OPTIMAL IMMUNIZATION STRATEGIES FOR GROUPS AT RISK IN VACCINE SUPPLY CHAIN MANAGEMENT

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Abstract

Annual influenza epidemics cause great losses in human and financial terms. Vaccination is the most effective way of protecting people from being infected. However, the impact of vaccination on the disease spread is dependent on the chosen immunization strategy and on functional, end-to-end vaccine supply chains *and logistics systems. This paper aims to determine the optimal combination of the various immunization strategies that lead to decrease of the disease burden. A supply-chain based model is proposed to address this problem. Computational results show that targeted vaccination significantly outperforms other strategies and prevails over them in terms of cost and efficacy.*

Keywords: *supply chain risk management, disaster logistics, operations management and scheduling*

1. INTRODUCTION

Influenza is an acute respiratory illness that rapidly spreads in seasonal epidemics and annually imposes great losses in both human lives and financial expenses. According to the World Health Organization (WHO) Global Influenza Surveillance and Response System [1], the impact of influenza in the USA only is currently estimated to be 25-50 million cases per year, leading to 150,000 hospitalizations and 40,000 cases of death. The average global burden of pandemic influenza in the rest of the world may be up to about 4-5 million cases of illness and 250,000-500,000 deaths annually. The WHO reports that costs in terms of healthcare, lost days of work and education, and social disruption have been estimated to vary between $1 million and $6 million per 100,000 inhabitants yearly in industrialized countries [1].

Vaccination is known as one of the most effective and widely distributed means of protecting people from being infected by infectious diseases (see [1]-[6], among others). In particular, the influenza vaccination can significantly reduce the transmission rate of infection from infected to the susceptible individual thereby decreasing the disease spread. This, in turn, results in lower morbidity and mortality among the population.

The effectiveness of nation-wide vaccination programs heavily depends on the structure and functioning of the corresponding vaccine supply chain (VSC). The role of the VSC is three-fold: (a) to ensure effective vaccine storage, handling, and stock management; (b) to guarantee effective maintenance of logistics management, and (c) to provide rigorous temperature control in the cold chain. The ultimate goal is to ensure the uninterrupted availability of quality vaccines from manufacturer to service-delivery levels so that opportunities to vaccinate are not missed because vaccines are unavailable [7]-[10]. Following studies in [11, 12], this paper is focused on defining the right quantity of the vaccine doses assigned to different population groups at risk of being infected.

2. VACCINE SUPPLY CHAINS

The vaccine supply chain considered in this study includes multiple manufacturers, several distribution centers (DCs), multiple clinics and multiple end-users that are different population groups at risk of being infected. The vaccination process starts at the moment when the World Health Organization (WHO) determines and announces the expected influenza epidemic risks, strain types, vaccine types and production rates (usually, this happens in January of the current year). After that, the vaccine manufacturers initiate the vaccine production process. After being produced, the vaccines should be tested, usually, the test lasts 45-60 days. Assume that the vaccine testing is performed in June-July and that vaccines are packed and ready to be shipped from the manufacturers in August. The planning horizon starts in August and terminates in March of the next year, with a total duration of 33 weeks. Details of the vaccine supply chain are given in [11]-[12].

Figure 1 borrowed from [11] schematically displays the main components of the vaccination supply chain, and material and information flow. Physical flows are marked by thick arrows; information flows are in broken lines. The set of DCs and the set of clinics are two main collective stakeholders ("players") in the healthcare organization (HCO), each having its own replenishment/service function.

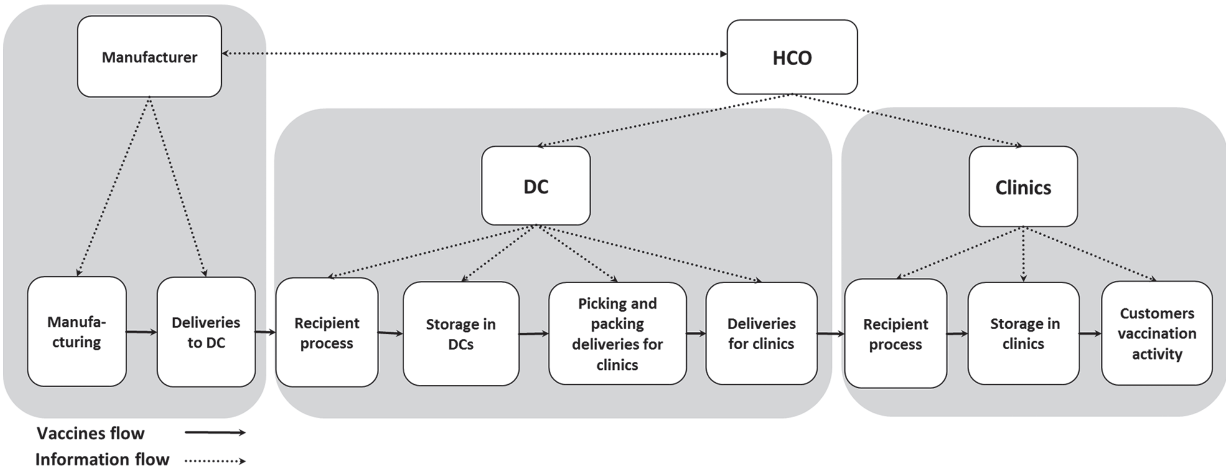

Figure 1 – Main supply chain components and process flows (the source: [11])

In order to improve the overall quality of vaccination services, a set of strategical decisions is to be done by the HCO before the start of the influenza vaccination season. In particular, the HCO is to decide how many vaccine doses should be ordered so that to minimize the total VCS costs (including direct/indirect medical/non-medical costs) while keeping the customer satisfaction and medical efficacy at predetermined levels. The customer satisfaction is associated with the public benefits of vaccination, i.e., an expected decrease in the number of lost working hours, decrease of visits to doctors and improvement of medical service during the influenza season. On the other hand, the medical efficacy is an integral characteristic of medical aspects of the vaccination program that are explicitly expressed by medical staff and medical organizations.

Since the population is heterogeneous (with respect to age, health conditions, and so on), the risk to be infected is varied from individual to individual. Therefore, in order to decrease the disease burden for less protected segments of the population (e.g., infants, seniors, medical personnel, etc.), it is on responsibility of the HCO to define what is a proportion of the vaccine doses to be allotted from the total ordered amount to each risk group of population. This decision strongly depends upon the choice of the vaccination strategy.

3. VACCINATION STRATEGIES

The right quantity of vaccines and, consequently, a major impact of influenza vaccination on the disease propagation in the VSCs is heavily dependent on the immunization strategies. For instance, the mass vaccination, wherein the aim to vaccinate large population groups over a short period of time, seems to be the most effective strategy when the budget is unlimited. However, in the real life, when the resources are scarce, such type of strategy is impractical. On the other hand, the random immunization means to randomly select a fraction of individuals to be vaccinated without accounting for their heterogeneity (age, occupation and so on). Such a strategy can lead to the vaccination of sustainable to disease individuals or persons who are in general isolated from the main mass of the population. Consequently, the impact of the random immunization on preventing the disease spread may be minor. Contrary to the mentioned immunization strategies, the targeted vaccination is directed toward the high-risk groups of individuals, which can be heavily affected by the disease (such as, e, g., elderly people, children, people with chronic illnesses, pregnant women) as well as the groups responsible for the disease spread (for instance, medical personal). Such a strategy allows to better utilize the scarce resources, such as vaccines, logistics resources, and a budget.

During the last decades, the effectiveness of the targeted vaccination was studied based on a variety of approaches. However, the literature devoted to the mathematical models for such type of vaccination still remains comparatively scarce. In particular, in [6, 7], the authors focused on identifying optimal vaccine allocation strategies to reduce influenza morbidity and mortality within the age-structured population. By implementing simulation, they found that vaccinating either younger children and older adults or young adults averts the most deaths. Similar results are obtained in [8].

In order to determine the optimal vaccination strategies for the heterogeneous population under uncertainty, the authors in [10] use a stochastic programming model. This model is an extension of the linear programming model proposed in [9] in which some parameters (e.g., vaccine efficacy and contact rate) are treated as random variables. The decisions regarding the number of individuals in each age group of the population that should be vaccinated are based on the relative infectivity and susceptibility of people in a group. A drawback of the paper is that the impact of the vaccination strategy on public benefits and medical efficacy is not considered. The authors in [16] find that prioritizing individuals on the basis of age and co-morbidities in along with considering individual infection history may have a greater impact on disease reduction in targeting and promoting influenza vaccinations. The advantage of the targeted vaccination was also shown for the non-influenza diseases (e.g., respiratory syncytial virus, see [15]), wherein vaccination of children less than 5 years old is the most effective strategy to avert disease in children and elderly.

While the authors in [6]-[8] consider only the impact of a vaccination strategy on epidemiological and economic outcomes, the present paper considers a more general model. Specifically, the optimal vaccination policies to minimize the total costs associated with vaccination are sought for, whereas the public benefits and medical efficacy are to meet a predefined level defined by decision makers. Similarly to [11-12], the new mathematical model includes public benefits and medical efficacy. At the same time, the present paper extends [11-12] by eliciting the impact of optimal vaccination strategies for each high-risk population sub-group. Moreover, the computational experiment comparing different types of immunization strategies (mass, random and targeted) is carried out demonstrating the advantages of the targeted strategy.

4. PROBLEM DESCRIPTION AND MATHEMATICAL FORMULATION

We consider influenza transmission and vaccination in a VSC containing a number of different risks-groups. The disease transmission takes place both inside the group (i.e., between the group's members) and between the different risks-groups as well. The population groups are heterogeneous (in the sense that the number of members in each group may be different); each group includes individuals with similar rates of susceptibilities and risks of morbidity and mortality. Most groups are assumed to be at high risk.

The main purpose of the proposed mathematical model is to find an optimal combination of different vaccination strategies for each risk group to prevent the disease outbreak. Note, that different individuals in the same risk group can be vaccinated by various immunization strategies. For instance, for some proportion of the individuals, one can use targeted vaccination, whereas the remaining persons are vaccinated under the mass or random immunization program. To estimate the effectiveness of the vaccination program, the researchers usually use a so-called post-vaccination reproduction number. This is the number of secondary cases that an initial infective can generate in the community of the susceptible individuals with partial vaccine coverage. When the number is less than one this means that the disease becomes endemic (i.e., the disease fades away with a time without additional interventions). Otherwise, the rate of disease spread increases and infection becomes an epidemic.

The specificity of the mathematical model to be designed is the presence of several conflicting criteria. The multi-criterion decision problem means that the model includes in the form of multiple objective functions three main characteristics: medical efficacy, public benefits, and vaccination program costs (see, for example, [9, 10]). Each of the three primary characteristics may be divided, in turn, into several partial objectives (called sub-objectives). Note, that in the suggested mathematical model, the public benefits are handled with the help of a general function called a vaccination coverage of the susceptible population. It implies that the larger the vaccination coverage, the fewer hospitalization cases are expected due to morbidity. Further, the medical efficacy is associated, in particular, with the total amount of hours needed for vaccination. The smaller the latter number, the higher the medical efficacy. Moreover, unlike the models considered in [9, 10], the best min-cost combination of the vaccine strategies is sought for.

The main initial (or strategic) decision variables treated in the considered VSC are the following:

- inventory size in the healthcare organization (HCO) r in period t, $t = 1,\ldots, T$, $r = 1,\ldots, R$;
- inventory size in clinic i at the end of period t, $i = 1,\ldots, I$, $t = 1,\ldots, T$;
- delivery (shipping) quantity of vaccines from manufacturer m to HCO r in period t;
- the delivery quantity of vaccine units from HCO r to clinic i in period t;
- the number of unused vaccines in sub-group j in period t in clinic i;
- vaccine consumption by sub-group j in clinic i in period t;
- amount of vaccine required by HCO r at period t.

Denote by $C(x)$, $E(x)$, and $B(x)$ three criteria above, that is, the vaccination costs, vaccination efficacy, and public benefits. In formal terms, a multi-criterion vaccination planning problem can be represented in the decision space of n variables as follows:

$$(\text{Min } C(\boldsymbol{x}), \text{ Max } E(\boldsymbol{x}), \text{ Max } B(\boldsymbol{x})) \tag{1}$$

$$\boldsymbol{x} \in \boldsymbol{X}, \ \boldsymbol{X} \subseteq \boldsymbol{R}^n \tag{2}$$

where $\boldsymbol{x}$ is the decision variable vector of size n, and $\boldsymbol{X}$ is the feasible set of variables.

For solving the multi-criterion problem (1)-(2), in this paper the method of principal criterion (also known as an epsilon-constrained approach, see [17]) is used wherein the vaccination costs are taken as the principal criterion and two other criteria considered as constraints with the right-hand side values provided by medical experts.

The following tactical decision variables, similar to those in the paper [10], are introduced:

x_{fv} - the proportion of the vaccinated individuals in the group at risk f under the policy v, where $f \in F$, $v \in V$. F is the set of risk-groups, and V the set of vaccine strategies (such as the mass vaccination, the random vaccination, the targeted vaccination, etc.)

Parameters in the model are the following:

w_f - the proportion of the number of individuals in a risk-group *f* from the entire population;
ω_{fv} - threshold (a minimal value) for a number of members from risk-group *f* to be vaccinated under strategy *v*; by allotting different values to ω_{fv}, various vaccination strategies can be derived;
α_{fv} - impact on disease spread in risk-group *f* vaccinated by policy *v* (see [9, 10], for details);
μ_F - the average size of the risk-group;
M - number of available vaccine doses *v*;
c_v - cost of vaccination strategy *v*;
η_v - the average time for vaccination under strategy *v*;
c_f - required vaccination coverage for risk-group *f*;
H_v - available medical personnel hours allotted to each vaccine strategy *v*.
Parameters for computingare α_{fv} similar to analogous parameters in [9, 10]:
m - the average contact rate of infected people;
u_f - the relative infectivity of individuals in risk-group *f* ;
s_f - the relative susceptibility of individuals in risk-group *f* ;
b - the transmission proportion;
ε - the vaccine efficiency;

$$\alpha_{fv} = mwf\,[u_f s_f\,[(1-b)(w_f - \varepsilon\omega_{fV}) + b\omega_{fv}\varepsilon(1-\varepsilon)] + bu_l s_f (w_f - \varepsilon\omega_{fV})^2]$$

The mathematical model can be now written as follows:

$$Min\ Z = \sum_{f \in F}\sum_{v \in V} c_{fv} w_f x_{fv} \quad (3)$$

subject to:

$$\sum_{v \in V} x_{fv} \le 1, \forall f \in F \quad (4)$$

$$\sum_{f \in F}\sum_{v \in V} a_{fv} x_{fv} \le 1 \quad (5)$$

$$\sum_{v \in V} x_{fv} \ge C_f, \forall f \in F \quad (6)$$

$$\sum_{f \in F} \mathsf{h}_v w_f x_{fv} \le H_v, \forall v \in V \quad (7)$$

$$\sum_{f \in F}\sum_{v \in V} w_f x_{fv} \le M \quad (8)$$

$$x_{fv} \ge 0, \forall v \in V; \forall f \in F \quad (9)$$

The objective function (3) minimizes the total vaccination cost. Eq. (4) ensures that the proportion of the vaccinated individuals in each risk-group *f* does not exceed one. To prevent the epidemic outbreak, constraint (5) holds, that is, the reproduction number is to be less than one. Constraint (6) ensures that the vaccination coverage for the risk-group *f* is no less than the predefined value C_f. Medical personal resource availability is demonstrated by constraint (7). Since the number of vaccine doses is limited, constraint (8) is used. Finally, constraint (9) guarantees that the decision variable is non-negative. Notice that constraint (6) reflects the public benefits whereas constraint (7) is associated with the medical efficacy.

5. COMPUTATIONAL EXPERIMENTS

Consider a fragment of the VSC CLALIT (see [11], [12], for details). The number of different groups at risk is 6 (1 stands for the low-risk group, …, 6 for the high-risk group); the set of vaccine policies includes 3 possible strategies of immunization: mass, random and targeted. The remaining data regarding the contact rate, relative infectivity/susceptibility, and others are borrowed from [10, 11]. The optimal solution of the linear program (3) -(9) is found by using the commercial software GAMS and CPLEX algorithm. The obtained computational results show that the targeted vaccination is superior with respect to the mass and random vaccination strategies as it has a smaller cost and a higher medical efficacy (see Figure 2). Another result is that the most prioritized risk groups are the following: elderly people, children (< 5 years), medical workers, and food-chain workers.

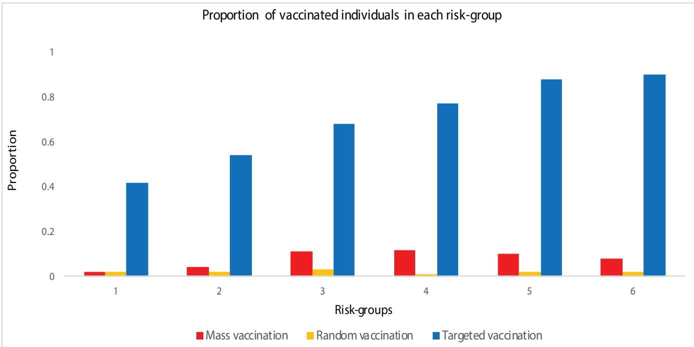

Figure 2 – The proportion of vaccinated individuals in each risk-group

6. CONCLUSION

Although the suggested mathematical model significantly differs from those known in the literature, the computational results obtained are very close to the earlier known ones, namely, the targeted vaccination strategy seems to be superior in comparison with the mass and random strategies (see, e.g., [6], [13]-[14]). It is worth noticing that the suggested model permits to find the best combination of several vaccination policies. In future work, it would be useful to further experiment with wider sets of vaccination strategies and population groups at risk. Moreover, investigating the influence of different transmission rates, e.g., saturated rates, on the optimal vaccination strategies may also be a very promising direction.

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