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A queuing model to address waiting time inconsistency in solid-organ transplantation

David A. Stanford [a,*], Jung Min Lee [a], Natasha Chandok [b,c], Vivian McAlister [b,d]

[a] Department of Statistical & Actuarial Sciences, The University of Western Ontario, 1151 Richmond St. N, London, ON, N6A 5B7, Canada

[b] Multi-Organ Transplant Program, London Health Sciences Centre, 1151 Richmond St. N, London, ON, N6A 5B7, Canada

[c] Department of Medicine, The University of Western Ontario, 1151 Richmond St. N, London, ON, N6A 5B7, Canada

[d] Department of Surgery, The University of Western Ontario, 1151 Richmond St. N, London, ON, N6A 5B7, Canada

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ABSTRACT

Organ transplantation is a vital therapy for the treatment of many patients. Due to blood compatibility rules, there has been a pattern in many jurisdictions for differing organ types where recipients of blood type O experience longer waiting times than those of other blood types, partly due to cross-transplantation of too many O organs to compatible donors of other blood types. In response to this, a recent development in some jurisdictions is a change in the rules to insist upon ABO-identical transplantation. The literature review herein enables us to conclude that unrestricted cross-transplantation has not achieved equity of access across all blood groups in any jurisdiction in which the problem has arisen. The present study next shows that ABO identical transplantation cannot achieve equity, either. It then presents a model for restricted cross-transplantation which indicates how comparable waiting times for all blood types could be achieved.

1. Introduction

Several prior studies assessing waiting times for solid-organ transplantation [1–8] have revealed a common and concerning pattern: recipients of blood type O wait on average substantially longer than blood type A, while those of blood type A in turn wait longer than patients with blood type AB. The waiting times for patients with blood type B are sometimes somewhat longer than type O, although this observation is inconsistent [1–8]. This waiting time pattern for solid-organ transplantation arises in many countries and/or health-systems, seemingly regardless of organ type. A Canadian perspective of what has come to be known as the "blood type O problem" (Glander et al. [3]) dates to our study of adult liver transplant waiting times in Canada from 2000 to 04 (Stanford et al. [8]), in which the average waiting time for transplanted O recipients was roughly 10 months, as opposed to 7 months for type B recipients, 6 months for type A recipients, and merely 3 months for type AB recipients. Such a discrepancy in waiting time for a life-saving intervention raises important ethical questions on equity of liver transplantation.

Two recent analyses further illustrate the blood type O problem. In 2010, Glander et al. [3] presented a review of transplantation related to end-stage renal disease (ESRD) in the Eurotransplant zone comprising the Benelux countries, Germany, Austria and Slovenia. Their study involved 1186 patients' waitlisted for their first kidney transplant at a single centre in the Eurotransplant zone between 1996 and 2008. As much as 14.1% of type-O donor kidneys were transplanted into non-O recipients, leading to a disparity of type-O patients on the waitlist relative to their proportion in the general population. Whereas the proportion of blood type O among waitlisted patients (36.6%) and donors (36%) closely reflected the general population, by the end of the study, as much as 47% of waiting patients were type O. This was accompanied by an 85-month median waiting time for type-O recipients as opposed to 59 months for the pooled grouping of A, B, and AB recipients. Investigators also examined whether the longer waiting times in type 0 recipients might translate into poorer clinical outcomes following renal transplantation and reported statistically significant increased rates of mortality and graft failure for type-O recipients. (As waiting time equity is our focus, we shall not comment in this study on the potential health consequences of longer waiting times. Instead, we will restrict our attention to possible causes of this inequity in waiting and propose solutions.)

A follow-up study involving a subset of the same authors, Liefeldt et al. [5], arrived at similar conclusions. In response to the

* Corresponding author. Tel.: +1 519 661 3612; fax: +1 519 661 3813.
E-mail address: stanford@stats.uwo.ca (D.A. Stanford).

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"gross imbalance" of O patients on the Eurotransplant Senior Program (ESP) list, as well as that reported by the Eurotransplant Kidney Allocation program (ETKAS) [5], new rules calling for exclusive ABO-identical transplantation [5] in the Eurotransplant zone were introduced in November 2010.

In Canada, deceased donor kidneys are allocated according to an ABO identical basis. In the case of liver transplantation, ABO compatible rules are allowed in the case of urgent transplants, which happen on the order of 10% of the time. Routine liver transplants are allocated on an ABO identical basis.

Many other studies – some indirectly – have addressed the blood type O problem. A list of countries and organ types that illustrates their diversity follows: Rexius et al. [7] [hearts in Sweden], Hussey et al. [4] [hearts in the UK], Barone et al. [1] [kidneys in the US] and Phelan et al. [6] [kidneys in Ireland]. In short, the blood type O problem occurs for numerous organ types in numerous jurisdictions, with, of course, differences in degree of disparity in waiting times.

These developments suggest that the impact of ABO-identical and ABO-compatible transplantation upon patient waiting times requires further study. The present work aims to address this from the perspective of a new queuing construct, which we name the "array of idealised transplant queues" (AITQ). The structure is so named because, unlike separate queues, we present a model in which donor organs of a particular type can be used for recipients of specified compatible blood groups, and as such, some of the four waitlists or queues are linked. The array is "idealised" in that, as a mathematical structure, not all aspects affecting the transplantation process are considered, and a number of simplifying assumptions are made (which are detailed in Section 2). Nonetheless, we have retained the key parameters in the wait list process from a queuing perspective, and we believe that we can properly infer the qualitative impact of deviations from the assumptions stated below in such situations as may present themselves.

In the next section, after defining the structure of the AITQ, we establish results which show that the time on the waitlist in such an idealised system is inversely proportional to the rate at which donor organs become available. The significance of this fact is that, in an AITQ operating under an ABO-identical policy, patients from the rarer blood groups of a given region would wait on average many times longer than the common blood types. For instance, in Canada where blood type O is about 15 times more common than blood type AB [9], the impact of an ABO-identical scheme, strictly adhered to, would be to see waiting times for AB patients on the order of 15 times longer than those of type O. The corresponding impact for blood type B patients would be a five-fold increase relative to blood type O.

While it has not been proven in the literature above that an unconstrained amount ABO-compatible cross-transplantation is in itself inherently incapable of leading to equity in access, we are convinced by the sheer variety of jurisdictions and organ types considered above that this will be the typical outcome when such a policy is employed. When combined with the results of Section 2 that show that comparable waiting times for the various blood types cannot be achieved under ABO-identical transplantation, we feel that the case has been made for a third option lying between these two extremes. In Section 3, we present what is required, from the perspective of the AITQ model, to achieve comparable waiting times for all blood groups. The central thrust of what we establish is that limited amounts of cross-transplantation must be allowed to achieve equity, but only between specified blood types, based uniquely upon the blood mix of the given jurisdiction. We use the Canadian blood mix to illustrate these concepts. We then illustrate how these results can be modified in other jurisdictions. We summarise our results and discuss future work in the final section of the paper.

While it is the problem of transplant waiting times that gave rise to the AITQ structure, the conclusions that we obtain herein apply to any array of queues in which the various component queues feature arrival rates and service capacity in a set proportion to each other, and in which some service capacity can be diverted from one of the queues to another.

We do not, in the present work, address issues relating to the development of transplantation policies to achieve the optimal amount of cross transplantation. First, such issues are properly addressed in the medical literature, which we hope to pursue in future work. Second, what is allowed in one jurisdiction may not be possible in another, for legislative, constitutional, or cultural reasons, among others.

2. Waiting times for an array of idealised transplant queues operating under an ABO-identical protocol:

2.1. Background on donor organ and recipient placement distributions:

In transplant queues, the service time constitutes the time between consecutive deceased donor organs becoming available. Stanford et al. [8], in their study of liver transplant waiting times in Canada from 2000–2004, observed that the process of deceased donor organs becoming available was adequately approximated by a Poisson process. The Poisson-arrivals assumption is widely borne out in large populations (say, of size n), in which individual members of the population each have a rare chance p of manifesting a particular characteristic (see Feller [10], page 153). Since inter-event times from a Poisson process are exponentially distributed (see Conway et al. [11]), this means that we are free to consider the time between consecutive deceased donor organs becoming available to be exponentially distributed.

In contrast, patient placements on the waiting lists are not Poisson, at least as was observed in the Canadian liver transplant context in Stanford et al. [8]. While the need for a transplant might well arise in the population at large, there are several subsequent steps involved prior to placement on a transplant waiting list: the patient's decision to seek treatment, the consult with their primary care provider, the referral to the specialist, and possible further delays. The length of the waiting list, at any time the decision to place is being considered, might itself play a role. The net result we observed in Stanford et al. [8] regarding the patient placement processes was such that the six regional Canadian waitlists all failed Poisson goodness of fit tests, after all of these factors have been taken into consideration. In some cases, a geometric distribution for the daily number placements was found to be suitable.

This combination of a non-Poisson arrival process and exponential service times would seem to suggest the use of a GI/M/1 queue for modelling purposes, as we shall see below.

2.2. The array of idealised transplant queues (AITQ) model:

We propose below an idealised transplant queue model which reflects the most important factors that affect waiting time. The resulting idealised model can be stated as follows.

Patients are placed on the waitlist for patients of blood-type i; $i = \text{O, A, B, AB}$ according to a renewal process (see Kleinrock [12]). The distribution of time between successive patient placements for the ith waitlist is given by

$$F_i(t) = Prob\{T_i \leq t\}; \quad t \geq 0; \ i = \text{O, AB, AB}$$

where T_i denotes the random variable representing the time between successive placements for waitlist i. We assume that the patient placement process has reached stationarity; i.e., there is no

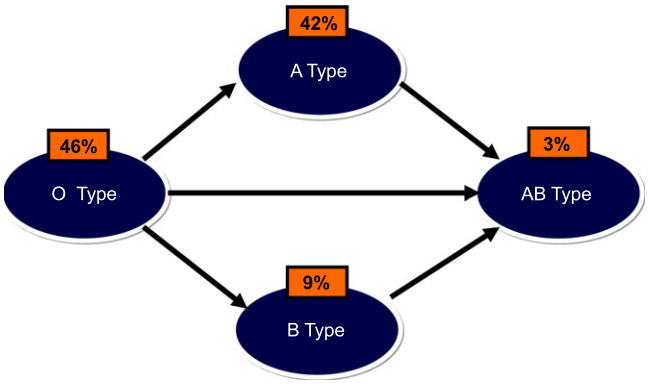

Fig. 1. Possible donor/recipient pairs (solid arrows).

growth from year to year in the long-term rate at which patients are added to the list. Patients on the ith waitlist are served in FCFS fashion, and there is a single server (representing the organ availability process of the ith blood type). The times between successive organs of the same blood type becoming available are exponentially distributed at rate μ_i; $i = \text{O, A, B, AB}$. We assume that each blood group has the same propensity to donate cadaveric organs and the same need for transplant and as such, each queue can be viewed as a time-scaled version of the others. Furthermore, we assume that the (common) long-run cadaveric supply for the four blood types is enough to meet the demand:

$$1/(\mu_i E\{T_i\}) = \rho < 1; \quad i = \text{O, A, B, AB.}$$

We further assume the existence of the moment generating functions $m_i(s)$ for the inter-placement time distributions (see Feller [10] p 285) defined by

$$m_i(s) = \int_{x=0}^{\infty} e^{sx} dF_i(x); \quad i = \text{O, A, B and AB.}$$

Last, to account for blood compatibility of select types of cross-transplantation, we observe that it is possible to re-assign service capacity from the O queue to A, B, and AB recipients; as well as from the A queue and the B queue to type AB recipients. The mechanism by which this service capacity is re-assigned is a coin toss with probability p_{ij} each time an organ of type i becomes available; $i = \text{O, A, B and AB}$. In the foregoing, j indicates the blood type of the compatible recipient class. We presume that the amount of redirected organs is sufficiently small that each of the queues remains stable. Typically, it is the case that the permissible p_{ij}'s will be small (on the order of, say, two to five percent for any donor class in total, as we show in Section 3).

The model we will be proposing illustrates these ideas in Fig. 1. The ABO-compatible pairings are those indicated by dashed or solid lines. The dashed lines indicate those pairings we will disallow, for reasons to follow. Hence, we set $p_{\text{OA}} = p_{\text{O(AB)}} = p_{\text{B(AB)}} = 0$ while allowing $p_{\text{OB}} > 0$ and $p_{\text{A(AB)}} > 0$.

For the AITQ model as constructed, we observe that each of the four idealised transplant queues operates as a GI/M/1 queue (see Kleinrock [12]). Before making use of this fact, we address several aspects in which the AITQ as formulated differs from transplant queues in reality and provide justification for our choices.

First, one could question the choice of an FCFS service discipline for the idealised model, when in many real situations sicker patients gain access to transplantation quicker than healthy ones. In the first instance, we observe that such models have been considered; we note in particular that Drekic et al. [13] considers a so-called "self-promoting" model in which customers of a regular priority are promoted to high priority upon the occurrence of a randomly-occurring health event. These events can also lead to abandonment from the regular queue due to either an improvement in health status such that transplantation is no longer desirable, as well as abandonment due to death or health degradation to the point that transplantation is no longer an option.

With regard to abandonments, it is true that long waiting times lead to a greater incidence of degraded health and death. Methodologically, a model incorporating abandonments would violate the GI/M/1 queue structure we use to establish the results that follow. A model that incorporates such aspects will yield shorter waiting times for patients who remain than an FCFS queue without abandonment would. The long waiting times that our model will forecast act as a good proxy for undesirable scenarios where abandonments are more likely to arise. Our focus here is to seek a cross-transplantation mechanism that can provide comparable access to patients of all blood types in a timely manner.

Remark. One referee's observation which we have not pursued herein warrants mention. The referee observes that as the need for transplants among the population at large is likely to resemble a Poisson process, an array of idealised M/M(n)/1 models would reflect the abandonment processes more accurately. Such a model would start the waiting time "clock" from time of need and could provide useful benchmarks for real-world systems. We are inclined to agree with the merit of this approach.

Patient health does affect their waiting time; for instance, the Modified End-Stage Liver Disease (MELD) score [14] is used widely to allocated livers. When prioritised systems are in effect in a system without abandonments, the overall average waiting time for a given blood type is unaffected, as guaranteed by the GI/G/1 conservation law (see Kleinrock [15]). In other words, while a prioritised system will provide better service to the patients most in need, there is no net benefit to a larger fraction of patients as a whole. The initial purpose of our AITQ model is to illustrate that ABO-identical transplantation will lead to shorter waiting times for larger blood groups than for the others. This effect is most easily illustrated in an FCFS environment.

We are certainly not recommending the abandonment of MELD-based allocation of livers. Assuming that transplantation is the desired therapy for all patients on the waitlist, and since the MELD score merely rearranges the order in which patients are transplanted, it is sufficient for us to consider a first-come, first-served (FCFS) queue in order to address the adequacy of an ABO-identical transplantation policy in the long term. MELD and similar sickest-first strategies will not correct a policy with profoundly differing waiting times for the various blood types.

Our coin toss mechanism is made purely for methodological reasons which will become apparent. It is the goal of this paper to establish that a strategy to allow a small, controlled amount of cross-transplantation can produce the desired balance yielding comparable waiting times for all classes. It is not our purpose herein to specify the details implementing such a strategy. The proper discussion on implementable strategies belongs in the medical literature.

As the dominant research questions here are (1) to establish that an ABO-identical policy cannot be maintained in the long run on the grounds of equity and fairness, and (2) to then establish that a model with restricted amounts of cross-transplantation can do so, we need a model that is sufficiently transparent to reveal the impact of the primary factors on waiting time (such as organ availability rates and chances of cross-transplantation). Thus, we need to avoid being opaque due to secondary yet important factors such as the stationarity and independence assumptions.

Indeed, it is unlikely in any given jurisdiction that the availability of donor organs and the need for transplantation are unaffected by public service campaigns to encourage donors signing

up, possible movements towards greater use of living donors, improvements in automobile safety, and medical advances that are saving more lives (and thereby depleting the sources of deceased donor organs). Unfortunately, the transient models required to reflect these developments more accurately are typically intractable, and even if they were tractable, they would almost certainly be opaque in terms of trying to discern the impact of the primary factors listed above.

As regards the independence assumption, we observe that the process of placing patients on the waitlist is certainly influenced by the human interaction. It is unclear whether the interactions of the attending physician and the multidisciplinary panel governing the waitlist, in seeking the best outcomes for a patient who could benefit from a transplant, might seek to place several of them on the list at an "opportune" time. Hence in fact the assumption of successive placement times being independent of each other may in fact be false. However, as the number of physicians involved is large, it is hard to imagine how one would be able to assess this interaction in a straightforward way. Primarily for reasons of tractability and transparency of the results in terms of the primary factors, it is necessary for us to proceed with the independence assumption.

The assumption that the long-run cadaveric supply for the four blood types is sufficient to meet the demand is difficult to assess in a simple manner. Certainly, at present notable numbers of patients die while waiting for many organ types in many jurisdictions, and it is likely the case that if none did, the waitlists would grow over time. This assumption is needed in order to invoke the stationary results for queues that we do.

We close this assessment by noting that such factors as organ size, and compatibility due to medical factors other than blood type have been ignored.

We turn now to our results. In what follows, we consider the AITQ as formulated and find that ABO identical transplantation is unsustainable in that, for the Canadian blood type mix (and Western nations with similar mixes), it penalises patients from blood groups B and AB. We then propose a modification to a strict ABO-identical policy in which limited amounts of transplantation are allowed between specific pairs of blood types and demonstrate that such a modified policy is sustainable in the long run.

2.3. Waiting times on the AITQ waitlists

Each of the queues comprising the AITQ features a renewal process for patient placements and has an exponential service mechanism for the organ inter-availability times. Based on these facts and the other assumptions noted above, each waiting list can be viewed as a stable GI/M/1 queue (see, for instance, Kleinrock [12]), so it follows that the sojourn time a patient spends on the relevant wait list is exponentially distributed. Defining $\mathcal{W}$ to be the time from arrival until completion of service for a randomly selected customer in the GI/M/1 queue, the sojourn time distribution satisfies

$$P(\mathcal{W} > t) = e^{-\mu(1-r_0)t}; \quad t \geq 0. \tag{1}$$

where $0 < r_0 < 1$ is the unique solution to the implicit equation $r_0 = m(-\mu(1-r_0))$. Hence the average sojourn time (which corresponds to a patient's average time on the waitlist) is given by

$$W = \frac{1}{\mu(1-r_0)}. \tag{2}$$

A notable consequence of Eqs. (1) and (2) is that any mechanism that manages to equate average waiting times between two components of the AITQ (such as, for instance, type O and type B) will also succeed in equating the percentiles of the waiting time distributions for all $t \geq 0$. (This fact will prove relevant in Section 3 below.)

2.4. Assessing waiting times under ABO-identical transplantation

Under an ABO identical policy, each of the four blood groups can be considered as its own transplant queue. We have assumed that there is no variation in the propensity to donate from one blood group to another, and that the per capita rate of patients requiring transplantation is the same from blood group to blood group. (The available data in the studies referred to in the Introduction seems to support these assumptions.) These assumptions imply that the donor rates and arrival rates are in the same proportion for all blood groups. The inter-placement time distributions are therefore scaled versions of each other with the same scale factor that links the donor rates, which is a (mild) condition (3) of the theorem that follows. While we illustrate the result for the case of blood groups O and B, the same conclusion results for type-A and type-AB patients if the same condition is satisfied. Let $r_0^{(O)}$ and $r_0^{(B)}$ denote the respective roots for the separate blood type O and type B systems, respectively.

Theorem. *Let $f = \mu_B/\mu_O$ be the ratio of organ availability rates for blood types* B *and* O *respectively. Furthermore assume that the moment-generating functions*

$$m_i(s) = \int_{x=0}^{\infty} e^{sx} dF_i(x); \quad i = O, B$$

exist for the patient inter-placement time distributions $F_O(t)$ and $F_B(t)$, and that these are scaled by the same factor that links the donor rates (f), i.e.

$$F_B(t) = Prob\{T_B \leq t\} = F_O(ft) = Prob\{T_O \leq ft\}, \quad \forall t \geq 0. \tag{3}$$

Then $r_0^{(O)} = r_0^{(B)}$.

Proof of Theorem. The root $r_0^{(B)}$ is the solution to the equation

$$r_0^{(B)} = m_B\left(-\mu_B\left(1 - r_0^{(B)}\right)\right).$$

In light of Eq. (3), it can be shown readily that

$$m_B(s) = m_O\left(\frac{s}{f}\right), \quad \forall s$$

so that

$$r_0^{(B)} = m_O\left(-\frac{\mu_B}{f}\left(1 - r_0^{(B)}\right)\right) = m_O\left(-\mu_O\left(1 - r_0^{(B)}\right)\right).$$

Thus $r_0^{(B)}$ is a solution to the defining equation for the root $r_0^{(O)}$. As the solution to this equation the interval (0,1) is unique, the result follows. ■

Lemma. *Let us use r_0 to denote the common value of $r_0^{(O)}$ and $r_0^{(B)}$ under the assumptions of the foregoing theorem. Then the average waiting times for type-* B *patients will be $(1/f)$ times larger than those of type* O*; that is:*

$$W_B = \frac{W_O}{f}. \tag{4}$$

Proof of Lemma. From Eq. (2) above we find immediately that

$$W_B = \frac{1}{\mu_B(1-r_0)} = \frac{1}{f\mu_O(1-r_0)} = \frac{W_O}{f}. \quad \blacksquare$$

Remark. The consequence of the foregoing theorem is that under an ABO identical policy, since O organs become available at roughly five times the rate that B organs do in the Canadian context, and fifteen times the rate that AB organs [9], Eq. (4) illustrates that

the average waiting time for blood type B and blood type AB patients will be, respectively, about five and fifteen times as long as that of blood O patients. Hence, an ABO-identical strategy is an unsustainable model if equity of access for all blood groups is an aim of the allocation policy.

We turn now to proposing a controlled model for cross-transplantation that does meet this objective.

3. Proposed model for limited cross-transplantation

Since the literature has shown that uncontrolled cross-transplantation adversely affects the blood type O population, on the one hand, and we have shown above on the other that an ABO-identical policy is inequitable on the other hand, one can conclude that an equitable policy must lie between these extremes. That is, it is necessary to allow some cross-transplantation to occur, but one must strive to keep its occurrence less frequent than under existing ABO-compatible policies which have negatively impacted type-O waiting times, in order to provide comparable access to organs for all blood types.

We propose a policy which permits limited amounts of cross-transplantation between specified pairings of donor and recipient blood types, while precluding all other ABO-compatible pairings. We illustrate the approach below in the Canadian context [9] (and anticipate similar outcomes in other jurisdictions with a similar blood mix). We then comment on what aspects would differ in jurisdictions whose blood type mixes are dissimilar to the Canadian case.

The process of identifying the donor and recipient blood types for permissible cross-transplantation is based upon the following logic that applies in the Canadian context (see Fig. 2):

1. Since blood group B deceased donor organs do not arise quickly enough to provide the same timely access for a transplant as the larger blood groups O and A, they must be supplemented by some amount of cross-transplanted organs — and the only compatible source is blood group 0.
2. Similarly, blood group AB deceased donor organs are too few in number to offer timely access, so they too must be supplemented by some cross-transplanted organs. While organs from all of blood groups O, A, or B are all compatible to type AB, it is preferable in practice for the greatest medical commonality to be preserved between the donor and the recipient. As such, donor organs of types A and B are preferred to those of type O.
3. Transplants for AB recipients from blood type B would only lead to more transfers from O to B to ensure timely access for type B patients. We need to limit the demand upon type O donors to type B patients who constitute 9% of the population. Hence, the logical source for the type AB recipients is blood group A.

The foregoing line of thought for the Canadian context can be adjusted for other jurisdictions having similar blood type mixes with higher proportions of O and A type blood, a substantially smaller proportion of B, and a very small proportion of type AB. In contrast, for countries whose blood mix includes almost equal proportions of O, A, and B type blood, such as Korea [16], the details of the solution using this approach would need to be modified accordingly. In Korea, the closer compatibility of AB type recipients to A and B type donors (as opposed to type O donors) would seem to suggest cross-transplantation based upon small numbers of A and B type donors to achieve equity of access to AB recipients.

The resulting policy we propose is a modification of an ABO-identical policy which allows for a small fraction p_O of type O organs to be transplanted into type B recipients, and another small fraction p_A of type A organs to be transplanted into type AB recipients (see Fig. 3).

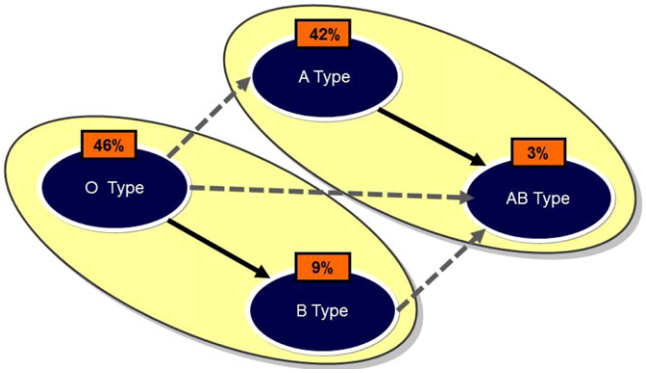

Fig. 2. Permissible donor/recipient pairs (solid arrows). Dashed arrows indicate the disallowed compatible pairs: O-type to AB-type not medically preferred; B-type to AB-type would lead to more transfers from O-type to B-type; and O-type to A-type disadvantages type-O patients.

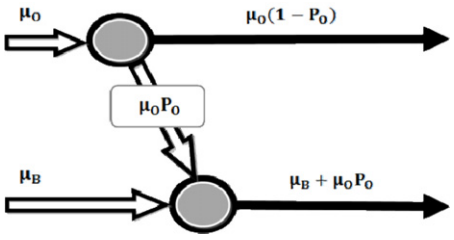

Fig. 3. Available donor organ flows & allocation to recipient groups (O-to-B case).

The resulting allocation of available deceased donor organs to type O and type B patients is evident in Fig. 3:

Using the properties pertaining to Poisson processes in Conway et al. [11], page 144, it can be shown directly that the process of O-type organs retained for O-type recipients is a Poisson process at rate $\mu_O\,(1 - p_O)$, and the process of O organs made available for B-type recipients is a Poisson process at rate $\mu_O p_O$, so long as the chance any given organ is selected for cross-transplantation remains at p_O, independently of all the others.[1] It also follows from the same page of Conway et al. [11] that the resulting aggregate process of deceased donor organs made available to type-B recipients is a Poisson process at rate $\mu_B + \mu_O\, p_O$.

The goal of ensuring fair access is achieved by equating the mean sojourn times W_O and W_B; this in turn will lead to the same probabilities of waiting t time units for a transplant. The resulting equation is

$$W_O = (\mu_O(1 - p_O - r_O))^{-1} = W_B = (\mu_B(1 - r_O) + \mu_O\, p_O)^{-1}.$$

Solving this equation for p_O in terms of the other parameters leads to the equation

$$p_O = \frac{(R-1)(1-r_O)}{2R}$$

where $R = \frac{\mu_O}{\mu_B} = 1/f$ is the ratio of the rates at which deceased donor organs of type O and type B become available. In the Canadian context in which $\mu_O \cong 5\mu_B$, this means that

$$p_O \cong 0.4\,(1 - r_O)\,.$$

Proceeding in the same way to determine p_A, since $\mu_A \cong 14\mu_{AB}$, we find that

$$p_A \cong 0.46(1 - r_O).$$

[1] This is purely a modelling assumption, and we are certainly not recommending it be the actual rule for determining the destination of the organs in practice. We comment further on this point in the discussion.

Table 1
Optimal cross-transplant probability p_O.

rho	D/M/1		M/M/1		H2/M/1	
	r_O	P_O	r_O	p_O	r_O	p_O
0.9	0.807	0.0772	0.9	0.04	0.955	0.0179
0.93	0.863	0.0547	0.93	0.028	0.969	0.0123
0.96	0.921	0.0316	0.96	0.016	0.983	0.0069
0.99	0.980	0.0080	0.99	0.004	0.996	0.0017

Table 1 determines the optimal p_O value as a function of the occupancy level, for deterministic arrivals, Poisson arrivals, and a particular hyper-exponential inter-arrival time distribution. The particular hyper-exponential distribution is the same as was used in Stanford et al. [8], featuring balanced means and a squared coefficient of variation of 3.77.

Since transplant waitlists are never empty, it is appropriate to presume a ρ value close to unity. Working with what we consider a very low estimate of $\rho = 0.9$, and observing that $r_O = \rho$ in the M/M/1 case, we find that p_O and p_A will not exceed 4% and 4.6% of organs respectively — and in fact are likely to be much smaller, ensuring that cross-transplantation is indeed kept rare.

As the table illustrates, p_O is typically about twice as large for deterministic arrivals as it is for Poisson arrivals. Conversely, it is typically only about half as large for the more variable hyper-exponential inter-arrival times. Since Stanford et al. [8] found that the patient placement process was more variable than a Poisson process, it is likely that one can use $p_O \cong 0.4\,(1-\rho)$ as an upper bound on the frequency of cross-transplantation of O organs to B patients. The specific optimal value will of course ultimately depend upon a host of other factors, such as the identification of a medically and ethically acceptable allocation mechanism, tested via extensive simulation, which will be pursued in future work in the medical literature.

4. Discussion

The foregoing analysis has established that it is possible to achieve comparable waiting times for solid-organ transplant in all blood groups by allowing a small amount of cross-transplantation from type O donors to type B recipients, and from type A donors to type AB recipients. The degree of cross-transplantation needs to be carefully controlled, however, to ensure it does not lead to a repetition of the practises that have given rise to the blood type O problem. The mechanism by which the allocation is done in the queuing model presented here — subjecting each organ as it becomes available to the same random chance of being cross-transplanted, independent of all other factors — was done for reasons of mathematical tractability of the results obtained. In reality, p_O and p_A must equal the long run fraction of cross-transplanted organs. From uniquely a waiting time perspective, the manner in which waiting times should be equalised should be dynamic, periodically allowing or disallowing the O $\rightarrow$ A and A $\rightarrow$ AB cross-transplantation so as to keep the waiting times on the waitlists in balance. However, such a perspective ignores all medical considerations beyond waiting time. Implementable strategies need to be developed which reflect medical decision-making first and foremost, with issues such as waiting times relegated to second place due to their long run impact on the health of patients awaiting transplantation. The development of such strategies will be pursued in future work: first in the context of liver transplantation in Canada, and then broadening in scope to consider other organs domestically, and in other jurisdictions. Thus, the conclusions obtained from the AITQ model presented herein have the potential to have broad implications for public health policy and issues of equity of access for transplant patients in general.

It is a non-trivial task to infer what the results would look like for any waitlist in which the patient placement rate exceeds the organ availability rate. What one can say is that any such waitlist only achieves "stability" by patients coming off the waitlist, due to death, becoming too ill to transplant, recovering one's health while waiting, and so on. In this context, one cannot ignore the priority aspects, as sicker patients will gain access sooner. In turn, healthy patients will wait longer, to the point that some of them suffer a degraded health status, and so on. Clearly, models to consider these interactions are a worthy area for future study. Nonetheless, the track record of the past decades reveals that ad hoc cross transplantation has been shown repeatedly to disadvantage patients of type O. On the other hand, we have shown that ABO-identical waitlists are such that there are too few organs from the smaller blood groups to provide comparable access on their own. Thus, while our model cannot determine mathematically what the ideal cross-transplantation frequency rate should be in such a context, one can nonetheless show that some cross-transplantation will be needed, and it is our opinion that it is likely to entail the pairings we have identified for many countries in Europe and the Americas, and possibly in Africa. As the Asian blood type mix is substantially different, a different arrangement would be needed.

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References

[1] M. Barone, A.W. Avolio, A. Di Leo, P. Burra, A. Francavilla, ABO blood group-related waiting list disparities in liver transplant candidates: effect of the MELD adoption, Transplantation 85 (2008) 844–849.
[2] G.M. Danovich, J.M. Cecka, Allocation of deceased donor kidneys: past, present, and future, Am. J. Kidney Dis. 42 (2003) 882–890.
[3] P. Glander, K. Budde, D. Schmidt, T.F. Fuller, M. Giessing, H.-H. Neumayer, L. Liefeldt, The 'blood group O problem' in kidney transplantation — time to change? Nephrol. Dial. Transplant. 25 (2010) 1998–2004.
[4] J.C. Hussey, J. Parameshwar, N.R. Banner, Influence of blood group on mortality and waiting time before heart transplantation in the United Kingdom: implications for equity of access, J. Heart Lung Transplant. 26 (2007) 30–33.
[5] L. Liefeldt, K. Budde, P. Glander, Accumulation of elderly ESRD patients with blood group O on the waiting list, letter to editors, Transplant. Int. 24 (2011) e83–e84.
[6] P.J. Phelan, P. O'Kelly, D. O'Neill, D. Little, D. Hickey, M. Keogan, J. Walshe, C. Magee, P.J. Conlon, Analysis of waiting times on Irish renal transplant list, Clin. Transplant. 24 (2010) 381–385.
[7] H. Rexius, F. Nilsson, A. Jeppsson, On the allocation of cardiac allografts from blood group-O donors, Scand. Cardiovasc. J. 36 (2002) 342–344.
[8] D.A. Stanford, E.M. Renouf, V.C. McAlister, Waiting for liver transplantation in Canada: waitlist history 2000–04 and sensitivity analysis for the future, Health Care Manag. Sci. 11 (2008) 184–195.
[9] Percentage of Blood Types In Canada. Retrieved from Canadian Blood Services website: http://www.blood.ca/centreapps/internet/uw_v502_mainengine.nsf/page/Percentage-of-Blood-Types-In-Canada?OpenDocument (accessed 31.10.13).
[10] W. Feller, An Introduction to Probability Theory and its Applications, Wiley, New York, 1968.
[11] R.W. Conway, W.L. Maxwell, L.W. Miller, Theory of Scheduling, Addison-Wesley, Reading, Mass, 1967.
[12] L. Kleinrock, Queueing Systems, Volume I: Theory, Wiley, New York, 1975.
[13] S. Drekic, D.A. Stanford, D.G. Woolford, A self-promoting priority model for transplant queues, Invited talk, in: 1st INFORMS Healthcare Conference, Montreal, Quebec, June, 2011.
[14] R. Wiesner, E. Edwards, R. Freeman, A. Harper, R. Kim, P. Kamath, et al., Model for end-stage liver disease (MELD) and allocation of donor livers, Gastroenterology 24 (2003) 91–96.
[15] L. Kleinrock, Queueing Systems, Volume II: Computer Applications, Wiley, New York, 1975.
[16] http://www.bloodbook.com/world-abo.html. Online search, November 8th 2012.