Liver Distribution Concepts

Background, Methods, and Results

John Lake, MD
Sommer Gentry, PhD
Dorry Segev, MD, PhD

Presentation to the OPTN/UNOS Liver and Intestinal Organ Transplantation Committee Public Forum on Redesigning Liver Distribution, September 16 2014

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History & Background

John R. Lake, MD
Professor of Medicine and Surgery
Executive Medical Director, Solid Organ Transplantation Program
University of Minnesota Medical School

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Final Rule: 42 CFR Part 121.8(b)

- (b) *Allocation performance goals.* Allocation policies shall be designed to achieve equitable allocation of organs among patients .., through the following performance goals:
- (1) Standardizing the criteria for determining suitable transplant candidates…
- (2) …from most to least medically urgent…
- (3) Distributing organs over as broad a geographic area as feasible …
- (4) … **reducing the inter-transplant program variance to as small as can reasonably be achieved in any performance indicator … as the Board determines appropriate…**

Final Rule: 42 CFR Part 121.8(a)

- *Policy development.* The Board of Directors established under §121.3 shall develop, in accordance with the policy development process described in §121.4, policies for the equitable allocation of cadaveric organs among potential recipients. Such allocation policies: …
- (2) **Shall seek to achieve the best use of donated organs**; …
- (5) Shall be designed to avoid wasting organs, to avoid futile transplants, to promote patient access to transplantation, and to promote the efficient management of organ placement;
- (8) **Shall not be based on the candidate's place of residence or place of listing…**

OPTN Board Direction

- **June 2010:** OPTN Board directed Liver/Intestine Committee to develop recommendations to reduce geographic disparities in waitlist mortality
- **November 2012:** OPTN Board resolution states that:
  - "The existing geographic disparity in allocation of organs for transplant is unacceptably high."
  - "The Board directs the organ-specific committees to define the measurement of fairness and any constraints for each organ system by June 30, 2013. The measurement of fairness may vary by organ type but must consider fairness based upon criteria that best represent patient outcome."
  - "The Board requests that optimized systems utilizing overlapping versus non-overlapping geographic boundaries be compared, including using or disregarding current DSA and region boundaries in allocation."

Policy Developments following the establishment of MELD prioritization in 2002

- 2005: Share 15 Regional policy implemented
- 2009: Proposals for elimination of local areas for allocation for MELD/PELD candidates (Region would be the first level of allocation. Proposal withdrawn.)
- 2010: Regional-National allocation of livers for Status 1 candidates
- June 2013: OPTN board approved
  - Share 15 National
  - Share 35 Regional
  - Liver-Intestine National Share

Previous SRTR Analyses

- June 2009: Evaluation of Allocation Systems using Regional Sharing or Concentric Circle Sharing above various MELD/PELD Thresholds
- February 2010: Data request models multiple allocation systems
- June 2010: LSAM evaluation of organ distance traveled for 27 proposed allocation systems
- October 2010: Simulated waiting list deaths by MELD/PELD for various allocation systems
- March 2011: Analysis of Region 8 Alternative Allocation System

Two Components of Allocation

Grouping

- Defines the set of candidates available for a given organ
- Currently based on DSA and region boundaries
- Balances access to transplantation and transport burden

Ordering

- Defines the sequence in which offers are made to those candidates
- Based on candidate and donor characteristics
- Balances illness severity, age, sensitivity, and other factors

Summative vs. Disparity (Fairness) Metrics

Summative Metrics

- Measure one outcome summarizing over the U.S.
- For instance: annual waitlist deaths, or total deaths

Disparity Metrics

- Measure differences in how liver candidates are treated across the country
- Candidates with MELD 38-39 have a 14% chance of death in 90 days in some OPOs, but have an 86% chance of death in 90 days in other OPOs.
- At some OPOs, median MELD at transplant is as low as 18; at some, it is as high as 36

(OPO-wise Variance in median MELD at transplant)

Methods & Approach

Sommer Gentry, PhD
Associate Professor, Mathematics
United States Naval Academy

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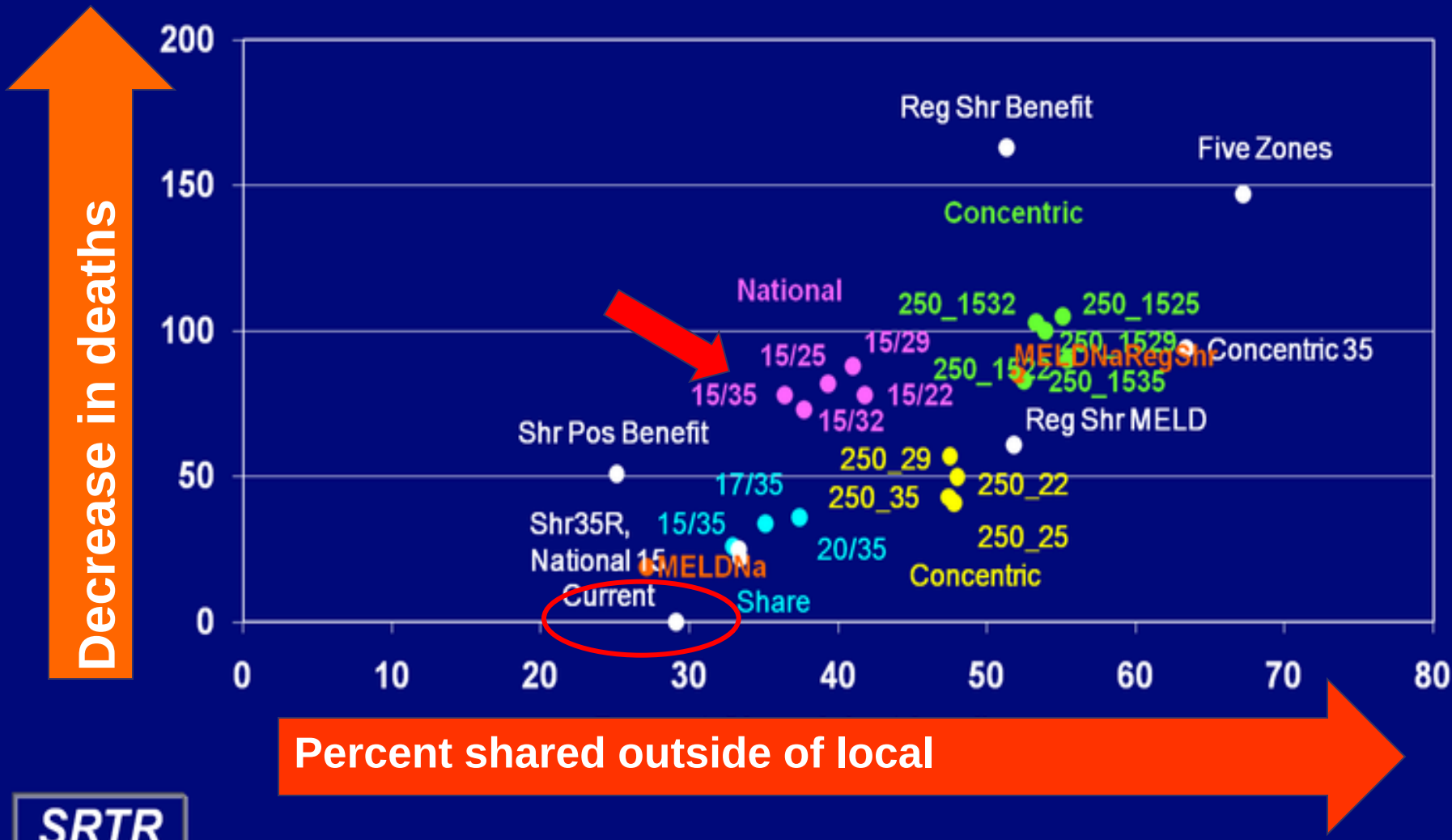
Percent Shared vs. Decrease in Total Deaths



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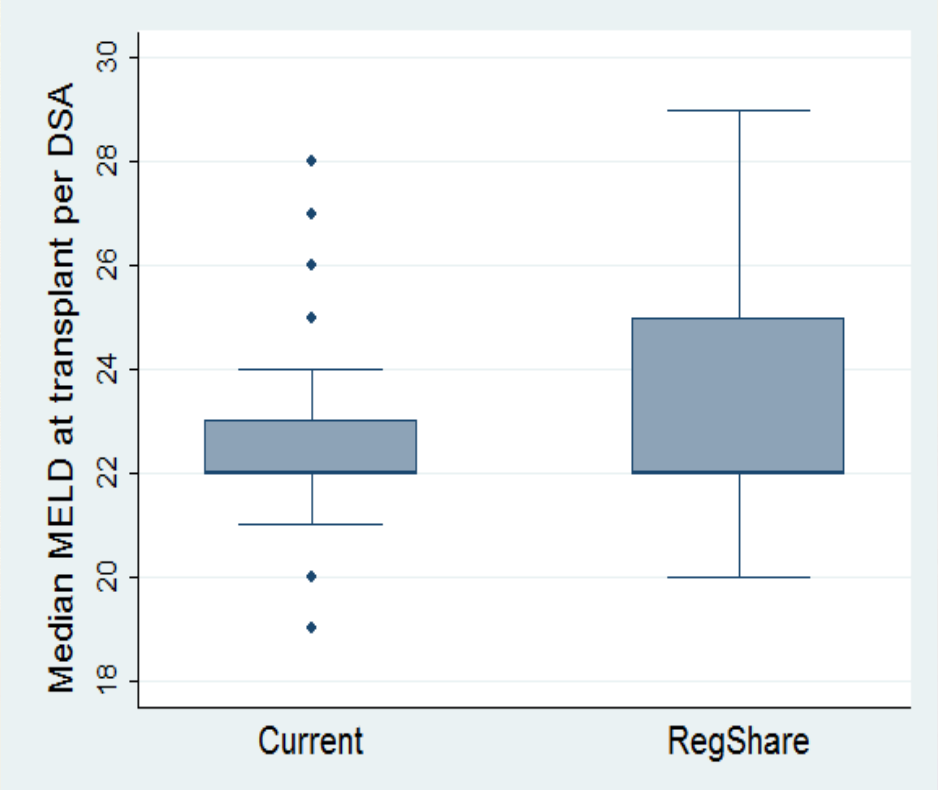
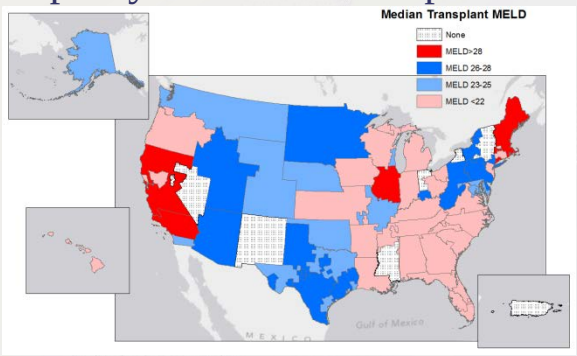
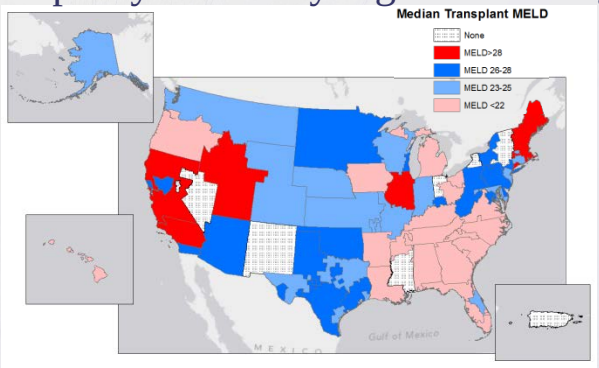
Broader sharing not sufficient to mitigate disparity -- actually worse with existing regions



Disparity in median transplant MELD

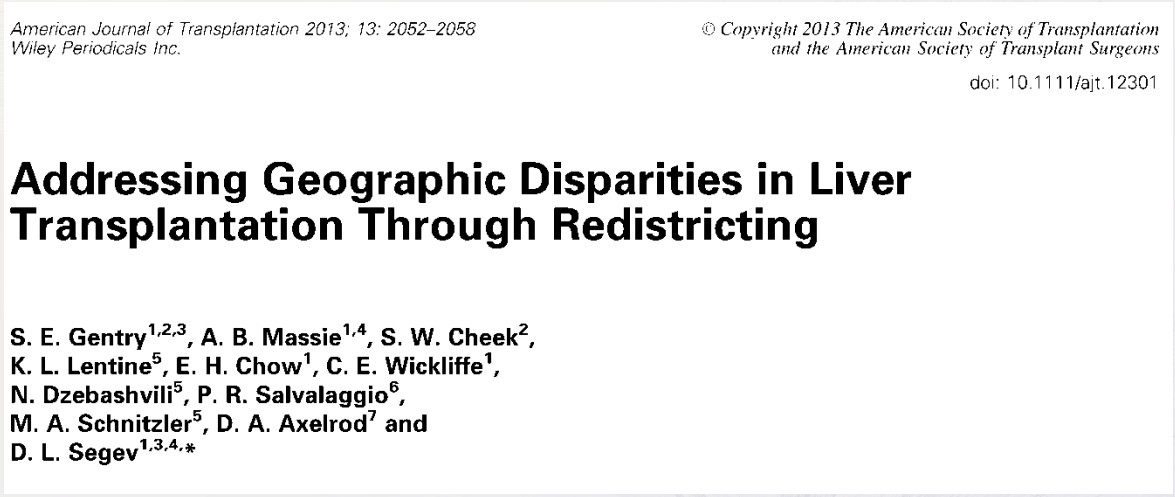


Disparity with fully regional sharing



Broader Sharing Alone not Sufficient

- Fully regional sharing would not decrease disparity in MELD at transplant; paradoxically, fully regional sharing increases disparity from variance of 11.2 to variance of 13.5
- Share-35 is a partial step toward regional sharing in the existing regions, so we do not expect Share-35 to mitigate geographic disparity



American Journal of Transplantation 2013; 13: 2052–2058
Wiley Periodicals Inc.

doi: 10.1111/ajt.12301

Addressing Geographic Disparities in Liver Transplantation Through Redistricting

S. E. Gentry[1,2,3], A. B. Massie[1,4], S. W. Cheek[2], K. L. Lentine[5], E. H. Chow[1], C. E. Wickliffe[1], N. Dzebashvili[5], P. R. Salvalaggio[6], M. A. Schnitzler[5], D. A. Axelrod[7] and D. L. Segev[1,3,4,*]

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Alternatives

- Redistricting
  - Reorganize current DSAs into optimal organ sharing districts
  - Math is developed; could be implemented immediately
- Beyond current DSAs
  - Optimal Concentric Circles (by distance or time or population)
  - Overlapping Amoebas (redistricting with districts that overlap)
  - Dynamic Scoring (no boundaries at all)
  - Math would take several years (not currently in progress)
  - Committee decided to go with redistricting (simpler, DSA structures remain intact)

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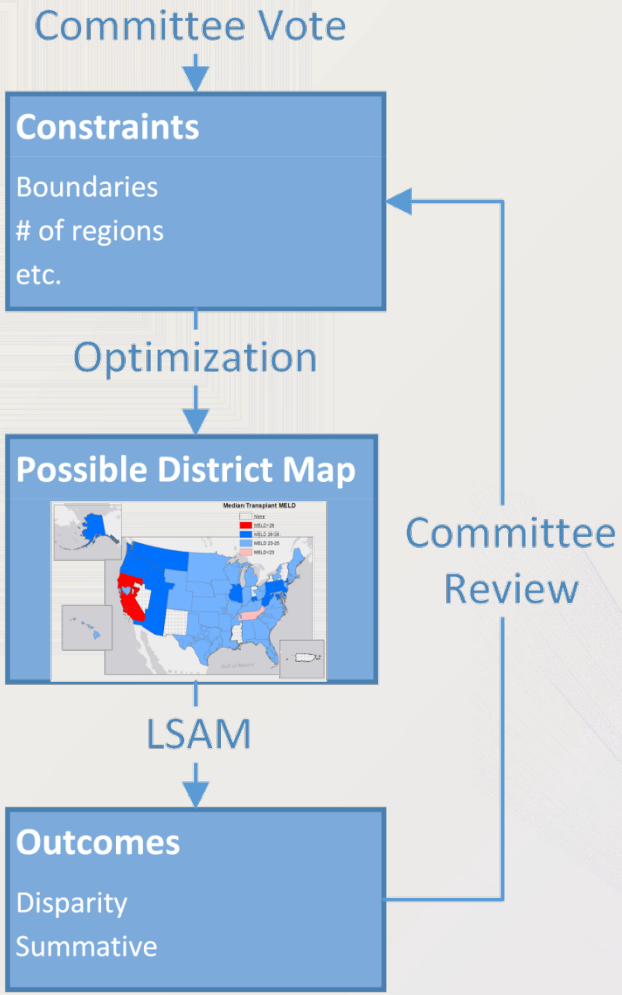
Redistricting Approach



- Iterative process
- Driven by Committee's chosen goals, constraints
- Multiple tools
  - Mathematical optimization: design districts
  - Travel time model
  - LSAM: generate summative and disparity metrics

Mathematical Optimization

- District layout designed by integer programming
- Disparity = difference between number of donors a region *should* have (if organs went to highest MELD patient anywhere in the country) and number of donors in a proposed district
- **Minimize** sum of these disparities over all districts:

$$\sum_{i \in DCT} |D_i - P_i|$$

- Subject to **constraints**:
  - District boundaries
  - Number of districts
  - Centers per district
  - Travel time

Mathematical Optimization for Redistricting

- The only data used for designing the sharing districts are the # donors per OPO versus # new liver transplant candidates at various MELDs (supply/demand per OPO)
  - Maps under consideration were designed using 2010 data
  - These counts are stable: maps designed using 2006 data also significantly reduced geographic disparity and reduced waiting list and total deaths when applied to 2010 simulations (Gentry et al., AJT 2013)
  - These counts seem to be stable even since Share-35

Transport Time Model

- Distance is very weakly correlated with cold ischemia time.
- The delay attributable to the distribution system is the transport time from donor hospital to transplant center.
- Transport model uses:
  - Geocoded locations of all donor/transplant centers
  - Google API for driving times
  - Fixed wing flight times and drive times to airport locations
  - Drive if drive time <2 hrs or if drive time < flying time

Impact of Broader Sharing on the Transport Time for Deceased Donor Livers, Gentry et al. Liver Transplantation, 2014.

Liver Simulated Allocation Model

- Discrete-event simulation
  - Draws from real donor and candidate data
  - Models organ offers, organ acceptance, MELD changes over time, waitlist survival, and post-transplant survival
  - Simulates the uncertainty associated with these events
- Used extensively by SRTR/OPTN to predict the impact of many proposed policy changes

LSAM Strengths and Limitations

Strengths

- Draws on real transplant data
- Simulates up to 5 years
- Multivariable acceptance and survival models
- Can compare multiple allocation and distribution systems

Limitations

- Predicts comparisons between alternatives, not specific outcomes
- Cannot account for changes in listing or acceptance behavior
- Cannot predict outcomes on a center-by-center basis
- Most recent input data files use data through 2011

LSAM predictions and Share-35 Actual Results

- LSAM predicted regional sharing increase from 32% to 35%; Share-35 increased regional sharing from 20.4% to 31.8%

- LSAM predicted transplants for MELD>35 increase from 21.3% to 23.1%; Share-35 increased transplants for MELD>35 from 23.1% to 30.1%

- LSAM predicted 344 pre-transplant deaths prevented over five years (annually); Share-35 decreased pre-transplant deaths by 104 over 9 months

LSAM predictions and Share-35 Actual Results

- LSAM predicted retransplants would not increase; retransplants did not increase under Share-35
- LSAM predicted discards would drop from 11.3% to 10.4%; Share-35 decreased discards from 9.9% to 9.3%
- LSAM predicted median transport would increase from 99 miles to 124 miles; Share-35 increased median transport from 59 miles to 85 miles
- LSAM predicted median transport time would not change; Share-35 did not increase median cold ischemia time

LSAM predictions: Take-Home Messages

- LSAM correctly predicted all *directions of change* in Share-35
- LSAM is not designed to predict *absolute* numbers, just designed to make *comparisons*
- Reminder: Redistricting math does NOT depend on LSAM

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Redistricting Metrics & Constraints

Parameters selected by committee vote:

- Disparity metric
  - Variance in median MELD at transplant
- Constraints
  - Contiguous districts using existing DSA boundaries
  - 4-8 districts
  - ≥6 centers per district
  - No increase in waiting list deaths
  - Maximum median travel time of 3, 4, 5 hours, or no limit

Selecting Options to Pursue

- We presented optimized maps and LSAM results using a variety of constraint settings within the Liver Committee's choices:
  - 4, 5, 6, 7, 8, 9, 10, or 11 districts;
  - Median volume-weighted transport time constraints between 3 hours, 4 hours, 5 hours, or no limit.
- Allowing longer transport times did not have much impact on disparity; committee selected 3 hours
- The committee chose 4 districts and 8 districts to pursue and explore in depth

Selecting Options to Pursue

- We presented LSAM results from concentric circle designs with 250 mile and 500 mile radius settings to compare with optimal redistricting designs
  - Concentric circles displayed a worse tradeoff between the transport impacts and the reduction in geographic disparity and deaths.
  - The Committee opted not to pursue concentric circles.

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Results

Sommer Gentry, PhD
Associate Professor, Mathematics
United States Naval Academy

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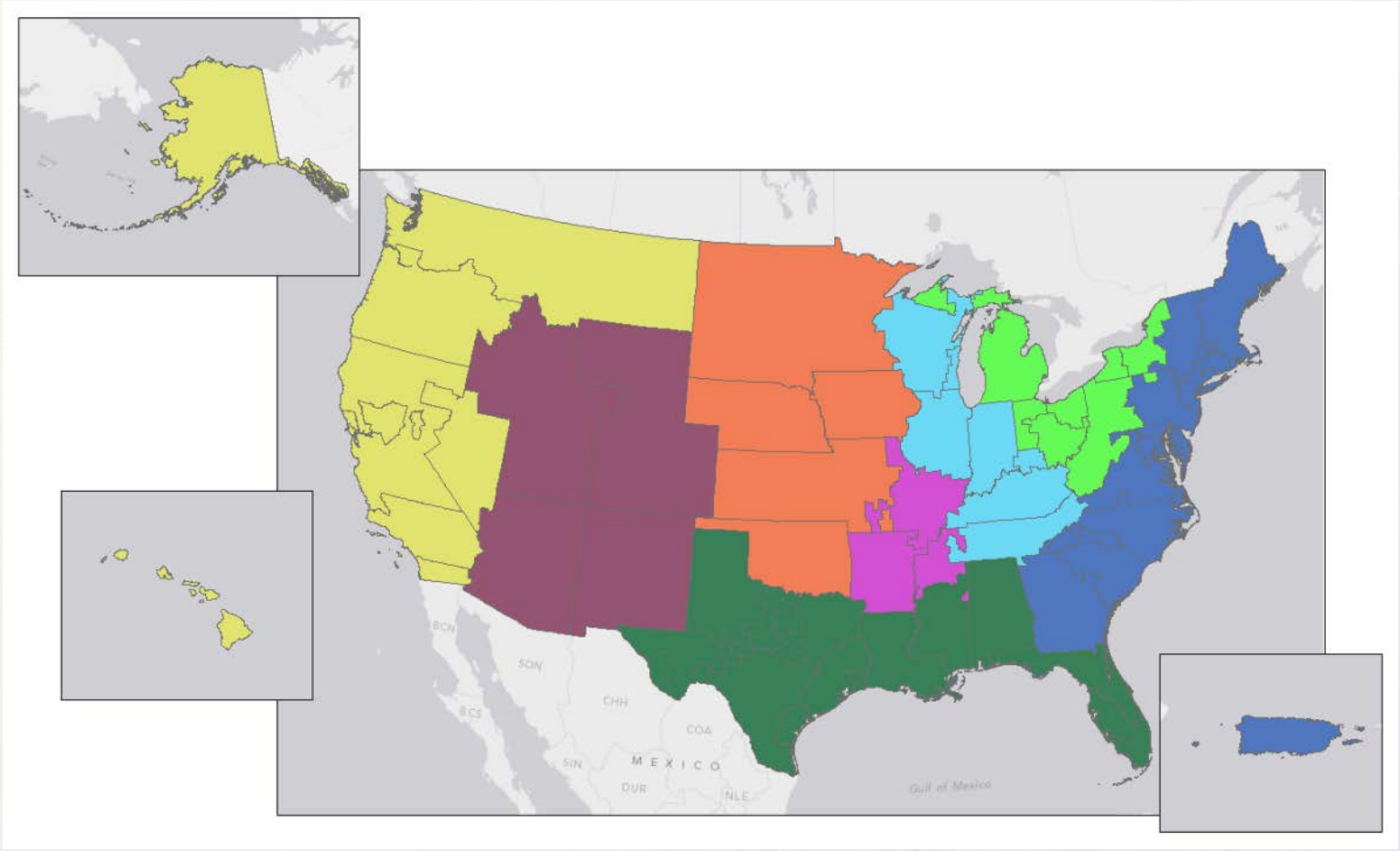
Optimal 8 District Map



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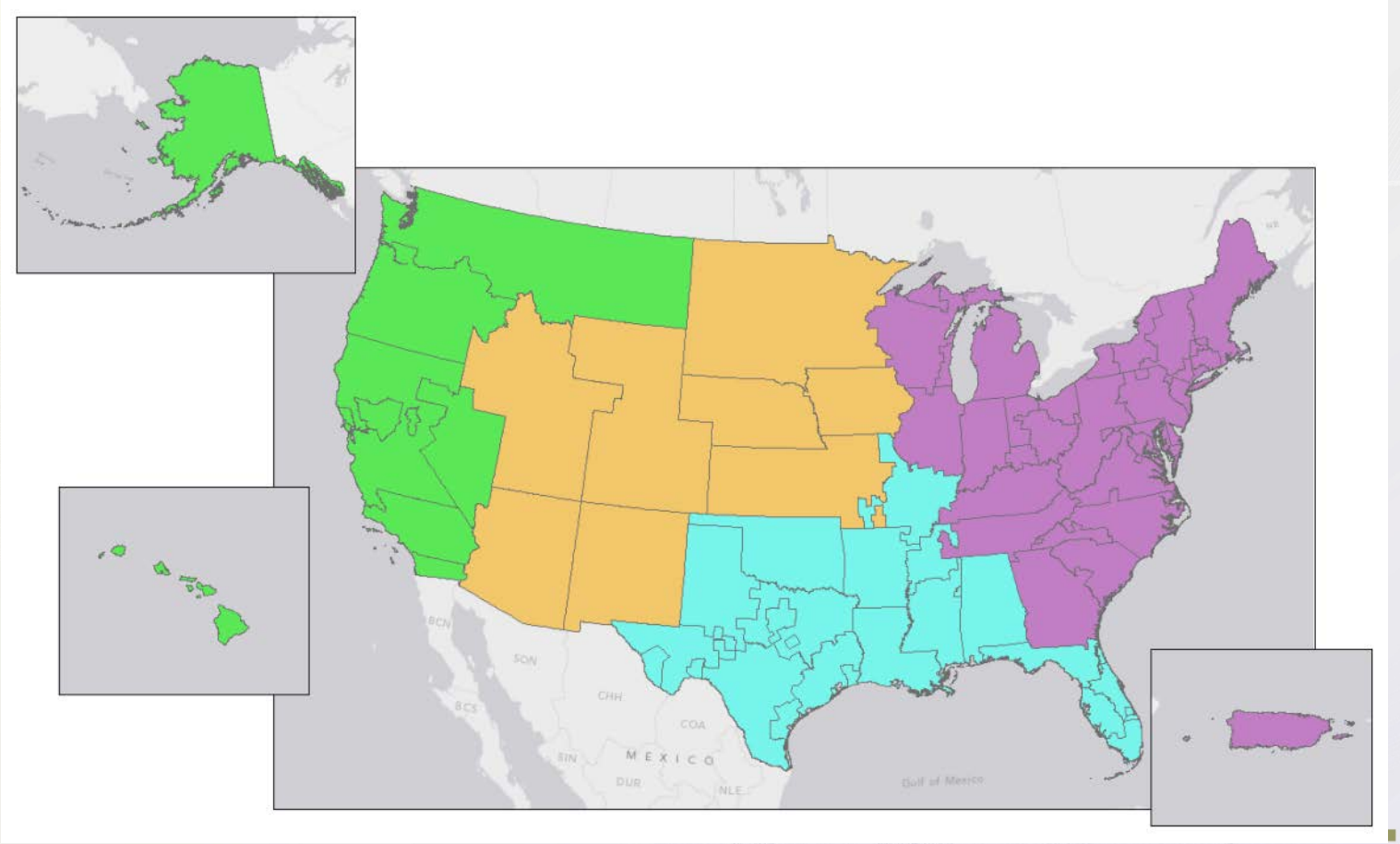
Optimal 4 District Map



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Allocation order for redistricting simulations

- Only two geographic tiers*
  - Within district:
    Status 1A/1B, descending order of MELD/PELD
  - National:
    Status 1A/1B, descending order of MELD/PELD

*The standard adjustments for donor blood type O and donor age younger than 18 were applied, but not Share-15 national rule

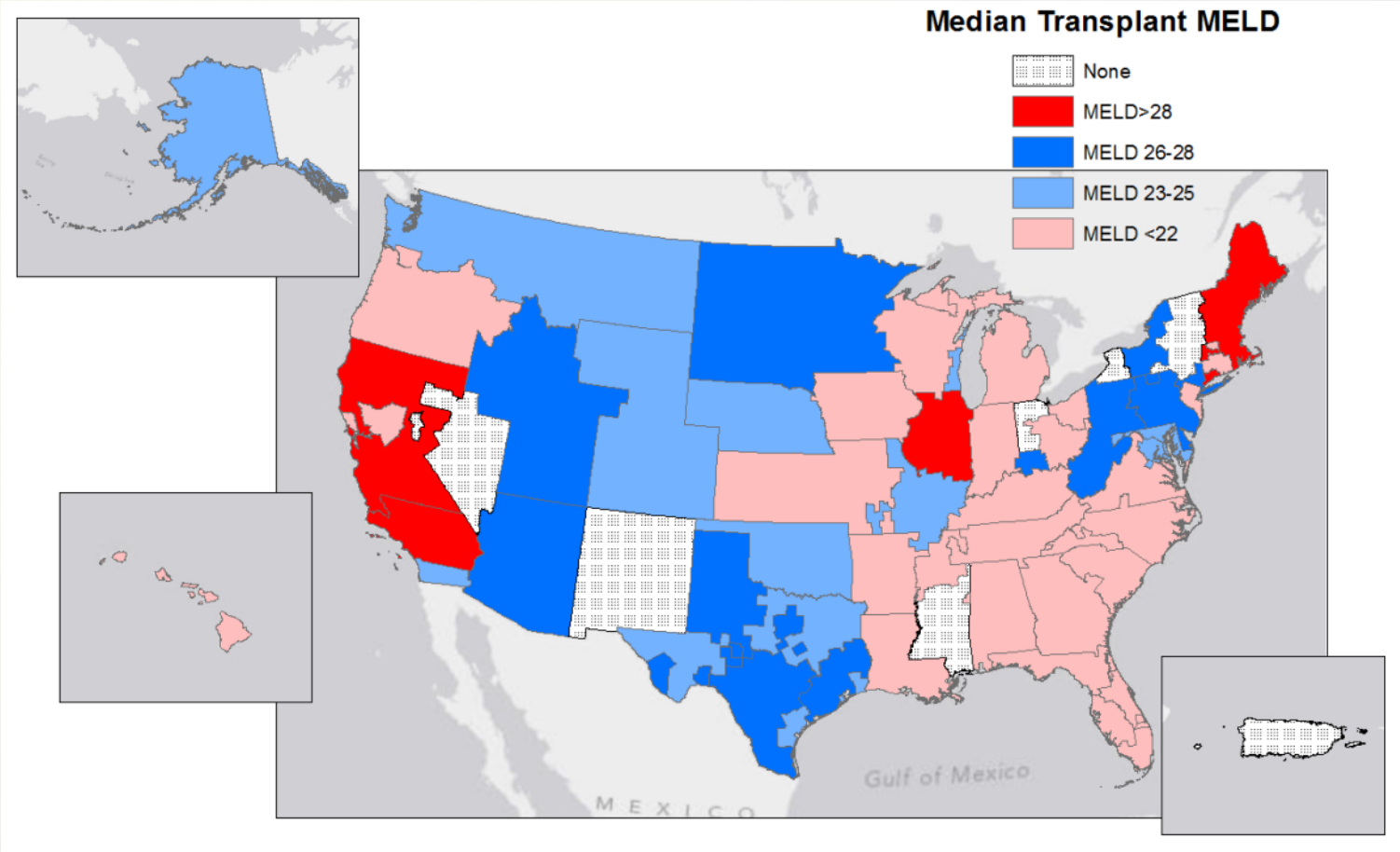
LSAM Results: Deaths and Disparity

	Discards	Waitlist and Removal Deaths Prevented	Total Pre- and Post-tx Deaths Prevented	Variance of Median Transplant MELD
Share 35	3510.5	reference	reference	7.55
Regional	4472.8	-208	-49	10.14
8 Districts	4443.7	111	296	3.61
4 Districts	4512.7	452	598	2.60
National	4894.1	921	556	0.84

LSAM Results: Transport and Sharing

	Local	Regional	Median Transport Time	Median distance (miles)	Flying	Variance Median Transplant MELD
Share 35	56.2%	34.5%	1.7	124	54.6%	7.55
Regional	35.7%	59.3%	1.8	194	67.6%	10.14
8 Districts	26.9%	69.6%	1.9	245	74.2%	3.61
4 Districts	16.4%	81.7%	2.2	419	84.3%	2.60
National	5.1%	8.1%	3.1	896	94.7%	0.84

Disparity in Transplant MELD, Local Distribution



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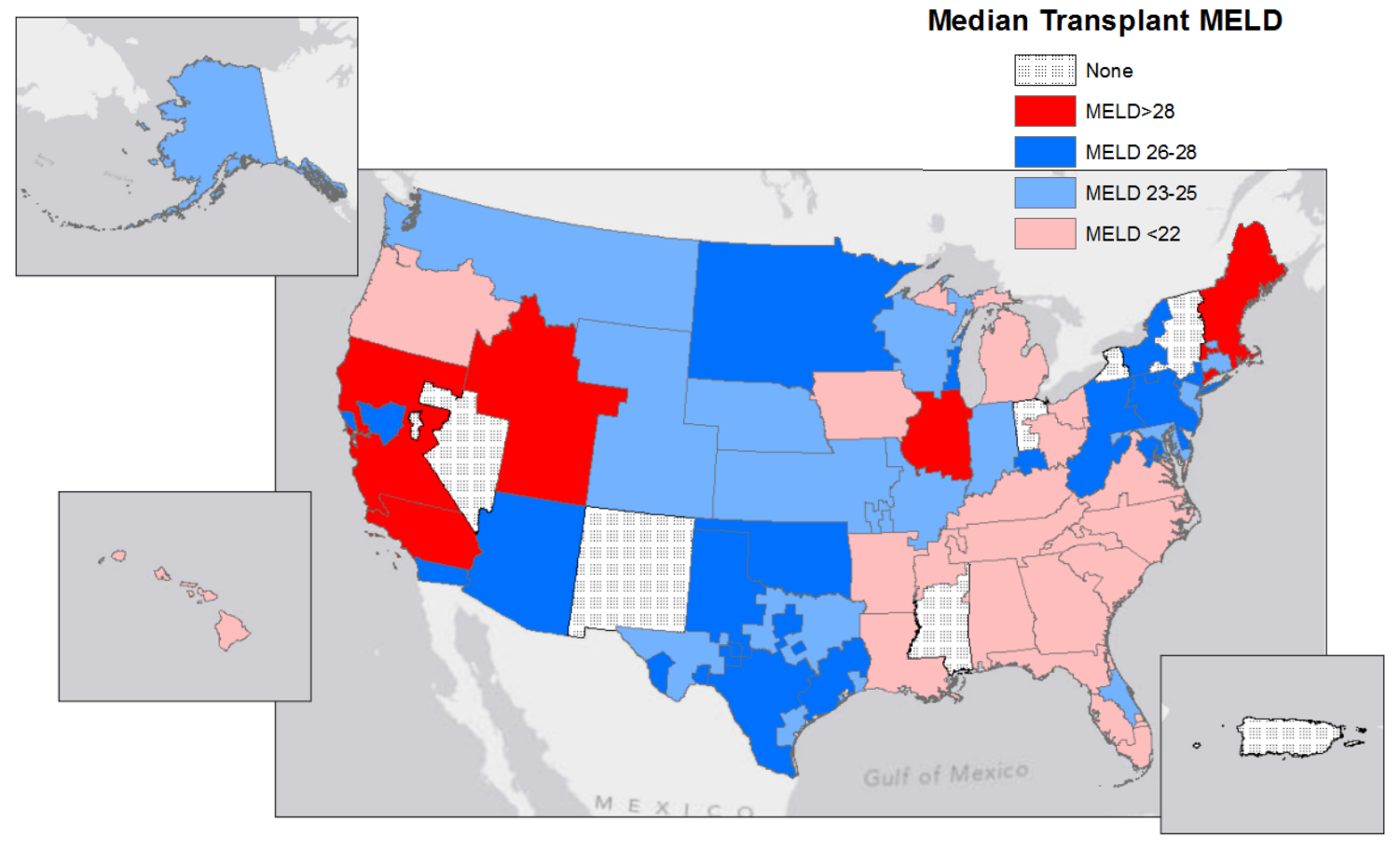
Disparity in Transplant MELD, Existing Regions, Fully Regional Sharing



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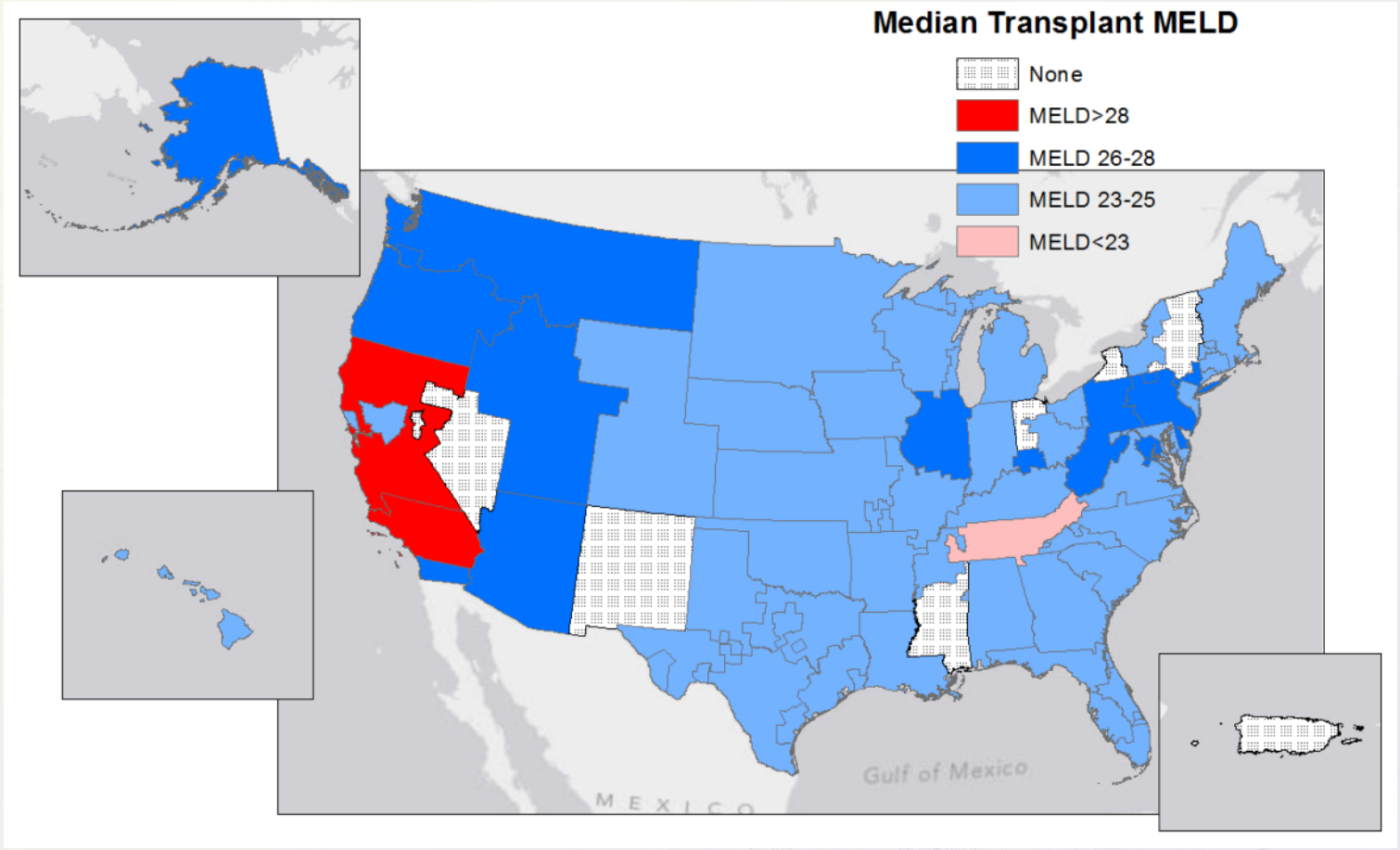
Disparity in Transplant MELD with 8 Districts



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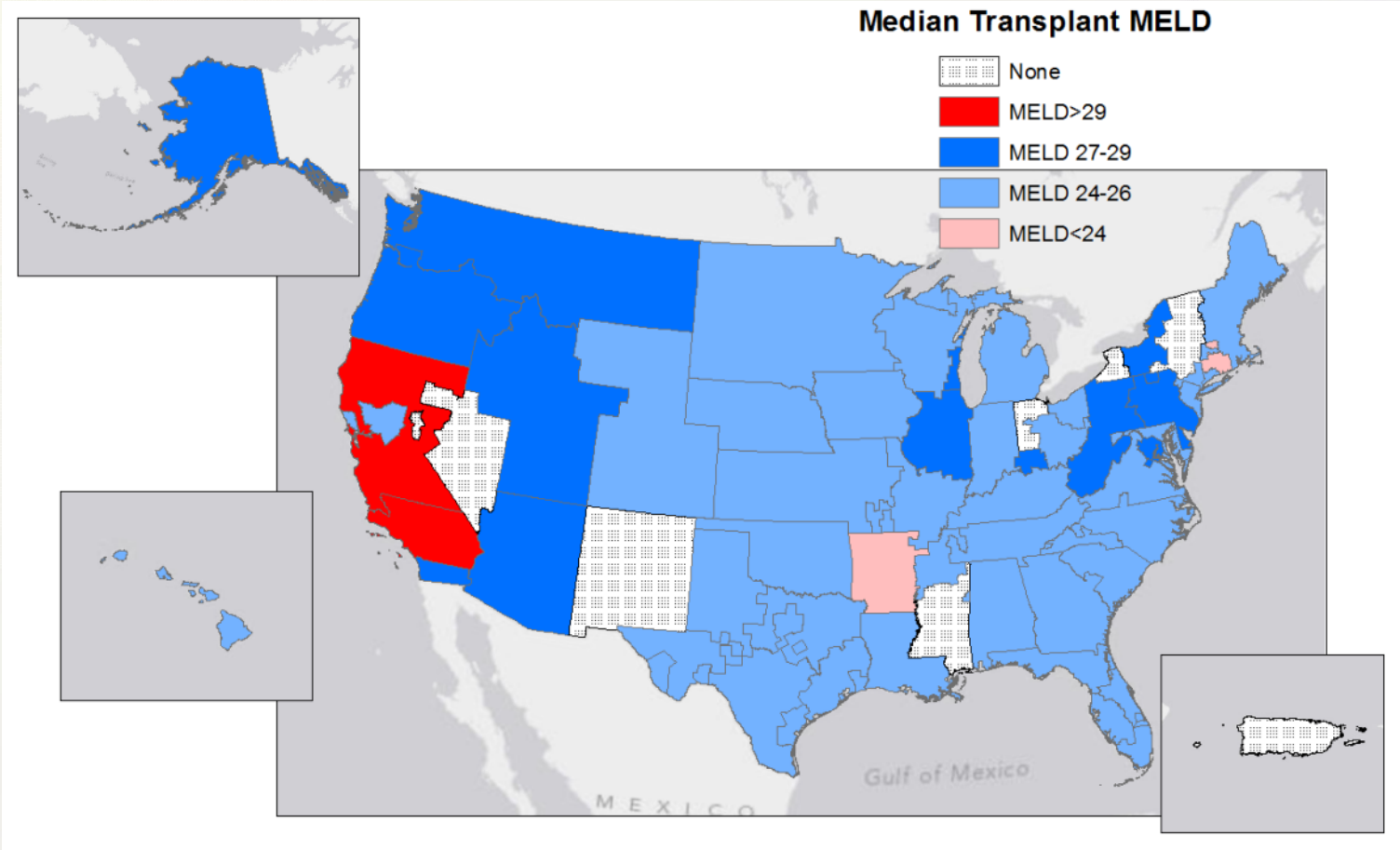
Disparity in Transplant MELD with 4 Districts



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Public Comment: Interest in Concentric Circles

- Responding to public comment, the Committee asked us to simulate concentric circle systems that would be similar in transport impacts to the 4 district and 8 district concepts.
  - We present results using 400 mile circles, which are comparable to the 8 district concept in terms of transport impacts, and using 700 mile circles, which are comparable to the 4 district concept.
  - Concentric circle designs require longer transport distances and more flying, and do not reduce total deaths or geographic disparity as effectively as redistricting.

Concentric Circles: Transport and Sharing

	Local	Regional	Median Transport Time	Median distance (miles)	Flying	Variance Median Transplant MELD
8 Districts	26.9%	69.6%	1.9	245	74.2%	3.61
Circles 400	23.7%	29.0%	1.9	261	77.4%	4.12
4 Districts	16.4%	81.7%	2.2	419	84.3%	2.60
Circles 700	14.6%	22.0%	2.2	440	85.6%	2.60

Concentric Circles: Disparity and Deaths

	Total Deaths Prevented	Variance of Median Transplant MELD
8 Districts	296	3.61
Circles 400	3	4.12
4 Districts	598	2.60
Circles 700	267	2.60

OPO Performance & Allocation

Dorry Segev, MD, PhD
Associate Professor of Surgery and Epidemiology
Vice Chair for Research
Department of Surgery
Johns Hopkins University

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OPO Performance and Allocation

- OPOs vary in the populations that they serve and in their conversion of eligible deaths to liver donations

- Standard metrics of OPO performance provided by the SRTR:
  - **observed : expected (O:E) liver yield**
  - **liver donor conversion ratio**

- Concerns have been raised about whether redistricting would transfer livers from better-performing OPOs to poorer-performing OPOs

Allocation Scenarios Tested

- Pre-share 35 (2010 data)
- Post-share 35 (June 18, 2013 – April 4, 2014)
- Redistricting: 4 optimized districts
- Redistricting: 8 optimized districts

Outcome: Net Import

- *(OPOs that do not serve a local liver transplant center are excluded from this analysis)*
- Net import of livers from adult donors per OPO is defined as

$$\frac{\text{livers imported} - \text{livers exported}}{\text{livers recovered}}$$

Potential Correlates

- Measures of OPO performance
  - Observed:Expected (O:E) Liver Yield *(how good you were at getting livers used from donors in your area)*
  - Liver Donor Conversion Ratio *(how good you were at getting eligible deaths to become donors)*

Potential Correlates

- Measures of disparity in supply/demand
  - O:E Eligible Deaths
    (how many more potential donors died in your area than in other areas)
  - O:E Incident Listings
    (how much more transplant demand is in your area than in other areas)

Liver Donor Conversion Ratio

- Liver donor conversion ratio is the unadjusted proportion of liver donations that are recovered from all eligible deaths within an OPO's service area.
- An eligible death is one that meets certain criteria for age, neurologic death, and other exclusions of infection or malignancy
- We use liver donor conversion ratio as reported by SRTR for 2010-2011.

Observed : Expected Liver Yield

- The observed liver yield is the actual number of liver donations from donors reported to SRTR for an OPO within a given time frame.
- The expected liver yield is a predicted number of liver donations from donors and is based on an adjusted logistic regression model.
- O:E Liver Yield is the ratio of the observed and expected liver yields.
- We use O:E liver yield as reported by SRTR for 2010-2011.

O:E Eligible Deaths

- We calculated an observed: expected ratio of eligible deaths for each OPO

$$\frac{OPO\ eligible\ deaths}{US\ eligible\ deaths} \Big/ \frac{pop.of\ OPO}{US\ pop.}$$

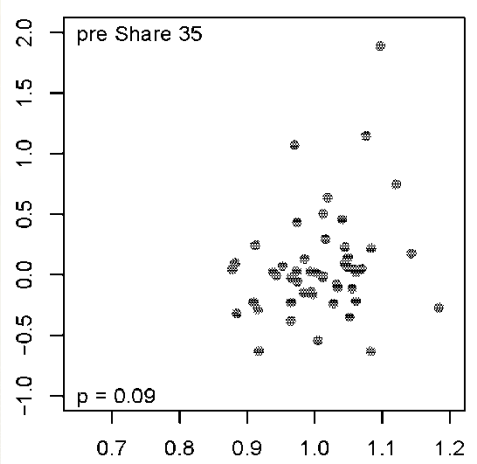
O:E Incident Listings

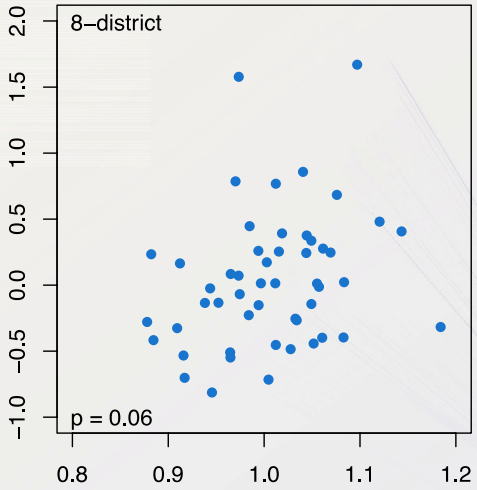
- Incident adult liver listings at MELD > 15
- We calculated an observed: expected ratio of incident listings, for each OPO

$$\frac{OPO\ incident\ listings}{US\ incident\ listings} \Big/ \frac{pop.\ of\ OPO}{US\ pop.}$$

Net Import vs. O:E Liver Yield

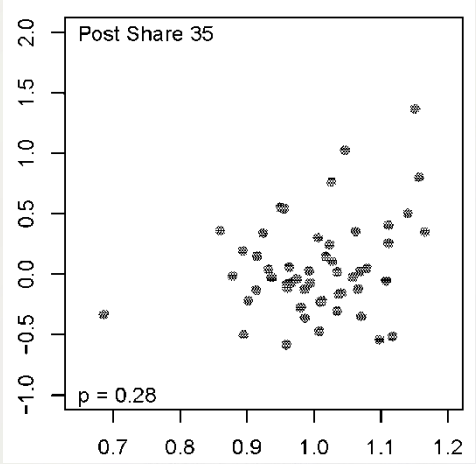
Pre- share 35

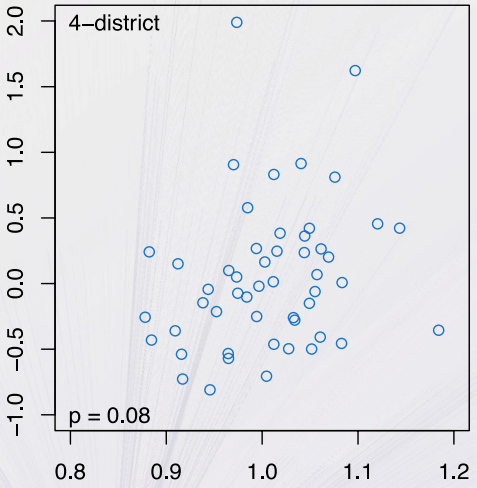




8 districts

Post- share 35





4 districts

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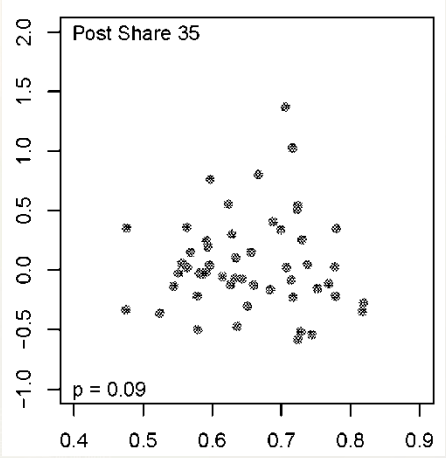
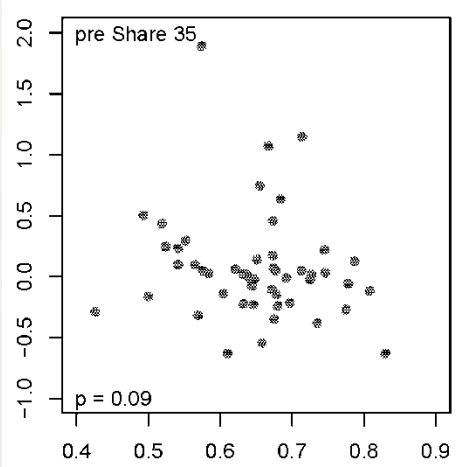
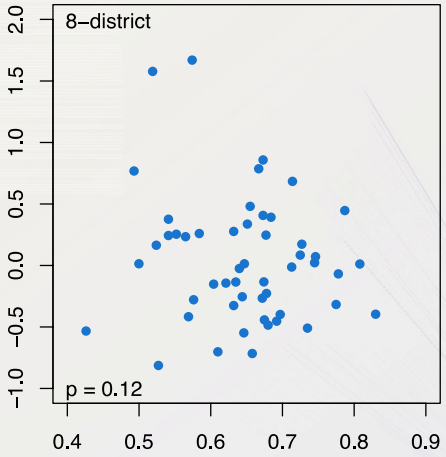
Net Import vs. Liver Donor Conversion Ratio

Pre- share 35

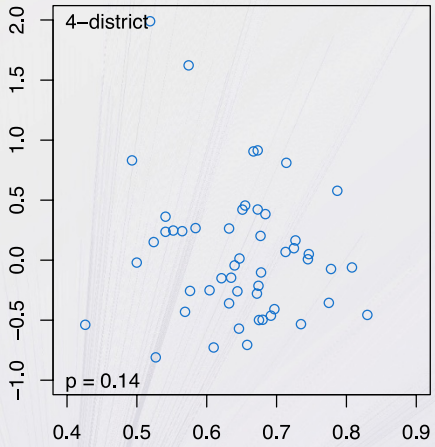


Post- share 35





8 districts



4 districts

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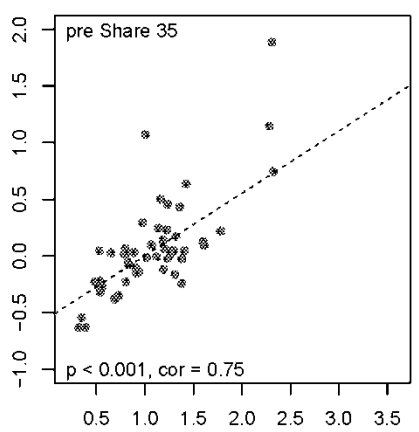
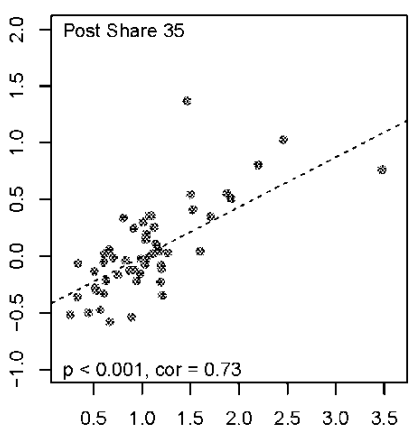
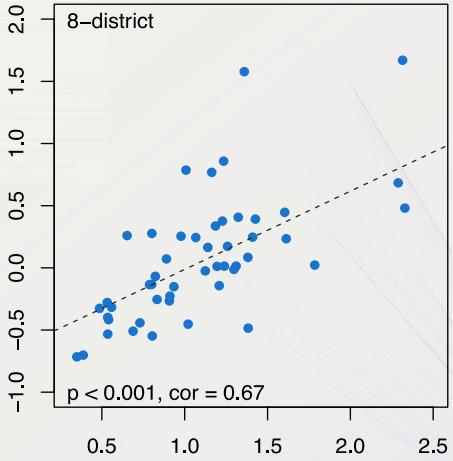
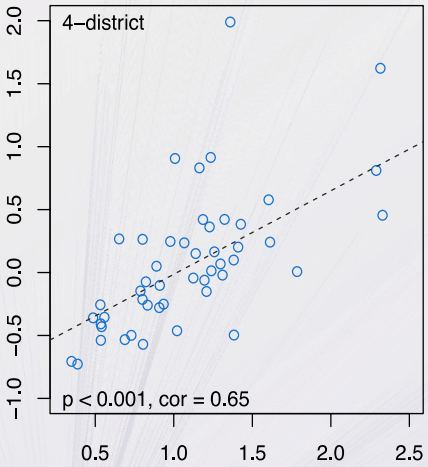
Net Import vs. Incident Listings

Pre- share 35 (p<0.001) Post- share 35 (p<0.001)









8 districts (p<0.001) 4 districts (p<0.001)

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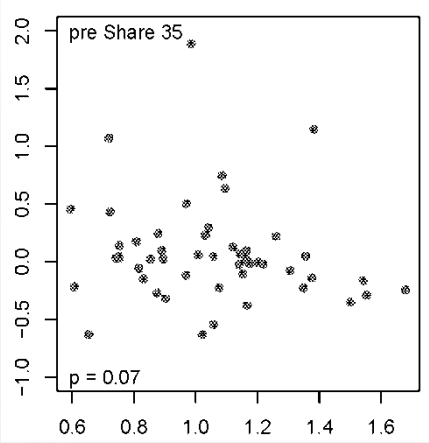
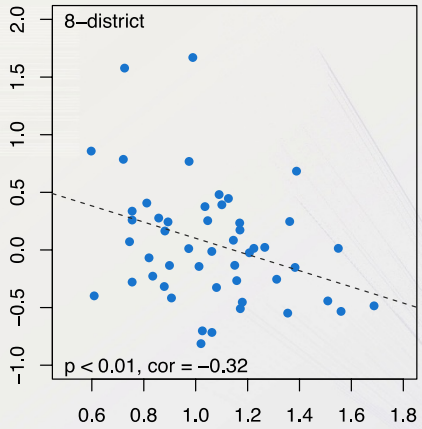
Net Import vs. Eligible Deaths

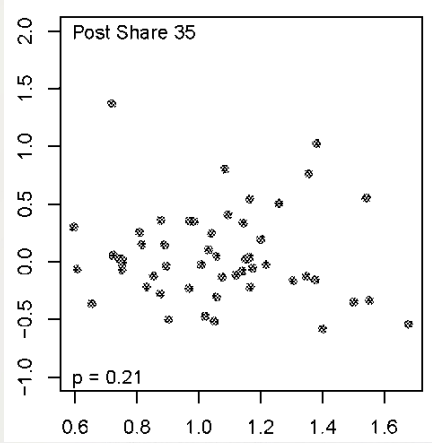
Pre- share 35

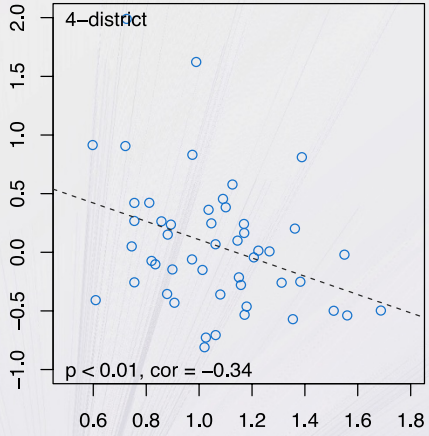




8 districts (p=0.004)

Post- share 35





4 districts (p=0.003)

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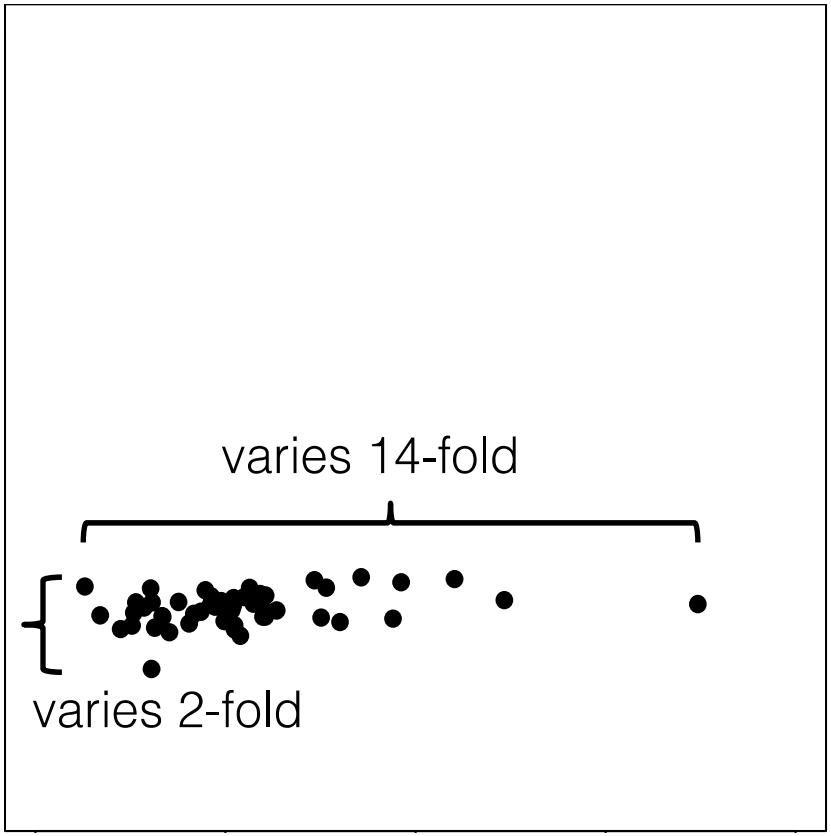
Listings vary much more than OPO Performance



Liver Flow: Conclusions

- There is no relationship between net import and OPO performance, either pre-Share35, post-Share35, or under redistricting. Organs do not, and would not, flow from better-performing OPOs to poorer-performing OPOs.
- Organs currently follow demand, flowing from areas with fewer listings than expected to areas with more listings than expected
- Under redistricting, organs would also follow supply, flowing from areas with higher rates of eligible deaths to areas with lower rates of eligible deaths

Thank You

Contact the Scientific Registry of Transplant Recipients:

Website: www.srtr.org

Email: srtr@srtr.org

Phone: 1.877.970.SRTR

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