Global Research in Chronic Health Issues

Access to Liver Transplantation: Gender, Race and Geographic Disparities...Policy Implications

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Learning Objectives

- To explore the effect of race, gender and geographical location on access to liver transplantation in the United States

- To explore the opportunities to influence health care policy from a global perspective
Liver Transplantation

- Treatment Modality for End Stage Liver Disease

http://aphilosopherstake.com/2012/06/12/organ-procurement-are-changes-needed-to-ensure-fairness/
United Network for Organ Sharing (UNOS)
Liver Transplantation in the United States
- Over 121,000 liver transplants have been performed since 1988
- Approximately 6,700 liver transplants performed annually
- Approximately 11,000 are added to the list each year
- Approximately 17,000 continue to wait for a liver transplant
- Approximately 1,400 are removed from the list annually due to death or becoming too ill

Demand Far Exceeds Supply!

US Federally Designated Organ Allocation System
- Era 1 (pre-1997): Time waiting/place
- Era 3 (2002-present): Model for End Stage Liver Disease (MELD)

MELD Score =
10 \{0.957 \text{Ln}(\text{Scr}) + 0.378 \text{Ln}(\text{Tbil}) + 1.12 \text{Ln}(\text{INR}) + 0.643\}
Progress Made & Problem Identification

- **MELD** (acuity based model with highest acuity prioritized for transplant)
  - Implementation February 27, 2002
  - Resulted in fewer End State Liver Disease (ESLD) patients being listed for transplant
  - Fewer ESLD patients dying on the waiting list

- Does geographic disparity (established by the Institute of Medicine in 1999) still exist?
- Are there other variables that influence access besides medical need/acuity?
- Significant GAP evaluating Current Allocation Era (MELD)
Theoretical Model: Access to Care

Anderson Behavioral Model: Phase 1 (1960s)

- Predisposing
- Enabling
- Need
- Use of Health Services

Demographic
- age
- gender

Social Structure
- education
- occupation
- race

Health Beliefs
- attitudes, values
- knowledge about health

Personal/Family
- “know-how” to navigate the system
- income
- insurance

Community
- facilities
- personnel
- distribution of resources
- geography

Perceived care seeking adherence

Evaluated Professional Measure and evaluation of need

MELD
- weight
- height
- blood type
- diagnosis
- body mass index

Anderson 1968, 1995
Study Purpose

- To increase the understanding and the effect of specific predisposing, enabling and need variables on access to liver transplantation
Methods

Secondary data analysis of large national research database: Scientific Registry of Transplant Recipients (SRTR) collected by the Organ Procurement and Transplantation Network (OPTN)

Population
- All individuals wait-listed for cadaveric liver transplant between 2002 to 2007
- Exclusions: <18 years old, Status 1 (acute liver failure), non-primary liver transplant, living donor recipients, split liver recipients, those removed from the list for reasons other than cadaveric transplant (death, deterioration, improvement, living donation, other)

Sample (total: 32,566):
- Wait listed patients: 15,448
- Transplanted patients: 17,118
Study Aims

**Aim 1:** Describe those who received a liver transplant between 2002 and 2007 compared with those who continue to wait for a liver transplant during this same period.

**Aim 2:** Examine the factors associated with hazard of transplant between 2002 and 2007, including those predisposing, enabling, need variables described including 11 geographical UNOS regions.
Statistical Methods

- **Aim 1**
  - To describe those liver transplants and candidates who continue to wait during the time-frame studied (2002-2007)
  
  - **Descriptive statistics** were used to address Aim 1 of the study.
Findings Aim 1

$H_0_1$: Higher rates of liver transplant will be associated with younger male Caucasians with higher incomes and higher education who are heavier, taller and with higher MELD scores.

- Male
- Caucasian
- Older
- Taller
- Heavier
- Higher MELD scores
Statistical Method

- **Aim 2**
  - To investigate the effects of the defined variables on hazard of transplant
  - To investigate the effects of the same predisposing, enabling and need variables on hazard of transplant for each of the 11 UNOS Regions
  - **Univariate and Multivariate Cox Regression Models**
Statistical Analysis

Cox Proportional Hazard Analysis

- Survival analysis that handles censoring
- Regression analysis that handles continuous predictors, categorical predictors (by encoding them as dummy variables) and time-varying covariates (MELD)
- The hazard function is the probability that an individual will experience the event (transplant) within a small time interval, given that the individual has survived up to that point. It can therefore be interpreted as the risk of transplant at time \( t \).

Cox Regression

\[
\lambda (t) = \lambda_0 (t) \exp (\beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_k X_k) = \lambda_0 (t) \exp (\beta_1 X \text{ predisposing} + \beta_2 X \text{ enabling} + \beta_3 X \text{ need}) = \lambda_0 (t) \exp (f(X))
\]
# Multivariate Model of Access to Liver Transplant

**UNOS Data 2002-2007**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Parameter Estimates</th>
<th>Standard Error</th>
<th>Hazard Ratio(CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Predisposing Factors</strong></td>
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</tr>
<tr>
<td>Gender$^1$</td>
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<td></td>
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</tr>
<tr>
<td>Female</td>
<td>-0.09609</td>
<td>0.2317</td>
<td>0.908** (.868-.951)</td>
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<tr>
<td>Race$^2$</td>
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<tr>
<td>African Am</td>
<td>-0.09253</td>
<td>0.02816</td>
<td>0.912* (0.863-0.963)</td>
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<tr>
<td>Hispanic</td>
<td>-0.18238</td>
<td>0.02612</td>
<td>0.833** (0.792-0.877)</td>
</tr>
<tr>
<td>Asian/Other</td>
<td>0.17437</td>
<td>0.02695</td>
<td>1.191** (1.129-1.255)</td>
</tr>
<tr>
<td>Age$^3$</td>
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<tr>
<td>31-45</td>
<td>0.13437</td>
<td>0.04797</td>
<td>1.144* (1.041-1.257)</td>
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<tr>
<td>46-60</td>
<td>0.16595</td>
<td>0.04577</td>
<td>1.118* (1.079-1.291)</td>
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<tr>
<td>61-75</td>
<td>0.23694</td>
<td>0.04833</td>
<td>1.267**(1.153-1.393)</td>
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<tr>
<td><strong>Enabling Factors</strong></td>
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<tr>
<td>Primary Payer$^4$</td>
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<tr>
<td>Medicaid</td>
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<td>1.039 (0.993-1.087)</td>
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<tr>
<td>Medicare/Public</td>
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<td>0.01971</td>
<td>0.995 (0.958-0.935)</td>
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<tr>
<td>Region$^5$</td>
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<tr>
<td>1</td>
<td>-0.48826</td>
<td>0.05178</td>
<td>0.614**(0.554-0.679)</td>
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<tr>
<td>3</td>
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<td>0.02691</td>
<td>2.028**(1.924-2.138)</td>
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<tr>
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<td>0.03158</td>
<td>1.119* (1.052-1.191)</td>
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<td>0.03049</td>
<td>0.555**(0.523-0.589)</td>
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<tr>
<td>6</td>
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<td>0.04613</td>
<td>1.401**(1.280-1.534)</td>
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<tr>
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<td>0.03250</td>
<td>0.884* (0.830-0.943)</td>
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<td>8</td>
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<td>0.03660</td>
<td>1.166**(1.086-1.253)</td>
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<tr>
<td>9</td>
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<td>0.03374</td>
<td>0.792**(0.741-0.846)</td>
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<tr>
<td>10</td>
<td>0.70594</td>
<td>0.03155</td>
<td>2.026**(1.904-2.155)</td>
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<td>0.31082</td>
<td>0.02455</td>
<td>1.365**(1.300-1.432)</td>
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<td><strong>Need Factors</strong></td>
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<td>Diagnosis$^7$</td>
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<td>HCC</td>
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<td>0.07071</td>
<td>1.783**(1.552-2.048)</td>
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<tr>
<td>MELD</td>
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<td>0.0007538</td>
<td>1.150**(1.149-1.152)</td>
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</table>

<table>
<thead>
<tr>
<th>UNOS Region</th>
<th>Hazard</th>
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<td>3</td>
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<td>10</td>
<td>2.026</td>
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<td>5</td>
<td>0.555</td>
</tr>
</tbody>
</table>
Hazard of Transplant by Region

UNOS Region

Hazard of Liver Transplant by Region

Hazard

UNOS Region
Findings Aim 2

$H_{o2}$: There will be differences in hazard of transplantation among 11 geographical UNOS regions.

- Increased likelihood of transplantation in Regions 3, 4, 6, 8, 10 & 11 by 104%, 12 %, 42%, 15%, 102%, and 43% respectively when compared to Region 2.

- Decreased likelihood of transplantation in Regions 1, 5, 7, & 9 by 39%, 43%, 10%, and 16%, respectively when compared to Region 2.
Findings Aim 2

- Ho$_3$: There will be disparity across race and gender in regard to access to liver transplantation among the entire population as well as among the 11 geographical UNOS regions.

- **Female Gender:** 10% less likely to be transplanted
  - Regional female gender: 3, 4, 8, and 11 ↓ by 13-20%

- **Race/AA:** 8% less likely to be transplanted
  - Regional AA: 1, 2, & 3 ↓ by 22% to 46%

- **Race/Hispanic:** 17% less likely to be transplanted
  - Regional Hispanic: 4, 5, 6, 8, & 9 ↓ by 16% to 47%

- **Race Asian:** 19% increased likelihood of transplanted
  - Regional Asian: 1, 2, 4, 5, & 9 ↑ by 22% to 120% and 10 showed ↓ by 22%
Discussion

Gender Disparity

- Current study showed differences in risk of transplant due to gender, when controlling for all other variables including acuity
- Supported potential systematic bias due to influence of creatinine in MELD acuity scale (Cholongitas, 2007)
- Possible provider-selection gender bias
- Organ Size Mis-match
- Educational Level
- Socioeconomic Status
Discussion

Racial Disparity

- Current study showed differences in risk of transplant due to race, when controlling for all other variables including acuity

- Pre-MELD implementation
  - Several studies found racial disparities
    - Race as an independent predictor of transplantation (Nair, 2002)
    - Findings by Reid (2004) and Gibbons (2003) differed which was attributed to single vs. changing MELD

- Post-MELD implementation
  - Several studies discussed racial disparities
    - Increasing rates of tx among AA and Asians (Freeman, 2004)
    - Differing trends in ethnicity across regions (Kemmer, 2008)
    - Increasing ablation and surgical resection among Asians (El-Serag, 2008)
    - Decreased percentages of Asians undergoing transplant (Siegel, 2007)
Discussion

- **Racial Disparity**
  - Racial Bias
  - Possible Provider-Selection Bias
    - Immunological Influence
    - Other
  - Socioeconomic Status
  - Educational Level (decreased and/or increased)
  - Language Literacy Issues
Discussion

Regional Disparity

- Current study reports geographic disparity associated with specific predictor variables by region

Regional Disparity existed pre-MELD
  - Differences in waiting times across regions and based on size of OPO
  - Regional Redistribution Recommendations never adopted

Post-MELD Studies
- Differences in acuity at transplant between large and small centers (Trotter, 2004)
- Center Selection and Allocation differences (Schaffer, 2003)
- Other Studies (Stahl, 2005; Roberts, 2006 etc.)
Discussion

- Limited change in regional distribution
  - Exception: MELD Share 15 Rule
- Increase in population of transplant programs
- Increase in numbers of transplant candidates (not evenly distributed)
- Differing ratios of transplant centers/donor service areas
- Differing ratios of donor service areas/region
- Existing System of Allocation not based on “geographic need” but rather historical convention
- Never been a study of “geographic need”
Limitations

- Secondary Data Analysis
  - Incomplete Data
    - Educational Level
    - More Accurate Measure of Socioeconomic Status
  - Data capture issues
    - Payer Status
- Analysis
  - Lack of Interactions
    - Region and MELD
    - Region and Race
    - Region and Gender
    - Education and Race
- Competing Risks
  - Wait list removals for death, clinical deterioration etc.
Policy Implications

- **Gender**
  - Reason(s) for disparity
  - If size/creatinine: how to correct for this?
  - Modeling to test for adjustments

- **Region**
  - Impact of DSA/Region?
  - Impact of Transplant Programs/Region?
  - Modeling Broader Sharing Proposals

- **Race**
  - Bias/Immunologic/Other
  - Testing for Interaction(s) with other variables
Future Research Initiatives

- Similar Studies at Various Levels of Allocation (DSA)
  - accounting for ratios of organ procurement organizations per region, transplant centers per donor service area, clinical expertise of transplant program, regional competition
  - may offer an opportunity to help define “geographic need”

- Quality of Life Studies to Inform Allocation Field
  - particularly in regard to age and HCC

- Studies to address the influence of language literacy, socioeconomic status and educational level on identified disparities
Future Research Initiatives

- Qualitative Work to Inform Areas of Gender and Racial Disparities
  - provider decision making process, regional allocation differences, center selection criteria and regional variances

- Outcome Analyses regarding Age, Race and Gender to Inform Potential Selection Bias

- Economic Studies to address the influence of payer type, reimbursement rate and institutional profit/non-profit status on likelihood of transplantation

- Potential International Collaborations
In Appreciation

- Sigma Theta Tau International
- Gordon and Betty Moore Foundation
- UCSF Graduate Student Research Award
- UCSF Century Club Award
- Samuel Merritt University
- Nu Xi Chapter of Sigma Theta Tau
- Inter Professional Mentors
  - Robert Newcomer PhD
  - Joe Mullan PhD
  - Peter Stock MD, PhD
  - Charlene Harrington PhD, RN
- Family and “Village” of Colleagues and Friends
  - Eric, Erin and Emily Fieberling
- Past and Future Patients
  - Amy (the 4 year old heart transplant recipient)
  - Joe (the 20-something kidney transplant recipient)
  - Wendy (the 30-something islet/pancreas transplant recipient)
  - Donor Families (known and unknown)
The moral test of any society is how it cares for the people in the dawn of life: the children; the twilight of life: the elderly; and the shadows of life: the sick and disenfranchised.

Hubert H. Humphrey
Questions