Optimizing Make-ahead Chemotherapy Drug Policies at an Outpatient Infusion Center

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INFORMS Healthcare Boston
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OUTLINE

• Motivation
• Model Description
• Probability of Wasting a Pre-mixed Drug
• Model Formulation
• Computation Experiments
• Conclusion/Future Work
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Reduce patient waiting time by mixing chemotherapy drugs before patients arrive in the system or at earlier stages in the process.
MOTIVATION

• Cancer
  • ~1.8 million new cases estimated in 2019
  • More than half require chemotherapy treatment
  • Variable infusion treatment times (30 min – 8 hr)

• Infusion centers
  • Increased outpatient demand leads to undesirable outcomes such as:
    • Increased patient waiting times
    • Overworked staff

OUTPATIENT INFUSION PATIENT FLOW

- Patient Arrives
- Phlebotomy
- Lab Processing
- Clinic
- Infusion
- Pharmacy
- Patient Discharged

Flow types:
- Patient Flow
- Information Flow
- Material Flow
WHAT IS CHEMOTHERAPY?

• Typically require solutions to be made in pharmacy
  • Hang-by time – time after drug is made until it must be administered

• Used to
  • Control
  • Cure
  • Ease

• Variable doses correlate to patient weight
• Solution administered by IV over time (variable)
• Drugs vary in cost ($10-$20,000+)
PRE-MIXING CHEMOTHERAPY DRUGS

• Anytime a drug is mixed before a patient is deemed ready to receive it

• Factors to consider:
  • Last minute cancellation may lead to wasting pre-mixed drug
  • Storage safety protocol
  • Tradeoff between waste cost and reduced patient waiting time
**PRE-MIXING CHEMOTHERAPY DRUGS**

University of Michigan Rogel Cancer Center (UMRCC)

- Will only pre-mix drugs during a fixed window of 6am-8am

- Pre-mix based on a fixed list of drugs
  - Based on cost and common use

- We expand this by considering patient probability of deferral and the number of patients scheduled for a particular drug
PRE-MIXING LITERATURE REVIEW


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OPTIMIZATION MODEL DESCRIPTION

• Chemotherapy Pre-mix Integer Program with hang-by time (CPIP-HT)
  • Verification – performed by pharmacists
  • Compounding – done by technicians

• Objective
  • Maximize the difference between expected saved wait time and waste cost
  • Two-hour window to pre-mix
OPTIMIZATION MODEL ASSUMPTIONS

• All drugs’ mixing times are deterministic

• Each patient is scheduled for only one drug

• Pharmacy task can be reduced to two steps

• Probability of deferral taken from BART
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PREDICTING PATIENT DEFERRALS

• Defining a patient *treatment deferral*
  • Patient arrives at the cancer center but is unable to receive their treatment (i.e. last minute cancellation)
  • Oncologist or nurse may deem them too ill for treatment after arrival
  • Unplanned treatment change
  • Social support
PREDICTING PATIENT DEFERRALS

• Prediction Model
  • Utilized patient specific data to predict their chance of deferral

PROBABILITY OF WASTING A DRUG

Let $S$ be defined as the set containing the probability of deferrals $p_i$ for all $i$ patients scheduled to receive the same drug. Given $m$ total patients ($i \in m$)

$S := \{p_1, p_2, \ldots, p_m\}$

$P(1) = \prod_{i \in S} p_i$
Let \( S \) be defined as the set containing the probability of deferrals \( p_i \) for all \( i \) patients scheduled to receive the same drug. Given \( m \) total patients \((i \in m)\)

\[
S := \{p_1, p_2, \ldots, p_m\}
\]

\[
P(1) = \prod_{i \in S} p_i
\]

\[
P(2) = \sum_{i \in S} \left[ (1 - p_i) \prod_{j \in S \setminus i} p_i \right] + P(1)
\]
PROBABILITY OF WASTING A DRUG WITH HANG-BY TIME

Pre-mix Window

Infusion Start

p_1 9:00am

p_2 11:00am

p_3 1:00pm
PROBABILITY OF WASTING A DRUG WITH HANG-BY TIME

\[ P(1) = p_1 p_2 \]

- Infusion Start
- \( p_1 \): 9:00am
- \( p_2 \): 11:00am
- \( p_3 \): 1:00pm
PROBABILITY OF WASTING A DRUG WITH HANG-BY TIME

\[ P(1) = p_1 p_2 \]

\[ P(2) = p_1 p_2 p_3 \]
PROBABILITY OF WASTING A DRUG WITH HANG-BY TIME

\[ P(1) = p_1 p_2 \]

\[ P(2) = p_1 p_2 p_3 + (1 - p_1) p_2 p_3 + (1 - p_2) p_1 p_3 = p_3 \]
PROBABILITY OF WASTING A DRUG WITH HANG-BY TIME

\[ P(1) = p_1p_2 \]

\[ P(2) = p_1p_2p_3 + (1 - p_1)p_2p_3 + (1 - p_2)p_1p_3 = p_3 \]
We then use the upper and lower time bounds on each dose to make sure the drug is made both early and late enough to be viable for a predetermined set of patients.
PATIENT ELIGIBILITY VECTOR

• $e_i^d$ is the $i^{th}$ eligibility vector of drug $d \in D$ Now suppose we have 3 doses of a drug $d$

$$e_1^d = [0 \ 0 \ 0]$$

• zero doses of this drug were pre-mixed
**PATIENT ELIGIBILITY VECTOR**

- $e_i^d$ is the $i^{th}$ eligibility vector of drug $d \in D$. Now suppose we have 3 doses of a drug $d$.

\[ e_{10}^d = [2 \ 3 \ 0] \]

- the first dose will only be viable for the first two patients while the second will be viable for all three patients. The third dose is not pre-mixed.
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OPTIMIZATION MODEL

• We first define our Expected Waste cost of a drug with the following:

\[
E^d_i [\text{Waste Cost}] = c_d \sum_{n=1}^{m_d} P_d(n, i) \quad E^d_i [\text{Saved Wait}] = \Delta_d \sum_{n=1}^{m_d} [1 - P_d(n, i)]
\]

**Parameters**
- \(\Delta_d\): the value of savings of drug \(d \in D\) (i.e., \((p_{d1} + p_{d2}) \times \text{dollar value of patient waiting time}\))
- \(c_d\): the cost of drug \(d\)
- \(p_{ds}\): the time it takes to process drug \(d\) at stage \(s\)
- \(m_d\): the number of doses needed for each drug \(d\)
- \(P_d(n, i)\): probability of wasting the \(n\) does of drug \(d\)

**Sets**
- \(D\): set of drugs \(d\) (e.g. 50 mg of Taxotere)
- \(E_d\): set patient eligibility vectors for all \(d \in D\)

**Variables**
- \(a^d_i = \begin{cases} 1 & \text{if we select patient eligibility vector } i \in E \text{ for drug } d \in D \\ 0 & \text{o.w.} \end{cases} \)
OPTIMIZATION MODEL

• We first define our Expected Waste cost of a drug with the following:

\[ E_i^d \text{[Waste Cost]} = c_d \sum_{n=1}^{m_d} P_d(n, i) \quad E_i^d \text{[Saved Wait]} = \Delta_d \sum_{n=1}^{m_d} [1 - P_d(n, i)] \]

• Then we maximize the difference between Projected Savings and Expected Waste

\[ \text{maximize} \sum_{d \in D} \sum_{i \in E} (E_i^d \text{[Saved Wait]} - E_i^d \text{[Waste Cost]})a_i^d , \]

**Parameters**
- \( \Delta_d \): the value of savings of drug \( d \in D \) (i.e., \( (p_{d1} + p_{d2}) \) dollar value of patient waiting time
- \( c_d \): the cost of drug \( d \)
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**Sets**
- \( D \): set of drugs \( d \) (e.g. 50 mg of Taxotere)
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- \( a_i^d = \begin{cases} 1 & \text{if we select patient eligibility vector } i \in E \text{ for drug } d \in D \\ 0 & \text{o.w.} \end{cases} \)
OPTIMIZATION MODEL CONSTRAINTS

• Only can select one eligibility vector for each drug

• All doses indicated in vector must be made if eligibility vector is selected

• All doses must be made within the time bounds associated with the eligibility vector
OPTIMIZATION MODEL CONSTRAINTS (CONT.)

- Limited number of pharmacists for verification
- Limited number of techs for drug compounding
- No preemptions allowed
- Must complete drug once started
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COMPUTATIONAL EXPERIMENTS

• How large is our integer linear program (i.e., number of variables and constraints)?

• What is the computational time needed to generate inputs and solve the model?

• How granular should we discretize time and still maintain a quality solution?
COMPUTATIONAL EXPERIMENTS

• Time discretization cases: 5 min, 2 min, 1 min

• Scenarios
  1. At most one dose of a drug is scheduled
  2. 2-5 doses of a drug are scheduled
  3. 10 doses of each drug scheduled

Note: We run 10 instances of each scenario in each case with a 2 hour time limit as well as a 1% optimality gap
### TIME DISCRETIZATION ANALYSIS

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Case</th>
<th>Number of Variables</th>
<th>Number of Constraints</th>
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<td></td>
<td>1 min</td>
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</table>

**Scenarios**

1. At most one dose of a drug is scheduled
2. 2-5 doses of a drug are scheduled
3. 10 doses of each drug scheduled
## TIME DISCRETIZATION ANALYSIS

### Scenarios
1. At most one dose of a drug is scheduled
2. 2-5 doses of a drug are scheduled
3. 10 doses of each drug scheduled

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Case</th>
<th>Median Load Time (sec)</th>
<th>Median Solve Time (sec)</th>
</tr>
</thead>
<tbody>
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<td>2</td>
<td>6</td>
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<tr>
<td></td>
<td>2 min</td>
<td>6</td>
<td>54</td>
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<tr>
<td>2</td>
<td>5 min</td>
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</tr>
</tbody>
</table>
TIME DISCRETIZATION ANALYSIS

Scenarios
1. At most one dose of a drug is scheduled
2. 2-5 doses of a drug are scheduled
3. 10 doses of each drug scheduled
• Determined discretizing time to 2 minutes was sufficient for our problem

• Problem size grows at factorial rate but is bounded in practice (i.e., never more than 10 doses of the same drug on a scheduled for a given day)

• Model formulations finds optimal solution providing a conservative estimate on patient wait time saved
CONCLUSIONS/FUTURE DIRECTIONS

• Developed a pre-mix optimization model utilizing the probabilities from the prediction model

• Address time dependencies and interdependences introduced by hang-by time

• Potential next steps include time dependent reward parameter
Thank you!

• Center for Healthcare Engineering and Patient Safety (CHEPS)

• CHEPS Chemo Team
  • Special thank you to Matt See for his hard work these past few years

• UMRCC Collaborators

• Rackham Merit Fellowship

• Bonder Foundation
COUNTING ELIGIBILITY VECTORS

• Total number of vectors = \( \sum_{d \in D} \binom{2m_d}{m_d} \) where \( m_d \) is the total number of patients scheduled for drug \( d \) on a given day

• Given \( m_d = 2 \) for a single drug \( d \), we might have the following vectors
  • \([0,0], [1,0], [2,0], [1,1], [1,2], [2,2]\)
  • Total number of vectors = \( \binom{4}{2} = 6 \)

• However what if we have \( m_d = 10 \) then the total number of vectors = \( \binom{20}{10} = 184,756 \)