Determining an optimal schedule for pre-mixing chemotherapy drugs

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Introduction

Cancer is the second leading cause of death in the U.S., with ~1.6 million cases estimated for 2015. Over 50% of cases require chemotherapy treatment. Increasing demand has led to increased patient waiting times and overworked staff. What if we could reduce these burdens by pre-mixing Chemo drugs?

What is Pre-mix?
Pre-mix is defined as the preparation of a drug before any patient is deemed ready to receive it. Generally, pharmacies/cancer centers/institutions do not pre-mix due to risk of wastage. In our model, we consider the tradeoff between waste cost and reduced patient waiting time.

Probability of Wasting a Drug

Let: $Prob(\text{Deferral or no show}) = p$
Assume: $m_d =$ patients scheduled to receive drug d on a given day

$$Prob(\text{Wasting nth dose}) = \sum_{i=1}^{n} \binom{m_d}{m_d - i + 1} p^{m_d - i + 1} (1-p)^{i-1}$$

What if the probability of deferral or no show depended on age, sex, treatment, type of cancer, etc.?

Let: $Prob(\text{Deferral or no show of patient } i) = p_i$
Let: $S_d =$ set of patients scheduled to receive drug d
∴ $S_d = \{1,2,\dots,m_d\}$

$$Prob(\text{Wasting 1}^{\text{st}}\text{ dose}) = \prod_{i \in S_d} p_i$$

$$Prob(\text{Wasting 2}^{\text{nd}}\text{ dose}) = \sum_{i \in S_d} \left[(1-p_i) \prod_{j \in S_d \setminus i} (p_j)\right] + \prod_{i \in S_d} p_i$$

$$Prob(\text{Wasting 3}^{\text{rd}}\text{ dose}) = \sum_{i \in S_d} \sum_{j \in S_d \setminus i} \left[(1-p_i)(1-p_j) \prod_{k \in S_d \setminus \{i,j\}} p_k\right] + \sum_{i \in S_d} \left[(1-p_i) \prod_{j \in S_d \setminus i} (p_j)\right] + \prod_{i \in S_d} p_i$$

Model

Parameters

Δ_d: the award or savings for mixing drug *d*
T: the total time units for the pre-mix period
c_d: the cost of drug *d*
N_d: the number of doses needed for each drug based on the scheduled patients
L: pre-mix capacity for any pre-mix period
M: a very large number

Sets

D: set of drugs *d* (e.g. 50 mg of Taxotere)
T: set of time units (each being 30 min)

Variables

$x_{nt}^d = \begin{cases} 1 & \text{if pre-mixing the } n\text{th dose of drug } d \text{ at time } t \\ 0 & \text{otherwise} \end{cases}$

$y_n^d = \begin{cases} 1 & \text{if not pre-mixing the } n\text{th dose of drug } d \\ 0 & \text{otherwise} \end{cases}$

Objective

Maximize the difference between expected reward and waste cost

$$\max \sum_d \sum_n \sum_t \left(\Delta_d - E_n^d[\text{waste cost}]\right) * x_{nt}^d, \quad \text{where } E_n^d[\text{waste cost}] = \sum_{w=1}^{n} c_d P_d(w)$$

Constraints

$$\sum_t x_{nt}^d + y_n^d = 1 \qquad \forall d,n \qquad (1)$$

$$y_n^d \le y_{n+1}^d \qquad \forall d, n = 1,\dots,N_d - 1 \qquad (2)$$

$$\sum_t t x_{nt}^d \le \sum_t t x_{(n+1)t}^d + M * y_{n+1}^d \qquad \forall d,n \qquad (3)$$

$$\sum_d \sum_n x_{nt}^d \le L \qquad \forall t \qquad (4)$$

$$\sum_t x_{nt}^d \le 1 \qquad \forall d,n \qquad (5)$$

(1) Relates the auxiliary variable to the decision variable
(2) Ensures that subsequent doses are not pre-mixed if a previous one is not pre-mixed
(3) Ensures the ordering of pre-mixed drugs
(4) Cannot pre-mix more than L drugs during any period
(5) Can only make the nth dose of a drug at most once

Results

Suppose we have patients scheduled to receive 15 different drugs. Below is a sample of the drugs highlighting the variability in price.

Table 1: Give an explanation of this table!

Drug	Hang by time	Price	Currently pre-mixed?	Treatment for
Carboplatin	12 hrs	$ 2.52	Yes	Cancer of the ovaries, head, and neck
Paclitaxel	12 hrs	$ 4.10	Yes	Cancer in the lungs, ovary, or breast
Cyclophosphamide	12 hrs	$ 879.00	Yes	Leukemia and lymphomas, and nephrotic syndrome
Folotyn	12 hrs	$ 4,637.21	No	T-cell lymphoma
Adcetris	12 hrs	$ 6,516.00	No	Treats Hodgkin's lymphoma and systemic anaplastic large cell lymphoma

Table 2: Give an explanation of this table!

	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
Reward	1 for all drugs	11.67 for all drugs	11.67 for all drugs	11.67 for all drugs	11.67 for all drugs
# of Doses	2 for each drug	2 for each drug	2 for each drug	1-2 lower cost 3-5 higher cost	1-2 lower cost 3-5 higher cost
$P_d(n)$	p=0.25 for all drugs	p=0.25 for all drugs	inverse to cost of drug ranging from 0.02 to 0.30	p=0.25 for all drugs	inverse to cost of drug ranging from 0.02 to 0.30

Table 3: Give an explanation of this table!

Drugs	Cost	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
A	$ 1.61	2	2	2	2	—
B	$ 2.52	1	2	2	2	1
C	$ 4.10	1	2	2	1	—
D	$ 6.80	1	1	1	1	1
E	$ 16.56	—	1	1	1	—
F	$ 83.40	—	—	—	—	—
G	$ 91.54	—	—	—	—	—
H	$ 155.56	—	—	—	—	—
I	$ 367.02	—	—	—	—	—
J	**$ 698.60**	**—**	**—**	**—**	**—**	**1**
K	**$ 879.00**	**—**	**—**	**—**	**1**	**2**
L	**$ 1,158.84**	**—**	**—**	**—**	**—**	**1**
M	$ 2,389.39	—	—	—	—	—
N	$ 4,637.21	—	—	—	—	—
O	$ 6,516.00	—	—	—	—	2
TOTAL	—	*5*	*8*	*8*	*8*	*8*

Future Work

Static Model
- Include the hang-by time for each drug
- Include the preparation time for each drug
- Continue working with data collection to run logistical regression
- How to categorize various types of patients

Dynamic Model
Goal: To find an optimal drug-mixing schedule throughout the day and update as we observe patient deferrals

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