A Short Course on Market Design and Matching

Özgür Yılmaz

College of Administrative Sciences and Economics
Koç University

KU Leuven
January 2018

Lecture 6: Kidney Exchange II

Do the 3-way exchanges increase the number of transplants?

A pair is denoted as type X-Y if the patient and donor are ABO blood-types X and Y, respectively.

Example (Roth et al, 2007): Consider the following pool of incompatible pairs:

- O-B, O-A, A-B, A-B, B-A (blood-type incompatible),
- A-A, A-A, A-A, B-O (positive crossmatch).

Assume there is is no tissue type incompatibility between patients and other patients' donors in the pool.

- If only two-way exchanges are possible: (A-B,B-A), (A-A,A-A), (O-B,B-O).
- If three-way exchanges are also feasible: (A-B,B-A); (A-A,A-A,A-A); (B-O,O-A,A-B).

Do the 3-way exchanges increase the number of transplants?

The three-way exchanges allow

- an odd number of A-A pairs to be transplanted (instead of only an even number with two-way exchanges), and
- O-type donors can facilitate three transplants rather than two.

Do the 3-way exchanges increase the number of transplants?

Let $\mathbf{odd}_X$ be equal to 1 if the size of the set X is odd, and 0 otherwise.

Proposition (Roth et al, 2007)

The effect of the three-way exchanges on the number of transplants is

$$odd_{A-A} + odd_{B-B} + odd_{AB-AB} + \#AB - O+$$

$$\min\{\#A - B - \#B - A, \#B - O + \#AB - A\}$$

Do the 4-way exchanges increase the number of transplants?

Example: Consider the following pool of incompatible pairs:

- O-A, A-B, B-AB (blood-type incompatible),
- AB-O (positive crossmatch).

Assume there is is no tissue type incompatibility between patients and other patients' donors in the pool.

- If only two-way and three-way exchanges are possible: (O-A, A-B, AB-O).
- If four-way exchanges are also feasible: (AB-O, O-A, A-B, A-AB).

Do the 4-way exchanges increase the number of transplants?

A type AB-O patient can form a four-way (AB-O, O-A, A-B, B-AB) exchange with three patients on the long side increasing the size of the maximal-size match by one.

Do the 4-way exchanges increase the number of transplants?

The number of exchanges is quite marginal since the frequency of AB type is very small.

Patient ABO Blood Type	Frequency
O	48,14
A	33,73
B	14,28
AB	3,85

Do the 4-way exchanges increase the number of transplants?

Let us recall the assumptions:

1. Large market assumption: No patient is tissue-type incompatible with another patient's donor.
2. Patient-donor pairs of types O-A, O-B, O-AB, A-AB, and B-AB are on the long side of the exchange in the sense that at least one pair of each type remains unmatched in each feasible set of exchanges.
3. Data suggests that (A-B) $>$ (B-A).
4. There is either no type A-A pair or there are at least two of them. The same is also true for each of the types B-B, AB-AB, and O-O.

No logistical constraints: all exchanges are possible

Theorem (Roth et al, 2007)

Consider a patient population for which Assumptions 1, 2, 3 and 4 hold and let μ be any maximal matching (when there is no restriction on the size of the exchanges). Then there exists a maximal matching ν that consists only of two-way, three-way, and four-way exchanges, under which the same set of patients get transplant as in matching μ.

Simulations

- Samples of incompatible pairs are generated.
- The characteristics such as the blood types of patients and donors, the PRA (percent reactive antibody) distribution of the patients, donor relation of patients, and the gender of the patients are generated using the empirical distributions of the U.S. Organ Procurement and Transplantation Network (OPTN) and the Scientific Registry of Transplant Recipients (SRTR) data.
- Whenever a pair is compatible (both blood-type compatible and tissue-type compatible), the donor can directly donate to the intended recipient and therefore this pair is not included in the sample.

Biologically Disadvantaged Groups for Transplantation

- Blood type O patients: Disadvantaged because of the natural injustice induced by ABO blood type compatibility
- Blood type B patients: More likely to be ethnic minorities who are more likely to suffer from kidney disease
  - % of patients transplanted within two years of going on the wait list:

O patients	22.4
B patients	18.3
A patients	38
AB patients	52.6

  - African American, Hispanic Asian ethnicities comprise the bulk of the B wait list (71 percent of the B list, and it is by far the highest among other blood type groups)

Kidney exchange: A new technology

Blood subtypes

- Antigen A has two major subtypes: A1 and A2.
- Patients of type B and O have usually very weak antibody response to A2 kidneys.
  - A2 kidneys can safely be transplanted to these patients as long as antibody response is weak.
  - The antibody response is measured by IgG titer value and a B or O patient's titer value must be below 1:8 to be eligible for a transplant from an A2 blood subtype donor.
  - A rough data on patients with low titer values:

	Percent of low titer value patients
B patients	80
O patients	35

Kidney exchange: A new technology

Blood Type A Subtyping

- Transplanting a subtype A2 kidney to a blood type B or blood type O patient requires two sets of tests, one set for the patient and another set for the kidney.
- Antibody Anti-A Titer Value Tests for Patients: Patient antibody Anti-A(IgG) titer value should be consistently below a certain threshold over a period, often over the last 6 months.
  Unless a patient hospital provides the documentation for consistently low antibody Anti-A (IgG) titer value, the patient is ineligible for subtype A2 kidneys.
- Subtyping Tests for Type A Kidneys
  1. Preliminary subtyping test: Not completely reliable. There is 3.5 percent odds that an A1 kidney will be tested as A2 (Bryan et al 2006).
  2. Confirmatory subtyping test: Reduces the frequency of mistakenly identifying an A1 kidney as A2 to 0.032 percent.

2014 US Reform on Deceased Donor Kidney Allocation

- Under the new deceased donor kidney allocation system, subtype A2 kidneys are preferentially allocated to blood type B patients.
- To benefit from increased access to kidneys, antibody Anti-A titer value tests are periodically conducted for blood type B patients.
  - To be eligible for a transplant from an A2 donor, a patient must have consistently low IgG titer values, approx. over 6 months.
  - Only 30 percent of patients have low IgG titer value. Thus, O patients have lesser incentives for building up a IgG titer value history; especially if they do not have a blood type A donor who may be of subtype A2.
  - O patients do not have a history of titer values since O patients are not eligible for A2 donors in the deceased donation context.

Rationale for Preferential Allocation: Equity in Access

- The Federal Final Rule, adopted in March 2000, provides a regulatory framework for the structure and operation of the OPTN:
  "The primary goal of the OPTN is to increase and ensure the effectiveness, efficiency, and equity of organ sharing in the national system of organ allocation, and to increase the supply of donated organs available for transplantation."
- While types B/O are both biologically disadvantaged, a type B patient is more likely to be a minority than a type O patient.
- The preferential allocation system is especially beneficial for the African American patient population which historically has the lowest access for transplant kidneys.

Rationale for Preferential Allocation: Practicality

- For a patient to be eligible for a subtype A2 kidney, his antibody Anti-A titer value should be consistently below a certain threshold over a period.
- Based on this medical criteria, more than 80 percent of type B patients are eligible to receive subtype A2 kidneys.
- In contrast, only 30-40 percent of type O patients are eligible for subtype A2 kidneys.

A recent finding (Sonmez et al, 2017)

- The preferential allocation of A2 kidneys to B patients in kidney exchange **potentially reduces**
  - the total number of living donor kidney transplants.
  - the number of living donor transplants across all ethnicities including the most disadvantaged groups such as the African American patient population.
- In contrast, making A2 kidneys available to both O and B patients will increase the total number of transplants.

Timing of Antibody Titer Value Tests Subtyping Tests

Antibody Titer Value Tests: Since a patient needs a history of antibody titer value tests to be eligible for an A2/A2B kidney transplant, these tests will be assumed to be carried out at the patient hospital before a potential recipient participates in kidney exchange.

Subtyping Tests (for A2/A2B) Living Donors: Two scenarios are considered.

1. Before Joining Kidney Exchange: Carried out at the hospital of the paired-patient of the type A paired-donor before the pair potentially participates in kidney exchange.
2. After Joining Kidney Exchange: Carried by the kidney exchange program (ex. by UNOS) once a pair joins the kidney exchange pool.

Formation of the Kidney Exchange Pool

- A patient with a paired living donor arrives to a hospital.
- If the pair is deemed (tissue, blood, and subtype) compatible given the available testing technology, the patient receives a transplant from his paired-donor.
- Otherwise the pair is transferred to the kidney exchange program.
- Exchange pool
  - blood type incompatible pairs (e.g. a pair of type O-B)
  - blood type compatible but tissue-type incompatible pairs (e.g. a pair of type B-O)

Assumptions on the Structure of the Kidney Exchange Pool

A pair is **underdemanded** (or, on the *long side of the exchange*) if at least one pair of the same type remains unmatched in each feasible set of exchanges. (Large population (**LP**))
(i) Under ABO compatibility, pairs of types O-A, O-B, O-AB, A-AB and B-AB are on the long side of the exchange.
(ii) Under A2-to-B compatibility, pairs of types O-A, O-B, O-AB, A-AB and B-A1B are on the long side of the exchange.
(iii) Under A2-to-O compatibility, pairs of types O-A1, O-B, O-AB, A-AB and B-AB are on the long side of the exchange.
(iv) Under full compatibility, pairs of types O-A1, O-B, O-AB, A-AB and B-A1B are on the long side of the exchange.

Assumptions on the Structure of the Kidney Exchange Pool

The next assumption is based on the following empirical observation for the US: The frequency of types A-B and B-A are 0.05 and 0.03 respectively (Terasaki, Gjertson, Cecka 1998). (Type Frequencies (**TF**))
The number of A-B pairs is greater than the number of B-A pairs.

Assumptions on the Structure of the Kidney Exchange Pool

The last assumption is justifed by Erdos-Renyi (1960) Random Graph Convergence Result for large kidney exchange pools:
(Upper-bound (**UB**))
(i) No patient is tissue-type incompatible with another patient's donor.
(ii) Each patient in the exchange pool has an IgG antibody titer value less than 1:8.

Analytical Results

Proposition 1: Consider the two-way exchange policy. If the compatibility protocol changes from ABO compatibility to A2-to-B compatibility, then
(i) the number of transplants via direct donation **increases** by $\#(B-A2)_{\checkmark}+\#(B-A2B)_{\checkmark}$,
(ii) the number of transplants via exchange **decreases** by

$$2\#(B-A2)_{\checkmark}-\#(AB-A2B)_{x}-\#(B-A2B)_{x}-\Lambda,$$

(iii) the total number of transplants **decreases** by

$$\#(B-A2)_{\checkmark}-\#(AB-A2B)_{x}-\#(B-A2B)-\Lambda,$$

where $\Lambda=(\mathbf{odd}_{(AB-AB)_{x}}-\mathbf{odd}_{(AB-A1B)_{x}})+(\mathbf{odd}_{(B-B)_{x}}-\mathbf{odd}_{(B-A2B)_{x}\cup(B-B)_{x}})$.

Proof

The structure of optimal matchings is given by the well-known Gallai-Edmonds Decomposition Theorem (Gallai (63, 64), Edmonds (65)).

The implication of this theorem for the current framework is as follows:

Lemma

(Gallai-Edmonds Decomposition (GED) Lemma)
In each maximal matching, a pair, which is not underdemanded and is compatible with an underdemanded pair, is matched with an underdemanded pair.

Intuition behind the proof

Switching to A2-to-B compatibility under the two-way exchange regime

- The number of A-B type pairs is weakly greater than the number of B-A type pairs.
- Long side of the market: pair of types O-A, O-B, O-AB, A-AB, B-A1B
- Long side of the market is shortened. But,

Intuition behind the proof

Switching to A2-to-B compatibility under the two-way exchange regime

- The number of A-B type pairs is weakly greater than the number of B-A type pairs.
- Long side of the market: pair of types O-A, O-B, O-AB, A-AB, B-A1B
- Long side of the market is shortened. But,
- **... short side of the market is also shortened.**

Analytical Results

Proposition 2: Consider the two-way exchange policy. If the compatibility protocol changes from ABO compatibility to A2-to-O compatibility, then
(i) the number of transplants via direct donation **increases** by $\#(O-A2)_{\checkmark}$,
(ii) the number of transplants via exchange **increases** by $\#(O-A2)_{x}+\#(A-A2)_{x}+\Theta$,
(iii) the total number of transplants **increases** by $\#(O-A2)+\#(A-A2)_{x}+\Theta$,
where
$\Theta=(\mathbf{odd}_{(O-O)_{x}}-\mathbf{odd}_{(O-O)_{x}\cup(O-A2)_{x}})+(\mathbf{odd}_{(A-A)_{x}}-\mathbf{odd}_{(A-A1)_{x}})$

Intuition behind the proof

Switching to A2-to-O compatibility under the two-way exchange regime

- AB-type donors and O-type patients are overrepresented.
- Higher demand for O than A (B) type donors and for A (B) than AB type donors.
- Long side of the market: pair of types O-A, O-B, O-AB, A-AB, B-AB
- Long side of the market is shortened.

Main result highlighted

- The allocation of A2 kidneys to B patients results in efficiency losses.
- The allocation of A2 kidneys to O patients results in efficiency gains.

Simulation Setup

- We randomly generate n non-blood related patient-donor pairs.
- Each patient is represented by the following set of characteristics: Race, blood type, A2 subtype compatibility status (for type O/B patients), and PRA status.
- Each kidney patient is assumed to arrive to a hospital paired with a non-biologically related donor.
- The donor can be a spouse or another non-biologically related donor. If the donor is a spouse, then she is assumed to be of the same race with the patient. Otherwise, her race is randomly generated using the US adult population race statistics.
- Based on the donor race, her other characteristics (blood type, A2 status, etc.) are randomly and independently generated.

Simulation Setup

- Upon generating a patient-donor pair, the donor is assumed to directly donate to her paired-patient if she is deemed compatible with the patient with the given technology. Otherwise the pair is assumed to be transferred to the kidney exchange pool.
- All assumptions used for the analytical analysis are dropped.

Patient-Donor Characteristics

3*	**US Races**				
	2***White**	2***Black**	2***Asian**	**Amer. Indian**	**Pacific Island.**
A. Patient $\rightarrow$ (Freq. %)	2*81.46	2*12.78	2*5.15	2*0.40	2*0.22
B. Other Donor $\rightarrow$ (Freq. %)	2*78.00	2*13.69	2*5.96	2*1.94	2*0.42
C. Blood Type $\downarrow$	Frequency (%)				
O	48.98	49.89	38.31	62.96	48.67
A	37.18	25.28	25.06	28.78	36.00
B	10.55	20.63	29.22	6.84	10.00
AB	3.29	4.19	6.41	1.43	5.33
D. Donor Relation	Frequency (%)				
Spouse	34.44	40.12	43.76	32.61	41.18
E. PRA Distribution $\downarrow$	Frequency (%)				
Low PRA	70.19				
Medium PRA	20.00				
High PRA	9.81				
F. A2 Subtype Comp.	Frequency (%)				
F.1. For *O* Patients	30				
F.2. For *B* Patients	80				

2-way Maximum Cardinality Exchange

Simulation Averages and Sample Standard Errors of $S = 500$ Simulations with $n = 2000$ Pairs						
Incomp. Pairs	Two-way Exchange					
	1. Without A Subtype Matching	2. With A Subtype Matching				
		Subtype Test Timing		$A2$ Transplant Protocol		
				i. $A2/A2B \to B$ only	ii. $A2 \to O$ only	iii. $A2/A2B \to B$ and $A2 \to O$
984.800 (23.2186)	**376.700 (22.3124)**	**(a) Before** Exchange Participation Decision	**Total Transplants**	**374.616 (23.1654)**	**424.852 (25.9950)**	**416.260 (25.4372)**
			B's receiving from own comp. $A2/A2B$ donors	12.180 (3.391)	-	12.180 (3.391)
			O's receiving from own comp. $A2$ donors	-	15.708 (3.833)	15.708 (3.833)
		(b) After Exchange Participation Decision	**Total Transplants**	**384.238 (23.1129)**	**425.374 (25.9735)**	**428.012 (26.1527)**
			B's receiving from own comp. $A2/A2B$ donors	1.022 (1.4034)	-	0.682 (0.7836)
			O's receiving from own comp. $A2$ donors	-	3.558 (2.2254)	3.882 (3.2902)

Table: Simulations for maximal two-way exchange (the numbers in parentheses are sample standard errors, to find the standard errors of the averages, divide the sample standard errors by $\sqrt{S} = 22.36$).

Welfare

- Roth, Sonmez, Unver (AER, 2007): Three-way exchanges contribute substantially.
- Roth, Sonmez, Unver, Saidman and Delmonico (AJT 2006): Simultaneous transplant constraint can be relaxed for good-samaritan donor chains (a.k.a. nondirected-donor chains), and thus substantially larger exchanges can be conducted.
- Sonmez Unver (2011): The impact of inclusion of compatible pairs in kidney exchange pool.
- The welfare gains from inclusion of compatible pairs is by far the largest of all. (Columbia University has adopted a program with compatible pairs.)
- Sonmez, Unver and Yilmaz (2017): The integration of blood subtyping technology into the exchange has adverse welfare effects.

Dynamic kidney exchange

Unver (RESTUD, 2010): In reality patients and donors arrive and leave the pool over time.

Unver considers how the transplantation center should decide who to match, when to match, etc.

Unver studies how to organize the dynamic kidney exchange mechanism. He shows

- When only two-way exchanges are feasible, it is optimal to conduct all exchanges as soon as they become available.
- When there is no limit on the size of the exchange, sometimes it is optimal not to conduct all the currently available exchanges and wait until more more patients can be matched.