Proceedings of the 1995 Winter Simulation Conference
ed. C. Alexopoulos, K. Kang, W. R. Lilegdon, and D. Goldsman

ORGAN TRANSPLANTATION POLICY EVALUATION

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ABSTRACT

This paper on the UNOS Liver Allocation Model (ULAM) describes the building of a simulation model that supports policy evaluation for a national medical problem. The modeling and simulation techniques used in building ULAM include: fitting donor and patient arrival processes having trend and cyclic rate components using non-homogeneous Poisson processes (NHPPs) having exponential rate functions which may include both a polynomial and some trigonometric components; fitting distributions to data on transition times between states of medical urgency; application of variance reduction techniques using common random-number streams and prior information; organizing data structures for efficient file searching and ranking capabilities; the use of bootstrapping techniques for attribute sampling; the building of submodels employing biostatistical procedures such as Kaplan-Meier and logistic regression; and the characterization of performance measures within a complex political, economic and social environment. ULAM provides a means for producing quantitative information to support the selection of a liver allocation policy.

1 DESCRIPTION OF THE MEDICAL PROBLEM

Organs for transplantation are a scarce resource. The number of people who donate organs has not kept pace with increasing demand. Thousands of people wait for organs every year, with many dying while they wait. The list of waiting patients continues to grow at a faster rate than the number of donors.

How to allocate such a scarce and valuable resource is indeed complex. Much is at stake among doctors, Organ Procurement Organizations (OPOs), transplant centers, and, without question, the potential recipients. Issues revolve around what is an equitable, efficient and effective means of organ distribution, that is, the trade-off between medical utility and justice among patients.

2 SYSTEM ENVIRONMENT

In 1987, the United Network for Organ Sharing (UNOS) was formed to develop and operate a nationwide system to allocate human organs to potential recipients. To this day, UNOS has maintained a leadership position in helping to establish and execute organ allocation policies in the United States.

The national system for collecting data on patients and organs, called the Organ Procurement Transplantation Network (OPTN), is operated by

UNOS. Organ allocation policies are constantly reviewed and changed to reflect the accelerated advances being made in science, medicine and communications. These changes are regularly reviewed and modified to ensure equity among those in the transplantation community and to instill confidence in the community at large.

Many issues arise with organ allocation. What may maximize medical benefit for one person may not necessarily result in equitable treatment for another. In pursuit of a policy to balance all aspects of this issue, UNOS operates through a Board of Directors and committees consisting of volunteers representing a broad cross section of the transplantation community and the general public. All organ allocation policies are developed by specialized committees, presented to the Board for approval and disseminated for public comment before implementation. Following a review of these comments, the Board of Directors votes to implement a recommended policy.

Because of the significance of the allocation process, the Federal Government has established a Division of Organ Transplantation (DOT) within the U.S. Department of Health and Human Services. DOT partially funds the National Organ Procurement and Transplantation Network and maintains oversight responsibility to ensure that medical utility and justice among potential recipients is maintained by organ allocation policies.

In 1993-94, UNOS initiated a simulation modeling program to compare proposed organ allocation policies before implementation. The intent of the program was to understand policy effects before policy implementation. Previously, UNOS could only assess policies in an ad hoc fashion. In 1995, Pritsker Corporation was selected by UNOS to build the Liver Allocation Model and to provide expertise in the evaluation of alternative policies for organ transplantation. Since an organ allocation policy specifies the patient to receive a donated organ graft at a transplant center, there are medical issues relating to the patients who do or do not receive grafts, economic considerations relative to the revenues associated with transplant centers, and political and legal issues relative to the distribution of a scarce resource to different segments of the population.

3 MODEL BUILDING PROCESS

The model building activities followed the process described in Pritsker, Sigal, and Hammesfahr (1994) and in Withers, Pritsker, and Withers (1993). Space does not permit a complete description of the modeling process and only the highlights are given.

3.1 Model Objective and Scope

The objective of model building was to develop the UNOS Liver Allocation Model (ULAM) for comparing proposed alternative allocation policies. The operative word in the objective is "comparing" as it allows the elimination of components which are presumed to not have an impact on the comparison of policies. A subobjective was to create a model that could be used and could be updated at UNOS headquarters to meet the future needs of the transplantation community.

3.2 Model Specification

A model specification document was written which describes the entities, events and component models for arrival streams of donors and patients, the patient status change process, the offering and acceptance of grafts by doctors/patients and the relist and survivability functions relating to patient post-transplantation status. A specification for the reports and displays to be included within ULAM was also detailed. The policies to be evaluated initially using ULAM were limited to those prescribed in terms of patient health status and the geographical areas where patients wait. SLAM-SYSTEM (Pritsker Corporation 1992) was selected as the simulation language for ULAM because of its flexibility and advanced data structure capabilities. The specification was presented to the Allocation Modeling Oversight Committee (AMOC) of UNOS. The Committee reviewed the specification and, after discussion and modifications, the specification document was approved.

4 OVERVIEW OF ULAM

A discrete event world view is used to implement ULAM. Modular modeling techniques are used in ULAM to allow component models or submodels to be inserted as new data is collected and as new component models are developed. Figure 1 presents an overview of ULAM. Starting on the left of Figure 1, we see that the arrivals to the system are donors and patients. Either historical or generated streams of arrivals can be processed with ULAM. Historical information was available from 1990-1994, and this data is stored within ULAM. To fit the interarrival distributions of donors to 65 OPOs and patients to 132 Liver Transplant Centers, we used an estimation procedure employing a non-homogeneous Poisson process (NHPP) having a rate function that is exponential-polynomial-trigonometric with multiple periodicities. For example, given the time t_i for the ith patient to arrive at transplant center 2 (expressed in days since the start of January 1, 1991),

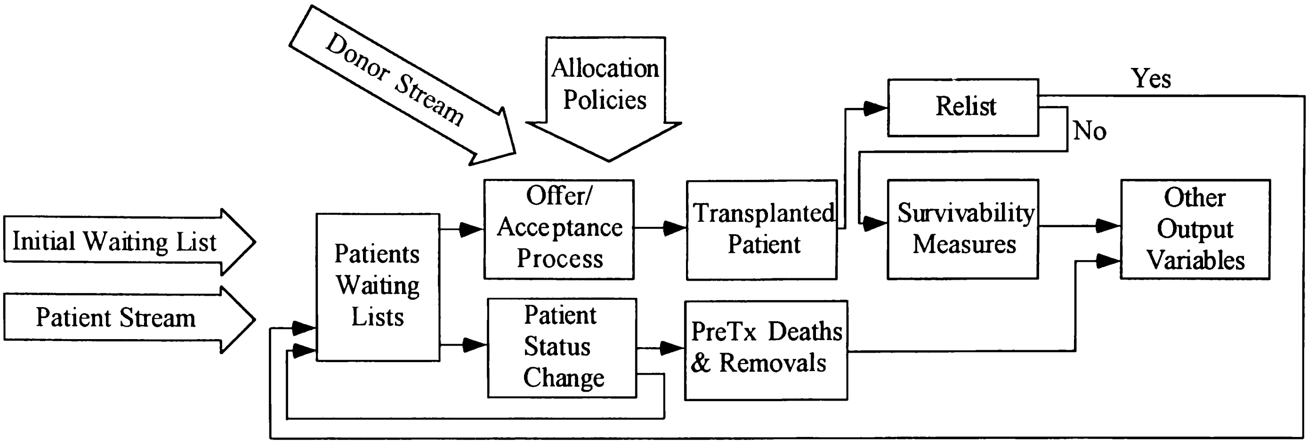

Figure 1: Overview of ULAM

the distribution function for the next arrival time t_{i+1} is

$$F_{t_{i+1}}(t) = 1 - \exp[-\int_{t_i}^{t} \lambda(z)dz]$$

where $\lambda(z) = -4.2747 + 0.00096752*z$
$+0.15562*\sin(z*2\pi/365+1.9728)$
$+1.2617*\sin(z*2\pi/7+0.45698)$
$+2.3340*\sin(z*2\pi-2.4037)$.

Notice that the three trigonometric rate components represent cyclic effects with periods of one year, one week, and one day, respectively. Details of the procedure are described in these proceedings (Kuhl, Wilson, and Johnson 1995). The characteristics of the donors are determined using a bootstrapping technique which randomly selects the characteristics of a generated donor from all donors in the 1990 to 1994 time frame. The characteristics of a donor include: age, weight, sex and blood type. This technique provides a set of generated donors with characteristics similar to the historical donors. When historical information is used, patients who have been relisted following an unsuccessful transplant are eliminated from the arrival stream as the time of arrival of a relisted patient is computed from a fitted relist function. The listing of a patient at multiple transplant centers is allowed in accordance with UNOS policies.

For the initial waiting list of patients, ULAM includes the actual waiting lists that existed at the beginning of each year from 1992 through 1994. A patient is added to the waiting list when the patient arrives. A patient is transplanted and taken off the waiting list when a graft is offered and accepted for that patient. An allocation policy ranks all patients waiting for a transplant in accordance with their medical urgency status and geographical location. This requires patient waiting lists to be organized by medical status and geographical location, and the lists are ranked in accordance with the policy being evaluated. The definitions of medical urgency status are:

Status	*Definition*
1	Patients must be in an Intensive Care Unit (ICU) due to acute or chronic liver failure and have a life expectancy of less than 7 days without a liver transplant.
2	Patients have been continuously hospitalized in an acute care bed for at least five days, or are ICU bound.
3	Patients require continuous medical care.
4	Patients are at home and functioning normally and for whom liver transplantation would be an elective procedure.
7	A patient listed as Status 7 is temporarily inactive; however, the patient continues accruing waiting time up to a maximum of 30 days.
8	A patient has died while waiting for a transplant.
9	A patient has been removed from the waiting list and is no longer considered as part of the UNOS system.

The policies employ a point ranking scheme where waiting time points are based on the rank of the longest waiting patient in the waiting list, that is, 10*(1+N−R)/N where N is the number of patients in the list and R is the patient's rank. The patient with the longest waiting time has rank N. In addition, points are assigned based on status (24, 18, 12, 6) and on blood type compatibility (10, 5, 0). This necessitates creating and reranking of the lists at every graft arrival. With as many as 6,000 patients on the waiting list and approximately 4,000 donors per year, the procedure for implementing the ranking of patients according to the allocation policy requires efficient data structures and computational procedures. A model built prior to ULAM required 4 hours on UNOS's mainframe computer for a 1 year run which ULAM performs in 40 seconds on a notebook computer. Further discussion of allocation policies is presented in a later section.

When a donor arrives, the quality of the graft harvested from the donor is assessed. Data available at UNOS permits the modeling of graft quality to be a function of the age of the donor. The graft is then offered to the patient ranked highest by the allocation policy taking into account the donor's and recipient's blood type, weight and age. The probability of accepting a graft by the doctor/patient is a function of recipient status. ULAM includes a Monte Carlo procedure for this acceptance process, where the probability of acceptance is a function of the medical status of the patient and the quality of the graft offered. If the graft is not accepted, then the next highest ranking patient is offered the graft. This continues until the graft is accepted or all patients have been considered. In the latter case, the graft is used for research or other medical purposes.

When the graft is accepted by a patient, the patient is transplanted and removed from the waiting list. The future status of the transplanted patient is then determined. First, it is determined whether the patient will require another transplant because of graft failure. In this case the patient is relisted at the transplant center that performed the transplant operation. Relist functions have been developed for each medical status using a technique developed by Kaplan and Meier (1974). The relist data was derived from the 1991-92 time period and allowed a two year follow-up period to determine if a patient was relisted. If the patient did not relist, their mortality following the transplant was determined. A logistic regression approach was employed for determining the mortality rate as a function of: (a) transplant center volume (number of transplants per year); (b) patient condition as reflected by the patient's medical status; and (c) whether the patient had a previous transplant. A similar analysis was performed for the relist function that revealed no significant effect of transplant center volume or previous transplant on the probability of relisting.

4.1 Status Change Event

As patients wait for a transplant, their medical status changes. When a patient arrives in the model an initial probability table is used to assign a medical urgency status to the patient. To model status change, a transition probability matrix, that is, a Markov chain, is constructed which models the probability of a change from one status to another in one day. The transition probabilities are estimated from a count of the number of times a daily transition was made from one status to another divided by the total number of daily transitions from the particular status. By assuming a Markov chain model, we are assuming that the time spent by a patient in each medial urgency status has a geometric distribution and that the probability of making a transition out of a given status after an additional day has elapsed is the same no matter how long the patient has already spent in the given status. Although the data revealed that this was not an appropriate assumption, validation studies showed that it was sufficient for comparing alternatives. Since transitions from the inactive state depend on the previous state of the patient, Status 7 was expanded to status' 70, 71, 72, 73 and 74 where the second digit represents the previous state and Status 70 indicates that the patient was initially placed in the inactive status.

At the current time, a semi-Markov model for status change is being developed. A holding time for each status transition has been fit using UNIFIT II (Law and Vincent 1994). Only forty percent of the holding times could be portrayed by one of the distribution types included in UNIFIT II. It was then decided to employ PrimeFit (Wagner and Wilson 1993) which fits Bezier distributions to the holding times. The semi-Markov approach to modeling status change is currently being validated.

4.2 User Interfaces

To build or modify ULAM, the standard SLAMSYSTEM modeler's interface is used. To run ULAM, SLAMSYSTEM's user interface was adapted to select policies and to specify control parameters such as run length, number of runs and data sources. Two of the five user screens adapted for ULAM are presented in Figures 2 and 3. In Figure 2, the policy to be run can be selected and the form of the input data, historical or generated, is made. The starting year and run length and whether to clear statistics can be input. The number of runs to be made is established and the editing of inputs and component modules can be done by selecting the EDIT INPUTS button. The selection of an animation is also allowed, and the SIMULATE button initiates the desired simulation.

On the bottom of this user interface screen are tabs for selecting the four other user interface screens. The SUMMARY screen allows the browsing of outputs from

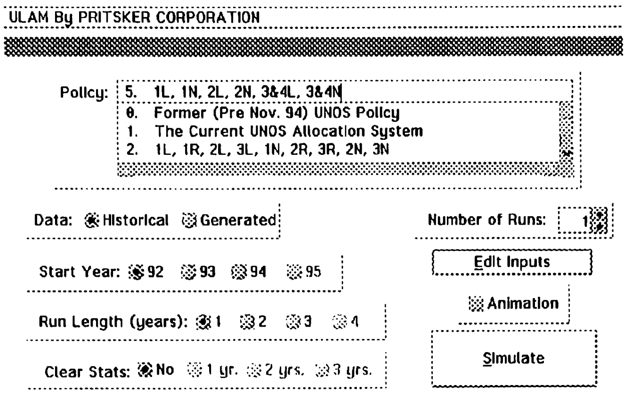

Figure 2: SIMULATE Screen of ULAM User Interface

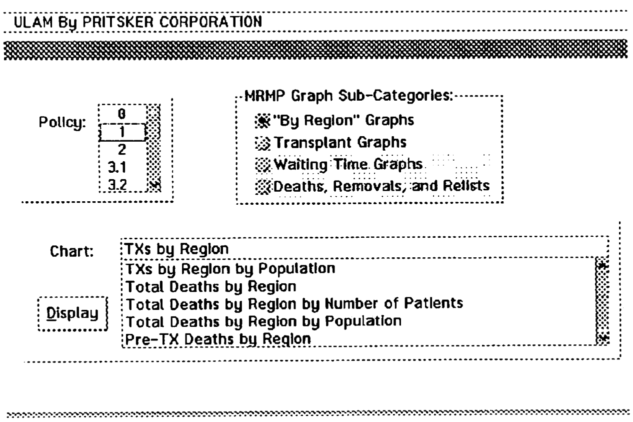

Figure 3: OUTPUT-MRMP Screen of ULAM User Interface

policy runs. The tab OUTPUT-SRSP provides access to displays of single-run, single-policy charts. Tab OUTPUT-SRMP allows the viewing of single-run, multiple-policy charts, and tab OUTPUT-MRMP allows the display of multiple-run, multiple-policy charts. Figure 3 presents the screen for the user interface associated with OUTPUT-MRMP, and shows the subcategories of graphs, that is, graphs comparing policies by regions, transplantation results, waiting time values, and the number of deaths, relists and removals.

4.3 Output Variables

The performance measurements used in evaluating the various allocation policies fall into the following categories:

Medical Utility

* Number of people transplanted
* Percentage of patients surviving transplantation
* Number of pre- and post-transplant deaths
* Surrogate measures of costs
* Number of patient-days in each medical status
* Percentage of transplants by medical status
* Distance the organs travel

Justice

* Percentage of patients transplanted by status
* Waiting time by patient and regional characteristics
* Number of pediatric patients transplanted

5 LIVER ALLOCATION POLICIES

Many allocation policies have been suggested. ULAM has been run for 15 different policies. Five policies were selected by the UNOS Allocation Modeling Oversight Committee for an initial detailed assessment. Each policy specifies a grouping of waiting patients according to a geographical area and a medical urgency status, for example, consider local patients in Status 1 (L1) first, then local patients in Status 2 (L2), etc. For policy specifications, local means patients waiting at Transplantation Centers associated with the OPO at which a donor arrives. Regional means the current UNOS regions. Super-Regions mean the U.S. divided into three major geographical areas (east, middle, west). National means the entire country. Note that a policy that specifies L1 first then R1 implies that ranking for Regional - Status 1 excludes Local - Status 1 patients. This complicates the ranking procedure for computing waiting time points as the waiting list changes depending on the location of a donor.

Policy 1 is the current allocation policy and is designed to balance patient need for a transplant with successful transplant outcome. In order to limit organ travel distance, the policy allocates liver grafts to the local patients first, followed by regional patients, and then patients on the national list. Patients who have the highest medical urgency for a liver transplant are looked at first in any given level. Status 3 and 4 patients are grouped together. Codes for each policy are given in the following form: [L1,2,3/4; R1,2,3/4; N 1,2,3/4].

Policy 3.2 allows for broader sharing of liver grafts to Status 1 and then Status 2 patients on a local and regional basis. Local allocation to Status 3 patients is made prior to national allocation to Status 1 patients. No transplants are made to Status 4 patients. [L1, R1, L2, R2, L3, N1, R3, N2, N3]

Policy 5 allocates liver grafts to local Status 1 patients first then national Status 1 patients followed by local Status 2 patients and national Status 2 patients, followed by local Status 3 and 4 patients, followed by national Status 3 and 4 patients. This policy resembles a single national list and allows broader national sharing to the most medically ill patients. [L1, N1, L2, N2, L3/4, N3/4]

Policy 8 allocates liver grafts to a local area defined by state boundaries, then to 3 super-regions and then nationally. This allows for more grafts to remain in the state of the donor and limits graft travel distance. This policy uses the medical urgency rules associated with Policy 3.2. [St1,SR1, St2, SR2, St3, N1, SR3, N2, N3]

Policy 9 allocates liver grafts to the local patients first, followed by patients listed within a super-region, and then to patients on the national list. This policy adapts the current policy Policy 1, by allowing for larger consideration of Status 1 patients after the local level. [L1,2,3/4, Super Region 1,2,3/4; N1,2,3/4]

6 VERIFICATION, VALIDATION AND ACCEPTANCE

The verification process involved testing each component model to determine if it operates properly. Extensive exploration of the allocation policies was performed to ensure that grafts were offered to the appropriate class of patients by status and location. Printouts of the matching of a donor to a patient and of the offering process were made and the models were verified.

An animation was developed which illustrates the flow of grafts to patients. Figure 4 is a snapshot of the animation screen showing the delivery of liver grafts to patients in accordance with UNOS regions. The color of the grafts and patients indicate their blood types. Also shown on the animation are the total distance traveled by all grafts and the current simulated time. A second animation shows a dynamic table which updates the number of transplants, pre-transplant deaths and patients removed from the waiting list by UNOS region. The animation helped to verify that ULAM operates the way it was intended.

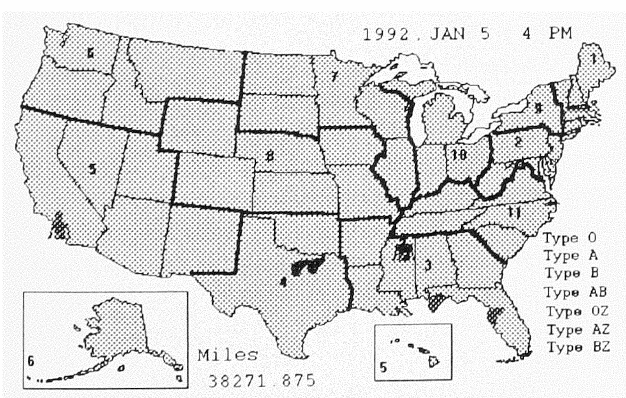

Figure 4: Snapshot of Animation Screen Showing the Routing of Livers to Patients

ULAM was validated by comparing each component model output as well as the total system model output to actual results over the 1992-94 time period. For example, for the donor streams, the stochastic process that was generated over four years (1991-94) was fitted with three years of data (1991-93) and used to project 1994 donor arrivals. The projection of 1994 was deemed acceptable.

The component models were developed using data in the same time period as that for which a validation was sought. This is necessitated due to major changes that occurred in liver transplantation from 1988-92. In verifying and validating the component modules, it was determined that the Markovian assumption for the status change component model was the most heroic and the most sensitive to parameter estimates. Thus, it became the focus of the validation effort. Markov transition probabilities were estimated for the time periods 1992, 1993, 1994, 1991-94 and 1992-94. Validation runs were made with each of these sets of transition probabilities. During preliminary runs of the model, it was determined that a three year period was necessary in order to compare policies. Thus, the validation runs were made for the period 1992 through 1994 with each of the transition probability matrices described above. In early validation runs, the fine detail of the model could not be reproduced and ULAM was rejected as a valid model for the liver transplantation process. In the validation runs, policy 1, the current policy, was used. After several weeks of performing validation exercises, it was uncovered that the policy in place from 1992 through November 1, 1994 differed from the current policy. The prior policy, named Policy 0, grouped Status 2, 3 and 4 patients together whereas the current policy only groups Status 3 and 4 patients together. Validation runs were then made with Policy 0 operating for the first two years and ten months of the third year, and then Policy 1 was in effect for the last two months of 1994. These validation runs produced results that were sufficiently close to actual results that a comparison of policies based on ULAM was deemed to be appropriate. The validation outputs for 1992-94 based on historical input streams and Markov chains based on both 1991-94 and 1992-94 data are presented in Figure 5.

To gain acceptance for the model, ULAM was presented to many individuals and groups within the transplantation community including the following UNOS committees: Allocation Modeling Oversight, Liver and Intestinal Organ Transplantation, Scientific Advisory, and Allocation Advisory. Throughout this period, changes and modifications and additional runs were made to promote understanding and to improve ULAM. Presentations were then made to the

Department of Organ Transplantation Oversight Committee and the UNOS Board of Directors. Each UNOS meeting is open and outside interested parties, and other modelers were in attendance. Their suggestions and recommendations were considered and included in ULAM after careful evaluation. Acceptance of the model was obtained through a review of the component models and through reviews of the outputs of ULAM for the various policy comparisons for which ULAM was built. This acceptance/auditing step is an important part of the simulation modeling process. (Withers, Pritsker, and Withers 1993)

6.1 ULAM Outputs and Performance Measures

An overview of the policy comparisons for the five policies assessed is given in Figure 6. These results are for historical donor and patient arrivals during 1992 through 1994. These outputs show that the number of non-repeated transplants, that is, the number of different patients that are transplanted, differs over the five policies. The difference increases as a policy transplants the sicker patients which have a higher relist probability. When a patient is relisted, a numerically lower medical urgency status is typically assigned, giving relisted patients a higher priority for transplantation. This is reflected in the model output in terms of the number of different patients transplanted as well as the number of Status 1 patients transplanted. Pediatric patients usually are assigned a numerically lower medical urgency status and this is reflected in the number of pediatric transplants that occur for those policies that transplant Status 1 and Status 2 patients nationally prior to treating Status 3 patients locally or regionally.

The number of days in status is a cost-related measure, as it indicates the number of days patients would be in the hospital and in intensive care units. It can be seen that there are a large number of patient-days in Status 3 which requires continuous medical monitoring and, if these patients are in the hospital, would reflect an added cost for those policies that have a low percentage of transplants for Status 3 patients.

The share type measures relate to the use of grafts locally. Currently there is a debate in the transplantation community as to whether a low percentage of grafts used locally would adversely affect the donor rate. If it does, there is a secondary effect, not included in ULAM, of a potential decrease in the donor arrival rate for such policies. In the outputs presented in Figure 6, the percent of transplants locally and regionally is given in accordance with the OPO definition of local and regional boundaries even though states and super-regions may be used in the allocation policy. Distance measures may have an impact on transplantation survival rates as the longer a graft is delayed before its use, the greater its possible deterioration.

With regard to death measures, ULAM presents quantitative information reflecting the intuitive and experiential nature of the different policies. Expectations were that the current policy would experience more pre-transplant deaths because it is not oriented to transplanting national Status 1 patients before local and regional patients. Policies 5 and 8 are more oriented to transplanting Status 1 patients first. Policy 3.2 is a compromise, and the output measures reflect this. By transplanting less sick patients, the number of post-transplant deaths is decreased and the quantitative values for this are shown. The total number of deaths occurring during the three year simulation period indicates the largest difference is 110 deaths between policies 5 and 1. For these two policies, the difference in the waiting list at the end of the simulation is 732 patients. The larger number of patients waiting at the end of the simulation reflects a negative performance for the policy. In an attempt to quantify deaths that occur after the simulation, the time of death for those patients transplanted was projected and then discounted back to the end of the simulation. For those on the waiting list, a projection of the number of pre-transplant deaths occurring after the simulation under the condition of no donor arrivals was made. This involved performing a Markov chain analysis to determine the expected number of deaths on a given day after the simulation period and then discounting it back to the final day of the simulation period. An analytic model was developed for this purpose to arrive at the discounted after simulation waiting list deaths. Results for a discount factor of 0.2 are shown in Figure 6. In ULAM's detailed output, values for discount factors of 0, 0.2 and 0.5 are presented. This use of an analytic model is an example of the use of prior information (the method of conditional expectations) as a variance reduction technique.

If the discounted after simulation "deaths" are added to the total pre- and post- transplant deaths, then the total simulation period "deaths" show a surprising similarity for the five policies evaluated. This was not expected as the five policies selected for evaluation were considered to be different with regard to the death measures included in the analysis. Another surprising result is that the number of patients removed from the list over the three year period are all similar. This was not the case for 1 and 2 year runs.

An extensive number of waiting time measures are estimated using ULAM. Only two such measures are presented in Figure 6. Other waiting time measures are time to removal, time in last status before transplant,

			VALIDATION RUNS			
Validation Period		1992-94	1992-94	REL. %	1992-94	REL. %
Transition Probabilities		Actual	1991-94	DIFF.	1992-94	DIFF.
Total Transplants		9990.0	9918.7	-1%	9920.1	-1%
Transplants by Status %	Status 1	23.0	24.9	8%	25.8	12%
	Status 2	25.1	27.1	8%	25.1	0%
	Status 3	49.1	46.1	-6%	47.0	-4%
	Status 4	2.7	1.8	-33%	2.1	-22%
Share Type %	Local	63.4	59.6	-6%	59.7	-6%
	Regional	16.9	27.0	60%	26.8	59%
	National	19.7	13.4	-32%	13.5	-31%
Distance (Miles)	Mean	270.8	291.1	7%	289.5	7%
	Median	110.6	126.0	14%	125.9	14%
	% > 1000	5.9	6.4	8%	6.3	7%
Pre-TX Deaths, by status	Status 1	394.0	342.4	-13%	290.1	-26%
	Status 2	289.0	322.2	11%	291.5	1%
	Status 3	320.0	388.2	21%	369.6	16%
	Status 4	151.0	168.4	12%	161.8	7%
	Status 7	605.0	713.9	18%	611.4	1%
	Total	1759.0	1935.1	10%	1724.4	-2%
Other WL Removals	Status 1	204.0	169.0	-17%	143.2	-30%
	Status 2	226.0	241.2	7%	223.3	-1%
	Status 3	409.0	465.7	14%	432.5	6%
	Status 4	292.0	306.3	5%	300.5	3%
	Status 7	738.0	831.5	13%	788.9	7%
	Total	1869.0	2013.7	8%	1888.4	1%
End Wait List Patients	Status 1	20.0	24.1	21%	26.0	30%
	Status 2	76.0	145.0	91%	143.0	88%
	Status 3	1898.0	2025.2	7%	2079.4	10%
	Status 4	1310.0	1105.3	-16%	1320.5	1%
	Status 7	755.0	660.7	-12%	738.5	-2%
	Total	4059.0	3960.3	-2%	4307.4	6%

Figure 5. ULAM Validation Outputs for 1992-94

		UNOS Liver Allocation Model Policy Comparison, 1992-1994, 10 Runs								
Policy	1	32	5	8	9		R32	R5	R8	R9
General Measures								RELATIVE % OF POLICY 1		
No. of Non Repeated Tx	8672.5	8460.7	8237.1	8336.6	8647.9		-2.44	-5.02	-3.87	-0.28
No. of Repeat Tx (Previous)	1239.9	1448.6	1677.7	1571.2	1266.3		16.83	35.31	26.72	2.13
Total Tx	9912.4	9909.3	9914.8	9907.8	9914.2		-0.03	0.02	-0.05	0.02
No. of Pediatric Tx	1443.4	1471.7	1568.2	1503.2	1445.7		1.96	8.65	4.14	0.16
No. of Post Tx Deaths < 12 months	1512.4	1639.1	1782.1	1708.7	1542		8.38	17.83	12.98	1.96
% Survival > 12 mos. (not relisted)	81.3	79.4	77.2	78.3	80.9		-2.34	-5.04	-3.69	-0.49
% Survival > 24 mos. (not relisted)	75.9	73.8	71.4	72.6	75.5		-2.77	-5.93	-4.35	-0.53
Cost Related Measures										
No. of Days in Status:										
Status 1	19805	11757.3	2953.8	7311.1	17633.1		-40.63	-85.09	-63.08	-10.97
Status 2	102740.2	86579.3	74463.4	76893.6	99125.6		-15.73	-27.52	-25.16	-3.52
Status 3	1597932	1749162	1957365	1857934	1637256		9.46	22.49	16.27	2.46
Status 4	965645.2	1058936	1070463	1066563	986030.4		9.66	10.85	10.45	2.11
% TX by Status:										
Status 1	25.2	32.4	41.2	36.3	27.1		28.57	63.49	44.05	7.54
Status 2	33.1	42.1	50.8	48.6	35.1		27.19	53.47	46.83	6.04
Status 3	39.6	25.4	7.9	15	36.2		-35.86	-80.05	-62.12	-8.59
Status 4	2.1	0	0.2	0	1.7		-100.00	-90.48	-100.00	-19.05
Share Type Measures										
% Tx Local	59.3	41.9	16.9	20	61.5		-29.34	-71.50	-66.27	3.71
% Tx Regional	26.9	36.9	5.5	4.8	2.5		37.17	-79.55	-82.16	-90.71
% Tx National	13.8	21.3	77.5	75.2	36		54.35	461.59	444.93	160.87
Distance Average (miles)	294.1	394	934.8	489.1	290.9		33.97	217.85	66.30	-1.09
Distance Median (miles)	126.5	211.9	774.2	362	126.7		67.51	512.02	186.17	0.16
% of Distances > 1000 miles	6.6	10.2	38.6	10.2	5.4		54.55	484.85	54.55	-18.18
% Blood Type Exact Match	71.5	68.1	72	68.8	71.2		-4.76	0.70	-3.78	-0.42
Death Measures										
No. Pre Tx Deaths	1679.2	1496	1313.9	1387.8	1627.6		-10.91	-21.75	-17.35	-3.07
No. Post Tx Deaths	1547.7	1661.5	1802.1	1736.2	1573.9		7.35	16.44	12.18	1.69
Total Deaths (Pre + Post)	3226.9	3157.5	3116.0	3124.0	3201.5		-2.15	-3.44	-3.19	-0.79
Discounted After Sim WL Deaths (.2)	1048.8	1130.6	1217.8	1178.8	1068.8		7.80	16.11	12.40	1.91
Discounted After Sim PostTX Deaths(	305.8	316.3	314.2	312.7	305.7		3.43	2.75	2.26	-0.03
Total Simulation Period "Deaths"	4581.5	4604.4	4648.0	4615.5	4576.0		0.50	1.45	0.74	-0.12
No. End Waiting List (Initial = 1675)	4413.4	4775.4	5145.2	4988.9	4494.4		8.20	16.58	13.04	1.84
No. Removed	1871.7	1829.2	1790.9	1804.1	1856.2		-2.27	-4.32	-3.61	-0.83
No. Relisted	1850.9	1975.4	2127.7	2053.1	1865.7		6.73	14.95	10.92	0.80
Total Waiting Time Measures										
Mean (Days from Arrival to Tx)	147.3	151.7	164.1	159.4	157.6		2.99	11.41	8.21	6.99
Median (Days from Arrival to Tx)	70.8	64.6	62.6	63.2	79.8		-8.76	-11.58	-10.73	12.71

Figure 6. ULAM Policy Comparisons for 1992-94

time to post-transplant death and time to relist. Each of these waiting time measures can be conditioned on status, geographical area, and patient attributes.

Based on the outputs produced by ULAM, it was decided not to make a policy change at the current time. Runs using the generated donor and patient arrival streams through 1997 are scheduled to be performed. In addition, several advanced modeling features are being investigated such as the use of a Semi-Markov model for transition probabilities and holding times.

7 SUMMARY

The process of modeling and simulation has been accepted by the UNOS transplantation community. ULAM has demonstrated how the formal modeling and simulation process can produce outputs that support policy evaluation for a national medical problem. Confidence in the model and its outputs for comparing alternative policies has been established. Refinements and extensions will further boost this confidence and the use of modeling and simulation in the transplantation community.

From a technical point of view, ULAM includes many advanced capabilities available from the simulation community. Common random-number streams and prior information are used as variance reduction techniques. Interarrival times and holding times were fit using developed techniques and programs. Bootstrapping methods were employed for attribute sampling. Statistical techniques were used for output variable estimation. SLAMSYSTEM with its capability for complex data structure development has produced a 240 to 1 decrease in running time, and SLAMSYSTEM's user interface provides a means to allow non-simulation personnel to make runs, to modify inputs in component modules, and to browse the outputs.

ULAM is a simulation program that can support the transplantation community in the evaluation of alternative policies which will yield improved medical utility and greater justice for waiting liver transplantation patients.

ACKNOWLEDGEMENTS

The authors wish to thank Gene A. Pierce, Executive Director, UNOS, and Walter K. Graham, Assistant Executive Director, UNOS, for their support and encouragement throughout this project. They have helped ensure that ULAM was developed in an unbiased fashion and permitted us total scientific leeway in the model development and use. The authors also wish to acknowledge the early efforts and contributions of Timothy J. Breen, Ph.D., in developing the fundamental concepts of the liver allocation model. Dr. Breen's suggestions and advice were invaluable in the development of the data systems used to support the modeling process. We also appreciate the constructive comments of Ms. Judy Braslow, Ms. Gwen Mayes and Mr. Remy Aronoff of the Division of Organ Transplantation, HRSA, DHHS.

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