

PANDEMIC INFLUENZA RESPONSE

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ABSTRACT

Recent incidents of avian flu (H5N1) in Asia and the pandemic influenza cases in history (1918, 1957 and 1968) suggest that a future pandemic influenza is inevitable and likely imminent. Governments and non-governmental organizations prepare response plans on how to react to a pandemic influenza. In this paper, we study the logistics side of the problem, specifically, food distribution logistics during the pandemic influenza. For this purpose, we develop a disease spread model that assists in estimating the food need geographically at a given time. Then, we develop an integrated solution approach called the *Dynamic Update Approach* to build the food distribution network. We run our integrated disease spread and facility location model for the state of Georgia and present the estimated number of infections and meals needed in each census tract for a one year period.

1 Introduction

Most of the experts think that a pandemic influenza will hit the world in the near future because of the cases that happened in the last few years (avian flu-H5N1) and the history of pandemic influenza (Morse, Garwin, and Olsiewski 2006). Epidemiologists warn that the next pandemic influenza could infect 33% of the population and kill millions (Gibbs and Soares 2005). According to the Centers for Disease Control and Prevention (CDC), there will be a \$71.3-165.5 billion economic impact on the United States Economy. The World Health Organization (WHO) estimates that 2-7.4 million people might die.

U.S. Department of Health & Human Services and U.S. Department of Commerce estimates that 20% of working adults may become ill, and there may be a 40% workforce loss during peak because of illness, fear of infection and the need to care infected family members or school-aged children. "If the refineries lose 30 percent of their people, they have to shut down. Transport and delivery would

be severely handicapped during a pandemic both because of gas shortages and the loss of workforce." says Dr. Michael T. Osterholm, the director of Center for Infectious Disease Research and Policy (Hoffbuhr 2006). Gas shortages will also trigger interruptions in services. Food and water supplies may be interrupted, and individuals may also be unable to get to a grocery store. Logistics of delivering these basic supplies to infected or quarantined households is an operations research question (Wu et al. 2006).

In this paper, we consider the problem of providing food to people who are not able to obtain it during a pandemic influenza. First, we develop a disease spread model to estimate the geographical spread of the disease and then construct a food distribution network based on these estimates. To the best of our knowledge, this is the first paper in the literature integrating a disease spread model and a food distribution model for planning purposes in the literature.

The remainder of the paper is organized as follows. In Section 2, we present the existing literature on the disease spread models and facility location problems. Then, the model follows that we construct to estimate the disease spread in Section 3. In Section 4, we present the facility location model and the solution approach proposed for the food distribution problem. In Section 5, the computational results for the state of Georgia are provided. Finally, we conclude with some future research directions in planning for a pandemic influenza.

2 Literature Review

There are two main streams of literature related to our problem: (i) disease spread models, and (ii) facility location and distribution models. In the literature, disease spread models have been thoroughly researched for different infectious diseases such as influenza, smallpox and SARS (see Ferguson et al. (2003) for a review of spread models for smallpox and Lipsitch and et al. (2003) and Riley and et al. (2003) for SARS). The disease spread models are developed to predict

the outbreaks in populations with complex social and spatial structures. There are two common ways to model the spread of an infectious disease in a population: (i) using differential equations (e.g. Cahill et al. (2005), Fraser et al. (2004)), and (ii) simulation modelling (e.g. Ferguson et al. (2006), Ferguson et al. (2005), Germann et al. (2006), Wu et al. (2006)).

We develop a simulation based spread model with heterogeneous mixing. The comparison of the relevant models in the literature and our model is provided in Section 3.

The second part of our problem, namely the facility location part, is determining the location of the food distribution facilities based on the geographical estimates on the food need obtained from the disease spread model. The problem we are dealing with is a hierarchical multi-period capacitated facility location problem where there are supply and demand nodes and two levels of facilities between supply and demand nodes. Multi-period facility location models have been extensively studied in the literature for the capacitated and uncapacitated version (Wesolowsky 1973; Roy and Erlenkotter 1982; Shulman 1991; Hinojosa, Puerto, and Fernández 2000). A popular solution approach for multi-period capacitated facility location problems is to generate the alternative solutions for the single period problem and look for the best combination of these alternative solutions by dynamic programming (Ballou 1968; Canel et al. 2001). However, all of these solution methods require solving a mixed integer problem which is not easy for a large-size problem like ours.

3 Disease Spread Model and Simulations

In this section, we explain the disease spread model developed for the pandemic influenza. We construct an individual-based continuous time stochastic model for influenza transmission. In the base model, we do not apply any intervention strategy. In addition to the base model, we investigate the effect of quarantine on the spread of the virus. In addition to food distribution, this model may also be useful for other purposes such as estimating the region-based hospital capacity needs for local governments for hospital capacity planning purposes.

Population heterogeneities such as age, density and geography are important in predicting the disease spread (Grais, Ellis, and Glass 2003); thus, we constructed a disease spread model that takes into account such population heterogeneities. First, the whole population is divided into communities that correspond to neighborhoods. Then, the population of each community is identified by five age groups, namely, 0-5, 6-11, 12-18, 19-64, 65+, since the previous research in this area claim that the progress of the disease depends on the age of the individual (Wallinga, Teunis, and Kretzschmar 2006), and the age of an individual determines his/her contact group. For example, children

are considered to play a major role in the transmission of influenza (Viboud et al. 2004) because they are assumed to be more susceptible due to lower immunity (although it depends on virus types) and to have more daily contacts in schools and play groups.

The disease spread model can be analyzed in two parts. The first one is the progress of the disease within an infected individual, and the second part is the spread of the virus among the members of the population.

In our model, an infected individual goes through the stages of the disease according to the natural history for pandemic influenza in Wu et al. (2006) (see Figure 1). According to Figure 1, each individual is assumed to be in one of the following stages at a given time; susceptible (S), exposed (E), presymptomatic (I_P), asymptomatic (I_A), symptomatic (I_S), hospitalized (I_H), recovered (R) or dead (D). When a susceptible individual is exposed, s/he passes to the exposed stage and then becomes presymptomatic. After the presymptomatic stage, the individual can develop symptoms with a certain probability based on his/her age. The probability of developing symptoms is 0.60 for working adults (19-64) and 0.75 for other individuals, which is consistent with other papers (Wu et al. 2006; Longini et al. 2005; Germann et al. 2006) on average but has an age-based structure. Asymptomatic individuals recover after the asymptomatic stage. A symptomatic individual will either recover or be hospitalized. The probability of hospitalization after developing symptoms is assumed to be 0.18 for children between 0 and 5, 0.12 for elderly and 0.06 for others (see Wu et al. (2006) for the base value of 0.06 and Longini et al. (2005) for the age-based adjustments). After hospitalization, the probability of death is 0.344 for children between 0 and 5 and elderly and 0.172 for others. (See Wu et al. (2006) for base values and Carrat et al. (2006) for age-based modifications.) The duration of the disease stages (E, I_P, I_A, I_S, I_H) are taken from Wu et al. (2006).

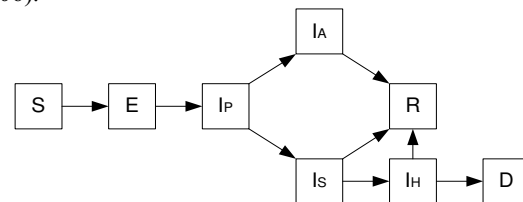


Figure 1: Natural disease history for influenza.

The natural history shows us how the disease progresses within an infected individual. The progress of the virus among the members of the population can be explained by the contact network. We start with a brief explanation of our contact network. In our model, all of the individuals mix in the community during the whole day. Other than

community mixing, individuals mix in households during the night and in peer groups during the day. The children in the first three age groups (0-5, 6-11, 12-18) mix with other children in kindergarten, elementary and secondary schools. The people in the age group 19-64 are considered as working adults, and they mix in work places with other adults. Elderly are not assumed to mix in peer groups. To sum up, a susceptible individual in the community can get infection from the other individuals in his/her household, peer group or in the community. In addition to three types of infections explained above, we challenge each community with a constant import rate (1.5 infected individuals per day per 100,000 people), which represents the infected people coming from outside the contact network.

The communities are linked to each other via peer groups which account for the inter-community spread of the disease. We incorporate a spatial component to our model by allowing individuals from different communities to mix in peer groups. An illustration of the contact network described above can be seen in Figure 2.

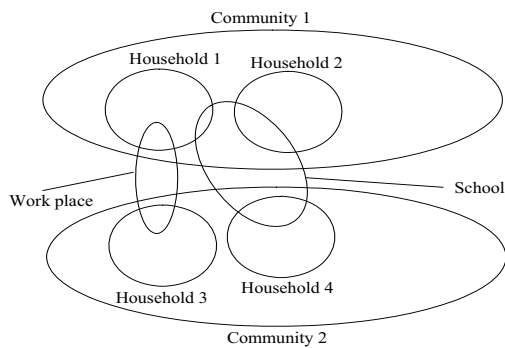


Figure 2: Example of interacting groups in a contact network.

Our disease spread model is generic and can be applied to any area. We take the state of Georgia as the test case and construct our model accordingly. We consider each census tract as a single community. We use 2000 U.S. Census data (www.census.gov/main/www/cen2000.html) to form the households and peer groups. There are 1615 census tracts in the state of Georgia, and the total population is 9,071,756.

Table 1 compares the most relevant models in the pandemic influenza literature and our disease spread model. In short, we develop a detailed SEIR disease spread model with a spatial component, age-based structure and night/day differentiation.

The details of the disease spread model and the explanation of relevant parameters are explained in Appendix A. To understand the results of the simulation better, here we provide basic concepts used in disease spread models.

The basic reproductive number R_0 is the average number of secondary cases caused by an infectious individual. This number determines the infectivity of the virus. For example, the basic reproductive number for Spanish flu in 1918 is estimated around 1.8. The parameters explained in Appendix A are determined mainly by this number.

We have done the simulations for a range of R_0 values to account for low ($R_0 = 1.5$), medium ($R_0 = 1.8$) and high ($R_0 = 2.1$) infectivity. The graph in Figure 3 shows the spread of the disease among the population of Georgia for different R_0 values.

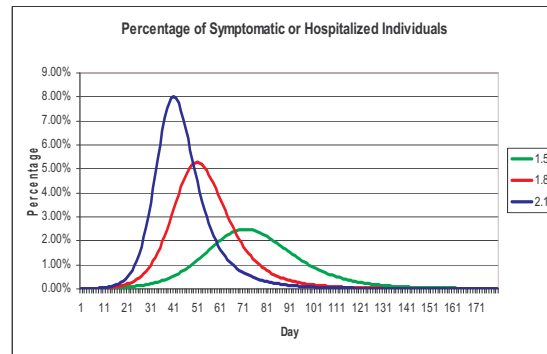


Figure 3: Simulation results under no intervention policy.

Table 2 summarizes the simulation results with no intervention policies. “Peak Infectivity” is the percentage of the individuals who are symptomatic or hospitalized when the spread peaks. “Peak Day” is the time when the spread peaks. “CAR” (Clinical Attack Rate) is the cumulative percentage of the people who have been symptomatic within the current year. “IAR” (Infection Attack Rate) is the cumulative percentage of the people who have been infected (can be symptomatic or asymptomatic) within the current year. Finally, “Death Ratio” is the percentage of the people who died because of influenza within the current year. “Peak Infectivity” is important for planning purposes since it determines “capacity” required (number of meals required in our case) in a response planning activity. On the other hand, “IAR” is used as a performance measure for evaluating the effectiveness of the intervention policies.

In addition to the base case with no intervention policy, we have investigated the effect of a limited quarantine. “Quarantine” is defined as keeping the individual(s) in their homes, which limits their peer group and community interactions. It is a voluntary quarantine, and the household is quarantined if an individual from that household develops symptoms and participates with a certain probability (0.5 in our case) or the individual is hospitalized. Other individuals in the quarantined household comply with the quarantine

Table 1: Comparison of the proposed model with the ones in the literature.

Reference	Natural History	Spatial Component	Age Based	Night/Day Differentiation
Wu et al. (2006)	Detailed SEIR	No	No	No
Ferguson et al. (2006), Ferguson et al. (2005), Patel, Longini, and Halloran (2005), Longini et al. (2005)	SEIR	Yes	Yes	No
Germann et al. (2006)	SEIR	Yes	Yes	Yes
Our Model	Detailed SEIR	Yes	Yes	Yes

Table 2: Results of the disease spread model with no intervention policy.

R_0 Value	Peak Infectivity	Peak Day	CAR	IAR	Death Ratio
1.5	2.48%	70	32.50%	49.65%	0.57%
1.8	5.27%	50	44.20%	67.49%	0.80%
2.1	8.01%	40	51.27%	78.27%	0.93%

independently with the same probability. Once a household is quarantined, if no other individual in the quarantined household develops symptoms or gets hospitalized for a week, the quarantine is released. Otherwise, the quarantine is extended for another week for that household. The quarantine is active for a given period of time (2-12 weeks) different from other papers in the literature (Wu et al. 2006; Longini et al. 2005) which assume that the quarantine is active for the entire time horizon.

We have investigated the effect of timing and length of quarantine on the peak infectivity and IAR for each R_0 value. Figure 4 shows the effect of the quarantine length and timing on the peak infectivity for $R_0 = 1.8$. As expected, the peak infectivity decreases as the length of the quarantine increases, but there is a diminishing rate of return. The peak infectivity in an 8-week quarantine is almost equal to that of a 12-week quarantine. Furthermore, we see that an 8-week quarantine is most effective in terms of peak infectivity if it is implemented starting from the beginning of the fourth week. However, the optimal timing is a little different if the performance measure is IAR. For example, for an 8-week quarantine, IAR is minimal if it is implemented at the beginning of the week 6. Similar analysis can be done for different R_0 values. Table 3 summarizes the results for an 8-week quarantine with an objective of minimizing the peak infectivity.

The next step in our problem is estimating the food requirement using the spread model. There can be several alternatives for calculating the food requirement depending on who to feed. One alternative is serving the households with all adults infected (symptomatic or hospitalized) since

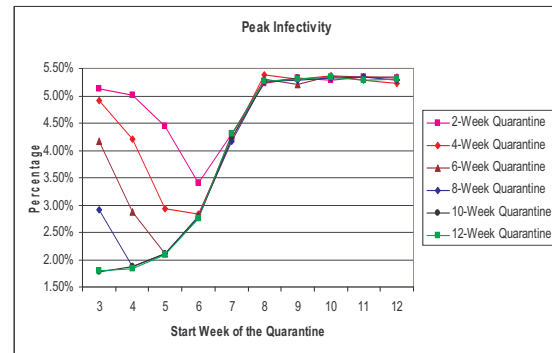


Figure 4: Effect of timing and length of quarantine on the peak infectivity.

the children in this household will not be able to feed themselves. In case of quarantine, serving the quarantined households is another alternative. In Figure 5, we present the daily number of meals needed for the state of Georgia and Metropolitan Atlanta Area for $R_0 = 1.8$ assuming an individual needs 3-meals a day, and the households with all adults infected are served (see Ekici et al. (2008) for the estimates using other alternatives to calculate the food requirement). We consider no intervention and an 8-week quarantine with the optimal timing (the beginning of fourth week). We consider the Metropolitan Atlanta Area because in the second part of the problem, we will construct a food

Table 3: Summary of the quarantine runs for an 8-week quarantine.

R_0 Value	Quarantine Start Week	Peak Infectivity	Peak Day	CAR	IAR	Death Ratio
1.5	7	0.80%	52	26.52%	40.46%	0.47%
1.8	4	1.86%	63	36.82%	56.14%	0.66%
2.1	3	3.97%	49	41.26%	62.87%	0.75%

distribution network for this area. In Figure 5, we observe two peaks for the 8-week quarantine, which is mainly due to the release of quarantine after 8 weeks.

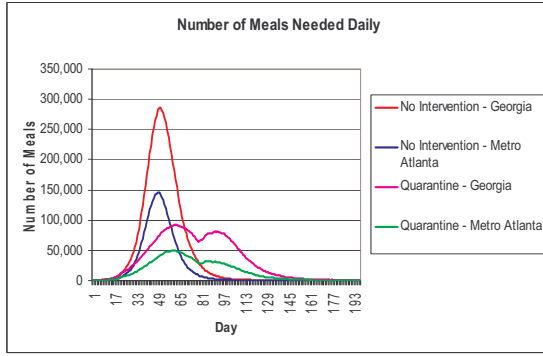


Figure 5: Food requirement assuming that households with all adults infected are served under no intervention or an 8-week quarantine policy.

4 Facility Location Model

In this section, we explain food distribution network that will be constructed and provide a mixed integer formulation for the facility location decisions.

First, we describe the problem setting and then explain the mathematical formulation. In our food distribution network, each census tract is considered as a demand node, and the amount of the demand is determined by the the number of individuals/households in need. There is a set of supply nodes that supply the food to major facility locations. After the food is processed and/or packed in these major facilities, it is sent to distribution centers. Then, the individuals/households who are in need get their food from these distribution centers. The major facilities and distribution centers can be opened and closed over time based on the demand. In our formulation, we consider closing and opening decisions on a weekly basis over one year.

Next, we present a mixed integer formulation for this facility location problem. Table 4 summarizes the notation. In this formulation, we assume that the demand is determin-

istic, that is, we know the number of meals needed ahead of time for a given day for each census tract. By running the disease spread model, we can obtain an estimate and treat this estimate as the true values.

The objective is to minimize the total cost while satisfying the demand. Variables used in the formulation are as follows:

$$x_{ijt} = \text{amount of food sent from node } i \text{ to node } j \text{ in period } t$$

$$i \in N_k, j \in N_{k+1}, k \in \{1, 2, 3\}, t \in \{1, \dots, T\},$$

$$y_{jt} = \begin{cases} 1, & \text{if facility at node } j \text{ is open during week } t \\ 0, & \text{otherwise} \end{cases}$$

$$j \in N_2 \cup N_3, t \in \{1, \dots, T\},$$

$$w_{jt} = \begin{cases} 1, & \text{if facility at node } j \text{ is opened} \\ & \text{at the beginning of week } t \\ 0, & \text{otherwise} \end{cases}$$

$$j \in N_2 \cup N_3, t \in \{1, \dots, T\},$$

$$z_{jt} = \begin{cases} 1, & \text{if facility at node } j \text{ is closed} \\ & \text{at the end of week } t \\ 0, & \text{otherwise} \end{cases}$$

$$j \in N_2 \cup N_3, t \in \{1, \dots, T\}.$$

Using these variables, the objective function can be written as:

$$\begin{aligned} \mathcal{O} \mathcal{F}(x, y, w, z) = & \sum_{t=1}^T \sum_{i \in N_1} \sum_{j \in N_2} (d_{ij} c_{ir}^1 x_{ijt} + c_o^1 x_{ijt}) \\ & + \sum_{t=1}^T \sum_{i \in N_2} \sum_{j \in N_3} (d_{ij} c_{ir}^2 x_{ijt} + c_o^2 x_{ijt}) \\ & + \sum_{t=1}^T \sum_{j \in N_3} \sum_{k \in N_4} d_{jk} c_{individual} x_{jkt} \\ & + \sum_{t=1}^T \sum_{j \in N_2} (F_j y_{jt} + f_j w_{jt} + g_j z_{jt}). \end{aligned}$$

The full mathematical formulation of the facility location problem is presented in Figure 6. In the formulation, expression (1) is the objective function, which is the summation of total transportation cost, handling cost, facility operating cost and facility opening-closing cost. Constraints (2) and (3) are the supply constraints and demand constraints, respectively. (4) represents the capacity constraints for each facility location (either a major facility or a distri-

Table 4: Notation used in the formulation.

T	:	number of weeks (time horizon)
N_1	:	set of supply nodes
N_2	:	set of major facility locations
N_3	:	set of distribution centers
N_4	:	set of demand nodes
S_i	:	amount of meals that can be supplied by the supply node at node i for $i \in N_1$
F_j	:	fixed cost incurred if the facility at node j is open during a week for $j \in N_2 \cup N_3$
f_j	:	cost of opening the facility at node j for $j \in N_2 \cup N_3$
g_j	:	cost of closing the facility at node j for $j \in N_2 \cup N_3$
c_o^1	:	unit material handling cost at a major facility
c_o^2	:	unit material handling cost at a distribution center
C_j	:	capacity of the facility that can be opened at node j for $j \in N_2 \cup N_3$
D_{kt}	:	demand of demand node k in period t for $k \in N_4, t \in T$
d_{ij}	:	distance (in miles) between node i and node j for $i \in N_k, j \in N_{k+1}, k \in \{1, 2, 3\}$
c_u^1	:	unit transportation cost from a supply point to a major facility per mile
c_u^2	:	unit transportation cost from a major facility to a distribution center per mile
$c_{individual}$:	unit transportation cost from a distribution center to a demand node per mile

bution center). Constraints (5) are flow balance constraints. Constraints (6) and (7) restrict service to open facilities. Constraints (8) and (9) set the initial and final values. Finally, (10)-(13) are the integrality and sign restrictions.

Next, we discuss two solution approaches to the food distribution logistics problem during pandemic influenza. The first one is called the *Deterministic Approach (DET-A)*. In this approach, the current spread of the disease is provided as an input to the disease spread model, and the food requirements of each demand node is estimated by running the disease spread model. We solve the facility location model assuming that the estimated demand values are true values and determine the opening and closing decisions of facilities accordingly. Then, the facility location decisions obtained for the estimated demand is implemented.

The second approach is called the *Dynamic Update Approach (DYN-A)*. By doing updates on the status of the spread in discrete times, we can improve the *DET-A*. That is, at the beginning of each week, we update our estimate on the amount of food needed by looking at the current spread of the disease. In this way, we decrease the deviation of the estimates from the real-world situation. In this approach, we apply only the decisions for the current week and then rerun the simulation in the next week for the remaining time horizon by providing the status of the real-world spread as an input to the simulation. We implement both of these solution approaches and present the results in the next section.

In the computational experiments, we assume that we serve households with all adults infected, but the approach is valid for any alternative used for calculating food requirement. In addition, we assume that we serve food to people when more than 0.5% of the population is infected at a given

time. Although the exact percentage is hard to estimate, the assumption is reasonable because the non-governmental organizations and/or governments will not construct a large food distribution network if the number of infections is under some threshold value.

5 Computational Results

In this section, we provide the results of the computational experiments. We compare the performances of the *DET-A* and the *DYN-A*.

We test our solution approaches for the Metropolitan Atlanta Area, which consists of 603 census tracts. Therefore, in the test instances, we have 603 demand nodes. We allow 10 potential major facility locations, 78 potential distribution centers and 28 supply nodes. The total capacity of major facilities is equal to that of distribution centers, and the total capacity of major facilities is approximately 2.5 times the estimated peak demand. The total capacity of the supply nodes is 2 times the estimated peak demand. Finally, we assume the opening, operating and closing costs are in proportion to the square root of the capacity of the corresponding facility type. The opening, operating and closing costs of a major facility is 100 (and 1000 for another setting) times that of a distribution center of the same size. This is reasonable because all the processing operations will be performed in the major facilities and the distribution centers, also called point of distribution, will be used only as a transshipment point.

To test the solution approaches, we run our simulation model to obtain spread patterns that will be taken as real-world spreads. Then, in the *DET-A*, we provide the spread

$$\begin{aligned}
 & \text{Minimize} && \mathcal{OF}(x, y, w, z) && (1) \\
 & \text{subject to} && \sum_{i \in N_1} x_{ijt} \leq S_i && i \in N_1, t \in \{1, \dots, T\} && (2) \\
 & && \sum_{j \in N_2} x_{jkt} \geq D_{kt} && k \in N_4, t \in \{1, \dots, T\} && (3) \\
 & && \sum_{j \in N_3} x_{ijt} \leq C_j y_{jt} && j \in N_{k+1}, k \in \{1, 2\}, t \in \{1, \dots, T\} && (4) \\
 & && \sum_{i \in N_k} x_{ijt} = \sum_{l \in N_{k+2}} x_{jlt} && j \in N_{k+1}, k \in \{1, 2\}, t \in \{1, \dots, T\} && (5) \\
 & && w_{jt} \geq y_{jt} - y_{jt-1} && j \in N_2 \cup N_3, t \in \{1, \dots, T\} && (6) \\
 & && z_{jt} \geq y_{jt} - y_{jt+1} && j \in N_2 \cup N_3, t \in \{1, \dots, T\} && (7) \\
 & && y_{j0} = 0 && j \in N_2 \cup N_3 && (8) \\
 & && y_{jT+1} = 0 && j \in N_2 \cup N_3 && (9) \\
 & && y_{jt} \in \{0, 1\} && j \in N_2 \cup N_3, t \in \{1, \dots, T\} && (10) \\
 & && w_{jt} \in \{0, 1\} && j \in N_2 \cup N_3, t \in \{1, \dots, T\} && (11) \\
 & && z_{jt} \in \{0, 1\} && j \in N_2 \cup N_3, t \in \{1, \dots, T\} && (12) \\
 & && x_{ijt} \geq 0 && i \in N_k, j \in N_{k+1}, k \in \{1, 2, 3\}, t \in \{1, \dots, T\} && (13)
 \end{aligned}$$

Figure 6: Mathematical formulation of the facility location problem.

status as an input to the simulation when more than 0.5% of the population is infected at a given time. Similarly, in the *DYN-A*, we provide the update of the demand as an input to the simulation when more than 0.5% of the population is infected at a given time, and we make weekly updates to the values. We use CPLEX 9.0 with a 10 hour time limit to solve the integer programs. In the test instances, the length of the time horizon is 8 weeks (between weeks 5 and 12), which corresponds to the interval in which more than 0.5% of the population is infected.

Figure 7 shows the number of major facilities operated over time for a single instance. In Figure 7, “Perfect Solution” is the solution obtained assuming that we know the real-world spread ahead of time. This is impossible to know but it provides a comparison base for our solution approaches.

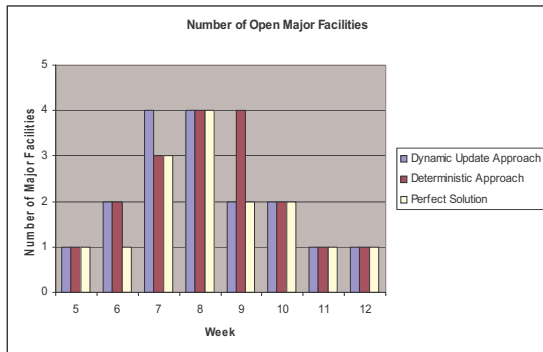


Figure 7: Number of major facilities open over time.

The optimality gap of the solutions obtained by the *DYN-A* is approximately 8.87% (when compared to “Perfect Solution”) and the *DYN-A* is 2.48% better when compared to the *DET-A* in terms of total cost. Another performance measure is the proportion of demand served within 10 miles. The proportion of demand served from a distribution center within 10 miles mainly depends on the transshipment costs but here we make a comparison in order to see how the proportion of demand served from a distribution center within 10 miles changes in different solution approaches. On average, 65% of the demand is served within 10 miles in the “Perfect Solution” and 67% of the demand served within 10 miles in the *DET-A* and *DYN-A*. We refer the reader to Ekici et al. (2008) for the results for larger sized problems.

6 Conclusion and Future Directions

In this paper, we construct a disease spread model with a spatial and an age-based structure for pandemic influenza that may be helpful for developing mitigation strategies and for planning purposes such as vaccine production/distribution planning and food distribution planning. In addition, using this model as a forecasting tool for determining the number of people who are in need of food, we construct a food distribution network model called the *Dynamic Update Approach*. To the best of our knowledge, we are the first to integrate a disease spread model and a facility location model on a dynamic basis. We run our model for the Metropolitan Atlanta Area. To utilize this spread model and *Dynamic Update Approach* in practice for a pandemic influenza, the real world data should be analyzed quickly to estimate the value of R_0 and other parameters.

In our disease spread model, we did not assume any seasonal effects or viral evolution, which may change the spread pattern of the virus. Another future direction is optimizing the intervention policies such as distribution of vaccines and antivirals. This may decrease the number of infected people as well as the amount of food requirement.

Finally, developing efficient and effective heuristic algorithms for the facility location decisions will enable us to solve larger-sized problems.

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A DETAILS OF THE DISEASE SPREAD MODEL

In this section, we explain the disease spread model details, and how we obtain the parameters used in the disease spread model. The details of the parameter calculations are explained in Wu et al. (2006). Here, we only present the age-based and night/day adjustments.

At the beginning of the simulation, every individual is assumed to be susceptible, and we introduce an initial number of infected individuals to the community, which represents the entrance of the virus to the population.

In the disease spread model, we simulate the time of next infection and choose the individual that will be infected. Next infection time is generated by calculating the “instantaneous force of infection” for each individual (Wu et al. 2006). We have adjusted the calculation of force of infection for our age-based model using the age-based parameters (see below for the calculation of the force of infection).

The coefficient of transmission (β), relative hazards of an infected individual at presymptomatic and asymptomatic stages (h_{PS} and h_{AS}) and relative hazards in peer groups and community to households (h_{PG} and h_C) are used to define different disease settings (Wu et al. 2006). We make age-based adjustments to the calculation of these parameters. As it is mentioned for the base case in Wu et al. (2006), we assume that the proportion of transmission that occurs at either presymptomatic or asymptomatic stage is 0.3, the proportion of infections generated by individuals who are never symptomatic is 0.15. Finally, we assume that 70% of the infections occur outside the household and half of these infections occur within the peer groups.

In our model, we assume that the relative infectivity of the children compared to adults is 1.5 and the relative susceptibility of the children compared to adults is 1.15 (Carrat et al. 2006). The susceptibility and infectivity parameters are normalized so that the expected susceptibility of an in-

dividual is 1.0, and the expected infectivity of an individual is 1.0, h_{PS} and h_{AS} for symptomatic, presymptomatic and asymptomatic cases, respectively.

Using these parameters, the force of infection experienced by the i^{th} individual during the day (λ_i^D) and during the night (λ_i^N) are calculated as follows:

$$\lambda_i^D = S_i \sum_{j=1}^{j=N} \delta_{ij}^{PG} m_j \epsilon_j h_{PG} \beta + \delta_{ij}^C \frac{m_j h_C \beta}{N_i},$$

$$\lambda_i^N = S_i \sum_{j=1}^{j=N} \delta_{ij}^H \frac{m_j \beta}{n_i^{HA}} + \delta_{ij}^C \frac{m_j h_C \beta}{N_i},$$

where S_C and S_A are the relative susceptibility values for a child and adult, respectively. Let q_A be the proportion of adults in our population, then S_C and S_A can be calculated using the following equations, which are explained above.

$$(1 - q_A)S_C + q_A S_A = 1.0$$

$$S_C = 1.15 S_A$$

N_i is the number of individuals in the i^{th} individuals community and N in the total number of people in the considered area. n_i^{HA} is the active household size of this individual where dead and hospitalized individuals are not counted. $\delta_{ij}^H, \delta_{ij}^{PG}$ and δ_{ij}^C are the indicator functions defined for households, peer groups and community, respectively. ϵ_j is the indicator variable showing whether j^{th} individual withdraws from work or school. Finally, m_j 's are defined as follows:

$$m_j = \begin{cases} I_X^C, & \text{if } j \text{ is a child at stage } X \\ I_X^A, & \text{if } j \text{ is an adult at stage } X \\ 0, & \text{otherwise,} \end{cases}$$

where I_X^C and I_X^A are the infectivity of an infected child and an adult at stage X (for $X \in \{I_P, I_A, I_S\}$), respectively. The values of these infectivity parameters are calculated as follows by using the expected relative hazard of an individual.

$$(1 - q_A)I_X^C + q_A I_X^A = \begin{cases} h_{PS}, & \text{if } X = I_P \\ h_{AS}, & \text{if } X = I_A \\ 1.0, & \text{if } X = I_S \end{cases}$$

$$I_X^C = 1.5 I_X^A$$

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