Analysis of the Renal Transplant Waiting List in the País Valencià (Spain)

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Abstract

In this paper we analyse the renal transplant waiting list of the País Valencià in Spain, using Queueing Theory. The customers of this queue are patients with end-stage renal failure waiting for a kidney transplant. We set up a simplified model to represent the flow of the customers through the system, and perform Bayesian inference through simulation to estimate parameters in the model. Finally, we consider several scenarios by tuning the estimations achieved and computationally simulate the behaviour of the queue under each one. The results indicate that the system could reach equilibrium at some point in the future and the model forecasts a slow decrease in the size of the waiting list in the short and middle term.

Keywords: Health services, Queueing, Simulation, Stochastic processes, Bayesian statistics.

1 Introduction

In general, the analysis of a queue is highly desirable. It allows managers to gain knowledge of its behaviour for planning purposes, and it also permits managers to have accurate information about the time clients are expected to spend in the queue. In health care, where waiting lists are very common, the queueing analysis becomes even more important since resources are usually scarce and must be optimised. In this paper, we focus on a transplant

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waiting list; specifically, we analyse the renal transplant waiting list of the País Valencià, one of the seventeen autonomous regions into which Spain is divided.

Patients with end-stage renal failure need to receive renal replacement therapy to keep them alive. The three main types of therapy are haemodialysis, peritoneal dialysis and kidney transplant. Under haemodialysis the patient has to go to hospital to use a kidney machine. They do that two or three times a week and they spend about three or four hours there each time. Peritoneal dialysis requires patients to carry a bag of sterile fluid that has to be changed every six to eight hours. Patients who receive a transplant are given immunosuppressive drugs indefinitely to reduce the risk of rejection, though in general it enables them to resume normal life activities and that is the reason why it is considered to be the best treatment. In this sense, several observational studies show that patients who undergo transplantation enjoy a longer and a better quality of life than those under either dialysis treatment (Port *et al.*, 1993, Matesanz, 1994, Eggers, 1998, Wolfe *et al.*, 1999). In addition to being the more convenient treatment from a social point of view, there is general agreement on the fact that it is also the cheapest one (Eggers, 1992).

Kidneys for transplantation usually come from cadaveric donors, although eventually they also can come from live ones (e.g. patients' relatives). Unfortunately, there is an imbalance between arrivals onto the waiting list and donors, the former being greater than the latter. This happens in the País Valencià, in Spain and in most countries around the world (see Table 1). This means list sizes grow, although at different speeds depending on the donation rate of the country. This shortage of organs is the reason why the allocation of kidneys to patients must be done very carefully.

The allocation of the cadaveric kidney among the candidates is done mainly on the basis of the affinity between the tissues of the donor and those of the potential recipients. The more compatible the tissues, the lower the risk of rejection. Firstly, their blood type must be compatible. Secondly, the tissue type (known as HLA-type) of the donor is cross-matched with that of the candidates. Finally, a test is performed to determine whether the candidate has antibodies to the proteins of the donor. This test must be negative for the candidate to be eligible. There are also other non-immunological features which have an influence on the graft outcome, such as age or gender (Chertow *et al.*, 1996), which have to be taken into account when allocating a kidney among the candidates.

Several analyses of renal transplant waiting lists can be found in scientific papers, using different numerical techniques and pursuiting quite distinct objectives. Considerable research has been devoted to the analysis of allocation policies which are able to guarantee equity (Wujciak and Opelz, 1993; De Meester *et al.*, Smits *et al.*, 1998, 2000; Zenios *et al.*, 2000). Papers focused on management can also be found, such as that by Davies and

Roderick (1998), which explores the overall demand for renal replacement therapy in the UK over the next 15 years.

For the Valencian Regional Health Authority the renal transplant waiting list in the País Valencià is an important concern. And that interest led them to promote a study, the scope of which was to gain knowledge about fairly basic issues such as whether or not the size of the queue would increase and, if so, its rate of growth, as well as the expected length of patients' waiting times. This paper shows a first approach to addressing this issue by means of statistical procedures and queueing modelling.

With regard to the renal transplant waiting list in the País Valencià, it is worth mentioning that there are 40 Transplantation Units in Spain, which are coordinated by the National Organization of Transplants (Matesanz and Miranda, 1996). Four of them are located in the País Valencià. The Spanish Network has one coordinator in each autonomous region, who is usually a member of the Regional Health Service, and one in every Hospital as well. Every Transplantation Unit is situated in a hospital and is responsible for procuring organs for all patients belonging to its geographical area of influence as well as for coordinating all steps involved in the transplantations. When there is an available kidney in a Unit, it is first offered to suitable candidates registered on its renal waiting list. If there are none, it is offered to the other Units in the same autonomous region. If there are still no compatible candidates, it is offered at national level, and in the case of the absence of appropriate recipients in Spain, it is finally offered to official transplant networks abroad.

The four waiting lists can be combined into a single one by just pooling them together, which could be considered as the renal transplant waiting list in the País Valencià. And that is actually the way the Regional Health Service considers it, as a single list that is analysed here from a statistical point of view for the first time.

2 Data

Data consisted of two sets of individual registries: the first one contained the information of patients with end-stage renal failure who arrived onto the Renal Transplantation Waiting List between January 1997 and December 1999, both inclusive; the second one comprised donations which were made throughout the same period. The information was supplied by the Registry of Transplantations of the País Valencià. For confidentiality reasons, data related to the identification of either patients or donors were not provided.

We chose the period mentioned above for homogeneity reasons, since there were only three Transplantation Units in the País Valencià until 1996, when the fourth one started its activity and greatly influenced the behaviour of the system. As for the length of the period, we chose it to be long enough to have sufficient data to carry out the statistical inference.

3 Queueing analysis

Queueing Theory is a natural framework for analysing the renal transplant waiting list as a system where 'customers' demand 'service'. The three key elements of a queue are the arrival pattern, the service mechanism and the queue discipline. From a statistical point of view, the process of arrivals and the process of service are considered to be stochastic and some inference is carried out through statistical procedures. An introduction to the statistical analysis of a queue can be found in Armero and Bayarri (2001).

The evolution of the renal transplant waiting list depends on two independent processes: the process of new arrivals onto the waiting list and the process of donations, together with the fact that a donor can give one or both kidneys. Before setting up our queueing model, we first identify its elements. In this sense, the *customers* are the patients who are waiting on the list for a transplant. An *arrival* occurs when a new patient with end-stage renal disease is admitted onto the waiting list and by the end of the study has been transplanted or is still waiting. A *departure* from the system happens when a donor's kidney is grafted onto a patient. The *service time* for a patient is the time that stretches from the transplantation of the preceding customer to their own transplant. Finally, the fact that a donor can give one or two kidneys leads to a *bulk service* of random size. Figures 1 and 2 show graphical representations of the time that a customer is queueing to be served, the service time and the total time spent in the system. Notice that two-kidney donations (Figure 2) allow two customers to be served at the same time.

With the elements defined above, we considered an $M/M^X/1$ queue (Hall, 1991) to model the renal transplant waiting list. This means we assume that the number of daily arrivals and the number of daily donations are two independent stochastic processes which follow Poisson distributions of rate λ and μ, respectively. Specifically, if $N_A(t)$ is the number of arrivals in t days and $N_D(t)$ the number of donations in t days, the model states

$$\begin{aligned} N_A(t) \mid \lambda &\sim \mathsf{Poisson}(\lambda t) \\ N_D(t) \mid \mu &\sim \mathsf{Poisson}(\mu t) \end{aligned} \tag{1}$$

It is worth remarking that λ not only governs the behaviour of the number of arrivals $N_A(t)$, but also that of T_A, the time between two consecutive arrivals. The same holds for μ with respect to the number of donations $N_D(t)$ and T_D, the time between two consecutive donations. Indeed, expression (1) is equivalent to

$$T_A \mid \lambda \sim \mathsf{Exponential}(\lambda)$$
$$T_D \mid \mu \sim \mathsf{Exponential}(\mu) \tag{2}$$

In addition, the donations come in groups whose size is a random variable X that may take values $X = 1$ and $X = 2$ such that

$$P(X = 2 \mid \theta) = \theta \tag{3}$$

Thus, the distribution of the number of transplants in t days $N_T(t)$, given the number of donations $N_D(t)$ and the proportion of two-kidney donations θ is

$$N_T(t) \mid N_D(t), \theta \sim N_D(t) + \mathsf{Binomial}(N_D(t), \theta) \tag{4}$$

Finally, we cannot assume that the discipline of the queue is FIFO (first-in-first-out), that is, customers are served in the same order in which they arrive into the system. This is due to the fact that patients are transplanted depending on criteria mainly related to compatibility with the donor. So it could be said that there is no typical discipline associated to this queue, since patients are reordered every time a new donation happens.

An important feature of any queue is the traffic intensity ρ, which is a measure of the congestion level of the system. Values lower than 1 indicate that the system will eventually reach equilibrium. Values equal to or higher than 1 indicate that the system is in a transient state and will become clogged. Under the assumptions above, expression (5) allows it to be computed.

$$\rho = \frac{\lambda}{\mu(1 + \theta)} \tag{5}$$

Note that the numerator of the traffic intensity is the arrival rate, whereas the denominator is the donation rate times the average number of kidneys per donation, which could be seen as the transplantation rate. So in this case, ρ simply compares the arrival rate to the transplantation rate. Therefore, a value lower than one means there are more transplantations than arrivals, which would imply equilibrium. A value higher than one would indicate just the opposite, as mentioned above.

Quantities λ, μ, θ and ρ, the parameters of the model, are unknown and need to be estimated using statistical tools. The statistical inference is performed from a Bayesian perspective. To do so, the information about the parameters provided by the data through the likelihood is combined with prior knowledge (if available). Both sources of information are merged by applying Bayes' theorem which gives rise to the posterior distribution of the parameters.

A very appealing feature of the Bayesian approach are the posterior predictive distributions. They allow us to forecast the values of possible future observations of the variables we are interested in, taking into account the data already observed. In Armero *et al.* (2003) the inference process that leads to the posterior predictive distributions of T_A, T_D, $N_A(t)$, $N_D(t)$ and $N_T(t)$ as well as to the posterior distribution of the parameters is explained in detail.

4 Results

During the period under analysis, 531 new patients were included in the renal transplant waiting list and 323 donations ocurred, 82 simple and 241 double, which gave rise to 564 kidneys. Figures 3 and 4 show the daily frequency of arrivals and donations, respectively. It can be seen that on most days there are no arrivals or donations, and when there are, there are usually one or at most two, further values being unlikely, although eventually possible. Figure 5 shows the daily number of available kidneys for transplantation. It reveals that usually both donor's kidneys are usable.

As for transplantations, 293 out of the 564 kidneys were transplanted to patients who entered the list during the period under study. The rest were grafted onto patients already on the list before 1997.

To check the assumption of the Poisson distribution for the processes of arrivals and donations, we used the Kolmogorov-Smirnov test. There was no evidence against that hypothesis for the donation process $(\mathrm{ks} = 0{,}0055, \mathrm{p} = 1)$ but there was some for the process of arrivals $(\mathrm{ks} = 0{,}0822, \mathrm{p} = 0{,}0011)$. This is because of the presence of some heterogeneity in the daily number of arrivals. It may be due to the fact that an arrival is more likely to happen on working days and improbably at weekends and holidays, in contrast to a donation, which can happen any day at any time.

The results above, together with the length of the period considered (1.095 days), determined both the posterior distributions of the parameters and the posterior predictive distributions of the variables.

4.1 Posterior distributions

With the aim of expressing our initial vague knowledge about the parameters in the model, and because we assumed independence between them, we considered independent non-informative prior distributions for λ, μ and θ. Specifically, we chose the following flat prior distributions:

$$
\begin{aligned}
\lambda &\propto \frac{1}{\lambda} \\
\mu &\propto \frac{1}{\mu} \\
\theta &\sim \mathsf{Uniform}(0,1)
\end{aligned}
\tag{6}
$$

Starting from the prior distributions in equation (6), the posterior distributions for the three parameters could be obtained analytically. They turned out to be as follows:

$$
\begin{aligned}
\lambda \,|\, \mathsf{data} &\sim \mathsf{Gamma}(\lambda \,|\, 531, 1.095) \\
\mu \,|\, \mathsf{data} &\sim \mathsf{Gamma}(\mu \,|\, 323, 1.095) \\
\theta \,|\, \mathsf{data} &\sim \mathsf{Beta}(\theta \,|\, 242, 83)
\end{aligned}
\tag{7}
$$

The posterior distribution of the intensity traffic ρ was obtained by simulation. For each parameter we generated 2.500 values from the corresponding posterior distribution in expression (7) and for every vector $(\lambda^{(i)}, \mu^{(i)}, \theta^{(i)}),\ i = 1, \ldots, 2.500$ we computed the corresponding value $\rho^{(i)}$ using expression (5), thus obtaining a sample $\{\rho^{(i)},\ i = 1, \ldots, 2.500\}$ from the posterior distribution of the traffic intensity $p(\rho \,|\, \mathsf{data})$.

Point estimators, such as the mean and the variance for the parameters can easily be computed from the distributions in expression (7) or from the numerical approximation to the posterior distribution of ρ.

Specifically, the posterior expected value and the variance for the daily rate of new arrivals λ were

$$
\begin{aligned}
E(\lambda \,|\, \mathsf{data}) &= 0{,}48493 \\
Var\,(\lambda \,|\, \mathsf{data}) &= 0{,}00044
\end{aligned}
$$

which means that, on average, 0,48 new persons per day arrive onto the list. Or equivalently (Armero et al., 2003), the expected time between two consecutive arrivals onto the list is $E(T_A \,|\, \mathsf{data}) = 1/0{,}48 = 2{,}06$ days, that is, approximately one arrival every two days. The small variance of the posterior distribution is indicative of an accurate estimation.

The resulting estimations for the daily rate of donations μ were

$$
\begin{aligned}
E(\mu \,|\, \mathsf{data}) &= 0{,}29498 \\
Var\,(\mu \,|\, \mathsf{data}) &= 0{,}00027
\end{aligned}
$$

They show that 0,29 donors per day are expected. Again, this means that the mean time between two consecutive donations is $E(T_D \,|\, \mathsf{data}) = 3{,}39$

days, which roughly speaking means that three donations happen every ten days. Again, the small value of the variance shows a high concentration of the posterior distribution.

As for the probability of a two-kidney donation θ,

$$E(\theta \,|\, \mathsf{data}) = 0{,}74462$$
$$Var\,(\theta \,|\, \mathsf{data}) = 0{,}00058$$

which tell us that, on average, 75% donors have both kidneys profitable. Results show high precision as well.

So, from the above results, in general terms we infer that in ten days, on average we would expect 5 new arrivals onto the list and 3 donors who would give 5,25 kidneys, which would suggest that the system could reach equilibrium in the long run. The traffic intensity ρ is the right measure to quantify this feature properly. From the sample of the posterior distribution for ρ, the following was obtained

$$E(\rho \,|\, \mathsf{data}) = 0{,}94900$$
$$Var\,(\rho \,|\, \mathsf{data}) = 0{,}00456$$

meaning that the system could achieve the steady-state, although there still remains a non-negligible chance for the system to get more and more congested, since $P(\rho < 1 \,|\, \mathsf{data}) = 0{,}788$ cannot be considered conclusive.

4.2 Simulation

The posterior distributions of the parameters allowed us to gain knowledge about some important features of the renal transplant waiting list. But managers are usually very concerned about forecasting too, mainly for planning purposes. So a further natural step consisted of predicting the behaviour of the renal transplant waiting list for some period in the near future. To address this issue, it is necessary to know the posterior predictive distribution of the number of people waiting for a transplant at time t, $p(N_W(t) \mid \mathsf{data})$. However, there is no analytical closed expression for such a distribution, because the distribution $p(N_W(t) \mid \lambda, \mu, \theta)$ is involved in the computation, and that distribution is unknown. So, we explored $p(N_W(t) \mid \text{data})$ through simulation.

To do so, we took the 2.500 values sampled from the posterior distributions of the parameters and for each vector $(\lambda^{(i)}, \mu^{(i)}, \theta^{(i)}),\ i = 1, \ldots, 2.500$ we simulated the evolution of the queue for the next year and a half (548 days), by means of time discrete event simulation (Law and Kelton, 2000) using ARENA software (www.arenasimulation.com). For every simulation $i = 1, \ldots, 2.500$, we recorded the daily number of people in the waiting list from 1st January 2000 to 31st July 2001 $\{N_W^{(i)}(t), t = 1, \ldots, 548\}$. All simulations started at $N_W(0) = 446$, the actual number of people waiting for a kidney transplant on 31st December 1999.

Then, for every t we averaged out the simulations to achieve the Monte Carlo estimator (Gilks *et al.*, 1996) for the expected value of $N_W(t)$

$$E\left(N_W(t) \mid \mathsf{data}\right) \approx \frac{1}{2.500} \sum_{i=1}^{2.500} N_W^{(i)}(t)$$

The resulting mean value and a 95% prediction band for $N_W(t)$ are shown in Figure 6. The graph confirms that, if the same conditions of the analysed period hold, the size of the queue is expected to decrease very slowly, although it also reflects that the further we go, the lower is the accuracy of the forecast.

We can also contrast our results with what has really happened, since the number of patients on the waiting list is available for the first day of every year. Indeed, the size of the list on 1st January 2001, 2002 and 2003 were 401, 415 and 378, respectively. It is remarkable that the actual behaviour of the waiting list roughly matched that predicted by the model we considered. However, since our simulations stopped on 31st July 2001, from a formal point of view we can only compare one observation, which is that corresponding to 1st January 2001, that is, the observed value for time $t = 367$. The model forecasted $E(N_W(367) \mid \mathsf{data}) = 428$ patients in the list, with a 95% prediction band $[360, 494]$, which includes the true observed value 401.

Finally, we set up several scenarios by tuning the conditions of the system and compared the results achieved with those obtained under the current conditions. Explicitly, we simulated the behaviour of the queue under the assumption of the three following increments in the donation rate:

Scenario 1 An average increase of 6 donations/year or, equivalently, one more kidney every two months. This implies changing the posterior expected value of μ from 0,29498 to 0,31142.

Scenario 2 An average increase of 12 donations/year (one more kidney every month). This involves changing the posterior mean of μ from 0,29498 to 0,32786.

Scenario 3 An average increase of 24 donations/year (two more kidneys every month), which means taking 0,36073 instead of 0,29498 as the posterior expectation of μ.

Figure 7 shows the comparison between the predicted mean of the size of the waiting list achieved under the current conditions and those obtained under the proposed scenarios. It can be seen how an increase in the donations rate cuts down the size of the waiting list. Specifically, under the current conditions, the model forecasts 428 people on average waiting for a kidney transplant after one year and a half. This means a reduction of around 4% in the size of the list . Under the conditions of scenario 1, the model predicts, again on average, 413 people waiting in the renal transplant waiting list after the same period, so that the reduction would be around 7%. Under scenario 2, the expected size of the list would be 397, that is, a reduction of around 11%. And last, under scenario 3, the model forecasts an expected value of 366 patients waiting for a kidney transplant, thus achiving a reduction in the original size of around 18%.

This pattern holds true as long as the process of arrivals remains unchanged. Indeed, a rise in the arrivals rate would compensate for the increments in the donations rate, keeping the size of the queue as it is or even increasing it if that increment is too pronounced. On the contrary, a decrease in the former would cause a steeper decrease in the size of list.

5 Discussion

In this paper we propose a simplified but sensible model that roughly represents the flow of the patients on the renal transplant waiting list. However, we are aware that the dynamics of the waiting system are considerably more complex than our model. In fact, patients can leave the queue for several reasons, either because they die, because they move to another waiting list in another Spanish autonomous region, or because they abandon treatment. It is also worth to remarking that there is no specific order of transplantation, since a donor's kidney is grafted onto the best suitable candidate according to compatibility matching. Besides that, children are special patients because either of the dialysis treatments impedes their normal growth, so they are prioritised on the list. In addition, when a graft fails the patient may be included on the waiting list again. As for donations, most donations become transplants, but a few of them do not because the kidney may be damaged due to too long period of ischaemia. But even though we did not account for these issues when we set up our model, the results obtained were quite coherent and provided an initial quantification of the main features of the system which, in turn, allowed us to forecast its evolution.

As mentioned previously, the length of the period was chosen as being long enough to have enough statistical power, but it was also short enough to avoid the impact of technological progress on the admission and transplantation policies. The latter is clearly reflected in the fact that the age limits for being admitted either as a patient on the list or as a donor have increased notably in recent years. This could suggest considering the arrival and transplantation rates as dynamic processes instead of constant during a period in a further approach.

The assumption of the Poisson process seems appropiate for the process of donations but not for that of arrivals, which shows overdispersion, probably due to some measurement error. However, the $M/M^X/1$ queueing model is very robust to this hypothesis, thus making inference reliable.

It is also worth remarking that the has always been a queue, since patients gathered on the list from the very beginning and so there has always been a 'stock' of patients waiting. This fact is also key to trusting the model.

Also, the discipline of the queue, that is the order in which patients are transplanted, does affect their waiting time in the system but has nothing to do with the size of the list. Since we were only concerned with making inferences about the latter, the true discipline of the queue becomes irrelevant.

We mentioned that both the number of arrivals and the number of donations are the two stochastic processes that determine the behaviour of the system. However, when we set up our scenarios, we just tuned the number of donations. We did so because managers can influence the process of donations much more than that of arrivals. Indeed, part of the work of the coordinators of the hospitals consists of convincing a potential donor's relatives to give the healthy organs of that potential donor for transplantation.

In summary, we believe the model we propose here picks up the main features of the renal transplant waiting list and provides a basic quantification of the situation of the system. It also allows its evolution to be forecasted in the short and middle term, achieving sensible results.

6 Future extensions

There is an ongoing project together with the Transplantation Units in the País Valencià to analyse the queue more deeply, considering a more realistic model that accounts for compatibility of tissues, age and sex between recipients and donors as well as potential abandonments of the queue. This involves updating the data and collecting new information from the clinical reports that was not present in the Registry of Transplants of the Regional Health Service.

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Country	New arrivals onto the list	Number of transplants	People in the list on 31-Dec-2002
País Valencià	Unavailable	196	378
Spain	Unavailable	2.032	4.014
Austria	539	410	774
Belgium	549	349	876
Cyprus	30	46	140
Denmark	194	171	375
Finland	223	172	214
France	2.637	2.255	5.227
Germany	3.372	2.184	9.623
Israel	172	165	594
Italy	3.711	1.588	8.434
Sweden	370	308	445
Switzerland	352	204	498
The Netherlands	803	560	1.287
UK	2.438	1.573	6.419
USA	22.603	14.722	53.880

Table 1: Number of new arrivals onto the renal transplant waiting list, number of transplants effected and size of the list in several countries in 2002. Source: Organización Nacional de Trasplantes (Spanish National Organization of Transplants.)

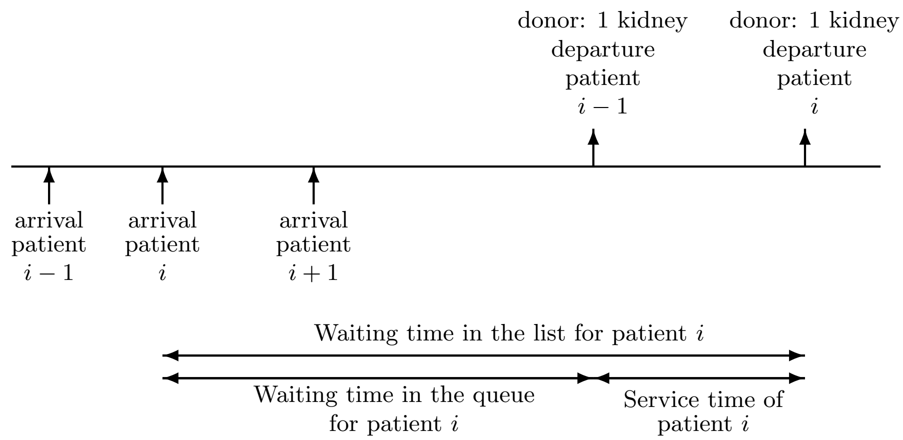

Figure 1: Graphical representation of queueing time, service time and total time spent in the system by a customer when only one kidney is obtained from the donor.

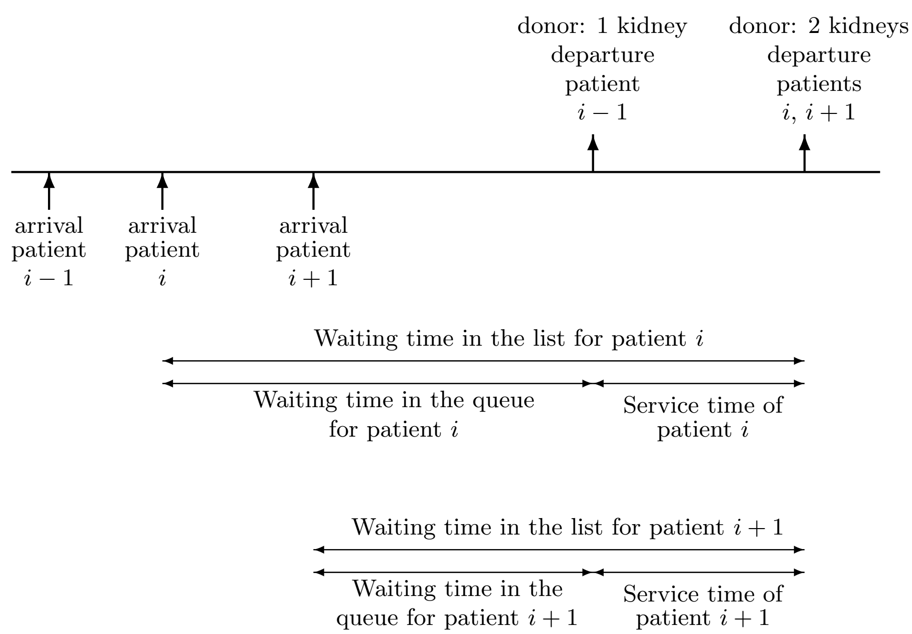

Figure 2: Graphical representation of queueing time, service time and total time spent in the system by the customers when the two kidneys are obtained from the donor.

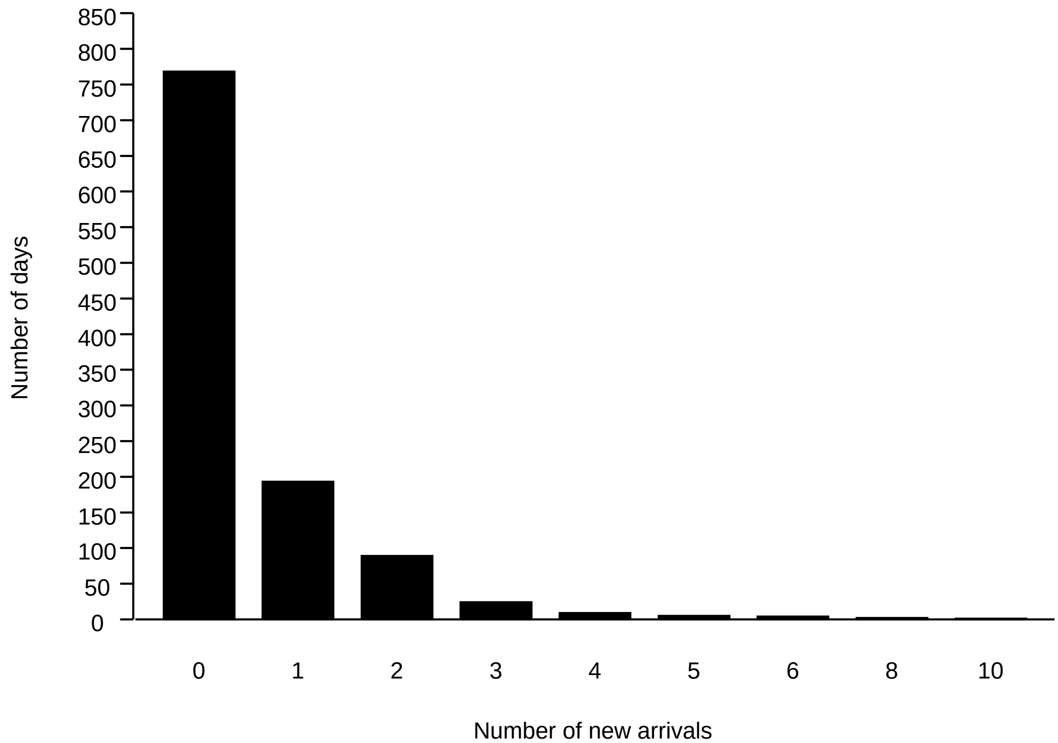

Figure 3: Daily frequency of new arrivals of patients onto the waiting list.

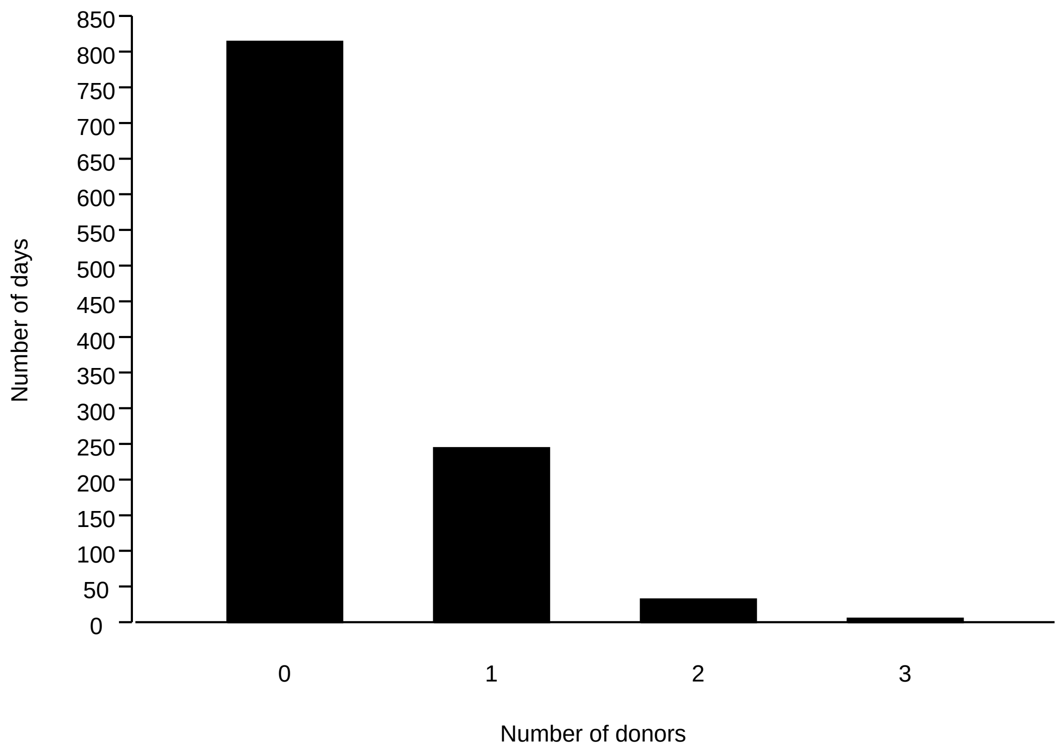

Figure 4: Daily frequency of the number of donors.

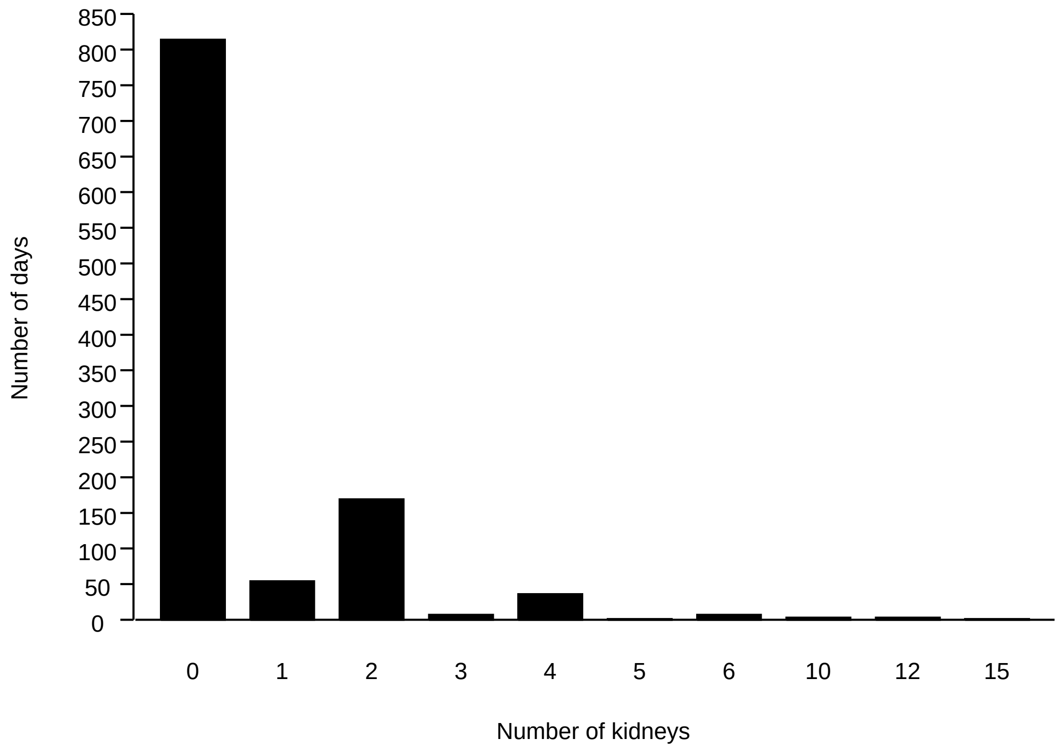

Figure 5: Daily frequency of the number of donated kidneys.

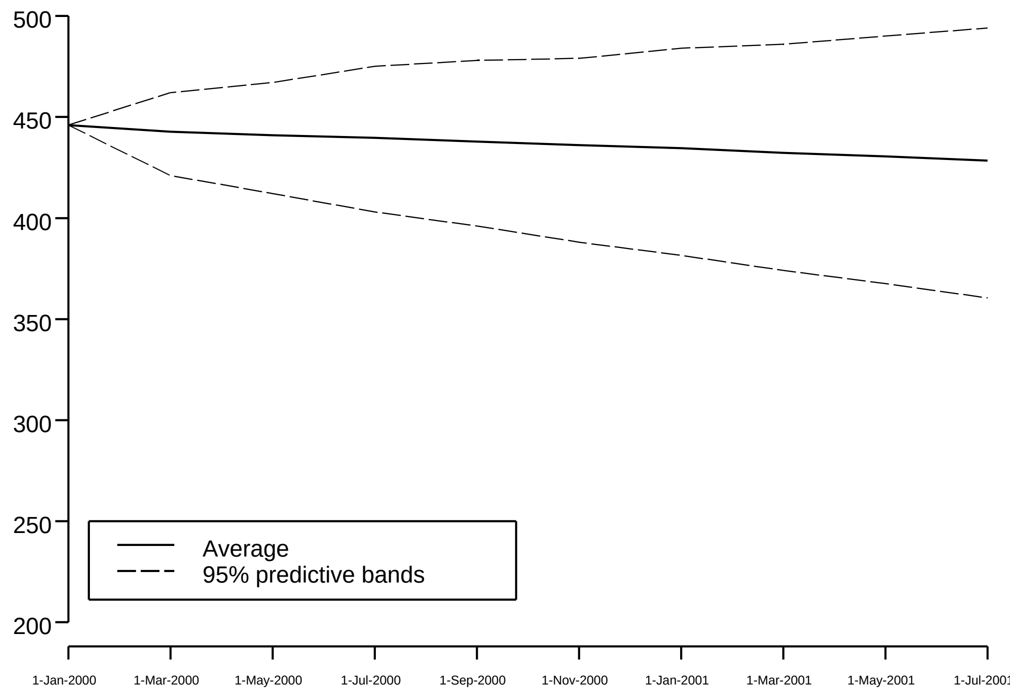

Figure 6: Predicted values of the size of the renal transplant waiting list for the period 1-Jan-2000 to 1-Jul-2001

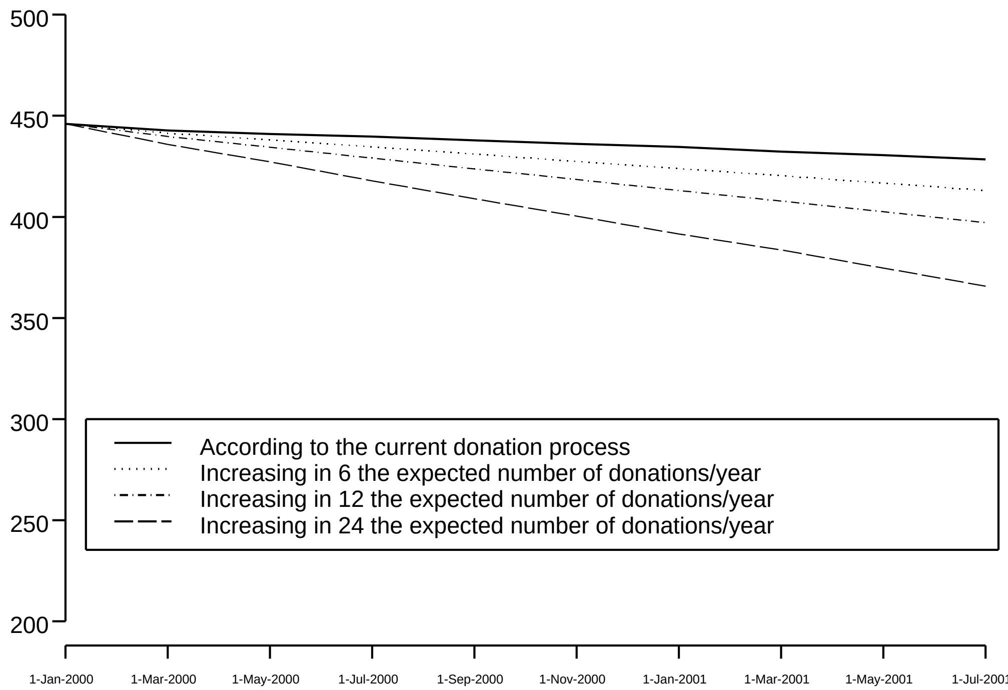

Figure 7: Predicted values of the size of the renal transplant waiting list for the period 1-Jan-2000 to 1-Jul-2001, according to the current process of donations and tuning it, by increases of 6, 12 and 24 in the expected number of donations/year.