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Innovative Applications of O.R.

Optimal two-phase vaccine allocation to geographically different regions under uncertainty

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ABSTRACT

In this article, we consider a decision process in which vaccination is performed in two phases to contain the outbreak of an infectious disease in a set of geographic regions. In the first phase, a limited number of vaccine doses are allocated to each region; in the second phase, additional doses may be allocated to regions in which the epidemic has not been contained. We develop a simulation model to capture the epidemic dynamics in each region for different vaccination levels. We formulate the vaccine allocation problem as a two-stage stochastic linear program (2-SLP) and use the special problem structure to reduce it to a linear program with a similar size to that of the first stage problem. We also present a Newsvendor model formulation of the problem which provides a closed form solution for the optimal allocation. We construct test cases motivated by vaccine planning for seasonal influenza in the state of North Carolina. Using the 2-SLP formulation, we estimate the value of the stochastic solution and the expected value of perfect information. We also propose and test an easy to implement heuristic for vaccine allocation. We show that our proposed two-phase vaccination policy potentially results in a lower attack rate and a considerable saving in vaccine production and administration cost.

1. Introduction

In case of an outbreak of an infectious disease, such as influenza, one of the most effective interventions is vaccinating the susceptible population. Vaccination is known to be more effective at the beginning of the epidemic (Khazeni, Hutton, Garber, Hupert, & Owens, 2009; Yarmand, 2010; Yarmand & Ivy, 2013; Yarmand & Ivy, in press; Yarmand, Ivy, & Roberts, in press). However, it is not always possible to vaccinate a large population in a short time due to insufficient available vaccine doses or limited capacity. For instance, during the 2010–2011 flu season in the United States influenza vaccine doses were administered continuously from August 2010 through May 2011 (Centers for Disease Control and Prevention (CDC), 2011a). The national vaccination coverage was estimated at 30% by the end of October and 43% by the end of May (the situation was similar for flu season 2009–2010) (CDC, 2011a). These observations suggest a new vaccination policy: to have two (or more) phases of vaccination in geographically different regions when the first phase occurs at the beginning of the epidemic (to have the maximum effect) and the vaccination level in the second phase in each region depends on the outcome of vaccination in the first phase in that region. Under this policy, which we refer to as the "two-phase vaccination policy", one critical question is "how many vaccine doses should be allocated to each region in each phase?".

The main advantage of the two-phase vaccination policy is to allow evaluation of the vaccination outcome after the first phase. Therefore phase two might not be necessary in some regions resulting in a potential decrease in vaccine production as well as possibility of redistribution of vaccine doses among regions which need the second phase. Note that this two-phase model is a special case of a more general multi-phase model. However having two phases is a reasonable assumption since it is unlikely such allocation decisions would be made on a frequent basis. Furthermore, evaluating the two-phase model provides a conservative estimate of the benefits of a more general multi-phase model.

In the United States, vaccine stockpiles in each state are centralized and controlled by the state health department. Under a two-phase vaccination policy the state health department would need to decide how many vaccine doses to allocate to each region (e.g., each county) in each phase, and hence how many vaccine doses to order for production. The allocation in the first phase is challenging because of uncertainty about the epidemic dynamics. The epidemic may progress, or die out in some regions with limited vaccination, or even without any vaccination. Due to uncertainty, we formulate the problem of allocating vaccine doses to different

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regions in different phases of vaccination as a stochastic resource allocation problem.

In this article, we consider seasonal influenza in geographically different regions (e.g., counties within a state). We present numerical results based on the 100 counties of the state of North Carolina. We examine the two-phase vaccination policy for a range of choices of model input parameters. We assume that health care officials have decided to have vaccination in two distinct time periods referred to as Phase-I and Phase-II. Based on the probability that the epidemic is contained in Phase-I in each region (estimated from the disease spread model discussed in Section 3.1), we formulate a two-stage stochastic linear program (2-SLP). The Phase-I vaccine allocation is determined in the first stage while the second stage determines Phase-II vaccine allocation according to the realizations of epidemic containment in different regions in Phase-I, hence providing flexibility in the Phase-II vaccine allocation. We use the special problem structure to reduce the developed 2-SLP to a linear program (LP) with a similar size to that of the first stage problem and therefore find the optimal allocation very efficiently.

We use our model for three purposes: (i) Estimating the saving in vaccine doses and the associated cost as a result of implementing the two-phase vaccination policy compared to the current continuous vaccination policy, (ii) estimating the optimal number of vaccine doses that should be ordered for production prior to the flu season, and (iii) estimating the associated value of the stochastic solution (*VSS*) and the expected value of perfect information (*EVPI*). The *VSS* provides an estimate of the usefulness of considering the stochastic nature of the problem while the *EVPI* provides an estimate of the value of epidemic detection and forecast systems. We also propose a heuristic for vaccine allocation based on our numerical results.

In addition to the 2-SLP formulation, we will also present a Newsvendor formulation of this problem. The Newsvendor formulation allows the identification of a closed form solution for the optimal allocation. It also provides insight into the structure of the optimal allocation that is not provided by the 2-SLP model; however, as we show this comes at the expense of requiring the complete distribution of demand, as opposed to just the mean demand for the 2-SLP mode (after it is reduced to an LP).

The remainder of this article is organized as follows. In Section 2 we present a review of relevant research. In Section 3 we present the problem definition and assumptions and present the 2-SLP and Newsvendor model formulations along with our solution methodology. In Section 4 we present and analyze the numerical results. Finally in Section 5 we conclude this article with summarizing the main findings and suggesting some directions for future research.

2. Literature review

Several aspects of flu vaccination have been analyzed by researchers including vaccine strain selection (e.g., Cho (2010), Kornish and Keeney (2008), and Wu, Wein, and Perelson (2005)), vaccine supply chain (e.g., Chick, Mamani, and Simchi-Levi (2008) and Deo and Corbett (2008)), vaccine market and the associated economic impacts (e.g., Brito, Sheshinski, and Intriligator (1991), Geoffard and Philipson (1996), and Philipson (2000, chap. 33)), and vaccination decisions among individuals (e.g., Bauch and Earn (2004), Chapman and Coups (1999), Galvani, Reluga, and Chapman (2007), Larson, Olsen, Cole, and Shortell (1979), and Reluga, Bauch, and Galvani (2006)) and households (e.g., Yarmand and Ivy (in press)).

In the context of vaccine supply chain management, the Newsvendor model has sometimes been used. For example, Chick et al. (2008) use a Newsvendor model for analyzing the influenza vaccine supply chain. In their Newsvendor model, the demand uncertainty is replaced by production uncertainty. Therefore they used the Newsvendor model in the production stage, and not the allocation stage.

In the context of epidemic control, a number of stochastic resource allocation models have been developed to determine optimal vaccination strategies. Becker and Starczak (1997) study vaccination policies in a stochastic SIR model (a model with susceptible, infective, and recovered population; see Hethcote (2000) for details) when the population has been divided into a community of households. They derive a closed form equation for the post-vaccination reproduction number, R_* (first introduced by Ball, Mollison, and Scalia-Tomba (1997)). Also they consider the constraint $R_* \leqslant 1$ and formulate and numerically solve an LP to find the minimum vaccination coverage under this constraint which ensures that the epidemic will die out.

Tanner, Sattenspiel, and Ntaimo (2008) present a stochastic programming framework for finding the optimal vaccination policy for controlling infectious disease epidemics under parameter uncertainty. They initially present a model to find the vaccination policy with the minimum cost under a chance constraint. The chance constraint requires $\Pr(R_* \leqslant 1) \geqslant \alpha$, where α is a predetermined parameter defined by the decision maker. They also present the problem formulation for two additional cases: (a) finding the optimal vaccination policy when vaccine supply is limited and (b) a cost-benefit scenario. They extend the LP formulation of Becker and Starczak (1997) to this stochastic programming framework.

Drawing upon the earlier work of Ball et al. (1997), Ball and Lyne (2002) consider the case of an all-or-nothing vaccine (i.e., a person is either completely immune following vaccination or the vaccine is completely ineffective). They show that if the sequence $\{n\mu_n\}$ is convex, where μ_n is the mean size of a local outbreak within a household of size n, then the optimal solution to the LP problem formulation of Becker and Starczak (1997) can be characterized explicitly.

Finally, Hill and Longini (2003) use a general framework that could apply to several epidemic situations including incorporation of latent periods (resulting in the SEIR model which also includes the exposed population; see Hethcote (2000) for details), diseases with permanent immunity (SIR model), or no immunity (SIS model in which infectives become susceptible again after recovery) with and without vital dynamics. They develop a method to derive optimal vaccination strategies for populations divided into heterogeneous subgroups.

We note that all of these models have considered only one phase of vaccination as opposed to two phases in our model. Therefore they do not allow evaluation of the vaccination outcome in the middle of the epidemic. Only a few of these models have considered vaccination cost in their analysis while our objective is to minimize the expected number of administered vaccine doses, and hence the expected cost of vaccination. In addition, most of these models have considered uncertainty in the disease parameters, while we have considered uncertainty in the vaccination outcome regarding the epidemic control which accounts for a different aspect of the stochastic nature of the problem in the context of resource allocation decisions. Finally, we will present a Newsvendor formulation of the vaccine allocation problem which, to the best of our knowledge, is the first application of the Newsvendor model for vaccine allocation.

3. Problem definition and assumptions

We assume that there are N regions to be vaccinated in an attempt to contain an epidemic (seasonal influenza in our study). Let $\mathcal{N} = \{1, 2, \ldots, N\}$ denote the set of indices of different regions