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PREDICTING THE BEHAVIOUR OF THE RENAL TRANSPLANT WAITING LIST IN THE PAÍS VALENCIÀ (SPAIN) USING SIMULATION MODELING

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ABSTRACT

A discrete event simulation model has been set up in order to analyze the renal transplant waiting list in the País Valencià, one of the autonomous regions in which Spain is divided. The model combines the information of the arrival of the patients onto the list and the process of donations, which also depend on the number of kidneys provided by each donor. Bayesian inference has been used to take into account the uncertainty about the parameters of the input distributions (acceptance, donation and transplantation rates). After validating the model, predictions about the future behaviour of the waiting list have been done. Results indicate a decrease in the size of the waiting list in a short and middle term. Comparison with other strategies of simulation has been done in order to confirm the problem of underestimation of the variance of the expected simulation output.

1 INTRODUCTION

It is well recognized that kidney transplantation is the best treatment for chronic kidney failure. Firstly, as several observational studies have shown (like the one performed by Port et al. 1993), it is the more convenient choice from a social point of view (results in a longer and a better quality of life for renal transplant recipients). In addition to this, there is the general agreement that it is the cheapest one (Eggers 1992).

Nevertheless, the supply of cadaveric kidneys for transplantation from the donors does not meet the potential candidates, resulting in an increasing size of the waiting list for a renal transplant in almost all the countries. This question has motivated several authors to study related questions such as the allocation of kidneys, the evolution of the waiting list or predictions on the future behaviour.

The difficulty of analyzing empirically this issues has made discrete event simulation a usual tool in transplantation literature. See for instance, Davies and Roderick (1998) for an analysis of the evolution of the number of patients needing a transplant, Zenios, Chertow, and Wein (2000) for an study about the equity of allocation policies, Taranto et al. (2000) for an allocation model for cadaveric kidneys, McLean (2001) for an study of risk strategies in renal transplantation, etc.

The main purpose of this work is gaining knowledge about the evolution of the renal transplant waiting list in the País Valencià from the past, in order to make predictions on its future behaviour. To do so, we use a discrete event simulation model that combines the information of two stochastic processes, the patients arrivals and the process of donations.

2 BACKGROUND

The renal transplant waiting list in the País Valencià is an important concern for the Valencian Regional Health authorities. This interest motivated them to promote a study whose main objective was to learn about the future behaviour of the size of the list, as well as the expected length of patientsâ waiting times. This work is an initial study of the first one of these issues.

In Spain there are 40 Transplantation Units, all coordinated by the National Organization of Transplants (Matesanz and Miranda 1996). Four of them are located in the País Valencià. 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. Each Unit has its own waiting list, although the four 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. This is the way the Regional Health Service considers it.

3 DATA

In order to computerize, manage and keep all the information relative to transplants in the País Valencià, the Valencian Regional Government created in 1992 the Registry of Transplants. The data for this analysis has been supplied by this Registry.

In particular, we have collected the daily number of patients entering the waiting list, the daily number of donors and the number of kidneys, one or two, provided by each donor. They were registered from January 1997 to December 1999. We ruled out data before January 1997 because in 1996 a new transplant hospital joined the network (making the actual total of four) and that modified the management of the waiting lists.

During the period under analysis (1095 days in all), 531 new patients were accepted onto the renal transplant waiting list. 564 kidney transplants coming from 323 donations were carried out. This apparent discrepancy between donations and kidneys is due to the fact that a donor can provide one or both kidneys. Specifically, we have noticed 241 double donations and only 82 single.

4 MODELING OF THE WAITING LIST

We have combined two sources of information in order to model the evolution of the renal waiting list of the País Valencià: the process of new arrivals onto the list and the process of donations, which also depend on the number of kidneys provided by each donor. Observed data confirmed the rather natural assumption that the donation process was a Poisson process. Nevertheless, there was some evidence against the fact that the arrival process was a Poisson process. This was maybe caused by 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 waiting list can be understood as a system in which an arrival occurs when a patient is admitted in the list and a departure means the graft of a donor's kidney onto a patient. Moreover, if we consider the patients as customers and the time between transplantation of two consecutive patients as the service time of the second patient, we can think of the waiting list as a queueing system with bulk service of random size (every donor can give one or two kidneys). See Figures 1 and 2 for graphical representations of the service mechanism of this system. This Markovian queue is denoted in Queueing Theory as $M/M^X/1$.

As our interest on this system is on its transient behaviour and Queueing Theory does not provide any analytical solution, simulation becomes necessary. We have built the simulation model using Arena software (<`http://www.arenasimulation.com`>).

5 BAYESIAN INFERENCE

One of the most important problems in the design of simulations is that of input modeling. In our model, and taking into account that input distributions are already delimited, the question becomes how to estimate their parameters. We use Bayesian methods to make inference about the input parameters (λ, the daily entrance rate; μ, the donation rate; and θ, the proportion of double donations). In other words, rather than using a single parameter estimation for the input parameters, we express our uncertainty about them via their posterior distribution.

With the aim of expressing our initial vague knowledge about the parameters in the model, and because we assumed independence between them, we considered the following independent non-informative prior distributions: $\lambda \sim \frac{1}{\lambda}$, $\mu \sim \frac{1}{\mu}$ and $\theta \sim \texttt{Uniform}(0, 1)$. From these prior distributions, the resulting posterior distributions for the three parameters are: $\lambda|\texttt{data} \sim \texttt{Gamma}(\lambda|531, 1095)$, $\mu|\texttt{data} \sim \texttt{Gamma}(323, 1095)$ and $\theta|\texttt{data} \sim \texttt{Beta}(\theta|242, 83)$. From these distributions, it is fairly easy to obtain point estimators (such as the posterior expectation and the posterior variance) and a central 95% posterior interval for the parameters. See Armero et al. (2003) for more details about this inferential analysis.

Bayesian methodology is not new in simulation input modeling. As Chick (1999) stands, "there are known pragmatic and theoretical difficulties associated with some standard approaches for input distribution selection. One difficulty is a systematic underestimate of the variance of the expected simulation output that comes from not knowing the *true* parameter values". He proposed Bayesian methods (in particular Bayesian model averaging) as an alternative, although acceptance of this methodology has not yet been achieved, in part because of increased computational demands, as well as challenges posed by the specification of prior distributions.

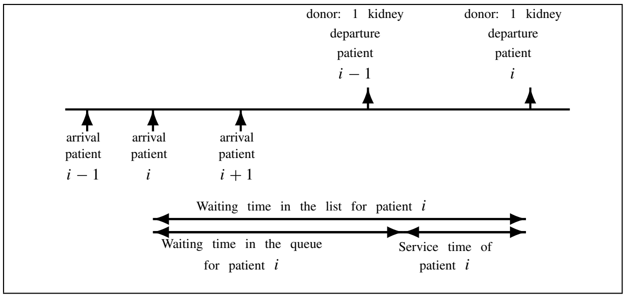

Figure 1: Graphical representation of the Queueing time, Service time and Waiting time on the List by a Patient When Only One Kidney is Obtained from the Donor

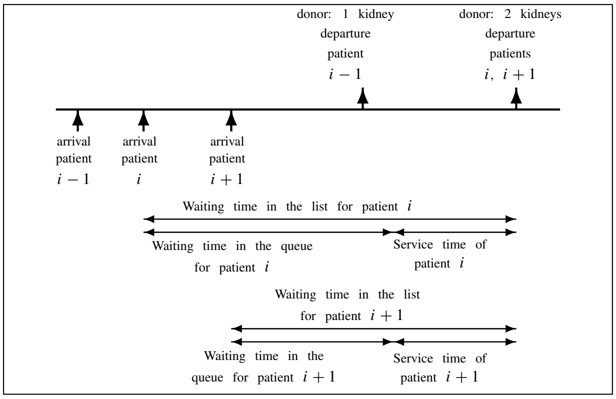

Figure 2: Graphical Representation of the Queueing Time, Service Time and Waiting Time on the List by a Patient When a Donor Provides Two Kidneys

6 SIMULATION ALGORITHM

Posterior distributions of the input parameters improved our knowledge about the renal transplant waiting list. But, decision-makers are also usually very concerned about forecasting figures of merit (e.g. the number of patients in the list), mainly for planning purposes (see for instance Roderick et al. 2003). In a similar way as Chick (2001), instead of using a single input parameter estimation, before performing each simulation replication, we sampled from the posterior distributions above mentioned.

More precisely, our main interest was predicting the number of patients $N_W(t)$ in the renal transplant waiting list at any instant t in the near future. This knowledge is expressed via the posterior predictive distribution $p(N_W(t)|\mathtt{data})$. To approximate this distribution, we first sampled 2500 values from the posterior distribution of the input parameters and for each sampled vector, we performed a simulation replication about the performance of the system for a period of one and a half year (548 days) starting in January 1st 2000. Validation of the model was performed based on data from period 1997 to 1999. Comparison with measures of performance in that period with simulated results confirmed the validity of the model proposed.

The result consisted of 2500 simulation replications, with replication i producing 548 random variables (daily number of people in the waiting list from 1st January 2000 to 31st July 2001), that is $\{N_W^{(i)}(t), i = 1, \ldots, 2500; t = 1, \ldots, 548\}$. 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, $\{N_W^{(i)}(t), i = 1, \ldots, 2500\}$ is a sample from the posterior predictive distribution $p(N_W(t)|\mathtt{data})$. Averaging out the simulations, we achieved the Monte Carlo estimator for the mean of $N_W(t)$

$$\mathrm{E}(N_W(t)|\mathtt{data}) \approx \frac{1}{2500}\sum_{i=1}^{2500} N_W^{(i)}(t)\,, \qquad (1)$$

and, similarly, for its variance

$$\mathrm{V}(N_W(t)|\mathtt{data}) \approx$$
$$\approx \frac{1}{2500}\sum_{i=1}^{2500}\left[N_W^{(i)}(t)\right]^2 - \left[\frac{1}{2500}\sum_{i=1}^{2500} N_W^{(i)}(t)\right]^2 . \qquad (2)$$

Figure 3 represents the box-plot of the 2500 simulated values of the posterior predictive distribution of the size of the renal transplant waiting list in various representative instants of the analyzed period. The graph confirms that, if the same conditions of the analyzed 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 $\mathrm{E}(N_W(367)|\mathtt{data}) = 428$ patients in the list, which is not far away from the true observed value 401. Indeed, a prediction 95% band for that value can be obtained as [360; 494], which includes the value 401.

7 OTHER STRATEGIES

In order to assess how this simulation algorithm is behaving in terms of a possible underestimation of the variance of the expected simulation output, our last efforts in this project

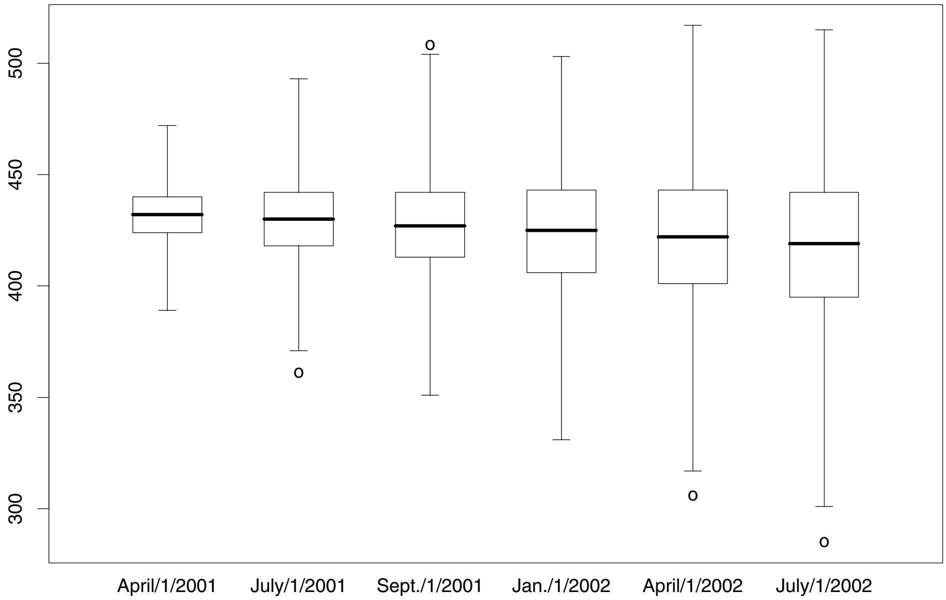

Figure 3: Box-plot of the 2500 Simulated Values of the Posterior Predictive Distribution of the Size of the Renal Transplant Waiting List in Various Instants of the Period 1-Jan-2000 to 1-Jul-2001

are in the way of analyzing the problem using different simulation strategies and how uncertainty about the input parameters influence in the predictions. In particular, to evaluate where the variance of the predictive number of patients in the list is coming from, we have performed different studies.

Firstly, we have compared results obtained by using different number of simulated values from the posterior distrib ution of the input parameters (keeping fixed the number of simulation replications). This comparison includes the usual (in simulation) situation in which there is only one starting input vector of estimated parameters (by means of the mean of the posterior distribution). In second place, maintaining the number of simulated values from the posterior distribution of the input parameters, we have compared results obtained by using different number of replicates. Finally, we have performed the same analysis of the last Section but based only on information from smaller periods (one or two last years, that is 98-99 period and 99 period).

In all cases, results indicated that the more confident in the parameters we are, the lower the variance of the expected output is. In particular, when performing simulation in the usual way, variance is rather smaller than when using simulation based on Bayesian inference. This happens because with the later procedure uncertainty about the input parameters is incorporated in the analysis. We must take into account that analysts are not usually so confident on their beliefs and so, their confidence about the parameters can result in underestimation of the variance of the output if they don't completely trust their beliefs.

8 CONCLUSIONS

This work, jointly with papers by Abellán et al. (2003) and Armero et al. (2003), are our first contributions to the statistical analysis of the waiting list for a renal transplant in the País Valencià. Up to now, we have a first model that combines information of the arrival process onto the list and the process of donations, from where we can make predictions about the future behaviour of the waiting list. Nevertheless, this model must be used with care if the interest is to make predictions about other measures of performance such as waiting time on the list of the patients, because it does not take into account differences between patients. Our next interests are on the way of developing 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. Other immediate efforts are going to be dedicated to better understanding the arrival, donation and transplant processes in relation to the age, geographical area of residence and date of entrance of the recipients and donors.

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