A Simulation-Optimization Framework To Improve The Organ Transplantation Offering System

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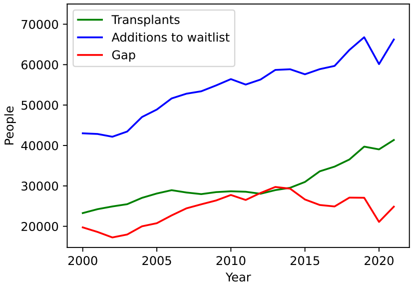
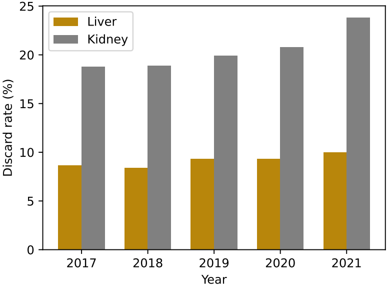
Motivation (1)

1. +105,000 patients in waiting list.
2. A new candidate $\sim$ every 10 minutes.
3. $\sim$ 17 people die each day waiting for an organ.
4. Large gap between organ supply and demand.
5. High discard rate on some organs.





Motivation (2)

Current system

Organ is procured → Quality check → Offered sequentially to patients on top of priority list → Organ accepted or offered until it is not viable anymore [Mankowski et al., 2019].

Why would an organ stop being viable?

Each organ has a maximum cold ischemia time (CIT; i.e. the time between the chilling of a tissue, organ, or body part after its blood supply has been reduced or cut off and the time it is warmed by having its blood supply restored).

Why do we have a high discard rate?

- Some organs are not deemed adequate for transplantation.
- "Undesirable" organs (specific attributes).
- Incentives to reject (medical doctors, transplantation centers).

Literature review

Priority list

Several articles have studied how to create "optimal" prioritized offering lists
[Zenios et al., 2000, Wolfe et al., 2007, Bertsimas et al., 2013].

Simulation models for the transplantation system

[Sandikçi et al., 2019] proposed and evaluated new models (national level), [Konrad, 2020] studied the roles of incentives.

Multiple simultaneous offers

[Mankowski et al., 2019] introduced the idea of multiple simultaneous offers, but did so at a high level, with fixed policies and without considering organ information.

Goal and contributions

Goal

Improve the organ offering system without having to change the prioritization or matching rules.

Contributions

We created a simulation-optimization methodology that maximizes the overall "gain" accrued by the transplantation system during the offering process. In particular:

1. Our model works for all organs and starts at the local (transplantation center) level, unlike previous work.
2. We incorporate batch-offering policies that are not fixed in advance, and also considers organ attributes and location.
3. We evaluate the quality of organs donated under our new policy to the overall quality of organs donated in the US.

Data sources

Three main data sources were used:

1. 2018–2019 public data for the waiting list (removals, new candidates, and average length), transplants performed, and expected acceptance ratio of organs per transplantation center (Scientific Registry of Transplant Recipients – SRTR).
2. Private data (2012–2014) involving the pool of organs donated and organs lost (Organ Procurement and Transplantation Network – OPTN).
3. Maximum cold ischemia times encountered in practice [Pan et al., 2018, Peters-Sengers et al., 2019].

Data preparation

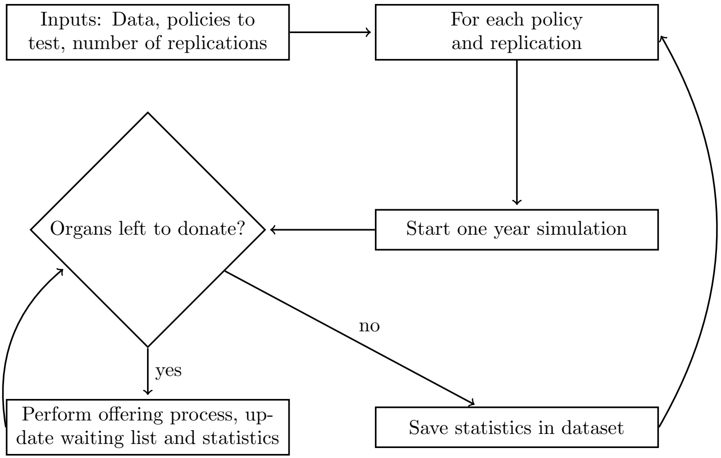
Organs' data:

1. Kidney categories: KDRI < 1.05, $1.05 \leq$ KDRI <1.75, and $1.75 \leq$ KDRI, where KDRI is the Kidney Donor Risk Index.
2. Liver categories: "Donor after cardiac death" (DCD), "Hepatitis C virus positive" (HCV+), and "Normal".
3. Arrival process was adjusted to reflect organs arriving at the transplantation center level.
4. Considered true discard rate because of organs exceeding the maximum CIT.

Transplantation centers' data:

1. Average waiting list information as starting point.
2. Average new candidate listings and removals to adjust waiting list size.
3. Offer acceptance ratio for organ categories at center level.

Methodology — Overview of the simulation model



Methodology — Simulation paramaters

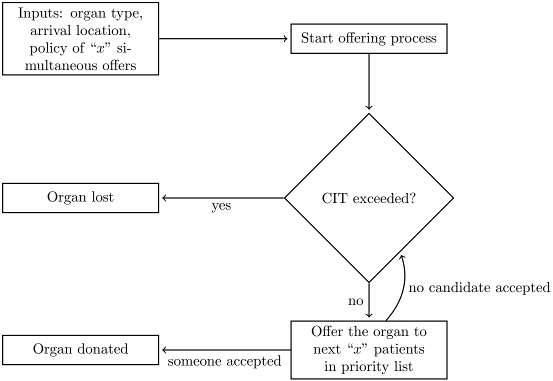
The following parameters exhibit a random behavior such as to mimic the variability exhibited by the centers' data (year over year):

- Initial length of waiting lists is within 20% of the average size of the waiting list that the center has experienced over time.
- Number of new listings and removals (waiting list) for each center during the year is also within 20% of average values.
- For each organ category, arrivals are also within 20% of average values. Arrivals are considered uniform over the year (consistent monthly donation data, and lack of granularity at day/week level).
- Finally, each organ (depending on its category) has a certain probability of being discarded for medical reasons.

Methodology — Offering process

Due to a lack of data we set:

1. A uniform (10, 60) minute response time for the first offer of a specific organ (center)
2. Subsequent uniform (0, 10) minute response times.



Methodology — Model validation

We validated our parameter choice for response times by setting our batching parameter x to 1 (current 1-offer-at-a-time policy).

Table 1: Validation of the liver model versus SRTR Data.

	1-offer simulation	SRTR data 2018
Organ utilization	90.95%	91.10%
Allocated organs	6,872	7,003
Total offers	168,109	168,159
Minutes to allocate	202	—

Table 2: Validation of the kidney model versus SRTR Data.

	1-offer simulation	SRTR data 2018
Organ utilization	80.80%	81.00%
Allocated organs	13,829	13,752
Total offers	1,563,116	1,562,014
Minutes to allocate	605	—

Methodology — Optimization

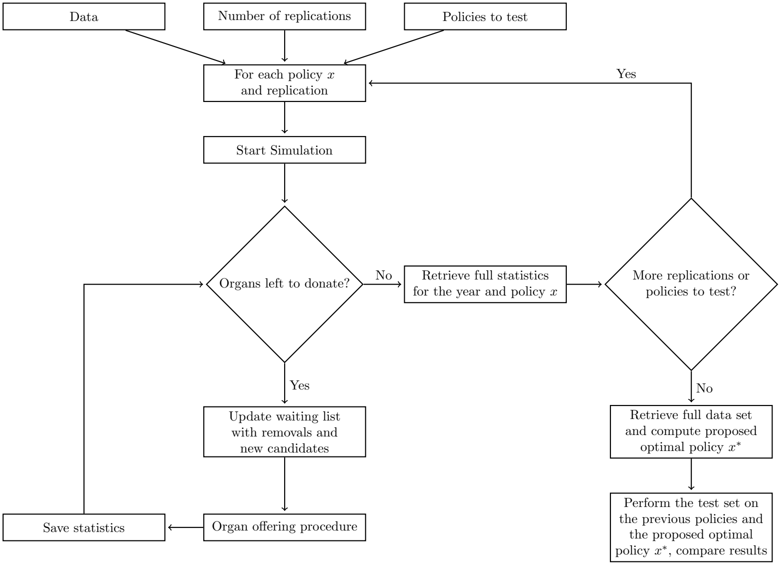
Positive and negative "gain" approach:

- Donating an organ returns a positive "gain" (1000 arbitrary units).
- First offer (-25 units), subsequent offers (-1 units) and disappointed patients (-300) return a negative "gain".

We seek to maximize the overall "gain". We proceed as follows:

1. Simulate many one-year period (replications) using different policies of x simultaneous offers.
2. For all replications record the net "gain" obtained for each organ (one sample in our training set).
3. Use the training set data to compute the expected value of a policy for a particular (organ category, location) pair.
4. Return the policy with the highest expected "gain" for all (organ category, location) pairs.

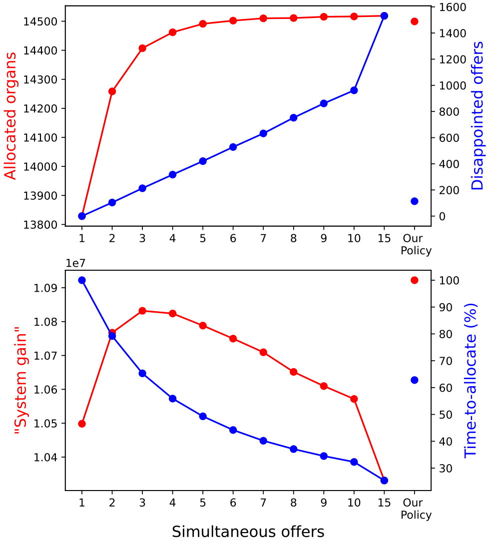
Methodology — Simulation-optimization approach



Test results — Kidney model

Over ten 1-year periods, our policy:

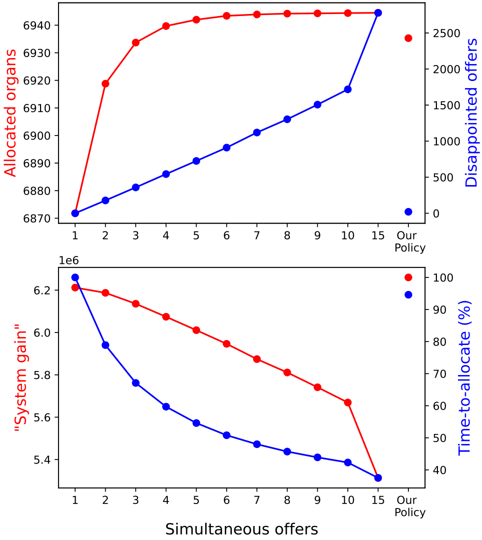
1. Maximizes the “gain” of the transplantation system.
2. Outperforms the benchmark (current) policy by around 650 donated kidneys per year.
3. Reduces the time needed to allocate the organs by 37.2%
4. Produces less disappointed offers than most of the other policies.



Test results — Liver model

Over fifty 1-year periods, our policy:

1. Outperforms the current policy by around 63 donated livers per year.
2. Reduces the time needed to allocate the organs by 5.3%
3. Allocates more organs than the $x = 2,\ 3$ policies with less offers, and has only 4% of the disappointed offers of the $x = 4$ policy.



Quality of discarded organs — Kidney

Table 3: Health markers for donated kidneys and kidneys discarded due to exceeding the maximum CIT.

	CIT discarded kidneys	Donated kidneys
DCD donors (%)	20.5%	13.9%
Donors with diabetes (%)	24.5%	7.2%
Donors with hypertension (%)	38.4%	73.3%
Mean body mass index of donors	28.3	27.0
Mean age of donors (years)	53.1	37.3
Age < 18 (%)	1.4%	11.2%
$18 \leq$ Age ≤ 34 (%)	9.8%	33.2%
$35 \leq$ Age ≤ 49 (%)	22.0%	27.9%
$50 \leq$ Age ≤ 64 (%)	46.8%	24.4%
$65 \leq$ Age (%)	20.0%	3.3%

Quality of discarded organs — Liver

Table 4: Health markers for donated livers and livers discarded due to exceeding the maximum CIT.

	CIT discarded livers	Donated livers
DCD donors (%)	78.8%	4.5%
Donors with diabetes (%)	9.6%	10.7%
Donors with hypertension (%)	74.9%	66.8%
Mean body mass index of donors	26.8	26.8
Mean age of donors (years)	37.8	39.5
Age $<$ 18 (%)	8.7%	9.6%
18 $\leq$ Age $\leq$ 34 (%)	37.5%	31.9%
35 $\leq$ Age $\leq$ 49 (%)	28.8%	25.5%
50 $\leq$ Age $\leq$ 64 (%)	20.7%	25.5%
65 $\leq$ Age (%)	4.3%	7.5%

Quality of discarded organs — Discussion

- All discarded organs had passed the quality approval process after being retrieved from the deceased donor.
- A study evaluating post-transplantation outcomes in more than 1,000 DCD and non-DCD livers donated found an insignificant difference in patient survival [Blok et al., 2016].
- Evidence of non-inferiority of DCD transplants found in [Cao et al., 2016].
- Countries such as Spain routinely and successfully use organs donated from patients over 70 years old (+23% from 70–79 age group, +10% from over-80 age group) [Matesanz et al., 2017].

These facts should ease the concerns about the pool of potential new organs to be donated, and suggest the discarded organs have good enough quality to provide value for recipients.

Conclusions and future work

We developed a model that:

1. Returns policies maximizing the "gain" of the transplantation system under all organs and set of parameters.
2. Provides granular policy recommendations based on organ categories and their arrival locations.
3. Yields better organ utilization and reduces the organ time-to-allocation versus the current system.

We also expect that more lives would be saved because of more donations, and further benefits could be expected because of lower time-to-allocation [Stahl et al., 2008, Cabello et al., 2011]. With respect to future work we should:

1. Extend the set of policies supported by our methodology.
2. Use new "gain" functions that represent better the trade-offs in the transplantation system.

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