Econometrica, Vol. 85, No. 5 (September, 2017), 1645–1671

DUAL-DONOR ORGAN EXCHANGE

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Owing to the worldwide shortage of deceased-donor organs for transplantation, living donations have become a significant source of transplant organs. However, not all willing donors can donate to their intended recipients because of medical incompatibilities. These incompatibilities can be overcome by an exchange of donors between patients. For kidneys, such exchanges have become widespread in the last decade with the introduction of optimization and market design techniques to kidney exchange. A small but growing number of liver exchanges have also been conducted. Over the last two decades, a number of transplantation procedures emerged where organs from two living donors are transplanted to a single patient. Prominent examples include dual-graft liver transplantation, lobar lung transplantation, and simultaneous liver-kidney transplantation. Exchange, however, has been neither practiced nor introduced in this context. We introduce dual-donor organ exchange as a novel transplantation modality, and through simulations show that living-donor transplants can be significantly increased through such exchanges. We also provide a simple theoretical model for dual-donor organ exchange and introduce optimal exchange mechanisms under various logistical constraints.

KEYWORDS: Market design, matching, complementarities, lung exchange, dual-graft liver exchange, simultaneous liver-kidney exchange.

1. INTRODUCTION

MOST TRANSPLANTS FROM LIVING DONORS REQUIRE only one donor for each procedure. There are, however, exceptions, including *dual-graft liver transplantation*, *bilateral living-donor lobar lung transplantation*, and *simultaneous liver-kidney transplantation*. For each of these procedures, grafts from two compatible living donors are transplanted. As such, these procedures are more involved from an organizational perspective than those with only one donor. Unfortunately, one or both of the donors can often be biologically incompatible with the intended recipient, precluding the transplantation. One way to overcome

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An earlier version of this paper was circulated under the title "Lung Exchange." Sönmez and Ünver acknowledge the financial support of the National Science Foundation through Grant SES #1426440. Sönmez acknowledges the support of Goldman Sachs Gives—Dalınç Arıburnu Faculty Research Grant. We thank Moshe Babaioff, four anonymous referees, and participants at NBER Market Design Meeting, Social Choice and Welfare Conference, WZB Market Design Workshop, Tsukuba Science Week, Osaka Market Design Conference, Australian Economic Theory Workshop, Conference on Economic Design, SAET Conference, Cologne-EUI Market Design Conference, RES-York Symposium on Game Theory, COMSOC Workshop, Florida State, Lafayette, Bilkent, ITAM, Arizona State, Dalhousie, St. Andrews, Glasgow, Manchester, Lancaster, York, William & Mary, and UT Austin, for comments.

© 2017 The Econometric Society DOI: 10.3982/ECTA13971

this potential barrier to transplantation is by an exchange of donors between patients. In addition to now-widespread kidney exchange, a small but growing number of (single-graft) liver exchanges have been conducted since the introduction of this transplantation modality in South Korea in 2003 (Hwang et al. (2010)). Despite the introduction of two-donor transplantation techniques, living-donor organ exchange has not yet been practiced, or even introduced, for these procedures. In this paper, we fill this gap as we

1. introduce *dual-donor organ exchange* as a potential transplantation modality for
(a) dual-graft liver transplantation,
(b) bilateral living-donor lobar lung transplantation, and
(c) simultaneous liver-kidney transplantation,
2. simulate the gains from exchange based on data from South Korea (for the applications of of dual-graft liver transplantation and simultaneous liver-kidney transplantation) and Japan (for the application of bilateral living-donor lobar lung transplantation),[1]
3. develop a model of dual-donor organ exchange, and
4. introduce exchange mechanisms under various logistical constraints.

As in kidney exchange, all operations in dual-donor organ exchange have to be carried out simultaneously. This practice ensures that no donor donates an organ or a lobe unless his intended recipient receives a transplant. As such, organization of these exchanges is not an easy task: A 2-way exchange involves six simultaneous operations, a 3-way exchange involves nine simultaneous operations, and so on. As shown by Roth, Sönmez, and Ünver (2007), most of the gains from kidney exchange can be obtained by exchanges that are no larger than 3-way. In this paper, we show that this is not the case for dual-donor organ exchange. Our simulations suggest that the number of transplants from larger than 3-way exchanges can approach to the number of transplants from 2-way and 3-way exchanges combined (see Table II). Therefore, exploring the structure of optimal exchange mechanisms is important under various constraints on the size of feasible exchanges.

Our model builds on the kidney-exchange model of Roth, Sönmez, and Ünver (2004, 2007). Medical literature[2] suggests that a living donor can donate an organ or a lobe to a patient if he is

1. *blood-type compatible* with the patient for the cases of kidney transplantation, liver transplantation, and lung transplantation,
2. *size-compatible* (in the sense that the donor is at least as large as the patient) for the cases of single-graft liver transplantation and lobar lung transplantation, and
3. *tissue-type compatible* for the case of kidney transplantation.

For our simulations, we take all relevant compatibility requirements into consideration in order to assess the potential welfare gains from dual-donor organ exchange under various constraints. For our analytical results on optimal exchange mechanisms, we consider a simplified model with blood-type compatibility only. With this modeling choice, our analytical model captures all essential features of dual-graft liver transplantation and lobar lung transplantation for pediatric patients, but it is only an approximation for the applications of lobar lung transplantation for adult patients and simultaneous liver-kidney transplantation. Focusing on blood-type compatibility alone allows us to define each pa-

[1]Simulations are conducted for countries where the respective transplantation modality is most prominent.

[2]For commonly practiced compatibility requirements, see Lee et al. (2001) and Florman and Miller (2006) for liver transplantation and McLean, Barr, and Starnes (2007) and Van Raemdonck et al. (2009) for lung transplantation. The need for tissue-type compatibility for kidney transplantation is well established, while tissue-type compatibility is not required in general for liver transplantation (Cecka, Zhang, and Reed (2005)). There is no well-established protocol on tissue-type compatibility for lung transplantation.

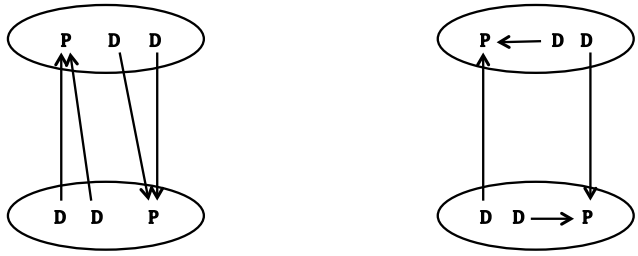


FIGURE 1.—Possible 2-way exchanges. Each patient (denoted by **P**) and her paired donors (each denoted by **D**) are represented in an ellipse. Carried donations in each exchange are represented by directed line segments. *On the left*, each patient swaps both of her donors with the other patient. *On the right*, each patient swaps a single donor with the other patient and receives a graft from her other donor.

tient as a triple of blood types (one for the patient and two for her incompatible donors), making our model analytically tractable.

While there are important similarities between kidney exchange and dual-donor organ exchange, there are also major differences. From an analytical perspective, the most important difference is the presence of two donors for each patient rather than only one as in the case of kidney exchange. For each patient, the two donors are perfect complements.[3] This key difference makes the dual-donor organ exchange model analytically more demanding than the (single-donor) kidney-exchange model. Even organizing an individual exchange becomes a richer problem under dual-donor organ exchange. For kidney exchange, each exchange (regardless of the size of the exchange) has a *cycle* configuration, where the donor of each patient donates a kidney to the next patient in the cycle. For dual-donor organ exchange, there are two configurations for a 2-way exchange (see Figure 1), five configurations for a 3-way exchange (see Figure 2), and so on. The richness of exchange configurations in our model also means that the optimal organization of these exchanges will be more challenging than for kidney exchange. Despite this technical challenge, we provide optimal mechanisms for (i) 2-way exchanges, (ii) 2-way and 3-way exchanges, and (iii) unrestricted exchanges (in Appendix E of the Supplemental Material (Ergin, Sönmez, and Ünver (2017))).

Due to compatibility requirements between a patient and each of her donors, living donation for dual-donor procedures proves to be a challenge to arrange even for patients with willing donors. But this friction also suggests that the role of an organized exchange can be more prominent for these procedures than for single-donor procedures. Our simulations in Section 3 and Appendix B of the Supplemental Material (Ergin, Sönmez, and Ünver (2017)) confirm this insight. An organized lung exchange in Japan has the potential to increase the number of living-donor lung transplants through 2-way and 3-way exchanges by 134–200%, saving as many as 40 additional lung patients annually (see last line of Table II in Section 3.1 and Table V in Appendix B.1 in the Supplemental Material). Even though dual-graft liver transplantation is a secondary option to single-graft liver transplantation, an organized dual-graft liver exchange has a potential to increase the number of living-donor liver transplants by 23–30% through 2-way and 3-way exchanges,

[3] In matching literature, there are not many models that can incorporate complementarities and find positive results. Most of the matching literature focuses on various substitutability conditions and shows negative results even in the existence of slight complementarities in preferences. For example, see Hatfield and Milgrom (2005), Hatfield and Kojima (2008), and Hatfield and Kominers (2016).

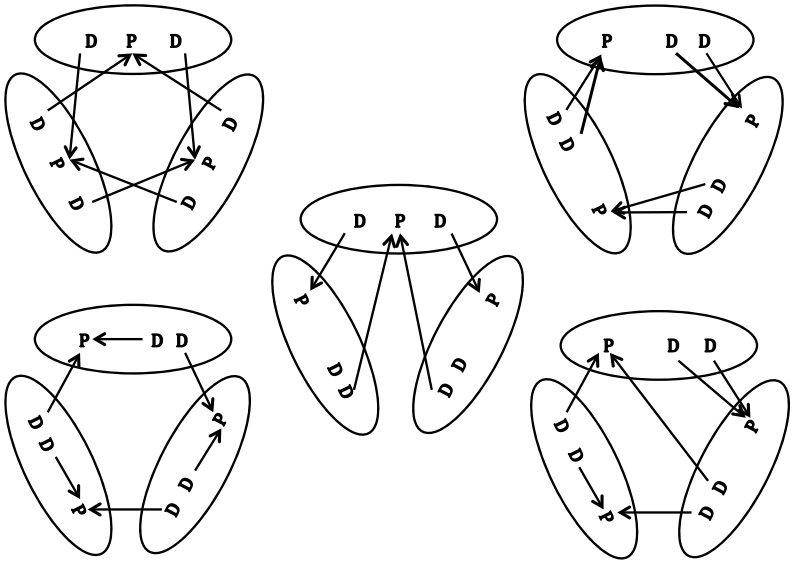


FIGURE 2.—Possible 3-way exchanges. *On the upper-left*, each patient trades one donor in a clockwise trade and the other donor in a counterclockwise trade. *On the upper-right*, each patient trades both of her donors in clockwise trades. *On the lower-left*, each patient trades one donor in a clockwise exchange and receives a graft from her other donor. *On the middle*, one patient is treated asymmetrically with respect to the other two: one patient trades both of her donors in two 2-way trades, one with one patient, the other with the other patient, while each of the other patients receives a graft from her remaining donor. *On the lower-right*, all patients are treated asymmetrically: one patient receives from one of her own donors, and one patient's donors both donate to a single patient, while the last patient's donors donate to the other two patients.

saving nearly 230–300 additional liver patients in South Korea alone (see the last line of Table IV in Section 3.2 and Table VI in Appendix B.2.

Increasingly, economists are taking advantage of advances in technology to design new or improved allocation mechanisms in applications as diverse as entry-level labor markets (Roth and Peranson (1999)), spectrum auctions (Milgrom (2000)), internet auctions (Edelman, Ostrovsky, and Schwarz (2007), Varian (2007)), school choice (Abdulkadiroğlu and Sönmez (2003)), kidney exchange (Roth, Sönmez, and Ünver (2004, 2005, 2007)), course allocation (Sönmez and Ünver (2010), Budish and Cantillon (2012)), affirmative action (Kojima (2012), Hafalir, Yenmez, and Yildirim (2013), Echenique and Yenmez (2015)), cadet-branch matching (Sönmez and Switzer (2013), Sönmez (2013)), refugee matching (Moraga and Rapoport (2014), Jones and Teytelboym (2016)), and assignment of arrival slots (Schummer and Vohra (2013), Schummer and Abizada (2017)). Our paper contributes to the emerging field of market design by introducing a new application in dual-donor organ exchange, and also to transplantation literature by introducing three novel transplantation modalities.

2. BACKGROUND FOR APPLICATIONS

There are four human blood types, O, A, B, and AB, denoting the existence or absence of the two blood proteins A or B in the human blood. A patient can receive a donor's transplant organ (or a lobe of an organ), unless the donor carries a blood protein that the patient does not have. Thus, in the absence of other requirements, O patients can receive a transplant from only O donors, A patients can receive a transplant from A and

O donors, *B* patients can receive a transplant from *B* and *O* donors, and *AB* patients can receive a transplant from all donors. For some of our applications, there are additional medical requirements. In addition to the background information for each of these applications, the presence or lack of additional compatibility requirements are discussed below for dual-graft liver transplantation and living-donor lobar lung transplantation. Background for simultaneous liver-kidney transplantation is discussed in Appendix C of the Supplemental Material.

2.1. *Dual-Graft Liver Transplantation*

The liver is the second most common organ for transplantation, after the kidney. Of nearly 31,000 U.S. transplants in 2015, more than 7000 were liver transplants. While there is the alternative (albeit inferior) treatment of dialysis for end-stage kidney disease, there are no alternatives to transplantation for end-stage liver disease. In contrast to western countries, donations for liver transplantation in much of Asia come from living donors. For example, in 2015, while only 359 of 7127 liver transplants were from living donors in the U.S., 942 of 1398 liver transplants were from living donors in South Korea. The low rates of deceased-donor organ donation in Asia are to a large extent due to cultural reasons and beliefs to respect bodily integrity after death (Lee (2010)). The need to resort to living-donor liver transplantation arose as a response to the critical shortage of deceased-donor organs and the increasing demand for liver transplantation in Asia, where the incidence of end-stage liver disease is very high (Lee et al. (2001)). For similar reasons, living-donor liver transplantation is also more common than deceased-donor liver transplantation in several countries with predominantly Muslim populations, such as Turkey and Saudi Arabia.

A healthy human can donate part of his liver, which typically regenerates within a month. Donation of the smaller left lobe (normally 30–40% of the liver) or the larger right lobe (normally 60–70% of the liver) are the two main options. In order to provide adequate liver function for the patient, at least 40% and preferably 50% of the standard liver volume of the patient is required. The metabolic demands of a larger patient will not be met by the smaller left lobe from a relatively small donor. This phenomenon is referred to as *small-for-size syndrome* by the transplantation community. The primary solution to avoid this syndrome has been harvesting the larger right lobe of the liver. This procedure, however, is considerably more risky for the donor than harvesting the much smaller left lobe.[4] Furthermore, for donors with larger than normal-size right lobes, this option is not feasible.[5] Even though the patient receives an adequate graft volume with right lobe transplantation, the remaining left lobe may not be enough for donor safety. Thus, unlike deceased-donor whole-size liver transplantation, size matching between the liver graft and the standard liver volume of the patient has been a major challenge in adult living-donor liver transplantation due to the importance of providing an adequate graft mass to the patient while leaving a sufficient mass of remaining liver in the donor to ensure donor safety.

Dual-graft (or dual-lobe) liver transplantation, a technique that was introduced by Sung-Gyu Lee at the Asan Medical Center of South Korea in 2000, emerged as a response

[4]While donor mortality is approximately 0.1% for left lobe donation, it ranges from 0.4% to 0.5% for right lobe donation (Lee (2010)). Other risks, referred to as donor *morbidity*, are also considerably higher with right lobe donation.

[5]For the donor, at least 30% of the standard liver volume of the donor is required. Beyond this limit, the remnant liver of the donor loses its ability to compensate, regenerate, and recover (Lee et al. (2001)).

to the challenges of the more risky right lobe liver transplantation (Lee et al. (2001)). Under this procedure, one (almost always left) liver lobe is removed from each of the two donors, and they are both transplanted into a patient. In the period 2011–2015, 176 dual-graft liver transplants were performed in South Korea, with the vast majority at the Asan Medical Center. Other countries that have performed dual-graft liver transplantation so far include Brazil, China, Germany, Hong Kong, India, Romania, and Turkey. The presence of two willing donors (almost always) solves the problem of size matching, rendering size compatibility inconsequential, but transplantation cannot go through if one or both donors are blood-type incompatible with the patient. This is where an exchange of donors can play an important role, making dual-graft liver transplantation an ideal application for dual-donor organ exchange with blood-type compatibility only. As an interesting side note, single-lobe liver exchange was introduced in 2003 at the Asan Medical Center, the same hospital where dual-graft liver transplantation was introduced. As such, it is a natural candidate to adopt an exchange program for potential dual-graft liver recipients.[6]

2.2. *Living-Donor Lobar Lung Transplantation*

As in the case of kidneys and livers, deceased-donor lung donations have not been able to meet the demand. As a result, thousands of patients worldwide die annually while waiting for lung transplantation. Living-donor lobar lung transplantation was introduced in 1990 by Dr. Vaughn Starnes and his colleagues for patients who are too critically ill to survive the waiting list for deceased-donor lungs. Since then, eligibility for this novel transplantation modality has been expanded to cystic fibrosis and other end-stage lung diseases.

A healthy human has five lung lobes: three lobes in the right lung and two in the left. In a living-donor lobar lung transplantation, two donors each donate a lower lobe to the patient to replace the patient's dysfunctional lungs. Each donor must not only be blood-type compatible with the patient, but, donating only a part of the lung, he should also weigh at least as much. Hence blood-type compatibility and size compatibility are the two major medical requirements for living-donor lobar lung transplantation. This makes living donation much harder to arrange for lungs than for kidneys, even if a patient is able to find two willing donors.

Sato et al. (2014) reported that there is no significant difference in patient survival between living-donor and deceased-donor lung transplantations. For a living donor, however, donation of part of a lung is "more costly" than donation of a kidney or even the left lobe of a liver. A healthy donor can maintain a normal life with only one kidney. And the liver regenerates itself within months after a living donation. In contrast, a donated lung lobe does not regenerate, resulting in a loss of 10–20% of pre-donation lung capacity. In large part due to this discouraging reason, there have been only 15–30 living-donor lobar lung transplants annually in the U.S. in the period 1994–2004. This already modest rate has essentially diminished in the U.S. over the last decade as the lung allocation score (LAS) was initiated in May 2005 to allocate lungs on the basis of medical urgency

[6]From an optimal design perspective, it would be preferable to combine our proposed dual-graft liver exchange program with the existing single-graft liver exchange program. When exchanges are restricted to logistically easier 2-way exchanges, such a unification can only be beneficial if a patient is allowed to receive a graft from a single donor in exchange for grafts from two of her donors. We leave this possibility to potential future research, in part because an exchange of "two donors for only one donor" has no medical precedence, and it may be subject to criticism by the medical ethics community.

and post-transplant survival. Prior to LAS, allocation of deceased-donor lungs was mostly based on a first-come-first-serve basis.

At present, Japan is the only country with a strong presence in living-donor lung transplantation. In 2013, there were 61 lung transplantations in Japan, of which 20 were from living donors. Okayama University Hospital has the largest program in Japan, having conducted nearly half of the living-donor lung transplants. Since September 2014, we have been collaborating with their lung-transplantation team to assess the potential of a lung-exchange program at Okayama University Hospital.

3. SIMULATIONS

We start our analysis with calibrated simulations to quantify the potential gains from dual-donor organ exchange.[7] Our methodology to generate patients and their attached donors is similar for all simulations. Each patient is randomly generated according to her respective population characteristics. For most applications, each patient is attached to two independently and randomly generated donors.[8]

The construction of the dual-donor exchange pool depends on the specific application, the most straightforward one being the case of lung transplantation. For this application, any patient who is incompatible with one or both of her attached donors is sent to the exchange pool. Once the exchange pool forms, an optimal algorithm is used to determine the transplants via exchange to maximize the number of transplants. For liver transplantation, we assume that single-graft transplantation is preferred to dual-graft transplantation because the former puts only one donor in harm's way rather than two. Therefore, for any patient, (i) direct donation from a single donor, (ii) exchange with a single donor, and (iii) direct donation from two donors will all be attempted in the given order before the patient is sent to the dual-graft liver-exchange pool.[9] We also conduct dynamic simulations and report their findings in Appendix B of the Supplemental Material.[10]

3.1. *Lung Exchange*

Since Japan leads the world in living-donor lung transplantation, we simulate patient-donor characteristics based on data available from that country. We failed to obtain gender data for Japanese transplant patients. Therefore, we assumed that half of the patient population is male and the other half is female. We use the aggregate data statistics in Table I to calibrate the simulation parameters.[11] Each patient-donor-donor triple is specified

[7]SLK-exchange simulations are reported in Appendix C of the Supplemental Material.

[8]For the case of simultaneous liver-kidney (SLK) exchange, there are kidney-only and liver-only patients who are in need of one donor only. A single donor is generated for these patients.

[9]For the application of SLK transplantation, we consider a scenario where the exchange pool includes not only SLK patients who are incompatible with one or both of their donors, but also kidney (only) patients and liver (only) patients with incompatible donors.

[10]See supplementary files for the Matlab program files and the data files used in simulations.

[11]For random parameters like height, weight, or left-lobe liver volume percentage in liver transplantation, we only have the mean and standard deviation of the population distributions. Using these moments, we assume that these variables are distributed by a truncated normal distribution. The choices of the truncation points are $\mu \pm c\sigma$ where μ is the mean, σ is the standard deviation of the distribution, and coefficient c is set to 3 (a large number chosen not to affect the reported variance of the distributions much). The truncated normal distribution PDF with truncation points for min and max, a and b, respectively, is given as $f(x;\mu,\sigma,a,b) = \frac{\frac{1}{\sigma}\phi(\frac{x-\mu}{\sigma})}{\Phi(\frac{b-\mu}{\sigma})-\Phi(\frac{a-\mu}{\sigma})}$, where ϕ and Φ are the PDF and CDF of standard normal distribution, respectively.

TABLE I

SUMMARY STATISTICS FOR LUNG-EXCHANGE SIMULATIONS FROM JAPANESE POPULATION[a]

Lung Disease Patients 2013		
Waitlisted at the Beginning of the Year	Arrived/Departed During the Year	Received Live-/Deceased-Donor Trans.
193	126–146/25–45	20/41
Adult Body Weight (kg.)		
Female	Mean: 52.9	Std Dev: 9.0
Male	Mean: 65.7	Std Dev: 11.1
Composite	Mean: 59.3	Std Dev: 10.1
Blood-Type Distribution		
O	30.05%	
A	40.00%	
B	20.00%	
AB	9.95%	

[a]This table reflects the parameters used in calibrating the simulations for lung exchange. We obtained the blood-type distribution for Japan from the Japanese Red Cross website http://www.jrc.or.jp/donation/first/knowledge/index.html on 04/10/2016. The Japanese adult weight distribution's mean and standard deviation were obtained from e-Stat of Japan using the 2010 National Health and Nutrition Examination Survey from the website https://www.e-stat.go.jp/SG1/estat/GL02010101.do?method=init on 04/10/2016.

by their blood types and weights. We deem a patient compatible with a donor if the donor is blood-type compatible with the patient and also as heavy as the patient. We consider population sizes of $n = 10$, 20, and 50 for the simulations.

Patients who are compatible with both donors receive two lobes from their own donors directly, whereas the remaining patients join the exchange pool. Then we find optimal 2-way, 2&3-way, 2–4-way, 2–5-way, and unrestricted matchings.

Simulation results are reported in Table II. When $n = 50$ (the last two lines), only 12.6% of the patients can receive direct donation, and the rest, 87.4%, participate in exchange (i.e., the remaining average of 43.7 patients). Using only 2-way exchange, an additional 10% of the patients can be matched, increasing the number of living-donor transplants by 78.5% (i.e., 4.96 divided by 6.31). Using 2&3-way exchanges, we can increase the number of living-donor transplants by 135% (i.e., 8.51 divided by 6.31). Of course, larger exchange sizes require more transplant teams to be simultaneously available and can test the limits of logistical constraints. Subject to this caveat, it is possible to match nearly 25% of all patients via 2–5-way exchanges, almost tripling the number of living-donor lung transplants. At the limit, that is, in the absence of restrictions on exchange sizes, a third of the patients can receive lung transplants through exchanges, facilitating living-donor lung transplantation to nearly 46% of all patients in the population (matching 16.5 patients in exchange in addition to the 6.31 patients who receive direct transplantation).

The effect of the population size on marginal contribution of exchange is very significant: For example, the contribution of 2&3-way exchange to living-donor transplantation reduces from 135% to 30% when the population size reduces from $n = 50$ to $n = 10$.

TABLE II

LUNG-EXCHANGE SIMULATIONS[a]

Population Size	Direct Donation	Exchange Technology				
		2-way	2& 3-way	2–4-way	2–5-way	Unrestricted
10	1.256	0.292	0.452	0.506	0.52	0.524
	(1.0298)	(0.72925)	(1.0668)	(1.1987)	(1.2445)	(1.2604)
20	2.474	1.128	1.818	2.176	2.396	2.668
	(1.4919)	(1.4183)	(2.0798)	(2.4701)	(2.7273)	(3.1403)
50	6.31	4.956	8.514	10.814	12.432	16.506
	(2.2962)	(2.9759)	(4.5191)	(5.3879)	(5.9609)	(7.1338)

[a]In these results and others, the sample standard deviations reported are reported under averages; for the standard errors of the averages, these deviations need to be divided by the square root of the simulation number, $\sqrt{500} = 22.361$.

3.2. *Dual-Graft Liver Exchange*

For simulations on dual-graft liver exchange, we use the South Korean population characteristics (see Table III).[12] The same statistics are used for the SLK-exchange simulations in Appendix C of the Supplemental Material.[13]

We restrict our attention to left-lobe transplantation only, a procedure that is considerably safer for the donor than right-lobe transplantation. The Korean adult liver left lobe volume distribution's moments are also given in Um et al. (2015) (see Table III). We randomly set the graft volume of each donor using these parameters. We consider the following simulation scenario in given order, as dual-graft liver transplants are considered only if a suitable single-graft donor cannot be found:

1. If at least one of the donors of the patient is blood-type compatible, and his graft volume is at least 40% of the liver volume of the patient, then the patient receives a transplant directly from this compatible donor (denoted as "1-donor direct" scenario).

2. The remaining patients and their donors participate in an optimal "1-donor exchange" program. We use the same criterion as above to determine compatibility between any patient and any donor in the 1-donor exchange pool. Specifically, patients form 2-way (or 2&3-way) exchanges in which each patient receives a graft that is at least 40% of her liver volume from a blood-type compatible donor of another patient in the same exchange.

3. The remaining patients and their coupled donors are checked for dual-graft compatibility. If a patient's donors are blood-type compatible with her and the sum of the donors'

[12]There is a selection bias in using the gender distributions of who receive transplants and who donate, instead of those of who need transplants and who volunteer to donate. We use the former in our simulations because this is the best data publicly available and we did not want to speculate about the underlying gender specific disease and behavioral donation models that generate the latter statistics.

[13]In generating patient populations, we assume that each patient is attached to two living donors. We determine the blood type, gender, and height characteristics for patients and their donors independently and randomly. Then, we use the following weight determination formula as a function of height: $w = ah^b$, where w is weight in kg, h is height in meters, and constants a and b are set as $a = 26.58$, $b = 1.92$ for males and $a = 32.79$, $b = 1.45$ for females (Diverse Populations Collaborative Group (2005)). This is the best formula we could find for a weight-height relationship in humans in this respect. This paper does not report confidence intervals; therefore, we could not use a stochastic process to generate weights. The body surface area (BSA in m^2) of an individual is determined through the Mostellar formula given in Um et al. (2015) as $BSA = \frac{\sqrt{hw}}{6}$, and the liver volume ($l_v$ in ml) of Korean adults is determined through the estimated formula in Um et al. (2015) as $l_v = 893.485BSA - 439.169$.

TABLE III

SUMMARY STATISTICS FOR DUAL-GRAFT LIVER-EXCHANGE SIMULATIONS FROM SOUTH KOREAN POPULATION[a]

Live-Liver Donation Recipients in 2010–2014		
Female	1492 (34.55%)	
Male	2826 (64.45%)	
Total	4318 (100.0%)	
Live-Liver Donors in 2010–2014		
Female	1149 (26.61%)	
Male	3169 (73.39%)	
Total	4318 (100.0%)	
Adult Height (cm.)		
Female	Mean: 157.4	Std Dev: 5.99
Male	Mean: 170.7	Std Dev: 6.4
Liver Left Lobe Volume as Percentage of Whole		
	Mean: 34.7%	Std Dev: 3.9%
Blood-Type Distribution		
O	37%	
A	33%	
B	21%	
AB	9%	

[a]This table reflects the parameters used in calibrating the simulations for dual-graft liver exchange. We obtained the blood-type distribution for South Korea from http://bloodtypes.jigsy.com/East_Asia-bloodtypes on 04/10/2016. The South Korean adult height distribution's mean and standard deviation were obtained from the Korean Agency for Technology and Standards (KATS) website http://sizekorea.kats.go.kr on 04/10/2016. The transplant data were obtained from the Korean Network for Organ Sharing (KONOS) 2014 Annual Report, retrieved from https://www.konos.go.kr/konosis/index.jsp on 04/10/2016.

graft volumes is at least 40% of the patient's liver volume, then the patient receives dual grafts from her own donors (denoted as "2-donor direct" scenario).

4. Finally, the remaining patients and their donors participate in an optimal "2-donor exchange" program. We use the same criterion as above to deem any pair of donors dual-graft compatible with any patient. Specifically, patients form 2-way (or 2&3-way) exchanges in which each patient receives two grafts that total to at least 40% of her liver volume from two blood-type compatible donors, at least one of whom is paired with a different patient in the same exchange.

Simulation results are reported in Table IV. For a population of $n = 250$ (in the last six lines in the table), on average 141 patients remain without a transplant following 1-donor direct transplant and 1-donor 2&3-way exchange modalities (as about 60 patients receive transplants from a donor of theirs and an additional 49 patients receive 1-donor exchange transplants as seen in the third line of $n = 250$). About 31% of these patients receive dual-graft transplants from their own donors under the 2-donor direct modality (i.e., around 43.5 patients receive 2-donor transplants from their own donors out of the 141 re-

TABLE IV
DUAL-GRAFT LIVER-EXCHANGE SIMULATIONS

Population Size	1-Donor Direct		1-Donor Exchange		2-Donor Direct		2-Donor Exchange	
			Number Matched	As % of Entrants	Number Matched	As % of Entrants	Number Matched	As % of Entrants
50	12.048 (3.0699)	2-way	3.92 (2.7204)	10.33%	10.634 (2.8256)	31.24%	4.64 (2.6872)	19.83%
		2&3-way	5.066 (3.4382)	13.35%	10.256 (2.8655)	31.19%	6.278 (3.6512)	27.74%
		Unrestricted	5.772 (3.9799)	15.21%	10.016 (2.9232)	31.12%	7.016 (3.9965)	31.65%
100	24.098 (4.4699)	2-way	10.656 (4.2073)	14.04%	20.45 (4.3129)	31.34%	10.028 (3.9322)	22.39%
		2&3-way	14.452 (5.6152)	19.04%	18.884 (4.4201)	30.73%	13.566 (5.2947)	31.87%
		Unrestricted	17.754 (6.4827)	23.39%	17.88 (4.39.32)	30.75%	14.284 (5.373)	35.47%
250	59.998 (6.9937)	2-way	35.032 (7.5297)	18.44%	48.818 (7.1265)	31.50%	26.096 (5.8167)	24.58%
		2&3-way	49.198 (10.37)	25.89%	43.476 (7.1942)	30.88%	34.796 (8.2052)	35.75%
		Unrestricted	60.672 (11.127)	31.93%	39.744 (7.0446)	30.73%	34.684 (7.8363)	38.71%

maining). An additional 24.5% of these patients are matched in the 2-donor 2&3-way exchange modality (i.e., around 35 additional patients receive 2-donor transplants through exchange out of the 141 remaining). This final figure corresponds to approximately 80% of the 2-donor direct donation, and thus, the contribution of exchange to dual-graft transplantation is highly significant. Moreover, the 2-donor 2&3-way exchange modality provides transplants for 70.5% of the number of patients who receive transplants through the 1-donor exchange modality. Therefore, the contribution of the 2-donor exchange modality to the overall number of transplants from exchange is also highly significant. Under 2&3-way exchanges, 2-donor exchange increases the total number of living-donor liver transplants by about 23% by matching 13.9% of all patients.

Since pools evolve differently depending on which exchange-size constraint is used, we also include three columns titled "As % of Entrants" in Table IV, which report patients who receive transplants under each modality (1-Donor Exchange, 2-Donor Direct, or 2-Donor Exchange) as the percentage of the patients who are present in the pool for the given transplant modality. Thus, the percentages in the last column can be used to compare gains from 2-Donor exchange for different population sizes and exchange-size constraints. For $n = 250$, by 2-way exchanges only, about 24.5% of the patients entering 2-Donor exchange receive transplants (i.e., 26 divided by 106, which is $n = 250$ minus the sum of patients matched in previous stages). By 2&3-way exchanges, 35.75% of the patients entering 2-Donor exchange pool receive transplants, and in the absence of exchange-size constraints, 38.7% of the patients entering 2-Donor exchange pool receive transplants. Thus, unlike in lung exchange, most of the gains from exchange are captured through 2&3-way exchanges in dual-graft liver exchange.

4. A MODEL OF DUAL-DONOR ORGAN EXCHANGE

Our simulations in Section 3 show that exchange is potentially important in the context of dual-donor organ transplants. We next present a simple theoretical model for its analysis.

We assume that each patient, who has two living donors, can receive transplant organs from her own donors if and only if both of them are blood-type compatible with the patient. That is, the two transplant organs are perfect complements for the patient. In our benchmark model, we assume that there are no size or tissue-type compatibility requirements; the only compatibility requirement regards the blood type. This assumption helps us to focus exclusively on the effect of the two-donor requirement on organ exchange, and it best fits our application of dual-graft liver transplantation.[14]

Let $\mathcal{B} = \{O, A, B, AB\}$ be the set of blood types. We denote generic elements by $X, Y, Z \in \mathcal{B}$. Let $\trianglerighteq$ be the partial order on blood types defined by $X \trianglerighteq Y$ if and only if blood type X can donate to blood type Y. Figure 3 illustrates the partial order $\trianglerighteq$.[15]

Each patient participates in the exchange with two donors, which we refer to as a *triple*.[16] The relevant information concerning the patient and her two donors can be summarized as a triple of blood types $X - Y - Z \in \mathcal{B}^3$, where X is the blood type of the patient, and Y and Z are the blood types of the donors. We will refer to each element in $\mathcal{B}^3$ as a *triple type* such that the order of the donors has no relevance. For example, an O patient with a pair of A and B donors counts as both a triple of type $O - A - B$ and also a triple of type $O - B - A$.

DEFINITION 1: An *exchange pool* is a vector of nonnegative integers $\mathcal{E} = \{n(X - Y - Z) : X - Y - Z \in \mathcal{B}^3\}$ such that:

1. $n(X - Y - Z) = n(X - Z - Y)$ for all $X - Y - Z \in \mathcal{B}^3$.
2. $n(X - Y - Z) = 0$ for all $X - Y - Z \in \mathcal{B}^3$ such that $Y \trianglerighteq X$ and $Z \trianglerighteq X$.

The number $n(X - Y - Z)$ stands for the number of participating $X - Y - Z$ triples.

The first condition in the definition of an exchange pool corresponds to the assumption that the order of the donors does not matter, that is, $X - Y - Z$ and $X - Z - Y$ repre-

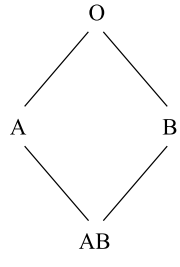


FIGURE 3.—The partial order $\trianglerighteq$ on the set of blood types $\mathcal{B} = \{O, A, B, AB\}$.

[14]When first introduced, the target population for lobar lung transplantation was pediatric patients. Since the lung graft needs of children are not as voluminous as those of adults, the application of lobar lung transplantation also fits our model well when the exchange pool consists of pediatric patients.

[15]For any $X, Y \in \mathcal{B}$, $X \trianglerighteq Y$ if and only if there is a downward path from blood type X to blood type Y in Figure 3.

[16]It is straightforward to integrate into our model patients who have one donor and who need one organ. We can do so by treating these patients as part of a triple where a virtual donor is of the same blood type as the patient.

sent the same type. The second condition corresponds to the assumption that compatible patient-donor triples do not participate in the exchange.

5. 2-WAY EXCHANGE

In this section, we assume that only 2-way exchanges are allowed. We characterize the maximum number of patients receiving transplants for any given exchange pool $\mathcal{E}$. We also describe an algorithm that achieves this maximum.

A 2-way exchange is the simplest form of dual-donor organ exchange, involving two triples exchanging one or both of their donors' grafts, and it is the easiest to coordinate. Thus, as a first step in our analysis, it is important to understand the structure and size of optimal matchings with only 2-way exchanges. There are forty types of triples after accounting for repetitions due to the reordering of donors. The following lemma simplifies the problem substantially by showing that only six of these types may take part in 2-way exchanges.[17] All proofs are relegated to Appendices A, D, and E.

LEMMA 1: *In any given exchange pool $\mathcal{E}$, the only types that could be part of a 2-way exchange are $A-Y-B$ and $B-Y-A$ where $Y \in \{O, A, B\}$.*

The six types of triples in Lemma 1 are such that every A blood-type patient has at least one B blood-type donor, and every B blood-type patient has at least one A blood-type donor. Therefore, A blood-type patients can only take part in a 2-way exchange with B blood-type patients, and vice versa. Furthermore, if they participate in a 2-way exchange, the $A-A-B$ and $B-B-A$ types must exchange exactly one donor; the $A-B-B$ and $B-A-A$ types must exchange both donors; and the $A-O-B$ and $B-O-A$ types might exchange one or two donors.

We refer to the six types in Lemma 1 as *essential types* and summarize the possible 2-way exchanges between them as the edges of the graph in Figure 4.

We next present a matching algorithm that maximizes the number of transplants through 2-way exchanges. The algorithm sequentially maximizes three subsets of 2-way exchanges:

ALGORITHM 1—Sequential Matching Algorithm for 2-Way Exchanges:

Step 1: Match the maximum number of $A-A-B$ and $B-B-A$ types.[18] Match the maximum number of $A-B-B$ and $B-A-A$ types.

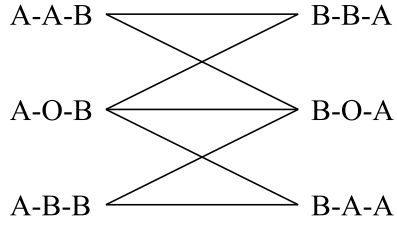


FIGURE 4.—Possible 2-way exchanges.

[17] While only six of forty types can participate in 2-way exchanges, nearly half of the patient populations in our simulations belong to these types due to very high rates of blood types A and B in Japan and South Korea.

[18] That is, match $\min\{n(A-A-B), n(B-B-A)\}$ type $A-A-B$ triples with $\min\{n(A-A-B), n(B-B-A)\}$ type $B-B-A$ triples.

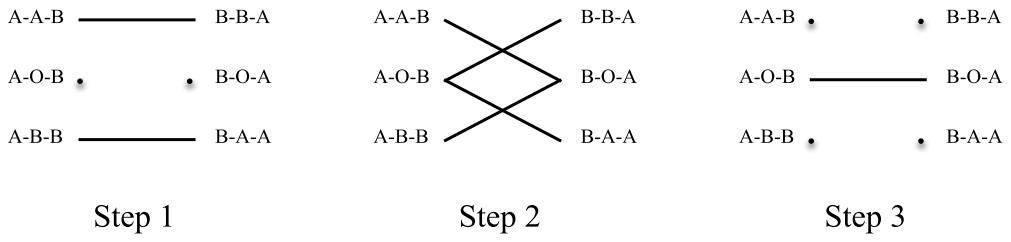


FIGURE 5.—The optimal 2-way sequential matching algorithm.

Step 2: Match the maximum number of $A-O-B$ types with any subset of the remaining $B-B-A$ and $B-A-A$ types. Match the maximum number of $B-O-A$ types with any subset of the remaining $A-A-B$ and $A-B-B$ types.

Step 3: Match the maximum number of the remaining $A-O-B$ and $B-O-A$ types.

Figure 5 graphically illustrates the pairwise exchanges that are carried out at each step of the sequential matching algorithm. The mechanics of this algorithm are very intuitive and based on optimizing the flexibility offered by blood-type O donors. Initially, the optimal use of triples endowed with blood-type O donors is not clear, and for Step 1 they are "put on hold." In this first step, as many triples as possible are matched without using any triple endowed with a blood-type O donor. By Step 2, the optimal use of triples endowed with blood-type O donors is revealed. In this step, as many triples as possible are matched with each other by using only one blood-type O donor in each exchange. And finally in Step 3, as many triples as possible are matched with each other by using two blood-type O donors in each exchange.

The next theorem shows the optimality of Algorithm 1 and characterizes the maximum number of transplants through 2-way exchanges.

THEOREM 1: *Given an exchange pool $\mathcal{E}$, Algorithm 1 maximizes the number of 2-way exchanges. The maximum number of patients receiving transplants through 2-way exchanges is* $2\min\{N_1, N_2, N_3, N_4\}$ *where*

$$N_1 = n(A-A-B) + n(A-O-B) + n(A-B-B),$$
$$N_2 = n(A-O-B) + n(A-B-B) + n(B-B-A) + n(B-O-A),$$
$$N_3 = n(A-A-B) + n(A-O-B) + n(B-O-A) + n(B-A-A),$$
$$N_4 = n(B-B-A) + n(B-O-A) + n(B-A-A).$$

Figure 6 depicts the sets of triple types whose market populations are N_1, N_2, N_3, and N_4.

6. LARGER-SIZE EXCHANGES

We have seen that when only 2-way exchanges are allowed, every 2-way exchange must involve exactly one A and one B blood-type patient. The following lemma generalizes this observation to K-way exchanges for arbitrary $K \geq 2$. In particular, every K-way exchange must involve an A and a B blood-type patient, but if $K \geq 3$, then it might also involve O blood-type patients.

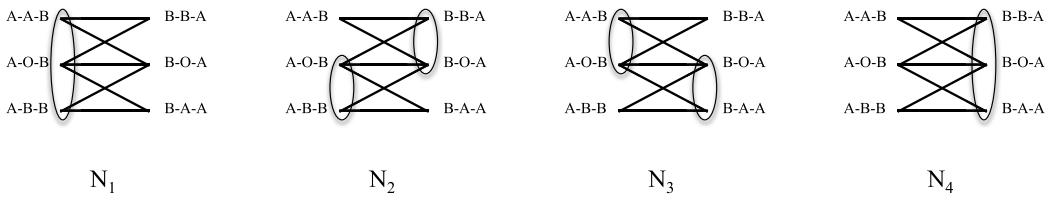


FIGURE 6.—Potential bottleneck groups for maximum number of 2-way exchanges.

LEMMA 2: *Fix $\mathcal{E}$ and let $K \geq 2$. Then, the only types that could be part of a K-way exchange are $O-Y-A$, $O-Y-B$, $A-Y-B$, and $B-Y-A$ where $Y \in \{O, A, B\}$. Furthermore, every K-way exchange must involve an A and a B blood-type patient.*

In kidney-exchange pools, O patients with A donors are much more numerous than their opposite type pairs, A patients with O donors. That is because O patients with A donors arrive for exchange all the time, while A patients with O donors only arrive if there is tissue-type incompatibility between them (as otherwise the donor is compatible and donates directly to the patient). This empirical observation is caused by the blood-type compatibility structure. In general, patients with less-sought-after blood-type donors relative to their own blood type become in excess and plentiful as the exchange pool grows in size. A similar situation will also occur in dual-donor organ exchange pools. For kidney-exchange models, Roth, Sönmez, and Ünver (2007) made an explicit long-run assumption regarding this asymmetry. We will make a corresponding assumption for dual-donor organ exchange below. However, our assumption will be milder, as it will be imposed only for two types of triples rather than all triple types with less-sought-after donor blood types than their patients.

DEFINITION 2: An exchange pool $\mathcal{E}$ satisfies the *long-run* assumption if for every feasible matching in the absence of exchange-size restrictions, there is at least one $O-O-A$ and one $O-O-B$ type that do not take part in any exchange.

Suppose that the exchange pool $\mathcal{E}$ satisfies the long-run assumption and μ is a matching composed of any size exchanges. The long-run assumption ensures that we can create a new matching μ' from μ by replacing every $O-A-A$ or $O-A-B$ type taking part in an exchange with an unmatched $O-O-A$ type, and every $O-B-B$ type taking part in an exchange by an unmatched $O-O-B$ type. Then, the new matching μ' is composed of the same size exchanges as μ, and it induces the same number of transplants as μ. Furthermore, the only O blood-type patients matched under μ' belong to the triples of types $O-O-A$ or $O-O-B$.

Let $\bar{K} \geq 2$ be the maximum allowed exchange size. Consider the problem of finding an *optimal* matching, that is, one that maximizes the number of transplants when only $2, \ldots, \bar{K}$-way exchanges are feasible. By the above paragraph, for any optimal matching μ, we can construct another optimal matching μ' in which the only triples with O blood-type patients matched under μ' are of types $O-O-A$ or $O-O-B$. We summarize this observation as the following lemma:

LEMMA 3: *Let $\bar{K} \geq 2$ be the maximum allowed exchange size and let the exchange pool $\mathcal{E}$ satisfy the long-run assumption. Then, there exists an optimal matching exclusively involving the two types $O-O-A$, $O-O-B$ and the six essential types $A-Y-B$, $B-Y-A$ where $Y \in \{O, A, B\}$.*

Also observe that, since the numbers of type $O-O-A$ and type $O-O-B$ triples are nonbinding by the long-run assumption, an optimal matching can be characterized just in terms of the numbers of the six essential types. In the next subsection, we use this approach to describe an algorithm that achieves the maximum number of transplants when $\bar{K}=3$.[19]

6.1. *2-&3-Way Exchanges*

We continue our analysis with a characterization of the types that can be part of a 3-way exchange. It turns out that ruling out the types $O-A-A$ and $O-B-B$ in the construction of an optimal matching is without loss of generality for the case of 3-way exchange. Not only can these triples not be matched under an optimal matching, they cannot be part of any 3-way exchange.

LEMMA 4: *Given an exchange pool $\mathcal{E}$, triples of types $O-A-A$ or $O-B-B$ cannot participate in any 3-way exchange.*

Thus, the only types that can participate in a 3-way exchange are $O-O-A$, $O-O-B$, $O-A-B$, and the six essential types $A-Y-B$, $B-Y-A$ where $Y\in\{O,A,B\}$.

For expositional simplicity, next we describe a collection of 2- and 3-way exchanges divided into three groups. We show in Lemma 6 in Appendix A that one can restrict attention to these exchanges when constructing an optimal matching.

DEFINITION 3: Given an exchange pool $\mathcal{E}$, a matching is in *simplified form* if it consists of exchanges in the following three groups:

Group 1: 2-way exchanges exclusively involving types $A-A-B$, $A-B-B$, $B-B-A$, and $B-A-A$. These exchanges are represented in Figure 7 by a regular (i.e., nonbold/nondotted end) edge between two of these types.

Group 2: 3-way exchanges exclusively involving types $A-A-B$, $A-B-B$, $B-B-A$, and $B-A-A$ represented in Figure 7 by an edge with one dotted and one nondotted end. A 3-way exchange in this group consists of two triples of the type at the dotted end and one triple of the type at the nondotted end.

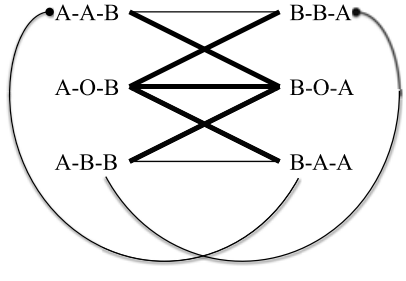


FIGURE 7.—Three groups of 2- and 3-way exchanges.

[19]Without additional structure, finding an optimal matching for fixed $\bar{K}\geq 3$ is a computationally hard problem in the sense that it is NP-complete (Abraham, Blum, and Sandholm (2007)). In contrast, exploiting the structure imposed above, we will provide a polynomial-time algorithm for $\bar{K}=3$ in the next subsection and for $\bar{K}=6$ in Appendix E of the Supplemental Material.

Group 3: 3-way exchanges involving two of the types $A-A-B$, $A-O-B$, $A-B-B$, $B-B-A$, $B-O-A$, $B-A-A$, and one of the types $O-O-A$, $O-O-B$, $O-A-B$. These exchanges are represented in Figure 7 by a bold edge between the former two types.[20]

We will show that when the long-run assumption is satisfied, the following matching algorithm maximizes the number of transplants through 2- and 3-way exchanges. The algorithm sequentially maximizes three subsets of exchanges:

ALGORITHM 2—Sequential Matching Algorithm for 2- and 3-Way Exchanges:

Step 1: Carry out group 1, group 2 exchanges in Figure 7 among types $A-A-B$, $A-B-B$, $B-B-A$, and $B-A-A$ to maximize the number of transplants subject to the following constraints $(*)$:

1. Leave at least a total $\min\{n(A-A-B)+n(A-B-B), n(B-O-A)\}$ of $A-A-B$ and $A-B-B$ types unmatched.
2. Leave at least a total $\min\{n(B-B-A)+n(B-A-A), n(A-O-B)\}$ of $B-B-A$ and $B-A-A$ types unmatched.

Step 2: Carry out the maximum number of 3-way exchanges in Figure 7 involving $A-O-B$ types and the remaining $B-B-A$ or $B-A-A$ types. Similarly carry out the maximum number of 3-way exchanges involving $B-O-A$ types and the remaining $A-A-B$ or $A-B-B$ types.[21]

Step 3: Carry out the maximum number of 3-way exchanges in Figure 7 involving the remaining $A-O-B$ and $B-O-A$ types.[22]

Figure 8 graphically illustrates the 2- and 3-way exchanges that are carried out at each step of the sequential matching algorithm. The intuition for our second algorithm is slightly more involved. When only 2-way exchanges are allowed, the only perk of a blood-type O donor is in his flexibility to provide a transplant organ to either an A or a B patient. When 3-way exchanges are also allowed, a blood-type O donor has an additional perk: He

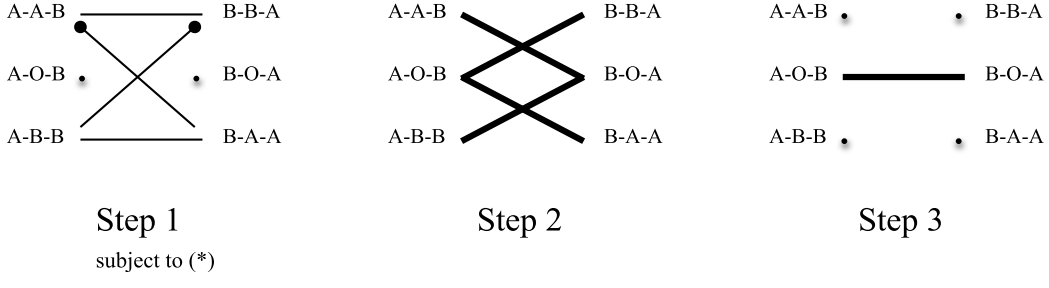


FIGURE 8.—The optimal 2- and 3-way sequential matching algorithm.

[20]There are five exchanges represented by bold edges in Figure 7. Four of these exchanges involve only one triple with an O donor. For those exchanges, the third triple of the 3-way exchange is uniquely defined either of type $O-O-A$ or of type $O-O-B$. The fifth exchange represented by a bold edge in Figure 7 has two triples with an O donor each. For this exchange, the third triple can be of any of the types $O-O-A$, $O-O-B$, or $O-A-B$.

[21]For each of these 3-way exchanges, the third triple is uniquely defined either of type $O-O-A$ or of type $O-O-B$.

[22]For these exchanges, the third triple could be of any of the types $O-O-A$, $O-O-B$, or $O-A-B$.

can help save an additional patient of blood type O, provided that the patient already has one donor of blood type O. For example, a triple of type $A-O-B$ can be paired with a triple of type $B-B-A$ to save one additional triple of type $O-O-A$. Since each patient of type $A-O-B$ is in need of a patient of either type $B-B-A$ or type $B-A-A$ to save an extra patient through the 3-way exchange, the maximization in Step 1 has to be constrained. Otherwise a 3-way exchange would be sacrificed for a 2-way exchange, reducing the number of transplants. The rest of the mechanics are similar between the two algorithms. For expositional purposes, we present the subalgorithm that solves the constrained optimization in Step 1 in Appendix D of the Supplemental Material. The following theorem shows the optimality of Algorithm 2.

THEOREM 2: *Given an exchange pool $\mathcal{E}$ satisfying the long-run assumption, Algorithm 2 maximizes the number of transplants through 2- and 3-way exchanges.*

6.2. *Necessity and Sufficiency of 6-Way Exchanges*

Although larger exchanges are logistically harder to organize, it is of theoretical interest to understand their potential role in dual-donor organ exchange. We next identify the types that can participate in an optimal matching in the absence of constraints on exchange size. In this setting, the only blood-type O patients that can be part of an optimal matching are of types $O-O-A$ or $O-O-B$.

LEMMA 5: *Given an exchange pool $\mathcal{E}$ satisfying the long-run assumption, $O-A-A$, $O-A-B$, and $O-B-B$ type triples are never matched in an optimal matching in the absence of exchange-size constraints.*

Thus, the only types that can participate in an optimal exchange are $O-O-A$, $O-O-B$, and the six essential types $A-Y-B$, $B-Y-A$ where $Y \in \{O, A, B\}$.

In our next result, we show that restricting attention to 2–6-way exchanges is sufficient to maximize the number of transplants through exchange. As part of the proof of this result, given in Appendix E of the Supplemental Material, we also provide an algorithm that achieves the maximum.

THEOREM 3: *Suppose that the exchange pool $\mathcal{E}$ satisfies the long-run assumption and exchange sizes are unrestricted. Then there exists an optimal matching that consists of exchanges no larger than 6-way.*

The following example shows that using 6-way exchanges is not only sufficient, but also necessary to find an optimal matching for some exchange pools.

EXAMPLE 1: Consider an exchange pool with one triple of type $A-O-B$, two triples of type $B-O-A$, and three triples of $O-O-B$.[23] Observe that all patients can receive two transplant organs of their blood type. Therefore, all patients are matched under an optimal matching. With three blood-type O patients and six blood-type O donors, all blood-type O organs must be transplanted to blood-type O patients (for otherwise not

[23]For the example to use the long-run assumption, we can assume there are also one additional $O-O-B$ triple and an $O-O-A$ triple. In this case, at least one $O-O-B$ and this $O-O-A$ triple remain unmatched in every matching.

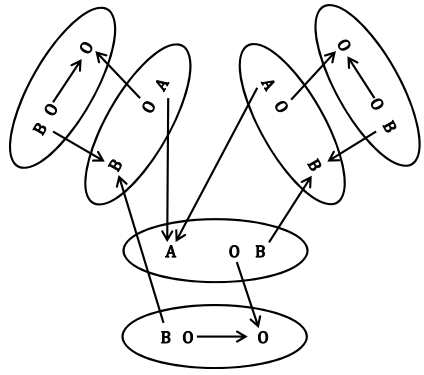


FIGURE 9.—An optimal matching for the pool in Example 1 always consists of a single 6-way exchange.

each patient would receive a transplant). This in turn implies that the two blood-type A organs must be transplanted to the only blood-type A patient. Hence, the triple of type $A-O-B$ should be in the same exchange as the two triples of type $B-O-A$. Equivalently, all triples with a non-O patient should be part of the same exchange. But patients of $O-O-B$ triples each are in need of an additional blood-type O donor, and thus $O-O-B$ triples should also be part of the same exchange. Hence, 6-way exchange is necessary to match all patients and obtain an optimal matching (see Figure 9).

Our simulations in Section 3 suggest that while the total number of transplants from exchanges larger than 3-way can be significant and approach those from 2-way and 3-way exchanges combined for the application of lung exchange, they are relatively modest for the application of dual-graft liver exchange. The contrast between the two sets of simulations suggests that the presence of size compatibility increases the role of larger than 3-way exchanges. Our theoretical results in the absence of size compatibility (and their proofs) provide some insight for the relatively modest role of larger than 3-way exchanges for the simulations on dual-graft liver exchange. Proposition 2 in Appendix E shows that when there are no exchange-size constraints, an optimal matching can be constructed using only 2- and 3-way exchanges provided that there are no blood-type O patients in the pool. Moreover, by Lemma 5, triples of type $O-O-A$ and $O-O-B$ are the only triples with blood-type O patients, who can be matched in an optimal matching. Each triple of these types requires a second O donor, which can only be supplied by $A-O-B$ or $B-O-A$ types. Thus, all welfare gains from exchanges beyond 3-way come from the ability of matching additional $O-O-A$ and $O-O-B$ types through the utilization of $A-O-B$ and $B-O-A$ types. In the absence of exchange-size constraints, a triple of $O-O-A$ or $O-O-B$ can be appended to any exchange for each triple of $A-O-B$ or $B-O-A$ that is part of the exchange (see, e.g., Figure 9 where three types of $O-O-B$ are appended to three types of $A-O-B$ or $B-O-A$). When only 2- and 3-way exchanges are feasible, only one triple of types $O-O-A$ or $O-O-B$ can be appended to any 2-way exchange that includes one or two triples of types $A-O-B$ and $B-O-A$. But that means that larger than 3-way exchanges can only increase the total number of transplants by the difference between (1) the maximum number of $A-O-B$ and $B-O-A$ types that can be matched in the absence of exchange-size constraints and (2) the maximum number of distinct 2-way exchanges that includes $A-O-B$ or $B-O-A$ types when no exchange can be larger than 3-way. The two types $A-O-B$

and $B-O-A$ are essential and they already play a key role under 2- and 3-way exchange. Hence the difference cannot be very high, limiting the role of larger than 3-way exchanges in our theoretical model as well as in our application of dual-graft liver exchange.

7. CONCLUSION

For any organ with the possibility of living-donor transplantation, living-donor organ exchange is also medically feasible. Despite the introduction and practice of transplant procedures that require two donors, organ exchange in this context is neither discussed in the literature nor implemented in practice. We propose dual-donor organ exchange as a new transplantation modality, focusing on the following three transplantation procedures: dual-graft liver transplantation, bilateral living-donor lobar lung transplantations, and simultaneous liver-kidney transplantation. We simulate the potential gains from dual-donor exchanges for these applications. We also formulate an analytical model of dual-donor organ exchange and introduce optimal exchange mechanisms under various logistical constraints.

Analytically, dual-donor organ exchange is a more challenging problem than kidney exchange since each patient is in need of two compatible donors who are perfect complements. Exploiting the structure induced by the blood-type compatibility requirement for organ transplantation, we introduce optimal exchange mechanisms under various logistical constraints. Abstracting away from additional medical compatibility considerations such as size compatibility and tissue-type compatibility, our analytical model best captures the specifics of dual-graft liver transplantation. For our calibrated simulations, however, we take into account these additional compatibility requirements (whenever relevant) for each application. Through these simulations, we show that the marginal contribution of exchange to living-donor organ transplantation is very substantial. For example, adopting 2-way exchanges alone has the potential to increase the number of living-donor lung transplants by 78.5% in Japan (see Table II).

The potential of an organized exchange for each medical application in a given society will likely depend on the following factors:

1. availability and expertise in the required transplantation technique;
2. prominence of living donation;
3. legal and cultural attitudes towards living-donor organ exchanges.

First and foremost, transplantation procedures that require two living donors are highly specialized and so far they are available only in a few countries. For example, the practice of living-donor lobar lung transplantation is reported in the literature only in the United States and Japan. Hence, the availability of the required transplantation technology limits the potential markets for applications of dual-donor organ exchange. Next, organized exchange is more likely to succeed in an environment where living-donor organ transplantation is the norm rather than an exception. While living donation of kidneys is widespread in several western countries, it is much less common for organs that require more invasive surgeries, such as the liver and the lung. Since all our applications rely on these more invasive procedures, this second factor further limits the potential of organized exchange in the western world. In contrast, this factor is very favorable in several Asian counties and countries with predominantly Muslim populations, where living donors are the primary source of transplant organs. Finally, the concept of living-donor organ exchange is not equally accepted throughout the world, and it is not even legal in some countries. For example, organ exchanges are outlawed under the German transplant law. Indeed, it was unclear whether kidney exchanges violate the National Organ Transplant Act of 1984 in

the U.S. until Congress passed the Charlie W. Norwood Living Organ Donation Act of 2007, clarifying them as legal. Clearly, dual-donor organ exchanges cannot flourish in a country unless they comply with the laws.

Based on these factors, we foresee the strongest potential for organized exchange for dual-graft liver transplantation in South Korea, for lobar lung transplantation in Japan, and for simultaneous liver-kidney transplantation in South Korea and in Turkey.

APPENDIX A: PROOFS OF LEMMAS 1, 2, 4, AND 5 AND THEOREMS 1 AND 2

PROOF OF LEMMA 1: Since AB blood-type patients are compatible with their donors, there are no AB blood-type patients in the exchange pool. This implies that no triple with an AB blood-type donor can be part of a 2-way exchange, since AB blood-type donors can only donate to AB blood-type patients.

We next argue that no triple with an O blood-type patient can be part of a 2-way exchange. To see this, suppose that $X-Y-Z$ and $O-Y'-Z'$ take part in a 2-way exchange. If X exchanges her Y donor, then Y can donate to O so $Y=O$. If X does not exchange her Y donor, then Y can donate to X. In either case, $Y \trianglerighteq X$. Similarly, $Z \trianglerighteq X$, implying that $X-Y-Z$ is a compatible triple, a contradiction.

From what is shown above, the only triples that can be part of a 2-way exchange are those where the patient's blood type is in $\{A, B\}$ and the donors' blood types are in $\{O, A, B\}$. If we further exclude the compatible combinations and repetitions due to reordering the donors, we are left with the six triple types stated in the lemma. It is easy to verify that triples of these types can indeed participate in 2-way exchanges (see Figure 4). *Q.E.D.*

PROOF OF THEOREM 1: Let N denote the maximum number of 2-way exchanges. Since each such exchange results in two transplants, the maximum number of transplants through 2-way exchanges is $2N$. We will prove the theorem in two parts.

Proof of "$N \leq \min\{N_1, N_2, N_3, N_4\}$*"*: Since each 2-way exchange involves an A blood-type patient, we have that $N \leq N_1$. Since $A-A-B$ types can only be part of a 2-way exchange with $B-B-A$ or $B-O-A$ types, the number of 2-way exchanges that involve an $A-A-B$ type is bounded above by $n(B-B-A)+n(B-O-A)$. Therefore, the number of 2-way exchanges involving an A blood-type patient is less than or equal to this upper bound plus the number of $A-O-B$ and $A-B-B$ types, that is, $N \leq N_2$. The inequalities $N \leq N_3$ and $N \leq N_4$ follow from symmetric arguments, switching the roles of A and B blood types.

Proof of "$N \geq \min\{N_1, N_2, N_3, N_4\}$*"*: We next show that the matching algorithm achieves $\min\{N_1, N_2, N_3, N_4\}$ exchanges. This implies $N \geq \min\{N_1, N_2, N_3, N_4\}$. Since $N \leq \min\{N_1, N_2, N_3, N_4\}$, we conclude that $N = \min\{N_1, N_2, N_3, N_4\}$, and hence, the matching algorithm is optimal.

Case 1. "$N_1 = \min\{N_1, N_2, N_3, N_4\}$": The inequalities $N_1 \leq N_2$, $N_1 \leq N_3$, and $N_1 \leq N_4$ imply that

$$n(A-A-B) \leq n(B-B-A)+n(B-O-A),$$

$$n(A-B-B) \leq n(B-A-A)+n(B-O-A),$$

$$n(A-A-B)+n(A-B-B) \leq n(B-B-A)+n(B-A-A)+n(B-O-A).$$

Therefore, after the maximum number of $A-A-B$ and $B-B-A$ types and the maximum number of $A-B-B$ and $B-A-A$ types are matched in the first step, there are

enough $B-O-A$ types to accommodate any remaining $A-A-B$ and $A-B-B$ types in the second step.

Since $N_1 \leq N_4$, there are at least $n(A-O-B)$ triples with B blood-type patients who are not matched to $A-A-B$ and $A-B-B$ types in the first two steps. Therefore, all $A-O-B$ triples are matched to triples with B blood-type patients in the second and third steps. The resulting matching involves N_1 exchanges, since all A blood-type patients take part in a 2-way exchange.

Case 2. "$N_2 = \min\{N_1, N_2, N_3, N_4\}$": Since $N_2 \leq N_1$, we have $n(A-A-B) \geq n(B-B-A) + n(B-O-A)$. Therefore, all $B-B-A$ types are matched to $A-A-B$ types in the first step. Similarly, $N_2 \leq N_4$ implies that $n(A-O-B) + n(A-B-B) \leq n(B-A-A)$. Therefore, all $A-B-B$ types are matched to $B-A-A$ types in the first step. In the second step, there are no remaining $B-B-A$ types, but there are enough $B-A-A$ types to accommodate all $A-O-B$ types. Similarly, in the second step, there are no remaining $A-B-B$ types, but there are enough $A-A-B$ types to accommodate all $B-O-A$ types. There are no more exchanges in the third step. The resulting matching involves N_2 2-way exchanges.

The cases where N_3 and N_4 are the minimizers follow from symmetric arguments exchanging the roles of A and B blood types. *Q.E.D.*

PROOF OF LEMMA 2: As argued in the proof of Lemma 1, no AB blood-type patient or donor can be part of a K-way exchange. Therefore, the only triples that can be part of a K-way exchange are those where its patient's and its donors' blood types are in $\{O, A, B\}$. After excluding the compatible combinations, we are left with the triple types listed above.

Take any K-way exchange. Since every triple type listed above has at least an A or a B blood-type donor, the K-way exchange involves an A or a B blood-type patient. If it involves an A blood-type patient, then that patient brings in a B blood-type donor, so it must also involve a B blood-type patient. If it involves a B blood-type patient, then that patient brings in an A blood-type donor, so it must also involve an A blood-type patient. It is trivial to see that all types in the hypothesis can feasibly participate in exchange in a suitable exchange pool.[24] *Q.E.D.*

PROOF OF LEMMA 4: Suppose that there exists a 3-way exchange that matches an $O-X-X$ type triple for any $X \in \{A, B\}$. This triple's O patient necessarily receives grafts from two O donors in this exchange. Then there exist two triples each with a single O donor in the same exchange, as $X-O-O$ types are compatible and are not present in $\mathcal{E}$. By Lemma 2, there should be an A and a B patient in any exchange. Thus, the other two triples that participate in this 3-way exchange are necessarily of types $A-O-B$ and $B-O-A$, respectively (as types with AB patients or donors and $A-O-O$, $B-O-O$, $A-O-A$, and $B-O-B$ types do not participate in exchange by Lemma 2). However, $O-X-X$, $A-O-B$, and $B-O-A$ types cannot form a feasible 3-way exchange among each other. This contradicts the existence of such a 3-way exchange. Hence, $O-X-X$ types cannot participate in a 3-way exchange. *Q.E.D.*

[24] We already demonstrated the possibility of exchanges regarding triples (of the types in the hypothesis of the lemma) with A and B blood-type patients in Lemma 1. An $O-A-A$ triple can be matched in a four-way exchange with $A-O-B$, $A-O-B$, $B-A-A$ triples (symmetric argument holds for $O-B-B$). On the other hand, an $O-A-B$ triple can be matched in a 3-way exchange with $A-O-B$ and $B-O-A$ triples. An $O-O-A$ or an $O-O-B$ type can be used instead of $O-A-B$ in the previous example.

Before proving Theorem 2, we first state and prove two lemmas that will be used in proving Theorem 2. Lemma 6 below states that, under the long-run assumption, one can restrict attention to the exchanges in Definition 3 to construct an optimal matching.

LEMMA 6: *Suppose that the exchange pool $\mathcal{E}$ satisfies the long-run assumption, and only 2- and 3-way exchanges are allowed. Then, there is an optimal matching that is in simplified form.*

PROOF: We first show that if a matching μ includes an exchange not represented in Figure 7, then there is a matching μ' that induces at least as many transplants and includes one more exchange of the kinds included in Figure 7. To see this, take any exchange in μ not represented as an edge in Figure 7. The exchange must be at most 3-way since larger exchanges are not allowed. Furthermore, by Lemma 2, the exchange includes two types $A-Y-Z$ and $B-Y'-Z'$ that are vertices of Figure 7. To create the matching μ', we first undo this exchange in μ, then create a weakly larger exchange that involves unmatched types and is represented as an edge in Figure 7.

Case 1. "There is a bold edge between the types $A-Y-Z$ and $B-Y'-Z'$ in Figure 7": Then we create the 3-way exchange that corresponds to that bold edge.

If there is no bold edge between $A-Y-Z$ and $B-Y'-Z'$ in Figure 7, then these types cannot be $A-A-B$ and $B-B-A$, because the only allowable exchange involving $A-A-B$ and $B-B-A$ is the 2-way exchange included in Figure 7. By an analogous argument, these types also cannot be $A-B-B$ and $B-A-A$. This leaves out two more cases:

Case 2. "$A-Y-Z=A-A-B$ and $B-Y'-Z=B-A-A$": The only allowable exchange involving these two types not represented in Figure 7 is the 3-way exchange where the third participant is $A-O-B$. In this case, we create the 3-way exchange that corresponds to the bold edge between the unmatched $A-O-B$ and $B-A-A$ types.

Case 3. "$A-Y-Z=A-B-B$ and $B-Y'-Z=B-B-A$": We omit the argument for this case, since it is symmetric to Case 2.

By the finiteness of the problem, there is an optimal matching μ that is not necessarily in simplified form. By what we have shown above, we can construct an optimal matching μ' that is in simplified form from the matching μ by iteratively replacing the exchanges that are excluded from Figure 7 with those that are included in it. *Q.E.D.*

LEMMA 7: *Suppose that the exchange pool $\mathcal{E}$ satisfies the long-run assumption and $n(A-A-B)+n(A-B-B)>n(B-O-A)$. If a matching μ is in simplified form and includes at least one 3-way exchange involving an $A-O-B$ and a $B-O-A$ type, then there is a matching μ' such that*: (i) *μ' is in simplified form*, (ii) *μ' induces at least as many transplants as μ, and* (iii) *μ' includes one less 3-way exchange involving an $A-O-B$ and a $B-O-A$ type compared to μ.*

PROOF: To construct μ', we first undo exactly one 3-way exchange in μ that involves an $A-O-B$ and a $B-O-A$ type. In the following, we will call these $A-O-B$ and $B-O-A$ types, "the $A-O-B$ type" and "the $B-O-A$ type." To finish constructing μ', we consider five cases:

Case 1. "There is an unmatched $A-A-B$ or $A-B-B$ type under μ": Then create a 3-way exchange involving that type and the $B-O-A$ type.

If we do not fall into Case 1, then all $A-A-B$ and $A-B-B$ types are matched under μ; but since $n(A-A-B)+n(A-B-B)>n(B-O-A)$, they cannot all be part of a 3-way exchange with $B-O-A$ types. That leaves four more cases:

Case 2. "An $A-A-B$ and a $B-B-A$ type are part of a 2-way exchange under μ": Then undo that 2-way exchange and create two new 3-way exchanges, one involving the unmatched $A-A-B$ type and the $B-O-A$ type, and another involving the unmatched $B-B-A$ type and the $A-O-B$ type.

Case 3. "Two $A-A-B$ types and a $B-A-A$ type are part of a 3-way exchange under μ": Then undo that 3-way exchange and create two new 3-way exchanges, one involving one of the two unmatched $A-A-B$ types and the $B-O-A$ type, and another involving the unmatched $B-A-A$ type and the $A-O-B$ type.

Case 4. "An $A-B-B$ and a $B-A-A$ type are part of a 2-way exchange under μ": Then undo that 2-way exchange and create two new 3-way exchanges, one involving the unmatched $A-B-B$ type and the $B-O-A$ type, and another involving the unmatched $B-A-A$ type and the $A-O-B$ type.

Case 5. "An $A-B-B$ type and two $B-B-A$ types are part of a 3-way exchange under μ": Then undo that 3-way exchange and create two new 3-way exchanges, one involving the unmatched $A-B-B$ type and the $B-O-A$ type, and another involving one of the two unmatched $B-B-A$ types and the $A-O-B$ type.

In each of the five cases considered above, the newly constructed matching μ' satisfies (i)–(iii) in Lemma 7. *Q.E.D.*

PROOF OF THEOREM 2: Define the numbers K_A and K_B by

$$K_A := n(A-O-B) - n(B-B-A) - n(B-A-A),$$
$$K_B := n(B-O-A) - n(A-A-B) - n(A-B-B).$$

We will consider two cases depending on the signs of K_A and K_B.

Case 1. "$\max\{K_A, K_B\} \geq 0$":

Suppose, without loss of generality, that $K_A \leq K_B$. Then, $K_B = \max\{K_A, K_B\} \geq 0$. This implies, by the definition of K_B, that $n(B-O-A) \geq n(A-A-B) + n(A-B-B)$. Therefore, all $A-A-B$ and $A-B-B$ types participate in 3-way exchanges with $B-O-A$ types in Step 2 of the algorithm.

The number of $A-O-B$ types that are not matched in Step 2 is given by

$$\begin{aligned} & n(A-O-B) - \min\{n(B-B-A) + n(B-A-A), n(A-O-B)\} \\ &= \max\{n(A-O-B) - n(B-B-A) - n(B-A-A), 0\} \\ &= \max\{K_A, 0\} \\ &\leq K_B = n(B-O-A) - n(A-A-B) - n(A-B-B). \end{aligned}$$

As a result, the number of $A-O-B$ types that are not matched in Step 2 is less than or equal to the number of $B-O-A$ types that are not matched in Step 2. Therefore, all $A-O-B$ types participate in 3-way exchanges in Steps 2 and 3 of the algorithm.

We have shown that the algorithm creates at least $3 \times [n(A-A-B) + n(A-B-B) + n(A-O-B)]$ transplants. Since each exchange consists of at most three participants and must involve an A blood-type patient, this is also an upper bound on the number of transplants through 2- and 3-way exchanges. Therefore, the outcome of the algorithm must be optimal.

Case 2. "$\max\{K_A, K_B\} < 0$":

By Lemma 6, there exists an optimal matching μ_0 that is in simplified form. Since $K_B < 0$, we have $n(A-A-B) + n(A-B-B) > n(B-O-A)$. Therefore, we can

iteratively apply Lemma 7 to μ_0 to obtain an optimal matching μ_1 in simplified form that does not include a 3-way exchange involving an $A-O-B$ and a $B-O-A$ type.

Let Δ_A denote the number of unmatched $A-O-B$ types in μ_1. Since $K_A<0$, that is, $n(B-B-A)+n(B-A-A)>n(A-O-B)$, there are more than Δ_A many participants with $B-B-A$ or $B-A-A$ types who do not take part in an exchange with $A-O-B$ types in μ_1. Choose an arbitrary Δ_A many of these $B-B-A$ or $B-A-A$ participants, undo the exchanges they participate in under μ_1, and create Δ_A new 3-way exchanges involving these participants and the unmatched $A-O-B$ types.

Similarly, let Δ_B denote the number of unmatched $B-O-A$ types in μ_1. Since $K_B<0$, i.e., $n(A-A-B)+n(A-B-B)>n(B-O-A)$, there are more than Δ_B many participants with $A-A-B$ or $A-B-B$ types who do not take part in an exchange with $B-O-A$ types in μ_1. Choose an arbitrary Δ_B many of these $A-A-B$ or $A-B-B$ participants, undo the exchanges they participate in under μ_1, and create Δ_B new 3-way exchanges involving these participants and the unmatched $B-O-A$ types.

The new matching μ_2 obtained from μ_1 in the above manner is in simplified form. Furthermore, μ_2 induces at least as many transplants as μ_1; therefore, it is also optimal. Note also that under μ_2, all $A-O-B$ types take part in a 3-way exchange with $B-B-A$ or $B-A-A$ types, and all $B-O-A$ types take part in a 3-way exchange with $A-A-B$ or $A-B-B$ types.

Let μ denote an outcome of the sequential matching algorithm described in the text. Since $K_A, K_B<0$, the constraint $(*)$ in Step 1 becomes equivalent to:

1. Leave at least a total $n(B-O-A)$ of $A-A-B$ and $A-B-B$ types unmatched.
2. Leave at least a total $n(A-O-B)$ of $B-B-A$ and $B-A-A$ types unmatched.

Therefore, in Step 2 of the algorithm, all $A-O-B$ types take part in a 3-way exchange with $B-B-A$ or $B-A-A$ types, and all $B-O-A$ types take part in a 3-way exchange with $A-A-B$ or $A-B-B$ types. This implies that the total number of transplants from exchanges involving $A-O-B$ or $B-O-A$ types is the same $(=3\times[n(A-O-B)+n(B-O-A)])$ for both matchings μ_2 and μ.

The restriction of the matching μ_2 to the 2- and 3-way exchanges represented as edges among $A-A-B$, $A-B-B$, $B-B-A$, and $B-A-A$ types in Figure 7 respects the constraint $(*)$. Therefore, the total number of transplants in μ_2 from exchanges not involving $A-O-B$ nor $B-O-A$ types cannot exceed the total number of transplants in Step 1 of the algorithm leading to μ. As a result, the total number of transplants under μ is at least as large as the total number of transplants under μ_2, implying that μ is also optimal. *Q.E.D.*

PROOF OF LEMMA 5: Suppose there are no exchange-size constraints and there exists an optimal matching μ that matches an $O-X-Y$ type triple i where $X, Y\in\{A,B\}$ in $\mathcal{E}$. By the long-run assumption, there exist an $O-O-X$ triple j and an $O-O-Y$ triple k that are unmatched in μ. We construct a new matching ν using μ by removing triple i and inserting triples j and k as follows (see Figure 10):

(i) the patient who originally receives from the X donor of i in μ now receives from the X donor of j in ν,

(ii) the patient who originally receives from the Y donor of i in μ now receives from the Y donor of k in ν,

(iii) the two O donors who originally donate to the patient of i in μ now donate to the patients of j and k in ν, respectively,

(iv) the O donors of j and k now donate to their own patients in ν, and

(v) the other donations in μ remain intact in ν.

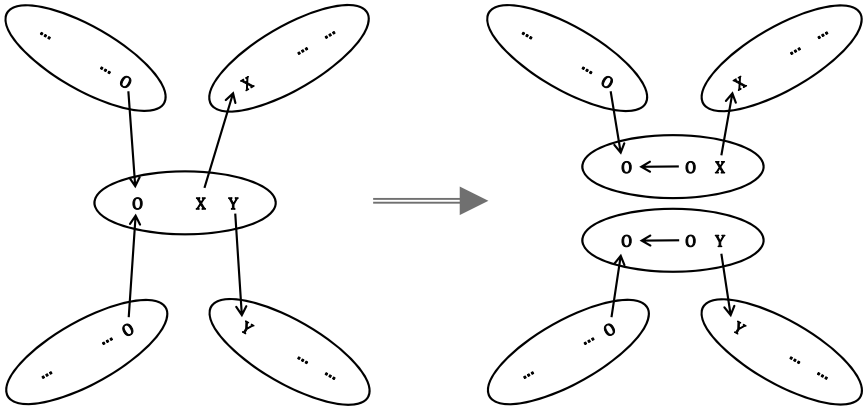


FIGURE 10.—The $O-X-Y$ triple in μ in the left is replaced with an $O-O-X$ triple and an $O-O-Y$ triple in ν in the right, which were originally unmatched in μ. Since triples with AB patients are absent in the exchange pool, the patients that X and Y donors donate in μ should also be of blood types X and Y, respectively. Moreover, although it is depicted in the figure as if these donors donate to two different patients in μ, when $X=Y$ it could also be the case that they donate to the same patient.

The new matching ν is feasible and matches one more triple than μ, which in turn contradicts the optimality of μ. *Q.E.D.*

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Co-editor Dirk Bergemann handled this manuscript.

Manuscript received 24 November, 2015; final version accepted 22 April, 2017; available online 12 May, 2017.