THE DONOR CRISIS: MODELING THE UNITED STATES ORGAN DONOR NETWORK

TEAM 1914

1. Summary

As the wait list of candidates for organ transplants in the United States continues to grow, policy makers, health care officials, individuals waiting for organs, and the general public alike become increasingly concerned about the efficiency and effectiveness of the organ transplant network in our country. Our team investigates the state of the organ transplantation system in the United States by utilizing an agent-based model to represent a wait list of candidates and a pool of organ donors. Our goal was to simulate the current system to enable the identification of weak spots. We developed a numerical simulation in MATLAB and then analyzed the wait list composition over time. We determined that the most daunting hurdle presented by the current system is simply the drastic shortage of donors. We consider how an individual might be influenced to donate and suggest some ways in which this dearth could be remedied.

Every agent in our model was described using the parameters of blood type, region, PRA value, HLA set, age, and amount of time spent on the waiting list. Our model simplified the problem at hand by ignoring such aspects as payback, local level priority, and racial and gender demographics. The principle assumptions we made included a very regular addition of candidates to the wait list and donors to the pool each day, a constant probability of death for all patients awaiting transplant, an ability to model multiple people with singular super-agents in the model, an equal probability of any HLA antigen appearing in the general population, and a nation-wide distribution of PRA values similar to the current waiting list distribution.

Our model design was an agent-based numerical simulation in MATLAB. We felt that this would best allow us to deal with individual donor-recipient matches that arise every day, as there are a relatively small number of people who can be described identically due to the range of parameters needed to adequately capture an individual. Our scheme began with the creation of a wait list of candidates possessing certain parameter values distributed according to current demographics of the organ wait list. Each time step of the model, additional candidates were added to the wait list and a set amount of donors were created. The candidates were first sorted according to the time they had been on the wait list, then by blood type. Considering candidates who had waited the longest first, keeping within a certain blood type, and prioritizing for high PRA values (except in the case of children, who were given priority regardless of PRA), we paired candidates with donors according to region, then HLA sets. If necessary to find a match, we would look at another region for a candidate to match a given donor. Finally, greater numbers of HLA mismatches would be accepted as a match if a national search

did not yield a pair. This method is in keeping with current national policy. After a match was made, both the donor and the candidate were removed from their respective matrix. To simulate death of wait list candidates, each time step we removed a number from the wait list, with a bias towards removing those who had been on the wait list the longest.

We subjected our model's super-agent property to multiple tests at various scaling factors to determine the resolution at which we could model multiple people with one super-agent. We examined time-based behavior of all characteristics of patients on the waiting list, such as PRA value, age, region, and blood type, and attempted to qualitatively analyze these predicted trends against our original data and knowledge of the problem space.

The super-agent model's strength's include scalability and in-depth investigation of multiple parameters. Weaknesses include heavy computational requirements and a limited ability to add functionality or consider additional variables with the existing model.

A large limitation with our particular implementation stems from the fact that we did not attempt to consider or evaluate patients after a transplant. As a result, we were unable to evaluate the survival or death of the patient after the operation, and thus could not evaluate the success or failure of our matching strategy against other matching strategies in terms of lives saved.

2. Problem Statement

As of February 2, 2007, 101,634 people in the United States were waiting for organ transplants.[3] Advanced-stage diseases such as Type I diabetes and cystic fibrosis can cause near-complete organ failure, necessitating a transplant to preserve a patient's life. While life-sustaining treatments have made tremendous strides in the past 20 years, the number of people waiting for organ transplants has doubled over the past decade.[4] The continued growth of national organ wait lists provides an area of concern for the medical community, policy-makers, and the general public.

In order to increase the efficiency of the system and improve the overall survival of patients on organ waiting lists, the U.S. federal government established OPTN, the Organ Procurement and Transplantation Network, to facilitate transplants on a national level. The United Network for Organ Sharing, a non-profit organization supported by the Department of Health and Human Services, maintains OPTN. The users of OPTN generally must follow its national policies, which establish a hierarchy of organ distribution guidelines that give priority to patients who are under 18 years-of-age or less likely to find a compatible match otherwise (such as those with high PRA values). These policies provide the most obvious starting point for a thorough understanding of national trends, as well as a framework from which to improve the system and suggest changes that would facilitate better donor-patient matching and ultimately save more lives.

A number of factors make it difficult to find enough organs for all those in need of transplants. By far the largest limiting factor is the number of donors who have legally consented to donate their organs upon death. In order to increase the number of consenting donors, some countries have implemented a policy of "presumed consent" in which a person is assumed to consent to donation upon death unless they make it otherwise known while living.

Medical factors also play a large role in determining the likelihood of a patient receiving an organ. For the most part, a patient's blood type must be compatible with a donated organ, so that the organ and body will interact well. In many cases, such as kidney or lung transplants, doctors must also ensure that the patient's immune system does not adversely react to the donor's organ. For patients with a high immuno-sensitivity, the wait for a compatible organ can be substantially exacerbated as they wait for donors who carry an exactly matching set of immune-system identification molecules. A convenient and popular test for determining the sensitivity of a patient's immune system is the panel reactive antibody test (PRA). A patient's PRA is expressed as a percentage, and indicates the portion of the U.S. population with which it would adversely react. Thus, a patient with a PRA of 0% represents an ideal case while one with a PRA of over 80% will have severe difficulty in finding a matching donor. In cases of patients with high PRA value, a donor's blood should ideally contain almost perfectly similar immune-system identification molecules, called human leukocyte antigens (HLAs), which signal to the patient's immune system that the organ belongs in the body. Lower PRA patients can afford some mismatches in HLA, since their immune systems are less likely to directly attack a new organ perceived as foreign. Because it can be so difficult to find a match for patients with high PRAs, these patients are currently given priority on the U.S. wait list for organs.

The geographical location of the patient can also influence the likelihood of a successful donation. Patients from rural areas far from a transplant center face both monetary and scheduling difficulties in reaching facilities to initiate the procedure. Donor pool size and donation policies can vary between medical centers, states, and regions, often throwing additional roadblocks at a patient's search for a donor.

Perceived barriers, such as the perception that one is too old or too sick to donate can impact donations as well. Religious beliefs may also play a role in discouraging eligible donors from consenting to donation, though many religious leaders, notably the late Pope John Paul II, have advocated organ donation.[7]

Our first step in accomplishing the tasks at hand was to create a model of the current U.S. organ transplant system for matching candidates with donors. Because this system is driven by the interactions of its members who are motivated by different properties, we decided that an agent-based simulation would yield an accurate model. We opted to develop a numerical simulation in MATLAB in which we could generate donor and patient populations based upon current transplant data and match donors to recipients based on established policies.

3. Assumptions

3.1. **Local Donations.** The first step in the process of finding a donor match for a patient is usually seeking local donors. Another option is enlisting the help of a nearby organ procurement organization (OPO). However, in modeling the matching of donors and recipients, it was difficult to ascertain accurate data by locality. In order to use more accurate data and capture national trends while simplifying the model, locality matching was ignored. Donors were matched only at the regional and national levels. This simplification may have affected results by increasing the number of pairings that involved candidates with high PRA factors regionally and nationally rather than patients with lower PRA factors waiting locally.

3.2. **"Payback".** Organ procurement organizations, or OPOs, collectively utilize a "payback" system to ensure that OPOs giving organs to other OPOs will eventually receive some organs in return for their donation. This "payback" system can provide incentive for locally unused organs to be used at a national level, since it is illegal in the United States to sell human organs. Because we have ignored any sub-regional donation activity, we have chosen to ignore these "payback" organs in the model. However, as a whole the bias of organs towards transplant candidates in an indebted OPO or region does not generally affect the probability of an organ being used, as it will go to another OPO if indebted OPOs cannot use the organ.

3.3. **"Deaths on Wait List".** Due to a lack of data regarding the exact rate at which candidates die while waiting for transplants on the wait list, the probability of death was approximated based upon available data. The probability of death for each agent of the model was correlated proportionally with time spent on wait list through a linear function. The function was calibrated such that there was a near certain chance of dying after 15 years on the wait list.

3.4. **PRA Value Modeling.** Panel reactive antibody values, or PRAs, help doctors determine the likelihood that a patient's immune system will react adversely to cells transplanted from outside the body. A patient's PRA is expressed as a percentage, and indicates the portion of the U.S. population with which it would adversely react. Thus, a patient with a PRA of 0% represents an ideal case, while one with a PRA of over 80% will have severe difficulty in finding a matching donor. In order to model the assignment of a PRA value to each newly generated patient, we examined a breakdown of the current U.S. waiting list population by high ($>$ 80%), medium (10-80%), and low ($<$ 10%) PRA values,[8] and generated new PRA values within each distribution according to probabilities given in the waiting list data. This method will most likely result in a higher than realistic percentage of PRA in our model, since patients with high PRA have a better chance of waiting longer for a donor match, and will thus be more represented on the waiting list. However, we reason that OPTN's policy of giving priority to high PRA value patients will substantially reduce this abnormality and bring it within reasonable tolerances, allowing our model of PRA values to better reflect current trends. At the very least, our model provides a "worst case" realistic scenario for modeling PRA values. Given this breakdown of PRA values of high, medium, and low, we then determined how many HLA matches a patient and donor must collectively have before a transplant can be allowed. We determined that high PRA value ($>$80%) patients require perfect HLA matches with a donor, while medium PRA value (10-80%) patients can accept a donor with at least 4 of their 6 HLA values in common and low PRA value ($<$10%) patients can use any donor, regardless of HLA matching.

3.5. **HLA Value Modeling.** Human leukocyte antigens, or HLAs, are inherited molecules that help the immune system distinguish between cells native to the body and those foreign. In patients with high PRA, meaning high immune system sensitivity, finding donors with matching HLA values is vital to ensuring a successful, unrejected transplant. A person has two sets of HLA values, one set inherited from the mother and one from the father. Each set contains three values, which occur at different points along the chromosome. Medical professionals call these points locus "A", locus "B" and locus "DR", respectively.[1] Based on data given by OPTN,

there are approximately 30 possible antigen values at the "A" locus, 65 possible "B" locus antigen values, and 21 possible "DR" locus antigen values.[2] When matching a patient and a donor using HLA, each of these loci represents a distinct case that cannot be equivalent to another case. For example, a donor with antigen 1 at locus "A" does not match with a patient who carries antigen 1 at locus "DR". Within each locus, however, some antigens can be substituted for one another. For example, at locus "A" a patient with antigen 10 can match with a donor who locus "A" carries antigen 10, antigen 26, or antigen 34 (antigens are not numbered consecutively). In order to model this multiple matching possibility within each locus, we assumed that all multiple matching scenarios were commutative. That is, if antigen 26 can substitute for antigen 10 at a given locus, then the reverse is also true, and antigen 10 can substitute for 26. This assumption is not always true according to the data,[2] but commutivity occurs well over half the time in our analysis. We therefore made the decision to model all substitutions as commutative, and thus were able to simplify the data by combining commutative antigens into one singular, more popular antigen. Using this strategy, we were able to reduce the number of possible antigens at each locus to 19 at "A", 40 at "B", and 10 at "DR". For lack of better data, we assume that, before commutativity is accounted for, all antigens are equally likely to occur in a given human, having no correlation with age, PRA, or any other properties of that person. From this assumption, it follows that, when we combine two commutative antigens into a single one, that singular antigen is twice as likely to occur than an antigen that has no equivalents for matching. Using this HLA model, we were able to randomly generate for each person in the model a 6 value HLA array containing two "A" values, two "B" values, and two "DR" values, representing the two sets of values every person inherits. The same is true for each donor in the model. When PRA circumstances necessitated a comparison with HLA, we were able to effectively model the attempt to match a donor with a patient by comparing "A", "B", and "DR" values independently and allowing transplants to occur when the total number of HLA mismatches was low enough (see PRA Values for details).

3.6. **Removal from Waiting List.** For numerous reasons, including death and disease progression, candidates placed upon the wait list for an organ may no longer be able to receive a transplant. In order to simplify the wide variety of factors and rates at which this can occur, all reasons for being removed from the wait list, such as an improving condition or a diagnosis that renders a patient medically unsuitable for donation, were lumped together and refer ed to as "death" in our model. In order to quantify this removal from the wait list an approximation of the probability of being removed from the wait list was created. It was determined that the probability of being removed from the wait list should correlate proportionally with the amount of time spent on the wait list such that:

$$P_{death}(t_{waiting}) = \frac{1}{y} t_{waiting}$$

This equation makes it such that the probability of death in a step, with respect to length of time on the wait list, increases linearly from no chance of death on the first day on the wait list to a 100% chance of dying on the last day of one's fifteenth year on the wait list. However, analysis reveals that while this approximation makes the probability of removal from the wait list proportional to time spent on the wait

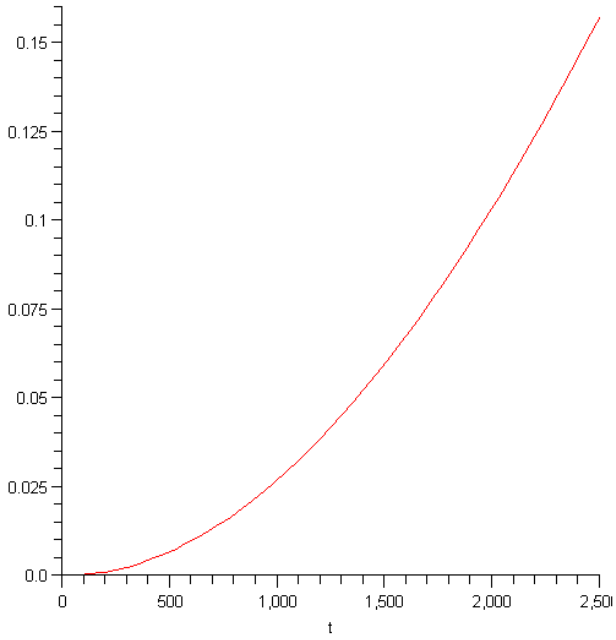

FIGURE 1. The cumulative probability of a recipient dying on the wait list after t days waiting, after correction.

list with respect to each step, there is actually a cumulative probability of having died prior to the step in question which effectively decreases the probability of surviving a given number of years on the wait list. Thus the function above gives a cumulative probability of death that approaches 100% logarithmically, arriving very close to 100% within a few hundred days.

Thus if it is desired that a candidate on the wait list have a 15% chance of living for seven years on the wait list it is necessary to adjust the function for probability of death in any step such that the cumulative probability of death based upon that function gives a 15% chance of death at seven years. Using symbolic algebra tools it was unfortunately not possible to solve exactly for the parameter that would give a perfect 15% cumulative chance of death after seven years on the wait list so a numerical "guess-and-check" algorithm was used to find a parameter value that was considered to be close enough for simulation purposes. As the median life expectancy while waiting for an organ was chosen somewhat arbitrarily, the parameter valued needed not be extremely accurate. Figure 1 shows the resulting function with a parameter of $50,000$.

3.7. **Blood Type Matching.** ABO blood type matching allows patients with A, B, and AB blood types to potentially receive organs from donors with other blood types. However, in the model it was computationally advantageous to first pair down the list of potential recipients for a donated organ to those candidates that had the same ABO blood type as the donor. While this is not perfectly accurate,

it is not unreasonable; OPTN Guidelines[1] strongly bias O and B donor kidneys towards recipients of the same blood type[2][3], thus leaving only the reasonable possibility that an A type organ will be given to an AB type recipient. For the purposes of this model, the possibility of A to AB donations of organs was ignored for the sake of simplicity, as was to possibility of zero-antigen mismatch organs leaving the O and B blood types. The results of the model should be minimally affected by this deficiency barring saturation of donors in which matches cannot be found in the donor blood type but might be found outside the donor blood type.

Additionally, blood types for persons added to the waiting list and persons donating organs were assumed to have a distribution of ABO blood types that mirrored that of the general United States population. An exception was made for the initial generation of waiting list that exists prior to the model beginning to execute, as the distribution of blood types in the existing transplant waiting list varied somewhat from the general population. The distributions of blood types for the waiting list used in initializing the model were taken from the actual United States organ transplant waiting list maintained on behalf of OPTN as of the end of year 2006.

3.8. **Further Assumptions.** The following assumptions and simplifications were also made when we created our model of the U.S. organ transplant system:

- There was no pre-existing donor population at the start of our simulation. Donors were added dynamically as the simulation progressed.
- We assumed a daily addition of 37 new donors each day. This value was taken from the yearly increase in the year 2006, divided by 365. In reality, this number would presumably not stay constant, but increase over time as the population increases.
- Demographics for the candidates on the wait list were assigned to mirror the actual demographics of the candidates on the U.S. wait list in the year 2006. We have no reason to suspect demographics would change significantly over the next 30 years, which is the upper bound of the time frame our model analyzes.
- Some demographics, such as race and sex, were not accounted for, as the need for organs was considered to be statistically independent of these demographics factors.
- We added a gradually increasing number of candidates to the wait list each day, starting at 122 (which matches 2006 statistics).
- We did not consider candidates removed from the wait list for reasons other than death (e.g., candidates who became too sick to perform the operation, or candidates whose condition improved). This may inflate our wait list slightly.
- In taking patient age into account, the candidates and donors were simply classified as children or adults, rather than being broken down into more specific age groups. Each of the 11 regions of the U.S. were assumed to have similar distribution of adult and children donors and candidates.

[1]Specifically sections 3.5.2, 3.5.3.3.1, and 3.5.3.3.2

[2]More precisely, the guidelines only allow O and B type donor kidneys to go to non-O and B type recipients in the case of a zero-antigen mismatch

Agent Parameter	Acceptable Values	Description
region	integer [1, 11]	The UNOS region in which the agent is located.
age	integer [1, 2]	The age group of the agent, 1 for and adult, 2 for a child.
blood type	integer [1, 4]	The ABO blood type of the agent, 1 for A, 2 for B, 3 for AB, or 4 for C.
PRA	float (0, 1)	The panel reactive antibody result of the agent, donor values are generated, but ignored.
HLA	6x1 integer array	The 6-part HLA code for the donor or recipient.
stepentered	integer (-infinity, infinity)	The time-step in which the agent entered the model, for recipients this is also the time-step on which they entered the wait list.
used	boolean	True if the donor's organ has been used or the recipient has received a transplant, false otherwise.
dead	boolean	True if the agent has died, false otherwise.

TABLE 1. The parameters associated with each agent in the model. The values for each of the parameters are generated based upon statistics for the population the agents will be represented.

- PRAs were assigned to candidates on the waiting list in three categories according to researched probabilities of each. The categories were PRA greater than 80%, PRA between 10% and 80%, and PRA less than 10%.
- We did not distinguish between different organs at this point. This was effectively like assuming that the demand for each organ was proportional to the supply of that organ in every region for each point in time, with an identical proportionality constant for each organ.

4. Model Design

4.1. **Overview of Model.** The model developed to simulate various types of transplant matching is based upon the construction and matching of large arrays of candidate and donor agents. These agents each carry certain properties, including a region of origin, a blood type, HLA markers, and others. (Table 1 contains a complete list of the parameters for each agent.) The model creates statistically representative arrays of recipients to add to the wait list while creating statistically representative arrays of donors to match with the wait list or recipients. In this way the model hold a representative agent for every person who needs to receive an organ transplant as well as for every donor for organ transplant. These individuals are individually matched using matching algorithms to perform transplants.

4.2. **Generating the Initial Wait List.** We began our simulation already having a wait list of candidates, containing whatever number of people we wanted to choose (ultimately, we matched this to the number of people on the wait list currently). Each person on the wait list was assigned a region from 1 to 11, based on actual data of how candidates on the wait list were geographically distributed in the year 2006. According to their region, each person was then given the amount of time he

or she had been waiting on the list by the starting time of our model. In reality, the waiting times vary from region to region, and this was taken into account. No one had been on the waiting list for more than 7.5 years at the start of our simulation. Blood types were assigned to each candidate based on data for the distribution of blood types on the current U.S. waiting list. Similarly, each candidate was given an HLA set and a PRA value. Each person was also designated as either a child or an adult, based on actual percentages on the current U.S. waiting list.

4.3. **Creating Donors and Candidates for the Wait List.** The time step of our model was one day, and each day we created 37 new donors, in keeping with probabilistic demographics. The number of candidates added each day increased over time, starting with a value of 122. The same qualities discussed above (age, blood type, region, HLA, and PRA) were given to each person created, both recipients and donors. A "death" function was put into place, which randomly removed people from the wait list with a bias towards those who had been on the wait list the longest.

4.4. **Matching Donors to Candidates.** Each time step the candidates on the wait list were sorted according to the time spent on the waiting list, so that those who had been waiting the longest would be on the top. Donors and candidates were sorted by blood type, and those with identical blood types were set aside as possible matches. People with matching blood types were then classified according to HLA values. From here on in, our sorting process more or less mirrored that currently used in the U.S. (with the assumptions listed above). Donor-candidate pairs with the most nearly matching HLA values in the same region in which the candidate had a PRA of greater than 80% were searched for first, and if such a pair was found, each was eliminated from the list. Next, donor-candidate pairs with nearly matching HLA values in which the candidate has a high PRA in different regions were searched for and eliminated if found. Then donor matches for the children on the wait list with nearly matching HLA values were attempted, regardless of the child's PRA. This was done first regionally, then nationally.

5. Model Verification

5.1. **Verification of Super-Agents.** In order to reduce computational overhead, it was deemed appropriate to allow each agent in the model to represent multiple recipients or donors. With such a methodology the number of agents in the model could be reduced by a scaling factor, significantly decreasing the computational cost of the model in terms of both processing and memory requirements, allowing our team to conduct more extensive testing and more thorough analysis of our model's performance.

In order to validate the simplification of computations using "meta-agents" it was necessary to quantify the amount of error introduced by the addition of these agents. To this end, short test simulations where executed with varying amounts of simplification. An overlay of some of these results can be seen in Figure 2 on the following page, showing the progressive use of one agent for every 25, 50, and 100 people. The output quantity compared is the total number of people on the wait list, though other simulation values compare similarly.

The comparison in Figure 2 shows that the wait list has the same to-scale behavior for reasonable numbers of people per agent. Though the noise of the values

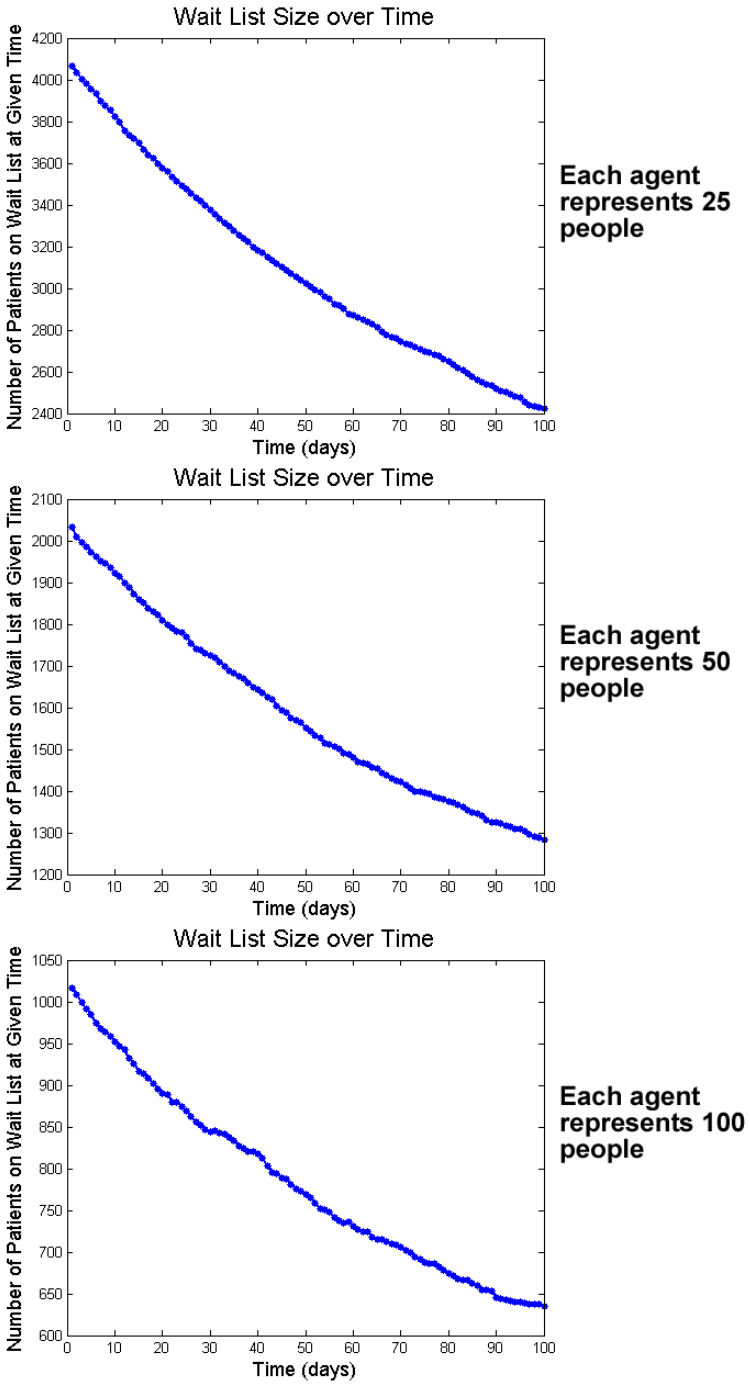

FIGURE 2. Comparison of the effect of various people per agent representations.

increases somewhat for 100 people per agent it is still a reasonably similar approximation of 25 people per agent. Due to computational limitations (specifically memory limits) the simulation was not run at a resolution of 12 or 1 people per agent, though it is believed the trend towards cleaner data would have continued.

There are certainly limitations to reducing the number of agents. Principally, the likelihood of precise HLA matches goes down as the number of agents decreases. The number of HLA combinations is fixed regardless of how many people are represented by each agent. Thus when their are more people per agent, and hence less agents, the probability of a donor with random HLA factors matching a reduced number of potential recipient agents goes down substantially. The indicator that this is happening is that donations are not being used, and in all but the most donor saturated simulations almost all donors were paired with a suitable recipient. This donor saturation was observed as the number of donors generated per day approached and exceeded the number of new recipients generated per day and the number of person on the wait list began to stabilize and decrease.

5.1.1. *Sorting Algorithms.* It is worth noting that a substantial amount of the time penalty incurred by decreasing the number of people (donors or recipients) represented by one agent results from sorting of the initial wait list. When the model is starting up a statistically representative wait list is generated that will be used to "prime" the model. This wait list is generated probabilistically from statistical data on the actual organ donation wait list at the end of 2006.

In order to make this in ital wait list useful for the model's matching algorithm, this wait list must be ordered based upon the amount of time each agent on it has been waiting for a transplant. As the list was probabilistically generated it is not in order by wait time and hence must be sorted.

For simplicity, the sorting algorithm implemented is a bubble sort, that uses element exchanges to "bubble up" the smallest values. Bubble sort is not particularly efficient, having a worst case run time of On^2 and a best-case run time of On. Given that the list is pseudo-randomly dispersed the operating time of the sort will be approximately its worst-case run time. The implementation of a more efficient sorting algorithm such as heapsort was considered, but discarded due to time constraints.

6. Model Analysis

6.1. **Wait List Characteristics.**

6.1.1. *Wait List Size.* As expected and in keeping with current trends, the number of candidates on the wait list increases over time. This is logical because we start with a fairly large initial wait list, and donors are added at a much slower rate than candidates are. Each day, our model was able to find every new donor a candidate match from the wait list that same day. Hence, in our simulation, our number of transplants per day is constant and every organ that is donated is used. This differs from reality, as logistics prevent every last organ donation from reaching a recipient. For example, in 2004, 6.4% of donated kidneys were not used because a match could not be found in time.[4] What this could imply is that the matching system currently in place is theoretically efficient enough at finding at least some

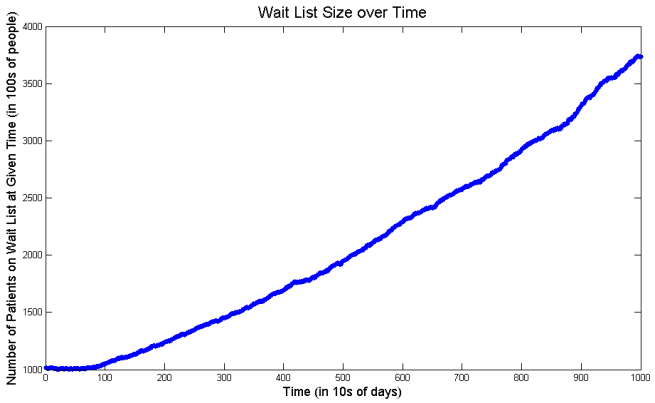

FIGURE 3. Waiting list size over time beginning at the end of 2006, as project by the model.

moderately acceptable match for every donation, but geographical distance, availability of surgeons, and other such factors are preventing each organ from being used.

6.1.2. *Blood Type.* Individuals of blood type O, which make up the largest percentage of the wild population, also made up the largest percentage of our model wait list. This was closely rivaled by candidates of blood type A, who seemed to be increasing on the wait list at about the same rate as blood type O candidates, though there were fewer A candidates. In reality, the percentage of candidates of blood type A on the wait list is significantly smaller than the wild type percentage, and the opposite is true for the percentage of candidates of blood type O. One reason a more distinct difference between the two blood types does not exist is that we did not allow for donors of blood type O to give to candidates of blood type A under any circumstance.

Candidates of blood types B and AB were less prevalent on the wait list, as expected. The rate of increase of each group was also much smaller than that of the other two blood types.

6.1.3. *Age.* As in reality, children make up only a small percentage of wait list candidates in our model. The rate of increase of children on the wait list is much less than that of adults, which is to be expected given that children are given priority in selecting organ matches.

6.1.4. *PRA.* By far, most wait list candidates in our simulation have a PRA of 0 to 9%, which makes sense given that this group also makes up the largest percentage of the wild type population. Additionally, candidates with higher PRAs are given preference since they are harder to pair. Interestingly, there is not all that much difference between the growth of the PRA group from 10 to 79% and that over 80%.

To further break down the distribution of PRA within the model, we examined how the amount of time spent on the wait list would affect the PRA value distribution. By comparing the short-term waiting list (less than 6 months) with the long-term list (more than 3 years), we can compare the distribution of PRA values

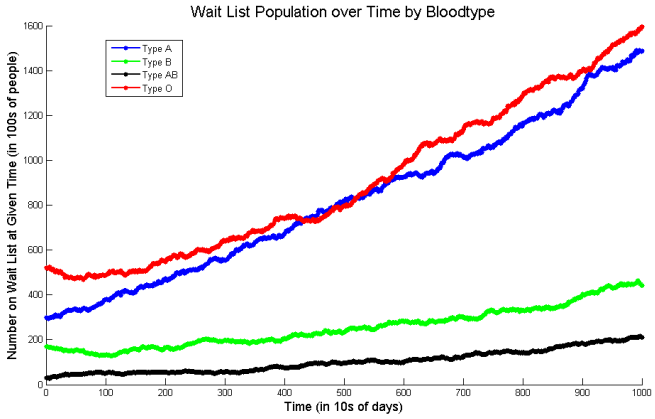

FIGURE 4. Waiting list population over time by blood type, beginning in 2006, as projected by the model.

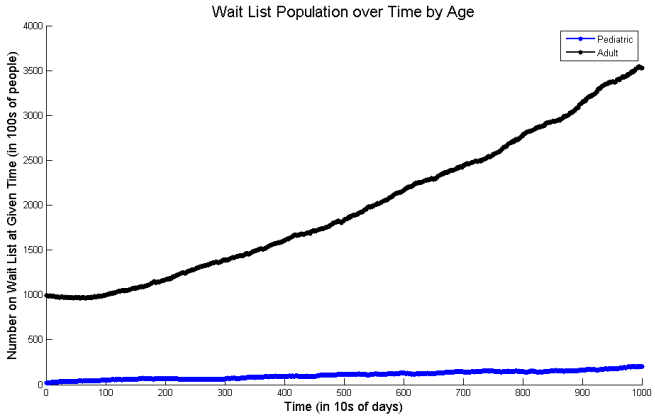

FIGURE 5. Waiting list population over time by age, beginning in 2006, as projected by the model.

and decide whether patients of certain PRA values are likely to wait on the list longer.

First, we examine the current short term data, which we have assumed to represent the standard distribution of PRA values in the current U.S. population. We notice that high PRA patients, with >80% PRA value, make up only 15% of the total short-term list population. Medium PRA value patients also occupy about 15% of the total short-term population. Low PRA patients are the most common, representing about of 69% of the population. We keep these relative values in mind to use as baseline estimates of the standard distribution of PRA values.

Without any policy giving high PRA values priority in donor matching, we would expect high PRA values to make up an increasing portion of the candidates who have been on the list the longest. However, the OPTN policy giving high PRA patients priority should dampen this effect somewhat. We notice from the figure

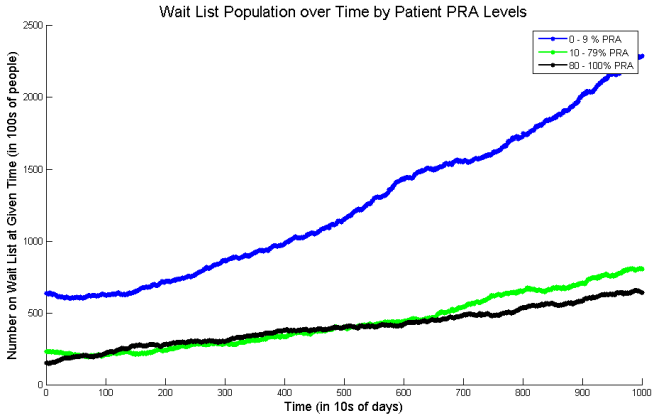

FIGURE 6. Waiting list population over time by PRA level groups, beginning in 2006, as projected by the model.

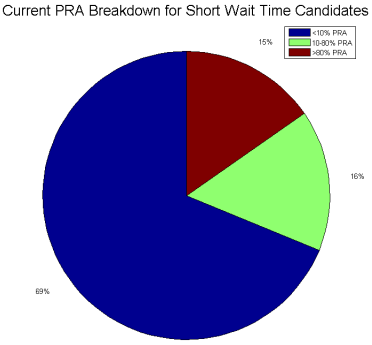

FIGURE 7. Current PRA breakdown for patients on waiting list for less thatn siz monthes.

that with this policy in place, the model predicts that after about 30 years the portion of long-term patients with high PRA values will increase slightly from 15% to 19%. Medium PRA patients will decrease some from current levels, but not to a significant degree. The proportion of low value PRA value patients who have been on the list for more than 3 years will also subtly increase.

These increases and decreases do not represent a significant departure from the baseline values described earlier, especially given the difficulty of finding a donor match for a high or medium PRA patient. The model thus indicates that for the next few years PRA patients of all levels will be evenly represented in the long-term wait list, using our assumed standards. From this we can conclude that, to the extent possible, the model's policy priorities keep high and medium PRA level patients off of the long-term waiting lists enough to ensure that the amount of time a patient waits to obtain an organ is not significantly affected by his or her PRA

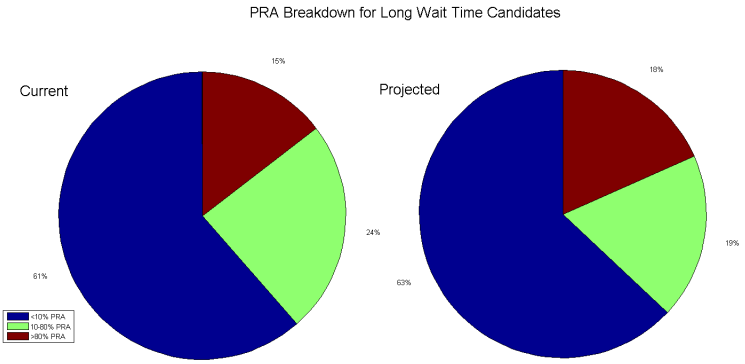

FIGURE 8. Current and 30-year projection for patients on waiting list for more than three years.

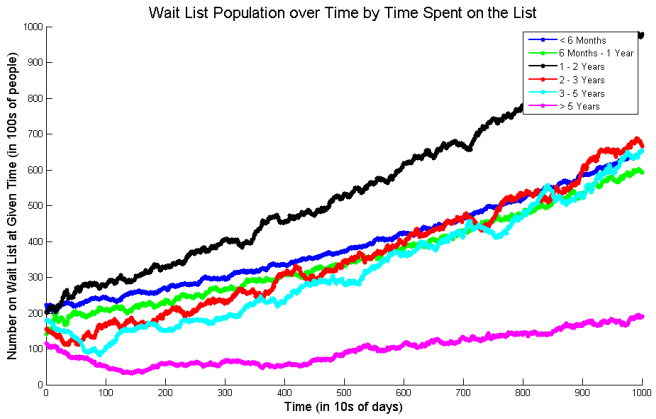

FIGURE 9. Waiting list population over time by time spent on waiting list, beginning in 2006, as projected by the model.

level. The policy's intent upon fairness to all patients regardless of PRA levels is thus substantiated.

6.1.5. *Time Spent on Wait List.* Most candidates on the wait list at the end of three years of our simulation fall into the category of having been on the list for one to two years. A minority of the candidates on the wait list have been on the list for more than five years.

It is important to keep track of the amount of time a candidate spends on the wait list in order to determine if current policy efficiently distributes organ donations to all candidates and prevents the list from becoming saturated with patients who have waited years for an organ because of difficulty finding a donor. For our analysis purposes, we have divided all wait-list candidates at a given time in the model into three groups: those who have waited less than 6 months, those who have waited between 6 months and 3 years, and those who have waited more than 3 years. We

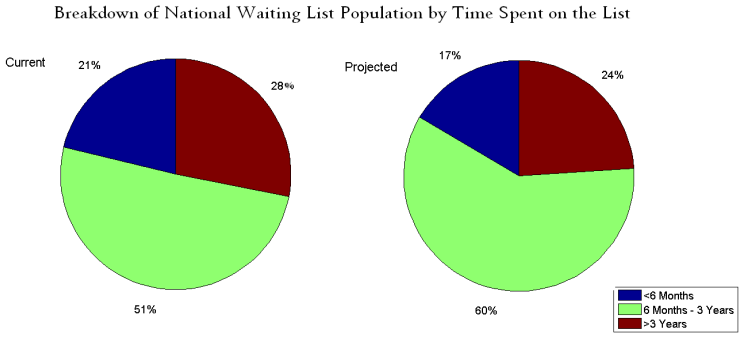

FIGURE 10. Current and 30 year projections of time spent on waiting list.

believe that analyzing these three groups, which we call the short-term, normal-term, and long-term wait lists, will help us determine the extent to which current policies affect the time a candidate spends on the waiting list.

When we examine the breakdown of current data for the list as well as our model's prediction for the wait list 30 years into the future, we first discover that the wait list is not becoming significantly saturated with donors who have waited for long periods of time. The long-term list actually decreases in size relative to the other lists over this time, from 28% to 24%. Furthermore, the model predicts that the future will maintain the current trend in which the majority of all candidates at any time on the list have waited from 6 months to 3 years. The relative number of patients on the short-term list will decrease from 21% to 17%.

Overall, our model indicates that current policies will achieve their objective in ensuring that the wait list is never predominantly made up of those who have waited for long periods of time (more than 3 years).

6.2. **Performance of Each Region.** From available data it is clear that the wait list candidates and donors are not evenly distributed over the eleven regions of the United States. We took this into account in our model. From our simulation runs, it was difficult to distinguish any particular problem regions. Each region started out with different percentages of the wait list in different categories of waiting time, but these regional values seemed to fall into similar national patterns over time.

We specifically examined the how region influenced the relative amount of time spent on the wait list compared with the national average discussed above. Our model is inconclusive as far as pinpointing regions that have disproportional wait list times and amounts of donors. We saw no significant trends in any region which deviated from the national trends. When examining the fraction of the candidates on the long-term wait list of each region, we found that it varied from 21% of Region 7 to 27% of Region 11. These values fall well within any expected random deviation from the national predicted value of 24%. Additionally, when looking at the fraction of each region represented on the short-term list, we found the model's predictions varied from 12% of Region 7 to 19% of Region 9. Again, this range of values falls within the expected deviation from the national predicted average that 17% of all patients will occupy the short-term list. With so little variation from region to region when compared to national averages, we cannot

identify any particular location that may be causing a "bottleneck" and inhibiting the efficiency of the network. Thus, we cannot provide any compelling reason to alter the organizational structure of the national organ donation network from its current state.

6.3. **Limitations.** One of the most important limitations of our model is that we have no way of assessing the quality of the outcome of each match, based on whether organs were from living or deceased donors, how good the match was according to HLA sets, and the state of the candidate's health at time of transplant (which could be worsened by long wait-list times). Our model lacked a definitive benchmark to use for deciding whether the current system is "good" or more efficient than another system. However, we were able to verify that the current system will to a great extent distribute organs evenly to patients relative to population size regardless of their time spent on the waiting list, regional location, or compatibility factors such as PRA.

7. The Donor Crisis

As stated previously, the candidates on the wait list drastically outnumber the donors. As such, any increase in organ donations from donors living or deceased would be welcomed. Presumed consent would result in a larger pool of organs from cadavers, whereas policy changes and awareness campaigns could generate further living donors.

7.1. **Obtaining More Donors: Presumed Consent.** In the United States, an individual or the individual's family must give consent to have his or her organs donated in case of death. Several other countries, including Austria, Belgium, Bulgaria, Czech Republic, Denmark, Finland, France, Greece, Hungary, Italy, Latvia, Luxembourg, Norway, Poland, Singapore, Slovak Republic, Slovenia, Spain, Sweden, and Switzerland, and use a system of presumed consent, in which every individual is considered for organ donation upon death unless he or she has explicitly declined to donate his or her organs prior to his or her death. The opt-out rate in the countries where this system is instituted is very small, at about 2%.[6] This results in many more donors than would otherwise be achieved. Many individuals in the United States never specify that they would like to donate their organs, even though they are not opposed to the idea; they simply never got around to designating themselves organ donors. Recently, some states of the U.S. have begun to implement presumed consent.

To explore how presumed consent in the United States may help alleviate the wait list load, we considered getting additional organ donors from a very common source: automobile fatalities. In the year 2003 in the United States there were 42,884 fatalities due to car accidents.[5] The number of deceased organ donors for the same year was 6547.[3] Even if only a quarter of the cadavers recovered from car accidents in 2003 were acceptable for harvesting organs, that number is still greater than the number of voluntary deceased organ donors. Furthermore, this does not even take into account that there are other forms of death that would still allow for organ donation. A bonus advantage of this system is that it would be more efficient to store the names of those few individuals who do not wish to be organ donors than the many of those who would donate their organs.

In order to control the growth of the wait list, more donors than candidates would have to be added each day. This means that sources other than car accidents would have to be investigated in order to obtain enough donors. Nevertheless, using organs from as many car fatalities as possible would certainly help to alleviate some of the growth.

7.2. **Influencing the Decision to Donate.** While each individual is born with two kidneys, only one is necessary for survival. A significant portion of kidney transplants involve kidneys from live donors. In fact, over the past 8 years, nearly 35% of all kidney transplants were from living donors.[3] As there is such a large (and continuously growing) waiting list for kidneys, it would clearly be beneficial if there were some way to influence more people to donate.

The decision to donate a kidney involves weighing many factors. Perhaps the main incentive for many living donors to give an organ is saving a loved one's life: less than 1% of the living donors in the last eight years were anonymous donors.[3] The remaining live donors were either family or acquaintances of the intended recipients. In cases where a donor's organ is not an ideal match for the intended recipient, sometimes paired kidney exchanges occur. This involves two donors giving their organs to the other's intended recipient, thereby helping two people instead of neither. While the donor is not donating to his or her loved one, his or her loved one is still receiving a transplant sooner because of the donor's gift.

It is possible that if more people were aware of the dire need for more kidney donors, some would be moved to donate even if for a stranger. Many people donate blood despite the discomfort involved because they feel good about coming to someone else's aid. Admittedly, organ donation is a much higher risk process and involves a much higher level of discomfort, but if the generosity of more individuals could be sparked, organ donations could increase.

Another incentive for someone to donate an organ could be monetary compensation, though this is not currently practiced in the U.S. The selling of organs, while permitted in some other countries such as India, is prohibited by law in the U.S. If individuals were paid to donate their organs without having intended recipients, the number of people willing to become anonymous donors would likely increase. However, one possible worry pertaining to organ sale is that the poor might be exploited by this practice.[9] Our government should perhaps investigate the organ market and reevaluate its policies to consider monetary compensation for organ donation. Organ donation might not be dissimilar to the current practices of egg and sperm donation if regulated properly.

An individual might be deterred from becoming a donor for fear of the medical consequences. Donating a kidney involves recovering from a surgery, and then subsequently being short one kidney for the rest of the donor's life. This is a sizable risk. Also, if someone is not adequately informed about organ donations, he or she may have invalid or unjustified reasons for not wanting to donate.

Based on the above considerations, we devised a simple formula for assigning each individual the likelihood that he or she will be willing to donate a kidney. Some factors, such as whether and how closely the donor is related to the recipient, cannot be altered. Others, such as an individual's awareness of organ donation or the compensation a donor receives, can be affected by campaigns and/or policy changes.

$$P = 0.1(4Q + 2AL + \frac{2A}{F+1} + \frac{2C}{I+1} - 4R) \tag{1}$$

where:

- P is the probability that a given individual will be willing to donate a kidney.
- Q is the acquaintance factor, a value from 0 to 1 designating how closely the donor is related to the recipient. The higher the number, the dearer the recipient is to the donor. A value of 0 would indicate that the donor is completely anonymous to the recipient. A mid-range value might be assigned in the case of paired-kidney exchanges where the donor's intended recipient would be helped, but the donor's actual recipient would not be an acquaintance. This term has the largest coefficient, as it is arguably the biggest incentive for a person to donate an organ.
- A is the awareness factor, a value from 0 to 1 measuring an individual's awareness of organ donation issues. It multiplies the altruism factor (an individual more aware of the need for organs would arguably become more sympathetic to the cause), and is divided by the fear factor (generally, the more informed someone is, the less they are afraid).
- L is the altruism factor, a value from 0 to 1. The more altruistic a person is, the larger his or her probability of donating an organ.
- F is the fear factor, a value from 0 to 1.
- C is the compensation factor, a value from 0 to 1 depending on how much compensation an individual is offered for donating an organ.
- I is the inconvenience factor, a value from 0 to 1 gauging the inconvenience associated with the surgery and post-operative recovery of donating an organ.
- R is the long-term health risk factor, a value ranging from 0 to 1 which could vary based on an individual's particular medical condition, as well as any medical advances that might be made in the future to help keep any organ donor in better health. This was seen as the biggest deterrent an individual might face to becoming a donor, hence the large negative coefficient for this term.

Theoretically, an array of the above factors could be determined for any individual. The probability of getting a certain number of donors (which could be based on how many candidates are on the wait list) could then be calculated. The factors which can be changed through campaigns and policy changes are of particular interest. Simulation experiments in which these factors are varied could be run to see if it might be reasonable to influence enough individuals to become donors to empty the wait list. Due to time constraints, we were unable to model this ourselves.

8. Report to Congress

After reviewing simulation data and considering policies of foreign countries with regards to organ transplantation, we submit the following reflection.

8.1. **Our Main Obstacle: Getting Donors.**

We have determined that the primary issue facing the U.S. in effectively reducing the size of the organ wait list is the lack of organ donors. Each day, the number of donors added to the system comes

to less than half the number of wait list candidates. This results in a seemingly endless trend of growth for the wait list. In order to reverse this trend, it is mandatory that the number of donors in the system drastically increase to outnumber the candidates on the wait list.

8.2. **Presumed Consent to Achieve More Deceased Donors.** Many other countries, and recently some states of the U.S., have instituted policies of presumed consent to augment the donor pool. Since the key to reducing the wait list is increasing the number of donors, this would certainly help. Such a policy would still not force people into becoming donors, as they could always choose to opt out, but it would almost certainly make more donors of individuals who wouldn't ordinarily opt in.

8.3. **Appealing to Living Donors.** For organs such as kidneys that can be donated by living individuals, it is preferential to have a live donor. Therefore, it would be beneficial to the organ transplantation system to not only increase the number of deceased donors, but also the number of living donors. This could be done through a few channels. First of all, awareness must be raised. A simple campaign to better introduce the general public to the dire need for organs and the basic issues surrounding organ transplantation could effectively spur people's desire to help as well as diminish fear. Secondly, monetary compensation for organ donors could serve to offset the inconvenience associated with donating organs. Anonymous organ donations make up only a tiny portion of live organ donations, and a good reason for this is that there is not enough of an incentive. Lastly, by making paired organ exchanges more widespread, donors whose organs aren't compatible with their intended recipients could help both their loved ones and other candidates (where the alternative would be for neither party to be served).

8.4. **Conclusion.** It is possible to reduce the size of the wait list for organ donations with a few simple policy changes. Presumed consent should be introduced in all states, an awareness campaign should be launched, some form of monetary compensation should be established, and paired organ exchanges should be encouraged.

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