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Maximum matchings in graphs for allocating kidney paired donation

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ABSTRACT

Living donors are often incompatible with their intended recipients. Kidney paired donation matches one patient and his or her incompatible donor with another pair in the same situation for an exchange. Let patient-donor pairs be the vertices of an undirected graph G, with edges connecting reciprocally compatible vertices. A matching in G is a feasible set of paired donations. Because the lifespan of a transplant depends on the immunologic concordance of donor and recipient, we weight the edges of G and seek a maximum edge-weight matching. Unfortunately, such matchings might not have the maximum cardinality; there is a risk of an unpredictable trade-off between quality and quantity of paired donations. We prove that the number of paired donations is within a multiplicative factor of the maximum possible donations, where the factor depends on the edge weighting. We propose an edge weighting of G which guarantees that every matching with maximum weight also has maximum cardinality, and also maximizes the number of transplants for an exceptional subset of recipients, while favoring immunologic concordance. We partially generalize this result to k-way exchange and chains, and we implement our weightings using a real patient dataset from Brazil.

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1. Introduction and motivation

The preferred treatment for end-stage renal disease is kidney transplantation, but there are not enough donor kidneys available to meet the need. As of November, 2018 there are 95,313 US candidates waiting for a kidney [1]. Often a family member or a friend offers to donate one of his or her two kidneys, but approximately one-third of such offers are ruled out because the donor's blood or tissue types are incompatible with the intended recipient. Kidney paired donation circumvents these barriers by matching an incompatible pair to another pair with a complementary incompatibility [2,3]. In simultaneous operations, the donor of the first pair gives to the recipient of the second pair, and vice versa.

A variety of operations research models have been applied for maximizing the benefits of kidney exchange [4–8]. The basic integer program formulations for kidney exchange were introduced by Roth et al. [9] and Abraham et al. [10]. More recent models cover broader aspects of kidney exchange, for instance, long chains in kidney exchange by Glorie et al. [11] and Anderson et al. [12] or international exchanges [13]. For further reading on the integer programming approach, we recommend surveys by Constantino et al. [14] and Mak-Hau [15].

Optimal two-way kidney paired donation can be formulated as a maximum matching problem in a weighted graph [4] or more generally as a cycle packing problem [16] if more than two pairs may be involved in any exchange. We primarily consider undirected graphs and two-way paired donation, but we also partially generalize to directed graphs representing k-way paired donation, involving up to k incompatible pairs.

Chains, in which a non-directed living donor donates to the recipient of an incompatible pair to start a sequence of living donations, can easily be incorporated into either model. We represent each non-directed donor as a node in the graph whose "recipient" is compatible with every paired donor in the pool.

The contribution of the paper is the design of clinically meaningful points systems for optimizing kidney paired donation. A paired donation allocation corresponds to a matching, or a cycle packing, in a graph which may have positive integer weights on either its vertices or edges. We argue that edge weights are necessary to capture important features of clinical paired donation such as matching pairs at the same hospital and the particularized risk of immunologic incompatibility. On an undirected graph, a maximum vertex-weight matching simultaneously maximizes the number of transplants performed. A maximum edge-weight matching, on the other hand, does not necessarily maximize the number of transplants performed. That is, accounting for factors such as the compatibility of each recipient with his or her donor

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might reduce the total number of transplants. On a directed graph, even weighting the vertices might decrease the number of transplants performed. Our work here is related to Dickerson et al. [17], which proved a theoretical bound and provided in-practice results showing the number of transplants overall that could be lost by requiring the maximum number of a special group of vertices to be included.

For maximum edge-weight matchings and cycle packings, we establish multiplicative bounds on the suboptimality of the number of transplants performed. Our results can be applied to generate edge weighting schemes that allow preference to be given to particularly good matches, with a guarantee that the number of transplants performed decreases by no more than a certain fraction. As a special case, we design an edge weighting that guarantees a maximum edge-weight solution will simultaneously maximize the number of transplants performed. For undirected graphs only, we also consider the case of a subgroup of recipients for whom a transplant is medically urgent, and design an edge weighting scheme that guarantees a maximum edge-weight matching will simultaneously maximize both the number of medically urgent recipients transplanted and the total number of transplants performed. Our proofs rely on elementary inequalities for matchings and cycle packings in edge-weighted graphs.

In Section 2, we consider various formulations of the objective for allocating kidney paired donation using maximum matchings. In Sections 3 and 4, we establish our main results on two-way matchings. In Section 5, we generalize to k-way kidney paired donation, using cycle packings on directed graphs. Computational results are presented in Section 6. We discuss the limitations of our analysis in Section 7.

2. Objectives for optimal matchings in KPD graphs

We represent reciprocal compatibility between incompatible pairs by edges in an undirected graph G. Each vertex of G represents an incompatible patient-donor pair, and there is an edge between two vertices of G whenever the donor of the first pair is compatible with the recipient of the second pair, and the donor of the second pair is compatible with the recipient of the first pair. We can represent non-directed donors that are available to start chains as vertices where the imaginary recipient would be compatible with the donor of any incompatible pair. We refer to G as a *KPD graph.*

2.1. Matchings in kidney paired donation graphs

A *matching* M in a graph G is a set of edges in G such that every vertex of the graph is incident with at most one edge of M. The *matching number* μ of G is the maximum number of edges in a matching in G. There is a vast literature on matchings, matching numbers, and their applications, including the classic paper by Edmonds [18], the book by Lovász and Plummer [19], and the survey by Pulleyblank [20].

Any feasible allocation of kidney paired donations within a KPD graph G is a matching. A KPD graph is not bipartite in general, since any incompatible pair may, in theory, be reciprocally compatible with any other.

There are several notions of optimality for the matching M. If all kidney paired donations are equally valuable, the matching M is optimal provided it has the maximum cardinality μ. We now discuss two variant notions of optimality in which *weights* (positive real numbers) are assigned to the vertices or edges of G to signify preferences among matchings.

The *vertex-weight* of a matching is the sum of the weights of the incident vertices. The *edge-weight* of a matching is the sum of the weights of its edges. Edge-weighted matchings include vertex-weighted matchings as a special case, in which the weight for each edge is defined as the sum of the weights of the vertices connected by that edge.

2.2. Factors that can be captured using vertex weights

To express priorities among patients, Roth et al. [21] proposed assigning a weight to each vertex of G. Organ allocation policy has long recognized special categories of transplant candidates: pediatric candidates, the medically fragile, or highly sensitized candidates. A medically fragile candidate is one whose need for a transplant has become urgent. A highly sensitized candidate is disadvantaged by a wide range of existing antibodies that make the search for a compatible donor like looking for a needle in the haystack [22]. Physicians recognize at least two objectives: maximizing transplants for prioritized patients, and maximizing transplants overall.

In the case of two-way matching on an undirected graph, there is no trade-off necessary to maximize both because maximum vertex-weight matchings always have maximum cardinality.

2.3. Factors that can only be captured as edge weights

The desirability of a particular paired donation allocation actually depends on both edge properties and vertex properties. To express priorities among feasible kidney exchanges, we proposed assigning a weight to each edge of the KPD graph G [4]. A maximum edge-weight scheme can also consider factors related to vertices, such as the pediatric or prior live donor status of a recipient, by adding the weight attributable to a vertex property to the weight of every edge incident on that vertex. Edge-weighted matchings are more general than vertex-weighted matchings, and more appropriate for KPD graphs.

KPD matching should favor better immunologic concordance between donor and recipient. Poor immune compatibility might trigger a response against the kidney, leading to graft rejection. Also, matches between pairs at geographically distant transplant centers require longer and more expensive organ transports. Both the distance and immunology must be modeled with edge weightings. Although kidney donors and recipients need not be related for a good outcome of the transplant, the extent of immunologic concordance between donor and recipient affects survival rates for the kidney [23]. Other factors such as the age and medical history of donor and recipient could be used to generate edge weights that express the expected gain in life-years for each particular donor and recipient pairing [24]. This would, for example, make it more likely that a kidney from a younger donor goes to a younger recipient who can take advantage of the graft's full usable lifespan [25].

Some centers can desensitize recipients to some incompatible donors, so edge weights might reasonably depend on the level of difficulty expected in desensitizing recipients to particular donors [26].

Furthermore, transplant centers strongly prefer to do an internal kidney exchange over matching their patients with candidates from another center [27]. The transplant centers must be assured that feasible matches between pairs who are both at their center will receive priority. Otherwise, large centers with the ability to perform many paired donations among their patients will have a disincentive to include their candidates and donors in a national registry.

For all of the considerations above, it is the fit between the donor and the recipient, which must be represented as an edge weight, that is critical to determining the benefit of an exchange.

3. Cardinality of maximum edge-weight matchings

In the worst case, the number of edges in a maximum edge-weight matching might be only half the number of edges in a maximum cardinality matching. In this section, we prove that

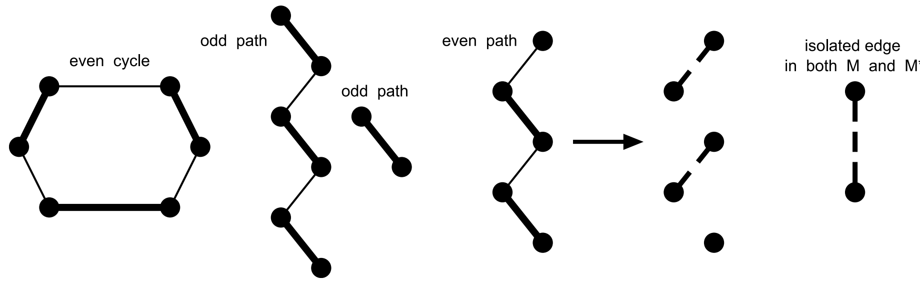

Fig. 1. Some components of the subgraph H in the proof of the Matching Lemma. The bold edges are in the maximum matching M, the unbolded edges are in the matching M^*, and the bold dashed edges are in both of the matchings M and M^*.

when there are only small differences between any two edge weights in the graph, a tighter multiplicative bound on the cardinality of the maximum edge-weight matching holds. We prove that, when all the edge weights are quite close together, in a sense we will describe, a maximum edge-weight matching has maximum cardinality.

3.1. Maximum vertex-weight matchings

The (vertex-) *weighted matching number* μ_v of G is the maximum number of edges among all matchings with maximum vertex-weight in G. The following result assures us that specifying higher priorities to some patients does not decrease the total number of patients receiving transplants in two-way paired donation.

Proposition 1. *In an undirected graph with positive vertex weights, any matching with maximum vertex-weight also has maximum cardinality. In other words, $\mu_v = \mu$, where μ of G is the maximum number of edges in a matching in G.*

We isolate the main idea of the proof of Proposition 1 in a lemma, which is a reformulation of a fundamental result in graph theory discovered by Berge [28,29]. We let $V(M)$ denote the set of vertices in a matching M.

Lemma 2 (*Matching Lemma*)**.** *Let G be a graph with matching number μ. Let M^* be any matching in G. Then there is a matching M with μ edges such that $V(M^*) \subseteq V(M)$.*

Proof. Proof of the Matching Lemma. Let M denote any maximum matching of G. We will replace some edges of M by an equal number of edges of M^* to bring about the containment $V(M^*) \subseteq V(M)$. It will not be necessary (and it may not be possible) to include all edges of M^* in a maximum matching M. Consider the subgraph H of G whose vertex set is $V(M^*) \cup V(M)$ and whose edge set is $M^* \cup M$. Each connected component of H is either an even cycle or a path with edges alternating between M and M^*, or an isolated edge belonging to both M and M^*. (See Fig. 1.)

The vertices of $V(M^*)$ in any even cycle are already in $V(M)$. In a path with an odd number of edges, the edge at each end must occur in M since M is a maximum matching, and it is clear that $V(M^*) \subseteq V(M)$. In paths with an even number of edges the two matchings use the same number of edges, and we may replace the edges of M by those of M^* (as illustrated in Fig. 1) to bring about the containment $V(M^*) \subseteq V(M)$. The vertices of $V(M^*)$ in an isolated edge belonging to both M^* and M are already in $V(M)$.

The Matching Lemma immediately implies Proposition 1. Let M_v be a maximum vertex-weight matching with μ_v edges. Then there is a maximum cardinality matching M that satisfies $V(M_v) \subseteq V(M)$. If $V(M_v) \neq V(M)$, then the vertex-weight of M is strictly greater than the vertex-weight of M_v, contrary to the definition of M_v. Therefore $V(M_v) = V(M)$, and thus $\mu_v = \mu$. The result in Proposition 1 is well-known; see [21] for a demonstration in a different context.

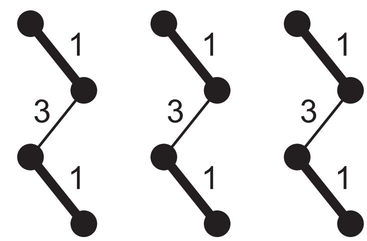

Fig. 2. A maximum cardinality matching (bold edges) has six edges, while a maximum weight matching has three edges. The labels are the edge weights.

3.2. Worst-case cardinality of maximum edge-weight matchings

The (edge-) *weighted matching number* μ_e of G is the maximum number of edges among all matchings with maximum edge-weight in G. Clearly,

$$\mu_e \leq \mu. \tag{1}$$

There are cases for which the inequality (1) is strict. For instance, the edge-weighted graph in Fig. 2 has matching number $\mu = 6$ and edge-weighted matching number $\mu_e = 3$. In this example, the ratio μ_e/μ equals 1/2.

Proposition 3. *In an edge-weighted graph with positive edge weights, a matching with maximum edge weight has at least half as many edges as a matching of maximum cardinality. In other words,*

$$\mu_e \geq \frac{1}{2}\mu. \tag{2}$$

Proof. Let M_e be a maximum edge-weight matching, and let M be a maximum matching of G. As in the proof of the Matching Lemma, consider the subgraph H of G with vertex set $V(M_e) \cup V(M)$ and edge set $M_e \cup M$. Again, each connected component of H is either an even cycle or a path. We will show that the inequality $\mu_e/\mu \geq 1/2$ holds for each connected component of H. The inequality (2) then follows.

An even cycle satisfies $\mu_e/\mu = 1$, as does an even path. Any odd path in H with k edges has its first, third, . . ., kth edge in M and its second, fourth, . . ., $(k-1)$th edge in M_e. There are $(k-1)/2$ edges of M_e and $(k+1)/2$ edges of M on an odd path with k edges, so we have $\mu_e/\mu = (k-1)/(k+1)$. This ratio is at least 1/2 unless $k = 1$. However, an odd path with one edge in H must belong to both M and M_e. An isolated edge in H belonging either to M or M_e but not both would violate either the maximum cardinality of M or the maximum edge-weight of M_e.

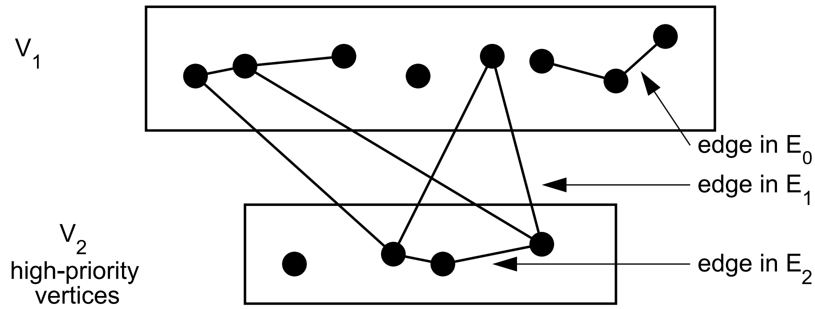

Fig. 3. Vertex and edge subsets.

The prospect of producing a maximum edge-weight allocation with μ_e near $\mu/2$ is likely to be unacceptable when arranging kidney exchanges. We proceed by restricting the class of edge weightings to obtain stronger guarantees. In Section 3.3 we will assign the edge weights in a manner that guarantees $\mu_e = \mu$.

3.3. A theorem on the cardinality of maximum edge-weight matchings

If the edge weights of an undirected graph G are all equal, then $\mu_e = \mu$, of course. We will show that the equality $\mu_e = \mu$ still holds provided the edge weights are nearly equal. Moreover, if the edge weights are not nearly equal, we give a lower bound for the fraction μ_e/μ.

Theorem 4. *Let G be an edge-weighted graph whose edge weights are all at least w and at most W $(0 < w \le W)$. Let μ and μ_e be the matching number and edge-weighted matching number of G. Then*

$$\mu_e \ge \left(\frac{w}{W}\right)\mu. \tag{3}$$

Also, if G has n vertices and $w \ne W$, then

$$\frac{W}{W-w} > \left\lfloor \frac{n}{2} \right\rfloor \quad \text{implies} \quad \mu_e = \mu. \tag{4}$$

Moreover, when the inequality in (4) holds, then every maximum edge-weight matching has maximum cardinality μ.

Proof. Consider two matchings M and M_e in G with maximum cardinality and maximum edge-weight, respectively. Of course, the weight of M is at most the weight of M_e. Also, the weight of M is at least $w\mu$, while the weight of M_e is at most $W\mu_e$. Therefore $W\mu_e \ge w\mu$, and inequality (3) follows.

Because μ and μ_e are integers, inequality (3) implies that $\mu_e = \mu$ if $(w/W)\mu > \mu - 1$. This latter inequality is equivalent to $W/(W-w) > \mu$ if we assume that $w \ne W$. In any graph the matching number satisfies $\lfloor n/2 \rfloor \ge \mu$, and thus the implication (4) holds. The argument remains valid when μ_e is replaced by $|M_e|$, the cardinality of an arbitrary maximum edge-weight matching. Thus, whenever the premise of (4) holds, every maximum edge-weight matching has maximum cardinality ($|M_e| = \mu$).

3.4. Edge weightings suggested by Theorem 4

Let G be a KPD graph with n vertices, matching number μ, and weighted matching number μ_e. The edge weight restriction of Theorem 4 forces the desirable equality $|M_e| = \mu_e = \mu$. It guarantees that every maximum edge-weight matching reflects a *quantitative efficiency* precept: Any two kidney paired donations are better than any single kidney paired donation.

Theorem 4 points the way to an allocation algorithm for kidney paired donation using the KPD graph G. We assign the weights

$$\begin{array}{llcll} & W & = & n+1 & \text{to each preferred edge of } G, \\ \text{and} & w & = & n-1 & \text{to each non-preferred edge of } G. \end{array}$$

An edge is *preferred* provided the two pairs have ready access to the same hospital, say, or the degree of immunologic concordance meets some desired threshold. Because $W/(W-w) = (n+1)/2 > \lfloor n/2 \rfloor$, by (4) we have $\mu_e = \mu$. Then the edges of M_e, any maximum edge-weight matching in G, give an optimal set of organ exchanges. This allocation maximizes the total number of kidney paired donations while simultaneously reducing travel and increasing immunologic concordance.

In the simplified method presented above, the edge weights take on just two values. No matching with maximum cardinality in G uses more preferred edges than M_e. In a more refined model we may specify degrees of preference by assigning edge weights to be real numbers in the closed interval $[n-1, n+1]$. We expand on this idea in Section 4.2.

4. Beyond the objectives of cardinality and edge-weight

4.1. Maximum edge-weight matchings with exceptional recipients

We might also want to maximize transplants for a very small group of exceptional recipients. Surgeons cite the example of patients who have run out of dialysis access and therefore cannot be dialyzed. For this group of recipients, a transplant is truly life-saving. Here, we consider an edge-weight system for two-way kidney exchange that parallels the one in Section 3.3, with the addition of an exceptional group of high-priority recipients.

4.1.1. A theorem on edge weights for exceptional recipients

Let $G = (V, E)$ be a KPD graph with n vertices. Consider the vertex partition $V = V_1 \cup V_2$, where each vertex in V_2 represents an exceptional recipient with his or her donor(s). We anticipate that V_2 will have smaller cardinality than V_1. A matching M has *maximum V_2-cardinality* provided no matching in G is incident with more vertices of V_2 than M. Our goal is to assign edge weights to reflect the high priorities of the vertices in V_2. Let the edge weight for each edge be the sum of: a number $b > 0$, a number $B > 0$ for each vertex in V_2 that is incident with the edge, and a number from the interval $[0, 2]$. Consider the edge partition $E = E_0 \cup E_1 \cup E_2$, where E_k is the set of edges of G with exactly k vertices in V_2 for $k = 1, 2, 3$. (See Fig. 3.) Then the edge weight of each edge in E_0, E_1, and E_2 lies in the respective closed interval

$$[b,\ b+2], \quad [b+B,\ b+B+2], \quad \text{and} \quad [b+2B,\ b+2B+2]. \tag{5}$$

The number b expresses the priority given to raw cardinality, the number B expresses the priority given to the vertices of V_2, and the number in $[0, 2]$ expresses any other desirable properties of a match, say, with larger weights corresponding to shorter travel distance or higher immunologic concordance.

Theorem 5. *Let G be an edge-weighted graph with vertex partition $V_1 \cup V_2$, edge partition $E_0 \cup E_1 \cup E_2$, and edge weights in the intervals in (5), with $b > 0$ and $B > 0$. Let G have matching number μ and edge-weighted matching number μ_e.*
(a) *If*

$$b \geq n-1, \tag{6}$$

then $\mu_e = \mu$, and every maximum edge-weight matching has maximum cardinality μ.
(b) *If*

$$B > n, \tag{7}$$

then every maximum edge-weight matching has maximum V_2-cardinality.

Part (a) asserts that, subject to condition (6) on b, every maximum edge-weight matching has maximum cardinality. Part (b) asserts that, subject to condition (7) on B, a maximum edge-weight matching also has maximum V_2-cardinality. If the premises (6) and (7) are both satisfied, then a maximum edge-weight matching has both maximum cardinality and maximum V_2-cardinality.

Preliminaries. Consider a vertex-weighted graph G_v, where every vertex in V_1 has weight $b/2$, and every vertex in V_2 has weight $(b/2) + B$. Let μ_v and μ be the matching number and vertex-weighted matching number of G_v. By Proposition 1, a maximum vertex-weight matching in G_v has maximum cardinality, and so $\mu_v = \mu$. Also, any maximum vertex-weight matching M_v has maximum V_2-cardinality. The Matching Lemma tells us that there is a maximum cardinality matching M with $V(M_v) \subseteq V(M)$. It follows that M has maximum V_2-cardinality. Because $B > 0$, M must have greater vertex weight than any maximum cardinality matching that does not have maximum V_2-cardinality, and so all maximum vertex-weight matchings must also have maximum V_2-cardinality.

We construct G_e, the edge-weighted graph corresponding to G_v, where the weight of each edge is the sum of the weights of the two incident vertices. From the argument above, M_e also has maximum cardinality and has maximum V_2-cardinality. Each edge weight of G_e equals b, $b+B$, or $b+2B$, depending upon the number vertices of V_2 incident with the edge.

We now amend the edge weights of the graph G_e, adding to each edge any number in the interval $[0, 2]$, to create a new graph G. Since the two graphs have the same set of edges, $\mu(G) = \mu(G_v)$. We use the generic μ to refer to the identical matching number of G and G_v. We will show that $\mu_e(G) = \mu$ if (6) holds, and that any maximum edge-weight matching in G has maximum V_2-cardinality if (7) holds.

Proof. Proof of (a). We proceed by contradiction. Assume that $\mu_e(G) < \mu$. Then because μ_e and μ are integers, $\mu_e(G) \leq \mu - 1$. Let the weight of every maximum edge-weight matching in G_e be K. The weight of a maximum edge-weight matching in G is at most $K - b + 2(\mu - 1)$, because it has one fewer edge (subtracting at least b) but might gain as many as $2(\mu - 1)$ units of weight from the amended weights of G. But by assumption (6), $K - b + 2(\mu-1) \leq K - n - 1 + 2\mu \leq K - n - 1 + 2\lfloor n/2 \rfloor < K$. The last inequality holds because $2\lfloor n/2 \rfloor \leq n$. Then the weight of a maximum edge-weight matching in G is strictly less than the weight of every maximum edge-weight matching in G_e, even though no edge weight in G_e exceeds the corresponding edge weight in G. This is a contradiction.

Proof. Proof of (b). We proceed by contradiction. Assume that some maximum edge-weight matching $M_e(G)$ does not have maximum V_2-cardinality. Again let the weight of every maximum edge-weight matching in G_e be K. The weight of a maximum edge-weight matching in G is at most $K - B + 2\mu$, because it contains at least one fewer vertex from V_2 (subtracting at least B), and might gain as many as 2μ units of weight from the amended weights in G. But by assumption (7), $K - B + 2\mu < K - n + 2\mu \leq K - n + 2\lfloor n/2 \rfloor \leq K$. Again the weight of a maximum edge-weight matching in G is strictly less than the weight of every maximum edge-weight matching in G_e, and we have a contradiction.

4.2. Edge weightings for clinical paired donation registries

Deciding what constitutes the best allocation is outside our scope. Those determinations must be made by the transplant community according to medical judgment and ethical principles. Theorems 4 and 5 provide guarantees regarding the effect of selecting particular numerical weights. If the correct clinical model is to order the cardinality objective(s) strictly ahead of other objectives, then policy-makers should select the edge weights from the specified intervals. Our theorems guarantee that the maximum edge-weight matchings solve the corresponding preemptive multi-objective problems.

The results presented here suggest a simple calculation to assign edge weight w_i to edge i in practice. Initially, assign a weight $\tilde{w}_i$ in the closed interval $[0, 2]$ to edge i. The number $\tilde{w}_i$ may be assigned on the basis of edge properties, such as the relative medical and geographic desirability of particular matches. Also, $\tilde{w}_i$ may be assigned on the basis of vertex properties, such as whether recipients are pediatric or prior live donors, when these recipients are not classified as exceptions.

Once n (the total number of patient-donor pairs) is known, add $b = n-1$ to each edge weight $\tilde{w}_i$ to get the weight w_i for edge i. If the consensus among physicians is that quantitative efficiency is required, then each edge weight falls in the interval $[n-1, n+1]$. The advantageous conclusion of Theorem 4 applies.

On the other hand, say that the desired allocation does not require quantitative efficiency, but a subset V_2 of exceptional vertices has been identified. Then we add $B = n+1$ to each edge weight $\tilde{w}_i$ for each vertex in V_2 incident with edge i. Thus either 0, $n+1$, or $2n+2$ is added to $\tilde{w}_i$. Because no edge should have weight zero, we add a small number to each edge, say, 1. The resulting edge weights are within the intervals

$$[1,\ 3], \qquad [n+2,\ n+4], \qquad \text{and} \qquad [2n+3,\ 2n+5]. \tag{8}$$

These edge weights might be suitable if there are some exceptional recipients, but policy-makers are willing to trade off overall cardinality to achieve, say, greater reductions in travel. Then part (b) of Theorem 5 applies, and as many exceptional recipients as possible will be matched.

If physicians require both quantitative efficiency and the maximum number of transplants for exceptional recipients, then we add $n-1$ to every edge, and we also add $B = n+1$ to each edge weight w_i for each vertex in V_2 incident with edge i. The edge weights will fall in the intervals

$$[n-1,\ n+1], \qquad [2n,\ 2n+2], \qquad \text{and} \qquad [3n+1,\ 3n+3], \tag{9}$$

and both of the reassuring conclusions of Theorem 5 hold. Donors and recipients can have confidence in an organ allocation system that maximizes the number of people who receive a transplant, and that gives absolute priority to exceptionally deserving recipients, and that also takes into account other important concerns.

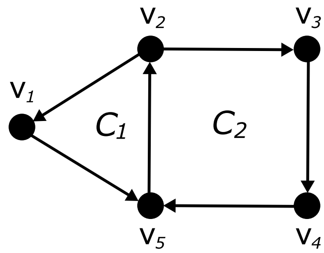

Fig. 4. A directed KPD graph with two directed cycles.

5. Kidney paired donation as vertex-disjoint cycle packing problem in a directed graph

To model kidney paired donation where three-way or k-way exchanges for $k > 2$ are permitted, we use a directed KPD graph $\mathcal{G}$ (See Fig. 4). There is an edge of $\mathcal{G}$ from one vertex to another vertex if the donor of the source vertex is compatible with the recipient of the target vertex. Then, any directed cycle in $\mathcal{G}$ is an opportunity for an exchange. In this case, the allocations are not matchings, but rather sets of vertex-disjoint cycles in the directed KPD graph $\mathcal{G}$. We formulate a problem of finding the best kidney exchanges as a vertex-disjoint cycle packing problem in directed graph [16]. A k-way cycle packing is a set of directed cycles involving only cycles of the length at most k. We define the cardinality of the cycle packing as the total number of edges involved in all cycles. Note that the analogous result to Proposition 1 does not hold: in Fig. 4, if the vertex weight of V_1 is greater than the sum of the vertex weights of V_3 and V_4, then the maximum vertex-weight cycle packing does not have maximum cardinality. We consider problems of finding k-way maximum cardinality cycle packings, and k-way maximum edge-weight cycle packings in the directed KPD graph.

Chains can still be represented, with a non-directed donor as a vertex with a dummy recipient that can receive a kidney from any donor except another non-directed donor. That is, there are edges pointing from each pair in the pool to each non-directed donor vertex.

In this setting, a maximum vertex-weight cycle decomposition might not have maximum cardinality. Dickerson et al. have provided a bound on the theoretical shortfall of cardinality (price of fairness) in these exchanges when including a side constraint that maximizes the number of included vertices of a given subset, given some assumptions about the structure of kidney paired donation graphs [17]. They also found that in practice the shortfall has been as large as 33.33%.

5.1. A theorem on the cardinality of maximum edge-weight vertex-disjoint cycles packing

We denote by $\bar{\mu}$ the number of edges in k-way maximum cardinality cycle packing in a directed KPD graph $\mathcal{G}$ for $k \geq 2$. We denote by $\bar{\mu}_e$ the maximum number of edges among all k-way cycle packings with maximum edge weight. Similarly to Section 3.3, we will provide a condition on edge weightings that guarantees $\bar{\mu} = \bar{\mu}_e$, along with a lower bound on the fraction $\bar{\mu}_e/\bar{\mu}$ for other edge weightings.

Theorem 6. *Let $\mathcal{G}$ be an edge-weighted directed graph whose edge weights are all at least w and at most W $(0 < w \leq W)$. Let $\bar{\mu}$ and $\bar{\mu}_e$ be the number of edges with in k-way maximum cardinality and k-way maximum edge-weight cycle packing of $\mathcal{G}$. Then*

$$\bar{\mu}_e \geq \left(\frac{w}{W}\right)\bar{\mu}. \tag{10}$$

Also, if $\mathcal{G}$ has n vertices and $w \neq W$, then

$$\frac{W}{W-w} > n \qquad \text{implies} \qquad \bar{\mu}_e = \bar{\mu}. \tag{11}$$

Moreover, when the inequality in (11) holds, then every k-way maximum edge-weight cycle packing has maximum cardinality $\bar{\mu}$.

Proof. Consider a k-way maximum cardinality cycle packing C and a k-way maximum edge-weight cycle packing C_e in $\mathcal{G}$ for $k \geq 2$. The weight of C is at most the weight of C_e. Also, the weight of C is at least $w\bar{\mu}$, while the weight of C_e is at most $w\bar{\mu}_e$. Therefore $w\bar{\mu}_e \geq w\bar{\mu}$, and inequality (10) follows.

Since $\bar{\mu}$ and $\bar{\mu}_e$ are integers, inequality (10) implies that $\bar{\mu}_e = \bar{\mu}$ if $(w/W)\bar{\mu} > \bar{\mu} - 1$. This latter inequality is equivalent to $W/(W-w) > \bar{\mu}$ if we assume that $w \neq W$. In any graph the cycle packing covers at most all n vertices, hence it satisfies $n \geq \bar{\mu}$, and thus the implication (11) holds. The argument remains valid when $\bar{\mu}_e$ is replaced by $|C_e|$, the cardinality of an arbitrary k-way maximum edge-weight cycle packing. Thus, whenever the premise of (11) holds, every k-way maximum edge-weight cycle packing has maximum cardinality $(|C_e| = \bar{\mu})$. All considered inequalities are oblivious to k, thus (10) and (11) hold for $k \geq 2$.

5.2. Edge weightings suggested by Theorem 6

Let $|C_e|$ be the number of edges in an arbitrary k-way maximum edge-weight cycle packing. Theorem 6 suggests an allocation algorithm for kidney paired donation using the KPD graph $\mathcal{G}$, if we want to guarantee that $\bar{\mu} = \bar{\mu}_e = |C_e|$. We assign the weights

$$\begin{array}{llll} & W = n+1 & \text{to each preferred edge of } \mathcal{G}, \\ \text{and} & w = n & \text{to each non-preferred edge of } \mathcal{G}. \end{array}$$

Because $W/(W-w) = n+1 > n$, by (11) we have $\mu_e = \mu$. Then the edges of C_e, any set of cycles of maximum edge-weight cycle packing in $\mathcal{G}$, give an optimal set of organ exchanges.

5.3. A wider interval of edge weights

The medical community might not prefer an allocation that maximizes the total number of transplants. Theorem 6 still offers a guarantee about the size of every maximum edge-weight cycle packing. If ethical considerations allow a cycle packing that contains a fraction $1-\epsilon$ of the number of edges in a maximum cardinality cycle packing μ, then by inequality (10) we may select our edge weights in any scaled version of the interval $[1-\epsilon, 1]$.

6. Computational experiments

To evaluate our proposal, we used real-life patient data acquired from one Brazilian hospital. Since KPD is still not permitted in any form in Brazil, this analysis also aims to provide evidence of increasing donation potential by allowing kidney exchanges.

6.1. Incompatible pairs data

Our single-center dataset contains 89 recipients, 11 of which had two incompatible donors available. We have data on the blood types of donors and recipients, and on the antigens for each donor and the donor-specific antibodies of each recipient. When a recipient has strong donor-specific antibodies against an antigen of the donor, then the kidney transplant is not compatible. Donor-recipient compatibility is evaluated using human leukocyte antigen (HLA) typing. All recipients were typed for HLA, but only 38 donors had HLA typing. For the remaining 62 donors, we randomly resampled HLA typing from over 500 past living donors from the same hospital.

A donor is assumed to be compatible with a recipient if they are blood-type compatible, and the recipient does not have strong donor-specific antibodies against the antigens of the donor. Each vertex of the graph represents a recipient and all of their incompatible donors.

A highly sensitized recipient is one that has preformed antibodies to most of the population, and so has difficulty finding any compatible donors. The panel reactive antibody (PRA) score approximates the percentage of the population with which the recipient is incompatible because of preformed antibodies. In our dataset, 21 candidates had PRA of at least 80%, and we considered them highly sensitized. Some of our weighting schemes prioritize highly sensitized recipients, because it is difficult to find matching donors for these recipients.

All pairs in our dataset are listed in one single transplant center. We simulated a multicenter pool by randomly assigning each pair to one of three notional cities. Some of our weighting schemes prioritize local (same-city) exchanges over those between multiple centers located in transplant centers in different cities.

6.2. Graph weighting

To model two-way KPD, we created an undirected edge between vertices in the KPD graph when the mutual exchange of kidneys was possible. To each edge, we variously assigned a numerical weight according to the schemes shown in Table 1.

To model two-and-three-way KPD as a cycle packing problem, we created a directed edge between vertices of the KPD graph, starting from a compatible donor to a potential recipient where the edge end. To each such edge, we assigned a numerical weight according to the schemes shown in Table 2.

In *Vertices* 1, all vertex-weights equal one. In *Vertices* 2, the exceptional recipients (sensitized or with past transplant) were awarded vertex-weight equal two, while the rest of vertices had vertex-weight one. The weight of each directed or undirected edge in *Vertices* 1 and *Vertices* 2 is the sum of the weights of the two incident vertices. For two-way KPD, *Vertices* 2 will have maximum cardinality, but for three-way KPD, *Vertices* 2 might not achieve this.

The *Edges* 1a scheme was suggested in Section 3.4 for matching and Section 5.2 for cycle packing problem, and it yields a maximum cardinality allocation that favors local exchanges. The *Edges* 1b has wider edge interval than *Edges* 1a (see Section 5.3). Using lower bound (3) for matching and lower bound (10) for cycle packing problem *Edges* 1b yields at least 70% of the maximum number of transplants in an allocation that favors local exchanges. The *Edges* 2 scheme weights edges in the intervals (8) of Section 4.2, and it yields a maximum V_2-cardinality matching (priority vertices) that does not necessarily have maximum cardinality. The *Edges* 3 scheme weights edges in the intervals (9) of Section 4.2, and it yields maximum cardinality and maximum V_2-cardinality allocations that local transplants edges. All schemes were tested for the matching problem, while we did not evaluate schemes *Edges* 2 and *Edges* 3 for cycle packing problem, since we did not offer theoretical results of this form for cycle packing.

6.3. Solution algorithm

The maximum cardinality and maximum edge-weight matching problems in undirected KPD graph are equivalent to maximum cardinality and maximum edge-weight cycle packing problems in an equivalent directed graph if only cycles of size two are allowed [16]. We represented an undirected KPD graph as a directed KPD graph, where each undirected edge becomes a cycle of two directed edges in a directed KPD graph. The weight of an undirected edge was split equally between two corresponding directed edges.

To solve a cycle packing problem, we used a simple integer program allowing participation of exactly two pairs in each cycle to model the matching problem, or at most three pairs in each cycle to model allocation with at most 3-way KPD [10]. Suppose G has n vertices, and p directed cycles, each with at most k edges. With the ith directed cycle, we associate the binary decision variable x_i. Let $x_i = 1$ if the ith cycle is included in the allocation, and let $x_i = 0$ if the ith cycle is not included in the allocation. Let the cycle index i be in the set Cyc(j) provided the ith cycle contains vertex j ($j = 1, 2, \dots, n$). Let the weight w_i represent the sum of edge weights of the ith cycle. Then the integer program to be solved is

$$\max \sum_{i}^{p} w_i x_i$$

$$\text{subject to: } \sum_{Cyc(j)} x_i \leq 1 \quad \text{for each vertex } j \text{ in } \{1, 2, \dots, n\}, \tag{12}$$

$$x_i \in \{0, 1\} \quad \text{for each cycle } i \text{ in } \{1, 2, \dots, p\}. \tag{13}$$

An optimal allocation was found using integer program solved by Gurobi Optimizer Version 8.1. from Gurobi Optimization, Inc [30].

Table 1
Two-way KPD edge weights for schemes *Vertices 1*, *Vertices 2*, *Edges 1*, *Edges 2*, and *Edges 3*.

Scheme	Edge weighting Two-way KPD	Weights	Weights ($n < 100$)
Vertices 1[a]	–	2	2
Vertices 2[a]	0 priority vertices	2	2
	1 priority vertices	3	3
	2 priority vertices	4	4
Edges 1a[a]	Unpreferred edge	$n-1$	99
	Preferred edge	$n+1$	101
Edges 1b	Unpreferred edge	$0.7n$	70
	Preferred edge	n	100
Edges 2	Unpreferred edge, 0 priority vertices	1	1
	Preferred edge, 0 priority vertices	3	3
	Unpreferred edge, 1 priority vertex	$n+2$	102
	Preferred edge, 1 priority vertex	$n+4$	104
	Unpreferred edge, 2 priority vertices	$2n+3$	203
	Preferred edge, 2 priority vertices	$3n+5$	305
Edges 3[a]	Unpreferred edge, 0 priority vertices	$n-1$	99
	Preferred edge, 0 priority vertices	$n+1$	101
	Unpreferred edge, 1 priority vertex	$2n$	200
	Preferred edge, 1 priority vertex	$2n+2$	202
	Unpreferred edge, 2 priority vertices	$3n+1$	301
	Preferred edge, 2 priority vertices	$3n+3$	303

[a]Overall maximum cardinality scheme.

Table 2
Three-way KPD edge weights for schemes *Vertices 1*, *Vertices 2*, *Edges 1*, *Edges 2*, and *Edges 3*.

Scheme	Edge weighting Three-way KPD	Weights	Weights ($n < 100$)
Vertices 1[a]	–	2	2
Vertices 2	0 priority vertices	2	2
	1 priority vertices	3	3
	2 priority vertices	4	4
Edges 1a[a]	Unpreferred edge	n	100
	Preferred edge	$n+1$	101
Edges 1b	Unpreferred edge	$0.7n$	70
	Preferred edge	n	100

[a]Overall maximum cardinality scheme.

Table 3
Comparison of numbers of transplants, preferred edges, and priority vertices matched with each weighting scheme for two-way KPD, using simulated donor-recipient pairs.

Weighting	Transplants			Preferred edge	Priority vertex
	Two-way	Three-way	Total	Local	Sensitized
Totals	89				21
Vertices 1	28.14	0	28.14	9.18	5.40
Vertices 2	28.14	0	28.14	9.30	8.45
Edges 1a	28.14	0	28.14	22.28	5.99
Edges 1b	28.14	0	28.14	22.28	5.97
Edges 2	27.70	0	27.70	20.90	8.45
Edges 3	28.14	0	28.14	20.42	8.45

Table 4
Comparison of numbers of transplants, preferred edges, and priority vertices matched with each weighting scheme for two- and three-way KPD allocation, using simulated donor-recipient pairs.

Weighting	Transplants			Preferred edge	Priority vertex
	Two-way	Three-way	Total	Local	Sensitized
Totals	89				21
Vertices 1	7.30	27.42	34.72	11.66	8.57
Vertices 2	8.98	25.70	34.68	11.72	10.16
Edges 1a	9.94	24.78	34.72	24.37	8.52
Edges 1b	9.70	24.66	34.36	25.45	8.35

6.4. Computational results

We tested our suggested edge weightings against vertex weightings. Table 3 shows the average results of 100 runs for a matching problem considering only two-way KPD. Table 4 shows the average results of 100 runs for a 3-way cycle packing problem considering two-way and three-way KPDs. Each row shows outcomes for a weighting scheme, and the columns reflect the average numbers of: incompatible pairs matched for 2-way KPD; incompatible pairs matched for 3-way KPD; total number of incompatible pairs that can be matched; incompatible pairs which match to another pair in the same hospital and thus do not need to travel; and incompatible pairs with sensitized recipient matched. The average number of pairs of each type who were matched for each paired donation allocation scheme should be compared to the numbers in the **Totals** row, which gives the average number of pairs of each type in the KPD graphs generated. For example, 21 out of 89 candidates were sensitized. It would not be meaningful to provide the number of preferred local (same-city) edges in this row.

The results suggest that vertex-weighting schemes would require most people or organs to travel long distances. Considering only two-way KPD (see Table 3), the vertex weighting shown is weakly Pareto-dominated by our edge weighting schemes. The *Edges* 1a weighting achieves the greatest number of local transplants but, since it gives the vertex properties zero weight, it matches fewer sensitized recipients.

In both three-way and two-way KPDs (see Table 4), edge weighting schemes (*Edges* 1a and *Edges* 1b) helped to prioritize local exchanges. Also, the wider edge weight interval (*Edges* 1b) decreases the total number of transplants, but does not violate the lower bound determined by the range of the edge weight interval — see Section 5.3 and Table 4.

The maximum edge-weight matching for any scheme in which all properties have positive weight is on the efficient frontier for this allocation problem [31]. Starting from any of the schemes shown in which all listed properties have positive weight (these are *Edges* 2, *Edges* 3), it will not be possible to increase one outcome measure without decreasing some other outcome measure.

7. Limitations

We will review some limitations of our analysis. If a KPD graph has smallest edge weight w and largest edge weight W, inequality (3) guarantees that $\mu_e \geq (w/W)\mu$. For realistic paired donation graphs, this lower bound is extremely conservative. For instance, in the simulation results of Table 3 for *Edges* 2 weightings, one cannot use inequality (3) to give tighter bounds than (2) gives, because for the aforementioned weightings the fraction w/W is less than $1/2$. These matchings nonetheless have almost maximum cardinality because they satisfy $\mu_e \geq 0.99\mu$. In a different case, that of two- and three-way kidney paired donation, Dickerson et al. [17] gave a theoretical result based on blood type distributions that showed we should expect the cardinality of such allocations to be within about 1.5% of the maximum possible cardinality in large enough groups of incompatible pairs, but they observed larger deviations in practice.

In a real kidney exchange program, recipients and their incompatible donors present to physicians on an ongoing basis. If every feasible paired donation were performed immediately, there would be no opportunity to take advantage of optimal matching algorithms, and fewer transplants could be performed. In this paper, we view the dynamic problem as a static optimization problem. Other researchers have investigated algorithms for dynamic optimization [32,33]. Actual match run frequency varies by country and transplant program, e.g., the UK, the Netherlands, and Australia run a match every three months, where US's United Network for Organ Sharing (UNOS) matches candidates weekly, and Ashlagi et al. [34] have studied the empirical effectiveness of these choices.

8. Conclusion

Organ allocation priorities have customarily been expressed through weighting systems that assign numerical values to each potential transplant. Kidney paired donation was no exception; the UNOS Kidney Pancreas Committee used a simulation tool to empirically explore the space of weighting schemes and decide weights for its Kidney Paired Donation Pilot Program. Physicians might not be experts at translating their judgments about the relative value of particular paired donation matches to numerical weights. Maximizing the total number of transplants might be required, but some circumstances might warrant decreasing the number of transplants to achieve other goals. We aim to help the transplant community express its allocation goals through the use of KPD graphs. To that end, we have provided weighting methods that give cardinality guarantees, while allowing the necessary edge preference structure.

We can recast Theorem 5 and the discussion in Section 4.2 as a preemptive (lexicographical) multi-objective optimization method. Klingman and Phillips [35] construct a similar method for a related model, a preemptive multi-objective assignment model.

The number of vertices in a matching M is $|V(M)|$. Let $|V_2(M)|$ be the number of vertices of M that are in the subset V_2. In decreasing order of importance, the objectives we consider for kidney paired donations are: $f_1(M) = |V_2(M)|$, the number of transplants for the highest priority recipients; $f_2(M) = |V(M)|$, the number of transplants overall; and $f_3(M)$, a function that may subsume various other vertex-associated objectives, such as the number of transplants for preferred but not exceptional recipients, as well as edge-associated objectives, like same-hospital transplant and immunologic concordance.

Let $\mathbb{M}$ be the set of all matchings in G. We express the constraints in the generic form: $M \in \mathbb{M}$. The general theory of multi-objective combinatorial optimization asserts [31] that for an ordered list of objectives $f_1(M)$, $f_2(M)$, …, $f_k(M)$ there exist preemptive weights C_1, C_2, …, C_k such that the preemptive multi-objective problem is equivalent to

$$\max_{M\in\mathbb{M}} \sum_{i=1}^{k} C_i f_i(M). \tag{14}$$

One may solve (14) using a maximum edge-weight matching algorithm.

Without loss of generality $C_k = 1$, and in our case $k = 3$. Theorem 5 provides exact values for C_1 and C_2. Write the maximum edge-weight matching problem as

$$\max_{M\in\mathbb{M}} \sum_{j\in M} w_j = \max_{M\in\mathbb{M}} \left((n+1)|V_2(M)| + (n-1)|V(M)| + \sum_{j\in M} \tilde{w}_j \right) \tag{15}$$

and note that the objective on the right hand side of (15) is a linear combination of the objectives f_1, f_2, and f_3. This yields $C_1 = n+1$ and $C_2 = n-1$ as preemptive weights for (14).

Alternatively, we may solve preemptive multi-objective problems as a sequence of single-objective problems. In that paradigm, first solve

$$F_1 = \max_{M\in\mathbb{M}} f_1(M) \tag{16}$$

and then solve

$$F_2 = \max_{M\in\mathbb{M}} f_2(M), \text{ subject to } F_1 = f_1(M), \tag{17}$$

which incorporates maximizing the most important objective as a constraint, and then solve,

$$F_2 = \max_{M\in\mathbb{M}} f_3(M), \text{ subject to } F_1 = f_1(M) \text{ and } F_2 = f_2(M), \tag{18}$$

and so on.

In the case of undirected graphs, the advantage of the former scheme with a single objective is that an efficient algorithm for matching can be used, whereas there is no obvious way to incorporate side constraints of the form in (17) into a maximum matching algorithm. Also, for directed graphs and k-way exchange, Dickerson et al. [17] note that the most efficient algorithms known cannot directly incorporate a side constraint requiring inclusion of the maximum number of vertices of a preferred subset. Our work gives an edge weighting function that implements this lexicographic ordering without adding a side constraint.

Thus, our results can be understood as specifying the correct preemptive weights for converting a clinically meaningful preemptive multi-objective optimization model to a single-objective model. Our points schemes appear in a format that is familiar and comprehensible to transplant policymakers. Further, the single-objective formulation facilitates the use of specialized, computationally efficient algorithms for these optimization problems.

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