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Customizing immunization clinic operations to minimize open vial waste

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ABSTRACT

Many multi-dose vaccine vials must be used within hours of reconstitution; unused doses are discarded as "open vial waste." Building on Mofrad et al. (2014), we evaluate operating strategies that maximize coverage by controlling open vial waste. We define novel metrics for determining thresholds on vaccination clinic operating hours and session frequency. We study the performance of optimal and heuristic policies in the presence of random vial yield. Cost analyses indicate significant potential savings. Because optimal strategies are context specific, we also develop a decision support tool (available online) to easily replicate the analysis for any problem setting.

1. Introduction

Organized routine immunization programs, especially those in the world's poorest countries, are critical for preventing the incidence of many diseases and for decreasing mortality rates. In many countries (e.g., Niger, India, Bangladesh), a substantial fraction of the clinics or health centers where immunizations occur are in remote locations from which it is difficult to access urban areas. Vaccine wastage is a major issue at such clinics because their stock of vaccines is limited and running out of vaccine before the next replenishment results in missed vaccination opportunities. Reduction in vaccine wastage also ensures the overall financial stability of immunization programs, especially in poor countries with limited budgets for these programs.

Vaccines used in worldwide immunization programs are typically manufactured in two forms: a liquid form that can be directly administered and a freeze-dried powder that must be reconstituted with a diluent before administration. In the powder form, the primary concern prior to reconstitution is the *shelf life* of the vaccine; it determines the expiration date of the vaccine. After reconstitution, the remaining lifetime of the vaccine is called *open vial life*, which is considerably shorter than shelf life. For example, a 10-dose vial of MMR vaccine has a 48-month shelf life, but only an 8-h open vial life [2]. When a multi-dose vial is reconstituted or "opened," but not completely used during its open vial life, the unused doses are discarded. This type of vaccine wastage is called *open vial waste* (OVW) [3]. OVW accounts for a large portion of overall vaccine wastage [7], which averages around 50% worldwide [16]. Vaccines are manufactured in a range of standard vial sizes, e.g., 1, 5, 10, 20 doses per vial. In general, vials with a greater number of doses are less expensive per dose due to their lower production, transportation and storage costs; however, they typically result in higher OVW.

A number of issues must be considered in designing an effective immunization program with low wastage. The majority of these issues are addressed at higher levels of decision making within governmental immunization organizations, e.g., determining the best vial size; designing the distribution chain; setting storage capacities, replenishment frequencies, and order quantities at various levels of the vaccine supply chain; and deciding on transportation modes and their capacities. Vial size and inventory considerations in particular have been examined in several previous studies. Refs. [7,8,11,17] perform economical analysis to determine the appropriate vial size. More specifically, Ref. [11] estimates the potential wastage cost associated with different vial sizes in various countries. Ref. [7] shows that the most economical vial size is a

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function of mean daily demand (i.e., vials with a greater number of doses produce less OVW as the mean daily demand increases). Ref. [8] determines a threshold on the mean daily demand for the adoption of a specific vial size; they also argue that using single-dose vials (which are physically larger on a per-dose basis) can severely constrain transportation capacity in the vaccine distribution supply chain and result in increased risk of vial breakage. Lastly, Ref. [17] investigates the economical impact of vial size using empirical data. Related to this work, Ref. [1] studies the impact of different vial sizes on the vaccine supply chain. Lastly, Ref. [3] integrates an optimization model and simulation to simultaneously determine vial size and ordering policy under the assumption of 100% coverage. Regardless of how vial size and replenishment frequency are determined, questions surrounding the downstream issue of how to best administer doses from multi-dose vials remain open.

In this paper, we focus on the lowest (i.e., clinic) level of the vaccine distribution chain, especially those in remote locations. Specifically, we focus on the development of vaccine administration policies when using multi-dose vials at these clinics. Most clinics currently operate under a policy that never turns away a patient as long as the requested vaccine is available; we refer to this policy, which typically results in high OVW, as the *greedy* policy. For example, if a patient arrives just as the clinic is closing and a new 20-dose vial is reconstituted, it is highly likely that 19 of these doses will be discarded. Thus, this type of myopic approach can result in significant OVW, which in turn can lead to missed opportunities for vaccinations. Improving the effectiveness of immunization programs requires tailored clinic operations and smarter vaccine administration policies that specifically address missed opportunities caused by a shortage of vaccines due to high OVW.

As previously stated, the existing literature on multi-dose vials is rather limited, and primarily focuses on the economic implications of single-vs. multi-dose vials. In contrast, Ref. [10] addresses another means for controlling OVW, namely that of vaccine *administration* from multi-dose vials, using a rigorous mathematical approach. They formulate a Markov decision process (MDP) model that maximizes the number of vaccinations between two consecutive vaccine stock replenishments (i.e., over one "replenishment cycle") by determining when to discontinue vaccinations as a function of time of day, the current vial inventory and the remaining number of vaccination sessions until the next inventory replenishment. We refer to such a strategy as a "vaccine administration policy." (Note that by "sessions" we mean the number of dedicated periods per cycle during which the clinic operates; a session typically corresponds to a working day, e.g., an 8-h session that runs from 8am to 4pm.) Although they consider the same decision making problem considered herein, the focus in Ref. [10] is on model formulation, policy structure and limited sensitivity analysis under the single objective of maximizing the mean number of vaccinations administered.

The contributions of this paper are five-fold. First, we pair combined analysis of the MDP model with simulation to perform descriptive analysis of the distribution of session duration induced by an optimal administration policy. We examine this novel metric of policy performance because a coverage-maximizing/waste-minimizing administration policy that induces large variability in a clinic's hours of operation may inconvenience patients and lead to undesirable long-term consequences. Second, we explore means by which a clinic can directly control patient convenience by imposing a minimum number of guaranteed hours per session or increasing the session frequency. We explore how these two means of control interact with each other as well as when the latter can counterintuitively affect coverage and wastage. Third, we propose a novel, easy to implement static heuristic policy that induces zero variability in session duration and compare its performance to that of two other heuristic policies. Fourth, we introduce the concepts of random vial-yield and vial failures to this problem setting and assess their impact on the performance of the optimal and heuristic policies. Lastly, we use data available for three countries to perform novel costs analyses for a single vaccine over all GAVI countries, which suggest potential savings on the order of $4.6 million.

The remainder of the paper is organized as follows. In Section 2, we provide an overview of the MDP model developed in Ref. [10] and a new simulation model created to evaluate additional performance metrics of interest. In Section 3, we conduct extensive computational analyses to generate insights on the relationships between day-to-day clinic operations and the vaccine administration policy. In Section 4, we present our heuristic policy analysis. We then, in Section 5, study the performance of the optimal policy and the heuristic policies in the presence of vial failures and random vial yield. In Section 6, we summarize the results in the form of some general operational recommendations based on the analysis in Sections 3 and 5 and estimate the procurement cost savings realized by switching to the optimal policy. Lastly, in Section 7, we discuss limitations of the work and possible future extensions.

2. Overview of models

In Section 2.1, we describe the MDP model developed in Ref. [10] which is used to generate optimal vaccine administration policies. In Section 2.2, we introduce a new simulation model that is used to simulate the performance of a clinic under a given vaccine administration policy generated by the MDP model.

2.1. Markov decision process model

To clarify the modeling approach used in Ref. [10] we present Fig. 1. Ref. [10] develops a finite horizon MDP model for vaccination sessions between two stock replenishments where Q vials are available at the beginning of each replenishment cycle and each vial consists of z doses. As seen in Fig. 1, the replenishment cycle is divided into T sessions and each session is divided into η timeslots of equal length. At each point in time, the state of the system is given by t, the number of sessions remaining until the next replenishment, q, the number of remaining vials and h, the current timeslot.

The MDP model determines when to discontinue opening new vials during a session as a function of the time of day, the current vial inventory and the remaining number of sessions until the next inventory replenishment. Ref. [10] shows that the MDP model results in an optimal vaccine administration policy that is of a threshold type. For convenience, we refer to this threshold as the clinic "closing time," although it is worth noting that the clinic will actually continue to vaccinate whenever there is a vial open and will remain open as long as other activities are being performed at the clinic. The model objective is to maximize the number of vaccinations administered over the replenishment cycle, given an initial inventory of vaccine vials. This objective results in low OVW while achieving the highest level of coverage, i.e., percentage of demand satisfied.

In the formulation of the finite horizon MDP model, the following assumptions are made (see Ref. [10] for more details):

- there is a single type of vaccine,
- the open vial life is greater than or equal to the maximum number of working hours per session [2,9],