Liver Organ Donations[1]

PART A: Who waits, Who receives…the multiple challenges in Organ Transplant decisions

Dr. Chris Kim looks up at his computer desk and sees a message appear - two patients arrived earlier in the day to the Emergency room of his hospital in El Paso, Texas as a result of a texting-while-driving car accident. Neither patient survived the head trauma they experienced and both designated themselves as organ donors. Dr. Kim knows that the teams in the hospital will be quickly harvesting the deceased organs and making them available for donation to the very very long list of patients waiting across the US. His job is to decide whom to contact and offer the two livers that are now available for transplant. Dr. Kim sees before him on the screen the information regarding 4 potential patients on the liver transplant waiting list.

Patient 1) Ventura Rodriguez is a 51 year old single father of a 14 year old daughter. His wife died when his daughter was very young. He works as a superintendent of a building complex in South Bronx. He loves to go to baseball games, he is very active in reading programs that target vulnerable youth populations and loves most to spend time with his daughter playing video games. Ventura was diagnosed with Hepatitis C at age 34. At that time, doctors put him on a drug treatment that worked well for 13 years. At age 47, he developed an abdominal hernia which led doctors to discover that he had cirrhosis of the liver and was in need of a transplant. While waiting for the transplant, Ventura's health has started to deteriorate, he is jaundiced and severely bloated and limited in his mobility. Analysis of his blood work has revealed that he has blood type B and has a MELD score of 29.

Patient 2) Leslie Waller is a 32 year old woman from San Diego, California who is engaged to David: they hope to wed in June 2021. Leslie is a marketing executive at a local pharmaceutical company and on the governing board of her church. Leslie was diagnosed with fatty liver disease at the age of 30 and she was put on the transplant wait list at that time. She was called 1 year ago and told that she might potentially be eligible for a transplant – she went through all of the steps to prepare herself for an imminent transplant. At the very last stage of the process, she was informed that the organ had been allocated to someone else; she is still waiting for her organ. Analysis of her blood work has revealed that she has blood type A and has a MELD score of 23.

Patient 3) Jamil Manuel is a 49 year old divorced father of two young boys (ages 17 and 19) from Baltimore. Jamil is an avid runner and gardener and currently is an OB/GYN physician in a free-clinic in downtown Baltimore. After running a half-marathon, Jamil found himself in the emergency room after experiencing a very high fever that evening. The doctors informed Jamil that he was suffering acute liver failure and have kept him in the Critical Care

[1] This case was written with the assistance of Shubham Akshat, Jonathan Southgate and Professors Pamela Armstrong, Maria Gisela Bardossy, and Wedad Elmaghraby

Unit as he awaits a transplant. Analysis of his blood work has revealed that he has blood type O and has a MELD score of 33.

Patient 4) Darcy Anderson is a 73 year old widower from Boise, Iowa. She is a mother of 4 and grandmother to 8 grandchildren, and retired librarian from the local public library - she now spends much of her time meeting up with friends in her needlepoint club and doing volunteer work for the National Society for the Daughters of the American Revolution. Darcy has been suffering from abdominal pain for several months and, after waiting several weeks to secure an appointment with Veterans Affairs medical facility (her husband served in the Army for 40 years), she was recently informed by her doctors that she has a rare form of liver cancer. Given the severity of her cancer, she is in need of a transplant very quickly. Analysis of her blood work has revealed that she has blood type AB and has a MELD score of 39.

The medical team harvesting the organs have informed him that that the two patients whose livers available for transplant are:

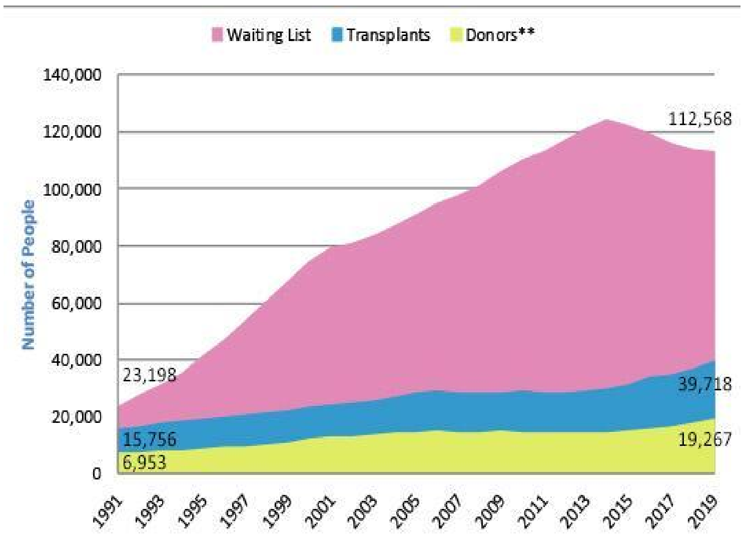
Donor 1) White, Female, Blood Type O, Age 39
Donor 2) African American, Male, Blood Type A, Age 75

What is Organ Transplantation?

Organ transplantation is the process of surgically transferring a donated organ to someone diagnosed with organ failure. As of March 2020, there are more than 112,000 candidates for transplant on the U.S. national waiting list.

There are significantly fewer donors (either living or deceased) and so the imbalance between the supply and the demand for organs continues to grow. In 2019, there were a total of 19,267 donors; 11,870 were deceased and 7,397 were living.[2]

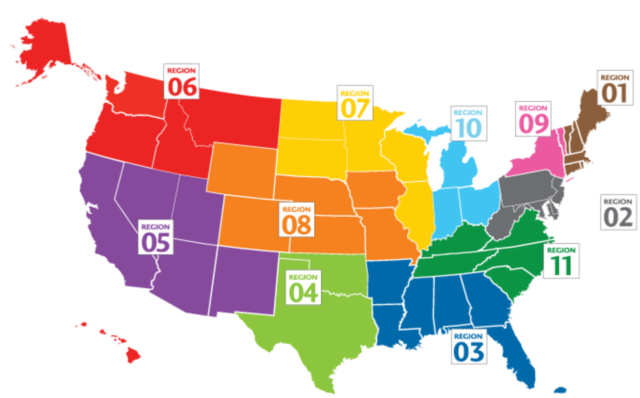
Each year, the number of people on the waiting list continues to be much larger than both the number of donors and transplants, which grow slowly. Deciding which patient gets which organ, and as a result, who does not, is a life and death decision. This scarcity decision is further complicated by the fact there can be thousands of medically compatible and available recipients for each organ.



In recognition of this allocation decision problem and the mismatch between supply and demand, the U.S. Congress passed the National Organ Transplant Act (NOTA) in 1984. According to this legislation, deceased donor organs are viewed as national resources in the U.S., and as such, their allocation has to be based on fair and equitable policies. Moreover, the sale of organs as well as money transfers of any nature in the acquisition of organs is strictly prohibited. Instead, the policy for allocating the organs should utilize waiting lists and a **priority method to assign organs to patients**.

The U.S. Congress established the Organ Procurement and Transplantation Network (OPTN) to maintain a national registry for organ matching and to develop allocation policies. In 2000, "the U.S. Department of Health and Human Services (HHS) implemented a Final Rule establishing a regulatory framework for the structure and operations of the OPTN."

Under this Final Rule, any organ allocation scheme is required to have "priority rankings based sound medical judgment", and at the same time, it should aim "to achieve the best use of donated organs, and avoid organ wastage" and should balance medical efficiency (extra life years) and equity (waiting time), without discriminating patients based on their race, age and blood type.



[2] https://www.organdonor.gov/statistics-stories/statistics.html

The United States is divided into 11 OPTN Regions. OPTN regional boundaries reflected patient referral and organ sharing patterns when they were created in 1986. Since that time, some regional boundaries have been adjusted to account for new relationships between Organ Procurement Organizations (OPOs) and transplant centers or to balance populations among regions. Regions are not uniform in size or population.

Each region is further divided into Organ Procurement Organizations (OPOs). OPOs are directly responsible for evaluating, procuring, and allocating donated organs within their respective region. Once an OPO procures an organ from a donor the OPTN national registry generates a list of potential recipients.

Challenge: Organ Allocation Part A

How would your team advise Dr. Kim to allocate these two donor liver organs? Your first challenge is to come up with an assignment of the two donor liver organs to the patients (note that you cannot split a liver and donate to more than one patient - a liver must be transplanted in its entirety). Within your project group, please come up with a consensus on a list of factors you would use to evaluate a particular donor and candidate pair? How would you evaluate the success (or failure) of a particular donor-patient allocation? What additional information would you like to have? What makes this assignment problem challenging? How would you make the assignment of these two donors' organs given the specific information you have been given about each patient and the information available regarding liver transplants in general (below). Please be prepared to explain and justify your allocation decision.

Resources

- Mayo Clinic: Liver Transplants
- WebMD: Liver Transplants
- UNOS Liver Facts
- UNOS Organ Matching (includes video overview)

PART B: Creating Models for Organ Allocation

Consider the set of 10 patients and 5 donors in the accompanying spreadsheet. Each patient and donor are described along several key attributes that have been identified as critical in assessing the potential success of a transplant. The list of attributes and their definitions can be found in the tables: Donors' Data and Candidates' Data.

One consideration in the allocation process is the potential success of a pairing. To help understand the association between each individual characteristic of a patient (candidate), donor and pair, doctors and the probability of survival, statisticians have run regression models and this knowledge is formalized in the following equation:

$$\text{Probability of survival} = S_0^{HR},$$

where S_0 is the baseline survival probability and *HR* is a hazard ratio calculated by multiplying various scores, $\mathbf{b_j}$, based on patient attributes, donor characteristics and patient-donor pairing. Each attribute ***j*** has an associated value $\mathbf{b_j}$. The hazard ratio for a particular patient-donor pair with *k* attributes is HR = $\prod_{j-1}^{k} b_j = b_1 b_2 b_3 ... b_k$.

Please note that the higher the hazard ratio, the lower the probability of survival for the patient. In addition, the higher the $\mathbf{b_j}$, the higher the hazard ratio; and consequently, the lower the likelihood of survival for the patient.

For the data and attributes provided in this case, the baseline probability of survival is 0.924 (P_0= 0.924). Then the survival probability of a specific candidate who receives an organ from a specific donor is determined to be 0.924 raised to the power of the product of their joint attribute values, i.e.,

Probability of survival = 0.924^$(b_{\text{donor age}} * b_{\text{donor race}} * b_{\text{donor cause of death}} * ... b_{\text{can MELD}} * b_{\text{can diabetes}} * ... * b_{\text{don-can height ratio}} * b_{\text{don-can blood match}} * b_{\text{don-can CIT}})$

Please see the example below for an illustrative example.

Table. Donors' Data

DONORS	
DONOR_ID	Unique identifier
DON_AGE	Donor's age when organ is harvested (in months)
DON_RACE	Donor's race
DON_DEATH	Donor's cause of death
DON_DCD	Was the donor deceased upon arrival at hospital?
DON_ABO	Donor's blood type (A, B, AB, O)
DON_HGT	Donor's height at time of death (in centimeters)
DON_GENDER	Donor's gender
DON_OPO	Donor's OPO (first two letters indicate state, e.g. **CA**OP is an OPO in California)
DON_REGION	Donor's OPTN region (1-11)

Table. Candidates' Data

CANDIDATES	
CAN_ID	Unique identifier
CAN_AGE	Candidate's age (in months)
CAN_RACE	Candidate's race
CAN_ABO	Candidate's blood type (A, B, AB, O)
CAN_HGT	Candidate's most recent height (in centimeters)
CAN_GENDER	Candidate's gender
CAN_OPO	Candidate's OPO (first two letters indicate state, e.g. **CA**OP is an OPO in California)
CAN_REGION	Candidate's OPTN region (1-11)
CAN_MELD	Candidate's latest MELD score. MELD (Model for End-stage Liver Disease) is a measure of how sick a candidate is. It is calculated from the results of a series of medical tests. MELD scores range from 6 to 40. The higher the number the more severe the case.
CAN_DIABETES	Does the candidate have diabetes?

Example

Candidate John Doe is a 58 year old white male with diabetes located in OPO **PA**TF, is 1.61 meters tall, with type A blood and a MELD score of 13. A match was identified with Donor Jane, who is an 84 year old African American woman who died from Anoxia while at the hospital in OPO **PA**DV. Donor Jane was 1.63 meters tall with type A blood.

If Donor Jane's liver is given to Candidate John Doe, his probability of survival post-transplant is calculated to be 86%. This is calculated as follows:

Hazard Ratio =
(1.44*1.14*1.07*1) * (1*1*0.959031444) * (0.98 * 1.105 * 1.13067) = 2.4222999

Probability of survival =
0.924 ^ = 0.86015637

DON_ID	53	
Attribute	**Data**	**Beta**
DON_AGE	1014	1.44
DON_RACE	African American	1.14
DON_DEATH	Anoxia	1.07
DON_DCD	No	1

CAN_ID	11470	
Attribute	**Data**	**Beta**
CAN_AGE	698	1.13067 [4]
CAN_RACE	White	0.98
CAN_MELD	13	1.105 [5]
CAN_DIABETES	Yes	1.16

Donor : Candidate	53 : 11470
Height Ratio	1 [1]
Blood Type	1 [2]
CIT (hrs)	0.959031444 [3]

(1) Height Ratio: **163** / **161** = 1.01242236. This ratio is greater than 0.88, hence the Beta coefficient is 1.

(2) Donor and candidate have identical blood type

(3) Step 1
Distance between **PATF** and **PADV** = 378.83237
Step 2
CIT: 5.771 + 0.001577 * **378.8323666** = 6.368418642
Step 3
CIT (hrs) : 1 + (**6.368418642** - 7.1)*0.056 = 0.959031444

(4) CAN_AGE : 1 + 0.016*(**58.1667** - 50) = 1.13067

(5) CAN_MELD : 1 + 0.015 *(**13** - 6) = 1.105

Challenge: Organ Allocation Modeling Part B

Given the categories and coefficients presented, propose an allocation of donors to patients given the 5 donors and 10 candidates in the accompanying spreadsheet. Develop an optimization formulation to assist you in determining your optimal allocation. Clearly specify and explain your objective function and constraints.

Based on your determined final solution, please reflect on the nature of your allocation.

- Create a plot of your allocations across the US (use a visual aid tool to illustrate from where and how far your organs are traveling).
- Be prepared to describe your assignment of organs across candidates based on their various characteristics/attributes (e.g., how many women received organs, African Americans, how old were your patients who received an organ, and those who did not…)
- Reflect on whether or not you find your allocation to be fair and/or efficient. How do you define efficiency? How are fairness and efficiency reflected in your objective function? Is there an aspect to your solution that you would like to change?

Challenge Part C: Efficiency and Fairness in Organ Allocation

Consider the optimization tool provided in the two spreadsheets **Part C-Set 1.xls** and **Part C - Set 2.xls**: Each spreadsheet contains an Integer Program that has been developed to determine an optimal allocation for TWO sample sets of 20 candidates and 10 donors each, based on the objective function Maximize *Cumulative Probability of Survival*.

Your assignment is to propose 2 additional objective functions (above and beyond the *Cumulative Probability of Survival* objective already present in the optimization formulation). You also have the option (but are not required) to propose additional constraints to better reflect your group's opinions regarding the importance of efficiency, fairness and any other allocation considerations as explored in Part A of this case. Please evaluate the outcomes of your new optimization models (with the updated objective functions and possible additional constraints) for each dataset, i.e., 2 objective functions for 2 dataset -> 4 outcomes.

Please address the following:

1) What criteria do your Objective functions 1 and 2 capture (each objective function may capture different sets of criteria)? How do you translate those criteria and your preferences into specific weights and metrics within your 2 proposed objective functions?

2) How does your allocation change based on your selected criteria and objective function(s) for each dataset?

3) How sensitive are your solutions to your proposed objective function(s), i.e., how well or robustly does your objective function capture fairness and/or efficiency for different datasets?

Ideas for Future Development:

Use Simulation to simulate arrival process of donors and candidates - stochastic nature of the problem.