Regulatory Realities – Redefining Benefit of Lung Transplant in the Current Era

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Disclosure

I have no conflicts of interest to declare
Background

Organ Allocation Principles

- Based upon medical urgency
- Avoid futile transplants
- Minimize the effect of waiting time
- Broader geographic sharing

DHHS. OPTN Final Rule. 42 CFR-Part 121. 1999
IOM Report 2000
Background
Lung Allocation Score (LAS) Development

- Developed by the lung allocation subcommittee of the OPTN & the SRTR
- Transplant candidates > 12 years of age
- Allocation based on a lung allocation score, rather than waiting time
- Implemented in May 2005

LAS Calculation

1. Waitlist urgency measure (WL\textsubscript{i}): Expected days lived in next year on waiting list
2. Post-transplant survival measure (PT\textsubscript{i}): Expected days lived during 1\textsuperscript{st} year post-transplant
3. Benefit\textsubscript{i} = PT\textsubscript{i} – WL\textsubscript{i}
4. Raw score = Benefit\textsubscript{i} – WL\textsubscript{i} = PT\textsubscript{i} – 2* WL\textsubscript{i} (Range $-730$ to $365$)
5. LAS is obtained by normalizing the raw score (Range 0 to 100)
LAS Calculation

1. Waitlist urgency measure (WL<sub>i</sub>): Expected days lived in next year on waiting list
2. Post-transplant survival measure (PT<sub>i</sub>): Expected days lived during 1<sup>st</sup> year post-transplant
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4. Raw score = Benefit<sub>i</sub> − WL<sub>i</sub> = PT<sub>i</sub> − 2* WL<sub>i</sub> (Range −730 to 365)
5. LAS is obtained by normalizing the raw score (Range 0 to 100)
Effects of LAS on Waitlist
Number of Candidates Awaiting Lung Transplant

Active
Inactive
All

Year
Candidates

0 1000 3000
Waitlist Mortality

Effects on Transplant Rates & Survival
Effect of LAS Implementation on Short-term Survival
US Experience

Early Survival

Ninety-day Mortality and Major Complications Are Not Affected by Use of Lung Allocation Score
Jonathan D. McCarr, MD,*, Josh Mooney, BS,* Jacob Quall, BA,* Amanda Arrington, MD,* Cynthia Herrington, MD,* and Peter S Dahlenberg, MD, PhD*

One-Year Survival

The impact of the lung allocation score on short-term transplantation outcomes: A multicenter study
Benjamin D. Kozower, MD,* Bryan F. Meyers, MD,* Michael A. Smith, MD,* Nitro G. De Oliveira, MD,* Stephen B. Cassel, MD,* Tracey J. Guthrie, RN,* Heekwon Wang, PhD,* Beverly J. Ryan, AGNP,* K. Robert Shen, MD,* Thomas M. Daniel, MD,* and David R Jones, MD*

Lung Allocation Score for Lung Transplantation*
Impact on Disease Severity and Survival
Cynthia J. Gries, MD, MSc; Michael S. Mulligan, MD, FCCP; Jeffrey D. Edelman, MD, FCCP; Ganesh Raghu, MD, FCCP; J. Randall Curtis, MD, MPH, FCCP; and Christopher H. Goss, MD, MSc, FCCP

• No difference in 90 day mortality or PGD
• 2008

• No difference in hospital or 1 year survival
• Higher PGD, ICU LOS
• Decreased waiting list#
• 2008

• No difference in 1 year survival
• No change in lung transplant candidates but significant change in recipient diagnosis
• 2007
Effect of LAS Implementation on Short-term Survival European Experience

Evaluation of Short-Term Outcome after Lung Transplantation in the Lung Allocation Score Era

- No difference in LOS, 90, 180 & 1 year mortality or PGD
- 2015

Introduction of the Lung Allocation Score in Germany

AJT 2014; 14: 1318-1327

- No difference in 90-day mortality
- Decreased waiting list time
LAS and Survival

Impact of U.S. Lung Allocation Score on Survival After Lung Transplantation

No difference in 1 year survival compared to historic cohorts
Significantly increased risk of death (HR 1.46) in quintile 5 (LAS > 46)

Increasing Lung Allocation Scores Predict Worsened Survival Among Lung Transplant Recipients

5331 UNOS Recipients into LAS Quartiles: <46, 47-59, 60-79, >80

OPTN/SRTR 2012 Annual Data Report: Lung
Lung Transplant Recipients Over Time

- **Age:**
  - <12
  - 12-17
  - 18-34
  - 35-64

- **Sex:**
  - Male
  - Female

- **Race:**
  - White
  - Black
  - Hispanic
  - Asian
  - Other/Look

- **PRA:**
  - 0%
  - 1%-19%
  - 20%-79%
  - 80%-85%
  - 85%-90%
  - 90%-95%
  - 95-100%
  - Unknown

- **Diagnosis group:**
  - A
  - B
  - C
  - D
  - Other/Look

Note: Patients receiving a transplant, including multi-organ transplants and pediatric patients. Retransplants are counted.
Concurrent Increase in Regulatory Oversight

- SRTR 1-year and 3-year mortality reports
- Centers for Medicare and Medicaid Services (CMS) “conditions for participation”
  - Proposed in 2005
  - Final rule implemented in 2007

## LAS and Long-Term Survival

### Impact of the Lung Allocation Score on Survival Beyond 1 Year

*AJT* 2014; 14: 2288-2294

#### Table 1: Baseline characteristics by temporal cohort

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total transplants</td>
<td>5081</td>
<td>4628</td>
<td>7437</td>
<td></td>
</tr>
<tr>
<td>Days of follow-up</td>
<td>1429 (337, 3303)</td>
<td>1817 (967, 2593)</td>
<td>714 (345, 1170)</td>
<td></td>
</tr>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recipient age</td>
<td>51.0 (40, 58)</td>
<td>55.0 (44, 60)</td>
<td>57.0 (47, 63)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Donor age</td>
<td>29.0 (19, 42)</td>
<td>30.0 (20, 44)</td>
<td>31.0 (21, 46)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>2542 (50.0%)</td>
<td>2328 (50.3%)</td>
<td>4337 (58.3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time on waitlist (days)</td>
<td>301 (123, 578)</td>
<td>298 (106, 640)</td>
<td>76 (23, 241)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinical status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical condition</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU</td>
<td>192 (3.8%)</td>
<td>163 (3.5%)</td>
<td>603 (8.2%)</td>
<td></td>
</tr>
<tr>
<td>Hospitalized</td>
<td>300 (6.0%)</td>
<td>207 (4.5%)</td>
<td>576 (7.7%)</td>
<td></td>
</tr>
<tr>
<td>Not hospitalized</td>
<td>4543 (90.2%)</td>
<td>4257 (82.0%)</td>
<td>6258 (84.1%)</td>
<td></td>
</tr>
<tr>
<td>On ventilator</td>
<td>153 (3.0%)</td>
<td>122 (2.6%)</td>
<td>449 (6.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>On ECMO</td>
<td>8 (0.2%)</td>
<td>28 (0.6%)</td>
<td>79 (1.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Candidate diagnosis</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>A</td>
<td>2602 (51%)</td>
<td>2311 (50%)</td>
<td>2341 (33%)</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>230 (4.5%)</td>
<td>182 (4%)</td>
<td>223 (3%)</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>861 (17%)</td>
<td>674 (15%)</td>
<td>935 (13%)</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>1183 (22%)</td>
<td>1411 (30%)</td>
<td>3778 (51%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>190 (6%)</td>
<td>50 (11%)</td>
<td>2 (0.03%)</td>
<td></td>
</tr>
<tr>
<td>Ischemic time (min)</td>
<td>265 (193, 323)</td>
<td>271 (207, 340)</td>
<td>398 (238, 363)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; Diagnosis groups are: A, obstructive lung disease; B, pulmonary vascular disease; C, cystic fibrosis or immuno deficiency disorder and D, restrictive lung disease. Median and interquartile range for continuous variables; counts and percentages for categorical.  
<sup>1</sup>Kruskal-Wallis and chi-square tests for continuous and categorical variables, respectively.
LAS and Long-Term Survival

LAS effect on the one-year threshold
At what cost?
Impact of the lung allocation score on resource utilization after lung transplantation in the United States

George J. Arnaoutakis, MD, a Jeremiah G. Allen, MD, a Christian A. Marlo, MD, MPH, b Brigitte E. Sullivan, MBA, a William A. Baumgartner, MD, a John V. Conte, MD, a and Ashish S. Shah, MD a

Table 2  Post-operative Outcomes According to LAS Group

<table>
<thead>
<tr>
<th>Variables</th>
<th>Q1-3 (N = 63)</th>
<th>Q4 (N = 21)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median hospital LOS, days (IQR)</td>
<td>15 (11-22)</td>
<td>35 (23-46)</td>
<td>0.003</td>
</tr>
<tr>
<td>Median ICU LOS, days (IQR)</td>
<td>3 (2-4)</td>
<td>6 (3-15)</td>
<td>0.01</td>
</tr>
<tr>
<td>Re-admissions, n (+SD)</td>
<td>3.4 (+2.9)</td>
<td>3.3 (+2.2)</td>
<td>0.9</td>
</tr>
<tr>
<td>In-hospital-treated rejection, n (+SD)</td>
<td>1 (+1.6)</td>
<td>0 (+0)</td>
<td>0.6</td>
</tr>
<tr>
<td>In-hospital infection, n (%)</td>
<td>38 (60%)</td>
<td>16 (76%)</td>
<td>0.1</td>
</tr>
<tr>
<td>Median time of mechanical ventilation, hours (IQR)</td>
<td>31 (21-41)</td>
<td>43 (29-121)</td>
<td>0.05</td>
</tr>
<tr>
<td>Re-intubation, n (%)</td>
<td>8 (12%)</td>
<td>7 (35%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Tracheostomy, n (%)</td>
<td>9 (14%)</td>
<td>7 (33%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Renal replacement therapy, n (%)</td>
<td>10 (16%)</td>
<td>4 (19%)</td>
<td>0.7</td>
</tr>
<tr>
<td>In-hospital mortality, n (%)</td>
<td>8 (12%)</td>
<td>2 (10%)</td>
<td>0.7</td>
</tr>
</tbody>
</table>

* p-value based on results of either 1-way Student's t-test (continuous variables) or chi-square test (categorical variables).

Figure 3  Breakdown of median charges according to LAS quartile. Rank-sum comparison shows index admission and total 1-year charges were higher for LAS Q6 patients compared with LAS Q1–3 patients (p = 0.004 for index admission and p = 0.008 for total 1-year charges).
Increased Resource Use in Lung Transplant Admissions in the Lung Allocation Score Era

Bryan G. Maxwell¹, Joshua J. Mooney², Peter H. U. Lee³, Joseph E. Levitt², Laveena Chhatwani², Mark R. Nicolls², Martin R. Zamora⁴, Vincent Valentine⁵, David Weill², and Gundeep S. Dhillon²

Table 2. Comparison of Lung Transplant Admissions from Two Temporal Cohorts before and after Data-derived Joinpoint

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>50.9 ± 0.7</td>
<td>54.4 ± 0.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male</td>
<td>3,279 (51.6%)</td>
<td>5,908 (59.5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td>0.0024</td>
</tr>
<tr>
<td>White</td>
<td>5,423 (85.3%)</td>
<td>8,091 (81.5%)</td>
<td></td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>45 (6.7%)</td>
<td>147 (1.5%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>447 (7.0%)</td>
<td>722 (7.3%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>319 (5.0%)</td>
<td>686 (6.9%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>127 (2.0%)</td>
<td>276 (2.8%)</td>
<td></td>
</tr>
<tr>
<td>Payer</td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Medicare</td>
<td>1,887 (29.7%)</td>
<td>3,944 (39.8%)</td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>499 (7.8%)</td>
<td>572 (5.8%)</td>
<td></td>
</tr>
<tr>
<td>Private/HMO</td>
<td>3,669 (57.7%)</td>
<td>4,838 (48.6%)</td>
<td></td>
</tr>
<tr>
<td>Self-pay/other</td>
<td>306 (4.8%)</td>
<td>568 (5.7%)</td>
<td></td>
</tr>
<tr>
<td>Major medical comorbidities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>1,324 (20.8%)</td>
<td>3,174 (32.0%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>746 (11.7%)</td>
<td>2,854 (28.8%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Clinical characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical status prior to transplant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not hospitalized</td>
<td>5,797 (81.1%)</td>
<td>8,157 (82.2%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>564 (8.9%)</td>
<td>1,765 (17.8%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>On ECMO</td>
<td>39 (0.6%)</td>
<td>103 (1.0%)</td>
<td>0.25</td>
</tr>
<tr>
<td>LAS primary diagnosis group</td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>A (obstructive lung disease)</td>
<td>2,874 (45.2%)</td>
<td>3,051 (30.8%)</td>
<td></td>
</tr>
<tr>
<td>B (pulmonary vascular disease)</td>
<td>277 (4.3%)</td>
<td>281 (2.8%)</td>
<td></td>
</tr>
<tr>
<td>C (CF/immunodeficiency)</td>
<td>933 (14.7%)</td>
<td>1,227 (12.4%)</td>
<td></td>
</tr>
<tr>
<td>D (restrictive lung disease)</td>
<td>1,995 (31.4%)</td>
<td>4,811 (48.5%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>282 (4.4%)</td>
<td>552 (5.6%)</td>
<td></td>
</tr>
</tbody>
</table>

Definition of abbreviations: CF = cystic fibrosis; ECMO = extracorporeal membrane oxygenation; LAS = lung allocation score; HMO = health maintenance organization.
Increased Resource Use in Lung Transplant Admissions in the Lung Allocation Score Era

Bryan G. Maxwell¹*, Joshua J. Mooney²*, Peter H. U. Lee³, Joseph E. Levitt², Laveena Chhatwani², Mark R. Nicolls², Martin R. Zamora⁴, Vincent Valentine⁵, David Welli², and Gundeep S. Dhillon²

Figure 1. Total hospital charges per admission for patients undergoing lung transplant (black) and other solid-organ transplant (gray). Dotted lines denote ±standard error.
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Figure 2. Percentage of admissions resulting in routine discharge to home, home health, or other facilities. LAS = lung allocation score.
In post-LAS era:
- Length of stay have increased
- Tracheostomy & ECMO rates post-transplant have increased
- Disposition to SNFs & rehab hospitals have increased
Since LAS implementation...

- Decreased number of wait list patients and waiting list time per patient
- Decreased waiting list mortality, initially, now increasing
- Recipient Characteristics Shift
  - Older patients
  - Sicker Patients
  - Group D / ILD recipient favored
- High LAS scores associated with increased post-transplant mortality
- But, No change in overall survival at 1 year
But ...

- Long-term survival appears to have worsened
- Increased resource utilization
- Indirect evidence of increased morbidity
Is there a pullback?
Candidates waiting for lung transplant by LAS

![Graph showing candidates waiting for lung transplant by LAS over years from 2004 to 2016 with different age groups represented by various symbols and lines. The graph indicates a decrease in the percentage of candidates waiting for lung transplant over the years, with a notable decline in the 40-50 age group.](image-url)
Total Lung Transplants by LAS

Year

Transplants
0 200 400 600

< 35
35-< 40
40-< 50
50-< 60
60-100

American Journal of Transplantation
pages 363-433, 2 JAN 2018 DOI: 10.1111/ajt.14562
Since 2014

- The percentage of candidates with LAS > 50 is decreasing
- The waitlist mortality for patients with LAS > 50 is rising
- The total number of transplants for LAS > 50 is decreasing
Survival Benefit of Lung Transplantation in the Modern Era of Lung Allocation

David M. Vock\textsuperscript{1}, Michael T. Durheim\textsuperscript{2,3}, Wayne M. Tsang\textsuperscript{4}, C. Ashley Finlen Copeland\textsuperscript{3}, Anastasios A. Tsiatis\textsuperscript{5}, Marie Davidian\textsuperscript{5}, Megan L. Neely\textsuperscript{2,6}, David J. Lederer\textsuperscript{7}, and Scott M. Palmer\textsuperscript{2,3}

Survival Benefit of Lung Transplantation in the Modern Era of Lung Allocation

David M. Vock¹, Michael T. Durheim²,³, Wayne M. Tsuang⁴, C. Ashley Finlen Copeland⁵, Anastasios A. Tsiatis⁶, Marie Davidian⁵, Megan L. Neely²,⁶, David J. Lederer⁷, and Scott M. Palmer²,³
Summary

- Implementation of LAS shifted the organs towards older & sicker patients
- Concurrent increase in regulatory pressures, probably led to:
  - Increased focus on 1-year survival
  - Worsening long term outcomes
  - Increased resource utilization to maintain 1-year outcomes
- Risk aversion leading to decreased number of transplants in the higher LAS groups
Thank You