

# Incentivized Kidney Exchange

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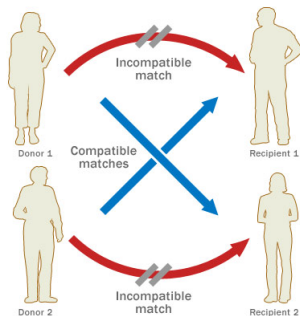
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- **Kidney Exchange** became a wide-spread modality of transplantation within the last decade (Roth, Sönmez, & Ünver 2004, 2005, 2007).
- More than 700 patients a year receive kidney transplant in the US along through exchange, more than 12% of all living-donor transplants.

# Kidney Exchange



- Human organs cannot be received or given in exchange for "valuable consideration" (US, NOTA 1984, WHO)
- However, **living donor kidney exchange** is not considered as "valuable consideration" (US NOTA amendment, 2007)

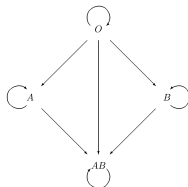
- Background and Contribution
  - Medical Institutions
  - Impact of (Non-)Inclusion of Compatible Pairs in Exchange
  - Efficiency and Access Equity As Two Transplantation Goals
  - Contribution of This Paper
- Model and Steady-State Derivations
  - Deceased Donation
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  - New Proposal: Incentivized Exchange
- Welfare and Equity Access Results
  - Efficiency and Equity Impact on Deceased-Donation Recipients
  - Efficiency and Equity Impact on Living-Donation Recipients
- Numerical Model Calibration Results

## BACKGROUND AND CONTRIBUTION

# Medicine of Kidney Donation: Compatibility

A donor needs to be pass two **compatibility** tests before transplantation can go through.

- **Blood-type Compatibility:** There are four blood types O, A, B, AB. Blood-type compatibility partial order:  $O \triangleright A, B \triangleright AB$ .



- **Tissue-type Compatibility:** Prior to transplantation, the potential recipient is tested for the presence of preformed antibodies against donor tissue type antigens, known as HLA.

If such antibodies exist above some threshold level, the donor is deemed **tissue-type incompatible**.

- **Deceased Donation:** Centralized priority allocation based on a points scheme. Waiting time is always prioritized. For kidneys  $\approx$  **first-in–first-out (FIFO)** queue based on geography except for patient with high tissue-type incompatibility chance and younger patients.
- **(Directed) Living Donation:** Mostly loved ones of the patient come forward. If one of them is compatible with the patient, then transplantation is conducted.
- **Living-Donor Organ Exchange:** If none of the living donors who came forward for their patient are compatible, kidney of one of them is **exchanged** with the compatible kidney from another incompatible patient-donor pair.

## (Non-)Inclusion of Compatible Pairs

- Typically a **blood-type compatible pair** participates in kidney exchange only when the donor is **tissue-type incompatible** with the patient.
- In contrast, a **blood-type incompatible pair** has no option for living donation other than kidney exchange.
- Hence, there are many more blood-type incompatible pairs in kidney exchange programs than blood-type compatible pairs.

**Number of O Patients  $\gg$  Number of O Donors**

- This disparity can be minimized if compatible pairs can also be included in kidney exchange.
- Most gains from kidney exchange will come from inclusion of compatible pairs rather than innovations in exchange formats or platforms.



In the US, the Organ Procurement and Transplantation Network (OPTN) is established to oversee equitable and efficient organ transplantation

*“With all of our collective efforts focused on patients, the goals of the OPTN are to:*

- ***Increase** the number of transplants*
- *Provide **equity in access** to transplants*
- *Improve waitlisted patient, living donor, and transplant recipient outcomes”*

- Three goals of OPTN for Equity in Access
  - Across blood types
  - Across tissue-type incompatibility levels
  - Across geographic regions
- Certain efficiency improving paradigms are abandoned because of inequity enhancing features
  - Example: ABO-incompatible indirect exchange

## New Proposal

*Incentivize compatible pairs to participate in exchange:*

*If a **compatible pair** with a more valuable donor blood type than patient blood type (such as A patient - O donor) participates in exchange, then give **priority** to the patient of this pair on the deceased-donor queue in case the patient's transplant fails in the future.*

- 15% of patients are reentrants for kidneys.
- Insure the patient of the compatible pair's altruism.
- All living donors already get such a **priority** for their altruism.

- A new **continuous-time continuum arrival** (a.k.a. **fluid**) model that can help us analyze the impact of all donation technologies together:
  - **deceased-donor allocation**,
  - **direct living donation**, and
  - **living-donor exchange**for all patient groups participating in different phases of the transplantation process.
- A new test-bed to quantify, predict, and estimate the **efficiency** and **equity** consequences of old and new transplant allocation policies.

## Contribution: Summary of Theoretical Results

In a homogeneous population (i.e., with uniform rates of donor arrivals per patient of the same blood type and with uniform tissue-type incompatibility probability), when reentry rates are sufficiently small:

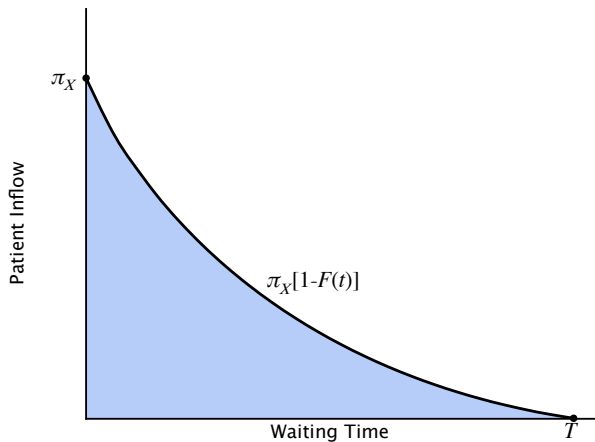
- When only **deceased donation** is available, all patients **wait for the same duration** for a transplant.
- When, in addition **direct living donation** becomes available,
  - every patient group **benefits**,
  - **access inequity to deceased donation arises**:  $t_O > t_B > t_A > t_{AB}$ .
- When, in addition, **(regular) exchange** becomes available,
  - every patient group **benefits**,
  - paired AB and O patients **benefit the least**, and paired B patients **benefit the most**,
  - **access inequity to deceased donation persists** for O:  
 $t_O > t_B = t_A > t_{AB}$ .
- When, in addition, **incentivized exchange** becomes available,
  - every patient group **benefits**,
  - all strictly with the exception of AB patients,
  - O patients **benefit the most**,
  - **access inequity to deceased donation decreases**.

## MODEL AND STEADY-STATE DERIVATIONS

- Each **patient** is represented by his blood type  $X \in \mathcal{T} = \{A, B, AB, O\}$ .
- Measure  $\pi_X$  of  $X$  blood-type **new patients** arrive every moment.
- $F(t)$ : The probability of a patient dying within  $t$  weeks after arrival such that  $F(T) = 1$  for some  $T$ .
- The **survival function** is  $1 - F(\cdot)$ : Living  $X$  blood-type patients at time  $t$  after arrival is

$$\pi_X[1 - F(t)].$$

# Patients with an Organ Failure

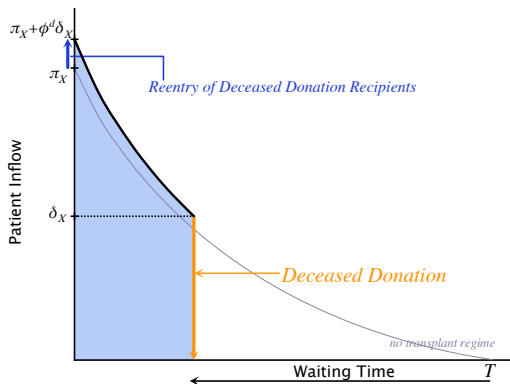




- Measure  $\delta_X$  of  $X$  blood-type **deceased donors** arrive every moment with  $\delta_X < \pi_X$ .
- **First-in-first-out (FIFO)** deceased-donor allocation protocol.
- $\theta < 1$ : The probability of a random donor having **tissue-type incompatibility** with a random patient (Tissue-type incompatibility probability could also be a distribution with mean  $\theta$  across the patient population, in the paper we consider this case).
- Blood-type allocation policy:
  - **ABO-i(dentical)**:  $X$  blood-type deceased-donor kidneys are only transplanted to  $X$  blood-type, compatible patients.
  - In the US, the policy is almost ABO-i, with the exception of A kidneys can be also transplanted to AB patients.

- At steady state, every moment a  $\phi^d$  fraction of the previous flow of deceased-donor transplants fail and those recipients **reenter** the queue.
- **Reentrant survival function** is assumed to be the same as that of new patients as  $1 - F(\cdot)$ .
- Thus,  $\phi^d \delta_X$  is the **flow of blood-type  $X$  reentrants**.

# Deceased Donation: Steady State



Demand = Supply

$$\left[ \pi_X + \phi^d \delta_X \right] \left( 1 - F(t_X^{\mathbf{d}, \text{dec}}) \right) = \delta_X$$
$$\Rightarrow t_X^{\mathbf{d}, \text{dec}} = F^{-1} \left( 1 - \frac{\delta_X}{\pi_X + \phi^d \delta_X} \right)$$

- To prove the above result, we need a new large market matching lemma regarding the possibility of **perfectly** matching

a flow  $\gamma$  of donors with a flow  $\gamma$  of patients,

who are blood-type compatible with these donors but can possibly be tissue-type incompatible with some.

- We prove such a lemma using a technique that uses **Gale's Demand & Supply Theorem**, assuming each patient has a **donor-tissue-rejection type**, and each rejection type's arrival flow goes to zero as the number of rejection types goes to infinity.
- We prove these types of lemmas for all of our results in the paper, i.e. for living-donor exchange as well.

- Fraction  $\lambda_X$  of blood-type  $X$  patients have a paired living donor, who is willing to donate to them.
- $p_X$  is the probability that the paired donor is of blood type  $X$ .
- We denote a pair type by patient-living donor blood types as  $X - Y$ .
- $p_Y \lambda_X \pi_X$  is the flow of pairs.
- $\phi^l < \phi^d$  is the reentering fraction of living donation recipients.

# Direct Living Donation

- Let  $p'_X$  be the probability of an  $X$  patient to be compatible with his living donor:

$$p'_O = (1 - \theta)(p_O)$$

$$p'_A = (1 - \theta)(p_O + p_A)$$

$$p'_B = (1 - \theta)(p_O + p_B)$$

$$p'_{AB} = (1 - \theta)(p_O + p_A + p_B + p_{AB}) = (1 - \theta)$$

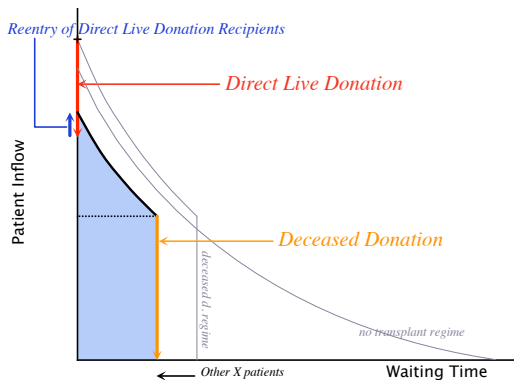
- In reality as  $p_B < p_A$ , we have

$$p'_O < p'_B < p'_A < p'_{AB}.$$

- Patient flow benefiting from direct living donation

$$I_X = p'_X \lambda_X \pi_X$$

# Direct Living Donation: Steady State



Demand = Supply

$$\left[ \pi_X - l_X + \phi^d \delta_X + \phi^l l_X \right] \left( 1 - F(t_X^{l,dec}) \right) = \delta_X$$

$$\Rightarrow t_X^{l,dec} = F^{-1} \left( 1 - \frac{\delta_X}{\pi_X - (1 - \phi^l) l_X + \phi^d \delta_X} \right)$$

- Only incompatible pairs participate.
- Only two-way exchanges are feasible.
- **Assumption:**
  - if  $Y \triangleright X$  then  $\theta p_Y \lambda_X \pi_X < p_X \lambda_Y \pi_Y$ .
  - $p_B \lambda_A \pi_A \leq p_A \lambda_B \pi_B$
- Categorize the pair types:
  - **Overdemanded types:** X-Y such that  $Y \triangleright X$  and  $Y \neq X$  & A-B
  - **Underdemanded types:** X-Y such that  $X \triangleright Y$  and  $Y \neq X$  & B-A
  - **Self-demanded types:** X-X



## Theorem (Optimal Living-Donor Exchange Rule)

*At steady state, a policy that dictates matching the longest-waiting pairs of a type  $X$ - $Y$  with their longest-waiting reciprocal type  $Y$ - $X$  pairs maximizes the flow of regular exchange transplants.*

- Self-demanded types and overdemanded types never wait in the exchange pool. They get matched immediately.
- Underdemanded types simultaneously wait in the **deceased-donor queue** and **exchange pool**.

In addition to flow of patients benefiting direct living donation,  $I_X$  found before, **flow of patients benefitting from exchange,  $e_X$** :

$$e_O = \theta p_O (\lambda_O \pi_O + \lambda_A \pi_A + \lambda_B \pi_B + \lambda_{AB} \pi_{AB})$$

$$e_A = \theta p_A (\lambda_A \pi_A + \lambda_{AB} \pi_{AB}) + \theta p_O \lambda_A \pi_A + p_B \lambda_A \pi_A,$$

$$e_B = \theta p_B (\lambda_B \pi_B + \lambda_{AB} \pi_{AB}) + \theta p_O \lambda_B \pi_B + p_B \lambda_A \pi_A, \text{ and}$$

$$e_{AB} = \theta (p_{AB} + p_A + p_B + p_O) \lambda_{AB} \pi_{AB} = \theta \lambda_{AB} \pi_{AB}.$$

- Introduce a tool for determining waiting times for deceased donation.
- Define a hypothetical *r*-ratio, a supply-to-demand flow ratio, as

$$r = \frac{\text{Flow of Donors}}{\text{Flow of Patients Who Demand These Donors}}$$

- As if all these donors will exclusively be allocated to these patients, a hypothetical waiting time for a group with supply-to-demand flow ratio *r*:

$$t = F^{-1}(1 - r).$$

decreasing in *r*.

Define the following  $r$ -ratios:

- For underdemanded type X-Y, they can participate in deceased donation or exchange. However, if they only participated in exchange the relevant  $r$ -ratio would be as follows:

- If  $X \triangleright Y$

$$r_{X-Y} = \frac{\theta p_X \lambda_Y \pi_Y}{\rho_Y \lambda_X \pi_X}$$

- If  $X-Y=B-A$

$$r_{B-A} = \frac{p_B \lambda_A \pi_A}{\rho_A \lambda_B \pi_B}$$

- For unpaired X patients, if all deceased donors were available to them because X-Y underdemanded pairs receive exclusively exchange:

$$r_X = \frac{\delta_X}{\pi_X - \lambda_X \pi_X + \phi^d \delta_X + \phi^l (\mathbf{I}_X + \mathbf{e}_X)} = \frac{\delta_X}{\pi_X^u}$$

- If  $t_X > t_{X-Y}$  then X-Y types will receive exclusively exchange transplants from Y-X and never receive deceased donation.

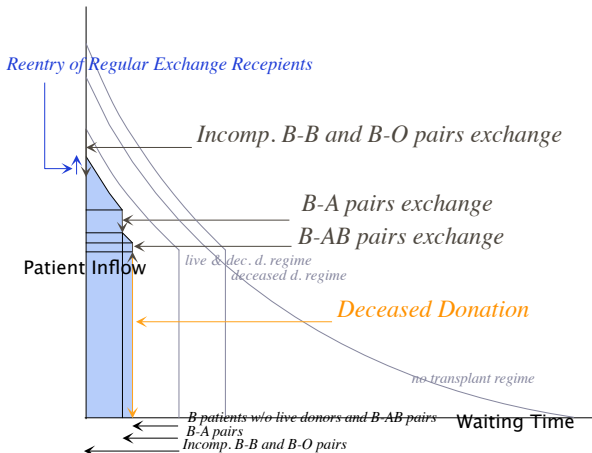
$$\implies t_X^{e,dec} = F^{-1}(1 - r_X)$$

- If  $t_X < t_{X-Y}$  then Y-X supply for X-Y demand is not enough to serve them all by exchange before a deceased-donor becomes available; thus, by assumption they are **pooled**:

$$r_{X,X-Y} = \frac{\delta_X + \pi_{Y-X}}{\pi_X^u + \pi_{X-Y}}$$

$$\implies t_X^{e,dec} = F^{-1}(1 - r_{X,X-Y})$$

# Regular Exchange: Blood-Type B Patients' Example



## New Policy: (Balanced) Incentivized Exchange

- A  $\rho_{X-Y}$  fraction of **compatible pairs** with type X-Y such that  $Y \triangleright X$  and  $Y \neq X$  participate in exchange, in return if their exchange transplant fails in the future, they receive **priority** in the deceased-donor queue upon reentry.
- **Balanced**: This measure of deceased donors of Y blood type will be reserved for X reentrants with **priority** for immediate transplantation.
- Waiting time for deceased donation is found similar to the case for regular exchange using the **pooling procedure**.



- No reentering patient gets a priority in AB deceased-donor queue.  
     $\implies$  Waiting time for AB deceased donation stays the same
- Reentering  $X \in \{A, B, AB\}$  patients of X-O get priority in O queue. If O-X were pooled for deceased donation under regular exchange in O deceased-donor queue: they begin dropping off of competition for deceased O donors, as incentivized X-O types facilitate more exchanges.  
     $\implies$  If  $\theta$  and  $\phi'$  are low, the waiting time for regular O deceased donation decreases
- Deceased-donor queues of B and A are similar to O's.

## WELFARE AND ACCESS EQUITY

## Theorem (Efficiency and Access Equity for Living Donation)

Let  $p_A > p_B$ . Suppose that all  $\lambda_X = \lambda$ ,  $\frac{\pi_X}{\pi_Y} = \frac{p_X}{p_Y}$  for all  $X$  and  $Y$ , and incentivized exchange participant fraction is uniform at  $\rho < 1$ . Then:

1. *Direct living donation:*

$$\frac{l_{AB}}{\pi_{AB}} > \frac{l_A}{\pi_A} > \frac{l_B}{\pi_B} > \frac{l_O}{\pi_O}$$

2. *Kidney exchange:*

$$\frac{e_B}{\pi_B} > \frac{e_A}{\pi_A} > \frac{e_{AB}}{\pi_{AB}} = \frac{e_O}{\pi_O}$$

With the inclusion of kidney exchange, overall access to living donation is ranked as

$$\frac{l_O + e_O}{\pi_O} < \frac{l_B + e_B}{\pi_B} = \frac{l_A + e_A}{\pi_A} < \frac{l_{AB} + e_{AB}}{\pi_{AB}} = \lambda$$

## Theorem (continued)

### 3. *Balanced incentivized exchange:*

$$\frac{i_O}{\pi_O} > \frac{i_A}{\pi_A} = \frac{i_B}{\pi_B} > \frac{i_{AB}}{\pi_{AB}} = 0$$

*and overall access to living donation is ranked as*

$$\frac{l_O + e_O + i_O}{\pi_O} < \frac{l_B + e_B + i_B}{\pi_B} = \frac{l_A + e_A + i_B}{\pi_A} < \frac{l_{AB} + e_{AB} + i_{AB}}{\pi_{AB}} = \lambda$$

## Theorem (Efficiency and Access Equity for Deceased Donation)

Let  $p_A > p_B$ . Suppose that all  $\lambda_X = \lambda$ ,  $\frac{\pi_X}{\pi_Y} = \frac{p_X}{p_Y} = \frac{\delta_X}{\delta_Y}$  for all  $X$  and  $Y$ , and incentivized exchange participant fraction is uniform at  $\rho < 1$ . Then:

1. With *deceased-donor transplantation only*, the waiting time at each deceased-donor queue is the same:

$$t_O^{\mathbf{d},dec} = t_A^{\mathbf{d},dec} = t_B^{\mathbf{d},dec} = t_{AB}^{\mathbf{d},dec}$$

2. Under *direct living-donor transplantation*, the waiting time at each deceased-donor queue decreases, and:

$$(t_{AB}^{\mathbf{d},dec} - t_{AB}^{\mathbf{l},dec}) > (t_A^{\mathbf{d},dec} - t_A^{\mathbf{l},dec}) > (t_B^{\mathbf{d},dec} - t_B^{\mathbf{l},dec}) > (t_O^{\mathbf{d},dec} - t_O^{\mathbf{l},dec})$$
$$t_{max}^{\mathbf{l},dec} = t_O^{\mathbf{l},dec} > t_B^{\mathbf{l},dec} > t_A^{\mathbf{l},dec} > t_{AB}^{\mathbf{l},dec} = t_{min}^{\mathbf{l},dec}$$

## Theorem (continued)

Further suppose that  $\theta$  and  $\phi^l$  are sufficiently small. Then:

3. Under *kidney exchange*, the waiting time at each deceased-donor queue decreases, and:

$$(t_{AB}^{\mathbf{d},dec} - t_{AB}^{\mathbf{e},dec}) > (t_A^{\mathbf{d},dec} - t_A^{\mathbf{e},dec}) = (t_B^{\mathbf{d},dec} - t_B^{\mathbf{e},dec}) > (t_O^{\mathbf{d},dec} - t_O^{\mathbf{e},dec})$$

$$t_{max}^{\mathbf{e},dec} = t_O^{\mathbf{e},dec} > t_B^{\mathbf{e},dec} = t_A^{\mathbf{e},dec} > t_{AB}^{\mathbf{e},dec} = t_{min}^{\mathbf{e},dec}$$

4. Under *balanced incentivized exchange*:

$$t_O^{\mathbf{b},dec} < t_O^{\mathbf{e},dec}; \quad t_A^{\mathbf{b},dec} = t_B^{\mathbf{b},dec} < t_A^{\mathbf{e},dec} = t_B^{\mathbf{e},dec}; \quad t_{AB}^{\mathbf{b},dec} = t_{AB}^{\mathbf{e},dec}$$

$$\underbrace{(t_{max}^{\mathbf{b},dec} - t_{min}^{\mathbf{b},dec})}_{=t_O^{\mathbf{b},dec}} < \underbrace{(t_{max}^{\mathbf{e},dec} - t_{min}^{\mathbf{e},dec})}_{=t_O^{\mathbf{e},dec}}$$

$$\underbrace{t_{max}^{\mathbf{b},dec}}_{=t_O^{\mathbf{b},dec}} < \underbrace{t_{max}^{\mathbf{e},dec}}_{=t_O^{\mathbf{e},dec}}$$

$$\underbrace{t_{min}^{\mathbf{b},dec}}_{=t_{AB}^{\mathbf{b},dec}} < \underbrace{t_{min}^{\mathbf{e},dec}}_{=t_{AB}^{\mathbf{e},dec}}$$

## NUMERICAL MODEL CALIBRATION RESULTS

*Calibration Parameters*

	O	A	B	AB	
ABO-i deceased-donor flows ( $\delta_X$ ) =	4982	3922	1225	314	Tissue-type incompatibility prob. $\theta$ = 0.0473
De-facto deceased-donor flows ( $\delta'_X$ ) =	4726	3818	1347	554	Reentry fraction of the recipients $\phi^l = \phi^d$ = 25.86%
New patient flows ( $\pi_X$ ) =	14693	9983	4466	1162	Incentivized-exchange particip. frac. ( $\rho$ ) = 25%, 50%, 100%
Paired-donor blood-type prob. ( $p_X$ ) =	0.456	0.378	0.126	0.040	Survival probability function $1 - F(t)$ = $0.9427e^{-0.1667t}$
Paired-donor fractions ( $\lambda_X$ ) =	43.07%	29.32%	31.74%	21.31%	

## 2009 US OPTN National Data and ESRD Survival Rates



<i>Model Outcomes: Patients Receiving Transplant</i>											
		O		A		B		AB		Overall	
Treatments		<i>Living-Donor Transplants</i>									
Living-donor transplantation ( $I_X$ )		2749.17	18.71%	2325.30	23.29%	785.76	17.59%	235.93	20.30%	6096.17	20.12%
Regular exchange ( $e_X + I_X$ )		2984.82	20.31%	2813.68	28.18%	1194.71	26.75%	247.65	21.31%	7240.85	23.89%
Incentivized ( $e_X + I_X + i_X$ )	$\rho = 25\%$	3483.52	23.71%	2835.97	28.41%	1202.14	26.92%	247.65	21.31%	7769.28	25.64%
	$\rho = 50\%$	3982.23	27.10%	2858.26	28.63%	1209.56	27.08%	247.65	21.31%	8297.71	27.38%
	$\rho = 100\%$	4979.65	33.89%	2902.85	29.08%	1224.42	27.42%	247.65	21.31%	9354.56	30.87%
Treatments	Dec. Donor A.	<i>Deceased-Donor Transplants</i>									
All except Balanced inc.	ABO-i ( $\delta_X$ )	4981.85	33.91%	3921.51	39.28%	1224.57	27.42%	314.07	27.03%		
	De facto ( $\delta'_X$ )	4726.00	32.16%	3815.00	38.21%	1347.00	30.16%	554.00	47.68%		
Balanced inc. $\rho = 25\%$	ABO-i	4852.86	33.03%	3997.96	40.05%	1262.47	28.27%	328.71	28.29%	10442.00	34.46%
	De facto	4597.01	31.29%	3891.45	38.98%	1384.9	31.01%	568.64	48.94%		
$\rho = 50\%$	ABO-i	4723.87	32.15%	4074.41	40.81%	1300.36	29.12%	343.35	29.55%		
	De facto	4468.02	30.41%	3967.9	39.75%	1422.79	31.86%	583.29	50.20%		
$\rho = 100\%$	ABO-i	4465.89	30.39%	4227.31	42.35%	1376.16	30.81%	372.64	32.07%		
	De facto	4210.05	28.65%	4120.79	41.28%	1498.58	33.56%	612.58	52.72%		

<i>Model Outcomes: Average Time to Nonprioritized Deceased-Donor Transplant</i>															
Dec.	O	A	B	AB	Overall	O	A	B	AB	Overall	O	A	B	AB	Overall
<b>Donor A.</b>	Deceased-donor transplantation					Incentivized $\rho = 25\%$					Balanced inc. $\rho = 25\%$				
ABO-i	6.64	5.83	7.82	7.90	6.51	5.16	4.70	6.52	7.23	5.20	5.30	4.58	6.33	6.94	5.20
De facto	6.93	5.98	7.28	4.79	6.51	5.41	4.85	5.98	4.04	5.21	5.56	4.72	5.81	3.88	5.19
	Living-donor transplantation					Incentivized $\rho = 50\%$					Balanced inc. $\rho = 50\%$				
ABO-i	5.82	4.81	7.04	6.99	5.62	4.70	4.83	6.73	7.53	5.06	4.97	4.59	6.35	6.94	5.05
De facto	6.11	4.95	6.51	3.92	5.62	4.94	4.91	6.17	4.20	5.05	5.23	4.74	5.82	3.88	5.05
	Regular exchange					Incentivized $\rho = 100\%$					Balanced inc. $\rho = 100\%$				
ABO-i	5.67	4.56	6.32	6.94	5.37	4.37	5.03	7.08	8.18	5.00	5.02	4.54	6.29	6.94	5.05
De facto	5.95	4.71	5.80	3.88	5.37	4.64	5.19	6.48	4.55	5.05	5.34	4.69	5.76	3.88	5.06

- New policy proposal: Incentivize compatible pair participation through prioritization of their patients in case he reenters the queue.
- To measure the welfare and equity effects formally, we introduce new machinery, a new dynamic entry-reentry model.
- We use the model for measuring, quantifying, estimating various effects of new and old policies on patient groups.