

Multi-Organ Exchange: The Whole is Greater than the Sum of its Parts

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Abstract

Kidney exchange, where candidates with organ failure trade incompatible but willing donors, is a life-saving alternative to the deceased donor waitlist, which has inadequate supply to meet demand. While fielded kidney exchanges see huge benefit from *altruistic* kidney donors (who give an organ without a paired needy candidate), a significantly higher medical risk to the donor deters similar altruism with livers. In this paper, we begin by proposing the idea of *liver* exchange, and show on demographically accurate data that vetted kidney exchange algorithms can be adapted to clear such an exchange at the nationwide level. We then explore cross-organ donation where kidneys and livers can be bartered for each other. We show theoretically that this *multi-organ* exchange provides linearly more transplants than running separate kidney and liver exchanges; this linear gain is a product of altruistic kidney donors creating chains that thread through the liver pool. We support this result experimentally on demographically accurate multi-organ exchanges. We conclude with thoughts regarding the fielding of a nationwide liver or joint liver-kidney exchange from a legal and computational point of view.

Introduction

The transplantation of organs from a deceased donor to a needy living candidate first occurred nearly sixty years ago, but only became popular in the 1970s due to the introduction of immunosuppressants that help prevent the rejection of foreign organs in a patient’s body. Since then, the majority of transplantation has occurred through a deceased donor waiting list consisting of needy patients who wait for any willing donor to die, resulting in the harvesting and subsequent transfer of a compatible organ from the donor’s cadaver to the living patient. There is a great supply shortage of cadaveric organs in most societies (including the US), and the imbalance between supply and demand keeps growing. As of April 2014, there were 100,019 patients waiting for a kidney, 15,770 waiting for a liver, and 9,047 for another organ (e.g., pancreas, joint pancreas-kidney, heart, lung, intestine) in the US alone.

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In recent years, *live* donation of organs has significantly increased the total number of organ transplants. In live donation, a donor gives one of his two kidneys, one of his two liver lobes, or a part of an intestine, etc., to the patient so both the donor and patient can live. The effect of live donation has been most prominent in kidney donation, where a recent advance—*kidney exchange* (Rapaport 1986; Roth, Sönmez, and Ünver 2004)—has provided renewed hope to even “hard to match” patients. In kidney exchange, patients bring willing but incompatible donors to a large waiting pool. Patients can then swap incompatible donors with other patients. Matching a candidate to a donor is difficult for a variety of reasons, including blood (ABO) type, tissue (HLA) type, age, and—due to the limitations of current medical knowledge—unknown exogenous factors. Nevertheless, kidney exchanges on the regional and national scale have seen marked success over the last few years.

In this paper, we explore the creation of living donor exchanges involving organs other than kidneys. We first propose *liver* exchange, which is similar to kidney exchange in some ways, but remains unexplored.¹ The major difference between kidney and liver exchange rests in the increased risk to live donors, with very high rates of donor morbidity (24%), “near-miss” events in surgery (1.1%), and mortality (0.2%) compared to live donor kidney transplantation (Cheah et al. 2013). Fielded kidney exchanges derive significant value from *altruistic* donors, who enter the exchange without a paired needy candidate and trigger long “chains” of donations within the pool. With such a high risk of complication from surgery in liver transplantation, we expect significantly fewer (or no, if deemed unethical by the medical community) altruistic donors in liver exchange.

With this in mind, we propose *multi-organ* exchange, where candidates in need of either kidneys or livers can swap donors in the same pool. We show theoretically that this combination provides linearly more transplants than running separate kidney and liver exchanges; this linear gain is a product of altruistic kidney donors creating chains that thread through the liver pool. We support this result experimentally on demographically accurate kidney, liver, and

¹A notable exception is that in Korea, 16 candidates hand-swapped willing donors in a single hospital over the course of six years. All swaps were arranged by hand. This shows the feasibility of the idea at a small scale (Hwang et al. 2010).

cross-organ exchanges. We conclude with thoughts regarding the fielding of a nationwide liver or joint liver-kidney exchange from a legal and computational point of view.

This paper provides the first foray into the theory and computational methods necessary to set the groundwork for a fielded nationwide liver or multi-organ exchange. It is clear that such exchanges would be highly beneficial for sustaining life and creating value in society.

Preliminaries

In order to develop a nationwide liver or multi-organ exchange, we must first accurately model the realities of such an exchange and design optimal, scalable clearing algorithms for it. In this section, we describe the creation of a *compatibility graph* representing the space of possible swaps among n candidate-donor pairs, based on traits of the candidates and donors. We then describe the *clearing problem*, a formalization of the process used to determine an optimal set of swaps.

Compatibility Graph

We begin by encoding an n -patient organ exchange as a directed graph. Construct one vertex for each incompatible candidate-donor pair. Add an edge e from one candidate-donor vertex v_i to another v_j , if the candidate at v_j can take a liver lobe or kidney from the donor at v_i . This process creates a compatibility graph for the general concept of barter exchange, where participants can swap items with each other. Within the compatibility graph, a cycle c represents a possible swap, with each vertex in the cycle obtaining the item of the next vertex. A matching is a collection of *disjoint* cycles; no vertex can give out more than one item (e.g., more than one kidney or liver lobe). Cycles ensure that donors give items if and only if their patients receive organs.

Fielded kidney exchanges also gain great utility through the use of *chains* (Rees et al. 2009). An altruistic donor initiates a chain by donating his organ to a patient, whose paired donor donates her organ to another patient, and so on. Due to significantly increased medical risk to living donors of other organs, we do not expect many (or possibly any) altruistic donors outside of kidney exchanges (Cheah et al. 2013).

The Clearing Problem

The *clearing problem* is that of finding a maximum-cardinality matching consisting of disjoint chains and cycles of length at most some small constant L . The cycle-length constraint is crucial since all operations in a cycle have to be performed simultaneously. Were this not the case, a donor might back out after his incompatible partner has received an organ. This backing out is legal because, in nearly all countries including the US, it is illegal to form a binding contract over the exchange of organs. The availability of operating rooms, doctors, and staff causes long cycles to be unexecutable. As is the practice in the US-wide kidney exchange and most other real kidney exchanges, we let $L = 3$. Chains need not be limited in length (and typically are not in practice); were a donor to renege before giving an organ but after his paired patient had received the organ, then no remaining

pair in the pool has lost its “bargaining chip”—although the collapse of the chain is not desired.

Denote the set of all (uncapped length) chains and all cycles of length no greater than L by $C(L)$. Let $|c|$ represent the number of candidate-donor pairs in a cycle or chain c . Then, given binary indicator variables $\forall c \in C(L)$, we must solve the following integer linear program:

$$\max \sum_{c \in C(L)} |c| x_c \quad s.t. \quad \sum_{c: v_i \in c} x_c \leq 1 \quad \forall v_i \in V$$

The clearing problem with any fixed $L > 2$ is NP-complete (Abraham, Blum, and Sandholm 2007). (The cases $L = 2$ with no chains and $L = \infty$ can be solved in polynomial time.) Significantly better (i.e., higher cardinality) results are found with $L = 3$ over $L = 2$, so solving the NP-complete version of the problem is necessary in practice (Roth, Sönmez, and Ünver 2007). The problem, at least with respect to kidneys, can be solved optimally in practice at the steady-state nationwide scale using a specialized tree search algorithm based on the branch-and-price framework for integer programming (Abraham, Blum, and Sandholm 2007). We will later discuss this algorithm in more detail as well as enhancements to it for liver exchange and multi-organ exchange.

Combining Exchanges Results in Linearly More Matches

In this section, we show that combining independent liver and kidney exchanges leads to a linear gain in the aggregate number of matches. We show this in an adapted version of a recent random graph model for kidney exchange due to Ashlagi et al. (2012). They adapt sparse Erdős-Rényi graphs to a model of kidney exchange with two classes of candidate: those with many incoming edges and those with very few incoming edges (intuitively, “easy-to-match” and “hard-to-match” candidates). That model mimics the basic structure of compatibility graphs seen in fielded kidney exchanges.

They build a random directed compatibility graph $D(n, \lambda, t(n), p_L, p_H)$ with n candidate-donor pairs, $t(n)$ altruistic donors, a fraction $\lambda < 1$ of the n candidate-donor pairs—representing *lowly-sensitized*, easy-to-match patients—who have probability p_L of an incoming edge from each vertex in the pool, and a fraction $1 - \lambda > 0$ of the n candidate-donor pairs—representing *highly-sensitized*, hard-to-match patients—who have probability p_H of an incoming edge from each vertex in the pool. We assume $p_L > 0$ is constant, and $p_H = \frac{c}{n}$ for some constant $c > 1$; thus, the graph induced by only those $1 - \lambda$ fraction of (sensitized) vertices with incoming edge probability p_H is sparse.

We assume, for kidney exchange compatibility graphs D_K , $t(n) > 0$; however, for liver exchange graphs D_L , $t(n) = 0$ (i.e., there are no altruistic liver donors). Finally, define the graph join operator $D = \text{join}(D_K, D_L)$ between a kidney exchange graph D_K and liver exchange graph D_L as follows: add directed edges between candidate-donor pairs in both pools in accordance with each pair’s associated probability (p_L or p_H); do not add edges from the

$t(n)$ altruistic donors in D_K to vertices in D_L (since altruistic kidney donors are unwilling to donate a liver).²

In the following theoretical results, we consider cycles of length at most some constant but chains of any length; this mimics current practice in kidney exchange, and would likely mimic that of fielded liver exchange. Thus, an *efficient matching* allocates the maximum number of transplants in cycles of size no more than some constant and chains of any length. Both results build on the work of Ashlagi et al. (2012), which considers only a single kidney exchange.

Proposition 1 assumes a linear (in the number of candidate-donor pairs) number of altruistic donors, while Proposition 2 works with just a constant number of altruistic donors. We omit the proof of Proposition 1 due to space, and contrast both theoretical results at the end of this section.

Proposition 1. *Consider $\beta > 0$ and $\gamma > 0$, kidney compatibility graph D_K with n_K pairs and $t(n_K) = \beta n_K$ altruistic donors, and liver compatibility graph D_L with $n_L = \gamma n_K$ pairs. Then any efficient matching on $D = \text{join}(D_K, D_L)$ matches $\Omega(n_K)$ more pairs than the aggregate of any such efficient matchings on D_K and D_L (with probability approaching 1 as n_K approaches ∞).*

Proposition 2. *Consider $\gamma > 0$, kidney compatibility graph D_K with n_K pairs and constant $t > 0$ altruistic donors, and liver compatibility graph D_L with $n_L = \gamma n_K$ pairs. Then there exists $\lambda' > 0$ such that for all $\lambda < \lambda'$, any efficient matching on $D = \text{join}(D_K, D_L)$ matches $\Omega(n_K)$ more pairs than the aggregate of any such efficient matchings on D_K and D_L (with constant positive probability).*

Proof sketch. For small enough λ and large enough c , with high probability there exists a set S_K (of size at least $n_K/2$) of highly-sensitized pairs in D_K that are “too far” away from lowly-sensitized pairs in D_K to be matched in a cycle of capped length and must be matched in a chain triggered by an altruist a or not matched at all (Ashlagi et al. 2012). By similar reasoning, there exists a larger set $S_{K\&L}$ of highly-sensitized pairs in the combined kidney and liver graph (of size at least $(n_K + n_L)/2 = (1 + \gamma)n_K/2$ that must be matched by an a -initiated chain or not at all.

We apply a general result on sparse random directed graphs from Krivelevich, Lubetzky, and Sudakov (2013): as c increases, a directed path of length approaching $|S_K|$ in S_K and $|S_{K\&L}|$ in $S_{K\&L}$ exists. Then with constant positive probability there exists an edge from a to one of the vertices in the first half of the directed path in S_K (Ashlagi et al. 2012); thus, the size of this a -initiated chain approaches at least $|S_K|/2 \geq n_K/4$ and at most $|S_K| \leq n_K$ as c increases. Similarly, with a different but still constant positive probability there exists an edge from a to one of the vertices in the first $(\gamma/2)|S_K|$ vertices of the directed path in $S_{K\&L}$ (recall that, in expectation, $1/(1 + \gamma)$ fraction of this portion of the path are in the original kidney graph D_K , and $\gamma/(1 + \gamma)$ in expectation are in D_L and thus have probability 0 of an incoming edge from a), resulting in a chain of length

²For the sake of clarity, we assume that the p_L (resp. p_H) for D_K equals the p_L (resp. p_H) for D_L . This is without loss of generality; all that matters is that p_L be constant and $p_H = \frac{c}{n}$ for $c > 1$.

approaching at least $(1 + \gamma/2)|S_K| > |S_K|$ in expectation (as $c \rightarrow \infty$). Thus, by combining pools, we see an increase approaching at least $\gamma/2|S_K|$, which is $\Omega(n_K)$. This is a linear increase in overall efficiency since $n_L = \gamma n_K$. \square

Intuitively, Propositions 1 and 2 show the theoretical efficacy of combining kidney exchange with alternate organ exchanges (where altruistic donation is less likely to be popular or deemed ethically acceptable).³ We will support Proposition 1 empirically in the coming sections.

On the dense model for organ exchange. Initial research on random graph models for organ exchange adapted *dense* (constant probability of an edge existing) Erdős-Rényi graphs to kidney exchange (Ashlagi and Roth 2011; Dickerson, Procaccia, and Sandholm 2012b). Fielded exchanges have proven to be sparse in practice—as in the theory above—and thus actual pools and their optimal matchings do not align with these dense models (Ashlagi et al. 2012; Ashlagi, Jaillet, and Manshadi 2013; Dickerson, Procaccia, and Sandholm 2013; 2014). Still, we note that the efficiency results in the dense model with chains (Theorem 1 of Dickerson, Procaccia, and Sandholm (2012b)) can be applied directly to independent liver exchange and multi-organ exchange to yield efficient matchings with linear expected overall gain from combining pools (given a linear number of altruists) for large enough compatibility graphs.

Generating and Clearing Demographically Accurate Pools

In this section, we describe our method for generating organ exchange graphs. We then describe the standard kidney exchange clearing algorithm and, motivated by generated realistic liver and kidney exchange graphs, present a tweak to this algorithm to decrease liver exchange solution time.

Data Generation

In order to create an at-scale nationwide liver or multi-organ exchange, we first have to develop a compatibility graph generator with which we can run simulations. First, we draw data from reliable sources (here, specific to the US). Second, this data is fed into a graph creation algorithm that probabilistically determines the existence of compatible and incompatible candidate-donor pairs, as well as compatibility constraints between different candidate-donor pairs. In the large, with high probability, graphs generated by this algorithm will mimic the demographics that would prevail in a large-scale fielded exchange in the US. (Plugging different raw data (e.g., age, weight, blood type distributions) into

³While Proposition 2 may seem like a stronger result due to its relaxed reliance on a constant number of altruistic kidney donors (instead of the linear number in Proposition 1), the numerator c in $p_H = c/n$ may be required to be quite large (although still constant), the λ sensitivity constant quite small, and the result also holds with constant positive probability instead of holding with probability approaching one. We feel this makes Proposition 1 a more relevant result overall than Proposition 2 for the composition (in terms of pool sensitization and number of altruistic donors) of currently fielded kidney exchanges.

the generator algorithm would provide realistic generation of non-US compatibility graphs.)

We generate kidney exchange compatibility graphs in accordance with Saidman et al. (2006); however, the compatibility of a potential liver donor with a candidate differs from that of a potential kidney donor in three critical ways. While a donor and candidate must be blood type (ABO) compatible, (a) they need not be HLA-compatible,⁴ (b) the age of the donor and candidate makes a significant difference in transplant success (Egawa et al. 2004), and (c) the donor must be heavier than the candidate (or else the donor’s liver, which must be cut in two before transplantation, will not be large enough to support the donor and candidate).

Graph generation is performed as follows. For each candidate and donor, we draw a gender (from the 2010 US Census Report⁵); conditioned on gender, we then draw candidate blood types from the OPTN (Organ Procurement and Transplantation Network⁶) distribution and donor blood types from the overall US population.⁷ We sample ages (dependent on gender) for candidates from the OPTN pool and for the donors from the 2010 US Census at a granularity level of one year. Then, given the age and gender (generated separately from OPTN data for candidate and US Census data for donors, as described earlier), we sample from a fine-grained table of weights released by the Center for Disease Control (McDowell et al. 2008). For candidates requiring a kidney, HLA is sampled from the OPTN databases. During edge generation, we include an exogenous “incompatibility factor” $f \in [0, 1]$ that randomly determines an edge failure even in the case of a compatibility success. This factor is common in the kidney literature (Ashlagi et al. 2011), and is used to account for incompleteness of medical knowledge and temporal fluctuations in candidate-donor compatibility.

The Clearing Algorithm

We now briefly discuss a scalable optimal kidney exchange clearing algorithm (Abraham, Blum, and Sandholm 2007), which is used in the US-wide kidney exchange; we adapt that algorithm for our liver and multi-organ exchange experiments based on characteristics of the graphs generated using the algorithm described above. At a high level, given a compatibility graph $G = (V, E)$, the algorithm enumerates all chains and cycles of length at most L and chooses the optimal disjoint set of these cycles and chains according to the objective function of maximizing match cardinality.

In reality the number of cycles is prohibitively large (cubic in $|E|$ for $L = 3$, and exponential in $|E|$ for unbounded chains) to write down in memory. Therefore, solving this problem hinges on a technique called *branch-and-price* (Barnhart et al. 1998), a method for incrementally gen-

⁴In kidney exchange, tissue type (HLA antibodies and antigens) are an important determinant of compatibility. A candidate and donor sharing antigen encodings on the same locus are more likely to result in a rejected kidney. Due to the use of suppressant drugs, this is a negligible factor in liver transplantation.

⁵<http://www.census.gov/compendia/statab/cats/population.html>

⁶<http://optn.transplant.hrsa.gov/data/>

⁷http://bloodcenter.stanford.edu/about_blood/blood_types.html

erating only a small part of the model during tree search, yet guaranteeing optimality by proving that all the promising variables have been incorporated into the model. The actual solver uses several additional techniques to make kidney exchange clearing scalable for memory and time (Abraham, Blum, and Sandholm 2007). It uses empirically and theoretically motivated heuristics to seed the initial cycle (i.e., variable) set used on the model, and then incrementally brings cycles into the model depending on their shadow price, a quantitative estimate of a cycle’s utility given the current model. Optimality is proven when no cycles can possibly increase the objective. The algorithm also uses specific branching heuristics and primal heuristics to construct feasible initial integral solutions at each branch. If these integral solutions match the (restricted, possibly fractional) LP solution, then the subtree can be pruned and optimality potentially proven.

A Liver-Specific Cycle Seeding Heuristic. The selection of the initial seed columns—representing individual cycles—is a heuristic process. The prior algorithm uses the cycles from two heuristically-generated feasible solutions (very few such cycles) and hundreds of thousands of randomly selected cycles from $C(L)$. Since enumerating $C(L)$ in its entirety is a costly ordeal, their sampling relies on a series of random walks. Starting at a randomly chosen vertex, a random walk takes steps to new vertices. At each step, if an edge exists leading back to the initial vertex, the corresponding cycle is added to the set of seed cycles and a new start vertex is chosen. This results in a randomized, but not uniformly random, sampling of all cycles.

We define a different sampling method for the cycle seeding problem. Our generated liver compatibility graphs tended to have many more vertices with low out-degree than the corresponding kidney exchange graphs. These candidates are difficult to match. With this in mind, we conduct a biased random walk sampling in the same spirit as the prior algorithm, except weighting the selection of the randomized start vertex inversely proportional to its out-degree. This biased sampling of the set of all cycles motivates the solver to branch on hard-to-match candidate-donor pairs. This can be done efficiently through an initial sorting of the vertices by out-degree, a process whose one-time $O(|V| \log |V|)$ runtime is overshadowed by the NP-hard clearing problem.

Experimental Results

We now provide computational results for a hypothetical nationwide liver or multi-organ exchange, using the realistic data generated above. First, we describe timing and matching results in the *static* case, where the algorithm sees the problem in its entirety up front. Second, we describe results for the *dynamic* case, where candidate-donor pairs arrive in the pool over time and are either matched or die waiting. We show results at sizes mirroring an estimated steady-state size of a US-wide liver exchange. Finally, we explore the possibility of a multi-organ exchange, where both liver- and kidney-needing candidates can swap donors in the same pool. This results in more lives being saved than were the nation to run separate liver and kidney exchanges.

Static Liver Exchange Experiments

In the static case, the generator outputs a single graph and the optimization engine solves the clearing problem on this graph exactly once. Figure 1 shows timing results on liver exchange graphs of various sizes $|V|$ and exogenous incompatibility rates f . Intuitively, when f is low (or zero), the optimizer must consider many more edges than when f is high, resulting in longer runtimes for denser graphs. As expected, the computation time increases drastically with graph size.

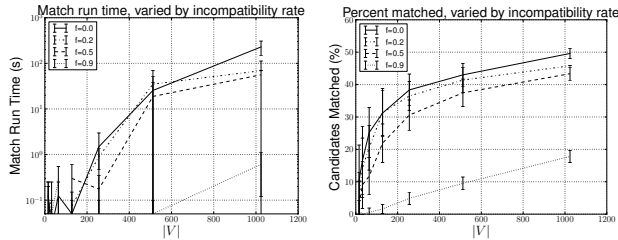


Figure 1: Match runtime (left) and percentage of candidates matched (right), varying incompatibility rate f and graph size $|V|$.

Figure 1 also shows the percentage of candidates matched (the number of candidates matched by the algorithm divided by the total number of candidates in the pool) as a function of compatibility graph size $|V|$ and exogenous incompatibility rate f . Intuitively, when f is held low, the percentage of candidates matched is higher than when the incompatibility rate is high. Of interest is the match behavior as $|V|$ increases. Regardless of f , the percentage of candidates matched increases with the size of the underlying compatibility graph. This behavior is similar to that seen in kidney exchange and motivates the need for a large (i.e., nationwide) liver exchange.

Addressing the needs of society. The estimated steady-state monthly size of the nationwide kidney exchange is 10,000 candidate-donor pairs (Abraham, Blum, and Sandholm 2007). The rate of live liver donation is 1/8th of the rate of live kidney donation (5% of all liver transplants involve live donors, compared to 40% for kidneys (Brown 2008)), although this number would hopefully increase due to the publicity of a successful exchange—we will conservatively estimate a factor of 1/2 as many live liver donors as kidney donors in steady-state. With 100,019 candidates currently waiting for a kidney and 15,770 candidates waiting for a liver in the US—and half as many live donors available—the steady-state for a US-wide liver exchange can be estimated at approximately half of $15,770 / 100,019 \approx 8\%$ of 10,000, or roughly 800 candidates. So, our clearing algorithm should be able to handle batch runs of a nationwide liver exchange.

Dynamic Liver Exchange Experiments

In the dynamic case, a variable number of candidates enter and leave the pool over a period of multiple time units. While the fielded nationwide kidney exchange currently operates under the static paradigm described earlier, recent work in the kidney exchange community has shown that optimizing in the dynamic setting leads to both more realistic and

higher cardinality matchings over time (Awasthi and Sandholm 2009; Ünver 2010; Dickerson, Procaccia, and Sandholm 2012a).

We start with a pool of $|V| = 800$ candidates assumed to be highly sensitized patients who built up in the system over time. These are matched myopically. Given a matched cycle by the algorithm, we then simulate that transplant actually succeeding in real life via an exogenous parameter set to $f = 0.7$. If any edge in a cycle fails, that entire cycle fails, and all candidates are returned to the pool (with the failed edge removed). We simulate candidates leaving the pool (either through finding a transplant or dying). On expectation $|V_{new}| = 226$ new candidates arrive in the pool per month, and the algorithm continues. We test over 24 months.

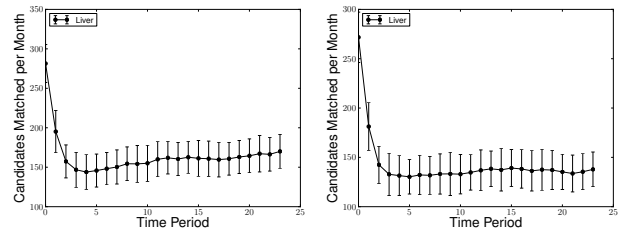


Figure 2: Number of candidates matched per time period in a dynamic setting over $T = 24$ months, with an expected lifetime per candidate of 10 years (left) or 1–2 years (right).

Figure 2 shows the number of candidates matched at each time period. This is the number of candidates matched by the algorithm, but before the virtual failures are taken into account. On the left, 12% of candidates will be alive after 10 years, corresponding to the expected lifetime of a kidney patient on dialysis waiting for a kidney (USRDS 2007). On the right, the probability of a candidate dying is set to an expected life of 1–2 years. This mimics the urgency of needing a liver transplant. While dialysis can be used to keep a patient with failed kidneys alive, no such treatment exists for livers. This corresponds to a drop in the number of candidates matched, due to the decreased number of candidates in the pool at each time period. (Note that a large number of candidates are matched per month in the beginning when the exchange goes live because there is a large pool that has accumulated. Soon thereafter a steady state is reached.)

Dynamic Bi-Organ Exchange Experiments

In this section, we expand beyond simulating a dynamic liver exchange to the novel concept of multi-organ exchange. In the long run, one could imagine exchanges of multiple different kinds of organs. However, to our knowledge, only kidneys and livers have ever been swapped (and only separately). Therefore, in this section we will focus on kidneys and livers. We show that combining an independent nationwide liver exchange with a nationwide kidney exchange into a joint kidney-liver exchange results in a statistically significant increase in the number of organ transplants, which aligns with Proposition 1.

We simulate a demographically accurate bi-organ exchange featuring candidates in need of either a kidney or a liver who can swap donors in a combined candidate-donor

pool. Approximately 85% of the candidates in the simulated pool need kidneys, while the other 15% need livers, as determined by the most recent OPTN waitlist data. We mimic the experiments in the previous section, with a starting pool size of $|V| = 800$ candidates who are highly sensitized and are assumed to have built up in the pool over time; we also include 100 altruistic kidney donors who enter the combined pool at an expected constant rate. We use the same exogenous transplant incompatibility parameter ($f = 0.7$) as in the previous section, and simulate candidate-donor pairs entering and exiting the pool in a similar fashion. To generate the candidates, we draw from the two different US distributions based on whether the candidate needs a kidney or a liver. Naturally, donors are drawn from the same US distribution in the two cases. We test over 24 months.

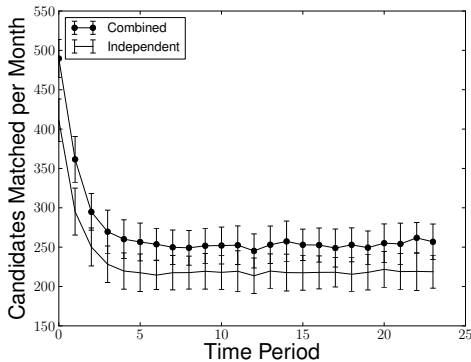


Figure 3: Number of matches in independent liver and kidney exchanges and a combined multi-organ exchange, per time period, in a dynamic setting over $T = 24$ months.

Figure 3 shows the number of candidates matched each month in the combined bi-organ exchange, as well as the aggregate number of candidates matched while keeping both liver- and kidney-needing candidates in separate pools. Clearly evident is the loss of life resulting from keeping both the liver and kidney pools independent, with the bi-organ exchange matching nearly 40 more candidates per month when compared to the two independent exchanges.

When we compare the *total* number of matches made over the entire period simulated above, the difference in lives saved between two independent pools and the combined bi-organ pool is more stark. In our experiments, the combined bi-organ pool produced 16.8% more matches than the sum of the two independent organ pools. An independent samples t -test revealed that the difference between the aggregate number of lives saved using independent, simultaneous liver and kidney exchanges and using a combined multi-organ exchange was significant, $t(46) = 31.37$, $p \ll 0.0001$.

Conclusions and Future Work

We explored the possibility of extending large-scale organ exchange to include liver lobes, either in conjunction with or independently of presently fielded kidney exchange. On demographically accurate data, vetted kidney exchange clearing algorithms (with a small tweak) can also clear liver exchanges at a projected US nationwide size. We explored the

prospect of multi-organ exchange, where candidates needing either a liver or kidney can swap willing donors in the same pool. We showed that such a combination matches linearly more candidates than maintaining two separate exchanges; this linear gain is a product of altruistic kidney donors creating chains that thread through the liver pool. This result is supported experimentally on demographically accurate multi-organ exchanges with high statistical significance.

This paper is intended as a first foray into automated liver and multi-organ exchange. As such, there is much room for future research (much of which is applicable to other organ exchange and even to barter exchanges beyond organs), and is motivated by experiences fielding the nationwide kidney exchange. One direction of future work is to take on the slow and politics-laden task of founding a liver exchange, or including livers in currently fielded kidney exchanges. Another is to develop scalable computational methods for the dynamic problem. Even for kidneys, the best current techniques are for simplified models (Ünver 2010; Ashlagi, Jaillet, and Manshadi 2013; Anshelevich et al. 2013) or face computational challenges (Awasthi and Sandholm 2009; Dickerson, Procaccia, and Sandholm 2012a).

Even for the static problem, scalability problems tend to get worse with the inclusion of a recent innovation in kidney exchange—donation chains started by altruistic donors. The cycle length cap L no longer applies to chains since they do not require simultaneous execution. Recent work explores this innovation, and hits computational limits experimentally with long chains (Ashlagi et al. 2012; 2011; Dickerson, Procaccia, and Sandholm 2012a; 2012b; Gentry and Segev 2011; Gentry et al. 2009). We do not expect altruistic donors in liver exchange due to increased risk for the donor compared to kidney donation, complicating the ethical considerations of even allowing altruistic donors in the pool (Woodle et al. 2010). However, that remains to be seen. In any case, one could include chains started by kidney-donating altruists into a bi-organ exchange—if the scalability challenges of chains can be adequately addressed.

Finally, this paper (and most papers on kidney exchange) deals with optimizing algorithmic organ matches; in reality, most algorithmic matches in fielded kidney exchanges do not result in an actual transplant. We expect this would be the case in liver and multi-organ exchange as well, although the exact failure rates for liver and multi-organ exchanges would be different than the observed failure rates in currently fielded kidney exchanges due to the medical and logistical differences in the organs and the transplant processes. Making organ exchange failure-aware is a critical step toward improving yield; recent work explores this notion (Blum et al. 2013; Dickerson, Procaccia, and Sandholm 2013) to both theoretically and empirically maximize the expected number of actual transplants (possibly with respect to some fairness constraints (Dickerson, Procaccia, and Sandholm 2014) that could try to balance factors including the increased risk of liver versus kidney donation) stemming from an algorithmic match.

Regardless, the urgent societal need for liver exchange is there today, and we hope to be able to address it through a dedicated or combined liver- or multi-organ exchange.

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References

- Abraham, D.; Blum, A.; and Sandholm, T. 2007. Clearing algorithms for barter exchange markets: Enabling nationwide kidney exchanges. In *ACM Conference on Electronic Commerce (EC)*, 295–304.
- Anshelevich, E.; Chhabra, M.; Das, S.; and Gerrior, M. 2013. On the social welfare of mechanisms for repeated batch matching. In *Proceedings of the National Conference on Artificial Intelligence (AAAI)*, 60–66.
- Ashlagi, I., and Roth, A. E. 2011. Individual rationality and participation in large scale, multi-hospital kidney exchange. In *ACM Conference on Electronic Commerce (EC)*, 321–322.
- Ashlagi, I.; Gilchrist, D. S.; Roth, A. E.; and Rees, M. 2011. Nonsimultaneous chains and dominos in kidney-paired donation—revisited. *American Journal of Transplantation* 11(5):984–994.
- Ashlagi, I.; Gamarnik, D.; Rees, M.; and Roth, A. E. 2012. The need for (long) chains in kidney exchange. NBER Working Paper No. 18202.
- Ashlagi, I.; Jaillet, P.; and Manshadi, V. H. 2013. Kidney exchange in dynamic sparse heterogeneous pools. In *ACM Conference on Electronic Commerce (EC)*, 25–26.
- Awasthi, P., and Sandholm, T. 2009. Online stochastic optimization in the large: Application to kidney exchange. In *Proceedings of the 21st International Joint Conference on Artificial Intelligence (IJCAI)*, 405–411.
- Barnhart, C.; Johnson, E.; Nemhauser, G.; Savelsbergh, M.; and Vance, P. 1998. Branch-and-price: column generation for solving huge integer programs. *Operations Research* 46:316–329.
- Blum, A.; Gupta, A.; Procaccia, A. D.; and Sharma, A. 2013. Harnessing the power of two crossmatches. In *ACM Conference on Electronic Commerce (EC)*, 123–140.
- Brown, R. S. 2008. Live donors in liver transplantation. *Gastroenterology* 134(6):1802–1813.
- Cheah, Y. L.; Simpson, M. A.; Pomposelli, J. J.; and Pomfret, E. A. 2013. Incidence of death and potentially life-threatening near-miss events in living donor hepatic lobectomy: A world-wide survey. *Liver Transplantation* 19(5):499–506.
- Dickerson, J. P.; Procaccia, A. D.; and Sandholm, T. 2012a. Dynamic matching via weighted myopia with application to kidney exchange. In *Proceedings of the National Conference on Artificial Intelligence (AAAI)*, 1340–1346.
- Dickerson, J. P.; Procaccia, A. D.; and Sandholm, T. 2012b. Optimizing kidney exchange with transplant chains: Theory and reality. In *International Conference on Autonomous Agents and Multi-Agent Systems (AAMAS)*, 711–718.
- Dickerson, J. P.; Procaccia, A. D.; and Sandholm, T. 2013. Failure-aware kidney exchange. In *ACM Conference on Electronic Commerce (EC)*, 323–340.
- Dickerson, J. P.; Procaccia, A. D.; and Sandholm, T. 2014. Price of fairness in kidney exchange. In *International Conference on Autonomous Agents and Multi-Agent Systems (AAMAS)*.
- Egawa, H.; Oike, F.; Buhler, L.; Shapiro, A.; Minamiguchi, S.; Haga, H.; Uryuhara, K.; Kiuchi, T.; Kaihara, S.; and Tanaka, K. 2004. Impact of recipient age on outcome of ABO-incompatible living-donor liver transplantation. *Transplantation* 77(3):403.
- Gentry, S. E., and Segev, D. L. 2011. The honeymoon phase and studies of nonsimultaneous chains in kidney-paired donation. *American Journal of Transplantation* 11(12):2778–2779.
- Gentry, S. E.; Montgomery, R. A.; Swihart, B. J.; and Segev, D. L. 2009. The roles of dominos and nonsimultaneous chains in kidney paired donation. *American Journal of Transplantation* 9(6):1330–1336.
- Hwang, S.; Lee, S.-G.; Moon, D.-B.; Song, G.-W.; Ahn, C.-S.; Kim, K.-H.; Ha, T.-Y.; Jung, D.-H.; Kim, K.-W.; Choi, N.-K.; Park, G.-C.; Yu, Y.-D.; Choi, Y.-I.; Park, P.-J.; and Ha, H.-S. 2010. Exchange living donor liver transplantation to overcome ABO incompatibility in adult patients. *Liver Transplantation* 16(4):482–490.
- Krivelevich, M.; Lubetzky, E.; and Sudakov, B. 2013. Longest cycles in sparse random digraphs. *Random Struct. Algorithms* 43(1):1–15.
- McDowell, M.; Fryar, C.; Ogden, C.; and Flegal, K. 2008. Anthropometric reference data for children and adults: United States, 2003–2006. *Nutrition* 10(10):1–45.
- Rapaport, F. T. 1986. The case for a living emotionally related international kidney donor exchange registry. *Transplantation Proceedings* 18:5–9.
- Rees, M.; Kopke, J.; Pelletier, R.; Segev, D.; Rutter, M.; Fabrega, A.; Rogers, J.; Pankewycz, O.; Hiller, J.; Roth, A.; Sandholm, T.; Ünver, U.; and Montgomery, R. 2009. A nonsimultaneous, extended, altruistic-donor chain. *New England Journal of Medicine* 360(11):1096–1101.
- Roth, A.; Sönmez, T.; and Ünver, U. 2004. Kidney exchange. *Quarterly Journal of Economics* 119(2):457–488.
- Roth, A.; Sönmez, T.; and Ünver, U. 2007. Efficient kidney exchange: Coincidence of wants in a market with compatibility-based preferences. *American Economic Review* 97:828–851.
- Saidman, S. L.; Roth, A.; Sönmez, T.; Ünver, U.; and Delmonico, F. 2006. Increasing the opportunity of live kidney donation by matching for two and three way exchanges. *Transplantation* 81(5):773–782.
- Ünver, U. 2010. Dynamic kidney exchange. *Review of Economic Studies* 77(1):372–414.
2007. United States Renal Data System (USRDS). <http://www.usrds.org/>.
- Woodle, S.; Daller, J.; Aeder, M.; Shapiro, R.; Sandholm, T.; Casingal, V.; Goldfarb, D.; Lewis, R.; Goebel, J.; and Siegler, M. 2010. Ethical considerations for participation of nondirected living donors in kidney exchange programs. *American Journal of Transplantation* 10:1460–1467.