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Cost utility analysis of end stage renal disease treatment in Ministry of Health dialysis centres, Malaysia: Hemodialysis versus continuous ambulatory peritoneal dialysis

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Data Availability Statement: The costs and utilities values in this study were imputed from the primary data which were collected as part of this study and the detailed methodology and results have been published. We have provided the dataset used in these analyses in the supporting documents section. Data on survival analysis are not publicly available because these data are provided by the National Renal Registry (NRR). We submitted official request to NRR in order to obtain that part

Abstract

Objectives

In Malaysia, there is exponential growth of patients on dialysis. Dialysis treatment consumes a considerable portion of healthcare expenditure. Comparative assessment of their cost effectiveness can assist in providing a rational basis for preference of dialysis modalities.

Methods

A cost utility study of hemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD) was conducted from a Ministry of Health (MOH) perspective. A Markov model was also developed to investigate the cost effectiveness of increasing uptake of incident CAPD to 55% and 60% versus current practice of 40% CAPD in a five-year temporal horizon. A scenario with 30% CAPD was also measured. The costs and utilities were sourced from published data which were collected as part of this study. The transitional probabilities and survival estimates were obtained from the Malaysia Dialysis and Transplant Registry (MDTR). The outcome measures were cost per life year (LY), cost per quality adjusted LY (QALY) and incremental cost effectiveness ratio (ICER) for the Markov model. Sensitivity analyses were performed.

Results

LYs saved for HD was 4.15 years and 3.70 years for CAPD. QALYs saved for HD was 3.544 years and 3.348 for CAPD. Cost per LY saved was RM39,791 for HD and RM37,576 for

of data mentioned above. Data release agreement was signed which highlighting the exclusive property of the dataset belongs to NRR. A processing fee was also charged. Other interested researchers can request data by submitting official request to the NRR secretariat at nrr@msn.org.my who will seek permission from the NRR steering committee, headed by Datuk Dr Ghazali ahmad https://www.msn.org.my/nrr/data_request.jsp. Researchers can replicate the study findings in their entirety by obtaining permission from NRR to use the survival dataset and following the protocol in the methods section. The dataset used in this study can be released to interested parties after a written approval is granted by NRR. Individual informed consent was not necessary since consent was waived as there was a public notice up on the walls of healthcare centres asking permission for the registry to collect data and patients have option to opt out. We also would like to confirm that authors did not have any special access privileges that others would not have.

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CAPD. The cost per QALY gained was RM46,595 for HD and RM41,527 for CAPD. The Markov model showed commencement of CAPD in 50% of ESRD patients as initial dialysis modality was very cost-effective versus current practice of 40% within MOH. Reduction in CAPD use was associated with higher costs and a small devaluation in QALYs.

Conclusions

These findings suggest provision of both modalities is fiscally feasible; increasing CAPD as initial dialysis modality would be more cost-effective.

1.0 Introduction

Renal replacement therapy (RRT) is the usual choice of treatment for patients suffering from end stage renal disease (ESRD), which includes dialysis, either hemodialysis (HD) or peritoneal dialysis (PD) and a kidney transplant. A kidney transplant is the best choice of treatment in patients suffering from ESRD, however, the waiting list for transplantation continue to grow despite kidney transplants from live donors due to the organ scarcity [1].

Dialysis modality selection in various countries is influenced by non-medical factors including financial and reimbursement policy [2–4]. Although both HD and PD are costly, specific advantages and disadvantages have been identified for each of them. Comparative assessment of their cost effectiveness can assist in providing a rational basis for preference of one or the others [5]. Economic evaluation of ESRD treatment and policy explorations have been performed recurrently in many settings [6]. However, economic evaluations of dialysis modalities in Malaysia are still lacking despite the continuous growth of ESRD patients at an alarming rate. Peritoneal dialysis is underutilized although it is considered a more cost-effective, if not, equally cost-effective treatment as compared to HD around the world [1, 7–9].

Hemodialysis is the main dialysis modality in Malaysia and there is an inequitable geographical distribution of provision. Economically developed west coast states of Peninsular Malaysia have higher rates compared to east coast states, Sabah and Sarawak [1]. Dialysis acceptance rates have reached a level equal to that of developed countries [1, 10]. According to the 24th report of the Malaysian Dialysis and Transplant Registry (MDTR), 6,662 new HD patients and 1,001 new PD patients were reported in 2016 representing an acceptance rate of 216 per million population (pmp) and 32 pmp respectively. Overall, the total number of HD and PD patients increased to 35,781 patients (1,159 pmp) and 3,930 patients (127 pmp) respectively in 2016 [11]. Dialysis provision in Malaysia is delivered by different agencies. Forty seven percent of all dialysis patients are being treated in private settings, 37% in MOH settings and the rest are dialyzing in other centres operated by non-governmental organizations (NGO) and university hospitals. The number of dialysis centres for the whole of Malaysia increased from 698 in 2011 to 814 in 2016, with a notable surge in private centres, which had trebled from 145 in 2005 to 435 in 2016 [11]. However, almost all (99%) PD patients are being treated in public settings and private facilities dominate HD provision.

Public health care services in Malaysia are funded through general taxation, with annual budgets allocated to the Ministry of Health (MOH) while within the private sector, individuals can purchase health insurance on voluntary basis. The government would reimburse civil servants and their dependents for dialysis in private centres. Public funds are also channelled through the Social Security Organization (SOCSO), a government-run social insurance body that receives mandatory contributions from private-sector employees earning below US$900 per month. The state-run Islamic social welfare organizations reimburse eligible patients for certain treatments including dialysis [1, 10]. MOH is the ultimate decision maker on the funding of its own dialysis programme. It also provides subsidies for HD centres run by NGOs centres. The government was the main source of funding for new and existing patients in 2016 [11].

ESRD has significant economic consequences with loss of gross domestic product (GDP) for its management. In developed countries, it was reported that the expenses for RRT provision were 2–3% of total healthcare expenditure while ESRD patients accounted for just 0.02–0.03% of the total population [12]. Although limited data is available for ESRD expenditure in Malaysia, the estimated costs of dialysis in 2005 were RM379.1 mil [1, 10]. A recent forecast estimates the cost incurred to treat 51,269 patients with dialysis in the year 2020 is RM1.5 billion (USD384.5 million) [13]. Given the low organ donation rate and continual growth of ESRD population, it is timely to carry out an economic evaluation of HD and PD.

The aim of this study is to compare the cost utility of HD and CAPD and to assess the cost utility of different dialysis provision strategies at varying levels of CAPD usage versus current practice using a Markov model simulation cohort.

2.0 Methods

This study used both primary and secondary data for HD and CAPD. The principal outcomes of interest were costs and utilities of HD and CAPD derived from the primary data collection as part of this study. The costs of 64 PD patients and 77 HD patients, none of whom changed modality, changed centre, dropped-out or died during their one-year assessment from five large MOH centres were collected from 1st October 2016 to 30th September 2017. The sample size calculation took the chance of drop-out into consideration. Patients were enrolled if they were above 18 years old, initiated dialysis between 2011 and 2015, and dialysis treatment is subsidized by MOH. The health utilities were collected during the last quarter of the study period. These results have been published [14, 15]. The secondary data for the survival analyses was sourced from the Malaysian Dialysis and Transplant Registry (MDTR). The perspective of this study was that of the MOH because it is the ultimate decision maker on the funding of its own dialysis programme. Sources of data used in the study are summarized in Table 1. A Markov model cohort simulation was developed to explore the cost utility of hypothetical dialysis provision strategies versus current practice.

2.1 Costs

The mean costs per patient per year were obtained in the cost analysis [14]. The costs were divided into components which include access surgeries, outpatient clinic care, dialysis consumables, staff emoluments, land, building and hospitalizations. All costs were presented in Malaysian Ringgit (RM) valued in the year 2017.

Table 1. Sources of data.

Data	Data Type	Source
Cost	Primary data	Surendra et al. 2018 [14]
Utilities (EQ-5D)	Primary data	Surendra et al. 2019 [15]
Life years (LY)	Secondary data	MDTR*
Transitional probabilities	Secondary data	MDTR*

*MDTR-Malaysia Dialysis and Transplant Registry

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2.2 Health utilities

Patient responses to the EQ-5D-3L were used to generate a health state profile that was converted to index-based values. The EQ-5D questionnaire comprises a visual analogue scale (VAS) and an EQ-5D descriptive system. The descriptive system contains 5 health dimensions; mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. It can be transformed into an index score [15].

2.3 Survival estimates

The Kaplan-Meier product-limit survivor function approach was used to estimate the mean survival rates (life years) for HD and CAPD patients because it best fits the available data. Transitional probabilities to death and change between the modalities were also estimated. The survival dataset was obtained from the MDTR. The samples were all HD and all CAPD patients who began dialysis in MOH centres between 2011 and 2015. The outcomes of interest are death and change of modality and the follow-up period ended on 31st December 2016.

2.3.1 Life years. Survival was not censored for change of modality based on first modality. This mean that patients were attributed to their first modality and they continue to be assigned to that modality even if they switch to the other modality at an early stage. Survival durations for patients were calculated from the date commencing the first modality till 31st December 2016 for patients who were still on dialysis. For patients who died, survival duration was calculated from date commencing the first modality, till date of death. All death outcomes whether occurring during first modality or after change in modality were considered for this analysis. Patients were censored if they had received a kidney transplant, recovered kidney function and were lost to follow up during the period.

2.3.2 Transition probability-change of modality. Annual change of modality rates was calculated by dividing the number of the events in a year by the estimated mid-year patient population. The proportion of cohort in each dialysis modality and transitioning between the modalities were imputed based on the observed mean dialysis change rates among HD and CAPD patients over the five years period. The rates were converted into an annual transition probability by using the following formula: $p = 1 - \exp(-r^{*}t)$ where p is the per cycle probability, r is the per-cycle rate, and t is the number of cycles. The probabilities were converted using the method on probabilities and rates by Drummond et.al. (2015) [16].

2.3.3 Transition probability-death. Annual death rates were calculated by dividing the number of deaths in a year by the estimated mid-year patient population. The annual transition probabilities from HD to death and from CAPD to death were determined based on the observed mean death rates over the five years period. The rates were converted into an annual transition probability by using the following formula; $p = 1 - \exp(-r^{*}t)$ where p is the per cycle probability, r is the per-cycle rate, and t is the number of cycles.

2.4 Markov model simulation cohort

The model was developed based on the Markov model designed by Villa et al. (2011) [17]. Only three health states were included in this model; HD, CAPD and death as shown in Fig 1. The theoretical model structure was built in the TreeAge Pro software version 2018 to run a computer-generated simulation on a hypothetical cohort of dialysis patients stating either HD or CAPD. In this study, the model simulated progression of renal outcomes in temporal horizons of five years. Each cycle consumes one year. Thus, this model runs in five cycles.

2.4.1 Scenario consideration. According to the de-identified MDTR data, 60% of all patients dialysing at MOH centres were on HD and 40% were on CAPD. Hence, this observed distribution was used as the base case scenario in this study. Alternative scenarios to Malaysia

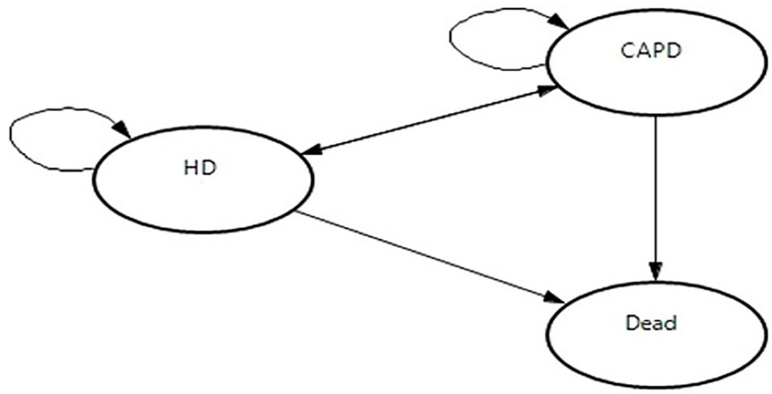

Fig 1. Markov model transition diagram.

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current practice included: Scenario 1, a model with an increased initial distribution of CAPD by 5%; Scenario 2: a model with an increased initial distribution of CAPD by 10%; Scenario 3: a model with a decreased initial distribution of CAPD by 10%.

2.4.2 Model assumptions. The underlying assumption of a Markov model in its standardized version is independent from past events, the Markovian property [16]. This means that irrespective of which state an individual in the model comes from, the patient will still face the same transition probabilities as someone who has another past state. A half-cycle correction was employed, which is equivalent to an assumption that, state transitions occur, on average, halfway through each cycle. Additionally, the model undertook the following assumptions; a) the Markov cohort comprised of ESRD patients aged 18 years and older, various racial/ethnic groups and clinical characteristics reflecting the characteristics of real world dialysis patients in Malaysia; b) the cohort starts with an initial distribution observed in each scenario; c) ESRD patients with no contraindications to any modality; d) patients' characteristics (other than age) remain unchanged during each cycle.

2.4.3 Model inputs. Relevant model data were incorporated based on primary data and secondary data as explained in the previous sections. The transition probabilities were assigned to each modality including death. Three health states (HD, CAPD, Death) were defined, with the chance of bidirectional transitions between all the states except death, which is an absorbent state. The total of probability must add up to one in each scenario. The initial prevalence was distributed among the modalities according to the proportions observed in the latest MDTR data. Based on those data, the future prevalence in each cycle (5 year) and state were determined by the application of a transition probabilities matrix (TPM). In the model, from one cycle to the next, the patient may stay on their current modality, switch to a different modality or die. Patients may die in any state (HD or CAPD) and only one movement was allowed per cycle. Once a patient die, he/she no longer accrue costs and benefits. Table 2 shows the model inputs.

2.4.4 One-way sensitivity analysis. One-way sensitivity analysis was used to investigate variability on all parameters included in the model. The plausible ranges of transition probabilities, health utilities and maximum/minimum value of cost components were included in this analysis. The results were presented in Tornado diagrams based on Net Monetary Benefit (NMB). A Tornado diagram is a special bar chart which is the graphical output of a comparative sensitivity analysis. It is comparing the relative importance of variables considered in the model [16]. The NMB was preferred due to the minute effectiveness differences between the strategies. It is calculated as (incremental benefit x threshold–incremental cost). A positive

Table 2. Parameter inputs for Markov model cohort simulation.

Parameter	Tornado diagram input labels[c]	Value (Mean)	Range	Parameter distribution[d]
Cost (RM), CAPD				Gamma (Alpha, Lambda)
Outpatient[a]	cCAPD_outpatient	4482.61	1842.79–12,401.07	
Access surgeries	cCAPD_access	477.26	199.80–1257.33	
Building and land	cCAPD_building_land	68.57	30.44–111.90	
Equipment	cCAPD_equipment	417.73	146.20–888.35	
Staff	cCAPD_staffing	3815.55	3011.47–4761.59	
Overheads	cCAPD_overheads	223.72	90.12–540.42	
Dialysis consumables	cCAPD_consumables	26486.05	25826.99–27171.01	
Hospitalization[b]	cCAPD_hosp	1604.55	0.00–17838.78	
Total		**37,576.03**	**31867.17–55,817.90**	
Cost (RM), HD				
Outpatient[a]	cHD_outpatient	5316.41	1993.95–11,399.97	
Access surgeries	cHD _access	1209.24	337.07–4865.86	
Building and land	cHD _building_land	783.95	162.94–2214.31	
Equipment	cHD _equipment	3299.05	2591.24–4424.78	
Staff	cHD_staffing	14818.36	11420.38–17499.80	
Overheads	cHD_overheads	1775.30	568.67–2914.41	
Dialysis consumables	cHD _consumables	11700.99	10803.51–12530.71	
Hospitalization[b]	cHD _hosp	887.28	0.00–18171.19	
Total		**39,790.58**	**30663.33–55996.57**	
Utilities				Beta (Alpha, Beta)
HD	uHD	0.854	0.290,1.000	
CAPD	uCAPD	0.905	0.564,1.000	

a = Outpatient costs include medications (including EPO), laboratory, radiology and clinic visits/referrals

b = Hospitalization costs include medications, blood products, referrals, laboratory investigations, imaging and procedures

c = Input labels for the one-way sensitivity analysis in the Markov model

d = Distribution used for the probabilistic sensitivity analysis in the Markov model

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NMB indicates that the imputed values are cost-effective at the given cost effectiveness threshold.

2.4.5 Probabilistic sensitivity analysis. To evaluate the impact of uncertainty on all the parameter values simultaneously, a probabilistic sensitivity analysis was performed by second order Monte Carlo simulations (1000 iterations). Each simulation provided one value of cost effectiveness. A gamma distribution for costs and a beta distribution for utilities and transition probabilities were used. Costs and outcomes were undiscounted or discounted at an annual rate of 3%. The result is presented in a cost effectiveness acceptance curve (CEAC).

2.5 Cost effectiveness threshold

Costs per QALY and LY less than three times and one-time gross domestic product per capita (GDP) are cost-effective and very cost-effective, respectively [18]. In Malaysia, the GDP per capita in 2017 was US$9,660 (≈RM40,000) [19]. Therefore, costs per LY or QALY should be lower than RM120,000 per patient to be cost-effective.

2.6 Incremental cost effectiveness ratio (ICER)

For the Markov model, the primary outcome is the Incremental Cost Effectiveness Ratio (ICER). Each intervention is compared to the next most effective alternative. The strategy is considered "dominated" when it generates higher costs and lower effectiveness compared to the alterative strategy. Cost effectiveness thresholds are one-time GDP per capita, US$9,660 (≈RM40,000) and three times GDP per capita, RM120,000.

2.7 Ethics approval

Ethics approvals were obtained from National University of Malaysia (JEP-2016-360) and the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (NMRR-16-1341-30856). This study was registered at ClinicalTrials.gov (NC T02862717). In the primary data collection, all research participants were provided with the Patient Information Sheet (PIS) and gave their permission to be part of the study by signing the informed consent form. Patients' participation was voluntary, and patients would continue to receive their dialysis treatment regardless of their enrolment in this study. All data was anonymized, with strict confidentiality and stored securely offline. Data validation checks were performed to ensure data quality. Data queries were generated and rectified with the investigators and research assistants at each site for missing values, out-of- range values and ambiguous data. The secondary data for survival analyses was de-identified and a data release agreement was signed with MDTR. Individual informed consent was not necessary since consent was waived as there was a public notice up on the walls of healthcare centres asking permission for the registry to collect data and patients have option to opt out.

3.0 Results

3.1 Survival analysis, life years and quality adjusted life years

The overall unadjusted one year and five years patients' survival (analysed as per ITT (initial modality of dialysis)) on dialysis were 94% and 48% respectively (Table 3). The unadjusted patient survival was marginally superior for those on HD compared to those on PD and this survival difference began to widen after the first year. At five years the unadjusted patient survival on HD was 53% compared with 39% in those on PD.

Table 4 shows the number of calculated LY and QALY. The average LY was 4.15 and 3.70 years for HD and CAPD respectively. Based on EQ-5D-3L index utility scores, average QALY for HD was 3.544 and 3.348 for CAPD.

3.2 Cost effectiveness and cost utility of HD and CAPD

The cost per LY for patients on HD was RM39,791, slightly higher than the cost per LY for patient on CAPD (RM37,576). The cost per QALY for patient in HD was RM46,595 and

Table 3. Unadjusted patient survival by dialysis modality.

Interval (month)	CAPD			HD			All		
	n	%survival	SE	n	%survival	SE	n	%survival	SE
0	3954	100		5614	100		9568	100	
6	3579	94	0.001	5213	94	0.001	8792	94	0.001
12	3191	87	0.001	4830	87	0.001	8021	87	0.001
24	1759	73	0.001	3218	76	0.001	4977	75	0.001
36	893	60	0.001	2092	67	0.001	2985	64	0.001
48	405	48	0.001	1215	60	0.001	1620	56	0.001
60	132	39	0.001	516	53	0.001	648	48	0.001
72	238			46			284		

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Table 4. Cost effectiveness and cost utility analysis.

Costs and outcomes	HD	CAPD
Life year (LY)	4.15	3.70
Quality adjusted life year (QALY)[a]	3.544	3.348
Cost per Life year (RM)[b]	39,791	37,576
Cost per QALY (RM)	46,595	41,527

a = Mean utility index for HD (0.854) and CAPD (0.905) [15]

b = Mean cost per patient per year, RM39,791 for HD and RM37,576 for CAPD [14]

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RM41,527 for patient in CAPD. The cost ratio of HD to CAPD per LY and per QALY was 1.06 and 1.12 respectively (Table 4).

3.3 Transitional probabilities

The annual death rate was higher in CAPD (0.134) than in HD (0.125). CAPD patients had a higher rate of switching dialysis modality (0.067) than HD patients (0.007) (Table 5).

3.4 Markov model

3.4.1 Projected costs, outcomes and cost effectiveness. Table 6 shows the results of the Markov model cohort simulation. Scenario 1 (55% HD and 45% CAPD) and scenario 3 (70% HD and 30% CAPD) were "dominated" strategies. The total undiscounted projected costs in scenario 2 were RM307,014 with 7.902 LYs and 7.041 QALYs. The base case scenario generated a higher undiscounted LYs (8.005) and QALYs (7.113) but with a higher cost (RM313,412). The ICER did not exceeded cost effectiveness threshold of three times GDP (RM120,000). However, the ICER exceeded the threshold for discounted costs and outcomes. Thus, scenario 2 appeared to be the most cost-effective strategy.

3.4.2 One-way sensitivity analysis. Figs 2 and 3 show the Tornado diagram with discounted costs and outcomes and undiscounted costs and outcomes respectively. In both sets of results, all imputed values are cost-effective at the cost effectiveness threshold (RM120,000). Health utilities, costs of hospitalizations and costs of outpatient clinic care in both modalities were the top predictors for the uncertainty of effectiveness in the Markov model.

3.4.3 Probabilistic sensitivity analysis. The CEAC of the Markov model (Fig 4) indicates that the probability of favouring base case or Scenario 2 is dependent on the level of the cost effectiveness threshold. At GDP of RM40,000-RM90,000, Scenario 2 was the best option. The

Table 5. Transitional probabilities.

Parameter	Tornado diagram input labels[a]	Rate[b] (Mean)	Range[a]	Parameter distribution[c]
Transitional probabilities[a]				Beta (Alpha, Beta)
CAPD-HD	pCAPD_HD	0.067	0.058,0.081	
CAPD-death	pCAPD_death	0.134	0.105,0.151	
HD-CAPD	pHD_CAPD	0.007	0.002,0.011	
HD-death	pHD_death	0.125	0.119,0.136	

a = Input labels for the one-way sensitivity analysis in the Markov model

b = Rates were converted to probability using the formula: $1\text{-}e^{(-rt)}$, where t = time, and r = rate.

The conversion was done automatically in the TreeAge Pro software.

c = Distribution used for the probabilistic sensitivity analysis in the Markov model

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Table 6. Costs, outcome and cost effectiveness.

Costs and outcomes	Base case	Scenario 1	Scenario 2	Scenario 3
HD:CAPD ratio	**60:40**	**55:45**	**50:50**	**70:30**
Undiscounted				
Projected cost, RM	313,412	308,032	307,014	311,086
Total LYs	8.005	7.910	7.902	7.933
Total QALYs	7.113	7.037	7.041	7.025
Discounted (3%)				
Projected cost, RM	94,425	93,517	93,236	94,361
LYs	2.417	2.407	2.407	2.410
QALYs	2.150	2.145	2.148	2.136
Cost effectiveness				
Cost per LY (discounted)	39,074	38,844	38,740	39,156
Cost per QALY (discounted)	43,919	43,591	43,399	44,172
Cost per LY (undiscounted)	39,151	38,943	38,852	39,214
Cost per QALY (undiscounted)	44,059	43,774	43,606	44,281
ICER				
Per LY (discounted)	120,160	355,207*	-	355,207*
Per QALY (discounted)	734,979	-92,909*	-	-92,909*
Per LY (undiscounted)	62,090	132,108*	-	132,108*
Per QALY (undiscounted)	87,864	-264,922*	-	-264,922*

ICER-incremental cost effectiveness ratio, QALY-quality-adjusted life year, LY-life Year

*"dominated" (worse outcomes, higher costs)

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base case was the best option if the accepted threshold is more than RM90,000. Irrespective of GDP threshold values, Scenario 1 and Scenario 3 were not cost-effective.

4.0 Discussion

This cost utility analysis study has provided a cost-analysis framework (micro-costing and step-down approach) and robust results of cost effectiveness of HD and CAPD in Malaysia. This is the first cost utility analysis of dialysis treatments for ESRD patients in Malaysia. The results indicate that CAPD is slightly more cost-effective than HD and the results are consistent with the previous economic evaluation of HD and CAPD in MOH centres in Malaysia [20].

However, the difference of costs per QALY or LY between HD and CAPD was small and not comparable to most developed and some developing countries [2, 21–24]. The ratio of HD to PD costs ranged from 0.70 in Nigeria to 1.90 in Canada [21]. The comparison of costs between HD and PD is presented in ratio forms to avoid possible biases introduced by heterogeneity in currency, eliminating the need for conversion rates and adjusting for inflation rate [21]. They highlighted that HD is generally more expensive than PD in developed countries, but data was not adequate to make any generalizations about the costs in developing countries. In developed countries, due to expensive labor and infrastructure costs, HD is frequently reported to be more expensive than CAPD [2]. For instance, Singapore has a 1.38 HD to PD cost ratio and the PD fluid is manufactured locally [24]. Just et al. (2008) reasserted their view that in developing countries where there are inexpensive labor costs and high imported equipment and solution costs, PD is more expensive than HD [2]. In Malaysia, the main cost

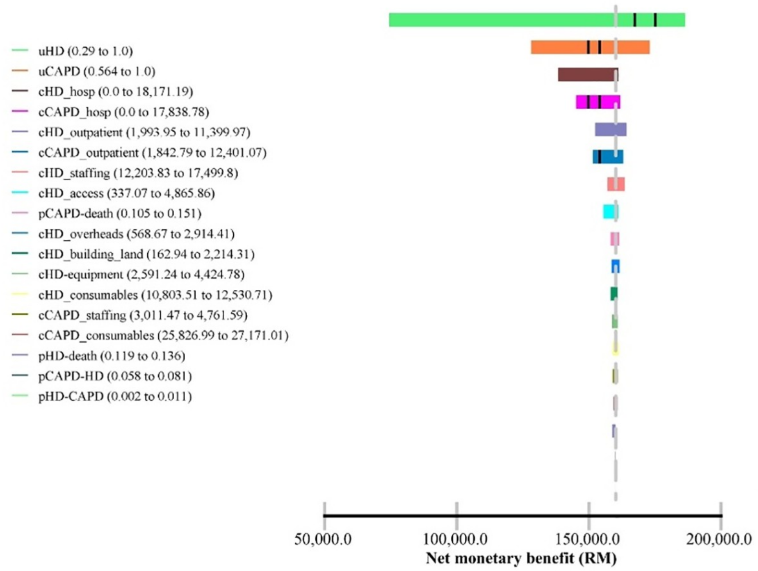

Fig 2. Tornado diagram (discounted). *Cost effectiveness threshold = RM120,000.

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component of HD is labor costs while dialysis consumables contribute a significant portion of total costs for CAPD [14].

The LYs and QALYs were higher in HD than in CAPD. The difference of survival between HD and CAPD may not be directly due to the dialysis modality. Survival rates are confounded by clinical and non-clinical factors [25–30]. In Malaysia, the apparent difference of the mortality risk between HD and CAPD is partly attributed to negative selection of PD patients [11]. The lesser LYs gained on CAPD was not compensated by a large increase in health utilities. Unlike in other countries utilities did not differ significantly in Malaysia [15]. In addition, the cost per QALY for both modalities exceeded RM40,000 which implies that both modalities are

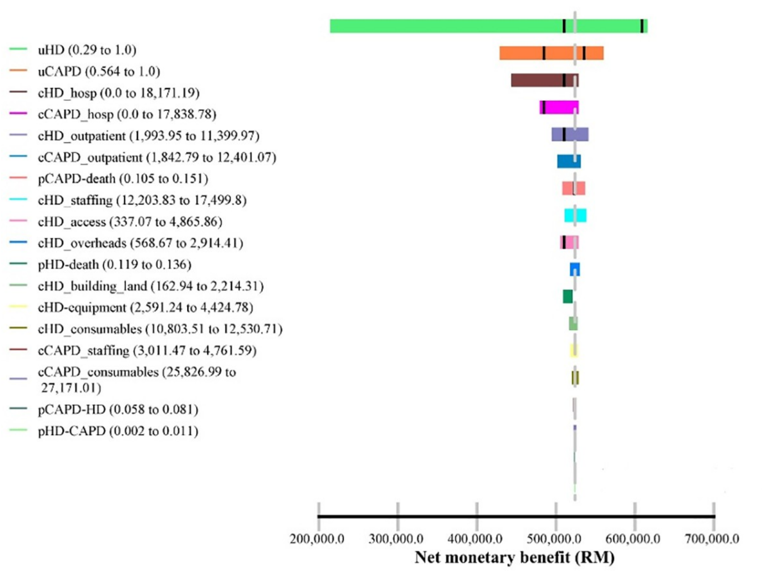

Fig 3. Tornado diagram (undiscounted). *Cost effectiveness threshold = RM120,000.

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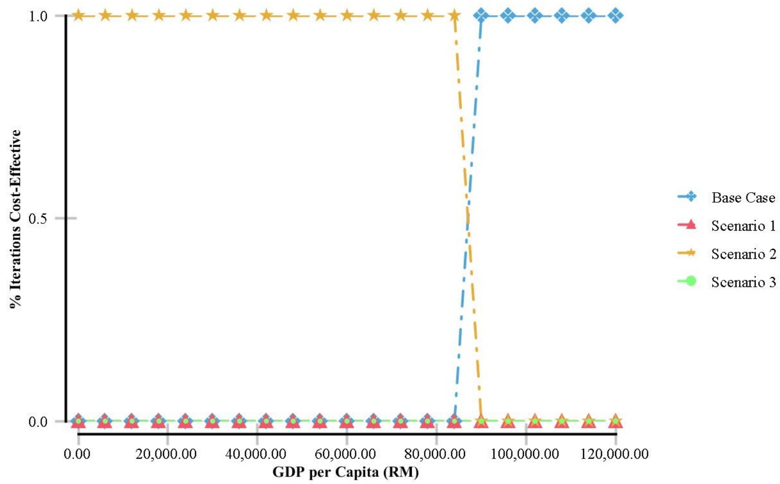

Fig 4. Cost effectiveness acceptability curve (discounted and undiscounted).

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not highly cost-effective. This does not reflect the true scenario since Malaysia is a country where the cost per QALY is low and the GDP is increasing yearly. Quoting the International Monetary Fund, GDP per capita for Malaysia rose from US$4,290 in 2000 to US$9,660 in 2017. Another important factor to consider in interpreting the results is that, the value of Ringgit Malaysia dropped significantly in the past few years with the lowest in a decade (US $1 = RM4.54) recorded in November 2016. Although the value of RM improved in 2017, it was still very low, average US$1 = RM4.30.

The Markov model is an analytical framework that is often used in decision analysis and is possibly the most common type of model used in economic evaluation studies [31]. Markov models are a popular form of decision-analytic model which distinguish patient cohorts based on a finite number of mutually exclusive "health states". The Markov model in this study shows that Scenario 2, 50% HD and 50% CAPD incident dialysis patients is the most cost-effective strategy. Scenario 2 incurred lesser costs but marginally lesser effectiveness than the base case scenario (60% HD and 40% CAPD). However, the ICER for the base case exceeded one-time GDP and three times GDP for undiscounted and discounted respectively. The Markov model is the first attempt to examine the cost utility of the different strategies of the dialysis provision in Malaysia.

The findings are consistent with the results reported by several countries on this topic in terms of PD expansion. The Markov model conducted by Treharne et al. (2014) analyzed the incident dialysis population to determine whether the proportion of patients on PD should be increased in United Kingdom. Compared with the reference scenario (22% PD, 78% HD), increasing PD use (39% PD, 61% HD) and (50% PD, 50% HD) resulted in reduced costs and better outcomes. Both strategies "dominated" the third scenario (5% PD, 95% HD) [32]. The study by Howard et al. (2009) in Australia reported that starting 50% of patients commencing RRT on PD resulted in significant cost savings and was at least as effective as the base case (12.5%) [33]. Similar observations were reported in Austria [34], Spain [17], Norway [35] and Indonesia [36]. In a budget impact analysis in Malaysia increasing PD provision contributes to cost savings. It will improve patients' access to dialysis in rural areas of Malaysia as the current funding model favours the setting up of HD centres in urban areas [37].

In the present study, an increase to 45% CAPD uptake is not a "dominant" scenario. In contrast, the Markov model developed by those countries mentioned above, showed favourable effectiveness and cost effectiveness in all scenarios when CAPD proportion is increased. This situation can be explained by several reasons. There is an apparent advantage of the mortality rate for HD in the current Markov model. In the other Markov models, PD had lower death risk than HD (the survival advantage favours PD). In countries where demographic and comorbidity data were comparable in both groups of patients, the disadvantage of survival on PD was not observed. Some countries adopt propensity cross matching approach to compare the relative effectiveness of both modalities. In such attempt by Chang et al. (2016), they postulated that the estimated life expectancy between HD and PD were nearly equal (19.11 versus 19.08 years) in the national cohort study with 14 years follow-up [25]. However, propensity score and adjustments were not pursued in the current study to reflect the current situation in Malaysia. Hence, the unadjusted mortality rate was higher in PD than HD in the current Markov model.

The rate of CAPD to HD transition used in this model was 6.70% (range 5.80% to 8.10%) annually. The 24th MDTR report stated that one-year PD technique survival was 79% and 24% at five years (uncensored for death and transplant) [11]. After excluding death, peritonitis persists as the commonest cause of technique failure over the last decade in Malaysia [11]. In a recent study of the risk of PD related peritonitis in Malaysia, the PD system and multiple patients' characteristics influence the risk of peritonitis [38]. The peritonitis rate was, however, well within the recommendation of 1 episode every 18 months or 0.67/year at risk according to the International Society for Peritoneal Dialysis (ISPD) [39]. Technique survival is crucial for PD programme expansion alongside other factors such as catheter placement and patients' education [40]. Most HD units keep one HD machine free for every 40 CAPD patients on treatment [20]. In contrast, transition rate of patients from HD to PD is minute. Another important factor to consider when interpreting the results is the insignificant difference in the cost between HD and CAPD in the current study. Other Markov models heavily favour PD expansion due to the large difference in the costs of dialysis accompanied by the positive effectiveness in PD.

The one-way sensitivity analysis via the Tornado diagram shows that health utilities, hospitalization costs and costs associated with outpatient clinic care relatively have a large impact on the net monetary benefits (NMB). Costs related to staffing, overheads, dialysis consumables, land and building have little to no sensitivity to the NMB. These findings accentuated the uncertainties in the Markov model and probably, the cost effectiveness relies on individual patient's characteristics. The probabilistic sensitivity analysis via the CEAC, indicates that Strategy 2 (50% CAPD) is a very cost-effective strategy. The base case is favourable if the cost effectiveness threshold is accepted in the region of above RM90,000. This would be unlikely considering the mean willingness to pay (WTP) among Malaysian population in one of the states in Malaysia was RM 29,080 (US$9,000) in 2010, per additional QALY gained [41].

The present study has several limitations. The lack of randomized controlled clinical trials means the causality between dialysis modality and mortality cannot be determined. Training costs of dialysis staff was not taken into the consideration in the cost analysis. It is recommended to include training costs in the cost analysis [16]. Kidney transplant was not included as one of the health states in the Markov model. Kidney transplant rate from deceased donors in Malaysia is very low and the annual probability of dialysis patients receiving kidney transplants from deceased donors is minute. The model was also kept simple without sub-group analysis and only the observed rates were used to minimise the complexity of the analysis while ensuring the research objectives were met. Finally, the study findings cannot be generalized to other providers, e.g. private.

5.0 Conclusion

In conclusion, both HD and CAPD are viable dialysis modalities in Malaysia. The Markov model favours incident CAPD expansion but with limitations. Hemodialysis and CAPD are established dialysis modalities that complement each other. A very important advantage of expanding home-based treatment like CAPD is that patients' disparities in access to dialysis can be improved particularly in less developed areas. The MOH through numerous agencies is already taking steps to encourage ESRD patients without contraindications to consider CAPD as a treatment option. Although reimbursements, economic considerations and government policies are imperative in dialysis provision, patient's preference cannot be overlooked. Patient selection is also key to a successful CAPD programme because patient's technique survival is still a major issue in CAPD.

Supporting information

S1 Dataset.
(XLSX)

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