Improving Geographic Equity in Kidney Transplantation Using Alternative Kidney Sharing and Optimization Modeling

Ashley Davis M.S. ^{1, 2}, Sanjay Mehrotra PhD ^{1, 2, 3, *}, John Friedewald M.D. ², Mark Daskin PhD ⁴, Anton Skaro M.D. PhD ², Michael Abecassis M.D. M.B.A, ² Daniela Ladner M.D. M.P.H. ²

¹ Industrial Engineering and Management Sciences, Northwestern University, Evanston, IL 60208

² Transplant Outcomes Research Collaborative (NUTORC), Comprehensive Transplant Center, Northwestern University Feinberg School of Medicine, Chicago, IL 60611

³Center for Engineering and Health, Northwestern University, Chicago, IL 60611

⁴ Industrial and Operations Engineering, University of Michigan, Ann Arbor, MI 48109

*Corresponding Author: Sanjay Mehrotra, PhD Professor, Industrial Engineering and Management Sciences Northwestern University 2145 Sheridan Road, Room C210 Evanston, IL 60208 Telephone: 847.491.3155 Facsimile: 847.491.8005 Email: mehrotra@northwestern.edu

Running Head: Improving Kidney Transplant Geographic Equity

Presented at: the 2011 American Transplant Congress, American Society of Nephrologists Conference, INFORMS Annual Meeting, and INFORMS Healthcare Conference

Word Count: 5,224 words, (Abstract: 218 words)

Key Words: Organ Allocation, Equity, Geography, Optimization

Financial support for this study was provided in part by a grant from the National Science Foundation, CMMI-1131568, from the Agency for Healthcare Research and Quality Health Services Dissertation Award, R36 HS021078-01, and from the Northwestern University Transplant Outcomes Research Collaborative. The funding agreement ensured the authors' independence in designing the study, interpreting the data, writing, and publishing the report.

Abstract:

The national demand for kidney transplantation far outweighs the supply of kidney organs. Currently a patient's ability to receive a kidney transplant varies depending on where they seek transplantation. This reality is in direct conflict with a federal mandate from the Department of Health and Human Services. We analyze current kidney allocation and develop an alternative kidney sharing strategy using a multi-period linear optimization model, KSHARE. KSHARE aims to improve geographic equity in kidney transplantation while also respecting transplant system constraints and priorities. KSHARE is tested against actual 2000-2009 kidney allocation using Organ Procurement and Transplant Network data. Geographic equity is represented by minimizing the range in kidney transplant rates around local areas of the country. In 2009, less than 25% of standard criteria donor kidneys were allocated beyond the local area of procurement, and Donor Service Area kidney transplantation rates varied from 3.0% to 30.0%, for an overall range of 27.0%. Given optimal sharing of kidneys within 600 miles of procurement for 2000-2009, kidney transplant rates vary from 5.0% to 12.5% around the country for an overall kidney transplant range of 7.5%. Nationally sharing kidneys optimally between local areas only further decreases the transplant rate range by 1.7%. Enhancing the practice of sharing kidneys by the KSHARE kidney sharing model may increase geographic equity in kidney transplantation.

1. Introduction

End Stage Renal Disease (ESRD) affects over 700,000 patients in the United States (US), with a three-fold rise in prevalence over the past decade (1). ESRD patients can receive treatment in two forms: dialysis and kidney transplantation. Compared to dialysis, kidney transplantation offers patients increased quality of life and decreased morbidity and mortality (2-11). Unfortunately, kidney transplantation demand far outweighs the supply of available kidney organs. While over 94,000 patients are currently waiting for a kidney transplant, only 16,813 patients received a kidney transplant in 2011 (12, 13).

The United Network for Organ Sharing (UNOS) oversees the procurement and allocation of all organs for transplantation within the Organ Procurement and Transplant Network (14). Since kidney transplant recipient outcomes improve with lessened time between procurement and transplantation, the country is subdivided to facilitate quick organ placement (15). The country is first divided into 11 UNOS groupings, which are groupings of neighboring states. Each region is further divided into 58 Donor Service Areas (DSAs) to facilitate all organ donation and allocation in their local area (16). Kidney allocation policy currently allocates a donated kidney first to patients in the same DSA of procurement (local allocation), then if necessary to patients in the same UNOS region of procurement (regional allocation), and ultimately nationally (national allocation) (16). Each DSA maintains its own kidney transplant waitlist. Patients are prioritized on each waitlist primarily based on their time on the transplant waitlist with some minor exceptions to increase transplant access for pediatric, multi-organ, and highly sensitized patients for whom it is more difficult to find a suitable kidney for transplantation (16).

A patient seeking transplantation does not necessarily have to list for transplantation in the DSA they reside in (17). A patient's waiting time to transplantation can vary by over four years depending on where they choose to seek transplantation (18). This geographic disparity has been increasing over time with respect to transplant waiting time, as well as transplant rates, waitlist mortality rates, and kidney quality (19). Given this geographic disparity, affluent patients, who are capable of traveling anywhere in the country for transplantation, can list for transplant in short waiting time DSAs to reduce their time to transplantation (20). UNOS is aware of this present inequity. In 1998, the Department of Health and Human Services released their "Final Rule" on organ transplantation, specifically disallowing geographic inequities (21). Since this ruling, UNOS has debated changes to allocation policy, but to date no changes to the geographic allocation strategy have been imposed (22).

While the transplant community agrees that the geographic equity issue needs to be addressed, many have reservations about changing current policy and have blocked finding a consensus to change (23). The American Society of Transplant Surgeons (ASTS) stated in 2009, "Whatever changes in kidney allocation policy are put forward, open and frequent communication, presentation and publication in peer-reviewed venues and careful planning for transition can go a long way to allay these fears... smaller stepwise implementation of changes may provide time for observation and stabilization of the system without a complete disruption of patients" (24). This statement embodies the transplant systems sentiment towards changes in geographic allocation policy. First, DSAs worry about the impact wider sharing will have on local kidney donation rates and their ability to transplant patients listed in their areas (25). Second, with thousands of patients currently awaiting transplantation (12), patients and policy makers alike worry about how wide-sweeping changes to allocation policy can be integrated into the current system without greatly affecting each currently listed patient's experience in the system (24). Finally, all changes to allocation policy must survive an extensive public comment approval period, where patients, transplant clinicians, policy makers, and the general public alike must clearly understand and approve of changes (26). Therefore, large, complex changes have traditionally not successfully been implemented (27).

A possible alternative to the kidney sharing framework proposed in this paper is to redesign all 11 UNOS regions to reduce geographic disparity. The regional redesign has been studied for liver (Stahl et al (28), Kong et al (29), and Gentry et al (30)). These works model the transplant system as a redistricting problem, similar to that used in political redistricting (31), to suggest a different regrouping of DSAs to form new UNOS regions. While geographic redesign preserves the general structure of geographic kidney allocation policy, it would impose a substantial change to the current UNOS system, which would be difficult (27). First, this change would be an immediate, non-incremental modification to the current system. As a result, it would greatly impact the experience of currently waitlisted patients and other stakeholders. Second, the regional patient population characteristics may change over time, which will require repeated restructuring of a complex system involving multiple stakeholders.

Our approach is different in many aspects since our primary focus is kidney transplantation. Kidney allocation differs from liver allocation because kidneys can tolerate a longer time from procurement to transplantation (cold ischemic time, or CIT), with an average CIT of 18 hours versus 8 hours, respectively (32). Therefore, kidneys can be allocated over farther distances than livers and hence do not need to rely as heavily on the regional allocation structure. This reality has led to a debate in the transplant community between those who urge for a national kidney transplant waitlist to facilitate national kidney sharing and those who urge that kidneys should still be prioritized for local allocation to benefit their local populations (25).

The KSHARE strategy studied in this paper addresses the equity over time. This has three major advantages: (1) It does not shock the current system abruptly; (2) Since regions are not redesigned, should unintended consequences arise, it will be easier to handle them by simply adjusting the fraction of shared organs across DSA, and (3) KSHARE strategy can be designed for an adaptive implementation with a gradual phase in, first within limited set of DSA before scaling it to the entire nation. The KSHARE strategy studied in this paper is also motivated from past evidence, where establishing partnerships among DSA seem to have helped reduce disparity within certain states, and then maintain low disparity levels over time. UNOS approved a statewide sharing variance for Florida (FL) and Tennessee (TN) in the early 1990s. This variance allowed for kidneys that are not allocated locally in the DSA of procurement, to be offered to other DSAs in the same state prior to regional and national allocation. Statewide sharing was markedly successful at decreasing the geographic disparity in the states in which it was implemented (33). The success of statewide sharing provides evidence that small structural changes to kidney allocation policy can result in significant improvements in geographic equity. KSHARE maintains features that are based on current organ usage and sharing practice. Specifically, KSHARE operates under the assumption that only those kidneys not currently allocated locally to DSAs with longer waiting times. Our model and study in this paper is intended to provide a system-level view, rather than offering a patient-level allocation policy that attempts to balances equity and utility (e.g., see Zenios et al (34), Su and Zenios (35,36), and Akan et al (37).

The KSHARE model discussed later also intends to study the possibility of improving national equity by sharing kidneys at various scales of local sharing (different radii of the sharing circle). On the other extreme, a national kidney sharing strategy has also been proposed by putting all patients on a single list (25). Unfortunately, it is not practical due to the biological limitations. Patient biological material is matched before a potential recipient is offered a procured kidney. The matching of the biological material for patients on a single list requires that all the biological material from all listed patients, as well as, donor kidney be present at a central location. This will require material from the procured kidneys to be flown to this central location before offering it to a patient. Bringing the material to a central location will add many hours to the time a procured kidney is out of a donor's body before being placed into a recipient

(called cold ischemic time (CIT)). The donated kidney quality worsens with CIT, which impacts overall kidney transplant outcomes (15). Bringing the biological material from patients to a central location is also not practical because of added logistical costs. There are other administrative reasons (e.g., insurance, patient pre and post-transplant checkup, etc.) that prevent a patient to fly into a centralized location for transplant. The above discussion provides the rationale used for the local-regional-national policy currently followed by UNOS.

The remainder of this paper is organized as follows. Section 2 formally introduces our alternative kidney sharing approach as well as the KSHARE model formulation. Section 3 provides a feasibility study of the KSHARE model in comparison to the actual kidney organ allocation policy using retrospective OPTN kidney transplant system data. Section 4 concludes the paper with a discussion of our results and outlines future research.

2. Methods

2.1. Overview of Approach

According to current kidney allocation policy, kidneys offered regionally and nationally are not prioritized for allocation in any specific DSA (16). We modify this portion of the policy as follows. Donated kidneys are still prioritized for local allocation. Prior to regional allocation, however, kidneys are offered to patients in certain DSAs that have a sharing partnership with the procuring DSA. By adding this prioritization, our primary goal is to optimally improve geographic equity over time. A secondary goal is to limit the number of sharing partnerships to be formed between DSAs to keep system implementation practical. Further, evidence that a limited number of sharing partnerships is more effective at reducing geographic inequity is given in (33), where we find that states with only two DSAs improved in geographic equity more rapidly than within states with four DSAs.

2.2. Kidney Sharing Strategy and Modeling Background

There is no general consensus on the definition of geographic equity in kidney transplantation. The Institute of Medicine (IOM) responded to the "Final Rule" (20), suggesting that kidney transplant rate was a meaningful indicator for equitable access to kidney transplantation (38). Annual kidney transplant rates are calculated for each DSA as the ratio between the number of annual kidney transplants in a DSA and the number of patients listed within the same DSA at the beginning of that year: $transplant rate_{DSA}(year) = \frac{transplants in DSA}{DSA Waiting List}$.

KSHARE aims to achieve its goals of improving equity while respecting the beliefs of the transplant community. First, only kidneys currently shared outside the DSA of procurement are eligible for reallocation in KSHARE, respecting the current system priority to not change current local allocation practices (25). Second, equity is achieved over many years, so as to not present a large, quick change to current local allocation practices (24). This was also the case in states implementing the Statewide Sharing local allocation variance (33). Finally, over this long phase-in period, sharing partnerships between DSAs will stay as consistent as possible to not present complex and variable sharing strategies for DSAs to follow (27).

Each DSA in the Continental US is located based on the location of their designated Organ Procurement Organization (OPO). An optimization model is used to find appropriate sharing partnerships, and understand the implications of the partnership arrangement on improving transplant rate equity. Since an objective of our study to understand the implication of "local partnerships" and "national partnerships", a distance metric is used to parameterize our model for constraining the region in which DSA partnerships are allowed to form. The distance between any two DSAs is approximated by the straight line distance between two DSA's corresponding OPOs. Given a pre-determined sharing radius of *r* miles, we define for each DSA the set of DSAs within *r* miles of the DSA. This will be a DSA's potential sharing partner set. For example, in Figure 1, the procuring DSA may share kidneys with a DSA having an OPO within the radius, DSAs 1, 2, or 3, but may not share them with DSA 4. From this set of potential sharing partners, KSHARE determines the optimal partnerships to be formed to minimize geographic inequity among all DSAs.

The kidney sharing radius of r allows for flexibility for the transplant community to decide on the appropriate distance for continual sharing. If geographic proximity is very important, then r is set small to allow kidney sharing only between geographically close DSAs. If distance is not important, then r is set larger to allow kidney sharing across longer distances.

2.3. KSHARE Formulation

KSHARE is a multi-period, linear, mixed integer optimization model that aims to minimize the range in kidney transplant rates among the DSAs after T years while maintaining consistent and stable DSA sharing partnerships during the T years of KSHARE implementation. We aim to create geographic equity after T years to following the preference of the ASTS towards phased-in changes over time (24). We now outline the KSHARE model formulation.

2.3.1. Model Assumptions

We make five assumptions about the present kidney transplantation system. First, we focus on DSAs in the Continental US and exclude the two DSAs based in Hawaii and Puerto Rico since their distance from other DSAs introduces significant bias to the results. Second, waitlisted patient growth and annual kidney procurement per DSA for each year is assumed to be the same as that in actual retrospective data. Third, KSHARE ignores the stochastic and time-varying nature of the system. In reality, we do not know the effect our change in policy will have on waitlisting and procurement rates. Fourth, the model treats all patients equally and does not focus on racial, age, and other patient subgroups individually. Realistically, patients of different minority subgroups are not prioritized differently on the transplant waitlist, so in

stabilizing the overall DSA kidney transplant rate, we intend to stabilize the rate across all patient groups. Fifth, KSHARE assumes that if a kidney is offered to a DSA, then a patient in that DSA will accept. In practice, a kidney may be offered to multiple DSAs prior to finding a willing recipient, but since we limit our feasibility study to standard criteria donor (SCD) kidneys that are traditionally easy to place, this practice is minimal (39). Sixth, we ignore blood type compatibility, which is left to future research.

In all these aspects, the current KSHARE model should be considered preliminary. However, our model does provide a framework from which to develop more advanced stochastic simulation optimization models to reduce geographic disparity nationally and among specific patient subgroups (40).

2.3.2. Optimization Model Formulation

The mixed integer optimization model for our problem is given in (1-12). In Objective (1), our goal is to achieve a feasible sharing assignment with minimal differences in sharing partners and sharing percentages over the phase-in period. Retaining a consistent sharing strategy is imperative for implementation. Constraint (2) sets the initial waiting list sizes in each DSA, while Constraint (3) updates the resulting listed population in each DSA at the beginning of each year t due to allocation procedure developed in the previous year. In Constraint (4), the total number of transplants within DSA i during year t is calculated. Constraint (5) restrains the amount of kidney sharing from DSA i during year t to be equal to the total amount of procured kidney organs at DSA i during year t, while constraint (6) maintains the current level of local allocation. By Constraint (7), the final, year T, transplant rate is restrained to be within the forced equitable transplant range. We aim to achieve equity by the end of year T so as to not force equity to occur immediately, but instead be improved over time. It will not be possible to maintain a consistent reduction in disparity each year since we maintain the current local allocation levels. Constraint (8) determines whether two DSAs are sharing partners throughout the sharing

process. If the model deems it optimal for DSA i to share with DSA j, then Y_{ij} is forced to be equal to one. Y_{ij} is otherwise forced to be equal to zero since the objective of the model is to minimize the number of sharing partnerships. In Constraint (9), the percentage of DSA i's supply shared with DSA *j* in year *t* is calculated. Constraint (10) determines the range in sharing quantity differences between DSA i and DSA j over the phase-in period. Finally, Constraints (11) and (12) ensure non-negativity and binary constraints on model variables.

$$\min \sum_{i \in I} \left(\sum_{j \in J_i} \varphi * Y_{ij} + E_{ij}^U - E_{ij}^L \right)$$
Subject To:
$$(1)$$

$$\begin{aligned} W_i(0) &= d_i , & \forall i \in I \\ W_i(t+1) &= W_i(t) + g_i(t) - P_i(t), & \forall i \in I, t \in 0, ..., T - 1 \\ P_i(t) &= \sum O_{ii}(t) , & \forall i \in I, t \in 0, ..., T \end{aligned}$$
 (2)

$$P_i(t) = \sum_{j \in J_i} Q_{ji}(t) , \qquad \forall i \in I, t \in 0, \dots, T$$
(4)

$$\sum_{i \in I_i} Q_{ij}(t) = s_i(t), \qquad \forall i \in I, t \in 0, \dots, T$$
(5)

$$\begin{aligned} &l_i * s_i(t) \leq Q_{ii}(t), & \forall i \in I, t \in 0, \dots, T \\ &x_L * W_i(T) \leq P_i(T) \leq x_U * W_i(T), & \forall i \in I \end{aligned} (6)$$

$$\sum_{t=0,\dots,T} Q_{ij}(t) \le M * Y_{ij}, \qquad \forall i \in I, j \in J_i$$
(8)

$$\begin{aligned} &Z_{ij}(t) * s_i(t) = Q_{ij}(t), &\forall i \in I, j \in J_i, t \in 0, ..., T \\ &E_{ij}^L \leq Z_{ij}(t) \leq E_{ij}^U, &\forall i \in I, j \in J_i, t \in 0, ..., T \\ &Q_{ij}(t), E_{ij}^L, E_{ij}^U, Z_{ij}(t), W_i(t), P_i(t) \geq 0 &\forall i \in I, j \in J_i, t \in 0, ..., T \\ &Y_{ij} \in \{0,1\} &\forall i \in I, j \in J_i \end{aligned}$$
(9)

$$\forall i \in I, j \in J_i \tag{12}$$

2.3.3. Parameters and Variables

Parameters: Define the set I as the set of all continental US DSAs. For each DSA i, define a set J_i which represents the set of all DSAs, including DSA *i* which lie within a feasible, predefined sharing distance r from DSA i. Let T represent the final year of the phase-in period. Additionally, let $s_i(t)$ represent the number of donated kidneys procured for transplantation during year t, and let l_i represent the percentage of such procurement which is typically allocated within a DSA *i* each year. Let d_i represent the total number of listed patients currently waiting within DSA *i* at the beginning of the phase-in period, year 0, and let $g_i(t)$ represent the growth in the transplant waitlist in DSA *i* during year *t*. Let x_L and x_U represent the calibrated upper and lower limits on the range of allowable transplant rates to be achieved by the end of year *T*. These parameters are calibrated to enforce maximal increases in geographic equity while maintaining model feasibility. Due to the size of this model, it is not feasible to solve a non-linear model that allows these parameters to be variable. Therefore to maintain model linearity, these upper and lower limits are iteratively tightened to the minimal range in DSA kidney transplant rates that does not cause model infeasibility. Finally, let φ represent a conversion factor of 10⁻⁸.

<u>Variables:</u> Define $W_i(t)$ to represent the total waitlisted population within DSA *i* at the beginning of year *t*. Let E_{ij}^L and E_{ij}^U represent the minimum and maximum percentage of DSA *i*'s kidney procurement shared with DSA *j* during any year of the phase-in period. Further, let $P_i(t)$ denote the number of donated kidneys transplanted in DSA *i* are allocated in year *t*. Let $Q_{ij}(t)$ represent the number of kidneys procured in DSA *i* and transplanted in DSA *j* during year *t* and define Y_{ij} as a binary variable equal to 1 if DSA *i* ever allocates a portion of its supply to DSA *j* throughout the phase-in timeframe. Finally, let $Z_{ij}(t)$ represent the percentage of DSA *i*'s procurement supply shared with DSA *j* during year *t*. Given $M \gg 0$ and φ is a scaling parameter, our multi-period model is formulated as follows. The inclusion of a constant M in the model is a commonly used technique in linear optimization (41).

Post-optimization using CPLEX (42), the transplant rate for each DSA *i* for year *t* is calculated by: $transplant rate_{DSA\,i}(t) = \frac{P_i(t)}{W_i(t)}$. Also, the annual kidney sharing strategy between any two DSAs, *i* and *j*, is captured in $Z_{ij}(t)$ for all years *t*.

3. Results

We test the feasibility and potential impact of KSHARE in comparison to actual SCD kidney allocation during 2000-2009. KSHARE is phased-in during the ten year period from 2000 to 2009. The choice of a ten year period was motivated from the analysis in Davis, Mehrotra, et al. (2013) (33). Davis, Mehrotra, et al. (2013) analyzed the implications of a statewide sharing variance that was given in the 1990s to the state of Tennessee and Florida. The statewide sharing variance allowed FL and TN to share non-locally used kidneys with the DSA within the state prior to offering it to the region. The analysis showed that a large portion of the reduction in disparity in Tennessee was achieved over five years, while that in Florida achieved over ten years. In fact, the analysis in Davis, Mehrotra, et al. (2013) shows that the disparity in other states with a similar number of DSAs either became worse, or the improvements were significantly less over the eighteen year period 1991-1999, for which the data was analyzed. The same number of kidney transplants occurs in the KSHARE and the actual SCD kidney allocation. The difference is that a fraction of kidneys are directed for transplant in a different DSA. We now compare the range and the ratio between the maximum and minimum DSA kidney transplant rates in the actual system, and the KSHARE based solution for each year between 2000 and 2009.

3.1. 2000-2009 OPTN Data

OPTN Standard Transplant and Research organ procurement and waitlisted patient information was analyzed during 2000-2009 (43,44). Annual SCD kidney procurement and transplantations, aggregated over all blood types, was calculated per DSA. The initial DSA kidney waitlist population was taken on January 1, 2000. The annual growth of a DSA's kidney waitlist size was taken for each year as the number of new kidney waitlist registrations minus the number of waitlist deaths. Patients who were removed from the waitlist for other reasons (e.g. living donor transplant, multiple-organ transplant, extended criteria donor transplant, or decided against transplantation) were excluded from the entire study population.

3.2. Effect of Kidney Sharing Radius

Optimal KSHARE kidney allocation was determined for feasible sharing radii from 370 to 2,700 miles. Sharing radii below 370 miles allows some DSAs to retain more procured kidneys over the ten year period than is necessary to transplant their entire local waitlisted patient population. A sharing radius of 2,700 miles is sufficiently large to allow for national kidney sharing. Table 1 gives the range in DSA kidney transplant rates in the terminal phase-in year (2009), for all sharing radii analyzed: r = 370, 450, 500, 550, 600, 900, 1,200, 1,500, and 2,700 miles.

Actual DSA kidney transplant rates varied in 2009 by 26.9%, from 3.0% to 29.9%. As the kidney sharing radius increases from 370 to 2,700 miles, the range in DSA kidney transplant rates falls from 25.7% to 5.8%. The incremental benefit in geographic equity, measured by a reduction in DSA kidney transplant rate range, diminishes as the kidney sharing radius increases. Extending the kidney sharing radius from 600 to 2,700 miles only reduces the range in DSA kidney transplant rates from 7.5% to 5.8%. We therefore focus the rest of this section on 600 miles KSHARE kidney sharing results.

3.3. Kidney Allocation Comparison: Actual versus KSHARE Kidney Sharing

In Table 2, we find a gradual reduction in DSA kidney transplant rate range from 2000 to 2009 according to KSHARE sharing. However, the magnitude of improvement varies from one year to another. A steady reduction is not attainable because the growth in waitlist registrations and kidney procurement varies over the ten years while DSA sharing partnerships remain consistent each year. In 2009, 600 mile KSHARE DSA kidney transplant rates range by 7.5% while actual DSA kidney transplant rates range by 26.9%. We point out that even though the range in actual DSA kidney transplant rates fall from 49.4% to 26.9% over time, this is because transplant rates have reduced naturally due to increased waitlist sizes. The ratio between the

maximum and minimum DSA kidney transplant rates remained relatively stable under current allocation. KSHARE allocation reduces this ratio from 7.9 to 2.5, a threefold improvement in geographic equity.

It is of note that a significant reduction in DSA kidney transplant rate range is unattainable at the end of ten year phase-in period. This is because KSHARE maintains current local allocation levels, creates a consistent kidney sharing policy, and sharing is restricted to 600 miles. However, since improvement is gained each year of the phase-in period, it is probable that over a longer period, geographic equity would continue to improve. Significant transplant rate equity will also be possible if the current local usage levels of a procured kidney are allowed to change.

We now comment on the simplified sharing structure generated from the KSHARE model (Figure 2). Currently, kidneys procured but not transplanted locally are accepted by an average of 19 other DSAs each year. By 600 mile KSHARE kidney allocation, no DSA shares kidneys with more than three geographically close DSAs. This creation of a small number of stable sharing partnerships may potentially have increased efficiency implications. Finally, the 600 mile KSHARE model increases the percentage of kidneys retained for local allocation from 76% to 79%.

4. Discussion

The preliminary results show that directed kidney sharing between DSAs can lessen the range in DSA kidney transplant rates from 26.9% to 7.5% over a ten year period. This result is achieved by only sharing between DSAs within 600 miles of each other rather than requiring national kidney sharing, which only further reduces the range in kidney transplant rates to 5.8% by 2009. In order to validate our results in this paper we performed a simulation study using the KSIM model described in (45). One hundred replications of KSIM model were performed.

Table 3 summarizes the disparity in the actual system and that those from the mean taken over the hundred replications. A comparison with results in Table 2 shows that the disparity observed from the deterministic optimization model, and that observed from the simulated system using the parameters of the deterministic optimization model are similar at the end of the ten year duration. Using the parameters recommended by the optimization model, we also calculated in-state (when multiple DSA are present within a state) and within region disparity in transplant rate. The transplant rate disparity was calculated by taking the ratio of the maximum transplant rate to the minimum transplant rate at a DSA within a state (region). The results of the actual system and those obtained from KSHARE are given in Tables 4 and 5, respectively. These results show that KSHARE disparity in all states except FL and TN is better than the actual, and has improved consistently. Recall that FL and TN received a statewide sharing variance in 1991 and 1992 respectively, and consequently, the DSAs within FL and TN were already sharing kidneys between 1991-1999 within the state prior to sending them to the region.

Note that the total number of transplants in the new system does not change. A reason for improvements in kidney transplant rate equity is that KSHARE directs more kidneys to the DSAs with smaller transplant rates, instead of letting any DSA within the region or the nation have access to the kidney that is not used locally. Consequently, it provides a better balance between the supply and the demand at each DSA. Since the model only allows sharing of a limited fraction of the kidneys which would have been shared since no matched recipient was found locally, the improvement in equity takes place gradually over time. Nevertheless, the results suggest that improvement in inequity can be achieved without requiring a major realignment of regions or placing increased sharing burden on any one area of the country. In creating stable DSA sharing partnerships between nearby DSAs, we may also increase the efficiency of kidney organ placements over time, and thereby improve kidney transplant recipient outcomes due to faster kidney placement (15). One may suspect that KSHARE

approach will cluster the DSAs. The KSHARE framework will not formally cluster DSAs into sets, because in an actual practical implementation, the policy derived from KSHARE model can be adapted over time after the equity issue has been resolved. More advanced policies based on advanced randomized versions of KSHARE are possible. For example, only a fraction of organs shared with a DSA will only be shared by generating a "random number", while the remaining will be used as usual.

5. Concluding Remarks

We have presented a framework for improving geographical equity in kidney transplant based on directing a fraction of the kidneys to donor service areas with small transplant rates. The fraction of directed kidneys to a donor service area are determined by an optimization model. The results from our study should be considered preliminary, and a step towards understanding the potential impact of organ sharing policies on geographic disparity. Future research aims to incorporate these additional measures of fairness, and extend our KSHARE model without our preliminary modeling assumptions. The discussion in the results section assumes a ten year period for improving geographic equity. In practice, this period will be chosen through discussions in the UNOS kidney committee. A more realistic model will consider the stochastic nature of the patient and organ arrival process, as well as improving geographic equity across different blood-types, patient ethnicity, socioeconomic status, kidney quality, and equity achieved over time different time periods. In addition, further modeling will incorporate differences in transplant center behavior. It is known that transplant centers differ in their acceptance of kidneys for transplantation that are poor in quality and can be more or less selective as to the type of patients they transplant (39). Current analysis makes a retrospective assumption on patient and kidney procurement dynamics. With ESRD prevalence changing (1), advanced KSHARE models must be robust against variability in future waitlisting and kidney procurement dynamics. Further, while transplant rate was proposed by the IOM as a realistic

geographic equity measure (38), other geographic equity measures need to be explored. Alternative measures of fairness include the waiting time to transplant, population mortality rate while waiting for transplant, transplanted kidney quality, and graft survival rates (19). Finally, the sharing radius concept does not prioritize DSA sharing partnerships that are within the same state or UNOS region. In the past, local allocation variances have never involved DSAs that are in different UNOS regions. The above model limitations of KSHARE kidney sharing strategy are currently being pursued by us in the framework of a simulation-optimization model. Our preliminary findings suggest that the broader conclusions of this paper that local sharing partnerships can significantly improve geographical equity continue to hold across multiple equity measures. We are finding that achieving transplant rate equity also results in a reduction of waiting time to transplant. This results in a significant saving in guality adjusted life years. Additionally, our research suggests that directed sharing of low quality kidneys will result in significant improvement in cold ischemic time for placing such kidneys. However, while developing a model under more realistic assumptions, we think that the research community may find our current modeling paradigm and the policy insights from our preliminary KSHARE kidney sharing model useful.

5. Acknowledgements

This work is funded by National Science Foundation award CMMI-1131568, Agency for Healthcare Research and Quality Health Services Research Dissertation Award R36 HS021078-01, and the Northwestern Transplant Outcomes Research Collaboration (NUTORC). The content of this work is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the US

Government.

The authors would like to thank the members of the Northwestern University Transplant

Outcomes Research Collaborative (NUTORC) for their opinions and suggestions for this work.

6. References

- U S Renal Data System, USRDS. 2010 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, *National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases,* Bethesda, MD, 2010.
- Mazzuchi N, Gonzalez-Martinez F, Carbonell E, et al. Comparison of survival for hemodialysis patients versus renal transplant recipients treated in Uruguay. Nephrol Dial Transplant 1999; 14(12): 2849-54.
- 3. Port FK, Wolfe RA, Mauger EA, et al. Comparison of survival probabilities for dialysis patients versus cadaveric renal transplant recipients. JAMA 1993; 270(11): 1339-43.
- Traynor JP, Thomson PC, Simpson K, et al. Comparison of patient survival in nondiabetic transplant-listed patients initially treated with hemodialysis or peritoneal dialysis. Nephrol Dial Transplant 2011; 26 (1): 245-252.
- Khauli RB, Steinmuller DR, Novick AC, et al. A critical look at survival of diabetics with end-stage renal disease. Transplantation versus dialysis therapy. Transplantation 1986; 41(5): 598-602.
- 6. Krakauer H, Spees EK, Vaughn WK, et al. Assessment of prognostic factors and projection of outcomes in renal transplantation. Transplantation 1983; 36(4): 372-8.
- Wolfe RA, Ashby VB, Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. N Engl J Med. 1999; 341(23): 1725-30.
- 8. Miskulin D, Bragg-Gresham J, Gillespie BW, et al. Key comorbid conditions that are predictive of survival among hemodialysis patients. Clin J Am SocNephrol 2009; 4:1818.
- 9. Laupacis A, Keown P, Pus N, et al. A study of the quality of life and cost-utility of renal transplantation. Kidney Int 1996; 50(1): 235-42.
- 10. Russell JD, Beecroft ML, Ludwin D, et al. The quality of life in renal transplantation--a prospective study. Transplantation 1992; 54(4): 656-60.
- 11. Simmons RG, Abress L. Quality-of-life issues for end-stage renal disease patients. Am J Kidney Dis 1990; 15(3): 201-8.
- 12. "Current U.S. Waiting List." Organ Procurement and Transplantation Network. January 4, 2013. *http://optn.transplant.hrsa.gov/latestData/rptData.asp*.

- 13. "U.S. Transplants Performed: January 1, 1988 October 31, 2012." Organ Procurement and Transplantation Network. January 14, 2013. http://optn.transplant.hrsa.gov/latestData/rptData.asp.
- 14. United Network for Organ Sharing. http://www.unos.org. Accessed January 14, 2013.
- 15. Salahudeen AK, Haider N, May W. Cold ischemia and the reduced long-term survival of cadaveric renal allografts. Kidney International 2004; 65: 713-718.
- Allocation of Deceased Kidneys [Organ Procurement and Transplantation Network web site]. 2010. Available at: http://optn.transplant.hrsa.gov/PoliciesandBylaws2/policies/pdfs/policy_7.pdf. Accessed February 17, 2010.
- 17. United Network for Organ Sharing. Questions and Answers for Transplant Candidates about Multiple Listing and Waiting Time Transfer. Available at: http://www.unos.org/docs/Multiple_Listing.pdf. Accessed April 27, 2011.
- 18. A Davis, S Mehrotra, J Friedewald, A Skaro, L McElroy, R Kang, E Wang, J Holl, M Abecassis, D Ladner. The Extent and Predictors of Geographic Inequity in Kidney Transplantation in the United States. *Working Paper*, 2013.
- Davis A, Mehrotra S, Friedewald J, et al. Has Geographic Inequity in Kidney Transplantation Changed Since the Final Rule," Technical Report. Department of Industrial Engineering and Management Sciences, Northwestern University, Evanston Illinois. 2013.
- 20. Grady D, Meier B. A Transplant That is Raising Many Questions. *The New York Times*. June 22, 2009.
- Department of Health and Human Services (1998). Organ procurement and transplantation network, Final Rule (40 CFR Part 121). Federal Register 63, 16296– 16338.
- 22. Proposal to Substantially Revise The National Kidney Allocation System. [Organ Procurement and Transplantation Network web site]. Available at: http://optn.transplant.hrsa.gov/PublicComment/pubcommentPropSub_311.pdf. Accessed January 13, 2013.
- 23. Stock P.G. Balancing Multiple and Conflicting Allocation Goals: A Logical Path Forward. Am J Transplant 2009; 9: 1519-1522.
- 24. Freeman RB, Matas AT, Henry M, et al. Moving Kidney Allocation Forward: The ASTS Perspective. Am J Transplant 2009; 9:1501-06.
- 25. Davis D, Wolitz R. A Staff Working and Discussion Paper: The Ethics of Organ Allocation. The President's Council on Bioethics. 2006.
- 26. Getting Involved in the Public Comment Process. [Organ Procurement and Transplantation Network web site]. Available at: http://optn.transplant.hrsa.gov/SharedContentDocuments/ PublicComment_FactSheet%281%29.pdf. Accessed April 27, 2011.
- 27. Wolfe RA, McCullough KP, et al. Calculating life years from transplant (LYFT): methods for kidney and kidney-pancreas candidates. *Am J Transplant*, 4 Pt 2: 997-1011, 2008.
- 28. Stahl JE, Kong N, Shechter SM, et al. A Methodological Framework for Optimally Reorganizing Liver Transplant Regions. *Medical Decision Making*, 25: 35-46, 2005.

- 29. Kong N, Schaefer AJ, Hunsaker B, Roberts MS. Maximizing the Efficiency of the US Liver Allocation Systems through Region Design. *accepted by Management Science*, 2010.
- Gentry S, Lentine K, Dzebiaahvili N, et al. Designing Geographic Allocation Regions for Equitable Access to Liver Transplant. *INFORMS Healthcare 2011 Oral Presentation*, 2011.
- 31. Garfinkel R, Nemhauser G. Optimal political districting by implicit enumeration techniques. *Management Science*, 16: 495-508, 1970.
- 32. 2009 Annual Report of the U.S. Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients: Transplant Data 1999-2008. U.S. Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation, Rockville, MD.
- 33. Davis A, Mehrotra S, McElroy L, et al. The Effects of the Statewide Sharing Variance on Geographic Disparity in Kidney Transplantation in the US. *working paper*. 2013.
- 34. Zenios SA, Chertow GM, Wein LM. Dynamic Allocation of Kidneys to Candidates on the Transplant Waiting List. *Operations Research*, 48(4): 549-569, 2000.
- 35. Su X, Zenios SA. Patient Choice in Kidney Allocation: The Role of the Queueing Discipline. *Manufacturing and Service Operations Management*, 6(4): 280-301, 2004.
- 36. Su X, Zenios SA. Patient Choice in Kidney Allocation: A Sequential Stochastic Assignment Model. *Operations Research*, 53(3): 443-455, 2005.
- 37. Akan M, Alagoz O, Ata B, Erenay FS. Optimizing Liver Allocation System Incorporating Disease Evolution. *Submitted for Publication*, 2008.
- Institute of Medicine. Organ Procurement and Transplantation: Assessing Current Policies and the Potential Impact of the DHHS Final Rule. National Academy Press. 1999.
- Massie AB, Stewart DE, Dagher NN, et al. Center-Level Patterns of Indicated Willingness to and Actual Acceptance of Marginal Kidneys. *Am J Transplant*. 2010; 10: 2472-2480.
- 40. Davis A, Mehrotra S, Kilambi V, et al. "Addressing US National Geographic Disparity in Kidney Transplantation By Creating Sharing Partnerships," Technical Report. Department of Industrial Engineering and Management Sciences, Northwestern University, Evanston Illinois. 2014.
- 41. Bertsimas, D, and Tsitsiklis JN. "Introduction to linear optimization." (1997)
- 42. IBM ILOG CPLEX Optimizer. (2013). Retrieved from www-01.ibm.com/software/integration/ optimization/cplex-optimizer/
- 43. United Network of Organ Sharing. UNOS Standard Transplant Analysis and Research Files: Kidney, Pancreas, and Kidney-Pancreas Waiting List. Created September 3, 2010.
- 44. United Network of Organ Sharing. *UNOS Standard Transplant Analysis and Research* Files: Deceased Donors. Created September 3, 2010.
- 45. Ashley Davis, Sanjay Mehrotra, John Friedewald, and Daniela Ladner (2013), "Characteristics of a Simulation Model to Investigate Geographic Disparities in the Kidney Transplant System" Proceedings of the Winter Simulation Conference, 2320-2329

Tables and Figures

			. ,
Sharing			
Radius (miles)	Range (%)	Δ (%)	д
370	4.3 - 30.0	25.7	7.0
450	4.5 - 15.0	10.5	3.3
500	4.6 - 12.5	7.9	2.7
550	4.8 - 12.5	7.7	2.6
600	5.0 - 12.5	7.5	2.5
900	5.8 - 12.5	6.7	2.2
1,200	6.3 - 12.5	6.2	2.0
1,500	6.5 - 12.4	5.9	1.9
2,700	6.6 - 12.4	5.8	1.9
Year 2009	3.0 - 29.9	26.9	10.0

Table 1: KSHARE Kidney Transplant Rates by Sharing Radius (2009)

 $\Delta = Maximum Transplant Rate - Minimum Transplant Rate$ $\partial = \frac{Maximum Transplant Rate}{Minimum Transplant Rate}$

Table 2: Comparison of Actual and 600 mile KSHARE Optimized Transplant Rates (2000-2009)

	Actual Allocation			KSHARE Allocation		
Year	Range (%)	Δ (%)	д	Range (%)	Δ (%)	д
2000	5.1 - 54.5	49.4	10.6	6.9 – 54.5	47.6	7.9
2001	5.1 - 54.6	49.5	10.8	5.9 – 40.3	34.4	6.9
2002	5.5 - 45.0	39.5	8.2	5.5 – 38.3	32.8	6.9
2003	4.7 - 44.1	39.4	9.4	5.4 – 37.1	31.7	6.9
2004	4.0 - 60.3	56.3	15	5.0 – 31.8	26.8	6.4
2005	3.9 - 45.8	42.0	11.9	4.4 – 25.1	20.7	5.7
2006	4.3 - 49.6	45.3	11.5	5.3 – 25.9	20.6	4.9
2007	4.4 - 37.7	33.3	8.6	4.4 – 23.4	19.0	5.3
2008	4.0 - 29.5	25.5	7.3	4.8 – 23.0	18.2	4.8
2009	3.0 - 30.0	27.0	10	5.0 - 12.5	7.5	2.5
Δ = Maximum Transplant Rate – Minimum Transplant Rate						
$\partial = \frac{Maximum Transplant Rate}{Minimum Transplant Rate}$						

Minimum Transplant Rate

	Actual Allocation			KSIM KSHARE Allocation		
Year	Range (%)	Δ (%)	д	Range (%)	Δ (%)	д
2000	5.1 - 54.5	49.4	10.6	5.0 – 51.8	46.8	10.4
2001	5.1 - 54.6	49.5	10.8	4.6 – 50.2	45.6	10.8
2002	5.5 - 45.0	39.5	8.2	5.2 – 43.1	37.9	8.3
2003	4.7 - 44.1	39.4	9.4	5.2 – 40.2	35.0	7.7
2004	4.0 - 60.3	56.3	15	5.0 – 35.6	30.6	7.1
2005	3.9 - 45.8	42.0	11.9	4.2 – 29.9	25.7	7.1
2006	4.3 - 49.6	45.3	11.5	4.7 – 26.4	21.7	5.6
2007	4.4 - 37.7	33.3	8.6	4.7 – 16.9	12.2	3.6
2008	4.0 - 29.5	25.5	7.3	4.4 – 15.4	11.0	3.5
2009	3.0 - 30.0	27.0	10	4.9 – 13.1	8.2	2.7

Table 3: Comparison of Actual and 600 mile KSHARE Optimized Transplant Rates Using a Simulation Model (2000-2009)

 $\Delta = \underset{A = Maximum Transplant Rate}{Maximum Transplant Rate} = \underset{Minimum Transplant Rate}{Minimum Transplant Rate}$

Table 4: Comparison of Actual and KSHARE Optimized Transplant Rate Disparity with States with more than One DSA (2000-2009). The disparity ratio $\partial = \frac{Maximum Transplant Rate}{Minimum Transplant Rate}$ is

calculated within each state with more than one DSAs.

	ACTI	JAL	KSHARE	
State	2000	2009	2000	2009
CA	2.495	2.847	2.437	1.003
FL	2.598	1.455	3.374	1.830
NC	2.090	1.825	1.027	1.000
NY	10.260	2.186	7.348	1.850
ОН	4.208	2.552	5.049	2.500
PA	2.271	1.911	1.507	1.021
TN	1.024	1.385	1.410	1.183
ТΧ	1.837	4.492	2.137	2.474
WI	1.193	3.177	1.123	1.330

Table 5: Comparison of Actual and KSHARE Optimized Transplant Rate Disparity withRegions (2000-2009). The disparity ratio $\partial = \frac{Maximum Transplant Rate}{Minimum Transplant Rate}$ is calculated within region.

	ACT	UAL	KSH	ARE
Region	2000	2009	2000	2009
1	1.783	1.051	1.525	1.000
2	4.059	2.181	1.945	2.154
3	3.834	8.323	4.634	2.340
4	1.837	5.854	2.473	2.474
5	7.434	10.576	4.480	2.500
6	2.271	1.665	2.237	1.012
7	1.554	3.379	1.448	1.491
8	3.017	2.831	2.972	2.402
9	10.260	2.186	7.348	1.850
10	4.268	2.552	5.049	2.500
11	2.865	3.002	3.172	2.500



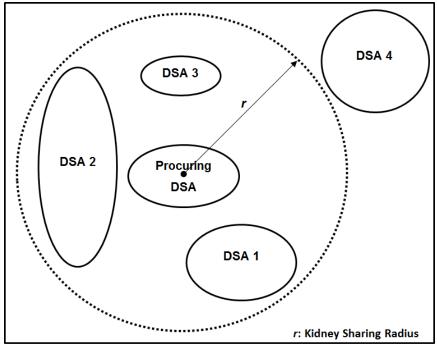


Figure 2: Actual versus 600 Mile KSHARE DSA Sharing Partnerships (2009)

