Optimization and organs: Computational methods for rationing transplantation

Computational Science Graduate Fellowship
Annual Program Review

Sommer Gentry

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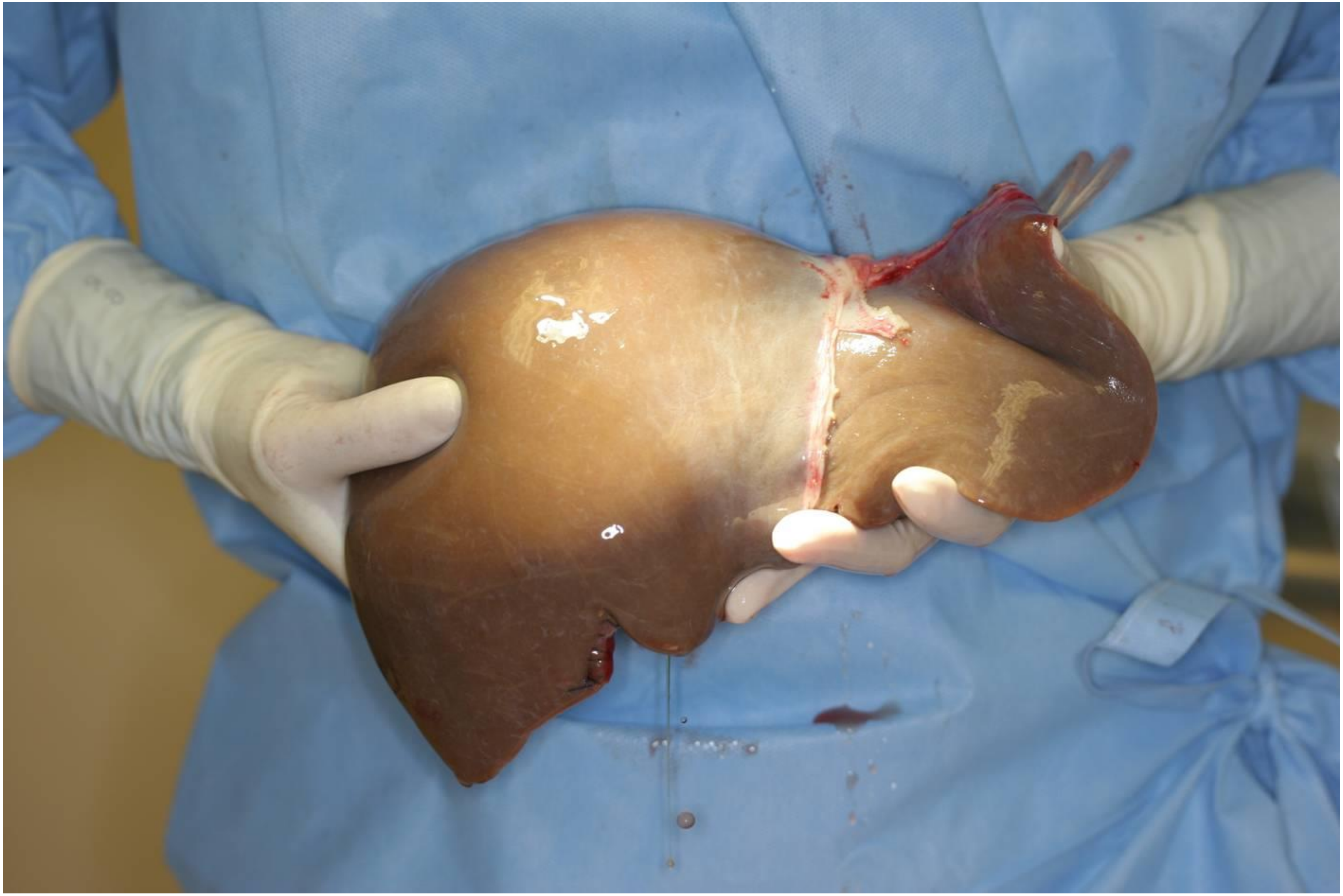
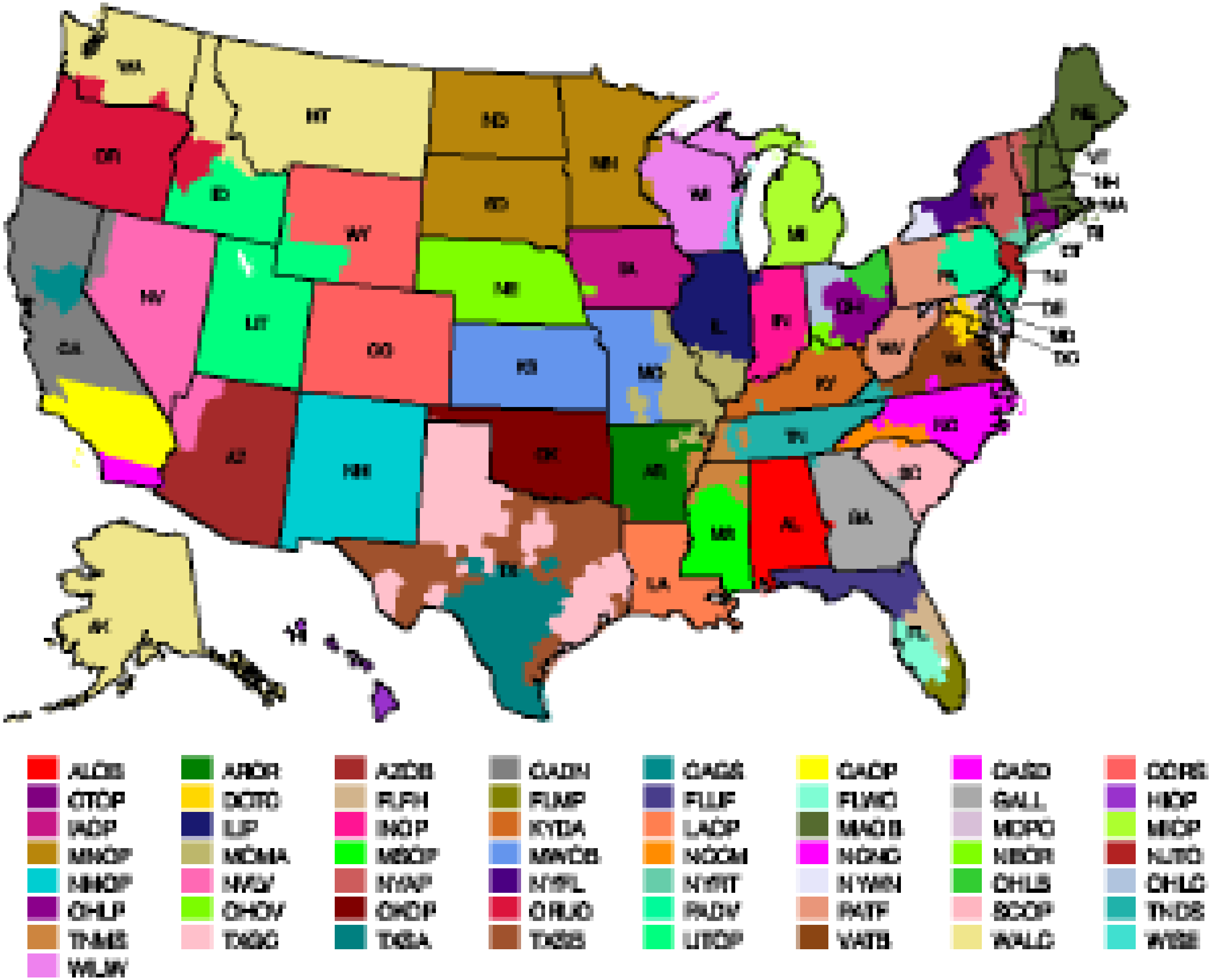
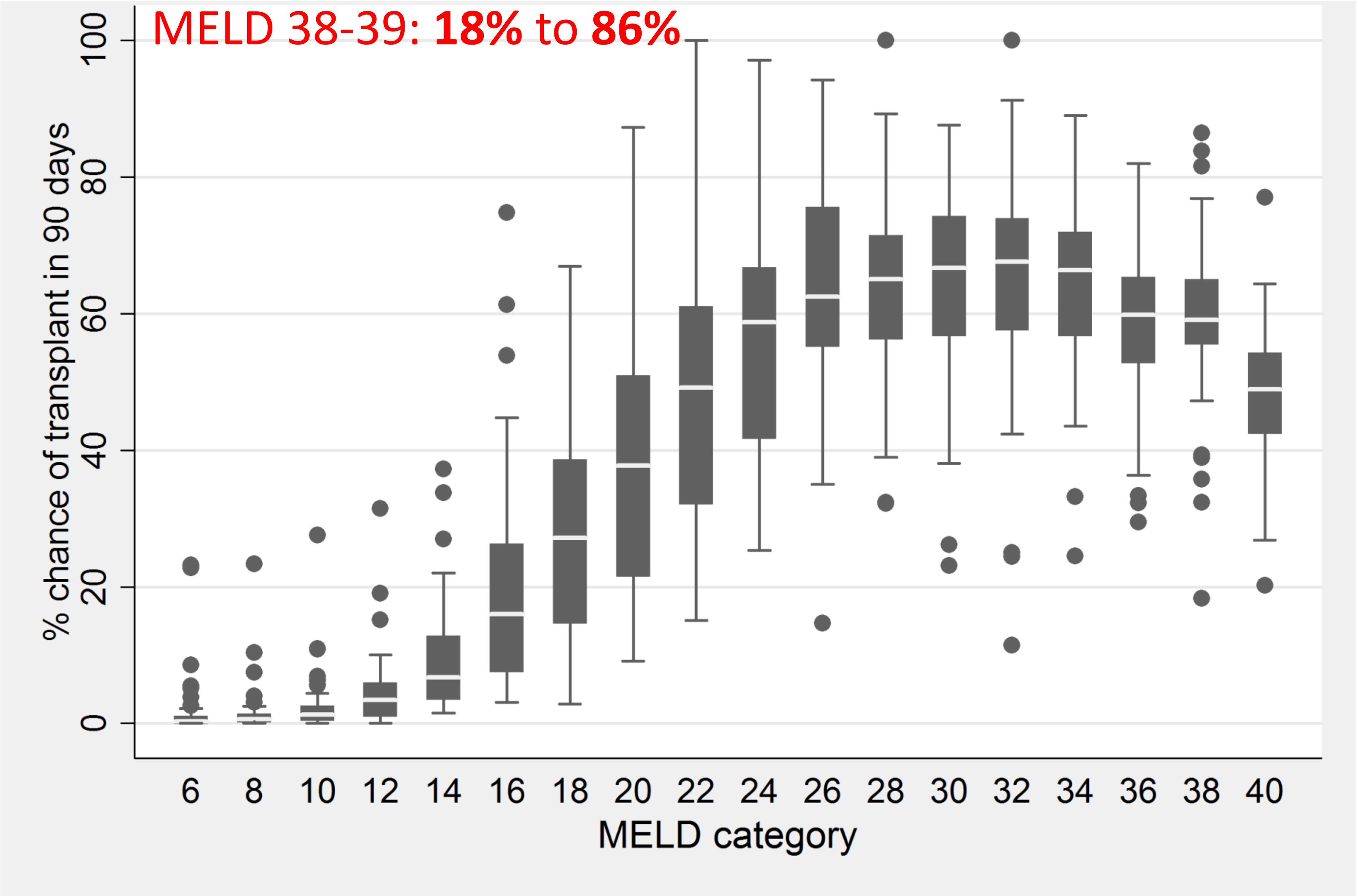


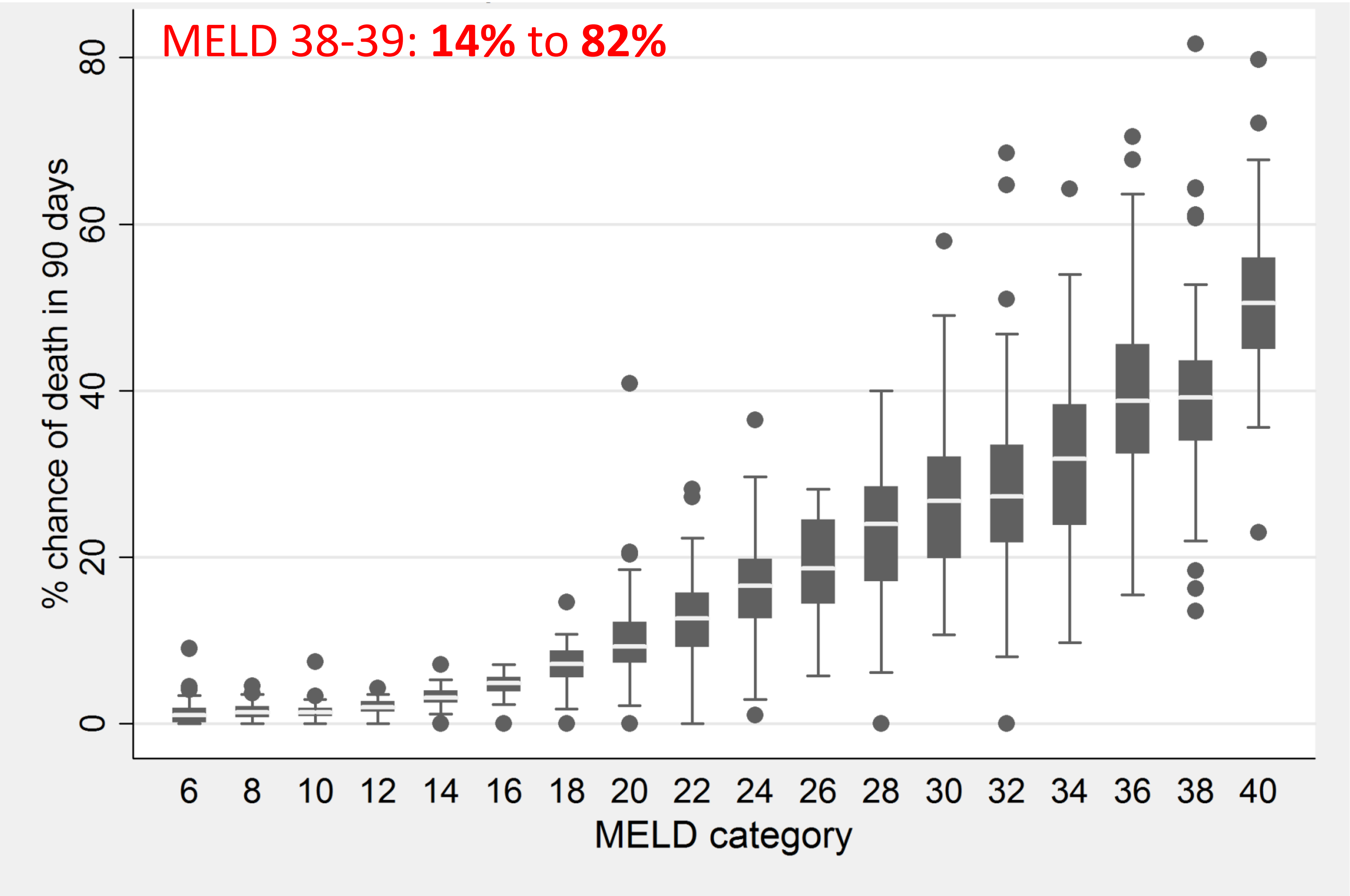
DSAs (donation service areas)



Range of transplant rates, by DSA



Range of waiting list death rate, by DSA



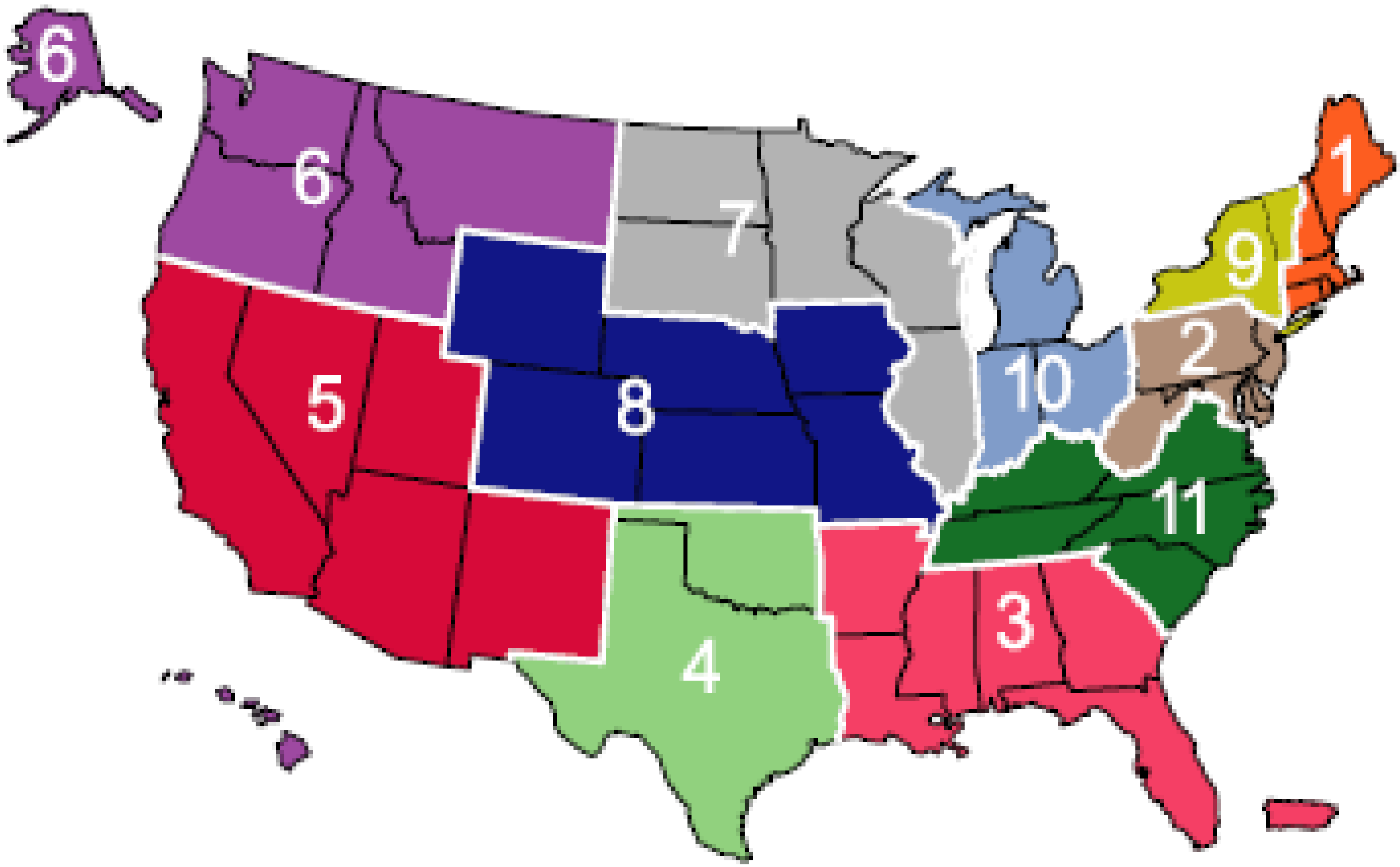
Geographic disparities are significant

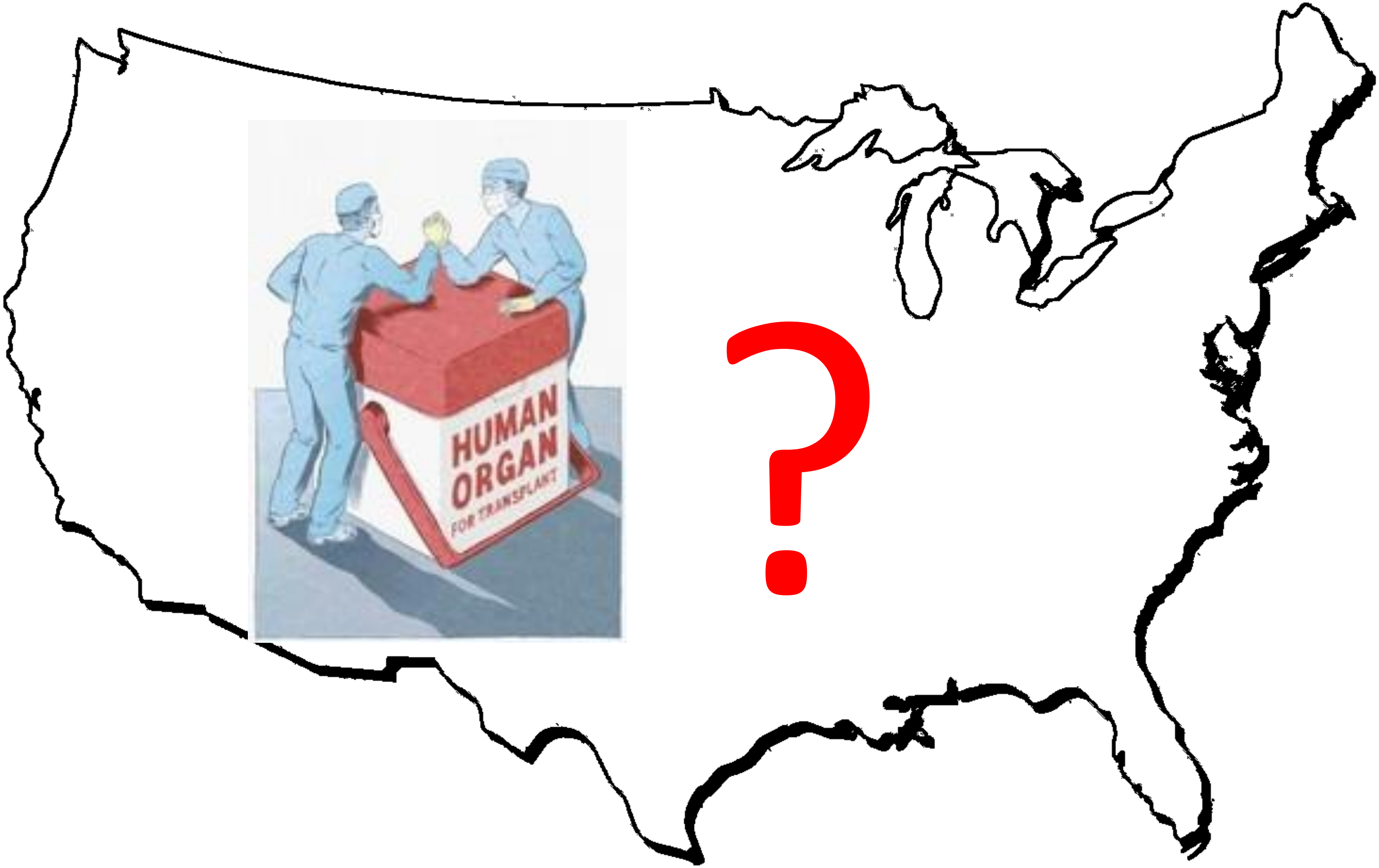
- Median MELD at transplant varies among OPOs by 10 points; 90-day survival for MELD 38 varies 4-fold
- Candidates have 20% lower risk of death and 74% higher chance of transplantation if they transferred from their initial listing OPO to a different one (Dzebisashvili et al. 2013)
  - Transferring to a different OPO is highly correlated with socioeconomic status
- Geographic disparities explain disparities between liver transplant rates for Caucasians and Hispanics, because these populations live in different places (Volk et al. 2009)

Department of Health and Human Services Final Rule (1998) 42 CFR Part 121.8(b)

"Neither place of residence nor place of listing shall be a major determinant of access to a transplant."

DSAs are partitioned into regions




HUMAN
ORGAN
FOR TRANSPLANT
?

The New York Times

December 29, 1999

Iowa Turf War Over Transplants Mirrors Feuds Across the Nation

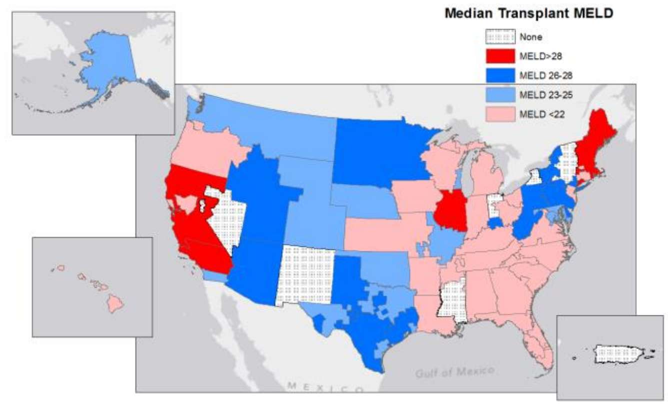
"But the debate is not just about saving lives... the fight, they say, is about which transplant centers -- not which patients -- will get the scarce organs, and the profits and prestige that go with them."

“Broader sharing” not sufficient; disparity is <u>worse</u> using existing regions

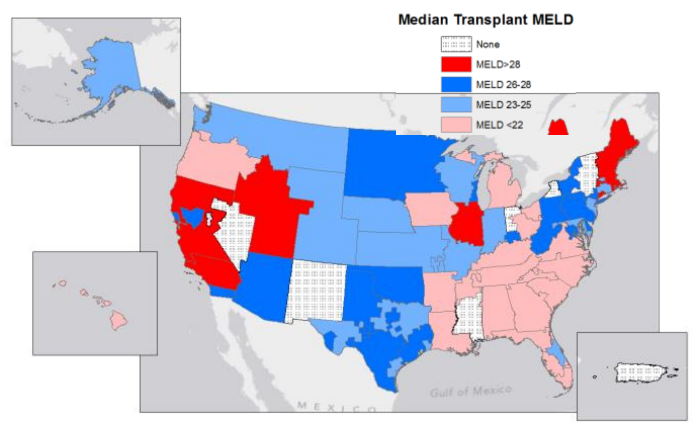
- Fully regional sharing is not predicted to reduce disparity in MELD at transplant!
- Paradoxically, <u>fully regional sharing increases disparity, as measured by variance of transplant MELD, from 7.55 to 10.14</u>

(Gentry et al. AJT 2013)

Disparity in median transplant MELD



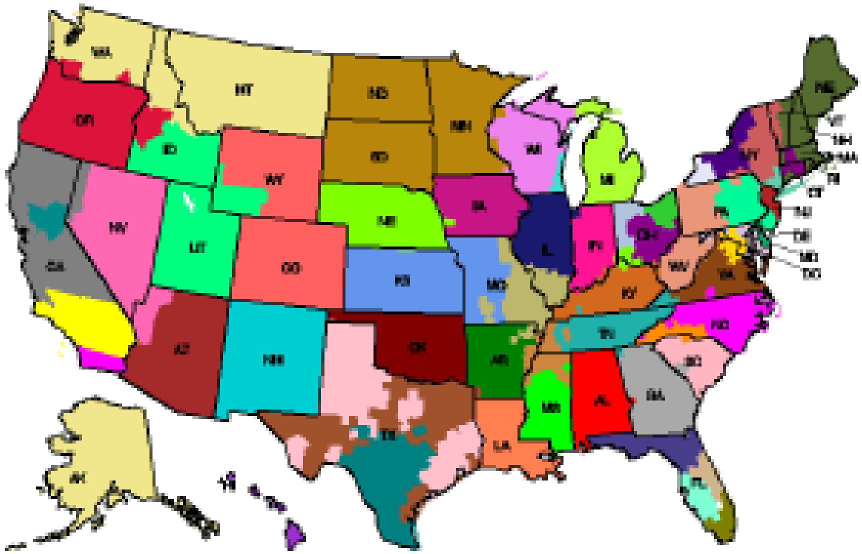
Disparity with fully regional sharing



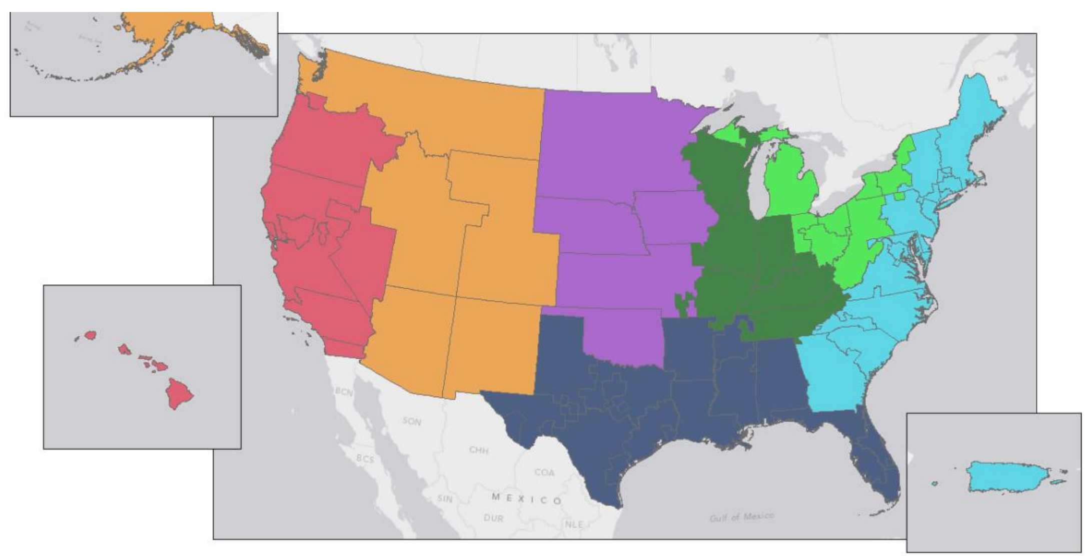
Optimal Redistricting

- Redistricting uses integer programming to design geographic boundaries that partition an area into smaller areas
  - There is a substantial body of OR literature on redistricting for voting districts and school districts, dating from 1950s to the present
- We partition the DSAs into new districts
  - design first (OPL/CPLEX), then analyze (LSAM)

Partition DSAs into districts



Under redistricting, livers would be allocated to the sickest candidate anywhere in the district



Redistricting Objective

- Minimize *misdirected livers*
  - A misdirected liver is one that goes to a different district than it would have if organs went to highest MELD patient anywhere in the country.
- Subject to constraints
  (least geographic disparity achievable through the allocation system is under national share)

Liver Committee's design constraints

- The number of districts should be at least 4 and no more than 8.
- Minimum number of transplant centers per district is 6.
- The maximum allowable median travel time between DSAs placed in the same district should be 3 hours.

w_{ik} = 1 if DSA *i* is in the district with center at DSA *k*, and 0 if not

Y_k = 1 if DSA *k* is selected as the center of a district, and 0 if not

c_k = active liver transplant centers in DSA *k*

d_k = donors available in DSA *k*

p_k = number of donors that should go to DSA *k* under proportional allocation

δ_{ij} = volume-weighted distance from DSA *i* to *j*

τ_{ij} = volume-weighted transport time between DSAs *i* and *j*

$$\text{Minimize:} \quad \sum_{k \in \mathcal{K}} \left| \sum_{i \in \mathcal{I}} p_i W_{ik} - \sum_{i \in \mathcal{I}} d_i W_{ik} \right|$$

Objective: minimize geographic disparity in liver availability by minimizing the sum of misdirected livers

$$\text{subject to:} \sum_{k \in \mathcal{K}} W_{ik} = 1 \qquad \text{for all } i \in \mathcal{I}$$

$$W_{ik} - Y_k \leq 0 \quad \text{for all } i \in \mathcal{I} \text{ and } k \in \mathcal{K}$$

Each DSA is assigned to one district

If a DSA k is assigned as the center of the district containing DSA i,
Y_k should be 1

$$\sum_{k \in \mathcal{K}} Y_k = N$$

$$\sum_{i \in \mathcal{I}} h_i W_{ik} \geq \bar{h} Y_k \quad \text{for all } k \in \mathcal{K}$$

Number of districts is N

Require at least $\bar{h}$
transplant centers in each district

$$W_{ik}\tau_{ik} \leq \bar{\tau} \quad \text{for all } i \in \mathcal{I} \text{ and } k \in \mathcal{K}$$

Maximum transport time from each district to its district center is $\bar{\tau}$

$$\sum_{k \in \mathcal{K}} \alpha_{ijk} W_{ik} \leq 1 - Y_j \quad \text{for all } i \in \mathcal{I} \text{ and } j \in \mathcal{K}$$

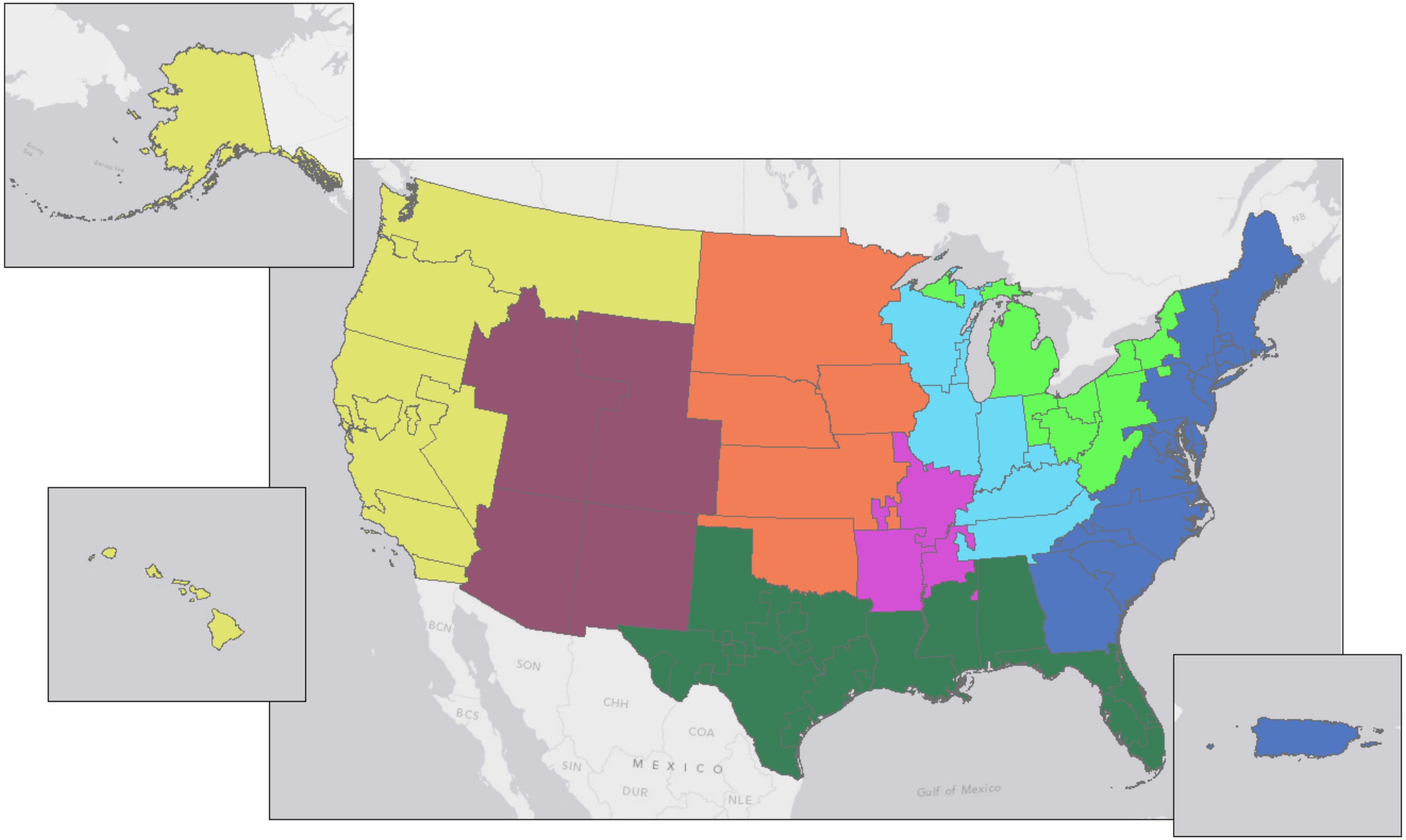
δ_{ij} = volume-weighted distance from DSA *i* to *j*

$\alpha_{ijk} = \{1 \text{ if } \delta_{ik} > \delta_{ij}, 0 \text{ if not}\}$

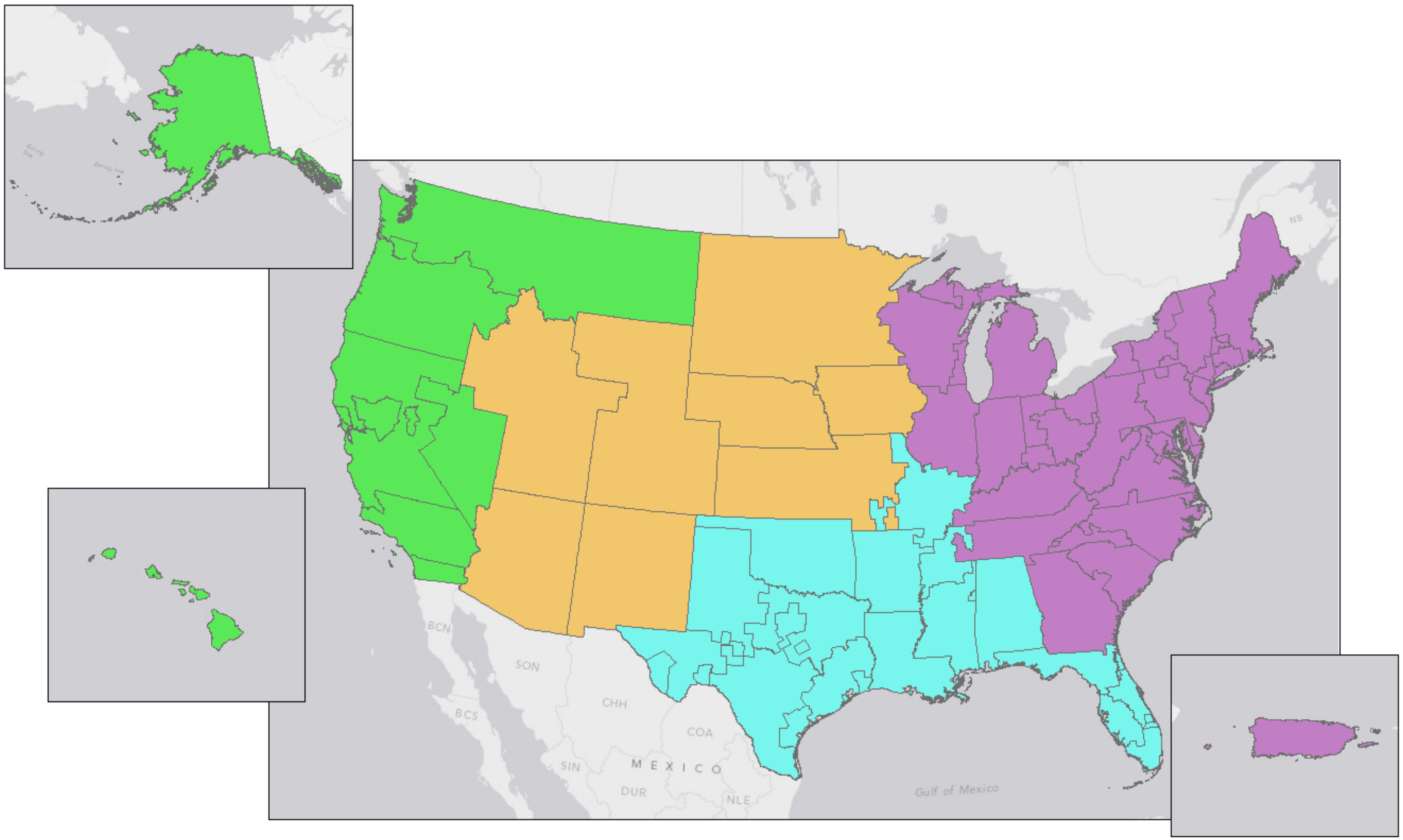
Every DSA is assigned to its nearest district center

(Daskin, Service Science, 2010)

8 districts, 3 hour limit



4 districts, 3 hour limit

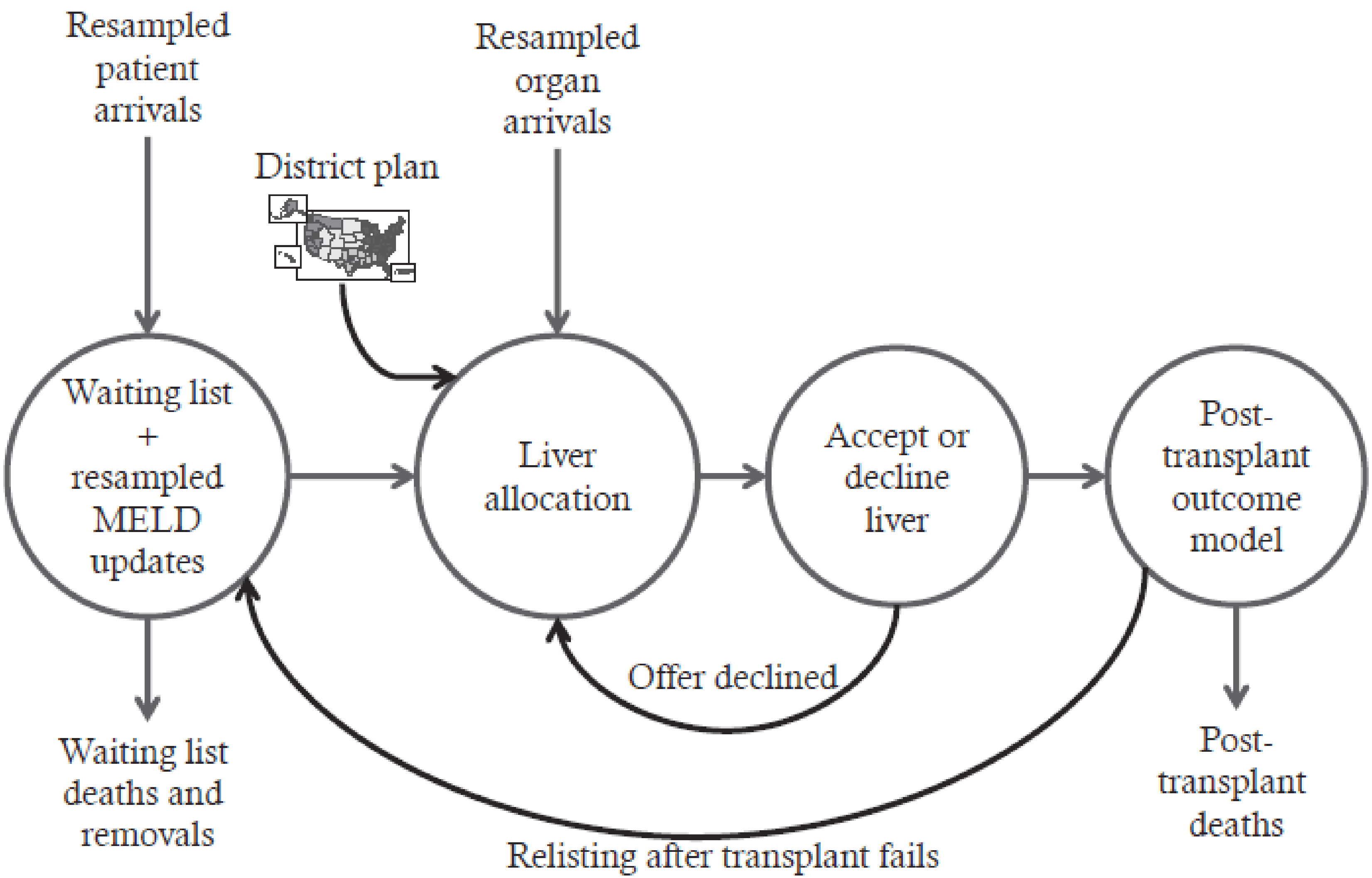


Liver Simulated Allocation Model

- The redistricting integer program is greatly simplified
  - Assume MELDs are fixed
  - Assume no deaths, no one becomes too sick
  - Assume all offers are accepted
- Liver Simulated Allocation Model re-introduces realistic clinical detail
  - Standard deviation of median MELD at transplant among DSAs is a geographic equity metric derived from LSAM data

Liver Simulated Allocation Model

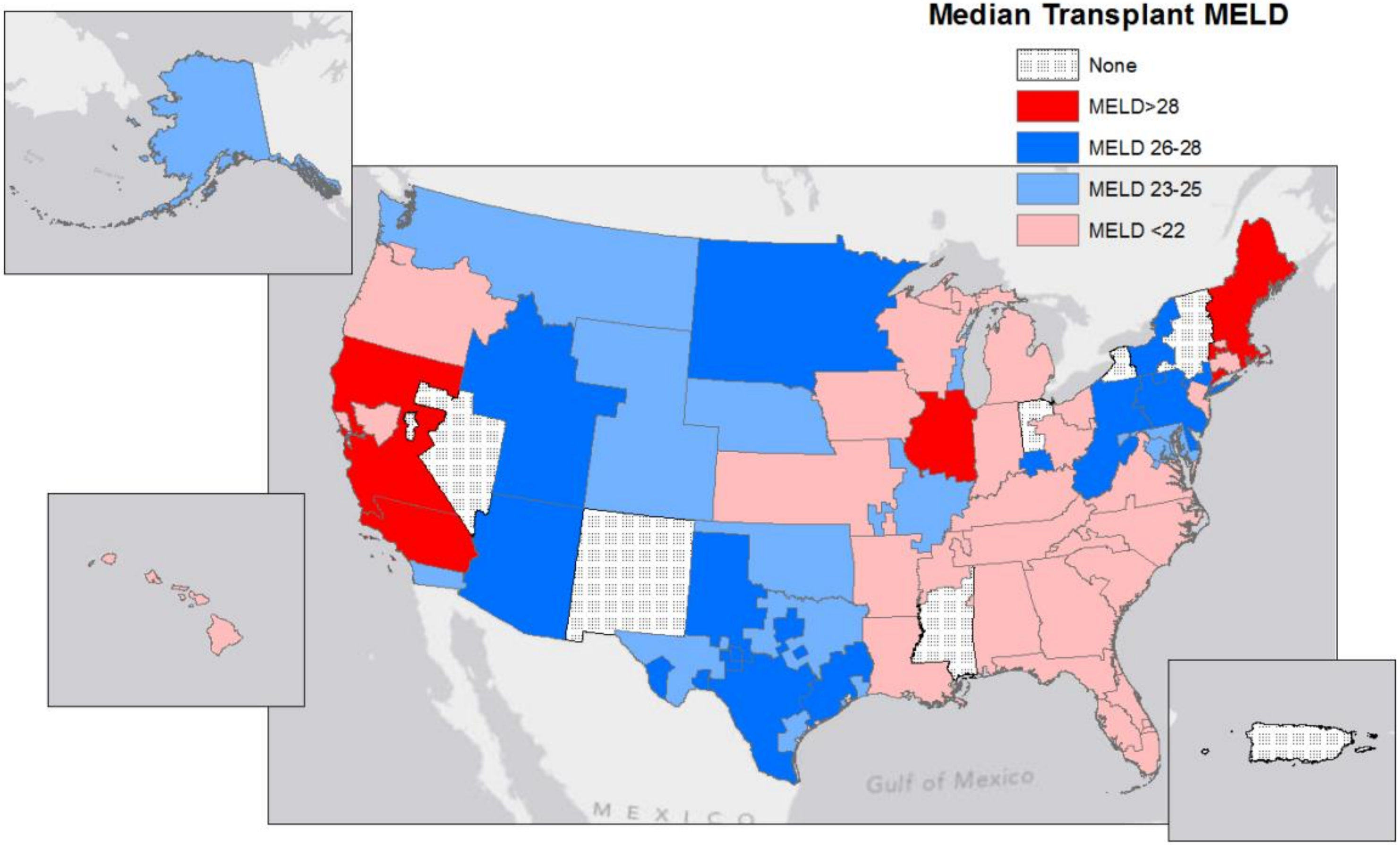
Thompson and Waisanen, 2004



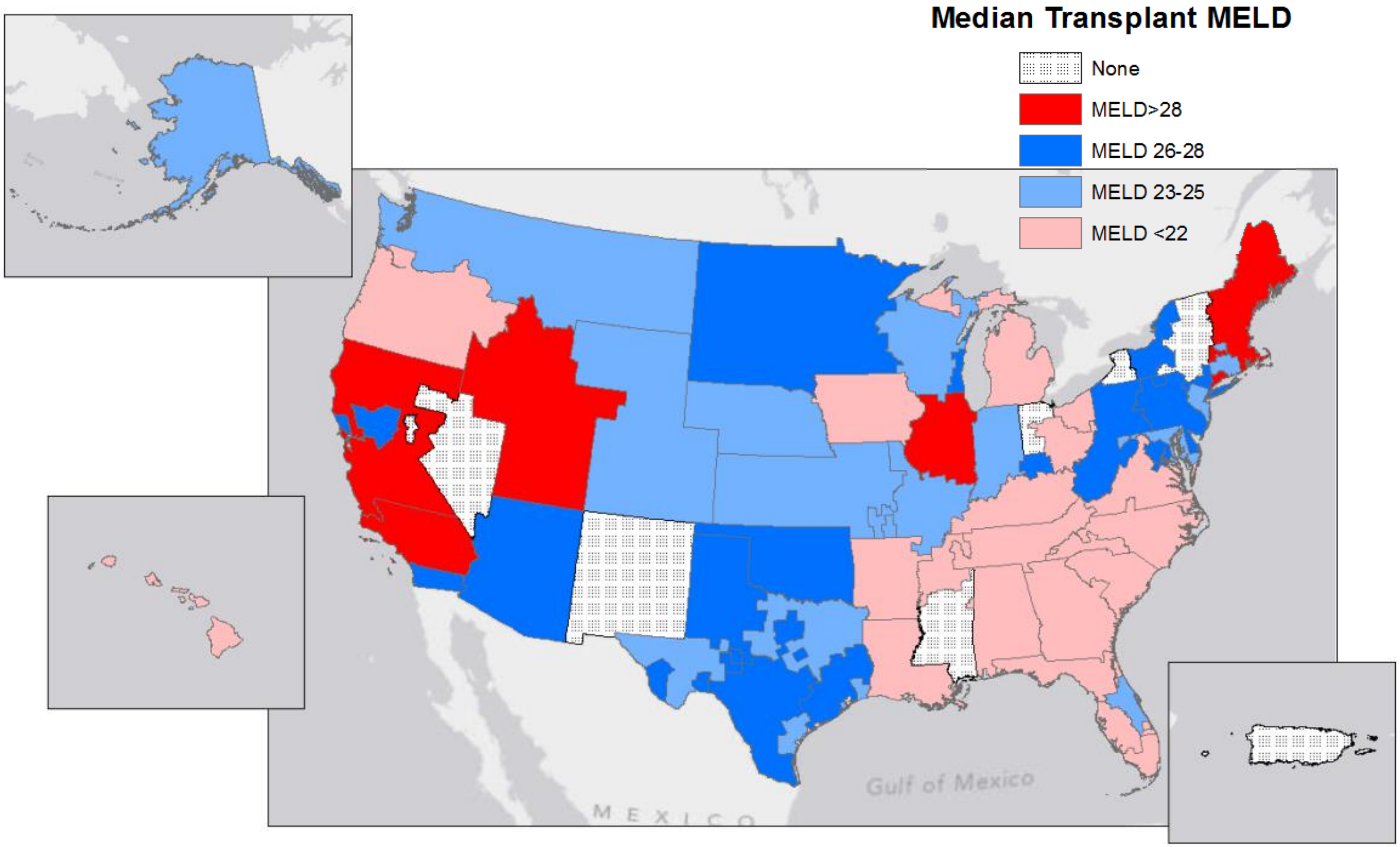
Simulated redistricting impacts

Allocation	Misdirected Livers	Std Dev MELD	Net Waitlist Deaths	Net Deaths
Local	2363	3.01	0	0
Regional	1317	3.26	-165	-122
National	0	1.66	-344	-510
4 Districts	128	1.87	-554	-581
8 Districts	156	2.08	-332	-342

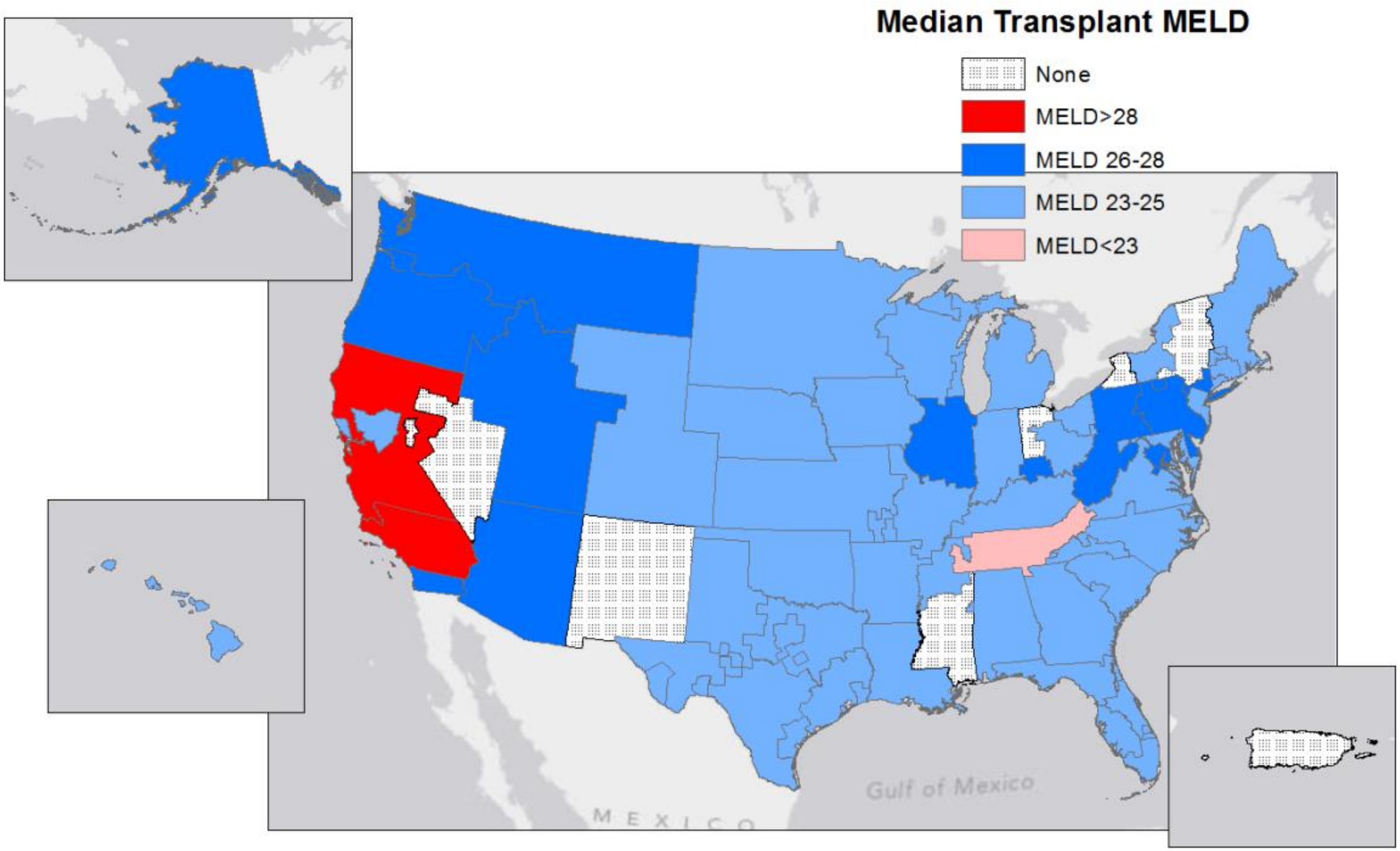
Disparity in transplant MELD, local



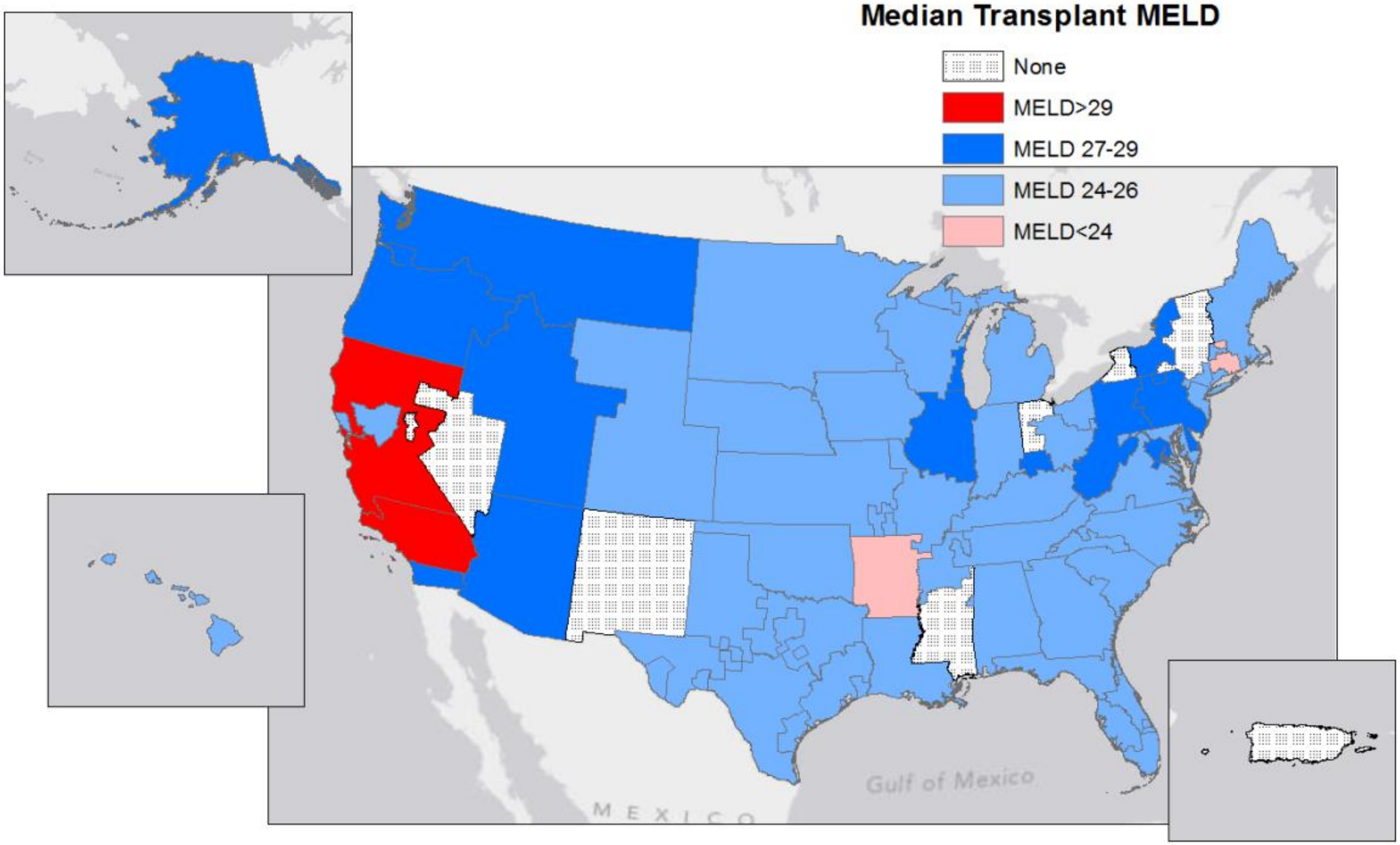
Disparity in transplant MELD, regional



Disparity in transplant MELD, 8 districts



Disparity in transplant MELD, 4 districts



Redistricting and organ transport

Allocation	Median Time	Median Distance	% Flying
Local	1.5 hours	68 miles	44%
Regional	1.7 hours	137 miles	61%
4 Districts	2.1 hours	340 miles	74%
8 Districts	1.8 hours	178 miles	64%

Redistricting is cost-saving

Allocation	Transport Cost	Pre-transplant Cost	Transplant Cost	Total Cost
Local	\$125 mil	\$1629 mil	\$3576 mil	\$5330 mil
Regional	\$165 mil	\$1487 mil	\$3468 mil	\$5120 mil
4 Districts	\$191 mil	\$1358 mil	\$3453 mil	\$5002 mil
8 Districts	\$176 mil	\$1387 mil	\$3462 mil	\$5025 mil

"In short, the unanimous vote taken on April 1st that sent two optimized redistricting plans forward for public comment was ***unprecedented***. I could not have imagined that every single member of the Liver Committee, including members representing transplant centers that are expected to do fewer liver transplants as a result of redistricting, would vote in favor."

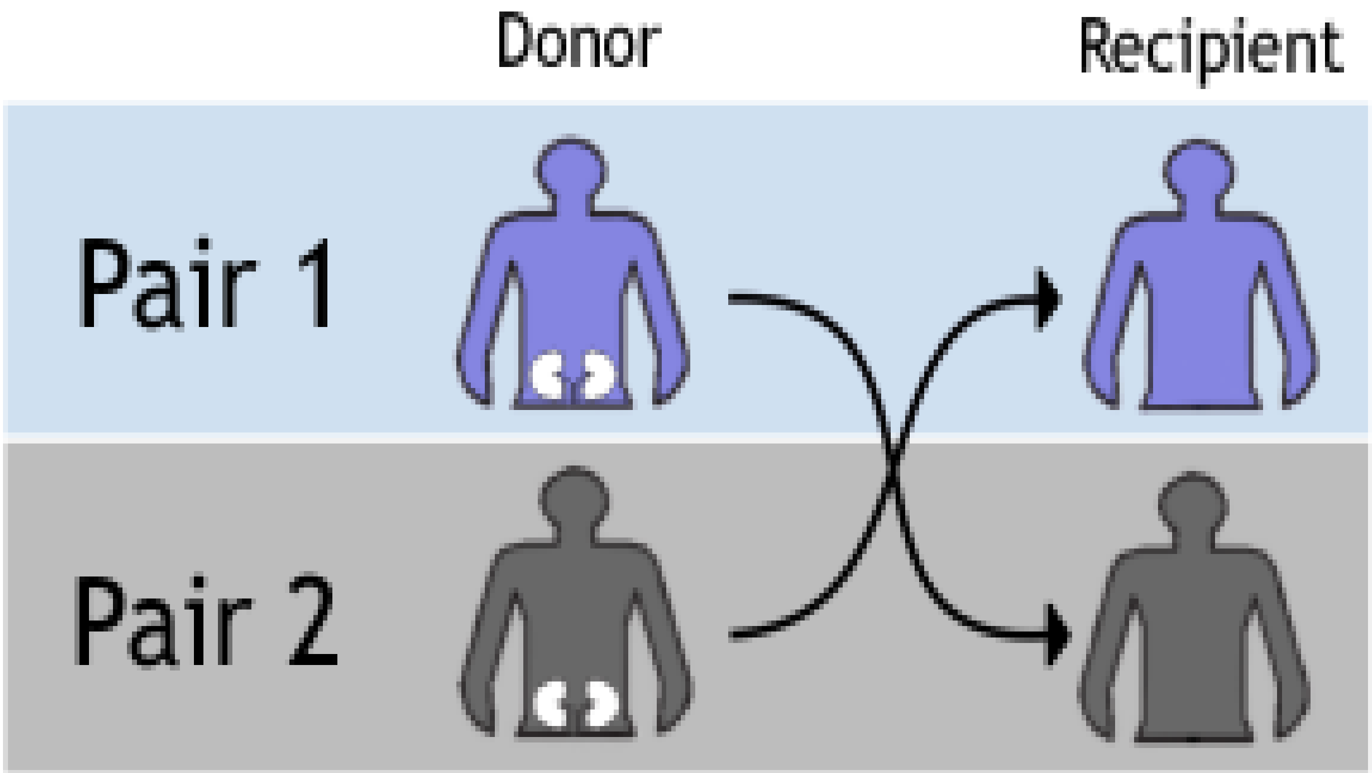
- Dr. David Mulligan, Chair, OPTN Liver and Intestinal Transplantation Committee

September 2014 public forum

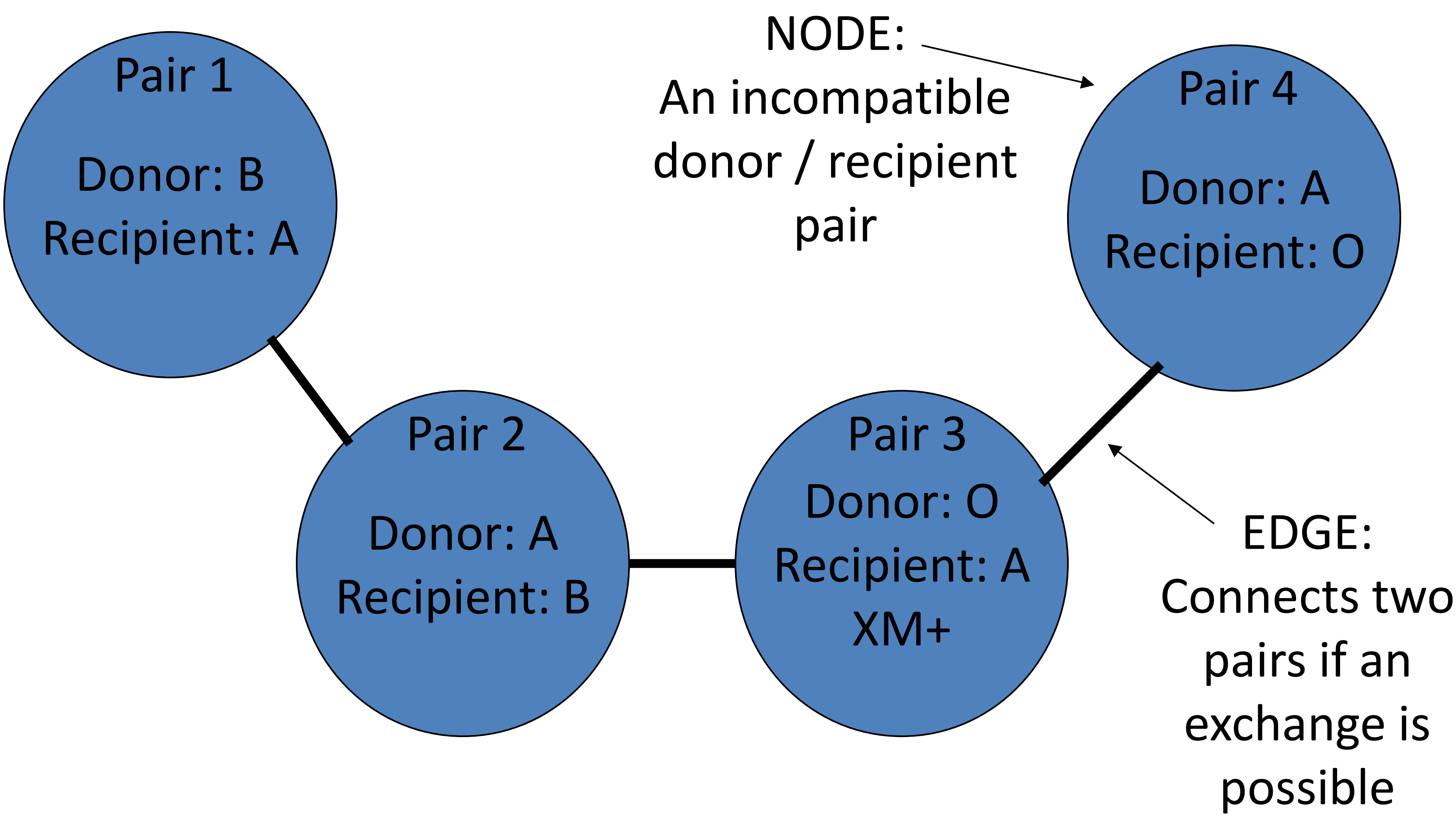
Lessons for implementing computational science solutions in healthcare

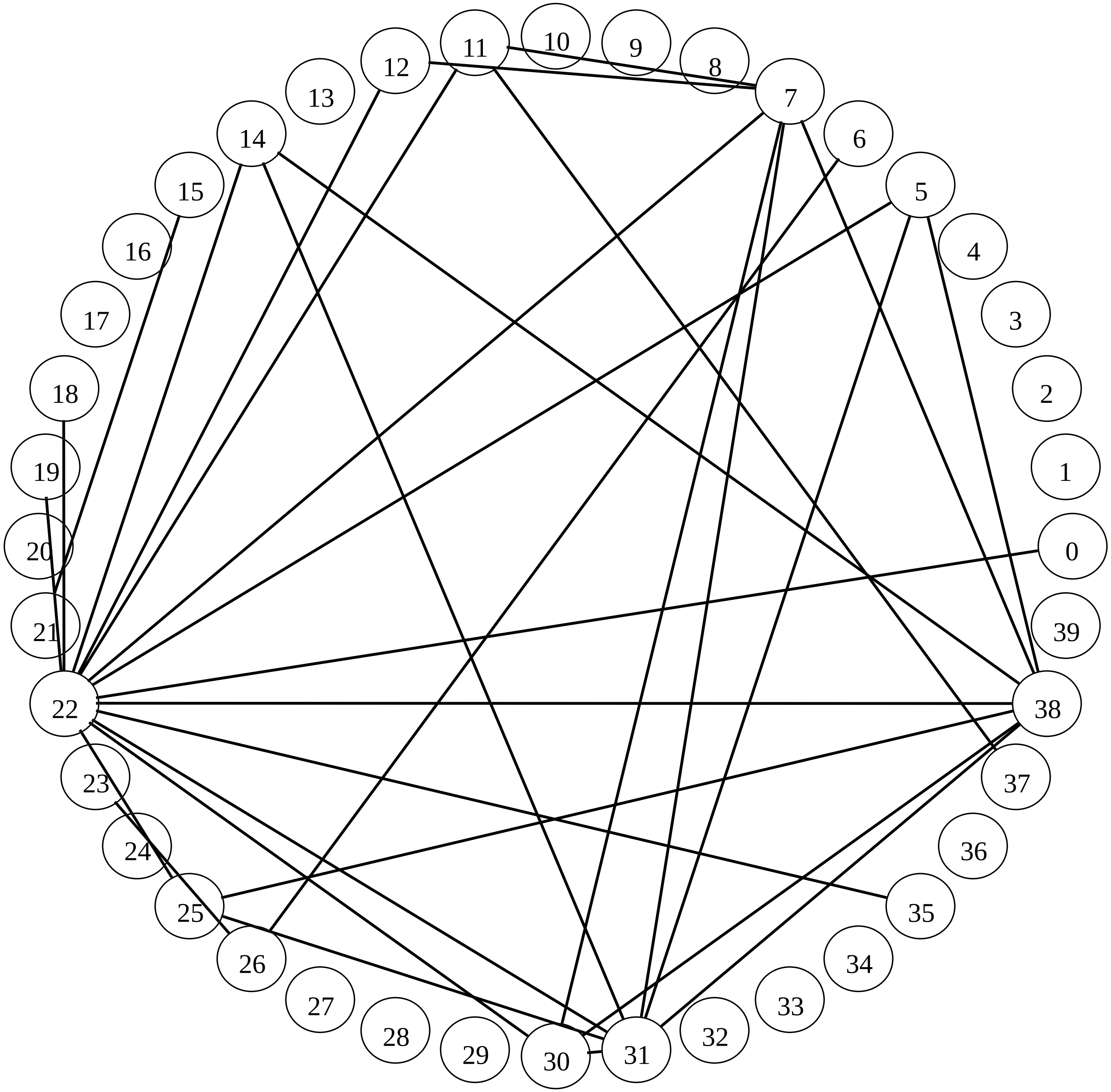
- Build transparent optimization models
- Enable decision-makers to focus on principles and objectives, not on constructing or critiquing ad hoc policies
- Make things as simple as they must be, but then use simulation to make them detailed enough to be plausible to clinicians

Kidney paired donation (KPD) or, kidney exchange



Graph: recipient / donor pairs





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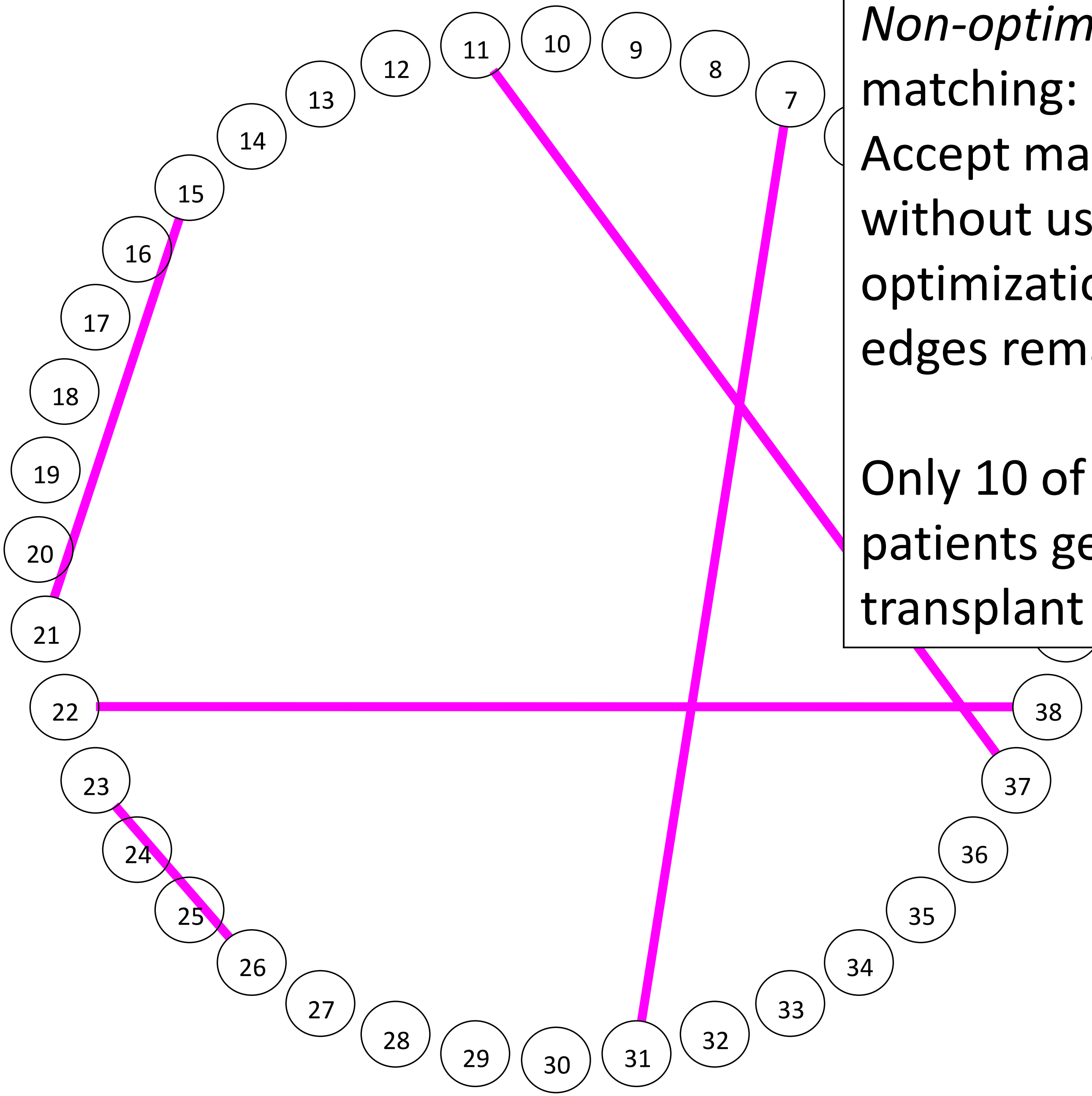
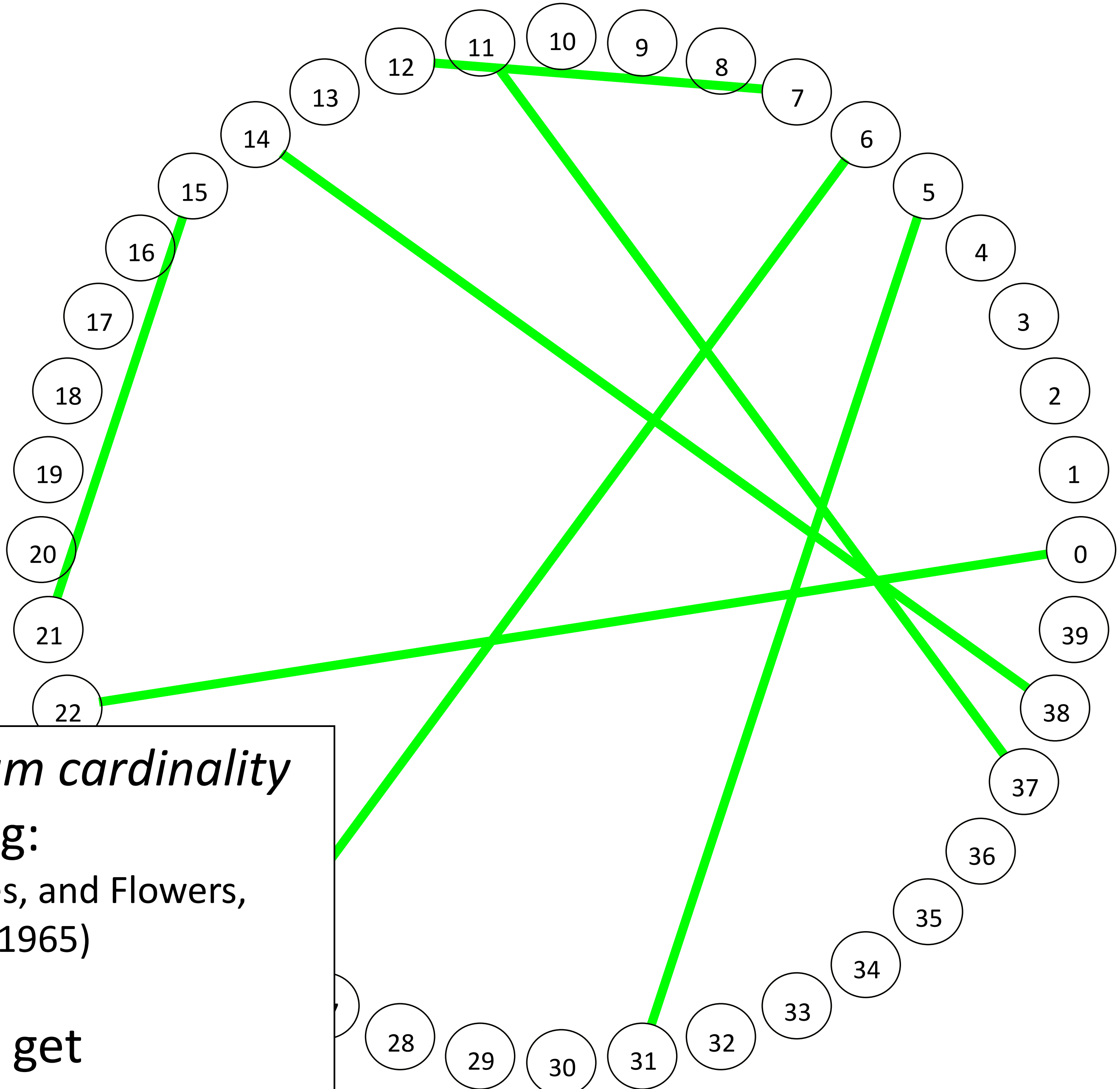


Non-optimal matching:
Accept matches without using optimization until no edges remain.

Only 10 of 40 patients get a transplant

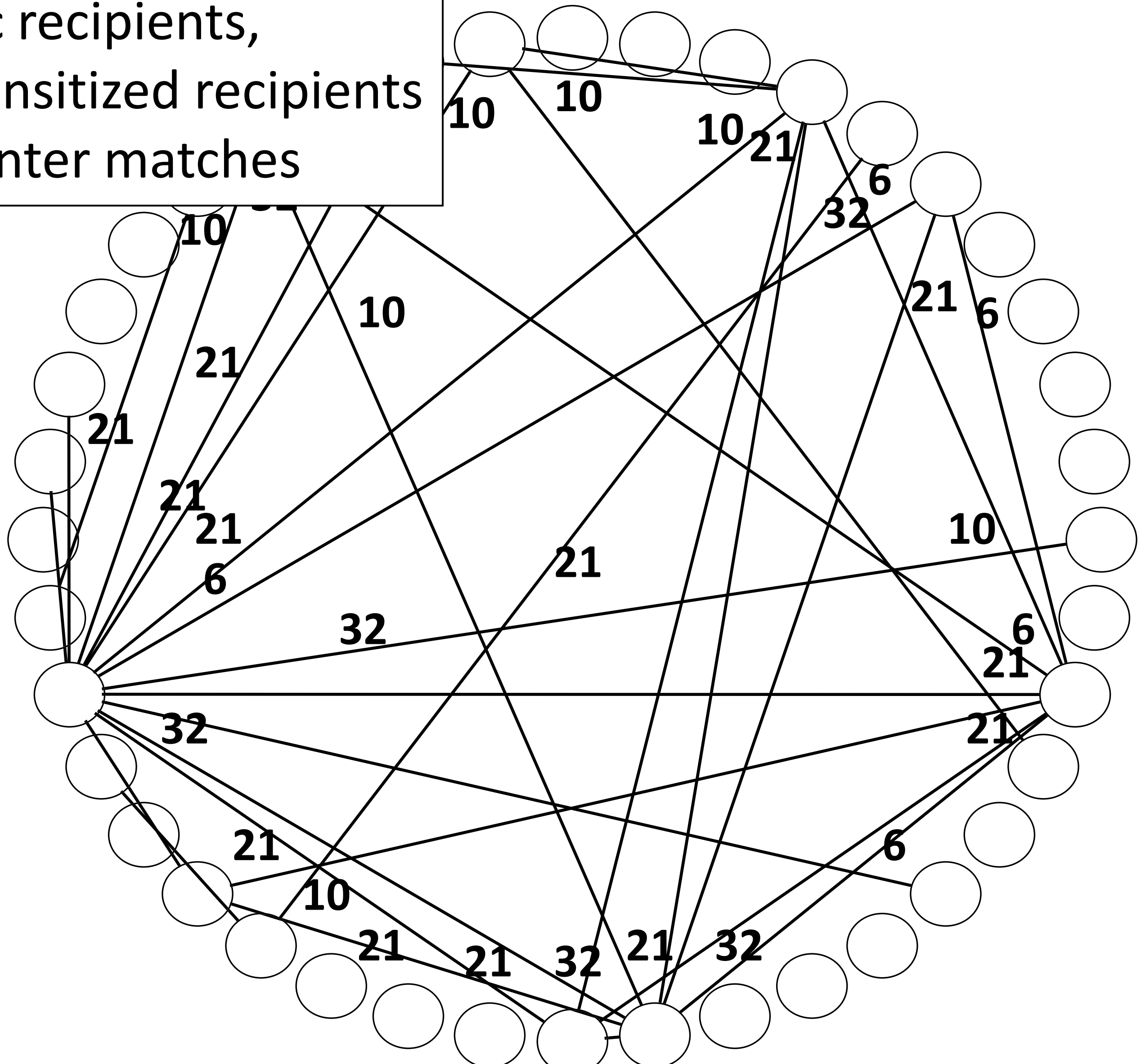


Maximum cardinality matching:

Paths, Trees, and Flowers, Edmonds (1965)

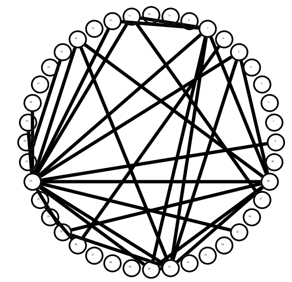
14 of 40 get transplants

Prioritization: 0-mismatch, pediatric recipients, highly sensitized recipients same-center matches

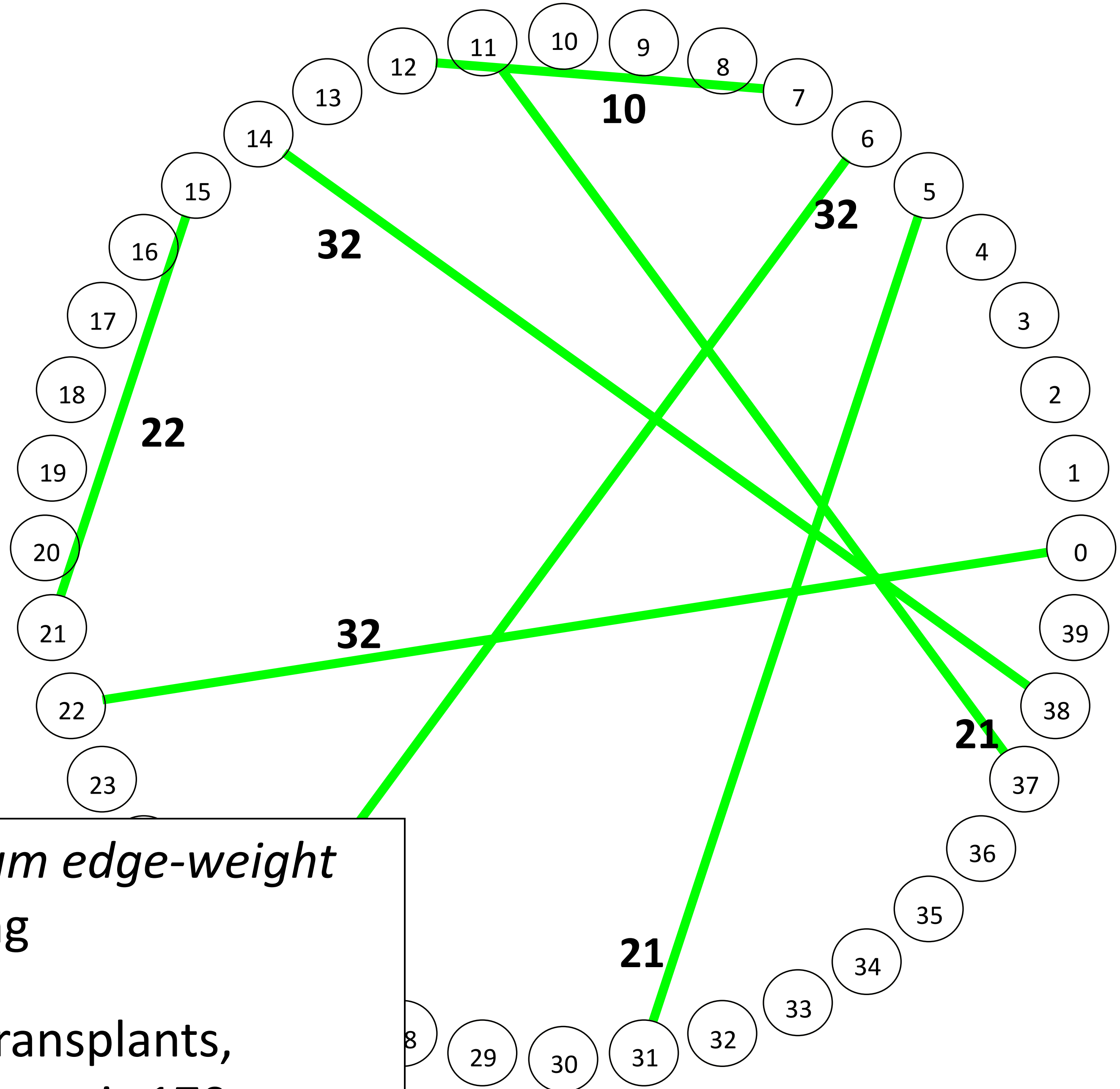



Donors
Recipients
FEB
APR
JUN
Donors
Recipients
25
11
10
26

Prioritized KPD matching



- *Decisions*: choose which incompatible pairs exchange (select edges in the graph)
- *Constraints*: each incompatible pair involved in only one match (one edge per node)
- *Objective*: maximize total benefit of transplants
  - *Benefit* will have to be defined by the scientific consensus, histocompatibility, medical judgment, patient and transplant center preferences, same-center match priority
  - *Edmonds' algorithm* finds the exchanges that yield the maximum benefit

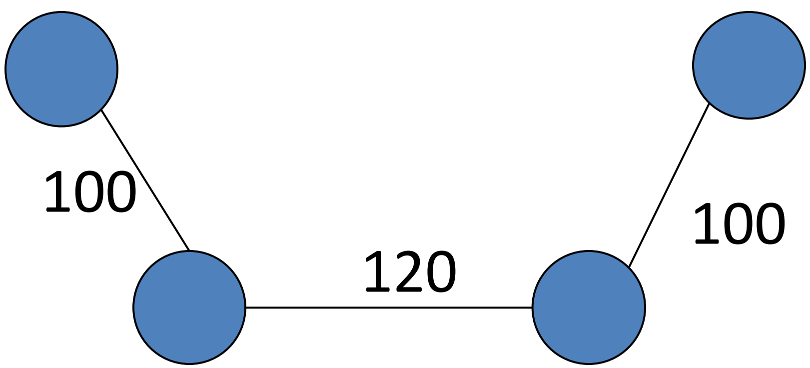


Maximum edge-weight matching

14 get transplants, benefit sum is 170

Greedy edge-rank heuristic

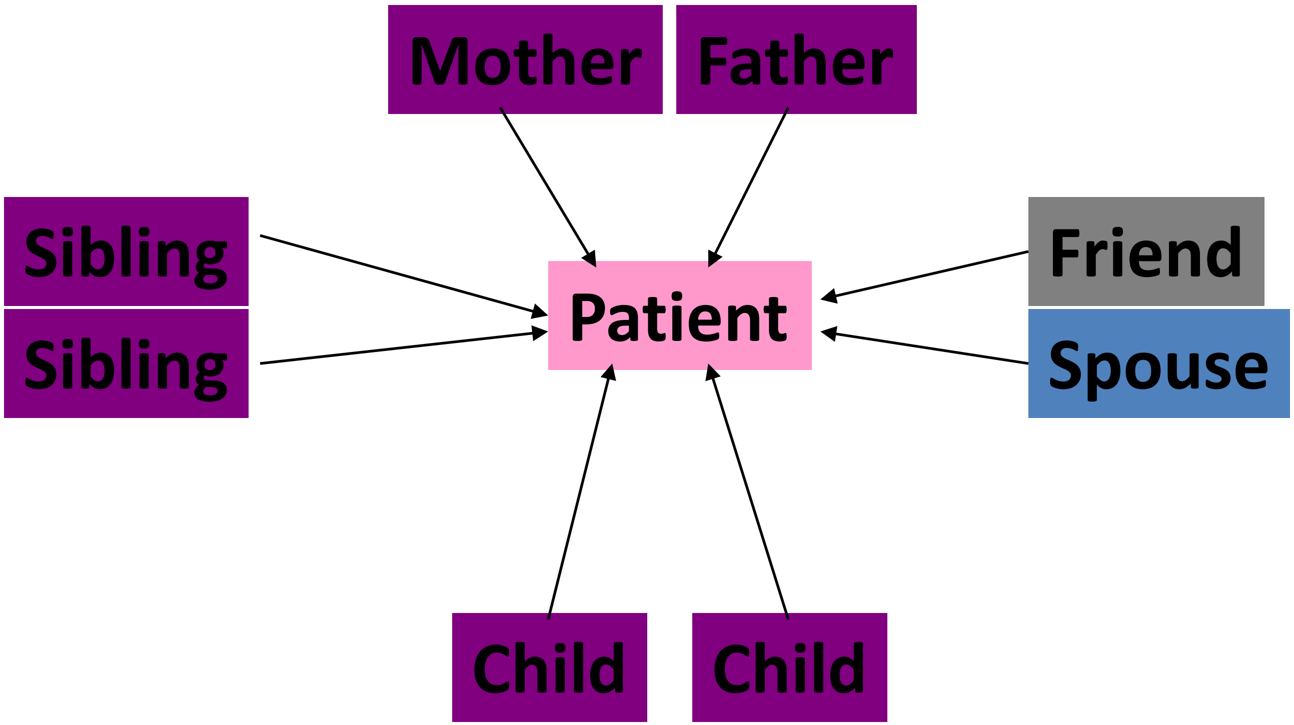
- Take best single paired donation match (edge) available, then next best edge, until no edges remain
  - neglects the connection structure of the graph; provably fails to find an optimal solution in many cases



KPD and the law

- National Organ Transplantation Act (1984) ordered that no one may donate an organ in exchange for valuable consideration

Simulated patients and social networks

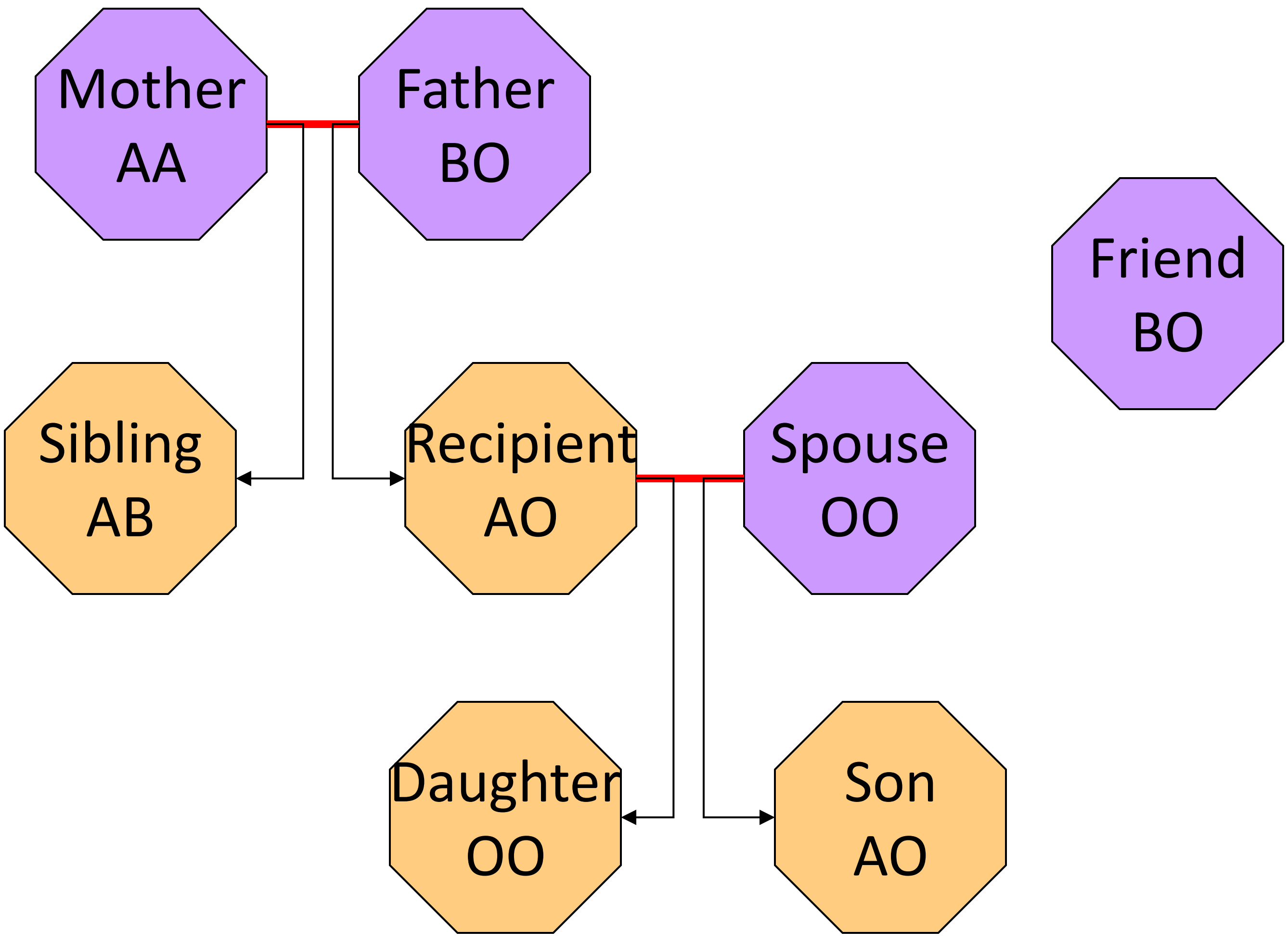


Relationship of Donor	%
Parent	19.7
Child	16.8
Sibling	42.4
Spouse	10.0
Unrelated	11.2

Each Patient has between 1-4 available donors

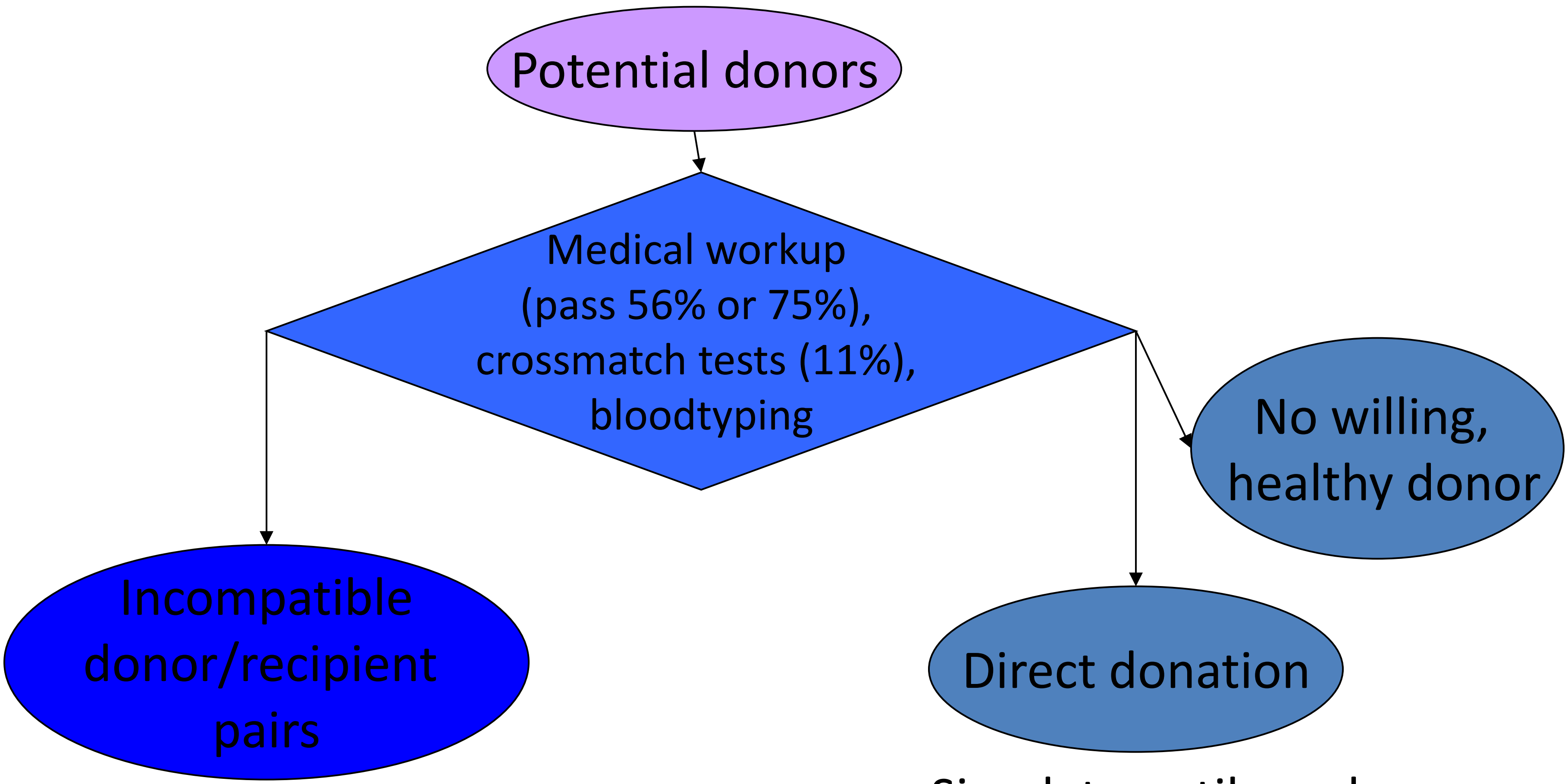
Gentry, Segev, et al. 2005. Am J Transplant.

Blood-type inheritance



Decision tree model of family

(Zenios, Woodle, Ross, Transplantation 72:4, 2001)



2406-4443 pairs annually

Simulate until reach
# of real live donors (6468)

Simulation and legislation

- 2406-4443 pairs predicted to present yearly
  - At least half of these pairs match for paired donation
- $340 million saved over dialysis using optimized matching for kidney paired donation
- 20% increase in living donor kidney transplantation

(Segev, Gentry, et al., JAMA, 2005)

- 2007 Charlie W. Norwood act legalized kidney paired donation for the first time in U.S.

Thank you to our colleagues at the **Scientific Registry for Transplant Recipients**

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