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Models: Principles of Robust System Design and their Applicability in Organ Allocation

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Sanjay Mehrotra, PhD

Professor, *Industrial Engineering and Management Science*
McCormick School of Engineering
Feinberg School of Medicine (by courtesy)

Director,
Center for Engineering and Health, Institute for Public Health and Medicine, Northwestern University

Background

Experience

- PhD, Operations Research, Columbia University (1986)
- Chair, Optimization Society, Institute for Operations Research and Management Science (2013-2014)
- Board of Directors, Institute for Operations Research and Management Science (2006-2007)
- Methodological interests in mathematical optimization, health systems engineering, and decision analysis
- Teach graduate and undergraduate courses in optimization, healthcare systems engineering, healthcare analytics, and healthcare management science.
- Past methodological research supported by National Science Foundation, Office of Naval Research, Department of Energy, and National Institutes of Health

Relevant Publications

- **Worked on geographic disparity in kidney transplantation for past five years**
- **Modeling the Allocation System: Principles for Robust Design before Restructuring, *Transplantation,* , editorial, 10.1097/TP.0000000000000656. PMID:25651120**
- **Improving Geographic Equity in Kidney Transplantation Using Alternative Kidney Sharing and Optimization Modeling, *Medical Decision Making* , online first, PMID: 25385750.**
- **The Effect of the Statewide Sharing Variance on Geographic Disparity in Kidney Transplantation in the US, *Clinical Journal of American Society of Nephrology*, 9(8):1449-60, doi: 10.2215/CJN.05350513. PMID: 24970871 Epub 2014 Jun 26.**
- **Changes in Geographic Disparity in Kidney Transplantation since the Final Rule, *Transplantation* , 98(9), 931-936. doi: 10.1097/TP.0000000000000446 PMID: 25286057.**
- **The Extent and Predictors of Geographic Disparity in Kidney Transplantation in the United States, *Transplantation,* PMID 24374790**
- **Characteristics of a Simulation Model to Investigate Geographic Disparities in the Kidney Transplant System, *Proceedings of the Winter Simulation Conference,* 2320-2329.**

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Disclosures

- I am neither affiliated with nor involved with any efforts regarding SRTR, UNOS, any transplant lobby, or patient support group. I do not receive any financial compensation from Northwestern Medicine's Comprehensive Transplant Center.

- My past work in organ (kidney) allocation is funded by a grant, titled Addressing Geographical Disparities in Transplant Organ Accessibility Across United States, from the National Science Foundation (2011-2015). The results are featured by the National Science Foundation in its Science, Engineering and Education Innovation highlights.

- I have an ongoing project in kidney transplantation funded by the Illinois Gift of Hope OPO and titled "Improving Utilization of High-KDRI Organs".

- I was invited to write an editorial on principles of robust system design and its application to organ allocation based on my past work. In this references were made to the methodology used in the current redistricting proposal. I received no financial compensation or any other special consideration for this.

  Modeling the Allocation System: Principles for Robust Design before Restructuring, (2015), *Transplantation,* editorial, 10.1097/TP.0000000000000656. PMID:25651120

- Collaborators in transplantation research:
  - *Northwestern University*: M. Abecassis, J. Friedewald, D. Ladner, A. Skaro
  - *Others*: R. Gilroy and B. Kaplan (University of Kansas), G. Klintmalm (Baylor Transplant Services),

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My Message to this Forum

- I neither wish to appear dismissive of redistricting outright nor the use of model-based methodologies for finding and evaluating solutions to disparities in transplantation. Both past and current efforts to frame the problem by such means are very important steps.

- I strongly believe that a prudent solution is required to fulfill the spirit of the Final Rule that "***organs and tissues ought to be distributed on the basis of objective priority criteria and not on the basis of accidents of geography***." Insofar as a proposed solution provides sufficient scientific evidence that it can best accomplish the above, it should be quickly implemented.

- I am here today to offer my scientific opinion and I might suggest that there is insufficient evidence and scientific validation to the current proposed solution meeting what is needed.

- The current model requires further independent, external evaluation to ensure that the desired goals will be achieved by it.

Outline

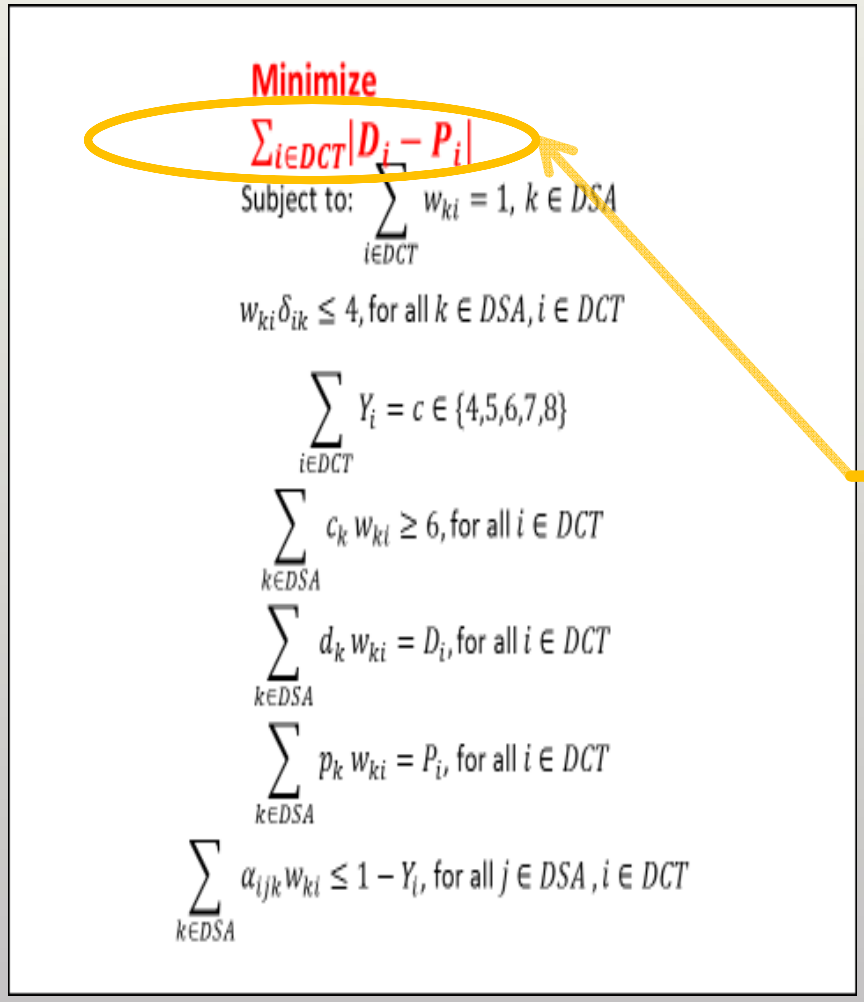
Review of Current Proposal

- Model needs further improvement
- Not dynamic or adaptive to future changes
- Needs an effective sharing policy

Suggestions to Forum

- Remarks for improving current proposal or for considering alternatives

Current Publically Available Mathematical Model for Redistricting in the Context of Principles for Robust System Design



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

$$\text{Subject to:} \quad \sum_{i \in DCT} w_{ki} = 1,\ k \in DSA$$

$$w_{ki}\delta_{ik} \leq 4, \text{for all } k \in DSA, i \in DCT$$

$$\sum_{i \in DCT} Y_i = c \in \{4,5,6,7,8\}$$

$$\sum_{k \in DSA} c_k w_{kl} \geq 6, \text{for all } i \in DCT$$

$$\sum_{k \in DSA} d_k w_{ki} = D_i, \text{for all } i \in DCT$$

$$\sum_{k \in DSA} p_k w_{ki} = P_i, \text{for all } i \in DCT$$

$$\sum_{k \in DSA} \alpha_{ijk} w_{ki} \leq 1 - Y_i, \text{for all } j \in DSA, i \in DCT$$

- The disparity exists at the DSA level. The model optimization is across districts.
- Questionable whether proportional allocation of MELD at transplant is consistent with reductions in disparities in waitlist mortality or waitlist attrition.
- Objective minimizing differences in liver supply and adjusted demand at regional level may not be ideal. It is preferable to minimize differences in the supply-demand ratios.

Note: The above is the most current version received from UNOS (as of 06/14/2015)

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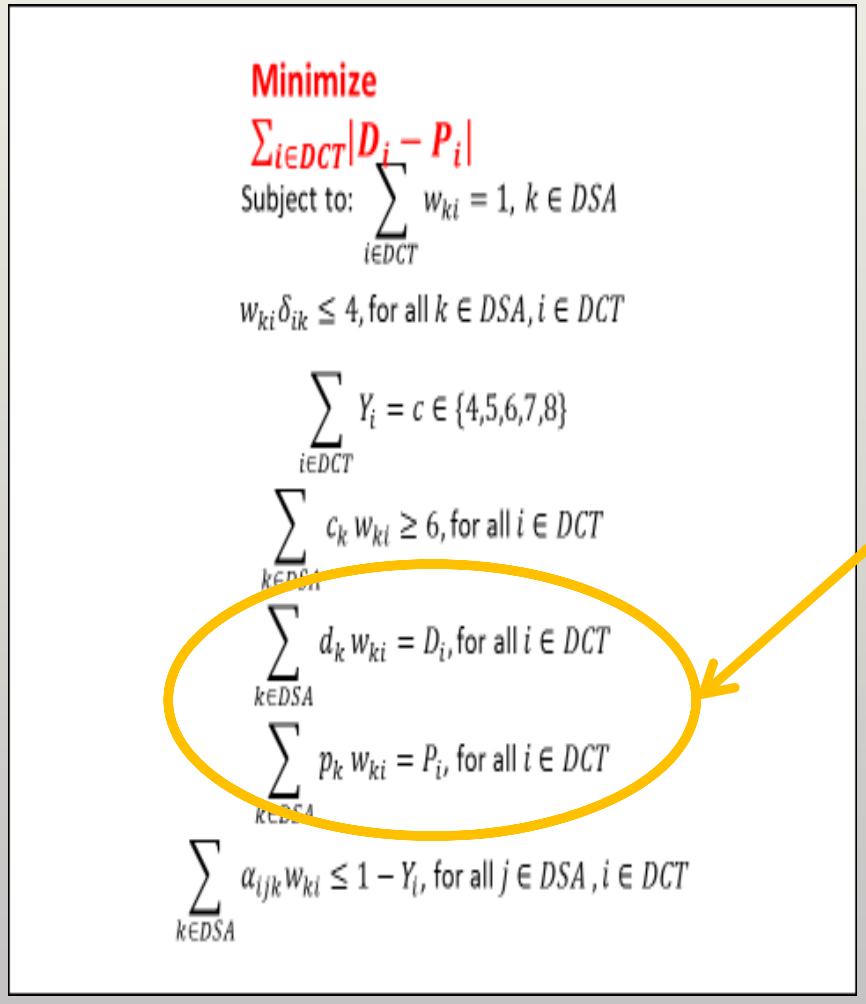

$$\text{Minimize} \quad \sum_{i \in DCT} |D_i - P_i|$$

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$$w_{ki}\delta_{ik} \leq 4, \text{for all } k \in DSA, i \in DCT$$

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- Liver supply and demand data in the model are based on 2010 data. These parameters (e.g., number of donors in a DSA) are uncertain and change is inevitable. Deterministic optimization problems can be very sensitive to such uncertainty, and the results may be suboptimal in the future.
- Model is not responsive to future transplant center behavioral changes and UNOS efforts to improve organ donations and ESLD patient access to transplant.
- Model is not adaptive to future policy changes by UNOS (e.g. changes to MELD exception point policies, or improvements in MELD score models)
  - The proposed solution might require redistricting routinely to be effective
- ***The engine for reducing disparity is organ sharing and listing behaviors. Redistricting alone is not the driver of disparity reductions***.

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Suggestions to this Forum

Recommended Steps
1. Engage a greater number of independent technical experts to collaborate on this important issue.
2. Develop an approach that improves disparity and adapts to future changes in transplant system behaviors and policies.
3. Employ rigorous “what-if” analyses for changes in organ supply/demand, wait listing behaviors, and organ acceptance behaviors to ensure solution stability and robustness.
4. This problem appears tractable and a more rigorous solution may be available in a short time.

APPENDIX

Additional Slides

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Principles for Robust Design

TABLE 1.

Principles of Complex System Design and Modeling in the Context of Liver Allocation System

	System Design Principles	Advantages
1	Explore design alternatives early	It will reduce the number of design iterations, improve reliability, and reduce cost.
2	Introducing risk, failure mechanisms, and uncertainty in system modeling	A systematic treatment of failures and risk will increase robustness of the designed system
3	Take a system-of-system approach, by first designing and testing subsystem individually, and then test them as a critical part of the overall system architecture	It will increase robustness of final integrated architecture, and better optimize the system performance.
4	Perform a detailed system modeling and validation to ensure that sub-system level functionality and behavior changes are appropriately incorporated in the model	It will prevents omission of important factors, and reduces negative effects of unintended consequences. The redesigned system performance is validated in a limited test environment.
5	Testability, Maintainability, and Recoverability prior to full deployment	A restoration to the original state is possible in the event of a design failure
6	Build a practical dynamic and adaptive control in the new system	It allows for corrective actions when model predicted and desired performance deviate, and significant changes from model assumptions are observed.
7	Perform cost-benefit analysis over the system life cycle	It will help understand the entire life-cycle cost and benefits, and will allows proper incorporation of system end-of-life costs

Source: Modeling the Allocation System: Principles for Robust Design before Restructuring, (2015), *Transplantation,* editorial, 10.1097/TP.0000000000000656. PMID:25651120

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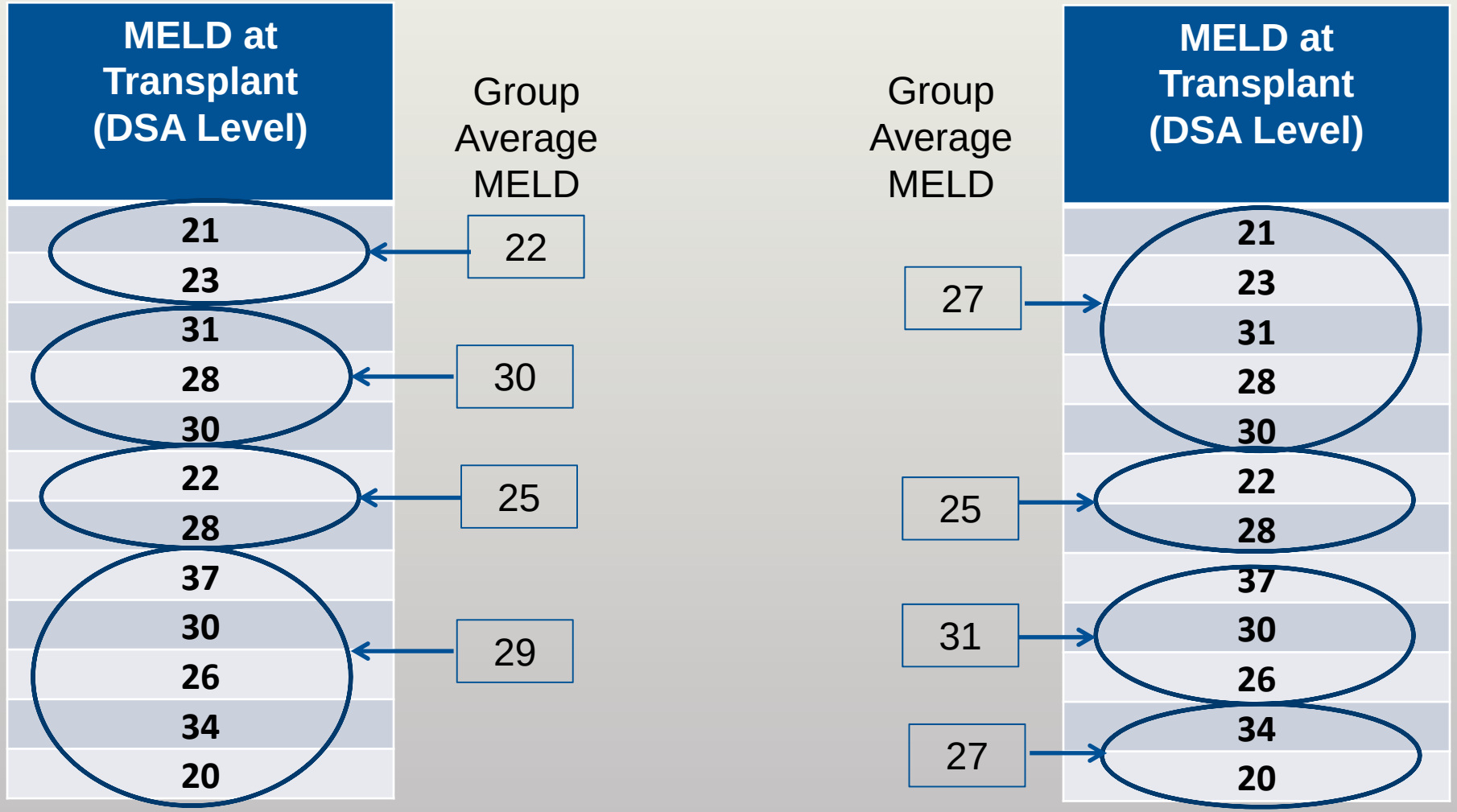
Simply Regrouping Does Not Change Disparity



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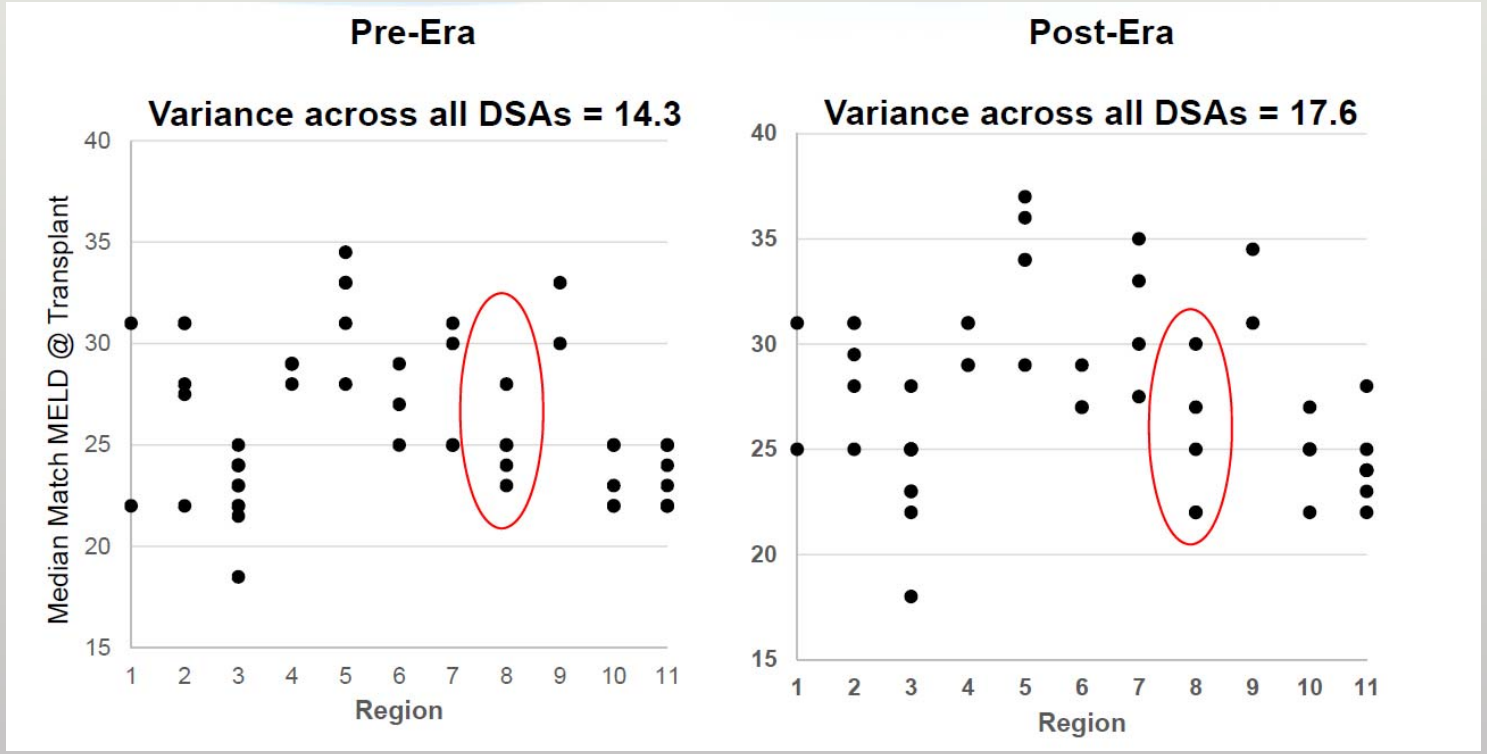
Is Variability in MELD at Transplant the Correct Type of Disparity Measure?

Variability across DSAs in MELD at transplant increased after Share 35 (Post-Era: 6/18/2013-6/17/2014) vs. Pre-Era (6/18/2012-6/17/2013)



Source: Share 35 Liver Policy Analysis at 1 Year. OPTN Report

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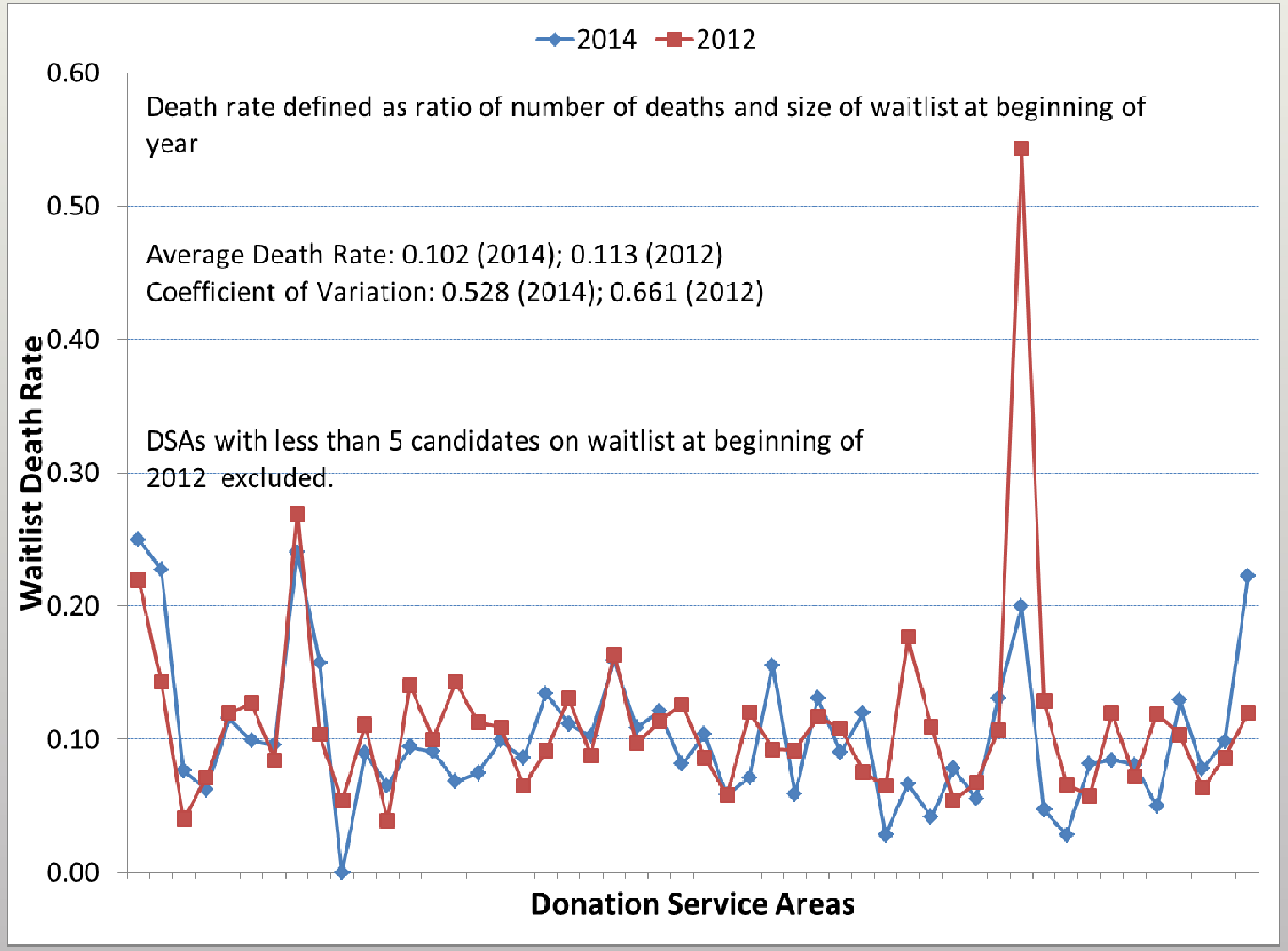
Disparities in Waitlist Mortality across DSAs decreased after Share 35



Note: Disparity measured using coefficient of variation, which is defined as the ratio of standard deviation to the mean. Results obtained from analyses of public data from SRTR website. Not peer-reviewed.

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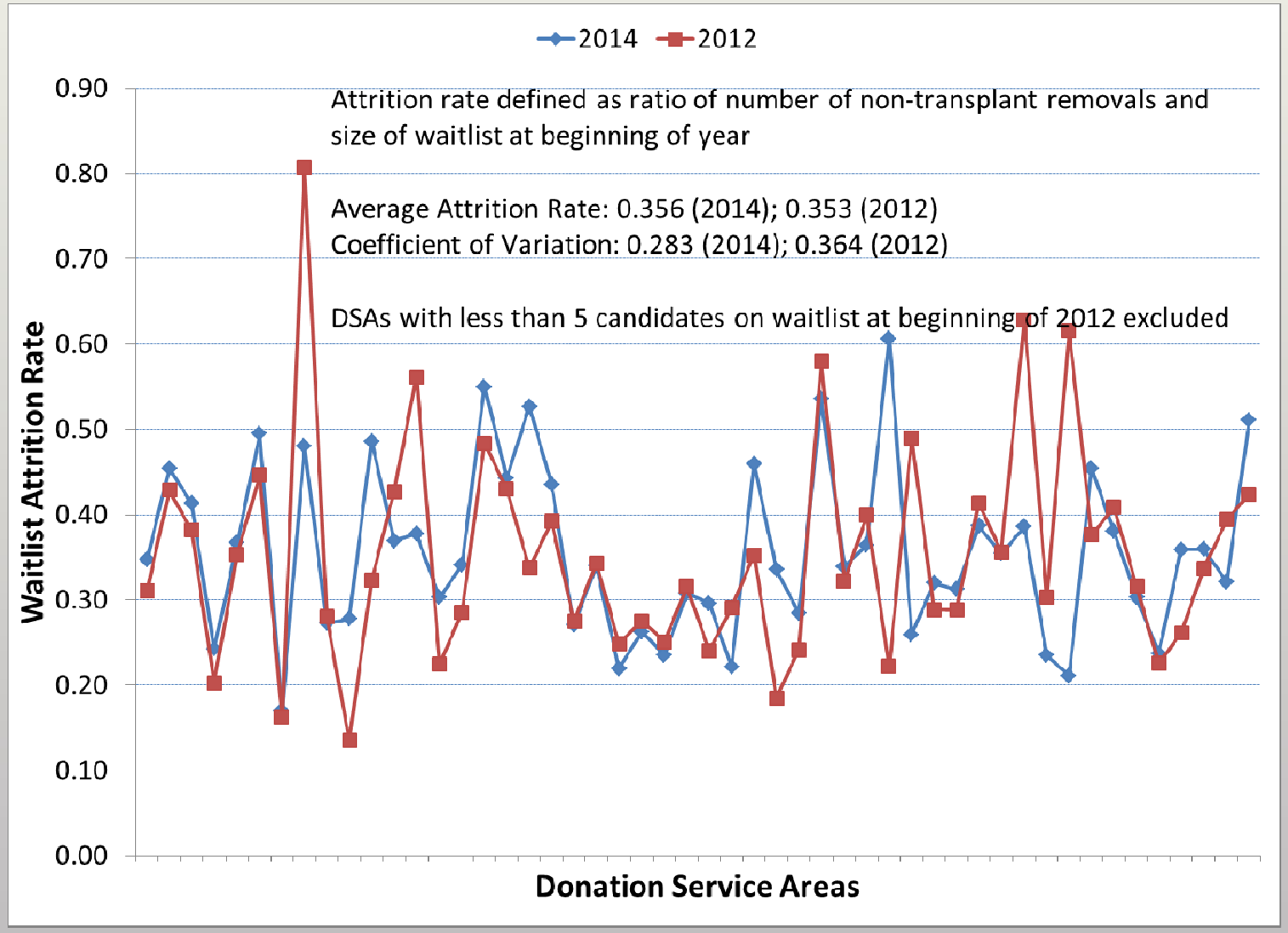
Disparities in Waitlist Attrition across DSAs decreased and after Share 35



Note: Disparity measured using coefficient of variation, which is defined as the ratio of standard deviation to the mean. Results obtained from analyses of public data from SRTR website. Not peer-reviewed.

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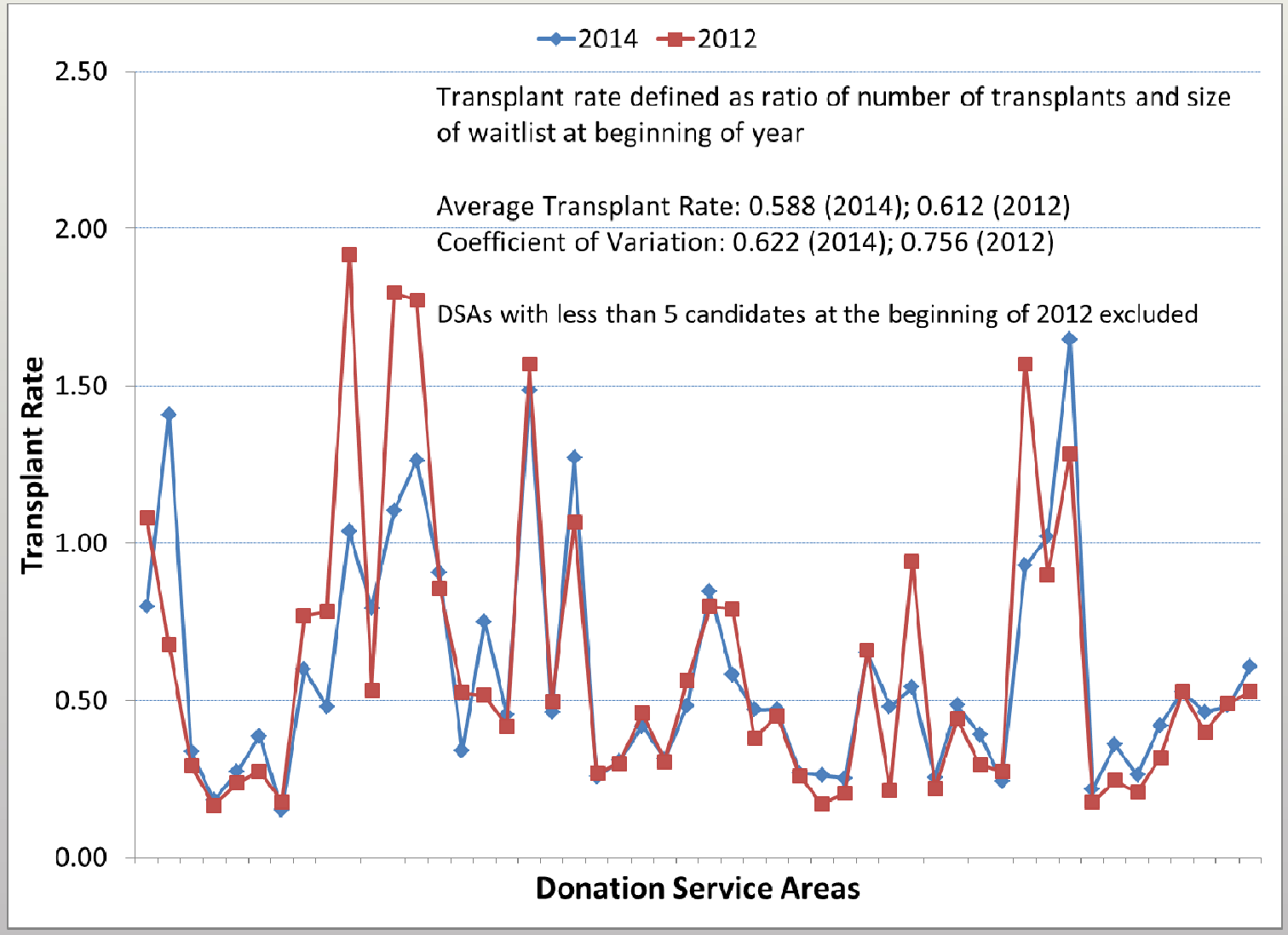
Disparities in Transplant Rates across DSAs decreased after Share 35



Note: Disparity measured using coefficient of variation, which is defined as the ratio of standard deviation to the mean. Results obtained from analyses of public data from SRTR website. Not peer-reviewed.

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Optimizing Ratios vs. Differences

- Minimize $\sum_{i=1}^{n} |D_i - S_i|$
- Reduces differences in the numbers of organs demanded by unit i and number supplied.
- Units with different magnitudes of supplies and demands may have very different *transplant rates*.
- In an uncertain, dynamic system involving waiting queues, the difference in service rate does not provide an appropriate measure for queue performance

- Minimize $\sum_{i=1}^{n} |\frac{D_i - S_i}{D_i}|$
- Reduces differences in the proportion of organ demand that is unsatisfied at unit i
- Preferable for disparity, because it ensures units will have more similar *transplant rates*.
- In an uncertain, dynamic system involving queues, the ratios of demand and supply rates do provide a more appropriate measure for queue performance

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Deterministic Optimization Model Solutions May be very Sensitive to Small Changes in Model Parameters

- Numerical Example:

Minimize:

$$-5500x_1 - 6100\,x_2 + 100x_3 + 199.9x_4$$

Subject to:

$$0.05x_1 + 0.6\,x_2 - 0.01x_3 - 0.02x_4 \leq 0$$

and other constraints…

- Optimal value is 8,820.

- Constraint now changes

Minimize:

$$-5500x_1 - 6100\,x_2 + 100x_3 + 199.9x_4$$

Subject to:

$$0.05x_1 + 0.6\,x_2 - 0.01x_3 - 0.0196x_4 \leq 0$$

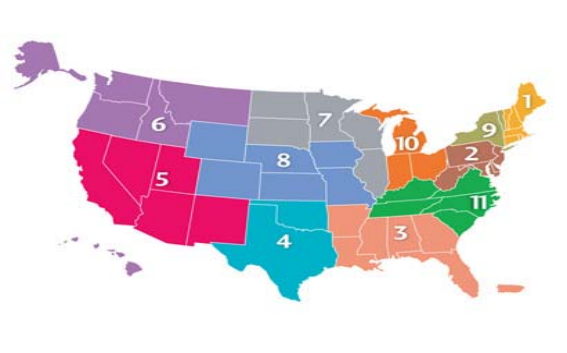
and other constraints…

- Optimal value is 6,929.
- 2% change in model parameter led to 21% decrease in objective!
- Techniques to generate more robust solutions are available for such problems. For an example with a practical network design applications that match supply to demand, see Robust distribution network reconfiguration,

Source: Ben-Tal A, El Ghaoui L, and Nemirovski A. Robust optimization. Princeton University Press, 2009.

Managing Listing Behaviors and Broader Sharing are Engine for Disparity Reductions

- **<u>Managing Listing Behaviors and Broader Sharing</u>** are the fundamental tools.



Adult Liver Allocation
Regional Status 1A
Regional Status 1B
Local/Regional MELD 40-35 [Share 35]
Local MELD >15 [Share 15]
…

A) Optimize Redistricting

B) Optimize Allocation Rules

C) Optimize DSA-to-DSA Sharing

Disparities occur at the DSA and transplant center levels. A prudent strategy would employ features of all of the above.

Sources: A) OPTN Website; C) **Improving Geographic Equity in Kidney Transplantation Using Alternative Kidney Sharing and Optimization Modeling,**

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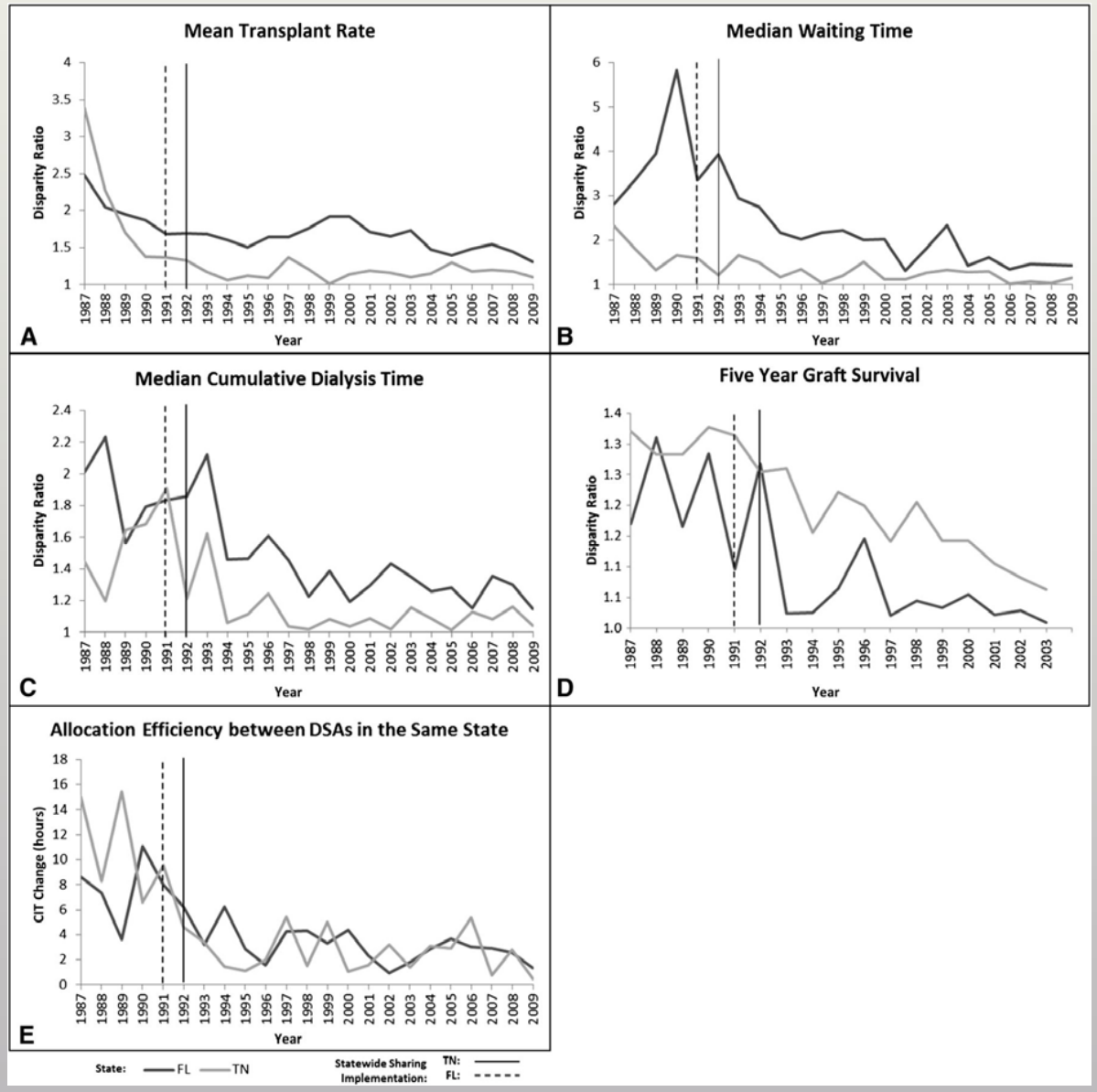
Historical Examples of Broader Sharing

- Share 15 (2005)
  - Offers deceased-donor liver to candidates with MELD $\geq$ 15 before making offer to a candidate listed at a local DSA where organ was procured.
- Share 35 (2013)
  - Promoted regional allocation for candidates with MELD $\geq$ 35
- Statewide Sharing (Kidney Transplantation; 1992)
  - Tennessee and Florida obtained a waiver from UNOS whereby local allocation was replaced by statewide allocation.

Statewide Sharing Results (Kidney Transplantation)



Improvement of geographic allocation disparity in Tennessee and Florida over time between 1987 and 2009. Florida (FL) and Tennessee (TN) implemented Statewide Sharing variances in 1991 and 1992, respectively (dotted and solid vertical line). Geographic disparity is measured for four disparity indicators (transplant rate, waiting time, dialysis time, and 5-year graft survival) using an allocation disparity ratio. Geographic disparity improves as the allocation disparity ratio nears 1.0. A disparity ratio of 1.0 suggests that there is no geographic disparity between DSAs within a state. Panel E illustrates allocation efficiency by demonstrating the drop in cold ischemic time (CIT) difference between locally transplanted kidneys and those transplanted statewide. DSA, donor service area.

Source: The Effect of the Statewide Sharing Variance on Geographic Disparity in Kidney Transplantation in the US,

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