Quantitative Analysis of the Kidney Allocation Policy in USA

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ABSTRACT

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Quantitative Analysis of the Kidney Allocation Policy in USA

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Kidney transplantation has become the preferred treatment option for people suffering from end stage renal disease (ESRD) since the successful kidney transplantation conducted by Dr. Joseph E. Murray in 1954. However, most ESRD patients are unable to undergo kidney transplantation due to the scarcity of cadaveric and living donor kidneys. People suffering from ESRD are enlisted on a kidney waiting list and prioritized based on a point scoring system. This scoring system attempts to balance equity and efficiency. For this reason the first kidney allocation policy in the United States was based on waiting time. However, this led to underutilization of kidneys. The Organ Procurement and Transplantation Network (OPTN) which is the body in charge of organ procurement and allocation has come out with a new kidney allocation policy which came into effect on December 4, 2014. This new policy was developed to improve equity and kidney utilization. However, the policy has no consideration for the allocation of kidneys under emergency situations. This problem was also observed by the National Kidney Foundation (NKF) in their comment about the effectiveness of the new policy. The policy also does not minimize the incentives for the rejection of kidney offers. This dissertation was carried out to develop and evaluate a point scoring model with consideration for kidney allocation under emergency. Attempt was also
made at minimizing the discard rate of kidneys through the application of penalty to candidates who reject kidneys that are later transplanted. Simulated results indicate that allocating kidneys with consideration for emergency situations may help to minimize death on waiting list while still prioritizing sensitive candidates and kidney utilization. It was also observed that the application of penalty function may help to minimize the kidney discard rate by 40%. The findings from the research are limited in the sense that the conclusions were drawn from simulated data which may not necessarily be the actual response from ESRD candidates. Also, legal, moral and ethical limitations may affect the implementation of the results from this research; hence, medical judgments must always be the decision maker in the acceptance or rejection of kidney offers.
DEDICATION

To my parents: “Charles Boachie Agyeman” and “Mary Badu”

To all my siblings, and my dearest friend: “Sabena C. Thomas”
ACKNOWLEDGEMENTS

I give thanks to the Almighty God for all the blessings. I thank Dr. Namkyu Park for the support and encouragement. His vision, patience and guidance helped me to understand the problem. Without the trust he had in me, this dissertation wouldn’t have come this far. I would also like to thank Dr. Gursel Suer for his motivation and the invaluable role he has played in my academic career. I will forever be grateful to him. I thank the members of my committee for their time and contributions to this research. It is an honor to have them serve on my committee.

I would also like to thank the entire faculty members of the Industrial and Systems Engineering department. You have always been supportive and I am most grateful for your guidance and the teaching opportunities. I thank Dr. Deborah McAvoy for her continuous support. Without her I might not have come this far.

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1. INTRODUCTION

End-stage Renal Disease (ESRD) is a terminal disease affecting over 500,000 in the United States [1]. The Johns Hopkins Health Systems [2] explains that ESRD occurs when the kidneys permanently cease to function. However, before this stage a kidney malfunctioning could be either acute renal failure or chronic renal failure. When the damage to the kidneys is sudden and reversible it is termed as acute renal failure [2]. It becomes chronic renal failure when the damage is insidious and worsens with time [2]. Chronic renal failure can lead to permanent damage of the kidneys at which stage one cannot rely on the kidneys for renal activities [2]. People suffering from ESRD have two major medical procedures to improve their lives: dialysis and transplantation [2].

Dialysis is the first treatment patients receive by visiting dialysis center at regular time intervals to take out excess body fluid [2]. This does not necessarily improve the condition but helps to control the spread of the disease. To resume active life ESRD patients must go through kidney transplantation [3]. Not only does successful kidney transplantation help improve ESRD patient’s life but it also minimizes their mortality rate [4]. In Port et al’s 1993 and 1994 papers [5, 6], the benefits of kidney transplantation far exceed that of dialysis. Dimitris et al. [3] also classify kidney transplantation as a “life-saving gift.” In addition to kidney, other organs are also transplanted to improve people’s life. The next section gives an overview of the evolution of organ transplantations.
1.1. Evolution of Organ Transplantation

Organ transplantation involves the substitution of a defective organ with a functioning organ. This idea was conceived several centuries ago; there is an account of a transplantation involving the removal of the leg of a patient by saint Cosmas and Damien in the 3rd century [7]. Although some researchers discredit this by arguing that the transplantation happened at a period of a foreknowledge, Zimmerman [8] has a great account of how the “sainted physicians” totally removed one of the white legs of a patient and miraculously replaced it with a black leg [8]. Zimmerman also explains that as early as 600BC plastic surgery was in practice; Gaspare Tagliacozzi one of the pioneers in plastic surgery, and together with his colleagues, they fruitfully conducted plastic surgeries in the 6th century [7]. They successfully conducted plastic surgeries by using parts of a person’s skin to replace a damaged skin of the same person [7]. Clyde and James [7] further explain that at that time the idea of graft rejection was not conceived since all the transplantations done involved “autogenous skin.” This is because autogenous skin comes from the same patient undergoing the transplantation.

Jacques-Louis Reverdin, a Swiss surgeon in 1869 also made a significant discovery which Clyde and James term as “almost a landmark.” Jacques-Louis was able to cover wounds and burns with his “pinch graft.” The pinch grafts were thin layers of skin that were also first implemented autogenously [9]. Successful grafts were later reported for homograft skins. At this period surgeons had surgically transplanted skins from other person to their patients. Winston Churchill attested to
the success of homograft when he helped heal the open wound of another officer by donating his skin [7].

Solid internal organ transplantation involving the surgical replacement of a defective internal organ with a healthy organ of the same kind and from the same species has now been highly researched. Various organs (kidney, kidney-pancreas, pancreas, liver, heart, lungs, and intestines) are now transplanted due to the advancement of knowledge. A French surgeon and biologist: Alexis Carrel [10] laid the platform for the transplantation of solid organs. Alexis who was a Nobel prize winner invented the surgical procedure surgeons use to stitch together blood vessels [11]. Erika [11] explains that Alexis' invention of vascular anastomosis in the 1900’s was the prerequisite for solid organ transplantation. As in most studies, in the early years animals were used to gain insight to the challenges of solid organ transplantation. This according to Starz [10] led to a major breakthrough in solid organ transplantation in humans.

One other factor that delayed internal solid organ transplantation in humans was the rejection of the organ by the recipient’s immune system. Although the transplanted organ is meant to save the recipient, the immune system treats the graft as a foreign object hence attacking and rejecting the organ. Erika [11] explains that the problem was understood after several studies on skin grafting which involves the transplantation of a section of one's skin. This according to Erika [11] led to the discovery that the rejection of solid organs by recipient’s immune system was an immunological event. Although the technique for sewing together human
tissues was discovered in the 1900's scientists gained a better understanding of solid organ rejection in the 1940's [11]. With this discovery of knowledge scientist were able to provide kidney transplantation as a better option to dialysis.

In comparison of dialysis to kidney transplantation Dimitris et al. [3] classify kidney transplantation as a "life-saving gift." The benefits of kidney transplantation also cut across economic boundaries; In 2003 Jordan et al. [12] concluded that the annual savings in kidney transplantation was 3 times greater than dialysis and its related cost. These advantages of kidney transplantation make it the preferred treatment option for ESRD patients, but due to the scarcity of kidneys, patients have to be placed on waiting list where they undergo dialysis until a kidney becomes available [13].

Dr. Joseph E. Murray in 1954 was the first person to succeed in kidney transplantation [14]. An American plastic surgeon Dr. Murray and his team at Peter Bent Brigham Hospital in Boston (now Brigham and Women's Hospital) successfully conducted a kidney transplantation between two identical twins [15]. At this time it was well understood that the greatest challenge to allograft survival was an immunological event [15]. Since the transplantation was between identical twins (who are genetically related), graft rejection due to immune system of the donor and the recipient wasn’t much of a concern hence the twins received no immunosuppressant [15] which helps to prevent graft rejection. For this major breakthrough in kidney transplantation Dr. Murray’s was recognized with the Nobel prize for physiology in 1990 [15]. To get more insight into the background of solid
organ transplantation the remaining section of this chapter talks about the processes one has to go through to be enlisted on the kidney waiting list to transplantation.

1.1.1. Enlistment on Kidney Waitlist to Transplantation

After Dr. Murray’s breakthrough, kidney transplantation became the preferred treatment for ESRD [13]. However, due to unavailability of kidneys, people suffering from ESRD (referred to as patients or candidates in this paper) who have no living donor have to undergo dialysis and wait until an organ becomes available for transplantation. Different countries have developed diverse ways of enlisting candidates on the kidney waitlist; In the United States of American to get on the waiting list one needs a referral from a medical professional to a dialysis/transplantation center after which several tests are conducted to ascertain the need for dialysis and kidney transplantation [16]. Once it is determine that one has a chronic renal disease and at a high risk of degenerating into ESRD, the person will be enlisted on the waiting list. Occasionally candidates are denied enlistment on the waitlist but the decision can be appealed for further consideration. This can be done at the same test center or the candidate can request for the tests to be conducted at a different center [16].

The United Network for Organ Sharing (UNOS) which is the body in charge of the management of kidney waitlist explains that a person can be listed on the transplant waitlist only when the glomerular filtrate rate (GFR) is below 20 mL/min/1.73m² [15]. The GFR is an indication of the performance of kidney and the
test determines the liquid flow rate through the kidney per minute [17]. Sherry et al. [17] explains that “the GFR is the best overall indicator of kidney function.” Table 1 adopted from Sherry et al. [17] gives further details about GFR and the recommended action to be taken at each level.
Table 1: Classification of chronic kidney disease (CKD) and action plan [17].

<table>
<thead>
<tr>
<th>CKD Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.73m²)</th>
<th>Action*</th>
</tr>
</thead>
<tbody>
<tr>
<td>At increased risk</td>
<td>Risk factors for CKD are present but without markers of kidney damage</td>
<td>&gt;90</td>
<td>Periodically test for CKD: treat modifiable risk factors for CKD</td>
</tr>
<tr>
<td>1</td>
<td>Kidney damage with normal or increased GFR</td>
<td>&gt;90</td>
<td>Diagnose and treat type of kidney disease; treat co-morbid conditions; slow progression of CKD; treat modifiable CVD risk factors; periodically restage</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with mild reduction of GFR</td>
<td>60-89</td>
<td>Adjust drug dosages for level of GFR</td>
</tr>
<tr>
<td>3</td>
<td>Moderate reduction of GFR</td>
<td>30-59</td>
<td>Evaluate for and treat complications of CKD; avoid nephrotoxic drugs</td>
</tr>
<tr>
<td>4</td>
<td>Severe reduction of GFR</td>
<td>15-29</td>
<td>Prepare for kidney replacement therapy</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt; 15 (or on dialysis)</td>
<td>Start kidney replacement therapy when uremia present</td>
</tr>
</tbody>
</table>

KEY: CKD: Chronic kidney disease; GFR: Glomerular filtration rate; CVD: Cardiovascular disease
*includes actions from preceding stages

Source: Adopted from Sherry et al. [17]

Factors that contribute to the estimation of GFR are weight of an individual, gender, race, age and creatinine. People free from CKD especially those between 20 – 30 years old, normally have GFR of nearly 125 mL/min/1.73m² [17]. To further
explain the general process the flow chart in figure 3 will be used to demystify the various stages from enlistment on the waitlist to receiving kidney transplantation.
Candidate arrives at transplant center

Test is conducted

Candidate needs transplantation?

Yes

Start waiting time counter (Score)

Candidate is enlisted on waiting list (Dialysis)

Is candidate sensitive?

Yes

Give High score

Give points for matching

Organ is compared to candidates for best match

No

Give low score

Candidate waits for organ

Organ available?

Yes

Candidate is transplanted

No

Candidate exits system

No

Candidates are ranked using the total points obtained

Candidate is transplanted

Candidate exits system

Candidate is enlisted on waiting list (Dialysis)

Conduct further tests

Is candidate sensitive?

Yes

Give High score

Give points for matching

Organ is compared to candidates for best match

No

Give low score

Candidate waits for organ

Organ available?

Yes

Candidate is transplanted

No

Candidate exits system

Candidate exits system

Candidate is enlisted on waiting list (Dialysis)

Conduct further tests

Is candidate sensitive?

Yes

Give High score

Give points for matching

Organ is compared to candidates for best match

No

Give low score

Candidate waits for organ

Organ available?

Yes

Candidate is transplanted

No

Candidate exits system

Candidate exits system

Candidate arrives at transplant center

Test is conducted

Candidate needs transplantation?

Yes

Start waiting time counter (Score)

Candidate is enlisted on waiting list (Dialysis)

Is candidate sensitive?

Yes

Give High score

Give points for matching

Organ is compared to candidates for best match

No

Give low score

Candidate waits for organ

Organ available?

Yes

Candidate is transplanted

No

Candidate exits system

Candidate exits system

Figure 1: Flow chart of the kidney allocation model
As observed from figure 1, when a candidate first arrives at a dialysis/transplantation center, a test is conducted to determine whether the candidate needs to be enlisted on the waitlist for dialysis. If it proves that there is the need for dialysis/transplantation (GFR < 20 mL/min/1.73m\(^2\)) the candidate will be enlisted on the waiting list, otherwise the candidate exits the system.

Once a person is enlisted on the waiting list or starts dialysis, he/she starts accumulating annual points for waiting time [13]. At this point other tests are conducted to determine the sensitivity level of the candidate. The sensitivity level is the degree to which a candidate’s antibody rejects a foreign object (organ) [13]. This can be improved by taking immunosuppressive medications [16]. For this reason highly sensitive candidates are prioritized on the current kidney allocation policy to avail them to a wider pool of organs. At this stage candidates wait until there is an organ during which time it is determined whether the candidate is active or inactive. Active candidates are those on the waitlist who are medically, economically, emotionally and physically capable of receiving kidney transplantation [18].

Various situations can lead to the classification of a candidate as inactive: for a candidate to be active he/she must be observed to be following medical directives, financially capable of post transplantation medication, physically in a good condition to go through transplantation and a host of other factors [16]. If these factors among others are not met, a candidate will not be offered a kidney
irrespective of the time spent on the waiting list [16]. This is not a one-time decision since a candidate’s status is not deterministic over time.

Transplant officials continuously examine waiting list candidates to determine their active or inactive status so that organs will be offered to only active candidates. As soon as an organ becomes available points are awarded to active candidates for tissue matching. This is literally the relationship between the organ and the prospective recipient [16]. The total points accumulated by each active candidate are then used to rank them. After this stage the organ is then offered to the topmost ranked candidate who has the option to accept the organ or otherwise. Whenever a candidate refuses to accept an organ, it is offered to the next candidate on the rank until the organ is accepted [13]. Since the kidney is highly perishable, it is soon discarded when it is not accepted by any active candidate. However, when it is accepted by an active candidate, the organ will be transplanted and the candidate will exit the system and continue with post transplantation treatments [19].

The points used to rank the candidates are awarded at three stages in the allocation system: the first stage is when a candidate is deemed qualified to be enlisted on the waiting list. Candidates start accumulating yearly points when they are enlisted on the waiting list database. This stage is highlighted in figure 2. This stage (highlighted by the oval) is a principal component of the current kidney allocation model. It is used as a means to satisfy the fairness constraint in the allocation policy.
Figure 2: First stage of point accumulation
The next stage on the allocation model where a candidate accumulates point is during sensitivity test. Highly sensitive candidates are prioritized by awarding them higher points to increase their chances of receiving an organ offer [13]. At this point the candidate has accumulated points for two parameters: waiting time and sensitivity which are highlighted in figure 3.
Figure 3: First and second stages of points accumulation
After stage 2 candidates will still remain on waiting list and undergo dialysis so as to prevent their condition from further deterioration. The next stage in the allocation policy for point accumulation is the stage when an organ becomes available. At this point tissues of candidates on the waitlist are compared to that of the donated organ. A higher point is awarded to the candidate whose tissue best matches that of the donor. A good tissue matching is a desired trait for allograft survival [11]. A candidate’s blood group also has a direct effect on tissue matching [11]. Starzl [10] explains that human lymphocyte antigen (HLA) are used in a “cross-matching tests.” This test is done to determine the immunological compatibility of the donated kidney and the active candidate. During the cross-matching tests, white blood cells (lymphocytes) from the donor are amalgamated with the serum of the recipient [11]. To minimize organ rejection immunosuppressive medications may be taken by the recipient. Erika [11] explains that three major immunosuppressive medications widely in used are found under glucocorticoid, an antimetabolite, and calcineurin inhibitor.

Although immunosuppressive medications help to boost graft survival, a good tissue matching is a desired property for graft survival [11]. For this reason ones blood type has a direct effect on tissue matching and also determines whom an organ can be offered. Table 2 shows the summary of the ABO blood type compatibility check with rhesus (Rh) factor.

From table 2 it can be concluded that a donor of blood group O can safely donate kidney to a recipient of any blood type without incompatibility issues [11].
However, for tissue compatibility concerns it is dangerous for a candidate of blood type A, B or AB to receive kidneys from a donor of non-A, non-B or non-AB blood type respectively. In 1954 when Dr. Murray first achieved the success in kidney transplantation, the transplant candidate did not take immunosuppressing medication because the kidney donor was a twin brother to the recipient [15] hence tissue incompatibility wasn't a major problem since the two were direct biological siblings.

Table 2: ABO blood type compatibility

<table>
<thead>
<tr>
<th>Transplant</th>
<th>Acceptability</th>
</tr>
</thead>
<tbody>
<tr>
<td>O to non –O</td>
<td>Safe</td>
</tr>
<tr>
<td>Rh- to Rh+</td>
<td>Safe</td>
</tr>
<tr>
<td>Rh+ to Rh-</td>
<td>Relatively safe</td>
</tr>
<tr>
<td>A to non –A</td>
<td>Dangerous</td>
</tr>
<tr>
<td>B to non –B</td>
<td>Dangerous</td>
</tr>
<tr>
<td>AB to non -AB</td>
<td>Dangerous</td>
</tr>
</tbody>
</table>


At this point candidates have accumulated points at three stages in the process: waiting time, sensitivity and for tissue matching. These stages are highlighted below in figure 4. The total score known as the kidney allocation score (KAS) is then used to prioritize the candidates for the kidney offer [19]. The
problem associated with the current kidney allocation policy in the United States, as well as the justification for this research, are explained in the next section.
Figure 4: The three stages of point accumulation
2. OVERVIEW, OBJECTIVES AND JUSTIFICATION OF RESEARCH

A recent report from the Organ Procurement and Transplantation Network (OPTN) and the Scientific Research of Transplant Recipients (SRTR) [20] indicates that kidney discard rate is still alarming and the earlier a solution is found the better. It states that the current discard rate for kidneys is 18% [20]. Although the major contributing factor to kidney discards is biopsy, the report acknowledges that this reason is contentious since suboptimal kidneys are more likely to be discovered before procurement, hence, they may not be procured at the first place. The pancreas has the highest rate of discard (25% to 30%) due to the fact that pancreatic diseases are less critical hence candidates have the luxury of time to wait for a better organ [20]. For this same reason ESRD patients have a high incentive to wait longer for a higher quality kidney since it is also less critical compared to heart related illnesses. Hearts have the least discard rate since diseases associated with hearts are critical hence the lowest rate (1%) of heart discards [20].

The OPTN/SRTR also stated in their annual report [20] that: “some relief of organ shortage may be possible by focusing efforts on minimizing the number of discarded organs recovered for transplant.” This research was undertaken to evaluate the current kidney allocation policy and develop novel ways by which the discard rate of kidneys may be minimized. This is in line with the current needs of OPTN. The research focuses on the kidney since ESRD has the largest number of people on the organ waitlist in the United States [16, 19, 21, 22].
This research also proposes a model for the allocation of kidneys under emergency medical conditions. The National Kidney Foundation (NKF) [23] explains in their publication about the new kidney allocation policy that the allocation of deceased donor kidneys still remains a challenge since the new kidney allocation policy has no provision for kidney allocation under emergency “such as dialysis failure” [23].

The new deceased donor kidney allocation policy approved by the Organ Procurement and Transplantation Network (OPTN) on June 24, 2013 took effect from December 4, 2014. This new policy based on simulation results has the potential to enhance post-transplant survival and access for highly sensitized candidates on the waitlist [24]. However, candidates aged ≥ 50 years are expected to receive fewer transplants. There is also no provision for the allocation of cadaveric kidneys in emergency situations such as dialysis failure. A typical situation is the case of Dr. Martin Salia: Dr. Salia was an American surgeon who contracted the deadly Ebola disease and was flown to a Nebraska hospital for treatment. According to Dr. Phil Smith, the medical director of the bio-containment unit of the Nebraska hospital, Dr. Martin arrived at the University of Nebraska Medical Center with no kidney function and was unresponsive [25].

The Ebola disease was “already extremely advanced” when Dr. Martin got to the University of Nebraska Medical Center, and although all attempts were made by the medical team to save his life, Dr. Martin’s condition was already critical hence kidney transplantation alone may not have been enough to save him, leading to the
waste of an organ. The question therefore is what happens if kidney transplantation was the only option to save his life? If Dr. Martin survived the Ebola virus, was he going to be enrolled on the waitlist and undergo dialysis until he accumulates enough points to rank first before being offered a kidney? What will happen if a pediatric patient suffers from a serious condition like this? Situations like these call for provision in the kidney allocation policy for the allocation of cadaveric kidneys in emergency situations.

Furthermore, the National Kidney Foundation foresees no improvement in the already high discard rate of cadaveric kidneys. A study in 2002 revealed that about 45% of kidneys were refused by the candidates who were first to be offered with kidney [26]. It suffices to conjecture that a kidney that has been rejected will have a higher probability of being discarded than one which has not been rejected before. Although this is not recorded in the literature, one can infer that a candidate will be highly skeptical of accepting a kidney that has been offered and rejected by another candidate ahead of him or her in the ranking order.

When a candidate is enlisted on the waitlist, the attributes of organs that will be accepted by the candidates are recorded. For example a candidate may specify that kidneys from donors of a certain age range, weight, diabetes and hepatitis C status etc. are the only kidneys that will be accepted. In doing this, candidates establish a minimum threshold which can be represented mathematically as:

\[ f(x, y, \ldots) \geq b \]  

(1)
Where \( f(x, y \ldots) \) represents all the attributes of the donor/organ that are of concern to the candidate and \( b \) is the lower limit of the quality of organs that will be accepted by the candidate. This differs for most candidates; hence, candidates with identical functions are grouped together when there is an organ available. For this reason candidates would always want to get the best possible organ which matches with their expectations or maximizes their expectations. To formulate this assume that a candidate’s interest relies only on the weight of the donor \((x)\) and number of years the donor has been smoking \((y)\). Also assume the two factors are assigned weights on an open scale with a higher number indicating desired trait for both variables. The candidate will therefore try to maximize the quality of organ that will be offered as formulated below.

\[
\text{Max} \quad f(x, y) \quad (2)
\]

\[
s.t. \quad \Theta_L \leq x \leq \Theta_U \quad (3)
\]

\[
\Phi_L \leq y \leq \Phi_U \quad (4)
\]

\( \Theta_L, \Theta_U, \) are the lower and upper limits of the weights assigned to the first factor of interest, and \( \Phi_L, \Phi_U, \) are the lower and upper limits of the weights assigned to the second factor of interest. Since every candidate has preference for the type of organs that will be accepted, this study offers recommendations on how to get transplant centers and candidates to have minimum incentive to reject kidney offers perceived as suboptimal. The study also proposes ways for kidney allocation under emergency situations.
This is necessary because there are thousands of people waiting for kidney transplantation in the United States. However, several thousands of kidneys procured for transplantation are discarded yearly while thousands of candidates die on the waiting list for non-availability of kidney. About 20,000 people died on the waitlist from 2009 to 2011 while over 4700 people got removed from the waitlist for becoming too sick to receive transplantation. Because of this problem the OPTN is looking for new ways to minimize the discard rate of cadaveric kidneys so that more people suffering from ESRD can have access to kidney transplantation. This research proposes ways which may help to minimize the discard rate of kidneys, and also proposes a model for kidney allocation under emergency medical situations. The next section discusses the literature about kidney allocation in the United States.
3. LITERATURE REVIEW

3.1. Kidney Allocation Policy

The National Organ Transplant Act (NOTA) laid the foundation for regulating kidney allocation in the United States. This act was passed by the US congress in 1984 [11]. The act established OPTN which is managed by a non-profit organization: United Network for Organ Sharing (UNOS) according to preset priority rules. UNOS manages a national kidney waitlist of all candidates needing transplantation [13]. Local organ procurement organizations (OPOs) who are also non-profit organizations procure kidneys and allocate them to candidates on their local waitlist based on UNOS/OPTN priority allocation rules. If no candidate is found the search is extended to nearby regions after which it becomes a nationwide search [13] [21]. Although the kidney allocation policy has gone through a series of evolutions, the principal ingredients of the policy remain intact. The major components of the current kidney allocation policy are waiting time, tissue matching and sensitivity [13].

The kidney allocation problem extends from unmatched demand and supply to high discard rate of expanded criteria donor (ECD) kidneys. In solving this problem researchers have worked on evaluating the performance of the allocation policy, the impact of surgeons and patients’ decision in accepting or rejecting kidney offer, and optimization of the allocation policy. The sections below throw more light on the different areas of research in the literature starting with surgeons and patients decision models.
3.1.1. Surgeons and Patients Decision model

The decisions made by surgeons and their patients play an important role in the utilization of kidneys. In 2002 about 45% of kidneys were refused by the candidates who were first to be offered with kidney [26]. Since the acceptance or rejection of organ depends on a collective decision making of candidates and their surgeons, models focusing on surgeon and patient decision making in the acceptance or rejection of an organ has also been studied; David and Yechiali [27] use optimal stopping criteria to model the patient–surgeon decision making. The patient-surgeon receives an offer for organ $X_j$ at a discrete decision epoch.

According to the authors the offer for organs follows a distribution function $F(x) = P(X \leq x)$ which is made up of organs offered in the sequence of independent but identically distributed stochastic variables [27].

At decision epoch $t_j$ there are two options that the patient and surgeon will have to choose from: accept the organ or reject of which one has to be made [27]. A reward $\beta(t_j)X_j$ is gained when the patient-surgeon accepts the offer. They explain that the discount function $\beta(t) \geq 0$ is a non-increasing function [27]. The discount function is the weight placed on the acceptance of the organ. They assume that the acceptance of the organ offer will positively enhance the patient’s life hence the reward is always greater than zero. This is a logical assumption since all parties in transplantation embark on it with the same assumption although some results in death. Transplant survival rates have also been increasing [18] which supports their
assumption. However, since transplantations do not always result in the positive outcome, the reward or the weight can be equal to zero which is equivalent to death. In this case there are no negative results associated with the acceptance of the organ offer [27].

When the offer is rejected, the process continues when there is another organ and terminates only when the patient dies or is removed from the waiting list for any other reason(s) [27]. Their model explains that patients are more selective when offers come more frequently [27]. This is intuitive since the chances of receiving an organ offer will be high. They further explain by assuming that the organ offer rate follows a uniform Poison process $\lambda$, an exponential rate of patient life $r$, and a reward $\beta(t) = e^{-\beta t}$. Under this situation the offer will be accepted only if $\beta(t) = e^{-\beta t} > \gamma$ where $\gamma$ is a reward threshold [26]. Zenios [26] explains that the optimal stopping time occurs when a solution is obtained for the equation:

$$\gamma = \frac{P(X \geq \gamma)\lambda}{\beta + r}$$  \hfill (5)

It can be deduced from the above equation that $\gamma$ decreases as the discount rate ($\beta$) and death rate ($r$) increases. However, $\gamma$ increases as offer rate increases. This means that more organs will be rejected when offers come often [26]. This is practical since people by nature are selective when there are more options to choose from. However, when death rate increases or when patient’s medical condition deteriorates, they are less likely to reject an organ. This is the situation
with heart disease patients. Since heart related illness are critical, candidates are less selective hence the discard rate of heart is the lowest among all organs [20].

To further enhance this model Ahn and Hornberger [28] did further work by classifying patients into 5 different states: “alive on dialysis waiting for transplant ($S_1$); not eligible for transplantation ($S_2$); received a functioning renal transplant ($S_3$), transplant failed ($S_4$); and death ($S_5$).” They observed that every patient on the waiting list at a point in time belongs to one of the above states and with time, transitions to another state through a Markovian process [26]. They assumed that within a month a patient may transition from one of the states to another and based on this, they calculated monthly transitional rates.

A patient can transition between $S_1$ and $S_2$, $S_1$ and $S_3$, $S_1$ and $S_4$, and $S_1$ to $S_5$. There is no direct transition between $S_2$ and $S_3$ since a patient not qualified for transplantation ($S_2$) cannot receive a renal transplant ($S_3$). These patients are the inactive patients on the transplant waitlist. For example, a candidate whose status is inactive due to financial constraint will not be offered a kidney. One can also stay in the same stage without transitioning to another stage. Patients can also transition from any of the states to $S_5$; however, there is no transition back from $S_5$ to any other state. At state $S_5$ the patient’s details are removed from the database since they became too sick to be considered for transplantation, or they died. These processes representing a Markov chain are illustrated in figure 5. The circles denote the states while the arcs denote the transitions between states.
They proposed the involvement of patients in the allocation policy with the aim of improving the utilization of organs. This was based on the results from empirical data which proved that a patient’s decision to accept or reject an organ depends on the patient’s knowledge about his/her state of health [28]. Although this is a laudable idea and has actually been the case in kidney allocation, it also has the potential to increase the discard rate of kidneys since candidates in a perceived good state will be tempted to wait for the best of organs. This might have contributed to the high discard rate of cadaveric kidneys for which transplant surgeons have expressed concerns [29, 30].

Surgeons are more likely to reject a perceived sub-optimal organ in anticipation for a higher quality organ for a relatively healthy patient [29]. Howard [31] has proven that transplant surgeons take into account the health of the patient...
in accepting or rejecting an organ. In his model, a surgeon makes a decision to accept or reject an organ when offered. This organ will be transplanted on a patient whose health state is \( h \in (0, \overline{h}) \), and of quality \( q \in (0, \overline{q}) \). According to the author the health of the patient goes through a first-order Markov process \( f(h' / h^2) \) in the event of a rejection of the organ by the surgeon/patient. The death of the patient is given by the state \( h=0 \), and \( q=0 \) is the state when there is no organ offer. This means there is no negative state in terms of patient’s health. The organs are offered from a quality distribution function \( f(q) \). Organ will be offered to the patient/surgeon from this function as organs become available until the patient is removed from the waiting list for accepting an organ, death, becoming too sick to receive transplantation or for any other reason that leads to the removal of the patient from the waiting list [31].

Due to the scarcity of organs, the state where \( q = 0 \) is the most frequent state that will be observed [31]. The probability \( p(h, q) \) where \( ph(h, q) > 0 \), \( Pq(h, q) > 0 \), \( p(0, q) = 0 \) and \( p(0, h) = 0 \) defines the event of a successful transplantation at period \( t + 1 \). This directly depends on the patient’s health at period \( t \) when the organ was offered [31]. To simplify the formulation Howard assumes that a transplantation results in two outcomes: a success with reward \( B \) and a failure (death) with reward of 0. His model also does not account for patients who experience graft failure who must be re-enlisted on the waitlist for a second transplantation. That’s every transplantation is classified as a success or failure. With a discount factor \( \delta \) and
utility factor \( u \), he further explains that if the organ is accepted by the patient/surgeon for transplantation at time \( t+1 \) the expected payoff is given by:

\[
EV^{TX}(h,q) = p(h,q)B
\]  

(6)

If the organ is rejected the patient remains on the waiting list with an expected payoff given by:

\[
EV^{W}(h) = \int_{q} \int_{h} V^{W}(h',q') f(h'|h) f(q'|q) dh' dq'
\]  

(7)

Where \( V^{W}(h,q) \) is defined by the Bellman equation given by:

\[
V^{W}(h,q) = u + \delta \max\{EV^{TX}(h,q), EV^{W}(h)\}
\]  

(8)

Since the surgeon and patient are interested in maximizing the reward after transplantation, the author explains that the organ will be accepted when the payoff for accepting the organ is greater than the payoff for refusing \( (EV^{TX}(h,q) > EV^{W}(h)) \). Howard further explains that the huge premium placed on survival rates of transplant candidates by policy regulators, patients and private insurance in awarding of contracts gives a hidden motivational factor to surgeons to reject organs perceived to be sub-optimal which may negatively affect the survival rate of their transplant centers [31]. He also suggests that transplant centers that reject organs but are eventually transplanted successfully by other transplant centers must be penalized. This is a wonderful proposal and a way to minimize the discard
rate of kidneys; however, it will be difficult to integrate into the kidney allocation model which has been built around patients and organ donors.

Alagoz et al. [32] modeled the patient/surgeon decision making problem for liver transplantation. A discounted Markov decision process (MDP) was used by the authors to model the problem as an infinite horizon, discrete-time, problem with the states defined by the patient health and quality of organ. They assumed that the probability of the surgeon/patient accepting a liver type \( l \) at time \( t \) for transplantation at time \( t + 1 \) is affected only by the patient health state at time \( t \) and is independent on the liver type \( l \) [32].

This is in contrast to Howard’s model [31] which considers the quality of the kidney as a deciding factor that affects the accept/reject decision making. In their model the decision maker at a state \( (h, l) \) has two options to choose from: “accept and transplant” the liver \( l \) or “wait for one more decision epoch.” If the organ is accepted, the patient receives a reward \( r(h, l) \), exits the process and moves to absorbing state “transplant” with absolute probability [32]. They further explain that an intermediate reward \( c(h) \) is received when the organ is rejected and moves to state \( (h', l') \in S \) with probability \( P(h', l'|h) \) where \( S \) is the state space. This is when the patient waits for another decision epoch for another offer. The intermediate reward can be viewed as the effect on the patient’s life for waiting further for another organ offer. They obtained the optimal solution by solving the following recursive equation [32, 33]:

\[
V(h) = \max_{l \in L} \left( r(h, l) + \beta \sum_{h' \in S} P(h' | h) V(h') \right)
\]
\[ V(h, l) = \max \left\{ r(h, l), c(h) + \lambda \sum_{(h', l') \in S} P(h', l' | h) V(h', l'), h \in \{1, \ldots, H\}, l \in S_L \right\} \] (9)

Where \( V(h, l) \) is the maximum total expected discounted reward that can be achieved by a patient in state \( h \) and offered with a liver \( l \) [32].

They introduced two control limits; one based on liver ("liver-based control limit") and one based on patient state ("patient-based control limit") for the optimal decision making. The liver-based control limit states that the liver \( l \) will be accepted for transplantation if and only if \( l \) is of type \( 1, 2, \ldots, i(h) \) for some liver state \( i(h) \) which is called liver-based control limit [32]. Also some patient state \( j(l) \) defines the patient limit control limit for the acceptance of the liver \( l \) if and only if the patient belongs to one of the states \( j(l), j(l) + 1, \ldots, H \) [32]. Comparing the optimal control limit for a patient in two distinct regions, they observed a lower optimal-liver based limits for the region where the patient receives better quality liver at a higher frequency. The other region which offers a lower quality liver at a lower frequency gives a higher optimal liver-based control limit [32]. The authors explain that a patient’s chances of receiving a liver offer, is directly dependent on the patient’s location; moreover, the liver-based control limit was always the optimal policy [33].

Besides decision based models, researchers have also researched about organ allocation with different focus. The next section discusses other research areas studied in the literature.
3.1.2. Other optimization approaches to organ allocation

The organ allocation policy has also been approached by various researchers from other perspectives. David and Yechiali [34] applied stochastic optimization to model the organ allocation problem as a sequence matching problem where a set of \( M \) offers arrive randomly for assignment to \( N \) waiting list candidates sequentially. The patient and organ have a finite set of attributes \( X = (X_1, X_2, ..., X_p) \) [34]. When an organ becomes available, the attributes of the patient and the organ are matched to determine the reward which is the total number of matching attributes. The attributes of the patient are known beforehand since the patient has been on the waiting list [34]. However, the organ attribute can be known only when it is procured. A patient receives a reward \( R \) when the attributes match with that of the organ. A mismatch yields a reward \( r \leq R \) [34].

In the organ allocation problem there are always more patients on the waitlist than organs. However, David and Yechiali first solved the general case where there are more organs \( (M) \) than the number of candidates on the waiting list \( (N) \). They solve this by allocating organs to each candidate on the waiting list at a fixed discount rate: \( 0 \leq \alpha \leq 1 \). They assign respective frequencies for \( P(X = a_1), ... P(X = a_N) \) of the \( N \) realizations, and are denoted by \( f_1, ... f_N \) with the assumption that \( f_1 \leq f_2 \leq ... \leq f_N \) [34]. The probability that there will be a mismatch for a random offer for all distinct candidates on the waiting list is denoted by
\[
\bar{f} = 1 - \sum_{i=1}^{N} f_i.
\]
They use the notations \((f)\) for \((f_1, \ldots, f_{N+1})\) and \((f_i)\) for \((f_1, \ldots, f_{i-1}, f_{i+1}, \ldots, f_{N+1})\) and formulate the optimality equations as:

\[
V_{N+1,M+1}(f) | X_1 = \max \begin{cases} 
R + \alpha V_{N,M}(f_{-i}) | \{X_1 = a_i\} & \text{(match)}; \\
\rho + \alpha \max_k V_{N,M}(f_{-k}) & \text{(a mismatch)}; \\
\alpha V_{N+1,M}(f) & \text{(rejection)}, 
\end{cases}
\]

The maximum expected total discounted reward is given by \(V_{N,M}(f)\) [34]. For the most realistic situation which is common for all solid organ \((N<M)\), thus, more waitlist candidates than organs, they indicate that assigning a match whenever possible is optimal. Under the same condition rejecting a mismatch is dependent on the following: \(\alpha \xi_i \geq r\) or \(\alpha \xi_i < r\) given \(\xi_i = f_i R + (1-f_i)r\) [34].

They also optimized other cases; when \(M=N\), thus, the number of organs is equal to the number of candidates on the waiting list which will rarely occur. Under this condition the optimal policy is to assign the organ to the candidate with the uncommonness of attributes [34]. Further details about the proof of their formulations and other scenarios can be found in [34].

Zenios et al. [35] applied dynamic programming to maximize clinical efficiency also called quality adjusted life years (QALY) while minimizing two other inequality functions: mean waiting time to kidney transplantation and chances of transplantation of distinct patient types [35]. The two functions respectively track fairness in average waiting time to kidney offer and fairness in access to kidneys among different groups of patients [35]. They apply a fluid model to model kidney
allocation in a continuous time, continuous space deterministic function [35]. The authors explain that the dynamism of their model allow it to track the changes in the waiting list over time. This leaves the model open without a closed form solution and not tractable [35].

Their model also classifies the candidates into groups based on demographics, immunological and physiological attributes. Unlike other models Zenios et al.’s. model considers re-enlistments [35]. Without loss of generality they assume that one group of patients belong to class \( k = 1, \ldots, k_w \). This class consists of patients on the waiting list. They join the list at the rate \( \lambda_k^j \) and leave either through receiving transplantation or death at the rate \( \mu_k \) per time unit [35]. The number of patients in each class at a time \( t \) is defined by the \( K \)-dimensional column vector

\[
x(t) = (x_1(t), \ldots, x_K(t))^T
\]  

[35]. They also assume \( K \) patients in the system who will receive organs from a set of \( J \) donors. A fraction \( \nu_{jk}^j(t) \) of organ \( j = (1, \ldots, J) \) with arrival rate \( \lambda_j^j \) is allocated to patients in class \( k \). When a patient receives the kidney and transplanted, there is a transition from the class \( k = 1, \ldots, k_w \) to class

\[
c(k, j) = (K_w + 1, \ldots, K).
\]  

A proportion of the candidates who received transplantation will rejoin the class \( k = 1, \ldots, k_w \) due to graft failure; the remaining portion will exit the system through death or successful transplantation [35].

They formulated the system state equation using linear differential equations as:
The limitations of this model as discussed by the authors are: no consideration for organ sharing among OPOs, unavailability of kidney recipients, and the ignoring of cross matching between recipient and donor. They also assume that the dynamics of the system is deterministic although the arrival or organs, transplantation and graft failure rates are all stochastic in nature. However, they argue that the model addresses the major factors in the then kidney allocation policy: efficiency and the imbalance in demand and supply [35].

The other two objectives: likelihood to receive transplantation and fairness in waiting time were integrated into the fluid system state equation and upon further approximations they obtained the objective function for the three criteria objectives [35]. The equation is shown below:

$$\max \text{imize } \int_0^T (\beta h' x(t) - (1 - \beta) x(t)' R x(t) + \gamma' D \mu(t)) dt$$

(13)

Where $\beta \in [0, 1]$

This equation does not provide a closed form solution and still remains difficult to solve mathematically [36] hence a dynamic index policy was used to offer
class \( j \) kidneys to class \( k \) candidates on the waiting list [36]. The performance of the dynamic index policy kidney allocation model can best be seen through simulation. The authors demonstrate its performance through simulation for a single OPO. By modifying the donor arrival rate, post transplantation and pre-transplantation mortality rates, distribution of patients (classes) and donor characteristics they concluded that the dynamic index policy minimizes waiting time and maximizes QALY [36].

Roth et al. [37] applied graph theory to model the kidney allocation problem as an exchange of living donor kidneys between a donor-recipient pair where each of the donors is incompatible with the original recipient. The edges (lines) of the graph link the patients whose donors are compatible with secondary recipients. The vertices of the graph also denote the patient and the original donor. They conclude that kidney exchange benefits both the patients who receive the paired kidneys and the other patients on the waiting list who have no live donor [37]. It minimizes waiting time for all candidates and also helps to increase the number of people who gain from the enormous benefits that come with transplantations involving living donor kidneys [37].

Su and Zenios [26] also modeled the kidney allocation by classifying waiting list candidates as either “autonomous or non-autonomous.” The former assumes that patients have no say in organ offer and must always accept any organ offered them at time \( t \) [26]. The latter also assumes that patients have the right to decide whether to accept or reject an organ. This represents the realities of the current
kidney allocation policy where patients have the right to either accept or reject an organ offer [13]. Candidates on the waiting list generally reject an organ in anticipation of a better quality organ [31]. The first condition will greatly improve organ utilization and reduce waiting time but the decision to accept/reject an organ does not always come from patients alone.

Transplantation centers are evaluated on survival rates hence an organ of a perceived lower quality has a higher chance of being rejected by a transplant surgeon so as to minimize the risk of post transplantation death which affects the center's survival rate [31]. Excellent survival rates are prerequisites for winning certain contracts [31]. The authors demonstrate that candidates' autonomy in kidney allocation makes it difficult to maintain the balance between equity and efficiency [31]. They explain that candidate's autonomy benefits only the individual but greatly degrades the effectiveness of the entire kidney allocation policy [26]. It is intuitive to agree with the authors since a candidate with the highest priority points on the waiting list has a higher chance of rejecting a kidney offer at time $t$ since another kidney at time $t+1$ will also first be offered to him before other candidates will be considered.

Stahl et al. [38] apply integer programming to determine the optimal size of OPOs and UNOS transplant regions using geographical equity and efficiency as performance measures. They consider the intramural regional communication between OPOs and respectively, measure efficiency and geographical equity by the frequency of transplants of intramural regions and minimum transplant rate among
OPOs within a region. They apply this model to liver allocation and model the
regions into a set of networks of nodes representing the OPOs which are joined
together by arcs. Since liver has short ischemia time they assumed that the decision
to accept or reject a liver offer depends only on cold-ischemia time (CIT) which
directly depends on the geographical distance from the OPO location to the
transplant center in the case of a cadaveric donor [38]. Unlike kidney allocation
where OPOs in one region can allocate organs to candidates outside of their
designated service area through the organ sharing and payback policy, their model
did not allow the allocation of liver to candidates outside of their region [38]. This
perhaps may be due to the fact that livers have short ischemic time compared to
kidneys [16]. They formulated the integer program model as:

\[
\left\{ \begin{array}{l}
\text{Max} \sum_{j \in J} c_j x_j : \sum_{j \in J} a_{ij} x_j = 1, i \in I; x_j \in \{0, 1\}, j \in J
\end{array} \right\}
\]

where

\[
x_j = \begin{cases} 
1 & \text{region } j \text{ chosen} \\
0 & \text{otherwise}
\end{cases}
\]

\[
a_{ij} = \begin{cases} 
1 & \text{OPO is in } J \\
0 & \text{otherwise}
\end{cases}
\]

The number of OPOs is represented by \( I \); \( J \) is a group of regions; and \( c_j \) is the sum of
regional intermural transplants for region \( j \). This model provides the optimal
number of regions that maximizes the total number of transplants [38].
Another integer programming model was formulated by the authors to solve the geographical equity objective; to formulate the model $\rho$ is defined as the importance patients/surgeons assign to transplant rate. To accommodate this factor the authors [38] modified the model to:

$$\left\{ \text{Max} \sum_{j \in J} c_{ij} x_j + \rho \lambda_{\min} \sum_{j \in J} a_{ij} x_j = 1, \; i \in I; \sum_{j \in J} f_{ij} x_j - \lambda_{\min} \geq 0, \; i \in I; x_j \in \{0,1\}, \; j \in J \right\}$$

(15)

The authors conclude that the optimal sets of regions are more inclined to highly populated areas. This perhaps might be due to the fact that OPOs and transplantation centers are rarely located in sparsely populated areas. They also explain that as the importance that decision makers place on minimum transplant rate across OPOs increases against intramural regional transplantations, the effect on the regional and OPO sizes (as at 2004) decreases [38].

A more recent work by Dimitris et al. [13] optimizes kidney allocation by focusing on equity, efficiency with flexibility in kidney allocation. In their paper the authors discuss some of the major challenges faced in modeling the kidney allocation policy. They explain that people will continue to disagree on the meaning of fairness due to its subjectivity; policy makers and academicians have not yet agreed on a common definition for fairness in kidney allocation [13].

To improve on the transparency of kidney allocation model the policy must be easy to communicate to the transplant community. The authors explain that this will help physicians, patients and their family to make informed decisions about transplantation options. A thorough understanding of the allocation policy will
enhance their abilities to estimate the chances of receiving organ offer hence kidney allocation model needs to be relatively simple to enhance easy communication [13]. Also to obtain the maximum benefits from kidney as a national resource, the kidney allocation policy must be efficient; this means that it must aim to maximize the life years gained from transplantation. For example, a kidney from a healthy 17 year old donor has a high probability of maximizing the gains if offered to a young recipient than a very old recipient.

In 2011 the OPTN released a request for information about the proposal to allocate the top 20% of kidneys to waiting list candidates < 35 years as a means of maximizing efficiency [39]. It is believed that the young-donor young-recipient pair called age matching will help to minimize the possibility of re-transplantation. This may also help to prevent the situation whereby transplanted candidates die with functioning kidneys [39]. Finally, the allocation policy must be easy to be implemented. This involves the collation and balancing of all the priority rules needed to formulate a unified allocation policy.

Dimitris et al. [13] in their paper adopted the current point scoring kidney allocation system and address the above challenges by proposing a model that allows the policy maker to decide on his/her own fairness constraint with flexibility [13]. This model will be reviewed in detail in the subsequent section.

3.1.3. The Current Kidney Allocation Policy

The OPTN is in charge of developing kidney allocation policy; however, every policy developed by OPTN needs approval from the U.S. Department of Health &
Human Services [40]. By legislative instrument the kidney allocation policy must meet legal, ethical, and economical requirements. In order to formulate kidney allocation policy, OPTN must ensure that the policy satisfies all the rules stipulated by the OPTN Rule [40]. Dimitris et al. [13] summarizes the regulations into four major rules stated below. The OPTN:

1. Shall seek to achieve the best use of donated organs, and avoid organ wastage;
2. Shall set priority ranking based on sound medical judgment;
3. Shall balance medical efficiency and equity, without discriminating against patients based on their race, age and blood type;
4. Shall be reviewed periodically and revised as appropriate.

To satisfy these regulations the OPTN allocates kidneys based on point scoring system [3, 13]. The candidates on the waiting list are ranked based on a calculated score called *Kidney Allocation Score* (KAS) [13]. Under this system each candidate receives a certain amount of points based on selected factors in the allocation policy. This system of kidney allocation has been used for over two decades [13]. The factors that go into the point scoring of the current kidney allocation policy are waiting time (also called dialysis time ($DT$)), life years from transplantation ($LYFT$), donor profile index ($DPI$), and calculated panel reactivity antibody ($CPRA$). Dimitris et al. [13] itemize in detail the components of a potential kidney allocation policy as:

1. Tissue matching or Human leukocyte antigen (HLA) matches which is the number of HLA shared by patient $p$ and organ $o$ [13]. HLA are proteins in the immune system
of humans, and a good match between the donor and a recipient’s HLA is a desired trait for best transplant outcomes [41]. HLA typing methods include: serology based typing and molecular based typing. For details about HLA the reader is referred to Schreuder et al. [42];

2. Age of patient $p$ and/or donor of organ $o$, denoted by $AGE(p)$ and $AGE(o)$;

3. Waiting time, which is equal to the number of years patient $p$ has been on the waiting list;

4. Dialysis time, which is equal to the years patient $p$ has spent on dialysis, denoted by $DT(p)$;

5. Blood group of patient and/or donor;

6. Expected post-transplant survival of patient $p$ from receiving organ $o$. This is the likelihood of survival of patient $p$ after receiving transplantation with organ $o$;

7. Expected waitlist survival of patient. This is an estimation of how long the patient can stay on the waiting list and still be classified as active candidate for future considerations in organ offer;

8. Life years from transplant, denoted by $LYFT(p, o)$ [13]. This is the benefits that patient $p$ is expected to gain when transplanted with organ $o$ as compared to patient $p$ remaining on dialysis [43];

9. Donor profile index, denoted by $DPI(o)$. This is a fraction ranging from 0 to 1. A kidney of highest quality has a $DPI$ equal to 0. The $DPI$ increases with a decrease in kidney quality. This means that a kidney of the lowest quality have a $DPI$ of 1;
10. Calculated panel reactive antibody, denoted by $CPRA(p)$. Unlike $DPI$, a candidate with CPRA equal to 0 has the lowest level of sensitivity. This is the degree to which the immune system of the recipient rejects/accepts a foreign object (kidney). A highly sensitive patient’s immune system rejects a lot of organs and has a $CPRA \geq 80$ [13, 43]. CPRA ranges from 0 to 100 [13].

The current kidney allocation policy assigns weights to some of these parameters to define the priority rule. This model first proposed in 2008 by OPTN (as cited in [13]) assigns static weights to $LYFT$, $DPI$, $DT$ and $CPRA$ [13]. The model is shown below:

$$KAS(p, o) = 0.8 \times LYFT(p, o) \times (1 - DPI(o)) + 0.8 \times DT(p) \times DPI(o) + 0.2 \times DT(p) + 0.04 \times CPRA(p).$$

This model is wonderfully formulated to alternate between efficiency ($LYFT$) and equity ($DT$). It ensures that for kidney with DPI equal to 0 indicating the highest quality kidney, priority is given to the patient with the highest $LYFT$ [13]. This is maximizing efficiency of the kidney so as to reduce the chances of re-transplantation. Moreover, for a kidney with a DPI equal to 1 the model prioritizes dialysis time (equity). This is also aimed at achieving the fairness constraint in the OPTN rule. Both the medical efficiency and fairness variables are assigned the same weight of 0.8. One only takes priority over the other depending on the quality of the kidney.

Because a DPI equal to 0 can annul the importance of the dialysis time, the model has another DT to serve as a recourse variable to satisfy the fairness
constraint; as seen in the equation above the $0.2DT$ is there to strengthen the importance of the time candidates spend on dialysis or waiting list. This term is independent on the quality of the kidney hence candidates with the longest time on dialysis still have a chance to be offered the highest quality kidney even if their LYFT is very small.

The last term in the allocation model (CPRA) is also there to give priority to highly sensitive candidates on the waiting list. Since highly sensitive candidates’ immune system rejects a lot of organs, they are naturally limited to a smaller pool of organs so this factor gives them the push to be considered at a higher frequency whenever an organ becomes available. This also poses a risk and may contribute to graft rejection. This was not a major factor when Dr. Murray achieved the first success in kidney transplantation since the donor and the recipient were siblings hence their tissues matched as desired [11].

Dimitris et al. [13] used the same parameters as in the current kidney allocation model and formulated a kidney allocation model to maximize LYFT subject to the fairness constraint. Their model offers flexibility to the policy maker to define the fairness constraints. Using historical data they show that their model maximizes efficiency and simulation results showed approximately 8% increase in LYFT when compared to the former national kidney allocation model [13]. The diagram below (adopted from [13]) shows how their model operates:
In figure 6 the score components are the donor profile index, calculated panel reactivity antibody and dialysis time is the fairness constraint. The weights assigned to the score components are derived from historical data. They explain that their model is flexible [13] for the policy maker to specify the fairness constraint which could also be a lower or upper bound such as allocating top 20% of kidneys to candidates < 35 years as proposed in 2012 by OPTN [21] or 40% of all organs to people of a specific blood group. The authors formulate their model in a sequence of stages described below:

They first assume that a set of patients and organs pairs \( C = (p, o) \) are compatible for transplantation at time \( t \) and are subject to a fairness constraint \( Ax \leq b \) where \( A \) and \( b \) are some matrix and vector respectively. The objective function for maximizing efficiency was formulated by the authors as:
where

\[ x_{(p,o)} = \begin{cases} 
1, & \text{if organ } o \text{ is assigned to patient } p, \\
0, & \text{otherwise.} 
\end{cases} \]

This model also assumes that patients have no autonomy hence every organ once offered must be accepted for transplantation [3, 13] although this does not represent the reality. They explain that when the candidates are given the autonomy to decide on accepting or refusing an offer, then \( x_{(p,o)} \) can take a fractional value between 0 and 1 [13].

Applying the concept of duality, they [13] also formulated the dual model as:

\[
\begin{align*}
\text{maximize} & \quad \sum_{(p,o) \in C} \text{LYFT}(p,o)x_{(p,o)} - y^T Ax + y^T b \\
\text{subject to} & \quad \sum_{o; (p,o) \in C} x_{(p,o)} \leq 1, \quad \forall p \\
& \quad \sum_{p; (p,o) \in C} x_{(p,o)} \leq 1, \quad \forall o \\
& \quad x \geq 0.
\end{align*}
\]
where $y$ is the optimal dual multiplier of the matrix in the fairness constraint. This then becomes a matching problem between recipients and donors by maximizing the expected results [13, 44, 45].

By representing

$$LYFT(p,o) - (y^TA)_{(p,o)} = K_{(p,o)}$$

$$\forall (p,o) \in C$$

where $K_{(p,o)}$ is the cost factor in the dual model an equivalent matching problem can be written as $K^Tx + y^Tb$ [13, 45]. The next section discusses kidney procurement and the complex organizational structure in kidney procurement and allocation.
4.0. KIDNEY PROCUREMENT AND ORGANIZATIONAL STRUCTURE

Kidney, a highly perishable organ has an ischemic period of approximately 36-48 hours [13], hence there is the need for specialist to transplant donated kidneys within the shortest possible time. Ischemia is the time the organ (kidney) stays without direct blood supply or oxygen from the donor [11]. In the case of a living donor this time is minimized since the donor can be transported to the surgical center where the recipient will be going through the transplantation. However, this is not always the case for deceased donor kidneys; in the case of a deceased donor (also known as cadaveric donor) the kidney has to be transported to the transplant center of the recipient.

Studies have shown that ischemia period has a direct effect on the quality of transplantation [46]. The “ideal” kidney is therefore the one donated by a living and healthy donor; however, due to the ever increasing number of ESRD patients and the unavailability if living donors, candidates on the kidney waitlist have to rely on kidneys from deceased donors [16]. Erika [11] explains that compared to two decades ago the advancement of knowledge in the fluids used for kidney preservation has helped to increase the length of time that a kidney can be preserved [11]. This helps to preserve (for a much longer period) kidneys from deceased donors from going bad hence increasing the pool of organs for the waiting list candidates.

Various organizations and regulations govern the procurement, allocation and transplantation of deceased and living donor kidneys. Among these
organizations are the Organ Procurement and Transplantation Network (OPTN), United Network for Organ Sharing (UNOS), and Organ Procurement Organizations (OPO). Some notable legislative instruments that also govern kidney procurement, allocation and transplantation are the Uniform Anatomical Gift Act (UAGA), National Organ Transplantation Act (NOTA), and Omnibus Budget Reconciliation Act (OBRA) [11]. The section below throws more light on the roles played by these organizations and legal instruments.

4.1 Organ Procurement and Transplantation Network

In 1984 the United States Congress created the Organ Procurement and Transplantation Network when it passed the National Organ Transplant Act. The NOTA entrusted OPTN with enormous responsibilities; among the responsibilities of OPTN as observed in [47] are:

1. Facilitation of organ matching. OPTN must use computerized system for organ matching and allocation which must be in service for 24 hours each day.

2. Providing professional and public education on organ donation and transplantation.

3. Developing general agreements and policies for the procurement, allocation and transportation of organs.

4. Collection of scientific data and management of the data related to organ donation and transplantation.

5. Providing scientific data to researchers for research on solid organ allocation and transplantation.
6. Finally, OPTN was also tasked to develop, maintain and provide security for a web-based computer system. This web-based computer system must contain recipient/donor organ characteristics and the candidates on the waiting list.

OPTN acts as the umbrella body for organ procurement, transportation, allocation and transplantation. As a federal law, Medicare funds can never be received by organ procurement organizations or transplantation centers unless they are part of OPTN [11, 47].

There are also other bodies that are members of the OPTN: independent histocompatibility laboratories with connection to organ transplantation, scientific organizations, professional organizations, voluntary health and patient advocacy organizations [11]. There are also members from the general public; these are people with keen interest in organ donation and/or transplantation [11, 47]. As a legislative requirement all transplantation centers and their affiliates are required to be members of OPTN [11] before they can operate in the sector. OPTN also ensures that its members comply with all the bylaws and maintains standards so as to guarantee public safety and to enhance public trust in the allocation system. To become a member of OPTN one needs to go through a formal application processes which are explained in the following section.

4.2. Application for OPTN Membership

The OPTN [21] explains that to become a member as an OPO or transplantation center there must be a formal application to the OPTN after which the OPTN Membership and Professional Standards Committee (MPSC) will
thoroughly review the prospective member’s application. This review is done by a “confidential medical peer” review team who advises the OPTN Board of Directors about the applicant’s level of readiness. Based on their recommendations the board decides whether to accept or reject the applicant’s application [21].

OPTN makes it clear that prospective applicants must agree to exhaust all internal administrative instruments before proceeding to the law court in case an application is rejected [21]. Without this declaration an application will be considered as incomplete and will not receive the attention and subsequent review by the MPSC [21]. An applicant is granted an interim membership when the MPSC members unanimously recommend to the OPTN board for the acceptance of the application [21]. This interim membership ceases to be legal when the board decides otherwise; however, when even one of the review committee members recommends that the application should be rejected, the applicant receives no interim membership and must wait for the final decision from the OPTN board of directors. Hospitals applying for OPTN membership as part of the requirement, must also apply as a transplantation center for at least one organ [21]. Such a hospital is also required to meet a staffing requirement; typically a hospital applying for membership should have a medical director, experienced transplant surgeon, transplant physicians, transplant coordinator, financial coordinator, and social support staff [11]. When a hospital is approved as a transplantation center, OPTN periodically reviews their transplantation survival rates to ensure that the best of service is offered to the public [21].
Hospitals that fall below an acceptable rate will have their membership status reviewed by the MPSC which can result in the suspension of membership [11, 21]. Unlike the MPSC and its subcommittee that rely on unanimous decisions to grant interim membership, the board of directors’ decision to reject or grant membership of an applicant is based on majority decision during a quorum meeting [21]. A quorum is formed when at least 50% of the Board of Directors who qualify to vote is present at a meeting [21]. One of the OPTN internal administrative tools that an applicant can utilize when an application is rejected is re-application.

A hospital applying to become a transplant program center or any other prospective member can re-apply for further considerations after initial rejection. During the re-application process the applicant will be required to show a proof that the circumstances that led to the initial rejection are resolved. This is achieved by submitting additional documentations to the MPSC or its representative [21]. The re-application goes through the same review process as the first application [21]. Figure 7 demystifies the processes that an individual or organization has to follow to become a member of OPTN.
Figure 7: Flow chart of OPTN membership application process
4.3. United Network for Organ Sharing

Another requirement established by the 1984 National Organ Transplantation Act is the creation of the OPTN to be run by a private non-profit organization under contract with the federal government. The Department of Health and Human Services (HHS) first awarded the contract to UNOS in 1986 since when UNOS has been managing the OPTN to date [22]. On October 25, 1999 UNOS launched a computerized database called UNetSM [16]. According to UNOS [22] this database is used to collect, analyze, store and publish list of waiting list candidates and information related to organ matching and transplantation in general [22]. The database has been updated to include all donated organs and transplantations that occurred from 1986 when UNOS was first contracted to administer OPTN [16]. The “fail-save” system can be accessed by transplant organizations on a 24/7 basis through the internet [16]. It is a secure mode where the transplant organizations can securely register patients to the waiting list and match organs to candidates on the waiting list. It also allows access for the management of waitlist candidates and transplant patients’ data; about 350 organ procurement organizations communicate with UNOS system each day [11].

To improve the accuracy and efficiency of organ transportation UNOS introduced DonorUNetSM in 2006 as an upgrade of the previous platform. With this upgrade when an OPO procures an organ, a message is transmitted electronically through the DonorUNetSM to transplantation hospitals [16]. This message comes with the organ properties and the candidates compatible with the organ. Before the
introduction of DonorUNet\textsuperscript{SM} UNOS had to rely on faxes and phone calls for the transmission of data among OPO’s and transplantation centers \cite{16}. It has helped to improve on the quality of organ allocation and transplantation since organ matching can now be done much quicker and effectively. Also multiple transplant centers can be offered an organ contemporaneously \cite{16}. This time saving is a great achievement since organs are highly perishable resources with some having ischemic time of 4 – 6 hours. Table 3 shows some solid organs and their ischemic time.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Ischemic Time (Hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>4 – 6</td>
</tr>
<tr>
<td>Liver</td>
<td>12 – 24</td>
</tr>
<tr>
<td>Kidney</td>
<td>48 – 72</td>
</tr>
<tr>
<td>Heart – Lung</td>
<td>4 – 6</td>
</tr>
<tr>
<td>Lung</td>
<td>4 – 6</td>
</tr>
</tbody>
</table>

Source: Adopted from UNOS \cite{16}:

Due to the short ischemic period of organs, allocation is mostly localized \cite{16}. Because of this UNOS has divided the U.S. into 11 regions each with a localized waiting list \cite{16}. When an OPO in a region procures a kidney, it first of all, searches
within its pool of active waitlist candidates to identify a potential candidate for the organ. If no candidate is found based on the allocation policy the search will be extended to nearby regions after which the search for a potential active candidate is extended to the entire nation for a more suitable candidate [16]. The search together with transportation (if required) of the organ must be completed within the ischemic period in order to preserve the quality of the organ, hence the zoning of the US into smaller regions. This adds to the complexity of kidney allocation since active candidates and in some cases relatives, transplantation centers, organ procurement organizations and other professionals must be well coordinated to achieve the common goal. The OPOs play a very important role in this coordination since they procure the organs [11].

Figure 8 shows a network of OPOs within a region. The OPOs (represented as triangles) are connected and communicate through the DonorUNetSM. As explained, whenever an OPO procures an organ and fails to find a match within its region, it will reach out to other OPOs within the region and prospect for a matching active candidate. The oval in figure 8 demonstrates the constraint or boundary of area where the OPO can procure an organ from. This is only a demonstration of an operational boundary. But realistically, the boundaries of operation for OPOs are not oval in shape. The OPOs within a region are connected through communication to allocate procured organs as shown by the lines in figure 8.
Figure 8: OPO search within a region

Figure 9 demonstrates the search procedure when no active candidate is found within the localized region where the organ was procured. At this point the search is expanded to include nearby regions to find a match for the organ [16]. This is demonstrated in figure 9 where the regions served by different OPOs are connected by communication during organ allocation. Of course, this is oversimplification of the model since there is no void between the OPO donation service areas.

Figure 9: Search among nearby regions
The final stage of the organ matching search is when the search is extended to the entire nation. This happens only when there is no match within the region that procured the organ and its adjoining regions [16]. The arrows emanating from the regions in figure 10 represent the extension of the search to include all regions. This search is always initiated at the OPO that procures the organ [16]; however, due to the short ischemic period of organs and logistical constraints the regional search will hardly be useful for organs with extremely short ischemic period such as heart and lungs. To further explain the processes, the entire search processes for organ matching with active candidate has been demystified in figure 11.

Figure 10: Nationwide search among all regions
Start with local search

A match found? [Yes → Terminate search, No → Expand search to nearby OPOs]

Expand search to nearby OPOs

A match found? [Yes → Terminate search, No → Expand search to nearby regions]

Expand search to nearby regions

A match found? [Yes → Terminate search, No → Nationwide search]

Nationwide search

A match found? [Yes → Terminate search, No → Terminate search and discard organ]

Figure 11: Flow chart of organ matching search processes.
UNOS’ DonorUNet\textsuperscript{SM} has helped to effectively reduce the time involved in organ matching by speeding up the transmission of information [16]. Other benefits from the regional system according to OPTN [21] are that the regional system helps to:

- Provide an effective communication mode among OPTN staff, Board of Directors and the transplant communities.
- Constitute the Board and other committees with geographically diverse transplant professionals.
- Improve transparency and consensus building through regional meetings.

Figure 12 shows graphically the OPTN regional map of the United States and its territories.

Figure 12: The U.S.A. regional map of the OPTN. Source: Adopted from OPTN [21], http://optn.transplant.hrsa.gov/members/regions.asp.
Region 1 consists of Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Eastern Vermont. Table 4 shows all the States and U.S. territories and their designated regions.

Table 4: States/territories and their region

<table>
<thead>
<tr>
<th>Region</th>
<th>States/Territories</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Eastern Vermont</td>
</tr>
<tr>
<td>2</td>
<td>Delaware, District of Columbia, Maryland, New Jersey, Pennsylvania, West Virginia, Northern Virginia</td>
</tr>
<tr>
<td>3</td>
<td>Alabama, Arkansas, Florida, Georgia, Louisiana, Mississippi, Puerto Rico</td>
</tr>
<tr>
<td>4</td>
<td>Oklahoma, Texas</td>
</tr>
<tr>
<td>5</td>
<td>Arizona, California, Nevada, New Mexico, Utah</td>
</tr>
<tr>
<td>6</td>
<td>Alaska, Hawaii, Idaho, Montana, Oregon, Washington</td>
</tr>
<tr>
<td>7</td>
<td>Illinois, Minnesota, North Dakota, South Dakota, Wisconsin</td>
</tr>
<tr>
<td>8</td>
<td>Colorado, Iowa, Kansas, Missouri, Nebraska, Wyoming</td>
</tr>
<tr>
<td>9</td>
<td>New York, Western Vermont</td>
</tr>
<tr>
<td>10</td>
<td>Indiana, Michigan, Ohio</td>
</tr>
<tr>
<td>11</td>
<td>Kentucky, North Carolina, South Carolina, Tennessee, Virginia</td>
</tr>
</tbody>
</table>
The OPO organ matching search process is analogous to tabu search. Starting from an encouraging solution \((x)\) tabu search moves to an improved solution \((x')\) within the adjoining regions of the initial promising solution [48]. As the search progresses the adjoining regions of each promising solution is explored by tabu search to prevent the temptation of settling on a local optimum or mediocre solution [48]. This is illustrated in figure 13; the numbers in figure 13 show the chronology of tabu search. For each stage all the adjoining regions (ovals) are explored for a better solution before moving on to the next stage [48]. Compared to the OPO search the ovals represent the various regions. The major difference between these two is that tabu search systematically searches all neighborhoods (regions) to avoid the temptation of settling on a local optimum while the OPO search terminates as soon as a match (solution) is found even when it is found during the first search [16].

Figure 13: Typical moves by a tabu search

Source: Adopted from Tsubakitani, S. and J.R. Evans [48]
4.4. Organ Procurement Organizations

The Organ Procurement Organizations (OPOs) are the other members of the Organ Procurement and Transplantation Network (OPTN). Erika [11] states that the OPOs are responsible for: seeking consent to procure organs and tissues of a deceased (cadaveric) donor form their relatives; donor testing; organ-tissue procurement and allocation; and transportation of the organs and tissues. She also emphasizes that the OPOs carry out education campaigns about organ donation within their communities. There are 58 OPOs serving the United States [49]. These are non-governmental organizations established to function as nonprofit agencies and are the only organizations with the right to procure organs for transplantation [49]. According to the OPTN bylaws, each OPO must meet the standards for “performance requirements, facility and services, personnel, and other additional requirements.” These requirements are explained in the subsequent sections.
5. REQUIREMENTS FOR ORGAN PROCUREMENT AND TRANSPLANTATION

5.1. Facility and Services Requirements

It is a requirement that a prospective OPO shows a connection with transplant hospital. These connections must be demonstrated by documentation showing the treaty between the OPO and the transplant and referral hospitals in the area that the OPO procures organs from. The areas known as Donation Service Area (DSA) are all regulated by the OPTN [47] which help to ensure efficient procurement, allocation and distribution of organs and tissues. There must also be a proof of laboratory testing capabilities that conforms to OPTN specifications so that donors’ tissues can be tested for tissue compatibility with that of prospective candidates on the waiting list. Furthermore, they must also have the resources to screen donors for diseases such as Human Immunodeficiency Virus (HIV) [21]. The OPOs must also demonstrate that they have the ability to prevent tissues from going waste by documenting its agreement with a tissue bank so that tissues procured can be stored and distributed efficiently in the future [21].

Since OPOs are the main bodies that procure organs, OPTN also requires that they show a documented proof of public and professional educational plans in the area of tissue and organ procurement. Finally, to satisfy the facility and services requirements each OPO must be equipped with computers and other equipment necessary for allocating organs fairly within its DSA. It must also have the ability to allocate organs to areas outside the DSA in case no much is found within the local
DSA [21]. The next section discusses the personnel requirement necessary for an OPO to become a member of OPTN.

5.2. Personnel Requirements

According to OPTN [21] the personnel requirements necessary for an OPO to become OPTN member includes an OPO administrative director, a medical director who “must be a physician licensed in at least one of the states within the OPO’s DSA”, board of directors, procurement coordinators and other dexterous professionals. For OPOs who are already members of OPTN, in situations of a personnel change such as change in medical director or administrative director, the onus lies on the OPO to formally communicate it to OPTN within 30 days, and must also furnish OPTN with the resume of the new person hired to occupy the position. If for any reason the vacant position is not occupied within 6 months the OPO must also communicate it to the MPSC [21]. The next section discusses the additional requirements that prospective OPOs must meet to become members of OPTN.

5.3. Additional Requirements

After meeting the facility, services and personnel requirements each OPO is also required to meet the following additional requirements: “patient confidentiality, donation service area, fiscal procedures, medical reimbursement, center for Medicare/Medicaid services (CMS) certificate, tax exemption and inactive status” requirements [21]. OPTN bylaws explain that since OPOs are non-profit agencies, there must be a proof of tax exemption “from federal income taxation under section 501 of the Internal Revenue Code of 1986” [21].
They must also prove their capability of protecting the data of organ donors in their DSA. Further details about the additional requirements can be found in the OPTN bylaws for OPOs [21]. All the OPOs serving the U.S.A. and their respective DSA are shown in table 5. The OPOs with no DSA as seen in table 5 have multiple centers and have the capacity to serve the entire state. For example the State of Alabama is served by only one OPO: Alabama Organ Center which has multiple centers within the state [49].
Table 5: U.S states, territories with their OPOs and DSA.

<table>
<thead>
<tr>
<th>State</th>
<th>Organ Procurement Organization(s)</th>
<th>Areas Served</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alabama</td>
<td>Alabama Organ Center</td>
<td></td>
</tr>
<tr>
<td>Alaska</td>
<td>Life Center Northwest</td>
<td></td>
</tr>
<tr>
<td>Arizona</td>
<td>Donor Network of Arizona</td>
<td></td>
</tr>
<tr>
<td>Arkansas</td>
<td>Arkansas Regional Organ Recovery Agency:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mid-America Transplant Services</td>
<td>Clay, Craighead, Greene, Independence, Lawrence Counties</td>
</tr>
<tr>
<td></td>
<td>Mid-South Transplant Foundation, Inc.</td>
<td>Crittenden, Cross, Lee, Mississippi, Phillips, St. Francis Counties</td>
</tr>
<tr>
<td></td>
<td>Southwest Transplant Alliance</td>
<td>Miller County</td>
</tr>
<tr>
<td>California</td>
<td>California Transplant Donor Network</td>
<td>Northern California</td>
</tr>
<tr>
<td></td>
<td>Golden State Donor Services</td>
<td>North Central California</td>
</tr>
<tr>
<td></td>
<td>LifeSharing: A Donate Life Organization</td>
<td>Imperial, San Diego</td>
</tr>
<tr>
<td></td>
<td>OneLegacy</td>
<td>Southern California</td>
</tr>
<tr>
<td>Colorado</td>
<td>Donor Alliance, Inc.</td>
<td></td>
</tr>
<tr>
<td>Connecticut</td>
<td>Life Choice Donor Services</td>
<td></td>
</tr>
<tr>
<td></td>
<td>New England Organ Bank</td>
<td>Southwestern Connecticut</td>
</tr>
<tr>
<td>Delaware</td>
<td>Gift of Life Donor Program</td>
<td></td>
</tr>
<tr>
<td>District of Columbia</td>
<td>Washington Regional Transplant Consortium</td>
<td></td>
</tr>
<tr>
<td>Florida</td>
<td>LifeLink of Florida</td>
<td>West</td>
</tr>
<tr>
<td></td>
<td>LifeQuest Organ Recovery Services</td>
<td>Northern Florida</td>
</tr>
<tr>
<td></td>
<td>TransLife/Florida Hospital</td>
<td>Eastern Florida</td>
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<tr>
<td></td>
<td>LifeAlliance Organ Recovery Agency</td>
<td>Southern Florida</td>
</tr>
<tr>
<td>Georgia</td>
<td>LifeLink of Georgia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tenness Donor Services</td>
<td>Catcoa, Dade, and Walker Counties</td>
</tr>
<tr>
<td>Hawaii</td>
<td>Legacy of Life Hawaii</td>
<td></td>
</tr>
<tr>
<td>Idaho</td>
<td>Intermountain Donor Services</td>
<td>Southern Idaho</td>
</tr>
<tr>
<td></td>
<td>LifeCenter Northwest</td>
<td>Northern Idaho</td>
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<tr>
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<td>Pacific Northwest Transplant Bank</td>
<td>West Central Idaho</td>
</tr>
<tr>
<td>Illinois</td>
<td>Mid-America Transplant Services</td>
<td>Southern Illinois</td>
</tr>
<tr>
<td></td>
<td>Gift of Hope Organ &amp; Tissue Donor Network</td>
<td>Northern and Central Illinois</td>
</tr>
<tr>
<td></td>
<td>University of Wisconsin Hospital and Clinic</td>
<td>Winnebago County</td>
</tr>
<tr>
<td>Indiana</td>
<td>Indiana Organ Procurement Organization, Inc.</td>
<td></td>
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<td></td>
<td>Kentucky Organ Donor Affiliates</td>
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<tr>
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Table 5: continued

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<tr>
<th>State</th>
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<tr>
<td>Kansas</td>
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<td>St. Francis Hospital and Medical Center, Topeka</td>
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<td>Washington Regional Transplant Consortium</td>
<td>Charles, Montgomery, Prince George's Counties</td>
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<td>Life Choice Donor Services</td>
<td>Franklin, Hampden, Hampshire Counties</td>
</tr>
<tr>
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<td>Berkshire County</td>
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<td>University of Wisconsin Hospital and Clinic</td>
<td>Northwestern Michigan</td>
</tr>
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<td>Minnesota</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>University of Wisconsin Hospital and Clinic</td>
<td>Houston County</td>
</tr>
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<td>Organ Recovery Agency</td>
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<td>Northern Mississippi</td>
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<td>------------------</td>
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<td>Eastern, Central North Carolina</td>
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<td></td>
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</tr>
<tr>
<td>Ohio</td>
<td>LifeBanc</td>
<td>Northeastern Ohio</td>
</tr>
<tr>
<td></td>
<td>Life Connection of Ohio</td>
<td>Northwestern, West Central Ohio</td>
</tr>
<tr>
<td></td>
<td>Lifeline of Ohio Organ Procurement Agency</td>
<td>Central, Southeastern Ohio</td>
</tr>
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<td></td>
<td>LifeCenter Organ Donor Network</td>
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<td>Pacific Northwest Transplant Bank</td>
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<td>Pennsylvania</td>
<td>The Center for Organ Recovery &amp; Education</td>
<td>Western Pennsylvania</td>
</tr>
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<td></td>
<td>Gift of Life Donor Program</td>
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<td>New York Organ Donor Network</td>
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<td>LifeLink of Puerto Rico</td>
<td>Pike County</td>
</tr>
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<td>Rhode Island</td>
<td>New England Organ Bank</td>
<td></td>
</tr>
<tr>
<td>South Carolina</td>
<td>LifePoint</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LifeLink of Georgia</td>
<td>Aiken, Edgefield Counties</td>
</tr>
<tr>
<td></td>
<td>LifeShare Of The Carolinas</td>
<td>York County</td>
</tr>
<tr>
<td>South Dakota</td>
<td>LifeSource, Upper Midwest Organ Procurement Organization, Inc.</td>
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<tr>
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<td>Mid-South Transplant Foundation, Inc.</td>
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<td>Northern and Southeastern Texas</td>
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<td>Texas Organ Sharing Alliance</td>
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<td>Northeastern, Southeastern and West Texas</td>
</tr>
<tr>
<td>Utah</td>
<td>Intermountain Donor Services</td>
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</table>
5.4. Judicial Framework of Organ Procurement

The first law to regulate organ procurement was enacted in 1968 [11] after the first successful heart transplantation by Dr. Christian Barnard [50]. This law: Uniform Anatomical Gift Act (UAGA) regulates the donation and procurement of organs. Since it was the first regulatory tool enacted to govern organ procurement,
all the states were governed by it; however, when it was revised in 1987 by the National Conference of Commissioners on Uniform State Laws (NCCUSL) only 26 states adopted the revised UAGA [50]. To ensure consistency in organ donation and procurement among all states the NCCUSL in 2006 started resolving the differences in the gift act [50]. The 2006 UAGA gives OPOs the power to access the registry of potential organ donors. This record kept by the Department of Motor Vehicles allows OPOs to save time by efficiently determining the status of an individual at the risk of brain death as a prospective organ donor or not [50].

NCCUSL [50] maintains that the gift act is not uniform since there are variations from state to state. This is a setback for OPOs that operate in more than one state. However, one thing (among others) which is uniform among all states is that the gift act prohibits the sale or purchase of organs of any form. An OPO or an individual cannot sell or buy an organ [50]. However, Barnieh et al. [51] have recently suggested that if the sale and buying of organs are allowed, it will increase the pool of living donors so that more people will enjoy the enormous benefits that come with living donor transplantation. This is a great suggestion but highly contentious owing to its moral and ethical implications. Organ sale is not new to the transplantation world but it was plagued with a myriad of challenges in countries like India and Philippines that used to allow organ trade. However, Barnieh et al. [51] explain that organ sale in the United States if legalized will help save $4,030 per patient and help increase the quality of life [51].
Since organs are not sold, consent is sought before they are procured from a cadaveric donor. Erika [11] explains that the UAGA “does not by law require the consent of next of kin for the procurement of organs from a brain dead” person who had previously agreed and have signed up in the registry of organ donors. Proof of this document is mostly found on the patient’s driver’s license. However, she further explains that OPOs as a requirement by OPTN must consult family members of the donor before any organ can be procured [11]. Hospitals are therefore required to notify their local OPOs of any patient who is at the edge of a brain death so that the OPO can seek consent of the family for organ procurement [11]. OPTN has established the hierarchy of next of kin from which consent must be sought: “spouse; adult son or daughter; parent; adult sibling; grandparent; legal guardian”; and any other person with the power to dispose of the body of the donor [11, 21]. UAGA also emphasizes that the decision to donate an organ or whole body for transplantation or research purposes is purely voluntary [21, 47]. Once consent has been sought the tissue or organs can be procured. The next section throws more light on the actual organ procurement and transplantation.

5.5. Organ Procurement and Transplantation

Since the first successful kidney transplantation was conducted in 1954, transplantation has become the best life-saving option for end stage renal disease patients. For this reason the number of people in need of organ transplantation keeps increasing each day. Averagely, the UNOS receives about 350 requests for waitlist enlistment and other transplant related activities daily [16]. As at 11:15 pm
on 09/16/2013 there were 119,606 candidates on the waiting list with 75,567 active candidates [21] of which kidney constitutes the greatest number of candidates. Table 6 shows a breakdown of the number of candidates for each organ as at 11:15PM on 9/16/2013. Since some candidates are in need of more than one organ, the sum of the numbers for all the individual organs is more than the total for all organs as shown in table 6 [16]. Active candidates are those candidates who are medically, financially, physically, psychologically and emotionally ready for transplantation [16].

Table 6: Organs and number of waitlist candidates [16]

<table>
<thead>
<tr>
<th>All</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>97,594</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1,175</td>
</tr>
<tr>
<td>Kidney/Pancreas</td>
<td>2,062</td>
</tr>
<tr>
<td>Liver</td>
<td>15,804</td>
</tr>
<tr>
<td>Intestine</td>
<td>253</td>
</tr>
<tr>
<td>Heart</td>
<td>3,555</td>
</tr>
<tr>
<td>Lung</td>
<td>1,623</td>
</tr>
<tr>
<td>Heart/Lung</td>
<td>49</td>
</tr>
</tbody>
</table>

The main bodies in charge of organ procurement are the Organ Procurement Organizations. Federal law requires each OPO to be affiliated with a transplantation
center and also hospitals are required by law to notify local OPOs of a patient who is at the risk of a brain death. This helps OPOs to start consent seeking for future procurement of the patient’s organs. There are two main sources of organ procurements: living donors and cadaveric donors [21]. The next sections discuss more about these types of organ donors.

5.5.1. Living Donors

Living donors are individuals who choose to donate an organ to a patient voluntarily. These donors are mostly close relatives of patients; friends also sometimes serve as living donors [13] but for tissue compatibility concerns, kidneys from close relatives (siblings and parents) are best matched to patient’s tissue which is a desirable feature for allograft survival [13]. Kidneys from live donors are mostly not procured by an independent OPO; these organs are mostly procured at the transplant center where the patient will undergo transplantation. This helps to minimize ischemic time which has a direct effect on the quality of the organ [3]. According to Erika [11] living donors normally donate kidneys; pancreases; small intestines; livers and lungs. It is however surreal for living donors to donate the whole of unitary organs in the human anatomy such as liver. It is therefore not surprising that kidney is the organ most donated by living donors [16].

Living donors first undergo psychological evaluation to ensure that they are not being coerced to donate. Professionals in mental health with thorough knowledge in transplantation, psychologically examine the donor to ascertain that he/she is of sound mental ability to give the consent for the donation. To avoid
conflict of interest these professionals are not supposed to be part of the team that will be caring for the donor and the recipient [52]. The cost involved in the donation is mostly covered by the insurance company of the living donor, thus if he or she is insured otherwise the End-Stage-Renal-Disease program covers the cost if the recipient qualifies [11]. All uncertainties must also be made known to the parties involved. This is to ensure that the donation is voluntary and that the donor understands that the donation exposes him/her to some level of risks [52].

Kidneys from living donors result in relatively better outcome than deceased donor kidneys. It takes about 21.6 years for half of the organs from living donors to stop operating as compared to 13.8 years in deceased donor kidneys [11]. As seen in figure 14 a lot more of recipients of cadaveric donor kidneys experience “incidence of acute rejection” after transplantation than recipients of living donor kidneys [20].

Figure 14: Incidence of acute rejection among adult kidney recipients: 2005 – 2009.

Source: OPTN/SRTR Annual Report as at 09/18/2013.

http://srtr.transplant.hrsa.gov
The OPTN/SRTR annual report [20] defines “incidence of acute rejection” as “a record of acute or hyperacute rejection, or a record of an antirejection drug being administered on either the Transplant Recipient Registration form or the Transplant Recipient Follow-up Form.” It further explains that only the first occurrence is recorded and is shown in figure 14. A contributing factor to the better outcome of transplants with kidneys from living donors is the decrease in ischemic time of living donor kidneys. Also, since most living donors are relatives of recipients, there is little risk of graft rejection due to mismatch in tissue typing.

Another factor is the fact that living donor kidneys are mostly procured from relatively healthy individuals. In the history of organ donation in the United States, kidneys from living donors first exceeded those from deceased donors in 2001 and this has not been the trend in recent years [11]. Living donors are mostly people between the ages of 18 to 70 years. As can be observed from figure 15, the year group 35 – 49 contributes to the greatest proportion of living kidney donors. In all, female living donors hold the majority spot with whites dominating in terms of race [20]. Further details about living donors can be found in figure 15.
Living organ donation has been increasing perhaps due to the benefits associated with it [21]. Although related donors are highly desirable, organs from this group of living donors have been decreasing since 2001 but it still exceeds other group of donors. Reference to figure 16 it can be observed that the number of transplants conducted with related living donor kidneys has steadily been decreasing since 2001. For the fact that the overall rate of living organ donations has been increasing in recent years, it is difficult to assign a cause to the dwindling observed in related living donor kidneys [20].
On the contrary, there has been a steady increase in unrelated living donors as seen in figure 16 although there was a decrease in 2007. Transplants conducted with kidneys from donors with no relationship to the recipients have also been increasing steadily from 1998 [20, 51, 53]. Unrelated living donors differ in the mode in which recipients on the waiting list get transplanted. Connie and Francis [54] explain that the non-directed donors (unrelated living donors) are classified under three branches: “live-donor paired exchange, live-donor/deceased donor exchange and altruistic donation.” They explain that the classification makes it easy for unrelated donors to donate to the candidates on the waiting list [54].

In a live-donor paired exchange, a donor who is incompatible with the planned recipient is arranged to donate to another recipient who also has an incompatible donor for the latter recipient’s original donor to also donate to the
former's recipient [54, 55]; thus, If living donors A and B intend to donate to recipients X and Y respectively but are both incompatible with their respective recipients, donors A and B are swapped so that A donates to Y while B donates to X. This is made possible only when compatibility is achieved for the pairs A and Y, and B and X. All the parties must also consent to the process before the transplantation can be performed. This has now become a common practice around the globe [54, 56, 57].

Live-donor/deceased-donor exchange also involves the trading of “privileged position” on the waiting list for living donor kidney. Under this system a living donor incompatible with the intended recipient is arranged to donate to a compatible candidate ranked highest on the waiting list so that the original recipient who was ranked low on the waitlist gets the opportunity to be offered the next available and compatible deceased donor kidney. This system was first introduced by the members in region 1 of the OPTN regions [54]. This has the advantage of opening up a lot of people to the benefits of living donor kidneys [54] instead of leaving the potential donor to walk away without donating because of his incompatibility with the intended recipient.

Altruistic donors are the donors with no intended recipients [54]. These are people who choose to donate their organs, mostly kidneys to recipients they have never known. Like other living donors they are made to go through several evaluations to ascertain their readiness for the organ donation. According to Connie and Francis [54] the altruistic donors are normally people with little to no
knowledge about the intricacies of organ donation. The authors explain that more than 60% of prospective altruistic donors who contact the University of Minnesota Medical facility to donate one of their kidneys cut off communication with the hospital after being enlightened on the risks and other details about organ donation [54]. For whichever category a living donor falls under, Delmonico et al. [54] explains that the transplant center is required by law to ensure that a living donor and recipient are well furnished with information concerning the inherent risk and alternative treatments that are available to the recipient. The next section discusses the deceased (cadaveric) donors.

5.5.2. Deceased Donor

Deceased donors are people who had consented to serve as organ donors upon their death [16]. When a hospital notifies a local OPO of a patient at the risk of a cardiac or brain death, the OPO will seek consent of the appropriate family member for the procurement of the patient’s organs. OPTN has set the priority in the people to contact for their consent to procure the organs of the patient: spouse; adult son or daughter; parent; adult sibling; grandparent; legal guardian;” and any other person with the power to dispose of the body of the donor [11, 21]. Although the Uniform Anatomical Gift Act does not require consent seeking, OPTN has made it a requirement hence no organ is procured from a registered cadaveric donor unless appropriate consent is sought from the right person [11].

The OPO will procure organ(s) only when the family agrees to the procurement for which only 54% of those families agree [58]. In 2002 if the families
of all consented cadaveric donors had agreed to the procurement, there would have been more than enough kidneys and hearts to equate the growth in waiting list [58]. However, at this same rate there would have been shortages in liver for the people on the waitlist [58]. Family members are less likely to agree to organ procurement when the donor is very old [58] as seen in figure 17. Families of younger donors are more likely to agree for the procurement of organs; this has been the case from the year 2000. Perhaps, younger donors families still see the donor as full of life that can potentially be more beneficial to recipients [58] as compared to older people. Just like the living donors that have been dominated by females, it is also the case for deceased donors. However, the difference is not as wide as it is in living donors. Hispanics and whites are respectively the majority contributors to deceased donor kidneys as observed in figure 17.

Thousands of these precious organs from cadaveric donors are discarded yearly although there are thousands of ESRD patients on the waitlist. The next section discusses in detail the discard rate of this group of kidneys.

Figure 17: Deceased donor kidney donation rates [20]
5.5.3. Discard Rate of Deceased Donor Kidneys

One major problem confronting kidney allocation is the high discard rate of deceased donor kidneys. Though there are thousands of candidates on the kidney waitlist, thousands of cadaveric kidneys that could benefit some candidates on the waiting list are discarded for various reasons. Figure 18 shows the discard rate of cadaveric kidneys from 1998 to 2011. Surprisingly, the highest discard rate comes from the group of people whose families are less likely to agree for the procurement of organs. It is generally perceived that kidneys from this group (older (55+ years) donors) are close to their salvage value even if they had remained in the natural bodies of their donors. Because of this most candidates on the waiting list prefer younger kidneys to older kidneys hence the high discard rate. Perhaps this is a contributing factor to the reason why those families refuse to agree to the procurement consent.

Figure 18: Discard rates for kidneys recovered from deceased donors for transplant.

Source: OPTN/SRTR Annual Report as at 09/18/2013.

http://srtr.transplant.hrsa.gov
Other reasons contributing to the high discard rate of deceased donor kidneys as stated by OPTN/SRTR [20] are biopsy findings, too long ischemic time and HIV positive status. Table 7 shows all the reasons for which deceased donor kidneys are discarded. It can be observed that a total of 2589 kidneys were discarded in 2011. If this trend continues it is likely to affect the interest of the public and has the potential to make families of deceased people reluctant to consent for the procurement of kidneys from their loved ones. I believe it will be morally debilitating for family members to realize that the organs recovered from their loved ones are only to be discarded. A system can be put in place to ensure that recovered kidneys are put into proper use. Kidneys which are not worthy to be transplanted for medical reasons such as HIV should not be recovered at the first place since HIV status can be determined before recovering the kidney.

Few organs were also discarded for having features “not as described” [20]; this reason is also not acceptable. This can be solved by adopted certain standard practices as in the aviation industry: air traffic controllers and pilots with diverse cultural background around the globe are able to communicate effectively in executing their task because there are standard words that form part of their daily vocabulary. Imagine the chaos that will happen if air traffic controllers or pilots start coming up with complaints that the other party does not describe things as it is during the take-off, landing, holding pattern or separation phase. This scenario may put fear in the public and will have detrimental effect on the aviation industry if it
occurs for a much longer period of time. Although these are two different industries, the standards of practice in the aviation industry can be adopted to improve kidney procurement and utilization. By this the OPO that procures the kidney sends the exact information needed to transplantation centers within its DSA or any other center that happens to have a candidate willing to accept the organ recovered.

Table 7: Reasons for the discards among kidneys recovered from deceased donors in 2011.

<table>
<thead>
<tr>
<th>Reasons for discard</th>
<th>Percent</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy findings</td>
<td>37.34</td>
<td>966</td>
</tr>
<tr>
<td>Other, specify</td>
<td>17.51</td>
<td>453</td>
</tr>
<tr>
<td>No recipient located - list exhausted</td>
<td>16.62</td>
<td>430</td>
</tr>
<tr>
<td>Poor organ function</td>
<td>9.24</td>
<td>239</td>
</tr>
<tr>
<td>Anatomical abnormalities</td>
<td>7.07</td>
<td>183</td>
</tr>
<tr>
<td>Diseased organ</td>
<td>3.48</td>
<td>90</td>
</tr>
<tr>
<td>Vascular damage</td>
<td>1.70</td>
<td>44</td>
</tr>
<tr>
<td>Organ trauma</td>
<td>1.24</td>
<td>32</td>
</tr>
<tr>
<td>Positive hepatitis</td>
<td>1.16</td>
<td>30</td>
</tr>
<tr>
<td>Too old on ice</td>
<td>1.08</td>
<td>28</td>
</tr>
<tr>
<td>Warm ischemic time too long</td>
<td>0.85</td>
<td>22</td>
</tr>
<tr>
<td>Too old on pump</td>
<td>0.70</td>
<td>18</td>
</tr>
<tr>
<td>Donor medical history</td>
<td>0.66</td>
<td>17</td>
</tr>
<tr>
<td>Recipient determined to be unsuitable</td>
<td>0.43</td>
<td>11</td>
</tr>
<tr>
<td>Organ not as described</td>
<td>0.27</td>
<td>7</td>
</tr>
<tr>
<td>Donor social history</td>
<td>0.23</td>
<td>6</td>
</tr>
<tr>
<td>Infection</td>
<td>0.19</td>
<td>5</td>
</tr>
<tr>
<td>Ureteral damage</td>
<td>0.15</td>
<td>4</td>
</tr>
<tr>
<td>Positive HIV</td>
<td>0.08</td>
<td>2</td>
</tr>
</tbody>
</table>

Source: OPTN/SRTR Annual Report as at 09/18/2013.

http://srtr.transplant.hrsa.gov

There have also been several instances where family members consent to the recovery of organs but the organs are not recovered for some of the same reasons that lead to the discard of some recovered kidneys. Figure 19 shows a graph of donors whose kidneys were not recovered for various reasons between 1998 and 2011. Generally this has been increasing from 1998 and 2005. However, form 2005
to 2011 there has been a decline in the number of kidneys not recovered from potential deceased donors. Table 8 shows the reasons for the non-recovery of kidneys from deceased donors.

The Scientific Registry of Transplant Recipient (SRTR) and OPTN [20] explain that “if the same reason was recorded for each kidney, it was only counted once.” It is important to note that as many as 534 representing 44.28% of the organs were not recovered due to poor organ functioning. If these were determined not to be worthy for transplantation and were not recovered, then there should be a way to identify those organs that were discarded for the same reason; as many as 239 organs were discarded in 2011 due to poor organ functioning which was discovered after the recovery. The high discard rate and the scarcity of kidneys mean that candidates must wait on the waitlist an average of 4 years until there is an organ; the next section discusses the kidney waitlist in detail.

Figure 19: Number of times kidneys not recovered from 1998 to 2011.

Source: OPTN/SRTR Annual Report as at 09/18/2013.

http://srtr.transplant.hrsa.gov
Table 8: Reasons for kidneys not being recovered at the time of another organ’s recovery in 2011.

<table>
<thead>
<tr>
<th>Reasons for non-recovery</th>
<th>Percent</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor organ function</td>
<td>44.28</td>
<td>534</td>
</tr>
<tr>
<td>Donor medical history</td>
<td>11.11</td>
<td>134</td>
</tr>
<tr>
<td>Other specify</td>
<td>9.29</td>
<td>112</td>
</tr>
<tr>
<td>Organ refused by all national programs</td>
<td>6.63</td>
<td>80</td>
</tr>
<tr>
<td>Ruled out after evaluation in OR</td>
<td>4.64</td>
<td>56</td>
</tr>
<tr>
<td>Diseased organ</td>
<td>4.48</td>
<td>54</td>
</tr>
<tr>
<td>Acute/chronic renal failure</td>
<td>3.73</td>
<td>45</td>
</tr>
<tr>
<td>Emotional</td>
<td>3.23</td>
<td>39</td>
</tr>
<tr>
<td>No recipient located</td>
<td>2.74</td>
<td>33</td>
</tr>
<tr>
<td>Organ refused by all regional programs</td>
<td>2.65</td>
<td>32</td>
</tr>
<tr>
<td>Donor age</td>
<td>2.32</td>
<td>28</td>
</tr>
<tr>
<td>Donor quality</td>
<td>1.24</td>
<td>15</td>
</tr>
<tr>
<td>Positive hepatitis</td>
<td>1.16</td>
<td>14</td>
</tr>
<tr>
<td>Donor social history</td>
<td>0.83</td>
<td>10</td>
</tr>
<tr>
<td>Family conflict</td>
<td>0.50</td>
<td>6</td>
</tr>
<tr>
<td>Anatomical abnormalities</td>
<td>0.41</td>
<td>5</td>
</tr>
<tr>
<td>Medical examiner restricted</td>
<td>0.33</td>
<td>4</td>
</tr>
<tr>
<td>Hemodynamically unstable donor</td>
<td>0.17</td>
<td>2</td>
</tr>
<tr>
<td>Surgical damage in OR</td>
<td>0.08</td>
<td>1</td>
</tr>
<tr>
<td>Time constraints</td>
<td>0.08</td>
<td>1</td>
</tr>
<tr>
<td>Trauma to organ</td>
<td>0.08</td>
<td>1</td>
</tr>
</tbody>
</table>

Source: OPTN/SRTR Annual Report as at 09/18/2013.

http://srtr.transplant.hrsa.gov

5.5.4. Kidney Waitlist

The kidney waitlist is made up of individuals suffering from ESRD who have no living donors [16]. These people are ranked based on the time they were enlisted for kidney transplantation and other parameters employed by the kidney allocation policy. The waitlist candidates are classified as either active or inactive candidate; this classification is not static since it depends on patient’s medical conditions and other stochastic factors. The active candidates are the waitlist candidates who are ready to be offered organs to undergo transplantation while inactive candidates are
hindered by different factor(s) [16]. Table 9 shows the reasons that led to the classification of waitlist candidates as inactive in 2011 as stated in the OPTN/SRTR 2011 annual report [20].

Table 9: Reasons for inactive status on the kidney waiting list in 2011.

<table>
<thead>
<tr>
<th>Reason for inactive status</th>
<th>Inactive w/ 7 days of listing</th>
<th>Active at listing, inact. on 12.31</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candidate work-up</td>
<td>8,029 69.0</td>
<td>5,414 29.1</td>
</tr>
<tr>
<td>Insurance issues</td>
<td>1,107 9.5</td>
<td>1,698 9.1</td>
</tr>
<tr>
<td>Too sick</td>
<td>897 7.7</td>
<td>6,596 35.5</td>
</tr>
<tr>
<td>Weight inappropriate for tx</td>
<td>553 4.8</td>
<td>1,057 5.7</td>
</tr>
<tr>
<td>Too well</td>
<td>542 4.7</td>
<td>870 4.7</td>
</tr>
<tr>
<td>Candidate choice</td>
<td>302 2.6</td>
<td>1,026 5.5</td>
</tr>
<tr>
<td>Tx pending</td>
<td>107 0.9</td>
<td>55 0.3</td>
</tr>
<tr>
<td>Medical non-compliance</td>
<td>47 0.4</td>
<td>635 3.4</td>
</tr>
<tr>
<td>Inappropriate substance use</td>
<td>37 0.3</td>
<td>276 1.5</td>
</tr>
<tr>
<td>Candidate could not be contacted</td>
<td>12 0.1</td>
<td>431 2.3</td>
</tr>
<tr>
<td>Physician/surgeon unavailable</td>
<td>3 0.0</td>
<td>2 0.0</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 0.0</td>
<td>535 2.9</td>
</tr>
<tr>
<td>Transplanted; removal pending data correction</td>
<td>1 0.0</td>
<td>- 0.0</td>
</tr>
</tbody>
</table>

Source: OPTN/SRTR Annual Report as at 09/18/2013.
http://srtr.transplant.hrsa.gov

In 2011 the factor that contributed to the highest number of inactive candidates is incomplete candidate work-up. This involves the diagnostic study of the individual to determine medical abnormalities that may adversely affect the quality of the transplantation [20]. Some candidates are also classified as inactive due to issues with their insurance providers. This bottleneck and the other factors
must be minimized to provide a bigger sample space for organs recovered from deceased donors.

The number of ESRD patients has been increasing for the past years so it is not surprising that the numbers of active candidates also keep increasing. There were 40,044 active candidates in the year 2000 but at the end of 2009 the active candidates were 52,516. As at 09/25/2013 as many as 76,734 active candidates were on the waitlist. Figure 20 shows the number of active candidates from 2000 to 2009. The number of active candidates is expected to keep growing since people receiving treatment for ESRD is also expected to keep growing [59].

```
<table>
<thead>
<tr>
<th>Year</th>
<th>Total Number of Active People on Waiting List</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>40,044</td>
</tr>
<tr>
<td>2001</td>
<td>42,309</td>
</tr>
<tr>
<td>2002</td>
<td>44,383</td>
</tr>
<tr>
<td>2003</td>
<td>45,614</td>
</tr>
<tr>
<td>2004</td>
<td>45,494</td>
</tr>
<tr>
<td>2005</td>
<td>46,431</td>
</tr>
<tr>
<td>2006</td>
<td>47,443</td>
</tr>
<tr>
<td>2007</td>
<td>49,114</td>
</tr>
<tr>
<td>2008</td>
<td>51,084</td>
</tr>
<tr>
<td>2009</td>
<td>52,516</td>
</tr>
</tbody>
</table>
```

Figure 20: Distribution of number of active waiting list candidates from 2002 to 2009.

The number of active candidates differs by blood group with blood group O constituting the highest number of active candidates which is followed by blood group A. The least number of active candidates are from the blood group AB. This
trend has been consistent from the year 2000 to 2009 and it is expected to continue
since it is proportional to the blood group distribution per the population of the
United States [60]. There haven't been significant proportional changes in the
number of active candidates from the various blood groups as seen in figure 21.

Although blood group AB has had the least number of active candidates from
the past years, they are more likely to stay longer on the waiting list than any of the
blood groups [3]. This is due to the fact that people in this blood group are very
sensitive: their immune system easily rejects foreign objects including transplanted
kidneys [3].

Figure 21: Distribution of number of active waiting list candidates by ABO blood
group from 2002 to 2009.

Candidates wait on the average of 4 years to receive kidney transplantation
[11, 20]. Some candidates are unable to be considered for kidney offer because they
get removed from the waitlist for various reasons; besides receiving kidney transplantation the other factor that leads to the removal of the next largest number of people from the waitlist is death. As many as 5,181, 5,172 and 5,139 adult candidates died on the waitlist in 2009, 2010 and 2011 respectively [20]. Some adult candidates after receiving no organ offer for months of waiting are also removed from the waiting list because they become too sick to receive kidney transplantation. This happens when it is medically determined that kidney transplantation will not be beneficial to the patient and may even worsen his/her medical condition. Such candidates are removed from the kidney waitlist [20]. Others are also removed from the waitlist because they choose not to receive kidney transplantation for religious and other personal reasons. This group of people has been increasing in the recent years: between 2009 and 2011 as many as 995 people were removed from the waiting list because they did not want to be considered for kidney transplantation. Table 10 shows the activities on the kidney waiting list for adults from 2009 to 2011.
Table 10: Adult patients' kidney waitlist activities.

<table>
<thead>
<tr>
<th></th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients at start of year</strong></td>
<td>74,572</td>
<td>79,365</td>
<td>83,879</td>
</tr>
<tr>
<td><strong>Patients added during year</strong></td>
<td>28,645</td>
<td>29,216</td>
<td>28,131</td>
</tr>
<tr>
<td><strong>Patients removed during year</strong></td>
<td>23,820</td>
<td>24,662</td>
<td>25,463</td>
</tr>
<tr>
<td><strong>Patients at end of year</strong></td>
<td>79,397</td>
<td>83,919</td>
<td>86,547</td>
</tr>
</tbody>
</table>

**Removal reason**

<table>
<thead>
<tr>
<th>Reason</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deceased donor transplant</td>
<td>9,713</td>
<td>9,980</td>
<td>10,399</td>
</tr>
<tr>
<td>Living donor transplant</td>
<td>5,170</td>
<td>5,235</td>
<td>4,922</td>
</tr>
<tr>
<td>Tx (type not specified)</td>
<td>54</td>
<td>89</td>
<td>81</td>
</tr>
<tr>
<td>Patient died</td>
<td>5,181</td>
<td>5,172</td>
<td>5,139</td>
</tr>
<tr>
<td>Patient refused transplant</td>
<td>271</td>
<td>318</td>
<td>406</td>
</tr>
<tr>
<td>Improved, tx not needed</td>
<td>131</td>
<td>101</td>
<td>135</td>
</tr>
<tr>
<td>Too sick to transplant</td>
<td>1,358</td>
<td>1,467</td>
<td>1,903</td>
</tr>
<tr>
<td>Changed to kid.-pan. list</td>
<td>165</td>
<td>191</td>
<td>194</td>
</tr>
<tr>
<td>Other</td>
<td>1,777</td>
<td>2,109</td>
<td>2,284</td>
</tr>
</tbody>
</table>


http://srtr.transplant.hrsa.gov

Reference to table 10 kidneys procured from deceased donors contribute most to kidney transplantation. The good news about this is that transplant rate
from deceased donors steadily increased between the years. Although the increase cannot compensate for the number of deceased donor kidneys discarded yearly, it is refreshing to know that more and more people are making use of deceased donor kidneys. Living donors only showed a slight increase in 2010 but dropped in 2011. This is not encouraging since the number of candidates on the waiting list keeps increasing and with the benefits that come with living donor kidney transplants, it will be better to see an increase in the number of people receiving living donor kidneys [20]. Since the majority of kidneys for transplantation come from deceased donors, they have been classified into groups for easy allocation depending on the age of the donor. The section below discusses further the various groups of deceased donors.

5.5.5. Classification of Kidney Donors

A kidney donor is classified as either belonging to the expanded criteria donor (ECD) or standard criteria donor (SCD) group [16]. According to UNOS [16] SCDs are 50 years old or less whereas ECDs are normally greater than 60 years. Dimitris et al. [13] explain that if a donor is over 50 years with at least two of the following, he/she is also classified as ECD: hypertension history, serum creatinine > 1.5 mg/dL or died from cerebrovascular disease [13]. Cerebrovascular diseases affect the brain when the blood vessels which supply blood to the brain fails to function properly [20]. These patients are referred to as brain dead and a hospital with such a patient is required by OPTN policy, to report to the OPO whose donor service area houses the hospital [20].
Majority of the kidneys that are discarded yearly belong to the ECD group [20]. Most candidates on the kidney waitlist perceive ECD kidney as inferior to SCD kidneys so it is not surprising that most candidates refuse to accept ECD kidneys. In 2011 46,418 candidates decided not to receive ECD kidney [20]. This constitutes approximately 54% of the active candidates on the waitlist in 2011 [20]. The next section discusses some resource allocation models which could be applied to locating kidney allocation/transplantation facilities.
6. RESOURCE ALLOCATION MODELS

The organ allocation problem is an area that attracts extensive interest, perhaps due to its direct effect on human life and also the gargantuan cost involved. The problem of organ allocation extends from location allocation problem to resource allocation problem. The location allocation problem is solved by selecting the optimal location for the establishment of dialysis and transplantation center or organ procurement center while the resource allocation problem is solved by searching for ways to better utilized resources such as solid organs in order to minimize discard rate of organs and maximize medical efficiency. Maximizing medical efficiency means reducing the rate at which transplanted candidates reenlist for another transplantation which is caused by the rejection of the organ or malfunctioning of the graft [13].

Medical efficiency also ensures that the number of transplanted candidates who die with a functioning kidney that can survive for several years are minimized [13]. In a summary, it strives to maximize the benefits from solid organ transplantation [13]. Since solid organs are perishable items, it is imperative to ensure that the locations of transplantation centers are optimal to the locations of organ procurement centers as well as the transplant community. Although the location allocation problem occurs less frequently compared to the organ (resource) allocation problem, it is a good step to discuss the location allocation problem since it has direct impact on the quality and cost in transplantation. This section reviews
some of the models in the literature about the location allocation problem, and the
resource allocation problem in relation to kidney allocation and transplantation.

6.1. Location-Allocation Models

The problem of location allocation is a strategic issue that confronts all
companies in various industries. This is a strategic decision problem which revolves
around locating the place that best serves a company’s interest. Many factors affect
the decision on where the best location is. Factors such as population density,
infrastructure, skilled personnel, operating cost, number of facilities, capacity of
facility, etc. have direct effect on the decision making for this problem [61]. The
objective of facility location-allocation problem therefore, is to determine the best
location(s) that brings the greatest return on investment by providing the best
possible services to the target customers.

The quality of the service delivered by a facility more or less depends on its
location. Wrongly locating a facility will negatively affect service delivery; especially
in the health sector where certain services cannot be delayed. A dialysis and
transplantation center must be as close as possible to the candidates on dialysis.
Also kidneys must be transported within a very short period of time to a
transplantation center in order to minimize the ischemic time which literally is the
time the kidney stays outside of the body. This helps to prevent the organ from
going bad so it can be viable for transplantation. This means that the distance from
the source of the organ, distance to customers and cost involved must be optimized.
If organ procurement centers are far from area of demand, it will have direct impact
on cost and will negatively affect the utilization of the facility and the quality of service. This means that organ procurement centers must be well distributed in order to better meet demand.

Decision makers therefore need decision supporting tools to make better decisions in location-allocation of organ procurement centers. Since several other factors such as services provided at a facility, working hours at a facility etc. also affect the decision on this problem, the decision must not only be based on shortest distance and time alone.

ARCGIS solves the location allocation problem by utilizing network analysis [62]. This commercial software only utilizes distance and time by minimizing total distance or travel time. For example it can find the location that minimizes total transportation cost to deliver a kidney to a transplantation center. This single objective capability of the software limits its applicability in solving the complex location-allocation problem in relation to kidney allocation. It also does not solve non distance based location allocation problems [63].

The location-allocation problem is a combinatorial optimization problem. Church and Murray [64] states that commercial application software are not using metaheuristics solution approach in solving the problem. Hossage and Goodchild [65] used genetic algorithm to solve the location allocation problem. Other metaheuristics searches such as tabu search, neighborhood search have also been applied to solve the problem [66]. Shamsul et al. [67] also used genetic algorithm and simulated annealing to solve the facility location-allocation problem. In
determining the capacity and location-allocation of a facility, they incorporated in their model users with and without preference. This is applicable to kidney allocation since candidates on the waitlist have the option to select a transplantation center and also the type of organ to accept or otherwise. Further details can be found in [67]. The next sections which are mainly based on Sunil's book [61] give detail descriptions of some of the location allocation models.

6.1.1. The Capacitated Facility Location Model

The location-allocation problem can be modeled as capacitated facility model to minimize the total cost involved in an operation. Total cost consists of fixed cost and variable cost. To formulate the problem the following parameters must be defined:

- $n =$ number of potential facility locations.
- $m =$ number of markets to be served.
- $D_j =$ annual demand for services from market $j$.
- $K_i =$ potential capacity of the facility at location $i$.
- $\bar{f}_i =$ annual fixed cost to operate facility $i$.
- $c_{ij} =$ cost of providing services to a customer from facility $i$ to market $j$.

The following decision variables must also be defined:

- $x_{ij} =$ number of people treated at facility $i$ for market $j$.
- $y_i =$ 1 if facility is allocated to a location $i$, 0 otherwise.

**Objective function**
The objective function of the above model minimizes fixed cost and variable cost [61]. The equation 16 constraint ensures that demand for all markets is met. Constraint in equation 17 ensures that services provided at a facility do not exceed the capacity of the facility. Equation 18 ensures that a facility is either located to a location or otherwise. From this model the location that comes with the lowest cost is the optimum location for the facility. In relation to kidney transplantation this location could be the location of a new organ procurement center, a dialysis center, transplantation center or a combination of them since some hospitals serve as both dialysis and transplantation centers.

The next section also talks about another location allocation model which uses the geographical coordinates of predetermine sites (possible locations for new facility) to determine the optimal location.
6.1.2. The Gravity Location Model

This model also starts with the identification of potential locations within a region for allocating the facility. A metric such as Euclidean distance is used by this model [68]. This model requires the determination of the geographical coordinates \((x, y) \in R^p \times R^p\) for a set of \(p\) facility locations [68]. The objective function of this model is to minimize the sum of weighted distances between the facilities and \(m\) market points. The gravity allocation model returns the minimum of the sum of the weighted distances to the market points \(k \in K\) in the set \((a_k, b_k)\) as the optimal solution which is the location with geographical coordinates \((x, y) \in R \times R\) [68]. The objective function of the model is formulated as:

\[
\text{Min } \sum_{k \in K} w_k d_k(x, y),
\]

Where

\[
d_k(x, y) = \sqrt{(x - x_k)^2 + (y - y_k)^2}
\]

\(w_k\) is the weighted cost factor for providing services at a facility to market point \(k\). The optimal location is the one with the minimum objective functional value which is the minimum distance travelled [68]. This is an intuitive way of locating a facility. However, it might be challenging to implement in the organ allocation sector since it sometimes involves air transportation of organs; with air transportation the route to traverse is not always at the discretion of the decision maker. The air space is highly regulated and the contingent must obey set out air space regulations. What this means is that the Euclidean distance between two locations may be the shortest
by road transportation but this does not in any way guarantee the shortest route in air transportation since the rules for air transportation are different from ground transportation. The next section also discusses a multi stage situation in location allocation.

6.1.3. Multi-Stage Location-Allocation Model

The hierarchical stages of transplantation permits the modeling of the location-allocation problem as a two stage capacitated facility location-allocation problem (TSCFLP) [68]. This can be seen in a situation where a transplantation center receives organ from other organ procurement centers. This is the exact case in kidney procurement and transplantation since all organ procurement organizations (OPO) are non-profit bodies that exist as separate entities [16]. This situation is illustrated in figure 22 where a transplantation center (rectangle) receives organs from organ procurement center (triangle). In this model organs procured at the procurement center are transported to be transplanted on the patients who are on dialysis awaiting kidney transplantation at the transplantation center. For a situation like this the total cost will consist of fixed cost at the transplantation center, variable cost at transplantation center and the variable cost for transporting organs from the procurement center to the transplantation center.

If the procurement center is under the same management as the transplantation center, then the fixed cost at the procurement center will also be added to the model. The formulation below considers the procurement and transplantation centers as two separate entities under different management;
hence, the objective function minimizes the costs at the transplantation center and the variable cost for the services the procurement center renders to the transplantation center.

Figure 22: Procurement center serving a transplantation center

To formulate the model the following parameters must be defined for the TSCFLP:

\( t_{ij} \) = transportation cost per unit from dialysis center \( i \) to transplantation center \( j \).

\( c_{kj} \) = cost per person for rendering services at transplantation center \( j \) to market point \( k \).

All other parameters have the same meaning as in the capacitated model described in section 6.1.1.

The following decision variables must also be defined:

\( x_{ij} \) = number of organs that will be transported from procurement center \( i \) with capacity \( p_i \) to transplantation center \( j \)

\( y_j = 1 \) if facility is allocated to a location \( j \), 0 otherwise

\( z_{kj} \) = number of people receiving services at transplantation center \( j \) from market point \( k \)

The model is formulated as:
\[
\text{Min} \sum \sum_{i \in I, j \in J} t_{ij}x_{ij} + \sum \sum_{k \in K, j \in J} c_{kj}z_{kj} + \sum f_jy_j
\]

Subject to

\[
\sum_{i=1}^{n} z_{kj} = 1 \quad \forall k \in K
\]  
(18)

\[
\sum x_{ij} \leq p_i, \forall i \in I
\]  
(19)

\[
x_{ij} - p_i y_i \leq 0, \forall i \in I, j \in J
\]  
(20)

\[
x_{ij} \geq 0, \forall i \in I, j \in J
\]  
(21)

\[
y_i = \{0, 1\}
\]  
(22)

\[
0 \leq z_{kj} \leq 1, \quad 0 \leq y_i \leq 1 \quad \forall k \in K, \quad j \in J
\]  
(23)

The TSCFLP returns the minimum of the objective functional value and the location with this value is the optimal center for the facility allocation.

The location-allocation models are helpful decision making tools but other factors such as political risk, population size and availability of land all have the potential to affect the decision of the location of a dialysis, transplantation or organ procurement center [61]. Political risk has the potential to impact the decision on facility location especially when there is a change in political administration. Under this situation commitments to the allocation of facility to a particular location might change to suit political interest. Also population size can sway the decision to locate a facility to an area of higher population. Furthermore, the cost and availability of land in a geographical region can potentially influence the decision on location.
allocation [61]; from the allocation models an area might be optimal for facility allocation but if there is no land available, or if the cost to purchase land is extremely expensive then the decision to locate the facility at that location will be reconsidered. Sensitivity analysis in addition to location-allocation models help decision makers to make decisions by considering these scenarios [61]. To demonstrate the application of the facility allocation model, a brief account of how genetic algorithm can be used to solve the gravity allocation (GA) model is demonstrated in the next section.

6.1.4. Using GA Approach to Solve the Gravity Allocation Model

Genetic algorithm approach has been used by other researchers to solve the location allocation problem. Hosage and Goodchild [65] solved the problem by considering it as a discrete space location problem. The authors solved a problem involving the allocation of 3 facilities and ran the algorithm with a population size of 25 for 120, 150, 180, and 210 generations. In all of these cases GA found 81.75% of correct solutions. The flexibility with GA is that the number of generations and population size can be increased to prevent the temptation of settling on a local optimum. This increases the possibilities of arriving at a global optimum in the solution space. However, this also has a direct impact on computational time which tends to increase with increase in the number of generations and population size [65].

To solve the gravity allocation model using GA, the steps [65] below will be followed:
1. Randomly generate initial population by randomly producing \( n \) sets of individuals. These individuals known as chromosomes represent an initial solution set from which GA will work to improve the solution quality until a termination stage is reached.

2. Evaluate fitness function of each individual in the population and assign reproduction probabilities.

3. Randomly pair chromosomes from previous population for mating.

4. Perform crossover or mutation or combination of the two to generate offspring.

5. Use a selection criterion to select a new population by determining which chromosomes from the offspring and/or parents make it to the next generation as parents.

6. Repeat from step 3 and continue iterations until a termination criterion is met.

Since the objective of the gravity location-allocation model is to minimize the weighted distance, the location with the lowest objective functional value which represents the minimum weighted distance will be selected for the \((n+1)^{th}\) facility when termination criterion of the GA is met. This will be the location where the new facility will be located. Assuming there are already \( n \) facilities in existence and we need to locate only one facility, the chromosome for the objective function can be represented as:
where $X_{n+1} Y_{n+1}$ represents coordinate pair for a potential new facility location. This approach was used by Dominguez et al. [69] when they solved the discrete ordered median problem. Since any of several locations can be selected for the $(n+1)^{th}$ facility location, a GA approach can be used to arrive at a more refined solution. To demonstrate this assume that the fitness function of 4 random potential locations from which one will be selected for the new location are 1000, 1050, 900, and 1200 for the initial population. Static scaling which is one of the GA tools for scaling fitness functions can be applied to the fitness functions by subtracting a constant factor (eg. 500) from each of the fitness functions. Applying the static scaling to the chromosomes (C1, C2, C3 and C4) the fitness functions after scaling are shown in Table 11.
Table 11: Chromosome fitness functional value after scaling

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Original Fitness Function</th>
<th>Fitness Function after Scaling</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>1000</td>
<td>1000 – 500 = 500</td>
</tr>
<tr>
<td>C2</td>
<td>1050</td>
<td>1050 – 500 = 550</td>
</tr>
<tr>
<td>C3</td>
<td>900</td>
<td>900 – 500 = 400</td>
</tr>
<tr>
<td>C4</td>
<td>1200</td>
<td>1200 – 500 = 700</td>
</tr>
</tbody>
</table>

Using the fitness function after scaling, reproduction probabilities will now be calculated for each chromosome after which chromosomes will be paired for mating followed by the other GA steps explained above. This will continue as explained until a termination criterion is met. At this stage the chromosome that comes up with the least objective function will be selected as the location for the \((n+1)^{th}\) facility location.

It is worth mentioning that other GA approaches such as dynamic scaling, sigma truncation, power law scaling exist that can also be used instead of static scaling. Also one can vary population size depending on the computational time available. Shamsul et al. [67] explain that larger population sizes increase the chances of arriving at a global solution but it also comes with an increased computational time [67]. The next section presents a numerical example for the gravity model.
6.1.5. Solving the Gravity Allocation Math Model

To show the results of the math model using the gravity model the following problem adopted from Sunil Chopra [61] is used: In this problem, a transplantation center has been serving an entire region for years. However, due to increase in demand the Organ Procurement Organization and the OPTN has decided to establish a new transplantation center to serve the regions (markets) A, B, C, D, and E (figure 24). This new facility will receive organs from existing organ procurement centers located at region F, G, and H. The estimated demand for each region, the geographical coordinates, the transportation cost, and the estimated number of organs from each source are given in table 12.
Table 12: Data for gravity model

<table>
<thead>
<tr>
<th>Markets/ Sources</th>
<th>Transportation Cost per Mile</th>
<th>Demand</th>
<th>Coordinates</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Markets</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>1.5</td>
<td>225</td>
<td>600</td>
<td>500</td>
</tr>
<tr>
<td>B</td>
<td>1.5</td>
<td>150</td>
<td>1050</td>
<td>1200</td>
</tr>
<tr>
<td>C</td>
<td>1.5</td>
<td>250</td>
<td>800</td>
<td>300</td>
</tr>
<tr>
<td>D</td>
<td>1.5</td>
<td>175</td>
<td>925</td>
<td>975</td>
</tr>
<tr>
<td>E</td>
<td>1.5</td>
<td>300</td>
<td>1000</td>
<td>1080</td>
</tr>
<tr>
<td>Source of Supply</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>0.9</td>
<td>500</td>
<td>700</td>
<td>1200</td>
</tr>
<tr>
<td>G</td>
<td>0.95</td>
<td>300</td>
<td>250</td>
<td>600</td>
</tr>
<tr>
<td>H</td>
<td>0.85</td>
<td>700</td>
<td>225</td>
<td>825</td>
</tr>
</tbody>
</table>

Source: Adopted from [61]

The problem is pictorially displayed in figure 24. There are 5 market regions (A, B, C, D, E) to be served by the potential transplantation facility. The new facility will rely on existing OPO facilities F, G, and H for organs to serve the markets. The problem therefore is to find the location for a new transplantation center that will minimize the cost of transporting organs from the OPOs to the transplantation center and the cost per travel from the market centers. The markets and sources in figure 24 are not drawn to scale but the new location can be anywhere within the
search space that minimizes the total weighted cost \((w_k)\) and distance as in the gravity location model. The weighted cost is made up of the cost from the source and market to the potential facility location.

Figure 24: Five markets (red) and 3 OPOs (yellow)

This problem was solved with the excel solver to minimize the objective function of the gravity location model. The results are shown in table 13.
Table 13: Solution of the gravity allocation math model

<table>
<thead>
<tr>
<th>Market/Source</th>
<th>Cost ($) / Mile</th>
<th>Demand</th>
<th>Coordinates</th>
<th>Distance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>Y</td>
</tr>
<tr>
<td>A</td>
<td>1.5</td>
<td>225</td>
<td>600</td>
<td>500</td>
</tr>
<tr>
<td>B</td>
<td>1.5</td>
<td>150</td>
<td>1050</td>
<td>1200</td>
</tr>
<tr>
<td>C</td>
<td>1.5</td>
<td>250</td>
<td>800</td>
<td>300</td>
</tr>
<tr>
<td>D</td>
<td>1.5</td>
<td>175</td>
<td>925</td>
<td>975</td>
</tr>
<tr>
<td>E</td>
<td>1.5</td>
<td>300</td>
<td>1000</td>
<td>1080</td>
</tr>
<tr>
<td>F</td>
<td>0.9</td>
<td>500</td>
<td>700</td>
<td>1200</td>
</tr>
<tr>
<td>G</td>
<td>0.95</td>
<td>300</td>
<td>250</td>
<td>600</td>
</tr>
<tr>
<td>H</td>
<td>0.85</td>
<td>700</td>
<td>225</td>
<td>825</td>
</tr>
</tbody>
</table>

Optimal Location

<table>
<thead>
<tr>
<th>X Coordinate</th>
<th>681.3034</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y Coordinate</td>
<td>881.9967</td>
</tr>
<tr>
<td>Cost ($)</td>
<td>1,265,235</td>
</tr>
</tbody>
</table>

The results in table 13 obtained from the gravity location model were obtained by entering the given data in spreadsheet as in figure 27 [61]. The equations in table 14 were then entered before the excel solver (figure 26) was ran.
Table 14: Formulae for cells in figure 25 [61]

<table>
<thead>
<tr>
<th>Cell</th>
<th>Cell Formula</th>
<th>Copied to</th>
</tr>
</thead>
<tbody>
<tr>
<td>G5</td>
<td>$\sqrt{((B16-E5)^2+(B17-F5)^2}$</td>
<td>GG5:G12</td>
</tr>
<tr>
<td>B19</td>
<td>SUMPRODUCT(G5:G12,D5:D12,C5:C12)</td>
<td>-</td>
</tr>
</tbody>
</table>

Figure 25: Snapshot of excel worksheet

Figure 26: Snapshot of excel solver
From table 13 the optimal location for the new single facility has the geographical coordinates (681.3034, 881.9967) and an associated cost of $1,265,235. The exact location for this coordinate can be identified by plotting the coordinates on a map. Although this location is the optimal location from the gravity model, other factors such as infrastructure and skilled personnel must be considered so that the facility can be located close to the optimal location [61]. Also there is the possibility of meeting other physical constraints such as unavailability of land at the optimal location for the construction of the new facility. For such situations the facility must be located as close as possible to the optimal location [61]. The next section will review how GA can also be used to solve resource allocation problem.
7. GENETIC ALGORITHM

Genetic algorithm (GA) which originated in the 1960s by John Holland [70] has been a very useful tool in solving optimization problems. Around the same time that Holland invented GA, Rechenberg and Schwefel also invented evolution strategy which is also used to search for solution to optimization problems [71, 72]. Other researchers also invented “evolutionary programming” which apply some of the basic ideas in GA such as mutation [73, 74]. Genetic Algorithm applies a series of steps which mimics biological evolution. These processes will be demonstrated by solving the gravity model as demonstrated in the section below.

7.1. Problem Definition and GA Procedure

In order to illustrate the GA processes multiple genes per chromosome will be used; assume that there are 16 different locations (genes) as shown in figure 27 from which 4 are to be selected to serve a single market or a region. These locations can randomly be grouped into 4 with each representing a potential solution. It is also assumed that a location cannot be duplicated hence each location can belong to only one group called chromosome. This constraint can be relaxed in a real world problem in order to allow the search for a global solution. Also in this problem a single market point was selected for simplicity but in reality, the facilities can serve multiple markets. From the gravity model the objective function is to select the chromosome that minimizes the total weighted cost. The chromosomes for the initial population are shown in table 15.
Suppose also that table 16 defines the distances and weighted cost per distance from each location (gene) to the market center. This means chromosome 1 consists of locations 1, 5, 9, and 12 with respective weighted costs $200, $2,450, $3,698, and $1,001. The fitness function for the chromosomes can be calculated and have been shown in table 17.

Table 15: Representation of chromosomes

<table>
<thead>
<tr>
<th>Chromosome 1</th>
<th>1</th>
<th>5</th>
<th>9</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosome 2</td>
<td>4</td>
<td>10</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Chromosome 3</td>
<td>11</td>
<td>15</td>
<td>13</td>
<td>7</td>
</tr>
<tr>
<td>Chromosome 4</td>
<td>0</td>
<td>14</td>
<td>6</td>
<td>3</td>
</tr>
</tbody>
</table>
Table 16: Distance and weighted cost per distance

<table>
<thead>
<tr>
<th>Location</th>
<th>Weighted Cost ($)</th>
<th>Distance to market (miles)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1500</td>
<td>55</td>
</tr>
<tr>
<td>1</td>
<td>200</td>
<td>78</td>
</tr>
<tr>
<td>2</td>
<td>2008</td>
<td>95</td>
</tr>
<tr>
<td>3</td>
<td>4000</td>
<td>99</td>
</tr>
<tr>
<td>4</td>
<td>300</td>
<td>102</td>
</tr>
<tr>
<td>5</td>
<td>2450</td>
<td>109</td>
</tr>
<tr>
<td>6</td>
<td>2564</td>
<td>109</td>
</tr>
<tr>
<td>7</td>
<td>2365</td>
<td>120</td>
</tr>
<tr>
<td>8</td>
<td>4562</td>
<td>158</td>
</tr>
<tr>
<td>9</td>
<td>3698</td>
<td>198</td>
</tr>
<tr>
<td>10</td>
<td>1459</td>
<td>201</td>
</tr>
<tr>
<td>11</td>
<td>6598</td>
<td>208</td>
</tr>
<tr>
<td>12</td>
<td>1001</td>
<td>257</td>
</tr>
<tr>
<td>13</td>
<td>5464</td>
<td>289</td>
</tr>
<tr>
<td>14</td>
<td>2008</td>
<td>325</td>
</tr>
<tr>
<td>15</td>
<td>4000</td>
<td>375</td>
</tr>
</tbody>
</table>
Fitness function sample calculation is shown below.

Fitness function: \( \min \sum_{k \in K} w_k d_k (x, y) \),

Using the data in table 15 and 16 the objective function for chromosome 1 can be computed as below:

Chromosome 1: \( = \text{Sum } [(200*78) + (2450*109) + (3698*198) + (1001*257)] = 2,306,113 \)

Objective functions for remaining chromosomes are shown in the table below:

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Objective function ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2,306,113</td>
</tr>
<tr>
<td>2</td>
<td>1,918,209</td>
</tr>
<tr>
<td>3</td>
<td>4,590,763</td>
</tr>
<tr>
<td>4</td>
<td>2,260,850</td>
</tr>
</tbody>
</table>

Optimal facility location is chromosome 2 since it has the minimum fitness function ($ 1,918,209). If this was the termination point for the GA then the four facilities will be located at the locations designated as 4, 10, 2, and 8 of chromosome 2. GA has the ability to find the best solution through a series of iterations.

To show the GA steps, assume that the chromosomes in table 15 respectively, represent chromosomes in the initial population (parents) which was generated
randomly. Reproduction probabilities can be calculated for each chromosome from their fitness functions as shown in table 18 after which the chromosomes will go through mating; the mating process has been explained in the subsequent paragraph.

Table 18: Reproduction probabilities of parent population

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Cumulative probability</th>
<th>Reproduction probability</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>0.001 – 0.270</td>
<td>=11075935/2306113=4.80</td>
<td>4.80/17.89=0.27</td>
</tr>
<tr>
<td>C2</td>
<td>0.271 – 0.590</td>
<td>=11075935/1918209=5.77</td>
<td>5.77/17.89=0.32</td>
</tr>
<tr>
<td>C3</td>
<td>0.591 – 0.730</td>
<td>=11075935/4590763=2.41</td>
<td>2.41/17.89=0.13</td>
</tr>
<tr>
<td>C4</td>
<td>0.731 – 1.000</td>
<td>=11075935/2260850=4.90</td>
<td>4.90/17.89=0.27</td>
</tr>
<tr>
<td>Total</td>
<td>11,075,935</td>
<td>17.89</td>
<td></td>
</tr>
</tbody>
</table>

To show the mating procedure cumulative probabilities for the chromosomes must be calculated from the reproduction probabilities. Four random numbers (RN) are then drawn to determine the mating pair from the parent population. This is shown below:

Cumulative probabilities (RN #s: 0.25, 0.29, 0.49, and 0.71)

- C1: RN# 1: 0.25
- C2: RN# 2: 0.29, RN# 3 0.49
- C3: RN # 4: 0.71
- C4: 0.731 – 1.000
The RNs are paired against the cumulative properties to determine the pairs for mating. Based on the chosen random numbers the chromosomes are paired as (C1 and C2), and (C2 and C3). Chromosome 4 (C4) is not paired with any chromosome because none of the random numbers falls within C4’s range of the cumulative probability. This means that C4 will not make it to the next GA stage. The chromosomes that go through to mating will then go through crossover.

For chromosomes to go through crossover first one has to determine the number of cut points available. This is given by \( n-1 \) where \( n \) is the number of genes per chromosome. Since there are 4 genes per chromosome, there are 3 possible cut points with a cut point probability \( (1/(n-1)) \) of 1/3 or 0.33. Assuming a crossover probability \( (p_c) \) of 0.7, a random number is again drawn to determine if the pair (C1, C2) will go through crossover. If the random number = 0.5, it means the pair will go through crossover since the RN is less than the \( p_c \). Another RN is selected to determine the cut point. Assuming the RN is 0.85, then cut point will be at the last possible cut point as shown in table 19. The genes ‘12’ and ‘8’ will go through crossover by swapping their positions to form 2 new offspring. This is shown in table 20. The same procedure is repeated for the other pair (C2 and C3). The next GA stage after crossover is mutation which has been described below:
Table 19: Cut point probabilities

<table>
<thead>
<tr>
<th>Cut Point Prob.</th>
<th>0.33</th>
<th>0.33</th>
<th>0.33</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cum Prob.</td>
<td>0.33</td>
<td>0.66</td>
<td>1.00</td>
</tr>
<tr>
<td>C1</td>
<td>1</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>C2</td>
<td>4</td>
<td>10</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 20: Offspring from C1 and C2

<table>
<thead>
<tr>
<th>Offspring 1</th>
<th>1</th>
<th>5</th>
<th>9</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Offspring 2</td>
<td>4</td>
<td>10</td>
<td>2</td>
<td>12</td>
</tr>
</tbody>
</table>

To demonstrate mutation an assumed mutation probability ($P_m$) =0.10 must be tested by drawing RNs to see if any of the genes in the offspring will go through mutation. A gene goes through mutation if its RN is less than the mutation probability and vice-versa. This process is applied to all the offspring. For this example it is assumed that the RNs are respectively 0.12, 0.25, 0.50, and 0.21 for the genes in offspring 1. This means that none of the genes will go through mutation. A similar test is conducted for the genes in the remaining offspring. Again, it is assumed that none of the offspring goes through mutation. This will preserve most of the characteristics of the parents in the offspring [75]. The next stage in GA after mutation is selection which is also described below.
Assuming the second pair (C2, C3) also went through crossover only at the last cut point, then 4 offspring will be produced. The new population becomes 8 in number (4 parents and 4 offspring). A selection criterion can now be used to determine which chromosomes make it to the next generation for the iteration to continue. Various selection strategies exist; for example the chromosomes with the best fitness functions can be selected to make it to the next generation. The problem with this strategy is that the algorithm can quickly run to a local optimum and the opportunity to get a global optimum will be missed [69]. Another strategy is to select the parent chromosomes to die and be replaced by the offspring. When this is done offspring will replace parents for the next iteration at the end of each generation. Table 21 shows the new population of 4 parents and 4 offspring (O1, O2, O3, and O4) from which 4 will be selected for the next iteration. The selected population for the next generation will go through the cycle over again until a preset termination condition is met [69].

Table 21: Parent and offspring parent population

<table>
<thead>
<tr>
<th>C1</th>
<th>1</th>
<th>5</th>
<th>9</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>C2</td>
<td>4</td>
<td>10</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>C3</td>
<td>11</td>
<td>15</td>
<td>13</td>
<td>7</td>
</tr>
<tr>
<td>C4</td>
<td>0</td>
<td>14</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>O1</td>
<td>1</td>
<td>5</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>O2</td>
<td>4</td>
<td>10</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>O3</td>
<td>11</td>
<td>15</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>O4</td>
<td>0</td>
<td>14</td>
<td>6</td>
<td>7</td>
</tr>
</tbody>
</table>
The next chapter discusses the application of the Mahalanobis distance (MD) to kidney allocation. The MD approach offers a holistic organ matching using multiple donor-patient attributes as an alternative to the single factor age matching which is currently implemented in kidney allocation. The MD approach may also offer virtually no incentive to for kidney rejection.
8. THE MAHALANOBIS DISTANCE APPROACH FOR KIDNEY ALLOCATION

The kidney allocation policy has gone through a series of evolutions for the past two decades. Although a lot of progress has been made, the achievement of optimality between equity and efficiency still remains a challenge [13]. The current kidney allocation policy alternates between equity and efficiency [13]; to maximize kidney utilization, efficiency takes precedence over equity during the allocation of kidneys of the highest quality.

Besides the balance between equity and efficiency other challenges faced by decision makers are the high discard rate of expanded criteria donor kidneys and the frequency of death on the waiting list [20]. In 2011 over 5,000 people died on the waiting list while discard rate also increased from 12.7% in 2002 to 17.9% in 2011 [20]. This section of the research discusses the prospects of minimizing the discard rate by applying the Mahalanobis distance model to kidney allocation. This model identifies patterns between the traits of organs and recipients of historical successful transplantations, and compares them to traits of waiting list candidates. This method may help to minimize the discard rate of kidneys since waiting list candidates are most likely to be offered with organs of virtually the same quality over time hence are presented with minimal incentive to reject an organ offer.

The Mahalanobis distance (MD) introduced by Professor P. C. Mahalanobis in 1930 is a statistical tool for identifying patterns between a known and unknown sample [76]. MD is used as a decision making tool by decision makers and has applications in patient monitoring, voice recognition, handwriting analysis,
manufacturing, quality control and earthquake forecasting [76]. To be able to identify the correlation between the known and unknown a system must be trained with standardized data. This is used as the basis for pattern recognition since the patterns which will be identified in the unknown will be compared to the trends identified in the known or the true data. Watanabe [76] defines patterns as the “opposite of chaos.” In the application of MD patterns are the items of interest that need to be identified. For example, in quality control the pattern of a process can be characterized as stable or unstable.

Mahalanobis – Taguchi (MT) system is an application of MD. MT is also used to derive a single value from MDs upon which a decision will be made. MD has a wide application in medical diagnoses; Nakajima et al. [77] explain that the processes that physicians diagnose diseases is an application of pattern recognition. This is because physicians collate information from patient’s medical history, physical examination and laboratory data to identify trends. If a pattern is identified then diagnosis is made by comparing the identified pattern(s) to known pattern(s) of other diseases to arrive at a diagnosis [77].

The uniqueness of MD is that it takes into account the correlation between all the involved parameters. The application of MD in medical diagnosis was first experimented by Kanetaka [77, 78]. Nakajima et al. [77] also applied MD to evaluate liver diseases and observed that the condition of the patients worsens with increase in MD and vice-versa. Using clinical data they concluded that MD is a useful decision
enhancement tool in medicine. The MD procedure starts from known to the unknown. To Determine the MD the following steps must be observed:

1. Collection of raw data (Table 22)
2. Normalization of data (Table 23)
3. Determination of correlation and the inverse matrix
4. Calculation of MD.

<table>
<thead>
<tr>
<th>Table 22: Format of raw data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Factor</strong></td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>...</td>
</tr>
<tr>
<td>m</td>
</tr>
<tr>
<td><strong>Total (Σ)</strong></td>
</tr>
<tr>
<td><strong>Average (µ)</strong></td>
</tr>
<tr>
<td><strong>Standard Deviation (σ)</strong></td>
</tr>
</tbody>
</table>
Table 23: Format of normalized data

<table>
<thead>
<tr>
<th>Factor</th>
<th>$X_1$</th>
<th>$X_2$</th>
<th>$X_3$</th>
<th>...</th>
<th>$X_n$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$x_{1,1}$</td>
<td>$x_{2,1}$</td>
<td>$x_{3,1}$</td>
<td>...</td>
<td>$x_{n,1}$</td>
</tr>
<tr>
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<td>$x_{2,2}$</td>
<td>$x_{3,2}$</td>
<td>...</td>
<td>$x_{n,2}$</td>
</tr>
<tr>
<td>3</td>
<td>$x_{1,3}$</td>
<td>$x_{2,3}$</td>
<td>$x_{3,3}$</td>
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<td>$x_{n,3}$</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>m</td>
<td>$x_{1,m}$</td>
<td>$x_{2,m}$</td>
<td>$x_{3,m}$</td>
<td>...</td>
<td>$x_{n,m}$</td>
</tr>
</tbody>
</table>

Where \[ X_{ii} = \frac{X_{ii} - \mu_{Xi}}{\sigma_{Xi}} \]

Numerical example for correlation matrix

The raw data must first be normalized from which the variance-co-variance matrix is computed. The correlation matrix $\rho_{xy}$ can then be computed from the variance-covariance matrix using equation below:

\[ \rho_{xy} = \frac{SS_{xy}}{\sqrt{SS_{xx}} \sqrt{SS_{yy}}} \]

Where $SS$ represents the co-variance.

Once the correlation matrix is known the inverse correlation matrix ($P_{xy}^{-1}$) can also be computed. Let $U = x_1, x_2, ... x_21$ represent the variables: donor age, donor height, donor weight etc. as respectively represented on the column headings in
table 25. This means that the variance-covariance matrix \( \Sigma \) for the 21 variables can be formulated as:

\[
\Sigma = \frac{1}{n-1} \begin{bmatrix}
SS_{x_{1j}} & SS_{x_{2j}} & SS_{x_{3j}} & \cdots & SS_{x_{21j}} \\
SS_{x_{1i}} & SS_{x_{2i}} & SS_{x_{3i}} & \cdots & SS_{x_{21i}} \\
SS_{x_{1i}} & SS_{x_{2i}} & SS_{x_{3i}} & \cdots & SS_{x_{21i}} \\
\vdots & \vdots & \vdots & \ddots & \vdots \\
SS_{x_{1i}} & SS_{x_{2i}} & SS_{x_{3i}} & \cdots & SS_{x_{21i}} 
\end{bmatrix}
\]

Where

\[
SS_{x_{ij}} = \sum_{i,j=1}^{n}(x_i - \bar{x})(x_j - \bar{x})
\]

From the covariance matrix the correlation matrix is also formulated as:

\[
\rho = \begin{bmatrix}
\frac{\text{Cov}(x_1, x_1)}{\sigma_1 \sigma_1} & \frac{\text{Cov}(x_1, x_2)}{\sigma_1 \sigma_2} & \cdots & \frac{\text{Cov}(x_1, x_n)}{\sigma_1 \sigma_n} \\
\frac{\text{Cov}(x_2, x_1)}{\sigma_2 \sigma_1} & \frac{\text{Cov}(x_2, x_2)}{\sigma_2 \sigma_2} & \cdots & \frac{\text{Cov}(x_2, x_n)}{\sigma_2 \sigma_n} \\
\frac{\text{Cov}(x_n, x_1)}{\sigma_n \sigma_1} & \frac{\text{Cov}(x_n, x_2)}{\sigma_n \sigma_2} & \cdots & \frac{\text{Cov}(x_n, x_n)}{\sigma_n \sigma_n}
\end{bmatrix}
\]

For simplicity, assume the covariance matrix for three variables is given as:

\[
\begin{bmatrix}
x_1 & x_2 & x_3 \\
2.6567 & 0.8552 & -0.1332 \\
0.8552 & 0.9510 & -0.0305 \\
-0.1332 & -0.0305 & 1.3756
\end{bmatrix}
\]

The correlation matrix will therefore be calculated as:

\[
\rho = \begin{bmatrix}
\frac{2.6567}{\sqrt{2.6567} \cdot \sqrt{2.6567}} & \frac{0.8552}{\sqrt{2.6567} \cdot \sqrt{0.9510}} & \frac{-0.1332}{\sqrt{2.6567} \cdot \sqrt{1.3756}} \\
\frac{0.8552}{\sqrt{2.6567} \cdot \sqrt{0.9510}} & \frac{0.9510}{\sqrt{0.9510} \cdot \sqrt{0.9510}} & \frac{-0.0305}{\sqrt{0.9510} \cdot \sqrt{1.3756}} \\
\frac{-0.1332}{\sqrt{2.6567} \cdot \sqrt{1.3756}} & \frac{-0.0305}{\sqrt{1.3756} \cdot \sqrt{0.9510}} & \frac{1.3756}{\sqrt{1.3756} \cdot \sqrt{1.3756}}
\end{bmatrix}
\]

\[
= \begin{bmatrix}
1.0000 & 0.5380 & -0.0697 \\
0.5380 & 1.0000 & -0.0267 \\
-0.0697 & -0.0267 & 1.0000
\end{bmatrix}
\]
To apply the Mahalanobis distance to kidney allocation raw data received from the Scientific Registry of Transplant Recipients (SRTR) were used. This is a large dataset expanding from 1986 to 2011 and has over 350,000 rows and 277 columns. Due to the large data size it was provided in SAS format. Fifty historical transplantation data were selected to demonstrate the Mahalanobis distance application. The traits considered for organ allocation using this method are: age, height, weight, antigens (A1, A2, B1, B2, DR1, DR2), donor panel reactivity antibody (PRA) and waiting time (DT). In this application DT was calculated as the difference between the time the recipient was enlisted on the waiting list and the time transplantation was conducted. The factors except waiting time and PRA were all collected for both the donor and recipient. The reason for selecting these factors is that the current kidney allocation model utilizes them to balance efficiency and utilization [13]. A factor such as antigen has various sub components. Table 24 shows the normalized data for the variables used in the MD experimentation.

The data were obtained from the kidney transplantations in 1991. Compared to other data sections this year’s data consistently had values for almost all the variables needed for the calculation of the MD. The next section presents the experimentation and results from the MD approach.

8.1. Example Problem

In this problem there are 10 people on the waitlist who qualify to receive a procured kidney with known traits. In order to allocate the kidney the traits of the waitlist candidates will be compared with historically successful transplants and
that of the arrival kidney to determine the candidate who will achieve the maximum benefits from transplantation when offered the kidney. The experiment utilizes 50 historical transplants in 1991 between August and October; this section of the data as explained is consistent and has almost all the data needed for the application of the Mahalanobis distance method. Compared to other sections it had fewer empty cells which were filled with random numbers by following the data structure as in each column. This approach focuses only on the allocation of the kidneys upon arrival. The importance of this approach is that candidates will be offered organs of similar qualities over time so they will be left with little incentive to reject an organ offer. The method and results (table 24 – 27) are presented in the sections below.

It is assumed that patients will always accept the organs once it is offered. Although this does not reflect reality as candidates on the national waitlist keep rejecting kidney offers, this assumption is logical since candidates will virtually be offered with kidneys of the same quality with time; there will then be little to no motivation to reject a kidney offer in the hope for a better quality kidney becoming available. The matching of the attributes of the candidates and the new kidney is also analogous to the approach used by David and Yichiali [79]. It is also similar to the age matching policy adopted by the current kidney allocation policy. In fact matching kidneys in this way is the optimal way in maximizing efficiency as has been proven by David and Yichiali [79]. This approach may help to minimize the discard rate of kidneys by ensuring that patients make a more informed decision in rejecting cadaveric kidneys.
The results from the MD method have been presented in the next section. Figure 28 shows the preprocessing of the data using Weka. Table 24 shows the normalized data which was necessary to bring all the data to a common comparable scale. Although the MD method is a non-parametric statistical approach the normalization is necessary since the data comes from different sources. From the normalized table the correlation matrix was also determined from which the inverse correlation matrix was calculated for determination of the MD.

8.2. Experimentation Results

“This study used data from the Scientific Registry of Transplant Recipients (SRTR). The SRTR data system includes data on all donor, wait-listed candidates, and transplant recipients in the US, submitted by the members of the Organ Procurement and Transplantation Network (OPTN), and has been described elsewhere. The Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors [20].”
Figure 28: Preprocessing of data
<table>
<thead>
<tr>
<th>DON_AGE_IN</th>
<th>DON_HGT</th>
<th>DON_WGT</th>
<th>DON_A1</th>
<th>DON_A2</th>
<th>DON_B1</th>
<th>DON_B2</th>
<th>DON_DRI</th>
<th>REC_HGT</th>
<th>REC_WGT</th>
<th>CAN_AGE_IN_MONTHS</th>
<th>REC_AGE_IN_MONTHS</th>
<th>REC_A1</th>
<th>REC_A2</th>
<th>REC_B1</th>
<th>REC_B2</th>
<th>REC_DRI</th>
<th>REC_DR2</th>
<th>REC_PRA</th>
<th>DT_in_Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.541083938</td>
<td>1.054804</td>
<td>0.093359</td>
<td>-0.0854</td>
<td>0.130252</td>
<td>0.142213</td>
<td>0.159949</td>
<td>0.013424</td>
<td>0.035465</td>
<td>0.014733</td>
<td>0.26563</td>
<td>-0.31705667</td>
<td>-0.331112924</td>
<td>-0.10836</td>
<td>0.145047</td>
<td>0.089757</td>
<td>0.104753</td>
<td>-0.23775</td>
<td>0.232174</td>
<td>0.153148</td>
</tr>
<tr>
<td>0.541083938</td>
<td>1.054804</td>
<td>0.093359</td>
<td>-0.0854</td>
<td>0.130252</td>
<td>0.142213</td>
<td>0.159949</td>
<td>0.013424</td>
<td>0.035465</td>
<td>0.014733</td>
<td>0.26563</td>
<td>-0.31705667</td>
<td>-0.331112924</td>
<td>-0.10836</td>
<td>0.145047</td>
<td>0.089757</td>
<td>0.104753</td>
<td>-0.23775</td>
<td>0.232174</td>
<td>0.153148</td>
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<tr>
<td>0.541083938</td>
<td>1.054804</td>
<td>0.093359</td>
<td>-0.0854</td>
<td>0.130252</td>
<td>0.142213</td>
<td>0.159949</td>
<td>0.013424</td>
<td>0.035465</td>
<td>0.014733</td>
<td>0.26563</td>
<td>-0.31705667</td>
<td>-0.331112924</td>
<td>-0.10836</td>
<td>0.145047</td>
<td>0.089757</td>
<td>0.104753</td>
<td>-0.23775</td>
<td>0.232174</td>
<td>0.153148</td>
</tr>
</tbody>
</table>

Table 25: Correlation matrix
| DON_AGE_IN_M | DON_HGT_CM | DON_WGT_KG | DON_A1 | DON_A2 | DON_B1 | DON_B2 | DON_DR1 | DON_DR2 | CAN_AGE_IN_MONTHS_AT_LISTING | REC_AGE_IN_MONTHS_AT_TX | REC_A1 | REC_B1 | REC_DR1 | REC_DR2 | REC_PRA_MOST_RECENT | DT_in_Months |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| 2.784388079 | -1.21363 | -0.36249 | 0.84068 | -0.75846 | -0.45972 | 0.029867 | -0.01719 | 0.33531 | -0.10764 | -0.166165215 | 0.35351 | -0.01764 | -0.166165215 | 0.35351 | -0.01764 | 0.343756263 | -0.21463 | 0.218651 | 0.794566 | 0.63223 | -0.72011 | 0.52820313 |
| 1.213639871 | 0.190873 | 0.163202 | -0.25196 | -0.0974 | 0.214786 | 0.189115 | 0.077883 | 0.12013 | 0.131718 | -0.186473 | 0.071803206 | -0.208968294 | 0.149923 | -0.22437 | -0.22279 | 0.087196 | 0.253444 | -0.369719143 |
| -0.36249741 | -0.0974 | 0.255222 | -0.50934 | 0.360582 | 0.026333 | 0.309497 | -0.56665 | 0.48957796 | -0.175642803 | 0.291156 | 0.408411 | 0.562822 | -0.61804 | -0.10939 | -0.39788 | -0.12635 | 0.34278394 |
| -0.840681 | -0.75846 | -0.45972 | 0.25579 | 0.288052 | 0.40668 | -0.44366 | -0.22818 | 0.18893 | 0.265189 | 0.34660783 | 0.26108903 | 0.738346 | -0.86413 | 0.21842 | -0.0452 | 0.215811 | 0.11402 | 0.588691999 |
| 0.251960747 | -0.0974 | 0.239326 | 0.29898 | 0.262989 | 0.44447 | -0.14361413 | -0.210878419 | 0.120717 | 0.096151 | 0.04581 | -0.07164 | 0.60568 | -0.08921 | 0.202580303 | 0.11416 | 0.230693738 |
| -0.0974 | 0.255222 | -0.64746 | 0.18604 | 0.255125 | 0.262767 | 0.719505 | 2.911445 | 2.12993 | -0.38925 | 0.56725 | 0.491399 | 0.61665 | 0.51587 | -0.88031 | -0.31465 | 0.391994042 |
| 0.214786 | 0.189115 | 0.18604 | 0.25579 | 0.288052 | 0.40668 | -0.44366 | -0.22818 | 0.18893 | 0.265189 | 0.34660783 | 0.26108903 | 0.738346 | -0.86413 | 0.21842 | -0.0452 | 0.215811 | 0.11402 | 0.588691999 |
| -0.0974 | 0.255222 | -0.50934 | 0.360582 | 0.026333 | 0.309497 | -0.56665 | 0.48957796 | -0.175642803 | 0.291156 | 0.408411 | 0.562822 | -0.61804 | -0.10939 | -0.39788 | -0.12635 | 0.34278394 |
| 0.251960747 | -0.0974 | 0.239326 | 0.29898 | 0.262989 | 0.44447 | -0.14361413 | -0.210878419 | 0.120717 | 0.096151 | 0.04581 | -0.07164 | 0.60568 | -0.08921 | 0.202580303 | 0.11416 | 0.230693738 |
| -0.0974 | 0.255222 | -0.64746 | 0.18604 | 0.255125 | 0.262767 | 0.719505 | 2.911445 | 2.12993 | -0.38925 | 0.56725 | 0.491399 | 0.61665 | 0.51587 | -0.88031 | -0.31465 | 0.391994042 |
| -0.36249741 | -0.0974 | 0.255222 | -0.50934 | 0.360582 | 0.026333 | 0.309497 | -0.56665 | 0.48957796 | -0.175642803 | 0.291156 | 0.408411 | 0.562822 | -0.61804 | -0.10939 | -0.39788 | -0.12635 | 0.34278394 |
| 0.33531 | -0.10764 | -0.166165215 | 0.35351 | -0.01764 | -0.166165215 | 0.35351 | -0.01764 | 0.343756263 | -0.21463 | 0.218651 | 0.794566 | 0.63223 | -0.72011 | 0.52820313 |
Table 27: Waiting list patients and new organ’s normalized data

| DON_AGE | DON_HGT | DON_WGT | DON_A1 | DON_A2 | DON_B1 | DON_B2 | DON_DR1 | DON_DR2 | REC_HGT | REC_WGT | CAN_AGE | REC_AGE | REC_A1 | REC_A2 | REC_B1 | REC_B2 | REC_DR1 | REC_DR2 | REC_PRA | DT_in_Months | D² |
|---------|---------|---------|--------|--------|--------|--------|--------|--------|--------|--------|---------|---------|--------|--------|--------|--------|--------|--------|--------|--------|----------|-----|
| P1      | 0.962034| 1.124662| 1.197557| -0.65487| -0.64563| -0.69026| -0.17306| -0.36804| -0.62914| 0.318976| -0.57888| -1.168715| -1.83086| -0.49726| -0.58038| -1.05201121| -2.0167| -0.43765| -0.27222| -0.60385| -0.82889| 7.280354+29 |
| P2      | 0.962034| 1.124662| 1.197557| -0.65487| -0.64563| -0.69026| -0.17306| -0.36804| -0.62914| -0.11887| -0.7634| -0.59195| -0.6735| -0.60489| 1.871948| 1.00353143| 1.782025| 0.474122| -0.3391| -0.60365| -0.5520| 3.97941+28 |
| P3      | 0.962034| 1.124662| 1.197557| -0.65487| -0.64563| -0.69026| -0.17306| -0.36804| -0.62914| -0.55673| 0.645725| -0.14194| 0.044291| -0.60489| -1.305883| 1.614376647| 0.79267| -0.64806| -0.3391| -0.60365| 1.584073| 2.93283E+24 |
| P4      | 0.962034| 1.124662| 1.197557| -0.65487| -0.64563| -0.69026| -0.17306| -0.36804| -0.62914| -0.13439| -0.77372| -1.51365| -1.64724| -0.60489| -1.30883| 1.178058634| 0.051494| -0.22724| -0.57319| -0.60365| -0.78229| 4.61308E+29 |
| P5      | 0.962034| 1.124662| 1.197557| -0.65487| -0.64563| -0.69026| -0.17306| -0.36804| -0.62914| 0.537902| 0.474603| 0.73602| 0.474603| 0.346017| 0.500559| -0.60489| -0.41494| -1.05201121| 0.051494| 0.33385| 2.43658| 0.54729| 1.21287| 2.22605E+27 |
| P6      | 0.962034| 1.124662| 1.197557| -0.65487| -0.64563| -0.69026| -0.17306| -0.36804| -0.62914| -1.59964| 2.06075| 0.749291| -2.09238| -0.60489| 1.871948| -1.05201121| -2.0167| 0.33385| -0.27222| -0.60365| -0.5967| 1.823962+27 |
| P7      | 0.962034| 1.124662| 1.197557| -0.65487| -0.64563| -0.69026| -0.17306| -0.36804| -0.62914| 1.417052| -0.34163| 0.644215| 0.661922| -0.49726| -0.38183| -0.76113253| 0.178118| -0.43765| -0.57319| 0.974627| 0.006496| 1.34929E+28 |
| P8      | 0.962034| 1.124662| 1.197557| -0.65487| -0.64563| -0.69026| -0.17306| -0.36804| -0.62914| -0.11887| -0.23215| 0.275534| 0.177833| -0.60489| -1.27669| -1.05201121| 0.87708| -0.64806| -0.40599| 0.60365| 0.87509| 1.78158E+26 |
| P9      | 0.962034| 1.124662| 1.197557| -0.65487| -0.64563| -0.69026| -0.17306| -0.36804| -0.62914| 0.77565| -0.17447| 0.471426| 0.871948| -1.05201121| 0.03292| 0.263713| -0.3391| -0.60365| -0.96789| 1.96744E+26 |
Assume that 10 patients on the waitlist who qualify to be offered the available organ are P1 to P10 as in table 27. What this means is that the patients’ blood and immune system support a successful transplantation with the arrival organ and that the attributes of the organ fall within the organ requirements of the candidates. This means that the patients have all agreed to accept an organ of the quality as the available organ. This model will therefore compare the characteristics of the organ to all the candidates and historical transplantations and calculate the MD. The smaller the MD the more closely related the organ is to the candidate’s traits and the higher the efficiency as compared to empirical successful transplants.

This means that the candidate with the lowest MD is the best to be offered the kidney if the objective is to maximize efficiency. The benefit of this system is that candidates who habitually reject an organ offer in anticipation of better quality organs will be presented with little incentive to reject an organ offer since this model will offer candidates organs of similar qualities over time. In the above results patient 3 (P3) should be offered with the organ since his MD is the smallest compared to the other nine candidates. This means that P3 is more genetically related to the organ donor than any of the candidates which is a desired feature for a successful transplantation; this was an important factor to Dr. Murray’s kidney transplantation breakthrough when he successfully transplanted a kidney from one sibling to the other [11]. The next section presents an allocation policy with penalty for rejecting a kidney offer.
9. KIDNEY ALLOCATION WITH PENALTY FOR REJECTION

The kidney allocation policy in the United States has gone through a series of policy reviews in recent years. This has resulted in the approval of a new policy which went into effect on December 4, 2014. Many changes have been made to address some of the problems that were inherent in the previous kidney allocation policy. The major factor in the former policy was waiting time. The policy prioritized and offered compatible kidneys to candidates that had waited the longest. Since waiting time was the major ranking factor, there were situations where several candidates died with functioning kidneys [16]

There were also cases where transplanted candidates had to re-enlist for kidney transplantation because the transplanted kidneys they received reached the end of their “useful life.” These problems occurred because some older candidates received much younger kidneys while younger candidates were given kidneys from older donors [16]; for example, kidney from a 25 year-old donor could be transplanted to a candidate as old as 75 years. This may result in the possibility of the candidate dying with a functioning kidney which may not be transplantable for medical reason.

The situation of re-enlistment may also occur due to graft failure or age mismatch. For example, if a kidney from a 70 year old donor is transplanted to a 25 year-old candidate, it increases the possibility of the graft reaching the end of its “useful life” even though the individual may be active with potentially more years to live. When this happens the person has to re-enlist for another transplantation [16].
This problem has direct effect on the number of people who will receive transplantation. It minimizes the number of kidneys that will be available to the candidates on the waiting list. To solve the problem the Organ Procurement and Transplantation Network (OPTN) has come up with intuitive policy modifications of which the principal components are explained in the next sections:

9.1. Age Matching

With the new policy, kidneys will be allocated to candidates within 15 years (+/-) of the donor’s age. For example: a kidney from a 45 year old donor will be offered to compatible candidates whose ages range from 30 to 60 years. This will help to prevent momentous mismatch of kidney and patient which may avoid re-transplantations and death with functioning kidney [16]. The National Kidney Foundation explains that this may not significantly affect the type of kidneys which most candidates on the waiting list will receive since most candidates are already offered kidneys within +/-15 years age range according to empirical data [23]. The next factor is the donor profile index (DPI).

9.2. Kidney Donor Profile Index

In the old kidney allocation policy which was used for over 2 decades [11], kidneys were classified as either expanded criterial donor kidney or standard criterial donor kidney. This system of classification led to the rejection and subsequent discard of kidneys which were potentially good kidneys for transplantation. Some kidneys of equivalent qualities were being utilized [23]. For example, a kidney from a 35 year old donor may be accepted and transplanted while
a kidney from a 60 year old donor may be rejected and discarded even if they are of the same quality.

It happened because a lot of emphasis was placed on the age of the donor. Intuitively, people may prefer kidneys from younger donors to much older donors. However, a lot of factors contribute into the survival of a kidney. For this reason the OPTN has come out with a point scoring system known as kidney donor profile index (KDPI) to help decision makers make the right decision about the quality of a kidney [24]. The following are the factors that contribute to the determination of the KDPI: “age, height, weight, ethnicity, history of high blood pressure, history of diabetes, cause of death, kidney function, hepatitis C status and donation after cardiac death versus donation after brain death” [24]. On a scale of 0 – 100%, a lower KDPI indicates a better quality kidney. This replaces the old classification of cadaveric kidneys as either expanded criterial donor kidneys or standard criterial donor kidneys [24]. This means that kidneys from a 35 and 60 year old donors could be of the same quality depending on the donor’s profile. This can happen if the 35 year – old donor had history of high blood pressure, history of diabetes etc. with nothing to show for the 60 year old donor.

Even though this is intended to improve the utilization of kidneys, there is still the possibility that candidates may reject kidneys from expanded criterial donors. This is because the parameters used in the determination of the KDPI in the current policy were already available to decision makers. One could infer that decision makers place different weight on each of the factors in the KDPI calculation.
For some candidates, age of the donor may be of a greater importance than a factor such as hepatitis C status; thus if the candidate is already a hepatitis C positive candidate. For a situation like this, a kidney from a donor who was also a hepatitis C positive may not be of a greater concern as a candidate who is already hepatitis C negative. For example: assume that a kidney with KDPI of 25% from a donor who was 35 year –old, hepatitis C positive, and with a history of high blood pressure is offered to a 45 year old with similar attributes as the kidney donor. Since this person is the first on the rank, it is possible for him/her to reject the kidney and wait for another offer which may have the same or similar KDPI but with an improvement in one of the factors such as normal blood pressure (i.e. no high blood pressure) even though another equally important factor might have caused the two to have the same KDPI. The remaining factor in the new policy prioritizes the expected benefit of the kidney/transplantation to the recipient and has been explained in the next section.

9.3. Expected Survival of Graft/Recipient

The new policy also offers kidneys of the highest quality (lower KDPI) to candidates who are expected to have the longest survival after the transplantation. This, similar to the age matching can literally be translated as the transplantation of younger kidneys to younger patients and older kidneys to older patients. This is expected to increase the number of organs available for transplantation since the likelihood of re-transplantation and people dying with functioning kidneys may be minimized. Since this is expected to increase the organ pool, it is difficult to
interpret it as age discrimination which is one of objectives stipulated by the UAGA to be met by organ allocation [80]. In order to predict the estimated kidney graft survival, the KDPI must be estimated from the kidney donor risk index (KDRI). This is done by utilizing the cox regression model [81] show below.

Let a continuous or discrete random variable $T$ represent the time to failure of a kidney. Also, let $F(t)$ represent the survival function of a kidney which is given by:

$$F(t) = \Pr(T \geq t)$$

The time to failure of the kidney $\lambda(t)$ according to Cox [81] may be defined as

$$\lambda(t) = \lim_{\Delta t \to 0^+} \frac{\Pr(t \leq T < t+\Delta t \mid T > t)}{\Delta t}$$

Further information can be found in Cox (1972) [81]. In order to determine the probability of failure, the factors that are in direct relationship with the organ must be determined. These have medically been determined to be “age, height, weight, ethnicity, history of high blood pressure, history of diabetes, cause of death, kidney function, hepatitis C status and donation after cardiac death versus donation after brain death” [82].

Let $x_j$ denote the set of pertinent attributes of $j$th kidney donor. This means that the above 10 factors can be represented as: $x_j = (x_{1j},...,x_{10j})$

Where $x_{ij}$ represents the $i$th donor attribute that has a direct effect on the survivability of the kidney from the $j$th donor. Cox [81] explains that the regression model for the time to failure can be modeled as:

$$\lambda(t : x) = \exp(x\beta)\lambda_0(t)$$
The final Cox regression model for the survivability of the kidney from the \( j^{th} \) donor is given by:

\[
\lambda_j(t) = \lambda_0(t)e^{\beta x_j}
\]  

(27)

Where \( \lambda_0(t) \) represents the baseline hazard function, \( \beta \) represents the regression coefficients, and \( x_j \) represents the variables (covariates) explained above. The baseline hazard function is observed when the covariates are equal to zero [81]. This could be considered as the case when there is no mitigation to improve the survival of the kidney. This indicates a direct relationship between survival [81] of a kidney and the baseline hazard rate.

Furthermore, the probability that the kidney from donor \( j \) will not survive, dies, or stop functioning, at time \( T_i \) can be defined to eliminate the effect of the baseline hazard function as explained by Cox (1972) [81]:

\[
P(T_i) = \frac{e^{\beta x_j}}{\sum e^{\beta x_j}}
\]  

(28)

The OPTN used kidney recipient data from 1995 – 2005 and estimated the beta for the 10 variables as shown in the table below:
Table 28: KDRI donor factors and model coefficients [82]

<table>
<thead>
<tr>
<th>Donor Characteristic</th>
<th>Applies to:</th>
<th>KDRI Coefficient (&quot;Beta&quot;)</th>
<th>KDRI &quot;XBeta&quot; Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (integer years)</td>
<td>All donors</td>
<td>0.0128</td>
<td>0.0128*(age-40)</td>
</tr>
<tr>
<td></td>
<td>Donors with age &lt; 18</td>
<td>-0.0194</td>
<td>-0.0194*(age-18)</td>
</tr>
<tr>
<td></td>
<td>Donors with age &gt; 50</td>
<td>0.0107</td>
<td>0.0107*(age-50)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>All donors</td>
<td>-0.0464</td>
<td>-0.0464*(hgt-170)/10</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>All donors w/ weight &lt; 80kg</td>
<td>-0.0199</td>
<td>-0.0199*(wgt-80)/5</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>African American donors</td>
<td>0.1790</td>
<td>0.1790</td>
</tr>
<tr>
<td>History of Hypertension</td>
<td>Hypertensive donors</td>
<td>0.1260</td>
<td>0.1260</td>
</tr>
<tr>
<td>History of Diabetes</td>
<td>Diabetic donors</td>
<td>0.1300</td>
<td>0.1300</td>
</tr>
<tr>
<td>Cause of Death</td>
<td>Donors w/ COD=CVA</td>
<td>0.0881</td>
<td>0.0881</td>
</tr>
<tr>
<td>Serum Creatinine</td>
<td>All donors</td>
<td>0.2200</td>
<td>0.2200*(creat-1)</td>
</tr>
<tr>
<td></td>
<td>Donors with creat &gt; 1.5 mg/dL</td>
<td>-0.2090</td>
<td>-0.2090*(creat-1.5)</td>
</tr>
<tr>
<td>HCV status</td>
<td>HCV positive donors</td>
<td>0.2400</td>
<td>0.2400</td>
</tr>
<tr>
<td>DCD Status</td>
<td>DCD donors</td>
<td>0.1330</td>
<td>0.1330</td>
</tr>
</tbody>
</table>

Numerical example adopted from OPTN [82] is shown below.

Given the data in table 29, the KDRI can be calculated as shown below.
Table 29: Attributes for calculating KDPI

<table>
<thead>
<tr>
<th>Variable</th>
<th>Status/Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>53</td>
</tr>
<tr>
<td>Height</td>
<td>5'11&quot;</td>
</tr>
<tr>
<td>Weight</td>
<td>175 lb</td>
</tr>
<tr>
<td>History of Hypertension</td>
<td>Donor has history of hypertension (Yes)</td>
</tr>
<tr>
<td>Diabetes Status</td>
<td>Donor has no diabetes history</td>
</tr>
<tr>
<td>Cause of Death</td>
<td>Cardiovascular accident (CVA)</td>
</tr>
<tr>
<td>Serum Creatinine</td>
<td>1.6mg/dL</td>
</tr>
<tr>
<td>HCV Status</td>
<td>Negative</td>
</tr>
<tr>
<td>DCD Status</td>
<td>Donor was DCD (Yes)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Hispanic/Latino</td>
</tr>
<tr>
<td>Cold Ischemic Time</td>
<td>4 hours</td>
</tr>
</tbody>
</table>

Note: The exponent beta (XBeta) = \[0.0128\times(53-40) + 0.0107\times(53-50)\] + 
\[0.0464\times(183-175)/10 + 0 + 0.1260 + 0 + 0.0881 + 0.2200\times(1.6-1) + -0.2090\times(1.6-1.5) + 0 + 0.1330 + (0.0108\times4) = 0.66278

KDRI = \(\exp(XBeta)\) [82]

Finally the KDRI is normalized by dividing it by the median KDRI of all kidney donors of the previous year. The KDPI is obtained by reading the corresponding KDPI for the calculated KDRI. In the above illustration, the normalized KDRI will be 1.94017854/1.24234410213776 = 1.561707853. Estimating the corresponding
KDPI of this value from the KDRI to KDPI mapping table yields a KDPI of approximately = 87%. This means that the kidney is a low quality kidney [82].

The problem with this system is that other factors that may potentially impact the quality of the kidney are not included in the calculation for the KDPI. A factor such as the cold ischemic time has a direct effect on the quality of a donated kidney. In fact this is a common reason given by transplant officials for the rejection of kidney offers [20]. This means that having a single number for transplant officials as in the KDPI will speed up the kidney quality evaluation process but decision makers may still look for further information to determine whether to accept or reject a kidney offer. The problem with cold ischemic time is that it is not readily available during the period when KDPI [82] is determined or during the period of organ allocation. However, expected value(s) may be included in the calculation of the KDPI as illustrated in the numerical example.

Another way to minimize the discard rate of kidneys is to provide a disincentive to decision makers so that kidneys perceived to be sub-optimal may be utilized. Since every transplant center tries to minimize the death rate of transplant patients, a transplant center can be made to pay a fine for any kidney that is rejected and later transplanted successfully at another transplant center [26]. However, this is not easy to integrate into the simulation model used by policy makers.

Another way to introduce a penalty function is to demote the candidate who was to receive the kidney offer. Varying degrees of penalty functions can be implemented. In the current system if an offer is rejected by a candidate on top of
the ranking system at a center, the same candidate will receive the priority to be offered an organ if the next available organ matches with his/her age and other allocation compatibility requirements. This may provide a hidden incentive for the candidate on top of the rank to wait for a kidney perceived as better quality kidney. A lesser penalty function will be the prioritization of the next candidate in the rank for the next available kidney instead of the candidate who refused the previous organ. Figure 29 will be used to explain the application of this penalty function for rejecting a kidney offer:

![Figure 29: Proposed ranking model](image)

In the figure above, it is assumed that the initial waiting list consists of a finite set of candidates A, B, C and D ranked in the order of highest KAS to the lowest, forming a discrete set. Also assume that the list consists of candidates with similar attributes who qualify to receive organs with similar qualities. This means that when a kidney becomes available, it will be offered to candidate A to form a candidate–organ pair (A, o) who can decide to either reject or accept the offer. If
candidate A accepts the offer, transplant will be conducted and A will exit the waiting list. However, if the offer is rejected, the next candidate will be offered with the kidney. If candidate B accepts the organ which was rejected by candidate A, then candidate B will undergo transplantation and exit the system. Since candidate A rejected the kidney offer and the organ was successfully transplanted for candidate B, the next available kidney will be offered to candidate C which means that candidate C. In other words, candidate C will be on top of the priority list. This scenario is depicted in stage 1 of figure 29.

Similarly, if both candidates A and B reject the offer, and the organ is accepted by candidate C for transplantation, candidate C will exit the system and candidates A and B will each be demoted by one level so that the next available kidney will first be offered to candidate D. This is depicted in stage 2 of the above diagram. Since the tendency for an organ to be accepted after going through a series of rejections is very small [26] by candidates with similar needs, it leads to the assumption of a necessary condition to terminate the application of the penalty after offering it to the fourth candidate on the waiting list. This is intuitive since decision makers have up to one hour to make a decision on any kidney offer. Kidneys also have high chances of being rejected when they have higher cold ischemic time [20]. For this reason no penalty function was applied after the fourth candidate. This means that if candidates A, B, C, and D all reject the same kidney offer and it is accepted by candidate E, none of those who rejected the organ will be demoted and will maintain their ranks on the waiting list. This is depicted in stages 3 and 4.
where candidates D or E accepts the kidney rejected by candidates A, B, C and A, B, C, D respectively.

Using 2010 kidney transplantation data obtained from the Scientific Registry of Transplant Recipients (SRTR) the penalty function was introduced into the current kidney allocation model and other notable models which are shown in the case studies in the next section. Some of the fairness constraints used in the simulation are shown below.

**Dialysis Time Fairness Constraints**

\[
\sum_{p:Dr(p)=0}^{1825} \sum_{o(p,o) \subseteq C} x_{(p,o)} \geq 0.57 \sum_{(p,o) \subseteq C} x_{(p,o)} \quad \forall p, o \\
\sum_{p:Dr(p)=1826}^{3650} \sum_{o(p,o) \subseteq C} x_{(p,o)} \geq 0.241 \sum_{(p,o) \subseteq C} x_{(p,o)} \quad \forall p, o \\
\sum_{p:Dr(p)=3651}^{5475} \sum_{o(p,o) \subseteq C} x_{(p,o)} \geq 0.14 \sum_{(p,o) \subseteq C} x_{(p,o)} \quad \forall p, o \\
\sum_{p:Dr(p)=5476}^{5475} \sum_{o(p,o) \subseteq C} x_{(p,o)} \geq 0.049 \sum_{(p,o) \subseteq C} x_{(p,o)} \quad \forall p, o \\
k \sum_{(p,o) \subseteq C} x_{(p,o)} \in \mathbb{Z}^+ \quad \forall (p,o) \subseteq C \\
\sum_{p:Dr(p)=0}^{5475} x_{(p,o)} \leq 1 \quad \forall (p,o) \subseteq C \\
\sum_{o:Dr(p)=0}^{5475} x_{(p,o)} \leq 1 \quad \forall (p,o) \subseteq C \\
C \subseteq \mathbb{Z}^+ \quad \forall (p,o) \subseteq C
\]
The dialysis time constraints were derived using the data from the transplantations in 2010. The constraints coefficients in front of the summation signs indicate the proportion (by dialysis) of people who received transplantation in 2010. 57%, 24.15, 14%, and 4.90% of people with waiting time (years) from 0 to 5, 6 to 10, 11 to 15, and greater than 15 years respectively received transplantation [82]. Also, in the above constraints, $x_{(p,o)}$ represents a candidate and patient pair. All candidate and organ pairs medically compatible for transplantation belong to the set of positive integers $C$. Dialysis time, patient and organ are denoted as $DT$, $p$ and $o$ respectively. $Z^+$ represents the set of positive integers. These fairness constraints were necessary constraints to ensure that the model simulates with conditions comparable to what occurred in 2010. However, the simulation model allows the decision maker to define other constraints. Similarly, age, gender, ethnicity and ABO blood group fairness constraints are shown in the next sections. The age fairness constraints ensure that kidneys are offered to candidates who are within +/- 15 years of the donor’s age.

**Age Fairness Constraints**

\[
\sum_{p \in \text{age}_p, 0}^{5} \sum_{o \in C} x_{(p,o)} \geq 0.027 \sum_{(p,o) \in C} x_{(p,o)} \quad \forall p, o
\]  

(37)

\[
\sum_{p \in \text{age}_p, 6}^{34} \sum_{o \in C} x_{(p,o)} \geq 0.146 \sum_{(p,o) \in C} x_{(p,o)} \quad \forall p, o
\]  

(36)

\[
\sum_{p \in \text{age}_p, 35}^{49} \sum_{o \in C} x_{(p,o)} \geq 0.237 \sum_{(p,o) \in C} x_{(p,o)} \quad \forall p, o
\]  

(37)
\begin{align}
\sum_{p,\text{Age} \leq 60} \sum_{(p,o) \in C} x_{(p,o)} & \geq 0.432 \sum_{(p,o) \in C} x_{(p,o)} \quad \forall p, o \tag{38} \\
\sum_{p,\text{Age} > 64} \sum_{(p,o) \in C} x_{(p,o)} & \geq 0.157 \sum_{(p,o) \in C} x_{(p,o)} \quad \forall p, o \tag{39} \\
k \sum_{(p,o) \in C} x_{(p,o)} & \in \mathbb{Z}^+ \quad \forall (p,o) \in C \tag{40} \\
\sum_{p,(p,o) \in C} x_{(p,o)} & \leq 1 \quad \forall (p,o) \in C \tag{41} \\
\sum_{o,(p,o) \in C} x_{(p,o)} & \leq 1 \quad \forall (p,o) \in C \tag{42} \\
C & \in \mathbb{Z}^+ \quad \forall (p,o) \in C \tag{43} \\
x_{o}^{Age} - 15 & \leq x_{p}^{Age} \leq x_{o}^{Age} + 15 \tag{44} \\
x_{o}^{Age} - 15 & = \begin{cases} Z^+ & \text{if } x_{o}^{Age} > 15 \\ 0 & \text{if } x_{o}^{Age} \leq 15 \end{cases} \tag{45} \\
x_{o}^{Age}, \quad x_{p}^{Age} & = z^+ \quad \forall (p,o) \in C \tag{46} \\
\end{align}

\textbf{Gender Fairness Constraints}

\begin{align}
\sum_{p,\text{Gender}_{(p)} = \text{Male}} \sum_{(p,o) \in C} x_{(p,o)} & \geq 0.603 \sum_{(p,o) \in C} x_{(p,o)} \quad \forall p, o \tag{47} \\
\sum_{p,\text{Gender}_{(p)} = \text{FM}} \sum_{(p,o) \in C} x_{(p,o)} & \geq 0.397 \sum_{(p,o) \in C} x_{(p,o)} \quad \forall p, o \tag{48} \\
k \sum_{(p,o) \in C} x_{(p,o)} & \in \mathbb{Z}^+ \quad \forall (p,o) \in C \tag{49} \\
\sum_{p,(p,o) \in C} x_{(p,o)} & \leq 1 \quad \forall (p,o) \in C \tag{50} 
\end{align}
\[
\sum_{o(p,o) \in C} x_{(p,o)} \leq 1 \quad \forall (p,o) \in C 
\] (51)

\[
C \in \mathbb{Z}^+ \quad \forall (p,o) \in C 
\] (52)

**Ethnicity Fairness Constraints**

\[
\sum_{p:Etn_{p,o} = W} \sum_{o(p,o) \in C} x_{(p,o)} \geq 0.518 \sum_{(p,o) \in C} x_{(p,o)} \quad \forall p, o 
\] (53)

\[
\sum_{p:Etn_{p,o} = Bk} \sum_{o(p,o) \in C} x_{(p,o)} \geq 0.263 \sum_{(p,o) \in C} x_{(p,o)} \quad \forall p, o 
\] (54)

\[
\sum_{p:Etn_{p,o} = Ht} \sum_{o(p,o) \in C} x_{(p,o)} \geq 0.147 \sum_{(p,o) \in C} x_{(p,o)} \quad \forall p, o 
\] (55)

\[
\sum_{p:Etn_{p,o} = As} \sum_{o(p,o) \in C} x_{(p,o)} \geq 0.053 \sum_{(p,o) \in C} x_{(p,o)} \quad \forall p, o 
\] (56)

\[
\sum_{p:Etn_{p,o} = Other} \sum_{o(p,o) \in C} x_{(p,o)} \geq 0.019 \sum_{(p,o) \in C} x_{(p,o)} \quad \forall p, o 
\] (57)

\[
k \sum_{(p,o) \in C} x_{(p,o)} \in \mathbb{Z}^+ \quad \forall (p,o) \in C 
\] (58)

\[
\sum_{p(o,p,o) \in C} x_{(p,o)} \leq 1 \quad \forall (p,o) \in C 
\] (59)

\[
\sum_{o(p,o) \in C} x_{(p,o)} \leq 1 \quad \forall (p,o) \in C 
\] (60)

\[
C \in \mathbb{Z}^+ \quad \forall (p,o) \in C 
\] (61)
ABO Blood Group Fairness Constraints

\[
\sum_{p:ABO(p,o)\neq O} \sum_{o \in C} x_{(p,o)} \geq 0.452 \sum_{(p,o)\in C} x_{(p,o)} \forall p,o \tag{62}
\]

\[
\sum_{p:ABO(p,o)\neq A} \sum_{o \in C} x_{(p,o)} \geq 0.362 \sum_{(p,o)\in C} x_{(p,o)} \forall p,o \tag{63}
\]

\[
\sum_{p:ABO(p,o)\neq B} \sum_{o \in C} x_{(p,o)} \geq 0.137 \sum_{(p,o)\in C} x_{(p,o)} \forall p,o \tag{64}
\]

\[
\sum_{p:ABO(p,o)=AB} \sum_{o \in C} x_{(p,o)} \geq 0.049 \sum_{(p,o)\in C} x_{(p,o)} \forall p,o \tag{65}
\]

\[
k \sum_{(p,o)\in C} x_{(p,o)} \in \mathbb{Z}^+ \forall (p,o)\in C \tag{66}
\]

\[
\sum_{p,(p,o)\in C} x_{(p,o)} \leq 1 \forall (p,o)\in C \tag{67}
\]

\[
\sum_{o,(p,o)\in C} x_{(p,o)} \leq 1 \forall (p,o)\in C \tag{68}
\]

\[
C \in \mathbb{Z}^+ \forall (p,o)\in C \tag{69}
\]

Using these fairness constraints, 2 kidney allocation models were evaluated with the penalty function. First of all, the models were run without the penalty function using the KPSAM and 2010 transplantation date for 10 iterations for 12 months. Survivability coefficients were obtained by running Cox regression model described above using SPSS statistical software. Although the current kidney allocation policy considers 10 factors to calculate the KDPI [82], attempt was made at adding a 11th factor (cold ischemic time) since this factor has direct effect on the quality of the kidney during transplantation [82]. The next chapter discusses the
models and presents the results of 3 case studies. My model which is an extension of the current kidney allocation model is also presented in the next section.
10. HEURISTIC FOR KIDNEY ALLOCATION UNDER EMERGENCY, AND CASE STUDIES

The new kidney allocation policy which came into effect on December 04, 2014 differs significantly from the old policy which was centered totally on waiting time [83]. However, this new policy has no provision for the allocation of kidneys under emergency medical situations such as dialysis failure which has been observed by the National Kidney Foundation [23]. This means that candidates who have no living donors and cannot survive the long waiting time of 4 years (averagely) will end up dying on the waiting list.

From 2009 to 2011, approximately 15,000 candidates died on the waiting list while 4,728 candidates became too sick to undergo kidney transplantation [20]. Although the number of kidneys discarded in the respective years wouldn’t have been enough to grant the lifesaving gift to these candidates even if all the discarded kidneys were utilized, the transplant community recognizes that the kidney discard rate is “unacceptable” [23]. The National kidney Foundation (NKF) is of the opinion that older Americans may increase their participation in organ donation if they realize that their organs will save lives and will not be procured only to be discarded [23]. NKF also stresses in their comment on the current kidney allocation policy concept paper that there is the need to formulate policies that will explicitly define how kidneys will be allocated in medical emergency situations such as “dialysis failure” [23].
This section proposes a model which extends the kidney allocation model to help allocate cadaveric kidneys for emergency situations. The extended kidney allocation model uses the same parameters used by the OPTN and UNOS in allocating cadaveric kidneys in the United States. The model was simulated with 2010 data through 10 iterations and compared with two other models and the current kidney allocation model. The case studies below shows the current kidney allocation model (case study 1) and the two other models that were compared to the proposed model (case study 4). Case study 2 and 3 were modelled by Dimitris et al. [13] and they observed a 8% increase in LYFT when case study 2 was simulated using 6 months data from transplantations conducted in 2008 [13]. The penalty function discussed in chapter 9 was applied to case studies 1 and 2 and the results are shown in figure 30. It can be observed that application of penalty function to the current allocation model results in approximately 3.95% increase in life years added, and a 40% decrease in the number of kidneys discarded.
As explained by Israni et al. [24], statistical comparisons are not carried out since the simulations used the same donor and transplant data making it inappropriate for independent statistical comparisons [24].

**Case Study 1 [82]**

\[ KAS_{(p,o)} = 0.8LYFT_{(p,o)}(1 - DPI_{(o)}) + 0.8DT_{(p)} DPI_{(o)} + 0.2DT_{(p)} + 0.04CPRA_{(p)} \]

**Case Study 2 [13]**

\[ KAS_{(p,o)} = LYFT_{(p,o)} + gDT_{(p)} + 0.08CPRA_{(p)} + 0.5I(Age_{(p)} \geq 50) \]

Where \( g(DT) = \begin{cases} 0.65DT & 0 \leq DT \leq 5, \\ DT - 1.75 & 5 \leq DT \leq 10, \\ 0.2DT + 6.25 & 10 \leq DT. \end{cases} \)
Case Study 3 [13]

\[ KAS_{(p,o)} = \text{MaxLYFT}_{(p,o)} \]

Case Study 4

\[ KAS_{(p,o)} = 
\left[ 0.8LYFT \times (1 - DPI_{(o)}) + (0.8\text{DT}_{(p)} \times DPI_{(o)}) \times \delta_{(p)}^{\text{ESBT}} \right] \\
+ 0.2\text{DT}(\delta_{(p)}^{\text{ESBT}}) \\
+ 0.04\text{CPRA} \\
+ (1 - \delta_{(p)}^{\text{ESBT}}) \times e^{\frac{LYFT}{46e}} \]

Where \( \delta_{(p)}^{\text{ESBT}} = \begin{cases} 
0 & \text{ESBT} \leq 183 \\
1 & \text{Otherwise} 
\end{cases} \)

For more information about case studies 1 – 3 the reader is referred to Dimitris et al. (2013) [13] and OPTN (2013) [13, 82]. In case study 4 candidates who cannot survive for more than 6 months are prioritized. Also, candidates with higher LYFT and younger are prioritized. The latter prioritization conforms to the objectives of OPTN. The utilization factor (last term in case study 4) was modelled as an exponential function.

Lemma: Let \( \Pi(t) \) represent the condition of a candidate at time \( t \) after the initial enlistment on the waiting list. Also, assume that the condition of the candidate will experience infinitesimal continuous growth over a time horizon or a Markovian change in state. The growth function \( \Pi(t) \) can therefore be written as an exponential growth function:

\[ \Pi(t) = \Pi_0 \times e^{rt} \]  
(70)
Where $I_0$ is the initial condition of the candidate, $r$ is the growth rate expressed as a decimal (rate of propagation of the candidate’s condition), and $t$ is the length of time under consideration (time between enlistment and arrival of kidney). Let $LYFT$ be equivalent to the time horizon under consideration. Also, let the rate of propagation be equivalent to the inverse of the candidate’s age. The result follows that:

$$\Pi(t) = I_0 * e^{LYFT/Age} \quad (71)$$

Where

$$\Pi_{(0)} = (1 - \delta^{ESBT}) \quad (72)$$

This means that when $\delta^{ESBT} = 0$, $\Pi_{(0)} = 1$. This condition is when a candidate is not expected to survive the average waiting period for a kidney offer which means that there is the need to prioritize him or her for emergency allocation. In microeconomics this condition may be explained as the critical stage when maximum resources (100%) are needed for investment in order to minimize opportunity cost. I conjecture that in the microeconomic world, a lot of attention is paid to the portfolio that takes or has the potential to take the largest investment of available resources. However, when $\delta^{ESBT} = 1$, $\Pi_{(0)} = 0$. This is the condition when the candidate can survive the expected waiting time and needs no prioritization for emergency points. This also means that the prospects for initial investment ($\Pi_{(0)}$) is null, hence, there is no need to spend precious time on that portfolio.
In case study 4, when $\Pi_{(0)} = 0$, the allocation model becomes the same as the current kidney allocation policy. However, that doesn’t have considerations for candidates who cannot survive the expected waiting time which is among the concerns expressed by National Kidney Foundation [23]. When a candidate cannot survive the expected waiting time, the model allocates kidneys according to sensitivity level, level of emergency, LYFT and age. Dialysis time and donor profile index are overruled under this condition. However, donor profile index is not eliminated since it is related to LYFT. Numerical example is shown below.

Let the 6 attributes and 4 instances data in table 30 represent the attributes of four active candidates on the waiting list who are medically compatible to receive a procured kidney $o$. This means that each of the candidates and the available organ can form a compatible patient–organ pair $x_{(p,o)}$. It can be seen in the table that all the candidates are expected to have the strength to undergo the expected waiting time as seen in the last column of table 30.
Table 30: Data for calculating KAS

<table>
<thead>
<tr>
<th>Candidates</th>
<th>$\text{LYFT}_{(p)}$</th>
<th>$\text{Age}_{(p)}$(years)</th>
<th>$\text{DT}_{(p)}$(months)</th>
<th>$\text{CPRA}_{(p)}$(%)</th>
<th>$\text{DPI}_{(o)}$</th>
<th>$\delta_{ESBT}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>5</td>
<td>52</td>
<td>24</td>
<td>80</td>
<td>0.82</td>
<td>1</td>
</tr>
<tr>
<td>B</td>
<td>8</td>
<td>38</td>
<td>12</td>
<td>70</td>
<td>0.82</td>
<td>1</td>
</tr>
<tr>
<td>C</td>
<td>10</td>
<td>37</td>
<td>4</td>
<td>75</td>
<td>0.82</td>
<td>1</td>
</tr>
<tr>
<td>D</td>
<td>4</td>
<td>53</td>
<td>5</td>
<td>60</td>
<td>0.82</td>
<td>1</td>
</tr>
</tbody>
</table>

Using case study 4, the KAS for the first candidate ($KAS_{(A,o)}$) can be calculated as shown below.

\[
KAS_{(A,o)} = (0.8 \times 5 \times (1 - 0.82) + (0.8 \times (24/12) \times 0.82)) \times 1 + (0.2 \times 24/12 \times 1) + (0.04 \times 80) + (1 - 1) \times e^{(5/52)} = 5.632.
\]

Similarly, the KAS for the other three candidates can be obtained as 4.808, 4.7253, and 3.3327 respectively for candidates B, C, and D. This means that candidate A will be at the top of the ranking. Candidate A was prioritized because of the long waiting time. The candidate (A) has stayed the longest (2 years) on the waiting list - and is therefore prioritized - followed by candidate B and then C. This example is analogous to the current kidney allocation ranking system. Assume that all the candidates have conditions that permit the application of the emergency factor; thus they are all expected to die before the arrival of the next kidney or become too sick for transplantation. For this situation the new $KAS_{(p,o)}$ for the candidates may be calculated using case study 4 as: 4.3009, 4.0343, 4.3103, and 3.4784 respectively. This means that candidate C who was ranked third previously
will now be ranked first and will receive the available kidney. The improvement in candidate C’s KAS can be attributed to the fact that he is younger and is expected to live longer (10 years) compared to the other candidates.

Candidate C’s sensitivity level is also higher than that of B and C hence the higher priority points. In both cases candidate D will be ranked last which is because the candidate has the lowest; 

\[ \text{LYFT}, \] highest age, and one of the lowest waiting time. The candidate also has the lowest sensitivity level which means that a smaller point will be earned for sensitivity. Table 31 summarizes the rankings for the two scenarios described above. The next section describes the organ acceptance probability calculation which was used in the KPSAM simulation.

<table>
<thead>
<tr>
<th>Candidate</th>
<th>( \delta_{EPB} = 0 )</th>
<th>( \delta_{EPB} = 1 )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>KAS</strong></td>
<td>Rank</td>
</tr>
<tr>
<td>A</td>
<td>4.3009</td>
<td>2\text{nd}</td>
</tr>
<tr>
<td>B</td>
<td>4.0343</td>
<td>3\text{rd}</td>
</tr>
<tr>
<td>C</td>
<td>4.3103</td>
<td>1\text{st}</td>
</tr>
<tr>
<td>D</td>
<td>3.4787</td>
<td>4\text{th}</td>
</tr>
</tbody>
</table>

10.1 Organ Acceptance Calculation

Organ acceptance in the simulation model was determined through the transformation of a calculated score into a number between 0 and 1 using the logit
transformation function. The factors used in the logit transformation function are:

“age, cause of death (COD), race, history of hypertension, history of diabetes, serum creatinine level, hepatitis C status (HVC), donation after cardiac arrest status, weight, height,” [20] and cold ischemic time (CIS). The raw value (before transformation) for the organ acceptance was calculated as follows [20]:

\[
\Phi = (0.148 \text{ if } 40 \leq \text{age} < 50) + (0.291 \text{ if } 50 \leq \text{age} < 60) + (0.502 \text{ if } 60 \leq \text{age} < 70)
\]

\[+ (0.319 \text{ if } \text{age} \geq 70) + (0.194 \text{ if } \text{COD} = \text{CVA}) + (0.127 \text{ if } \text{COD} = \text{other})
\]

\[+ (-0.210 \text{ if } \text{race} = \text{Black or African American}) + (0.304 \text{ if } \text{race} = \text{other})
\]

\[+ (-0.134 \text{ if } \text{history of hypertension} = \text{Yes}) + (0.314 \text{ if } \text{HVC status} = \text{positive})
\]

\[+ (0.208 \text{ if } \text{history of diabetes} = \text{Yes}) + (-0.013 \text{ if Serum creatinine} > 1.5 \text{mg/dL})
\]

\[+ (0.149 \text{ if } \text{DCD status} = \text{Yes}) + (0.014((170 - \text{height})/10)) + (0.035((\text{weight} - 80)/5))
\]

\[+ (0.0108 \times \text{Cold time}) + (0.135 \text{ if } \text{regional share}) + (0.256 \text{ if } \text{national share})
\]

Where \( \Phi \) represents the output from the equation; COD stands for cause of death, and CVA stands for cerebrovascular accident. The height of the organ donor in the above equation is measured in centimeters. The result of the above equation will be transformed using the logit transformation and the outcome will be compared to a random number drawn between 0 and 1. If the logit transformed number is greater than or equal to the random number, then the organ is accepted. It is rejected when the number is less than the random number.
To show the logit transformation, consider $\Phi$ as a dependent variable that needs to be predicted from $n$ independent variables such as: age, cold time, height, weight, serum creatinine, history of hypertension, history of diabetes, DCD status, race, CVA status, and HVC. If the dependent and independent variables are linearly related with coefficients ($\beta_i$) in the form:

$$\Phi = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \ldots + \beta_n x_n$$

(73)

Then the logistic function of $\Phi$ between 0 and 1 is given by the inverse logit of the function as shown below:

$$\log \frac{\Phi}{1 - \Phi} = \log \frac{1}{1 + e^{-(\beta_0 + \beta_1 k_1 + \beta_2 k_2 + \beta_3 k_3 + \ldots + \beta_n k_n)}}$$

(74)

$$= \log \frac{1}{1 + e^{-(\beta_0 + \sum_{i=1}^{n} \beta_i k_i \gamma_i)}}$$

(75)

Numerical example

In the above example, the kidney* with attributes in the table below will be offered to candidate C (in table 31) if there is an emergency factor. If the organ is offered to candidate C, the probability that the organ will be accepted by the candidate is calculated below using the data in table 32.
Table 32: Sample data for acceptance probability calculation [24]

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 ≤ Age* &lt; 50</td>
<td>0.148</td>
</tr>
<tr>
<td>50 ≤ Age &lt; 60</td>
<td>0.291</td>
</tr>
<tr>
<td>60 ≤ Age &lt; 70</td>
<td>0.502</td>
</tr>
<tr>
<td>Age ≥ 50</td>
<td>0.319</td>
</tr>
<tr>
<td>Race* = Black or African American</td>
<td>-0.210</td>
</tr>
<tr>
<td>COD = CVA</td>
<td>0.194</td>
</tr>
<tr>
<td>History of Hypertension</td>
<td>No</td>
</tr>
<tr>
<td>HVC Status</td>
<td>No</td>
</tr>
<tr>
<td>History of Diabetes</td>
<td>No</td>
</tr>
<tr>
<td>Serum Creatinine (&gt;1.5mg/dL)</td>
<td>-0.013</td>
</tr>
<tr>
<td>DCD Status</td>
<td>0.149=Yes</td>
</tr>
<tr>
<td>Height</td>
<td>67cm</td>
</tr>
<tr>
<td>Weight</td>
<td>(0.035) for 150lb</td>
</tr>
<tr>
<td>Cold Time</td>
<td>4 hours</td>
</tr>
<tr>
<td>Regional Share</td>
<td>0.135</td>
</tr>
<tr>
<td>National Share*</td>
<td>0.256</td>
</tr>
</tbody>
</table>

\[ \Phi = 0.148 - 0.210 + 0.194 + 0 + 0 - 0.013 + 0.149 + (0.014(170-67)/10) + (0.035((150-80)/5)) + (0.0108*4) + 0.256 = 1.2014 \]
The logit of $\Phi$ is calculated as: 
$$
\frac{1}{1 + e^{-1.2014}} \approx 0.77
$$

To determine whether the organ will be accepted by the candidate ($C$) or not a random number between 0 and 1 will be drawn and compared to the logit of $\Phi$. If the random number is greater than or equal to the logit of $\Phi$, then the organ will be accepted by the candidate. It will be rejected if the logit of $\Phi$ is less than the random number. Assuming a random number equal to 0.52 is drawn, then, the organ is accepted by the candidate. The output from the heuristic for allocating kidneys under emergency situations and the current model are presented in table 33, figure 30, figure 31, figure 32, and figure 33. From figure 34 it can be observed that allocating kidneys with preemption for emergency candidates may decrease the waiting list death rate by 2% with minimal effect on kidney discard rate. Also, older candidates (candidates who are 50 years or older) may experience a decrease in kidney offer as seen in table 33 and figure 31 due to the age matching policy which aims to improve kidney utilization. However, the expectations from the age matching of kidneys with candidates if realized, may increase the kidneys available for allocation and could offset the decrease in organ offer to this group of candidates. Figure 32 and figure 33 respectively show the distribution of kidneys for race/ethnicity and ABO blood group.
Table 33: Simulated model summary and actual transplant recipients in 2010

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ABO Blood Group</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>3551</td>
<td>3214</td>
<td>3230</td>
</tr>
<tr>
<td>AB</td>
<td>556</td>
<td>631</td>
<td>637</td>
</tr>
<tr>
<td>B</td>
<td>1357</td>
<td>1918</td>
<td>1921</td>
</tr>
<tr>
<td>O</td>
<td>4686</td>
<td>5101</td>
<td>5122</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18</td>
<td>455</td>
<td>451</td>
<td>471</td>
</tr>
<tr>
<td>18-34</td>
<td>975</td>
<td>1661</td>
<td>1665</td>
</tr>
<tr>
<td>35-49</td>
<td>2565</td>
<td>3012</td>
<td>3025</td>
</tr>
<tr>
<td>50-64</td>
<td>4185</td>
<td>4029</td>
<td>4033</td>
</tr>
<tr>
<td>&gt;=65</td>
<td>1970</td>
<td>1711</td>
<td>1716</td>
</tr>
<tr>
<td><strong>Race/Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black/African American</td>
<td>3472</td>
<td>3818</td>
<td>3830</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1493</td>
<td>1651</td>
<td>1666</td>
</tr>
<tr>
<td>White</td>
<td>4378</td>
<td>4653</td>
<td>4662</td>
</tr>
<tr>
<td>Other/Unknown</td>
<td>807</td>
<td>742</td>
<td>752</td>
</tr>
</tbody>
</table>
Figure 31: Distribution of transplants by age

Figure 32: Distribution of transplants by race
The next section summarizes the main findings from this research.
11.0 SUMMARY

The findings from the research and recommendations for future work to extend the project have been summarized in this section.

11.1 Summary of Findings in this Research

In this paper the kidney allocation policy in the United States has been analyzed. Extensive literature review has been conducted to evaluate the contributions of researchers who have approached the problem from various perspectives. The KPSAM developed by SRTR [84] was used to simulate different case studies. Attempt was also made to formulate a model for allocation of kidneys under emergency situations which is a major concern expressed by NKF [23] about the current kidney allocation policy. The major findings from this research are summarized below:

1. A model for the allocation of cadaveric kidneys under emergency situations such as dialysis failure [23] has been proposed. The current kidney allocation model does not consider the fact that not all candidates can wait for the 3 to 5 years for kidney offer.

2. Chapter 6 discusses some location allocation models and how they can be applied to locating kidney procurement, dialysis and transplantation centers. Example problem was solved.

3. Chapter 7 describes a Genetic Algorithm (GA) application to solving the kidney allocation problem. A problem with a single market (patient) and multiple
sources (OPOs) was solved. It was observed that distances play a critical role in kidney allocation since it has a direct effect on cold time.

4. Mahalanobis distance (MD) application to kidney allocation was discussed in chapter 8. Historical data from successful transplantations was used to demonstrate how the MD approach can be used for kidney allocation. This approach will ensure that kidneys are paired with candidates in an effective way to minimize re-transplantations and the situations where candidates die with functioning kidney. It is analogous to the age matching policy adopted by the current kidney allocation policy, but MD approach matches not only age, which is a single factor, but also can match multiple patients’ organ attributes.

5. Chapter 9 discusses kidney allocation with penalty function for the rejection of kidney offers. Simulation results indicate that the penalty function may help reduce the discard rate of cadaveric kidneys by 40%.

6. Chapter 10 describes the model for kidney allocation under emergency. Attempt has been made to incorporate the estimated years a patient can survive on the waiting list for cadaveric kidney offer. This may help to minimize the number of people who die on the waiting list or become too sick to receive transplantation. Simulated results of the model compared to simulated results of the current kidney allocation policy indicate that the model may help to decrease death on waiting list by 2.19%

7. The number of cadaveric kidneys may be increases if a law could be enacted to prevent family members and relatives from revoking the permission to procure
the organs of a registered organ donor upon their death. Approximately 54% of people contacted for their consent to procure the organs of registered donors at risk of brain death decline to the procurement [58]. Furthermore, a law could be passed to automatically enroll people as organ donors as done in some European countries such as Spain [85]. This “opt-out” [58] approach to organ donation may also help to provide some relief to the organ scarcity problem.

11.2 Limitations of the Research

The research used simulated data to draw conclusion and this may not be the actual reflections in reality. Moreover, some of the instances in the data with omissions were deleted; hence, the data used may not be a perfect reflection of transplantations in 2010. Furthermore, the simulated cold time may not be available at the time of kidney allocation although it has an effect on the acceptance/rejection of kidney offers. Finally, the penalty function discussed in chapter 9 may not be ethically or morally acceptable; hence in all cases medical judgment should be the ultimate decision maker in the allocation of kidneys and the acceptance or rejection of a kidney offer.

11.3 Future Work

The proposed model for the allocation of kidney under emergency situations presented in chapter 10 may be explored further in relation to liver and heart allocations to see how it affects organs that require more immediate transplantation than kidneys. For this situation the function for the estimated survival before transplantation (ESBT) could be broken down further as a step function into months
or even days for different ESBT instead of the binary case discussed in chapter 10. This may be necessary since heart and liver transplants are more of emergency situations and require preemption than the need for kidney transplantation [20].

11.4 Disclaimer

“The data reported here have been supplied by the Minneapolis Medical Research Foundation (MMRF) as the contractor for the Scientific Registry of Transplant Recipients (SRTR). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should it be seen as an official policy of or interpretation by the SRTR or the U.S. Government.” [13]
REFERENCES


(accessed, 04/24/2011)


82. Organ Procurement and Transplantation Network, *Policies*.


