2015 Healthcare Engineering and Patient Safety Symposium

CENTER FOR HEALTHCARE ENGINEERING & PATIENT SAFETY
UNIVERSITY OF MICHIGAN

Determining an Optimal Schedule for Pre-Mixing Chemotherapy Drugs

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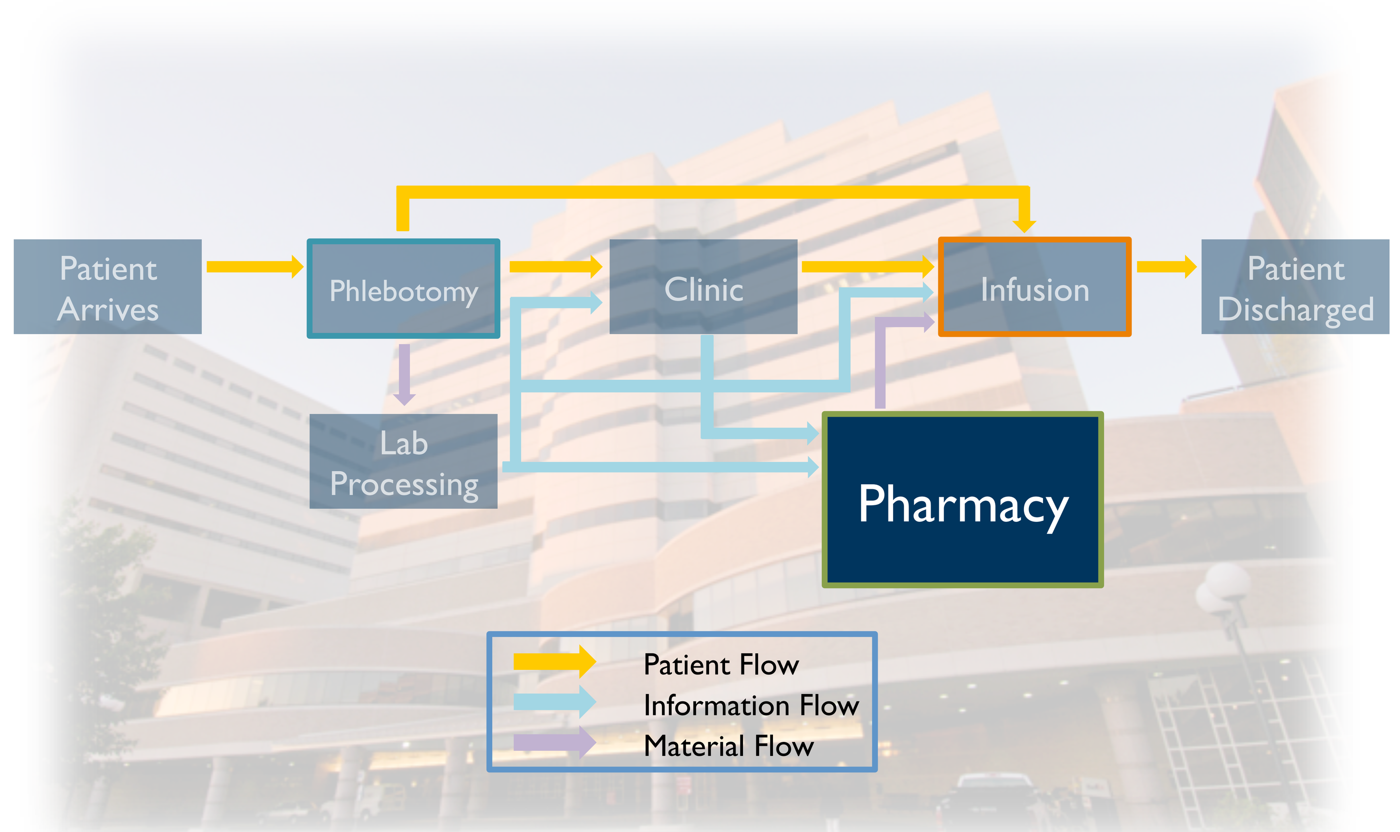
Problem Statement

- Cancer
  - Second leading cause of death in the U.S.
  - ~1.6 million estimated cases in 2015
  - More than half require chemotherapy treatment
- Infusion centers
  - Increased outpatient demand leads to undesirable outcomes such as:
    - Increased patient waiting times
    - Overworked staff



What is Pre-Mix?

- Anytime you mix a drug before a patient is deemed ready to receive it
- Generally you don't pre-mix drugs due to risk in wastage cost
- Consider the trade off between waste cost and reduced patient waiting time

UMCCC current Pre-mix policy

- Will only mix drugs during a fixed window of time before patients arrive
  - 6am-8am
- Have a fixed list of drugs they are willing to mix
  - Based on cost and common use

Probability of Wasting a Drug

Let $Prob(\text{Deferral/no show}) = p$

Assume m_d = patients scheduled to receive drug d on a given day

Then the probability of wasting the n^{th} dose of drug d is given by

$$P_d(n) = \sum_{i=1}^{n} \binom{m_d}{m_d - i + 1} p^{m_d - i + 1} (1-p)^{i-1}$$

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

Let $Prob(\text{Deferral/no show of patient } i) = p_i$

Let S_d = set of patients scheduled to receive drug d

$\therefore S_d = \{1, 2, \dots, m_d\}$

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

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

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

Model

Sets

D: set of drugs d (e.g. 50 mg of Taxotere)

Variables

$$x_{nt}^d = \begin{cases} 1 & \text{if we mix the } n\text{th dose of drug } d \text{ at time } t \\ 0 & \text{o.w.} \end{cases}$$

$$y_n^d = \begin{cases} 1 & \text{if we don't mix the } n\text{th dose of drug } d \\ 0 & \text{o.w.} \end{cases}$$

Objective

Maximize the difference between our expected reward and waste cost

Parameters

- Δ_d: the reward or savings for mixing drug d
- T: the total time units for the premix 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

$$E_n^d[\text{waste cost}] = c_d P_d(w)$$

$$\max \sum_d \sum_n \sum_t (\Delta_d - E_n^d[\text{waste cost}]) * x_{nt}^d$$

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 our auxiliary variable to the decision variable
(2) If you don't make the previous dose you cant make the next
(3) Does ordering
(4) Only make L at a time
(5) Can only make the nth dose of a drug once

Results

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

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

AMPL Results

	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 values	p=.25 for all drugs	p=.25 for all drugs	inverse to cost of drug ranging from .02 to .30	p=.25 for all drugs	inverse to cost of drug ranging from .02 to .30

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

Acknowledgements

Collaborators: Pamela Martinez, Matt Rouhana, Ajaay Chandrasekaran, Jonathan Zhou, Hassan Abbas
This research is generously supported by the Center for Healthcare Engineering and Patient Safety and the Rackham Merit Fellowship Program.