# The Effects of Socioeconomic Status on Liver Transplantation Listing

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## A. Introduction

The first reference to liver transplantation which appears in medical literature is credited to C. Stuart Welch who outlined the procedure in canines in 1955.[1] The surgical techniques perfected in animal models were then applied to human subjects in 1963.[2] Though these early attempts at liver transplantation were utterly unsuccessful, they set the stage for the treatment now considered standard of care for patients with acute hepatic failure, decompensated chronic liver disease and progressive liver pathology unlikely to remit. With the advent of cyclosporine and FK506 in the 1980s, liver graft survival skyrocketed, thereby establishing liver transplant as a feasible and lasting alternative to medical therapies.[2] At that time, since the surgical technology and pharmacology of rejection therapy were greatly improved, the existing limitation was organ availability.

In 1984, the United States Congress recognized the need for a governing organization which would efficiently and fairly distribute all organ donations. Under the National Organ Transplant Act (NOTA) of 1984, the Organ Procurement and Transplantation Network (OPTN) was born. The goals of OPTN are the following: 1) to increase the effectiveness and efficiency of organ sharing and equity in the national system of organ allocation and 2) to increase the supply of donated organs for transplantation.[3] Currently, the United Network of Organ Sharing carries out the OPTN mandate, thereby orchestrating the listing and appropriation of available organs. This system operates via a point system in which the sickest patients are designated status 1 and are therefore placed at the top of the waiting list. This strategy, while considering the sickest patients first as they have the shortest mean survival, mandates a long and arduous waiting process for other patients who are also becoming less and less medically stable.

With regards to the need for liver transplantation, the number of individuals awaiting liver transplants has increased from 1,527 in 1991 to 16,874 in 2000.[4] As you can imagine, the number of organs has not risen comparably. The number of recipients of cadaveric transplants for 1991 was 2,931 and 4,579 for 2000, thereby satisfying only 27% of the demand.[4] In an effort to increase the number of organs available, transplant centers have been moving towards more living-related liver transplants. With new surgical expertise in right hepatic lobe transplant, it is projected that hundreds of patients a year will benefit from living-related donations.

Despite all of the innovations and the omnipotent presence of OPTN, people of color and the economically disadvantaged all less likely to be listed for transplants and eventually obtain transplants than their counterparts. Though the role of racial inequities has been explored in the body of liver transplantation research, the role of socioeconomic status has not. It is for this reason that the role of socioeconomics in liver transplantation is to be explored herein.

## B. Rationale

Though there is an abundance of research supporting racial biases in the access to liver transplantation, the impact of socioeconomic status has not been explored. In the wealth of literature concerning renal transplantation, such a relationship has clearly been established.[6,7] In a study on the effect of gender, race, and poverty on the renal transplant process, Alexander *et. al.* found that those below the poverty line were less likely to progress to listing (33% vs. 41%) than their more wealthy counterparts.[7] As this seems to be the standard difference found in most of such studies, it is likely that this difference also occurs in the realm of liver transplantation. We hypothesize that patients of lower

socioeconomic status, as determined by level of education, parental education, household income, and insurance, are less likely to be placed on the liver transplant list.

**C. Study Design/ Procedure**

This study is a prospective cohort study to be conducted at all of the liver transplant centers in the United States. All candidates being evaluated for a possible liver transplant will be asked to complete a questionnaire regarding race, socioeconomic status and etiology of liver disease (see attached sheet 1). The transplant committee will complete a separate questionnaire regarding medical status of the applicant (see attached sheet 2). Both of these questionnaires will be sent to an independent organization for analysis. All patients will be followed until an initial decision is made concerning acceptance or rejection from the transplant list. Those individuals excluded on the basis of medical criteria will be excluded from the analysis. Those patients excluded for "social" criteria will be compared to those individuals placed on the liver transplant waiting list. This data will then be analyzed by multiple logistic regression analysis to determine whether lower socioeconomic status results in a lower rate of placement on the transplant list. In the renal literature, an approximate difference of 8% was found. Extrapolating the following data, the sample size will have to be the following for a power of 80%:

$$n = 8 \left( \frac{p_1 q_1 + p_2 q_2}{\text{effect}^2} + \frac{2}{\text{effect}} \right) + 2$$

$$n = 8 \left( \frac{(0.33)(.67) + (.41)(.59)}{(.08)^2} + \frac{2}{0.8} \right) + 2$$

$$n = 8 \, (0.2211 + 0.2419/ 0.0064) + 27$$

$$n = 606$$

Though only 606 patients are required in each group to demonstrate a statistically significant difference, the inclusion of patients from all transplant centers will not only increase the number of participants but also address the problem of generalizability of results.

**D. Study Drugs**

Not applicable.

**E. Medical Device**

Not applicable.

**F. Study Questionnaires**

Please see attached sheets. Questionnaire 1 will be submitted by possible liver transplant candidates and questionnaire 2 will be submitted by the transplant committee evaluating the patient being evaluated.

**G. Study Subjects**

Patients may be included in the study if they are between the ages of 18 and 65, have a progressive and irreversible liver disease and one of the following:

1. Ascites refractory to diuretics
2. Spontaneous bacterial peritonitis
3. Increasing fatigue interfering with ADLs
4. Hepatic encephalopathy
5. Malnutrition and/ or wasting
6. Recurrent bacterial cholangitis
7. Hepatorenal syndrome
8. Fulminant hepatic failure
9. History of variceal bleeding
10. Metabolic bone disease in the setting of documented fractures
11. Worsening synthetic function as documented by decreasing albumin (<2.5 g/dl) and increasing prothrombin time

Patients will be excluded from the study of they have any of the following:

1. HIV positivity
2. Evidence of an extrahepatic malignancy
3. Infection outside of the biliary tract
4. Advanced cardiac or pulmonary disease (specifically pulmonary hypertension)
5. Hepatocellular carcinoma with a lesion of 5 cm or greater
6. Active alcohol or drug abuse

**H. Recruitment of Subjects**

Questionnaires will be sent to transplant committees across the nation. The questionnaires are then distributed to the patients being evaluated and the physicians evaluating the patient. The information will be mailed back to an independent reviewer. The reviewer will then follow the UNOS listing to locate patients who are accepted to the transplant list. The questionnaires of those individuals not found on the list will then be examined for medical suitability. In the event that they were medically suitable, the reviewer will conduct a phone interview to elicit the status of that patient's bid for a transplant. This group of patients will represent group 1 and those actually listed for transplant will represent group 2.

**I. Confidentiality of Subjects**

All of the information will be collected and analyzed by an independent organization. In addition, all applications would be coded with numbers and correlated with patient data only to ascertain whether a patient is listed on the UNOS transplantation list.

**Potential Conflict of Interest**

Potential conflicts of interest are minimized by having the questionnaires coded and the data analyzed by an independent organization.

**J. Location of the Study**

Clinical areas in the individual transplant centers.

**K. Potential Risks**

No risks are involved in filling out the various questionnaires or responding to a phone survey.

**L. Potential Benefits**

The potential benefit of the study will be to identify the socioeconomic disparities present in the initial phase of evaluation for liver transplant and thereby identify barriers to access to care for the disadvantaged.

**M. Alternative Therapies**

Not applicable.

**N. Compensation to Subjects**

No compensation will be offered for completing questionnaires or completing a phone interview.

**O. Cost to Subjects**

The participants will not incur any cost in the study. All questionnaires will be attached to stamped and self-addressed envelopes for mailing.

**P. Minors as Research Subjects**

This is not applicable to the study population outlined above.

**Q. Radiation and Radioactive Substances**

Not applicable.

**R. References**

1. Welch, CS. A mote on transplantation of the whole liver in dogs. Transplant Bull 2:54-55, 1955.
2. Busuttil, R. and Klintmalm, G. Transplantation of the Liver. Philadelphia, W.B. Saunders, 1996.
3. OPTN: Organ Procurement and Transplantation Network. http://www.optn.org/optn.
4. OPTN: Organ Procurement and Transplantation Network. http://www.optn.org/data/annualReport.asp
5. Trotter, J., Wachs, M., Everson, G., Kam, I. Adult-to-adult transplantation of the right hepatic lobe from a living donor. *New England Journal of Medicine*. 346 (14):1074-1082, 2002.
6. Caleb Alexander, G., Sehgal, A. Barriers to cadaveric renal transplantation among blacks, women, and the poor. *JAMA*. 280(13): 1148-1152, 1998.
7. Kasiske, B., London, W., Ellison, M. Race and socioeconomic factors influencing early placement on kidney transplant waiting list. *Journal of American Society of Nephrology*. 9:2142-2147, 1998.
8. Cottler, S., Jensen, D. Patient selection for liver transplantation. Up-to-date (www.utdol.com).
9. Crippin, J. Liver Transplantation: The Hepatology perspective. www.centerspn.org/pubs/liver/crippin1.htm.

# Liver Transplant Candidate Information Sheet

(Please print all information and use a black or blue ink pen)

**Candidate Registration Number**:

_____

**Zip Code**:_____
**Gender**:_____

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**Date of Diagnosis of Liver Disease**: _____
**Cause of Liver Disease**: _____

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**Ethnicity**: _____
**Race**: _____

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**Highest Level of Education: (Select one)**

_____ None
_____ Associates or Bachelors Degree
_____ Grades 0 – 8
_____ Post-College Graduate Training
_____ Grades 9-12
_____ Post-College Graduate Degree
_____ Completed some college courses
_____ Other

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Mother's Highest
**Level of Education: (Select one)**

_____ None
_____ Grades 0 – 8
_____ Grades 9-12
_____ Completed some courses
_____ Associates or Bachelors Degree
_____ Post-College Graduate Training
_____ Post-College Graduate Degree
_____ Other

Father's Highest
**Level of Education: (Select one)**

_____ None
_____ Grades 0 – 8
_____ Grades 9-12
_____ Completed some college courses college
_____ Associates or Bachelors Degree
_____ Post-College Graduate Training
_____ Post-College Graduate Degree
_____ Other

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**Employment Status**:

_____

**Yearly Household Income** (Select one):

_____ $ 0 - $10,000
_____ $ 10,001 - $20,000
_____ $20,001 - $30,000
_____ $30,001 - $40,000
_____ $40,001 - $50,000
_____ $50,001 - Greater

**Number of Adults in Household**:_____

**Number of Children in Household**: _____

**Name of insurance Carrier**
_____

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Please note that you may be selected for a follow-up phone interview. If you do not wish to participate in such an interview, please check here. _____

# Liver Transplant Candidate Medical Eligibility

(Please print all information using a blue or black ink pen)

**Candidate Registration Number:**

_____

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**Primary Diagnosis**:

_____

**Secondary Diagnosis**:

_____

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**Comorbid States:** (Please answer yes or no)

_____ Diabetes Mellitus
_____ Hypertension
_____ Coronary Artery Disease
_____ Cerebrovascular Disease
_____ Peripheral Vascular Disease
_____ Pulmonary Disease/ Hypertension
_____ Extrahepatic Malignancies
_____ HIV
_____ Hepatocellular Carcinoma

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**Severity of Liver Disease:** (Check the following that apply)

_____ Encephalopathy
_____ Variceal Bleeding
_____ Ascites
_____ Spontaneous Bacterial Peritonitis
_____ Malnutrition/ Muscle Wasting
_____ Portal Vein Thrombosis
_____ TIPS
_____ Pruritus
_____ Recurrent Bacterial Cholangitis
_____ Metabolic Disease/ Fractures

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**Laboratory Information:** (Most Recent)

_____ Creatinine
_____ Albumin
_____ PT
_____ AFP

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Has patient informed you of a history of alcohol or drug abuse? YES NO

Has patient informed you of drug or alcohol use in the last six months? YES NO