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Optimizing the timing and number of batches for compounded sterile products in an in-hospital pharmacy

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ABSTRACT

Hospital pharmacy departments have traditionally batched the production of a category of medications called Compounded Sterile Products (CSP). Since the batches are intended to satisfy several hours, or even a day's worth of demand, the cancellation of orders by physicians can lead to the waste of a considerable amount of medication. The manager of the pharmacy department can choose to produce the CSP medication in one or more batches per day. In making this decision the manager is trading off two sorts of costs: (a) the "holding cost" of carrying inventory, which in this context is largely the cost of wasted doses, and (b) the "set up cost" of the labor for delivering the prepared medication to the various units of a hospital. Although this trade-off superficially resembles that of a classic batching problem, it turns out to be quite different. This is primarily because the sequence of batches must repeat in a 24-hour cycle and the holding cost, related to the waste of CSP medications, varies over the 24-hour cycle according to the pattern of order cancellations, which in turn depends on the schedule of physicians' reevaluating the treatments of patients under their care. In addition, the setup cost, related to the cost of the delivery, varies slightly with the cost of labor at different times of the day. While previous work has looked at the benefits of multiple batches per day, the problem has not been addressed in a mathematically rigorous manner. The contribution of this work is twofold. Firstly, it extends the considerable literature on lot sizing by introducing a formulation for deciding the optimal number and timing of batches as an integer programming problem that caters for, and minimizes, the novel forms of holding and setups costs described above. In doing so the inventory curves over time are modeled precisely. Secondly, a dynamic programming methodology for the optimization problem is developed that is solvable with just a few minutes of computing time. Thus the pharmacy manager can make rational decisions about the optimal number and timing of CSP production batches based on the specific patterns of costs and work practices found in his or her hospital.

1. Introduction

One of the functions performed by in-hospital pharmacies is the preparation of custom Compounded Sterile Products (CSP) for both in-patients and out-patients (e.g., those receiving chemotherapy). Most CSP medications are chemically stable for a relatively short time after they have been prepared. Thus, they are usually manufactured in powder or concentrate form and custom compounded prior to use. Since these medications are usually administered directly into a patient's blood stream, strict sterility procedures must be followed in their preparation. With a rise in the cost of CSP ingredients the waste of prepared doses of this type of medication has become a salient issue for pharmacy managers [1,6,8,10,15].

Because preparing and delivering CSP doses one at a time would be very inefficient, they are typically produced and delivered to hospital units in batches. A batch consists of doses that are to be administered over a certain period of time, e.g., from 16:00 on one day until 15:59 on the following day. As the pharmacy starts to prepare a batch of CSP medications its pharmacy information system (PIS) typically prints out labels for all of the doses needed to fulfill all the orders to be administered over the next period. Note that there may well be several doses associated with each order. The labels are distributed to pharmacy technicians who prepare all the doses required. After being checked by a pharmacist, the prepared batch of medication is delivered to the nursing units.

Some patient-specific doses end up being dispensed but not administered. Dispensed doses may not be administered for a number of reasons. For example, a patient's condition could change and the medication may no longer be appropriate, or the medication could be delivered to a wrong unit or otherwise be misplaced resulting in the compounding and delivery of a replacement. However, the cancellation (or change) of orders is the largest cause of CSP waste — simply because order cancellations are very common. For example, examining three months of data from an 830-bed hospital in New York State, revealed

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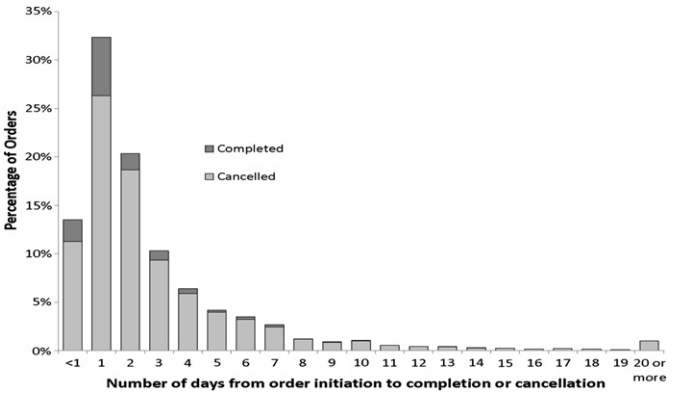

Fig. 1. Distribution of number of days from order initiation to completion or cancellation.

that only 12% of CSP orders are actually completed; the rest are canceled prior to the initially specified end date. As can be seen from Fig. 1, 80% of orders are canceled within seven days of initiation. Doses for canceled orders are seldom recycled. For recycling, doses would have to be returned to the pharmacy, inventoried, then retrieved and relabeled when another patient needs the same custom compounded medication. If there is not another patient that needs the same prescription before the dose expiry date, the medication would still be wasted. Because the logistics of collecting unused CSP doses is complex, the formulation is patient-specific, and many CSPs have short shelf lives, unused CSPs are usually wasted. Given the cost of raw materials, the estimated annual waste from dispensed-but-not-administered CSP medication amounted to over one-third of a million dollars in this one hospital.

Waste can affect not only the doses that are stored in the nursing unit when the cancellation arrives, but also the doses that are in the batch production process. With the pharmacy information systems most widely used at the time of writing, cancellations during batch production also result in waste. A cancellation of an order is signaled to the pharmacy with the automatic printing of a "cancellation" label. This label is intended to alert the pharmacy not to produce the doses associated with the order. However, in practice, it is difficult to prevent compounding after the job labels have been printed at the start of batch preparation: an employee would have to search through hundreds of production labels already distributed to technicians. As a result, doses canceled during the batch preparation process are routinely produced and subsequently wasted.

Some institutions have attempted to reduce CSP waste by increasing the number of daily production batches. Reports of such initiatives have prompted other pharmacy managers to ask what is the *optimal* number of batches for their institutions [2], as the answer has not been readily available.

In deciding on the number of daily CSP batches, managers must trade off the reduction in medication waste against the increase in employee hours needed for the preparation and delivery of additional batches. There is no single optimal solution for every hospital of a certain size with a given mix of cases. In selecting batch schedules, we have found that pharmacy managers have either made their decisions intuitively or employed labor-intensive methodologies such as trying different implementations and cataloging CSP waste by physically collecting it or by tracking it through an IT system. At least one pharmacy used a trial-and-error approach to find that waste reduction from going to six batches per day was more than offset by the additional labor required [8].

The decision on the optimal number of batches relates to the large literature on capacitated lot sizing which was recently reviewed by Karimi, Fatemi Ghomi and Wilson [9]. Based on their taxonomy our problem has the following attributes:

- An infinite planning horizon
- Single level (from pharmacists to patients)
- Capacitated (by the physical facilities such as the hoods in the pharmacy)
- "Simple" setup — i.e. not sequence dependent

Further problem classification merits discussion. The demand is uncertain in the sense that demand from a patient disappears if an order is canceled. However, the critical nature of the medication makes shortages unacceptable. So, the pharmacy must produce based on the orders and the period being covered, and ignore the possibility that some orders may be canceled. Waste of doses that were dispensed but never administered grows with the inventory of doses, and thus cancellation-induced waste can be thought of as a *holding cost*. The delivery of drugs to hospital units is largely independent of the quantity delivered and can therefore be conceptualized as a *setup cost*.

We would further classify the CSP problem as a *single item* lot-sizing problem, rather than custom production. Although producing individual medication orders for patients makes it look like custom production or at least multiproduct production, the setup (i.e., medication delivery) is joint across all orders, so it is sensible, at some level, to model this problem as a single item lot-sizing problem. Also here we note, that the demand for doses from any particular patient is steady, e.g., one injection per day or 3 bags per day for example, and the total number of orders is relatively steady, driven as it is by the number of beds in the hospital.

Given the attributes we discussed, the problem of determining batch size for the production of CSP doses looks similar to a classic batching problem trading off holding versus setup costs. Yet, the similarity is superficial: both the holding and the setup costs vary over time, typically following a cyclic pattern that repeats daily. Setup costs vary because labor costs for technicians vary by shift. The holding costs vary over time because the rate of order cancellation is not uniform over a 24-hour period: it is driven by physicians' work schedules. The peak in order cancellation is related to the timing of physicians' "rounds" when each patient's status and medical orders are reviewed and often changed. Further, the schedule of batches must repeat every 24 h so that the pharmacy staff will have a regular work schedule. It is worth noting that because the set of batches picked must repeat every 24 h the problem bears some resemblance to the ELSP (see [3] and [5] for reviews of this problem). Yet for all these formulations the length of the cycle is determined endogenously by the trade-off in the problem, where for our problem it is specified exogenously by the work schedule.

While there is a large literature on batching problems with holding costs that vary over time [11,13,16], all of the papers we are aware of deal with perishable inventory and holding costs that vary with the age of the inventory. Our problem is different because the holding cost varies by the time of day but not by the age of the inventory per se. Our product, compounded medication, does perish. However, this does not affect the solution because the batching cycle time (typically a day) is much less than the lifetime of the product (days or weeks), so accounting for perishability is unnecessary. Despite being an infinite horizon problem, the cyclic nature of the time-varying holding costs requires that we model all the batching decisions for a day, and not just for a single batching decision. Finally because production takes a significant amount of time the compounding of CSP medications for the next administration period must be scheduled for the current period. These aspects make this problem quite distinct from any other batching problem of which we are aware.

Others have looked at the decision to batch CSP production in hospitals without optimizing batch scheduling [1,6,7,14]. We offer mathematical formulation and solution methodology for finding batch schedules that jointly minimize the cost of waste and cost of batch production staffing. In Section 2 we introduce an optimization model for CSP preparation, to determine optimal start times and the batches