INSTITUTO DE ECONOMÍA

DOCUMENTO de TRABAJO

382
2010

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www.economia.puc.cl • ISSN (edición impresa) 0716-7334 • ISSN (edición electrónica) 0717-7593

Versión impresa ISSN: 0716-7334
Versión electrónica ISSN: 0717-7593

PONTIFICIA UNIVERSIDAD CATOLICA DE CHILE
INSTITUTO DE ECONOMIA

Oficina de Publicaciones
Casilla 76, Correo 17, Santiago
www.economia.puc.cl

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Javier Domínguez
Rodrigo Harrison*
Raimundo Atal

Documento de Trabajo Nº 382

Santiago, 2010

*harrison@uc.cl

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Javier Domínguez;. Email: javierdomi@hotmail.com

Rodrigo Harrison; Institute of Economícs, Pontificia Universidad Católica de Chile. Email: **harrison@uc.cl**

Raimundo Atal; Institute of Economics, Pontificia Universidad Católica de Chile. Email: ratal@uc.cl

Name of the departments to which the work should be attributed

Facultad de Medicina, Departamento de Urología. Pontificia Universidad Católica de Chile.

Facultad de Economia Instituto de Economía Pontificia Universidad Católica de Chile.

Contact information for the corresponding author:

Javier Dominguez

Pontificia Universidad Catolica de Chile Departamento de Urologia. Marcoleta 350. Santiago. Chile.

Phone: 56 2 3543468. Fax: 56 2 6384413 E-mail: javierdomi@hotmail.com (may be published)

Reprint requests:

Javier Dominguez

Pontificia Universidad Catolica de Chile Departamento de Urologia. Marcoleta 350. Santiago. Chile.

Phone: 56 2 3543468. Fax: 56 2 6384413 E-mail: javierdomi@hotmail.com (may be published)

Number of figures and tables: **1 table and 2 figures**

Cost-Benefit estimation of cadaveric kidney transplantation, the case of a developing country.

Abstract

In this paper we estimate cost savings for the health-care system and quality of life improvement for patients from an increase in the number of kidney transplants in Chile. To do so, we compare the present value of dialysis and transplantation costs and quality of life in a 20-year horizon.

We used Markov models and, in addition, introduce some degree of uncertainty in the value of some of the parameters that build up the model and, using Montecarlo simulations, estimate confidence intervals for our results.

Our estimates suggest that an additional kidney transplant has an expected savings value of US$ 28,000 for the health-care system. If quality of life improvement is also considered, expected savings rise to US$ 102,000. These results imply that, increasing donation rate by one donor per million people would turn into an estimated cost saving of US$ 827,000 per year, or near US$ 3 million per year if the effect in the quality of life is considered.

These results demonstrate that kidney transplants, along with a better quality of life for patients are a cost saving decision in developing countries.

Introduction

Kidney transplantation is nowadays the treatment of choice for end stage renal disease. Refinements in immunosuppression and care of severely ill patients have resulted in a significant improvement in graft survival and quality of life over dialysis **[1]**.

Dialysis expenditures in turn represent an important part of healthcare system budgets in many countries**.** For example, in 2006, expenditures in dialysis in Chile were near US$ 160 million, while 1800 people were officially in waiting list for a kidney transplant **[2]**. So, in a developing country with limited resources it is valuable to determine whether an important contribution could be made by increasing kidney donation and hence transplantation.

We try to address this issue in Chile, where cadaveric donation rates have been constantly low. In fact, in 2010 there were 5.4 donors per million people (pmp) in Chile, while 14 and 34 cadaveric donors pmp were recorded in Argentina and Spain, respectively. In 2009 in turn, there were 19 and 26 cadaveric donors pmp in Uruguay and the United States (U.S.), respectively. **[2, 3, 4, 5, 6].**

Previous studies have found that significant cost-saving could stem from increasing transplantation from cadaveric (Germany and Canada) and living (U.S.) donors. **[8, 9, 10]**. The authors interpret their results as an investment threshold, that is, the maximum value that authorities should be willing to invest in order to increase organ donation rates in the first case. Cost savings from living donation, in turn, are interpreted as the maximum payment that should be given to a living donor in order to induce his/her donation.

All these papers also suggest that there is a substantial improvement in quality of life for kidney recipients, measured as the Quality Adjusted Life Years (QALYs) gained **[1].**

In this paper, we perform the exercise of calculating these net benefits using Markov processes like the studies mentioned above, in a developing country, Chile.

Methododology

We developed a Markov model similar to the one used in previous studies **[8, 9]** in order to estimate the net present value of cumulative costs for both alternative treatments: transplantation and dialysis, and an approximation of the improvement in quality of life, measured as life years gained weighted by a quality factor, which results in Quality Adjusted Life Years (QALYs). This type of model is broadly used in medical related literature for a large number of problems and decision making analysis **[11, 12, 13, 14, 15]**.

Briefly, these models typically assume that, at any point in time, a patient is in one of a finite number of health states and that, from one period to the next, he/she can shift to another health state with a known probability (transition probability). Any health state is then assigned a utility and/or financial cost, and the evaluation of the Markov process gives an expected present value of utility and/or financial costs for a given time horizon **[16]**.

We compare expected utility and financial costs associated with two alternatives: one in which the patient gets a transplant in the first period and the other in which the same patient does not get a transplant in any period. We consider one-year cycles and a time horizon of 20 years.

In addition, given the nature of the data, we find necessary to consider —as opposed to the studies cited above— the fact that there is a certain degree of uncertainty in some of the parameters used in the model. To do so, we assume some distribution for these parameters and use Montecarlo simulations to obtain a 95% confidence interval for our results. This, in our view, represents a better approximation to real policy-makers' decisions than estimating just a mean value.

Data

Data for parameters used in the model are presented in table1. Survival rates were obtained from the Instituto de Salud Publica (ISP) **[17]**, the Chilean institution that manages the waiting list, assigns donors to recipients and records transplant outcomes. Utility values at each health state —dialysis and transplantation— were obtained from the literature **[18]**. The death health state is assigned with a utility value of zero. These values were used to weight expected life years spent in each state by quality, and obtain a QALY.

Parameters for which we assumed some degree of uncertainty are, mainly, survival and graft rejection probabilities, obtained from ISP and the literature. We assumed normal distributions truncated at one, with standard deviations equal to 10% of the mean reported in different studies.

Transplantation costs include: immunosuppressive treatment, initial surgery costs, previous studies and follow-up of transplanted patients. Meanwhile, among considered dialysis costs are: hemodialysis, peritoneal dialysis and vascular access.

An important remark is that, as these costs are those effectively considered by the public health-care system because they represent the amounts assigned to each hospital that performs each of those services, we do not consider uncertainty for these values **[19]**.

We consider one additional assumption that is worth mentioning: Dialysis cost is a weighted average between hemodialysis and peritoneal dialysis costs, in which weights are assigned according to the proportion of patients that use each of these treatments today. Nearly 90% of the population under dialysis was under hemodialysis in Chile at the time of study **[20]** and we consider substitution towards peritoneal dialysis in our study's time horizon of 20 years until 30% of patients are treated under peritoneal dialysis. We thus consider a constant transition rate of one percentage point per year, to reach that proportion. However, to properly address this estimation, we consider some degree of uncertainty for this transition factor, as presented in table 1.

Results

Estimation results are presented in figures 1 and 2.

Figure 1 describes cumulative cost-savings and increase in quality of life obtained from an additional transplant. It shows the initial un-saving due to high initial surgery costs of transplantation versus dialysis maintenance costs and subsequent positive net cost savings due to smaller maintenance costs of a transplanted patient versus dialysis. In all the relevant time horizon there is a better quality of life associated with a transplanted patient.

Figure 2 describes cost-savings and improvement in quality of life as a function of additional donors per million people. These results are interpreted as the investment threshold for any organ donation program as a function of incremental donors the program is actually capable to get **[8, 9].**

Dotted lines in both graphs represent 95% confidence intervals for our results, stemming from assumed distributions for some of the parameters considered in the model.

Our estimates suggest that the expected present value of costs associated with dialysis is approximately US$134,000, while the expected costs of a transplant amount to nearly US$106,000. In the same way, receiving a kidney implies 7.30 QALYs, while staying in dialysis is estimated to report only 4.32 QALYs. This means that an additional transplant implies a net saving of US$28,000 and 2.98 QALYs gained. If a US$25,000 valuation of a life year in perfect health condition is considered **[1]** then an additional transplant implies an estimated total saving of US$ 102,000.

With these results, and considering an average of 1.77 kidneys procured by each cadaveric donor **[2]**, our estimates indicate a net saving of around U$ 827,000 per year from an increase in the donation rate of one donor pmp. If gained QALYs are considered, these net savings rise to approximately US$ 3 million a year.

Discussion

Our results indicate that cadaveric renal transplant has a high cost-saving potential for the health-care system in Chile. Previous studies have found similar results for developed economies, like Canada and Germany **[8, 9]**. This paper uses Markov modelling in order to explore these issues in a developing country and we find that lower transplant costs, relative to dialysis are also present. Although health care costs are considerably less in Chile, the relative benefit of transplantation over dialysis in Chile (21% of dialysis cost saved by transplantation) is similar to that reported in other studies performed with the same methodology in Germany (38%) and Canada (26%).

These figures are of major relevance as actual cadaveric donation rates in Chile (5,4 donors pmp) are well below those in other countries of the region like Argentina, (14 donor pmp) or Uruguay (19 donors pmp in 2009) and those in developed countries like the US, Canada, or Germany, for which, as stated earlier, estimation of cost-savings using Markov modelling have already been calculated.

We also stress the point that these results may underestimate the actual cost-saving potential of increasing organ donation because of the fact that we only consider kidney transplant **[8]**. However, additional cost-savings —when the improvement in quality of life is considered— could stem from other organ transplants, like livers, hearts and lungs, for example **[25, 26, 27].** Actually, in 2008, along with 206 kidneys, 74 livers, 19 hearts ant 9 lungs were transplanted in Chile **[2].**

Costs used in this study were obtained in large part from Chilean health authorities and represent what is effectively disbursed by the public health-care system. We try to assess uncertainty regarding some of the parameters used in the model by using Montecarlo simulation which, in our view, is a major contribution to the literature, and we expect to see further development in this sense in the future.

The main conclusion of this paper is that cost savings are positive and substantial, with a high (95%) level of confidence even for a single incremental donor. To put figures in perspective, if Chile reached the donation rates of Argentina, Uruguay, the U.S. or Spain, cost-savings would rise to near US$ 7, 11, 17 or 24 million per year, respectively. If QALYs gained are considered, expected cost-savings would rise to US$ 27, 42, 63 or 87 million per year, respectively.

These results can rightly be interpreted as an investment threshold for organ donation initiatives that, in our view, could be highly cost-effective in a country with low donation rates, like Chile, as opposed to countries with high donation rates, like Spain, where additional donors can only be reached at significant additional costs. We are confident that this is not the case in Chile, where, in addition to low donation rates, opinion surveys suggest that near 80% of the population is favorable to donation **[28]**.

Specific policies aimed at increasing organ donation rates in Chile are not discussed in this paper, but should be the subject of future research that encompasses specific characteristics of the Chilean reality in transplantation.

Preliminary research has found that the major challenge facing the system in Chile is its low ability to actually identify potential donors due to a lack of capital and human resources dedicated to this activity inside hospitals **[2, 29, 30].**

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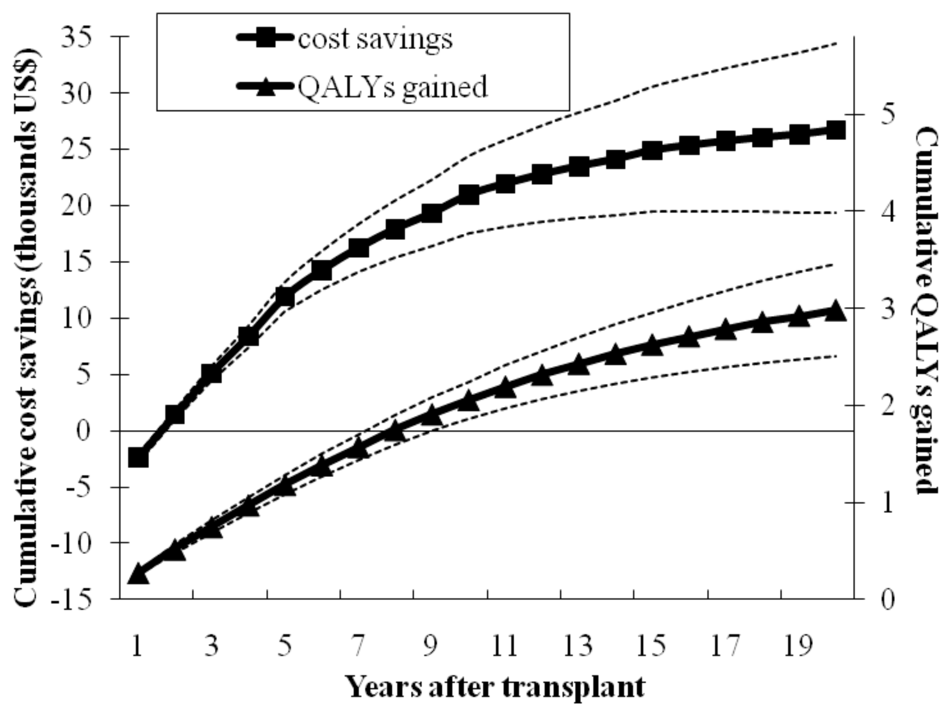
Table 1 Inputs for Markov Model		
	Input values and assumed distributions (percentage, unless otherwise indicated)	**Source**
Dyalisis utility	50.0	**[18]**
Transplant utility (at year 1 after transplant)	80.0	
Transplant utility (at year 2 after transplant)	80.0	
Cadaveric transplant cost	US$ 11,186	**[19]**
Organ procurement cost	US$ 3,162	
Maintenance cost - transplantation (at year 1)	US$ 2,610	
Maintenance cost - transplantation (after year 1)	US$ 8,745	
Immunosuppresive treatment cost (after 2nd year)	US$ 7,661	
Graft rejection cost	US$ 10,818	
Maintenance cost - hemodyalisis	US$ 14,624	
Maintenance cost - peritoneal dyalisis	US$ 17,639	
Maintenance cost - dyalisis failed graft	US$ 14,624	
Proportion of hemodyalisis patients of total dyalisis patients	90.0	**[20]**
Transition rate to peritoneodyalisis	BETA(0.0%; 1.0%; 2.0; 1.2)	
Discount rate	8.0	**[21]**
Currency	US$ 2009	
Exchange rate	Ch$/US$ 520	**[22]**
Population	16.5 Million	**[23]**
Number of cadaveric donors	116 donors	**[2]**
Procured kidneys per cadaveric donor	1.77 kidneys	**[2]**
Cadaver graft survival at year 1	N(86.0; 8.6)	**[17]**
Cadaver graft survival at year 2	N(83.0; 8.3)	
Cadaver graft survival at year 3	N(81.0; 8.1)	
Cadaver graft survival at year 4	N(79.0; 7.9)	
Cadaver graft survival at year 5	N(77.0; 7.7)	
Cadaver graft survival at year 6	N(74.0; 7.4)	
Cadaver graft survival at year 7	N(71.0; 7.7)	
Cadaver graft survival at year 8	N(68.0; 6.8)	
Cadaver graft survival after year 8 (percentage of previous year)	N(95.2; 9.52)	**[8]**
Average graft life	15 years	
Rejection probability at year 1	N(20; 2.0)	**[24]**
Rejection probability at year 2	N(10; 1.0)	
Rejection probability at year 3	N(5.0; 0.5)	
Rejection probability at year 4 and ahead	N(3.0; 0.3)	
Death with functioning graft	N(28; 2.8)	

Patient mortality after graft loss (at year 1)	N(24; 2.4)	**[8]**
Patient mortality after graft loss (after year 1)	N(11; 1.1)	
Dyalisis patient mortality	N(4.52; 0.452)	
Life expectancy in waiting list	15 years	
Life expectancy after transplant	20 years	

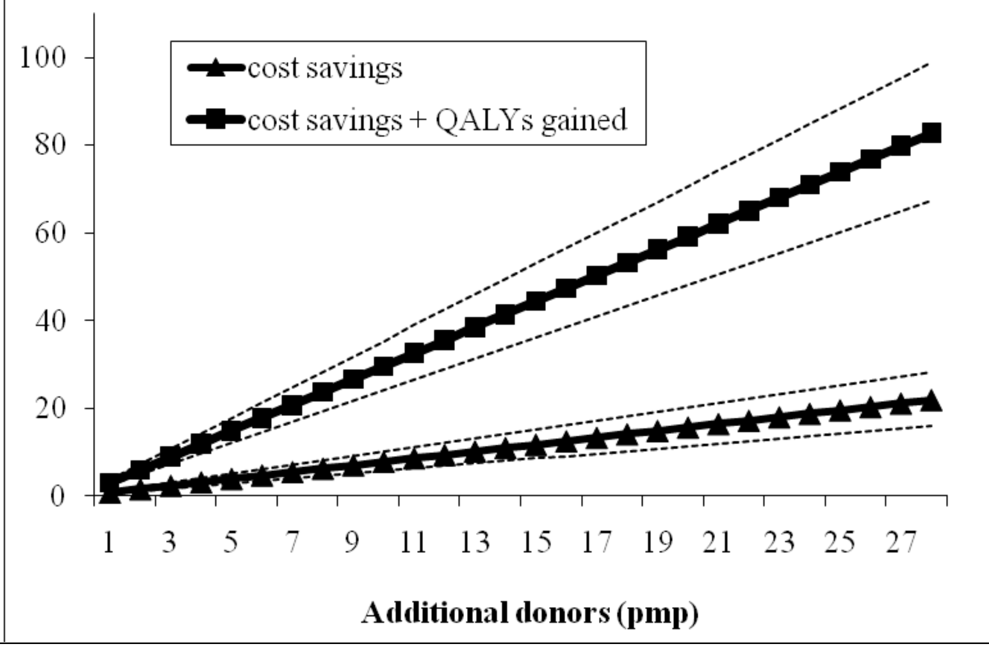
Note: The second column shows distribution assumptions for parameters used in the model. Mean values were obtained from sources shown in column 3, and we assumed 10% of the mean as standard deviations.
N(a,b) indicates Normal Distribution truncated at 1 with mean “a” and variance of “b”, BETA(a,b,p,q) indicates Beta Distribution with a minimum value of “a”, maximum value of “b” and (“p”,”q”) shape parameters.

Figure 1 Incremental quality adjusted life years (QALYs) gain and cost savings of transplantation**.**



Note: solid lines indicate estimation mean, and dotted lines reflect 95% confidence intervals.

Figure 2 Investment thresholds in Chile (millions of US dollars).



Note: solid lines indicate estimation mean, and dotted lines reflect 95% confidence intervals