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Kidney Exchange With Immunosuppressants

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Abstract

We investigate the implications of introducing immunosuppressants to the kidney exchange problem. Immunosuppressants relax biological constraints between patients and donors, allowing patients to receive transplants from any donor. Given the limited availability, we propose how to assign immunosuppressants and how to match patients to donors to facilitate transplants. We ask whether there exist Pareto efficient solutions that satisfy additional requirements of monotonicity and maximal improvement. We propose modifications of the top-trading cycles solutions to achieve these requirements. To quantify the welfare improvement as per our proposal, we conduct counterfactual analyses using transplant data from South Korea. Our result suggests that the current use of immunosuppressants could have been reduced by 55 percent.

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Keywords: immunosuppressants, kidney exchange, top-trading cycles rules, Pareto efficiency, monotonicity, maximal improvement

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1. Introduction

When a patient suffers from end-stage renal disease and has to receive a kidney transplant, several options are available depending on the immunological compatibility of the patient with her own donor.[1] If the patient is compatible with the donor, a direct transplant within this pair can be performed. Otherwise, the patient has to look for other ways to receive a transplant. One option is that the patient is registered on a waitlist to receive a transplant from a deceased donor. Another option, developed in the last decade, is to participate in a kidney exchange program where patients swap their donors to form compatible pairs (Roth et al., 2004). Unfortunately, the possibility of receiving transplants from deceased donors or through exchanges is quite limited relative to the increasing number of patients in the waitlist, as illustrated in Table 1 of data from the KONOS (Korean Network for Organ Sharing) program.

Recent developments in immunosuppressive protocols have introduced a new option for transplants from *incompatible* donors. Immunosuppressants (suppressants, for short) have been commonly used to prevent rejections after compatible transplants. Since 1980s, they have been developed to eliminate blood-type compatibility constraints (Alexander et al., 1987) and more recently, they are being used to eliminate *all* immunological compatibility constraints – blood-type, tissue-type, and positive crossmatch – that patients might have against donors (Gloor et al. (2003), Kawai et al. (2008), and Montgomery et al. (2011)). If a patient uses a suppressant, she becomes compatible with *any* donor, so is able to receive a transplant even from an incompatible donor, which we call an *incompatible kidney transplant*.

To receive an incompatible transplant, a patient takes rituximab, an immunosuppressive drug inactivating a part of white blood cells, and receives a plasmapheresis treatment to remove certain antibodies from the blood. Intravenous immunoglobulin (IVIG) is also added to prevent potential infections. Although a precise timing of this procedure and the dose of drugs may vary across patients, incompatible transplants have been reported quite successful. For blood-type incompatible transplants, the long-term survival rate is shown equivalent to that of compatible transplants.[2] The tissue-type incompatible transplants and transplants with positive crossmatch are also reported quite satisfactory and regarded as good alternatives of standard transplants or dialysis.[3]

In recent years, the number of patients using suppressants has increased in many countries. In Korea, for example, the proportion of blood-type incompatible kidney transplants has increased from 4.7 percent

[1] Immunological compatibility is mostly determined by biological characteristics of patients and donors, such as ABO blood types, tissue (Human Leukocyte Antigen; HLA) types, and the crossmatch. The ABO blood type is determined by the inherited antigenic substances on the surface of red blood cells. For example, if a patient's antigen is type A, then her blood type is type A and her antibody is type B; if a patient's antigen is type AB, then blood type is AB and she has no antibody. A patient with antibody of type X cannot receive a transplant from a donor with type X antigen. For example, if a person's blood type is A, then her antibody is type B, and thus, she cannot receive a transplant from any donor having a type B antigen, namely, blood types B and AB. Similarly, if a person's blood type is O, then her antibodies are types A and B; therefore, she cannot receive a transplant from any donor of blood types A, B, or AB. The tissue (HLA) type is determined by a patient's and a donor's HLAs, which are proteins on the surface of cells that are responsible for immunological responses. If the patient and the donor have the same HLAs, they are called an *identical match*, which is rare between unrelated persons because the number of possible combinations of HLAs is very large. For more information, see the Genetics Home Reference website, provided by the U.S. National Library of Medicine, at http://ghr.nlm.nih.gov/geneFamily/hla. A patient's antibodies and a donor's HLAs also determine the "crossmatch": If the crossmatch is positive, then the patient's antibodies react to the donor's HLAs, thereby making a transplant unsuccessful.

[2] According to the KONOS Annual Report in 2014, the five-year survival rate of ABO-incompatible living-donor kidney transplants is 95.2 percent and that of ABO-compatible living-donor kidney transplants is 96.4 percent. Other papers show similar results: Takahashi et al. (2004), Tyden et al. (2007), Montgomery et al. (2012), and Kong et al. (2013).

[3] For tissue-type incompatible transplants, see Kawai et al. (2008), Montogomery et al. (2011), and Laging et al. (2014). For transplants with positive crossmatch, see Gloor et al. (2003), Thielke et al. (2009), and Jin et al. (2012).

Table 1: Kidney transplantation in Korea.

Year	Patients in waitlists	Total transplants	Transplants from deceased donors	Transplants from living donors
2009	4,769	1,238	488	750
2010	5,857	1,287	491	796
2011	7,426	1,639	680	959
2012	9,245	1,788	768	1,020
2013	11,381	1,761	750	1,011
2014	13,612	1,808	808	1,000

Table 2: Three types of living-donor kidney transplants in Korea.

Year	Transplants from living donors	Direct transplants of ABOc pairs	Direct transplants of ABOi pairs	Exchange transplants
2009	750	675 (90.0%)	35 (4.7%)	40 (5.3%)
2010	796	689 (86.6%)	78 (9.8%)	29 (3.6%)
2011	959	828 (86.3%)	113 (11.8%)	18 (1.9%)
2012	1,020	827 (81.1%)	193 (18.9%)	0 (0.0%)
2013	1,011	795 (78.6%)	212 (21.0%)	4 (0.4%)
2014	1,000	783 (78.3%)	212 (21.2%)	5 (0.5%)

(ABOc means blood-type compatible; ABOi means blood-type incompatible.)

to 21.2 percent of the total living-donor transplants during 2009-2014, as shown in Table 2.[4] In contrast, the proportion of transplants through kidney exchanges has decreased from 5.3 percent to nearly 0 percent during the same period. The proportion of compatible transplants has also decreased by more than 10 percent. As can be seen, suppressants have largely replaced other types of living-donor transplants in Korea.

As the number of patients using suppressants increases, the expenditure of the National Health Insurance Service (NHIS) to subsidize these incompatible transplants also increases. Since the NHIS has a limited budget, we should ask how suppressants are currently being used and if there is a better way to use suppressants to facilitate transplants.

In this paper, we propose to use suppressants as a part of the kidney exchange program. For an illustration, consider an example in which compatibility is determined only by ABO blood type. A pair consists of a patient and a donor, X-Y, where the patient's blood type is X and the donor's type is Y. Suppose that there are three pairs: A-B, B-AB, and O-AB. Due to the immunological constraints, a patient of type A can receive a transplant only from a donor of type A or O, a patient of type B can receive a transplant only from a donor of type B or O, and a patient of type O can receive a transplant only from a donor of type O.

Because each patient is incompatible with her own donor, in the absence of suppressants, each of them can only receive a transplant from someone else. In a kidney exchange program, on the other hand, the patients swap their donors to form compatible pairs. Unfortunately, in this example, no such exchanges

[4]This sharp increase is partly because the NHIS of Korea has covered a large fraction of the total cost of suppressants since 2009. Patients pay a small share of the total cost, as low as 20 percent depending on their medical conditions. The cost of suppressants in Sweden, Germany, and Japan is also covered by the public health insurance to a large extent.

are possible, because the patients in the A-B and O-AB pairs are incompatible with all three donors.

Now suppose that at most two patients can use suppressants. One easy way to use suppressants is to choose any two patients as recipients and have them receive transplants directly from their own donors. In the example, for instance, the patients in the B-AB and O-AB pairs can be provided suppressants and receive direct transplants from their donors, in which case, the patient in the remaining A-B pair does not receive a transplant. This is how suppressants are currently used in South Korea, which is summarized in the fourth column of Table 2.

However, there is a better way to use suppressants, which enables all patients to receive transplants. Indeed, the pairs A-B and B-AB form a "chain" in a sense that the donor in the A-B pair is compatible with the patient in the B-AB pair, while the remaining patient of type A and the remaining donor of type AB are not compatible. Such a chain can be viewed as a trading cycle with a "missing link": If the donor in the B-AB pair and the patient in the A-B pair were compatible, these pairs would have formed a cycle along which they could swap donors and form compatible pairs. Providing a suppressant to the patient of type A fills in this missing link and transforms the chain into a trading cycle between A-B and B-AB. Then, the patient of type B receives a transplant from the donor of type B and the patient of type A receives a transplant from the donor of type AB, the latter transplant being made possible by the use of a suppressant. The remaining suppressant can now be provided to the patient in the O-AB pair so that she receives an incompatible transplant from her own donor.

A key feature of our proposal is that patient-donor pairs, who *become* compatible through the use of suppressants, still participate in the kidney exchange pool. Note that in the example, when the patient in the A-B pair uses a suppressant, she can receive a transplant directly from her own donor, and so need not participate in the exchange program. Nevertheless, the participation of this pair can eventually benefit all participants: the patient in the B-AB pair now receives a compatible transplant and the patients in the A-B and O-AB pairs receive incompatible transplants. Provided that it does not make a significant difference from whom a patient receives a transplant when using a suppressant, the pair A-B would be willing to participate in the exchange program, especially given that the patient in this pair has to use a suppressant anyway to receive a transplant. Such an "altruistic" participation of compatible pairs has also been studied in the standard kidney exchange context (Sönmez and Ünver (2014), Roth et al. (2005), and Gentry et al. (2007)).[5]

We begin with the standard kidney exchange model without suppressants as a benchmark. We introduce two Top-Trading Cycles rules (TTCs) associated with a priority ordering over patients.[6] Both rules are defined by means of an algorithm in which patient-donor pairs form trading cycles in each step. In our setting, however, there can be multiple overlapping cycles because preferences are coarse. For each

[5]The term "altruistic pairs" in Sönmez and Ünver (2014) refers to compatible pairs who participate in a kidney exchange even though a direct transplant between themselves is possible. Because participation is voluntary, our proposal further prevents a negative externality that tissue-type suppressants may have on kidney exchange programs. As Sönmez and Ünver (2013) have observed, when tissue-type suppressants become available, the shortage of donors of a particular blood type – usually, blood type O – can get even worse. This is because type O donors are blood-type compatible with all patients and therefore appear in the exchange pool only when they are tissue-type incompatible with their own patients. Therefore, as tissue-type suppressants become available, these donors can be crowded out from the exchange program. In our proposal, however, all donors in incompatible pairs stay in the pool even after their patients use any types of suppressants.

[6]Shapley and Scarf (1974) propose TTC for a general model with indivisible goods. Roth et al. (2004) develop TTC for the kidney exchange problem by considering chains formed with patients on the waitlist. As in Roth et al. (2004), we impose no constraint on the size of cycles in kidney exchanges. For more discussion on the size of exchanges, see Roth et al. (2007) and Saidman et al. (2006).

rule, we propose how to choose trading cycles when there are multiple.

We next extend the model by introducing suppressants. To accommodate the limited availability of suppressants, we assume that at most K patients can use the suppressants. For each compatibility profile of patients and donors, we first determine which patients are to receive the suppressants. We update the compatibility profile accordingly, as the recipients of suppressants become compatible with any other donors. Based on this new profile, we lastly choose matchings between patients and donors.

As there are many ways to implement our idea of identifying chains and transforming them to cycles, we consider additional requirements to better use suppressants. We first consider efficiency for matching. *Pareto efficiency* says that for any assignment of suppressants and the corresponding compatibility profile, there should be no other matching that makes all patients weakly better off and at least one patient strictly better off.

We also define efficiency for the assignment of suppressants: suppressants should be used so as to maximize the transplants. We introduce two variants of this idea depending on how we define "maximal" transplants. Consider two groups of potential recipients. Identify the sets of patients receiving transplants when each group is provided suppressants. *Maximal improvement* requires that if the first group enables more transplants than the other in terms of *set inclusion*, then the latter group should not be chosen as recipients of suppressants. *Cardinally maximal improvement* modifies this requirement by comparing the *total number of transplants* that they facilitate, rather than comparing them in terms of set inclusion.

In addition to efficiency, we consider a requirement that no patient be made worse off by the availability of suppressants. We regard this requirement as fairness, as it says that no participant has to be penalized by introducing this new technology. This is especially so when no patient is responsible for the development of transplant technologies. If a patient gets worse off than before, while some others benefit, she would find it unfair. This idea, often referred to as "solidarity", has been studied extensively in various resource allocation problems.[7] More broadly, this requirement can also be viewed as a necessary condition to reach a consensus on an "institutional" change in kidney transplantation problem. We are proposing a new system for transplants by introducing suppressants: a patient would agree to switch to it only if she is not made worse off than before. We call this requirement "monotonicity" and define its two variants. *Strong monotonicity* requires all patients to be weakly better off after suppressants are introduced, *no matter who receives them*. In contrast, *monotonicity* requires that there be *some* way of allocating suppressants so that all patients become weakly better off.

We check the compatibility of these requirements. Our first result is that Pareto efficiency and strong monotonicity are incompatible. The second result is that even if strong monotonicity is weakened to monotonicity, we cannot satisfy it together with Pareto efficiency and cardinally maximal improvement.

In view of these impossibilities, we weaken cardinally maximal improvement to maximal improvement and ask if this weaker requirement is compatible with Pareto efficiency and monotonicity. To show that it is, we introduce two solutions by modifying TTCs defined earlier. Each solution operates in four steps. First, apply a TTC to the initial compatibility profile, assuming that no one uses suppressant. No actual allocation is made at this step, but identify the set of patients who are to receive no transplants.

[7]For a detailed survey on solidarity or monotonicity requirements, see Thomson (2013). The underlying idea of these requirements is that all agents' welfare has to be affected in the same direction – either all worse off or all better off – when there is an exogenous change in the economy. The exogenous changes can be variable populations ("population monotonicity"), a change in the available resource ("resource monotonicity"), or the introduction of a new technology that we consider in this paper.

Second, modify the initial priority ordering so that the patients identified in the previous step have lower priorities than the other patients. Third, choose the recipients of suppressants. This is done by selecting cycles and chains according to the modified priority ordering. The patients at the head of these chains are provided suppressants. Finally, update the compatibility profile and apply TTC associated with the modified priority ordering to this profile.

As this solution satisfies monotonicity, any patient who could initially receive a compatible transplant in the absence of suppressants will receive a transplant again in the presence of suppressants – but possibly, an incompatible transplant. We further refine monotonicity and check if it is possible to guarantee that this patient receives a *compatible* transplant in the presence of suppressants. We show that a subsolution of the aforementioned TTC solution satisfies this refined requirement.

To assess the welfare improvement as per our proposal, we conduct a simple counterfactual analysis using the recent transplant data. The use of suppressants for incompatible transplants is a relatively new phenomenon and, as yet, there are not much data. However, the KONOS data set from South Korea is an exception. It collects all pairs who received living-donor kidney transplants, either compatible or incompatible, as well as their blood-type profile during the four-year period (2011-2014). Using this information, we show that our proposal could have made a significant improvement from the current practice.[8]

Unfortunately, there are two restrictions that make it hard to apply our theoretical results directly to the data. First, the KONOS only publishes the blood-type profile of the patient-donor pairs, but other biological information – such as tissue-type or crossmatch – is not available. We therefore simplify the model by assuming that compatibility is determined only by blood-types. This is an assumption adopted in other kidney exchange papers and regarded acceptable in a large exchange pool (Roth et al. (2007) and Sönmez et al. (2016)). Although we do not put any restrictions on the size of chains and cycles, this assumption results in a limited variety of cycles and chains. Second, the KONOS can only collect the pairs whose patients *already* received transplants. Before patients receive transplants, their donors remain unidentified; only after transplants are operated, the patient-donor pairs are added to the KONOS data and become identifiable as pairs. As we do not have the information of the entire population in the exchange pool, we cannot directly apply our TTC solutions defined earlier.

We still implement the idea of transforming chains to cycles by using suppressants in this analysis, but we introduce a "dual" problem to overcome these restrictions. Instead of maximizing transplants as the TTC solutions do, we aim to minimize the use of suppressants, given a target group of patients receiving transplants. We first identify all pairs in the data who have used suppressants for incompatible transplants. Taking these patients as a target group for transplants, we minimize the use of suppressants. Our results show that only 340 patients have to use suppressants as per our proposal, whereas 757 patients actually used suppressants in the KONOS data. This is a reduction of 55.1 percent, which is confirmed by our robustness check.

The literature on kidney exchange stems from the seminal work by Roth et al. (2004) and most papers have taken the compatibility profile as a fixed primitive of the problem. More recently, possible changes of compatibility profile are taken into considerations due to the technological advances in medical science. A

[8]In this paper, we make use of the KONOS data as much as possible to measure the welfare improvement. An alternative approach, when there is no available data, is to run simulations on hypothetical populations. Sönmez et al. (2016) and Andersson and Kratz (2016) provide good examples of this approach in kidney exchange problems.

recent paper by Andersson and Kratz (2016) deepens our understanding of suppressants from a different perspective, complementing our analysis. When suppressants are used to relax blood-type incompatibility only – but not tissue-type incompatibility – and the supply is *unlimited*, they provide a way to minimize the use of suppressants, while maintaining the maximal number of transplants. Sönmez et al. (2016) is also closely related to ours, as they consider a "blood subtyping" technology that enables transplants between certain incompatible blood-types. This technology is different from suppressants, however, in that it is used for *all* patients to identify more detailed biological characteristics once adopted in practice. They analyze the welfare impact of this technology on kidney exchanges by calculating a possible increase of transplants as well as a potential negative externality.

The rest of this paper is organized as follows. Section 2 introduces the standard kidney exchange model without suppressants and defines two versions of TTC. Section 3 extends the model by introducing suppressants and establishes our two impossibility results. Section 4 defines two modifications of TTC and studies their properties. Section 5 presents our counterfactual analyses based on Korean experience. Section 6 adds a few concluding remarks.

2. Kidney Exchange Model without Immunosuppressants

There is a finite set N of patient-donor pairs. Let n be the number of pairs in N. Each pair i consists of patient i and donor i. A patient is either compatible or incompatible with a donor depending on immunological characteristics. Patient i has a dichotomous preference R_i over the pairs: She prefers pairs whose donors are compatible with her to pairs with incompatible ones; all pairs with incompatible donors are equally desirable and so are all pairs with compatible donors. For simplicity, we can only specify pairs with compatible donors in each patient's preference list. A kidney exchange problem, or simply a **problem**, is defined as a preference profile $R = (R_i)_{i \in N}$.[9]

We introduce a graph whose nodes are the pairs in N. A graph is a collection of directed arcs between the nodes. If patient i is compatible with donor j, we draw a directed arc $j \to i$ to represent a possible transplant from donor j to patient i. We allow self-directed arcs for patients who are compatible with their own donors. Each problem is then represented as a graph.

A list of distinct pairs $i_1, \ldots, i_k$ forms a **cycle** if $i_1 \to i_2 \to \cdots \to i_k \to i_1$. Note that the smallest possible cycle is a self-cycle $i \to i$. Similarly, a list of distinct pairs $i_1, \ldots, i_k$ forms a **chain** if $i_1 \to i_2 \to \cdots \to i_k$ and patient i_1 is incompatible with donor i_k, i.e., $\neg(i_k \to i_1)$. Given a chain $i_1 \to i_2 \to \cdots \to i_k$, patient i_1 is called the **head** of this chain. We say that a collection of cycles are **jointly feasible** if no pair appears in more than one cycle. Similarly, a collection of cycles and chains are **jointly feasible** if no pair appears in more than one chain or cycle. For each R, let $\mathcal{C}(R)$ be the collection of all sets of jointly feasible cycles and let $\mathcal{H}(R)$ be the collection of all sets of jointly feasible cycles and chains.

Example 1. Consider the following problem with three pairs:

R_1	R_2	R_3
2	1, 3	2, 3

[9] Bogomolnaia and Moulin (2004) study dichotomous preferences in a general matching context. They examine randomized matchings to achieve efficiency, fairness, and strategic requirements when only two-way exchanges are allowed.

Let $R = (R_1, R_2, R_3)$. Each patient is compatible with the donors listed in her preference list. There are three cycles, $1 \to 2 \to 1$, $2 \to 3 \to 2$, and $3 \to 3$. The first and the third cycles are jointly feasible, so the set consisting of these cycles is in $\mathcal{C}(R)$. There are four chains, 1, 2, $1 \to 2 \to 3$, and $3 \to 2 \to 1$. The chain composed of pair 1 and the cycle composed of pairs 2 and 3 are jointly feasible, so the set consisting of this chain and this cycle is in $\mathcal{H}(R)$.

A matching specifies which patient is matched to which donor. Each patient is matched either to a compatible donor or to her own incompatible donor. A patient receives a transplant if and only if she is matched to a compatible donor. A patient (weakly) prefers a matching to another if and only if she (weakly) prefers the donor matched at the former to the donor matched at the latter.

Each pair is given a certain priority according to a linear ordering over N.[10] We denote this linear ordering by $\succ$ and write $i \succ j$ if and only if patient i has a higher priority than patient j.

A matching rule determines the set of matchings for each problem. Let φ be a generic matching rule. A matching rule is *essentially single-valued* if all matchings chosen for each problem are equally desirable for all patients. In other words, patients receiving transplants are the same across all matchings chosen for each problem.

A matching is *Pareto efficient* at a preference profile if there is no other matching that is weakly preferred by all patients and is strictly preferred by at least one patient. A matching rule is *Pareto efficient* if it selects *Pareto efficient* matchings for each problem. We now define Top-Trading Cycles (TTC) rules adapted to this model.[11]

> **Top-trading cycles rule associated with** $\succ$ (simply, $TTC_\succ$):
>
> Let $\mathcal{C}_0$ be the collection of all sets of jointly feasible cycles. If there is none, all patients are matched to their own donors. Otherwise, proceed to the following step.
>
> **Step** t (≥ 1): In $\mathcal{C}_{t-1}$, identify all sets of jointly feasible cycles including the patient with the t-th highest priority at $\succ$. If there is such a set, let $\mathcal{C}_t$ be the collection of all these sets. Otherwise, let $\mathcal{C}_t \equiv \mathcal{C}_{t-1}$.
>
> This process terminates at Step n. For each set in $\mathcal{C}_n$, all patients in the cycles of this set are matched to the donors along the directed arcs. All other patients are matched to their own donors.

Note that this rule can be viewed as a "sequential priority" rule since we first identify all matchings at which the patient with the highest priority receives a transplant, then all matchings at which the patient with the second highest priority does, and so on. If patients are restricted to participate in only two-way exchanges, such a sequential priority rule is *Pareto efficient* and maximizes the number of transplants.[12] If we allow more than two-way exchanges, however, *Pareto efficient* matchings do not necessarily maximize the number of transplants. Given this, we formulate another version of the TTC rule.

[10] For more detailed discussion on these priorities, see Roth et al. (2005).

[11] For related studies on TTC rules, see Jaramillo and Manjunath (2012), Alcalde-Unzu and Molis (2011), and Saban and Sethuraman (2013).

[12] The structure of matchings that maximize the number of transplants is studied in Bogomolnaia and Moulin (2004) and Roth et al. (2005) when all cycles consist of at most two pairs. To identify such matchings, Okumura (2014) and Andersson and Kratz (2016) introduce weighted graphs using priorities.

Top-trading cycles rule maximizing the number of transplants (simply, $\overline{TTC}_{\succ}$):

Let $\mathcal{C}_0$ be the collection of all sets of jointly feasible cycles maximizing the number of transplants. If there is none, all patients are matched to their own donors. Otherwise, proceed to the steps described above when defining $TTC_{\succ}$.

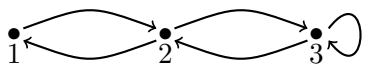
Proposition 1. *For every priority ordering $\succ$, $TTC_{\succ}$ and $\overline{TTC}_{\succ}$ are essentially single-valued and Pareto efficient.*

3. Kidney Exchange Model with Immunosuppressants

We introduce suppressants to the standard kidney exchange model. If patient i receives a suppressant, she becomes compatible with all donors, including her own. We denote by R_i^* the preference of patient i after receiving a suppressant. For each $S \subseteq N$, let $R_S^* \equiv (R_i^*)_{i \in S}$. For each problem R and each $S \subseteq N$, let $R(S) \equiv (R_S^*, R_{-S})$ denote the preference profile derived from R when patients in S receive suppressants. All definitions in the previous section carry over to this setting by replacing R with $R(S)$.

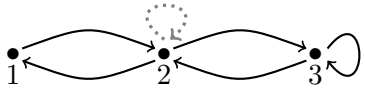
Example 2. (Example 1 continued) The problem in Example 1 is given as follows:

R_1	R_2	R_3
2	1, 3	2, 3



Now suppose that patient 2 uses a suppressant. Then, the problem changes into:

R_1	R_2^*	R_3
2	1, 2, 3	2, 3



Now, there is one additional cycle, $2 \to 2$, while a chain composed of pair 2 disappears. All other three cycles and three chains remain the same.

To accommodate the limited availability of suppressants, we introduce a non-negative integer K, an upper bound on the number of patients receiving suppressants. If $K = 0$, this model coincides with the standard kidney exchange model.

A **solution** of this model is now defined as a pair of a **recipient choice rule**, which selects at most K recipients of suppressants for each problem, and a **matching rule**, which selects matchings after updating these recipients' preferences. Let (σ, φ) be a generic solution where σ is a recipient choice rule and φ is a matching rule. For each problem R, patients in $\sigma(R)$ are provided suppressants and the problem changes to $R(\sigma(R))$. The resulting matchings are given as $\varphi(R(\sigma(R))$. Let $\varphi^\sigma(R) \equiv \varphi(R(\sigma(R))$ be the set of resulting matchings.

As before, a matching rule φ is *Pareto efficient* if it selects *Pareto efficient* matchings for each problem. Note that *Pareto efficiency* says nothing about how we assign suppressants. It simply requires no further improvement from the matchings chosen by a matching rule for each given set of recipients. A solution (σ, φ) is *Pareto efficient* if for each problem R, φ selects *Pareto efficient* matchings at $R(\sigma(R))$.

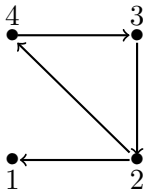
Our next requirement says that, no matter which recipient choice rule we have, a matching rule should make all patients weakly better off after suppressants are introduced.[13]

> **Strong monotonicity**: For each non-negative integer K, each problem R, and each recipient choice rule σ, each matching in $\varphi^{\sigma}(R)$ is weakly preferred to each matching in $\varphi(R)$ by all patients.

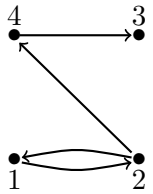
This requirement is convincing especially when we cannot choose a particular recipient set, for example, when patients individually decide whether they use suppressants or not. This is in fact the current practice in South Korea: Any K patients of incompatible pairs can use suppressants and they receive direct transplants from their own donors after using suppressants. This practice satisfies *strong monotonicity*, whereas $TTC_{\succ}$ and $\overline{TTC}_{\succ}$ do not.

Example 3. ($TTC_{\succ}$ and $\overline{TTC}_{\succ}$ violate *strong monotonicity*.) Consider two problems with four pairs defined as follows:

R_1	R_2	R_3	R_4
2	3	4	2



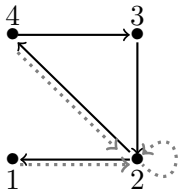
$\bar{R}_1$	$\bar{R}_2$	$\bar{R}_3$	$\bar{R}_4$
2	1	4	2

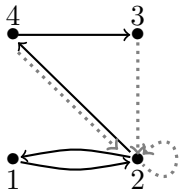


Let $1 \succ 2 \succ 3 \succ 4$ for both problems. Since there is only one cycle for each problem, $TTC_{\succ}(R)$ and $\overline{TTC}_{\succ}(\bar{R})$ match the patients and the donors as follows:

$$TTC_{\succ}(R): \begin{bmatrix} \text{patient 1 – donor 1} \\ \text{patient 2 – donor 3} \\ \text{patient 3 – donor 4} \\ \text{patient 4 – donor 2} \end{bmatrix} \qquad \overline{TTC}_{\succ}(\bar{R}): \begin{bmatrix} \text{patient 1 – donor 2} \\ \text{patient 2 – donor 1} \\ \text{patient 3 – donor 3} \\ \text{patient 4 – donor 4} \end{bmatrix}$$

Now suppose that $K = 1$ and consider a choice rule choosing patient 2 for both problems. As patient 2's preference changes to R_2^*, the graphs change into:





For these new profiles $R' = R(\{2\})$ and $\bar{R}' = \bar{R}(\{2\})$, $TTC_{\succ}$ and $\overline{TTC}_{\succ}$ choose the following matchings:

[13] The two monotonicity requirements can be viewed in relation to "welfare-dominance under preference replacement" in allocation problems. It requires when a person changes her preferences, all the remaining people be affected in the same direction (see Thomson (1999) for a thorough survey of this requirement). Since the use of suppressants by a group of patients changes their preferences, our requirements share a similar idea as welfare-domination under preference replacement, but there is no direct logical relation between them. In our requirements, first, at most K patients may change their preference at the same time when they use suppressants. Second, when patient i's preference changes, it always changes only to R_i^*. Third, when preferences change, all patients, *including those who use suppressants*, should be affected in the same direction. Lastly, all patients should be affected in a particular direction – they are made weakly better off.

$$TTC_{\succ}(R'): \begin{bmatrix} \text{patient 1 – donor 2} \\ \text{patient 2 – donor 1} \\ \text{patient 3 – donor 3} \\ \text{patient 4 – donor 4} \end{bmatrix} \qquad \overline{TTC}_{\succ}(\bar{R}'): \begin{bmatrix} \text{patient 1 – donor 1} \\ \text{patient 2 – donor 3} \\ \text{patient 3 – donor 4} \\ \text{patient 4 – donor 2} \end{bmatrix}$$

Under $TTC_{\succ}$, patients 3 and 4 are made worse off. Under $\overline{TTC}_{\succ}$, patient 1 is made worse off.

This observation generalizes to our first impossibility result.

Proposition 2. *No matching rule jointly satisfies Pareto efficiency and strong monotonicity.*[14]

Proposition 2 implies that the current practice in South Korea necessarily violates *Pareto efficiency* as it satisfies *strong monotonicity*.

Before we proceed, let us take a closer look at Example 3 above. At R, suppose that patient 1, instead of patient 2, is provided a suppressant. Then, patient 1 newly forms a self-cycle, while the existing cycle $2 \to 4 \to 3 \to 2$ still remains the same. Similarly, at $\bar{R}$, suppose that patient 4, instead of patient 2, is provided a suppressant. Then, patients 3 and 4 form a new cycle $3 \to 4 \to 3$, while the existing cycle $1 \to 2 \to 1$ still remains the same. Summarizing, in this example, there is a way to choose a recipient to make all patients weakly better off than before. Given this observation, we now ask if it is possible to make all patients weakly better off with a particular recipient choice rule. Consider a solution (σ, φ).

> **Monotonicity**: For each non-negative integer K and each problem R, each matching in $\varphi^{\sigma}(R)$ is weakly preferred to each matching in $\varphi(R)$ by all patients.

We note that *monotonicity* is trivially satisfied by many solutions. For example, consider a solution (σ, φ) with an *essentially single-valued* matching rule φ and a recipient choice rule σ that never chooses any patient. Then, $\varphi = \varphi^{\sigma}$ and the solution (σ, φ) satisfies *monotonicity*. Obviously, this is not an effective way of using suppressants, so it is reasonable to require that such cases be prevented.

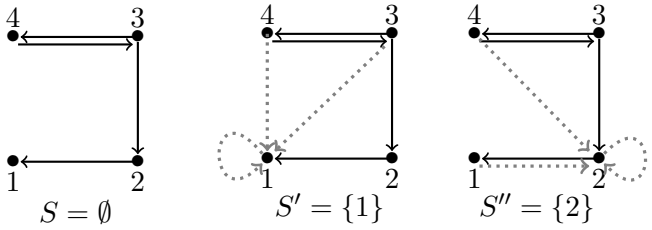
We thereby formulate a new efficiency requirement pertaining to the assignment of suppressants. It says that the recipients of suppressants should be chosen so that the set of patients receiving transplants is maximal in terms of set inclusion.

> **Maximal Improvement**: For each non-negative integer and each problem, consider two potential groups of recipients. If the first group results in a set of transplants that properly includes a set of transplants that the second group results in, the second group should not be chosen by σ.

Example 4. (Illustration of Maximal Improvement) Consider the following problem with four pairs and $K = 1$. Consider three potential sets of recipients, S, S', and S'':

[14] Since a matching rule φ may not be single-valued, there is another way to define *strong monotonicity*: For each non-negative integer K, each problem R, and each recipient choice rule σ, a matching in $\varphi^{\sigma}(R)$ is weakly preferred to a matching in $\varphi(R)$ by all patients. This alternative definition is weaker than *strong monotonicity* and incompatible with *Pareto efficiency* and *essentially single-valuedness*.

R_1	R_2	R_3	R_4
2	3	4	3



Consider a solution (σ, φ) satisfying *maximal improvement* where φ is a matching rule choosing all *Pareto efficient* matchings. For each set of recipients, the matching rule chooses the following matching:

$$\varphi(R(\{1\})) : \begin{bmatrix} \text{patient 1 – donor 1} \\ \text{patient 2 – donor 2} \\ \text{patient 3 – donor 4} \\ \text{patient 4 – donor 3} \end{bmatrix} \qquad \varphi(R(\{2\})) : \begin{bmatrix} \text{patient 1 – donor 2} \\ \text{patient 2 – donor 1} \\ \text{patient 3 – donor 4} \\ \text{patient 4 – donor 3} \end{bmatrix}$$

Also, $\varphi(R(\{1\})) = \varphi(R)$. When no patient uses a suppressant, patients 3 and 4 receive transplants. When patient 1 is provided a suppressant, patients 1, 3, and 4 receive transplants. When patient 2 is provided a suppressant, all patients receive transplants. Therefore, the recipient choice rule σ should not choose $\emptyset$ and $\{1\}$ for this problem.

As discussed in Section 2, we can also consider the number of transplants in formulating this requirement. Then, the aforementioned requirement can be defined as follows.

> **Cardinally Maximal Improvement**: For each non-negative integer and each problem, consider two potential groups of recipients. If the first group results in a greater number of transplants than the second group, the second group should not be chosen by σ.

From the definition, *cardinally maximal improvement* implies *maximal improvement*. Unfortunately, we have the second impossibility result.

Proposition 3. *No solution jointly satisfies Pareto efficiency, monotonicity, and cardinally maximal improvement.*

In view of impossibility results in Propositions 2 and 3, we weaken *cardinally maximal improvement* to *maximal improvement* and ask whether it is compatible with *Pareto efficiency* and *monotonicity*.

4. Top-Trading Cycles Solutions with Immunosuppressants

We propose two solutions based on the TTC rules defined in Section 2. We first determine the recipients of suppressants and then choose matchings between patients and donors. Consider a problem.

> **Extended top-trading cycles solution** (simply, $eTTC_{\succ}$):
>
> **Step 1.** Apply $TTC_{\succ}$ to the problem and identify the set of pairs whose patients do not receive transplants at a resulting matching. Denote this set by $\bar{N}$ and the set of remaining pairs by $N \setminus \bar{N}$. No actual allocation is made at this step.

Step 2. Let $\succ^*$ be the priority ordering induced from $\succ$ such that all pairs in $\bar{N}$ have lower priorities than those in $N \setminus \bar{N}$, while the relative priorities within $\bar{N}$ and $N \setminus \bar{N}$, respectively, remain the same as in $\succ$.

Step 3. Let $\mathcal{H}_0$ be the collection of all sets of jointly feasible cycles and at most K chains.[15] Proceed to the following steps.

Substep t (≥ 1): In $\mathcal{H}_{t-1}$, identify all sets of jointly feasible cycles and at most K chains including the patient with the t-th highest priority at $\succ^*$. If there is such a set, let $\mathcal{H}_t$ be the collection of all these sets. Otherwise, let $\mathcal{H}_t \equiv \mathcal{H}_{t-1}$.

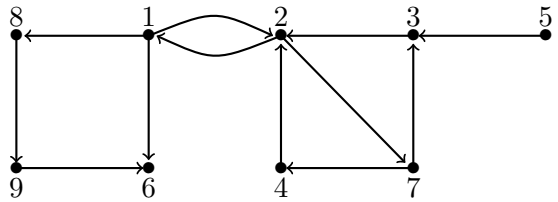
This process terminates at Substep n. Choose a set in $\mathcal{H}_n$ and choose the patients at the head of the chains in this set to be the recipients of suppressants.

Step 4. Update these recipients' preferences and apply $TTC_{\succ^*}$ to the new preference profile.

In Step 1, we apply $TTC_{\succ}$ to the initial preference profile and find the set of patients $\bar{N}$ who do not receive transplants at the step. Since $TTC_{\succ}$ is *essentially single-valued*, the sets of patients receiving transplants remain the same across all matchings selected by $TTC_{\succ}$. In Step 2, we modify the initial priority ordering $\succ$ to $\succ^*$. As long as the pairs in $N \setminus \bar{N}$ have higher priorities than those in $\bar{N}$, the cycles or chains including these patients will be selected when applying $TTC_{\succ^*}$ later. This guarantees that these patients receive transplants even after the suppressants are used. In Step 3, we determine the recipients of suppressants. This is done by selecting cycles and at most K chains according to the modified priority ordering and assigning suppressants to the patients at the head of these chains. In the last step, we update the preference profile and apply TTC associated with the modified priority ordering. It is straightforward from the definition that $eTTC_{\succ}$ is *essentially single-valued*. Therefore, the sets of patients receiving transplants remain the same across all matchings selected by $eTTC_{\succ}$ for each problem.

Example 5. ($eTTC_{\succ}$) Consider the following problem with nine pairs:

R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	R_9
2	$1, 3, 4$	$5, 7$	7	$\emptyset$	$1, 9$	2	1	8



Suppose that $1 \succ 2 \succ \cdots \succ 9$. There are three cycles $1 \to 2 \to 1$, $2 \to 7 \to 4 \to 2$, and $2 \to 7 \to 3 \to 2$. Among these, $TTC_{\succ}$ chooses the first cycle including the pair with the highest priority, which is pair 1. The resulting matching is:

[15] Such $\mathcal{H}_0$ is always non-empty. This is because (i) patients outside $\bar{N}$ form cycles among themselves and (ii) patients in $\bar{N}$ do not form cycles, but only chains, among themselves. (If there were any cycle among patients in $\bar{N}$, such a cycle should have been chosen in Step 1 of the algorithm, making these patients not belong to $\bar{N}$.) Therefore, we can choose the cycles from (i) and at most K chains from (ii).

$$\begin{bmatrix} \text{patient 1 – donor 2} \\ \text{patient 2 – donor 1} \\ \text{other patients – their own donors} \end{bmatrix}$$

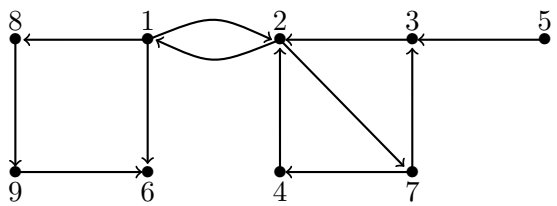
So, $\bar{N} = \{3, 4, \ldots, 9\}$ and we modify $\succ$ into $\succ^*$, which happens to coincide with $\succ$.
(1) Suppose that at most one patient can receive a suppressant ($K = 1$). We identify the collection of all sets of jointly feasible cycles and a chain, including pair 1, and then among them, we identify the sets including pair 2. Among them, again, we identify the sets including pair 3: $\{5 \to 3 \to 2 \to 1 \to 8 \to 9 \to 6\}$ and $\{7 \to 3 \to 2 \to 1 \to 8 \to 9 \to 6\}$. Among these, we next identify the sets including pair 4. Since there is none, we move on to pair 5 and choose the first set. We choose the patient at the head of this chain, patient 5, to be a recipient of suppressant. We then update patient 5's preference and apply $TTC_{\succ^*}$ to this new profile. A resulting matching is determined along a cycle, $5 \to 3 \to 2 \to 1 \to 8 \to 9 \to 6 \to 5$. All patients in the cycle are matched to the donors along the directed arcs. All other patients are matched to their own donors.
(2) Suppose instead that at most two patients can receive suppressants ($K = 2$). As above, we identify the set of cycles and at most two chains according to the modified priority ordering $\succ^*$. We end up with the following two sets: $\{5 \to 3 \to 2 \to 1 \to 8 \to 9 \to 6,\ \ 7 \to 4\}$ and $\{7 \to 4 \to 2 \to 1 \to 8 \to 9 \to 6,\ 5 \to 3\}$. Suppose that we choose the first set. Then, patients 5 and 7 are the heads of the chains in this set and we choose them to be recipients of suppressants. We then update these patients' preferences and apply $TTC_{\succ^*}$ to this new profile. The resulting matching is determined along the two cycles, $5 \to 3 \to 2 \to 1 \to 8 \to 9 \to 6 \to 5$ and $7 \to 4 \to 7$. Suppose instead that we choose the second set. Then, patients 5 and 7 are the heads of the chains in this set and we choose them to be recipients of suppressants. The resulting matching is determined along the two cycles, $7 \to 4 \to 2 \to 1 \to 8 \to 9 \to 6 \to 7$ and $5 \to 3 \to 5$. For both sets, all patients receive transplants, confirming that $eTTC_{\succ}$ is *essentially single-valued*.

We can also define a version of the extended top-trading cycles solution by adapting $\overline{TTC}_{\succ}$.

> **Extended top-trading cycles solution maximizing the number of transplants** (simply, $e\overline{TTC}_{\succ}$):
>
> **Step 1.** Apply $\overline{TTC}_{\succ}$ to the problem and identify the set of pairs whose patients do not receive transplants at a resulting matching. Denote this set by $\bar{N}$ and the set of remaining pairs by $N \setminus \bar{N}$. No actual allocation is made at this step.
>
> **Steps 2 to 4.** All these steps are exactly the same as above when defining $eTTC_{\succ}$.

Again, it is straightforward from the definition that $e\overline{TTC}_{\succ}$ is *essentially single-valued*.

Example 6. ($e\overline{TTC}_{\succ}$) Consider the problem in Example 5:



Among the three cycles, $\overline{TTC}_{\succ}$ chooses the cycle maximizing the number of transplants; $2 \to 7 \to 4 \to 2$ and $2 \to 7 \to 3 \to 2$. Since there are more than one, the second cycle is chosen since it includes the patient with a higher priority at $\succ$, which is patient 3. The resulting matching is:

$$\begin{bmatrix} \text{patient 2 – donor 3} \\ \text{patient 3 – donor 7} \\ \text{patient 7 – donor 2} \\ \text{other patients – their own donors} \end{bmatrix}$$

So, $\bar{N} = \{1, 4, 5, 6, 8, 9\}$ and we modify $\succ$ into $\succ^*$ such that $2 \succ^* 3 \succ^* 7 \succ^* 1 \succ^* 4 \succ^* 5 \succ^* 6 \succ^* 8 \succ^* 9$.
(1) Suppose that at most one patient can receive a suppressant ($K = 1$). We identify the collection of all sets of jointly feasible cycles and a chain, including pair 2, and then among them, identify the sets including pair 3. Among them, again, we identify the sets including pair 7, and so on. Then, we end up with the following two sets: $\{1 \to 8 \to 9 \to 6,\ \ 2 \to 7 \to 3 \to 2\}$ and $\{7 \to 3 \to 2 \to 1 \to 8 \to 9 \to 6\}$. Suppose that we choose the first set. Patient 1 is at the head of a chain in this set, so we choose her to be a recipient of suppressant. We then update this patient's preference and apply $TTC_{\succ^*}$ to the new profile. A resulting matching is determined along two cycles, $1 \to 8 \to 9 \to 6 \to 1$ and $2 \to 7 \to 3 \to 2$. All patients in the cycles are matched to the donors along the directed arcs. All other patients are matched to their own donors.
(2) Suppose that at most two patients can receive suppressants ($K = 2$). As above, we identify the collection of sets of jointly feasible cycles and at most two chains according to the modified priority ordering $\succ^*$. We end up with the following two sets: $\{5 \to 3 \to 2 \to 1 \to 8 \to 9 \to 6,\ \ 7 \to 4\}$ and $\{7 \to 4 \to 2 \to 1 \to 8 \to 9 \to 6,\ \ 5 \to 3\}$. Depending on which set we choose, we obtain two resulting matchings, as shown in (2) of Example 5.

These solutions satisfy the following requirements.

Theorem 1. *$eTTC_{\succ}$ and $e\overline{TTC}_{\succ}$ satisfy Pareto efficiency, monotonicity, and maximal improvement.*

So far, we assume that a patient is indifferent between compatible transplants and incompatible transplants. This assumption is plausible as long as both types of transplants are equally desirable.

Patients, however, may prefer compatible transplants to incompatible transplants due to, for instance, a higher medical cost or potential side effects. If we are to make all patients weakly better off by introducing suppressants when patients have such preferences, the following requirement must hold.

> **Monotonicity***: For each non-negative integer K and each problem R, (i) each matching in $\varphi^\sigma(R)$ is weakly preferred to each matching in $\varphi(R)$ by all patients and (ii) any patient who receives a transplant in a matching in $\varphi(R)$ is not in $\sigma(R)$.

Consider the patients who receive transplants even in the absence of suppressants. Condition (i) says that they should still receive transplants when suppressants become available, which is exactly what *monotonicity* requires. For that, these patients should be either in cycles or in chains chosen for a matching when suppressants are used. Condition (ii) says that none of them should be the head of a chain. Otherwise, they would feel worse off, because they are now receiving incompatible transplants while they used to receive compatible transplants. *Monotonicity** guarantees that any patient who could initially receive a compatible transplant still receives a compatible transplant.

It is straightforward from the definition that *monotonicity** implies *monotonicity*. To achieve this requirement, we make a small modification on Substep n of Step 3 in the definition of $eTTC_{\succ}$:

> **Step 3.** Let $\mathcal{H}_0$ be the collection of all sets of jointly feasible cycles and at most K chains. Proceed to the following steps.
>
> **Substep t** (≥ 1): In $\mathcal{H}_{t-1}$, identify all sets of jointly feasible cycles and at most K chains including the patient with the t-th highest priority at $\succ^*$. If there is such a set, let $\mathcal{H}_t$ be the collection of all these sets. Otherwise, let $\mathcal{H}_t \equiv \mathcal{H}_{t-1}$.
>
> This process terminates at Substep n. *Choose a set in $\mathcal{H}_n$ such that no pair in $N \setminus \bar{N}$ is the head of a chain in the set.* Choose the patients at the head of the chains in this set to be the recipients of suppressants.

We denote this solution by $eTTC^*_{\succ}$. The difference between $eTTC_{\succ}$ and $eTTC^*_{\succ}$ is in the choice of recipients of suppressants: $eTTC_{\succ}$ chooses any set of cycles and chains from $\mathcal{H}_n$ in Substep n, whereas $eTTC^*_{\succ}$ chooses a particular one from $\mathcal{H}_n$ such that no pair in $N \setminus \bar{N}$ is a head of a chain. The existence of such a particular set is the key to the proof of the following result.

Proposition 4. *$eTTC^*_{\succ}$ satisfies monotonicity*. Moreover, for each problem, the set of patients who receive transplants under $eTTC^*_{\succ}$ is the same as that under $eTTC_{\succ}$.*

5. Counterfactual Analysis

To measure the welfare improvement as per our proposal, we now conduct counterfactual analyses based on the recent transplant data from South Korea. We implement the same idea of using suppressants to transform chains to cycles as in the previous section. However, given the restrictions that we discussed in Introduction, we now assess how much use of suppressants could have been reduced from the current practice.

In what follows, we assume that immunological compatibility is only determined by ABO blood types.[16] We do not put any restrictions on the size of chains and cycles, but this assumption results in a limited variety of cycles and chains which we explain below. Note again that a patient of type A can receive a transplant only from a donor of type A or O, a patient of type B can receive a transplant only from a donor of type B or O, and a patient of type O can receive a transplant only from a donor of type O, while a patient of type AB can receive a transplant from any donor.

We represent a pair of patient and donor by X-Y where the patient's blood type is X and the donor's type is Y. Let #(X-Y) be the number of pairs of type X-Y. We draw a directed arc from one pair to another if the patient of the latter is compatible with the donor of the former. A ***k*-cycle** is a cycle consisting of k pairs and a ***k*-chain** is a chain consisting of k pairs.

5.1. Counterfactual analysis based on the KONOS data

We use the KONOS data on living-donor kidney transplants during the four-year period (2011-2014). The data set collects all patient-donor pairs – either compatible or incompatible – who received transplants

[16] Some analytical results in Roth et al. (2007) and Sönmez et al. (2016) are also based on this assumption. This assumption is plausible when the exchange market is large enough and the tissue-type restriction does not bind.

Table 3: Profile of blood types of living kidney transplants in 2012.

Type	A	B	O	AB	Total
A	210	35	80	24	349
B	28	172	77	24	301
O	38	39	164	5	246
AB	34	37	20	33	124
Total	310	283	341	86	1020

(Patients' types are in leftmost column; donors' types are in top row.)

Table 4: Blood types of incompatible pairs in 2012.

Type	A-B	B-A	A-AB	B-AB	O-A	O-B	O-AB	Total
# of pairs	35	28	24	24	38	39	5	193

during this period. It also collects their ABO blood types. Because almost no transplants were made through exchanges, as shown in Table 2, these patients should have received transplants directly from their own donors.

In 2012, for example, there were 1,020 living-donor kidney transplants in total. Table 3 summarizes the blood-type profile of these pairs. For instance, there were 210 compatible pairs of type A-A whose patients received transplants directly from their donors; there were 35 incompatible pairs of type A-B whose patients received transplants from their donors by using suppressants.

In this blood-type restricted setting, there are 16 types of pairs in total. Among them, 7 types of pairs are incompatible: A-B, B-A, A-AB, B-AB, O-A, O-B, and O-AB. We collect the profile of these 193 incompatible pairs as in Table 4. Since the patients in these incompatible pairs received transplants directly from their own donors, the total number of these patients coincides with the number of patients who used suppressants in 2012.

Given these incompatible pairs, we now propose an algorithm that computes the minimal quantity of suppressants needed to ensure that all these pairs still receive transplants. This algorithm finds the smallest number of chains to achieve this goal.

Minimum chains algorithm. For each set of incompatible pairs and their blood type profile:

Step 1. Find all 2-cycles. Since only pairs of types A-B and B-A can form cycles, the number of all 2-cycles is min {#(A-B),#(B-A)}. Remove all pairs in these 2-cycles from the pool.

Step 2. Find all 3-chains, which are the longest chains in the setting. If #(A-B) > #(B-A) in Step 1, these 3-chains must be of the form O-A $\rightarrow$ A-B $\rightarrow$ B-AB. If #(A-B) < #(B-A) in Step 1, the 3-chains must be of the form O-B $\rightarrow$ B-A $\rightarrow$ A-AB. If #(A-B) = #(B-A) in Step 1, there is no remaining pairs of types A-B and B-A and no 3-chain can be formed. Remove all pairs in these 3-chains from the pool.

Step 3. Find all 2-chains. These chains must be one of O-A $\rightarrow$ A-B, O-A $\rightarrow$ A-AB, O-B $\rightarrow$ B-A, O-B $\rightarrow$ B-AB, A-B $\rightarrow$ B-AB, and B-A $\rightarrow$ A-AB, depending on which types of pairs remain in the pool. Remove all pairs in these 2-chains from the pool.

Step 4. Find all 1-chains.

Lastly, calculate the number of chains identified in Steps 2 to 4.

In Step 1, pairs A-B and B-A form trading cycles. Any patient included in these cycles can receive a transplant even without suppressants. Once all these 2-cycles are formed and removed, at most one type of A-B and B-A pairs exists.

In Step 2, if A-B pairs exist but B-A pairs do not, the longest possible chain is a 3-chain, O-A $\rightarrow$ A-B $\rightarrow$ B-AB. Similarly, if B-A pairs exist but A-B pairs do not, the longest possible chain is a 3-chain, O-B $\rightarrow$ B-A $\rightarrow$ A-AB. If there are no pairs A-B and B-A, no 3-chain can be formed.

In Step 3, if there are no remaining pairs A-B and B-A, the longest chain is a 2-chain of the forms O-A $\rightarrow$ A-AB and O-B $\rightarrow$ B-AB. If A-B pairs exist but B-A pairs do not, then at most one of the two pairs O-A and B-AB may exist. This is because, if both O-A and B-AB pairs exist, they form a 3-chain O-A $\rightarrow$ A-B $\rightarrow$ B-AB and this chain should have been removed in Step 2. Therefore, 2-chains are either all O-A $\rightarrow$ A-B or all A-B $\rightarrow$ B-AB. Similarly, if B-A pairs exist, but A-B pairs do not, then at most one of the two pairs O-B and A-AB may exist. Therefore, 2-chains are either all O-B $\rightarrow$ B-A or all B-A $\rightarrow$ A-AB.

After all 2-chains are formed and removed, each remaining pair forms a 1-chain in Step 4. Collect all chains from Step 2 to Step 4 and let the patients at the head of these chains use suppressants. We show that this algorithm minimizes the use of suppressants.

Theorem 2. *The minimum chains algorithm minimizes the use of suppressants while ensuring that all incompatible pairs receive transplants.*

Table 5 summarizes these steps of the minimum chains algorithm applied to the data in 2012. There are 28 2-cycles, 7 3-chains, 41 2-chains, and 34 1-chains, adding up to 82 chains in total. In Table 5, the numbers in the parentheses represent the number of the corresponding pairs who still remain after cycles or chains are formed and removed. The result shows that the use of suppressants could have been decreased from 193 to 82, while ensuring that all incompatible pairs still receive transplants.

The outcomes in other years are similar, as summarized in Table 6. During 2011-2014 in total, the number of recipients of suppressants 757 could have been reduced to 340, ensuring that all incompatible pairs still receive transplants.[17] This is a reduction of 55.1% from the current practice.

5.2. Counterfactual analysis based on the hypothetical population

As a robustness check, we redo our analysis for a slightly different specification of patient-donor pairs in this section. The KONOS data only collects pairs (either compatible or incompatible) whose patients have already received transplants. Since some incompatible pairs did not perform transplants, the KONOS data may underrepresent the population of incompatible pairs.

In the analyses above, on the other hand, we applied the minimum chains algorithm to the incompatible pairs in each *annual* data. This bases the assumption that the patients and the donors in each annual

[17] We calculated this number based on the assumption that compatibility is only determined by blood types. However, there may well be pairs who used suppressants due to tissue-type incompatibility. Those pairs are not captured in Table 4, but if they are added to the pool, our proposal will result in an additional reduction of suppressants. Therefore, the reduction from 757 to 340 calculated above can be viewed as a lower bound of reduction.

Table 5: Minimum chains algorithm for incompatible pairs in 2012.

Type	A-B	B-A	A-AB	B-AB	O-A	O-B	O-AB	Total
# pairs	35	28	24	24	38	39	5	193
2-cycle	28(7)	28(0)						56
3-chain	7(0)			7(17)	7(31)			21
2-chain			24(0)		24(7)			48
2-chain				17(0)		17(22)		34
1-chain					7(0)			7
1-chain						22(0)		22
1-chain							5(0)	5

(The number of remaining pairs is noted in parentheses.)

Table 6: Results of the minimum chains algorithm during 2011-2014.

	# pairs	2-cycle	3-chain	2-chain	1-chain	# Suppressants
2011	131	17	2	30	31	63
2012	193	28	7	41	34	82
2013	216	29	10	38	52	100
2014	217	34	3	48	44	95

data can participate in the exchange pool together. This assumption excludes a possibility that that these pairs have operated transplants and have left the pool at different times within a year.

To avoid a possible bias of population or any subtle timing issue, we now assume that patients and donors arrive randomly in an arbitrary time period, which can be very short. We construct a hypothetical population of 1,001 pairs using the average distribution of ABO blood types in South Korea: Blood type A is about 34.0 percent, type B about 27.0 percent, type O about 28.0 percent, and type AB about 11.0 percent of the total population. The types of patients and donors are assumed identically and independently distributed (i.i.d.) according to this distribution. Out of 1,001 pairs, we obtain 453 incompatible pairs. Table 7 summarizes the profile of blood types of these pairs.[18]

From this table, we collect all incompatible pairs and apply the minimum chains algorithm. Because of the i.i.d. assumption, there are as many pairs of type A-B as those of type B-A, and therefore, there is no 3-chain in Step 2. Tables 8 and 9 summarize the result. By applying our algorithm, 453 recipients of suppressants could have been reduced to 202. This is a reduction of 55.4%.

Remark. As another robustness check, we also consider a population including some compatible pairs in the exchange pool, which we excluded so far. For this case, we can obtain a larger reduction than 55 percent. The result is deferred to the online supplement.

[18]The number of pairs of each type is rounded to the nearest integer, with the total equal to 1,001.

Table 7: Profile of blood types of a hypothetical population.

Type	A	B	O	AB	Total
A	116	92	95	37	340
B	92	73	76	30	271
O	95	76	78	31	280
AB	37	30	31	12	110
Total	340	271	280	110	1001

(Patients' types are in leftmost column; donors' types are in top row.)

Table 8: Minimum chains algorithm for incompatible pairs in a hypothetical population.

Type	A-B	B-A	A-AB	B-AB	O-A	O-B	O-AB	Total
# pairs	92	92	37	30	95	76	31	453
2-cycle	92(0)	92(0)						184
3-chain								0
2-chain			37(0)		37(58)			74
2-chain				30(0)		30(46)		60
1-chain					58(0)			58
1-chain						46(0)		46
1-chain							31(0)	31

(The number of remaining pairs is in parentheses.)

	# pairs	2-cycle	3-chain	2-chain	1-chain	# Supp.
Hypothetical population	453	92	0	67	135	202

6. Conclusion

In this paper, we take a first step to investigate the implications of introducing suppressants to the kidney exchange problem. We propose several requirements for assigning suppressants and matching patients to donors. We introduce two extended TTC solutions and show that they satisfy Pareto efficiency, monotonicity, and maximal improvement. By using transplant data from South Korea, we lastly show that the use of suppressants can be significantly reduced from the current practice.

There remain several interesting questions. First, we may think of different procedures of assigning suppressants, instead of assigning K suppressants all at once as we do in this paper. For instance, suppose that we assign suppressants sequentially, one by one (or more generally, several unites by several). Each time, we apply the extended TTC solution to assign one unit of suppressant and let all patients who receive transplants leave the pool. We show in an example (which we defer to the online supplement) that no patient is better off and that some patients may end up worse off under sequential assignment than under simultaneous assignment.

Second, we can adapt the deferred acceptance (DA) solution to our setting. Since there is a single priority ordering over patients, the DA solution can be defined as follows: Among all sets of jointly feasible cycles and at most K chains, choose ones including a patient with the highest priority; among the resulting collections, choose ones including a patient with the second highest priority; and so on. From what we obtain, we choose the patients at the head of chains to be recipients of suppressant and we let patients receive kidneys from donors along the directed arcs in the cycles and chains. Note that there is no pre-matching step such as Steps 1 and 2 of $eTTC_{\succ}$. From DA, we obtain a "stable" assignment: If a patient does not receive a transplant, then either (i) all patients with lower priorities do not receive transplants, or (ii) all available suppressants are assigned to patients with higher priorities. This solution also satisfies *Pareto efficiency* and *maximal improvement*. However, it violates *monotonicity*, which can easily be verified with the example in the proof of Proposition 3 after switching the labels of patients 1 and 6 except for the priority ordering.

Third, the assumption of dichotomous preferences can be relaxed, for example, to tri-chotomous preferences. Although compatibility based on ABO blood types is binary, there are different levels of compatibility when tissue types (or HLA types) are taken into account, according to which the immuno-suppressive treatments should vary. If patients prefer compatible donors to less compatible ones, which they again prefer to incompatible donors, the structure of the problem changes significantly. This will be an interesting and non-trivial extension of our analysis.

Lastly, there remains the participation issue. According to Proposition 4, the recipients chosen by $eTTC^*_{\succ}$ are those who should use suppressants anyway to receive transplants. They would easily accept to use suppressants, but they may still prefer transplants received directly from their own donors, declining to remain in the exchange pool. As their participation benefits other patients, it would be reasonable to introduce a (monetary or non-monetary) compensation to promote their participation.

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A Appendix. Proofs

Proof of Proposition 1

Proposition 1: For every priority ordering $\succ$, $TTC_{\succ}$ and $\overline{TTC}_{\succ}$ are *essentially single-valued* and *Pareto efficient*.

Proof: It is straightforward from the definitions that $TTC_{\succ}$ and $\overline{TTC}_{\succ}$ are *essentially single-valued.*

Suppose, by contradiction, that $TTC_{\succ}$ is not *Pareto efficient*. Then, there are a problem and a matching chosen by $TTC_{\succ}$ for this problem, from which further Pareto improvement can be made. That is, there is a matching at which all patients who receive transplants at $TTC_{\succ}$ also receive transplants and at least one patient newly receives a transplant. Among all patients newly receiving transplants, choose the one with the highest priority under $\succ$. From the definition, $TTC_{\succ}$ should have chosen cycles at which this patient receives a transplant, a contradiction.

Suppose, by contradiction, that $\overline{TTC}_{\succ}$ is not *Pareto efficient*. By the same argument, there is a matching at which all patients who receive transplants at $\overline{TTC}_{\succ}$ also receive transplants and at least one patient newly receives a transplant. From the definition, $\overline{TTC}_{\succ}$ should have chosen matchings maximizing the number of transplants, a contradiction.

Proof of Proposition 2

Proposition 2: No matching rule jointly satisfies *Pareto efficiency* and *strong monotonicity*.

Proof: The proof is by means of an example with three pairs. Consider the following preferences of three patients:

R_1	R_2	R_2'	R_3
2	1	3	2

Let $R \equiv (R_1, R_2, R_3)$ and $R' \equiv (R_1, R_2', R_3)$. Let φ be a *Pareto efficient* matching rule. Suppose first that $K = 0$. By *Pareto efficiency*:

$$\varphi(R): \begin{bmatrix} \text{patient 1 – donor 2} \\ \text{patient 2 – donor 1} \\ \text{patient 3 – donor 3} \end{bmatrix} \qquad \varphi(R'): \begin{bmatrix} \text{patient 1 – donor 1} \\ \text{patient 2 – donor 3} \\ \text{patient 3 – donor 2} \end{bmatrix}$$

Now suppose that $K = 1$. Consider a recipient choice rule choosing patient 2 for both problems. Then, both problems change to (R_1, R_2^*, R_3). To make everyone weakly better off at this new problem than at R, we should have $\varphi(R)$ for the new problem. Similarly, to make everyone weakly better off at the new

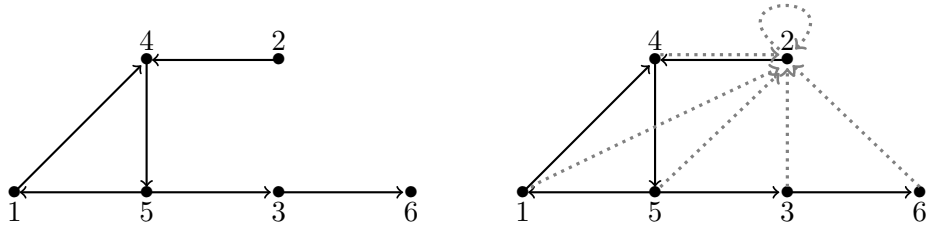
problem than at R', we should have $\varphi(R')$ for the new problem. Altogether, both $\varphi(R)$ and $\varphi(R')$ should be chosen for the new problem. However, patient 1 is worse off at $\varphi(R')$ than at $\varphi(R)$ and patient 3 is worse off at $\varphi(R)$ than at $\varphi(R')$, a contradiction to *strong monotonicity*.

Proof of Proposition 3

Proposition 3: No solution jointly satisfies *Pareto efficiency*, *monotonicity*, and *cardinally maximal improvement*.

Proof: The proof is by means of an example with six pairs. Consider the following problem and consider a solution (σ, φ) satisfying the three requirements:

R_1	R_2	R_3	R_4	R_5	R_6
5	$\emptyset$	5	1, 2	4	3



Suppose first that $K = 0$. By *Pareto efficiency*, pairs 1, 4, and 5 form an exchange cycle and these patients are matched with the donors along the directed arcs. Next, suppose that $K = 1$. To satisfy *cardinally maximal improvement*, patient 2 has to use a suppressant and all pairs except for pair 1 form a cycle. The resulting matchings are:

$$\varphi(R): \begin{bmatrix} \text{patient 1 – donor 5} \\ \text{patient 2 – donor 2} \\ \text{patient 3 – donor 3} \\ \text{patient 4 – donor 1} \\ \text{patient 5 – donor 4} \\ \text{patient 6 – donor 6} \end{bmatrix} \quad \varphi(R(\{2\})): \begin{bmatrix} \text{patient 1 – donor 1} \\ \text{patient 2 – donor 6} \\ \text{patient 3 – donor 5} \\ \text{patient 4 – donor 2} \\ \text{patient 5 – donor 4} \\ \text{patient 6 – donor 3} \end{bmatrix}$$

Since patient 1 is made worse off, *monotonicity* is violated.

Proof of Theorem 1

Theorem 1: $eTTC_{\succ}$ and $e\overline{TTC}_{\succ}$ satisfy *Pareto efficiency*, *monotonicity*, and *maximal improvement*.

Proof: (Pareto efficiency) For each problem, $eTTC_{\succ}$ chooses the recipients of suppressants and update the preference profile, to which $TTC_{\succ^*}$ is applied. By Proposition 1, the resulting matchings are *Pareto efficient* at the updated preference profile. The same argument applies to show that $e\overline{TTC}_{\succ}$ is *Pareto efficient*.

(Monotonicity) Note that at each matching, no patient who receives a transplant can be made strictly better off and no patient who receives no transplant can be made strictly worse off. Therefore, for each problem R, it is enough to show that all patients who received transplants at $TTC_{\succ}(R)$ still receive transplants at $eTTC_{\succ}(R)$. Suppose, by contradiction, that there is a patient who receives transplant at

$TTC_{\succ}(R)$, but not at $eTTC_{\succ}(R)$. If there is more than one such patient, then choose the one with the highest priority at $\succ^*$. Call this patient i^*.

Since patient i^* received a transplant at $TTC_{\succ}(R)$, she is in one of the jointly feasible cycles that $TTC_{\succ}$ chooses. When suppressants are assigned to the recipients, all these jointly feasible cycles still remain jointly feasible at the new compatibility profile. Note also that all patients receiving transplants at $TTC_{\succ}(R)$ have higher priorities than all the remaining patients at $\succ^*$. Therefore, any patient whose priority is higher than i^* at $\succ^*$ must have received a transplant at $TTC_{\succ}(R)$.

Case 1. If all patients receiving transplants at $eTTC_{\succ}(R)$ have higher priorities than patient i^* at $\succ^*$, then these patients are the ones who received transplants at $TTC_{\succ}(R)$. However, this contradicts Step 3 of the $eTTC_{\succ}$ algorithm: a set of cycles and chains should have been chosen so that patient i^* is also included together with these patients. There does exist such a set: for example, the set of jointly feasible cycles that $TTC_{\succ}(R)$ chooses.

Case 2. If there is a patient receiving a transplant at $eTTC_{\succ}(R)$ who has a lower priority than patient i^* at $\succ^*$, then this again contradicts Step 3 of the $eTTC_{\succ}$: a set of cycles and chains should have been chosen so that patient i^* is included ahead of the patient with a lower priority. There does exist such a set: for example, the set of jointly feasible cycles that $TTC_{\succ}(R)$ chooses.

Altogether, there should be no such patient i^*, completing the proof. The same argument applies to show that $e\overline{TTC}_{\succ}$ is *monotonic*.

(Maximal improvement) Suppose, by contradiction, that for a problem R, there is a set S of patients whose use of suppressants results in a matching with more transplants than a matching in $eTTC_{\succ}(R)$ in terms of set inclusion. Let H be a set of cycles and chains that results in this matching at $R(S)$. Then, all patients who receive transplants at $eTTC_{\succ}(R)$ also receive transplants when S is chosen. There should also be a patient who receives a transplant when S is chosen, but not at $eTTC_{\succ}(R)$. If there is more than one such patient, then choose the one with the highest priority at $\succ^*$. Call this patient i^*.

Case 1. If all patients receiving transplants at $eTTC_{\succ}(R)$ have higher priority than patient i^* at $\succ^*$, then this contradicts Step 3 of the $eTTC_{\succ}$: a set of cycles and chains should have been chosen so that patient i^* is also included together with these patients. There does exist such a set: for example, H.

Case 2. If there is a patient receiving a transplant at $eTTC_{\succ}(R)$ with a lower priority than patient i^* at $\succ^*$, then this again contradicts Step 3 of the $eTTC_{\succ}$: a set of cycles and chains should have been chosen so that patient i^* is included ahead of the patient with a lower priority. There does exist such a set: for example, H.

Therefore, there should be no such patient i^*, completing the proof. The same argument applies to show that $e\overline{TTC}_{\succ}$ satisfies *maximal improvement*.

Proof of Proposition 4

Proposition 4: $eTTC^*_{\succ}$ satisfies *monotonicity**. Moreover, for each problem, the set of patients who receive transplants under $eTTC^*_{\succ}$ is the same as that under $eTTC_{\succ}$.

Proof: Consider Substep n of Step 3 under $eTTC^*_{\succ}$. From the definition, $\mathcal{H}_n$ is the collection of *all* sets of cycles and at most K chains that include the same set of pairs. It is sufficient to show that there is $H \in \mathcal{H}_n$ in which no pair in $N \setminus \bar{N}$ is the head of a chain.

Choose any $H \in \mathcal{H}_n$. If no pair in $N \setminus \bar{N}$ is the head of a chain in H, we are done. Otherwise, let i^*

be a pair in $N \setminus \bar{N}$ who is the head of a chain in H. Let $i^* \to i_1 \to \cdots \to i_k$ be this chain. We show that we can rearrange the cycles and chains of H into another set in $\mathcal{H}_n$ in such a way that i^* is not the head of a chain any more.

Choose a set of jointly feasible cycles chosen in Step 1 of $eTTC^*_{\succ}$. Since $i^* \in N \setminus \bar{N}$, there is a cycle including i^* in this set. Let j^* be the pair that points to i^* along this cycle (it is possible that $j^* = i^*$ in case $i^* \to i^*$). There are two cases.

Case 1. j^* is one of the pairs in $i^* \to i_1 \to \cdots \to i_k$. Let $j^* = i_m$ for some $m \in \{1, \ldots, k\}$. Then, rearrange this chain into a cycle $i^* \to i_1 \to \cdots \to i_m \to i^*$ and form another chain $i_{m+1} \to \cdots \to i_k$, while keeping all other chains and cycles as in H. Then, the resulting set of cycles and chains is still in $\mathcal{H}_n$ and i^* is now in a cycle.

Case 2. j^* is not one of the pairs in $i^* \to i_1 \to \cdots \to i_k$. Since $j^* \in N \setminus \bar{N}$, j^* also has to receive a transplant at $eTTC_{\succ}(R)$. Therefore, she is either in a cycle or a chain of H.

Subcase 1. If j^* is in a cycle of H, say $j^* \to j_1 \to \cdots \to j_l \to j^*$, then, rearrange this cycle and the chain $i^* \to i_1 \to \cdots \to i_k$ into a chain $j_1 \to j_2 \to \cdots \to j^* \to i^* \to i_1 \to \cdots \to i_k$, while keeping all other chains and cycles as in H. Then, the resulting set of cycles and chains is still in $\mathcal{H}_n$ and i^* is not the head of a chain.

Subcase 2. If j^* is in a chain of H, say $j_1 \to \cdots \to j_l \to j^* \to j_{l+1} \to \cdots \to j_t$. Reorganize this chain and the chain $i^* \to i_1 \to \cdots \to i_k$ into two chains $j_1 \to j_2 \to \cdots \to j^* \to i^* \to i_1 \to \cdots \to i_k$ and $j_{l+1} \to \cdots \to j_t$, while keeping all other chains and cycles as in H.[19] Then, the resulting set of cycles and chains is still in $\mathcal{H}_n$ and i^* is not the head of a chain.

If there is any pair in $N \setminus \bar{N}$ who is again the head of a chain in the resulting set of cycles and chains, we repeat the same process as above for that pair. In the end, we obtain a set in $\mathcal{H}$ such that no pair in $N \setminus \bar{N}$ is the head of a chain of the set.[20]

The second statement follows immediately from the fact that $\mathcal{H}_n$ is a collection of sets of cycles and chains including the same pairs, whose patients receive transplants.

Proof of Theorem 2

Theorem 2: The minimum chains algorithm minimizes the use of suppressants, ensuring that all incompatible pairs receive transplants.

Proof: Among all sets of jointly feasible chains and cycles including all incompatible pairs, let $\mathcal{H}$ be the collection of all such sets that have the smallest number of chains. Choose any $H \in \mathcal{H}$ and let h^* be the number of chains in H.

[19] Patient j^* can be in a self-cycle in Subcase 1. Patient j^* can also be at the head of a chain in H in Subcase 2. If so, j^* newly becomes the head of a chain as we rearrange chains and/or cycles. Since j^* is in $N \setminus \bar{N}$ and is now at the head of a chain, we repeat the same process for j^*.

[20] As we repeat this process, i^* never becomes the head of a chain again, and therefore, we only need to repeat this process at most n times. The reason is as follows. After rearranging chains and/or a cycle as above, j^* gets connected to i^* and there can be at most one pair who newly becomes the head of a chain. From the construction, such a new head appears only when j^* points to this pair in H, while j^* points to i^* in the cycle chosen in Step 1 of the $eTTC^*_{\succ}$ algorithm. We apply this observation to i^*. Since j^* is connected to i^* in the rearranged cycle or chain, for i^* to be a new head as we repeat the process, there has to be another pair k^* to which j^* points in the cycle chosen in Step 1 of the $eTTC^*_{\succ}$ algorithm. However, j^* cannot point to two distinct pairs in this cycle.

Claim 1: It is possible to keep the same number of chains h^* by forming an additional 2-cycle with pairs from the chains in H, if any.

Proof of Claim 1: Note that 2-cycles can be formed only by pairs A-B and B-A in this setting. Choose a A-B pair and a B-A pair from the chains in H if any. We show that it is possible to maintain the same number of chains by forming an additional 2-cycle and reorganizing the remaining pairs in the chains to which A-B and B-A pairs belong in H. There are four types of chains that may include this A-B pair in H: A-B, O-A $\rightarrow$ A-B, A-B $\rightarrow$ B-AB, and O-A $\rightarrow$ A-B $\rightarrow$ B-AB. (Similarly, there are four types of chains that may include this B-A pair in H: B-A, O-B $\rightarrow$ B-A, B-A $\rightarrow$ A-AB, and O-B $\rightarrow$ B-A $\rightarrow$ A-AB.)

Case 1. the A-B pair is a 1-chain in H: We show that the B-A pair should be in O-B $\rightarrow$ B-A $\rightarrow$ A-AB in H. Suppose otherwise. If B-A is a 1-chain in H, then the A-B and B-A pairs could have formed a cycle from H, reducing the number of chains by 2. This is a contradiction to $H \in \mathcal{H}$. If the B-A pair is in O-B $\rightarrow$ B-A, then the A-B and B-A pairs could have formed a cycle and the O-B pair could have formed a 1-chain from H, reducing the number of chains by 1. This is again a contradiction. If the B-A pair is in B-A $\rightarrow$ A-AB, then the same argument applies. Summarizing, if this A-B pair is a 1-chain in H, then the B-A pair should be in the 3-chain in H. Let the A-B and B-A pairs form a cycle and the remaining pairs in the 3-chain, O-B and A-AB, form two 1-chains. Keep all other cycles and chains as before. The number of chains does not change, while an additional cycle is formed.

Case 2. the A-B pair is in O-A $\rightarrow$ A-B: We show that the B-A pair should be either in O-B $\rightarrow$ B-A or in O-B $\rightarrow$ B-A $\rightarrow$ A-AB. If the B-A pair is in B-A $\rightarrow$ A-AB, then the A-B and B-A pairs could have formed a cycle and the remaining pairs, O-A and A-AB, could have formed a 2-chain from H, reducing the number of chains by 1. This is a contradiction to $H \in \mathcal{H}$. A similar argument applies if the B-A pair is a 1-chain in H. Now, suppose that the B-A pair is in O-B $\rightarrow$ B-A. Let the A-B and B-A pairs form a cycle and the remaining pairs, O-A and O-B, form two 1-chains. Keep all other cycles and chains as before. The number of chains does not change, while an additional cycle is formed. Suppose that the B-A pair is in the 3-chain. Let the A-B and B-A pairs form a cycle and the remaining pairs in the chains, O-A, A-AB, and O-A, form a 2-chain O-A $\rightarrow$ A-AB and a 1-chain O-B. Keep all other cycles and chains as before. The number of chains does not change either.

Case 3. the A-B pair is in A-B $\rightarrow$ B-AB: We show that B-A should be either in B-A $\rightarrow$ A-AB or in O-B $\rightarrow$ B-A $\rightarrow$ A-AB. Otherwise, we can reduce the number of chains by 1 as above, a contradiction. The same argument as in Case 2 applies to show that the number of chains does not change when the A-B and B-A pairs form a cycle and the remaining pairs are rearranged.

Case 4. the A-B pair is in O-A $\rightarrow$ A-B $\rightarrow$ B-AB: In this case, the B-A pair may be in any type of chains. Suppose that the B-A pair is in O-B $\rightarrow$ B-A $\rightarrow$ A-AB. Let the A-B and B-A pairs form a cycle and the remaining pairs in the chains form two 2-chains, O-A $\rightarrow$ A-AB and O-B $\rightarrow$ B-AB. Then the number of chains does not change, while an additional cycle is formed. A similar argument applies to the other types of chains that may include the B-A pair, so we omit them.

Proof of Theorem 2: (continued) By Claim 1, we can find another set of cycles and chains in $\mathcal{H}$ by forming as many 2-cycles as possible, without changing the total number of chains. Denote by H' a resulting set of cycles and chains. Then, a A-B pair and a B-A pair cannot exist in the chains in H'. Otherwise, we can form an additional 2-cycle with these pairs by applying Claim 1.

Claim 2: It is possible to keep the same number of chains h^* by forming an additional 3-chain with pairs

from the 2-chains or the 1-chains in H', if any.

Proof of Claim 2: We consider the following three cases.

Case 1. no A-B pair and no B-A pair exist in any chain in H'. Then, each chain in H' consists of some of O-A, O-B, A-AB, B-AB, and O-AB pairs. However, no additional 3-chain can be formed by these pairs and therefore we are done.

Case 2. some A-B pairs exist in some chains in H', but no B-A pair exists in any chain in H'. Then, each chain in H' consists of some of O-A, O-B, A-B, A-AB, B-AB, and O-AB pairs. An additional 3-chain among these pairs will be O-A $\rightarrow$ A-B $\rightarrow$ B-AB, if any. Note that the O-AB pairs always remain as 1-chains, so we can set them aside.

We focus on the remaining five types of 2-chains and 1-chains in H': O-A $\rightarrow$ A-B, A-B $\rightarrow$ B-AB, O-A, A-B, and B-AB. Let the number of each type of chain in H' be

$$n_1 \equiv \#(\text{O-A}\rightarrow\text{A-B}), \qquad n_2 \equiv \#(\text{A-B}\rightarrow\text{B-AB}),$$
$$n_3 \equiv \#(\text{O-A}), \qquad n_4 \equiv \#(\text{A-B}), \qquad n_5 \equiv \#(\text{B-AB}).$$

Since the number of chains cannot be further reduced from H', we have the following observations.

(i) At least one of n_3 and n_4 should be zero. Otherwise, the two 1-chains, O-A and A-B, could have changed to a 2-chain, reducing the number of chains by 1 from H'. This is a contradiction.

(ii) At least one of n_4 and n_5 should be zero, by the same argument as in (i).

(iii) At least one of n_2 and n_3 should be zero. Otherwise, a 2-chain A-B $\rightarrow$ B-AB and a 1-chain O-A could have changed to a 3-chain, reducing the number of chains by 1 from H'. This is again a contradiction.

(iv) At least one of n_1 and n_5 should be zero, by the same argument as in (iii).

Given these observations, we consider the following subcases.

Subcase 1. $n_4 > 0$. By (i) and (ii), we have $n_3 = n_5 = 0$. Suppose that either n_1 or n_2 is zero. Then no additional 3-chain can be formed. Suppose that $n_1, n_2 > 0$. Choose one O-A $\rightarrow$ A-B chain and one A-B $\rightarrow$ B-AB chain. Let O-A, A-B, and B-AB pairs form a 3-chain. Let the remaining pair A-B form a 1-chain. Then, the number of chains does not change, while an additional 3-chain is formed.

Subcase 2. $n_4 = 0,\ n_3 > 0,\ n_5 > 0$: Then, by (iii) and (iv), we have $n_2 = 0$ and $n_1 = 0$. No additional 3-chain can be formed.

Subcase 3. $n_4 = 0,\ n_3 > 0,\ n_5 = 0$: Then, by (iii), we have $n_2 = 0$. No additional 3-chain can be formed.

Subcase 4. $n_4 = 0,\ n_3 = 0,\ n_5 > 0$: Then, by (iv), we have $n_1 = 0$. No additional 3-chain can be formed.

Subcase 5. $n_4 = n_3 = n_5 = 0$: Suppose that either n_1 or n_2 is zero. Then no additional 3-chain can be formed. Suppose that $n_1, n_2 > 0$. The symmetric arguments as in Subcase 1 apply here to show that the number of chains does not change, while an additional 3-chain is formed.

Case 3. some B-A pairs exist in some chains in H', but no A-B pair exists in any chain in H'. The symmetric arguments as in Case 2 apply here to complete the proof. We omit it.

Proof of Theorem 2: (continued) From Claims 1 and 2, we can find another set of cycles and chains in $\mathcal{H}$ by first forming all possible 2-cycles and then forming all possible 3-chains, without changing the total number of chains. Denote by H'' a resulting set of cycles and chains. No additional 2-chains can be formed with pairs from the 1-chains in H''. Indeed, if there were any, then the number of chain could have been reduced further, a contradiction to $H'' \in \mathcal{H}$.

Summarizing, all cycles and chains in H'' can be identified in four steps. First, identify as many 2-cycles as possible among the pairs and set them aside. Second, among the remaining pairs, identify as many 3-chains as possible and set these 3-chains aside. Third, among the remaining pairs, identify as many 2-chains as possible. Lastly, identify all remaining 1-chains. These cycles and chains are those in H'' and the number of chains is exactly h^*. This process is exactly how the minimum chains algorithm operates.

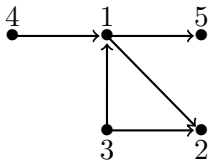
B Online Supplement

Sequential assignment versus simultaneous assignment

We present an example to show that no patient is better off and that some patients may end up worse off under sequential assignment than under simultaneous assignment. Consider the following problem:

Let $1 \succ 2 \succ \cdots \succ 5$. Suppose that at most two patients can use suppressants. (1) Simultaneous assignment: We apply $eTTC_{\succ}$ by setting $K = 2$. There are several sets of feasible chains that include all patients. Let us choose $\{4 \to 1 \to 5,\ \ 3 \to 2\}$ among others. Then, patients 3 and 4 are provided suppressants and the patients in these chains receive transplants along the two cycles, $4 \to 1 \to 5 \to 4$ and $3 \to 2 \to 3$. All patients receive transplants.

R_1	R_2	R_3	R_4	R_5
$3, 4$	$1, 3$	$\emptyset$	$\emptyset$	1



(2) Sequential assignment: We first apply $eTTC_{\succ}$ by setting $K = 1$. There is only one set of feasible chains chosen according to $\succ$, which is $\{3 \to 1 \to 2\}$. Then, patient 3 is provided a suppressant and the patients in this chain receive transplants along the cycle $3 \to 1 \to 2 \to 3$. We apply $eTTC_{\succ}$ by setting $K = 1$ to the remaining patients. There is only one set of feasible chain chosen according to $\succ$, which is $\{4\}$. Then, patient 4 is provided a suppressant and receives a transplant from his own donor. Patient 5 ends up with not receiving a transplant.

Counterfactual analysis based on the KONOS data when "altruistic" compatible pairs participate

In the counterfactual analysis, we collected incompatible pairs when applying the minimum chains algorithm, excluding all compatible pairs from the population. The use of suppressants could be reduced further, however, when some compatible pairs participated in the exchange pool, facilitating transplants even more. Such compatible pairs are called "altruistic" pairs (Sönmez and Ünver, 2014). For example, if AB-O pairs participate in the pool, then 3-chains can be transformed into 4-cycles AB-O $\to$ O-A $\to$

Table 9: Results of the minimum chains algorithm when AB-O pairs participate.

	#pairs	#AB-O	2-cycle	4-cycle	3-cycle	2-chain	1-chain	#Supp
2011	131	20	17	2	18	12	31	43
2012	193	20	28	7	13	28	34	62
2013	216	17	29	10	7	31	52	83
2014	217	11	34	3	8	40	44	84
Hypothetical population	453	31	92	0	31	36	135	171

A-B → B-AB, and 2-chains can be transformed into 3-cycles AB-O → O-A → A-AB or AB-O → O-B → B-AB. Table 9 summarizes the results of the minimum chains algorithm when compatible pairs of type AB-O participate in the exchange pool.

As can be seen, the use of suppressants during 2011-2014 could have been reduced from 757 to 272, a larger reduction than what we obtain in Section 5. If we add other compatible pairs to the pool, even larger reduction would be obtained.

Counterfactual analyses of other years

We present the details of counterfactual result of 2011, 2013, and 2014, which we omit in Section 5.

Table 10: Profile of blood types of living kidney transplants in 2011.

Type	A	B	O	AB	Total
A	219	19	76	13	327
B	17	148	73	19	257
O	33	21	195	9	258
AB	34	30	20	33	117
Total	303	218	364	74	959

(Patients' types are in leftmost column; donors' types are in top row.)

Table 11: Minimum chains algorithm for incompatible pairs in 2011.

Type	A-B	B-A	A-AB	B-AB	O-A	O-B	O-AB	Total
# pairs	19	17	13	19	33	21	9	131
2-cycle	17(2)	17(0)						34
3-chain	2(0)			2(17)	2(31)			6
2-chain			13(0)		13(18)			26
2-chain				17(0)		17(4)		34
1-chain					18(0)			18
1-chain						4(0)		4
1-chain							9(0)	9

(The number of remaining pairs is noted in parentheses.)

Table 12: Profile of blood types of living kidney transplants in 2013.

Type	A	B	O	AB	Total
A	192	39	93	24	348
B	29	138	70	24	261
O	51	44	173	5	273
AB	37	42	17	32	128
Total	309	263	353	85	1010

(Patients' types are in leftmost column; donors' types are in top row.)

Table 13: Minimum chains algorithm for incompatible pairs in 2013.

Type	A-B	B-A	A-AB	B-AB	O-A	O-B	O-AB	Total
# pairs	39	29	24	24	51	44	5	216
2-cycle	29(10)	29(0)						58
3-chain	10(0)			10(14)	10(41)			30
2-chain			24(0)		24(17)			48
2-chain				14(0)		14(30)		28
1-chain					17(0)			17
1-chain						30(0)		30
1-chain							5(0)	5

(The number of remaining pairs is noted in parentheses.)

Table 14: Profile of blood types of living kidney transplants in 2014.

Type	A	B	O	AB	Total
A	193	37	84	26	340
B	34	143	54	25	256
O	46	40	185	9	280
AB	54	31	11	28	124
Total	327	251	334	88	1000

(Patients' types are in leftmost column; donors' types are in top row.)

Table 15: Minimum chains algorithm for incompatible pairs in 2014.

Type	A-B	B-A	A-AB	B-AB	O-A	O-B	O-AB	Total
# pairs	37	34	26	25	46	40	9	217
2-cycle	34(3)	34(0)						68
3-chain	3(0)			3(22)	3(43)			9
2-chain			26(0)		26(17)			52
2-chain				22(0)		22(18)		44
1-chain					17(0)			17
1-chain						18(0)		18
1-chain							9(0)	9

(The number of remaining pairs is noted in parentheses.)