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A Simulation Based Comparison of Point of Care Testing and Central Laboratory Testing

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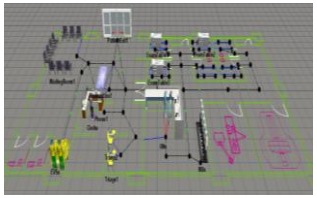
Operations Research Group @ Dartmouth

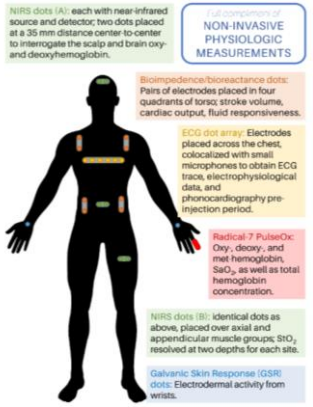
Transportation

Applications

- Schedule Design
- Network Planning
- Disruption Management
- Pricing
- Consensus Building
- Predictive Diagnostics

Healthcare





Models and Methods

GAME THEORY AND MECHANISM DESIGN

APPLIED MACHINE LEARNING

SIMULATION MODELING

INTEGER OPTIMIZATION

OPTIMIZATION UNDER UNCERTAINTY

FAST ALGORITHMS AND HEURISTICS

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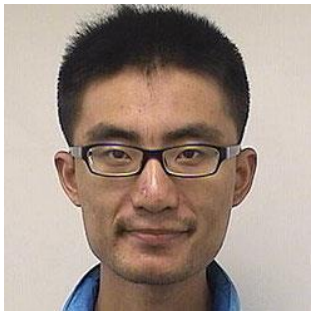
Reed Harder



Keji Wei

Dr. James Stahl

NIH National Institute of Biomedical Imaging and Bioengineering
Creating Biomedical Technologies to Improve Health

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Consortia for Improving Medicine with Innovation & Technology

FDA NEWS RELEASE

COVID-19 U… …rizes First Diagnostic Test Where Results Can Be Read Directly From Testing Card

For Immedi… …2020

Silver Spring, … Food and Drug Administration issued an emergency use aut… antigen test where … be read directly from the testing card, a similar design to some p… simple design is fast and efficient for healthcare providers and patients and does not need the use of … analyzer.

"This new COVID-19 antigen test is an important addition to available tests because the results can be read in minutes, right off the testing card. This means people will know if they have the virus in almost real-time. Due to its simpler design and the large number of tests the company anticipates making in the coming months, this new antigen test is an im… …nt in our fight against the pandemic," said Jeff Shuren, M.D., J.D., director of the FDA's Center for D… …l Health.

HOW …

A healthca… provider swabs the patient's nose and twirls that sample… …d with a testing reagent added. After waiting 15 minutes, the healthcare provider reads the results directly from the testing card. One line indicates a negative result; two lines indicate a positive result.

WHERE IT CAN BE USED:

This test could be used at point-of-care settings, like a doctor's office, emergency room or some schools. This test has been authorized for use in patients suspected of COVID-19 by their healthcare provider within seven days of symptom onset. Given the simple nature… …likely th… …uld be made broadly available. According to the test manufacturer, Abbo… …p to… …able monthly in the U.S. at the beginning of October 2020.

TEST DETAILS:

In general, antigen tests are very specific, but are not as sensitive as molecular tests. Due to the potential for decreased sensitivity compared to molecular assays, negative results from an antigen test may need to be confirmed with a molecular test prior to making treatment decisions. Negative results from an antigen test should be considered in the context of clinical observations, patient history and epidemiological information.

*Colors added for emphasis

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… Other Recent Headlines

Speed

Cost

- *"New saliva-based Covid-19 test could be a fast and cheap 'game changer'"*

Convenience

16, 2020

- *"S ? At-home coronavirus test kits are an option"*

False Positives

- Boston 25 News, August 20, 2020

- *"All 77 false-positive COVID-19 tests came back negative, NFL testing partner cites 'isolat nation'"*

False Positives

- CBS Sport 24, 2020

- *"Sweden uncovers 3,700 false positives fr 9 test kit"*

False Negatives

- *MedicalExpress.com, Augus*

- *"COVID-19 Story Tip: Beware of False Negatives in Diagnostic Testing of COVID-19"*

- *Johns Hopkins Medicine Newsroom, May 26, 2020*

*Colors added for emphasis

Background

- US has the highest annual per-capita health expenditures of the OECD[1], yet still faces significant health challenges.
- Changes are being proposed to:
  - Produce higher quality care at reduced cost
  - Shift focus to patient-centered early care for better outcomes and lower utilization of more expensive specialized medical resources
- Evolving new delivery models have patients more involved in decision-making and self-care.[2]
- These require the development of inexpensive and easy-to-use medical devices and information sharing tools that provide timely health status information at the point of care.
- National Institute of Biomedical Imaging and Bioengineering (NIBIB) created → the Point-of-Care Technologies Research Network (POCTRN) in 2007.

[1]OECD: Organization for Economic Co-operation and Development

[2]www.POCTRN.org

Systems Engineering Perspective

- Technologies do not exist in isolation but rather within systems of other technologies, which in turn influence their effectiveness and likelihood of success or failure.
  - *The National Academies of Sciences, Engineering and Medicine* have called for the introduction of systems engineering tools into healthcare to help solve problems
  - Industrial/Systems Engineering (ISyE)
- POCT is potentially disruptive, changing **where**, **when** and **how** we deliver care – a great case-in-point for the systems engineering perspective!

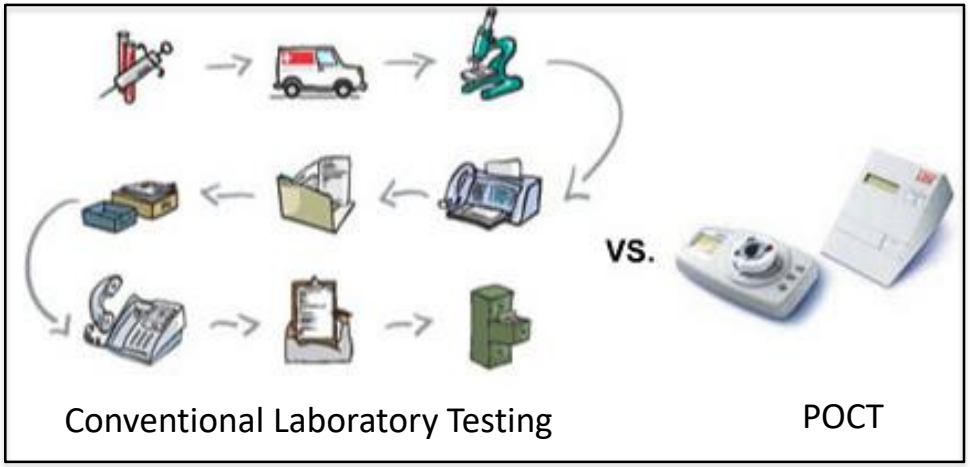
Diagnostic Testing in Primary Care Medicine

- Direct costs estimated to be low (around 4% of average hospital budget), but estimated to indirectly affect 2/3rd of this budget (Lee-Lewandrowski and Lewandrowkski, 2009)
- Improvements can have a big impact on downstream processes (patient flow, diagnoses, outcomes)

Courtesy of ACEP Now

What is Point of Care Testing (POCT)?

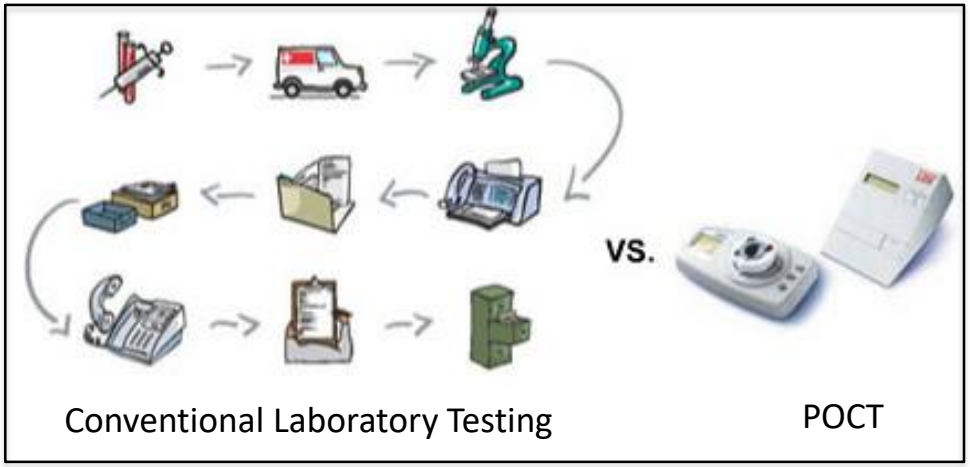
- Diagnostic testing close to the point of care, instead of sending samples or patients to a central lab for testing
- Empirically faster turnaround times than use of central lab (e.g., Renaud et al., 2008)



Courtesy of Whitmire Medical (www.whitmiremedical.com)

The Potential of Point of Care Testing (POCT)

- Common in Europe, rapidly expanding use in the US: projected to grow at a rate of 15% per year (Scalise, 2006)
- Applications include testing for streptococcus, HIV, pregnancy, blood glucose, malaria, cardiac biomarkers, drug screens, cancer, hepatitis C, stroke, syphilis, and COVID-19



Courtesy of Whitmire Medical (www.whitmiremedical.com)

Why not use POCT wherever possible?

- Typically more (directly) expensive per test
  - For example, Lee-Lewandrowski and Lewandrowski (2013) estimate approximately $10 vs. $5 for a creatinine test

- Often assumed to provide lower quality diagnostic information
  - Worse testing characteristics/higher error rates (Nichols et al., 2000)
  - E.g., prone to insufficient sample volumes
  - More prone to provider error (O'Kane et al., 2011)
  - Short turnaround time reduces opportunity for error correction

Why not use POCT wherever possible?

POCT

- Fast turnaround times reduce time to treatment
- Generally higher cost, lower quality than central lab

Central Lab Testing

- Generally slower turnaround times
- Economies of scale: lower cost, higher quality

Empirical results (Bradburn et al., 2012) show mixed results between hospitals on patient outcomes: clinical setting matters!

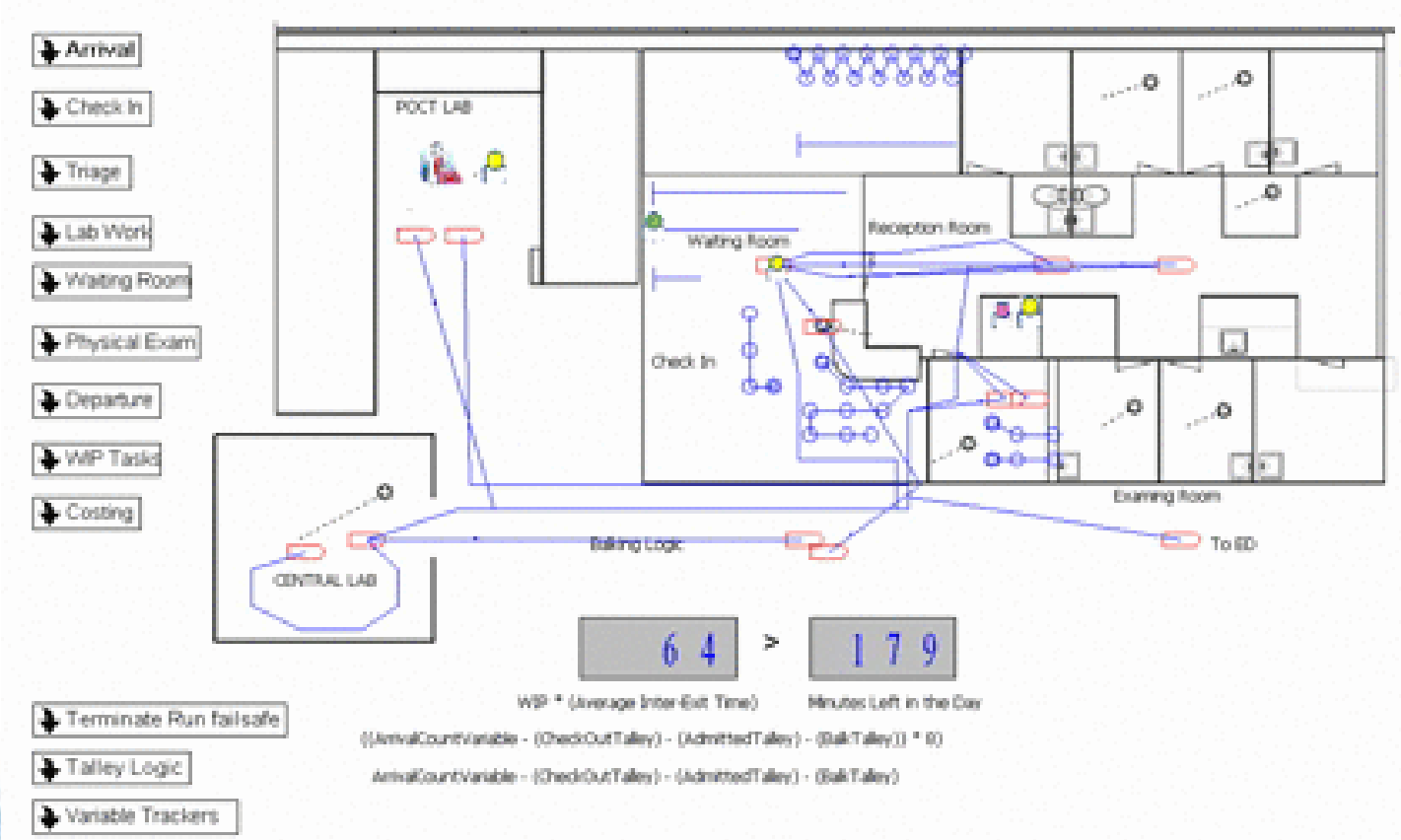
Literature Review: Two Relevant Areas

- **Empirical evaluations**: generally reduced turnaround time (Renaud et al., 2008), mixed patient outcomes (Bradburn et al., 2012)

- **Clinical Simulation:** literature evaluating diagnostic testing is limited
  - Storrow et al. (2008) simulated an emergency clinic with varied test turnaround times, quantified improvement in patient flow
  - Powell and Reinhart (2007) evaluated introduction of POCT in emergency clinic on patient flow
  - Little attempt to evaluate tradeoffs in cost and quality, or evaluate varied clinical settings, or model outcomes/societal costs

Discrete-Event Simulation in ARENA Software

- For holistic comparison of different testing regimes
  - Evaluation of patient flow, outcomes and costs



Overview of Simulation

- System parameters taken from direct observation, expert knowledge and health care delivery literature
- National Survey of the Society of General Internal Medicine (Stahl et al., 2003)
- National Ambulatory Medical Care Survey (Rui and Okeyode, 2015)
- A series of studies on Real-Time Location Systems (RTLS) in health care delivery (Stahl et al., 2011a; 2011b; 2013)
- Triangular distributions used for stochastic model inputs for which data for parametric fitting of distributions was not available (Law and Kelton, 1991)
- Additionally, conducted several sensitivity analyses of the main assumptions and input parameters

Inter-Arrival and Exam Times

- Some patients have an underlying target illness, others don't
  - Both may show symptoms with 3 severity levels

Variable Name	Severity	Value
Established Patient Inter-arrival Time	1	N(129,60) (min)
Established Patient Inter-arrival Time	2	N(61,60) (min)
Established Patient Inter-arrival Time	3	N(144,60) (min)
New Patient Inter-arrival Time	1	N(596,60) (min)
New Patient Inter-arrival Time	2	N(303,60) (min)
New Patient Inter-arrival Time	3	N(722,60) (min)
New Patient Exam Time	1	N(15,9) (min)
New Patient Exam Time	2	N(17,8) (min)
New Patient Exam Time	3	N(42,16) (min)
Established Patient Exam Time	1	N(13,6) (min)
Established Patient Exam Time	2	N(15,5) (min)
Established Patient Exam Time	3	N(42,16) (min)
Time to Fill Out Paper Work	All	Tri(10,15,20) (min)
Probability of a Patient Having Target Condition	1	0.2
Probability of a Patient Having Target Condition	2	0.4
Probability of a Patient Having Target Condition	3	0.75
Probability of Testing a Patient	1	0.5
Probability of Testing a Patient	2	0.7
Probability of Treating a Patient	3	0.9

Target Condition and Testing Probabilities

- Probability of having underlying illness and being tested positively correlated with severity

Variable Name	Severity	Value
Established Patient Inter-arrival Time	1	N(129,60) (min)
Established Patient Inter-arrival Time	2	N(61,60) (min)
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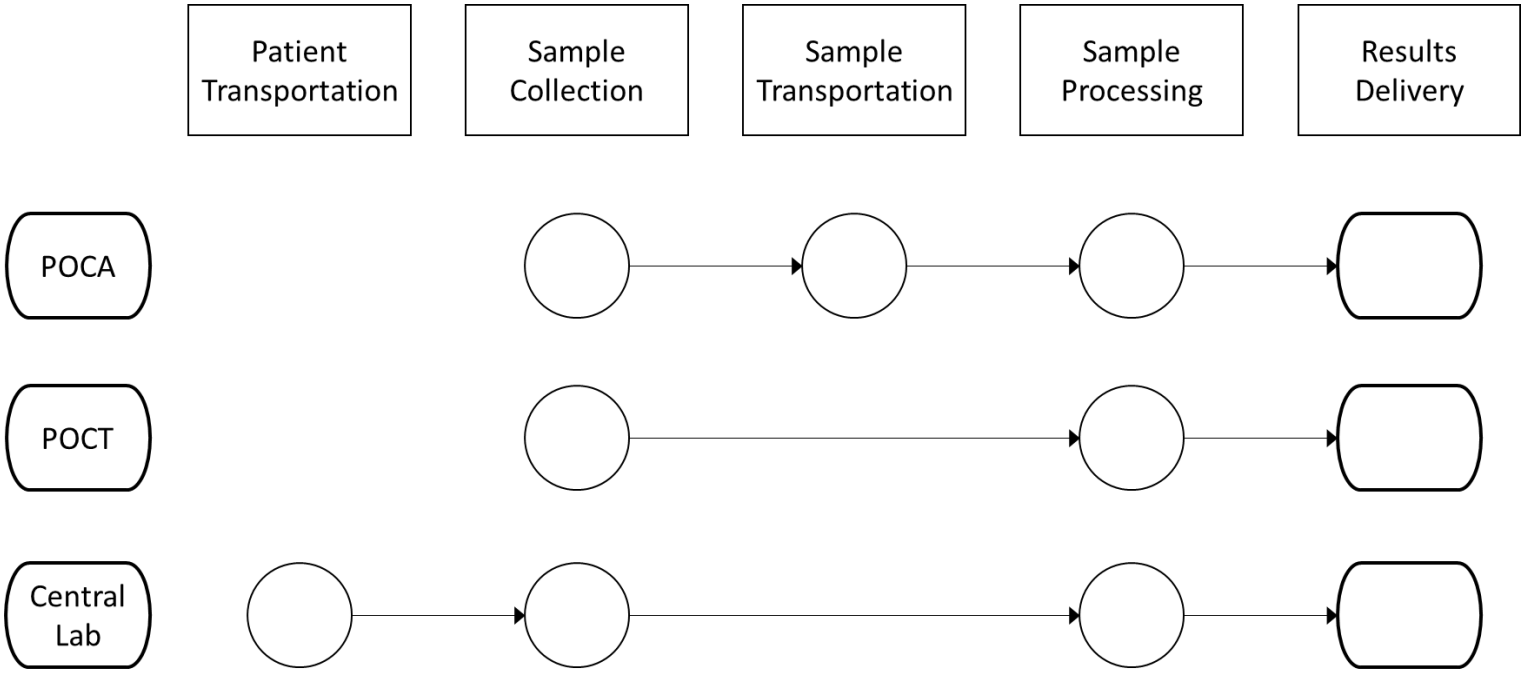
Probability of Treating a Patient	3	0.9

Testing Regimes Overview



*POCA: Point-Of-Care sample Acquisition

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Clinical Scenarios Overview

Rural

Test Regime	Subprocess: Patient Transportation (hr)	Sample Collection (min)	Sample Transportation (hr)	Sample Processing (min)	Result Delivery (hr)
POCT	0	Tri(20,30,40)	0	Tri(10,30,50)	0
POCA	0	Tri(20,30,40)	Tri(8,16,24)	Tri(5,15,25)	Tri(4,8,12)
Central lab	Tri(8,16,24)	Tri(20,30,40)	0	Tri(5,15,25)	Tri(2,4,6)

Community

Test Regime	Subprocess: Patient Transportation (hr)	Sample Collection (min)	Sample Transportation (hr)	Sample Processing (min)	Result Delivery (hr)
POCT	0	Tri(20,30,40)	0	Tri(10,30,50)	0
POCA	0	Tri(20,30,40)	Tri(2,4,6)	Tri(5,15,25)	Tri(4,8,12)
Central lab	Tri(2,4,6)	Tri(20,30,40)	0	Tri(5,15,25)	Tri(2,4,6)

Hospital-Based

Test Regime	Subprocess: Patient Transportation (hr)	Sample Collection (min)	Sample Transportation (hr)	Sample Processing (min)	Result Delivery (hr)
POCT	0	Tri(20,30,40)	0	Tri(10,30,50)	0
POCA	0	Tri(20,30,40)	Tri(0.5,1,1.5)	Tri(5,15,25)	Tri(0.2,1,1.8)
Central lab	Tri(0.2,1,1.8)	Tri(20,30,40)	0	Tri(5,15,25)	Tri(0.2,1,1.8)

Error Rates

- Sensitivity and specificity as proxies for test quality (for example, 80% vs 95%, for Pneumonia)

Variable Name	Pneumonia Test	Opiate Test	Chlamydia Test	Cholesterol Test
POCT Sensitivity (%)	80	75	80	90
POCT Specificity (%)	80	70	80	90
POCA Sensitivity (%)	95	95	95	97
POCA Specificity (%)	95	95	95	97
Central Lab Test Sensitivity (%)	95	95	95	97
Central Lab Test Specificity (%)	95	95	95	97
Per-patient Treatment Cost ($)	61	5,980	66	68

Patient Time Lost

- Patients who test positive for illness are treated
- They lose further productive days in recovery
- Work days lost according to distribution on severity, underlying illness, treatment

Target Condition	Treated?	Severity	Pneumonia Test	Opiate Test	Chlamydia Test	Cholesterol Test
Yes	Yes	1	DISC(0.5,0,0.5,1)	DISC(0.9,0,0.1,1)	0	0
Yes	Yes	2	Tri(0,2,5)	Tri(0,0.5,3)	Tri(0,0.2,1)	Tri(0,0.2,0.5)
Yes	Yes	3	Tri(0,5,10)	Tri(0,1,5)	Tri(0,0.5,1)	Tri(0,0.2,1)
Yes	No	1	Tri(0,3,6)	Tri(0,2,10)	Tri(0,1,2)	Tri(0,0.2,0.5)
Yes	No	2	Tri(5,10,15)	Tri(0,3,20)	Tri(0,1.5,2.5)	Tri(0,0.5,1.5)
Yes	No	3	Tri(10,14,18)	Tri(0,5,30)	Tri(0,2,3)	Tri(0,1,5)
No	Yes or No	1	DISC(0.5,0,0.5,1)	DISC(0.95,0,0.05,1)	0	0
No	Yes or No	2	Tri(0,1,2)	Tri(0,0.5,2)	Tri(0,0.2,0.5)	0
No	Yes or No	3	Tri(0,3,6)	Tri(0,2,5)	Tri(0,0.5,0.75)	0

Pneumonia Test Details

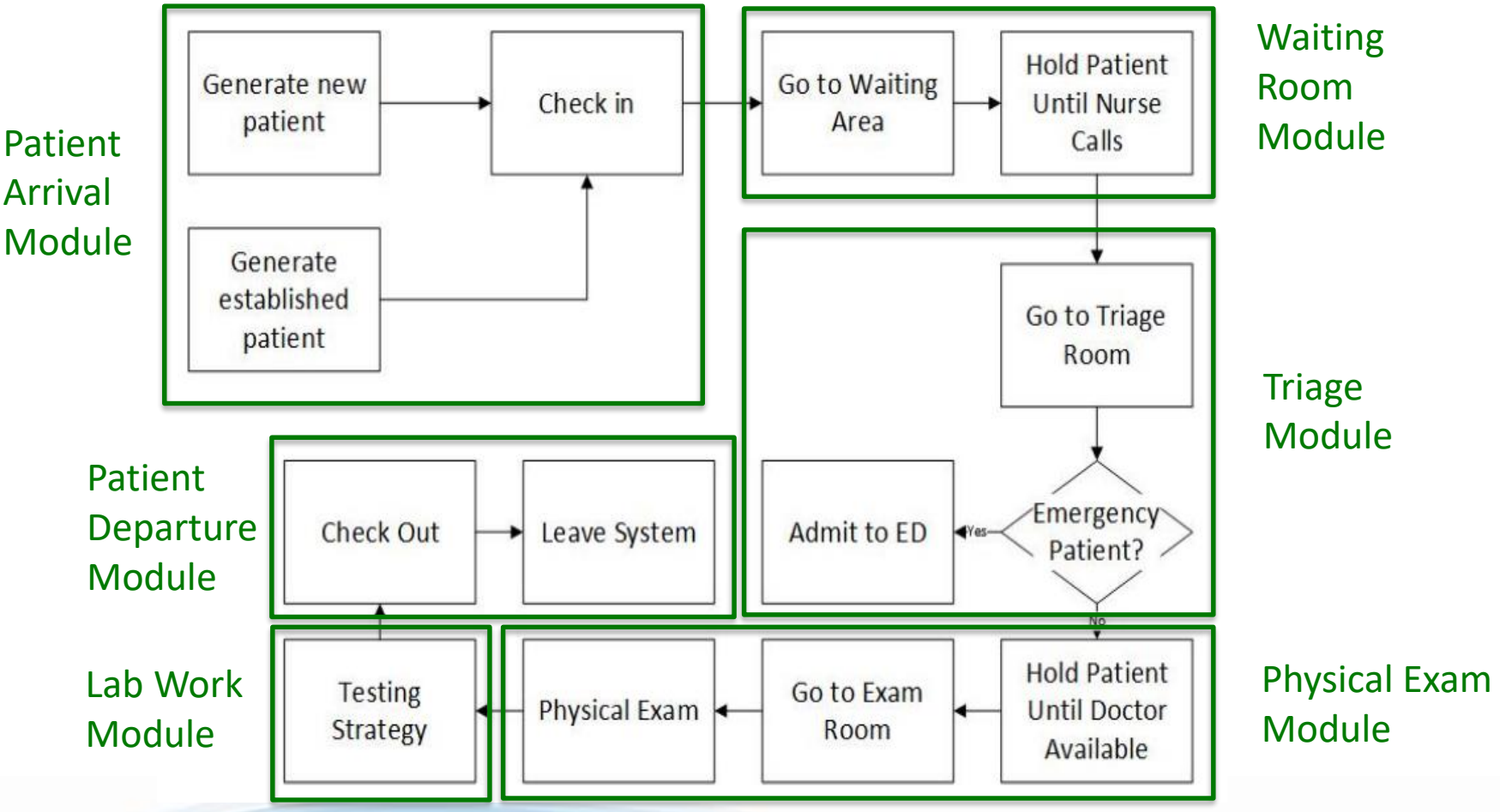
- Three types of tests for Pneumonia: Blood, X-Ray and Urine
  - Severity level 3 automatically treated

Indicator Severity	*P*(Blood Test Only)	*P*(X-ray Test Only)	*P*(All Three Tests)
1	0.30	0.60	0.10
2	0.60	0.10	0.30

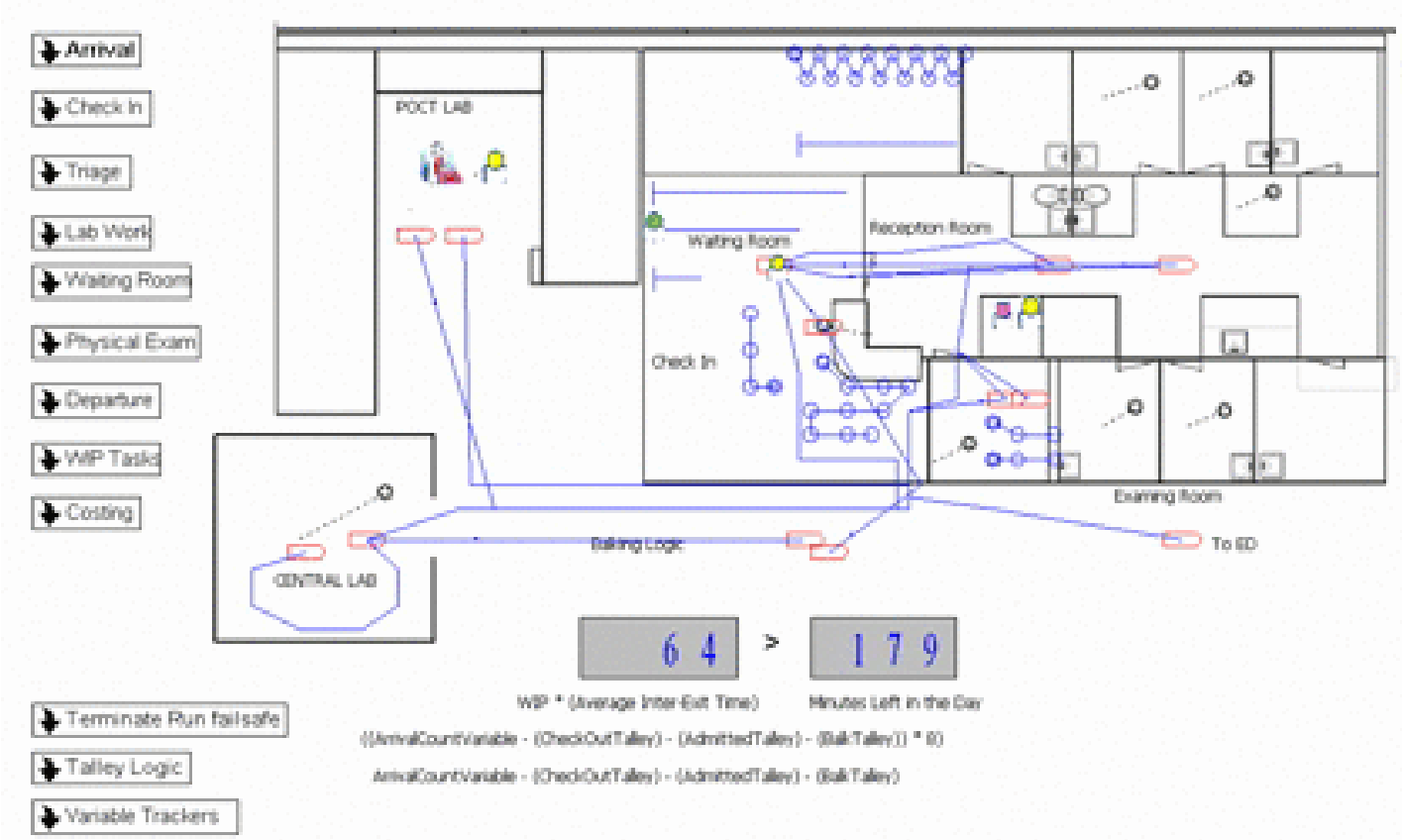
- Test costs ($):

Regime	Procedure		
	Blood Test	X-Ray Test	Urine Test
POCT	323	138	108
POCA	308	123	25
Central lab	303	118	88

Overview of Simulation



Overview of Simulation



- 120 year-long (1 work year = 240 eight-hour work-days) replications for each scenario

Simulation Results

Avg. time in the clinical system per patient (Hr) – Pneumonia Testing

	Rural	Community	Hospital-Based
POCT	1.69 (0.01)	1.69 (0.01)	1.69 (0.01)
POCA	17.17 (0.57)	10.28 (0.81)	2.74 (0.01)
Central Lab	15.62 (0.86)	6.78 (0.20)	2.74 (0.01)

Simulation Results

Avg. subsequent productive days lost per patient – Pneumonia Testing

	Rural	Community	Hospital-Based
POCT	1.73 (0.01)	1.73 (0.01)	1.73 (0.01)
POCA	1.51 (0.01)	1.53 (0.01)	1.53 (0.01)
Central Lab	1.52 (0.01)	1.52 (0.01)	1.52 (0.01)

Simulation Results

Avg. total lost productive hours per patient – Pneumonia Testing

Combining two previous tables: *Time in Clinical System*+8*(*Subsequent Productive Days Lost*)

	Rural	Community	Hospital-Based
POCT	15.50 (0.08)	15.50 (0.08)	15.50 (0.08)
POCA	29.29 (0.57)	22.49 (0.81)	14.97 (0.08)
Central Lab	27.80 (0.87)	18.93 (0.21)	14.92 (0.08)

Simulation Results: Overall Cost

1) Avg. direct cost per tested patient ($)

	Rural
POCT	361.12 (0.58)
POCA	315.26 (0.45)
Central Lab	328.09 (0.5)

2) Time Costs transformed using average hourly wages + fringe benefits (~$36/hr in 2018)

3) Treatment Costs

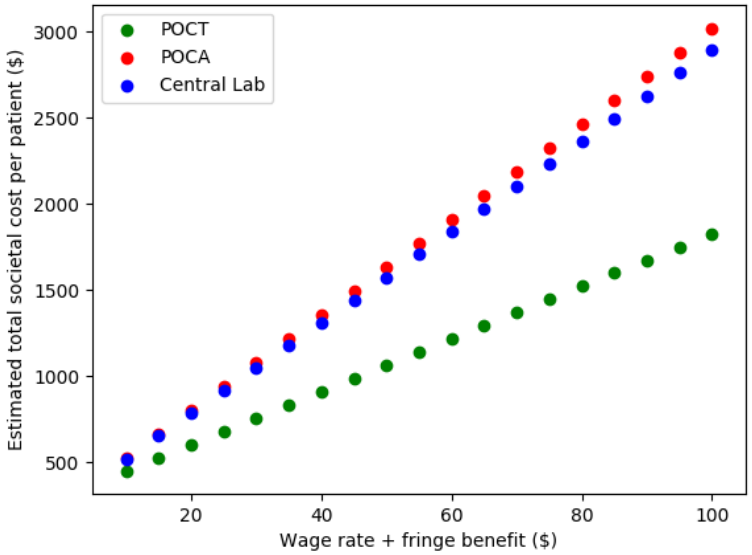
	False Positive Treatments (% of Total)	True Positive Treatments (% of Total)
POCT	12.24	16.38
POCA	9.57	18.95
Central Lab	9.69	18.83

Total societal costs per patient ($) – Pneumonia Testing

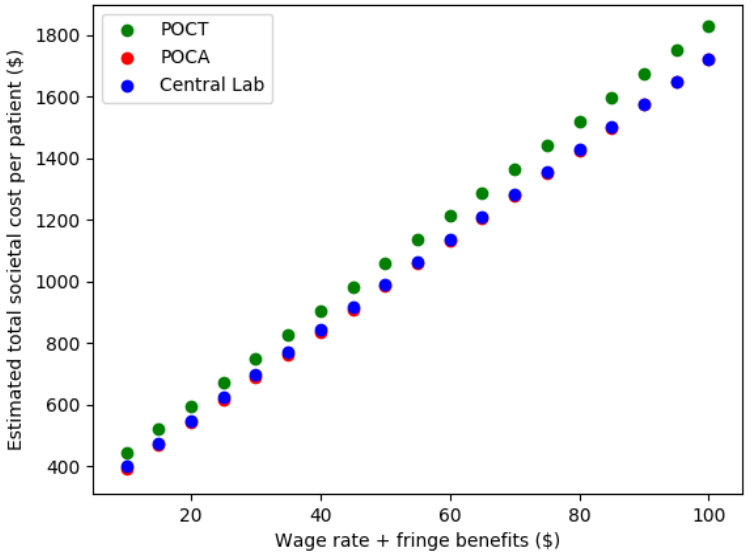
	Rural	Community	Hospital-Based
POCT	842.97 (3.24)	842.97 (3.24)	842.97 (3.24)
POCA	1244.61 (21.51)	1024.14 (29.36)	778.13 (3.22)
Central Lab	1203.92 (30.99)	916.63 (9.42)	784.39 (3.23)

Sensitivity Analysis: Wage Rate

Rural



Hospital-Based



Increasing wage rate enhances the advantages of lower lost productive hours

- Amplifies POCT advantages in the Rural scenario
- Amplifies POCT disadvantages in the Hospital-Based scenario

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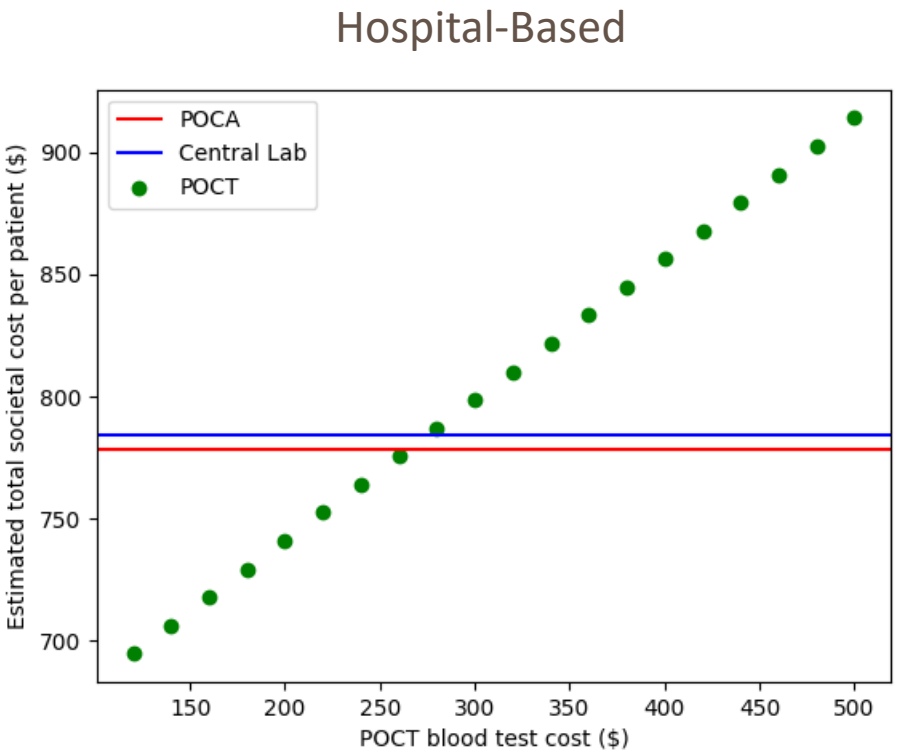
Sensitivity Analysis: Test Cost



At somewhere between $260 and $280, POCT becomes cheaper than POCA and central lab

Alternate Conditions: Total Societal Costs

Opiate Addiction

	Rural	Community	Hospital-Based
POCT	**2,335.24 (3.21)**	**2,335.24 (3.21)**	**2,335.24 (3.21)**
POCA	**2,415.02 (44.39)**	**2,146.52 (40.47)**	**1,864.79 (3.53)**
Central Lab	**2,413.77 (51.26)**	**2,065.82 (22.82)**	**1,913.10 (3.53)**
POCT	355.13 (0.33)	355.13 (0.33)	355.13 (0.33)
POCA	885.62 (33.34)	636.14 (33.34)	367.27 (0.65)
Central Lab	831.63 (39.55)	537.52 (25.82)	366.57 (0.65)

Lower Quality POCT (75%/70% Sens./Spec.) and high treatment costs: POCT worse even in community settings

Alternate Conditions: Total Societal Costs

	Rural	Community	Hospital-Based
POCT	2,335.24 (3.21)	2,335.24 (3.21)	2,335.24 (3.21)
POCA	2,415.02 (44.39)	2,146.52 (40.47)	1,864.79 (3.53)
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Central Lab	**831.63 (39.55)**	**537.52 (25.82)**	**366.57 (0.65)**

Cholesterol

High Quality POCT (90% Sens./Spec.) and relatively mild short term health outcomes: POCT performs best in all scenarios

Takeaways

- Simulation framework for evaluating tradeoffs in patient outcomes for different testing regimes in different clinical scenarios
- Recapitulate empirical work: clinical setting can greatly affect testing regime considerations
- Limitations:
  - Other outcome measures – e.g., staff utilization, clinic revenue – are ignored
  - Parameters dependent on settings and patient populations
  - Longer term modeling of patient health outcomes needed
- Future work needed, and is ongoing, to expand the flexibility, scope, and accessibility of models of this type

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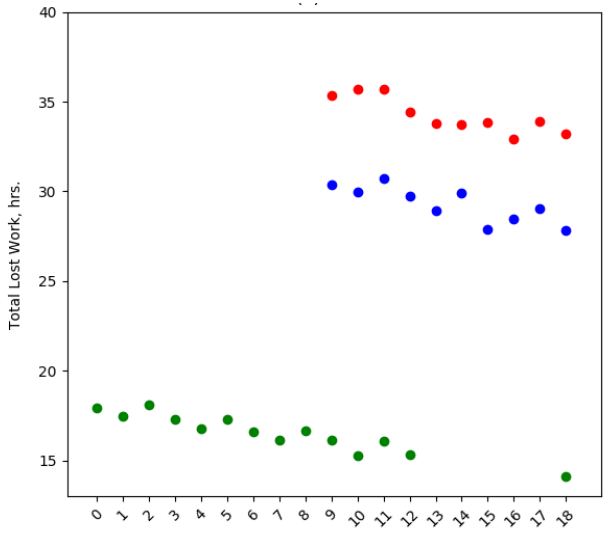
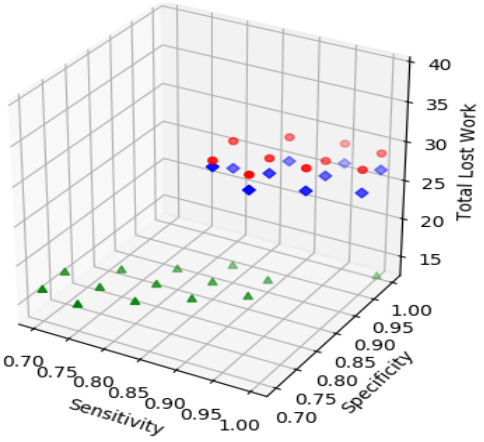
Thank You

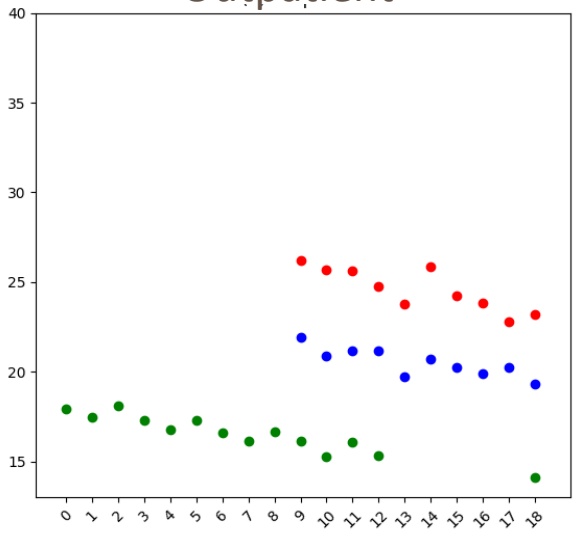
Sensitivity Analysis: Test Efficacy

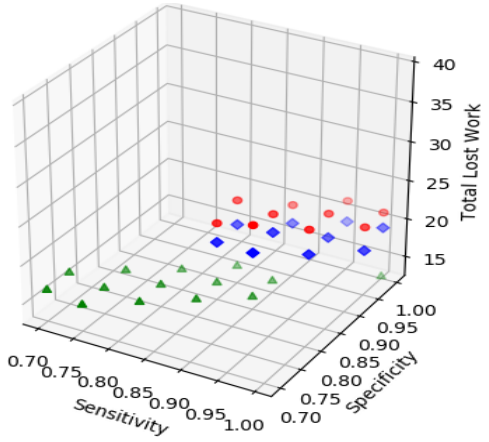
Rural





Outpatient





Hospital-Based