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Improving Chemotherapy Make-ahead Policies through Discrete-event Simulation

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CENTER FOR
HEALTHCARE ENGINEERING & PATIENT SAFETY
UNIVERSITY OF MICHIGAN

Research Team/Collaborators

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Key Goal

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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

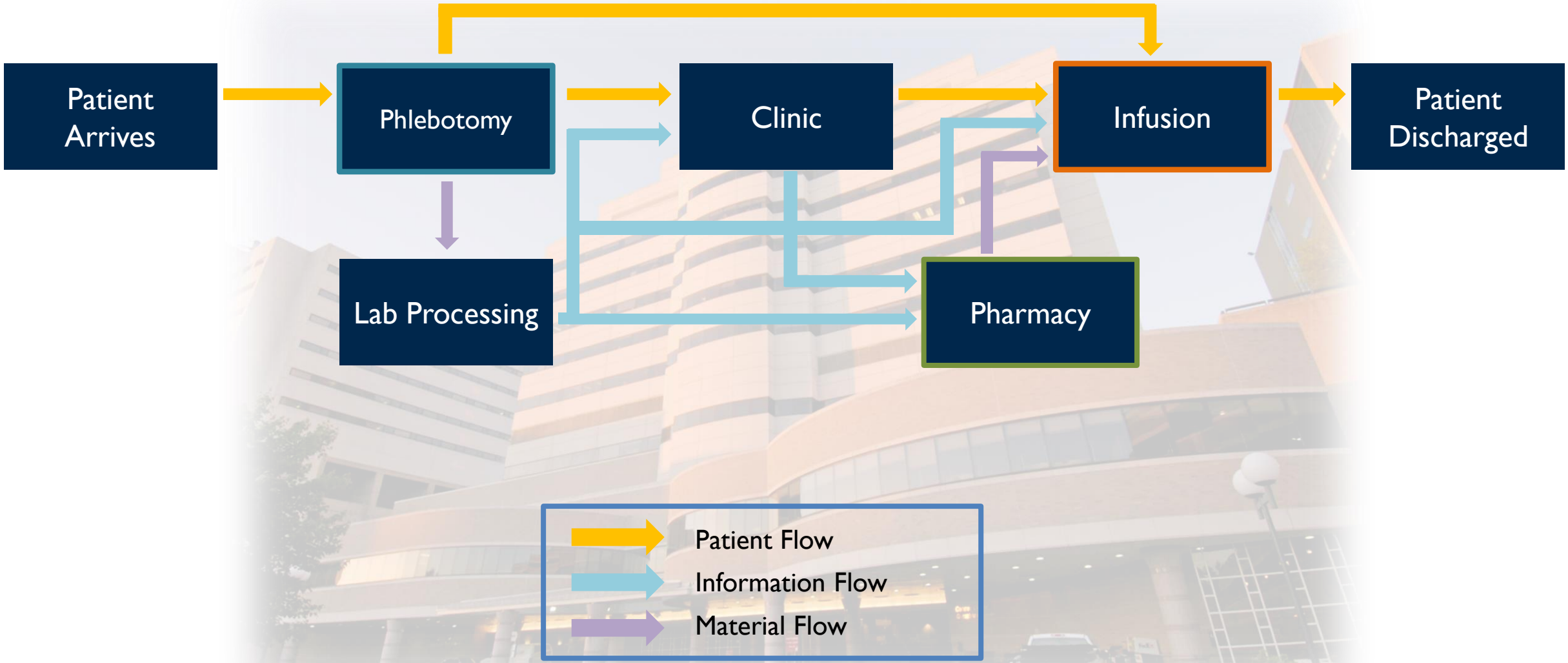
Motivation

- Cancer
  - ~1.7 million new cases estimated in 2018
  - 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

Source:
American Cancer Society (2018) http://www.cancer.org

Outpatient Infusion Patient Flow



Discussion of Chemotherapy

- Typically require solutions to be made in pharmacy
- Used to
  - Control
  - Cure
  - Ease
- Variable doses correlate to patient weight
- Solution administered by IV over time (variable)
- Drug vary in cost ($10-$20,000+)

What is Pre-mix?

- Anytime a drug is mixed before a patient is deemed ready to receive it
- Due to risk in wastage cost, drugs are generally not pre-mixed
- Consider the trade off between waste cost and reduced patient waiting time

What is Pre-mix?

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UMCCC current Pre-mix policy

- Will only pre-mix drugs during a fixed window of 6am-7:30am

- Have a fixed list of drugs they are willing to mix
  - 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.

Problem Statement

- UMRCC Pharmacy has a goal to keep the order turnaround-time (TAT) under 1 hour for each patient.
  - Current TAT can be as much as 2 hours.

- Our focus is to improve the drug TAT in the pharmacy and in turn reduce the overall time in the system for patients
  - We propose various pre-mix policies ranging in risk tolerance
  - Must asses the trade off of saved timed vs drug waste if a patient defers

Outline

- Background
  - Motivation
  - Problem Statement
- Prediction Model
  - Patient Deferrals
  - Data Description
- Simulation Model
  - Condition
  - Simulation flow
  - Inputs/Outputs
- Summary/Future Work

Patient 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

Prediction Data

Covariate	Description	Mean	St. Dev	Min	Max
Length	Scheduled infusion appointment length in minutes	195.6	133.2	30	780
Age	Patients age in years	59	13.6	16	95
Total Pervious Cancellations	Number of cancellations since the patient's last completed visit	.8	1.4	0	21
Days since Last Cancellation	Number of days since the last cancelled visit	27.3	59.5	0	504
Total Previous Visits	Number of the patient's previously completed visits	8.4	9.2	0	83
Days since Last Visit	Number of days since the patient's last completed Visit	15.3	23.3	0	448
BMI (kg/m^2)	Patient's last recorded BMI	28	6.8	12.7	78.7

Prediction Data

Factor	Levels	Description
Status (Response)	2	Appointment completed or deferred/no-show
Sex	2	Either male or female
Race	8	Patient's Race: White or Caucasian (WC), Black or African American (BA), Asian, American Indian and Alaska Native (AA)/Native Hawaiian and Other Pacific Islander (NO), BA and other, Multi-racial and WC, WC/BA, and Multi-racial
Ethnicity	4	Patient's Ethnicity: Non-Hispanic, Hispanic, Patient Refused, Unknown
Marital Status	8	Patient's Marital Status: Single, Married, Legally Separated, Divorced, Widowed, Unknown, Significant other, Other
Protocol	51	The various treatment protocols a patient is prescribed by an oncologist. This consists of the type of chemotherapy drug, solution, frequency of treatment, and additional treatment regimen notes.
Region	10	Region of the U.S. that the patient's permanent address is reported

Prediction Model

- BART Model
  - Example decision threshold at probability 0.75
  - Correctly predicted 93% of completed appointments and 21% of deferrals/no shows
  - Overall prediction accuracy of 84%.
- Probabilities incorporated in simulation
- Additional details on model selection
  - Richardson, D. B., Guikema, S. D., & Cohn, A. E. (2017). Predicting Patient Treatment Deferrals at an Outpatient Chemotherapy Infusion Center: A Statistical Approach. *JCO Clinical Cancer Informatics*, *1*, 1-8.

Outline

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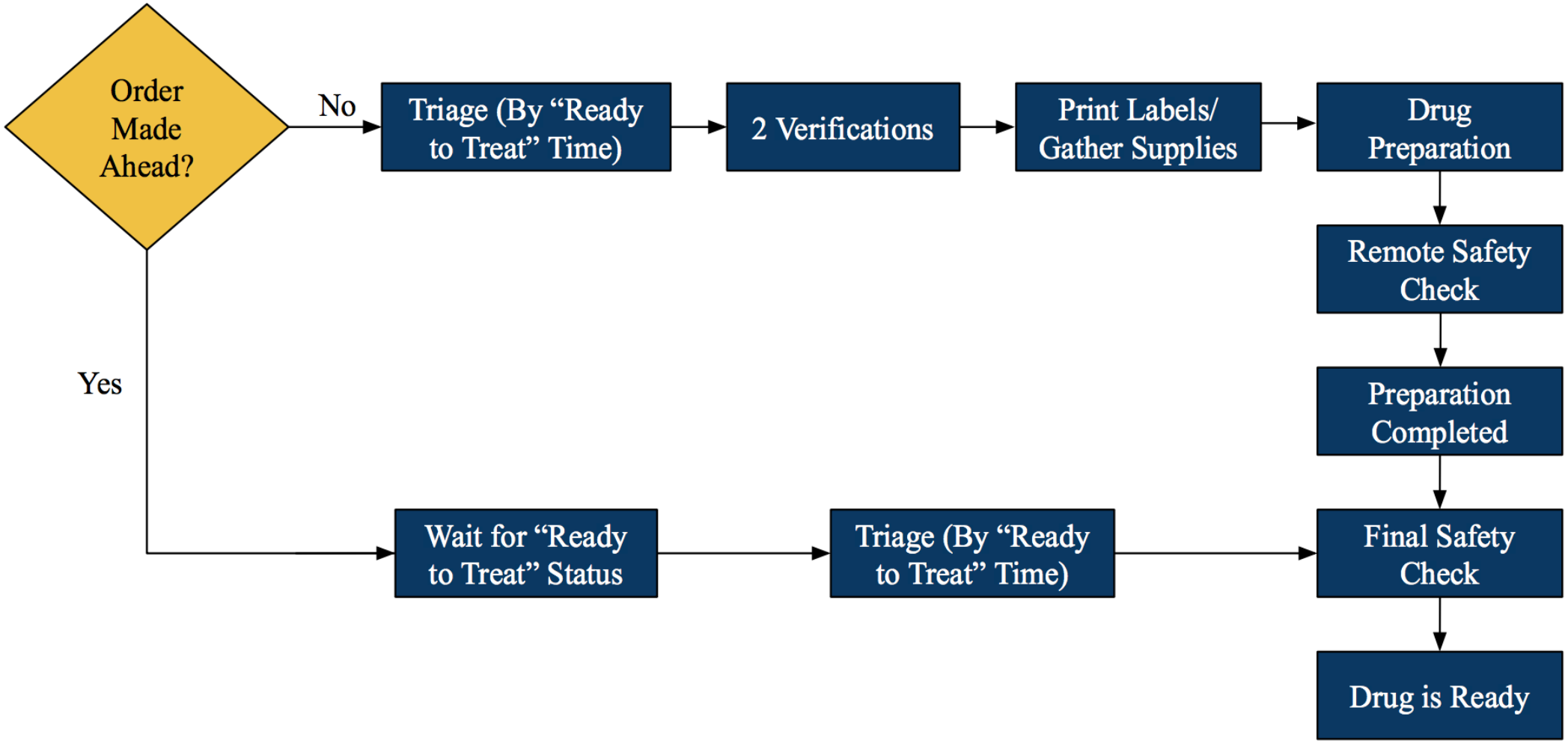
Simulation Flow



Modeling Conditions

- Pre-mix from 6:00am-7:30am, then service patients from 7:30am until finished
- We assume that all pre-mixed orders will not expire before they are administered if the patient appointment is at noon or before
- All arrivals are deviated from patient appointment times (no walk-ins)
- We assume a single drug order for each patient with a drug compounding probability of failure of 5%.
- There is also a chance for pre-mixed orders to be wasted if a patient defers or doesn't show.

Estimated Input Parameters

Process	Distribution	Description
Patient Arrivals	JohnsonSU (-0.43, 1.41, -2.77, 45.51)	Negative values=early arrival Positive=late arrival
First Verification	Triangular (1, 2, 15)	Expert Opinion in min
Second Verification	Triangular (1, 2, 5)	Expert Opinion in min
Print Labels/Kit	Triangular (1, 3, 5)	Expert Opinion in min
Drug Mix Time	Beta (1.78, 47.89, 0, 240)	Historical Data
Safety Check	Pearson3(2.509, 3.583, 3.240)	Historical Data

Test Case Overviews

- Case 1
  - Pre-mix drugs for first 20 patients who have a probability of deferral/no-show of 0.1 or lower
- Case 2
  - Pre-mix proportionally based on appointment time (i.e. if 10% of appointments between 9-10 am mix the first 2 drugs in that hour)
- Case 3
  - Combination of Case 1 and 2

Test Case Outputs

Time in System and Wasted Drug Results

Metrics		Scenarios
Days		No Pre-mix
1	Average	52.79
	CI	(49.51, 56.07)
2	Average	85.63
	CI	(80.79, 90.46)
3	Average	58.04
	CI	(54.74, 61.34)
4	Average	38.10
	CI	(36.3, 39.89)
5	Average	47.86
	CI	(44.95, 50.78)
Avg of Avg # of Drugs Wasted		0

Test Case Outputs

Time in System and Wasted Drug Results

	Metrics	Scenarios	
Days		No Pre-mix	1
1	Average	52.79	30.70
	CI	(49.51, 56.07)	(29.53, 31.87)
2	Average	85.63	46.60
	CI	(80.79, 90.46)	(44.43, 48.8)
3	Average	58.04	35.44
	CI	(54.74, 61.34)	(33.65, 37.22)
4	Average	38.10	24.78
	CI	(36.3, 39.89)	(24.18, 25.37)
5	Average	47.86	28.32
	CI	(44.95, 50.78)	(27.53, 29.09)
Avg of Avg # of Drugs Wasted		0	2.81

First 20 below probability of deferral threshold

Test Case Outputs

Time in System and Wasted Drug Results

Days	Metrics	No Pre-mix	Scenarios 1	2
1	Average	52.79	30.70	26.64
	CI	(49.51, 56.07)	(29.53, 31.87)	(26.23, 27.05)
2	Average	85.63	46.60	41.73
	CI	(80.79, 90.46)	(44.43, 48.8)	(39.21, 44.25)
3	Average	58.04	35.44	37.69
	CI	(54.74, 61.34)	(33.65, 37.22)	(34.87, 40.51)
4	Average	38.10	24.78	22.82
	CI	(36.3, 39.89)	(24.18, 25.37)	(22.35, 23.33)
5	Average	47.86	28.32	25.73
	CI	(44.95, 50.78)	(27.53, 29.09)	(25.27, 26.19)
Avg # of Avg # of Drugs Wasted		0	2.81	3.13

Pre-mix proportionally based on appointment time

Test Case Outputs

Time in System and Wasted Drug Results

	Metrics	Scenarios			
Days		No Pre-mix	1	2	3
1	Average	52.79	30.70	26.64	26.17
	CI	(49.51, 56.07)	(29.53, 31.87)	(26.23, 27.05)	(25.65, 26.68)
2	Average	85.63	46.60	41.73	38.19
	CI	(80.79, 90.46)	(44.43, 48.8)	(39.21, 44.25)	(36.19, 40.19)
3	Average	58.04	35.44	37.69	27.47
	CI	(54.74, 61.34)	(33.65, 37.22)	(34.87, 40.51)	(26.59, 28.35)
4	Average	38.10	24.78	22.82	22.43
	CI	(36.3, 39.89)	(24.18, 25.37)	(22.35, 23.33)	(22.06, 22.81)
5	Average	47.86	28.32	25.73	25.70
	CI	(44.95, 50.78)	(27.53, 29.09)	(25.27, 26.19)	(24.71, 26.7)
Avg of Avg # of Drugs Wasted		0	2.81	3.13	2.32

Combination of 1 and 2

Summary

- Utilized patient specific data to predict their chance of deferral
- Simulated pharmacy orders from order arrival to patient delivery patient
- Presented “rule of thumb” policies and showed their improvement compared to not pre-mixing

Future Work

- Order arrival Stream
- Test optimization model
- Simulation optimization to explore dynamic policies

Thank You!

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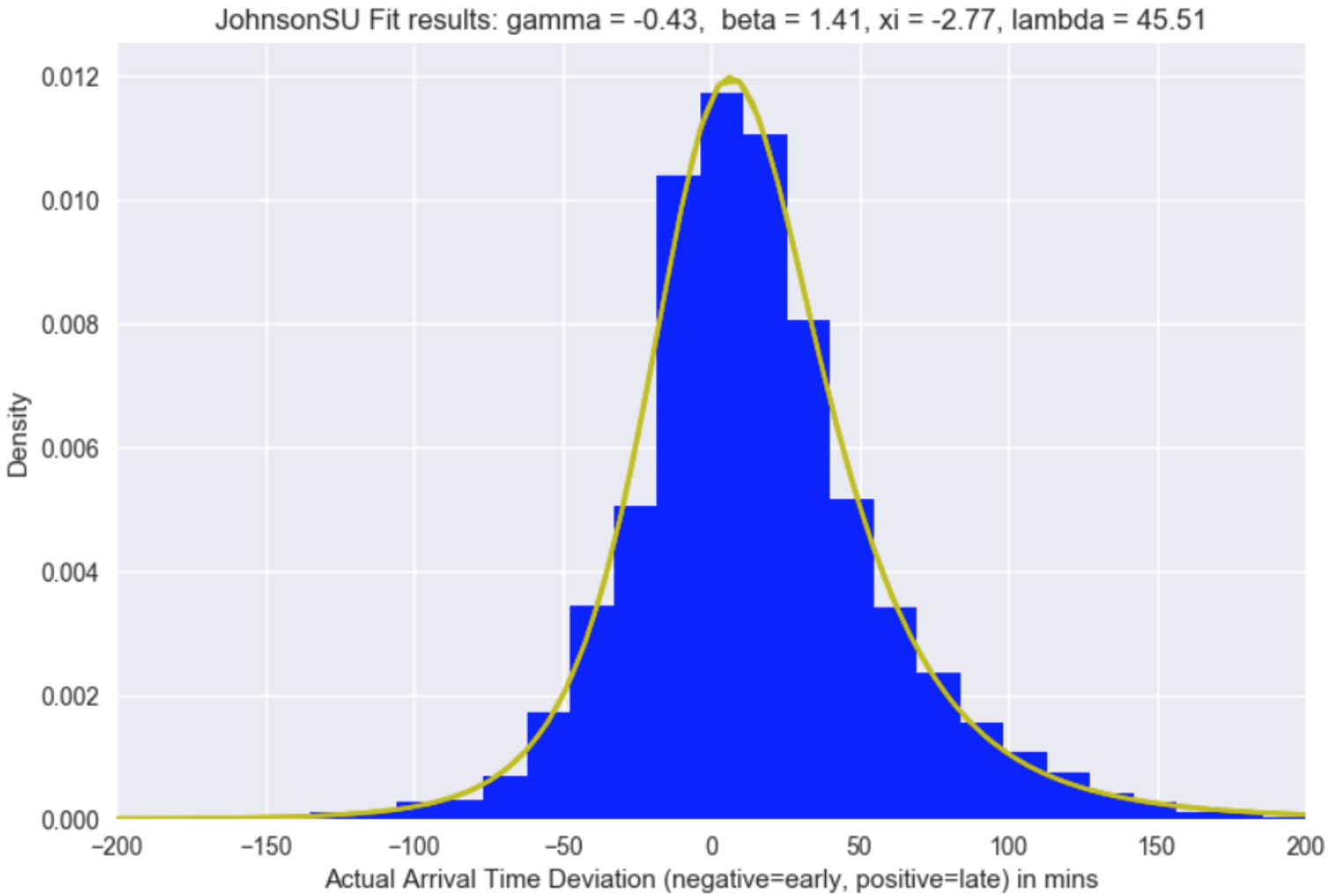
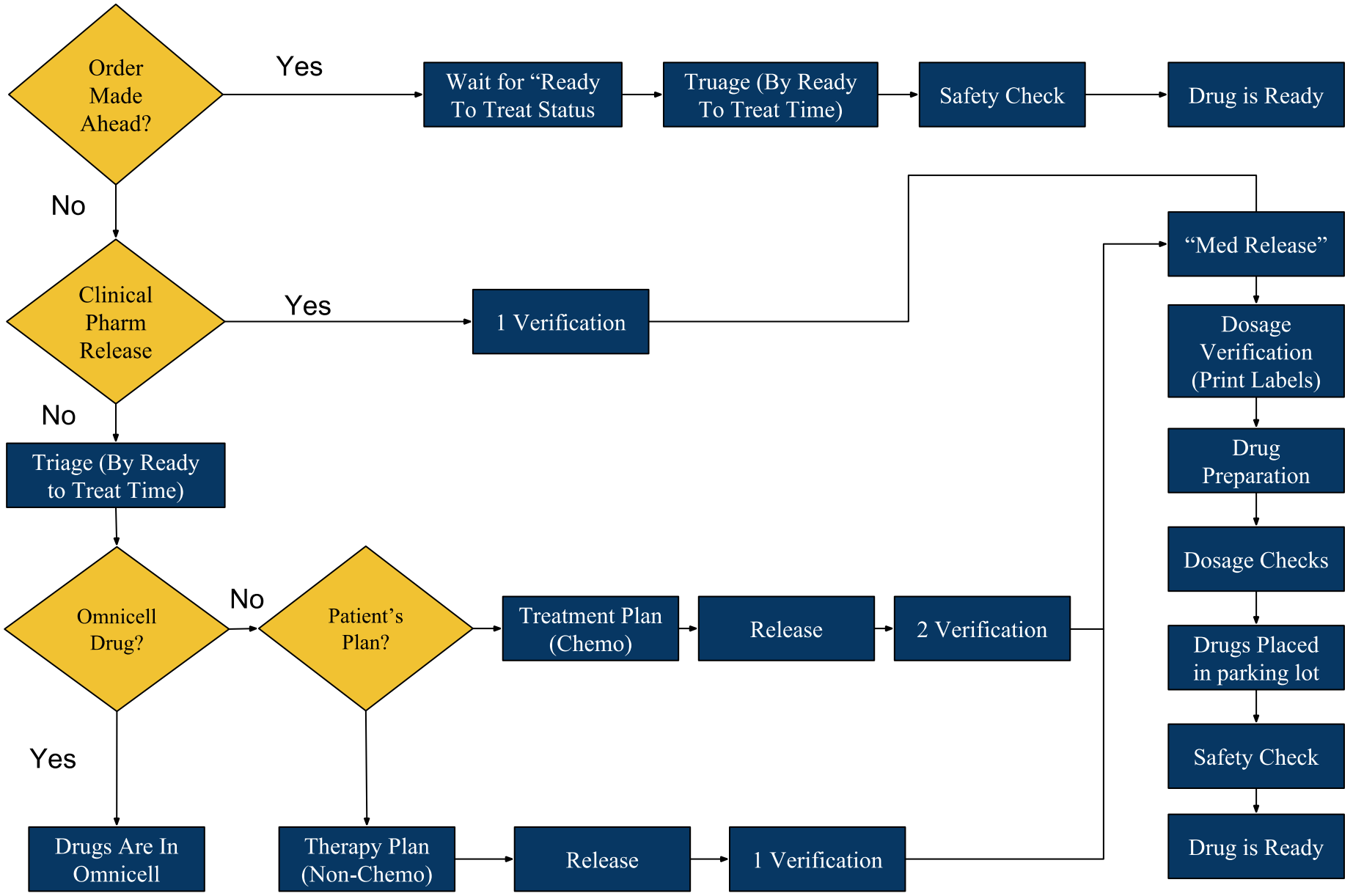
Estimated Input Parameters



Pharmacy Work Flow



Questions

- Current Simulation in Python using Simpy, would you have any reasons this would not be a good approach?
- Suggestions on implementing dynamic polices we would not be able to define transition probabilities to utilize an MDP?