ABSTRACT

YAYLALI, EMINE. A Two-Agent Stochastic Alert Threshold Model for Identifying a Potential Disease Outbreak: A Case Study for H1N1. (Under the direction of Dr. Julie S. Ivy).

Influenza pandemics are considered one of the most significant and widely spread threats to public health. In this research, we explore the relationship between local and state health departments with respect to issuing alerts and responding to a potential disease outbreak such as H1N1. We modeled the public health system as a two-agent (or decentralized) partially observable Markov decision process where local and state health departments are decision makers. The model is used to determine when local and state decision makers should issue an alert or initiate mitigation actions such as vaccination in response to the existence of a H1N1 threat. The model incorporates the fact that health departments have imperfect information about the exact number of infected people. The objective of the model is to minimize both false alerts and late alerts while identifying the optimal timing for alerting decisions. Providing such a balance between false and late alerts has the potential to increase the credibility and efficiency of the public health system while improving immediate response and care in the event of a public health emergency. Using data from the 2009-2010 H1N1 influenza outbreak to estimate model parameters including observations and transition probabilities, computational results for near optimal solutions are obtained. In order to gain insight regarding the structure of optimal policies at the local and NC levels, various model parameters including false and late alerting costs are explored.
A Two-Agent Stochastic Alert Threshold Model for Identifying a Potential Disease Outbreak: A Case Study for H1N1

by
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DEDICATION

To my family for their support and love
Emine Yaylali was born on January 29, 1984. She grew up in a seaside city in Turkey. After graduating from high school specialized on science and mathematics, she continued her studies at Bogazici University, Turkey. She earned a Bachelor of Science degree on Industrial Engineering in 2007 and her interest on mathematical modeling led her to being a graduate student on Operations Research Program in North Carolina State University. She is currently working as a research assistant and her interests are sequential decision making under uncertainty with multiple decision makers and optimization for emergency preparedness and healthcare applications.
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CHAPTER 1

Introduction

1.1 Public Health Emergency Preparedness & Response

Recent events such as the 9/11 attacks, the anthrax attacks, the flu vaccine shortage of 2004-2005, the outbreaks of SARS and West Nile Virus, and the response to Hurricane Katrina have increased the concerns about public health infrastructure. These events highlighted the importance of emergency preparedness given the inevitable threat to public health from natural or manmade disasters. A prepared health system should have the ability to prevent, detect, alert, respond to, and recover from a large-scale public health crisis. It should have the capacity to reduce morbidity and mortality arising from intentional terrorist attacks, large-scale transmission of naturally occurring agents, and natural disasters. In an effort to develop such a public health system and address gaps in preparedness, the U.S. government has spent approximately $5 billion since September 2001 to introduce surveillance systems, purchase equipment and develop preparedness plans (Seid et al., 2007).

Threats and hazards to public health can emanate from a variety of diverse sources such as biological agents, natural disasters, environmental exposures, chemical and radiological materials, or explosions. Biological agents include parasites, bacteria, and viruses that cause illness or death in people, animal or plants. Influenza pandemics, such as the bird and swine flus, are one area of growing concern with respect to this type of threat. Natural disasters such as hurricanes and earthquakes are costly and continue to grow in expense with a current estimated cost of US $600 billion over a 27-year period. The release of chemical or radiological materials can have similarly huge economic impact because
thousands of people are displaced or evacuated after the occurrence of such a release (CDC, 2009). Although the nature, occurrence and consequence of these event categories are different, the Federal Emergency Management Agency (FEMA) and the CDC recommend a single, comprehensive and all-hazards approach to emergency preparedness.

After a threat occurs, it may affect public health in several ways. First, it may cause deaths or illnesses that exceed the capacities of local or state health services. Second, health infrastructure may be damaged as a result of threat. It also affects the psychological and social behavior of the community that indirectly alters public health structure. Another possible outcome of a threat can be large, spontaneous or organized population movements to the areas where health services cannot deal with the situation (Noji, 1997). An emergency preparedness plan for public health should consider all possible outcomes. This can only be possible if emergency response is carefully planned and executed. In this research, we consider the alerting phase of an emergency plan.

1.2 Background on North Carolina Health Alert Network

The North Carolina Health Alert Network (NC HAN) is an internet-based alerting system providing 24/7 flow of critical health information among North Carolina's state and local health departments, hospital emergency departments, and law enforcement officials (NC office of public health preparedness and response). NC HAN is an outcome of the public health infrastructure development described earlier. The North Carolina Division of Public Health created NC HAN in conjunction with the Centers for Disease Control and Prevention (CDC) in October 2002. It provides highly secure alerts through simultaneous use of phone, fax, email, etc. The main focus for the initial development of such a system was bioterrorism
preparedness. However, it has evolved into a system with broader coverage such as providing notification regarding communicable disease outbreaks, hurricanes and other types of disasters and diseases (Baker & Porter, 2005). NC HAN is part of the national HAN system that was developed by CDC to connect all 50 states connected and provide vital health information and the infrastructure to support information flow at state and local levels, and beyond (Health alert Network). NC HAN is a component of the North Carolina Public Health Information Network (NC PHIN). In addition to NC HAN, NC PHIN includes surveillance programs such as the North Carolina Electronic Disease Surveillance System (NCEDDS), the Prehospital Medical Information System (PreMIS), the Epidemic Information Exchange (Epi-X) which is responsible from the communication between the CDC and the state, Disease Event Tracking and Epidemiologic Collection Tool (NC DETECT), and program area modules (e.g. TB, hepatitis, etc.). There is no physical connection between NC HAN and the other surveillance systems of NC PHIN. Hence, the same information could be reported via different tools to health care officials. Although, the main goal of the HAN (national or state level) is to improve the communication network, it can be used not only before or during the emergency event, but also after the event. It can be used to coordinate response activities such as de-escalation, debriefing and revising response actions (Doniger, Labowitz, Mershon, & Gotham, 2001). The main focus of this research is the utilization and optimization of alerting systems such as NC HAN and we do not explicitly model the effect of other surveillance systems on overall emergency response to a threat.
The public health entities in North Carolina that have direct access to NC HAN and some other elements of NC PHIN can be summarized from local to state level as shown in Figure 1:

Figure 1: NC Public Health Structure from Local to State

Eighty-five local health departments and NC Department of Health and Human Service (hereafter referred to as the State Health Department) are the primary decision makers in the alerting process since they are responsible for reporting through NC HAN. One unique aspect of this research is that we model the public health system from the perspective of these two decision makers. In doing so, we can explore the relationship between these two decision makers in terms of alerting decisions. It is reasonable to assume the magnitude of a threat that leads to issuing an alert differs on local and state levels because of population size and
geographical factors. A threat that is significant at the local level may not be as important for state level. Similarly, a state level alert may not affect a county that does not have any cases related to the threat. Therefore, alerting decisions and alert thresholds if they exist may be different for local and state level. We describe the effect of this relation on our modeling process in detail in Section 3.2.

1.3 Relationship between Local and State Health Departments

Local health departments are autonomous in their decision process. In other words, they have guidelines, recommendations or information that they receive from the State Health Department and they report back to it; however they are not required to follow the State Health Department’s advice. Thus, in our model we allow for the possibility that local and State alerting decisions may differ.

The information flow between local and State is another crucial part of an emergency preparedness plan in general. In our research this translates to the alerting process and NC HAN. Interviews conducted with local health department personnel acknowledged a time lag in the flow of information between state and local health departments. In order to realistically represent the relationship between local and state health departments, our model incorporates the lead-time between these entities.

Our analysis of NC HAN alerts suggests that there is a discrepancy in utilization and usage frequency of NC HAN at the local and the state health departments. The local health directors interviewed all indicated that there are no existing guidelines regarding when and how to use NC HAN. As a result, some local health departments report every single case; some do not even report outbreaks. This leads to a lack of uniformity in the NC HAN data
and loss of reliability. Some health directors refer NC HAN as “the boy who cried wolf” because the majority of issued alerts are not relevant to their counties or are not important enough. We would like to address this issue by developing guidelines for the optimal timing of alerting decisions.

1.4 H1N1 and how to determine level of a threat

Pandemic influenza outbreaks are considered one of the most important and widely spread threats to public health (Osterholm, 2005; Webby & Webster, 2003). Because of the recent H1N1 outbreak and the availability and accessibility of data on the topic, we have selected H1N1 as our focus threat. The parameters of the model are estimated from data derived from syndromic influenza surveillance and NC HAN. In this research we seek to determine alerting thresholds for identifying an H1N1 outbreak.

H1N1 and other pandemic outbreaks may have a significant impact on the public health system resulting with human casualties and economic burden. In the U.S. alone, previous flu outbreaks, the 1918 Spanish flu, the 1957 Asian flu, and the 1968 Hong Kong flu resulted in more than 500,000, 70,000 and 34,000 deaths, respectively (Longini Jr, Halloran, Nizam, & Yang, 2004). H1N1, originating from animal influenza viruses, is the latest outbreak of an influenza virus. As of March 21, 2010 worldwide more than 213 countries and overseas territories or communities have reported laboratory confirmed cases of the pandemic influenza H1N1 2009, including over 16,931 deaths (WHO 2009).

Determining the level of H1N1 threat is a key step in estimating the model parameters such as transition probability matrices and information matrices. However, there is more than one criterion strategy for declaring a type of influenza (novel or existing) as a pandemic
outbreak. Different variables such as geographical spread, severity, mortality and the effect of the disease in the high-risk populations such as infants, the elderly and chronically ill patients, are used to classify a pandemic threat. According to WHO, on an international level a pandemic can be classified with a six-phase system that describes the process by which a novel influenza virus moves from the first few infections in humans through to a pandemic outbreak. These phases are summarized in Table 1. Phases 5 and 6 are acknowledged as “global outbreak”. A pandemic moves to Phase 5 if the virus caused outbreaks in two or more countries in one WHO region (WHO 2009).

Table 1: WHO Pandemic Phase Descriptions (WHO 2009)

<table>
<thead>
<tr>
<th>PHASE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHASE 1</td>
<td>No animal influenza virus circulating among animals have been reported to cause infection in humans.</td>
</tr>
<tr>
<td>PHASE 2</td>
<td>An animal influenza virus circulating in domesticated or wild animals is known to have caused infection in humans and is therefore considered a specific potential pandemic threat.</td>
</tr>
<tr>
<td>PHASE 3</td>
<td>An animal or human-animal influenza reassortant virus has caused sporadic cases or small clusters of disease in people, but has not resulted in human-to-human transmission sufficient to sustain community-level outbreaks.</td>
</tr>
<tr>
<td>PHASE 4</td>
<td>Human to human transmission of an animal or human-animal influenza reassortant virus able to sustain community-level outbreaks has been verified.</td>
</tr>
</tbody>
</table>
Table 1 Continued

<table>
<thead>
<tr>
<th>PHASE 5</th>
<th>The same identified virus has caused sustained community level outbreaks in two or more countries in one WHO region.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHASE 6</td>
<td>In addition to criteria defined in Phase 5, the same virus has caused sustained community level outbreaks in at least one other country in another WHO region.</td>
</tr>
<tr>
<td>POST PEAK PERIOD</td>
<td>Levels of pandemic influenza in most countries with adequate surveillance have dropped below peak levels</td>
</tr>
<tr>
<td>POST PANDEMIC PERIOD</td>
<td>Levels of influenza activity have returned to levels seen for seasonal influenza in most countries with adequate surveillance</td>
</tr>
</tbody>
</table>

1.5 Research Objectives

In this research, we propose to develop alert response thresholds to determine appropriate alert levels as a function of the potential for an adverse event and the extent of impact using a partially observable Markov decision process (POMDP). NC HAN attempts to provide alerts regarding current threats in a timely manner in order to optimize response actions while trying to minimize false alarms on the local and the state level. The main question we answer is when a local and state health department should issue an alert or initiate mitigation actions such as vaccination in response to the existence of a threat (H1N1 in this particular research), given that health departments have imperfect information about exact number of infected people (i.e., the system’s state). For various levels of threat, does there exist a threshold for issuing an alert, if so how does the threshold change for local and state health departments? What is the probability of a false alarm and what is the cost of a false alarm? What percentage of threats where an alert is not issued become true positives (i.e. true threat or outbreak) and what is the cost of such situation associated with? To answer
such questions we propose to model North Carolina system “health” where health corresponds to the level of pandemic (H1N1) threat, in order to optimize response actions (i.e. waiting, alerting or mitigation) at the local and state level while minimizing false alerts and late alerts. Providing such a balance between false and late alerts in the system increases the credibility and efficiency of the system while improving immediate response and care in the event of a public health emergency.

We develop a partially observable Markov decision process (POMDP) to determine optimal policies for alerting decisions and response actions. The POMDP formulation incorporates two types of uncertainty. The first is the stochastic nature of the system, i.e., the state of the system dynamically changes. The second is the uncertainty stems from the partial observability of the system due to incomplete or imperfect information. The POMDP framework is appropriate for the structure of our system since the system states, which are defined as “pandemic threat levels”, change dynamically with some probability, it is impossible to know the true level of pandemic spread in the system with certainty and the outcome of alerting decisions is not deterministic. It is only possible to observe signals that provide clues about the true state of the system. Such signals could be the number of deaths, the number of hospitalizations, the spread of disease in high-risk populations (infants, elderly etc.), the geographical spread, or the number of infected people. Here, we use the number of infected people diagnosed by a medical center as observations.

The remainder of this thesis is organized as follows. Chapter 2 provides a brief literature review about emergency preparedness and related methodologies including POMDPs and multi-agent systems. Chapter 3 presents the POMDP model in detail. In
Chapter 4, the methodology and data used in our model are described. Chapter 5 presents the numerical experiments performed and Chapter 6 briefly reviews the limitations of the model, discusses the main findings and possible future work.
CHAPTER 2

Literature Review

Because this research seeks to improve effectiveness of emergency preparedness and response, we explore previous models for emergency preparedness and response. In addition, we discuss the relevant literature including POMDP and multi agent sequential decision making.

2.1 Emergency Preparedness and Response

The literature on emergency preparedness ranges from empirical studies to mathematical or simulation models. Some studies focus on developing guidelines and frameworks for emergency preparedness management (See (McLoughlin, 1985), (Perry & Lindell, 2003)) whereas other studies use modeling tools to create disaster response models. Disaster response models are mostly developed for a specific type of disaster. Although, our model is developed for pandemic flu, it can be adapted to other type of disasters given data to estimate transition probabilities and model parameters. Models in the literature explore different problems that may occur after an earthquake (Barbarosoglu & Arda, 2004), (Paul, George, Yi, & Lin, 2006), hurricane (Regnier, 2008), pandemic influenza (Medema et al., 2004), anthrax (Zaric et al., 2008) or nuclear attack (Papazoglou & Christou, 1997) such as location decisions, logistics problems, vaccination strategies by using different modeling techniques. None of the models mentioned above deal with the importance of timing in alerting decisions or how it affects the response strategies for the given disaster. They consider scenarios where a disaster occurs and its magnitude is known to decision makers. Our model, in contrast, incorporates imperfect knowledge about the disaster’s condition and
time is considered as one of the key variables in determining the best possible response action. For surveys on disaster modeling, see (Altay & Green III, 2006) and (Brandeau et al., 2009).

Pandemic influenza literature includes the studies on developing mitigation strategies (Ferguson et al., 2006), (Germann et al., 2006), modeling the economic impact of pandemic influenza (Medema et al., 2004; Meltzer, Cox, & Fukuda, 1999), estimating the mortality associated with influenza (Murray et al., 2007; Simonsen et al., 1998) etc. The research most related to our work is that on models that investigate intervention strategies to minimize the impact of outbreak. Simulation or compartmental models such as deterministic SEIR differential equations (Hethcote, 2000) are traditional methodologies for modeling epidemics. The SEIR model consists of four compartments labeled as S (for susceptible), E (for exposed), I (for infectious) and R (for recovered). Different mitigation techniques are introduced in these models to evaluate disease spread or quantify the costs and benefits of these techniques. In most models, the mitigation strategies are implemented as soon as the first case of influenza is observed. Mitigation strategies involving vaccination must also consider the possibility that vaccination is not available (i.e. if the pandemic strain is novel). Then, vaccination should be initiated with a time lag in the model (Germann et al., 2006). In our model, we allow for the implementation of mitigation strategies depending on the severity of influenza pandemic and the time to initiate a mitigation strategy is not fixed. Therefore, false alarms and unnecessary mitigation are minimized. Next, we review POMDP and multi-agent models that are methodologically related to our model.
2.2 Partially Observable Markov Decision Process (POMDP)

A POMDP is a generalization of Markov decision processes (MDPs) in which there is incomplete information and uncertainty regarding the current state of the Markov process. Incomplete information regarding the state of process affects the optimal choice of actions. Physical constraints, noise corrupted readings in the observation of the state, or the high cost of observing the state can result in uncertainty. Some examples for which the uncertainty of the state is a realistic assumption include machine maintenance, learning theory, artificial intelligence, and health care. Shiryaev (1963) initially formulated a detection problem with a random process whose parameters were unknown and explored applying a Markov process as a special case of this problem. Drake (1962), Astrom (1965) and Sondik (1971) defined explicit formulations for a POMDP. Since then, the theory of POMDPs including solution techniques and structural characteristics has been an active research topic. While numerous articles provide theoretical contributions to the analysis and characterization of POMDPs, there is also significant research that applies POMDPs to practical problems. Several problems in a wide variety of areas with imperfect state information and stochastic nature can be formulated as POMDPs. Monahan’s (1982) and Cassandra’s (1998) surveys provide summarizes of the literature for several of these applications. To our knowledge, there is no other POMDP application that models public “health” as a pandemic threat level in order to explore alerting decisions.

However, there are some applications of POMDP to health care related topics (Hu, Lovejoy, & Shafer, 1996), (Hauskrecht & Fraser, 2000), (Maillart, Ivy, Ransom, & Diehl, 2008). Smallwood, Sondik and Offenseend (1971) are the first to propose the utilization of
POMDP while defining patient health as an unobserved state pairing with the physician state of information which are called twin states. Patient state is described as the internal physiological or psychological state of the patient which is usually unobservable, while the physician state of information corresponds to the physician’s belief regarding the patient state and depends on the physician, his prior experience and his knowledge of the patient. The physician will have data available (diagnostic tests etc.) that influence his state of information about the patient’s state. The authors explore a broad range of healthcare system problems such as medical diagnosis and treatment, individual facility design, health service programs and regional health system design as promising areas to integrate the twin state definition.

Another application domain that is analogous to our model is machine maintenance. In the machine maintenance problem, a machine or a system which is observed periodically deteriorates over time. Since deterioration includes internal parts of the machine/system, the true condition of the machine/system is unknown to decision maker. It is possible to disassemble the machine in order to determine its true state; however, this procedure can be costly or unproductive. Observations such as outputs of the machine, outcomes of the system, and inspection of the machine/system can be used as a basis for maintenance or replacement decisions. The decision maker attempts to determine optimal maintenance/replacement actions while minimizing the chance of failure. For additional discussion of solution methods associated with machine maintenance applications, see (Girshick & Rubin, 1952), (Eckles, 1968), (Ross, 1971), (Smallwood & Sondik, 1973), (Rosenfield, 1976), (Pierskalla & Voelker, 1976), (Wang, 1976; Wang, 1977), (White, 1977), (White III, 1978; White III,
1979), (Valdez-Flores & Feldman, 1989), (Chen & Feldman, 1997), (Banjevic, Jardine, Makis, & Ennis, 2001), (Ivy & Pollock, 2005). In our model, the decision maker seeks optimal alerting actions while minimizing false alerts (unnecessary maintenance) and late alerts (failure). Similarly, it is impossible to know the nature or level of outbreak, thus the model is partially observable. The assumption of an ordering of the states as increasing health threat level resembles two-state or multi-state deteriorating systems depending on the number of the states.

### 2.3 Multi-agent models

One of the unique aspects of our model that differs from existing POMDP models is that our model is defined on two levels which are dependent. Our model is a system of two POMDP models that interact with each other in every decision epoch. The idea of including multiple interacting decision makers (also known as agents) into a POMDP model has been explored by the artificial intelligence community in recent years. Several models have been developed in the area of decentralized control of multiple agents under uncertainty which is a generalization of POMDPs. We discuss these models and how they differ from our model next.

The common characteristic of multi-agent modeling frameworks (that is discussed later) is the decentralized control of multiple agents. In addition, all frameworks are used to model stochastic systems where agents have partial observability about the system’s state. The difference in the formulations of the frameworks lies in the several factors such as modeling communication between agents (i.e. explicit or implicit), and demonstrating the
belief state of agents and reward functions (e.g. cooperative if agents have a global reward function or non-cooperative if agents receive their own rewards).

Some real-life problems that motivate the research on multi-agent systems are the control and coordination of planetary rovers (Zilberstein et al., 2002), decentralized control of service sharing (Cogill et al., 2006), the communicative team decision problems such as coordinated helicopter flights (Pynadath & Tambe, 2002), multiple access broadcast channels (Ooi & Wornell, 1996), distributed sensor networks (Lesser, Ortiz, & Tambe, 2003), (Nair et al., 2005), and planning the movements of mobile robots (Bernstein et al., 2002).

The decentralized partially observable MDP (DEC-POMDP) or distributed POMDP is one of the frameworks that are developed for multi-agent systems. It was first proposed by Bernstein et al. (2000). In this framework, agents (two or more) communicate implicitly, in other words the model does not have an explicit set of actions for each agent but has one general action set. In this model, in every step, each agent chooses an action, a state transition happens and each agent observes locally. The model also allows joint observations between agents. It is a cooperative system where all agents work toward a global reward function instead of having their own private reward functions. States are defined as a general set for all agents, thus all agents share a common environment and changes in the environment are modeled as the state transition in the model. Similar to POMDP, DEC-POMDP can be used for finite horizon or infinite horizon problems. The DEC-POMDP is extended to include explicit communication actions by Goldman and Zilberstein (2003) and referred as DEC-POMDP-COM. After observing the environment, agents in DEC-POMDP-COM model send an instantaneous message to other agents and incur a cost associated with transmitting the
message. Information shared between agents can be regarding whether a certain goal has been achieved or simply the agents’ observation about the system’s state. When and what to communicate provides a communication policy for the model. The difference between these frameworks and our formulation is that the state space is a common shared set for all agents whereas in our model we define two state spaces, one for the local level and one for the North Carolina level. In addition to this, DEC-POMDP models have a global reward defined for all agents while agents in our model (local and NC level) accumulate their rewards according to their own reward function.

If the DEC-POMDP model is extended to be a non-cooperative one, all agents in the system are allowed to compete against each other towards possibly conflicting goals and have their private reward function. This extension can be formulated as a partially observable stochastic game (POSG), where a POSG with one agent is equivalent to a POMDP (Hansen, Bernstein, & Zilberstein, 2004). Similar to our formulation, POSG defines an action set, an observation set and a reward function indexed for agents. The deviation from our model lies in the definition of set of states. In POSG, all agents share the same environment, and thus have a global state space. The state space is distinguished for each agent and is defined separately for each agent in our model.

A network distributed POMDP (ND-POMDP) is another multi-agent sequential decision making tool under uncertainty that was introduced by Nair et al. (2005). The motivation was to capture local interactions between agents. Distributed sensor networks and distributed satellites are some examples where agents interact extensively with a small group of neighboring agents. Therefore exploiting local agent interaction in these domains is a key
factor. In this framework, similar to our formulation, the state space includes local states of agents. In addition, ND-POMDP has a set of unaffected states which cannot be affected by the agents’ actions such as environmental factors. Action and observation sets are a joint set of actions available for agents and a joint set of observations of agents, respectively. The agents’ observations and state transitions are assumed to be independent of other agents’ actions. This is the difference between our formulation and the ND-POMDP framework. In our model, the local agent is assumed to be affected by the NC agent’s actions and the NC agent is affected by the observations of the local agent. In this framework, the reward function is defined as the sum of the rewards of sub-group of agents. These sub-groups are determined from interactions of agents and emphasize the importance of locality in the framework.

A different approach to formulating a multi-agent problem is to explicitly identify belief states. The interactive POMDP (I-POMDP) was developed by Gmytrasiewicz and Doshi (2005) to include belief states of agents not only regarding their own local state but also regarding other agents’ states. I-POMDP is more expressive and flexible than DEC-POMDP since it is possible to formulate belief over underlying states and belief over the other agents in terms of their preferences, capabilities and beliefs. In addition, cooperative and non-cooperative models can be modeled by I-POMDP framework. In order to model explicit belief states, the interactive state space is defined as a joint set which includes a set of states representing the physical environment and a set of possible models of agents. Actions, observations and transitions are defined for each agent and the set of joint actions, observations and transitions are modeled as three components of the I-POMDP. Some
simplifying assumptions are made over the set of observations and transitions in order to guarantee the agents’ autonomy. The model’s non-manipulability assumption over the transition model ensures that agents’ actions do not change the other agents’ models directly. One agent affects other agents by changing the physical state of the environment, therefore changing the agents’ beliefs. The model non-observability assumption over the observation set ensures that agents cannot observe other agents’ models directly. Our model resembles I-POMDP framework with respect to the way in which the actions, observations, transitions and rewards of agents is formulated explicitly. However, our model allows one agent to observe the other agent’s observations directly and also knowing one agent’s action affects the beliefs of other agent.

In Table 2, we present the multi agent frameworks and how they differ from our model.

Table 2: Multi-agent Frameworks

<table>
<thead>
<tr>
<th>FRAMEWORK</th>
<th>REFERENCE</th>
<th>OUR MODEL</th>
</tr>
</thead>
</table>
| DEC-POMDP (Distributed POMDP)  | Bernstein et al. (2000)          | • Each agent has its own reward function  
• Each agent has its own state space |
| Partially Observable Stochastic Game (POSG) | Emery-Montemerlo et al. (2004) | • Each agent has its own state space  
• Agents are not competing for resources |
| Networked Distributed POMDP (ND-POMDP) | Nair et al. (2005)   | • Agents are not independent, the actions of agents affect each other |
| Interactive POMDP (I-POMDP)    | Gmytrasiewicz and Doshi (2005)   | • Agents interact and are able to observe the other agent’s observations(actions) directly and these observations (actions) affect each others’ belief states |
In this section, we explained different frameworks to model multi agent systems and how they resemble to our model or how they differ from our formulation. Table 2 summarizes these differences such as reward function, state space definition and agents’ interaction with each other.
CHAPTER 3
Stochastic Alert Threshold Model

In this chapter, we introduce our model formulation and its variants. The model is developed to determine thresholds for any type of threats. However, different types of threats will behave differently and will have different parameters in the model. In this research, we assume that the threat explored is H1N1 since there is data on pandemic flu cases and they are relatively easy to access.

3.1 Core Process Model: States and Levels

We model the level of pandemic threat using a Markov chain with the following two states: no pandemic threat (0) and pandemic threat exists (1) where the pandemic is assumed to be H1N1. We set \( S \equiv \{0,1\} \) be the set of possible threat levels, and \( S_t \in S \) be the state of the system at time \( t, t = 1,2,3,... \)

From state \( i, i = 0,1 \) a state transition occurs at the NC level to state \( j, j = 0,1 \), with probability \( p_{ij} \). Similarly, from state \( i, i = 0,1 \), a state transition occurs at the local level to state \( j, j = 0,1 \), with probability \( q_{ij} \). These transition probabilities collectively form 2x2 transition probability matrices \( P = [p_{ij}] \) and \( Q = [q_{ij}] \) for \( i = 0,1 \) and \( j = 0,1 \). For the sake of simplicity, we suppress the time index \( t \) in the formulation. A schematic of this Markov chain for NC and the local level is shown in Figure 2.
The local level is assumed to be analogous to the local health departments (LHDs). These LHDs are assumed to be mutually independent for the sake of simplicity in the model.

3.2 Relationship between Local and NC Level

To model the relationship between NC and local level, the local observation vector and the NC response action vector are denoted by $O^{LS}_t$ and $R^{SL}_t$, respectively. $O^{LS}_t$ are defined to be observations which are collected at every time, $t = 1,2,3,...$ at the local level and reported to the NC level. Based on these observations from the local level, the NC level
updates its belief state. We define \( R_t^{SL} \) to be response actions that NC level officials (State Health Department) advise LDHs to do based on the current threat level of NC. As we mentioned, LHDs are autonomous. Therefore, if the NC level recommends a response action against a certain type of threat, the local level takes this recommendation into consideration, but it is possible that they do not have this type of threat present in their county and hence the LHD may not issue an alert. We should also mention that there are separate observations associated with the NC level that also affect the transition of the state. We discuss these observations in the following sections within the context of the POMDP formulation of each level.

### 3.3 POMDP Formulation

#### 3.3.1 States

One can never truly know the magnitude of the pandemic threat (i.e. which state the system is in) or when changes occur with respect to the risk of the pandemic threat (i.e. transitions between states). We assume the decision maker’s knowledge of the system’s condition is uncertain or probabilistic. Moreover, the observations available to provide information about the nature of threats are imperfect. Thus, the core-process model, defined in Section 3.1, is partially observable. We formulate this model as a POMDP. We define the state occupancy probabilities \( \pi^L_i(t) \) as the probabilities that the system is in core states \( i = 0,1 \) at time \( t \) where \( \sum_{i=0}^{1} \pi^L_i(t) = 1 \) and \( \pi^L_i(t) \geq 0 \) for \( i = 0,1 \) at the local level and \( \pi^L(t) = [\pi^L_0(t), \pi^L_1(t)] \) is the state occupancy distribution for the local level. Similarly, the
state occupancy probabilities, $\pi^S_i(t)$, are defined as the probabilities that the system is in core states $i = 0,1$ at time $t$ where $\sum_{i=0}^{1} \pi^S_i(t) = 1$ and $\pi^S_i(t) \geq 0$ for $i = 0,1$ at the NC level and $\pi^S(t) = [\pi_0^S(t), \pi_1^S(t)]$ is the state occupancy distribution for the NC level. Next, we introduce observations and their associated probabilities.

### 3.3.2 Observations and Information Matrix

At every decision epoch, observations related to the system’s health are observed. $X^L_t$ is defined to be the observation vector that is collected at time $t$ at the local level and similarly $X^S_t$ is the observation vector at time $t$ at the NC level. Specifically, the number of H1N1 influenza virus isolates (cases) identified by the State Laboratory of Public Health for the local level and the number of influenza-like illnesses (ILI) obtained from hospital emergency departments (ED) and outpatient clinics participating in the influenza sentinel provider network (SPN) for the NC level are observed (NC DHHS 2007-2010) and indexed by the observation vectors $X^L_t$ and $X^S_t$, respectively. We assume no cost is incurred for observations. By observing $X^n_t$ at time $t$ for level $n$, information which is needed to capture the true value of $S^n_t$ is obtained. Since the NC level has two types of observations (i.e. within the NC level ($X^n_t$) and from the local level to the NC level ($O^{LS}_t$), we use these in estimating the underlying state for the NC level. Suppose that $S^L_t = i$, at the local level, an observation has the value $k$ with probability $\beta^L_{ik}$ at time $t$, then

$$\beta^L_{ik} = \Pr\{X^L_t = k \mid S^L_t = i\} \quad \text{for } \forall i, k.$$
For the NC level, if $S_i^S = i$, an observation at the NC level has the value $k$ and an observation from the local level that has been reported to the NC level has value $m$ with probability $\beta_{ik}^S$, i.e.,

$$\beta_{ik}^S \equiv \Pr\{X_i^S = k, O_i^{LS} = m \mid S_i^S = i\} \quad \text{for } \forall i, k, m.$$  

Note that, $\beta_{ik}^S$ also depends on the value $m$, however for notational convenience we suppress it and define the information matrices $B^L = \left[ \beta_{ik}^L \right]$ for $\forall i, k$ of the local level and $B^S = \left[ \beta_{ik}^S \right]$ for $\forall i, k, m$ of the NC level. Actions available to the system are discussed in the next section.

### 3.3.3 Actions

One can control the system by choosing actions. Let $A$ be a finite set of all actions available. At every decision epoch, one of three possible actions from $A$ is chosen: wait ($a = 0$), issue a type 1 alert ($a = 1$), or issue a type 2 alert ($a = 2$). These actions are available on both the local and the NC level. Similarly, $R_t^{SL}$, the recommendation sent from the NC level to the local level, can be either wait, issue a type 1 alert or issue a type 2 alert. Then, the action set is $A = \{a_t^L, a_t^S, R_t^{SL}\}$ for $\forall t$. There is a slight difference between $\{a_t^L, a_t^S\}$ and $R_t^{SL}$ since the set $\{a_t^L, a_t^S\}$ are the actions that are chosen at time $t$ by the local and NC level respectively, but $R_t^{SL}$ represents the action that is recommended to the local level by the NC level at time $t$. Depending on time lag between the local and the NC level, $R_t^{SL}$ may have been chosen as the optimal action for the NC level at some previous $t$ (i.e. $t-1$).
The difference between type 1 and type 2 alerts is based on magnitude of the response actions. A type 1 alert corresponds to informing key health personnel and initiating active surveillance on the disease of interest while a type 2 alert also includes mitigation actions that are costlier than surveillance. For H1N1, the mitigation action is assumed to be vaccination. We define time horizon and the transition probabilities associated with actions in the next section.

3.3.4 Time Horizon and Transition Probabilities

Let $T$ denote the set of decision epochs, $T = \{0, 1, 2, \ldots, M\}$ where $M$ is the problem horizon. We assume an action is selected at the beginning of each decision epoch. Let $P(a) = [p_{ij}(a_i^S)]$ denote the state transition probabilities when action $a_i^S \in A$ is chosen at the NC level at time $t$, in other words the system moves to state $j$ from state $i$ with probability $p_{ij}(a_i^S)$ if action $a_i^S$ is chosen at time $t$. We let $Q(a) = [q_{ij}(a_i^L, R_i^{SL})]$ denote the state transition probabilities when action $a_i^L \in A$ is chosen at the local level at time $t$ and $R_i^{SL} \in A$ is chosen at the NC level prior to time $t$ and conveyed to the local level at time $t$. In the next section, we provide the formulations for updating the belief states according to the observations.

3.3.5 Bayesian Update of States

The information provided by observations, $X_i^L$ and $X_i^S$, and the actions chosen, $a_i^L, a_i^S, R_i^{SL} \in A$ are used to update the state occupancy probabilities $\pi^L(t)$ and $\pi^S(t)$. Let $k_i^n$ and $a_i^n, R_i^{SL} \in A$ be the value of $X_i^n$ observed and the actions taken at time $t$ for level
n, respectively. Using Bayes’ formula, the belief state is updated from time \( t \) to \( t+1 \) according to the following relationship:

\[
T_i(\pi^L_i | j, a^L_i, R_{i}^{SL}) \equiv \pi^L_i(t + 1) = \frac{\beta^L_{ij} \sum_k q_{kb}(a^L_i, R_{i}^{SL}) \pi_k(t)}{\sum_h \beta^L_{ih} \sum_k q_{kh}(a^L_i, R_{i}^{SL}) \pi_k(t)}, \quad i = 0,1 \text{ for local level}
\]

\[
T_i(\pi^S_i | j, a^S_i) \equiv \pi^S_i(t + 1) = \frac{\beta^S_{ij} \sum_k p_{si}(a^S_i) \pi_k(t)}{\sum_h \beta^S_{ih} \sum_k p_{sh}(a^S_i) \pi_k(t)}, \quad i = 0,1 \text{ for NC level}
\]

where \( \beta^L_{ij} \) and \( \beta^S_{ij} \) are the \((i,j)\)th elements of \( B^L \) and \( B^S \), and \( q_{kb}(a^L_i, R_{i}^{SL}) \) and \( p_{si}(a^S_i) \) are the \((k,i)\)th elements of \( Q(a^L_i) \) and \( P(a^S_i) \), respectively.

\[Q(a) = [q_{ij}(a^L_i, R_{i}^{SL})]\] is assumed to have the following linear form:

\[
Q(a^L_i, R_{i}^{SL}) = \begin{cases} 
Q(a^L_i) & \text{if } R_{i}^{SL} = 0 \\
Q(a^L_i) \pm k_1 & \text{if } R_{i}^{SL} = 1 \\
Q(a^L_i) \pm k_2 & \text{if } R_{i}^{SL} = 2 
\end{cases}
\]

where \( k_1, k_2 \in \mathbb{R} \) and \( k_1 \leq k_2 \). Figure 3 illustrates the schematics of iterative update process of the local and NC level. The belief state of NC level updates itself using its observation, action and observation of the local level and then the local level updates its belief state from its observation, action and the action of the NC level.
Figure 3: The iterative update process of the local and NC level.

A collection of decision rules that prescribe one of these actions for each occupancy distribution, for all epochs, is called a policy. We let $\pi_n^*(\pi)$ denote the optimal policy where $\pi$ is the state of the system and $n$ is the NC or the local level. Our objective is to find such an optimal policy for both the NC and the local level that minimizes total expected cost.

### 3.3.6. Cost Structure

In this thesis, we explore the tradeoff between false and late alarms. Because we do not have enough data to accurately estimate the cost of false and late alarms, these costs are treated as relative weights associated with the actions chosen. We investigate the behavior of model under the various weight schemes. In practice, we would leave the choice of weights that are close to the realities of North Carolina to public health experts.

We define the following immediate rewards given the selected action is known:
Then, the immediate reward for the belief state is
\[ C^n_i(i^n, a^n) = \sum_{i^* \in S} C^n_{i^*}(i^n, a^n) \pi^n_i(i^n) \]

For \( n = \text{local, NC} \) and \( \forall t \):

\[
\begin{align*}
C^n_i(i^n = 0, a^n = 0) &= 1 - c^n_{\text{falsealert1}} \\
C^n_i(i^n = 0, a^n = 1) &= 1 - c^n_{\text{falsealert2}} \\
C^n_i(i^n = 0, a^n = 2) &= 1 - c^n_{\text{truealert}} \\
C^n_i(i^n = 1, a^n = 0) &= 1 - c^n_{\text{falsealert}} \\
C^n_i(i^n = 1, a^n = 1) &= 1 - c^n_{\text{truealert1}} \\
C^n_i(i^n = 1, a^n = 2) &= 1 - c^n_{\text{truealert2}}
\end{align*}
\]

Since a type 2 alert involves more costly mitigation actions than a type 1 alert, the following inequalities hold for \( n = \text{local, NC} \):

\[
\begin{align*}
c^n_{\text{falsealert2}} &> c^n_{\text{falsealert1}} \\
c^n_{\text{truealert2}} &> c^n_{\text{truealert1}}
\end{align*}
\]

Furthermore, the weight of false alerting should be larger than the weight of timely alerts of the same type because when a false alert is triggered, we incur the cost of the timely alert by initiating the response process in addition to extra cost due to losses caused by false alerting. This relationship is presented in the following inequalities for \( n = \text{local, NC} \):

\[
\begin{align*}
c^n_{\text{falsealert2}} &\geq c^n_{\text{truealert2}} \\
c^n_{\text{falsealert1}} &\geq c^n_{\text{truealert1}}
\end{align*}
\]

We discuss the relationship vectors between the local and NC level in the next section.
3.3.7. Lead Time between Local and NC Level

The information flow between the state and local levels is not in real time, but is subject to a time lag. We use the relationship variables, \( O_t^{LS} \) and \( R_t^{SL} \) to incorporate this delay into our formulation. The observation vector from local to NC level at time \( t \) is assigned to be \( X_{t-1}^L \), which means the NC level updates its local level knowledge according to observations from the local level obtained in the prior decision epoch. Similarly, response actions from the NC level to the local level are based on the NC level actions from previous interval, \( a_{t-1}^S \).

The following relationship holds:

\[
O_t^{LS} = X_{t-1}^L \quad \text{and} \quad R_t^{SL} = a_{t-1}^S \quad \text{for all} \; t \in T
\]

The optimal value function is presented in the next section.

3.3.8. Value Function

We formulate a dynamic programming formulation for the alert threshold model that minimizes the total expected cost which is a function of the belief states, \( \pi^L_t, \pi^S_t \) and observations \( X_t^L \) and \( X_t^S \). The optimal value functions for the local and NC levels, respectively, can be written as:

\[
V^*_t(\pi^L_t) = \max \begin{cases} 
C^L_t(a^L_t = 0 | \pi^L_t(t)) + \sigma E_X[V^*_t+1(\pi^L_t(B_t^L, R_t^{SL}, a^L_t)), \\
C^L_t(a^L_t = 1 | \pi^L_t(t)) + \sigma E_X[V^*_t+1(\pi^L_t(B_t^L, R_t^{SL}, a^L_t)), \\
C^L_t(a^L_t = 2 | \pi^L_t(t)) + \sigma E_X[V^*_t+1(\pi^L_t(B_t^L, R_t^{SL}, a^L_t))]
\end{cases}
\]

\[
V^*_t(\pi^S_t) = \max \begin{cases} 
C^S_t(a^S_t = 0 | \pi^S_t(t)) + \sigma E_X[V^*_t+1(\pi^S_t(B_t^S(O_t^{LS}), a^S_t)), \\
C^S_t(a^S_t = 1 | \pi^S_t(t)) + \sigma E_X[V^*_t+1(\pi^S_t(B_t^S(O_t^{LS}), a^S_t)), \\
C^S_t(a^S_t = 2 | \pi^S_t(t)) + \sigma E_X[V^*_t+1(\pi^S_t(B_t^S(O_t^{LS}), a^S_t))]
\end{cases}
\]
where $0 \leq \sigma < 1$ is the discount factor and $E_X$ denotes the expectation operation given the belief state, $\pi$. The solutions, $V^*(\pi^L)$ and $V^*(\pi^S)$ yield optimal policies, $\delta^*_L(\pi)$ for the local level and $\delta^*_L(\pi)$ for the NC level.

The POMDP formulation with one decision maker is modified in order to accommodate the local and NC level decision makers. This chapter summarized the core state model and the nested POMDP formulation with multiple decision makers. The model characterizes the relationship and interactions between these two levels. The remainder of this thesis describes model parameters estimation procedures and investigates the behavior of the model under these parameters.
CHAPTER 4
Methodology

In this chapter, we introduce the data sets that are used in estimating the parameters and our parameter estimation methods. Finally, the solution technique that is implemented is explained.

4.1 Data

To estimate the distributions for the observations conditional on the underlying system state at the NC and local levels, we use three datasets from systems that report the number of H1N1 cases for their monitored population weekly as shown in Table 3. Although, the target populations of the first three datasets are same, the number of H1N1 cases reported each differs significantly. This is due in part to: (i) the limited capacity of the State Laboratory (Data Set 1), (ii) the reporting of unconfirmed cases and the possible inclusion of seasonal flu cases (Data Set 2) and (iii) underreporting (Data Set 3).

Table 3: Data sources

<table>
<thead>
<tr>
<th>Data Source</th>
<th>Target Population</th>
<th>Date</th>
<th>Local or State Level</th>
<th>Total number of observed cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC Department of Human and Health Services identified by State Laboratory (2008-2010)</td>
<td>NC</td>
<td>10/2008 - 03/2010</td>
<td>Both</td>
<td>1869 (confirmed)</td>
</tr>
</tbody>
</table>
### 4.2 Estimation of Parameters

In this section, we analyze the datasets in order to estimate the appropriate values for the model parameters. The transition probability matrices for each possible action and the information matrices are calculated with the datasets. Both matrices are determined for the local and NC level separately. The transition probability matrices provide the probabilities that the system moves between the core states while the information matrices are the indicators of observing a certain value given that the system is in one for the core states.

The datasets span a time interval of approximately 60 weeks. After analyzing these datasets, we conclude that the time span of the data was not long enough to establish the time dependency in the transition probability matrices. Therefore, we assume the transition probability matrices for the local and NC level are stationary. The assumption that the transition probability is stationary is a limitation of our model due to lack of better data. However, keeping the time horizon of the model short enough allows us to overcome this problem and analyze the results for this simplified model.
### 4.2.1 Transition probability Matrix for the NC Level

The transition probability matrix $P = [P_{ij}]$ for the NC level is assumed to be stationary and is conditional on the selected action. There are three matrices to estimate, namely $P_{a=0}$, $P_{a=1}$, and $P_{a=2}$. Data from CDC’s FluView report (2007-2010) are used to estimate $P_{a=1}$ and $P_{a=2}$ because $P_{a=1}$ and $P_{a=2}$ involve active surveillance as a response action. FluView is a weekly report produced from information on influenza activity in the United States by the Epidemiology and Prevention Branch in the Influenza Division at CDC since 1997. Information in five categories is collected in a collaborative effort between CDC and its many partners in state, local, and territorial health departments, public health and clinical laboratories, vital statistics offices, healthcare providers, clinics, and emergency departments. (for more information see [http://www.cdc.gov/flu/weekly/fluactivity.htm](http://www.cdc.gov/flu/weekly/fluactivity.htm)). One of the five categories tracks influenza related illnesses through the US Outpatient Influenza-like Illness Surveillance Network (ILINet). ILINet reports the number of patients with influenza-like illness (ILI) by age group and the weighted percentage (on the basis of the state population) of ILI patient visits to healthcare providers weekly at regional and national levels. The baseline percentage is the mean percentage of patient visits for ILI during non-influenza weeks for the previous three seasons plus two standard deviations. The weekly percentage is compared to this baseline (national baseline is 2.3%). Due to wide variability in the regional level data, region specific baselines are calculated. Region 4 includes North Carolina with a baseline of 2.0%. We assume that this baseline is the indicator of the core state transition. Weeks that have lower percentage than the regional baseline are assumed to be in core state
0, “No pandemic threat”, and weeks with a higher percentage than regional baseline are in core state 1 “Pandemic threat exists”. Data between March 2009 (Week 09 of 2009) and October 2009 (Week 42 of 2009) are used to estimate $P_{a=1}$. March 2009 was chosen because the first case of H1N1 was reported in March (Morbidity and Mortality Weekly Report CDC April 2009). The release of H1N1 vaccine (October 19th of 2009 in NC - NC DHHS H1N1 Vaccine FAQ 2009) was defined as the last period for the estimation of $P_{a=1}$ since vaccination is included as a mitigation action for alert type 2 (a=2). We perform the estimation process as follows. Let $T_{a=1}$ be the weeks between March 2009 and October 2009, then $T_{a=1} = \text{Week}\{09\_09, 10\_09, ..., 41\_09, 42\_09\}$ and $T_{a=2}$ be weeks between October 2009 and April 2010, then $T_{a=2} = \text{Week}\{43\_09, 44\_09, ..., 51\_09, 52\_09, 01\_10, 02\_10, ..., 13\_10\}$ defining $pt_i$ as the weighted percentage for Region 4 on week $t$ for $t \in T_{a=1}$ and $t \in T_{a=2}$. Indicator variable $I_t(i)$ is defined as

$$I_t(i = 0) = \begin{cases} 1 & \text{if } pt_i \leq \text{regional baseline} \\ 0 & \text{otherwise} \end{cases} \quad \text{and} \quad I_t(i = 1) = \begin{cases} 1 & \text{if } pt_i \geq \text{regional baseline} \\ 0 & \text{otherwise} \end{cases}$$

Then, the transition probability between $i \in S$ is calculated as follows:

$$p_a(i|\emptyset) = \sum_{i \in T_a} \sum_{i \in S} I_t(i') I_{t+1}(i), \quad \text{for } a = 1,2$$
Then, \( P_{a=1} \) and \( P_{a=2} \) are
\[
\begin{bmatrix}
0.955 & 0.045 \\
0.083 & 0.917
\end{bmatrix}
\text{and}
\begin{bmatrix}
0.667 & 0.333 \\
0.286 & 0.714
\end{bmatrix}
\]

The “Wait” action \((a=0)\) does not involve active surveillance, therefore estimating \( P_{a=0} \) from active surveillance data is not appropriate. The effectiveness of active surveillance on spread of pandemic influenza is used to derive \( P_{a=0} \) from \( P_{a=1} \). Although it is clearly stated in many sources that active surveillance of influenza is important for detecting outbreaks and responding in a timely manner (Langmuir, 2004), (Thacker et al., 1986), (Brownstein, Freifeld, & Madoff, 2009), there is little direct empirical evidence regarding the efficacy or effectiveness of surveillance and case reporting in the context of influenza (Aledort, Lurie, Wasserman, & Bozzette, 2007). Thus, we use a controlled trial of disease surveillance strategies conducted in Monroe County, New York (Thacker et al., 1986). According to this study, active surveillance improved the reporting of measles, rubella, salmonellosis, and hepatitis by 51 percent. Assuming the same percentage is preserved for pandemic influenza, particularly H1N1, and increased reporting of disease decreases the probability of a transition of the core state from State 0 to State 1 by a factor \( h = 0.51 \). The transition from State 1 to State 0 is also affected by early reporting, hence early response to outbreak increases the transitions from State 1 to State 0 by the same factor. Therefore, we can calculate \( P_{a=0} \) from \( P_{a=1} \) by multiplying \( p_{01}(a = 1) \), \( p_{10}(a = 1) \) by \( 1/h \) and \( h \), respectively. This relationship is summarized as follows:
The resulting transition probability matrix is

\[
P_{a=0} = \begin{pmatrix}
1 - p_{01}(a = 1)/h & p_{01}(a = 1)/h \\
p_{10}(a = 1)/h & 1 - p_{10}(a = 1)/h
\end{pmatrix}
\]

Next, we present how the transition probability matrices for the local level are estimated.

### 4.2.2 Transition Probability Matrix for Local Level

Similar to \( P = [p_{ij}] \), the transition probability matrix for local level, \( Q = [q_{ij}] \) is also assumed to be stationary and dependent on the selected action. Because population characteristics of NCSU students such as homogeneity, close proximity and smaller size of the population resembles the county level population, NCSU Health Service Data (2009) is used to estimate the transition probability matrices, \( Q_{a=1} \) and \( Q_{a=2} \). We ignore age groups, other behavioral characteristics and their effect on disease spread. NCSU Health Service reports the confirmed cases of H1N1 that are observed in the student population weekly. Information reported includes the total number of cases, their age, sex, residence, academic category and class. The data collected between August 2009 and November 2009 (15 weeks) have a mean of 109 cases per week. Similar to the baseline approach for the NC Level, we assume that the weekly average defines the transition between core states. In other words, weeks that have a lower number of cases than the average are assumed to be in core state 0, no pandemic threat, and weeks with higher case number than the average are in core state 1, pandemic threat exists. \( Q_{a=1} \) was estimated from data before October 19th and the weeks after this date are used to estimate \( Q_{a=2} \). This dataset clearly has a shorter time horizon than
FluView. As a result, our estimate of the transition probability for the local level is less reliable than the NC level. However, in the absence of better data, we use these estimated values.

Analogous to the NC level formulation, we develop the estimation process for the local level as follows. Let $T_{a=1}$ be the weeks prior to October 19th and $T_{a=2}$ be weeks after October 19th. We define $n_t$ as the number of H1N1 cases at NCSU on week $t$ for $t \in T_{a=1}$ and $t \in T_{a=2}$. The indicator variable $I_t(i)$ is defined as

$$I_t(i = 0) = \begin{cases} 1 & \text{if } n_t \leq \text{average cases per week} \\ 0 & \text{otherwise} \end{cases}$$

and

$$I_t(i = 1) = \begin{cases} 1 & \text{if } n_t \geq \text{average cases per week} \\ 0 & \text{otherwise} \end{cases}$$

The transition probability between $i \in S$ is calculated as follows:

$$p_a(i|i') = \frac{\sum_{t \in T_a} I_t(i')I_{t+1}(i)}{\sum_{t \in T_a} \sum_{i \in S} I_t(i')I_{t+1}(i)}, \quad \text{for } a = 1, 2$$

Then, $Q_{a=1}$ and $Q_{a=2}$ are

$$Q_{a=1}(i|i') = \begin{pmatrix} 0.75 & 0.25 \\ 0.2 & 0.8 \end{pmatrix} \quad \text{and } Q_{a=2}(i|i') = \begin{pmatrix} 0.5 & 0.5 \\ 0.633 & 0.333 \end{pmatrix}$$

Similar to the estimation of $P_{a=0}$, $Q_{a=0}$ is determined from $Q_{a=1}$ by using the same factor $h$.

Then, the transition probability matrix is

$$Q_{a=0}(i|i') = \begin{pmatrix} 0.510 & 0.490 \\ 0.102 & 0.898 \end{pmatrix}$$
On the local level, it is assumed that the transition probability matrices have been perturbed linearly by scalars \( k = (k_1, k_2) \) depending on the NC level optimal actions. We selected arbitrarily small values for \( k = (k_1, k_2) \). Choosing \( k_1 = 0.001 \) and \( k_2 = 0.0015 \), the following transition probability matrices of wait action are obtained:

\[
Q(a^L_t = 0, R_{t}^{SL} = 1) = \begin{pmatrix} 0.511 & 0.489 \\ 0.103 & 0.897 \end{pmatrix} \quad \text{and} \quad Q(a^L_t = 0, R_{t}^{SL} = 2) = \begin{pmatrix} 0.5115 & 0.4885 \\ 0.1035 & 0.8965 \end{pmatrix}
\]

The transition probability matrices of type 1 alert and type 2 alert when the NC level optimal action is known can be easily calculated using the same procedure.

The observations on the local and NC levels help us to update our belief on underlying core state of the system. In the next two sections, we determine the probabilities of observations for the local and NC levels.

### 4.2.3. Information Matrix for NC Level

We estimate the information matrix for the NC level, \( B^S \), using the number of influenza like illnesses (ILI) in North Carolina reported by the Sentinel Provider Network weekly. The NC DHHS Influenza Sentinel Provider Network Data between March 2009 (9th Week of 2009) and April 2010 (13th Week of 2010) consists of 23793 ILI cases including seasonal influenza and unconfirmed cases. Thus, the number of H1N1 cases is a subset of the number of ILI. However, we assume the real number of H1N1 cases does not have a significantly different trend from the ILI cases and the number of ILI is a close enough approximation for the H1N1 cases. The number of ILI per week has a maximum of 1477 and a minimum of 47.
In order to estimate $B^S$ from NC DHHS Influenza Sentinel Provider Network Data, we also need to know when the system is in the state 0 (no pandemic threat) or State 1 (pandemic threat exists). For estimation of the transition probability matrices, we develop a condition for classifying the core state 0 or 1 and determined the core state for each week between March 2009 and April 2010 based on the FluView report of the CDC. Since the data span the same time interval, the same classification is assumed to be true in the estimation of information matrices. Then we estimate the probability of observing the number of ILI given the system is in core state 0 and core state 1. The information matrix for NC level is

$$B^S = \begin{pmatrix} 0.9355 & 0.0645 & 0.0000 \\ 0.2308 & 0.3077 & 0.4615 \end{pmatrix}$$

The rows of $B^S$ correspond to core states 0 (no Pandemic threat) and 1 (threat exists) respectively; the columns of $B^S$ correspond to intervals of number of ILI $[0, 300)$, $[300, 800)$ and $[800, \infty)$ respectively. In Section 3.3.2, we defined $B^S$ to depend on both observations from the NC level and observations from local level, $O_{LS}$. (i.e. $\beta_{ik}^S \equiv \Pr\{X_i^S = k, O_{t}^{LS} = m | S_i^S = i\}$ for $i, k, m$). However, to simplify the estimation process, we suppress this relationship. Hence, the definition of $B^S$ is altered as follows:

$$\beta_{ik}^S \equiv \Pr\{X_i^S = k | S_i^S = i\} \text{ for } i, k$$

The estimation of the information matrix of the local level is discussed in the next section.
4.2.4. Information Matrix for Local Level

The information matrix $B^l$ for the local level shows the probability of observing a certain value that corresponds to the number of H1N1 cases originating from the counties and identified by the State Laboratory given the core state is known. NC DHHS State Laboratory reports influenza cases, their virus type and which county they are from weekly. NC DHHS State Laboratory Data between 03/07/2009 and 04/01/2010 consists of 1869 confirmed influenza cases. 1500 of these were identified as Type A (H1N1) pandemic virus. These 1500 cases originated from 92 counties with a minimum of 1 isolate and a maximum of 13 isolates of the same virus from the same county. Similar to $B^s$, we use the identified core states which are known according to our analysis on the transition probability matrix. In other words, the weeks that are assumed to be in core state 0 with respect to the baseline (or weekly average) analyses are assumed to be in core state 0 for the information matrix estimation. Then the information matrix for the local level is

$$B^l = \begin{pmatrix} 0.9459 & 0.0342 & 0.0199 \\ 0.9451 & 0.0485 & 0.0063 \end{pmatrix}$$

The rows of $B^l$ correspond to core state 0 (no pandemic threat) and core state 1 (threat exists) respectively; and columns of $B^l$ correspond to intervals of the number H1N1 cases $[0,5), [5,10)$ and $[10, \infty)$ respectively. After developing the model and estimating the necessary parameters, the next step is to solve the model. We discuss how to solve the POMDP model in the next section.
4.3 Solution Method

POMDPs generalize MDPs; however this generalization increases the computational complexity by adding an additional dimension due to the uncertainty of states. In comparison to MDPs, POMDPs have an infinite state space. Furthermore, an optimal policy for a POMDP is defined over a continuous state space. These features of a POMDP increase the computational effort and memory required to solve the model optimally. In addition, our model has a nested two level structure which doubles the size of the model and increases its computational complexity. Thus, we use an approximation algorithm called the fixed-finite-grid method (For detailed information on solution techniques of POMDPs, see Lovejoy’s (1991) and White’s (1991) surveys). In this method, the belief space $\pi$ is discretized by grids and belief state values that lie between grid points are interpolated. The grid size is an important factor with respect to the performance of the algorithm. The smaller the grid size is, the better the approximation. However, computational time also increases for smaller grid sizes. We define $\hat{V}_i(\pi^n)$ as the finite-grid approximation of the optimal value function $V_i^*(\pi^n)$. Then, it can be shown that $\hat{V}_i(\pi^n) \geq V_i^*(\pi^n)$ (Hauskrecht, 2000). Thus, grid-based approximation yields to an upper bound on the optimal solution.

The finite-grid method was developed for POMDPs with one decision maker. In order to implement this approximation technique for our two-level nested model, we produce an iterative scheme. The iterative solution scheme starts by evaluating the optimal value function with the finite-grid technique for the initial decision epoch of the time horizon at the NC level and produces the optimal solution of the NC level. The solution of the NC level is
fed to the local level as the value of $R_t^{SL}$ and is used to update the belief state at the local level. Thus, the optimal action of the NC level affects the optimal action of the local level. After obtaining the optimal solution of the local level, we proceed with the NC level for the next decision epoch. Since the effect of the local observations on the NC level’s information matrix is ignored, sending the local observation values to the NC level is not required. Figure 4 presents the iterative solution scheme.

![Figure 4: The iterative solution procedure of the local and NC level](image)

The global optimality of solutions in both levels are not guaranteed due to the heuristic nature of the designed iterative solution procedure.

In the next chapter, we use the estimated parameters to solve the model according to the finite-grid approximation technique and present the numerical results.
CHAPTER 5

Numerical Results

The fixed-finite-grid approximation method is implemented in C++ and a grid size of 100 was used for all experiments. Solutions were found in less than one minute using a computer with a 2.39 GHz Intel® Core(TM)2 Quad CPU and 3.25 GB of RAM. To measure the value function of belief values that are between grid points, linear approximation of adjacent grids is used. Dataset used for the parameter estimation includes the influenza surveillance of approximately 1.5 years. Based on the data span, time horizon is set to 100 weeks. The model is not discounted, in other words, discount factor \( \sigma \) is assumed to be 1. The reasons we chose a non-discounted reward function are that the immediate reward function involves the relative weights of the different type of alerting instead of the actual costs of alerting and the time horizon is relatively short length. In the following sections, we introduce the test set for the numerical experiments and present the optimal solutions for the NC and local levels. We also illustrate how the system responds to changes in the values of several parameters.

5.1 Test Set

As mentioned in Section 3.3.6, the reward function is developed to measure the effect of different weight schemes with respect to the cost values of false, late and timely alerting. All weight values are assumed to be between 0 and 1 (i.e. \( c_{n_{\text{alert\_type}}}^{n} \in [0,1] \) for \( \forall \text{alert\_type} \) and \( n=\text{local, NC} \)) since they represent the relative relationship of the cost of different alert types. We develop a test set as illustrated in Table 4 to explore the effect of different orderings between false and late alerts. Hence, in this test set we rank the weight of
late alert, the weight of false alert 1 (of type 1 alert) and the weight of false alert 2 (of type 2 alert) are varied while keeping the weight of timely alerts (type 1 and type 2) at a fixed value. In addition, all weight values in the test set satisfy the relationship inequalities defined in Section 3.3.6 so that the weights associated with type 1 alerts are smaller than the weights associated with type 2 alerts and also the weight of false alerts are larger than the weight of timely alerts. The weights in the test set are varied by small increments for the base case and the other cases. Later, they are systematically increased to the values close to 1 as we conduct the sensitivity analysis in order to evaluate the effect of such increase. The weights are kept the same for the local and NC level while solving the model iteratively.

Table 4: Test Set

<table>
<thead>
<tr>
<th>Case</th>
<th>Weight structure</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base Case</td>
<td>False alert 2 &gt; False alert 1 = Late alert</td>
<td>$[c_{late}, c_{false1}, c_{false2}, c_{alert1}, c_{alert2}]$</td>
</tr>
<tr>
<td>Case 2</td>
<td>False alert 2 = Late alert &gt; False alert 1</td>
<td>[0.25, 0.2, 0.25, 0.1, 0.15]</td>
</tr>
<tr>
<td>Case 3</td>
<td>Late alert &gt; False alert 2 &gt; False alert 1</td>
<td>[0.3, 0.2, 0.25, 0.1, 0.15]</td>
</tr>
<tr>
<td>Case 4</td>
<td>False alert 2 &gt; Late alert &gt; False alert 1</td>
<td>[0.25, 0.2, 0.3, 0.1, 0.15]</td>
</tr>
<tr>
<td>Case 5</td>
<td>False alert 2 &gt; False alert 1 &gt; Late alert</td>
<td>[0.2, 0.25, 0.3, 0.1, 0.15]</td>
</tr>
</tbody>
</table>

In the following section, the optimal policies under the weights of the test set for the NC level are presented.

5.2 Numerical Results for NC Level

The results of the test cases are shown in Figures 5 through 9. The figures show the graph of the (approximate) optimal policy of the NC level as a function of time and belief.
state. Since there are only two core states in the model, we can easily calculate the belief of being in State 0 if we know the belief of being State 1 or vice versa. Observing a new value at the NC level (the number of ILI cases), the belief state can be derived from the information matrix. The belief state in the figures represents the probability of being state 0 (no pandemic). The area under the graphs is colored according to the optimal actions for each case. Areas colored in red, yellow or green indicates that the optimal action is to issue a type 2 alert, to issue a type 1 alert or wait, respectively. Figure 5 illustrates the optimal actions of the base case where the weight of false alert 1 is equal to the weight of late alert.

Figure 5: The optimal policy of the NC level when $c_{\text{false alert 1}}$ and $c_{\text{late alert}}$ are 0.2 and $c_{\text{false alert 2}}$ is 0.25
The optimal policies at the NC level include all three types of actions. The wait action becomes the optimal action in the last eight decision epochs starting with belief states larger than 0.335 at time 100 and at time 93, the optimal action is “Wait” if the belief of being in no pandemic state is larger than 0.975.

Figure 6 demonstrates the approximate optimal solutions of case 2 where the weight of late alerts is increased to 0.25 while the weight of false alert 1 and false alert 2 is kept same as the base case (0.2, 0.25 respectively).

Figure 6: The optimal policy of the NC level when $C_{falsealert2}^n$ and $C_{falsealert1}^n$ are 0.25 and $C_{falsealert1}^n$ is 0.20.

The optimal policy of case 2 is similar to the base case. The only difference between these cases is that the threshold probability of being no pandemic state between type 1 alert and
waiting is greater at case 2 than the base case (i.e. at time 100, the threshold probability is 0.425 for case 1, while it was 0.335 for the base case). Therefore, the system tends to issue more type 1 alerts than waiting which is expected since the weight of late alert is greater for case 2 than the base case.

If we keep increasing the weight of late alert, we observe a similar pattern as the probability of waiting decreases more as shown in Figure 7. For case 3, wait is the optimal action if the belief state of being no pandemic is greater than 0.505 at time 100. This result is intuitive because the late alerts are penalized more than false alerts; in response the system issues alerts more instead of waiting.

![Figure 7: The optimal policy of the NC level when $c_{\text{late alert}}^{n} = 0.3$, $c_{\text{false alert 2}}^{n} = 0.25$ and $c_{\text{false alert 1}}^{n} = 0.20$.](image)

Figure 7: The optimal policy of the NC level when $c_{\text{late alert}}^{n} = 0.3$, $c_{\text{false alert 2}}^{n} = 0.25$ and $c_{\text{false alert 1}}^{n} = 0.20$. 

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In Case 4, we slightly increased the weight of false alert while the weight of late alert
and false alert 1 are fixed at the base case. The effect of this change on the optimal policy
with respect to the base case is seen at the threshold between wait and type 1 alert again (i.e.
0.335 and 0.425 at time 100 for the base case and case 4, respectively). The optimal policy
is illustrated in Figure 8. Although it is hard to see from the figure, the area of type 2 alert
decreases compared to the base case. However, the threshold probability between type 1 and
type 2 alert stays the same in the long run.

Figure 8: The optimal policy of the NC level when $c^n_{falsealert2}$ is 0.3, $c^n_{latealert}$ is 0.25
and $c^n_{falsealert1}$ is 0.20.

In the last case (Case 5), the weight of false alert 2 is set as the largest weight and the
weight of false alert 1 is increased above the weight of a late alert. This is the case where the
area of wait action is the largest, presented in Figure 9. In case 5, it is 0.285 whereas it is 0.335 in the base case. We also observe that wait becomes the optimal action for a longer time interval (i.e. in all other cases, the last decision epoch with wait being an optimal action is 93 while in case 5, this is 91).

Figure 9: The optimal policy of the NC level when $C_{false\_alert\_2}^n$ is 0.25, $C_{false\_alert\_1}^n$ is 0.2 and $C_{late\_alert}^n$ is 0.25.

The optimal policies in the test set are similar to each other due to the small magnitude of the changes in the weights for the cases. We also observed that wait is the optimal action for a shorter time while type 1 and type 2 action often dominate wait action. We hypothesize that the reason for this behavior is that the estimated transition probability matrices of wait and type 1 alert are close to each other. When the weight of false alert 1 is
not significantly large, wait is dominated by the type 1 alert because the similarity between
the transition probabilities. The transition probability associated with wait was developed
from the transition probability associated with type 1 alert and the factor $h$. Depending on the
magnitude of $h$, the similarity between the transition probabilities may change. Another
significant finding is that in all cases the system converges to the same threshold probability
between type 1 and type 2 alert which is 0.405. The stationary transition probability matrices
and supressing the effect of the local level on the NC level could be two possible causes of
the existence of the long run threshold between type 1 and type 2 alert at the NC level.

In the following section, we explore the optimal policies of the local level for the
same test set.

5.3 Numerical Results for Local Level

The local optimal actions in every decision epoch are shaped by its observations
$(X_i^L)$, reward function $(C_i^L)$ and the optimal action of NC level one decision epoch prior
$(R_i^{NC})$. We used the same weights with the NC level (i.e. $c_j^L = c_j^S, \forall j$) and the following
results are obtained. The results are presented in the Figures 10 and 11. Figure 10 has with
the same format of the NC level figures. Similar to the NC level, the belief state can be
calculated from observing a new value at the local level (H1N1 cases identified at the State
Labs) and according to the belief state and time, the optimal action can be detected.

The optimal policy of the base case is shown in Figure 10. This is the case where the
weights of late alert and false alert 1 are equal and the weight of false alert 2 has the greatest
value.
Figure 10: The optimal policy of the local level when $C_{\text{false alert } 1}^n$ and $C_{\text{late alert}}^n$ are 0.2 and $C_{\text{false alert } 2}^n$ is 0.25.

The optimal policy of the local level for the base case consists of wait and type 1 alert. The threshold between wait and type 1 alert for a fixed decision epoch increases over time, but the increase is not monotonic (i.e. at time 100, if the belief of being in a no pandemic state is smaller than 0.335, the optimal action is type 1 alert, while at time 80, this value is observed as 0.225).

In order to compare how the different weights of alerts change the optimal policies at the local level, the optimal policies of all test cases are shown in Figure 11. For the selected case, the optimal action is to wait for the belief states that are on the right side of the line and to issue a type 1 alert for those that are on the left side.
If we compare case 2 and case 4, because we only increase the weight of false alert 2 (i.e. 0.25 for case 2, 0.3 for case 4) and type 2 alert is not the optimal action at the local level, the optimal policies of case 2 and case 4 are equivalent to each other.

When we increase the weight of late alert from 0.25 (the base case with the blue line) to 0.3 (cases 2&4 with red&green lines), as expected the system tends to issue more type 1 alerts than waiting in order to decrease the possibility of late alerts which are penalized with the larger weight. This trend continues as we increase the weight of late alerts as demonstrated in Case 3 (purple line) which has the smallest area associated with the wait action.
These experiments show that small changes in the weight of false alert 2 do not have a significant affect on the optimal policy. On the other hand, the small changes in the weight of the false alert 1 have an impact on the shape of the optimal policy. The optimal policy with the least Type 1 alerting, case 5, happens when we increase the weight of false alert 1 and false alert 2 compared to the base case.

Because of the effect of the NC level optimal actions on the local level, we observe a different pattern in the threshold between wait and alerting than the NC level. This threshold does not converge to a value in the long run for the test set. The optimal policy of any belief state or time does not involve Type 2 alerts. One possible cause of this may be the estimated transition probability matrices of the local level. The local level transition probability matrix of type 2 alert does not distinguish with the local level transition probability matrix of type 1 alert. Thus, it is mostly dominated by type 1 alert if the weights of type 1 and type 2 alerts are not significantly different from each other. We explore in the next section whether the change in the weights or other parameters produces optimal policies with different structures in the NC and local level.

5.4 Sensitivity Analysis

The model is populated with the parameters from various sources. Some parameters such as the transition probability and information matrices are derived directly from datasets; some are adopted from the literature. As in the case of the cost parameters, we determine them as the relative weights and leave the choice of right values to public health experts. However, the variation in these parameters may lead to changes in the optimal policy. Therefore, we conduct one-way sensitivity analysis on the cost parameters, \( h \) (the factor
used for estimating the transition probability matrices of wait action) and \( k = (k_1, k_2) \) (the scalars that shape the effect of the NC level on the local level). Table 5 summarizes the base case values of these parameters and the lower-upper bound values they varied between.

Table 5: The Base, Lower Bound and Upper Bound Values of Parameters for the Sensitivity Analysis

<table>
<thead>
<tr>
<th>Cost Parameters</th>
<th>Sensitivity on</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Base</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[LB - UB]</td>
</tr>
<tr>
<td>The weight of late alert</td>
<td>0.2</td>
<td>[0.05 – 0.8]</td>
</tr>
<tr>
<td>The weight of false alert 1</td>
<td>0.2</td>
<td>[0.05 – 0.8]</td>
</tr>
<tr>
<td>The weight of false alert 2</td>
<td>0.25</td>
<td>[0.05 – 0.8]</td>
</tr>
<tr>
<td>The weight of alert 1</td>
<td>0.1</td>
<td>[0.025 – 0.6]</td>
</tr>
<tr>
<td>The weight of alert 2</td>
<td>0.15</td>
<td>[0.025 – 0.6]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Transition Probability Factors</th>
<th>Sensitivity on</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Base</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[LB - UB]</td>
</tr>
<tr>
<td>( h )</td>
<td>0.51</td>
<td>[0.3 – 0.9]</td>
</tr>
<tr>
<td>( k = (k_1, k_2) )</td>
<td>(0.001,0.0015)</td>
<td>[(0.001,0.0015) – (0.05,0.0075) – (0.01,0.015) – (0.05,0.075)]</td>
</tr>
</tbody>
</table>

The results of sensitivity analysis are presented in the following sections.

5.4.1 Sensitivity on Cost Parameters

The cost parameters that are determined as the weights of late alerts, false alerts and timely alerts are varied between lower and upper values depending on the base case value of that parameter. Since there are some relationship inequalities between these weights that must hold in every case, it is impossible to carry out one-way sensitivity analysis for some parameters (i.e. when the weight of false alert 1 is increased, the weight of false alert 2 should be increased to a value that is larger than the weight of false alert 1).
The weight of late alert in the base case is set as 0.2. Figure 12 is a one-way sensitivity analysis on the effect of weight of the late alert by varying $C^S_{latealert}$ from 0.05 to 0.8 at the NC level.

**Figure 12: The optimal policies of the NC level for various $C_{late alert}$ values**

In Figure 12, T1 lines present the threshold probabilities that the optimal action is type 1 alert for the belief values on the left side of the T1 line and wait for the belief values on the right side of line. Similarly, T2 lines distinguish the threshold probabilities of the optimal action being type 2 alert or type 1 alert. The system seems to be robust with respect to changes in the weight of late alert. While type 2 alert is mostly unaffected by the weight of the late alert, the area where wait is the optimal action increases (decreases) as the weight of late alert decreases (increases).
Figure 13 shows the optimal policies of the local level when the weight of late alert is varied from 0.05 to 0.8 and the base weight is 0.2.

![The optimal policies of the local level for various $C_{\text{late alert}}$](image)

The optimal policy for the local level involves only type 1 alert and wait. The right side of each line correspond to the belief states where wait is the optimal action and for the belief states that are on the left side of the lines, the optimal action is type 1 alert. Although the optimal policy in all cases does not contain a type 2 alert, the change in the weight of late alert has a significant impact on the overall policy. The smaller the weight of late alert is, the less likely type 1 alert is the optimal action. Eventually, when the value is 0.05, the optimal policy is to wait for all belief states. When we consider the transition probability matrices of the local level and the effect of the NC level actions on the local policy, the results are intuitive since the weight of late alert is one of the factors that drives system to issue alerts.
The weight of false alert 1 is one of the cost parameters that is bounded by the other weights. As a result, we cannot carry out one-way sensitivity analysis for $C_{falsealert1}^n$. The lower value for the weight of false alert 1 is $C_{falsealert1}^n = 0.05$. To satisfy relationship inequalities, keeping the ratio of $C_{falsealert1}^n / C_{alert1}^n$, the weight of type 1 alert (timely), $C_{alert1}^n$ is decreased to 0.025. At NC level, the optimal policy is shown in Figure 14. As expected, decreasing the value of false alerting and the cost of alerting for type 1 alert reduces the cases where wait is the optimal action.

Figure 14: The optimal policy of the NC level when $C_{falsealert1}^n$ is 0.05 and $C_{alert1}^n$ is 0.025.
The effect of decreasing type 1 alert related weights on the local level is similar to that found for the NC level where the system tends to issue more type 1 alerts than waiting, as shown in Figure 15.

![Figure 15](image)

**Figure 15:** The optimal policy of the local level when $c_{falsealert_1}^n$ is 0.05 and $c_{alert_1}^n$ is 0.025.

The upper bound on $c_{falsealert_1}^n$ is 0.8. To ensure that the weight of false alert 2 is greater than the weight of false alert 1, we also increase $c_{falsealert_2}^n$ to 0.85. We report the optimal policies of the NC level and local level when the weight of false alert 1 is increased to the upper bound and the weight of false alert 2 is adjusted accordingly in Figure 16 and Figure 17, respectively.
Figure 16: The optimal policy of the NC level when \( c_{false alert 1}^{n} = 0.8 \) and \( c_{false alert 2}^{n} = 0.85 \).

The weights of false alerts in the test set produced fairly robust optimal policies that consisted of type 2 alerts and type 1 alerts for a large belief state set for the NC level. However, when we increase the weight of false alerts to the upper bounds, we observe a different behaviour where type 1 alerts are dominated by “Wait” for larger values of the belief states. The area associated with type 2 alerts in the optimal policy is not affected by the change of the weights of false alerts because the weights of timely alerts \( (c_{alert 1}^{n}, c_{alert 2}^{n}) \) are small.
Figure 17: The optimal policy of the local level when $c_{false alert 1}^n$ is 0.8 and $c_{false alert 2}^n$ is 0.85.

As a result of penalizing the false alerts with a large weight, the optimal policy is less likely to alert than wait. One interesting result at the local level policy is that this is the first case we observe type 2 alert being one of the optimal decisions. Since the optimal policies are influenced by the weights of alerts as well as the transition probability matrices and the information matrices, it is difficult to predict or explain why one action becomes optimal or dominates the other actions in different scenarios.

The weight of false alert 2 is bounded below by the other alerting weights. The one-way sensitivity analysis is possible if only we increase its value, however the other weights in the system need to be adjusted if the weight of the false alert 2 is reduced. Using the same
upper and lower bounds (0.05, 0.8), the optimal policies of the NC level is presented in Figure 18. The base case \( c_{falsealert2}^n = 0.25 \) and the upper bound case \( c_{falsealert2}^n = 0.8 \) have the same weights for all other alerting types whereas the weight set in the lower bound case is modified in order to comply the relationship inequalities while the ratios \( c_{falsealert1}^n/c_{alert1}^n \) and \( c_{falsealert2}^n/c_{alert2}^n \) are kept same as for the base case.

![The Optimal Policies of the NC level for various False Alert 2](image)

Figure 18: The optimal policy of the NC level for various \( c_{falsealert2}^n \) values

The same weights of false alert 2 generated the optimal policies shown in Figure 19 in the local level. The base case and upper bound case produced the same optimal policy since type 2 alert is not favorable even when its weight was smaller than the upper bound. The probability transition matrices associated with type 2 alert and type 1 alert seems to be one of the reasons that type 2 alert is not one of the optimal actions of the base case in the
local level. For the lower bound case, the optimal policy consists of type 1 alert and wait but the type 1 alert is the optimal action for a smaller set of belief states compared to the base case. This is due to the weights associated with the type 1 alert and false alert 1 which are reduced to compensate for the decrease in the weight of false alert 2.

![The optimal policies of the local level for various $C_{false\ alert2}$ values](image)

Figure 19: The optimal policy of the local level for various $C_{false\ alert2}$ values

The weight of alert 1, $C_{alert1}^n$, is assumed to be 0.1 for all cases of the test set. Sensitivity analysis of this weight is presented in Figures 20 and 21 for the NC level. When the weight is assigned to its lower bound (0.025), the optimal policy and the base case optimal policy (demonstrated in Figure 20) resemble each other. Type 1 alert is observed more frequently for the lower bound case due to the small weight corresponding to issuing a type 1 alert.
Figure 20: The optimal policy of the NC level for various $C_{\text{alert}1}^n$ values

When the weight of alert 1 is at its upper bound, $C_{\text{alert}1}^n = 0.6$, and the rest of weights are altered accordingly, the optimal policy in the NC level (as shown in Figure 21) eliminates the type 1 alert and replaces it with waiting because of the high cost of issuing a type 1 alert (false or timely).
Figure 21: The optimal policy of the NC level when $c_{false\text{alert}1}^n$ is 0.8 and $c_{alert1}^n$ is 0.6.

The optimal policies for the local level corresponding to the different values of $c_{alert1}^n$ are presented in Figure 22. For the upper bound, waiting is optimal for all belief states. This is the case where all weights associated with type 1 alert and type 2 alert (false and timely) are increased in order to accommodate the weight of a type 1 alert. As the weight of alert 1 decreases, the optimal policy includes type 1 alert for more belief states.
Figure 22: The optimal policies of the local level for various $C_{alert1}$ values

If the weight of alert 2 is subject to same upper and lower values as the weight of alert 1, the optimal policies of the NC level change as shown in Figure 23. The increase in the weight of alert 2 and false alert 2 (at the upper bound) results in a smaller threshold probability between type 1 and type 2 alert while no change occurs between wait and type 1 alert. On the other hand, the optimal policy of the lower bound is close to the optimal policy of the base case with a smaller set of belief states for which waiting is the optimal action. We should also consider the fact that the weight of alert 1 is also decreased when the weight of alert 2 is set to its lower bound.
Figure 23: The optimal policies of the NC level for various $C^n_{\text{alert } 2}$ values

For the local level, increasing the weight of alert 2 (along with its weight of false alert 2) provided an equivalent optimal policy with the base case, as seen in Figure 24. Because type 2 alert is still not favorable in comparison to type 1 alert and wait. The optimal policy when the weight of alert 2 is set to the lower bound has more type 1 alerts than the base case because the weight of alert 1 is decreased along with alert 2 in order to maintain the ordering defined in Section 3.3.6.
When we compare the changes in the optimal policies for the local and NC levels, the local level seems to be more sensitive to the changes in the cost-related parameters. In contrast, the NC level has the same structure of optimal policy in most cases although there are some examples of optimal policies with different structure in the NC level as seen in Figures 16 and 21.

**5.4.2 Sensitivity on $h$**

The factor, $h$, is that is used to construct the transition probability matrices of corresponding to wait action at the local and NC levels from the estimated transition probability matrices of the type 1 alert. From the literature, $h$ is assumed to be 0.51 (Thacker et al., 1986). Figure 25 is a one-way sensitivity analysis on $h$ for the NC level (in which the lower and upper bounds are 0.1 and 0.9, respectively).
Figure 25: The optimal policies of the NC level for various $h$ values

The transition probability matrices of wait is closely related to the transition probability matrices of type 1 alert and $h$. Thus, the change in $h$ affects the optimal policy regarding the “wait” and “type 1 alert” actions. When $h$ is equal to the upper bound, the wait action is optimal when the belief state is greater than 0.335 at time 100 and 0.685 at time 1. On the other hand, the lower bound reduces the cases when wait is the optimal action. When $h$ is 0.1, wait is the optimal action only at time 100.

Figure 26 shows the one-way sensitivity analysis for $h$ on the local level. The transition probability matrices associated with the wait action are determined by $h$. Increasing $h$ means that alerting (type 1 alert) is more effective than waiting. Thus, there are more type 1 alerts for the upper bound and more waiting for the lower bound.
Figure 26: The optimal policies of the local level for various $h$ values

From the above discussion it is clear that the transition probability matrices have a significant influence on the optimal policies on the NC and local levels. Although we only change the relationship between wait and type 1 alert, the optimal policies, especially on the NC level, significantly differ from the base case.

5.4.3 Sensitivity on $k = (k_1, k_2)$

The factors, $k = (k_1, k_2)$ model the effect of the NC level on the local level. This is formulated as a linear effect on the transition probabilities of the local level depending on the optimal action of the NC level in Section 3.3.5. The larger $k = (k_1, k_2)$ are the greater the influence of the NC level on the local level. Figure 27 shows the threshold probabilities
between the type 1 alert and wait to be the optimal action of the local level for various multipliers of \( k = (k_1, k_2) \). The multipliers of \( k = (k_1, k_2) \) are determined as follows:

\[
ak = (a \cdot k_1, a \cdot k_2)
\]

where \( a = 5, 10, 50 \)

![Wait and Type 1 alerts of the local level for various k](image)

Figure 27: The threshold probabilities of wait and type 1 alert of the local level for various \( k = (k_1, k_2) \) values

As \( k = (k_1, k_2) \) increases, the difference between the threshold probabilities of the wait and the type 1 alert actions of two consecutive decision epochs increases at the end of the time horizon. In the beginning of the time horizon, the optimal policies seems to be insensitive to the changes in \( k = (k_1, k_2) \). Another interesting result is that type 2 alert is one of the optimal actions for the larger \( k = (k_1, k_2) \). Although the type 2 alert is the optimal action for a few decision epochs, these are some cases that the optimal policy for the local level includes type
2 alert. Table 6 presents the decision epochs where the type 2 alert is one of the optimal actions.

Table 6: Cases where the optimal policy includes type 2 alerts.

<table>
<thead>
<tr>
<th>$k = (k_1, k_2)$</th>
<th>Decision Epoch</th>
<th>Belief States Associated With The Optimal Action:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Wait</td>
</tr>
<tr>
<td>10$k = (0.01, 0.015)$</td>
<td>99</td>
<td>(0.345-1)</td>
</tr>
<tr>
<td>50$k = (0.05, 0.075)$</td>
<td>99</td>
<td>(0.415-1)</td>
</tr>
<tr>
<td></td>
<td>98</td>
<td>(0.355-1)</td>
</tr>
<tr>
<td></td>
<td>97</td>
<td>(0.355-1)</td>
</tr>
</tbody>
</table>

The optimal action is type 2 alert within the intervals of the belief states, specified in the last column of Table 6. One major finding is that the ordering on the optimal actions is non-monotonic. At time 99 of $10k = (0.01, 0.015)$ and time 97 of $50k = (0.05, 0.075)$, the optimal action sequence is as follows: type 1 alert, type 2 alert, type 1 alert and wait. Therefore, the optimal policy for the local level is not of a control limit type with respect to belief states because of the increased effect of the NC level.

5.4.3 Summary of Sensitivity Analysis

The weights of cost parameters affect the optimal policy. While some of them significantly change the shape of the optimal policy, others affect the threshold probabilities.
between type 1 alert - type 2 alert and type 1 alert – wait. The NC level seems to be more robust with respect to the changes in the cost weights. h-sensitivity analysis show that the transition probabilities are as important as the cost parameters in constructing the optimal policy. The optimal policy of the local level is affected by the the effect of the NC level on the local level. When it is increased, non-monotonic optimal policies are found.
CHAPTER 6

Conclusion

We develop a novel model to explore the dynamics of local and state health departments under the potential threat of a pandemic influenza outbreak, particularly a H1N1 outbreak. The model seeks to capture the relationship between local and state entities as well as the disease spread and how this relationship affects the optimal policy of responding for an outbreak. The control action we investigate is alerting, we study the effect of the cost of late alerts and false alerts on the optimal policy.

One key conclusion can be derived from our experiments is that local level is more sensitive to the changes in the weights of late alerts and false alerts than the NC level. Although, the shape of optimal policy – “Wait” until a threshold value then “Issue a type 1 alert” afterwards- stays the same for all experiments, it is evident that when the assigned weights of late alerts are increased then the threshold of “Issue a type 1 alert” increases.

At the NC level, the system is not sensitive to the weights of late and false alerts in the long run. One interesting result for NC level is that all experiments converge to same threshold value (Belief of being no pandemic threat=0.405). The optimal policy is to “Issue a type 1 alert” for belief values greater than the threshold value in all cases. The different weights for late and false alerts only affect the end of time horizon decisions, namely the “wait” action. The long run threshold value could provide a useful insight for public health policy makers.
From the sensitivity analysis, we observed that the optimal policy is sensitive to the weights of cost parameters. While some of them only cause small changes in the optimal policy (i.e. the weight of late alert on the NC level policy), some results in significantly different optimal policies (i.e. the weight of false alert 1 on the local and NC level policy). Similar to the testset, the local level policy is more influenced by the cost weights than the NC level policy. The sensitivity analysis on \( h \) confirms that the transition probability matrices shape the optimal policy as well as the cost parameters. With a different set of estimated transition probabilities, we may determine different types of optimal policies on the local and NC level. The sensitivity on \( k = (k_1,k_2) \) shows that increasing the effect of the NC level on the local level reduces the smoothness of the threshold probabilities between the type 1 alert and wait actions. It also produces non-monotonic optimal policies on the belief states for larger \( k = (k_1,k_2) \).

The optimal policies of all numerical experiments except \( 10k = (0.01,0.015) \) and \( 50k = (0.05,0.075) \) appear to be control-limit type with respect to belief states as a function of time. In other words, there is an ordering of the optimal actions depending on their severities and the optimal actions for the belief states at a given decision epoch follow this ordering. The control limit type of optimal policy is an expected for a two-state POMDP, but the fact that the relationship between the local and NC levels can remove this property is interesting. It is difficult to deduce the iterative effect of levels on the optimal policies of each other.
There are some limitations to this research. Several simplifying assumptions reduce the level of realism in the model. Data that are used to estimate transition probabilities are another limitation to the model since they are collected by varying entities and even for the same target population, the magnitude of observations are significantly different.

The core state definition (i.e. when system is in “No pandemic threat” or “Pandemic threat exists”) is open to discussion since there is no current estimate in the literature that defines the transition of an outbreak. In this model, we only use one variable to identify the state of the system, whereas there are more variables such as mortality, hospitalizations, affected age groups, etc. that are indicators of an outbreak, i.e. being in the “Pandemic threat exists” state. Furthermore, the stationary assumption of the transition probability matrices seems unrealistic due to nature of an outbreak. Future work could capture the disease pattern better if an in-depth data set is used to estimate non-stationary transition probability matrices.

In addition, increasing the number of states could bring the model into a more realistic setting. The Department of Homeland Security has a color-coded threat level system which has five levels of threat: Depending on likelihood of a threat, these levels are low, guarded, elevated, high, and severe (dhs.gov). A similar scheme for our model could be future research.
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