# Social and Utilitarian Considerations for Allocating Organs within a National Organ Sharing System: A Computerized Simulation Model for Policy Decision-Making*

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## Abstract

**Background:** An organ-sharing system should achieve fairness and optimal graft longevity. Balancing between social and utilitarian considerations is a sensitive ethical, public and medical issue that requires a means to examine the consequences of any allocation policy or planned changes thereof.

**Objective:** To evaluate the performance and applicability of a computerized simulation model by examining the impact of two opposing organ allocation policies (social or utilitarian) on predicted organ distribution regarding age, waiting time, recipient sensitization measured by panel reactive antibody level, and overall donor-recipient tissue matching (measured by the number of HLA antigen mismatches).

**Methods:** Using a computerized simulation model, virtual donors and recipients were emulated and organs were allocated according to either social algorithms or utilitarian policies. The resulting number of HLA mismatches, PRA, age, and waiting time distributions were compared between allocation strategies.

**Results:** Simulating allocation of 7,000 organs to 17,000 candidate recipients and implementing social policies yielded donor-recipient compatibility comparable to utilitarian policies (0–1 mm: 19.4% vs. 28%) while allocating 66.7% of organs to long waiters (>48 months).

**Conclusion:** This computerized simulation model is a valuable tool for decision-makers establishing or modifying organ allocation policies.

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Viewing transplantable organs as a precious national resource dictates that their allocation within any national or regional organ-sharing system be just, fair and impartial. The determinant parameters in any allocation scheme are both social and biological (utilitarian). Thus the relative weight given to donor-recipient tissue compatibility and the candidate recipient pre-sensitization levels (panel reactive antibody) on one hand, and the importance given to age and waiting times on the other, may vary and reflect the social philosophy and values of a given community [1]. The ideal allocation algorithm should achieve complete social fairness and optimal graft longevity at the same time. However, since this goal is probably unachievable, an optimized approach combining both social values and utilitarian considerations should be sought.

The implementation of any given allocation algorithm in real life will require the passage of many years in order to evaluate the impact of any change in policy or the relative weight of any parameter. Thus, a simulation model can provide the decision-makers with a valuable tool that will obviate the need for a long-term observation.

The present study examines the performance of an adaptable and comprehensive simulation model, by evaluating the impact of two opposing approaches to allocation – social and utilitarian – on overall donor-recipient tissue compatibility, waiting times, age, and PRA levels of the recipients. This model and its application are proposed as a valuable tool for policy decision-making in national organ-sharing organizations.

## Material and Methods

A simulation model with two separate phases was developed, using the SAS System for Windows (Carey, NC, USA).

### Donors and recipients

The first phase consisted of creating virtual donors and recipients having specific attributes in proportions comparable to their prevalence in the general population. This was achieved by generating a set of random numbers for each attribute of every emulated donor and recipient entity. The attribute was assigned according to this number, representing the frequency of each specific attribute in the general population. Thus, each virtual donor and recipient entity appeared with age, ABO blood group and tissue antigens (HLA-A, -B and -DR configuration); recipient entities had, in addition, PRA level and waiting time. HLA configuration includes two specific antigens in each -A, -B and -DR HLA loci. Ten sets of donors and recipients were created independently using different random number seeds for each set in order to repeat the simulation 10 times independently.

### The allocation process

The second phase of the simulation consisted of allocating the virtual organs according to two policies. The first is a social policy, which includes the scoring of waiting time, PRA levels and age, and either disregarding HLA altogether (1a) or scoring HLA match by cross-reacting groups (1b). The second is a utilitarian policy,

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including the scoring of age, PRA and HLA matching by either gene to gene (2a) or CREG (2b) methods, and disregarding waiting time entirely. GTG match is defined as the number of specific antigens shared by both donor and recipient, measured by the number of mismatches. The CREG system defines clusters of specific HLA Class I (-A and -B) antigens that do not react against each other. Matching according to the CREG method is computed by summing the number of mismatched CREG in addition to the number of mismatched HLA-DR antigens. Thus the CREG system is more relaxed since it does not require precise antigenic matching; rather, belonging to the same CREG is considered a match between donor and recipient.

For each organ a stepwise search among all candidates was conducted and a compatibility score was calculated for each candidate.

- *Blood type:* ABO identity was obligatory for matching. All candidates with non-identical ABO blood groups were excluded at this point.
- *Cross-match:* The probability of a positive cross-match was calculated according to the PRA level of the candidate recipients in proportions comparable to real-life data. A positive cross-match excluded a candidate from eligibility at this point in the search algorithm.
- *Waiting time:* Waiting time was divided into four categories: 0–24 months, 25–48 months, 49–96 months, and 96 months and more.
- *PRA:* Panel reactive antibody level was also divided into four separate groups: 0–25%, 26–50%, 51–75%, and 76–100%. The different PRA groups were scored equally in the two policies.
- *Age:* Candidates were divided according to age group as well: 0–16 years, 17–40 years, 41–60 years, and over 60. The score for the different age groups did not differ between the policies.

Each organ was allocated to the recipient with the highest score. The simulation was run 10 times independently and the results were then averaged in order to achieve a high confidence level. The scoring point systems for each policy are depicted in Table 1.

## Evaluation of the results

The resulting distribution of PRA levels, recipients' age, and waiting time were analyzed. Donor-recipient HLA compatibility outcome was measured in two ways: number of mismatches in individual HLA -A, -B and -DR antigens and number of mismatches in CREG class I and HLA-DR antigens. When HLA was taken into account in the allocation process (1b, 2a and 2b), the resultant compatibility was assessed by the number of mismatches and measured using the parallel HLA matching method (GTG or CREG respectively).

Statistical analysis was performed to evaluate significant differences between the various allocation methods using the SAS package.

## Results

The model created 7,000 organs and 17,000 virtual organ candidate recipients in 10 runs of simulation; thus 7,000 donor-recipient pairs were available for analysis. The distribution of age, blood groups,

CREG = cross-reacting groups
GTG = gene to gene

**Table 1.** The scoring system for the different allocation algorithms

| Allocation policy | | | | Social | | Utilitarian | |
|---|---|---|---|---|---|---|---|
| | | | | 1a | 1b | 2a | 2b |
| Age group (yrs) | | | 0–16 | 4 | 4 | 4 | 4 |
| | | | 17–40 | 2 | 2 | 2 | 2 |
| | | | 41–60 | 1 | 1 | 1 | 1 |
| | | | >60 | 0 | 0 | 0 | 0 |
| PRA level (%) | | | 0–25 | 0 | 0 | 0 | 0 |
| | | | 26–50 | 2 | 2 | 2 | 2 |
| | | | 51–75 | 4 | 4 | 4 | 4 |
| | | | 76–100 | 6 | 6 | 6 | 6 |
| Waiting time (mos) | | | 0–24 | 2 | 2 | 0 | 0 |
| | | | 25-48 | 4 | 4 | 0 | 0 |
| | | | 49-96 | 6 | 6 | 0 | 0 |
| | | | >96 | 8 | 8 | 0 | 0 |
| HLA matching method: # of mm* | | | | None | CREG | GTG | |

| DR | B | CERG-B | Total | None | CREG | GTG |
|---|---|---|---|---|---|---|
| 0 | 0 | | 0 | 0 | 7 | 6 |
| 0 | | 0 | 0 | 0 | 6 | |
| 0 | 1 | | 1 | 0 | 5 | 5 |
| 0 | | 1 | 1 | 0 | 4 | |
| 0 | 2 | | 2 | 0 | 3 | 4 |
| 0 | | 2 | 2 | 0 | 2 | |
| 1 | 0 | | 1 | 0 | 5 | 3 |
| 1 | | 0 | 1 | 0 | 4 | |
| 1 | 1 | | 2 | 0 | 3 | 2 |
| 1 | | 1 | 2 | 0 | 2 | |
| 2 | 2 | 1 | 3 | 0 | 1 | 0 |

Organs were assigned to the candidate with the highest score.
* Only CREG- B without CREG-A was included in order to compare with conventional B and DR matching.

PRA levels, waiting times, and ages were very similar to their actual distribution in the real-life population of transplant candidates [Figure 1].

## Waiting time

Policy 1 ("social") allocated 65.7% (1a) and 66.7% (1b) of all organs to recipients waiting more than 48 months. In contrast, the utilitarian policy allocated only 35.1% (2a, CREG) and 29.8% (2b, GTG) to long waiters ($P = 0.0005$).

## PRA

There was no difference between the two policies regarding allocation to low and high PRA candidates. Thus, with each policy approximately 30% of organs were allocated to high PRA recipients.

## Age

There was no difference in the proportion of organs allocated to each age group: 77% were allocated to recipients aged 10–50 years, 9% to pediatric patients, and approximately 14% to older recipients (age >50).

## Donor-recipient compatibility

Donor-recipient compatibility using the various algorithms is summarized in Table 2. The resulting donor-recipient compatibility
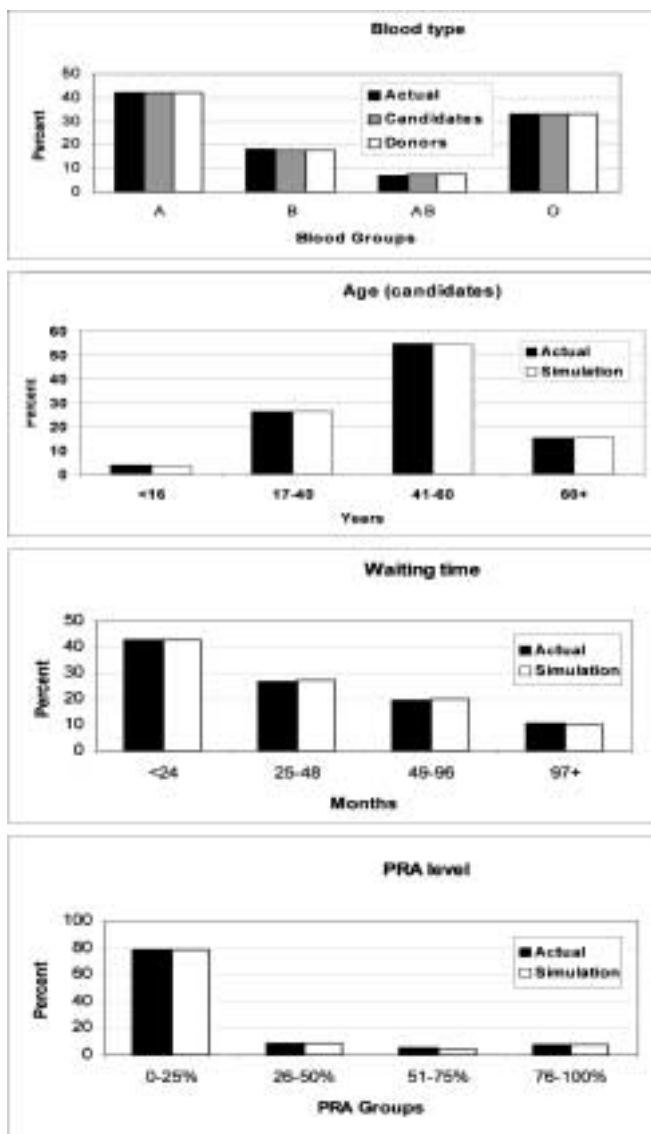
**Figure 1.** Distribution of blood type groups, age groups, PRA levels and waiting time. The simulated candidates vs. the actual statistics of the Israeli national waiting list for renal transplantation.

occurring randomly in policy 1a, namely, ignoring HLA matching in the allocation process, was the worst, achieving a low 0.1% of 0–1 mm, and as high as 88.6% of 4–6 mm when evaluated by strict GTG, or 6.1% of 0–1 mm and 40.2% of 4–6 mm when assessed by CREG. Implementing policy 1b, i.e., allocating organs by the CREG method using the social policy resulted in 19.4% of 0–1 mm, 43.4% of 2–3 mm and 37.1% of 4–6 mm. Thus, the social policy, which considers both waiting time and the level of CREG match, yields a significantly higher proportion of 0–1 mm and lower fraction of 4–6 mm ($P = 0.0001$).

The "utilitarian" policy, which disregarded waiting time and allocated organs by CREG (2a) yielded, expectedly, the highest fraction of 0–1 mm (28%) and the lowest of 4–6 mm (10.7%). The same policy using the GTG (2b) allocation scheme resulted in 7.7% of 0–1 mm and 31.6% of 4–6 mm ($P = 0.0005$ and $P = 0.0001$, respectively).

**Table 2.** Distribution (%) of the number of mismatches (mm) between the various allocation algorithms

| Group | 1a | | 1b | 2a | 2b |
|---|---|---|---|---|---|
| Allocation by | Pure social | | Social + CREG | Utilitarian by CREG | Utilitarian by GTG |
| Evaluated by | GTG* | CREG* | CREG | CREG | GTG |
| # of mm | | | | | |
| 0–1 | 0.1 | 6.1 | 19.4 | 28 | 7.7 |
| 2–3 | 11.3 | 53.7 | 43.4 | 61.3 | 60.7 |
| 4–6 | 88.6 | 40.2 | 37.1 | 10.7 | 31.6 |

\* Since HLA was not included in the allocation scheme, the figures actually represent the random matching achieved within the donor-recipients pairs.

## Discussion

The increasing gap between the availability of and demand for transplantable organs requires the use of an allocation algorithm that is both just and efficient. The relative weight given to each parameter in the allocation scheme is a crucial factor affecting the final allocation decision.

When community values and preferences were studied, it appeared that age, prognosis (expected graft longevity), and parenthood were the most influential deterministic factors to rank priority for organ allocation [1]. Implementation of such priority ranking values in the United Network for Organ Sharing allocation policies – by giving extra points for waiting time and pediatric status and eliminating points for certain HLA match grades – resulted in an increase in the number of transplants in minorities and long waiters in the mandatory sharing group of 0 mm [2]. However, since implemented in this group specifically, it did not have any effect on waiting time on non-mandatory sharing recipients.

The use of computer simulation models in an attempt to fine-tune allocation algorithms has been suggested and implemented before. Zenios at al. [3] used a computer simulation model to compare alternative allocation schemes to the UNOS policy in effect. Implementing distributive efficiency algorithm and considering waiting time, expected graft survival and quality of life, and promoting allocation to disadvantaged minorities resulted in shortening the mean waiting time and increased the overall likelihood of transplantation [3]. A simulation-derived allocation model was implemented in Eurotransplant in 1996, aiming at giving higher priority to long waiters while optimizing HLA matching [4]. Analyzing the actual results showed a decrease in waiting times, higher transplant rates in pediatric patients, yet the fraction of 0 mm transplants remained constant [4]. Others, who claimed that the waiting time parameter is devaluated, thus casting doubt regarding fairness, justice and equability in organ allocation [5], raised the issue of relative weight given to waiting time. Delmonico et al. [6], who combined both level of HLA match and population distance in their algorithm, reported their adoption of a policy with higher weight for waiting time.

UNOS = United Network for Organ Sharing

Moreover, the use of the cross-reacting groups method was suggested as a means to achieve better matching in candidate recipients with uncommon HLA phenotypes that decreased the overall likelihood of transplantation [7,8]. The impact of CREG matching on graft survival is under debate. While some authors see an advantage only in a small percentage of overall transplants performed [9,10], others report superiority in 3 year graft survival as well as in cost-saving [11,12].

The positive CREG matching effect on graft survival in Europe was attributed to the underlying effect of conventional HLA matching [13]. However, a positive effect of CREG matching in sensitized, re-transplant recipients in the United States was observed [14]. It seems that even if CREG matching yields a marginal effect in terms of graft survival, it allows for better matching in a limited donor and recipient pool size.

The definition of "social" and "utilitarian" policies in this study is obviously arbitrary. However, due to the flexibility of the model, the values assigned to any parameter in any approach can be modified in accordance with the specific priority ranking of the relevant society. The simplest method of achieving absolute social fairness would seem to be the use of waiting time alone, disregarding all other parameters; in other words: first in, first transplanted. However, this would put at a disadvantage the highly sensitized candidates and the pediatric patients and will result in a low degree of donor-recipient compatibility. This in turn is expected to decrease expected graft survival, and the need for re-transplants would grow. In contrast, the ultimate utilitarian approach would be to allocate organs to recipients with the highest probability of long-term graft survival. Thus, candidates with a high degree of HLA matching, low PRA and shorter waiting times (associated with less co-morbidity) would rank highest in the priority scale. Socially, this would be unacceptable. In the present model, each approach contained elements of its counterpart. Thus, the social approach did consider tissue matching using the more relaxed CREG method, and giving a higher score to waiting time, while the utilitarian approach considered age and pre-sensitization. In contrast to other studies describing simulation models [3,6], the endpoint of this model was not the prediction of survival and quality of life. Rather, being a flexible tool in determining allocation strategy, it looks at the impact of policy changes on parameters such as waiting time, overall donor-recipient compatibility, and likelihood of transplantation in the various age groups and as a function of candidates' pre-sensitization.

The results obtained with the social strategy regarding waiting time show a threefold increase of such likelihood in long waiters. Yet, the use of the CREG class I and DR match combined in this policy (1b) resulted in an impressive proportion of 0–1 mismatch (19.7%) and a relatively low proportion of low level 4–6 mismatches (12.6%). These results are not far from those obtained with the utilitarian approach and by measuring compatibility using the CREG system (28 and 10.7%, respectively). Thus, an allocation algorithm that favors the much disadvantaged long waiters but still maintains a high level of donor-recipient compatibility can be identified.

## Conclusion

We have proposed a computerized simulation model to serve as a valuable tool for decision-making in the sensitive and elusive field of efficient yet fair and just organ allocation. The results of our study suggest, with a high confidence level, the feasibility of this simulation model to evaluate alternative allocation algorithms, striving at optimal graft longevity and addressing social fairness at the same time. Thus, using the CREG matching system and giving higher weight to social parameters such as waiting time will result in comparable overall donor-recipient compatibility, while at the same time addressing an important social issue in organ allocation.

## References

1. Browning CJ, Thomas SA. Community values and preferences in transplantation organ allocation decisions. *Soc Sci Med* 2001;52(6): 853–61.
2. Leffell MS, Zachary AA. The national impact of the 1995 changes to the UNOS renal allocation system. United Network for Organ Sharing. *Clin Transplant* 1999;3(4):287–95.
3. Zenios SA, Wein LM, Chertow GM. Evidence-based organ allocation. *Am J Med* 1999;107(1):52–61.
4. De Meester J, Persijn GG, Wujciak T, Opelz G, Vanrenterghem Y. The new Eurotransplant Kidney Allocation System: report one year after implementation. Eurotransplant International Foundation. *Transplantation* 1998;15;66(9):1154–9.
5. Koch T. Normative and prescriptive criteria: the efficacy of organ transplantation allocation protocols. *Theor Med* 1996;17(1):75–93.
6. Delmonico FL, Harmon WE, Lorber MI, et al. A new allocation plan for renal transplantation. *Transplant Proc* 1999;31(1-2):358–9.
7. Thompson J, Thacker L, Takemoto S. CREG matching for first kidney transplants performed by SEOPF centers between October 1987 and September 1995: an analysis of outcome and prospective benefit. *Transplant Proc* 1997;29:1435–7.
8. Takemoto S, Terasaki PI, Gjerston DW, Cecka JM. Equitable allocation of HLA-compatible kidneys for local pools and minorities. *N Engl J Med* 1994;331(12):760–4.
9. Stobbe I, van der Meer-Prins EM, de Lange P, et al. Cross-reactive group matching does not lead to a better allocation and survival of donor kidneys. *Transplantation* 2000;15;70(1):157–61.
10. Starzl TE, Eliasziw M, Gjertson D, et al. HLA and cross-reactive antigen group matching for cadaver kidney allocation. *Transplantation* 1997;15;64(7):983–91.
11. Hollenbeak CS, Woodward RS, Cohen DS, et al. The economic benefit of allocation of kidneys based on cross-reactive group matching. *Transplantation* 2000;15;70(3):537–40.
12. Thompson JS, Thacker LR. CREG matching for first cadaveric kidney transplants (TNX) performed by SEOPF centers between October 1987 and September 1995. Southeastern Organ Procurement Foundation. *Clin Transplant* 1996;10(6 Pt 2):586–93.
13. Wujciak T, Opelz G. Evaluation of HLA matching for CREG antigens in Europe. *Transplantation* 1999;27(8):1097–9.
14. Takemoto SK, Cecka JM, Terasaki PI. Benefits of HLA-CREG matching for sensitized recipients as illustrated in kidney regrafts. *Transplant Proc* 1997;29(1-2):1417.

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