Geographic disparities in liver transplantation: How current metrics may fail to address the disparity

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Potential Conflicts of Interest

• Funding mechanism: 1K08DK098272
• These views are my own, and not those of the NIH or the University of Pennsylvania
• Receive no external funding for this research
• Practice in UNOS Region 2
  – DSA estimated to get increase in number of LTs
In principle, I support changes that provide lifesaving transplant to patients in greatest need.

I have concerns about the current proposal:
- Metrics of disparities
- Definitions of demand and supply/demand mismatch
- Technical aspects of the models and its outputs

Overall goal is to present data in order for the transplant community to create a system that is best for all patients.

Although data may be viewed as critical of certain regions, that is not my intention. Presenting data to inform the community on how we feel we should view disparities.

Medical School (Mt. Sinai) and Internal Medicine Residency (Columbia) in NY

I believe our system has other needs (i.e., MELD inflation, access to care, DSA-level differences in donation rates) that will have an impact that dwarfs that of redistricting.

Once metrics have been identified to evaluate novel strategies, the AST supports the use of evidence-based medicine to evaluate the objective, measurable outcomes of interest.

The AST believes that any new organ allocation policy must be evaluated for its demographic, geographic, and socioeconomic impact on liver transplantation.

Any systematic changes must give due consideration to effects on pediatric populations.

Ongoing efforts should be made to minimize and standardize MELD exceptions when possible.

The AST supports well-defined and accurate data collection that are required to make decisions regarding liver organ allocation.

Ensuring the accurate collection of data before and after change implementation is critical.

Transparency of analytic methodology, applicability, and limitations is necessary.
Stated guiding principles of UNOS

• UNOS Vision Statement: To promote long, healthy and productive lives for persons with organ failure by promoting maximized organ supply, effective and safe care, and equitable organ allocation and access to transplantation.

• UNOS Mission Statement: To advance organ availability and transplantation by uniting and supporting its communities for the benefit of patients through education, technology and policy development.
Unique aspects in evaluating geographic disparities in liver transplantation

• What is metric of access
  – Getting onto waitlist
  – Getting transplant if have disease
  – Severity of illness at transplantation
  – Dying on a waitlist
  – Dying overall

• Who is population at-risk
  – All patients with end-stage organ disease
  – All patients with end-stage organ disease deemed ‘transplantable’
  – All patients waitlisted

• How do define population at risk
  – Renal: USRDS
  – Liver, lung, heart....
• Message 1: Allocation MELD is neither the appropriate marker of severity of illness at transplant, nor the metric that should define geographic disparities.
• Message 2: The current system of organ allocation leads one group to be disadvantaged above all others:
• The ‘sickest’ patients.
Where are the sickest patients being transplanted?

According to OPTN/UNOS data as of 3/27/2015.
What contributes to the large differences in measures of severity of illness at transplantation between the Northeast and the Southeast regions of the country?
Percentage of deceased donor transplant recipients with whose allocation MELD is at least 10 points higher than their lab MELD, 2012-2014

According to OPTN/UNOS data as of 3/27/2015
Where are the sickest transplant recipients: Lab vs allocation MELD for all adult OLT recipients; 2012-2014

<table>
<thead>
<tr>
<th>Region</th>
<th>Median lab MELD</th>
<th>Median match MELD</th>
<th>OLT recipients with exception points</th>
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<tbody>
<tr>
<td>1</td>
<td>17</td>
<td>31</td>
<td>41.0%</td>
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<td>36</td>
<td>34.5%</td>
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• Message 3: The current MELD exception system contradicts a major recommendation of the Final Rule and must be overhauled before making major policy changes.

• Point 3 of the Final Rule: “Establishment of an objective scoring system for prioritizing patients for liver transplantation”

1-OPTN Final Rule, 42 CFR part 121, Page 14; October 20, 1999
Who is the sicker transplant recipient?

56 year-old male with decompensated HCV cirrhosis
Lab MELD=22
Allocation MELD=22

56 year-old owner of several gyms; HCV cirrhosis complicated by HCC; treated with TACE 18 months ago
Lab MELD=8
Allocation MELD=34
Flaws with allocation MELD: Not a measure of severity of illness (all exceptions)

Waitlist outcomes based on MELD exceptions from 2005-2012*

- Listed with MELD exception
- Listed without MELD exception

*Adapted from Northup et al, Hepatology 2015;
Lab MELD is the predictor of transplant survival benefit: HCC versus non-HCC

Thus, the HCC MELD exception policy unintentionally resulted in a dramatic reduction in transplant-related survival benefit leading to **thousands of years of cumulative “lost” survival benefit** as compared to transplanting patients with high MELD scores.

• Message 4: Number of waitlisted patients is a flawed metric of demand.
Who is ‘disadvantaged’ and not accounted for in waitlist metrics defining organ demand

Percentage of 5-state Medicaid beneficiaries with decompensated cirrhosis or HCC waitlisted for LT, 1999-2009

1-Goldb; 97; 4-Mathur AK, et al. Transplantation 2014; 98(1): 94-99
Who may be ‘advantaged’ in waitlist metrics due to higher rates of waitlisting

• Patients with end-stage liver disease living in areas with:
  – Greater transplant center density
  – Increased market competition

• Transplant center density leads to:
  – Increased listing for organ transplant
  – Increase allocation MELD at transplant

Percentage of 5-state Medicaid ESLD patients listed for LT based on local LT center density, 2006-2014

p<0.001
Percentage of 5-state Medicaid ESLD listed for LT based on distance to closest LT center, 2006-2014

\[ p < 0.001 \]
LI 9.3 Centers performing adult liver transplants in 2011, within OPTN regions
Best metric of true demand: Age-adjusted death rates from HCC and chronic liver disease based on CDC death data, 2010-2013*

UNOS Vision Statement:
To promote long, healthy and productive lives for persons with organ failure by promoting maximized organ supply, effective and safe care, and equitable organ allocation and access to transplantation.

Where do geographic disparities in care for persons with organ failure really exist?

<table>
<thead>
<tr>
<th>Age adjusted death rate per 100,000 population, 2010-2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.0-14.9</td>
</tr>
<tr>
<td>15.0-17.5</td>
</tr>
<tr>
<td>17.7-19.7</td>
</tr>
<tr>
<td>20.3-34.2</td>
</tr>
</tbody>
</table>


Hawaii, Alaska not shown
Message 5: Measures of organ demand, and supply/demand ratio heavily influenced by waitlisting practices. Hence, waitlist demand ≠ true demand.
Supply/demand ratio of eligible deaths/listed patients, 2012

- >0.8
- 0.55-0.75
- 0.25-0.49
- <0.25

Hawaii, Alaska not shown

* Consistent with definition used by SRTR

Supply/demand ratio for 2012

Supply = eligible deaths; Demand = Patients on waitlist from ESLD or HCC in 2012

Lower supply/demand ratio = greater shortage of organs

* Based on CDC cause-of-death data

Supply/demand ratio of eligible deaths/deaths from liver disease, 2012

- 0.40-0.45
- 0.30-0.23
- 0.25-0.49
- <0.25

Hawaii, Alaska not shown

* Consistent with definition used by SRTR
Measures of waitlist mortality do not necessarily capture true burden of death from liver disease:

% of waitlist deaths among total number of deaths from liver disease, 2012*

Higher percentage suggests overestimation of burden of mortality from liver disease based on waitlist data alone

<table>
<thead>
<tr>
<th>Area</th>
<th>Deaths from ESLD</th>
<th>Waitlist deaths</th>
<th>% all liver deaths captured by waitlist deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1,000</td>
<td>100</td>
<td>10%</td>
</tr>
<tr>
<td>2</td>
<td>1,000</td>
<td>50</td>
<td>5%</td>
</tr>
<tr>
<td>3</td>
<td>1,000</td>
<td>25</td>
<td>2.5%</td>
</tr>
</tbody>
</table>
Absolute number of deaths from liver disease on the waitlist versus the overall population

% of waitlist deaths among total number of deaths from liver disease, 2012*

*Deaths on the waitlist defined as the number adults removed from the waitlist for death or clinical deterioration in 2012 according to OPTN/UNOS data; number of overall deaths defined by CDC cause-of-death data from chronic liver disease or HCC in 2012 according to cdcwonder.gov

Higher percentage suggests overestimation of burden of mortality from liver disease based on waitlist data alone

% of waitlist deaths among total number of deaths from liver disease, 2012:
- >11.5%
- 6.2-9.9%
- 3-5.9%
- ≤2.7%

Hawaii, Alaska not shown

- 2,083 total deaths from liver disease
- 308 waitlist deaths
- 15 million adults

- 1,807 deaths from liver disease
- 209 waitlist deaths
- 10 million adults

- 3,238 deaths from liver disease
- 77 waitlist deaths
- 14.8 million adults
Message 6: Under redistricting, the greatest increase in transplants will shift to the donor service areas with the lowest donation rates.
Sharing and Shifting of Livers Across OPOs

• Published literature states redistricting will not transfer livers from high-performing OPOs to low-performing OPOs.
  – Metrics of OPO performance had limitations
    • O:E liver yield: Only includes donors with at least one organ transplanted
      – OPO doesn’t obtain consent, can’t be donor, not in O:E yield
    • Unadjusted liver donor conversion ratio (not standard SRTR metric)
      – (Livers transplanted) / (eligible deaths)

• Categorization of importer or exporter considered binary
  – Net import or export of 5 vs 100 organs considered same

• What about other metrics?
  – Authorization rates
  – Replicate unadjusted liver donor conversion ratio
  – Donors per million

• What about volume of imports and exports over 5 years?

Low performance, highest importer

Projected changes in transplant volume over 5 years with 4 districts, 3 points, 150 miles

Intermediate to high performance, highest exporter
Message 7: LSAMs constraints and assumptions may prevent the software from appropriately accounting for the realities of the current allocation system.
2.4.2 Standardized Behavior

The OPTN allocation guidelines are extensive, but they do not eliminate all ambiguity. In practice, there is some amount of variation in policy and behavior between different OPOs and transplant centers. However, LSAM assumes that all centers and OPOs implement allocation policies in the same way and exhibit the same organ acceptance behavior. LSAM also does not model any directed or expedited allocation of donated organs.

2.4.3 Status Matching and HCC

Patients who underwent transplant in real life have no status updates in their patient records past the transplant date, so status updates from other patients were appended to fill out their LSAM patient histories in the SRTR-provided status input file. These patients are matched on expected mortality but not on specific diagnosis, so LSAM’s ability to predict outcomes in diagnosis subgroups (such as HCC patients) is limited.

2.4.4 Single Listings, Single Organs

LSAM does not model patients who list at multiple transplant centers or who are listed for multiple organs. LSAM also does not model multi-organ transplants or split livers.
LSAM Constraints

1. “LSAM also does not model any directed or expedited allocation of donated organs.”

- 59 (1.0%) of organ offers in 2012 considered “bypasses”
- 108 (1.8%) of organs transplanted at positions ≥500

2. “LSAM does not model patients who list at multiple transplant centers”

- 1,354 (5.2%) of adults on list in 2012 waitlisted at >1 transplant center

3. “LSAM does not model patients who are listed for multiple organs”

- 2,132 (8.0%) of all adults on list in 2012

4. “LSAM also does not model multi-organ transplants”

- 471 (8.4%) of all adult LTs in 2012

5. “LSAM assumes that all centers and OPOs implement allocation policies in the same way and exhibit the same organ acceptance behavior.”
Five considerations for future changes to system of liver transplantation

1. Severity of illness metrics need to consider who is truly the sickest and not artificially sick from “MELD inflation”
2. Overhaul MELD exception system and determine the impact of this before changing policies.
   • Recently accepted policies (HCC cap) do not go far enough
3. Need to consider outcomes of broader population with ESLD
   • Centers should submit data on all OLT referrals and decisions to measure true demand and listing rates
   • ? New UNOS metric
   • Create collaborative/national effort to create liver-equivalent of USRDS
4. Refine LSAM to simulate the current system of organ allocation
5. Focus on improving donation rates in areas with lowest rates
   • Certain areas with lowest rates have greatest gains with redistricting
   • Change metrics of OPO performance and reported OPO data
   • Do not dis-incentivize OPO risk-taking (single-organ older donors)