

MODELLING THE RESPONSE OF A PUBLIC HEALTH DEPARTMENT TO INFECTIOUS DISEASE

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ABSTRACT

We present a discrete-event simulation model of the response of a local public health department (LHD) to pertussis cases. We take a comprehensive view of public health actions, beginning with detection of an individual patient, confirmation of the case by physician and lab tests, and contact tracing and isolation of contacts by LHD personnel. We explicitly model the information transfer between providers, laboratories and LHDs, and examine the effect of different alerting strategies on the number of confirmed cases encountered. The effect of limited resource availability for contact tracing is also examined. Given our results, we suggest that resource availability has significant impact on the progression of a disease outbreak, as do information delays at various stages of the process.

1 INTRODUCTION

The role of public health personnel, especially those from local public health departments (LHDs), in emergency preparedness is widely recognized. However, most LHD personnel are engaged in significant routine duties in addition to those associated with emergency preparedness, such as monitoring outbreaks of infectious diseases and implementing countermeasures when such are identified. State laws require many infectious diseases such as pertussis, various sexually transmitted diseases, food borne illnesses and tuberculosis to be reported to the LHD or state health department within 24 hours of diagnosis by any

health provider in that LHD's jurisdiction. LHD personnel must follow up on all such reported cases, making sure that necessary measures are taken to prevent wider transmission and to treat patients already infected. One of the most common types of countermeasures used by LHDs in the face of an infectious disease is contact tracing, where contacts of infected patients are identified, located and either treated, vaccinated or isolated to prevent their infecting additional patients. Given that there are many different infectious diseases that a LHD must potentially be monitoring at any given time, surveillance of the population to detect an outbreak and the execution of countermeasures such as contact tracing constitute a very significant fraction of the workload of an LHD. This routine workload, in turn, must by necessity affect the ability of the LHD to rapidly detect emergency situations such as an outbreak of a new disease (such as the H1N1 influenza) or a bioterrorism attack. Hence an effective characterization of the ability of a LHD to react to an emergency situation must begin with a thorough understanding of the routine workload of its personnel; only then can we begin to assess the ability of the LHD to recognize and react to a new situation in a timely manner.

In this paper we develop a simple simulation model that combines an epidemiological model of disease transmission with a discrete event model of the process undergone by infected patients and their contacts in a LHD. We explicitly model the limited resources available for contact tracing as a multiserver queue, allowing us to capture the effect of workload on the time required for contact tracing, and hence the number of additional infections caused by infected patients (secondary infections). We examine the effect of the level of resource availability and initiation of contact tracing on the total number of confirmed cases in an outbreak. Pertussis (whooping cough) is used as the testbed due to the prevalence of this disease in the workload of LHDs, its highly infectious nature and the availability of prior studies on its epidemiology. Our results indicate that the level of LHD resource availability significantly affects the number of confirmed cases in an outbreak, as well as its duration. In addition, the rapidity with which the start of an outbreak is recognized and contact tracing initiated also has significant effect on outbreak magnitude, and thus on the workload of the LHD.

2 LITERATURE REVIEW

The epidemiology of pertussis has been studied in the public health and medical communities for several decades, starting early in the 20th century (Stocks 1933). Among the large number of publications addressing this disease, Wendelboe et al. (2007a,b) study the transmission of the disease in young infants, while Wendelboe and Van Rie (2006) review available diagnostic tools.

Extensive prior research has used continuous simulation models (also referred to as system dynamics models) to study the spread and transmission of infection through populations to determine the effectiveness of vaccination strategies within the United States (Hethcote 1999; Van Rie and Hethcote 2004). An extensive review of mathematical modeling techniques for the study of different aspects of infectious diseases is given by Hethcote(2000), while an excellent overview of various aspects of system dynamics modeling is given by Sterman(Sterman 2000). Koopman (2004) discusses the uses of computer modeling of infectious diseases from a public health perspective.

To model the spread and transmission of infectious diseases, age-structured compartmental models are used. These consist of 12-16 distinct subpopulations or compartments based on the susceptibility of the individuals within the compartment such as fully susceptible individuals, those with varying levels of infection, varying levels of vaccinated immunity, and waning immunity. A theoretical population of constant size whose age distribution has reached steady state is used to populate these compartments, using 32 distinct age groups. Each of these age groups has an associated daily death rate and daily outflow rate representing aging into the next age group, as well as a fertility rate to add newborns to the population. Movements between compartments occur when there is adequate contact of a susceptible individual with an infective individual for transmission to occur, an age increase results in vaccination, or vaccination efficacy wanes due to an age increase. Transmission between infected individuals and susceptible individuals is based on estimated force of infection parameters and a contact mixing matrix that specifies the age distribution of contacts for individuals from each age group (Hethcote 1997). The resulting mathematical

model contains over 380 differential equations giving the rate of daily transfers between age groups and compartments. The computer simulations are conducted using the numerical solutions of these differential equations and the daily incidence of pertussis from the year 1940-2040. The models are used to examine different vaccination strategies to determine if it were possible to eradicate pertussis within the United States (Hethcote 1999; Van Rie and Hethcote 2004).

A number of models have also examined the effects of different contact tracing policies on the spread of infectious diseases (Eames and Keeling 2003; Eames 2006). Much of this work focuses on the structure of the network of contacts that must be traced, in terms of how many contacts a given individual may have. Several different approaches to contact tracing have been proposed. In single-step contact tracing, a fixed fraction of the contacts of an index case (the patient identified as being infected) are identified and treated. The key parameter here is the fraction of treated contacts, and Eames (2006) demonstrates the very limited ability of this type of contact tracing to eradicate the infection from the population. Under iterative contact tracing, on the other hand, all contacts of the index case are treated as index cases themselves, with all their contacts being traced and treated, so that contact tracing progresses through the population along the paths of infection. This approach to contact tracing has been shown to be more effective than single-step contact tracing, and is the approach taken by most LHDs in North Carolina. Hence our model focuses on an iterative contact tracing policy. Other authors (Armbruster and Brandeau 2007; Armbruster and Brandeau 2010) have examined the optimal mix of screening and contact tracing required for cost effective control of endemic and chronic diseases.

The model presented in this paper differs from those previously discussed. While the previous models discussed have focused on the spread and incidence of pertussis in a steady state environment for vaccination purposes, this paper focuses on the effect of different public health responses have on an outbreak within a defined area, specifically the jurisdiction of an LHD. The model presented in this paper is designed to focus more on modeling the effects of information delays and resource capacity within an outbreak than on the spread of pertussis within a larger population. It does not use a compartmental design but does incorporate the age-structured design of the previously discussed models as well as uses the force of infection parameter estimates derived by Hethcote in his work (Hethcote 1997; Hethcote 1999).

3 MODEL OVERVIEW

3.1 Model Overview

Our simulation model was developed to study how the levels of resource availability within an LHD may affect the spread and mitigation of pertussis within their local geographic jurisdiction. It is developed as a discrete-event computer simulation model using the time and resource based delays modules within the *Arena* modeling software. The model begins by creating a single entity corresponding to the index case (the first infected patient in the population). This index case then comes into contact with other individuals, creating other entities (contacts), some of whom are infected based on the force of infection model used. These contacts, in turn, come into contact with others, creating additional contact entities. Over time, most of the infected contacts will seek treatment from a physician. However, some contacts in older age groups may not seek treatment due to milder symptoms, busy lifestyles, lack of insurance, etc. If the physician suspects that the contact entity may have pertussis, they will order a culture or polymerase chain reaction (PCR) test (Wendelboe and Van Rie 2006) whose results are transmitted to the physician when the test is complete. If the results of the test are positive the physician will then report a confirmed case of pertussis to the LHD. Once the LHD receives a certain number of confirmed cases, they will begin contact tracing, a process in which health department staff, usually communicable disease (CD) nurses, will try to locate and contact all known direct contacts with the confirmed cases and advise them on the correct course of action to be taken. Contacts are usually advised to isolate themselves and take medication, preventing them from infecting additional patients, and their vaccination histories are reviewed and brought up to date. This results in more confirmed cases as those who feel they have come in contact

with an infected individual will seek out medical attention. Eventually as more and more contacts are tracked down and isolated, fewer new infections arise, and the outbreak will be contained.

3.2 Age Structured Design

Within the model decisions are made on each contact entity that affect its movement between modules in the model. These decisions are whether or not the contact entity is infected based on symptoms, the number of direct contacts the entity will create, what kind of medical test is ordered, and the type of results of the test. These attributes are assigned based upon data obtained from the North Carolina Division of Public Health (NCDPH). The data covered all pertussis cases reported in North Carolina in the years 2007 and 2008. The population was divided into 11 different age groups: < 1 year, years 1-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-39, 40-49, 50-59, and 60+ based on the data, and an empirical probability distribution was determined for each attribute based on the total number of cases and the number of cases per age group with the pertussis data provided. Using the data and these age groups, four other probability distributions were also determined for each specific each group:

- Symptom Distribution: Determines whether the patient is infected or not, based on age group and Hethcote's force of infection estimates (Hethcote 1997).
- Contact Distribution: Determines the number of direct contacts a given patient will have, based on the NCDPH data.
- Test Distribution: Determines whether a patient diagnosed by a physician will have a culture or PCR test ordered for them, based on the NCDPH data.
- Culture Result Distribution: Determines whether the culture test ordered has a positive or negative result, given the patient's age group and symptoms, based on the NCDPH data.
- PCR Result Distribution: Determines whether the PCR test ordered has a positive or negative result, given the patient's age group and symptoms.
- Culture Negative Result Distribution: Determines whether a negative culture test result is a true negative or false negative, based on the NCDPH data.
- PCR Negative Result Distribution: Determines whether a negative PCR result is a true negative or false negative, based on the NCDPH data.

These distributions are used to assign the specific attributes to each contact entity based upon their age group that collectively control the decisions determining their movement through the model.

3.3 Force of Infection Parameters

We use Hethcote's estimates of force of infection rate parameters by age group (Hethcote 1997) to determine whether the contacts created were infected or not. These rates were broken down into age groups which fit with the age-structured design of the model. The force of infection rate parameter λ_i for the i th age group determines the percentage of the total number of contacts C_i created by an infected patient in the i th age group are infected, yielding a number of infected patients in age group i of $\lambda_i C_i$.

3.4 Time and Resource Based Delays

The model uses a combination of time and resource based delays to model the movements of patient entities between modules of the model. The only resource based delay models the contact tracing process as a multiserver queue whose servers represent the LHD personnel who track down and contact all known direct contacts with suspected or confirmed pertussis. Entities representing identified confirmed cases wait until they are contacted by one of the contact tracing resources on a first in first out basis. The average duration of an entity in this queue is determined by the rate at which confirmed cases are identified and the rate at which the contact tracing resources can process them by identifying and notifying all their

contacts. This representation of contact tracing differs substantially from that used in most of the literature on contact tracing, e.g., (Eames and Keeling 2003; Eames 2006), which does not explicitly model the resources used in contact tracing or the associated queuing phenomena, treating contact tracing as a simple time delay.

All other delays in the model are simple time-based delays. These include an incubation period of the infection, waiting to get an appointment with a physician, and the physician waiting for test results. These delays were estimated from multiple sources, notably interviews with public health personnel from the NCDPH and were mainly estimated using triangular distributions. All infection related delays such as the incubation period of pertussis and the period of communicability were derived from the *Control of Communicable Diseases Manual* (Heymann 2008). All other delays were estimated after extensive conversations with health department employees and pertussis domain experts.

3.5 Assumptions

The following specific assumptions were needed to define how certain parts of the model operate:

- A certain percentage of entities aged 25 years or older would not attempt to seek treatment from a physician even if they were infected and showing symptoms of pertussis. This assumption is made due to the fact that older individuals are less likely to see a doctor even if they do have an illness due to busy schedules, lack of insurance, etc.
- A certain percentage of entities that do seek treatment from a physician will be misdiagnosed.
- A certain percentage of contact entities will not be located once contact tracing has begun.
- Contact entities who have a pertussis test ordered for them will undergo either a culture test or a PCR test, but not both.

3.6 Model Flow

To better describe the model we shall organize our discussion around three principal sections:

- Index Case and Contact Creation
- Physician Treatment, Lab Results, and Health Alert
- Contact Tracing

3.6.1 Index Case and Contact Creation Section

This section, the first of the model, starts with an entity representing the index case being created. Once the entity is created, it is first assigned an age group based on the age group probability distribution. It is then assigned the attributes of its symptoms as well as the number of contact entities it will generate, based upon its age group. The index entity then moves to the incubation period time delay module, and while doing so causes a number of entities corresponding to the index case's number of contacts to be created. Although all the index entity's contacts are created simultaneously, they are released individually into the model after a different random time delay, simulating the fact that the index case would make direct contact with them at different times during its infectious period.

After a contact entity is released into the model it follows a process very similar to that of the index case. It is first assigned an age group attribute, then, based on the age group, its symptoms and the number of contacts it generates. After these contacts have been generated, we determine whether each contact is infected or not based upon its symptoms. Contact entities that are not infected move to the contact tracing section of the model and wait in a hold module for contact tracing to begin. If the entity is infected and contact tracing has not begun, the entity moves into the incubation period time delay module. This time delay represents the amount of time elapsing between the patient becoming infected and their displaying symptoms severe enough to seek treatment from a physician. There is a probability that some of these in-

ected entities will not seek treatment. Figure 1 shows an overview of the flow of entities through this section of the model.

3.6.2 Physician Treatment, Lab Results, and Health Alert Section

This section of the model begins with entities moving from the incubation period time delay module to a delay module representing the time elapsing between the patient exhibiting symptoms and their seeking care from a physician. Once the patient sees a physician, a diagnosis event occurs for each entity. Entities are either misdiagnosed as not having pertussis, or recognized as a possible pertussis case. Misdiagnosed (false negative) entities move to the contact tracing section of the model to await contact tracing in a hold module. These entities continue to create additional contacts if they are still in their infectious stage of pertussis (Heymann 2008), a period of roughly three weeks time from infection. The entities that are classified as possible cases are then duplicated to represent both the flow of information and the flow of entities within the model. One set of the duplicate entities moves to the contact tracing section of the model to serve as the contact entities. The other set moves to an attribute assignment determining what type of test will be ordered (PCR or Culture) to confirm whether the patient has pertussis. These entities represent the flow of information regarding the entities (medical records, test results, etc.) that go to seek treatment. After the type of test is assigned, the information entities move to a delay module to wait for the test to be completed. This time delay depends on which type of test is ordered. Once the test result is obtained, the information entities are assigned a test result attribute - positive, negative, or false negative. If the result is a true negative, the entity simply exits the model. If the result is a false negative, there is possibility that the contact entity can create additional contacts. If the test result is positive, it is returned to the ordering physician after a time delay. After another delay the confirmed case of pertussis is reported to the LHD. After enough confirmed cases are reported to the health department to reach the health alert threshold, the contact tracing section of the model will be triggered to begin after a short delay. Figure 2 is an overview of the flow of entities through this section of the model.

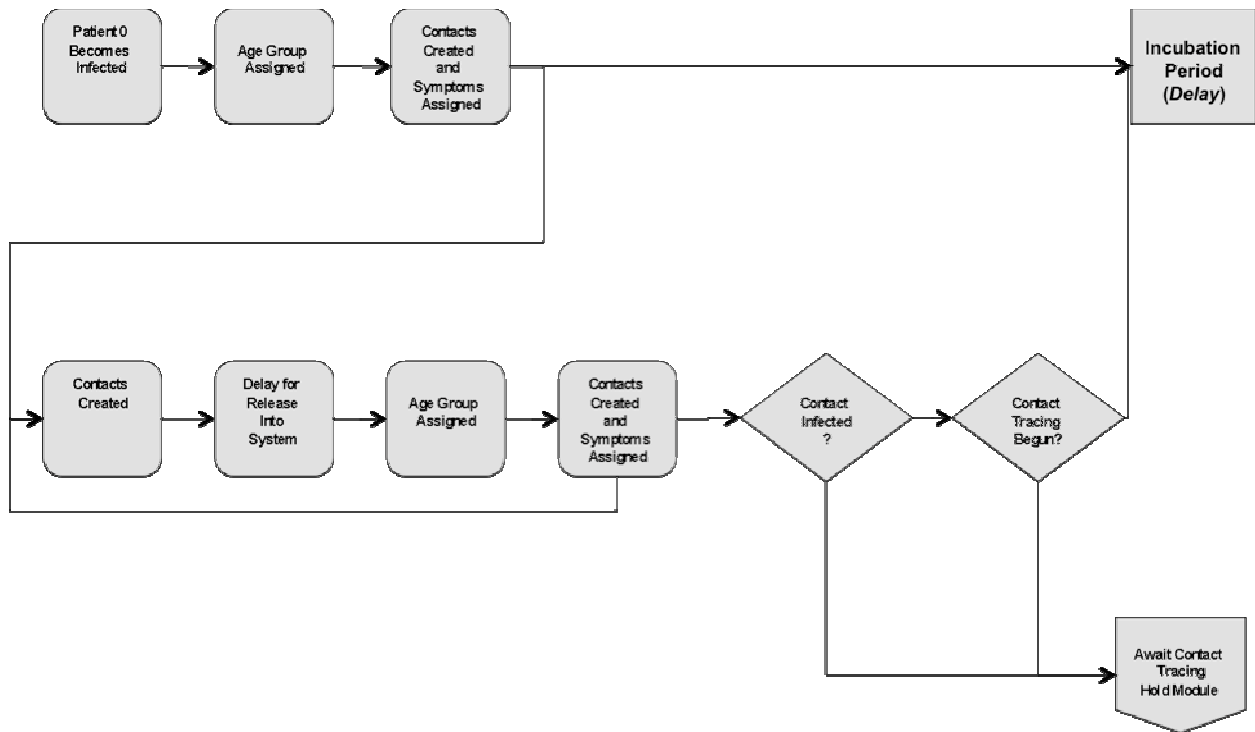


Figure 1: Index Case and Contact Creation Section Flow Diagram

3.6.3 Contact Tracing Section

Once the contact tracing section of the model is initiated, all the contact entities that have moved to this section of the model and are waiting in the hold module begin to be processed by the contact tracing server. This server is a resource-based delay unlike the time based delays discussed in Section 3.4. The initiation of contact tracing has two additional effects on the model. Once this section is triggered all newly created infected contact entities do not move to the incubation period time delay, but instead they move directly to the contact tracing server queue. In addition, before newly created contact entities are assigned a number of contacts to create the contact tracing server queue is examined. If the number in queue is under 15, the contact entity will not create any additional contacts, under the assumption that they will be contacted by the LHD very shortly after creation before infecting others. This hopefully over time will completely stop the infection. After being processed by the contact tracing server, entities that did not choose to seek treatment initially or those that were misdiagnosed will now receive treatment, and after a delay for processing their diagnostic test, will now become a confirmed case, and the entities will then be disposed of. The other entities that were already confirmed cases or were not infected will then after being processed by the contact tracing server be disposed of, ending their flow through the model. Figure 3 is an overview of the flow of entities through this final section of the model.

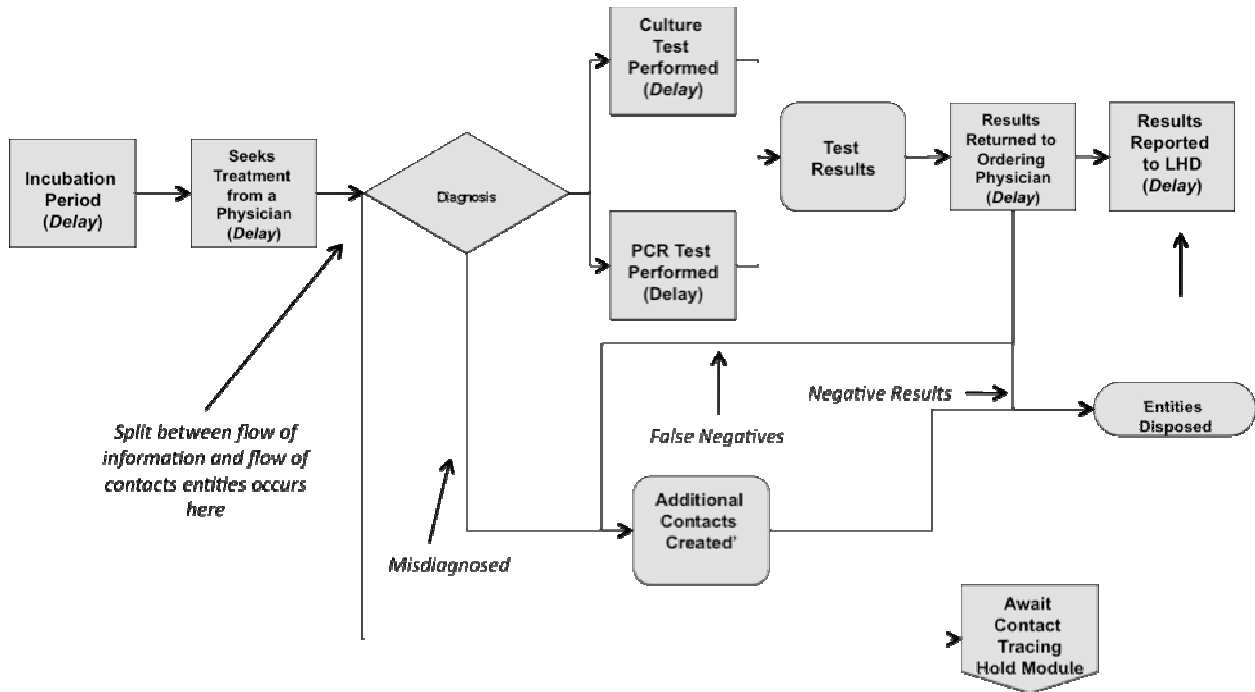


Figure 2: Physician Treatment, Lab Results, and Health Alert Section Flow Diagram

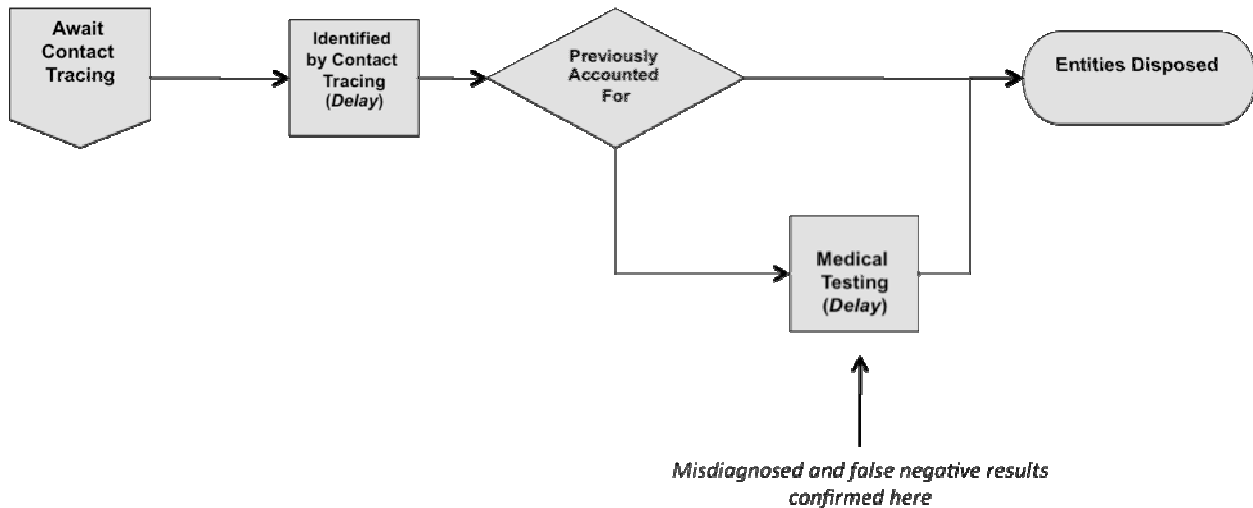


Figure 3: Contact Tracing Section Flow Diagram

4 FEATURED RESULTS

4.1 Effect of Confirmed Case Threshold for Initiation of Contact Tracing

To examine the results of the simulation model, output data were collected on the number of confirmed cases per day. The model was first used to study the effects of the number of confirmed cases required for the LHD to recognize a public health threat and begin contact tracing. A base case was established under which the LHD has 3 resources available 24 hours a day seven days a week to perform the contact tracing. Scenarios were run with the base case parameters with confirmed case threshold levels requiring 1, 2, 3, and 4 confirmed cases to trigger the contact tracing. The simulations ran for 200 days with 500 replications for each scenario due to the terminating nature of the outbreak being simulated.

As seen in Figure 4, a threshold of one confirmed case results in the lowest average cumulative confirmed cases, and the curve begins to level off earlier in the simulation than the other curves. As the confirmed case threshold is increased, the average number of cumulative confirmed cases increases from 36 cases with a threshold of one confirmed case to 46 cases with four confirmed cases. The biggest average increase occurs when the threshold is increased from one confirmed case to two. The curves themselves also begin to level off later in the simulation, although with minimal increase. These results are intuitive: the earlier contact tracing is begun, the sooner infected patients can be located and isolated, reducing the overall number of confirmed cases that will occur.

The results in Figure 5 show that once contact tracing has begun, there is an increase in the average number of confirmed cases per day that occur for roughly three weeks, after which the outbreak is controlled and the number of confirmed cases per day decreases rapidly to zero. Again, the earlier contact tracing is begun the sooner the increase in confirmed cases per day begins, with lower average numbers of confirmed cases per day.

4.2 Resource Capacity and Availability

This model was designed as a tool to study the effects of varying levels of resource capacity and availability on the spread and mitigation of a pertussis outbreak. To demonstrate the ability of this tool to model these effects, a specific threshold level was examined by varying the levels of resource (personnel) availability. These scenarios were:

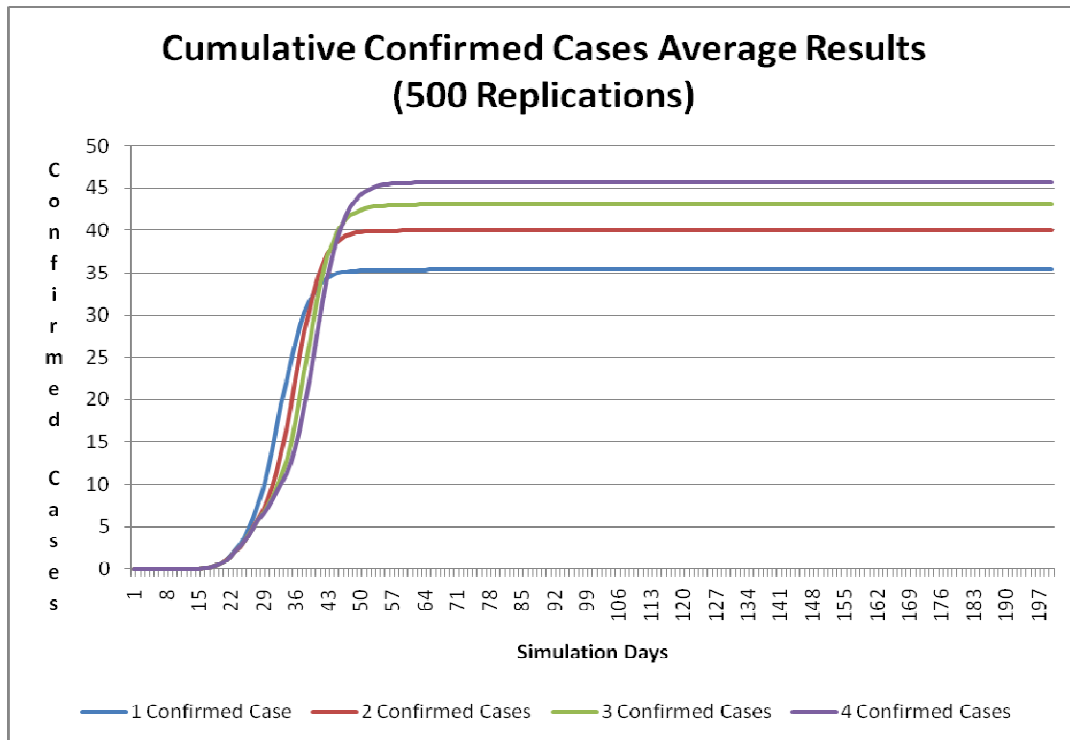


Figure 4: Average cumulative confirmed case generated over 200 days

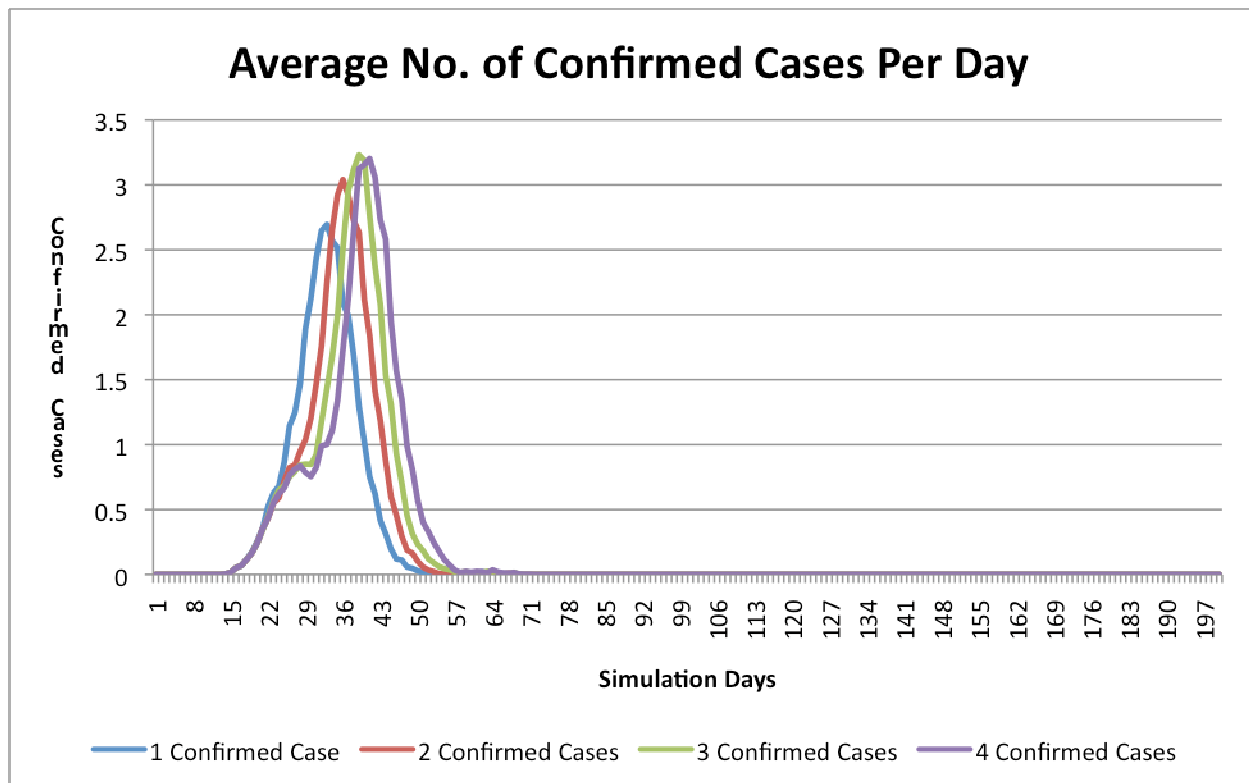


Figure 5: Average confirmed cases per day generated over 200 days

- Base Case: 3 resource capacity of the health department available 24 hours a day 7 days a week
- 3 Resources: 3 resource capacity of the health department available 8 hours a day 7 days a week
- 4 Resources: 4 resource capacity of the health department available 8 hours a day 7 days a week
- 5 Resources: 5 resource capacity of the health department available 8 hours a day 7 days a week

As seen in Figure 6, the lowest average number of cumulative cases arises under the base case, leveling off around 35 cases. Although the base case has only 3 resources, these resources are available around the clock, allowing contact tracing to occur quickly. Under the remaining scenarios, resources are available for 8 hours a day but vary in number. With each decrease in capacity their respective curves level off at higher cumulative averages, and later in the simulation. The scenario with five resources levels off around 60 cases, a significant increase from the 35 cases of the base case and almost 30 days later. The four resource scenario levels off around 95 cases. Interestingly, the three resource scenario never levels off, suggesting that the outbreak is never controlled. However, the growth appears to be approximately linear, suggesting that an approximate equilibrium between new infections and identified and isolated contacts is achieved.

The results in Figure 7 indicate that as in Figure 5, once contact tracing is begun there is an increase in the number of confirmed cases per day that lasts for a period of time before decreasing to zero. However, as resource availability decreases relative to the base case, the increase occurs later and lasts longer, and in the case of the three resource capacity remains at almost a constant level through the end of the simulation.

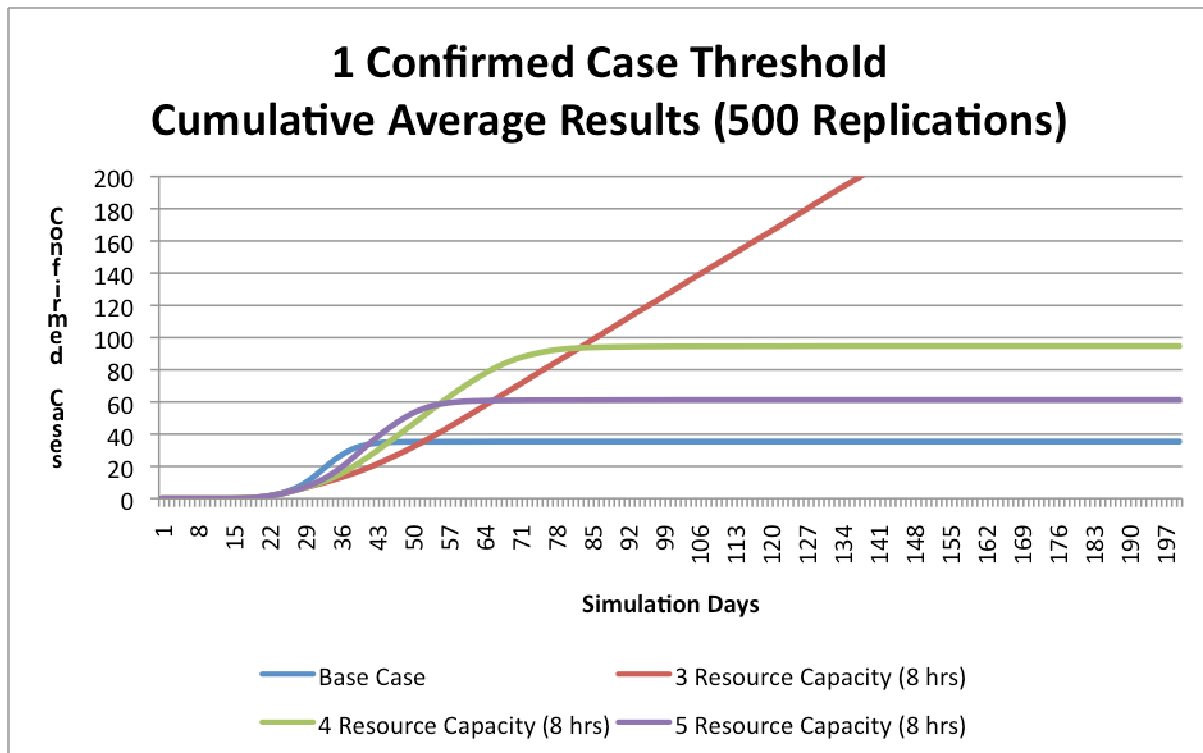


Figure 6: Average cumulative confirmed cases generated over 200 days

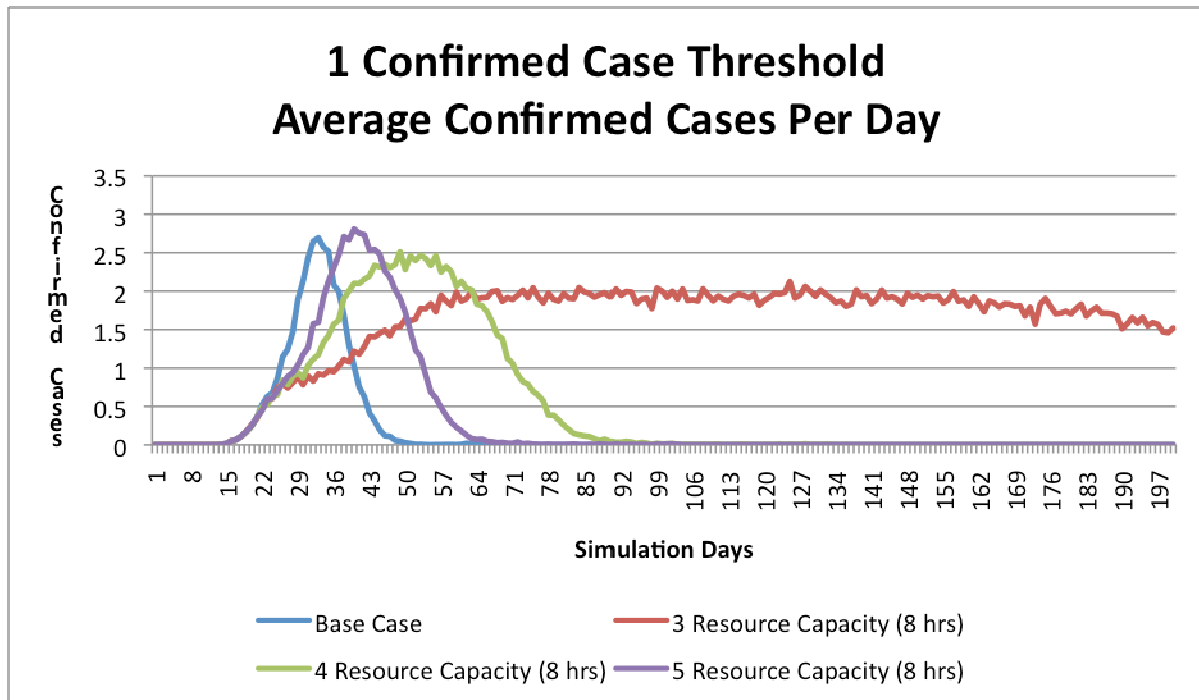


Figure 7: Average confirmed cases per day generated over 200 days

The above results indicate that the level of resources available for contact tracing has a significant impact on the degree to which a local health department can control and mitigate a pertussis outbreak. The lower the resource availability of the LHD, the longer it will take on average for contact tracing to be performed. This longer time to identify and isolate contacts results in a higher number of infections, since infectious patients are able to expose more contacts. These results are consistent with those of Eames(2006), who points out that contact tracing is of little value when the time to perform contact tracing is so long that infected individuals have time to transmit the disease to a large number of their contacts. The results in Figure 7 corresponding to three available resources approaches this condition – the contact tracing is unable to remove infectious individuals from the population fast enough to reduce the number of infected patients.

It is also interesting to note that the average confirmed cases per day represent a rough measure of the daily workload imposed on the LHD by the outbreak. Figure 7 clearly shows that when the available resources are insufficient to bring an outbreak under control, a heavy, ongoing workload is imposed on the local health department which may compromise its ability to recognize and react to other types of emergencies in its domain.

5 CONCLUSIONS AND FUTURE WORK

5.1 Conclusions

A formal, quantitative validation of our model against actual case data remains an ongoing challenge. In particular, the average size of an outbreak in terms of the number of confirmed cases appears to be too high. This may be due to a number of factors which we continue to explore: incomplete modeling of the network structure representing the number and age groups of contacts of different individuals; inaccuracies in the estimates of force of infection due to differences between Hethcote’s assumptions and the population represented in the NCPDH data; and failure to model the many informal redundancies routinely operative in the operations of a local health department that might lead to infected individuals being discovered more rapidly than our model suggests. However, the results presented above indicate that the

model is capable of representing the basic dynamics of a pertussis outbreak in a qualitatively correct manner, and has been verified as such by public health experts. The consensus of our public health colleagues who have reviewed this model is that while its precise quantitative predictions may not be totally accurate, it has the potential to serve as a tool to compare different scenarios, such as the effects of reducing certain time delays through improved information technology or, as illustrated here, of different levels of resource availability.

5.2 Future Work

Our future work will be directed along two parallel paths. The first of these will be the ongoing refinement and validation of the model against data from actual outbreaks. This data can be potentially obtained from two sources: the NCDPH case data used to develop the initial model is now available for the year 2009, providing a new data set that can be used for validation. In addition, data from the North Carolina Health Alert Network (NC-HAN) provides data on health alerts issued in North Carolina together with the associated number of cases. We will also continue to work with public health researchers and practitioners to refine the epidemiological parameters of the model to improve its quantitative predictions.

The second principal direction of our future work will be to incorporate the effects of improved information technology on the magnitude and duration of outbreaks. This enhancement will allow the model to be used to examine the benefits of several information technology investments in the North Carolina Public Health Information Network that have been made in the recent past, and suggest directions for how these networks may be extended. Finally, we would like to incorporate a second infectious disease into the model, allowing us to study the effect of how local health departments allocate their time between different surveillance and contact tracing tasks.

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