

Original Article

Economic impact of extended time on peritoneal dialysis as a result of using polyglucose: the application of a Markov chain model to forecast changes in the development of the ESRD programme over time

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Abstract

Background. The use of polyglucose as a peritoneal dialysis (PD) fluid extends time on PD treatment. It is anticipated, therefore, that the share of patients treated with PD will be positively influenced. The relationship between extension of PD treatment time and an increase of the PD treatment share, however, is complex and needs further investigation. In this paper, a Markov chain model was applied to investigate the impact of extended time on PD treatment for the PD share in all dialysis patients in The Netherlands. Furthermore, the economic impact of the extended time on treatment (ETOT) was explored.

Methods. Scenarios were forecast over a 10 year period using aggregate data from the End-Stage Renal Registry in The Netherlands (Renine). Three scenarios were simulated in which the median PD technique survival was extended by 8, 10 and 12 months. Two other scenarios explored the impact of the combined effect of ETOT of 10 months together with a 10% and 20% increase of PD inflow shares. Reductions of costs to society due to ETOT were estimated using Dutch cost data on renal replacement therapies.

Results. PD share increases from 30.0% in the null scenario to 34.5% in the scenario with an ETOT of 10 months and an increased PD inflow share of 20%. The reduction in total costs to society of the renal replacement therapies is 0.96%. The average societal costs per discounted patient year for haemodialysis (HD) are €84 100. For PD, these costs are €60 300.

A shift from HD to PD results in average cost savings of 28% per patient year.

Conclusions. In view of high dialysis costs to society, a reduction of 0.96% can be considered to be relevant for healthcare policy makers.

Keywords: economic evaluation; extended time on treatment; Markov chain modelling; peritoneal dialysis; polyglucose

Introduction

Although glucose is the principal osmotic agent used in peritoneal dialysis (PD), it is sometimes associated with a relatively short duration of effective ultrafiltration. Research has shown that the use of polyglucose as a PD fluid extends time on PD treatment [1]. It can therefore be expected that the PD share in dialysis patients will be positively influenced. This implies that the annual costs of an end-stage renal disease (ESRD) programme will decrease, because costs to society of PD are lower than costs of haemodialysis (HD) [2].

In this paper a Markov chain model was applied, to investigate the impact of extended time on PD treatment (ETOT) in The Netherlands. Anonymous and aggregated data from the Dutch Renal Disease Registry (Renine) was used to forecast patient numbers over a 10 year period in six different scenarios. A null scenario describes a situation where there is no impact resulting from ETOT. To model the effects of ETOT, three scenarios were defined where the transition rates in the Markov chain model were adapted. In addition, two scenarios described the effects of ETOT together with increased PD inflow shares. The effect measures

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were: the PD share in total ESRD patients at the end of the 10 year model period; the discounted patient years shifted from HD to PD over the model period; and the impact of this shift in patient years on the costs of the ESRD programme.

Subjects and methods

In general, patients in an ESRD programme are vulnerable to competing risks. A patient has a certain probability of staying on the same treatment, being transferred to other treatments, recovering his/her renal functioning or dying. If technique survival on PD is extended through the use of polyglucose in all patients, ETOT could be directly translated into a higher PD share. However, polyglucose is only effective in reducing technique failure in patients suffering from ultrafiltration failure. Other patients leave PD treatment for different reasons, such as peritonitis. Moreover, patients can receive a kidney transplant or die during the additional time they could have stayed on PD treatment as a result of using polyglucose. Consequently, the benefits of ETOT are not transparent.

The total effect of the use of polyglucose in ultrafiltration patients can be divided into direct and indirect effects. The direct effect results from the increase in PD treatment time. The indirect effect results from the increase in the number of patients starting on PD instead of HD. It is expected that more patients will start on PD because the chances of staying for a longer period on stable PD treatment are higher.

Markov chain model

A Markov chain model simulates the dynamics in a patient population, distributed over a number of treatment and age groups. Continuous time is divided into a sequence of discrete periods. The model estimates the number of patients in the different treatment and age groups at the end of each period. In this application of the Markov chain model, a period equals 1 month. Consequently, a scenario covering 10 years consists of 120 periods. In the first month of the model period, the calculations begin with a known distribution of patients over treatment and age groups. The number of patients per treatment and age groups at the end of the

month are derived from: (a) the number of patients entering the ESRD treatment—this is the inflow; (b) the distribution of inflow over the treatment and age groups; (c) the application of the transition rates that indicate the number of patients moving to another treatment or age group within the period; and (d) the transition rates of patients ending the treatment—this is the outflow from the model.

The transition rates and the relative distribution of the new patients over the groups are exogenously determined. The transition rates were calculated from the actual transitions that occurred in The Netherlands in the period 1997–1999. The relative distribution of the new patients over the groups equals the average relative distribution over the years 1997–1999.

Figure 1 shows a simplified representation of the Markov chain for three treatment groups and two calculation periods. The number of patients in each group at the end of the month is used as a starting point for the calculations in the next period. Again, the patients entering the different treatment and age groups are added to the patient numbers at the start and the transition rates are applied.

Since transitions differ over age, four age groups were distinguished in the model: 0–44, 45–64, 65–74 and 75+ years. Patients can move from a younger age group to an older group. Five modes of treatment were distinguished: full care-centre haemodialysis (FCCHD); limited care-centre haemodialysis (LCCHD); home haemodialysis (HHD); PD; and living with a functioning donor kidney (KTX).

Within treatment groups, two sub-treatments were distinguished for transitions occurring in the first year of treatment and transitions occurring in later years. The reason for this is that in some treatments, transitions in the first year are higher than in later years. The model has a total of 40 different groups (4 age groups \times 5 modes of treatment \times 2 sub-treatments) to describe developments in the patient population. In addition to the 40 treatment groups, the model has two ‘absorbing states’. These states are related to death and to recovery of patients’ own kidney function. Both death and recovery constitute the ‘outflow’ from the model.

Data

Anonymous and aggregated data were provided by the End-Stage Renal Registry in The Netherlands (Renine). Renine

Markov Chain

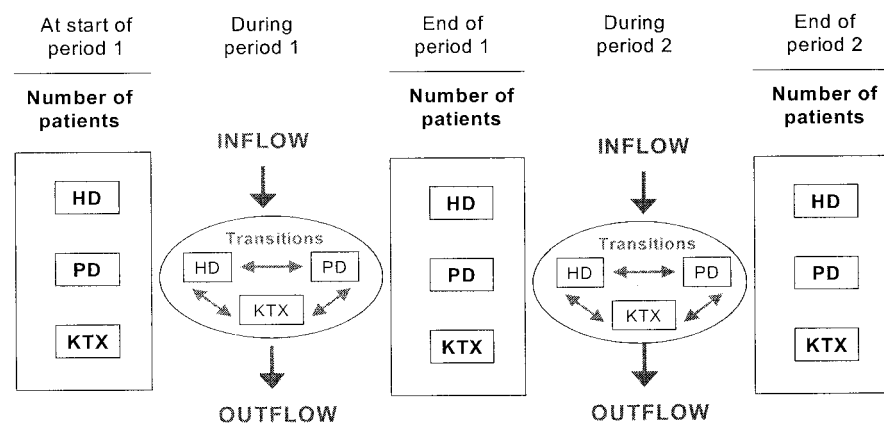


Fig. 1. The Markov chain.

has data available for transitions between modes of treatment, incidence in the ESRD programme and mortality [3]. These data were used to calculate the transition rates and the distribution of the new patients over the treatment and age groups

On the basis of the number of new patients per age group in the period 1990–1999, a linear trend was estimated describing the incidence in the four age groups per million of the population. This trend, combined with predictions of the age-specific growth of the Dutch population, was used to calculate the absolute number of new patients per age group in the 10 year model period [4,5].

The null scenario

The null scenario explores the developments without ETOT. The incidence per million of the age-specific population in the 10 year model period is assessed according to the calculated linear trend. The distribution of these new patients over treatment groups is equal to the average distribution in the period 1997–1999. In the null scenario, the transition rates are the average transition rates from the 3 year period 1997–1999. Monthly transition rates were calculated as the ratio of the transitions actually observed in a month and the number of patients at the beginning of that month.

Scenarios with extended time on PD

Three scenarios were defined to explore the direct effects of ETOT. These scenarios differ from the null scenario in the transition rates from PD to HD. For the period 1990–1999, technique survival on PD was calculated. Figure 2 shows the technique survival on PD, for patients starting their PD treatment in the period 1990–1999. Using the Renine data, it was found that for The Netherlands, median time on PD until a transition to HD was 3.9 years for all PD patients. In PD patients with ultrafiltration failure, Wilkie *et al.* [1] found a median extension of technique survival on PD of 22 months as a result of the use of polyglucose as a dialysis fluid. Peers *et al.* [6] found an extended continuous ambulatory peritoneal dialysis (CAPD) technique survival of at

least 1 year. It was estimated that incidence of ultrafiltration failure in PD patients is 5% in the first year of treatment, 30% after 3 years of PD treatment and 50% after 4 years [7,8]. To represent these estimates in the Markov model, the transition rates from PD to HD in the first year of treatment were kept constant. The assumption is that in the first year of treatment there is no effect of the use of polyglucose. In one scenario it was assumed that the median time until technique failure on PD increases by 10 months for all PD patients. This corresponds with ~22 months of ETOT for the 50% of patients with ultrafiltration failure. Two other scenarios were defined, a scenario with a lower median ETOT of 8 months and a scenario with a higher extension of median technique survival of 12 months.

The monthly transition rates for later years on treatment in the Markov model were adjusted to express the increased time on PD treatment in such a way that the median time on PD of 3.9 years increased by 8, 10 and 12 months. Figure 2 shows the survival curve for the scenario with the ETOT of 10 months, compared with the observed survival curve in the period 1990–1999.

The adjusted transition rates were obtained by correcting for the adjusted failure rate as an impact of ETOT. The theoretical survival (s_t) can be defined as:

$$s_t = (1 - r)^t \quad (1)$$

where r is the failure rate and t is the number of periods. If T is the median time on PD in months, the failure rate r can be described as:

$$r = 1 - e^{(\ln(0.5)/T)} \quad (2)$$

The extended median time is $T_e = T + \text{extension}$. The adjusted failure for each ETOT can be described as:

$$r_e = 1 - e^{(\ln(0.5)/T_e)} \quad (3)$$

where r_e is the adjusted failure rate for ETOT.

The adjusted transition rates were calculated by multiplying all transition rates from PD to HD with a factor r_e/r . With a median time on PD of 3.9 years, the monthly failure rate (r) is equal to 0.0147 and the failure rate for an extended

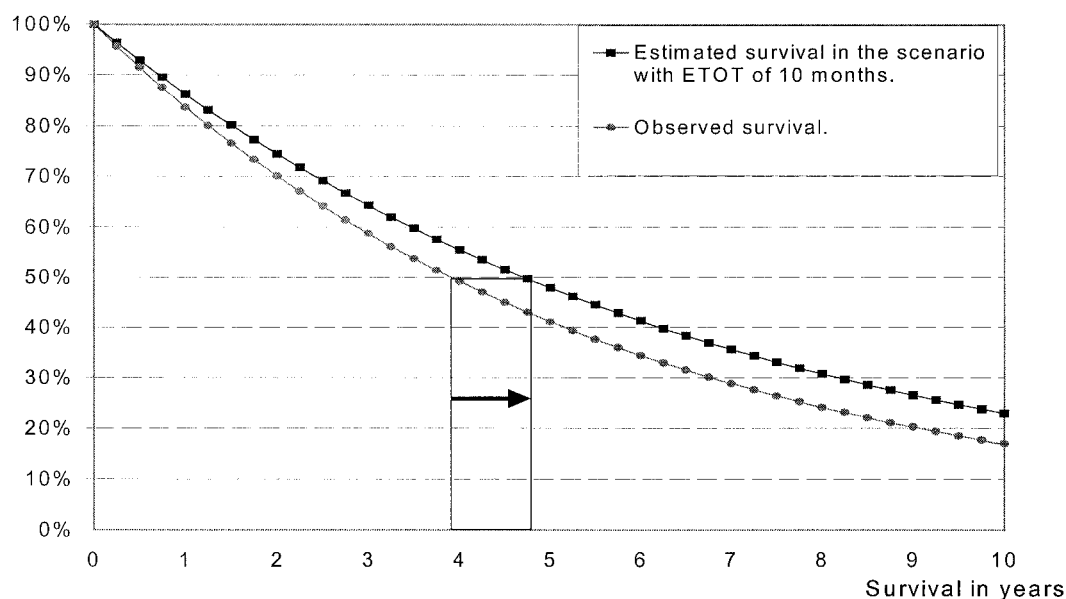


Fig. 2. Technique survival on PD with adjusted failure-rate.

time on PD (r_e) of 8 months is equal to 0.0126. As a consequence, the correction factor for all transition rates from PD to HD is 0.8649. For the extended times of 10 and 12 months, the correction factors for all transition rates are 0.8366 and 0.8101, respectively.

Scenarios with increased PD incidence and extended time of 10 months

Because of ETOT, PD treatment will be more attractive to patients and doctors. It can therefore be anticipated that the share of patients starting their renal replacement therapy with PD will increase. The relationship between ETOT and increasing incidence in PD is unknown. Two scenarios have been defined in which the PD incidence increases by 10% or by 20% compared with the inflow share in the null scenario. The relative distribution of PD incidence over the age groups has been kept equal to this distribution in the null scenario. Compared with the null scenario, total ESRD incidence does not change. Also, the share of transplants in the new patient does not differ. In these two scenarios with increased PD incidence, the extended time on PD treatment is 10 months.

Costs

To estimate the cost impact of extended time on PD treatment, total costs of the renal replacement programme in five scenarios were compared with total costs in the null scenario.

The cost estimates were based on a cost study in The Netherlands [5]. In this study, total costs to society were calculated per patient per year for different treatment and age groups. Treatment groups were: FCCHD, LCCHD, HHD, CAPD, continuous cycling peritoneal dialysis (CCPD) and KTX; age groups were: 0–44, 45–64, 65–74 and 75+ years. The costs of PD used in the estimates consisted of a weighted average of CAPD and CCPD costs. The weights were the age-related shares of CAPD and CCPD patients in total PD patients. Costs to society included costs of dialysis, other dialysis-related healthcare costs and patient costs. Costs of home adaptation for PD patients and travel costs for HD and PD patients were also included.

Costs in the first year on treatment and costs in the later years on treatment were distinguished for each treatment and age group. Total costs in the first year of treatment were higher than in the later years. In the first year, costs of hospitalization, vascular access operations and of training of patients are higher than in later years. In the dialysis treatment groups, costs in the two older age groups of 65–74 and 75+ are higher than costs in the two younger age groups. This is due to the higher costs of hospitalization in the older age groups.

In the original cost study, additional costs of polyglucose were not taken into account. In The Netherlands, these costs amount to €3313 per patient per year. The extra costs of polyglucose were added to the costs of PD for the additional patient years as a result of ETOT. In general, resource use was valued at real cost to society, not at reimbursement rates. Originally costs were calculated at a 1996 price level. Using a price index for healthcare services, costs have been updated to 1999 prices. To calculate total costs of dialysis over a 10 year period in the six scenarios, yearly costs were discounted using a rate of 4%.

Results

Figure 3 presents total estimated inflow per million of the population per age group of ESRD patients in the period 1990–2009. Figures from 1990 to 1999 are actual inflow figures. The figures from 2000 to 2009 are estimates using linear trend extrapolations for the 10 year period. This estimated trend has been used to calculate the total number of new patients in the estimation period.

The estimated trend indicates a stronger growth of incidence in ESRD patients per million of the population in the older age groups of 65–74 and 75+ compared with the age groups 0–44 and 45–64.

Table 1 summarizes the distribution of total number of new patients over HD and PD treatment in shares of total new patients per age group. The shares in the

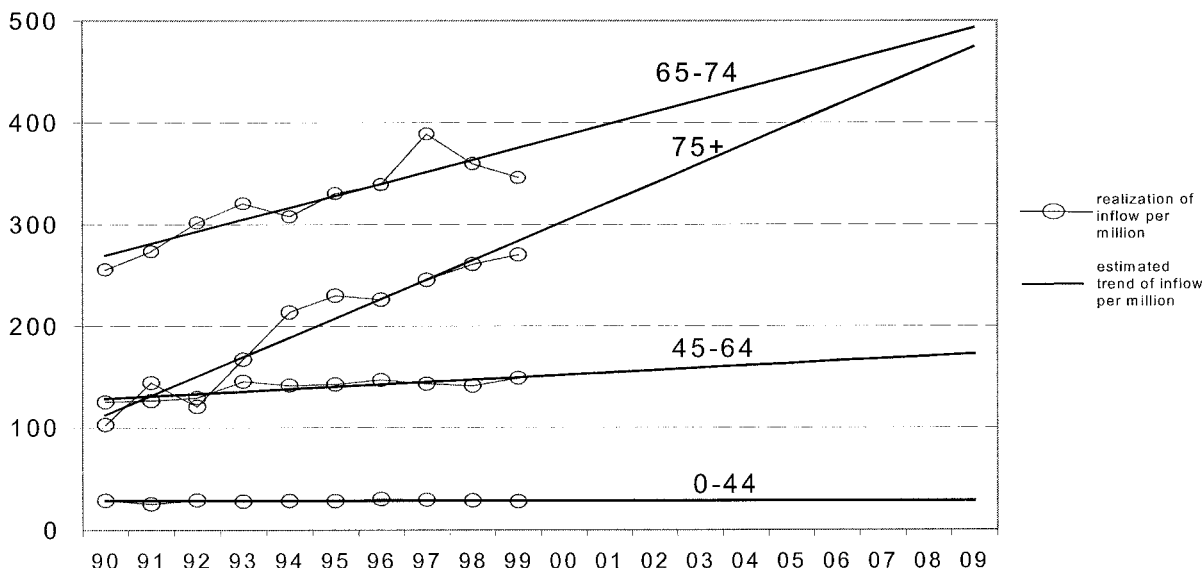


Fig. 3. Inflow of ESRD patients per age group per million of the population. Realized inflow in the period 1991–1999 and estimated trend.

Table 1. Incidence per age group in the null scenario and the two scenarios with increased inflow shares, in shares of total new patients per age group

Age group	Scenarios	HD	PD	KTX
0–44	Null scenario	52.3	41.5	6.2
	10% increased PD inflow share + ETOT of 10 months	48.2	45.7	6.2
	20% increased PD inflow share + ETOT of 20 months	44.0	49.8	6.2
45–64	Null scenario	60.9	35.5	3.7
	10% increased PD inflow share + ETOT of 10 months	57.3	39.1	3.7
	20% increased PD inflow share + ETOT of 20 months	53.7	42.6	3.7
65–74	Null scenario	76.6	23.0	0.4
	10% increased PD inflow share + ETOT of 10 months	74.3	25.3	0.4
	20% increased PD inflow share + ETOT of 20 months	72.0	27.6	0.4
75+	Null scenario	84.6	15.4	0.0
	10% increased PD inflow share + ETOT of 10 months	83.1	16.9	0.0
	20% increased PD inflow share + ETOT of 20 months	81.5	18.5	0.0

null scenario are derived from the average relative distribution of new patients over treatment and age groups in the period 1997–1999 in The Netherlands. Table 1 also presents the relative distribution in the two scenarios with a 10% or 20% increased PD inflow share.

Figure 4 presents the development of the PD shares in the six scenarios in the 10 year model period from 2000 to 2009. The realized PD shares for 1999 are also presented. The predicted PD share in the null scenario initially increases from 30.5% at the beginning of 2000 to 31.0%, but decreases to 30.0% at the end of 2009 as a result of changes in the age distribution of the dialysis population. The scenarios in which the median time on PD treatment was increased by 8, 10 and 12 months, result in PD shares at the end of 2009 increasing to 30.8%, 31.0% and 31.1%, respectively. If the PD inflow share increases by 10% or 20%, the share of PD in total dialysis patients increases to 32.7% or 34.5% at the end of 2009.

Extended time on PD treatment results in a shift of life years from HD to PD. The increase of PD inflow shares enhances this shift of life years from HD

to PD. In Table 2, the total number of discounted life-years on HD for the different scenarios over the 10 year modelling period are presented. The decrease of patient years in HD equals the shift to PD. In the scenario with an ETOT of 10 months, 1.0% of the discounted life-years in the null scenario shifts from HD to PD. In the scenarios with an ETOT of 8 or 12 months, this shift is 0.8% and 1.1%, respectively. In the scenarios with an ETOT of 10 months and increased inflow shares of 10% or 20%, the proportion of shifted discounted life-years is 2.9% and 4.9%, respectively.

Table 3 shows the total discounted costs to society of HD and PD treatment forecasted in different scenarios.

In the ‘median survival + 10 months’ scenario, the reduction in total costs is 0.19% compared with the null scenario. In the ‘median survival + 8 months’ and in the ‘median survival + 12 months’ scenarios, the cost reduction is 0.15% and 0.22%, respectively. In the scenarios where the PD inflow share increases by 10% and 20% together with an ETOT of 10 months, the cost reduction is 0.58% and 0.96%, respectively. In the null scenario the total costs per discounted patient

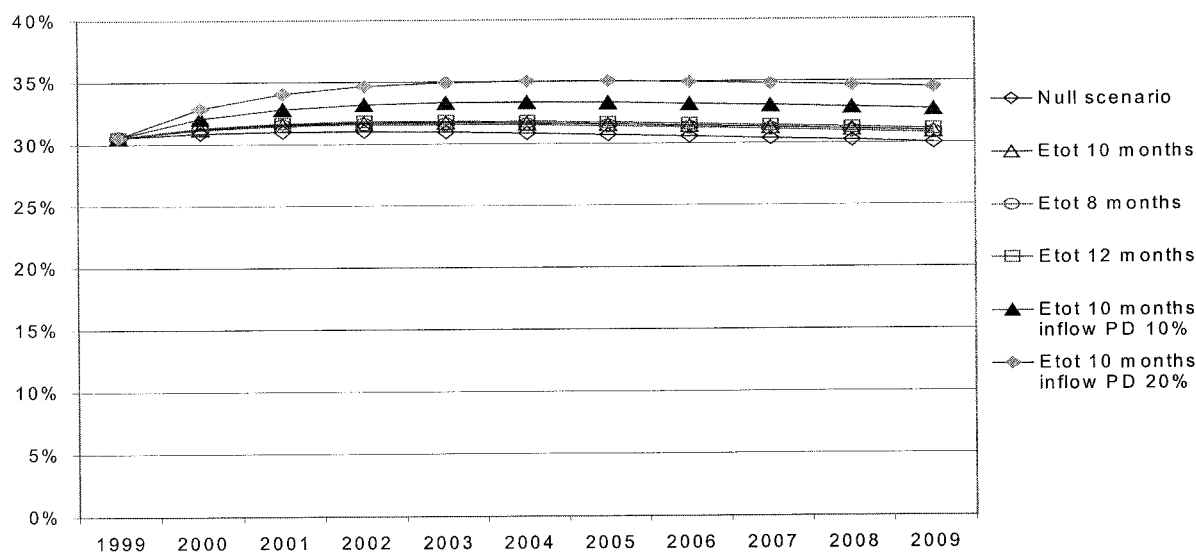
**Fig. 4.** The PD share in the six scenarios over a 10 year model period (2000–2009) and the start value for the analysis at the end of 1999.

Table 2. Discounted patient years shifted from HD to PD over the 10 year model period

Scenarios	Total number of discounted patient years in HD patients	Discounted patient years shifted from HD to PD	Share of discounted patient years shifted from HD to PD
Null scenario	33641.7		
ETOT of 8 months	33374.9	266.8	0.8%
ETOT of 10 months	33316.7	325.0	1.0%
ETOT of 12 months	33261.4	380.3	1.1%
10% increased PD inflow share + ETOT of 10 months	32654.2	987.5	2.9%
20% increased PD inflow share + ETOT of 10 months	32004.2	1637.5	4.9%

Table 3. Discounted societal costs of dialysis over the 10 year model period (millions of Euros)

Scenarios	HD	PD	Total costs	Cost savings compared with the null scenario	Savings as % of total costs
Null scenario	2828.9	898.6	3727.5		
ETOT of 8 months	2806.5	915.3	3721.8	5.7	0.15%
ETOT of 10 months	2801.6	918.9	3720.5	7.0	0.19%
ETOT of 12 months	2797.0	922.4	3719.4	8.1	0.22%
10% increased PD inflow share + ETOT of 10 months	2746.2	959.6	3705.8	21.7	0.58%
20% increased PD inflow share + ETOT of 10 months	2691.9	1000.2	3692.1	35.4	0.96%

year for HD are €84 100. The total costs per discounted patient year for PD are €60 300. These costs constitute average HD and PD costs over the model period, weighed by the total patient years per treatment and age group. In the model period, a shift from HD to PD results in cost savings of on average 28% per patient year.

Discussion

A Markov chain model was used to estimate the effect of the use of polyglucose as a dialysis fluid in patients with ultrafiltration failure over a 10 year period. The total effect was distinguished between a direct effect and an indirect effect. The direct effect results from the extended time on PD treatment and the indirect effect occurs as the impact of increased PD inflow shares. These increasing PD inflow shares are expected

to result from the improved perspective for patients who stay longer on a stable PD treatment. Three scenarios were defined in which the direct effect of ETOT was modelled by increased median technique survival of 8, 10 and 12 months for all PD patients. Two other scenarios combined the extended time of treatment of 10 months with increased PD inflow shares of 10% and 20%. The null scenario was based on technique success for HD, PD and KTX, as it was observed in the Dutch ESRD registry in the period 1997–1999. The effect measures were: the increased PD share in the total ESRD programme at the end of the 10 year period; the shift of discounted patient years from HD to PD in the model period; and the cost impact as a result of ETOT.

In the scenarios in which the median time on PD treatment increases by 8, 10 and 12 months, the predicted PD share at the end of 2009 increases to 30.8%, 31.0% and 31.1%, respectively. The scenario with the 10 months extended time on PD treatment and a 10% increase of the PD inflow shares shows a PD share of 32.7% at the end of 2009. When the PD inflow share increases by 20%, the share of PD in total dialysis patients increases to 34.5% at the end of the model period.

Compared with the null scenario, the scenarios in which median technique success increases by 10 months combined with increased PD inflow shares of 10% and 20%, show a shift in discounted patient years from HD to PD of 2.9% and 4.9%, respectively. Although this seems to be low, the absolute number of discounted patient years shifted from HD to PD is 988 and 1638 patient years respectively. The scenarios with an ETOT of 8, 10 and 12 months show a shift in patient years from HD to PD of 0.8%, 1.0% and 1.1%, respectively. In the model period, average societal costs per patient on PD are estimated to be 28% lower than average societal costs per HD patient (PD: €60 300 per year; HD €84 100 per year). Total societal costs of dialysis can decrease by 0.6% to 1.0% as a result of both the direct and indirect effects. This implies for The Netherlands that societal costs decrease by €35.4 million in the scenario with an ETOT of 10 months and an increased PD inflow share by 20%.

The analysis indicates that the impact resulting from increased inflow shares is larger than the direct effect of the ETOT. An additional analysis was performed to investigate the sensitivity of different assumptions for our conclusion. In this sensitivity analysis, a number of scenarios was used to investigate the influence of increasing PD inflow shares and increased time on treatment on the overall PD share. In one group of scenarios, the PD-inflow share was increased by 50%, in 10 steps of 5%. In another group of scenarios the time on treatment was increased in 36 steps of 1 month. The model results from these scenarios were used to estimate the influence of increased PD-inflow shares and ETOT on overall PD shares. Ordinary least square regressions were applied to estimate these relationships. The regressions

indicated that an increase of the PD inflow by 1% causes the PD shares to increase by 0.57%. An increase of the technique survival on PD by 1% causes the PD share to increase by 0.11%. The sensitivity analysis confirmed our conclusion that the influence of increasing PD shares is larger than the influence of ETOT.

It is possible that PD patients with ultrafiltration failure switch to CCPD when using polyglucose to extend time on PD treatment. This could have an impact on costs because CCPD is more expensive than CAPD. It is unknown whether ETOT would result in a substantial increase in CCPD. The possible cost impact has already been partially incorporated into our cost estimates. The PD costs per patient per year used in the cost estimates are an average of CAPD and CCPD costs weighted by the age-specific shares of CAPD and CCPD in total PD patients. The question is whether ETOT changes these age-specific shares. The relationship between ETOT and a switch from CAPD to CCPD needs further investigation before a possible impact on costs can be estimated.

This study concentrated on the effect the use of polyglucose has on PD shares in total renal replacement therapy. The results from the Markov modelling indicated higher PD shares. Consequently, direct and indirect effects of extended time on PD treatment result in cost savings that can amount to 1.0% of the total cost of dialysis treatment in The Netherlands. Although the relative cost savings are low, the absolute cost savings are substantial. These cost savings make it possible to offer dialysis treatment to more patients with equal budgets. In The Netherlands, the cost savings would allow for 452 more HD patient years or 635 more PD patient years in the 10 year model period. On a worldwide scale, the dialysis budget is estimated to be \$100 billion [9]. In view of these high dialysis

costs to society, a saving of 1.0% can be considered to be relevant for healthcare policy makers.

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