A Model for the Ordering and Distribution of the Influenza Vaccine

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Abstract
The system for the production and distribution of the United States supply of influenza vaccine has experienced disruptions during past influenza seasons. The identification of elements of the influenza vaccine is different each year and must be researched and identified each year prior to the influenza season. The manufacturing of the vaccine is a complicated process with many potential problems. This paper identifies two different policies for use in a normal influenza season to determine how many companies are required to provide a sufficient amount of influenza vaccine, the percentage distribution policy and the strict priority distribution policy. The majority of the influenza seasons could be covered by purchasing fewer than 108 million doses, as in the percentage distribution policy, making sure that the vaccine dose orders are spread out evenly over four companies and distributed evenly by age group percentage, but could be reduced to as little as 24.5 million total vaccine doses during a shortage caused by production problems with minimal cost and loss of life using a strict priority distribution policy.

1. Introduction
Each year there is an estimated 36,000 deaths and 200,000 hospitalizations [1] in the United States due to health problems stemming from the influenza virus. Ninety percent of deaths related to underlying respiratory and circulatory illnesses associated with the influenza virus occur among adults older than 65 years of age [2]. An untreated flu pandemic could cause widespread sickness and death in the United States among all age groups if the country is not ready for the possibility. However, during a normal influenza season panic can still occur if there is a shortage of influenza vaccine for distribution. In 2004, a limited supply of the flu vaccine developed a panic in the United States. Mostly the elderly were affected by waiting in long lines for the opportunity to receive the influenza vaccine. An elderly woman actually died in line waiting with her husband [3]. Chiron Corporation, one of the two companies licensed to provide the flu vaccine in the United States at the time, had to withdraw 48 million doses of the inactivated vaccine (Fluvirin®) that the company expected to deliver in 2004. That turned out to be half of the 100 million doses that were expected to cover the United States population [4]. Luckily, the flu season ended up as being mild and the limited supply of the vaccine did not appear to cause additional deaths [5]. However, what steps can be taken to minimize the risks of this type of situation?

The range of annual demand for flu vaccine is usually 75 to 115 million doses [6]. The type of flu season, from mild to bad, will alter the number of shots demanded by the public. The demand, therefore, can be said to be unknown from year to year as can the supply. The average amount of influenza vaccine ordered, the overall supply chain and the number of United States suppliers were used in the development of a model to determine how many companies there should be and the number requested from each company to provide a sufficient supply.

The purpose of this paper is to determine the number of doses of influenza vaccine required to order from a determined number of manufacturers to prepare for influenza vaccine shortages in the future like the shortage in the 2004 flu season. The paper also looks at how to use the vaccine on hand when a shortage occurs to minimize overall cost. Two policies are presented to distribute the influenza vaccine: a strict priority distribution policy and a percentage distribution policy.

A systems engineering approach to the production of the vaccine and the supply and demand chain is utilized to develop a model to minimize cost by spreading the vaccine production over several companies and focusing the distribution of the vaccine produced to specific target age groups. The process is simply to deliver the required vaccine to the customer when required to avoid death. This becomes difficult when there is a limited supply of vaccine. Understanding the production difficulties, the supply process of the vaccine to the distributors and then to the customers, and the customer demand are all
important aspects of the system. This model is theoretical and would be difficult to check without the backing of the CDC and all other stakeholders.

1.1. Deadly Influenza Seasons

Influenza A and B are the two types of influenza strains that cause human illness. Influenza B viruses are not categorized into subtypes. Influenza A viruses are categorized on the basis of their two surface antigens. Hemagglutinin (HA) is an antigenic glycoprotein found on the surface of the Influenza virus and is responsible for binding the virus to the cell that is being infected. Neuraminidase (NA) is an antigenic glycoprotein enzyme found on the surface of the Influenza virus. The three types of human influenza viruses are H1N1, H1N2, and H3N2. Influenza type A viruses are constantly changing and this requires the manufacture of a completely new vaccine batch each year.

Influenza and pneumonia were ranked number eight on the list of causes of deaths among the United States population in 2006 [7]. Usually, the virus each year only affects small children, the elderly, and those with existing medical conditions but four times in the last 100 years there has been an influenza pandemic, or a world-wide epidemic, which has affected the United States. These were caused by new influenza A virus subtypes that emerged during the 20th Century.

The first to affect the United States was the “Spanish Influenza” in 1918-19. It is believed to be caused by a type A (H1N1) virus [8]. The Spanish Influenza epidemic caused an estimated 22 million deaths around the world according to the CDC.

In 1957-58 there was an influenza pandemic called the “Asian Flu”. This was caused by an influenza A (H2N2) type virus [8]. An estimated 1 million people died worldwide of the Asian influenza, 70,000 in the United States.

The “Hong Kong Flu” occurred in 1968-69 and was caused by an A (H3N2) type virus [8]. It is estimated that 750,000 people worldwide died of the virus and 34,000 of those deaths occurred in the United States. Both the 1957-58 and 1968-69 pandemics were known to be caused by viruses containing a combination of genes from a human influenza virus and an avian influenza virus.

The most recent H1N1/09 influenza identified as a pandemic by CDC killed over 12,000 in the United States in 2009-10. It mostly affected those with chronic diseases, pregnant women, and children [9].

1.2. Vaccine Development and Production

The Vaccines and Related Biological Products Advisory Committee (VRBPAC) of the Food and Drug Administration (FDA) meet each year to determine the formulation of the influenza vaccine in the United States for that year. The recommendations are based on antigenic analysis of recently isolated influenza viruses. Post–vaccination serologic studies are also used to develop the vaccine [10]. Influenza vaccine effectiveness depends on the age and the health, or immune status, of the patient being vaccinated. It also depends heavily on the match of the strains of the virus chosen for the vaccine for that year. The vaccine will be more effective if the strains used in the vaccine matches what is currently circulating in the United States.

The vaccine has been found to be 70% to 90% effective in preventing infection in healthy adults under 65 and 30% to 40% effective in preventing infection in adults over 65 based on the National Foundation for Infectious Disease reports [11][12]. The American Medical Directors Association (AMDA) reports that generally the influenza vaccine is 50% to 60% effective in preventing influenza related hospitalization among those that are 65 and older, and 80% effective in preventing influenza related death among those that are 65 and older [13].

2. Vaccine Supply and Demand

The uncertainty in vaccine production amounts, the uncertainty in customer demand, and the supply and demand chain all add to the problem of getting the influenza vaccine to where it is needed each year. The architecture of the influenza vaccine distribution system, including inflow and outflow requirements, is analyzed by utilizing the rational method [14]. Mathematical principles, equations, and estimated costs associated with potential deaths are utilized to develop an optimized solution.

The CBO identified several problems in the influenza vaccine supply chain [15]. The lengthy egg-based manufacturing process means that production cannot be scaled up. Demand for the vaccine each year varies and can depend on outside factors like the severity of the previous year and media coverage. The manufacturing process is prone to contamination.

The United States market is by far the largest demand of influenza vaccine for the world’s producers. The United States population is around 300 million which is larger than the population of the whole of the European Union and 10 times greater than Canada. The target supply for the United States is somewhere between 68 million and 99 million doses of the influenza vaccine [6].

The number of influenza vaccine doses produced in any given year is limited by the capacity of the
production facilities, the availability of eggs used for the production, and the yield of influenza virus from each egg. All three of those variables can be easily disrupted. Private companies are required to plan the amount of vaccine they will produce well in advance. Any disruption of the production schedule may lead to a delay in the availability of the vaccine and result in a customer relation nightmare. The manufacturing process is currently very rigid and does not allow much room for error in ordering.

The demand for the vaccine fluctuates from year to year. The most influenza shots ordered prior to 2005 was 83 million [16]. In 2004, only 57 million doses were eventually distributed. In 2005, the estimate for vaccination production with production from three companies will be from 71 million to 97 million doses [17]. In a pandemic situation that number would at least double to 180 million. The amount of 185 million comes up frequently as the number of vaccine doses that the CDC would like to have on hand or at their disposal during the regular influenza season [16]. During the 2009-10 swine flu pandemic 162 million H1N1 specific vaccines were produced and distributed in the United States, but only 90 million were used by customers [9].

The influenza vaccine system for the United States will be identified as comprised of the Government and Health Care industry that requests the vaccines for patients and the companies that manufacture the vaccine. In the middle of the two is the distribution process which includes private distribution companies. These private distribution companies search out vaccine supplies after all the direct orders have been purchased through the manufacturers and act as a clearinghouse for any vaccine remaining at the manufacturing facilities. The amounts a purchaser pays may differ depending upon such variables as the quantities purchased, contractual arrangements, and source of purchase. The Congressional Budget Office identified the distribution process as inadequate [15].

A simplified distribution system is used to model the manufacturing, distribution, and use of the influenza vaccine. For the model, each company is considered to have one batch of vaccine that they produce. This makes the vaccine for that company good or bad and not partially good or bad. Chances are that if there is a manufacturing problem or contamination it will shut down the plant. A delay will be modeled as a good batch that arrives in time to utilize. The model also simplifies the distribution to eliminate the private distributors and focuses on the manufacturer to health care provider line. The assumption is that the vaccine will find the paying customer if there is still vaccine left in the market.

3. Vaccine Model

3.1. Vaccine Model Introduction

The Vaccine Model can be used to identify the correct number of vaccines to be ordered from each company. The vaccine order quantities are based on the number of companies available for the production of the influenza vaccine and divided equally between those companies to minimize overall cost. The Vaccine Model determines the number of customers based on the population of the United States and their age, and then determines how many companies are needed to spread out the purchase to ensure that enough is available for the determined amount of customers. Finally, the Vaccine Model then determines which age groups should receive the vaccinations first to minimize total cost. A goal of this research is to help minimize cost while providing sufficient vaccinations to those who request it.

The Vaccine Model calculations are implemented in Excel and calculations are produced using the Frontline’s Solver in Microsoft Excel. The total cost of the vaccine program cell is minimized. The total cost includes the cost of the vaccine purchased and the cost of the deaths associated with the influenza virus. Two policies were used in the distribution of the vaccine. One policy uses a strict priority that was developed for the distribution of the vaccine. The other policy would be to distribute the vaccine by population percentage as the customers came to receive the vaccine. The Vaccine Model is also used to look at a pandemic situation in which more than usual percentages would request a vaccine in each age group identified.

The number of potential customers is based on the population of the United States (U.S. Census 2000 released 5/15/01) and is set at 80,679,143 as a default. The number is developed by dividing the total population of the United States into age groups and using the past percentages of vaccination in each age group to determine the potential total customers.

3.2. Vaccine Model Development and Distribution Policies

Customers are defined for the purpose of the model as the total number of United States citizens that request a vaccine. Non-customers are defined as the United States citizens that do not actively seek a vaccination during the influenza season. The customers are divided into age groups and are placed into high-risk or a low-risk category. On any given influenza season the number of customers requesting vaccination ranges from 70 to 90 million depending on the severity of the season. In a pandemic situation that
number would at least double to 180 million. The amount of 185 million comes up frequently as the number that the CDC would like to have on hand or at their disposal during the regular influenza season [16].

The Vaccine Model calculations are used to determine how many companies are required and how many vaccine doses from each company should be ordered to have an adequate supply of vaccine on hand during the influenza season. It is important to get a large amount of the vaccine out to the public as early as possible due to the tapering off of customer demand because the influenza season usually peaks in February [5]. The mortality rate also peaks by the end of February [18]. The Vaccine Model is set up using the indices, parameters, decision variables, constraints, and objective function identified in section 3.7.

The Decision Variables for the Vaccine Model are the total inactivated vaccine purchased $R$, and the total number of companies to purchase the vaccine from $N$. The variable $n$ is the number of companies that develop a bad batch of vaccine that can not be used. If the vaccine can not be used it will not be delivered, and therefore, not paid for. The $N$ value must be smaller or equal to the number of companies that currently have a license to sell vaccine in the United States market.

Parameters for the Vaccine Model include the cost per inactivated influenza vaccine dose $V$, the total number of customers $T$, which is the sum of the customer totals of each age subgroup $X_{\text{inNR}}$, the number of companies that fail to produce useable vaccine $n$ from a total number of $N$ companies, the probability of contamination with each order of vaccine $P$ (see Table 3-3), the probability of death given a vaccine shot $Q'$, and the probability of death given no shot for low risk and high risk customers $Q$, and the total number of customers receiving a vaccine $Y_{\text{inNR}}$. The percentages of each age group in the general United States population and the percentage of those in each age group requesting vaccination on any given year divided by high and low risk groups is used to determine the number of customers that will require an influenza vaccine. The Vaccine Model is primarily developed on the basis of the number of customers. The number of potential customers $T$ is based on the population of the United States and is set at 80,679,143 as a default. This number is developed by dividing the total population of the United States into age groups and using the past percentages of vaccination in each age group to determine the potential total customers. This number can be changed by changing the observed percentage of each age group that requests a vaccine. The cost of the inactivated influenza vaccine $V$ as set by Medicare’s 2009 Physician Fee Schedule is $11.17 to $19.70 [19]. A cost of $18.31 was used by the model.

The question to be answered is how many influenza shots should be ordered from a set number of companies to minimize the effect of a shortage, to cover as many customers as possible, and to minimize the overall cost of vaccination orders and lost earnings from all deaths. The number of vaccines ordered should minimize cost while covering the demand.

### 3.3. Vaccine Model Age Categories and Priority

Age categories have been identified for use in modeling affects of influenza. Meltzer identified 0-19 years, 20-64 years, and 65+ years categories [20]. These categories were assigned present value earnings lost by Meltzer, as well as illness and hospitalization costs.

Table 3-1 identifies each age category and the percentage of each age category in the total population of the United States in 2000. The percentage of high-risk and low-risk customers from each age group is determined by the United States population. Table 3-1 is based on the past percentages of customers (i.e. persons looking for an influenza vaccine). The average number of persons in each age category requesting a vaccination varies but is estimated by past percentages. The vaccination percentage has been significantly improved along with other childhood disease vaccinations for young children at 81% for 2003-2004 [21]. The percentage of adults 65 years and older that are vaccinated ranged from 40% to 70% in 1999, but has increased to 60% to 70% in 2009 [20][22].

For each age category and risk level, the percentage of those in each age group who usually request vaccination in the United States was multiplied by the number of persons in each category to determine the potential number of customers $X_{\text{inNR}}$ that would show up at a distribution point for a vaccination.

<table>
<thead>
<tr>
<th>Age</th>
<th>US Pop (Mil)</th>
<th>US Population Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>19.18</td>
<td>6.82%</td>
</tr>
<tr>
<td>5-19</td>
<td>61.30</td>
<td>21.78%</td>
</tr>
<tr>
<td>20-49</td>
<td>124.09</td>
<td>44.10%</td>
</tr>
<tr>
<td>50-64</td>
<td>41.86</td>
<td>14.87%</td>
</tr>
<tr>
<td>65+</td>
<td>34.99</td>
<td>12.43%</td>
</tr>
</tbody>
</table>

The health impact of individual seasons can vary widely on the basis of the size of the susceptible population, the prevalence of influenza infections, the type and strain of the annual viruses introduced into the population during the influenza season, and the match between the current virus strains and the strains used in
the vaccinations. The Vaccine Model estimates how many customers in each group will likely request a vaccine based on population of the United States and the population of each age group.

Two policies for the distribution priority of the vaccine are used in the Vaccine Model. The strict priority distribution policy uses a rigid priority to distribute the influenza vaccine. If the higher risk groups are targeted first in a set strict priority, and the distribution is limited to those groups only, you can limit the deaths associated with a shortage of the vaccine and overall cost. A study of the percentage of persons in each category, the potential for death, and the cost of death associated with each age category was accomplished to develop a priority of vaccination. This priority of vaccination are based on the calculated probabilities of death for each age group. Information on the probabilities of death is provided in the next section and in Table 3-2. The CDC vaccination priority was used strictly in the Vaccine Model to distribute vaccine first to the high risk groups that will reduce expected total cost. This form of distribution could be used in an influenza vaccine shortage or pandemic situation in which there was not enough time to produce additional vaccine to cover the increased demand.

The second, a percentage distribution policy, provides the vaccine to customers as they request it. In a normal influenza season, customers come to request vaccine based on their age categories and risk group. Each age and risk group has a percentage that searches for a vaccine. The vaccine is then distributed based on the percentage of customers that request a vaccine. No one group is completely vaccinated but the majority of all high risk groups are vaccinated.

### 3.4. Influenza Virus Attack and Death Rates

$Q_{Ai}$ is the fraction of the vaccinated, attacked population in age group $i$ that dies due to the influenza virus. $Q_{Mi}$ is the fraction of unvaccinated, attacked population rate of deaths due to the influenza virus. The Attack Rate $A$ is the attack rate in the United States for all people in all age groups and is assumed to be homogeneous across all age groups and risk categories. The attack rate is defined as the percentage of the United States population, customers and non-customers, which will be attacked by the influenza virus strain during the influenza season. In the Vaccine Model, the normal influenza season is modeled using a 20% attack rate [15][20][23][24]. The attack rate multiplied by the percentage of each population death rate if attacked gives the fraction of each age group that dies of the influenza virus.

The overall death rates used by the Vaccine Model are taken from Meltzer [20] and are considered the upper bound of the expected death rates. These death rates are identified in Table 3-2 and are not homogeneous.

The effectiveness of the influenza vaccine is a topic for discussion. The Advisory Committee on Immunization Practices (ACIP) stipulates that the effectiveness of the inactivated influenza vaccine depends “primarily on the age and immunocompetence of the vaccine recipient and the degree of similarity between the viruses in the vaccine and those in circulation” [25]. The effectiveness of the vaccine is dependent upon the health of the person being vaccinated and the guess made of the influenza strains that will be circulated during the influenza season. Taking into account the barriers to effectiveness and the past studies completed, an estimation of the vaccine effectiveness was developed and used in the Vaccine Model. The percentage used for vaccination effectiveness in the Vaccine Model is 60%. This assumption can be changed when definitive numbers are produced by the CDC. This is slightly lower than the published CDC number of 70% [25].

The customer category is based upon cost per loss of life in that age category generated by the Vaccine Model explained below. The cost per loss of life is highest for 0-4 and 5-19 high risk age group, and is lowest for the older than 65 low risk group. The customer category rank is shown in Table 3-2.

Table 3-2 shows overall death rates for the 10 age and risk groups.

### Table 3-2. Age Groups and Death Risk Probabilities

<table>
<thead>
<tr>
<th>Age</th>
<th>Risk Level</th>
<th>Death Rates*</th>
<th>Cust. Cat. (i)</th>
<th>$Q_{i}$ (unvaccinated)</th>
<th>$Q_{i}'$ (Vaccinated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>High</td>
<td>7.65</td>
<td>1</td>
<td>.00153</td>
<td>.000459</td>
</tr>
<tr>
<td>0-4</td>
<td>Low</td>
<td>0.125</td>
<td>6</td>
<td>.000025</td>
<td>.000015</td>
</tr>
<tr>
<td>5-19</td>
<td>High</td>
<td>7.65</td>
<td>2</td>
<td>.00153</td>
<td>.000459</td>
</tr>
<tr>
<td>5-19</td>
<td>Low</td>
<td>0.125</td>
<td>7</td>
<td>.000025</td>
<td>.000015</td>
</tr>
<tr>
<td>20-49</td>
<td>High</td>
<td>5.72</td>
<td>3</td>
<td>.001144</td>
<td>.0003432</td>
</tr>
<tr>
<td>20-49</td>
<td>Low</td>
<td>0.09</td>
<td>8</td>
<td>.000018</td>
<td>.0000108</td>
</tr>
<tr>
<td>50-64</td>
<td>High</td>
<td>5.72</td>
<td>4</td>
<td>.001144</td>
<td>.0003432</td>
</tr>
<tr>
<td>50-64</td>
<td>Low</td>
<td>0.09</td>
<td>9</td>
<td>.000018</td>
<td>.0000108</td>
</tr>
<tr>
<td>65+</td>
<td>High</td>
<td>5.63</td>
<td>5</td>
<td>.001126</td>
<td>.0004504</td>
</tr>
<tr>
<td>65+</td>
<td>Low</td>
<td>0.54</td>
<td>10</td>
<td>.000108</td>
<td>.0000756</td>
</tr>
</tbody>
</table>

*Death Rates are taken from Meltzer per 1,000 [20].

### 3.5. Company Rate of Batch Contamination

An estimate for the probability of contamination is required for the Vaccine Model due to the uncertainty of the manufacturing process. A 10% estimate of batch contamination was used. The probability of contamination with each vaccine order $P$ is shown in
Table 3-3 for one, two, three, and four companies. The probability of a good batch with each vaccine order would then be \((1 - P)\). The probability of a bad batch given an order is modeled as a binomial distribution where \(P_{13}\) is the probability that one batch is bad when you order from three companies. The influenza vaccine production was significantly slowed or reduced by contamination or manufacturing problems three times between 2001 and 2005. Therefore, a ten percent probability is a reasonable estimate for \(P\).

### 3.6. Vaccine Model Death Costs

The goal of the Vaccine Model developed is to minimize the cost of death and the cost of the vaccine used under the current situation of limited resources and a time constraint for the production of the vaccine. The only way to do this is to identify an amount of money for each potential life lost and then use that to develop a function based on those dollar amounts, and then minimize it based on the amount of deaths using a certain amount of vaccine and the cost of the vaccine program itself.

#### Table 3-3. Binomial Probabilities for Individual Company Contamination

<table>
<thead>
<tr>
<th>Binomial (P_{nN})</th>
<th>Probability of Contamination</th>
</tr>
</thead>
<tbody>
<tr>
<td>(P_{n1})</td>
<td>0.9 0.1</td>
</tr>
<tr>
<td>(P_{n2})</td>
<td>0.81 0.18 0.01</td>
</tr>
<tr>
<td>(P_{n3})</td>
<td>0.729 0.243 0.027 0.001</td>
</tr>
<tr>
<td>(P_{n4})</td>
<td>0.6561 0.2916 0.0486 0.0036 0.0001</td>
</tr>
</tbody>
</table>

For each age category, Meltzer [20] placed a price on the lost wages over a lifetime of persons that have died. The average cost of a death in 1995 US dollars of one under 19 was $1,019,536, 20-64 years was $1,045,278, and only $74,146 for someone 65 years old and older. The cost of death was estimated in 2006 by Lee at $1.9 million for those 65 years old and older. The focus of this paper is on the cost of death and developing a number of available vaccines so that the right amount of vaccine is provided to each age group to reduce potential deaths. \(C_i\) could be calculated for each age group resulting in a prorated \(C_i\) for all ages which could then be inserted into the calculations. Calculations would be based on annual earnings and work histories for low and high risk customer categories. The use of a prorated \(C_i\) would greatly increase the utility of the Vaccine Model and is considered for future research.

### 3.7. Vaccine Model Structure

The indices used in the Vaccine Model are: \(i = \) Customer category \((i=1, 2… 10)\), \(j = \) Customer category \((j=1, 2… (i-1))\), \(n = \) Number of companies with a bad vaccine batch \((n=1, 2, 3, 4)\), \(N = \) Number of companies total \((N=1, 2, 3, 4)\), \(R = \) Number of doses of vaccine purchased \((R\geq 0)\).

The Vaccine Model needs to solve the problem of selecting \((R, N)\) to minimize the expected value of the cost of the vaccine purchased \(f_1\), the cost of those dying after they receive a vaccine \(f_2\), the cost of those dying that did not receive a vaccination \(f_3\) after requesting it, and the cost of those dying that never looked for a vaccine, \(\text{Cost}_t\). Thus, the equation to minimize is Equation 1:

\[
\text{Total Cost } = E(f_1(r,n,N) + f_2(r,n,N) + f_3(r,n,N)) + \text{Cost}_t
\]

The constant \(\text{Cost}_t\) is the cost associated with the non-customers, the population that does not seek a vaccination. This is calculated by multiplying the amount of population not seeking a vaccine by the percentage of death for unvaccinated persons. \(\text{Cost}_t\) does not have to be added into Equation 1, since it is not affected by the amount of vaccine available, but is included here for completeness.

The variables \(R\) and \(N\) are constrained to be nonnegative.

\[
R \geq 0, N \geq 0 \quad \text{Equation 2}
\]

The overall death rates for unvaccinated customers \(Q_i\) is given by Equation 3 below.

\[
Q_i = Q_{Xi}A
\]

Equation 3

Let \(D_{iNR}\) be \(f_1+f_2\), the cost of all customer deaths. There are \(X_{iNR}\) customers in group \(i\), but only \(Y_{iNR}\) of them are vaccinated, so Equation 4 is;
\[ D_{nNR} = \sum_{i} C_{i}[ (Q_{i} Y_{inNR}) + (Q_{i} (X_{inNR} - Y_{inNR}) ] \]

The first part of Equation 4 is the cost of the vaccinated customers. The second part of Equation 4 is the cost of the customers that were not vaccinated.

We can now write Equation 1, \( \text{TotalCost} \), as the sum of those that do not seek a vaccination \( \text{CostF} \), the cost of purchasing the vaccine itself, and the cost of the customers that seek a vaccination and either receive it and still die or do not have the chance to receive it (by restrictions or shortage) and die. This is given in Equation 5 below.

\[ \text{TotalCost} = \text{CostF} + R \sum_{n=0}^{N} P_{nN} \left[ V\left( \frac{N-n}{N} \right) + D_{nNR} \right] \]

The cost of vaccine purchased itself and the cost of the customers that do and do not receive a vaccination is calculated in the second part of Equation 5. The variables \( R \) and \( N \) should be selected to minimize this total cost.

We will consider two policies for vaccine distribution: A percentage distribution policy and a strict distribution policy. Both distribution policies use the Equations 1 through 5 above. The difference in the policies is the way that the vaccine is distributed once the number of customers is calculated. The equations below are used to determine how many vaccines there are to distribute and which customers receive them.

Equation 6 is used for the strict priority distribution policy:

\[ Y_{inNR} = \min\left( X_{inNR}, R\left( \frac{N-n}{N} \right) - \sum_{j=1}^{i-1} X_{jnNR} \right) \]

And \( Y_{inNR} \geq 0 \)  \hspace{1cm} \text{Equation 6}

Equation 6 reduces the vaccine available as the customers get them based on a strict priority distribution. Once all the customers in the first highest risk group based on their customer category are covered completely, the vaccine is then passed on to the next highest customer category that has customers not yet vaccinated. The amount of vaccine that was purchased \( R\left( \frac{N-n}{N} \right) \) is reduced during each step by the vaccine already used for higher risk groups. The vaccination of customers continues by priority until the limit of \( R\left( \frac{N-n}{N} \right) \) number of vaccines is reached.

This limit takes into account the reduction of the vaccine ordered but not purchased due to batch contamination.

Where for the percentage distribution policy:

\[ Y_{inNR} = R \frac{N-n}{N} \frac{X_{inNR}}{T} \]

When

\[ R \frac{N-n}{N} < T \]  \hspace{1cm} \text{Equation 7}

\[ Y_{inNR} = X_{inNR} \]

When

\[ R \frac{N-n}{N} \geq T \]  \hspace{1cm} \text{Equation 8}

The percentage of customers that receive the vaccine for each age and risk category are calculated using the percentage of the total customers in each category divided by the total number of customers in all categories. In this manner most customers in each category receive the vaccination but all the customers in each category are never completely vaccinated.

3.8. Recommendations

Based on the fact that there is no discount for volume, the more companies that can spread the vaccination purchases is the best scenario. For the 2006-2007 influenza season the model calculated the number of vaccine doses that were required to minimize cost under the assumptions that all inactive vaccine is used appropriately for each age group, and the vaccine purchased in the United States can be divided equally into four companies. Using four companies, the purchase of 24,335,875 influenza vaccine doses provides an average death total of 44,985 and total cost of $34.6 billion in a normal influenza season if a strict priority distribution is used as in Table 4-1, Scenario 1.

If you had enough vaccine to distribute to all who wanted a dose you could save additional lives. Utilizing the method of providing a vaccination when any member of any population comes to purchase one the amount of vaccine needed goes up to 107,572,140 vaccine doses, which provides a death toll of 43,631 at a cost of $35.5 billion dollars as in Table 4-2, Scenario 2. Chances are, however, that there will not be enough time to manufacture and stockpile enough vaccine for the entire United States population. Therefore it is recommended that you aggressively target the vaccine doses to the high risk groups that will reduce overall total cost.

For example, in the best case scenario of all four companies having good batches and using the strict
priority vaccination policy identified above you need only 24,335,875 vaccine doses to limit the total deaths to 10,908. If you distribute 80,679,143 doses to cover all the potential customers the death toll will drop to 9,548 deaths. This is only a reduction of 1,360 deaths with an additional 56,343,268 vaccine doses purchased. This suggests that a strict priority for vaccination should be considered even during seasons where shortages have not occurred.

Based on the Vaccine Model calculations and using four companies you would order 6,083,967 doses from each of the four companies for the normal scenario utilizing the strict priority distribution policy and 52,085,151 from each of the four companies in a pandemic situation. Under the percentage distribution policy all requesting customers can be vaccinated and there is not a shortage until more than one company defaults on their shipment of vaccine.

3.9. Risk Assessment

The argument can be made that all life no matter what age should be considered equal. Under a shortage condition, a strict priority distribution policy would be used to distribute the influenza vaccine. If the cost of life is changed and made equal for the normal influenza season with priority distribution then the total cost of the program increases to $45.23 billion from $34.6 billion with an additional 12 million vaccine doses required to minimize total cost. Table 3-4 outlines the cost associated with each scenario outcome and the total expected cost of the program using the priority distribution policy. The average number of deaths would be 44,618, which are approximately 300 less than using a reduced amount for the cost of life for those 65 and older.

The cost of vaccine on average would be $613.58 million versus $409.05 million for the reduced cost of all persons 65 and older. The cost of the vaccine, cost of each life lost, and the total cost of the program must be reviewed to assess the risks and costs that the country as a whole are willing to take on to adequately distribute supply of the vaccine when required. The first row in Table 3-4 corresponds to N=1 through N=4 with each column corresponding to the number of companies n that result in contaminated vaccine batches that cannot be used.

4. Conclusions and Recommendations

4.1. Key Points and Recommendations

Each influenza season is different in severity and the number of customers seeking a vaccine. A pandemic situation would add additional uncertainty to the problem. Over the past few years, however, it is clear that not enough vaccine is being produced to cover the demand. Only one out of the last four years has seen a surplus of vaccine after the conclusion of the influenza season.

<table>
<thead>
<tr>
<th>Companies</th>
<th>Average Cost</th>
<th>all Good</th>
<th>1 Bad Batch</th>
<th>2 Bad</th>
<th>3 Bad</th>
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</tr>
</thead>
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</table>

Four companies distributing the inactivated vaccine doses evenly could provide coverage for the population of the United States if a strict priority distribution policy is in place. Distributing the vaccine without a priority would cause the amount of the vaccine required to increase significantly.

A pandemic would require at minimum an order of around 208 million doses of vaccine spread over four companies to cover the United States population adequately if there was a 10% chance of contamination from each company. This is based on the assumption of a strict priority distribution policy. This is based on the assumption that a much higher percentage of people in each age group and category would be looking for the vaccine. If the priority distribution is not used the number of vaccines required goes up to 300 million.

The majority of the influenza seasons could be covered by purchasing fewer than 108 million doses, as in the percentage distribution policy, making sure that the doses are spread out evenly over four companies and distributed by percentage but could be reduced to as little as 24.5 million doses if necessary using a strict priority distribution policy.

Under the assumption that you can not enforce a strict priority for vaccine distribution, ordering around 26.89 million vaccine doses from four separate companies should reduce the effect of shortages in annual vaccine doses during a normal influenza season.

4.2. Vaccine Model Results

The number of vaccinations given to customers in Scenario 1 and Scenario 3 for the Vaccine Model is based on a strict priority distribution policy. Using four companies, the purchase of 24,335,875 influenza vaccine doses provides an average death total of 44,985 and total cost of $34.6 billion in a normal
influenza season if a strict order of vaccination is used. This is Scenario 1 and Table 4-1. The number of vaccinations given in Scenario 2 and Scenario 4 were based on percentage distribution policy. Utilizing this policy, the amount of vaccine needed in a normal influenza year goes up to 107,572,140 vaccine doses which provide a death toll of 43,631 at a cost of $35.5 billion dollars. This is Scenario 2 and Table 4-2.

The result of not providing a large-scale immunization program based on the Vaccine Model developed would result in a cost of $41 billion and around 58,000 deaths during a normal influenza year as shown in Tables 4-1 and 4-2 when there are no good batches to use.

Table 4-1. Scenario 1: Normal Influenza Season Cost in Billions, Priority Distribution policy, 44,985 Deaths

<table>
<thead>
<tr>
<th>Companies</th>
<th>Average Cost</th>
<th>All Good</th>
<th>1 Bad</th>
<th>2 Bad</th>
<th>3 Bad</th>
<th>4 Bad</th>
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</table>

Table 4-2. Scenario 2: Normal Influenza Season Cost in Billions, Percentage Distribution policy, 43,631 Deaths

<table>
<thead>
<tr>
<th>Companies</th>
<th>Average Cost</th>
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<td>41.01</td>
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4.3. Pandemic Situation

If a pandemic occurs under the current production process there would most likely be a shortage situation due to the fact that most of the population would seek out a vaccination if it was available. The pandemic influenza is modeled using a 35% attack rate. Nobody can predict the attack rate of a future pandemic but it is estimate that it would be higher than a normal influenza season [19]. That scenario would double or even triple the current requests for vaccinations. The assumption used is that 80% of the population will search for a vaccination, or an estimated 225.1 million customers. A priority must be identified and followed for either shortage situation, production difficulties or a pandemic. The distribution must also be made under the current system at least at first until other more drastic government regulations are put into place or technology progress makes the manufacturing process adaptive.

With four companies and a strict priority distribution into a pandemic situation where 80% of the population would be looking for a vaccine the amount of vaccine to be purchased would be 208,340,603 providing an average death toll of 54,798 using four companies at a cost of $41.36 billion. This is Scenario 3 and Table 4-3. If you had all the vaccine that you needed for all the customers that wanted a vaccine you could save more lives. Using a percentage distribution policy, 300,181,334 vaccine doses would be needed to cover the amount of customers that would come in for a vaccine estimated at $225.14 million. Based on the Vaccine Model calculations and using four companies you would order 52,085,150 doses from each of the four companies in a pandemic situation using the strict priority distribution policy.

Using the percentage distribution policy in the Vaccine Model calculations and using four companies you would order 75,045,334 from each of the four companies in a pandemic situation. A total of 300,181,334 vaccine doses would need to be ordered to cover the amount of customers that would come in for a vaccine. Using four companies, there would be 53,400 deaths at a cost of $43.01 billion dollars. This is Scenario 4 and Table 4-4.

Table 4-3. Scenario 3: Pandemic Influenza Season Cost in Billions, Priority Distribution, 54,798 Deaths

<table>
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<th>Companies</th>
<th>Average Cost</th>
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Table 4-4. Scenario 4: Pandemic Influenza Season Cost in Billions, Percentage Distribution, 53,400 Deaths

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4.4. Summary

By CDC calculation, 185 million doses should be available each year to make sure an adequate supply gets to those customers who should be getting that vaccine. The Vaccine Model estimates that around 108
million on an average year are needed to minimize cost to the economy and loss of life. If the cost of life is changed and made equal for the normal influenza season with priority distribution then the total cost of the program increases to $45.23 billion from $34.64 billion with an additional 12 million vaccine doses required to minimize total cost. The Vaccine Model found that four companies can adequately produce the vaccine required even if one of the companies fails. Using the percentage distribution policy no shortage would occur unless more than one company failed to produce the requested vaccination doses. The strict distribution policy reduces the amount of vaccine doses required by under a third of that required using the percentage distribution policy in a normal influenza year.

The total cost of the vaccine program under the strict priority distribution policy would be $34.64 billion for a normal vaccination year to $41.36 billion for a pandemic year. Minimum cost and loss of life in a pandemic situation would be accomplished if a strict priority distribution policy was used. Under shortage conditions, the risk of not being able to cover all customers in a pandemic situation is minimized by using the strict distribution policy and a decrease in overall cost of $1.7 billion dollars versus the percentage distribution policy with around 208 million doses ordered. The use of a strict priority distribution in a shortage situation limits loss of life to an average 1,300 United States citizens under a pandemic situation if the production of vaccine is spread over four companies. Actual vaccine costs are reduced by over $1 billion dollars during a normal influenza season and over $600 million during a pandemic year by using the strict priority distribution.

The result of not providing a large-scale immunization program based on the Vaccine Model developed would result in a cost of $41 billion and around 58,000 deaths during a normal influenza year based on the results of the Vaccine Model. No vaccine immunization program during a pandemic would result in an economic loss of $71.8 billion and over 100,000 deaths based on the results of the Vaccine Model.