A Methodological Framework for Optimally Reorganizing Liver Transplant Regions

James E. Stahl, MD, CM, MPH, Nan Kong, MS, Steven M. Shechter, MS, Andrew J. Schaefer, PhD, Mark S. Roberts, MD, MPP

Background. The United States is divided currently into 11 transplant regions, which vary in area and number of organ procurement organizations (OPOs). Region size affects organ travel time and organ viability at transplant. Purpose. To develop a methodologic framework for determining optimal configurations of regions maximizing transplant allocation efficiency and geographic parity. Methods. An integer program was designed to maximize a weighted combination of 2 objectives: 1) intraregional transplants, 2) geographic parity—maximizing the lowest intraregional transplant rate across all OPOs. Two classes of functions relating liver travel time to liver viability were also examined as part of the sensitivity analyses. Results. Preliminary results indicate that reorganizing regions, while constraining their number to 11, resulted in up to 17 additional transplants/year depending on the travel-viability function; when not constrained, it resulted in up to 18/year of increase. Conclusion. Our analysis indicates that liver transplantation may benefit through region reorganization. The analytic method developed here should be applicable to other organs and sets of organs. Key words: transplant regions; organ procurement organizations; liver transplants.

End-stage liver disease, that is, chronic liver disease and cirrhosis, is the 10th leading cause of death among adults in the United States, accounting for more than 25,000 deaths in 1998 alone. At present, the only therapy available is liver transplantation. Fortunately, patients at almost any stage of their disease receiving a liver transplant can expect an 80% to 90% 5-year survival rates. Unfortunately, liver transplantation is both costly and limited by the supply of viable donor organs. The acute hospitalization alone has been estimated between $145,000 and $287,000.

The number of patients registered with the United Network for Organ Sharing (UNOS) for liver transplantation has increased over 12-fold in the past decade to more than 16,000 in 2002. During this same period, the pool of donated organs only doubled, and supply has not been able to keep pace with demand.

UNOS.org). In 2002, even though more than 5300 people received a liver transplant, nearly 7000 died while waiting for one. It should be noted, however, that even though the registration rate for liver transplant is rising faster than the transplant rate, fewer than 2000 of those registered died from causes directly attributed to their end-stage liver disease. Fewer than 400 of these deaths were patients who were critically ill. Currently, the donation rate and transplant rate are closely matched, and the deaths per year has leveled off (see Figure 1).

Surprisingly, many donated livers are never actually transplanted. Between 1988 and 1998, more than 3600 livers were lost to transplant because of poor matching, refusal by transplant centers, or allocation delays, resulting in time-related loss of organ viability. On average, procured livers remain viable for only 12 to 18 h once harvested. Therefore, reducing the time needed to match and transport livers should increase the number of viable livers available for transplantation. This should then improve the net survival in patients suffering from end-stage liver disease.

Because of the severe shortage of livers and their fleeting nature, both allocation procedure and policy...
are critically important for the welfare of end-stage liver disease patients. Livers, as well as other types of organs, are currently allocated through a hierarchical geographic allocation system with 3 levels: Organ procurement organization (OPO) level, regional level, and national level. There are approximately 300 hospitals that perform transplantation. These are supplied by 59 OPOs organized into 11 regions (Figure 2). Specifically, a liver is first offered to the most critical patients (status 1)—first at the OPO level and then at the regional level. If no match is found, then the liver is offered to the remaining patients in the local OPO level followed by the same region, in descending order of urgency. Finally, if still no match is found, the liver is offered to the most urgent patient in the rest of the country (Figure 3).

The organ shortage also makes the control and equity of access to organs critical. Since the late 1990s, a vigorous debate has existed between the federal government, which has advocated for a national allocation system, and states such as Louisiana, Wisconsin, Texas, Arizona, Oklahoma, Tennessee, and South Carolina, which have either sued the government or introduced legislation requiring organs procured within a state to be used within the state. Since 1989, the percentage of procured organs used locally has increased from 31.5% to more than 65%, whereas the number of organs shared across procurement areas has decreased from 59% to 25% (www.UNOS.org).

The size of the region affects the distance organs must travel and thus the cold-ischemia time (CIT) of the procured organ, which in turn affects the viability of the organ at transplant. Consequently, region size potentially affects the number of successful transplants. The current size and configuration of the transplant regions do not explicitly consider organ type, the duration of organ viability, and intermediate technologies such as dialysis in their design, but rather were developed for administrative purposes (www.UNOS.org). The regions currently encompass varying numbers of OPOs (median = 5, range = 2 to 11), from which the organs are supplied.

A regional structure that optimizes the tradeoff between CIT and administrative demands may maximize intraregional matches, help alleviate demand, and reduce the risk of losing organs. Currently, an organ may be offered to many patients, with each step consuming administrative and logistical time. Because their viability decreases over time, unless regions are carefully designed, patients may lose potentially life-saving organs. Larger regions can share more organs, within region, which increases the chance of having an intraregional match, but increased size may result in more travel time. On the other hand, smaller regions require less travel time but have smaller donor pools, making an intraregional match less likely. This increases the likelihood that an extraregional match must be sought, which costs administrative and logistical time.

The purpose of this research is to provide a basic modeling framework for improving organ allocation and optimizing transplant allocation efficiency and geographic equity, focusing strictly on region design.
This initial modeling framework focuses on 2 objectives. The 1st objective is to maximize the total number of intraregional transplants. This measure serves as a proxy for transplant allocation efficiency. The 2nd objective is to maximize the minimum OPO intraregional transplant rate. This rate is defined as the number of intraregional transplants in an OPO divided by the number of patients on the OPO waiting list. This rate serves as a proxy measure for geographic equity.

To explain our concept of geographic equity further, we assume that improving geographic equity, that is, making patient access to organs as equal as possible across all OPOs, can be accomplished by maximizing the intraregional transplantation rate of the OPO with the lowest intraregional rate. Specifically, across all OPOs, improving the lowest ratio of intraregional transplants in an OPO to the number of patients on the waiting lists of that OPO will result in a more equitable distribution of organs. In other words, if 2 region designs produce equal numbers of successful intraregional transplants, but 1 produces a higher minimum intraregional transplant rate across OPOs, that design would be preferred.

Therefore, this preliminary analysis has 2 important objectives: 1) maximize total intraregional transplants nationwide and 2) provide equitable access to transplants across the country, avoiding significant disparities. Hence, we do not necessarily want to optimize total intraregional transplants alone. At the same time, we do not want to penalize regions for high transplant allocation efficiency for the sake of equity, either. Therefore, another objective is to address the tradeoff between total intraregional transplants and the lowest OPO intraregional transplant rate across all OPOs.

METHODS

We considered 2 strategies for reorganizing the existing OPOs into transplant regions. First, we constrained the number of transplant regions to 11, the same number as in the current system. This strategy examined the hypothesis that the current size and configuration of regions were already optimal with regard to either of our objectives. Second, we relaxed this constraint and allowed the number of regions to vary. This examined the hypothesis that the optimal number of regions should be 11.

For the purposes of these basic analyses, we modeled the country as a simple network (Figure 4). In this model, OPOs are represented as the nodes of a network. Arcs connecting OPOs indicate that they are contiguous. We made several further simplifying assumptions. First, we defined a hypothetical region as a set of no more than 9 contiguous OPOs. This limit was chosen because of computational constraints—the time to complete an analytic run and the needed computer memory rises very rapidly as the maximum number of OPOs allowed within a region increases. Second, an OPO was only allowed to supply livers to the region containing it. Third, each OPO was assumed to have only 1 transplant center. This simplified the estimation of the distance an organ would need to travel, though multiple transplant centers could be easily incorporated in the model. We also assumed that there were 59 OPOs as being representative of the period of time from which our data were derived (1993–2000). Finally, for this analysis, we assumed that both transplant allocation efficiency and geographic equity could be represented as factors in a function linking CIT and liver transport distance (LTD).

Livers may be rejected and thus lost based on a combination of objective and subjective criteria used by transplant surgeons at the recipient institution, for example, poor quality, which results in a high risk of primary nonfunction. Because UNOS has limited data available on the reasons a surgeon or transplant center rejects a liver, we made the simplifying assumption that the probability of rejecting a liver, measured by the liver’s viability, was solely dependent on its CIT. Because the probability of primary nonfunction is positively correlated with CIT and CIT is positively correlated with LTD, the distance a liver must travel affects
its viability and the probability that it is rejected, and this in turn is affected ultimately by the size and configuration of regions. We also assumed that any liver offered to a transplant center that was not rejected was transplanted. Therefore, the size and configuration of transplant regions affect both factors considered in this study that are influenced by liver viability. Because the functional relationship of liver viability to CIT is not completely known, we tested 2 different functional relationships between primary nonfunction and CIT: linear and polynomial (Figure 5). These 2 functions were fitted from data obtained through a meta-analytic review of the literature (search terms: liver transplant, cold-ischemia time, graft dysfunction, patient and graft survival, etc.; Medline, 1966 to present).

These functional forms were believed, by expert opinion, to be clinically reasonable and would bound the true function, modeling the relationship between liver viability and CIT. For the relationship between CIT and LTD, we used CIT (in hours) = 9.895 + 0.003 × LTD (in miles). Geographic data, such as the number and current configuration of regions, OPOs and transplant centers, were used from publicly available sources.

The next step in the analysis was to identify all possible regional configurations. A depth-first search (DFS) algorithm was performed to identify all hypothetical regions where each individual region comprised 9 or fewer contiguous OPOs (see appendix). Given 59 existing OPOs, there are more than 311,000 hypothetical regions that could be constructed, with between 1 and 9 OPOs per region. For any OPO within a given region, the number of transplants contributing to the intraregional transplant traffic was the number of livers offered to that OPO from other OPOs within the region minus those lost in transport. For any given region, the number of intraregional transplants was the sum of the inter-OPO transplants within that region (see appendix). This estimation was done for all hypothetical regions. The optimization problem, however, is even more complex. There are billions of possible ways to combine these regions into potential solutions that span the entire United States. Two sets of integer programs were solved over these regions to find the optimal transplant regional configuration with respect to the proposed objectives in our experiments. Integer programs are standard models in operations research for making decisions over discrete variables. Integer programming is particularly useful when trying to model packing, partitioning, logistical, or travel problems when there are a finite number of options to choose from. Our analysis is, in essence, a partitioning problem, but the method may be applied in other areas. For example, integer programming has been usefully applied in policy areas as diverse as political redistricting, crew scheduling, EMS location, optimizing surgical scheduling, and network design.

In our analysis, we first examined the effect of maximizing transplant allocation efficiency on regional configuration. We solved an integer program to find the optimal set of regions such that the total number of intraregional transplants was maximized (see appendix). Next we considered the effect of geographic equity on transplant allocation efficiency. As discussed above, this meant for this analysis, the integer program objective function was maximizing the intraregional transplant rate of the worst-off region, that is, the one with the lowest rate. The intraregional transplant rate for an OPO, denoted by λ, was defined as the number of intraregional transplants preserved in an OPO divided by the number of patients in the OPO waiting for transplants. We denoted λ_{min} to be the intraregional transplant rate of the worst-off OPO, that is, the minimum λ across all OPOs. Therefore, the objective of the geographic equity analysis is to maximize λ_{min} across OPOs.

There is a tradeoff between transplant allocation efficiency and geographic equity. Improving one often comes at the expense of the other. To quantify this tradeoff, we defined a new constant ρ and then searched for a set of regions that maximizes the number of intraregional transplants plus ρ, multiplied by the minimum intraregional transplant rate across OPOs, that is, the number of intraregional transplants + ρ.
The value assigned to $\rho$ is based on how much importance we place on the minimum transplant rate across OPOs versus intraregional transplants (higher values of $\rho$ mean more weight is given to $\lambda_{\text{min}}$). Hence, $\rho$ provides a mathematical means of balancing the 2 conflicting factors, transplant allocation efficiency and geographic equity. $\rho$ may be considered a function of the total interregional waiting list, and any changes in $\rho$ represent changes in the efficiency of the waiting list. For any value of $\rho$, a decision maker would be indifferent between increasing the total intraregional transplants by 1 and increasing the intraregional transplant rate in the worst OPO by $1/\rho$.

We denoted $\rho_c$ to be the number of intraregional transplants divided by the minimum $\lambda$ with respect to the current regional configuration. Then with the value of $\rho_c$, a decision maker would be indifferent between increasing the total intraregional transplants by 1 and increasing the minimum $\lambda$ by $1/\rho_c$. We chose $\rho = 0$ and $\rho_c$ in the analysis. In fact, the case $\rho = 0$ is equivalent to the 1st experiment in which we did not incorporate geographic equity.

RESULTS

Results without the Consideration of Geographic Equity

Table 1 displays the preliminary results for both cases in which the number of regions in the optimal configuration was fixed at 11 and when the number was unrestricted. In the 2nd column of the table, the intraregional transplants increase per year is presented for the former case. The intraregional transplants increase per year, and the number of regions in the optimal regional configuration is presented in the 3rd and 4th columns of the table, respectively, for the latter case.

It appears that regardless of the liver viability function chosen (linear or polynomial), the optimal regional configuration obtained from our model resulted in more intraregional transplants. It should be noted that the regions chosen by our search strategy were not the same regions that currently exist (see Figure 6). Relaxing the constraint on the number of regions slightly increased the number of intraregional transplants over the scenario where the number of regions was fixed to 11.

Results with the Consideration of Geographic Equity

Table 2 shows the preliminary results for 2 cases incorporating the factor modeling geographic equity. Again, the 1st case is when the number of regions in the optimal configuration was restricted; the 2nd is when the number was unrestricted. For the 1st case, the 2nd column presents the primary outcome—the intraregional transplants increase per year. For the 2nd case, the 4th and 5th columns present the primary outcome and the number of regions in the optimal regional configuration. In addition, we report the minimum intraregional transplant rate across OPOs for both cases, shown in the 3rd and 6th columns, respectively.

With regard to the primary outcome, similar conclusions were drawn as in the cases where geographic equity was not considered. It should be noted that the minimum intraregional transplant rate across OPOs was significantly higher than that in the current regional configuration given the $\rho$ value.

Comparing the 2 sets of experiments reflected in Tables 1 and 2 and Figures 7–9, we observed that the increase in intraregional transplants over the current...
configuration diminished as the value of $\rho$ increased. However, the minimum intraregional transplant rate across OPOs increased as the value of $\rho$ increased. This observation reflects the tradeoff between transplant allocation efficiency and geographic equity. As the weight assigned to the equity increases, equity becomes a more important issue for region reorganization as opposed to efficiency.

**Sensitivity Analyses**

Because the liver viability is a key parameter of our model, we conducted sensitivity analyses in which we varied the underlying function modeling the relationship between CIT and primary nonfunction and in which we systematically varied the parameters in the models within ±2 standard errors (see Table 3). The sensitivity analyses indicated that the primary outcome was not very sensitive to the varying underlying relationship between CIT and primary nonfunction, regardless of whether the number of regions in the optimal configuration was restricted to 11 (see Figure 7). We also observed that the optimal regional configuration was nearly identical in most of the sensitivity analyses to the base case optimal configuration, though not the same as the current configuration.

### Table 2  Base Case Primary Outcome Results (with consideration for geographic equity)

<table>
<thead>
<tr>
<th>PNF Function</th>
<th>Number of Regions Fixed</th>
<th>Number of Increase</th>
<th>Minimum $\lambda$</th>
<th>Number of Regions Not Fixed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear</td>
<td>13.0/year</td>
<td>0.345</td>
<td></td>
<td>13.0/year</td>
</tr>
<tr>
<td>Polynomial</td>
<td>12.2/year</td>
<td>0.337</td>
<td></td>
<td>12.2/year</td>
</tr>
</tbody>
</table>

Note: OPOs = organ procurement organizations; PNF = probability of liver primary nonfunction. For the consideration of geographic equity, the minimum intraregional transplant rate across OPOs (minimum $\lambda$) in the current regional configuration is 0.060 for the linear PNF function and is 0.059 for the polynomial PNF function; the weighting parameter $\rho$ was assigned to be $\rho_\lambda$, and thus its value is 154,160 for the linear PNF function and is 153,978 for the polynomial PNF function.

Figure 7  Additional transplants per year with reconfigured regions. *$\rho$ may be considered functionally related to the total national waiting list.
OPTIMALLY REORGANIZING LIVER TRANSPLANT REGIONS

Figure 8 Minimum intraregional transplant rate v. \( \rho \). "\( \rho \) may be considered functionally related to the total national waiting list." \( \lambda \), minimum intraregional transplants/intraregional waiting list size.

Figure 9 Optimal number of regions v. \( \rho \). "\( \rho \) may be considered functionally related to the total national waiting list."
DISCUSSION

Although our model is necessarily a simplification of reality, this framework gives us a means for estimating the effect of various strategies for organizing OPOs into regions. In this model, the optimal sets of regions tend to group densely populated areas. For example, unlike the current system, in each of the optimal sets, the New York metropolitan area and New Jersey appear in the same region. This is due to the fact that the benefit of grouping denser populated regions, that is, the resulting increase of intraregional transplants in the denser populated regions, tends to outweigh any losses from having larger, less densely populated regions. In addition, the optimal transplant regions based on the relationship between liver viability and transport distance modeled in our preliminary analysis appear to be different from the current system of regions regardless of which relationship was assumed, and they appear to improve the number of intraregional transplants. Finally, incorporating considerations of geographic equity may reduce the total number of intraregional transplants and vice versa. This implies that regulations aimed at transplant allocation efficiency (i.e., increasing the total transplants by restricting their transport) and those aimed at equity should be examined carefully before being considered for implementation. In the future, we will make refinements to this model by including more accurate and comprehensive demographic data.

The main purpose of this study is to establish methods and principles that can be applied to a more detailed and wide-ranging study of region design. Therefore, we only focused here on liver transplantation. However, we believe the optimal regional configurations produced from this framework may differ by organ type, owing to the availability and viability of the organ. With this framework, it may be feasible to generate an optimal regional configuration for each organ type. It may also be feasible to generate an overall optimal regional configuration based on the weight assigned to each type of organ, considering the scarcity of the organ and the availability of any replacement therapy. For example, organs such as livers that are relatively rare and have no replacement therapy available may be weighted more than organs such as kidneys, which have an intermediate therapy in dialysis.

In our models, we only considered the uncertainty on 1 factor, organ viability as a function of distance the organ needs to travel. There are many other areas of uncertainty in our models for which we did not perform sensitivity analyses. However, because the main point of this study was to establish an analytic framework rather than a definitive answer, we did not elaborate on the sensitivity analysis. Our models also do not currently build in health care costs, which might have an effect on the tradeoff between region size and the willingness to transplant organs across OPOs. We felt this a reasonable omission in that the cost of administering a region is negligible when compared to the cost of a single transplant. We also only considered liver transplantation within the United States. Although it is possible that organs might be transported across national borders, this is very unusual. We therefore felt that this was reasonable to exclude. This being said, any application of this framework to a multinational situation such as the European Union would have to consider this possibility.

One major limiting factor in our study was computing capacity. We were unable to exactly solve problems containing some hypothetical regions consisting of more than 9 OPOs. This precluded comparisons to any hypothetical configurations containing larger regions. We are currently exploring methods for approximately solving larger problems. However, considering larger regions will only improve our solutions, which already seem to indicate that the existing configuration is not optimal.

In the current hierarchical system employed by UNOS, there are local, or OPO-level transplants, re-
gional transplants, and national transplants. We assumed that the number of local transplants was unaffected by the regional configuration. However, given the current allocation scheme, the effect of region design on the transplantation at the local level may not be negligible but is difficult to model. Although the framework provided in this article is able to maximize total intraregional transplants, it is unable to consider the number of national transplants. This is important because more intraregional transplants result in fewer national transplants. These issues will be addressed in future research.

In conclusion, liver transplantation provides a relatively simple example with which to test the validity of this modeling framework: 1) livers can remain outside the body for up to 18 h, 2) the CIT increases as the LTD increases, and 3) the liver quality decreases as the CIT increases. In comparison, hearts and lungs must be transplanted almost immediately, and kidneys have a much longer CIT and an intermediate technology in dialysis to relieve the time pressure. The lessons learned here, however, should be applicable to other individual organ types and the organ allocation system in general. This framework will also provide the means to estimate the effect of new preservation and organ replacement technologies that may alter the constraints of the allocation system considerably. In addition, even apparently modest gains resulting from reorganizing the regions may substantially change the transplant environment. Annually, there are approximately 1200 patients in the most urgent clinical categories on the waiting list and less than 400 with a projected life expectancy of less than 1 month. On any given day, there are typically less than 20 patients in this most urgent category.10 This has been relatively stable for the past 5 years. An additional 15 to 25 organs/year could save the lives of 5% or more of those in most urgent need and shift the profile of the overall transplant waiting list toward the less ill and start reducing the waiting list. However, because there will undoubtedly be monetary and nonmonetary costs associated with a regional reorganization, which are as yet unknown, this preliminary analysis cannot yet answer whether this is cost-effective relative to other means to balance supply and demand, such as improved procurement, alternate technologies, or improved preservation techniques, but this framework gives us the means to do so. This will be the focus of future work.

GLOSSARY

Cold Ischemia Time (CIT): The time interval beginning when an organ is cooled with a perfusion solution at the organ procurement surgery and ending when the organ is reperfused at implantation.

Organ Procurement and Transplantation Network (OPTN): The unified transplant network established by the US Congress.

Organ Procurement Organization (OPO): OPOs serve as the vital link between the donor and recipient and are responsible for the identification of donors and the retrieval, preservation, and transportation of organs for transplantation.

Organ Transplant Region: The national UNOS membership is divided into 11 geographic regions. This region structure was developed to facilitate organ allocation and provide individuals with the opportunity to identify concerns regarding organ procurement, allocation, and transplantation.

United Network for Organ Sharing (UNOS): A private, non-profit organization to administer OPTN under contract with Health and Human Services. It establishes an organ-sharing system that maximizes the efficient use of organs through fair and timely allocation.

Depth-First Search (DFS): Any search algorithm, which considers outgoing edges of a vertex before any neighbors of the vertex, that is, outgoing edges of the vertex’s predecessor in the search.

Integer Program: An optimization in which the decision variables are required to be integer-valued.

Objective Function: The function to be optimized in an optimization problem.

Local Transplant Rate ($\lambda$): The rate that a patient receives intraregional transplant in the perspective OPO.

Weighting Parameter ($\rho$): The coefficient that reflects the decision-making tradeoff between transplant allocation efficiency and geographic equity.

Depth-first search to enumerate all region sets:

All regions composed of up to 9 contiguous organ procurement organizations (OPOs) were enumerated. To enumerate all possible solutions, that is, sets of regions, a depth-first search (DFS) algorithm was run with the OPO network to identify all hypothetical regions, in which each individual region was composed of less than or equal to 9 contiguous OPOs. A DFS is a type of network search algorithm that examines the state-space search tree recursively, in this case, the search tree constructed by sets of OPOs, by proceeding down 1 branch of the tree until a solution state or a dead-end state (i.e., no more moves are possible from that state) is encountered. When a dead-end state is encountered, the DFS algorithm then backs up to the last decision it made and makes another choice of which direction to pursue downward in the search tree.

Variables:

For every possible region \( j \), once enumerated, a variable \( x_j \) is created. This variable may only take on the values 0 or 1. The value \( x_j = 1 \) is interpreted as region \( j \) being chosen, and the value \( x_j = 0 \) is interpreted as region \( j \) not being chosen.

Objective function:

Our 1st objective was to find the set of regions that maximizes the total number of intraregional transplants. The chance that an individual patient is able to receive a liver offer from other OPOs within the same region was estimated as the ratio of patient population in the patient’s OPO to the patient population of the entire region, excluding the OPO where the liver is offered.

The coefficients in the objective function are described below:

- \( \text{Patients}(i) \) = the number of patients who register in any waiting list in OPO \( i \).
- \( \text{Organs}(i) \) = the number of organs procured in OPO \( i \) and shared outside the OPO.
- \( \text{PNF}(\text{cit}) \) = the probability of a liver’s primary nonfunction given its cold ischemia time.
- \( \text{CIT}(i,j) \) = the cold ischemia time of a liver that transports from OPO \( i \) to OPO \( j \).

Assume region \( r \) contains OPO \( j_1, j_2, \ldots, j_m \). Then the total number of intraregional transplantations for region \( r \) may be estimated by

\[
C_r = \sum_{k=1}^{m} \sum_{j=1}^{m} \frac{\text{Patients}(j_k)}{\text{Patients}(r) - \text{Patients}(j_k)} \times \text{Organs}(j_k) \times (1 - \text{PNF}(\text{CIT}(j_k, j_l)) \text{)}.
\]

and the intraregional transplant rate in OPO \( j_k \) contained in region \( r \), may be estimated by

\[
f_{k} = \sum_{j=1}^{m} \frac{1}{\text{Patients}(r) - \text{Patients}(j)} \times \text{Organs}(j) \times (1 - \text{PNF}(\text{CIT}(j_k, j_l)) \text{)}.
\]

Formulation:

Let \( I \) and \( J \) be the sets of all OPOs and hypothetical regions, respectively. The matrix \( A \) is defined by \( a_{ij} = 1 \) if region \( j \) contains OPO \( i \), and 0 otherwise. The number of rows of this matrix is the number of OPOs, and the number of columns of this matrix is the number of hypothetical regions. For the cases in which the geographic equity is not considered, we solved the following integer program:

Max \( \sum_{j \in J} c_j x_j \)

subject to \( \sum_{j \in J} a_{ij} x_j = 1 \), \( i \) in \( I \).

\( x_j \) in (1), \( j \) in \( J \).

This model maximizes the number of intraregional transplants while ensuring that each OPO belongs to exactly 1 region. If the number of regions was required to remain at 11, the constraint \( \sum_{j \in J} x_j = 11 \) was added.

When the geographic equity is incorporated in the objective, we solve the following problem. Here the matrix \( F \) is composed by \( f_{ij} \), and \( \lambda_{\text{min}} \) is denoted as the minimal local transplant rate.

Max \( \sum_{j \in J} c_j x_j + \rho \lambda_{\text{min}} \)

subject to \( \sum_{j \in J} a_{ij} x_j = 1 \), \( i \) in \( I \).

\( \sum_{j \in J} f_{ij} x_j - \lambda_{\text{min}} \geq 0 \), \( i \) in \( I \).

\( x_j \) in (1), \( j \) in \( J \).

This model maximizes a weighted sum of the number of intraregional transplants and the minimum intraregional transplant rate across OPOs. If the number of regions was required to remain at 11, the constraint \( \sum_{j \in J} x_j = 11 \) was added.