COST-EFFECTIVENESS ANALYSIS OF THE SPANISH RENAL REPLACEMENT THERAPY PROGRAM

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◆ **Background:** We undertook a cost-effectiveness analysis of the Spanish Renal Replacement Therapy (RRT) program for end-stage renal disease patients from a societal perspective. The current Spanish situation was compared with several hypothetical scenarios.

◆ **Methods:** A Markov chain model was used as a foundation for simulations of the Spanish RRT program in three temporal horizons (5, 10, and 15 years). The current situation (scenario 1) was compared with three different scenarios: increased proportion of overall scheduled (planned) incident patients (scenario 2); constant proportion of overall scheduled incident patients, but increased proportion of scheduled incident patients on peritoneal dialysis (PD), resulting in a lower proportion of scheduled incident patients on hemodialysis (HD) (scenario 3); and increased overall proportion of scheduled incident patients together with increased scheduled incidence of patients on PD (scenario 4).

◆ **Results:** The incremental cost-effectiveness ratios (ICERs) of scenarios 2, 3, and 4, when compared with scenario 1, were estimated to be, respectively, –€83 150, –€354 977, and –€235 886 per incremental quality-adjusted life year (Δ QALY), evidencing both moderate cost savings and slight effectiveness gains. The net health benefits that would accrue to society were estimated to be, respectively, 0.0045, 0.0211, and 0.0219 Δ QALYs considering a willingness-to-pay threshold of €35 000/ Δ QALY.

◆ **Conclusions:** Scenario 1, the current Spanish situation, was dominated by all the proposed scenarios. Interestingly, scenarios 3 and 4 showed the best results in terms of cost-effectiveness. From a cost-effectiveness perspective, an increase in the overall scheduled incidence of RRT, and particularly that of PD, should be promoted.

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At the end of 2010 in Spain, more than 55 000 patients diagnosed with end-stage renal disease (ESRD) were receiving renal replacement therapy (RRT), representing an incidence of 137 patients [hemodialysis (HD): 85%; peritoneal dialysis (PD): 13%; kidney transplantation (Tx): 2%] and a prevalence of 1079 patients (HD: 45%; PD: 5%; Tx: 50%) per million population. The economic impact of the RRT program on Spanish society was estimated to be about €1 829 million that same year (1).

The choice of dialysis modality depends largely on the patients, because they choose the modality that best satisfies their needs. The information available to patients is a determining factor in their choice, and information availability has been associated with an increase in the preference for PD over HD (2). Provision of information about treatment alternatives is considered to be highly relevant to patients, because a lack of freedom at the time that the RRT modality is chosen reduces health related quality of life (HRQoL), particularly in the psychological dimension (3). Nevertheless, no significant differences in clinical outcome have been detected in a comparison of those two alternatives (4).

It has been observed that the larger proportion of patients on HD might be a result of a lack of information provided to patients (5). Consequently, the importance of early detection of renal disease should be emphasized. Early referral of ESRD patients to nephrologists allows those patients to make a more informed decision about the RRT modality that they will receive. Furthermore, it

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helps to delay progression of the pathology, reducing morbidity and facilitating clinical follow-up (6–13)—and as a result also reducing costs (1).

Several organizations—such as the U.K. Renal Association, the U.S. National Kidney Foundation, the Spanish Society of Nephrology (SEN) (2), and the Spanish Society of Family and Community Medicine (14)—have issued recommendations related to the diagnosis of ESRD and the therapeutic objectives that should be established. These organizations recommend referral to nephrologists for patient evaluation and follow-up. As has already been mentioned, late referral of patients to nephrologists has important economic consequences, given that a non-scheduled (non-planned or urgent) start to RRT turns out to be more costly than a scheduled (planned or elective) start (1).

As mentioned earlier, a scheduled dialysis start has been associated with greater choice of PD over HD [relative risks of 2.09 and 1.68 computed from data presented by Marrón and colleagues (5,15)]. According to the existing literature, between 51% and 54% of the dialysis starts in Spanish patients (omitting Tx) are scheduled. Scheduled starts in patients starting HD range between 43% and 53%, and those in patients starting PD range between 81% and 90% (5,15,16).

As for the total cost of the RRT program in Spain, it should be mentioned that, according to a recent estimate carried out by Villa *et al.* (1), most of the estimated costs in the year 2010 were attributable to HD (73%); only small percentages were attributable to PD (6%) and to Tx (21%). According to the authors, this cost distribution is a consequence of both the larger number of patients treated with HD and the higher estimated average cost of that modality. The authors concluded that, from a cost minimization perspective, it would be favorable to increase the number of patients on PD.

In the present study, we aimed to determine whether better clinical and economic outcomes could be obtained by increasing the proportion of scheduled patients (those eligible for a planned start) in the Spanish RRT program, using various scenarios simulated in three temporal horizons (5, 10, and 15 years). In the first simulation, the overall proportion of scheduled incident patients was increased. In the second simulation, the proportion of scheduled incident patients on PD was increased, keeping the overall scheduled incidence constant. Finally, in the third simulation, the preceding two scenarios were combined. Our overall objective was to conduct a cost-effectiveness analysis of the Spanish RRT program for ESRD patients from a societal perspective. Using a Markov chain model we were able to compare the current Spanish situation with our hypothetical scenarios.

METHODS

We developed a Markov chain model for the Spanish RRT program. Markov models are useful for representing random processes that evolve over time; they are therefore suited to modeling the progression of chronic diseases. A specific disease is structured as a chain of various health states, in which movements between the states over given time periods (“cycles”) occur with a given probability (“transition probability”). Estimates of costs and health outcomes are attached to each state in the model. By running the model over a large number of cycles (the “temporal horizon”), long-term costs and health outcomes associated with a disease are obtained (see Briggs and Sculpher (17) for a detailed introduction to Markov modeling).

In our particular case, four health states [HD, PD, Tx, Death (D)] were defined, with the chance of bidirectional transitions between all the states except D, which is an absorbent state. The model simulated progression of renal pathology in three temporal horizons (5, 10, and 15 years). Based on the opinion of an expert panel, 4 scenarios were considered:

- Scenario 1: A model that reflects the current situation of the Spanish RRT program.
- Scenario 2: A model with an increased overall proportion of scheduled incident patients (to 75% from 57%).
- Scenario 3: A model in which the overall proportion of scheduled incident patients was held constant (at 57%), but in which the relative proportion of scheduled incident patients on PD was increased (to 30% from 10% of all incident patients). As a consequence, the proportion of incident patients on HD decreased.
- Scenario 4: A model that combined scenarios 2 and 3. The overall proportion of scheduled incident patients was increased (to 75% from 57%), and the proportion of scheduled incident patients on PD was also increased (to 30% from 10% of all incident patients).

The simulation was set to start at the beginning of 2010, using data from a recent forecast of ESRD incidence and prevalence figures at the end of 2009 in Spain (1). The initial prevalence was distributed among the RRT modalities according to the proportions observed in that forecast: HD, 46%; PD, 5%; and Tx, 49%. Based on those data, the future prevalence in each cycle (1 year) and state was determined by the application of a transition probabilities matrix (TPM).

It was estimated that the number of incident patients grows at a constant rate of 2% with respect to the previous cycle and also that the initial incidence is distributed

among the RRT modalities according to the proportions observed in the forecast: HD, 86%; PD, 13%; and Tx, 1%. According to Ortega *et al.* (16), 53% of Spanish incident patients on HD are scheduled. Moreover, based on expert panel opinion and on the existing literature (5,15), it was assumed that 10% of all incident patients are scheduled and started on PD, accounting for 83% of the incident patients on PD. Incident patients on Tx were always regarded as scheduled. Based on those percentages, it was possible to derive the overall proportion of scheduled incident patients. On the whole, it was estimated that 57% of incident patients on any RRT modality were scheduled.

The TPM determines the likelihood of patient flows between the defined health states from year to year (Figure 1). The TPM parameters were estimated based mainly on data recorded by the SEN registry. Exceptions included the probabilities of remaining on HD and on PD (18) and of making a transition from Tx to HD or to PD (19). Compared with non-scheduled patients, the scheduled patients on HD appear to have a lesser risk of death (relative risk: 0.39) (16). Mortality rates for HD were therefore computed as weighted averages of the mortality rates associated with scheduled and non-scheduled patients. The model also included a kidney Tx queue, ensuring that future transitions to Tx do not exceed the number of available organs (maximum of

4000 kidney transplantations annually, according to the expert panel).

The predictive validity of the TPM was checked by comparing the simulated data with the data available in the SEN registry for the period 1996 – 2009. An accumulated squared prediction error close to 5% was observed throughout that entire period, meaning that the predictive power of the matrix was considered to be very high, encompassing almost 95% of all variations registered in the prevalence. There was also evidence of a stable trend between the data taken from the SEN registry and the predictions provided by the model, further validating the established TPM (Figure 2).

Figure 1 — Transition probabilities. HD = hemodialysis; PD = peritoneal dialysis; Tx = kidney transplantation; D = death.

Figure 2 — Prevalence of end-stage renal disease in Spain. Weighted registry data (1996 – 2009), model forecast (2010 – 2024), and trends. HD = hemodialysis; PD = peritoneal dialysis; Tx = kidney transplantation.

To obtain information about clinical effectiveness, expressed in quality-adjusted life years (QALYs), we conducted a literature review. That review was complemented with data from a proprietary database obtained from the Sanitary Research Fund Project 96/1327, which was funded by the Spanish Ministry of Health. Health utilities were assigned values on a scale from 0 (worst state or death) to 1 (optimal or perfect health). The utilities were calculated based on the Project 96/1327 database, whose content was drawn from administration of the SF-36 health questionnaire. Using the methodology proposed by Rebollo *et al.* (20) and implemented in Spain, SF-36 HRQoL scores were converted into SF-6D health utilities. No statistically significant differences in means were found between the HD and PD utilities (0.69) at the 95% confidence level. The Tx utility (0.81) was significantly higher in comparison with the other two modalities. Those findings accord with results from previous studies (21,22). As for the possible difference in effectiveness between continuous ambulatory PD (CAPD) and automated PD (APD), we decided, based on the review carried out by Rabindranath *et al.* (23), not to perform individualized analyses for those modalities.

For each RRT modality, QALYs were defined as the product of the survival rate in a cycle and the health utility associated with the particular modality. As stated, the attributed costs were gathered from a previous study (1). Direct and indirect costs were both included from a societal perspective. Table 1 shows the costs (in euros at January 2010) and the health utilities considered in the model. Costs and health utilities were both discounted at a 3.5% rate. With regard to the cost-effectiveness comparisons, incremental cost-effectiveness ratios (ICERs) and net health benefits (NHBs), assuming a willingness-to-pay threshold of €35 000 per incremental QALY (Δ QALY), were both computed.

To evaluate the robustness of the results, a univariate sensitivity analysis was carried out. In addition, focusing

on scenario 4, a bivariate “worst case” sensitivity analysis was conducted, in which the costs of PD were increased by 10%, and the utility of PD was decreased by the same percentage.

RESULTS

Aiming for concision and unless otherwise stated, all results mentioned in this section relate to the long-term temporal horizon (15 years). Although our findings are consistent across the three temporal horizons considered, the interested reader can find detailed results of all simulations in Tables 2 and 3. Moreover, “discounted average per-patient (if applicable) annual” figures are simply called “average” figures.

SIMULATED PREVALENCE, INCIDENCE, AND TRANSITIONS

Compared with scenario 1, the average prevalence of HD remains almost constant in scenario 2 (29 880 and 30 006 respectively), but the prevalence of PD (3 099 vs 3 436) and Tx (34 108 vs 34 551) increases. In scenarios 3 and 4, the average prevalence of HD falls off (27 005 and 27 583 respectively), and once again, the average prevalence of PD (5 803 and 5 683) and Tx (35 157 and 35 414) increase.

Because the prevalence of PD is higher and, furthermore, because PD patients have a higher probability of receiving a graft than HD patients do (0.12 vs 0.07), in all 3 scenarios, more transitions to Tx also occur. In scenario 2, the transitions to PD remain constant compared with those in scenario 1; in scenarios 3 and 4, those transitions fall off. The fall-off is mainly the result of the reduction in the prevalence of HD. Furthermore, in scenario 4 (compared with scenario 3), the number of patients on PD declines because more scheduled incident patients are on Tx and HD, and in relative terms, the scheduled incidence of the patients on PD represents a lower proportion than is present in scenario 3. The number of transitions to Tx never exceed the maximum number of available organs as defined by the expert panel.

COST ANALYSIS

Compared with scenario 1 (€24 448), average costs fall off moderately in scenarios 2 (€24 337), 3 (€23 774), and 4 (€23 780), an effect attributable to the increase in the prevalence of both PD and Tx, combined with the significant fall-off in HD. Compared with the current situation, scenarios 3 and 4 imply annual cost savings of €32 million and €18 million respectively. However, scenario 2 suggests added costs of €10 million, because

TABLE 1
Model Parameters: Costs and Health Utilities

Parameter	HD	PD	Tx
Scheduled incidence cost (€)	928	1 808	38 313
Non-scheduled incidence cost (€)	4 595	1 808	
Transition cost (€)	928	1 808	38 313
Prevalence cost (€)	37 968	25 826	6 283
Indirect cost (€)	8 929	7 429	5 483
Health utilities	0.69	0.69	0.81

HD = hemodialysis; PD = peritoneal dialysis; Tx = kidney transplantation.

TABLE 2
Average Annual Figures, 15-Year Horizon

	Overall	HD	PD	Tx
Scenario 1				
Prevalence	67 087	29 880	3 099	34 108
Incidence	7 434	6 364	962	108
Survival rate	0.8571	0.8109	0.8637	0.9053
Total cost (€ millions)	1 657	1 213	98	346
Per-patient cost (€)	24 448	36 417	25 971	11 244
Per-patient QALYs	0.5317	0.4627	0.4907	0.6117
Scenario 2				
Prevalence	67 993	30 006	3 436	34 551
Incidence	7 434	6 157	1 137	141
Survival rate	0.8588	0.8143	0.8633	0.9046
Total cost (€ millions)	1 666	1 206	109	351
Per-patient cost (€)	24 337	36 314	25 981	11 277
Per-patient QALYs	0.5330	0.4649	0.4907	0.6117
Scenario 3				
Prevalence	67 965	27 005	5 803	35 157
Incidence	7 434	4 933	2 394	108
Survival rate	0.8588	0.8082	0.8624	0.9037
Total cost (€ millions)	1 625	1 073	194	357
Per-patient cost (€)	23 774	36 444	26 023	11 316
Per-patient QALYs	0.5336	0.4613	0.4907	0.6117
Scenario 4				
Prevalence	68 679	27 583	5 683	35 414
Incidence	7 434	4 967	2 327	141
Survival rate	0.8601	0.8123	0.8623	0.9034
Total cost (€ millions)	1 639	1 088	190	360
Per-patient cost (€)	23 780	36 325	26 022	11 335
Per-patient QALYs	0.5345	0.4638	0.4907	0.6117

HD = hemodialysis; PD = peritoneal dialysis; Tx = kidney transplantation; QALY = quality-adjusted life year.

the reduction in the total cost of HD does not offset the larger costs observed in PD and Tx, caused by a higher incidence in those modalities and also by higher overall survival.

An increase in the average cost of HD is observed in scenario 3 compared with scenario 1 (€36 444 vs €36 417). In scenario 3, the proportion of scheduled incident HD patients is lower. In scenario 2, the opposite situation occurs, leading to the average cost of HD being lower (€36 314). In scenario 4, the average cost of HD is lower again (€36 325), because the cost increase observed in scenario 3 is offset by the cost reduction observed in scenario 2.

As for the average cost of PD, a slight increase compared with the cost in scenario 1 (€25 971) is observed in scenarios 2 (€25 981), 3 (€26 023), and 4 (€26 022). Those cost increases are caused by the

higher relative proportion of incident PD patients. Incident patients present larger costs derived from creation of the peritoneal access and delivery of training. Likewise, the current average cost of Tx (€11 244) is observed to increase in scenarios 2 (€11 277), 3 (€11 316), and 4 (€11 335), a result of the higher proportion of incident patients on that modality, presenting larger costs.

EFFECTIVENESS ANALYSIS

Compared with scenario 1 (0.8571), scenarios 2 (0.8588), 3 (0.8588), and 4 (0.8601) evidence a slight increase in the discounted survival rate, providing 0.5317, 0.5330, 0.5336, and 0.5345 discounted QALYs respectively. With regard to the therapeutic modalities, greater effectiveness of Tx compared with

TABLE 3
Cost-Effectiveness Results for Three Temporal Horizons

		Overall		HD		PD		Tx		
	ICER	NHB	Average cost	QALYs	Average cost	QALYs	Average cost	QALYs	Average cost	QALYs
Scenario 1										
15 Years			24 448	0.5317	36 417	0.4627	25 971	0.4907	11 244	0.6117
10 Years			27 596	0.5750	39 449	0.5011	28 131	0.5315	12 228	0.6626
5 Years			29 116	0.6234	42 842	0.5441	30 547	0.5771	13 336	0.7194
Scenario 2										
15 Years	−83 150	0.0045	24 337	0.5330	36 314	0.4649	25 981	0.4907	11 277	0.6117
10 Years	−76 993	0.0045	27 489	0.5764	39 336	0.5035	28 146	0.5315	12 265	0.6626
5 Years	−71 565	0.0045	29 010	0.6249	42 717	0.5567	30 573	0.5771	13 375	0.7194
Scenario 3										
15 Years	−354 977	0.0211	23 774	0.5336	36 444	0.4613	26 023	0.4907	11 316	0.6117
10 Years	−372 050	0.0193	26 977	0.5767	39 474	0.5096	28 209	0.5315	12 310	0.6626
5 Years	−504 913	0.0164	28 580	0.6244	42 856	0.5425	30 690	0.5771	13 413	0.7194
Scenario 4										
15 Years	−235 886	0.0219	23 780	0.5345	36 325	0.4638	26 022	0.4907	11 335	0.6117
10 Years	−229 076	0.0204	26 976	0.5777	39 346	0.5024	28 207	0.5315	12 333	0.6626
5 Years	−238 238	0.0180	28 566	0.6257	42 718	0.5555	30 686	0.5771	13 439	0.7194

ICER = incremental cost-effectiveness ratio; NHB = net health benefit; HD = hemodialysis; PD = peritoneal dialysis; Tx = kidney transplantation; QALY = quality-adjusted life year.

HD and PD is observed. Barely any differences separated the latter modalities, basically because the health utility was considered to be the same (0.69) in both cases. Even so, the effectiveness of PD is somewhat greater in all scenarios because of the greater survival of patients on the PD modality. The average effectiveness for PD and Tx does not vary between the scenarios, because in no scenario did the survival rate vary. Conversely, the average effectiveness of HD varies because the rate of survival varies as the proportion of scheduled and non-scheduled incident patients on the HD modality changes.

COST-EFFECTIVENESS ANALYSIS

The ICERs of scenarios 2, 3, and 4, when compared with scenario 1, were estimated as -€83 150, -€354 977, and -€235 886 per ΔQALY respectively, demonstrating both moderate cost savings and slight effectiveness gains. The NHBs accruing to society were estimated at 0.0045, 0.0211, and 0.0219 ΔQALYs respectively, considering a willingness-to-pay threshold of €35 000/ΔQALY. Scenario 1 is therefore dominated by all the other scenarios proposed. Interestingly, scenarios 3 and 4 show the best results in terms of cost-effectiveness.

SENSITIVITY ANALYSIS

In the univariate sensitivity analysis, the ICERs resulting from scenarios 2 and 3 did not change significantly, despite application of variation rates of ±10% in each of the parameters individually. Focusing on scenario 4, the univariate sensitivity analysis reflected a possible impact on the results from changes in the utility and costs of PD.

Quantification of changes in an ICER resulting from variation in a single parameter is not very reliable because the interactions of the various parameters are not taken into account. To test the robustness of the model, a bivariate "worst case" sensitivity analysis was carried out within scenario 4. The costs and utilities of PD were both modified: PD utilities were lowered by 10%, and PD costs were incremented by 10%. Gains in QALYs (0.5294 vs 0.5289) and cost savings (€24 053 vs €24 592) were both still observed in comparison with scenario 1.

DISCUSSION

In the present study, the Spanish RRT program was simulated in three temporal horizons (5, 10, and 15 years). In light of the current situation (scenario 1), three hypothetical scenarios were compared in terms

of cost-effectiveness: an increased overall proportion of scheduled incident patients (scenario 2); a constant overall proportion of scheduled incident patients, but an increased proportion of scheduled incident patients on PD (scenario 3); and an increased overall proportion of scheduled incident patients combined with an increased proportion of scheduled incident patients on PD (scenario 4).

With regard to costs, the average costs are moderately lower in scenario 2 than in scenario 1. However, this decrease in the average cost does not completely offset the costs derived from the increase in the number of prevalent patients. Compared with scenario 1, scenarios 3 and 4 both show cost savings in average and in total terms alike. In both the latter scenarios, survival increases, but a decrease in the average cost offsets the total cost derived from the larger prevalence. With regard to effectiveness, scenarios 2, 3, and 4 provide more QALYs (even though the gains are modest) than does the alternative of taking no action to change the current situation.

The cost-effectiveness indicators show that scenarios 3 and 4 are the most efficient options, dominating scenarios 1 and 2. Therefore, if the number of scheduled incident patients were to be increased, and if patients were to be allowed to receive PD therapy, not only would a greater number of QALYs be obtained, but the intervention would bring about a lower cost than that obtained with the policies currently being followed. In this way, society would obtain a more efficient distribution of the resources invested to treat renal disease.

The importance of early detection and early referral to a nephrologist in ESRD has also been emphasized (6–13), because early detection and referral present an advantage both for the HRQoL of patients and for the economic costs. Similarly, early detection and referral give the patient the opportunity to become informed about the various treatment modalities—a situation that would be expected to increase the number of patients choosing PD (4).

CONCLUSIONS

In the cost analysis carried out by Villa *et al.* (1), the authors concluded that, from a cost-minimization perspective, it would be favorable to increase the number of incident patients on PD. In the present work, in which the costs and the effectiveness of the various RRT modalities have both been considered, a result favorable to PD has also been observed. Given that the NHB is positive, society should assume the costs of introducing the proposed scenarios, considering a willingness-to-pay threshold of €35 000/ΔQALY.

DISCLOSURES

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REFERENCES

1. Villa G, Rodríguez-Carmona A, Fernández-Ortiz L, Cuervo J, Rebollo P, Otero A, *et al.* Cost analysis of the Spanish renal replacement therapy programme. *Nephrol Dial Transplant* 2011; :[Epub ahead of print].
2. Arrieta J, Bajo MA, Caravaca F, Coronel F, García-Pérez H, González-Parra E, *et al.* Guidelines of the Spanish Society of Nephrology. Clinical practice guidelines for peritoneal dialysis (Spanish). *Nefrologia* 2006; 26(Suppl 4):1–184.
3. Szabo E, Moody H, Hamilton T, Ang C, Kovithavongs C, Kjellstrand C. Choice of treatment improves quality of life. A study on patients undergoing dialysis. *Arch Intern Med* 1997; 157:1352–6.
4. Liem YS, Bosch JL, Hunink MG. Preference-based quality of life of patients on renal replacement therapy: a systematic review and meta-analysis. *Value Health* 2008; 11:733–41.
5. Marrón B, Martínez Ocaña JC, Salgueira M, Barril G, Lamas JM, Martín M, *et al.* Analysis of patient flow into dialysis: role of education in choice of dialysis modality. *Perit Dial Int* 2005; 25(Suppl 3):S56–9.
6. Górriz JL, Sancho A, Pallardó LM, Amoedo ML, Martín M, Sanz P, *et al.* Prognostic significance of programmed dialysis in patients who initiate renal substitutive treatment. Multicenter study in Spain (Spanish). *Nefrologia* 2002; 22:49–59.
7. Górriz JL, Sancho A, Pallardó LM, Amoedo ML, Barril G, Salgueira M, *et al.* Longer pre-dialysis nephrological care is associated with improved long-term survival of dialysis patients. More facts. *Nephrol Dial Transplant* 2002; 17:1354–5.
8. Roderick P, Jones C, Tomson C, Mason J. Late referral for dialysis: improving the management of chronic renal disease. *QJM* 2002; 95:363–70.
9. Gallego E, López A, Lorenzo I, López E, Llamas F, Illescas ML, *et al.* Influence of early or late referral to nephrologist over morbidity and mortality in hemodialysis (Spanish). *Nefrologia* 2003; 23:234–42.
10. Caravaca F, Arrobas M, Luna E, Pizarro JL, García C, Espárrago JF, *et al.* Progression of renal insufficiency in the pre-end-stage renal disease setting (Spanish). *Nefrologia* 2003; 23:510–19.
11. Stack AG. Impact of timing of nephrology referral and pre-ESRD care on mortality risk among new ESRD patients in the United States. *Am J Kidney Dis* 2003; 41:310–18.
12. Kazmi WH, Obrador GT, Khan SS, Pereira BJ, Kausz AT. Late nephrology referral and mortality among patients with end-stage renal disease: a propensity score analysis. *Nephrol Dial Transplant* 2004; 19:1808–14.

13. Khan SS, Xue JL, Kazmi WH, Gilbertson DT, Obrador GT, Pereira BJ, *et al.* Does predialysis nephrology care influence patient survival after initiation of dialysis? *Kidney Int* 2005; 67:1038–46.
14. Alcázar R, Egocheaga MI, Orte L, Lobos JM, González Parra E, Alvarez Guisasola F, *et al.* SEN–SEMFYC consensus document on chronic kidney disease (Spanish). *Nefrologia* 2008; 28:273–82.
15. Marrón B, Ortiz A, de Sequera P, Martín–Reyes G, de Arriba G, Lamas JM, *et al.* Impact of end-stage renal disease in planned dialysis start and type of renal replacement therapy: a Spanish multicentre experience. *Nephrol Dial Transplant* 2006; 21(Suppl 2):ii51–5.
16. Ortega T, Ortega F, Díaz–Corte C, Rebollo P, Ma Baltar J, Alvarez–Grande J. The timely construction of arteriovenous fistulae: a key to reducing morbidity and mortality and to improving cost management. *Nephrol Dial Transplant* 2005; 20:598–603.
17. Briggs A, Sculpher M. An introduction to Markov modelling for economic evaluation. *Pharmacoeconomics* 1998; 13:397–409.
18. Antolín A, Miguel A, Pérez J, Gómez C, Zurriaga O, Blasco MJ, *et al.* Analysis of survival in dialysis: hemodialysis versus peritoneal dialysis and the significance of comorbidity (Spanish). *Nefrologia* 2002; 22:253–61.
19. UNIPAR. *Information Unit for Kidney Patients of the CAPV 2005* (Spanish). Vitoria–Gasteiz, Spain: Central Publication Service of the Basque Government; 2006. [Available online at: http://www.osakidetza.euskadi.net/v19-hbas0003/es/contenidos/informacion/hbas_nefrologia/es_hbas/adjuntos/enfermos_renales_pais_vasco.pdf; accessed 10 May 2011]
20. Rebollo P, Morís J, Ortega T, Valdés C, Ortega F. Estimating utility values for health status using the Spanish version of the SF-36. Validity of the SF-6D index vs EQ-5D (Spanish). *Med Clin (Barc)* 2007; 128:536–7.
21. Cleemput I, Kesteloot K, Vanrenterghem Y, De Geest S. The economic implications of non-adherence after renal transplantation. *Pharmacoeconomics* 2004; 22:1217–34.
22. Pacheco A, Saffie A, Torres R, Tortella C, Llanos C, Vargas D, *et al.* Cost-utility study of peritoneal dialysis and hemodialysis in Chile. *Perit Dial Int* 2007; 27:359–63.
23. Rabindranath KS, Adams J, Ali TZ, MacLeod AM, Vale L, Cody J, *et al.* Continuous ambulatory peritoneal dialysis versus automated peritoneal dialysis for end-stage renal disease. *Cochrane Database Syst Rev* 2007; (2):CD006515.