Global Research in Chronic Health Issues

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

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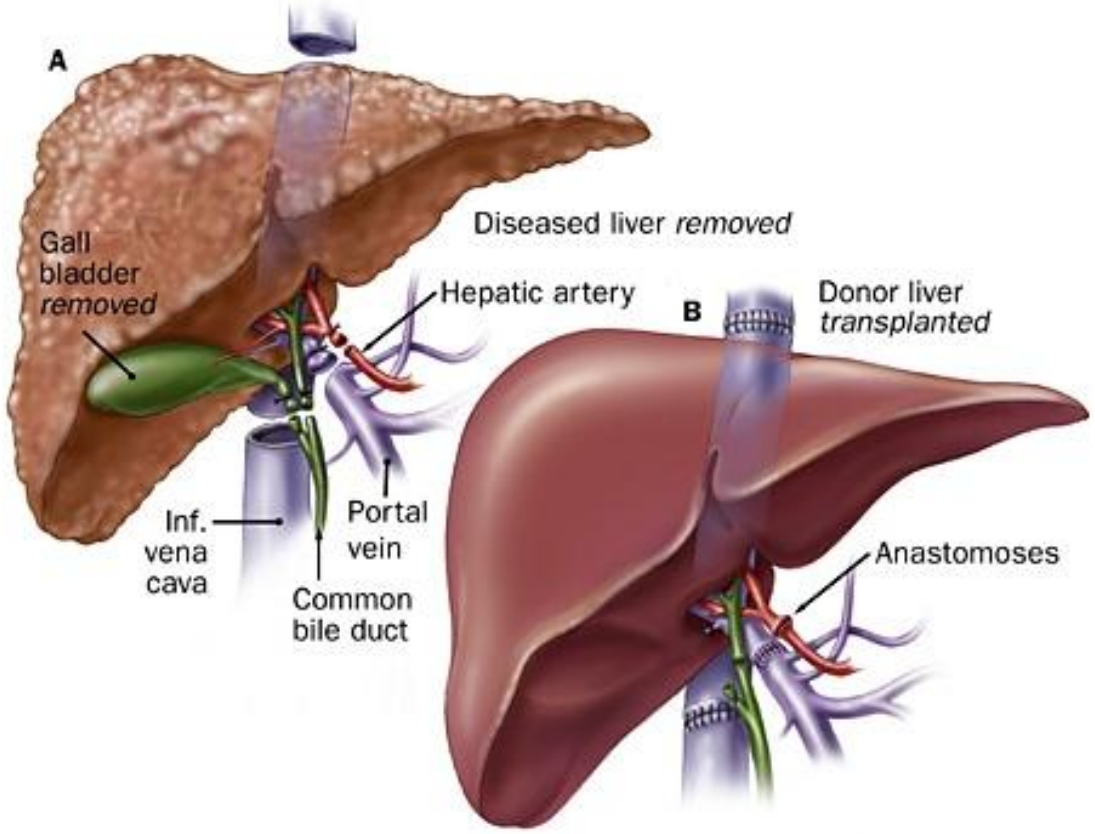
Learning Objectives

- 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

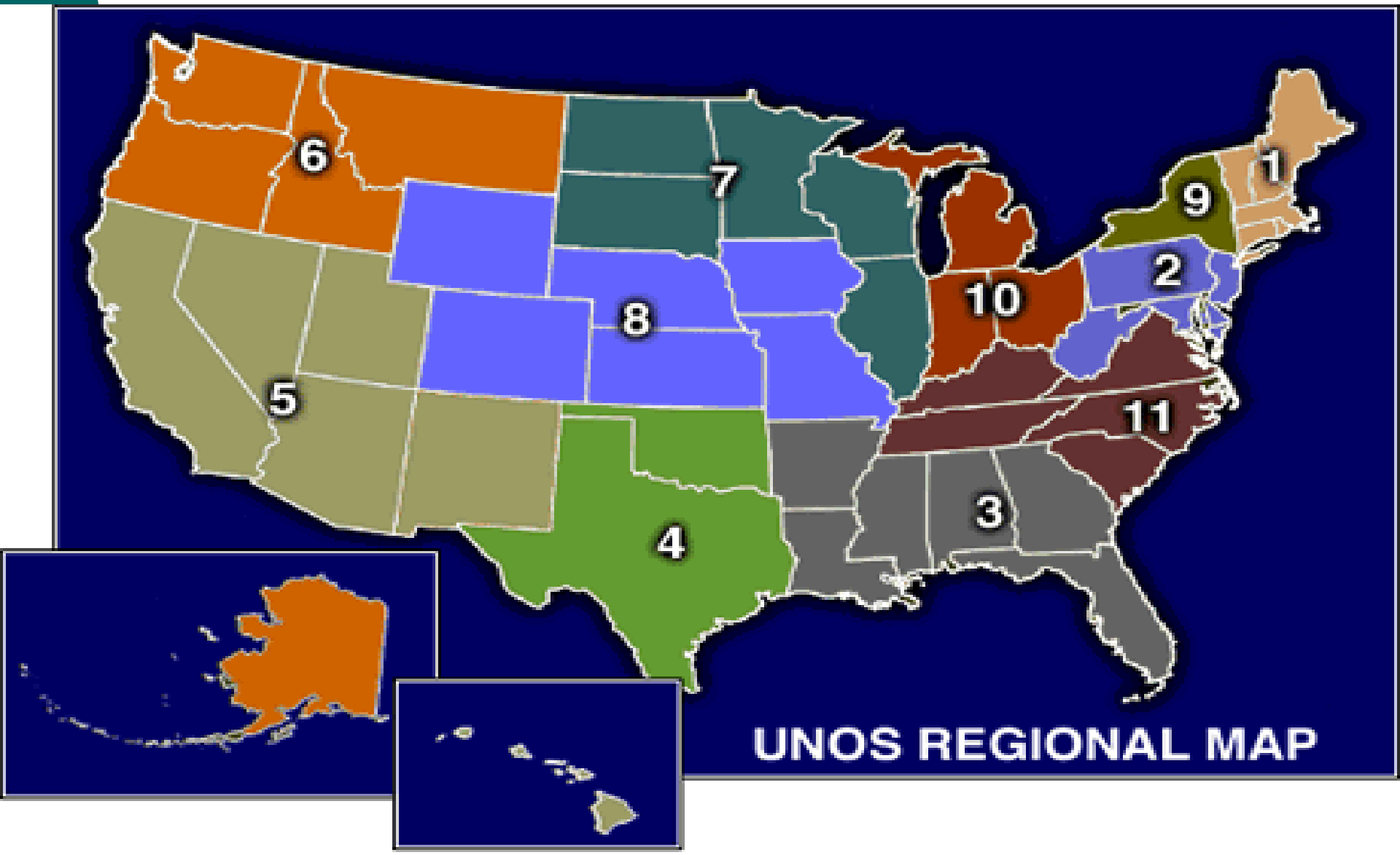
Liver Transplantation

- 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)



Background and Significance

- **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 2 (1998-2002):** Child Pugh Score and subjective measures (encephalopathy and ascites)
  - **Era 3(2002-present):** Model for End Stage Liver Disease (MELD)

MELD Score =

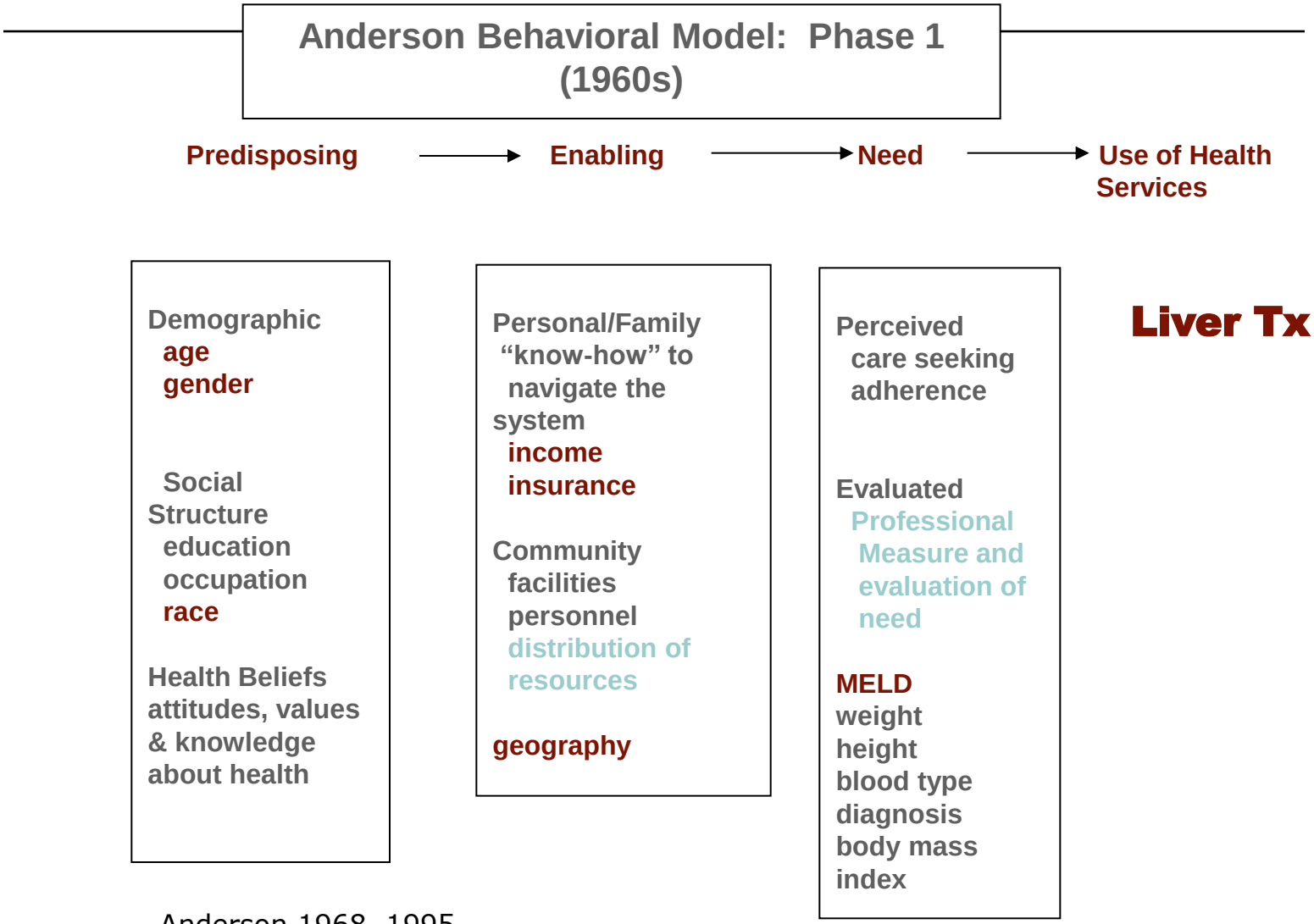
10 {0.957 Ln(Scr) + 0.378 Ln(Tbil) + 1.12 Ln(INR) + 0.643}

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 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 f**or 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

- Ho_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

$$\lambda(t) = \lambda_o(t)\exp(\beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_k X_k)$$

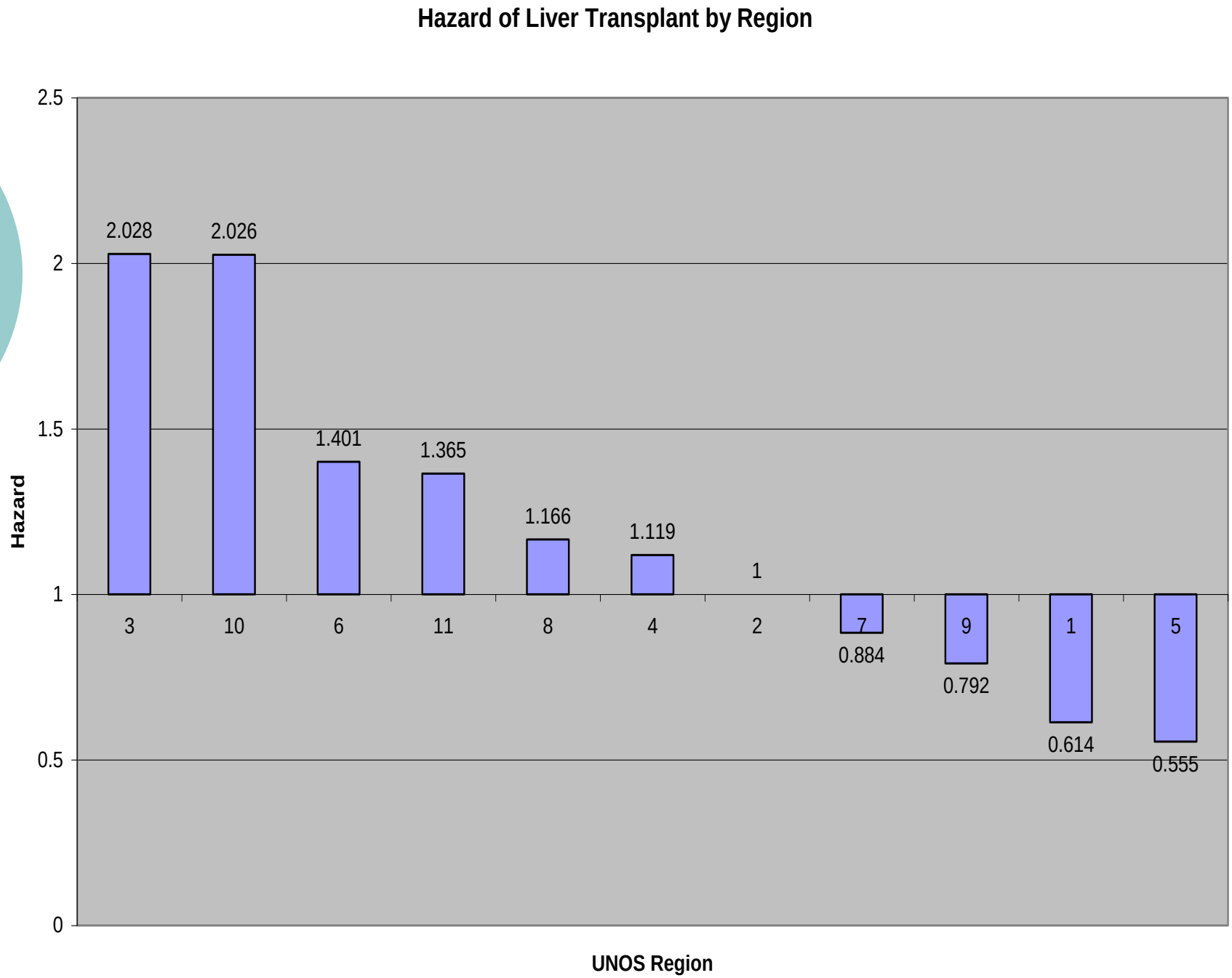
$$= \lambda_o(t)\exp(\beta_1 X_{predisposing} + \beta_2 X_{enabling} + \beta_3 X_{need})$$

$$= \lambda_o(t)\exp(f(X))$$

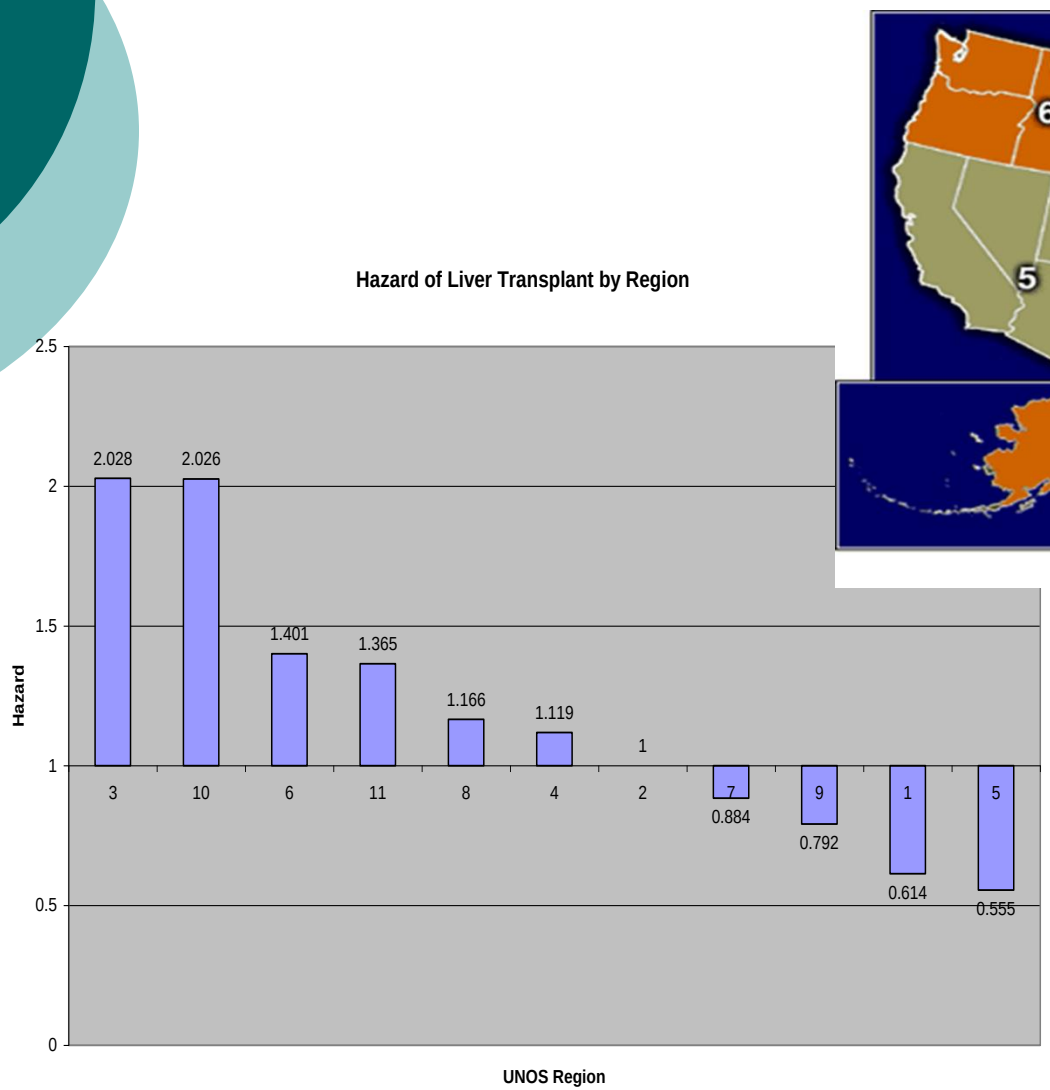
Multivariate Model of Access to Liver Transplant UNOS Data 2002-2007

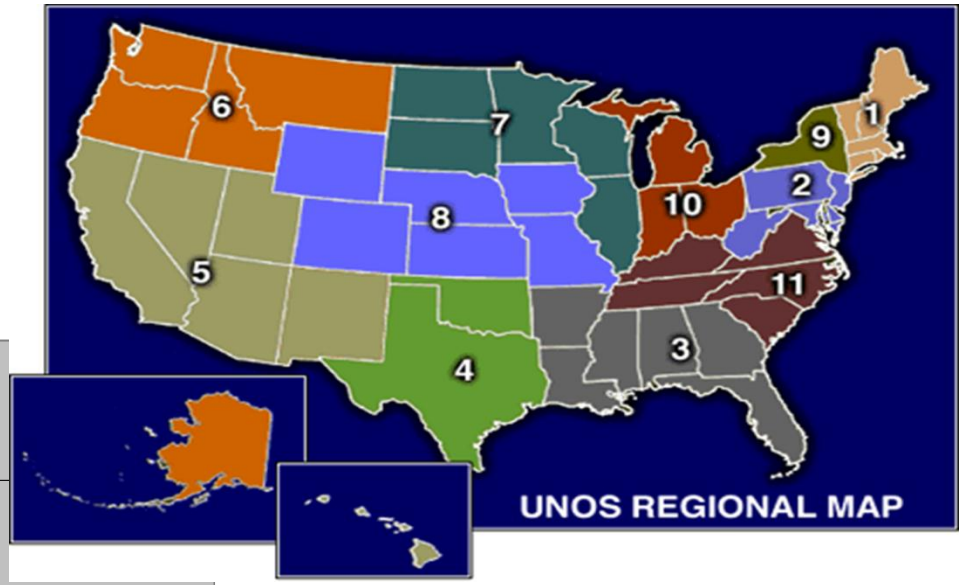
Variable	Parameter Estimates	Standard Error	Hazard Ratio(CI)
Predisposing Factors			
Gender[1]			
Female	**-0.09609**	**0.2317**	**0.908** (.868-.951)**
Race[2]			
African Am	**-0.09253**	**0.02816**	**0.912* (0.863-0.963)**
Hispanic	**-0.18238**	**0.02612**	**0.833** (0.792-0.877)**
Asian/Other	**0.17437**	**0.02695**	**1.191** (1.129-1.255)**
Age[3]			
31-45	**0.13437**	**0.04797**	**1.144* (1.041-1.257)**
46-60	**0.16595**	**0.04577**	**1.118* (1.079-1.291)**
61-75	**0.23694**	**0.04833**	**1.267**(1.153-1.393)**
Enabling Factors			
Primary Payer[4]			
Medicaid	0.03826	0.02299	1.039 (0.993-1.087)
Medicare/Public	-0.00465	0.01971	0.995 (0.958-035)
Region[5]			
1	**-0.48826**	**0.05178**	**0.614**(0.554-0.679)**
3	**0.70702**	**0.02691**	**2.028**(1.924-2.138)**
4	**0.11257**	**0.03158**	**1.119* (1.052-1.191)**
5	**-0.58854**	**0.03049**	**0.555**(0.523-0.589)**
6	**0.33730**	**0.04613**	**1.401**(1.280-1.534)**
7	**-0.12291**	**0.03250**	**0.884* (0.830-0.943)**
8	**0.15380**	**0.03660**	**1.166**(1.086-1.253)**
9	**-0.23341**	**0.03374**	**0.792**(0.741-0.846)**
10	**0.70594**	**0.03155**	**2.026**(1.904-2.155)**
11	**0.31082**	**0.02455**	**1.365**(1.300-1.432)**
Need Factors			
Diagnosis[7]			
HCC	**0.57840**	**0.07071**	**1.783**(1.552-2.048)**
MELD	**0.14018**	**0.0007538**	**1.150**(1.149-1.152)**

Comparison Groups: 1. Gender: Male 2. Race: White 3. Age: 18-30 4. Primary Payer: Private 5. Region: 2 6. Diagnoses: Cirrhosis 7. Height: <165.5 8. Weight: <71 9. ABO Group: O (*p<.05; **p<.0001); ***Likelihood Ratio Chi-Square=27068.8788 (p<.0001)***


Hazard of Liver Transplant by Region
2.5
2
1.5
1
0.5
0
Hazard
2.028
2.026
1.401
1.365
1.166
1.119
1
0.884
0.792
0.614
0.555
3
10
6
11
8
4
2
7
9
1
5
UNOS Region

Hazard of Transplant by Region





Findings Aim 2

- Ho_2: **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**
    - IOM Report of 1999 (Gibbons, 2003)
      - 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