# How (not) to Integrate Blood Subtyping Technology to Kidney Exchange*

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**Abstract**

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# 1 Introduction

Following a series of collaborations between members of the transplantation community and researchers in market design, kidney exchange became an important source of transplant kidneys over the last decade.[1] By 2010, transplants from kidney exchanges in the US exceeded 550 (Massie, Gentry, Montgomery, Bingaman, and Segev, 2013) which accounts for about 10 percent of all living donor kidney transplantations, and to more than 3 percent of all kidney transplantations. Given the persistent shortage of kidneys for transplantation throughout the world, analysis of policies and procedures that could increase the contribution of kidney exchange to the number of kidney transplants became an active area of research not only in the transplantation community, but also among the researchers in market design. In this paper we analyze the potential spillovers of a recent policy change in allocation of deceased donor kidneys on the number of transplants from living donors including those from kidney exchanges. We will show that, if care is not taken, extension of this policy to kidney exchange can result in a reduction of the number of transplants from living donors (due to a reduction of transplants via exchanges) even though a number of its variants have great potential to increase this number. In order to explain the policy change and its potential effect on the number of transplants from living donors, we shall give some basic background on transplant immunology.

The most widely used blood type classification is known as the ABO grouping. Under this classification, there are two antigens (antigens A, B) and two antibodies (antibodies anti-A, anti-B) that are responsible for the ABO blood types. The specific combination of these four components determines an individual's blood type. For example, people with type A blood have only the A antigen on the surface of their red cells, and as a result, anti-A antibodies are not produced by them (for otherwise they would cause the destruction of their own blood.) Thus, only antibody anti-B is produced by blood type A people. Similarly blood type B people have antigen B along with antibody anti-A, whereas blood type O people have neither antigen while having both antibodies, and blood type AB people have both antigens while having neither antibodies. Blood type compatibility is a major factor for the successful transplantation of kidneys, and this immunologic asymmetry between different blood types along with the relative scarcity of type B kidneys for transplantation have historically resulted in an unfavorable situation for blood type O and B patients. The impact of this unbalance has not been uniform across different ethnicities, and it has especially disadvantaged African American patient population which has nearly 70 percent presence in blood types O and B.

The above mentioned ABO blood type induced imbalance is well-known and well-analyzed. What is less known is, antigen A has two major subtypes A1 and A2, and different immunologic

[1] Citations here.

properties of these subtypes have started to play an important role in allocation of deceased donor kidneys in the US since 2014. When donated to type B or O patients, subtype A2 kidneys result in significantly weaker antibody response than subtype A1 kidneys.[2] The resulting distribution of antibody response in patient population is such that, A2 kidneys can be safely transplanted to more than 80 percent of type B patients and to approximately 30 percent of type O patients. This medical possibility is the basis of a recent policy change in the US to provide greater kidney access to blood type B patients: In 2014, UNOS approved a new national deceased donor kidney allocation system that preferentially allocates A2 kidneys to B patients. While both O and B patients can potentially receive subtype A2 kidneys, the preferential allocation is limited to only blood type B patients. This has two major reasons.

1. *Equity in Access:* One of the primary goals of the OPTN is to increase and ensure the equity of organ sharing in the national system of organ allocation.[3] As we mentioned above, blood type B/O patients have significantly less access to transplant kidneys than blood type A/AB patients. And while both disadvantaged blood types are overrepresented among minorities, a blood type B patient is more likely to be a minority than a blood type O patient. Hence the preferential allocation of subtype A2 deceased donor kidneys to blood type B patients is the best possible utilization of deceased donor A2 kidneys for the minority population as a whole, and especially the African American patient population which historically had the lowest access for transplant kidneys.

2. *Practicality:* For a patient to be eligible for a subtype A2 kidney, his IgG antibody titer value should be consistently below a certain threshold over a period.[4] Based on this medical criteria, more than 80 percent of type B patients are eligible to receive subtype A2 kidneys. In contrast, only 30-40 percent of type O patients are eligible for subtype A2 kidneys. Hence directing A2 kidneys to B patients requires regular IgG antibody testing for only blood type B patients, who are more likely to be eligible for these kidneys.

Transplants from deceased donors is not the only source of transplant kidneys. Transplants from living donors, directly or via kidney exchanges, are the two other sources. One implication of the preferential allocation of subtype A2 deceased donor kidneys to blood type B patients

[2]In the US approximately 40% of the population is of blood type A. Of this 40%, about 80% is of subtype A1 and 20% is of subtype A2. There are also rare subtypes that are immunologically similar to subtype A2. These rare subtypes, combined, account to less than 1% of the blood type A population.

[3]The federal Final Rule, adopted in March 2000, provides a regulatory framework for the structure and operation of the OPTN: The primary goal of the OPTN is to increase and ensure the effectiveness, efficiency, and equity of organ sharing in the national system of organ allocation, and to increase the supply of donated organs available for transplantation.

[4]The threshold is 1:8 in the US.

is, these patients are now routinely tested for their level of IgG antibodies. On the other hand, establishing an IgG antibody test history for blood type O patients may easily be deemed to be unnecessary, especially if they do not have a blood type A donor who may be of subtype A2. This encourages preferential allocation of subtype A2 kidneys to type B patients not only for deceased donor kidneys, but also for kidney exchange. That is because, unlike type B patients, type O patients will often lack an established IgG antibody testing history necessary to receive a subtype A2 kidney. Critically, this has an important efficiency implication for kidney exchange, unlike for deceased donor allocation where preferential allocation of subtype A2 kidneys to B patients is mostly a distributional matter. In this paper we show that extending the preferential allocation of A2 kidneys to blood type B patients in kidney exchange not only potentially reduces the total number of living donor kidney transplants, BURASI YUMUSATILACAK **but also potentially reduces the number of living donor transplants across all ethnicities including the most disadvantaged groups such as the African American patient population**. In contrast, making subtype A2 kidneys available to patients of both blood types B and O will unambigously benefit patients of all ethnicities. This will require blood type O patients with incompatible living donors to have a history of testing for IgG antibodies, similar to type B patients who have these tests to benefit from the preferential allocation of subtype A2 kidneys under the national deceased donor kidney allocation system.

The organization of the rest of the paper is as follows: In Section 3 we build on the theoretical model of Roth, Sönmez, and Ünver (2007) to theoretically analyze the impact of availability and timing of various blood subtyping technologies on the number of living donor kidney transplants. Our theoretical results in Section 3 are based on a number assumptions on the distribution of patient-donor blood types motivated by some of the features of living donor kidney transplantation. In Section 4, we drop these assumptions and show via computational simulations that all our theoretical results are verified using kidney donation data from the US. In Section 5 we conclude. The Appendix is devoted to proofs (Appendix A), the extended analysis allowing for 3-way kidney exchange in addition to 2-way exchange (Appendix B), and additional results related to simulations (Appendix C).

## 2 A Model of Kidney Exchange

A pair of type X-Y denotes a pair of X-blood type patient and Y-blood type donor. If there is no medical incompatibility for a patient-donor pair, the donor donates to the patient via direct donation; otherwise, the pair participates the exchange pool for kidney paired donation. Thus, the set of incompatible pairs constitute the exchange pool. Whether a pair is incompatible (thus, participates the exchange pool) is determined with respect to certain medical criteria

and also the policies and protocols adopted by the transplant centers and exchange programs.

The standard medical criteria for transplantation is the **ABO blood type compatibility**, or simply **ABO compatibility**. According to this criteria, there are four blood types A, B, AB, and O, (representing the presence of proteins A or B, or both, or neither, respectively) and a patient may not receive the kidney of a donor whose blood contains one of the A, B proteins that the patient does not have. Under ABO compatibility, a patient with blood-type O (simply, an O patient) has the most difficulty finding a compatible donor, while O donors never have a blood-type incompatibility with any patient. Similarly, it is difficult (relative to other types) to match an AB donor with a patient, while AB patients do not have blood type incompatibility with any donor. Thus, in a large population, there is a higher demand for O kidneys than AB kidneys; also, an O-AB pair demands a kidney in high demand and offers a kidney in low demand and is at a disadvantage. A pair is **underdemanded** (or, on the *long side of the exchange*) if at least one pair of the same type remains unmatched in each feasible set of exchanges. For example, an O-AB pair is *underdemanded* in a large population. Similarly, since there is a higher demand for O kidneys than A kidneys (or B kidneys), an O-A pair (O-B pair) is also *underdemanded*.

The national kidney allocation program has been recently revised to incorporate new features of extended access for certain blood type candidates so that these candidates can accept kidneys from A and AB donors whose blood types satisfy certain subtype characteristics. Based on the success rates of the transplantations from these blood-subtype donors, it has been discussed to extend the ABO compatibility by adding these new compatibilities. One such extended access policy is to allow transplantation from the donors with A2 (technically, "non-A1") subtype of type A (simply, A2 donors) to O patients. We refer to this policy as **A2-to-O compatibility**. Another policy of extended access is such that A2 donors and A2B (technically, "non-A1B") donors can donate to B patients. We refer to this compatibility structure as **A2-to-B compatibility**. Another policy is the combined compatibility to allow transplantation from A2 donors to O and B patients, and from A2B donors to B patients. We refer to this compatibility structure as the **full compatibility**.

We analyze the impact of blood subtyping technologies on the **maximum number of living donor kidney transplants**. The theoretical part of this analysis is based on a number assumptions on the distribution of patient-donor pairs (Section 3). Then, we drop these assumptions and show via computational simulations that our theoretical results are verified (Section 4).

The number of A-O pairs in the exchange pool is determined by the probability of a patient having a positive crossmatch probability with a donor. From the national patient characteristics, the ratio of tissue-type incompatible A-O pairs is less than 20% of all A-O pairs (see

PRA distribution in Table 1 in Roth, Sönmez, and Ünver (2007)). Also, eighty percent of blood type A are subtype A1. Thus, under A2-to-O compatibility, the number of O-A1 pairs is considerably greater than the number of tissue-type incompatible A-O pairs in the exchange pool. An A2 donor can donate to an O patient. Thus, an O-A2 pair can be matched with a pair of the same type or an O-O pair. This implies that tissue-type incompatible O-A2 pairs in the exchange pool are not *underdemanded*.

A similar argument holds for A2-to-B compatibility as well and B-A1B pairs are on the long side of the exchange. Moreover, since an A2B donor can donate to a B patient, a B-A2B pair can be matched with another pair of the same type or a B-B pair. This implies that tissue-type incompatible B-A2B pairs are not *underdemanded*.

We analyze efficiency implication of various compatibility policies in large population. The next large population (**LP**) assumption reflects the set of *underdemanded* pairs based on the corresponding compatibility protocol.

**Assumption 1** *(Large population (**LP**))*
*(i) Under ABO compatibility, pairs of types O-A, O-B, O-AB, A-AB and B-AB are on the long side of the exchange.*
*(ii) Under A2-to-B compatibility, pairs of types O-A, O-B, O-AB, A-AB and B-A1B are on the long side of the exchange.*
*(iii) Under A2-to-O compatibility, pairs of types O-A1, O-B, O-AB, A-AB and B-AB are on the long side of the exchange.*
*(iv) Under full compatibility, pairs of types O-A1, O-B, O-AB, A-AB and B-A1B are on the long side of the exchange.*

The number of transplants under any compatibility policy depends also on the balance between A-B pairs and B-A pairs. In the US, the frequency of A-B pairs is higher than the one of B-A pairs (Teresaki, Gjertson, and Cecka, 1998). Moreover, the frequency of AB type is substantially low. The following on type frequencies (**TF**) takes population characteristics of type distributions into account.

**Assumption 2** *(Type Frequencies (**TF**))*
*(i) The number of A-B pairs is greater than the number of B-A pairs.*
*(ii) The frequency of AB donor type is substantially low (around 3 percent).*

We analytically derive the effects of compatibility policy change on the maximum number of transplants by ignoring the tissue-type incompatibilities. Moreover, while a pair with a blood subtype donor might not qualify for a live donation under a blood subtype compatibility policy because the patient has a titer value higher than 1:8, we ignore this type of incompatibility

in the exchange pool. Theoretically, this is a strong assumption. But, in a large population, there are selection opportunities and as the population gets larger, this assumption becomes less consequential. For example, under A2-to-O compatibility, both O-A2 pairs and O-O pairs can be matched with O-O pairs. Thus, in a large population, O-O pairs with the patient having lower titer value can be selected to be matched with O-A2 pairs, while others are matched with other O-O pairs. The simulations on the US population characteristics show that this selection effect almost fully compensates the following upper-bound (**UB**) assumption.

**Assumption 3** *(Upper-bound (**UB**))*
*(i) No patient is tissue-type incompatible with another patient's donor.*
*(ii) Each patient in the exchange pool has an IgG antibody titer value less than 1:8.*

Let $(X-Y)$ be the set of pairs of type X-Y. Let #T denote the cardinality of the set T. Let $(X-Y)_c$ be the set of tissue-type compatible X-Y pairs and $(X-Y)_i$ be the set of tissue-type incompatible X-Y pairs. For any nonnegative number $k$, let $\lfloor k \rfloor$ denote the integer part of $k$, i.e. the greatest integer no larger than $k$. For a set $T$, let $\mathbf{odd}_T$ be equal to one if the cardinality of $T$ is odd, and zero if it is even.

# 3 Integrating blood subtyping technology to kidney exchange

The OPTN Board of Directors approved a variance to enable the transplantation of blood type A2 and A2B deceased donor kidneys into blood type B candidates. Since 2014, this variance has been implemented in the deceased donation context. Based on the success rates of kidney donation from A2 and A2B donors to B patients, the UNOS has decided to integrate blood subtyping technology also to kidney exchange via a Kidney Paired Donation Pilot Program.

A medical criterion for donation based on blood subtype is that to be eligible to receive an A2 or A2B kidney, the candidate would need to have two consecutive quarterly anti-A titers performed demonstrating low isoagglutinin titers (anti-A IgG titer less than 1:8); any candidate with a titer value of 1:8 or higher will be excluded. Since only A2-to-B compatibility has been implemented under deceased donation, this data is available mostly for B patients. Thus, there is a selection of B type patients (rather than O type patients) eligible for transplants based on blood subtype compatibility. Thus, as a first step, we focus on the effects of blood subtyping technology under A2-to-B compatibility.

The current proposal of the UNOS Kidney Paired Donation Pilot Program does not specifically require participating transplant programs/hospitals to provide the OPTN with the ABO subtype information. Thus, if a patient-donor pair turns out to be blood-type (or blood-subtype

compatible) and tissue-type compatible, transplant occurs via direct donation and this pair does not enter the exchange pool.

Our first insight suggests that the preferential matching of A2 or A2B kidney donors with B patients has an adverse effect on efficiency in the exchange context. While the expectation is that integrating the subtyping technology into kidney exchange will lead to efficiency improvements, the realized effect is the opposite: we argue that this policy shift potentially reduces the total number of living donor kidney transplants.

**Proposition 1** *Assume LP(i), LP(ii), TF, UB. Consider the two-way exchange policy. If the compatibility protocol changes from ABO compatibility to A2-to-B compatibility, then*
*(i) the number of transplants via direct donation* ***increases*** *by* $\#(B-A2)_c + \#(B-A2B)_c$,
*(ii) the number of transplants via exchange* ***decreases*** *by*

$$2\#(B-A2)_c - \#(AB-A2B) - \#(B-A2B)_i - \Lambda,$$

*(iii) the total number of transplants* ***decreases*** *by*

$$\#(B-A2)_c - \#(AB-A2B) - \#(B-A2B) - \Lambda,$$

*where* $\Lambda = (\boldsymbol{odd}_{(AB-AB)} - \boldsymbol{odd}_{(AB-A1B)}) + (\boldsymbol{odd}_{(B-B)} - \boldsymbol{odd}_{(B-A2B)_i \cup (B-B)})$.

The intuition for this result is quite simple: if subtyping tests suggests that an B-A pair is blood-subtype compatible (and tissue-type compatible), then the transplant occurs via direct donation at the transplant hospital. This is possible due to subtype technology and it increases the number transplants via direct donation. But, this direct donation prevents a paired kidney donation including this B-A pair and an A-B pair in the exchange pool. Thus, while the number of transplants via direct donation increases, the number of transplants via paired kidney exchange decreases twice as much and overall, the number of transplants decreases.

This argument is only for compatible B-A pairs (that is, for tissue-type compatible B-A2 pairs) and does not carry over the O-A pairs. The effect of A2-to-O compatibility is quite different. A blood-subtype compatible (and tissue-type compatible) O-A2 pair would be on the long-side of the exchange, if entered the exchange pool rather than a direct donation. Thus, such a pair would be *underdemanded* in the exchange pool and does not prevent a paired kidney donation by not participating the exchange. Moreover, each incompatible O-A2 pair (either due to the high IgG antibody titer value of the patient or tissue-type incompatibility) enters the exchange pool and since this pair can be matched with an O-O pair via paired kidney donation, this increases the matches with O-O patients and hence the overall number of transplants via paired kidney donation.

**Proposition 2** *Assume LP(i), LP(iii), UB. Consider the two-way exchange policy. If the compatibility protocol changes from ABO compatibility to A2-to-O compatibility, then*
*(i) the number of transplants via direct donation* ***increases*** *by* $\#(O-A2)_c$,
*(ii) the number of transplants via exchange* ***increases*** *by* $\#(O-A2)_i + \#(A-A2) + \Theta$,
*(iii) the total number of transplants* ***increases*** *by* $\#(O-A2) + \#(A-A2) + \Theta$,
*where* $\Theta = (\boldsymbol{odd}_{(O-O)} - \boldsymbol{odd}_{(O-O)\cup(O-A2)_i}) + (\boldsymbol{odd}_{(A-A)} - \boldsymbol{odd}_{(A-A1)})$

These two results have a very important implication regarding the efficiency of integrating subtyping technology to exchange: under the current protocol of subtype testing by hospitals, A2-to-B compatibility leads to a decrease in the number of transplants (than ABO compatibility), while A2-to-O compatibility leads to an increase. This points to a crucial difference between deceased donation and exchange. While A2 donors are made available only for B patients in deceased donation and this preferential allocation achieves the desired distributional outcome, the same policy has adverse effect on efficiency in the exchange context. On the other hand, encouraging A2-to-O compatibility by testing O patients regularly for their anti-A IgG titer values increases the number of transplants and leads to unambiguous efficiency gains.

The effects of A2-to-O compatibility and A2-to-B compatibility on live donation are mutually exclusive. Similarly, the sets of pairs affected in exchange by A2-to-O compatibility and by A2-to-B compatibility are mutually exclusive. Thus, the combined effect of A2-to-B compatibility and A2-to-O compatibility on the number of transplants is just the direct sum of these effects of these compatibilities and the following corollary is obtained.

**Corollary 1** *Assume LP(i), LP(iv), TF, UB. Consider the two-way exchange policy. If the compatibility protocol changes from ABO compatibility to full compatibility, then*
*(i) the number of transplants via direct donation* ***increases*** *by*

$$\#(O-A2)_c + \#(B-A2)_c + \#(B-A2B)_c,$$

*(ii) the number of transplants via exchange* ***changes*** *by*

$$\#(O-A2)_i + \#(A-A2) - 2\#(B-A2)_c + \#(AB-A2B) + \#(B-A2B)_i + \Theta + \Lambda,$$

*(iii) the total number of transplants* ***changes*** *by*

$$\#(O-A2) + \#(A-A2) - \#(B-A2)_c + \#(AB-A2B) + \#(B-A2B) + \Theta + \Lambda,$$

*where* $\Theta = (\boldsymbol{odd}_{(O-O)} - \boldsymbol{odd}_{(O-O)\cup(O-A2)_i}) + (\boldsymbol{odd}_{(A-A)} - \boldsymbol{odd}_{(A-A1)})$ *and* $\Lambda = (\boldsymbol{odd}_{(AB-AB)} - \boldsymbol{odd}_{(AB-A1B)}) + (\boldsymbol{odd}_{(B-B)} - \boldsymbol{odd}_{(B-A2B)_i\cup(B-B)})$.

The number of transplants under full compatibility could increase or decrease depending on which compatibility has a stronger effect. Even if the amount of increase in the number transplants due to A2-to-O compatibility exceeds the amount of decrease due to A2-to-B compatibility (this implies that the number of transplants increases overall compared to ABO compatibility), the adverse effect of blood subtype compatible B-A pairs cannot be removed by switching to full compatibility. Thus, exchange programs cannot fully utilize blood subtyping technology even under full compatibility. We argue that via a different protocol of blood subtype tests, there is a way such that integrating blood subtyping technology will unambiguously benefit all patients.

## 3.1 Subtype test timing: after participating to exchange

In 2008, a kidney donated from a living donor, whose ABO subtyping completed prior to the donation was reported as A2, was transplanted into a blood type O recipient resulting in immediate graft rejection and organ failure. Repeat subtype testing of the donor indicated the actual subtype to be A1 (see the OPTN document at http://optn.transplant.hrsa.gov/PublicComment/pubcommentPropSub_281.pdf). Actually, the error rates associated with subtyping exceed those for ABO determination. The probability of the true subtype being A1 (or A1B) given a single subtype test indicates A2 (A2B) was estimated to be about 3.5 percent (Bryan, Polesky, Eisenbrey, Sesok-Pizzini, Luger, Smith, and Susskind, 2006). If a confirmatory test also indicates A2 (A2B) the estimated error rate drops dramatically, to approximately 0.032 percent.

Based on this high error rate and importance of the repeat testing, the current OPTN policy requires that the hospital subtyping a living donor whose initial subtype test indicates the donor to be non-A1 (negative for A1) or non-A1B (negative for A1B), must ensure that a confirmatory test is performed prior to living donation to assess the accuracy of the result. "... Blood samples for subtype testing must be taken on two separate occasions, defined as two samples taken at different times. Samples tested must not be taken after a blood transfusion. When the initial and second determination subtypes are the same result, the result can be used to determine transplant compatibility with the intended recipient or any other potential recipient. If the initial and second determination subtyping results are not the same, the donor must be allocated based on the primary blood type, A or AB" (the OPTN Policies brochure, available at http://optn.transplant.hrsa.gov/ContentDocuments/OPTN_Policies.pdf#nameddest=Policy_08).

The difference between ABO blood type testing and blood subtype testing has important policy implications. How to control and monitor the blood subtype testing has been widely discussed and several alternatives have been proposed. The Membership and Professional

Standards Committee (MPSC) in OPTN requested that the Operations and Safety Committee (OSC) examine current OPTN policies to evaluate whether the current blood subtype testing restrictions are adequate to ensure that subtypes of both deceased and living donors are accurately determined and verified (see the OPTN document at http://optn.transplant.hrsa.gov/PublicComment/pubcommentPropSub_281.pdf). We argue that if the OPTN requires the timing of subtype testing (and the associated confirmatory testing) to be after the pairs participate the exchange pool, blood subtyping technology can be fully utilized to unambiguously benefit all patients. Our proposal is as follows: All the medical tests except blood subtype tests are done by hospitals before the pair is registered at the OPTN. If a patient-donor pair turns out to be blood-type and tissue-type compatible, transplant occurs via direct donation. Otherwise, the pair participates the exchange pool and the blood subtype tests are monitored by the OPTN/UNOS KPD Program. Our next result shows that this change in the timing of subtype tests benefits all patients and the number of transplants increases under A2-to-B compatibility, which, under the current subtype test timing, leads to efficiency losses (see Proposition 1).

**Proposition 3** *Assume LP(i), LP(ii), TF, UB. Consider the two-way exchange policy. If the compatibility protocol changes from ABO compatibility to A2-to-B compatibility, then*
*(i) the number of transplants via direct donation* ***increases*** *by*

$$\max\{0, \#(B-A2B)_c - \boldsymbol{odd}_{(B-A2B)_i \cup (B-B)}\},$$

*(ii) the number of transplants via exchange* ***increases*** *by*

$$\#(AB-A2B) + \#(B-A2B)_i + \min\{\#(B-A2B)_c, \boldsymbol{odd}_{(B-A2B)_i \cup (B-B)}\} + \Lambda',$$

*(iii) the total number of transplants* ***increases*** *by*

$$\#(B-A2B) + \#(AB-A2B) + \Lambda',$$

*where*

$$\begin{aligned}\Lambda' =& (\boldsymbol{odd}_{(AB-AB)} - \boldsymbol{odd}_{(AB-A1B)}) + \\ & (\boldsymbol{odd}_{(B-B)} - (1 - \min\{1, \#(B-A2B)_c\})\boldsymbol{odd}_{(B-A2B)_i \cup (B-B)}).\end{aligned}$$

The change in the timing of subtype tests has an important efficiency implication: a blood subtype compatible B-A pair can now be matched with an A-B pair so that two patients receive a transplant instead of only the patient in the B-A pair. Thus, the efficiency loss due to B-A pairs not participating exchange under A2-to-B compatibility can be prevented. Moreover, the efficiency gains due to pairs with A2 or A2B donors are maintained. Thus, the full potential of blood subtyping technology is achieved under this alternative protocol of subtype test timing.

We argued that blood subtyping technology leads to efficiency improvements under A2-to-O compatibility (see Proposition 2). The next result shows that the effect of changing the timing of subtype tests is marginal in the case of A2-to-O compatibility.

**Proposition 4** *Assume LP(i), LP(iii), UB. Consider the two-way exchange policy. If the compatibility protocol changes from ABO compatibility to A2-to-O compatibility, then*
*(i) the number of transplants via direct donation* ***increases*** *by*

$$\max\{0, \#(O-A2)_c - \boldsymbol{odd}_{(O-O)\cup(O-A2)_i}\},$$

*(ii) the number of transplants via exchange* ***increases*** *by*

$$\#(A-A2) + \#(O-A2)_i + \min\{\#(O-A2)_c, \boldsymbol{odd}_{(O-A2)_i\cup(O-O)}\} + \Theta',$$

*(iii) the total number of transplants* ***increases*** *by* $\#(O-A2) + \#(A-A2) + \Theta'$,
*where*

$$\begin{aligned}\Theta' =&(\boldsymbol{odd}_{(A-A)} - \boldsymbol{odd}_{(A-A1)})+\\ &(\boldsymbol{odd}_{(O-O)} - (1-\min\{1, \#(O-A2)_c\})\boldsymbol{odd}_{(O-O)\cup(O-A2)_i}).\end{aligned}$$

The effect of extended access is similar to the case, where the blood subtyping tests are at the discretion of the hospitals and done before the pairs participate the exchange pool: The effects of A2-to-O compatibility and A2-to-B compatibility on live donation are mutually exclusive. Similarly, the sets of pairs affected in exchange by A2-to-O compatibility and by A2-to-B compatibility are mutually exclusive. Thus, the combined effect of A2-to-B compatibility and A2-to-O compatibility on the number of transplants is just the direct sum of these effects of these compatibilities and the following corollary is obtained. But, there is substantial difference: The extended access yields full utilization of blood subtyping technology under the new timing of blood subtyping tests.

**Corollary 2** *Assume LP(i), LP(iv), TF, UB. Consider the two-way exchange policy. If the compatibility protocol changes from ABO compatibility to full compatibility, then*
*(i) the number of transplants via direct donation* ***increases*** *by*

$$\begin{aligned}&\max\{0, \#(B-A2B)_c - \boldsymbol{odd}_{(B-A2B)_i\cup(B-B)}\}+\\ &\max\{0, \#(O-A2)_c - \boldsymbol{odd}_{(O-O)\cup(O-A2)_i}\},\end{aligned}$$

*(ii) the number of transplants via exchange* ***increases*** *by*

$$\begin{aligned}&\#(AB-A2B) + \#(B-A2B)_i + \min\{\#(B-A2B)_c, \boldsymbol{odd}_{(B-A2B)_i\cup(B-B)}\} + \Lambda'+\\ &\#(O-A2)_i + \#(A-A2) + \min\{\#(O-A2)_c, \boldsymbol{odd}_{(O-O)\cup(O-A2)_i}\} + \Theta',\end{aligned}$$

*(iii) the total number of transplants* ***increases*** *by*

$$\#(O-A2)+\#(A-A2)+\#(AB-A2B)+\#(B-A2B)+\Theta'+\Lambda',$$

*where*

$$\begin{aligned}\Lambda' =&(\boldsymbol{odd}_{(AB-AB)}-\boldsymbol{odd}_{(AB-A1B)})+\\ &(\boldsymbol{odd}_{(B-B)}-(1-\min\{1,\#(B-A2B)_c\})\boldsymbol{odd}_{(B-A2B)_i\cup(B-B)}),\end{aligned}$$

*and*

$$\begin{aligned}\Theta' =&(\boldsymbol{odd}_{(A-A)}-\boldsymbol{odd}_{(A-A1)})+\\ &(\boldsymbol{odd}_{(O-O)}-(1-\min\{1,\#(O-A2)_c\})\boldsymbol{odd}_{(O-O)\cup(O-A2)_i}).\end{aligned}$$

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# 4 Simulations

In this section, we report the results of simulations using the US patient statistics obtained from the Organ Procurement and Transplantation Network (OPTN) database to demonstrate the magnitudes of potential welfare benefits and harms of subtype A2 matching with B or O patients in exchange under a number of different scenarios.

## 4.1 Simulation Setup

In each simulation, we randomly generate $n$ non-blood related patient-donor pairs as follows. Each patient is represented by a set of characteristics, namely, his ethnic background (i.e., his race), his blood type, his A2 subtype compatibility status (for O and B blood type patients), and his probability of having tissue type incompatibility with a random donor (known as his panel reactive antibody or simply PRA level). Each patient is assumed to come paired with a non-biologically related donor. The donor can be either his spouse or another donor. If she is his spouse, then we assume she has the same race with the patient. Otherwise, we randomly generate her race using the US adult population race statistics. Based on her race, we randomly and independently determine her other characteristics, such as her blood type, her A2 status (if she is A blood type). The probability distributions used are reported in Table 1.

In each simulation, after a patient-donor pair is generated, if the donor is compatible with the patient (without considering A2 compatibility), she immediately donates to her patient and the pair does not participate in exchange. Otherwise the pair becomes a potential entrant to exchange.[5]

We no longer make the large market assumption that we used in our theoretical study. Hence, each patient can have tissue-type incompatibility against not only his own donor but also

[5] We use the same blood type distribution for both the donors and patients of a given race.

| | US Races | | | | |
|---|---|---|---|---|---|
| | **White** | **Black** | **Asian** | **Amer. Indian** | **Pacific Island.** |
| **A. Patient →** (Freq. %) | 81.46 | 12.78 | 5.15 | 0.40 | 0.22 |
| **B. Other Donor →** (Freq. %) | 78.00 | 13.69 | 5.96 | 1.94 | 0.42 |
| **C. Blood Type ↓** | Frequency (%) | | | | |
| $O$ | 48.98 | 49.89 | 38.31 | 62.96 | 48.67 |
| $A$ | 37.18 | 25.28 | 25.06 | 28.78 | 36.00 |
| $B$ | 10.55 | 20.63 | 29.22 | 6.84 | 10.00 |
| $AB$ | 3.29 | 4.19 | 6.41 | 1.43 | 5.33 |
| **D. Donor Relation** | Frequency (%) | | | | |
| Spouse | 34.44 | 40.12 | 43.76 | 32.61 | 41.18 |
| **E. PRA Distribution ↓** | Frequency (%) | | | | |
| Low PRA | 70.19 | | | | |
| Medium PRA | 20.00 | | | | |
| High PRA | 9.81 | | | | |
| **F. A2 Subtype Comp.** | Frequency (%) | | | | |
| F.1. For $O$ Patients | 30 | | | | |
| F.2. For $B$ Patients | 80 | | | | |

Table 1: **Patient and living donor distributions used in simulations:** Distribution A is the frequency of patient races that received live donation, Distribution C is the blood type frequencies among races of new candidates to the kidney deceased donor waiting list, and Distribution D is obtained from non-biological donations except kidney exchanges; all three from OPTN data for the year 2014 `http://www.optn.org` retrieved on 07/10/2015. Distribution B is 18-60 year-old adult population race distribution in the US and based on 2010 US census retrieved from `http://www.census.gov/data.html` on 07/10/2015. OPTN/SRTR Annual Report in 2003, for the period 1993-2002, retrieved from `http://www.optn.org` on 11/22/2004 is used for distribution E. We used relatively less recent data report for this distribution, as it was the most detailed data statistic we could find. Distribution F.1 is taken from XXXX. The arrow direction (when used) shows the cell direction along the column or row entries adding up to frequency 100%. For the Bernoulli distributions of D, F.1, and F.2, the alternative event and its probability are omitted for brevity.

other donors. Depending of the PRA of the patient as low, medium, or high, which shows how likely a patient will develop tissue type incompatibility against a randomly selected donor from the US population, his (and any other blood-type compatible donor) is independently tested for tissue-type incompatibility. A PRA value below 10% is considered low (i.e., against less than 10% of the population, the patient will have tissue-type incompatibility); PRA values between 10-80% are considered as medium; and PRAs above 80% are considered as high according to the OPTN annual report. [6]

Frequencies of low, medium, and high PRA patients reported in the OPTN database are given in Table 1. A more detailed PRA distribution is unavailable in the medical literature. Thus, we assume that:

- each low PRA patient has a tissue-type incompatibility probability of 5% with a random donor,
- each medium PRA patient has a tissue-type incompatibility probability of 45% with a random donor, and
- each high PRA patient has a tissue-type incompatibility probability of 90% with a random donor.

After the pool of incompatible patient-donor pairs are determined, these pairs become eligible for exchange. We consider different dimensions of simulation scenarios, consistent with our theoretical analysis and the chronological development of A2 matching for deceased donation practices.

For A2 matching, we consider three different treatments:

i. Only A2/A2B to B transplantation is allowed.

ii. Only A2 to O transplantation is allowed.

iii. Both A2/A2B to B and A2 to O transplantation are allowed.

Using these treatments, we consider seven scenarios differentiated across three dimensions:

1. **Without A subtype matching**: This is the control scenario and identical to optimized exchange with incompatible pairs.

[6] These statistics refer to the PRAs of the existing patients in the deceased-donor waiting list. New entrant PRA distribution is not readily available from these reports.

2. **With A subtype matching**: These six scenarios are grouped across two dimensions: timing of A subtype testing and availability of subtype A2 to blood type O or B transplantation. In either scenario, antibody titer-level determination tests are conducted for all B and O patients as soon as they become sick, as it takes up to 6 months with frequent testing to determine suitability to receive non-A1 subtype organs (which we refer to as A2 in the rest of this section for notational convenience).

   (a) **Timing of the A subtype test**; **before the decision to participate in exchange**: When patients become sick, the subtype testing is done for all A and AB type paired donors. Depending on one of the three subtype matching protocols below, if the patient is A-subtype compatible and tissue-type compatible with his own donor, then the donor directly donates to his patient, and the pair does not participate in exchange. Otherwise, the pair becomes available for exchange. Compatibilities among all donors and patients are determined using tissue-type compatibility tests and blood-type compatibility tests including possible A2 or A2B donor matching. We consider the three A subtype matching scenarios discussed above during initial transplantation phase and exchange phase.

   (b) **Timing of the A subtype test is after the decision to participate in exchange:** The subtype testing is done for all A and AB type donors only during the exchange phase. (Hence possible newly determined donors with subtype A2 and tissue-type and A2-compatible patients cannot opt out of the exchange.) Compatibilities among all donors and patients are determined using tissue-type compatibility tests and blood-type compatibility tests including possible A2 or A2B donor matching. We consider the three A2 matching scenarios discussed above during the exchange phase.

We consider two different exchange technologies for these 7 simulation scenarios: Optimal two-way and optimal two&three-way exchange.[7,8]

[7]For two-way exchange simulations we use $n = 2000$ as the sample size. On the other hand, since determining a maximal two&three-way exchange is an NP-hard problem, we use a sample size of $n = 500$ instead of 2000.

[8]In our simulations, to find the maximal number of patients who can benefit from an exchange (for both two and two&three-way exchange) we use the CPLEX integer programming software. We refer the reader to the Appendix of Roth, Sönmez, and Ünver (2007) for the formulation of optimal exchange problem as an integer program. When compatible pairs are also included in exchange for scenarios 2(b)i-iii, the formulation stands. However, all feasible single-pair cycles are also included in two-way and two&three-way exchange integer program. Also see Sönmez and Ünver (2014) for the structure of optimal matchings when compatible pairs are included into two-way exchange.

## 4.2 Simulation Results

We report the results of two-way exchange simulations as averages and sample standard errors of $S = 500$ simulations in Table 2.[9]

If A2/A2B to B transplantation is used alone and the donor subtype tests are done uncoordinated with exchange, i.e., before the exchange participation decision, the average number of transplants achievable through two-way exchange (and direct donation if needed) decreases from Scenario 1 – the current exchange practice – to Scenario 2(a)i – the use of deceased donation A2 matching protocol for live donation uncoordinated with exchange – as predicted by Proposition 3. This decrease is statistically significant with a paired t-test for degrees of freedom 499 with t-statistic 4.3366 that leads to a p-value less than $10^{-5}$.

When how the effect of this possible myopic transition from the current exchange practices to the deceased donation is shared across patients of different ethnical backgrounds (see Table 3), we observe that for Whites, there is a decrease, which is statistically significant (with a paired t-test p-value less than $10^-5$). For Blacks, Asians, and Pacific Islanders, there is a slight decrease, for American Indians, there is a slight increase, none of which are statistically significant at 10% level.

The direction of other changes across all treatments are in accordance with theoretical results as seen in Table 2. In particular the average number of transplants significantly increases from Scenario 1 and 2(a)i to 2(a)ii and 2(a)iii (cf. Proposition 2), while there is a significant decrease from Scenario 2(a)ii to 2(a)iii (cf. Proposition 1). The same pattern is true for all races (see Table 3). This corresponds to 13.74% increase from only A2/A2B to B transplantation to only A2 to O transplantation (from Scenario 2(a)i to 2(a)ii). Moreover, when the A2 subtype transplantation is done uncoordinated with exchange before the exchange participation decision, even the full A2 matching brings a substantial decrease to the number of transplantation, with respect to A2 to O only transplantation a 2% decrease is observed in the number of transplants (from Scenario 2(a)ii to 2(a)iii).

When exchange programs are run coordinated with A2 transplantation, the corresponding number of transplants from (a) to (b) scenarios increases and the signs and statistical significance of differences across scenarios are as predicted by the theoretical results. What is striking is that the maximum average number of transplants under optimal two-way exchange and live donation (Scenario 2(b)iii), the maximum achievable is not too much different (although the increase is highly statistically significant) from the uncoordinated only A2 to O transplantation (Scenario 2(a)ii), the difference is only 0.7%. If A2/A2B to B transplantation could totally be eliminated for live donation and we could only conduct A2 to O live-donor transplants, even

[9] In Appendix C, we report the results of simulations for two&three-way technology in Tables 4, 5, and 7.

| Simulation Averages and Sample Standard Errors of $S = 500$ Simulations with $n = 2000$ Pairs | | | | | | |
|---|---|---|---|---|---|---|
| | Two-way Exchange | | | | | |
| | 1. Without $A$ Subtype Matching | 2. With $A$ Subtype Matching | | | | |
| | | | | $A2$ Transplant Protocol | | |
| Incomp. Pairs | | Subtype Test Timing | | i. $A2/A2B \to B$ only | ii. $A2 \to O$ only | iii. $A2/A2B \to B$ and $A2 \to O$ |
| 984.800 (23.2186) | **376.700 (22.3124 )** | **(a) Before** Exchange Participation Decision | **Total Transplants** | **374.616 (23.1654)** | **424.852 (25.9950)** | **416.260 (25.4372)** |
| | | | $B$'s receiving from own comp. $A2/A2B$ donors | 12.180 (3.391) | - | 12.180 (3.391 ) |
| | | | $O$'s receiving from own comp. $A2$ donors | - | 15.708 (3.833) | 15.708 (3.833) |
| | | **(b) After** Exchange Participation Decision | **Total Transplants** | **384.238 (23.1129)** | **425.374 (25.9735)** | **428.012 (26.1527)** |
| | | | $B$'s receiving from own comp. $A2/A2B$ donors | 1.022 (1.4034 ) | - | 0.682 (0.7836) |
| | | | $O$'s receiving from own comp. $A2$ donors | - | 3.558 (2.2254) | 3.882 (3.2902) |

Table 2: Simulations for maximal two-way exchange (the numbers in parentheses are sample standard errors, to find the standard errors of the averages, divide the sample standard errors by $\sqrt{S} = 22.36$).

if we cannot coordinate exchange programs with A2 matching, we would lose very little with respect to the optimal policy recommendation. This result also holds across all race groups. Two&three-way simulations are very similar (as reported in Tables 4 and 5, respectively, in Appendix C.[10]

[10]We also how different pair types are affected by different scenarios in Appendix C in Table 6 for two-way exchange and Table 7 for two&three-way exchange.

| Races | Total Number of Pairs | | Number of Patients of Each Race Matched in Two-way Exchange out of $n = 2000$ Pairs | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | 1. Without | 2. With $A$ subtype matching | | | | | |
| | | | | (a) $A$ subtype test done **before** participation decision in exchange | | | (b) $A$ subtype test done **after** participation decision in exchange | | |
| | Comp. | Inc. | $A$ subtype | | | | | | |
| | (w/o $A$ subtype matching) | | matching | i. $A2/A2B \to B$ only | ii. $A2 \to O$ only | iii. $A2/A2B \to B$ and $A2 \to O$ | i. $A2/A2B \to B$ only | ii. $A2 \to O$ only | iii. $A2/A2B \to B$ and $A2 \to O$ |
| **White** | **833.1060** (23.3396) | **795.1440** (23.0033) | **299.6800** (19.3555) | **297.7780** (19.7659) | **339.3600** (22.2173) | **332.3660** (21.8758) | **305.9440** (19.7554) | **340.0200** (22.2719) | **341.9880** (22.6046) |
| **Black** | **126.3580** (10.5689) | **130.5120** (11.1098) | **51.5260** (7.3608) | **51.4080** (7.2456) | **57.6660** (7.4497) | **56.5180** (7.3210) | **52.3240** (7.3320) | **57.4220** (7.7379) | **57.9120** (7.4857) |
| **Asian** | **49.5580** (7.2818) | **53.0260** (7.1113) | **23.3540** (5.0095) | **23.2900** (4.8918) | **25.3700** (5.1945) | **24.9720** (5.1886) | **23.8200** (5.0138) | **25.5380** (5.2026) | **25.6700** (5.1160) |
| **American Indian** | **4.0420** (2.0564) | **3.9020** (1.9452) | **1.3000** (1.1852) | **1.3080** (1.1558) | **1.5140** (1.2510) | **1.5020** (1.2430) | **1.2980** (1.1747) | **1.4380** (1.2382) | **1.4940** (1.2382) |
| **Pacific Islander** | **2.1780** (1.5083) | **2.1740** (1.3621) | **0.8400** (0.8740) | **0.8320** (0.8997) | **0.9420** (0.9531) | **0.9020** (0.9392) | **0.8520** (0.9032) | **0.9560** (0.9633) | **0.9480** (0.9397) |
| **TOTAL** | **1015.200** (23.2186) | **984.800** (23.2186) | **376.700** (22.3124 ) | **374.6160** (23.1654) | **424.852** (25.9950) | **416.260** (25.4372) | **384.238** (23.1129) | **425.374** (25.9735) | **428.012** (26.1527) |

Table 3: Averages for **two-way exchanges** (Table 2) broken down according to races of the patients

# 5 Conclusion

# Appendix A Proofs

The structure of optimal matchings is given by the well-known Gallai-Edmonds Decomposition Theorem (Gallai (1963, 1964), Edmonds (1965)). We use (directly or indirectly) the insight provided by this characterization result. The implication of this theorem in our model is as follows:

**Lemma 1** *(Gallai-Edmonds Decomposition (GED) Lemma)*
*In each maximal matching, a pair, which is not* underdemanded *and is compatible with an* underdemanded *pair, is matched with an* underdemanded *pair.*

**Proof of Proposition 1:**
(i) Since A2 donor can donate to a B patient, each tissue-type compatible B-A2 pair does not participate the exchange and the transplant is via direct donation. This holds for the tissue-type compatible B-A2B pairs. Thus, the number of transplants via direct donation increases by the number $\#(B-A2)_c + \#(B-A2B)_c$.
(ii) By Assumption UB(i), each B-A pair is compatible with each A-B pair. Moreover, by Assumption TF(i), each B-A pair is matched with an A-B pair under the ABO compatibility. Under A2-to-B compatibility, some of the B-A pairs (tissue-type compatible B-A2 pairs) do not participate the exchange. Thus, Assumption TF(i) holds for the pairs in the exchange pool as well, which implies that the B-A pairs are on the short side of the exchange pool and each such pair is matched with an A-B pair. Thus, the number of pairwise exchanges decreases by

the number of tissue-type compatible B-A2 pairs and the number of transplants via exchange decreases by $2\#(B-A2)_c$.

Under the A2-to-B compatibility, there are new matches, which are not possible under the ABO compatibility. First, note that each (tissue-type incompatible) AB-A2B pair can be matched with a B-A1B pair. By Assumption LP(ii), an AB-A2B pair is not *underdemanded*. By Assumptions UB(i) and UB(ii), such a pair is compatible with any B-A1B pair, which is *underdemanded* by Assumption LP (ii). This implies that, by Lemma 1, an AB-A2B pair is matched with an *underdemanded* pair, e.g. a B-A1B pair. If the number of AB-A1B pairs is odd, then at most one such pair remains unmatched in a maximum matching and an AB-A2B pair can be matched with an AB-A1B pair. Since B-A1B pairs are on the long side of the market, for each maximum matching where an AB-A2B and an AB-A1B pair are matched, one can obtain another maximum matching where the AB-A2B pair is matched with a B-A1B pair, and an AB-A1B pair remains unmatched. Thus, we can assume without loss of generality that each AB-A2B pair is matched with a B-A1B pair. Since under the ABO compatibility, each AB-AB pair is matched only with another AB-AB pair, A2-to-B compatibility increases the number of transplants (via exchange including an AB-AB pair) by the number of (tissue-type incompatible) AB-A2B pairs. Moreover, each AB-A1B pair is matched with a pair of the same type. Also, by Assumption UB, each B-A2B pair is compatible with a B-B pair implying that each B-B or B-A2B pair can be matched with a B-B or B-A2B pair. Thus, the number of transplants via exchange from the ABO compatibility to the A2-to-B compatibility changes by the following number:

$$2\#(AB-A2B)+2\lfloor\frac{\#(AB-A1B)}{2}\rfloor+2\lfloor\frac{\#(B-A2B)_i+\#(B-B)}{2}\rfloor-$$
$$2\lfloor\frac{\#(AB-AB)}{2}\rfloor-2\lfloor\frac{\#(B-B)}{2}\rfloor-2\#(B-A2)_c.$$

Since $2\lfloor\frac{\#T}{2}\rfloor=\#T-\mathbf{odd}_T$ and $\#(AB-AB)=\#(AB-A1B)+\#(AB-A2B)$, this number is equal to

$$\#(AB-A2B)+\#(B-A2B)_i-2\#(B-A2)_c-$$
$$\mathbf{odd}_{(AB-A1B)}-\mathbf{odd}_{(B-A2B)_i\cup(B-B)}+\mathbf{odd}_{(AB-AB)}+\mathbf{odd}_{(B-B)}$$

Let $\Lambda=\mathbf{odd}_{(AB-AB)}+\mathbf{odd}_{(B-B)}-\mathbf{odd}_{(AB-A1B)}-\mathbf{odd}_{(B-A2B)_i\cup(B-B)}$ and note that $\Lambda\in\{-2,-1,0,1,2\}$. Moreover, by Assumption TF(ii), this number is negative. Thus, the number of transplants via exchange decreases by the following number:

$$2\#(B-A2)_c-\#(AB-A2B)-\#(B-A2B)_i-\Lambda$$

(iii) The result follows from the fact that $\#(B-A2B)=\#(B-A2B)_i+\#(B-A2B)_c$.

**Proof of Proposition 2:**

(i) Since an A2 donor is compatible with an O patient, each tissue-type compatible O-A2 pair does not participate the exchange and the transplant is via direct donation.

(ii) By Assumption UB, each incompatible O-A2 pair can be matched with an incompatible O-A2 or O-O pair. Since, under ABO compatibility, each O-A pair is on the long side, O-A2 pairs being matched with each other and with O-O pairs increases the number of transplants at least by $2\lfloor \frac{\#(O-A2)_i}{2} \rfloor$.

By Assumption LP(ii), the number of O-A1 pairs is greater than the number of A-O and A-A2 pairs and each O-A1 pair is *underdemanded*. Thus, by Lemma 1, each A-O and A-A2 pair is matched with an O-A1 pair. While A-A pairs (including A-A2 pairs) are matched with each other under the ABO compatibility, each A-A2 pair is matched to an *underdemanded* pair (in particular, an O-A1 pair) under the A2-to-O compatibility. Thus, the number of transplants including an O-A1 pair increases by $\#(A-A2)$. Thus, the number of transplants via exchange increases by $\#(O-A2)_i+\#(A-A2)$ and a residual term. The residual term depends on whether the cardinalities of certain sets are odd or even. Under the ABO compatibility, an O-O pair remains unmatched if the cardinality of the set of O-O pairs is odd. The same is true for A-A pairs. Under the A2-to-O compatibility, A-A1 pairs are matched to each other. Thus, such a pair remains unmatched if the cardinality of the of the set of A-A1 pairs is odd. Similarly, each pair in the set $(O-O)\cup(O-A2)_i$ is matched with a pair in the same set. Thus, if the cardinality of this set is odd, then one of these pairs remain unmatched.

(iii) The result follows directly from (i) and (ii).

**Proof of Proposition 3:**

The number of transplants increases compared to the case where the subtype testing is done before the participation to the exchange. The reason is simple: if the test is done before, then some pairs do not participate the exchange because of subtype compatibility. A compatible B-A2 pair does not participate the exchange, yet this pair would be matched to an A-B pair if the subtype compatibility is ignored, which would increase the number of transplants since the A-B pair is on the long side of the market. Thus, this type of losses is prevented by having the test after the participation to the exchange; these subtype compatible pairs on the short side are matched with the corresponding pairs on the long side rather than setting them for direct donation. Moreover, if compatible, the B-A2B pairs can be set for direct donation; otherwise, they can be matched with B-A2B pairs or with B-B pairs. Thus, each such pair is matched. The only exception for a direct donation of a compatible B-A2B pair is that if the total number of incompatible B-A2B and B-B pairs is odd, a compatible B-A2B pair is matched with the remaining pair from the pool of incompatible B-A2B pairs and B-B pairs to prevent any such

loss. This two-way exchange is subject to not only the total number of incompatible B-A2B and B-B pairs being odd, but also to the number of compatible B-A2B pairs being positive. This conditional increase is captured by the term:

$$\max\{0, \#(B-A2B)_c - \mathbf{odd}_{(B-A2B)_i \cup (B-B)}\}.$$

The increase in the number of transplants via exchange is captured by the following term:

$$\#(B-A2B)_i + \min\{\#(B-A2B)_c, \mathbf{odd}_{(B-A2B)_i \cup (B-B)}\} + \mathbf{odd}_{(B-B)}.$$

To explain this term, suppose there exists at least one compatible B-A2B pair and the total number of incompatible B-A2B and B-B pairs is odd (otherwise, it is trivial). Under A2-to-O compatibility, all the incompatible B-A2B pairs and B-B pairs are matched, one of them being matched with a compatible B-A2B pair. Thus, the number of transplants via these exchanges is $\#(B-A2B)_i + \#(B-B) + 1$. Since under the ABO compatibility, the number of transplants in exchanges with B-B pairs is $\#(B-B) - \mathbf{odd}_{(B-B)}$, the difference is equivalent to $\#(B-A2B)_i + 1 + \mathbf{odd}_{(B-B)}$, the second term standing for $\mathbf{odd}_{(B-A2B)_i \cup (B-B)}$. Also, an AB-A2B pair can be matched with a B-A1B pair, which, by Assumption LP(ii), is on the long side of the market.

**Proof of Proposition 4:**
The result is almost the same as the result in Proposition 2 and the reason is the O-A pairs being on the long side of the market so that direct donation is optimal for compatible O-A2 pairs. The only exception for a direct donation of a compatible O-A2 pair is that if the total number of incompatible O-A2 and O-O pairs is odd, a compatible O-A2 pair is matched with the remaining pair from the pool of incompatible O-A2 pairs and O-O pairs to prevent any such loss. Clearly, such a two-way exchange is subject to the existence of at least one compatible O-A2 pair. Note that this corresponds to the case under A2-to-B compatibility, where a compatible B-A2B pair is matched with the remaining pair from the pool of incompatible B-A2B pairs and B-B pairs. The same argument in Proposition 3 holds here as well and the term capturing the increase in the number of direct donation is as follows:

$$\max\{0, \#(O-A2)_c - \mathbf{odd}_{(O-A2)_i \cup (O-O)}\}.$$

Similarly, the increase in the number of transplants via exchange is given by the following term:

$$\#(O-A2)_i + \min\{\#(O-A2)_c, \mathbf{odd}_{(O-A2)_i \cup (O-O)}\} + \mathbf{odd}_{(O-O)}.$$

# Appendix B Two-way and three-way exchanges

We reproduce our main results on two-way exchanges for two-way and three-way exchanges[11] under blood subtype compatibility protocols. First, we analyze the efficiency implications of blood subtyping technology under the current implementation of blood subtype tests (Appendix B.1). Second, we consider these implications under the change in timing of subtype tests (Appendix B.2).

## B.1 Subtype test timing: before exchange participation

**Proposition 5** *Assume LP(i), LP(ii), TF, UB. Consider the two-way and three-way exchange policy. Let*

$$\Delta = \#(B-O) + \#(AB-A) - (\#(A-B) - \#(B-A)).$$

*If the compatibility protocol changes from ABO compatibility to A2-to-B compatibility, then (i) the number of transplants via direct donation* ***increases*** *by* $\#(B-A2)_c + \#(B-A2B)_c$*, (ii) the number of transplants via exchange* ***changes*** *by*

$$\begin{aligned} &\#(AB-A2B) + \#(B-A2B)_i - 2\#(B-A2)_c + \\ &\max\{0, \min\{\Delta, \#(B-A2)_c + \#(A-A2B)\}\}, \end{aligned} \tag{1}$$

*(iii) the total number of transplants* ***changes*** *by*

$$\begin{aligned} &\#(AB-A2B) + \#(B-A2B) - \#(B-A2)_c + \\ &\max\{0, \min\{\Delta, \#(B-A2)_c + \#(A-A2B)\}\}. \end{aligned}$$

**Proof.** (i) Given that the subtype test timing is before the exchange participation, the direct donations are selected independently from whether three-way exchanges are feasible or not. Thus, by part (i) of Proposition 1, the number of transplants via direct donation increases by $\#(B-A2)_c + \#(B-A2B)_c$.

(ii) There are increases in the number of transplants via the following two-way exchanges: the AB-A2B pairs (who are matched with the same type under ABO compatibility) are matched with B-A1B pairs (who are *underdemanded* by Assumption LP(ii)) and B-A2B pairs (who are on the long side of the exchange under ABO compatibility, but not *underdemanded* under A2-to-B compatibility) are matched with other B-A2B pairs or with B-B pairs. On the other hand, since the compatible B-A2 pairs do not participate the exchange and the A-B pairs are

[11] The feasibility of three-way exchanges prevents any potential efficiency loss due to the number of pairs being odd and one pair of this type remaining unmatched. Since there are no remaining pairs for this reason, there is no residual term in each following result.

*underdemanded* by Assumption TF(i), there is a decrease in the number of two-way exchanges by an A-B pair and an B-A pair.

The following three-way exchanges are possible: a B-O pair, an O-A pair and an A-B pair (or an A-A2B pair); an AB-A pair, an A-B pair (or an A-A2B pair) and a B-AB pair. In each of these exchanges, two *underdemanded* pairs (an O-A pair and an A-B pair (or an A-A2B pair) in the first one, and a B-AB pair and and A-B pair (or an A-A2B pair) in the second one) are matched. These three-way exchanges potentially compensates the efficiency loss due to the compatible B-A2 pairs not participating the exchange.

**Case 1:** $\Delta \leq 0$.
Under ABO compatibility, all B-O and AB-A pairs are matched via three-way exchanges including an A-B pair. This implies that each A-B pair which is not matched with a B-A pair via a two-way exchange, remains unmatched under A2-to-B compatibility. Similarly, no A-A2B pair is matched via a three-way exchange. Thus, since there are not enough B-O and AB-A pairs to match with the remaining A-B pairs (not matched with B-A pair via a two-way exchange) via three-way exchange, switching to the A2-to-B compatibility policy does not increase the number of transplants via three-way exchange.[12] The efficiency loss due to the compatible B-A2 pairs not participating the exchange cannot be recovered under A2-to-B compatibility.

**Case 2:** $\Delta > 0$.
Under ABO compatibility, each A-B pair, not matched with a B-A pair via a two-way exchange is matched either with B-O pair or an AB-A pair via three-way exchange. Since $\Delta > 0$, the same three-way exchanges are feasible under A2-to-B compatibility as well. Moreover, there are $\Delta$ of B-O and AB-A pairs available for further three-way exchanges and $\#(B-O)+\#(AB-A)$ of the A-B pairs who are not matched to B-A pairs, can be matched via three-way exchange. These pairs can be matched with the A-B pairs, which are matched with compatible B-A2 pairs via two-ways exchange under ABO compatibility (but not under A2-to-B compatibility due to the compatible B-A2 pairs not participating the exchange), or with the A-A2B pairs. Thus, the total number of A-B pairs and A-A2B pairs available for three-way exchange with the remaining B-O pairs and AB-A pairs is equal to $\#(B-A2)_c+\#(A-A2B)$. Since the number of these new three-way exchanges is bounded above by $\Delta > 0$, the number of transplants via

[12]Note that under A2-to-B compatibility, a new three way exchange is possible: an O-A2B pair, a B-AB pair and an AB-O pair. Since each AB-O pair is part of a three-way exchange with two pairs from the long side of the exchange (an O-B pair and a B-AB pair), this new exchange does not increase the number of transplants. Other feasible three-way exchanges under A2-to-B compatibility are via an A-A2 pair, a B-O pair and an O-A pair, or via an A-A2 pair, an AB-A pair and a B-AB pair. Since an A-A2 pair is not *underdemanded* and is matched with the same type in each matching, these three-way exchanges do not increase the number transplants.

three-way exchange increases by $\min\{\Delta, \#(B-A2)_c + \#(A-A2B)\}$.
(iii) The change in the total number of transplants is equal to the sum of the change in the number transplants via direct donation and the change in the number of transplants via exchange. Thus, it is equal to the sum of the terms in part (i) and (ii). ■

**Proposition 6** *Assume LP(i), LP(iii), UB. Consider the two-way and three-way exchange policy. Let*

$$\Delta = \#(B-O) + \#(AB-A) + \#(B-A) - \#(A-B).$$

*If the compatibility protocol changes from ABO compatibility to A2-to-O compatibility, then*
*(i) the number of transplants via direct donation* ***increases*** *by* $\#(O-A2)_c$,
*(ii) the number of transplants via exchange* ***increases*** *by*

$$\begin{aligned} &\#(O-A2)_i + \#(A-A2) + \#(B-A2) + \\ &\max\{0, \min\{\Delta, \#(AB-A2)\}\}, \end{aligned} \tag{2}$$

*(iii) the total number of transplants* ***increases*** *by*

$$\begin{aligned} &\#(O-A2) + \#(A-A2) + \#(B-A2) + \\ &\max\{0, \min\{\Delta, \#(AB-A2)\}\}, \end{aligned}$$

**Proof.** (i) Given that the subtype test timing is before the exchange participation, the direct donations are selected independently from whether three-way exchanges are feasible or not. Thus, by part (i) of Proposition 2, the number of transplants via direct donation increases by $\#(O-A2)_c$.
(ii) Each tissue-type incompatible O-A2 pair can be matched with another pair of the same type via two-way exchange. Similarly, each A-A2 pair is matched with an O-A1 pair and the remaining A-A pairs (that is, the A-A1 pairs) are matched with each other such that there is at most one three-way exchange (only if the cardinality of the set of A-A1 pairs is odd) and there is no unmatched pair in this set. Thus, the total number of transplants via exchange with O-A2 pairs increases by $\#(O-A2)_i + \#(A-A2)$.

There are new three-way exchanges under A2-to-O compatibility, which are not feasible under ABO compatibility. The first one is via the pairs of type B-A2, O-A and A-B. Note that under A2-to-O compatibility, each B-A2 pair participates the exchange. Since A-B pairs and O-A1 pairs are *underdemanded* by Assumptions TF(i) and LP(iii), respectively, each B-A2 pair is matched with an O-A1 pair and an A-B pair via a three-way exchange. Since there are two *underdemanded* pairs in this three-way exchange (as opposed to only one *underdemanded* pair (an A-B pair) in the two-way exchange of A-B and B-A pairs under ABO compatibility), this increases the number of transplants by $\#(B-A2)$.

Another new three-way exchange is via the pairs of type AB-A2, O-B and B-AB; or type AB-A2, O-A and A-AB. Since O-B pairs and B-A1B pairs (also, O-A pairs and A-A1B pairs) are *underdemanded* by Assumptions LP(i) and LP(iii), respectively, each AB-A2 pair is matched with an O-B pair and a B-A1B pair (or with an O-A pair and an A-A1B pair) via a three-way exchange. Since there are two *underdemanded* pairs (O-B and B-A1B pairs, or O-A and A-A1B pairs) in this three-way exchange (as opposed to only one *underdemanded* pair (an A-AB pair) in the two-way exchange of AB-A and A-AB pairs under ABO compatibility), this increases the number of transplants by $\#(AB-A2)$. But, a two-way exchange with AB-A and A-AB pairs is not the only exchange where AB-A2 pairs are matched under ABO compatibility. Some of the AB-A2 pairs are matched with an A-B pair and a B-AB pair in a three-way exchange under ABO compatibility. Thus, we need to take the number of these exchanges into account in calculating the increase in the number of transplants via this new type of three-way exchanges including an AB-A2 pair.

**Case 1:** $\Delta \geq \#(AB-A2)$.
Since $\#(AB-A) = \#(AB-A1) + \#(AB-A2)$, we have $\#(B-O) + \#(AB-A1) \geq \#(A-B) - \#(B-A)$. Also, note that, each B-A2 pair is matched via a three-way exchange including an A-B pair. Thus, each B-A1 pair is matched with an A-B pair via a two-way exchange, each B-A2 pair is matched via a three-way exchange including an A-B pair and the remaining A-B pairs are matched either with a B-O pair or with an AB-A1 pair via a three-way exchange. Since there is no remaining A-B pair, each AB-A2 pair can be matched with an O-B pair and a B-AB pair, or with an O-A pair and an A-AB pair, in a three-way exchange, each of which increases the number of transplants by one compared to ABO compatibility. Thus, the number of transplants increases by $\#(AB-A2)$.

**Case 2:** $\Delta < \#(AB-A2)$.
In this case, $\#(B-O) + \#(AB-A1) < \#(A-B) - \#(B-A)$. Note that each B-A1 pair is matched with an A-B pair via a two-way exchange, each B-A2 pair is matched via a three-way exchange including an A-B pair and $\#(B-O) + \#(AB-A1)$ of the remaining A-B pairs are matched either with a B-O pair or with an AB-A1 pair via a three-way exchange. The number of the remaining A-B pairs to be matched with AB-A2 pairs is the same under ABO compatibility and A2-to-O compatibility. Since the number of three-way exchanges including an A-B pair and an AB-A2 pair is bounded by the number of AB-A2 pairs, the number of transplants via three-way exchanges with AB-A2, O-B and B-AB pairs (or AB-A2, O-A and

A-AB pairs) increases by the number:[13]

$$\#(AB-A2)-\max\{0,\min\{\#(AB-A2),\#(AB-A2)-\Delta\}\}$$

which is equivalent to

$$\max\{0,\min\{\Delta,\#(AB-A2)\}\}.$$

(iii) The change in the total number of transplants is equal to the sum of the change in the number transplants via direct donation and the change in the number of transplants via exchange. Thus, it is equal to the sum of the terms in part (i) and (ii). ■

**Proposition 7** *Assume LP(i), LP(iv), TF, UB. Consider the two-way and three-way exchange policy. Let*

$$\Delta=\#(B-O)+\#(AB-A)+\#(B-A)-\#(A-B).$$

*If the compatibility protocol changes from ABO compatibility to full compatibility, then*
*(i) the number of transplants via direct donation* ***increases*** *by*

$$\#(O-A2)_c+\#(B-A2)_c+\#(B-A2B)_c,$$

*(ii) the number of transplants via exchange* ***changes*** *by*

$$\#(AB-A2B)+\#(B-A2B)_i-2\#(B-A2)_c+ \tag{3}$$
$$\#(O-A2)_i+\#(A-A2)+\#(B-A2)_i+ \tag{4}$$
$$\max\{0,\min\{\Delta,\#(B-A2)_c+\#(A-A2B)+\#(AB-A2)\}\}, \tag{5}$$

*(iii) the total number of transplants* ***changes*** *by*

$$\#(AB-A2B)+\#(B-A2B)-\#(B-A2)+$$
$$\#(O-A2)+\#(A-A2)+$$
$$\max\{0,\min\{\Delta,\#(B-A2)_c+\#(A-A2B)+\#(AB-A2)\}\}.$$

**Proof.** (i) The increase in the number of transplants via direct donation is the sum of the terms in part (i) of Propositions 5 and 6. This follows directly from the argument in part (i) of the proofs of these results.

[13]Note that we assume that under ABO compatibility, an A-B pair, if matched with an AB-A pair in a three-way exchange, is matched with an AB-A2 pair if only if all the AB-A1 pairs in the exchange pool are already matched. Without this assumption, this number is the upper bound on the number of increase in the number of transplants via the three-way exchanges with AB-A2, O-B and B-AB pairs (or AB-A2, O-A and A-AB pairs).

(ii) Parts (3) and (4) follow from part (1) in the expression of Proposition 5(ii) and part (2) in the expression of Proposition 6(ii), respectively. The only difference is that there is $\#(B-A2)_i$ in part (4), instead of $\#(B-A2)$ in part (2) in the expression of Proposition 6(ii). The reason is that since under full compatibility, the compatible B-A2 pairs do not participate the exchange, only incompatible B-A2 pairs can be matched via a three-way exchange including O-A and A-B pairs.

**Case 1:** $\Delta \geq \#(B-A2)_c + \#(A-A2B) + \#(AB-A2)$.
Since $\#(AB-A) = \#(AB-A1) + \#(AB-A2)$, we have $\#(B-O) + \#(AB-A1) \geq \#(A-B) - \#(B-A)$. That is, under ABO compatibility, each A-B pair, not matched with a B-A pair via a two-ways exchange, is part of a three-way exchange including either a B-O pair or an AB-A1 pair. Under full compatibility, each AB-A2 pair can be matched in a three-way exchange including an O-B pair and a B-AB pair, or with an O-A pair and an A-AB pair, in a three-way exchange, each of which increases the number of transplants by one compared to ABO compatibility. Moreover, under full compatibility, since $\#(B-A2)_c$ of B-A pairs do not participate the exchange, there are $\#(B-A2)_c$ A-B pairs not matched with a B-A pair via a two-way exchange. Similarly, a A-A2B pair can be matched in a three-way exchange including a B-O pair or an AB-A1 pair. Thus, in total, there are potentially $\#(B-A2)_c + \#(A-A2B)$ pairs which can be matched via three-way exchange including a B-O pair or an AB-A1 pair. Since $\Delta - \#(AB-A2) \geq \#(B-A2)_c + \#(A-A2B)$, there are enough number of B-O and AB-A1 pairs to be matched with these pairs in a three-way exchange. Thus, under full compatibility, each unmatched A-B pair and each A-A2B pair are matched in a three-way exchange, each such exchange increases the number of transplants by one. Thus, the number of transplants increases by $\#(B-A2)_c+\#(A-A2B)+\#(AB-A2)$ via these three-way exchanges.

**Case 2:** $\Delta < \#(B-A2)_c + \#(A-A2B) + \#(AB-A2)$.
Suppose $\Delta < 0$. This implies that under ABO compatibility, all B-O and AB-A pairs are matched with A-B pairs via three-way exchange. Thus, under full compatibility, neither an A-B pair (matched via two-ways exchange under ABO, but not under full compatibility) nor an A-A2B can be matched in a three-way exchange including one of the B-O and AB-A pairs. Thus, there is no increase in the number of transplants via three-way exchanges including a B-O pair or an AB-A pair.
If $0 < \Delta$, then under ABO compatibility each A-B pair unmatched via a two-ways exchange is matched in a three-way exchange including a B-O pair or an AB-A pair. There are $\#(A-B) - \#(B-A)$ such exchanges. Under full compatibility, each AB-A2 pair is matched in a three-way exchange including an O-B pair and a B-AB pair, or an O-A pair and an A-AB pair,

thus there are $\#(AB-A2)$ of these exchanges.
Suppose $0<\Delta<\#(AB-A2)$. Since $\#(B-O)+\#(AB-A1)<\#(A-B)-\#(B-A)$, all B-O and AB-A1 pairs are matched in three-way exchanges including an A-B pair and there are $\#(B-O)+\#(AB-A1)$ of these exchanges. Thus, under full compatibility, the number of transplants increases by $\Delta$.
Suppose $\Delta>\#(AB-A2)$. Since $\#(B-O)+\#(AB-A1)>\#(A-B)-\#(B-A)$, there are $\#(A-B)-\#(B-A)$ three-way exchanges including an A-B pair. There are $(\#(B-O)+\#(AB-A1))-(\#(A-B)-\#(B-A))=\Delta-\#(AB-A2)$ remaining pairs of type B-O or AB-A1 available for three-way exchanges with A-B pairs (there are $\#(B-A2)_c$ such pairs) and A-A2B pairs (there are $\#(A-A2B)$ such pairs). Since $\Delta-\#(AB-A2)>0$, there is positive number of these exchanges under full compatibility. Since $\Delta-\#(AB-A2)<\#(B-A2)_c+\#(A-A2B)$, the number of these additional exchanges is $\Delta-\#(AB-A2)$. Thus, under full compatibility, the number of transplants increases by $\Delta$.
(iii) The change in the total number of transplants is equal to the sum of the change in the number transplants via direct donation and the change in the number of transplants via exchange. Thus, it is equal to the sum of the terms in part (i) and (ii). ■

## B.2 Subtype test timing: after exchange participation

**Proposition 8** *Assume LP(i), LP(ii), TF, UB. Consider the two-way and three-way exchange policy. Let*

$$\Delta=\#(B-O)+\#(AB-A)+\#(B-A)-\#(A-B).$$

*If the compatibility protocol changes from ABO compatibility to A2-to-B compatibility, then*
*(i) the number of transplants via direct donation* ***increases*** *by* $\#(B-A2B)_c$,
*(ii) the number of transplants via exchange* ***increases*** *by*

$$\#(AB-A2B)+\#(B-A2B)_i+\max\{0,\min\{\Delta,\#(A-A2B)\}\},$$

*(iii) the total number of transplants* ***increases*** *by*

$$\#(AB-A2B)+\#(B-A2B)+\max\{0,\min\{\Delta,\#(A-A2B)\}\}.$$

**Proof.** The compatible B-A2 pairs are matched via direct donation if the blood subtyping tests are before the participation to exchange. Since each such direct donation prevents a pairwise exchange with an A-B pair, this results in a decrease in the number transplants. Thus, given the timing is after the participation to exchange, compatible B-A2 pairs are matched with A-B pairs in exchange. Thus, part (1) in the expression of Proposition 5(ii) does not include the term $-2\#(B-A2)_c$. For three-way exchanges and the case $\Delta<0$, the same argument in Case 1 in the

proof of Proposition 5(ii) holds here as well. For the case $\Delta > 0$, the only difference is that the total number of A-B pairs and A-A2B pairs available for three-way exchange with the remaining B-O pairs and AB-A pairs is equal to $\#(A-A2B)$ instead of $\#(B-A2)_c+\#(A-A2B)$. Thus, the increase in the number of transplants via three-way exchanges with B-O and AB-A pairs is equal to the following:

$$\max\{0, \min\{\Delta, \#(A - A2B)\}\}.$$

Since the other exchanges are not effected by the timing of the tests, the result follows. ■

**Proposition 9** *Assume LP(i), LP(iii), UB. Consider the two-way and three-way exchange policy. Let*

$$\Delta = \#(B - O) + \#(AB - A) + \#(B - A) - \#(A - B).$$

*If the compatibility protocol changes from ABO compatibility to A2-to-O compatibility, then*
*(i) the number of transplants via direct donation* ***increases*** *by* $\#(O - A2)_c$,
*(ii) the number of transplants via exchange* ***increases*** *by*

$$\#(O - A2)_i + \#(A - A2) + \#(B - A2) + \max\{0, \min\{\Delta, \#(AB - A2)\}\},$$

*(iii) the total number of transplants* ***increases*** *by*

$$\#(O - A2) + \#(A - A2) + \#(B - A2) + \max\{0, \min\{\Delta, \#(AB - A2)\}\},$$

**Proof.** The compatible O-A2 pairs are matched with via direct donation under A2-to-O compatibility. Moreover, since B-A2 pairs are not compatible under A2-to-O compatibility, these pairs participate the exchange. Thus, there is no difference between the two scenarios in terms of the timing of blood subtyping tests. Thus, the result is equivalent to the one in Proposition 6. ■

**Proposition 10** *Assume LP(i), LP(iv), TF, UB. Consider the two-way and three-way exchange policy. Let*

$$\Delta = \#(B - O) + \#(AB - A) + \#(B - A) - \#(A - B).$$

*If the compatibility protocol changes from ABO compatibility to full compatibility, then*
*(i) the number of transplants via direct donation* ***increases*** *by* $\#(O - A2)_c + \#(B - A2B)_c$,
*(ii) the number of transplants via exchange* ***increases*** *by*

$$\#(O - A2)_i + \#(A - A2) + \#(AB - A2B) + \#(B - A2B)_i + \#(B - A2) + \max\{0, \min\{\Delta, \#(AB - A2) + \#(A - A2B)\}\},$$

*(iii) the total number of transplants* ***increases*** *by*

$$\#(O - A2) + \#(A - A2) + \#(AB - A2B) + \#(B - A2B) + \#(B - A2) + \max\{0, \min\{\Delta, \#(AB - A2) + \#(A - A2B)\}\}.$$

# Appendix C Remaining Simulation Results

| Averages and Standard Errors of $S = 500$ Simulations with $n = 500$ Pairs | | | | | | |
|---|---|---|---|---|---|---|
| Incomp. Pairs | Two&Three-way Exchange | | | | | |
| | 1. Without $A$ Subtype Matching | 2. With $A$ Subtype Matching | | | | |
| | | Subtype Test Timing | | $A2$ Transplant Protocol | | |
| | | | | i. $A2/A2B \to B$ only | ii. $A2 \to O$ only | iii. $A2/A2B \to B$ and $A2 \to O$ |
| 246.430 (23.2186) | **96.956 (11.6453 )** | **(a) Before** Exchange Participation Decision | **Total Transplants** | **97.240 (12.0308)** | **117.292 (12.9746)** | **114.878 (13.1884)** |
| | | | $B$'s receiving from own comp. $A2/A2B$ donors | 12.180 (3.391) | - | 12.180 (3.391 ) |
| | | | $O$'s receiving from own comp. $A2$ donors | - | 15.708 (3.833) | 15.708 (3.833) |
| | | **(b) After** Exchange Participation Decision | **Total Transplants** | **98.358 (11.6661)** | **117.292 (12.9746)** | **118.596 (13.0767)** |
| | | | $B$'s receiving from own comp. $A2/A2B$ donors | 1.022 (1.4034 ) | - | 0.682 (0.7836) |
| | | | $O$'s receiving from own comp. $A2$ donors | - | 3.558 (2.2254) | 3.882 (3.2902) |

Table 4: Simulations for maximal two&three-way exchange (the numbers in parentheses are sample standard errors, to find the standard errors of the averages, divide the sample standard errors by $\sqrt{S} = 22.36$)

| Races | Total Number of Pairs | | Number of Patients of Each Race Matched in Two&three-way Exchange out of $n = 500$ Pairs | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | 1. Without | 2. With $A$ subtype matching | | | | | |
| | | | | (a) $A$ subtype test done **before** participation decision in exchange | | | (b) $A$ subtype test done **after** participation decision in exchange | | |
| | Comp. | Inc. | $A$ subtype | | | | | | |
| | (w/o $A$ subtype matching) | | matching | i. $A2/A2B \to B$ only | ii. $A2 \to O$ only | iii. $A2/A2B \to B$ and $A2 \to O$ | i. $A2/A2B \to B$ only | ii. $A2 \to O$ only | iii. $A2/A2B \to B$ and $A2 \to O$ |
| **White** | **207.8560** (11.8609) | **198.8320** (11.3236) | **76.9180** (9.9465) | **77.2800** (10.3015) | **93.9140** (11.0920) | **92.0640** (11.4244) | **78.2440** (9.9796) | **93.9760** (11.1348) | **95.0840** (11.2439) |
| **Black** | **31.5340** (5.4129) | **32.7300** (5.4398) | **13.3880** (3.7924) | **13.3560** (3.7381) | **15.8100** (4.2040) | **15.4240** (4.0449) | **13.4940** (3.7596) | **15.7840** (4.1795) | **15.9480** (4.1795) |
| **Asian** | **12.5540** (3.3295) | **13.2520** (3.6572) | **6.0740** (2.4990) | **6.0480** (2.4604) | **6.8340** (2.6526) | **6.7000** (2.5906) | **6.0640** (2.5292) | **6.8040** (2.6075) | **6.8740** (2.6759) |
| **American Indian** | **1.0680** (1.0685) | **1.0200** (1.0206) | **0.3400** (0.6428) | **0.3360** (0.6260) | **0.4280** (0.6524) | **0.4060** (0.6679) | **0.3420** (0.6307) | **0.4240** (0.6731) | **0.4040** (0.6706) |
| **Pacific Islander** | **0.5580** (0.7535) | **0.5960** (0.7307) | **0.2360** (0.4866) | **0.2200** (0.4605) | **0.3060** (0.5486) | **0.2840** (0.5440) | **0.2140** (0.4697) | **0.3040** (0.5515) | **0.2860** (0.5336) |
| **TOTAL** | **253.570** (23.2186) | **246.430** (23.2186) | **96.956** (11.6453 ) | **97.240** (12.0308) | **117.292** (12.9746) | **114.878** (13.1884) | **98.358** (11.6661) | **117.292** (12.9746) | **118.596** (13.0767) |

Table 5: Averages for **two&three-way exchanges** (Table 2) broken down according to races of the patients

| Pair Types (Patient-Donor) | Total Number of Pairs | | Number of Pairs Matched in Two-way Exchange out of $n = 2000$ Pairs | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | 1. Without $A$ subtype matching | 2. With $A$ subtype matching | | | | | |
| | | | | (a) $A$ subtype test done **before** participation decision in exchange | | | (b) $A$ subtype test done **after** participation decision in exchange | | |
| | Comp. | Inc. | | i. $A2/A2B \to B$ only | ii. $A2 \to O$ only | iii. $A2/A2B \to B$ and $A2 \to O$ | i. $A2/A2B \to B$ only | ii. $A2 \to O$ only | iii. $A2/A2B \to B$ and $A2 \to O$ |
| | (w/o $A$ subtype matching) | | | | | | | | |
| $O - O$ | **372.7320** (17.6297) | **101.5100** (9.8058) | **58.9120** (7.6607) | **58.8780** (7.6635) | **58.9380** (7.7121) | **58.9340** (7.7230) | **58.8560** (7.6540) | **58.8840** (7.7153) | **58.8840** (7.7153) |
| $O - A1$ | | **270.2700** (15.7888) | **34.6260** (5.8664) | **36.1920** (5.6932) | **46.3740** (7.0664) | **46.5800** (6.6901) | **36.1820** (5.9200) | **45.7520** (6.8258) | **46.0080** (6.9418) |
| $O - A2$ (subtype inc.) | | **51.7920** (7.3204) | **6.4720** (2.5920) | **8.0160** (2.9903) | **23.6880** (5.2147) | **25.1860** (5.7037) | **9.0360** (3.1321) | **25.4520** (4.8603) | **27.1200** (4.8910) |
| $O - A2$ (subtype comp.) | | **15.7080** (3.8330) | **2.2480** (1.4829) | **2.7940** (1.7509) | **15.7080** (3.8330) | **15.7080** (3.8330) | **3.0840** (1.8611) | **15.7080** (3.8330) | **15.7080** (3.8330) |
| $O - B$ | | **125.6440** (10.5425) | **15.6140** (3.8213) | **11.4060** (3.6600) | **25.0940** (6.4206) | **14.8680** (4.7783) | **10.9080** (3.4092) | **23.1160** (5.8202) | **19.3040** (5.1327) |
| $O - A1B$ | | **27.9400** (5.4321) | **1.0480** (1.1333) | **0.8180** (1.1133) | **0.7360** (1.0586) | **0.7140** (1.0838) | **0.3160** (0.6364) | **0.2980** (0.5270) | **0.2780** (0.5379) |
| $O - A2B$ | | **6.9740** (2.7159) | **0.2840** (0.5403) | **0.5640** (0.7792) | **0.1600** (0.4180) | **0.6560** (0.8289) | **0.4520** (0.6846) | **0.0860** (0.3013) | **0.8500** (0.8906) |
| $A - O$ | **268.2200** (15.0193) | **72.9260** (8.3058) | **42.5720** (6.4944) | **42.5720** (6.4944) | **42.5720** (6.4944) | **42.5720** (6.4944) | **42.5720** (6.4944) | **42.5720** (6.4944) | **42.5720** (6.4944) |
| $A - A1$ | **154.4480** (11.9961) | **41.6840** (6.4541) | **24.0900** (4.9127) | **24.1520** (4.8839) | **23.9940** (4.9151) | **24.0000** (4.9182) | **24.1800** (4.9087) | **23.9720** (4.9079) | **23.9720** (4.9079) |
| $A - A2$ | **38.8980** (6.2152) | **10.1460** (3.3019) | **5.8480** (2.5804) | **5.8320** (2.5902) | **5.9200** (2.5789) | **5.9200** (2.5789) | **5.8360** (2.5523) | **5.9200** (2.5789) | **5.9200** (2.5789) |
| $A - B$ | | **89.5340** (8.7918) | **76.4120** (7.2652) | **67.2600** (8.1389) | **71.2260** (8.1420) | **65.6220** (7.6577) | **75.9820** (7.2279) | **73.7380** (6.9693) | **71.7020** (7.0969) |
| $A - A1B$ | | **19.7340** (4.4052) | **2.4040** (1.4728) | **2.0400** (1.5580) | **1.6480** (1.3914) | **1.5880** (1.4221) | **1.9980** (1.5462) | **1.3020** (1.1548) | **1.2900** (1.1630) |
| $A - A2B$ | | **5.0040** (2.3313) | **0.6180** (0.7857) | **3.5800** (1.9625) | **0.4440** (0.6956) | **3.5220** (1.9466) | **4.1080** (2.1367) | **0.3380** (0.5731) | **3.7760** (1.9974) |
| $B - O$ | **97.6120** (9.5863) | **26.2360** (5.1856) | **15.4380** (3.7601) | **15.4380** (3.7601) | **15.4380** (3.7601) | **15.4380** (3.7601) | **15.4380** (3.7601) | **15.4380** (3.7601) | **15.4380** (3.7601) |
| $B - A1$ | | **69.9880** (7.9492) | **60.8940** (6.7840) | **63.1980** (7.5089) | **63.1300** (7.4318) | **63.2000** (7.5026) | **63.2160** (7.5368) | **63.1500** (7.4311) | **63.2020** (7.5048) |
| $B - A2$ (subtype inc.) | | **6.3500** (2.4972) | **4.6880** (2.1410) | **4.8280** (2.1973) | **4.8360** (2.2015) | **4.8360** (2.2015) | **4.8360** (2.2015) | **4.8360** (2.2015) | **4.8360** (2.2015) |
| $B - A2$ (subtype comp.) | | **11.0540** (3.2018) | **10.5180** (3.0621) | **11.0540** (3.2018) | **10.8980** (3.1660) | **11.0540** (3.2018) | **11.0540** (3.2018) | **10.8980** (3.1660) | **11.0540** (3.2018) |
| $B - B$ | **27.9140** (5.4105) | **7.4760** (2.7026) | **4.0640** (2.1830) | **4.1820** (2.1722) | **4.0380** (2.1702) | **4.1000** (2.1576) | **4.4020** (2.1647) | **4.0020** (2.1660) | **4.3620** (2.1809) |
| $B - A1B$ | | **7.6160** (2.7763) | **0.9800** (1.0304) | **1.4060** (1.1366) | **1.0540** (1.0475) | **1.3520** (1.1811) | **1.3460** (1.1666) | **0.9860** (1.0373) | **1.3060** (1.1502) |
| $B - A2B$ (subtype inc.) | | **0.7640** (0.8705) | **0.0800** (0.2716) | **0.5500** (0.7270) | **0.0880** (0.3040) | **0.5500** (0.7407) | **0.5740** (0.7548) | **0.0800** (0.2859) | **0.5720** (0.7576) |
| $B - A2B$ (subtype comp.) | | **1.1260** (0.9839) | **0.1640** (0.3917) | **1.1260** (0.9839) | **0.1720** (0.4083) | **1.1260** (0.9839) | **1.1260** (0.9839) | **0.1560** (0.3847) | **1.1260** (0.9839) |
| $AB - O$ | **26.9920** (4.9656) | **7.4660** (2.5896) | **4.3440** (2.0134) | **4.3440** (2.0134) | **4.3440** (2.0134) | **4.3440** (2.0134) | **4.3440** (2.0134) | **4.3440** (2.0134) | **4.3440** (2.0134) |
| $AB - A1$ | **15.0560** (3.9002) | **4.1440** (2.0366) | **2.3920** (1.5241) | **2.3920** (1.5241) | **2.3920** (1.5241) | **2.3920** (1.5241) | **2.3920** (1.5241) | **2.3920** (1.5241) | **2.3920** (1.5241) |
| $AB - A2$ | **3.9220** (2.0120) | **1.0900** (1.0354) | **0.6080** (0.7665) | **0.6080** (0.7665) | **0.6080** (0.7665) | **0.6080** (0.7665) | **0.6080** (0.7665) | **0.6080** (0.7665) | **0.6080** (0.7665) |
| $AB - B$ | **7.4720** (2.6128) | **1.9940** (1.4636) | **1.1820** (1.1293) | **1.1820** (1.1293) | **1.1820** (1.1293) | **1.1800** (1.1234) | **1.1820** (1.1293) | **1.1820** (1.1293) | **1.1820** (1.1293) |
| $AB - A1B$ | **1.6200** (1.3233) | **0.4420** (0.6749) | **0.1500** (0.4380) | **0.1140** (0.4164) | **0.1280** (0.4195) | **0.1200** (0.4218) | **0.1200** (0.4218) | **0.1200** (0.4122) | **0.1160** (0.4182) |
| $AB - A2B$ | **0.3560** (0.5709) | **0.1460** (0.3646) | **0.0500** (0.2182) | **0.0900** (0.2865) | **0.0420** (0.2008) | **0.0900** (0.2865) | **0.0900** (0.2865) | **0.0440** (0.2053) | **0.0900** (0.2865) |
| **TOTAL** | **1015.200** (23.2186) | **984.800** (23.2186) | **376.700** (22.3124 ) | **374.6160** (23.1654) | **424.852** (25.9950) | **416.260** (25.4372) | **384.238** (23.1129) | **425.374** (25.9735) | **428.012** (26.1527) |

Table 6: Averages for **two-way exchanges** (Table 2) broken down according to pair types

| Pair Types (Patient-Donor) | Total Number of Pairs | | Number of Pairs Matched in Two&three-way Exchange out of $n = 500$ Pairs | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1. Without $A$ subtype matching | 2. With $A$ subtype matching | | | | | | |
| | | | | (a) $A$ subtype test done **before** participation decision in exchange | | | (b) $A$ subtype test done **after** participation decision in exchange | | | |
| | Comp. (w/o $A$ subtype matching) | Inc. (w/o $A$ subtype matching) | | i. $A2/A2B \to B$ only | ii. $A2 \to O$ only | iii. $A2/A2B \to B$ and $A2 \to O$ | i. $A2/A2B \to B$ only | ii. $A2 \to O$ only | iii. $A2/A2B \to B$ and $A2 \to O$ |
| $O-O$ | **93.5140** (8.8839) | **25.7380** (5.0842) | **15.0540** (3.8252) | **15.0540** (3.8252) | **15.0540** (3.8252) | **15.0540** (3.8252) | **15.0540** (3.8252) | **15.0540** (3.8252) | **15.0540** (3.8252) |
| $O-A1$ | | **67.4540** (7.8147) | **8.7260** (4.5471) | **10.8300** (3.7552) | **16.2260** (5.4518) | **15.8220** (4.9213) | **10.3540** (3.8007) | **16.2280** (5.4331) | **16.9140** (5.3325) |
| $O-A2$ (subtype inc.) | | **12.8660** (3.4843) | **1.6300** (1.3744) | **2.4040** (1.5315) | **10.9800** (3.0289) | **11.0480** (3.0582) | **2.3720** (1.5870) | **11.0200** (3.0447) | **11.0800** (3.0660) |
| $O-A2$ (subtype comp.) | | **3.8840** (1.9540) | **0.5720** (0.7733) | **0.8220** (0.8831) | **3.8840** (1.9540) | **3.8840** (1.9540) | **0.8200** (0.9345) | **3.8840** (1.9540) | **3.8840** (1.9540) |
| $O-B$ | | **31.4640** (5.3988) | **4.8080** (4.8549) | **1.6160** (2.3340) | **4.9720** (4.9708) | **2.5760** (3.6208) | **2.1180** (2.6733) | **4.9560** (4.9176) | **4.0120** (4.4298) |
| $O-A1B$ | | **6.9220** (2.5677) | **0.0020** (0.0447) | **0.0020** (0.0447) | **0.0080** (0.0892) | **0.0060** (0.0773) | **0.0080** (0.0892) | **0.0100** (0.0996) | **0.0180** (0.1331) |
| $O-A2B$ | | **1.6600** (1.2711) | **0.0000** (0.0000) | **0.0720** (0.2810) | **0.0000** (0.0000) | **0.1200** (0.3433) | **0.0780** (0.3035) | **0.0020** (0.0447) | **0.1840** (0.4411) |
| $A-O$ | **67.1660** (7.5142) | **18.4060** (4.2972) | **10.7540** (3.2109) | **10.7540** (3.2109) | **10.7540** (3.2109) | **10.7540** (3.2109) | **10.7540** (3.2109) | **10.7540** (3.2109) | **10.7540** (3.2109) |
| $A-A1$ | **38.0680** (6.1991) | **10.3020** (3.1999) | **5.9600** (2.4037) | **5.9600** (2.4037) | **5.9600** (2.4037) | **5.9600** (2.4037) | **5.9600** (2.4037) | **5.9600** (2.4037) | **5.9600** (2.4037) |
| $A-A2$ | **9.7780** (3.0337) | **2.5620** (1.5885) | **1.5020** (1.2120) | **1.5020** (1.2120) | **1.5020** (1.2120) | **1.5020** (1.2120) | **1.5020** (1.2120) | **1.5020** (1.2120) | **1.5020** (1.2120) |
| $A-B$ | | **22.4280** (4.5030) | **19.3020** (3.7899) | **18.0800** (3.5489) | **19.2320** (3.7489) | **17.9980** (3.5501) | **19.0480** (3.6999) | **19.2180** (3.7441) | **18.9340** (3.6716) |
| $A-A1B$ | | **4.9020** (2.2527) | **0.8660** (1.0030) | **0.8980** (1.0686) | **0.8260** (0.9724) | **0.9400** (1.0839) | **1.0200** (1.1464) | **0.8600** (1.0249) | **1.0440** (1.1228) |
| $A-A2B$ | | **1.2940** (1.0798) | **0.2620** (0.5195) | **1.0160** (0.9621) | **0.2820** (0.5469) | **1.0440** (0.9777) | **1.0980** (1.0012) | **0.2620** (0.5156) | **1.1080** (1.0171) |
| $B-O$ | **24.3260** (4.8994) | **6.6460** (2.5647) | **3.8920** (1.9961) | **3.8920** (1.9961) | **3.8920** (1.9961) | **3.8920** (1.9961) | **3.8920** (1.9961) | **3.8920** (1.9961) | **3.8920** (1.9961) |
| $B-A1$ | | **17.4860** (4.2234) | **15.6940** (3.8275) | **15.8100** (3.9579) | **15.7420** (3.8732) | **15.8000** (3.9491) | **15.8120** (3.9618) | **15.7280** (3.8585) | **15.7820** (3.9086) |
| $B-A2$ (subtype inc.) | | **1.5220** (1.3164) | **1.1600** (1.1406) | **1.1660** (1.1459) | **1.1660** (1.1459) | **1.1660** (1.1459) | **1.1660** (1.1459) | **1.1660** (1.1459) | **1.1660** (1.1459) |
| $B-A2$ (subtype comp.) | | **2.7180** (1.6492) | **2.6600** (1.6117) | **2.7180** (1.6492) | **2.6820** (1.6402) | **2.7180** (1.6492) | **2.7180** (1.6492) | **2.6820** (1.6402) | **2.7180** (1.6492) |
| $B-B$ | **6.8540** (2.5718) | **1.8440** (1.3621) | **1.1020** (1.0439) | **1.1020** (1.0439) | **1.1020** (1.0439) | **1.1020** (1.0439) | **1.1020** (1.0439) | **1.1020** (1.0439) | **1.1020** (1.0439) |
| $B-A1B$ | | **1.8880** (1.3825) | **0.5940** (0.7226) | **0.7900** (0.8362) | **0.5940** (0.7578) | **0.7380** (0.7991) | **0.7300** (0.7965) | **0.5780** (0.7273) | **0.7360** (0.7820) |
| $B-A2B$ (subtype inc.) | | **0.2280** (0.4565) | **0.0640** (0.2450) | **0.1800** (0.4049) | **0.0600** (0.2377) | **0.1800** (0.4049) | **0.1800** (0.4049) | **0.0680** (0.2520) | **0.1800** (0.4049) |
| $B-A2B$ (subtype comp.) | | **0.2960** (0.5338) | **0.0840** (0.2777) | **0.2960** (0.5338) | **0.1160** (0.3388) | **0.2960** (0.5338) | **0.2960** (0.5338) | **0.1060** (0.3209) | **0.2960** (0.5338) |
| $AB-O$ | **6.7020** (2.4774) | **1.8900** (1.4135) | **1.1080** (1.1220) | **1.1080** (1.1220) | **1.1080** (1.1220) | **1.1080** (1.1220) | **1.1080** (1.1220) | **1.1080** (1.1220) | **1.1080** (1.1220) |
| $AB-A1$ | **3.8900** (1.8903) | **1.0560** (1.0426) | **0.6180** (0.7676) | **0.6180** (0.7676) | **0.6180** (0.7676) | **0.6180** (0.7676) | **0.6180** (0.7676) | **0.6180** (0.7676) | **0.6180** (0.7676) |
| $AB-A2$ | **0.9940** (1.0100) | **0.3060** (0.5186) | **0.1520** (0.3863) | **0.1520** (0.3863) | **0.1520** (0.3863) | **0.1520** (0.3863) | **0.1520** (0.3863) | **0.1520** (0.3863) | **0.1520** (0.3863) |
| $AB-B$ | **1.7620** (1.2444) | **0.5100** (0.7006) | **0.3060** (0.5412) | **0.3060** (0.5412) | **0.3060** (0.5412) | **0.3060** (0.5412) | **0.3060** (0.5412) | **0.3060** (0.5412) | **0.3060** (0.5412) |
| $AB-A1B$ | **0.4360** (0.6684) | **0.1060** (0.3391) | **0.0600** (0.2540) | **0.0580** (0.2505) | **0.0520** (0.2396) | **0.0600** (0.2540) | **0.0580** (0.2505) | **0.0560** (0.2470) | **0.0580** (0.2505) |
| $AB-A2B$ | **0.0800** (0.2996) | **0.0520** (0.2222) | **0.0240** (0.1532) | **0.0340** (0.1814) | **0.0220** (0.1468) | **0.0340** (0.1814) | **0.0340** (0.1814) | **0.0200** (0.1401) | **0.0340** (0.1814) |
| **TOTAL** | **253.570** (23.2186) | **246.430** (23.2186) | **96.956** (11.6453 ) | **97.240** (12.0308) | **117.292** (12.9746) | **114.878** (13.1884) | **98.358** (11.6661) | **117.292** (12.9746) | **118.596** (13.0767) |

Table 7: Averages for **two&three-way exchanges** (Table 6) broken down according to pair types

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