

ORIGINAL ARTICLE

Effect of match-run frequencies on the number of transplants and waiting times in kidney exchange

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Numerous kidney exchange (kidney paired donation [KPD]) registries in the United States have gradually shifted to high-frequency match-runs, raising the question of whether this harms the number of transplants. We conducted simulations using clinical data from 2 KPD registries—the Alliance for Paired Donation, which runs multihospital exchanges, and Methodist San Antonio, which runs single-center exchanges—to study how the frequency of match-runs impacts the number of transplants and the average waiting times. We simulate the options facing each of the 2 registries by repeated resampling from their historical pools of patient-donor pairs and nondirected donors, with arrival and departure rates corresponding to the historical data. We find that longer intervals between match-runs do not increase the total number of transplants, and that prioritizing highly sensitized patients is more effective than waiting longer between match-runs for transplanting highly sensitized patients. While we do not find that frequent match-runs result in fewer transplanted pairs, we do find that increasing arrival rates of new pairs improves both the fraction of transplanted pairs and waiting times.

KEYWORDS

donors and donation: paired exchange, economics, ethics and public policy, health services and outcomes research, kidney transplantation/nephrology, organ procurement and allocation

1 | INTRODUCTION

Kidney exchange, also called kidney paired donation (KPD), enables candidates with incompatible living donors to obtain transplants from other living donors, such as nondirected donors (NDDs) or donors belonging to other incompatible pairs.^{1–12} KPD programs perform match-runs that use optimization to find cyclic exchanges among incompatible pairs, and chains initiated by a NDD. Intuitively, an important factor that impacts the number of transplants is the size of the pool, which may be affected by the length of time between match-runs.

While the timing for deceased organ allocation is determined by the availability of organs, the timing of match-runs in KPD is more flexible. Longer intervals between match-runs allow for the

accumulation of more pairs in the pool and may allow more potential matches. However, we will see that there is an important difference between pool size and composition. A larger pool of patient-donor pairs who have not previously failed to match provides many more matches than an equally large pool that includes many pairs for whom no matches were accomplished in previous match-runs, and this will reduce the benefits of delaying match-runs in mature pools that contain many hard-to-match pairs. Furthermore, infrequent match-runs may also slow down the complex process of identifying matches and carrying out transplants. This problem is amplified by the large fraction of proposed virtual matches that fail because of immunological, logistical, and other reasons.^{11,13} Furthermore, additional time on the waiting list is undesirable for candidates.¹⁴

Abbreviations: APD, Alliance for Paired Donation; KPD, kidney paired donation; NDD, nondirected donor; PRA, panel reactive antibodies.

National KPD programs in the United Kingdom, The Netherlands, Australia, and Canada conduct infrequent match-runs. In the United Kingdom, The Netherlands, and Australia, a match-run is conducted every 3 months and in Canada every 4 months.¹⁵⁻¹⁹ In the United States, KPD programs typically match very frequently: multicenter programs such as the Alliance for Paired Donation (APD) and National Kidney Registry match daily, United Network for Organ Sharing finds matches weekly, and also single-center programs such as Methodist at San Antonio (MSA) search for matches whenever a new pair becomes available. In the United States, competition among KPD programs to produce transplants may have incentivized programs to perform match-runs at high frequency, which raises a major concern that such frequent matching may lead to fewer transplants.¹³ In particular, matching frequently may lead to inefficient use of easy-to-match donors and missed opportunities for the most sensitized candidates.

This article studies the impact of matching frequencies on the number of potential transplants and on the average waiting time to transplant in a pool of candidate-donor pairs. While matching frequency may affect outcomes by changing the pool size, other factors that determine pool size include acquisition rate and departure rate. This article further explores how these factors impact the fraction of the pool transplanted. We use the set of enrolled pairs from both the APD over a 9-year period and the MSA over a 3.5-year period.

The MSA and APD provide us with 2 distinct, nonoverlapping datasets with very different pools of participating pairs (eg, number of: blood type O donors, easy-to-match pairs, NDDs, and compatible pairs) and different operational practices that significantly impact the connectivity of the respective pools. These different datasets allow us to evaluate the effects of match-run frequency in very different environments, thus providing a robustness check for the policies studied.

2 | METHODS

2.1 | Data

The APD data consist of the characteristics of all incompatible pairs, NDDs and patients without a donor who enrolled in the APD registry between January 1, 2007 and August 11, 2016, including 1571 incompatible pairs and 50 NDDs. The MSA data consist of similar data for pairs entering from July 1, 2013 to February 1, 2017 including 592 pairs and 4 NDDs. The pairs' ABO distribution is given in Table 1 (for patients with multiple donors we select 1 donor randomly for this distribution) and Pool panel reactive antibodies (PRA) distribution in Table 2.

The compatibility between a patient and a donor is determined by their blood types and a virtual crossmatch test, which compares the patient's antibodies (as entered by the patient's transplant center) and the donor's human leukocyte antigen. In addition to the virtual crossmatch, transplant centers perform a crossmatch to verify compatibility. Finally, proposed offers fail to culminate in transplants for a variety of reasons that we model with failure rates described below. The 2 main types of failures occur due to positive crossmatch and rejection of the proposed donor by the recipient's center.¹³

TABLE 1 Pairs type distribution in the APD and MSA data. First and second columns are the patient and donor ABO blood types, respectively

pABO	dABO	APD	MSA
AB	AB	0.32	0
AB	B	0.45	0
AB	A	0.7	1.01
AB	O	0.7	1.35
B	AB	1.15	0.68
B	B	2.16	1.35
B	A	6.62	4.05
B	O	4.33	5.57
A	AB	1.4	1.35
A	B	3.95	4.05
A	A	9.42	7.26
A	O	8.53	16.89
O	AB	2.42	0.68
O	B	8.4	7.43
O	A	28.64	21.79
O	O	20.81	26.52

APD, Alliance for Paired Donation; MSA, Methodist at San Antonio.

TABLE 2 Pool PRA distribution in the MSA and APD pools

	0-90	90-98	98-100
MSA	0.5845	0.0946	0.3209
APD	0.6416	0.1286	0.2298

APD, Alliance for Paired Donation; MSA, Methodist at San Antonio; PRA, panel reactive antibodies.

2.2 | APD versus MSA data composition

This study does not allow us to compare the efficiency of the APD and MSA. Part of the value of these 2 datasets is the real differences in the connectivity of the pools' compatibility graphs between APD and MSA (ie, to the extent to which pairs are likely to be able to exchange with others in the pool). For example, the MSA dataset does not have to take into account discretionary exclusion criteria by different transplant centers as is done in the APD, which lowers the connectivity of the APD pool. MSA further allows higher mean fluorescence intensity (MFI) cutoffs than APD centers allow, which translates to more compatibilities between donors and patients and hence a more connected compatibility graph (ie, more possibilities of donation from 1 pair to another). In addition, the MSA dataset has more compatible pairs participating compared to APD and no "selection" in that all pairs participate in the MSA system, whereas the APD loses easy-to-match and compatible pairs due to internal matching outside the APD. MSA also has a higher percentage of pairs with multiple donors than APD, again increasing possibilities of donation from 1 pair to another.

Because of the substantial differences between the 2 pools, the computational experiments we conduct on each pool will be informative by providing "within-experiment" comparisons of different match

frequencies, etc. within each pool. The 2 very different pools will in turn allow us to explore the impact of match-run frequency in the presence of differences such as arrival rate, composition of the pool (ie, number of blood type O donors, easy-to-match pairs, number of NDDs, number of compatible pairs) and departure rate, as well as the connectivity of the pools discussed above.

2.3 | Optimization

For each match-run, we execute the matching algorithm on the available pool of incompatible pairs and NDDs to find a maximum “weighted” solution. One type of sensitivity analysis we conduct is to vary the priorities assigned to different patients based on their level of sensitization. We tested 3 strategies (S1, S2, S3) that use different weights assigned to a given patient’s transplant based on the patient’s calculated PRA (cPRA) (Table 3). Waiting time was not prioritized in these strategies because in the steady state, this will not change the *average* waiting time, due to Little’s Law.²⁰ Our matching algorithm allows for cycles/loops of length at most 3 and chains of any length. The last donor of a chain becomes a “bridge donor” who continues the chain in the next match-run. A chain is terminated if the bridge donor remains in the pool for 3 months, by assuming the bridge donor donates to a patient on the deceased donor waiting list who does not have an incompatible donor. We do not include the chain-ending transplant in our analysis in order not to bias the outcomes of transplanted patients in the pool (eg, the large number of patients on the deceased donor waiting list allows ending chains with very highly sensitized patients).

2.4 | Simulation design

For each set of parameters, we run Monte Carlo simulations for 50 iterations. In each iteration we simulate the arrival of 5000 pairs and a small fraction of NDDs. The goal is to analyze the steady state that is reached by having a departure rate as described below. Each time period (number of days) we sample from the data pairs and NDDs with replacement according to some fixed arrival rate. In the base case, a pair or an NDD joins the pool every 2 days. We also simulate the departure of pairs and NDDs from the pool without being matched as observed in the data.

For the APD, we set the number of NDDs that join the pool (during the arrival of 5000 pairs) to 160. The base case departure rate for the

TABLE 3 Base weights assigned by strategies 1 through 3 (S1-S3). Strategies S1, S2, S3 set the weight only according to the recipient’s cPRA

cPRA	S1	S2	S3
98-100	1.05	2	10
90-98	1.05	1.5	5
80-90	1.05	1.05	2
0-80	1	1	1

cPRA, calculated panel reactive antibodies.

APD data is estimated using a Cox model, and on average a pair or NDD remains in the pool for 420 days (this rate varies only slightly across different types of pairs). In particular, each pair or NDD leaves the pool with probability 1/420 per day independently for reasons other than a match within the pool. We further conduct sensitivity analysis both on arrival rates and departure rates. For the MSA data we do not have good estimates and set the base case average stay in the pool to 800 days. This was chosen to be larger than the estimated departure rate of the APD because pairs at the MSA do not enroll in competing exchange programs (but here too we conduct a sensitivity analysis). Due to the very small number of NDDs in the MSA data, we restrict attention only to pairs and thus assume there are no chains when using MSA data (however, we also conducted simulations with chains and found similar qualitative results).

While the simulation is run until all pairs have arrived, statistics are measured only for pairs that arrived after the 100th pair arrived to decrease the biases at the “beginning” of the simulation and capture steady-state results. Simulations were run for different matching frequencies.

We model the failure rate of match offers being converted to transplants. In APD, after the matching algorithm identifies a match, each candidate’s center has up to 1 day to accept the *offer* or not. Some offers are turned down by centers for nonimmunological reasons despite the fact that they should have preselected only donors that are acceptable for their patients. If all offers within a chain or a loop are accepted, centers are asked to conduct the actual cross-matches and exchange more extensive patient and donor medical records. Using estimates from Fumo et al,¹³ 1-way offers are estimated to be rejected 27% of the time; the involved pairs are returned to the pool after keeping them inactive for the time it takes to add 1 pair to the pool. Actual crossmatch failures were set to occur with a probability of 38% for patients with cPRA >90 and 10% for all other patients. The transplants in the chain were conducted until the first failure. Two types of models are simulated for realizing and resolving failures motivated by practices in single and multihospital exchange programs:

No-delay model: Failures are realized immediately, allowing for instantaneous reoptimization. This model concentrates on the impact of waiting between match-runs. This model is equivalent to reoptimizing immediately after every failure over the entire pool. (A similar reoptimization approach is adopted in single-center programs such as MSA and partially in national programs such as the United Kingdom and The Netherlands.)

Delay model: Failures are resolved over time as observed in US multihospital KPD registries. In our simulations, a pair becomes inactive during an offer stage until 2 days elapse and during a crossmatch stage it is inactive until 7 more days elapse. Patients were considered transplanted if there were no failures in the chain or cycle.

All the simulations using MSA data assume the no-delay model, as MSA is a single-center program that can reoptimize immediately after some failure occurred. In fact, most simulations are conducted

under the no-delay model in order to evaluate the impact of policies on transplants in “best-case” scenarios.

3 | RESULTS

The measured simulation outcomes are the fraction of patient-donor pairs transplanted and the average waiting time to transplants experienced by the candidates over the entire study. Simulations were run with the intervals between match-runs of 2, 4, 7, 14, 30, 60, and 120 days.

3.1 | Impact of match-run frequency under different prioritization strategies

We first test the effect of varying the interval between match-runs under different prioritization strategies. Figure 1 describes outcomes under the delay model (failures are resolved over time) and Figure 2 describes outcomes under the no-delay model (immediate resolution of failures).

The top left plots of Figures 1 and 2 show that under both models, regardless of the prioritization strategy, the average fraction of

transplanted patients decreases as the interval between match-runs exceeds 7-14 days. Top right plots of these figures show that the average waiting time increases as the interval between match-runs increases. The effect of change is more significant in Figure 1 than in Figure 2 because the time required to resolve failures harms the match rate and the waiting time. This is most evident in the bottom right plots, which show the average waiting time for overdemanded (easy-to-match pairs); these pairs can match immediately when failures are resolved immediately (explaining why the average waiting time is about half the length of interval between match-runs), but have to wait significantly more to be part of a cycle or a chain when failures take time to resolve.

Some prioritization may help the most highly sensitized patients (middle plots in Figures 1 and 2). However, in those cases fewer low sensitized patients and fewer underdemanded pairs are transplanted (patients-donor pairs with ABO types X-Y are underdemanded if they need a scarcer kidney than they are offering in exchange (ie, if X is ABO compatible with Y but Y is not ABO compatible with X); that includes O-A, O-B, O-AB, A-AB, B-AB). We report very similar qualitative results using MSA data (Figure 3). While the qualitative observations are similar, there are large differences

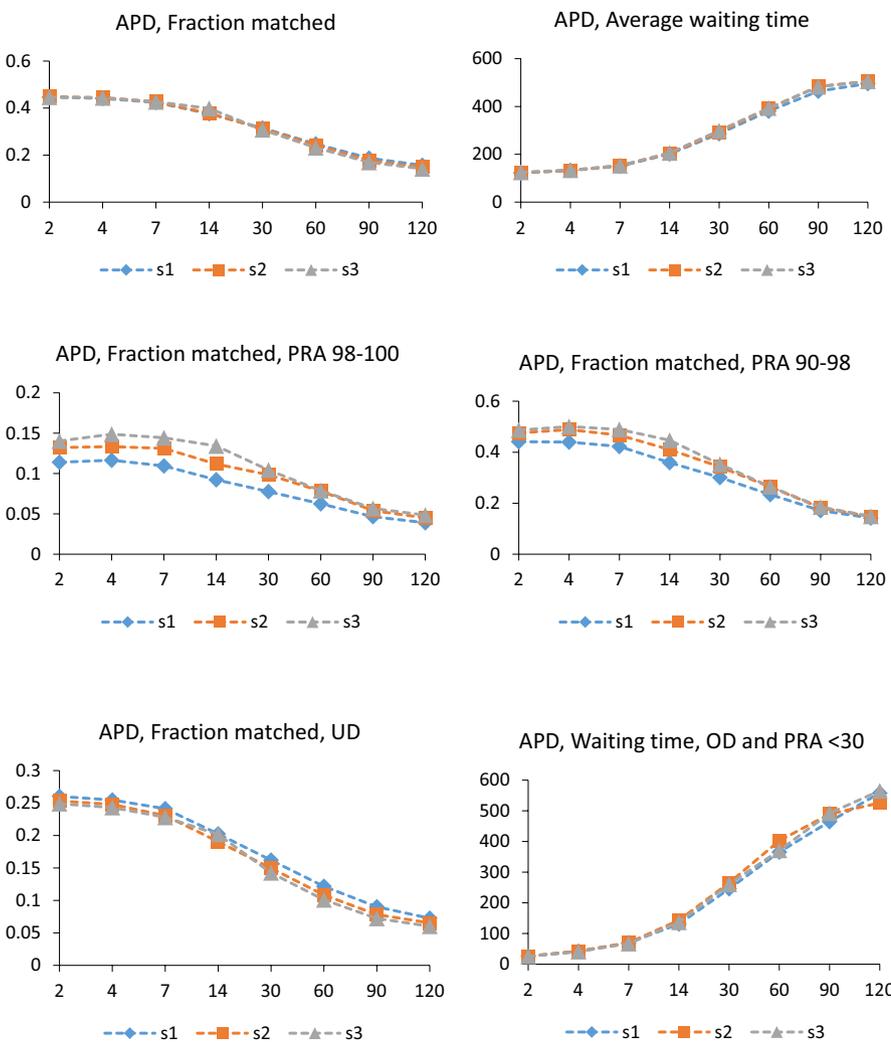


FIGURE 1 Statistics under the delay model using APD data. The x-axis represents the time interval between 2 match-runs. Strategies S1-S3 are defined in the “strategies” section and Table 3. (Top left) Fraction of matched pairs. (Top right) Average waiting time. (Middle) Fraction of match patients with high PRA. (Bottom) Fraction of underdemanded pairs matched and the average waiting time of overdemanded pairs with low PRA. APD, Alliance for Paired Donation; OD, overdemanded; PRA, panel reactive antibodies; UD, underdemanded [Color figure can be viewed at wileyonlinelibrary.com]

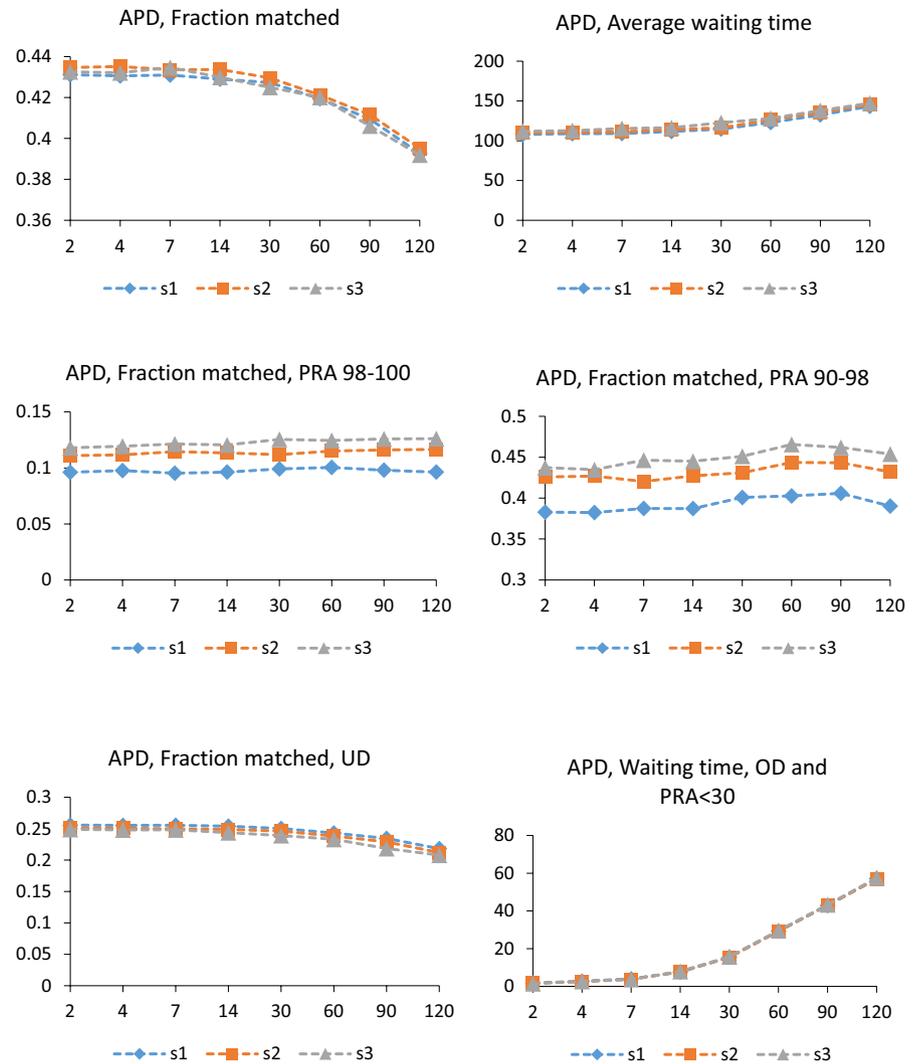


FIGURE 2 Statistics under the no-delay model using APD data. The x-axis represents the time interval between 2 match-runs. Strategies S1-S3 are defined in the “strategies” section and Table 3. (Top left) Fraction of matched pairs. (Top right) Average waiting time. (Middle) Fraction of match patients with high PRA. (Bottom) Fraction of underdemanded pairs matched and the average waiting time of overdemanding pairs with low PRA. APD, Alliance for Paired Donation; OD, overdemanding; PRA, panel reactive antibodies; UD, underdemanded [Color figure can be viewed at wileyonlinelibrary.com]

between the MSA and APD (for instance, 11% difference in the fraction of matched pairs, Figures 2 and 3, under the no-delay model). This difference in the fraction of matched pairs is due to differences in the connectivity of the pools. Note that in Table 1, the ratios of O donors to O patients are .57 and .89 in the APD and MSA pools, respectively. Also, 34.4% of APD pairs contain an O donor, whereas 50.3% of the MSA pairs have an O donor, which strongly impacts the difference in fraction matched and the difference in fraction of underdemanded matched. Thus, independent of the pool connectivity, matching infrequently does not increase the fraction of matched pairs.

We emphasize that a low matching frequency under the delay model is not very practical since this requires the KPD program to wait with failed matches (without reoptimizing) until the next match-run.

We next focus on the no-delay model where failures are resolved immediately (if infrequent matching is not helpful for this model, it is not expected to be helpful under the delay model). For simplicity we also present the next results only for strategy S2 as we find no qualitative differences between the 3 strategies in the simulations. For clarity we present the next results only under strategy S2 as we find no qualitative differences in the simulations.

3.2 | Varying arrival and/or departure rates

We conduct sensitivity analysis on the arrival rate of new pairs (base case is 1 arrival every 2 days = 1 period) and report in Figure 4 simulation results under the no-delay model when a pair arrives every t periods ($t = 1, 2, 4, 7, 14$). For each arrival rate, the fraction of transplanted pairs does not increase as the interval between match-runs increases. However, the greater the arrival rate, the greater the fraction of transplanted pairs and the lower the waiting time (note: the larger the t , the lower the arrival rate). The bottom plots provide a different view of the results. Note that the arrival rate is a major factor determining the fraction of transplanted patients, whereas the matching frequency plots essentially coincide (except the lowest frequencies). The lower the arrival rate the more benefit there is to increase arriving pairs. This benefit is minor for very high arrival rates (after 350-700 pairs annually).

We also varied the average time a pair remains in the pool in MSA and APD ($x = 420, 800, 1000$). The results (Figure 5) show that as the departure rate becomes large ($1/x$), the smaller the fraction of pairs that are transplanted. However, for every departure rate, matching frequently does not harm the fraction of matched pairs. Like the

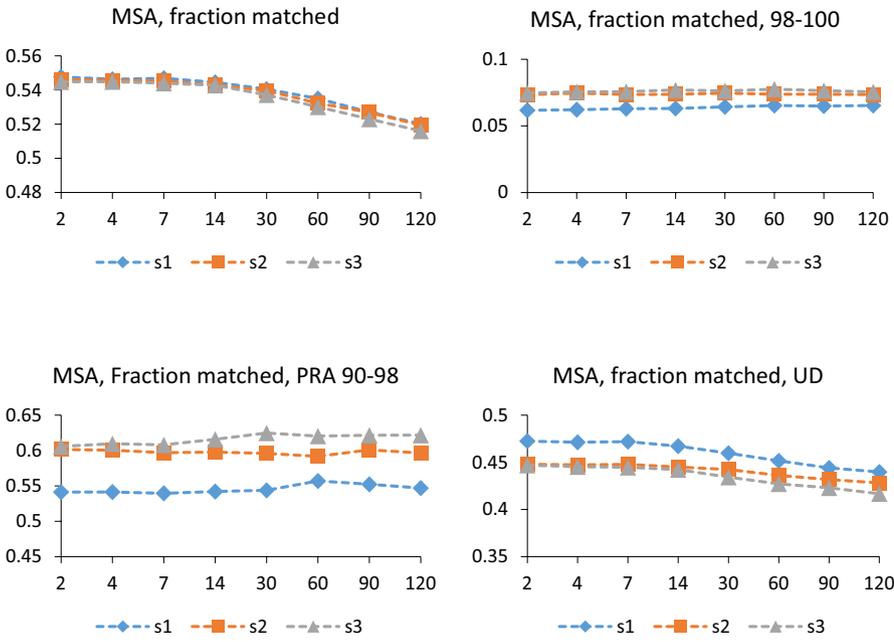


FIGURE 3 Statistics under the no-delay model using MSA data. The x-axis represents the time interval between 2 match-runs. Strategies S1-S3 are defined in the “strategies” section and Table 3. (Top left) Fraction of matched pairs. (Top right) Fraction of matched patients with PRA 98-100. (Bottom left) Fraction of match patients with PRA 90-98. (Bottom right) Fraction of matched underdemanded pairs. MSA, Methodist at San Antonio; PRA, panel reactive antibodies; UD, underdemanded [Color figure can be viewed at wileyonlinelibrary.com]

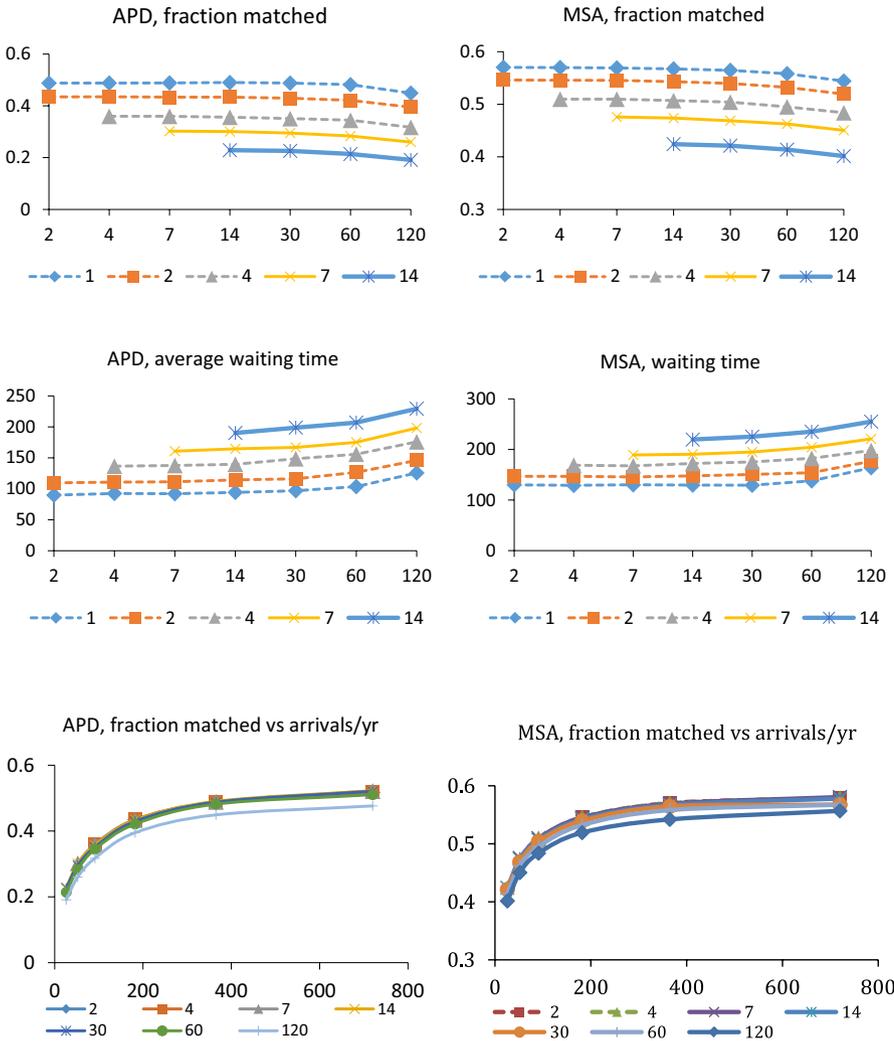


FIGURE 4 Sensitivity analysis over arrival rates under the no-delay model and strategy S2 in APD and MSA datasets. In the first 4 figures, each curve represents an arrival rate by the number of days between the arrival of each pair or NDD, and the x-axis represents the time interval between 2 match-runs. The 2 bottom figures are similar to the top 2 figures only the x-axis represent the number of pairs arriving per year and each curve represents the interval length between 2 match-runs. APD, Alliance for Paired Donation; MSA, Methodist at San Antonio; NDD, nondirected donor [Color figure can be viewed at wileyonlinelibrary.com]

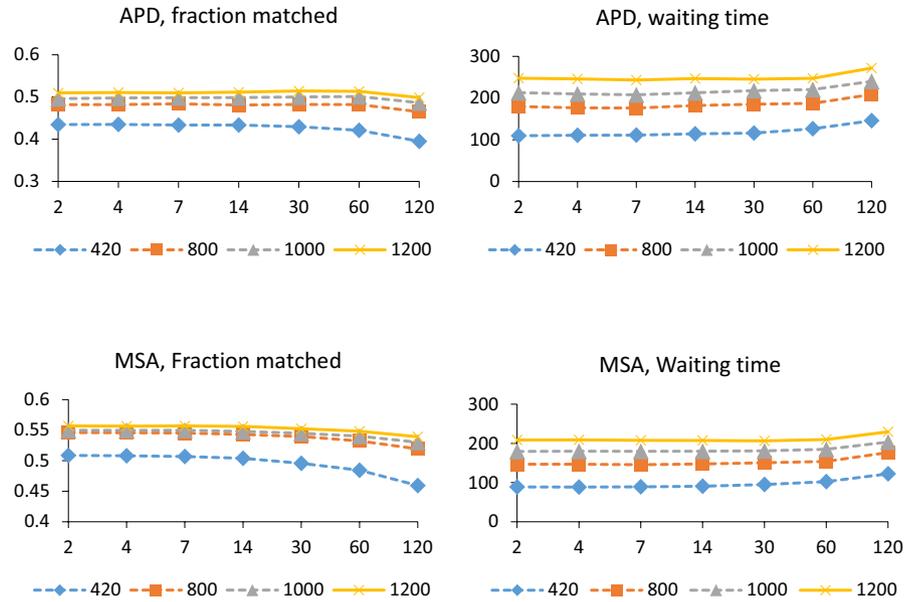


FIGURE 5 Sensitivity analysis over departure rates under the no-delay model and strategy S2 in the APD and MSA data. The x-axis represents the time interval between 2 match-runs. Each line represents a different departure rate where the numbers correspond to the average number of days a pair remains in the pool without being matched. (Left) Fraction of matched pairs. (Right) Average waiting time. APD, Alliance for Paired Donation; MSA, Methodist at San Antonio [Color figure can be viewed at wileyonlinelibrary.com]

impact of arrival rate, decreasing departure rate increases the fraction of transplanted patients.

rates. However, increasing the arrival rate results in a higher blood type O match efficiency.

3.3 | Varying practical constraints: NDDs and cycle length

We ran similar simulations to explore different constraints. Simulations assuming no NDDs in the APD result in similar patterns (Figure 6 left). We relaxed the maximum cycle length to allow for 4-way cycles, and, while the fraction of patients transplanted increases, frequent matching does not harm the fraction of transplanted pairs (Figure 6 right).

4 | DISCUSSION

As KPD has become more widely used, the databases of patients and donors have grown rapidly and they contain a large fraction of highly sensitized patients.²¹ It is therefore important to evaluate the effect of increasing the pool size in order to create more opportunities for these patients. To do so we vary the match-run frequencies (which can be determined by the KPD program) but also vary the exogenous arrival rate (which is a consequence of participation and collaboration).

3.4 | Match efficiency

One indicator of the matching efficiency of a KPD program is the fraction of blood type O donor kidneys that are transplanted into blood type O patients (intuitively, in a very large pool all blood type O donor kidneys would be transplanted into blood type O patients). Figure 7 shows that using longer match-run intervals does not increase this measure under different prioritization strategies and different arrival

Using the accumulated patient/donor pool at the APD and MSA databases, we modeled running a matching algorithm, making match offers, accounting for rejected offers, and simulated laboratory cross-matches. We varied the match-run frequency, the arrival rate to the pool, and the departure rate from the pool. Sensitivity analyses were performed for pool connectivity, priorities assigned to highly sensitized patients, failure rates, use of NDDs, and chain/cycle length. We

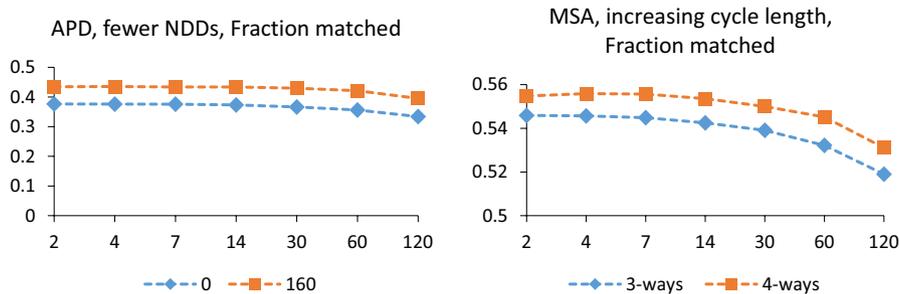


FIGURE 6 Different number of NDDs (left) and different cycle length (right). Both simulations use the no-delay model and strategy S2. The x-axis represents the time interval between 2 match-runs. Testing base case arrival of NDDs (160) and no NDDs at all. (Left) Testing both 3-way and 4-way cycles. (Right) Average waiting time. APD, Alliance for Paired Donation; MSA, Methodist at San Antonio; NDDs, nondirected donors [Color figure can be viewed at wileyonlinelibrary.com]

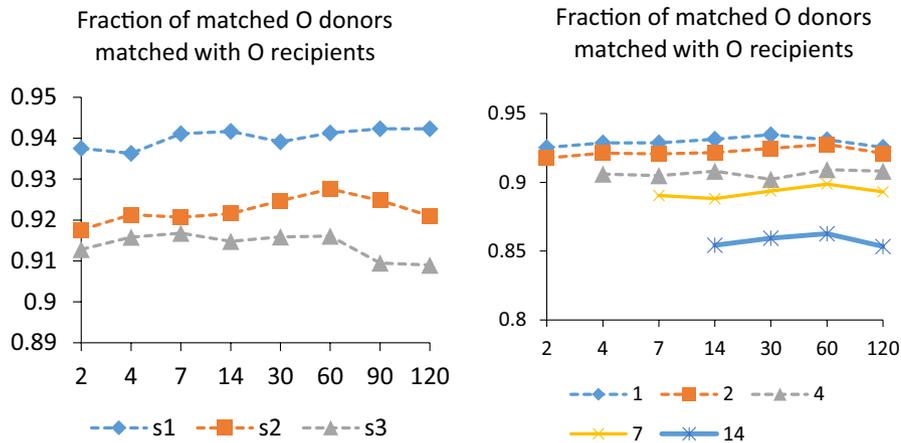


FIGURE 7 Fraction of matched O donors that are matched with O patients. The left plots different prioritization strategies and the right plots different arrival rates for strategy S2. The x-axis represents the time interval between 2 match-runs [Color figure can be viewed at wileyonlinelibrary.com]

find that matching frequently does not reduce the fraction of the pool matched. Importantly, however, the fraction of the pool transplanted does increase as either the arrival rate increases or the departure rate decreases. In fact, increasing arrival rate is the most important modifiable factor to increase the fraction of the pool transplanted, particularly for low arrival rates. While the exact numbers might differ across datasets, the general principles will still hold.

These results help illustrate why the size of the pool is not by itself a good indicator of the fraction of patients who can be transplanted. A large arrival rate means a large pool with many matchable pairs, while a low fraction of transplantable patients can also produce a large pool, but of hard-to-match pairs.

The lesson for the United States is that KPD programs should consider efforts to collaborate to increase their arrival rate. While waiting 1-2 weeks between match-runs does not reduce the fraction of pool transplanted, using this time to clarify competing matches for easy-to-match pairs by using different strategies may help to achieve predetermined goals such as more transplants for hard-to-match patients. For non-US KPD programs that perform match-runs less frequently than every month and have nonnegligible departure rates, it may be worth experimenting with more frequent match-runs. Finally, non-US programs with a low acquisition rate and low match rate may benefit from international collaboration to increase their acquisition rate. This is likely to have a much larger impact on the fraction of the pool they match than does match frequency. The logistics of international exchange currently serve as a barrier to broader collaboration, and strategies to overcome these barriers should become an active area of research.

Intuitively, matching frequently does not harm the fraction of transplanted patients because both underdemanded pairs (such as O-A patient-donor pairs) and highly sensitized patients accumulate in the pool. When, for example, a patient-donor A-O pair arrives, if the patient is low sensitized the pair can match immediately with an O-A pair, which is an efficient match. If the A patient is highly sensitized and cannot match with any of the accumulated O-A pairs, it is also unlikely that this patient can match any pair arriving in the near future, so it does not increase the total number of transplants to postpone matching other pairs until a donor compatible with this patient arrives. Put differently, when the departure rate is low, many hard-to-match

pairs accumulate in the pool and so waiting with a newly arriving easy-to-match pair is unnecessary since it is likely to match to one of the already present hard-to-match pairs. And when the departure rate is high, matching infrequently will result in many departures of easy-to-match pairs.

Moreover, that a low arrival rate yields a match rate below the maximum is a result of both departures of unmatched pairs and sub-optimal matching, which would not have happened in a thicker pool. For example, with a low arrival rate, some O donors might match A patients, but with a large arrival rate such A patients could be matched by A donors and such O donors could match O patients. Finally, it is worth noting Little's Law,²⁰ which states that in steady state, the average pool size equals the arrival rate multiplied by the average time a pair remains in the pool (whether matched eventually or not). So for a given arrival rate, one may artificially increase the pool size by waiting between match-runs. However, this can increase the average waiting time as well, which may lead to more departures.

Since matching at some KPD programs in the United States is more aligned with the delay model, it is reasonable to use high matching frequencies. Our results suggest that even under the no-delay model (where failures are resolved before the next match run), high matching frequency is a reasonable strategy.

Our approach is very different from that of Segev et al.²² In our approach the pool evolves dynamically with arrival and departures modeled over time. Segev et al.²² examined a large static pool, and compared matching pairs sequentially using a "first-accept" approach, to optimizing over the entire pool (a single match-run). Matching frequently in our (steady-state) model is thus different from their first-accept approach. The key difference lies in the composition of the pool: When we match frequently and seek to match an easy-to-match pair, our evolving pool contains mostly hard-to-match pairs, while in their model, which considers a single matching cycle, there could be many other easy-to-match pairs in the pool and matching easy-to-match pairs with each other is often inefficient. While we model departures, our findings hold even for very low departure rates. Finally, we always optimize while prioritizing hard-to-match pairs, regardless of the matching frequency.

KPD programs vary in the priorities they use. Our findings suggest that while prioritization of highly sensitized patients increases the percentage of these patients transplanted, it does not significantly increase the total number of transplants. However, guidelines for how to prioritize pairs can come from studying unmatched departures.

Some strategies used by MSA affect matching frequency and are driven by other factors. Donors may have strong preferences over when to donate, so it is important to prioritize donors whose window for donation closes soon. Moreover, compatible pairs should be given high priority, otherwise they may choose to depart to conduct a direct transplant. These strategies are consistent with matching frequently.

This study has limitations. Only a limited number of strategies are considered and some other strategies may perform better. Strategies that consider the future may have benefits over strategies that optimize in the current pool.^{23,24} However, this is unlikely when the arrival rate is high, since it will be possible to match easy-to-match pairs upon arrival to hard-to-match pairs due to the accumulation of the latter. Also, while patient data are taken from actual KPD registries, we made simplifying assumptions that may weaken our conclusions. We assumed failure rates are independent, and assumed a steady influx of pairs into the database. However, we emphasize that while we report only a representative set of simulations, we found similar qualitative findings under a much broader set of strategies and with lower failure rates. Also, while frequent and infrequent match-runs result in a similar fraction of matched pairs, matching infrequently may allow an increase in match quality. Additionally, departure rates in our simulations are identical for all pairs. If frequent matching for a given KPD program is a good strategy with identical departure rates, it would remain a good strategy also when easier-to-match pairs depart faster than harder-to-match pairs since these pairs match quickly in our simulations. Finally, some departures are due to transplants, which are good outcomes. Thus, the reasons for departures from a KPD pool should be studied.

We also do not explicitly study competition between KPD programs. However, we predict the following effects: When patients do not cross-register, the existence of multiple programs reduces the arrival rate of each; when some patients cross-register, departure rates may be influenced by match rates at competing programs. So matching frequency, by affecting the match rate, affects departures and arrivals at competing programs, and the overall chance of a pair to match should be further studied.

In summary, while we do not find that frequent match-runs result in fewer transplants, we do find that increasing arrival rates and decreasing departure rates improves both the fraction of matched pairs and waiting times. So while the fraction of matched patients (and their waiting times) may be harmed by competition among KPD programs, it is unlikely due to the high frequency of match-runs, but rather due to low arrival rates of pairs and high departure rates.

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DISCLOSURE

The authors of this manuscript have conflicts of interest to disclose as described by the *American Journal of Transplantation*. Michael Rees and Alvin Roth have an ownership interest in Rejuvenate Healthcare, LLC, which seeks to provide consulting services regarding care for end-stage renal disease patients and may gain or lose financially as a result of this publication. The other authors have no conflicts of interest to disclose.

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