28th Annual INCOSE international symposium

Washington, DC, USA
July 7 - 12, 2018

Rajesh Ganesan (George Mason University); Wen-Chi Hung (University of California, Davis); Tzu-Yi Peng (Trendforce Corp.); Chun-Hung Chen and Naoru Koizumi (George Mason University)

A Hybrid Liver-Candidate Transportation System to Improve Accessibility and Extend Organ Life in Liver Transplantation

Session: 8.3.2 - Healthcare Applications

Grants

- NIH Grant 1R21DK088368-01
- NSF Award CMMI-1233376
- Department of Energy Award DE-SC0002223
- National Science Council of Taiwan Award NSC-100-2218-E-002-027-MY3.

An Application of Modeling and Simulation (M&S) to System Engineering

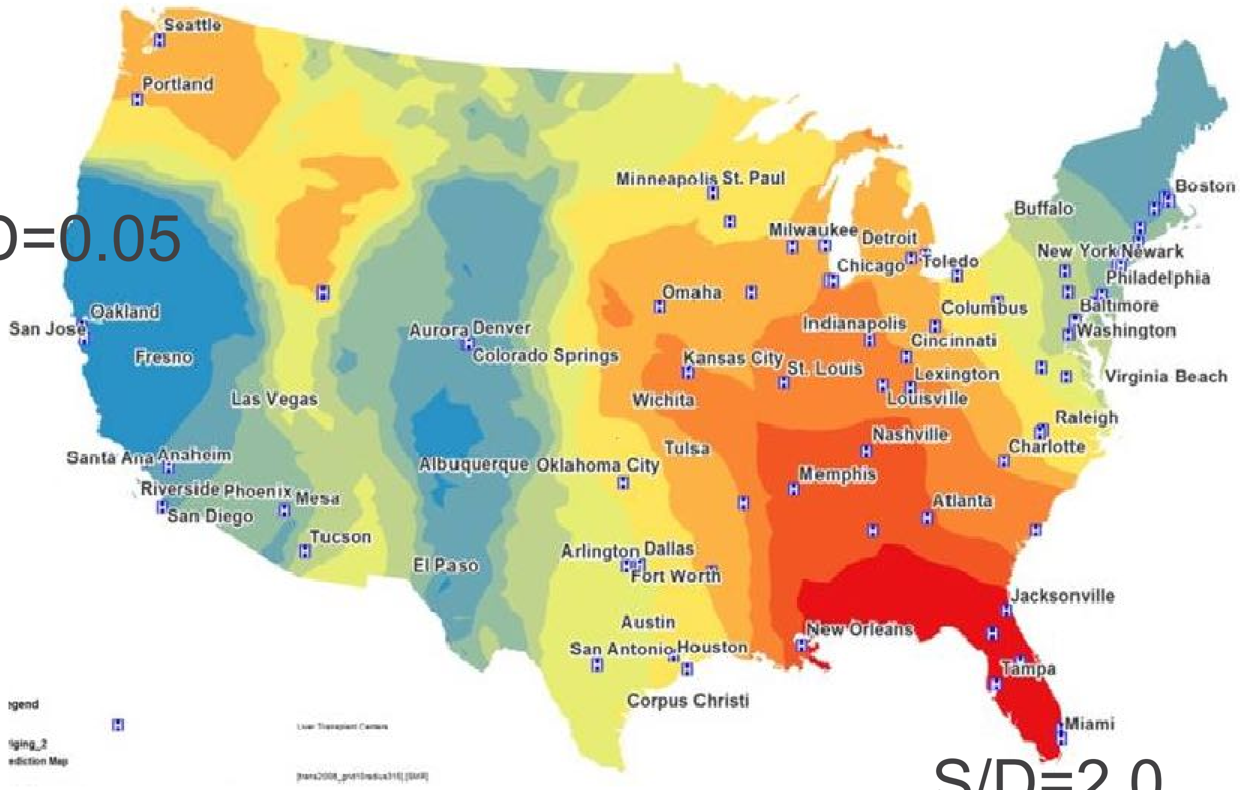
Background

Spatial Analysis

- Geocoded entire transplant donors (37,240) and candidates (65,600) between 2003 and 2013 at the zip level.
- Mapping Organ supply-demand ratios across US counties
- Kriging based on variant radius circles.
- FL- (Red is Best) 2 livers available for each waiting candidate
- CA - (Blue is worst) 1 liver available for 20 waiting candidates

Liver Supply-Demand S/D Ratios: Contiguous US

S/D=0.05



S/D=2.0

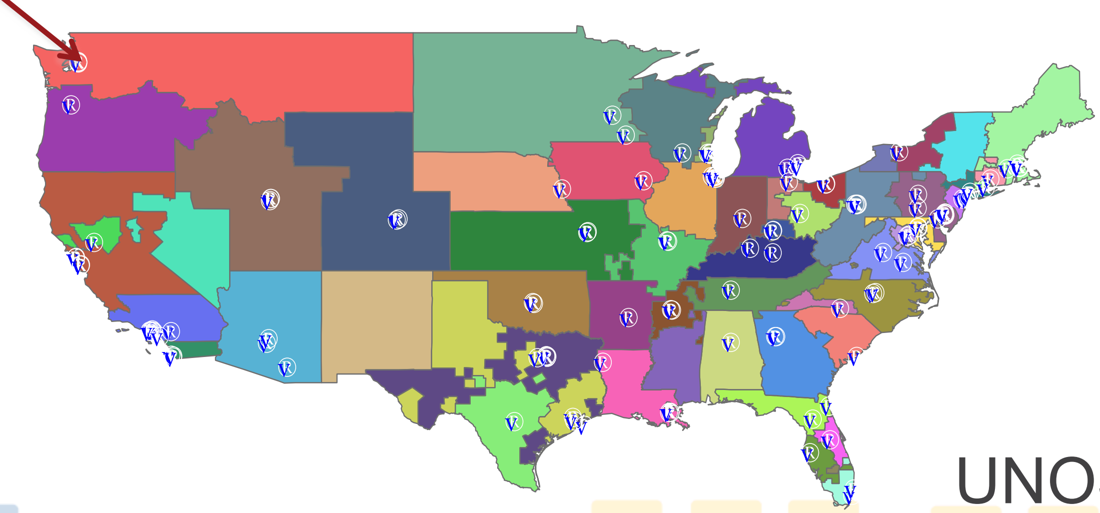
Issue: Geographical Disparity in access to a Liver

Current Allocation Systems

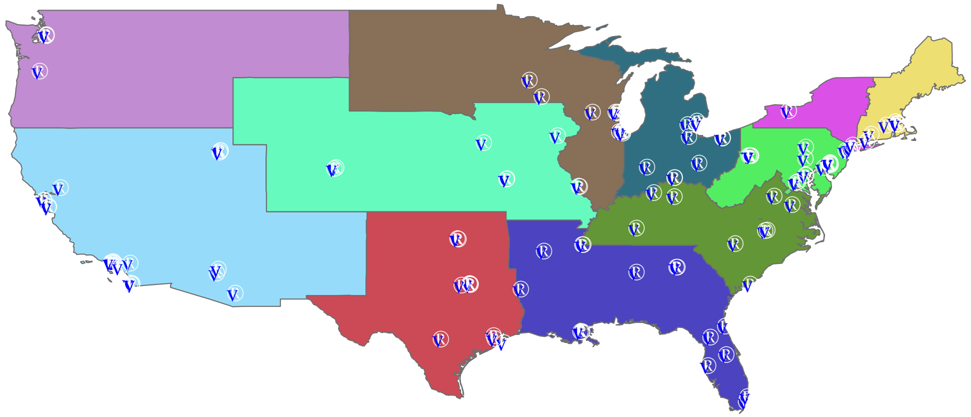
- Geography disparity due to **administratively** determined organ allocation boundaries
- 3 levels of allocation boundaries: Organ procurement organization (OPO)'s Donation Service Area (DSA) → UNOS regions → National (US)

TX- transplant center

58 DSAs

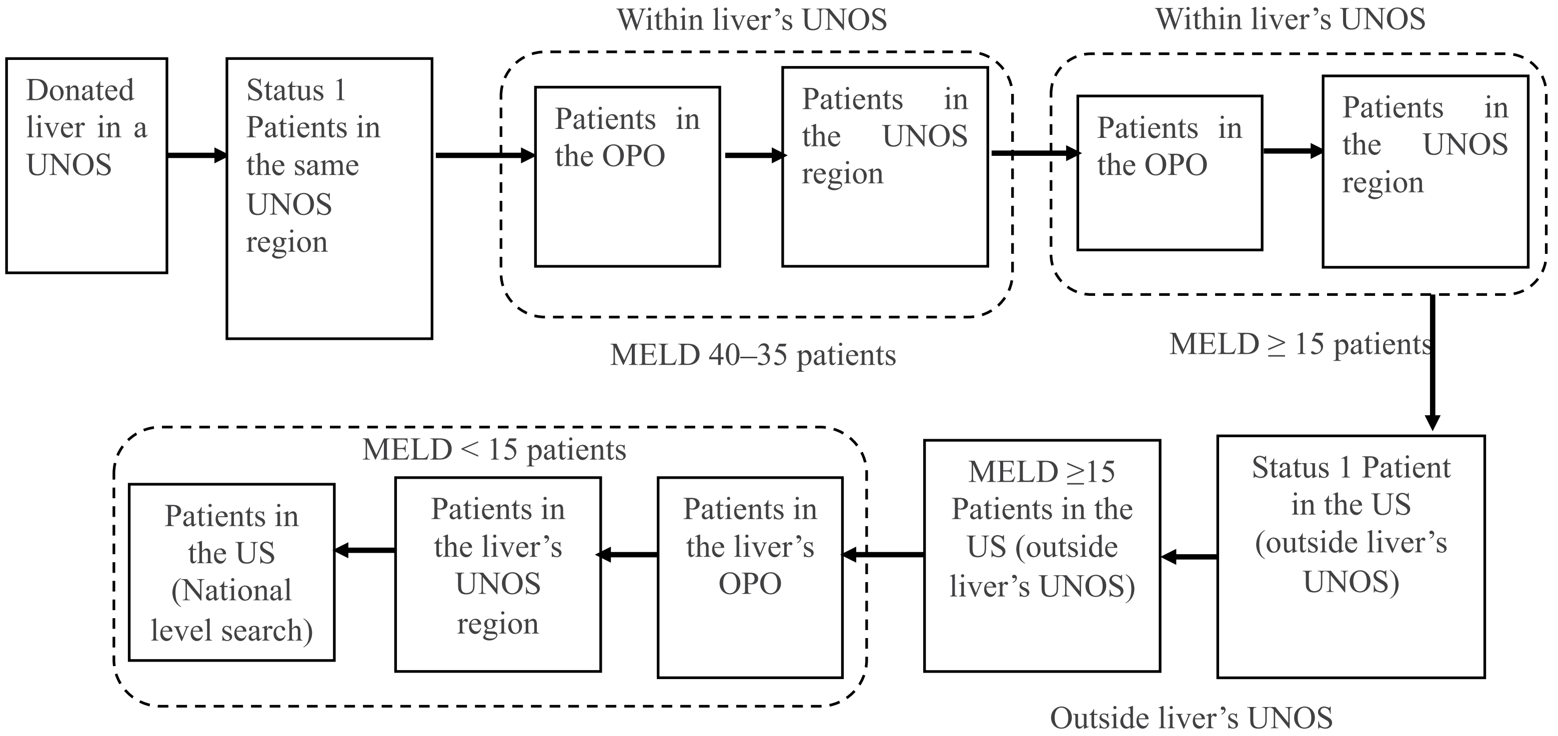


11 UNOS regions



UNOS – United Network for Organ Sharing

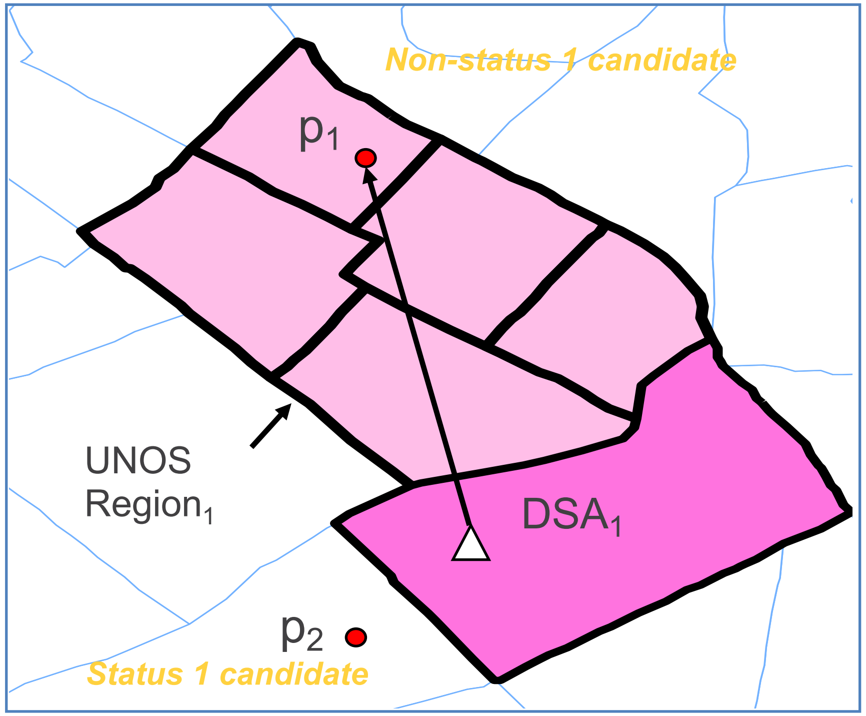
Recommendation by Health and Medicine Division (formerly Institute of Medicine) of the National Academies



- Within each category of patients, a liver is offered in the descending order of MELD score and waiting time.
- Other considerations include blood type, existence of malignant cancer, size, (age) etc.

Status 1 – high priority (risk of imminent death), High MELD to Low MELD Score
MELD Score (Model For End-Stage Liver Disease)

Problems with the Current System in which p_1 (non-status 1) receives the liver and liver travels a longer distance



By giving the liver to p_2 not only is a status 1 candidate getting the liver but also the liver travels shorter distance and can be transplanted sooner

Summary of Other Issues in the Current System

Apart from geographical disparity in access to liver, other issues include

- Long System Waiting time (typically in years)
  - Low supply also contributes to this (lack of aggressive initiatives at the state-level to enlist as "Organ Donor")
- Lack of Broader Organ Sharing
  - Organ Allocation Boundaries limit reachability to those who are in critical need
  - Reachability is also limited by the liver's shelf life
    - Cold Ischemia Time – Time between harvest from a cadaver to transplant (max 8 hrs but post-graft failure probability increases exponentially by the hour)

An Application of Modeling and Simulation (M&S) to System Engineering

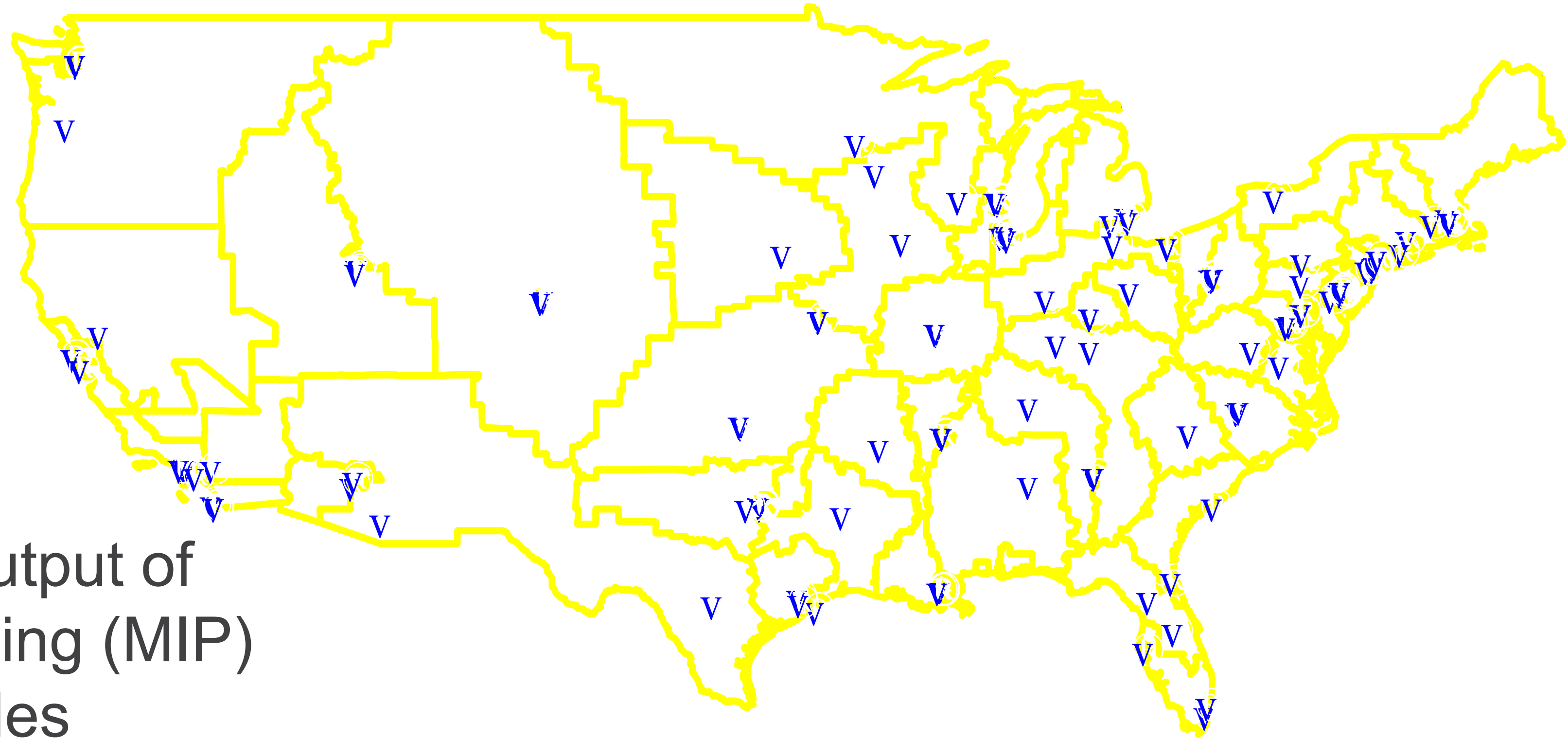
Solution 1

One of the Approaches to Mitigate the Issues – Redraw the boundaries

- Analyzing geographic disparity at the national level
  - Exploratory Spatial Data Analysis
- Building better allocation boundaries
  - Mixed Integer programming (MIP) approach
- Evaluating the new allocation boundaries
  - Discrete Event Simulation approach

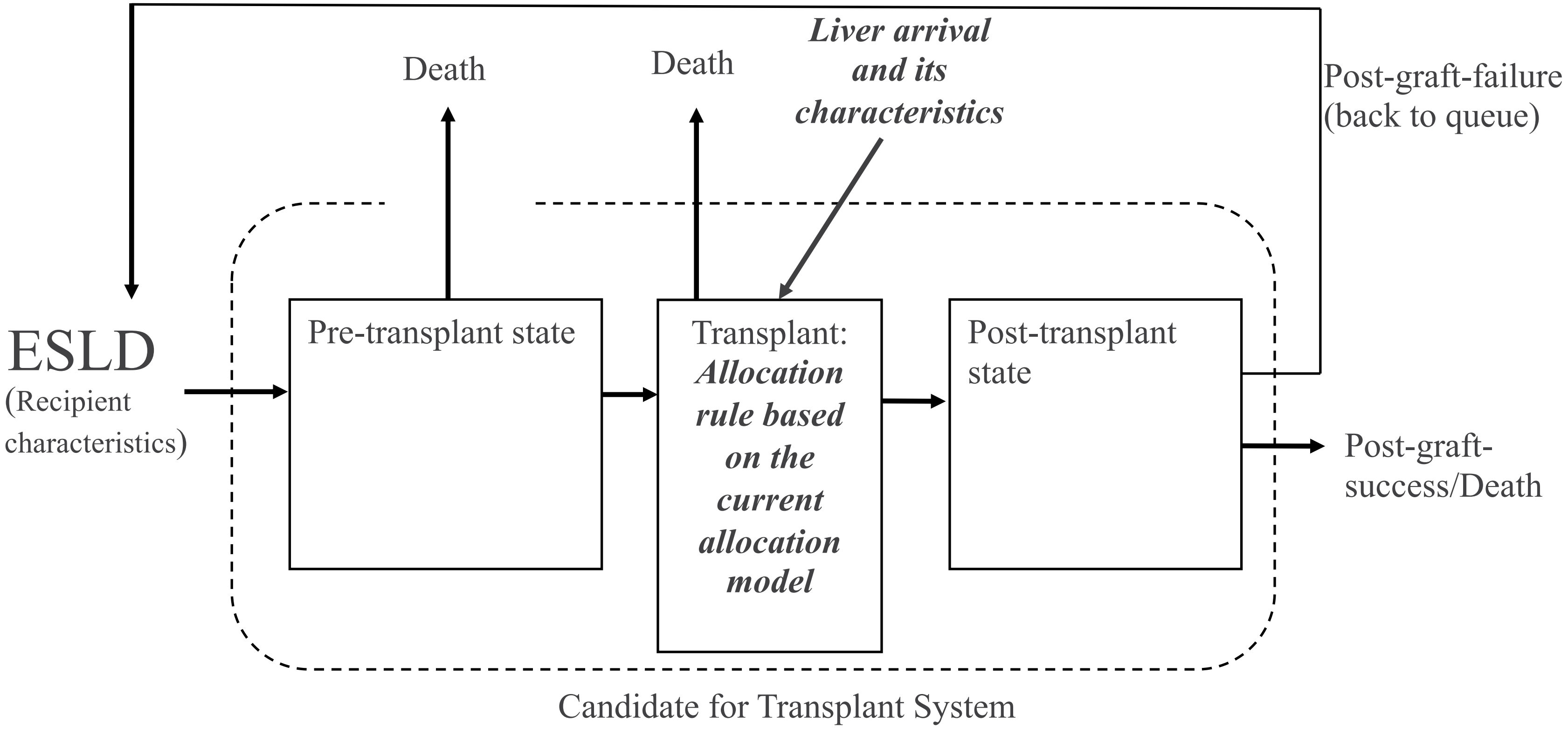
Boundary Analysis & Result

Maintained 58 Second level (DSAs) but redrew their boundaries

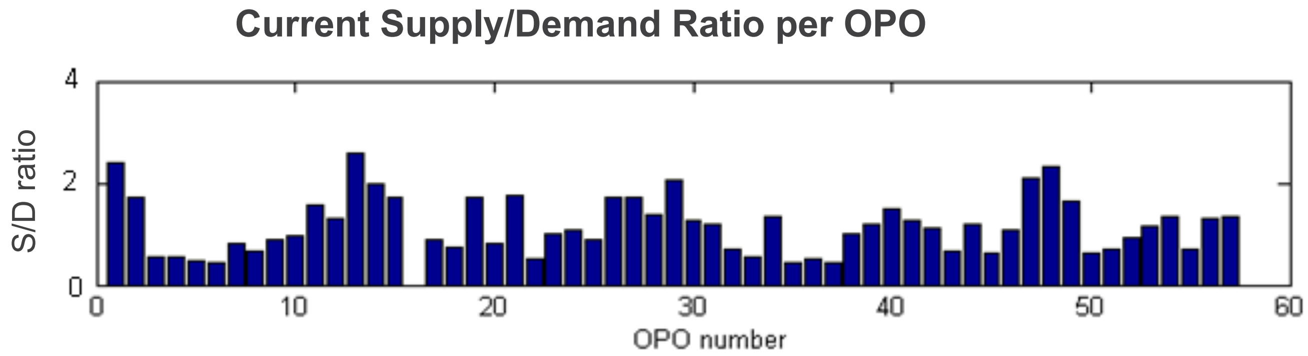


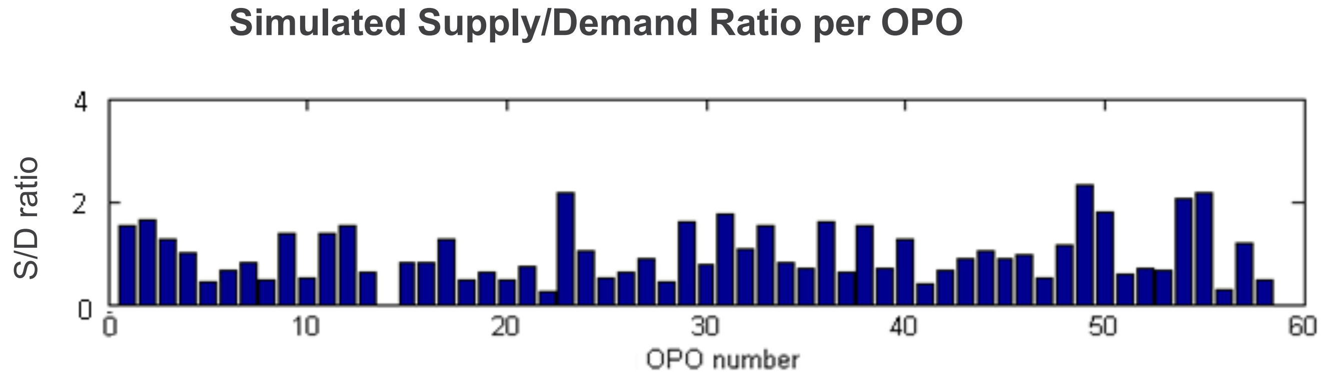
Yellow boundaries are the output of the Mixed Integer programming (MIP) algorithm and the color shades represent the current boundary

Discrete Event Simulation Model



Simulation Result 1





- Reduced geographic disparity (measured in terms of mean sq. error of OPO supply-demand ratio) by 15% (reduced variability in the S/D ratio by redrawing the boundaries)

Simulation Result 2

- Reduced the mean waiting time for
  - Current Status 1 patients (those that need a liver within 7 days to survive): reduced by 39%
- MELD <15 had their mean waiting time increased by 20%
  - However, as their liver worsened they would be moved to a higher MELD bracket where they would see a reduction in the overall mean waiting time.

Conclusions from Solution 1

- Findings (some improvements)
  - The alternative boundary system moved toward an evenly distributed S/D ratio among OPOs
  - Observed a reduction in mean waiting time for severe patients
  - Broader organ sharing was not achieved
- Extensions – Hybrid Liver-Candidate Transportation System

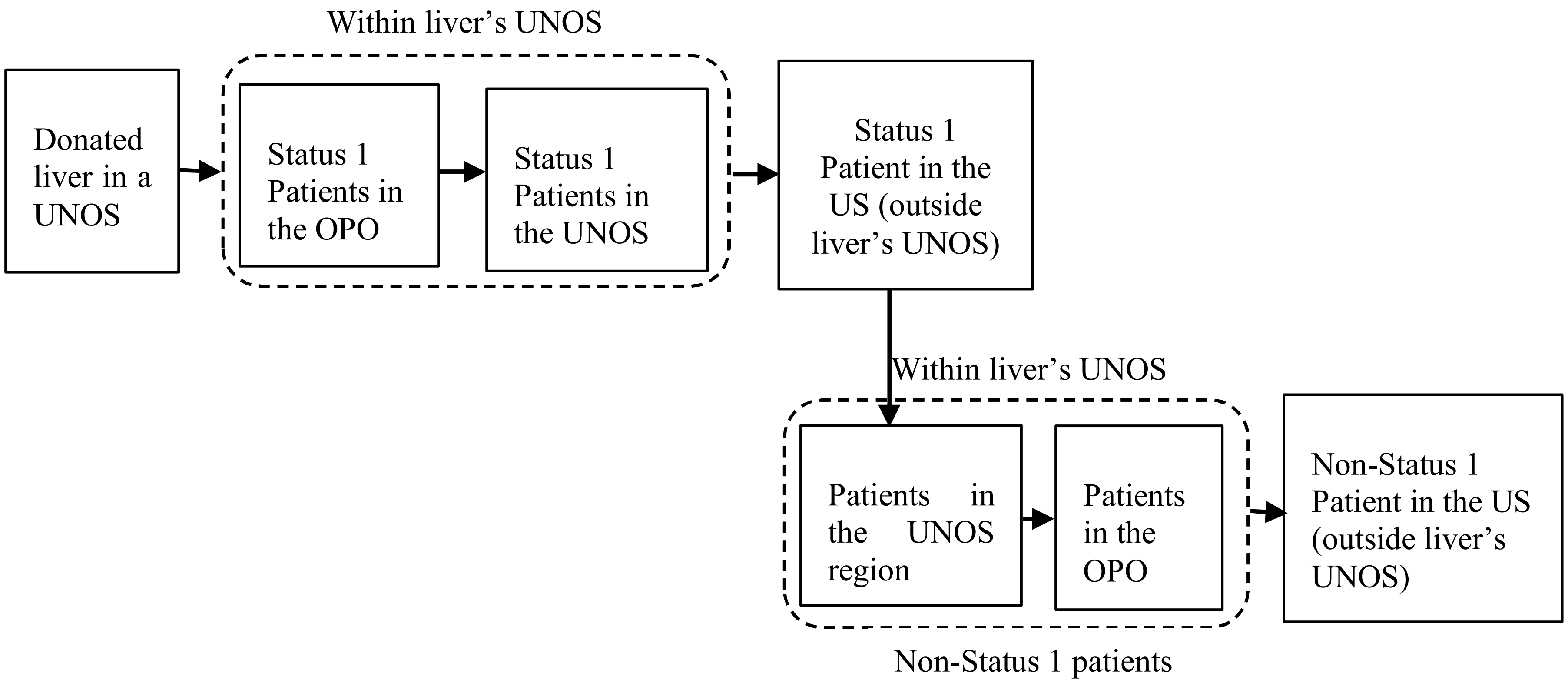
An Application of Modeling and Simulation (M&S) to System Engineering

Solution 2

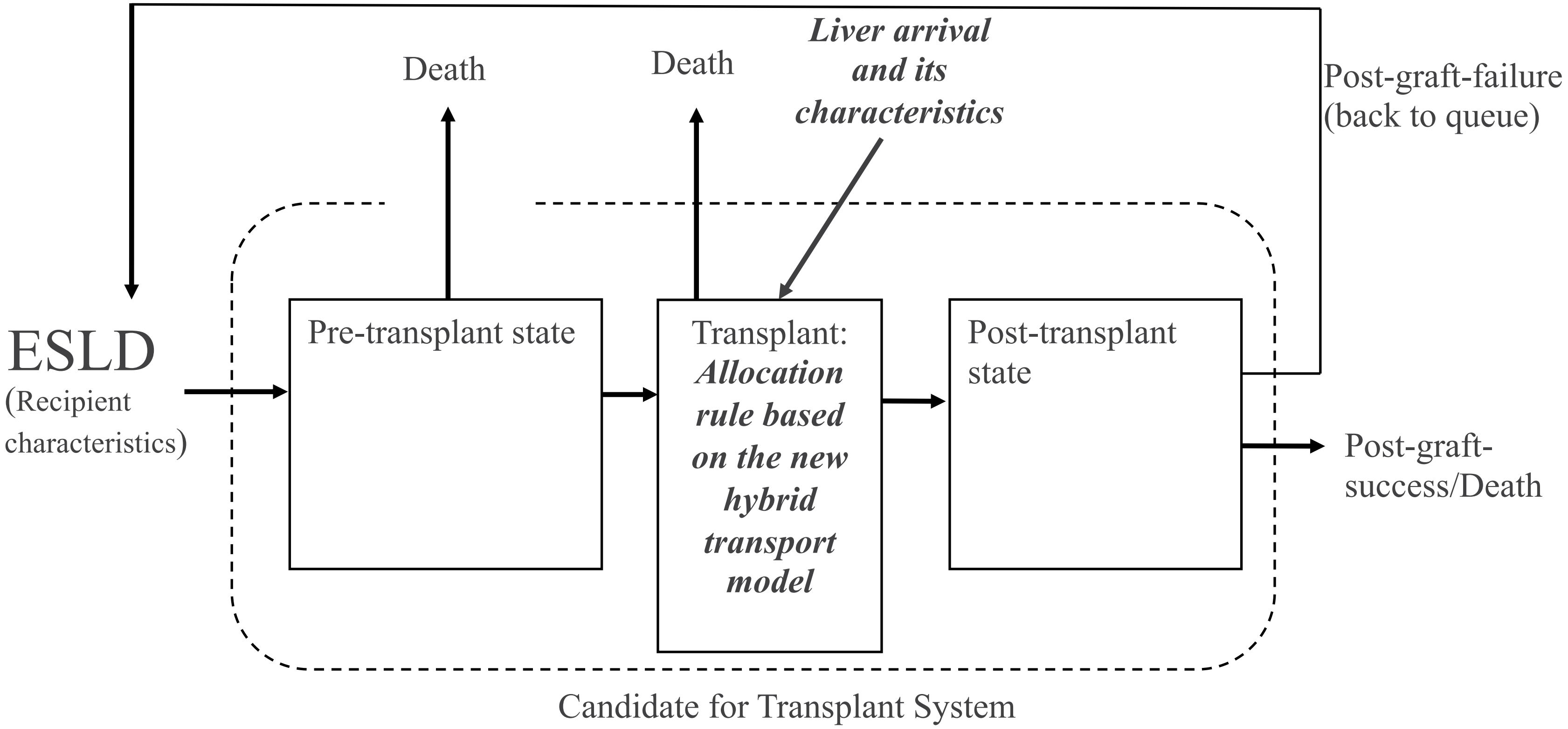
Hybrid Liver-Candidate Transportation System

- Reduce the dependency on boundary based allocation
  - Keep boundaries only for admin purposes but not for decision making in liver allocation
  - Can non-status 1 candidates move?
    - Gives the transplant center in the DSA the opportunity to serve
- Improved Transportation modes for livers to minimize cold ischemia time and increase reachability
  - For status 1 who cannot move to other transplant centers (already hospitalized)

Hybrid Liver-Candidate Transportation System



Discrete Event Simulation Model



Data for Modeling and Simulation

- The actual data is obtained from the UNOS database
  - consists of waiting list candidates as of January 1st 2010, and the new candidate arrivals and liver arrivals of 2010.
- The actual data is used to create probability distributions on each attribute of the candidate and donor.
  - When a candidate or donor is created as per the arrival time distributions, their attribute values are also generated using the attribute distributions for each individual attribute.
  - It should be noted that each candidate simulated from the distribution has the following characteristics (attributes): Identity number, TX zip code where registered, blood type, MELD score, status 1 status, age, date of registration, race, and two 0-1 indicator variables that indicate alive (1)/deceased (0) and received liver (1)/waiting for liver (0).
  - The donor characteristics (attributes) were as follows: Identity number, donor hospital zip code, blood type, race, age, and a 0-1 indicator variable to indicate whether their livers were transplanted (1) or rejected/wasted (0).
- Results presented are averages overs 50 simulation runs

Table 1: Average Number of Candidates/Livers Transported

Performance Metric	Baseline model (current)	Hybrid liver-candidate transport model
Average number of livers that were transplanted in an OPO outside the donor OPO (all categories) by transporting livers	627 (12%)	-
Average number of livers that were transplanted to Status 1 among all Status 1 candidates by transporting livers outside the donor OPO in the same or different UNOS	351 (89%)	-
Average number of candidates (all categories) that received livers within their OPO. Note: Very few OPOs don't have any TX, instead they use the nearest TX.	5076 (100%)	4544 (90%)
Average number of candidates (all categories except status 1) transported outside their OPO but within the same UNOS	-	210 (4%)
Average number of candidates (all categories except status 1) transported outside the OPO to a different UNOS	-	322 (6%)
Average number of livers for Status 1 candidates among all Status 1 candidates that were transported outside their OPO – in the same or different UNOS	-	361 (92%)

Broader Organ Sharing

Table 2: Distance Travelled in kms by the Liver or Candidate Outside their Current OPO for Transplant

Performance Metric	Baseline Model All Livers (Donor Hospital to final TX)	Baseline Model Livers for Status 1 (Donor Hospital to final TX)	Hybrid Model All Candidates except status 1 (Registered TX to final TX)	Hybrid Model All Status 1 (Registered TX To liver OPO)	Hybrid Model Status 1 (Registered TX in the liver's UNOS To liver OPO)	Hybrid Model Status 1 (Registered TX Outside liver's UNOS To liver OPO)
Mean	44.56	54.45	26.38	34.49	34.1	35.2
Std. Dev	60.07	67.92	38.48	41.54	39.56	42.5
Median	33.94	42.93	11.05	18.3	17.85	19.5
Max	448.96	448.96	383.90	169.63	154.52	169.63
Min	0.58	0.58	0.33	0.33	0.33	15.5
Count	627	351	532	361	241	120

Distance travelled is higher in baseline as compared to the hybrid approach

Table 3: Waiting Time Statistics in Days

Performance Metric	Baseline model (current scenario)	Hybrid liver-candidate transport model (new scenario)
Status 1		
Median	1	1
Mean	2.3	1
Standard Deviation	4.8	0
MELD<15		
Median	1139	480
Mean	1211	743
Standard Deviation	944	729
MELD≥15		
Median	300	397
Mean	508	651
Standard Deviation	561	627

Table 4: Geographical Disparity among OPOs - No significant change

Geographical disparity Supply/Demand ratio among 58 OPOs	Baseline- liver transport	Hybrid liver-candidate transport	$H_o: m_1=m_2$ $H_1: m_1 \neq m_2$
Median	0.449	0.437	p= 0.51
Mean	0.464	0.462	
Standard Deviation	0.231	0.201	
Maximum	1.013	0.985	
Minimum	0.000	0.058	
Mean Squared Error	0.053	0.052	

Summary

Category	Baseline	Solution 1	Solution 2
	Current boundary	Redraw boundary	Hybrid transport
	Liver is transported	Liver is transported	Liver is transported for status 1 and candidate for non-status 1
Waiting time status 1	Up to 5-7 days	39% reduction	57% reduction
Waiting time non-status 1		MELD < 15 increased by 20%	MELD >15 increased by 23%
Broader Organ sharing	X	X	√ (mostly status 1)
Geographical disparity in terms of Supply/Demand ratio among the 58 OPOs	High	15% reduction	Same as Baseline

Ways Forward

- A combination of solution 1 for improved geographical disparity and solution 2 for broader organ sharing that benefits the neediest among all is one way to move forward
  - Solution is at least better than current system
  - Keep boundaries for admin reasons but not for decision making in liver allocation
- Enlist more people as Organ Donors (increase supply)
- Faster transportation- both liver and candidate

Papers

- Ganesan, R., Hung W-C., Peng T.-Y., Chen C.-H., Koizumi, N.,A Hybrid Liver-Candidate Transportation Approach to Improve Accessibility and Extend Organ Life in Liver Transplantation, *Proceedings of the 28th Annual INCOSE International Symposium,* Washington DC, July 2018, to appear.

- Koizumi, N., Gentili, M., Ganesan, R. Chen., C.-H., Melancon, K., and Waters, N., Mathematical Optimization and Simulation Analyses for Optimal Liver Allocation Boundaries, in *Healthcare Analytics: From Data to Knowledge to Healthcare Improvement,* Yang Hui and Eva K. Lee (eds.), John Wiley & Sons, Inc., pp.451-475, 2016.

- Koizumi, N., Ganesan, R. Gentili, M., Chen., C.-H., Melancon, K., and Waters, N., Redesigning Organ Allocation Boundaries for Liver Transplantation in the United States, *Proceedings of the International Conference on Health Care Systems Engineering, Springer Proceedings in Mathematics & Statistics*, 2014, Vol. 61, pp 15-27, 2014.

Thank You

Q & A

Rajesh Ganesan (George Mason University); Wen-Chi Hung (University of California, Davis); Tzu-Yi Peng (Trendforce Corp.); Chun-Hung Chen and Naoru Koizumi (George Mason University)

A Hybrid Liver-Candidate Transportation System to Improve Accessibility and Extend Organ Life in Liver Transplantation

Session: 8.3.2 - Healthcare Applications

28th Annual INCOSE international symposium

Washington, DC, USA

July 7 - 12, 2018

www.incose.org/symp2018