number of true cases are given the wrong treatment, resulting in both elevated cost and mortality. Especially when a doctor’s sensitivity and specificity are relatively low (i.e. the
assumed 0.4) in the Status Quo, more patients with pneumonia will be diagnosed to be otherwise compared to the POC Strategy in which the device is better at catching true cases with the higher sensitivity (i.e. 0.7). From Figure 4.4.2, it can be observed that the cost of the Status Quo continues to rise as the probability of prescribing antibiotics approaches 1. Since the POC strategy is associated with a lower cost overall and doctors in this strategy prescribe antibiotic according to the result of the device, the POC strategy is not affected by pDrug and maintains a cost advantage at all times. When more than half of the patients are given antibiotics as shown in Figure 4.4.3, the mortality of the Status Quo will be lower compared to the POC Strategy. This result follows a similar logic from the first scenario: as more antibiotics are prescribed, fewer patients with pneumonia will be given the wrong treatment due to misdiagnoses. This is as if scaling up antibiotic use were compensating for the lower sensitivity caused by the lack of diagnostics, which would lower the mortality rate of the Status Quo.

The variable pA, which is the probability that an antibiotic works, also has significant influence on the model outputs. If it is increased/decreased, then cost and mortality become lower/higher for both strategies. Since we consider antibiotics are very good at treating bacterial pneumonia (which may not always be true as discussed in Chapter 5), this variable is treated as a constant variable and therefore its sensitivity analysis is not discussed here.

The POC diagnostic lowers cost mainly by shifting the distribution of the patient from false
negative to true positive branches. By having a better sensitivity, the device is able to detect from a population more patients with pneumonia, who are otherwise falsely diagnosed in the Status Quo. This results in more patients receiving the right treatment and thus fewer needing to return for further treatment which is costly. Saving is also derived from the true negative branch where patients are not given antibiotics but only symptom-relieving drugs or no treatment at all, both of which are cheaper. Savings of drug cost is secondary and varies based on the cost difference between antibiotics and the test. Indeed, if the cost of antibiotics is reduced to below $1, the cost per patient will be $0.19 higher. This is similar to Scenario 1 but the loss is at a smaller magnitude due to the additional effect of the diagnostic in shifting patient distribution.

The POC strategy can also make mistakes through giving all patients with false negative results symptom-relieving drugs. However, from the result that the mortality difference has become much smaller, it can be seen that the mistakes doctors make without the diagnostic in the Status Quo is contributing to a significant portion of the mortality. Furthermore, even with the assumed parameters, the mortality of the POC strategy is still slightly higher. The mortality rate can be lowered if the sensitivity of the device can be improved. As shown in Figure 4.4.4, unlike in the previous case where only a perfect test can match the mortality rate of the Status Quo, in this scenario, a slight increase in sensitivity from 0.7 to 0.76 will result in the POC strategy having a lower mortality rate. This finding makes the POC device very promising in solving the existing pneumonia problem cost-effectively and making the slight increase in cost justifiable.
Overall, the POC strategy can generate savings if doctors follow the test results from the diagnostic. Even though the cost of antibiotic could be lower, the cost of testing could also be much lower with a higher patient volume, making it very likely for POC diagnostics to achieve a cost advantage. In addition, with slightly better test characteristics, the POC strategy can achieve lower mortality than the Status Quo. Therefore, the diagnostic is very promising in this situation to potentially lower both the cost and mortality of treating a patient with pneumonia.

4.5 Modelling the POC Diagnostic and Transportation to Urban Hospitals

Scenario 3: This scenario builds on the decision tree structure of Scenario 2 with an additional possibility of transportation to urban hospitals. It is assumed that when patients present at any outpatient clinics and are critically ill, they will be transported by ambulance to a more sophisticated urban facility for treatment.
Figure 4.5.1: Structure of the decision tree form Scenario 2 with the additional possibility of transporting critically ill patient directly to a more sophisticated urban hospital for treatment.
Patients entering with symptom

\[
p_A = 0.9 \\
p_{\text{Drug}} = 0.1 \\
p_{\text{POCdirect}} = 0.1 \\
p_{\text{PTNR}} = 0.7 \\
p_{\text{PTPR}} = 0.7 \\
p_{\text{Pos}} = 0.006 \\
p_{\text{SQPos}} = 0.006 \\
p_{\text{SQTNR}} = 0.4 \\
p_{\text{SQTPR}} = 0.4 \\
p_{\text{SQdirect}} = 0.1
\]

Rural Hospitals With POC Diagnostics

D +

pPos

False Negative and send home with symptoms relieving drugs

True Positive

pPTPR

Not referred

Send home with Antibiotics

Deemed very serious and transported

\[
p_{\text{POCdirect}}
\]

False Positive and send home with antibiotics

Deemed Severe and transported

pPOCdirect

Antibiotics and Send home

pPTNR

Patients Return and further treatment

True negative and send home without treatment

\[
p_{\text{POCdirect}}
\]
Figure 4.5.2: Sensitivity analysis of the percentage of patient transported (pSQdirect) on the mortality rate of both strategies.

4.5.1 Result Analysis and Recommendation for Scenario 3

The healthcare facilities in rural India are often limited by resources and therefore lack necessary equipment and health workers capable of treating severe pneumonia cases. During our visit, we were told that most urgent cases are directly transported to district or urban hospitals, both far away from rural areas. Since an ambulance can be very expensive in India, it is useful to evaluate if the diagnostic can generate savings by reducing the volume of patients being transported.

With the assumed parameters introduced in Section 4.2, I build upon Scenario 2 by adding another
option for patients with positive diagnostic test results. Now when patients have a positive test result, they can either be transported to an urban hospital or remain in the rural hospital for care. Cost of transportation is assumed to be $40 since acquiring an ambulance is very expensive compared to other types of services in the hospital. The tree structure implicitly assumed an ambulance is always available if needed, which may not be true in some areas.

When both variables, pSQdirect and pPOCdirect, which dictate the portion of patients being transported in both strategies, are set to be the same, the preferred strategy is the POC strategy which is similar to Scenario 2 but with an overall higher cost and mortality associated with the transportation branch. As the percentage of transported cases increases for one strategy, its cost also increases significantly (Figure 4.5.2). This high sensitivity suggests that if a small number of patients, who would be deemed critical and transported, can remain at local hospitals for treatment with the existence of the POC diagnostic, the cost can be reduced significantly.

From the above analysis, it can be seen that the special feature of a POC diagnostic to offer information on the severity of the disease presents another way that could more dramatically impact this transportation scenario. Currently, image based POC diagnostics are believed capable of producing such information. Provided that the diagnostic can distinguish patients whose condition is suitable for treatment at local hospitals, it is recommended to avoid the costly long-distance transportation of less urgent patients to urban hospitals.
4.6 Modeling the Secondary Facility: Device vs. X-ray

Scenario 4 & 5: Both scenarios focus on secondary facilities where X-ray is available. The effect of using it in combination with the POC diagnostics is evaluated.

Additional assumptions for scenario 4 and 5:

- We assume in resource limiting environment X-ray is the gold standard of diagnosing pneumonia as it provides the most reliable information for the diagnosis of PNA, meaning there is no false positives or false negatives;
- We assume X-ray may not be available due to breakdown or doctor’s reluctance to order

Dual diagnostics has been a popular algorithm in for testing many diseases. For example, the use of HIV rapid test followed by a more advanced testing method to confirm the results has been studied and shown to improve the lower sensitivity and specificity of the first test (Klarkowski et. al. 2009). The dual arrangement is also valuable in saving health resources as the rapid test applied first is considerably cheaper than a more sophisticated diagnostic or full-blown laboratory test. With the stressed health system due to the high demand of service, the benefit of dual diagnostics is more pronounced in India because the rapid test could potentially ameliorate the prolonged waiting time until a patient can be treated. With all the above reasons, we construct a model to evaluate the effect of dual arrangement on the management of pneumonia in the context of India.
The amount of modeling complexity increases substantially when the device is implemented at two levels simultaneously due to the multiple rounds of decision making which soon expands the decision tree to an unmanageable size. Therefore, the secondary level is modeled in its own without distinguishing patient populations between those from PHCs and those referred by themselves.

Using methods of evaluating dual diagnostics suggested by Pooran et al. (2010), a decision tree is constructed with the POC diagnostic applied on patients before the X-ray. Prior probabilities (i.e. what percentage of patients will have positive/negative result) of both the POC diagnostic and X-ray were calculated based on prevalence rate, sensitivity and specificity of the test using the Bayes’ formula shown in assumption 10 of Section 2.3. For simplicity, I have combined the two scenarios in one tree. The tree has three strategies: the Status Quo (X-ray only strategy), the X-ray after positive POC diagnostic result strategy (Positive Strategy hereafter) and X-ray after negative POC diagnostic result strategy (Negative Strategy hereafter). In the Status Quo, all patients are diagnosed with X-ray when it is available. If not available, the doctor will make the decision to treat at his discretion, which has a lower accuracy. In the Positive Strategy, if the rapid diagnostic gives a positive result, then X-ray is applied to confirm the case. In contrast, for the Negative Strategy, the pattern is reversed with X-ray applied to confirm negative cases.
Figure 4.6.1: Decision tree structure for dual diagnostic application and X-ray breakdown analysis

Status Quo (X-ray Only):

- **D+**
  - **pSR**
    - Send Back with Antibiotics
    - 
    - Send Back Home with Symptom Relieving Drugs
  - **D**
    - 
    - Send Back Home with Symptom Relieving Drugs

- **D**
  - **pDOC**
    - Send Back Home with Symptom Relieving Drugs
  - **pBreak**
    - Patients return and get hospitalized
      - **pNH**
        - Patient return and get antibiotics and send home
Confirming Positive Diagnostics Result by X-ray:

- **X-ray available**
  - **Device +**
    - **pDP**
      - **pDP**
        - **X-ray + / Device +**
          - **Hospitalized**
            - **pH**
              - **Send Back with Antibiotics**
                - **#**
        - **pXP**
          - **True negative and send home with symptom relieving drugs**
    - **Device -**
      - **#**
  - **pDNPV**
    - **Patients return and get hospitalized**
      - **pNH**
        - **Patient return and get antibiotics and send home**
  - **False Negative (1-NPV) send home with symptom relieving drugs**

- **X-ray after POCT positive result at Secondary**
  - **Device +**
    - **pDP**
      - **pDP**
        - **True Positive (PPV)**
          - **Hospitalized**
            - **pH**
              - **Send Back with Antibiotics**
                - **#**
      - **False Positive (1-PPV)**
        - **#**
    - **Device -**
      - **#**
  - **False Negative (1-NPV) send home with symptom relieving drugs**
    - **pDNPV**
      - **Patients return and get hospitalized**
        - **pNH**
          - **Patient return and get antibiotics and send home**

- **X-ray break down**
  - **pBreak**
    - **Device +**
      - **pDP**
        - **Device +**
          - **pDP**
            - **X-ray + / Device +**
              - **Hospitalized**
                - **pH**
                  - **Send Back with Antibiotics**
                    - **#**
            - **pXP**
              - **True negative and send home with symptom relieving drugs**
        - **Device -**
          - **#**
    - **Device -**
      - **#**
  - **False Negative (1-NPV) send home with symptom relieving drugs**
    - **pDNPV**
      - **Patients return and get hospitalized**
        - **pNH**
          - **Patient return and get antibiotics and send home**

- **True negative (NPV) and send home with symptom relieving drugs**

- **pDNPV**
  - **Patients return and get hospitalized**
    - **pNH**
      - **Patient return and get antibiotics and send home**
Confirming Negative Diagnostics Result by X-ray:

- X-ray available
  - Device +
    - False Positive (1-PPV)
      - Hospitalized
        - pH
        - Send Back with Antibiotics
  - Device -
    - X-ray + / Device -
      - Hospitalized
      - pH
      - Send Back with Antibiotics
    - X-ray - / Device -
      - True negative / device - and send home with symptom relieving drugs

- X-ray after POCT
  - Negative result at Secondary
    - Device +
      - True Positive (PPV)
        - Hospitalized
        - pH
        - Send Back with Antibiotics
      - False Positive (1-PPV)
        - Hospitalized
        - pH
        - Send Back with Antibiotics
    - Device -
      - True negative (NPV) and send home with symptom relieving drugs
        - pDNPV
        - False Negative (1-NPV) send home with symptom relieving drugs
          - pNH
            - Patients return and get hospitalized
            - Patient return and get antibiotics and send home

- X-ray broken
  - pBreak
Table 4.6.1: Transition probabilities, and mortality rate of Scenario 5.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Base Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence (pSR)</td>
<td>0.006</td>
<td>Kotwani and Holloway</td>
</tr>
<tr>
<td>Hospitalized at Secondary (pH)</td>
<td>0.5</td>
<td>Assumed</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.0013</td>
<td>Rudan I. et al.</td>
</tr>
<tr>
<td>Mortality Given Antibiotics</td>
<td>0.0005</td>
<td>Assumed</td>
</tr>
<tr>
<td>Mortality at Secondary</td>
<td>0.010</td>
<td>Assumed</td>
</tr>
<tr>
<td>Mortality of Returning Patients</td>
<td>0.018</td>
<td>Assumed</td>
</tr>
<tr>
<td>Sensitivity of Doctor (pDOC)</td>
<td>0.4</td>
<td>Assumed</td>
</tr>
<tr>
<td>Sensitivity of Device</td>
<td>0.7</td>
<td>Assumed</td>
</tr>
<tr>
<td>Specificity of Device</td>
<td>0.7</td>
<td>Assumed</td>
</tr>
<tr>
<td>Specificity of X-ray</td>
<td>0.85</td>
<td>Assumed</td>
</tr>
<tr>
<td>Specificity of X-ray</td>
<td>0.85</td>
<td>Assumed</td>
</tr>
<tr>
<td>Device Gives Positive (pDP)</td>
<td>0.3024</td>
<td>Calculated</td>
</tr>
<tr>
<td>Device Negative Predicted Value (pDNPV)</td>
<td>0.9974</td>
<td>Calculated</td>
</tr>
<tr>
<td>Device Positive Predicted Value (pDPPV)</td>
<td>0.01235</td>
<td>Calculated</td>
</tr>
</tbody>
</table>

Table 4.6.2: Costs data used for Scenario 5.

<table>
<thead>
<tr>
<th>Cost</th>
<th>Value (U$)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics</td>
<td>5</td>
<td>Assumed</td>
</tr>
<tr>
<td>Symptom-relieving Drugs</td>
<td>2</td>
<td>Assumed</td>
</tr>
<tr>
<td>X-Ray cost</td>
<td>7</td>
<td>Madsen et al.</td>
</tr>
<tr>
<td>Supportive Care</td>
<td>6</td>
<td>Madsen et al.</td>
</tr>
<tr>
<td>Cost of Visit Secondary</td>
<td>30</td>
<td>Assumed</td>
</tr>
<tr>
<td>Device Cost/Visit</td>
<td>2</td>
<td>Assumed</td>
</tr>
<tr>
<td>Hospitalization at Secondary</td>
<td>125.2</td>
<td>Madsen et al.</td>
</tr>
</tbody>
</table>
**Table 4.6.3:** Cost calculations for all terminal nodes in Scenario 5.

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost (US$)</th>
<th>Calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Status Quo (X-ray)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalized at Secondary</td>
<td>125.2</td>
<td>125.2*</td>
</tr>
<tr>
<td>Send Home with Antibiotics</td>
<td>48</td>
<td>30+5+7+6</td>
</tr>
<tr>
<td>Send Home with Symptom Rx</td>
<td>45</td>
<td>30+2+7+6</td>
</tr>
<tr>
<td>POCT at Secondary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D+ T+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalized at Secondary</td>
<td>139.2</td>
<td>125.2+2+10+2</td>
</tr>
<tr>
<td>Send Home with Antibiotics</td>
<td>46</td>
<td>30+5+3+6+2</td>
</tr>
<tr>
<td>D+ T-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalized at Secondary</td>
<td>125.2</td>
<td>125.2</td>
</tr>
<tr>
<td>Send Home with Antibiotics</td>
<td>49</td>
<td>30+5+3+6+5</td>
</tr>
<tr>
<td>Send Home with Symptom Rx</td>
<td>41</td>
<td>30+2+3+6</td>
</tr>
<tr>
<td>D- T-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Send Home with Symptom Rx</td>
<td>43</td>
<td>30+2+3+6+2</td>
</tr>
<tr>
<td>D- T+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalized at Secondary</td>
<td>125.2</td>
<td>125.2</td>
</tr>
<tr>
<td>Send Home with Antibiotics</td>
<td>49</td>
<td>30+5+3+6+5</td>
</tr>
</tbody>
</table>

*125.2 is an aggregate cost at secondary hospital cited from Madsen et al. including the cost of transportation, X-ray, supportive cost and therefore no other costs were added to this value.

### 4.6.1 Dual Diagnostics Combining POC Diagnostics and X-ray

Because of the lack of resources in India, the use of X-ray has been very limited due to the high cost of the test and the maintenance. POC diagnostics on the other hand are considerably cheaper and offer a significant cost advantage. In response to the resource-poor condition, we hypothesized that by employing a dual diagnostic arrangement combining POC diagnostics and X-ray, health outcomes could be improved at a lower cost. Motivated by the hypothesis, I evaluate the effect of cost and mortality of the dual diagnostic arrangement when X-ray is only applied to confirm either...
positive or negative cases from a POC test.

For this section, we set the pBreak to be 0 and compare only the X-ray available branches of each strategy to evaluate the effect of dual arrangements. The Status Quo has the lowest cost and mortality because X-ray is assumed to be a perfect test and therefore there are no returning patients due to misdiagnoses. Both dual diagnostic strategies are shown to have a higher cost and mortality compared to the Status Quo. The elevated cost and mortality are inevitable as the diagnostics has less diagnostic power than the X-ray.

The cost/mortality outputs for Positive and Negative strategies are 46.26/0.26 and 62.28/0.16 respectively. It can be seen that confirming the positive cases resulted in a lower cost and higher mortality compared to confirming the negative cases. The increase in cost stems mostly from those who are falsely diagnosed to be positive and either hospitalized or given treatment. This can be observed from the expected cost of treating false positives in the Negative Strategy and the equivalent branch in the Positive Strategy (86.6 vs 49.0). Given a very low prevalence rate, the false positive rate is high with the assumed sensitivity and specificity. This also contributes to the higher false positive rate of the Negative Strategy. On the other hand, the Negative Strategy enjoys a lower mortality because false negative cases missed in the Positive Strategy are detected by X-ray. Therefore the higher mortality associated with delayed treatment is avoided.
The analysis of this scenario suggests that if dual diagnostics are pursued in light of limited capacity for X-ray, confirming positive cases will achieve a cost advantage while confirming negative cases will achieve a lower mortality. Cost savings of the dual diagnostic arrangement purely depend on the cost difference between the diagnostics and X-ray. If the cost of POC testing can be significant lower than X-ray, there is a potential to reduce overall cost. However, from our observation, many local facilities need to expand their working staff and space for the diagnostics to fully function. Therefore cost saving may not be a good argument for the dual arrangement. In the context of resource-poor settings, the fact that the Negative Strategy will result in a substantial higher cost makes this strategy less favorable, if viable at all, even with the decreased mortality.

4.6.2 POC Diagnostics When X-ray is Not Available

Many medical professionals rely on chest X-ray to confirm pneumonia (Bahl and Bahn, 1994). However, in resource-poor countries where high demand of healthcare is not met by the supply, it is simply not feasible for the doctor to order X-ray for every patient who deserves it. In addition to the limited capacity to offer X-ray to patients in need, we observed that in many facilities the X-ray is frequently broken down due to the lack of maintenance. Therefore, when X-ray is not available to patients, the POC diagnostics may offer a way to improve diagnosis accuracy and lower mortality. In this section, I evaluate when the existence of POC diagnostic as an alternative to X-ray could be beneficial by varying the value of pBreak, probability of X-ray being unavailable, which was set to 0 in the last section.
Figure 4.6.2: Sensitivity analysis of pBreak (probability of X-ray being unavailable) on mortality for the Positive Strategy.

Figure 4.6.3: Sensitivity analysis of pBreak (probability of X-ray being unavailable) on cost for the Positive Strategy.
Figure 4.6.4: Sensitivity analysis of $p_{\text{break}}$ (probability of X-ray being unavailable) on mortality for the Negative Strategy.

Sensitivity Analysis

Figure 4.6.5: Sensitivity analysis of $p_{\text{break}}$ (probability of X-ray being unavailable) on cost for the Negative Strategy.
A sensitivity analysis was performed on pBreak to decide the rate at which X-ray must be unavailable before the POC diagnostic can achieve lower cost and mortality compared to when X-ray is the sole diagnostic. From Figure 4.6.3 and Figure 4.6.5, it can be seen that the cost of Status Quo rises at a much faster rate than that of both the Positive and Negative Strategy. The Positive Strategy and Negative Strategy starts to show cost advantage when 12.8% and 28.5% of X-ray are unavailable respectively. This is mainly because as X-rays become unavailable in the Status Quo, the doctors are making all the diagnosis without the aid of any equipment, resulting in significantly reduced accuracy. However, when both POC diagnostics and X-ray exist, doctors are still left with the POC diagnostic which offers better sensitivity and specificity than his or her own judgment. As a result, the number of patients who receive the wrong treatment will grow at a faster rate in the Status Quo than in the Positive Strategy as X-ray become less available.

There is also a point at which the mortality of the Status Quo surpasses that of the Positive Strategy. When 32.8% of X-ray equipment become unavailable, the Positive Strategy achieves a lower mortality because fewer patients are sent home without treatment when they actually have the disease (Figure 4.6.2). Those who return for further treatment are tagged with a higher mortality as they have missed an early intervention and the disease has progressed. The low return rate of patients is what drives the lower mortality of the POC diagnostics strategy.

Given the low mortality of the Negative Strategy associated with missing fewer false negatives
mentioned in the last section, it can be seen in Figure 4.6.4 that the Status Quo quickly loses its advantage in terms of mortality as doctors start to make diagnosis on themselves without the support of any diagnostics. With the assumed high mortality rate of those with PNA who are misdiagnosed, the Negative Strategy trumps the Status Quo with lower mortality beyond the X-ray breakdown rate of 1.2%.

The results from this scenario suggest that the POC diagnostic is a worthwhile investment at places where X-ray is frequently not available to patient due to either equipment breakdown or doctors’ reluctance to order the test. Even though the addition of the POC diagnostic will be more costly as indicated by previous scenarios, the savings derived from downstream treatment can be substantial, making the diagnostic potentially favorable.

5. Shaping the Policy: Policymaking in Light of Findings

The last chapter detailed the analysis of several key implementation strategies of POC diagnostics in resource-poor environments. In particular, I evaluated the scenarios focusing on four broad issues:

- Antibiotic use and resistance
- Cost of pneumonia treatment
- Mortality of pneumonia in infants
- Effective resource allocation
In designing policies, policymakers need deeper insights into the barriers of scaling up a POC diagnostic, the necessary characteristics for such a diagnostic to generate health impact and effective allocation of resources for its implementation. In this chapter, I summarize the findings from previous analyses and then discuss the recommendations with an eye toward policymaking in an attempt to address the above issues. At the end, whether POC diagnostics are worthwhile and under what conditions are described in light of all the discussion.

5.1 Summary of Findings and Recommendations from Policy Simulation

Scenario 1: When all patients are prescribed antibiotics, the POC diagnostic is not recommended as it cannot lower either cost or mortality.

Scenario 2: When doctors prescribe antibiotics and sometimes symptom-relieving drugs, the diagnostics can become an attractive method to lower mortality. The POC diagnostic helps to identify which patient’s illness would not benefit from antibiotics, because viral agents don’t respond to antibiotics. Therefore, with the more accurate diagnosis that comes with the diagnostic, more patients would receive the proper treatment. However, whether the diagnostic has a cost advantage depends on the cost of antibiotics and the probability that doctors provide symptom-relieving drugs.
**Scenario 3:** POC diagnostics which provide severity information on target diseases can be employed in rural health centers and facilitate proper treatment onsite to avoid transportation to urban hospitals, therefore generating savings.

**Scenario 4:** This scenario showed that confirming positive cases can result in a moderate improvement in mortality with a limited rise in cost and confirming the negative cases can result in a substantial improvement in mortality with a significant rise in cost. Therefore, when a dual diagnostic arrangement is employed, limited X-ray should be applied to confirm positive cases in the presence of significant budget limits. Otherwise, negatives cases should be confirmed by X-ray to achieve a greater improvement in mortality rate.

**Scenario 5:** If X-ray is not available due to the high patient volume or equipment breakdown, compared to when X-ray is the only diagnostic to aid the diagnosis, the existence of POC diagnostics as an alternative can achieve superior health outcome and cost advantage when the percentage of X-ray breakdown reaches 12.8%.

**5.2 Policy Implications for Antibiotic Use and Resistance**

As mentioned in Section 1.3, both antibiotic misuse and resistance continue to escalate in many developing countries and present a major risk to public health, especially in India (Figure 5.2.1). Policymakers have put forward policies to promote the quality of antibiotics as well as “evidence-
based” practice of medical professionals to ameliorate the issue. New technologies such as the POC diagnostics can become another policy lever to ensure more effective use of antibiotics. Both the Ministry of Health and Family Welfare in India and the CDC in the US have recommended the use of advanced diagnostics to promote evidence-based medicine (EBM) as a strategy to control antibiotic resistance. In most developed countries, EBM is the main approach for clinicians to make medical decisions in providing patient care. The key element of this approach is the emphasis on acquiring clinical evidence to reach a diagnosis before giving therapies to treat. In India and other developing countries, such practice is not well-developed, which is contributing to the abuse of antibiotics and the rising resistance. POC diagnostics with superior test characteristics clearly have the ability to offer better clinical evidence and improve the accuracy of diagnosis in most developing countries. Therefore, if physicians are able to follow the guidance of the diagnostic in making prescription decisions, there will be fewer wrongly prescribed antibiotics, thus slowing down the growing antibiotic resistance. The correcting effect of the diagnostics on antibiotic misuse will be most profound in rural areas where physicians have limited equipment to aid their diagnoses. In situations where the prescription pattern of antibiotics is highly irrational, policymakers can also mandate the use of POC diagnostics and full compliance to limit antibiotic misuse.
Figure 5.2.1 Unit of different types of antibiotics sold in India from 2005 to 2009 (Bharuch, 2009).

Given the positive effect of the diagnostic on antibiotic use, there are nevertheless many cultural challenges that hinder the effort to reduce antibiotic resistance. For example, doctors’ habit of prescribing antibiotics to any patient with a fever has become deeply rooted. While it is partially because they are concerned that the patient will not return for follow up, the behavior is also the manifestation of a complex systematic problem which involves factors including but not limited to non-optimal regulations, poorly-designed financial incentives and ineffective stimulation for innovation, all of which are hard to change and require a multifaceted approach to improve. Further, this habit is reinforced by the patients’ expectation to be given antibiotic or any type of drug during
a doctor’s visit for which they need to wait for hours. Without a permanent change in the prescribing behavior of the professionals and in the mindset of the patients, the diagnostic by itself can never solve the problem of antibiotic misuse. Therefore, policies promoting education of health professionals and patients about antibiotic use and resistance are required to complement the implementation of advanced diagnostics. Besides the cultural issue, the poor selection of available antibiotics, which is responsible for patients not receiving the right drugs, is also one of the key drivers of antibiotic resistance. From our observation in India, many health workers continue to provide the wrong antibiotics which are ineffective against the causative organisms. Insufficient supply of antibiotics which target the disease-causing bacteria not only contributes to greater morbidity and mortality but also generates higher downstream costs of care. Therefore, policies should be designed to improve the supply chain of quality antibiotics which target prevalent bacterial strains to preserve the power of other antibiotics. When such policies go along with the new diagnostics, the increase in treatment efficiency will also lead to less antibiotic use, limiting the spread of antibiotic resistance.

While antibiotic resistance may be a secondary issue in the eyes of governments as their top priority is to combat the high death rate of PNA, the issue is of great importance and could influence strongly the view of NGOs and potential donors. As NGOs and donors nowadays play a key role in delivering novel technologies to poor countries, the issue of antibiotic resistance should be emphasized by policymakers in developing countries in order to gather a wider support for the
adoption of POC diagnostics in their respective countries.

5.3 Impact of the POC Diagnostic on Cost of Pneumonia Treatment

Introducing a new POC diagnostic will likely add a cost burden to the health care system based on the analyses in this study. In general, cost savings can only be achieved if the cost of antibiotics is expensive (~$3 or more) which is not the situation in most rural areas. Cost savings from shifting patient distribution to avoid returning patients are also marginal and can be easily offset by the additional cost of expanding the limited capacity and the reduced patient throughput to accommodate the diagnostic.

From our observations in India, the current demand for healthcare service far exceeds the supply, especially in rural areas. This large demand has caused each patient visit to be very short in order to accommodate more people waiting in the line. With cheaper services and lower out-of-pocket payment, a doctor visit in the public system is even more time-constrained relative to the private system due to higher volume. Public hospitals in rural India typically host one four-hour session per day. For each of the sessions, 80 to 100 patients are seen by one doctor, averaging less than 3 minutes per patient. Patients are rarely asked about their past medical history and discussion with the doctors about their condition is minimal. Patients with a fever are generally given a course of antibiotics with limited diagnostic assessment being performed. The length of a patient visit is not much longer even in the private clinics which have eight-hour sessions and see the same number
of patients as public hospitals per day (Based on our visit to India). Under such a condition, in order for the POC diagnostic to generate health impacts, it will require significant changes in the structure of practice by which patients are seen. Potential change could be extending the time of each patient visit, hiring additional health professionals or treating fewer patients per session. Even if implemented without the suggested changes to the existing system, the POC diagnostic could inevitably increase the cost burden of the healthcare system as applying the diagnostic introduces an additional cost to all suspected cases. Therefore, when considering implementing such a device, policymakers need to take into account the cost associated with the accompanied changes that would have to be made before the diagnostic can realize its potential.

Another potential way a POC diagnostic can generate savings is to substitute for X-ray use. This idea has been proven not viable as our experience revealed that practitioners in outpatient clinics in India rarely order X-ray for diagnosing pneumonia. It was also observed that X-ray equipment frequently breaks down due to poor maintenance. Therefore, employing POC diagnostics would largely represent an added cost instead of an offset of X-ray cost.

Nevertheless, the diagnostic can benefit the patients clinically if extra workers are employed to perform the test on patients before they are seen by the doctor. Although hiring new staff and occupying extra space will inevitably lead to a higher expense, the diagnostic may still be worthwhile as the cost savings from providing treatment to fewer patients without pneumonia may
offset the increase in expense. Further, incorporating such a triage process could ensure the most
critical cases be dealt with first. As a result, a prioritization mechanism is built into the system
which can help avoid potential downstream treatment cost associated with severe cases which is
often very high.

5.4 Trade-offs of Implementing POC Diagnostics: Cost vs. Mortality

Even with the most sophisticated engineering and science, POC diagnostics still suffer from lower
sensitivity and specificity due to technical and operational constraints, compared to, for example
X-ray, but higher sensitivity and specificity than the current manner of clinical diagnosis, based on
symptoms and signs. This results in a trade-off between accessibility and accuracy. In other words,
policymakers are forced to make a decision between maximizing the number of people in rural
areas who will begin the proper treatment and minimizing the number of patients who will not
receive proper treatment due to less accurate medical decisions. In areas where the existing
technology offers better test characteristics, policymakers should decide if benefits from broader
access outweigh the cost of wasted treatment and patient lives due to inaccurate diagnoses.

However, in this study the background is rural areas in developing countries where existing
diagnostic technology, if it exists at all, offers poorer accuracy compared to the POC diagnostics.
Therefore, by expanding patient access to more accurate decisions, the trade-off is effectively
avoided. Although this trade-off will not become an issue in most parts of India, when considering
implementation policies, policymakers should devote great attention to areas with diagnostic
capability similar to or above that of the new diagnostic under consideration.

At the individual diagnostic level, there is yet another trade-off between cost and mortality, which is crucial in designing implementation policies. As shown in the analysis, for many instances the POC diagnostic was able to reduce the mortality but led to an increase in cost (Scenario 2 and 4). Given the ultimate goal to treat patients more effectively and improve the health of the entire population, mortality should be prioritized over the cost. Therefore, in light of anticipated budgetary limits, policymakers should adjust their policy to allow for the greatest number of devices to be implemented in high prevalence areas, maximizing the number of patients treated to ameliorate the epidemic.

5.5 Externalities and Implications of the Diagnostics for Other Diseases

The study evaluates the effect of an innovative diagnostic on cost and mortality. However, on top of these measurable effects, there are positive externalities associated with the introduction of a new technology. Policymakers need to take into account these externalities as indirect costs or benefits are often significant enough to affect policy outcome. For example, when a doctor encounters a negative result suggested by the diagnostic, he or she will quickly act to examine the patient for other potential diseases such as malaria, which can also be fatal if not treated in time. These are termed "informational externalities" and have been examined in studies concerning new surgery procedures (Escarce, 1996). The study also suggests that if a government advisory panel
finds that a technology offers superior clinical benefit for one disease, it will likely revise the often-biased expectations for new technologies and turn doctors in favor of adopting technologies for other diseases. This generates momentum for introducing other novel technologies which may solve broader health issues. Such positive externalities associated with the POC diagnostics could potentially create a much greater health impact than the device itself.

However, new technologies also bring negative externalities. In particular, as discussed above doctors are likely to spend more time reaching a diagnosis with the new technology. This can in turn delay the treatment of other diseases not only from a single-patient perspective but also from a population level because patient throughput is reduced. In addition, health workers and physicians need to be trained to operate the technology and understand how it works. The extra time burden associated with the technology can be intolerable with the severe shortage of the health workforce in some of the rural areas.

5.6 Resource Allocation for Implementing Novel POC Diagnostics

With the greatest potential to improve the health care in rural areas, resources need to be carefully planned and allocated to ensure a well-functioning diagnostic. The aforementioned issues such as expanding the workforce and facility capacity to carry out the test will require substantial resource commitment. In addition, even with the highly portable design and the less stringent requirement for transportation environment, the distribution of POC diagnostics to the vastly scattered rural health centers can be costly.
Rather than focusing solely on the purchasing and transporting of the diagnostic itself, many complementary systems are equally important and deserve particular attention. In order for the diagnostic to reach its maximum value, it requires a supporting system and necessary infrastructures currently lacking in many resource-poor environments. For instance, due to lack of training for health professionals, the result of a thermal-camera-based POC diagnostic in the form of an image may need interpretation by an expert radiologist who is more likely to work in urban hospitals. This remote assistance service would only be possible if a reporting system of medical information between rural and urban hospitals exists. The system will also be critical in emergency situations where the doctor at the destination hospital needs the patient’s medical information to prepare and execute treatment in a timely manner. Such a reporting system heavily relies on the existing electrical and IT infrastructure which most developing countries lack. According to Gupta and Sathaye (2009), India’s 1 billion population is serviced by only five interconnected electricity grids, leading to a 17% shortage of supply in more than 20 of the 28 states. Many areas outside the coverage of the grid have either no electricity at all or limited accessibility, leaving a huge obstacle for building a reporting system. Resources should also be devoted to form a technical support team. Especially in poor environmental conditions such as high temperature and humidity, the diagnostics involving electrical components may have glitches or breakdowns. A remote or on-site technical support team needs to be in place when doctors encounter difficulties with the device, especially under emergency conditions.
Whether the diagnostics can improve health outcome is highly dependent on the infrastructure and support system which demand considerable resources to establish. Therefore, all of the above factors should be considered by policymakers in budget planning for implementing a new diagnostic.

5.7 When is a POC Diagnostic Worthwhile in Resource-Poor Countries?

This study represents the first attempt in exploring the implementation strategies of novel POC diagnostics for PNA within the complex tiered healthcare system structure of developing countries. From the analyses of policy scenarios, it can be seen that POC diagnostics are worthwhile in primary outpatient settings where doctors prescribe symptom-relieving drugs for patients who are believed not to have PNA and where transportation of urgent cases from rural to urban areas are frequent. The diagnostic could also be useful in secondary outpatient settings when employed in combination with X-ray or as an alternative diagnostic in the absence of X-ray.

While the scenarios highlight the impact of POC diagnostics at a micro-level, the models offer insights merely in terms of cost and mortality which did not capture the more complex issues of practical considerations, behavioral changes and social implications, not to mention the assumptions they are built upon. Practical considerations such as expanding capacity, establishing complementary supporting systems and meeting the budget are all critical in the efficient functioning of the diagnostic. Besides practical concerns which seem to be the biggest obstacle to
realizing the benefits of POC diagnostics, other considerations are in favor of its wide adoption. Positive behavioral changes such as improved doctors’ prescribing patterns and patients’ health seeking behavior are all beneficial for the disease diagnosis and treatment. The indirect social implications associated with the new diagnostic including the clinical benefits to other diseases’ diagnosis, improved attitude towards the adoption of other novel technologies and the moderating effect on antibiotic resistance also suggest POC diagnostics to be a worthwhile investment. Therefore, if practical issues are adequately addressed, POC diagnostics are well justified to be implemented with their positive health implications to the society.

Although findings are subject to substantial uncertainty, the current study suggests that, overall, the implementation of POC diagnostics could reduce the burden of PNA due to poor diagnosis and treatment. However, it depends on not only the accuracy of the device itself but also many factors within the healthcare system and the society as a whole. The ability of such novel diagnostics to reduce cost associated with PNA management is limited due to resources required to effectively integrate them into the clinical decision-making process. In order to design policies to achieve maximum impact of novel diagnostics, a clear understanding of the interaction between the diagnostic and various complex aspects of the healthcare system is essential and needs to be evaluated in future studies.
6. Future Directions of Studies on POC Diagnostics

This work represents an initial analysis of the impact of POC diagnostics in resource-poor countries such as India and others sharing the same tiered structure of public healthcare system. In addition to the aspects that the model did not capture mentioned in the limitations section, there are several additional factors that should be examined to address the issues with PNA. In developing countries, there are unique physical constraints and demographic characteristics which hamper the effective treatment of PNA. Some of these factors such as healthcare seeking behavior, pairing of new technologies, socioeconomic status and the private health sectors were not presented in this study but may play major roles in the deployment of POC diagnostics. Building on the initial framework and insights offered by this study, future studies should incorporate the following considerations.

6.1 Innovative Diagnostics and Healthcare Seeking Behavior

Reluctance to seek healthcare has contributed to the higher mortality rate of pneumonia in many developing countries (Luque et al., 2008). When the treatment is delayed, a mild cold or early stage PNA can progress quickly and eventually become fatal. A good-quality diagnosis leading to an effective downstream treatment plays a key role in stimulating care-seeking behavior when parents observe their children to be sick. Currently in Africa and India, more than 70% of pneumonia cases do not present initially to healthcare facilities (Luque et al., 2008). Most of the households only seek help at health centers after self-treatment which is ineffective and could
potentially worsen the child’s illness. The low rate of healthcare-seeking behavior is largely associated with the cost that patients have to bear when the care they receive in the end provides insignificant value (Amexo et al, 2004).

Researchers claim that parents can prevent these illnesses from developing into severe cases by treating the illness early on. In order to ensure this takes place, first and foremost parents needs to be educated to recognize symptoms of pneumonia and when to take action to seek medical care; but more importantly, health officials of the region need to improve the quality of diagnosis and treatment at local health centers to change the current negative perception of parents (Edmundson and Harris, 1989). In the future, having the POC diagnostic closer to rural villages could gradually change the healthcare seeking behavior of the rural population and encourage villagers to visit health centers more frequently. Such a behavioral change can generate significant impact on the mortality rate of PNA and should be incorporated into the analysis when it comes to determine the optimal strategy to introduce a POC diagnostic.

6.2 Pairing with Malaria Diagnostics

As noted in Section 4.6, the POC diagnostics for pneumonia have great implications for the diagnosis and treatment of other infectious diseases prevalent in developing countries. In this study, the application of dual diagnostics where the second diagnostics was traditional X-ray was evaluated and shown to be an effective means to increase treatment efficiency and lower cost. In
countries such as India, malaria is another major threat to the society and reducing mortality due to this disease has been an ongoing effort. Since malaria and pneumonia can share striking clinical similarities, particularly in children who cannot be expected to provide a useful medical history, making an accurate diagnosis to distinguish them can be difficult. Currently, there have been many studies examining the use of rapid diagnostics to diagnose malaria. Most studies claim the rate of misdiagnosis is high especially in the population with high pneumonia prevalence (Amexo et al., 2004). However, if both types of diagnostics are available, applying them simultaneously can potentially increase the probability of catching both diseases. The results from the current study warrant a further analysis of dual diagnostics of pneumonia and malaria in resource-poor environments.

6.3 Socioeconomics Factors and High Risk Areas

The prevalence of several risk factors in India has contributed to the higher incidence rate of pneumonia. Socioeconomic status (SES) plays a key role, for example, in determining care seeking behavior when parents observe their children to be sick. The term SES refers to the income level, educational background and type of occupation of the family members in a household. As most of the population residing in rural areas have low SES, their children are subject to higher risks when affected by PNA. Edmundson and Harris (1989) suggest that SES has a significant impact on morbidity and mortality of young children because low SES families are likely to be associated with malnutrition, poor housing and ventilation, and overcrowding, all of which increase the risk
of contracting infectious diseases. The demographic distribution of SES is important because it underlines the areas or the population at high risk of diseases such as PNA. By knowing the distribution of risk, we can direct more effort to policymaking focusing on these risk groups in order to improve their health status.

6.4 Implementation in the Private Sector

As mentioned earlier, the Indian healthcare system, as well as those of most other developing countries, are comprised of a public and a private component. This study did not consider the private sector because we did not visit enough private clinics to collect the data required for the analysis. However, the private sector serves a significant portion of the patients. A doctor at a PHC described the situation where if an M.D. refers 10 people, 6 will go to private clinics and 4 will go to public ones. Even though the number can vary widely as our sample size is limited, the significance of the private sector cannot be underestimated (Based on our interviews in India).

Earlier in this thesis, it was pointed out that in order to exploit the full potential of the POC diagnostic, there is likely a need for extra workers to be hired and extra space occupied. Given that the public hospitals are already functioning close to their maximum capacity, adoption of these technologies can be difficult regardless of their cost and mortality implications. On the other hand, private hospitals often own larger facilities and employ more medical staff. The existing conditions could facilitate the more rapid adoption of this technology in private health care settings. In
addition, the cost advantage of POC diagnostics can be even more pronounced if placed in these private clinics as the antibiotics and the service they provide cost up to three times more than ones dispensed in public clinics. Therefore, future studies should develop and evaluate implementation strategies in private clinics which can potentially make more economic sense.
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Appendix A: Interview Questions for Nagpur Satellite Clinics

CLINICAL CARE PATHWAY

Pneumonia

How do children usually appear when they come to your clinic?

When they appear in this way, what are their likely illnesses?

What other types of illnesses do children in this area have?

When children present with fever and high respiratory rates, what do you do to examine them?
What diagnostic tools do you have?

How often, roughly, are children that present with fever and difficulty breathing diagnosed with pneumonia?

How and how often is pneumonia diagnosed in your clinic?

When children are diagnosed with pneumonia, what happens to them next?

How long does the pneumonia usually last in children here?

How is mild/severe pneumonia normally treated at this stage?

Do many children die from pneumonia? How many?

Before arriving to this clinic, do children have any other form of health evaluation? Midwives? If midwives, how do they make diagnoses?

How often do children come here and never receive a diagnosis?

How long do children wait at this clinic to see a healthcare worker?

Is there a hierarchical pattern within the healthcare facility in Nagpur/India based on level of sophistication?

Are advanced facilities located mostly in the urban area? Are there any difficulties for patients to access these facilities?
Is it possible to refer a patient directly to the highest level of facility?

Are patients reluctant to travel to the referred hospital due to difficulties in access (i.e. lack of transportation)?

About what percentage of children have healthcare seeking behaviour once symptoms appear?

What do you think the greatest barrier to care in pneumonia/malaria is in your community?

If a hand-sized device was developed to diagnose pneumonia, do you think it would be helpful? At what level of the care pathway would it make the most difference? How would your treatment/care change if you had an accurate diagnostic tool?

**Malaria**

How is malaria diagnosed?

How frequently do you see malaria cases in children?

How is malaria treated?

Do you use rapid diagnostic tests? If not, why not?

How quickly can lab results be processed and returned to patients?

Do you have an idea for how accurate those results are?

How often do you think a diagnosis was mistakenly applied?

At what level in the health care pathway are anti-malarial drugs accessible?

What do you think would change if rapid diagnostic tests could be used at the ASHA level?

**COST**

How much do patients pay to visit this clinic?

How do you determine the cost for each visit?

What do pneumonia antibiotics cost?
What do anti-malarials cost?

Where does this clinic get funding?  How does it operate from the top/down?

What would a visit cost at this stage for a child with mild/severe pneumonia?

Does the price for this treatment vary significantly between satellite clinics?

Do any patients have insurance?

What sorts of claims do they normally make?

Do you have a billing system for patients?

How are medicines stored? How are they delivered to the clinics?

Has the cost of things changed much in the past 5/10 years?  How so?  How do you think it will change in the future?

What treatments are given regardless of a diagnosis?

Are there any vaccination programs implemented for pneumonia as preventative measure?

Has there been any studies on indirect costs for pneumonia patients? (i.e., travel, leisure forgone)

What are the potential indirect costs special to patients in Nagpur?

What are the costs for a healthcare provider at each level of hospitals?

MODEL

Out of a hundred patients, how many can be referred to different level of hospitals (i.e. how many positive can get referred, how many can actually reach the level of hospital they are referred)

If patients are diagnosed to be negative, out of 100, how many of them voluntarily seek medical treatment. (i.e. go to hospital themselves) This needs to be asked for each level and expected to be lower as the level of hospital gets higher due to financial reasons).
What are the false positive and false negative rate of diagnosis? (Out of 100 patients, how many having the disease is not diagnosed. How many do not have the diseases but are diagnosed.)

Out of 100 of patients, how many are able to get to the referred level of hospital and receive treatment?

Out of 100 patients, how many can be cured, or died at each point of care?

Out of the patients who are not referred, what are the survival and death rate?

What are the survival and death rate at each level of hospital?

What is the percentage of mild, moderate and advanced pneumonia in the patient population?

How many instances of pneumonia do you see in a given month? Year?