

1 **Full title**

2

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

5

6 **Short title:**

7

8 **Cost utility analysis of dialysis in Malaysia**

9

10 Naren Kumar Surendra<sup>1\*</sup>¶, Mohd Rizal Abdul Manaf<sup>1¶</sup>, Lai Seong Hooi<sup>2¶</sup>, Sunita  
11 Bavanandan<sup>3¶</sup>, Fariz Safhan Mohamad Nor<sup>4&</sup>, Shahnaz Shah Firdaus Khan<sup>5&</sup>, Ong Loke  
12 Meng<sup>6&</sup>, Abdul Halim Abdul Gafor<sup>7&</sup>

13

14 <sup>1</sup>Department of Community Health, Faculty of Medicine, Pusat Perubatan Universiti  
15 Kebangsaan Malaysia, Kuala Lumpur, MALAYSIA

16

17 <sup>2</sup>Hospital Sultanah Aminah, Ministry of Health, Johor Bahru, Johor, MALAYSIA

18

19 <sup>3</sup>Hospital Kuala Lumpur, Ministry of Health, Kuala Lumpur, MALAYSIA

20

21 <sup>4</sup>Hospital Tengku Ampuan Afzan, Ministry of Health, Kuantan, Pahang, MALAYSIA

22

23 <sup>5</sup>Hospital Tengku Ampuan Rahimah, Ministry of Health, Klang, Selangor, MALAYSIA

24

25 <sup>6</sup>Hospital Pulau Pinang, Ministry of Health, Penang, MALAYSIA

26

27 <sup>7</sup>Nephrology Unit, Faculty of Medicine, Pusat Perubatan Universiti Kebangsaan Malaysia,  
28 Kuala Lumpur, MALAYSIA

29

30 \*Corresponding author

31 [naren.cruise@gmail.com](mailto:naren.cruise@gmail.com)

32

33 ¶These authors contributed equally to this work.

34 &These authors also contributed equally to this work.

35

36

37

38 **Abstract**

39

40 **OBJECTIVES**

41

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

45

46 **METHODS**

47

48 A cost utility study of hemodialysis (HD) and continuous ambulatory peritoneal dialysis  
49 (CAPD) was conducted from a Ministry of Health (MOH) perspective. A Markov model was  
50 also developed to investigate the cost effectiveness of increasing uptake of CAPD to 55% and  
51 60 % versus current practice of 40% CAPD in a five-year temporal horizon. A scenario with  
52 30% CAPD was also measured. The costs and utilities were sourced from published data which  
53 were collected as part of this study. The transitional probabilities and survival estimates were  
54 obtained from the Malaysia Dialysis and Transplant Registry (MDTR). The outcome measures  
55 were cost per life year (LY), cost per quality adjusted LY (QALY) and incremental cost  
56 effectiveness ratio (ICER) for the Markov model. Sensitivity analyses were performed.

57

58 **RESULTS**

59

60 LYs saved for HD was 4.15 years and 3.70 years for CAPD. QALYs saved for HD was 3.544  
61 years and 3.348 for CAPD. Cost per LY saved was RM39,791 for HD and RM37,576 for  
62 CAPD. The cost per QALY gained was RM46,595 for HD and RM41,527 for CAPD. The  
63 Markov model showed commencement of CAPD in 50% of ESRD patients as initial dialysis

64 modality was very cost-effective versus current practice of 40% within MOH. Reduction in  
65 CAPD use was associated with higher costs and a small devaluation in QALYs.

66

67 **CONCLUSIONS**

68

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

71 **1.0 Introduction**

72

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

78

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

88

89 Dialysis provision is dominated by HD in Malaysia and there is an inequitable distribution of  
90 its provision. Dialysis acceptance rates have reached a level equal to that of developed countries  
91 [1, 10]. According to the 24<sup>th</sup> report of the Malaysian Dialysis and Transplant Registry  
92 (MDTR), 6,662 new HD patients and 1,001 new PD patients were reported in 2016  
93 representing an acceptance rate of 216 per million population (pmp) and 32 pmp respectively.  
94 Overall, the total number of HD and PD patients increased to 35,781 patients (1,159 pmp) and  
95 3,930 patients (127 pmp) respectively in 2016 [11]. The number of dialysis centres for the

96 whole of Malaysia increased from 698 in 2011 to 814 in 2016. This was attributed by the private  
97 dialysis centres which had trebled from 5 pmp in 2004 to 14 pmp in 2016 [11].

98

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

107

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

111

## 112 **2.0 Methods**

113

114 The study used both primary and secondary data for HD and CAPD. The primary outcomes of  
115 interest were costs and utilities of HD and CAPD derived from the primary data collection as  
116 part of this study and these have been published [15, 16]. The survival data was sourced from  
117 the Malaysian Dialysis and Transplant Registry (MDTR). The perspective of the study was that  
118 of the MOH because it is the ultimate decision maker on the funding of its own dialysis  
119 programme. Sources of data used in the study are as shown in Table 1.

120

121 A Markov model cohort simulation was developed to explore the cost utility of hypothetical  
122 dialysis provision strategies versus current practice.

123 Table 1: Sources of data

<b>Data</b>	<b>Data Type</b>	<b>Source</b>
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

124 \*MDTR-Malaysia Dialysis and Transplant Registry

125

## 126 **2.1 Costs**

127

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

132

## 133 **2.2 Health utilities**

134

135 Patient responses to the EQ-5D-3L were used to generate a health state profile that was  
136 converted to index-based values. The Malaysian value-set was used, and the results have been  
137 published [15].

138

## 139 **2.3 Survival estimates**

140

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

147

### 148 **2.3.1 Life years**

149

150 Survival was not censored for change of modality based on first modality. Survival durations  
151 for patients were calculated from the date commencing the first modality till 31<sup>st</sup> December  
152 2016 for patients who were still on dialysis. For patients who died, survival duration was  
153 calculated from date commencing the first modality, till date of death. All death outcomes  
154 whether occurring during first modality or after change in modality were considered for this  
155 analysis. Patients were censored if they had received a kidney transplant, recovered kidney  
156 function and were lost to follow up during the period.

157

### 158 **2.3.2 Transition probability-change of modality**

159

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

168

169

### 170 **2.3.3 Transition probability-death**

171

172 Annual death rates were calculated by dividing the number of deaths in a year by the estimated  
173 mid-year patient population. The annual transition probabilities from HD to death and from

174 CAPD to death were determined based on the observed mean death rates over the five years  
175 period. The rates were converted into an annual transition probability by using the following  
176 formula;  $p = 1 - \exp(-r*t)$  where  $p$  is the per cycle probability,  $r$  is the per-cycle rate, and  $t$  is  
177 the number of cycles.

178

## 179 **2.4 Markov model simulation cohort**

180

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

187

### 188 **2.4.1 Scenario consideration**

189

190 According to the MDTR data, 60% of all patients dialysing at MOH centres were on HD and  
191 40% were on CAPD. Hence, this observed distribution was used as the base case scenario in  
192 this study. Alternative scenarios to Malaysia current practice included: Scenario 1, a model  
193 with an increased initial distribution of CAPD by 5%; Scenario 2: a model with an increased  
194 initial distribution of CAPD by 10%; Scenario 3: a model with a decreased initial distribution  
195 of CAPD by 10%.

196

### 197 **2.4.2 Model assumptions**

198

199 The underlying assumption of a Markov model in its standardized version is independent from



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

210

### 211 **2.4.3 Model inputs**

212

213 Relevant model data were incorporated based on primary data which were collected as part of  
214 this study and the detailed methodology and results have been published elsewhere [14, 15].

215

216 Transition probabilities were estimated according to an analysis of a de-identified dataset from  
217 MDTR as described above. The transition probabilities were assigned to each modality  
218 including death. Three health states (HD, CAPD, Death) were defined, with the chance of  
219 bidirectional transitions between all the states except death, which is an absorbent state. The  
220 total of probability must add up to one in each scenario. The initial prevalence was distributed  
221 among the modalities according to the proportions observed in the latest MDTR data. Based  
222 on those data, the future prevalence in each cycle (5 year) and state were determined by the  
223 application of a transition probabilities matrix (TPM). In the model, from one cycle to the next,  
224 the patient may stay on their current modality, switch to a different modality or die. Patients  
225 may die in any state (HD or CAPD) and only one movement was allowed per cycle. Once a

226 patient dies, he/she no longer accrue costs and benefits. Table 1 shows the model inputs.

227

#### 228 **2.4.4 One-way sensitivity analysis**

229

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

239

#### 240 **2.4.5 Probabilistic sensitivity analysis**

241

242 To evaluate the impact of uncertainty on all the parameter values simultaneously, a  
243 probabilistic sensitivity analysis was performed by second order Monte Carlo simulations  
244 (1000 iterations). Each simulation provided one value of cost effectiveness. A gamma  
245 distribution for costs and a beta distribution for utilities and transition probabilities were used.  
246 Costs and outcomes were undiscounted or discounted at an annual rate of 3%. The result is  
247 presented in a cost effectiveness acceptance curve (CEAC).

248

249

250 **2.5 Cost effectiveness threshold**

251

252 Costs per QALY and LY less than three times and one-time gross domestic product per capita  
 253 (GDP) are cost-effective and very cost-effective, respectively [18]. In Malaysia, the GDP per  
 254 capita in 2017 was US\$9,660 (≈RM40,000) [19]. Therefore costs per LY or QALY should be  
 255 lower than RM120,000 per patient to be cost-effective. The combined data of costs and utilities  
 256 are shown in Table 2.

257 Table 2: Parameter inputs for Markov model cohort simulation

Parameter	Tornado diagram input labels <sup>b</sup>	Value (Mean)	Range	Parameter distribution <sup>c</sup>
<b>Cost (RM), CAPD</b>				Gamma (Alpha, Lambda)
Outpatient <sup>a</sup>	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	cCAPD_hosp	1604.55	0.00-17838.78	
<b>Total</b>		<b>37,576.03</b>	<b>31867.17-55,817.90</b>	
<b>Cost (RM), HD</b>				
Outpatient <sup>a</sup>	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	cHD_hosp	887.28	0.00-18171.19	
<b>Total</b>		<b>39,790.58</b>	<b>30663.33-55996.57</b>	
<b>Utilities</b>				Beta (Alpha, Beta)
HD	uHD	0.854	0.290,1.000	
CAPD	uCAPD	0.905	0.564,1.000	

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

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

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

261

262

## 263 2.6 Incremental cost effectiveness ratio (ICER)

264

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

270

## 271 2.7 Ethics approval

272

273 Ethics approvals were obtained from Pusat Perubatan Universiti Kebangsaan Malaysia (JEP-  
274 2016-360) and the Medical Research and Ethics Committee (MREC), Ministry of Health  
275 Malaysia (NMRR-16-1341-30856). This study was registered at ClinicalTrials.gov (NC  
276 T02862717).

277

## 278 3.0 Results

279

### 280 3.1 Life years and quality adjusted life years

281

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

285 Table 3: Cost effectiveness and cost utility analysis

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

286 <sup>a</sup>=Mean utility index for HD (0.854) and CAPD (0.905) [15]

287 <sup>b</sup>=Mean cost per patient per year, RM39,791 for HD and RM37,576 for CAPD [14]

288

289

## 290 3.2 Cost effectiveness and cost utility of HD and CAPD

291

292 The cost per LY for patients on HD was RM39,791, slightly higher than the cost per LY for  
 293 patient on CAPD (RM37,576). The cost per QALY for patient in HD was RM46,595 and  
 294 RM41,527 for patient in CAPD. The cost ratio of HD to CAPD per LY and per QALY was  
 295 1.06 and 1.12 respectively (Table 3).

296

## 297 3.3 Transitional probabilities

298

299 The annual death rate was higher in CAPD (0.134) than in HD (0.125). CAPD patients had a  
 300 higher rate of switching dialysis modality (0.067) than HD patients (0.007) (Table 4).

301 Table 4: Transitional probabilities

Parameter	Tornado diagram input labels <sup>a</sup>	Rate <sup>b</sup> (Mean)	Range <sup>a</sup>	Parameter distribution <sup>c</sup>
<b>Transitional probabilities<sup>a</sup></b>				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	

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

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

304 The conversion was done automatically in the TreeAge Pro software.

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

306

## 307 3.2 Markov model

308

### 309 3.2.1 Projected costs, outcomes and cost effectiveness

310

311 Table 5 shows the results of the Markov model cohort simulation. Scenario 1 (55% HD and  
 312 45% CAPD) and scenario 3 (70% HD and 30% CAPD) were dominated strategies. The total  
 313 undiscounted projected costs in scenario 2 were RM307,014 with 7.902 LYs and 7.041  
 314 QALYs. The base case scenario generated a higher undiscounted LYs (8.005) and QALYs  
 315 (7.113) but with a higher cost (RM313,412). The ICER did not exceeded cost effectiveness  
 316 threshold of three times GDP (RM120,000). However, the ICER exceeded the threshold for

317 discounted costs and outcomes. Thus, scenario 2 appeared to be the most cost-effective  
 318 strategy.

319 Table 5: Costs, outcome and cost effectiveness

<b>Costs and outcomes</b>	<b>Base case</b>	<b>Scenario 1</b>	<b>Scenario 2</b>	<b>Scenario 3</b>
<b>HD:CAPD ratio</b>	<b>60:40</b>	<b>55:45</b>	<b>50:50</b>	<b>70:30</b>
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*

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

321 \*Dominated (Worse outcomes, higher costs)

322

### 323 3.2.2 One-way sensitivity analysis

324

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

330

### 331 3.2.3 Probabilistic sensitivity analysis

332

333 The CEAC of the Markov model (Figure 4) indicates that the probability of favouring base  
 334 case or Scenario 2 is dependent on the level of the cost effectiveness threshold. At GDP of

335 RM40,000-RM90,000, Scenario 2 was the best option. The base case was the best option if the  
336 accepted threshold is more than RM90,000. Irrespective of GDP threshold values, Scenario 1  
337 and Scenario 3 were not cost-effective.

338

#### 339 **4.0 Discussion**

340

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

346

347 However, the difference of costs per QALY or LY between HD and CAPD was small and not  
348 comparable to most developed and some developing countries [2, 21-24]. The ratio of HD to  
349 PD costs ranged from 0.70 in Nigeria to 1.90 in Canada [21]. The comparison of costs between  
350 HD and PD is presented in ratio forms to avoid possible biases introduced by heterogeneity in  
351 currency, eliminating the need for conversion rates and adjusting for inflation rate [21]. They  
352 highlighted that HD is generally more expensive than PD in developed countries, but data was  
353 not adequate to make any generalizations about the costs in developing countries. In developed  
354 countries, due to expensive labor and infrastructure costs, HD is frequently reported to be more  
355 expensive than CAPD [2]. For instance, Singapore has a 1.38 HD to PD cost ratio and the PD  
356 fluid is manufactured locally [24]. Just et al. (2008) reasserted their view that in developing  
357 countries where there are inexpensive labor costs and high imported equipment and solution  
358 costs, PD is more expensive than HD [2]. In Malaysia, the main cost component of HD is labor  
359 costs while dialysis consumables contribute a significant portion of total costs for CAPD [14].

360

361 The LYs and QALYs were higher in HD than in CAPD. The difference of survival between  
362 HD and CAPD may not be directly due to the dialysis modality. Survival rates are confounded  
363 by clinical and non-clinical factors [25-30]. In Malaysia, the apparent difference of the  
364 mortality risk between HD and CAPD is partly attributed to negative selection of PD patients  
365 [11]. The lesser LYs gained on CAPD was not compensated by a large increase in health  
366 utilities. Unlike in other countries utilities did not differ significantly in Malaysia [15]. In  
367 addition, the cost per QALY for both modalities exceeded RM40,000 which implies that both  
368 modalities are not highly cost-effective. This does not reflect the true scenario since Malaysia  
369 is a country where the cost per QALY is low and the GDP is increasing yearly. Quoting the  
370 International Monetary Fund, GDP per capita for Malaysia rose from US\$4,290 in 2000 to  
371 US\$9,660 in 2017. Another important factor to consider in interpreting the results is that, the  
372 value of Ringgit Malaysia dropped significantly in the past few years with the lowest in a  
373 decade (US\$1=RM4.54) recorded in November 2016. Although the value of RM improved in  
374 2017, it was still very low, average US\$1=RM4.30.

375

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



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

398

399 In the present study, an increased 5% CAPD uptake is still a dominated scenario. In contrast,  
400 the Markov model developed by those countries mentioned above, showed favourable  
401 effectiveness and cost effectiveness in all scenarios when CAPD proportion is increased. This  
402 situation can be explained by several reasons. There is an apparent advantage of the mortality  
403 rate for HD in the current Markov model. In the other Markov models, PD had lower death risk  
404 than HD (the survival advantage favours PD). In countries where demographic and comorbidity  
405 data was comparable in both groups of patients, the disadvantage of survival on PD was not  
406 observed. Some countries adopt propensity cross matching approach to compare the relative  
407 effectiveness of both modalities. In such attempt by Chang et al. (2016), they postulated that  
408 the estimated life expectancy between HD and PD were nearly equal (19.11 versus 19.08 years)  
409 in the national cohort study with 14 years follow-up [25]. However, propensity score and  
410 adjustments were not pursued in the current study to reflect the current situation in Malaysia.

411 Hence, the unadjusted mortality rate was higher in PD than HD in the current Markov model.

412

413 There is low technique survival in PD patients in Malaysia which means there is a high  
414 probability of PD patients converting to HD annually. The rate of CAPD to HD transition used  
415 in this model was 6.70% (range 5.80% to 8.10%) annually. The 24<sup>th</sup> MDTR report stated that  
416 one-year PD technique survival was 94% and 66% at five years (censored for death and  
417 transplant) [11]. Technique survival is crucial for PD programme expansion alongside other  
418 factors such as catheter placement and patients' education [38]. In contrast, HD patients enjoy  
419 excellent technique survival in Malaysia. The one-year HD technique survival was 99% and  
420 97% at five years (censored for death and transplant) [11]. Because of the high technique failure  
421 in CAPD patients in Malaysia, the HD unit must be prepared to cater for patients who are likely  
422 to fail CAPD. Most HD units keep one HD machine free for every 40 CAPD patients on  
423 treatment [20]. Another important factor to consider when interpreting the results is the  
424 insignificant difference in the cost between HD and CAPD in the current study. Other Markov  
425 models heavily favour PD expansion due to the large difference in the costs of dialysis  
426 accompanied by the positive effectiveness in PD.

427

428 The one-way sensitivity analysis via the Tornado diagram shows that health utilities,  
429 hospitalization costs and costs associated with outpatient clinic care relatively have a large  
430 impact on the net monetary benefits (NHB). Costs related to staffing, overheads, dialysis  
431 consumables, land and building have little to no sensitivity to the NHB. These findings  
432 accentuated the uncertainties in the Markov model and probably, the cost effectiveness relies  
433 on individual patient's characteristics. The probabilistic sensitivity analysis via the CEAC,  
434 indicates that Strategy 2 (50% CAPD) is very cost-effective strategy. The base case is  
435 favourable if the cost effectiveness threshold is accepted in the region of above RM90,000.

436 This would be unlikely considering the mean willingness to pay (WTP) among Malaysian  
437 population in one of the states in Malaysia was RM 29,080 (US\$9,000) in 2010, per additional  
438 QALY gained [39].

439

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

449

## 450 **5.0 Conclusion**

451

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

462 **Acknowledgements**

463

464 The authors would like to gratefully acknowledge all the people that have made this study  
465 possible. First and foremost, we would like to thank the sub principal investigators and research  
466 assistants comprise of nurses and medical assistants at each centres for their valuable input and  
467 data collection; Dr Liu Wen Jiun, Ms. Jamilah Sarif, Mr. Norisham bin Mohd Dom (Hospital  
468 Sultanah Aminah), Dr Kiren Kaur A/P Bhajan Singh, Ms. Rozana Bt Zainol Rasid, Ms. Bistari  
469 Binti Zubir (Hospital Tengku Ampuan Afzan), Mr. Amirul Nizam bin Mohtar, Mr. Mohd  
470 Patrival bin Zahari, Ms. Jamaiyah binti Supar, Ms. Vijaya A/P Lakayan (Hospital Kuala  
471 Lumpur), Ms. Lim Siew Kim, Mr. Khairul Nul Hakim bin Hazman, Norhazliza binti Hashim  
472 Hospital Pulau Pinang, Mr. Ratneswaran A/L Naganathan, Ms. Noriah binti Othman (Hospital  
473 Tengku Ampuan Rahimah). Second, we would like to acknowledge Dato' Dr. Tan Chwee  
474 Choon, former Head of Nephrology Service, Ministry of Health Malaysia and Datuk Dr.  
475 Ghazali Ahmad, Head of Nephrology Department, Hospital Kuala Lumpur for providing us  
476 with their able assistance and allowing us to conduct this research. Besides, we would like to  
477 thank National Renal Registry, in particular, Madam Lee Day Guat in providing patients' list  
478 for sampling. Finally, the authors thank the Director General of Health in Malaysia for  
479 permission to publish this paper.

480

481

## 482   **References**

- 483
- 484   1. Rizal AM, Surendra NK, Abdul Gafor AH, Seong Hooi L, Bavanandan S. Dialysis  
485    provision and implications of health economics on peritoneal dialysis utilization: a review  
486    from a Malaysian perspective. *Int J Nephrol*. 2017;2017:5819629.  
487
- 488   2. Just PM, de Charro FT, Tschosik EA, Noe LL, Bhattacharyya SK, Riella MC.  
489    Reimbursement and economic factors influencing dialysis modality choice around the  
490    world. *Nephrol Dial Transplant*. 2008;23(7):2365–2373.  
491
- 492   3. Lameire N, Peeters P, Vanholder R, Van Biesen W. Peritoneal dialysis in Europe: an  
493    analysis of its rise and fall. *Blood Purif*. 2006;24(1):107-114.  
494
- 495   4. Wauters JP, Uehlinger D. Non-medical factors influencing peritoneal dialysis utilization:  
496    the Swiss experience. *Nephrol Dial Transplant*. 2004;19(6):1363-1367.  
497
- 498   5. Arogundade FA, Ishola DA Jr, Sanusi AA, Akinsola A. An analysis of the effectiveness  
499    and benefits of peritoneal dialysis and hemodialysis using Nigerian made PD fluids. *Afr J*  
500    *Med Sci*. 2005;34(3):227-233.  
501
- 502   6. Teerawattananon Y, Mugford M, Tangcharoensathien V. Economic evaluation of palliative  
503    management versus peritoneal dialysis and hemodialysis for end-stage renal disease:  
504    evidence for coverage decisions in Thailand. *Value Health*. 2007;10(1):61-72.  
505
- 506   7. Liu FX, Quock TP, Burkart J, Noe LL, Inglese G. Economic evaluations of peritoneal  
507    dialysis and hemodialysis: 2004–2012. *F1000 Research*. 2013;2(273):1-13,  
508
- 509   8. Karopadi AN, Mason G, Rettore E, Ronco C. Cost of peritoneal dialysis and hemodialysis  
510    across the world. *Nephrol Dial Transplant*. 2013;28(10): 2553-2569.  
511
- 512   9. Grapsa E. Is the underutilization of peritoneal dialysis in relation to hemodialysis, as renal  
513    replacement therapy, justifiable worldwide? Yes or No. *Hippokratia*. 2011;15(1): 13-15.  
514
- 515   10. Lim TO, Goh A, Lim YN, Mohamad Zaher ZM, Suleiman AB. How public and private  
516    reforms dramatically improved access to dialysis therapy in Malaysia. *Health Aff*  
517    (Millwood). 2010;29(12):2214-2222.  
518
- 519   11. Wong HS, Goh BL (eds) 24<sup>th</sup> Report of the Malaysian Dialysis and Transplant Registry  
520    2016, Kuala Lumpur 2018, <https://www.msn.org.my/nrr/mdtr2016.jsp>  
521
- 522   12. Levey AS, Atkins R, Coresh J, Cohen EP, Collins AJ, Eckardt KU, et al. Chronic kidney  
523    disease as a global public health problem: approaches and initiatives - a position statement  
524    from Kidney Disease Improving Global Outcomes. *Kidney Int*. 2007;72(3):247-259.  
525
- 526   13. Bujang MA, Adnan TH, Hashim NH, Mohan K, Kim Liong A, Ahmad G, et al. Forecasting  
527    the incidence and prevalence of patients with end-stage renal disease in Malaysia up to the  
528    Year 2040. *Int J Nephrol*. 2017;2017:2735296.  
529
- 530

- 531 14. Surendra NK, Rizal AM, Hooi LS, Bavanandan S, Mohamad Nor FS, Shah Firdaus Khan  
532 S, Ong LM, et al. The cost of dialysis in Malaysia: hemodialysis and continuous ambulatory  
533 peritoneal dialysis. *Malaysian Journal of Public Health Medicine* 2018;18(Suppl 2): 70-81.  
534
- 535 15. Surendra NK, Rizal AM, Hooi LS, Bavanandan S, Mohamad Nor FS, Shah Firdaus Khan  
536 S, Ong LM, et al. Health related quality of life of dialysis patients in Malaysia:  
537 Hemodialysis versus continuous ambulatory peritoneal dialysis. *BMC Nephrol.* 2019;  
538 30;20(1):151.  
539
- 540 16. Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. *Methods for the*  
541 *Economic Evaluation of Health Care Programmes* (4<sup>rd</sup> ed). Oxford. New York: Oxford  
542 University Press: 2015.  
543
- 544 17. Villa G, Rodríguez-Carmona A, Fernández-Ortiz L, Cuervo J, Rebollo P, Otero A, et al.  
545 Cost analysis of the Spanish renal replacement therapy programme. *Nephrol Dial*  
546 *Transplant.*2011;0: 1–6.  
547
- 548 18. Marseille E, Larson B, Kazi D, Kahn J, Rosen S. WHO thresholds for the cost–  
549 effectiveness of interventions: alternative approaches. *Bull World Health Organ.*  
550 2015;93:118–124.  
551
- 552 19. International Monetary Fund.2017. Available from  
553 <https://www.imf.org/external/index.htm>  
554
- 555 20. Hooi LS, Lim TO, Goh A, Wong HS, Tan CC, Ahmad G, et al. Economic evaluation of  
556 centre hemodialysis and continuous ambulatory peritoneal dialysis in Ministry of Health  
557 hospitals, Malaysia. *Nephrology.* 2005;10:25-32.  
558
- 559 21. Karopadi AN, Mason G, Rettore E, Ronco C. Cost of peritoneal dialysis and hemodialysis  
560 across the world. *Nephrol Dial Transplant.* 2013;28(10):2553-69.  
561
- 562 22. Li PK, Chow KM. The cost barrier to peritoneal dialysis in the developing world--an Asian  
563 perspective. *Periton Dialysis Int.* 2001;21(3):S307-313.  
564
- 565 23. Liu FX, Quock TP, Burkart J, Noe LL, Inglese G. Economic evaluations of peritoneal  
566 dialysis and hemodialysis: 2004–2012. *F1000 Research.* 2013; 2 (273):1-13.  
567
- 568 24. Karopadi AN, Mason G, Rettore R, Ronco C. The role of economies of scale in the cost of  
569 dialysis across the world: a macroeconomic perspective. *Nephrol Dial Transplant.* 2014;  
570 29(4): 885–892.  
571
- 572 25. Chang YT, Hwang JS, Hung SY, Tsai MS, Wu JL, Sung JM, et al. Cost-effectiveness of  
573 hemodialysis and peritoneal dialysis: A national cohort study with 14 years follow-up and  
574 matched for comorbidities and propensity score. *Sci Rep.* 2016;21(8):669-677.  
575
- 576 26. Heaf JG, Wehberg S. Relative survival of peritoneal dialysis and hemodialysis patients:  
577 effect of cohort and mode of dialysis initiation. *PLoS ONE.* 2014;9(3):e90119.  
578
- 579

- 580 27. Kim H, Kim KH, Park K, Kang SW, Yoo TH, Ahn SV, et al. A population-based approach  
581 indicates an overall higher patient mortality with peritoneal dialysis compared to  
582 hemodialysis in Korea. *Kidney Int.* 2014;86(5):991-1000.  
583
- 584 28. Liem YS, Wong JB, Hunink MG, de Charro FT, Winkelmayer WC. Comparison of  
585 hemodialysis and peritoneal dialysis survival in The Netherlands. *Kidney Int*  
586 2007;71(Suppl 2):153–158.  
587
- 588 29. Yang F, Khin LW, Lau T, Chua HR, Vathsala A, Lee E, et al. Hemodialysis versus  
589 peritoneal dialysis: a comparison of survival outcomes in South-East Asian patients with  
590 end-stage renal disease. *PLoS ONE.* 2015;10(10):e0140195.  
591
- 592 30. Weinhandl ED, Foley RN, Gilbertson DT, Ameson T J, Snyder JJ, Collins AJ. Propensity-  
593 matched mortality comparison of incident hemodialysis and peritoneal dialysis patients. *J*  
594 *Am Soc Nephrol.* 2010;21:499-506.  
595
- 596 31. Briggs AH, Ades AE, Price MJ. Probabilistic sensitivity analysis for decision trees with  
597 multiple branches: use of the Dirichlet distribution in a Bayesian framework. *Med Decis*  
598 *Making.* 2003;23(4):341-50.  
599
- 600 32. Treharne C, Liu FX, Arici M, Crowe L, Farooqui U. Peritoneal dialysis and in-centre  
601 hemodialysis: a cost-utility analysis from a UK payer perspective.  
602 *Appl Health Econ Health Policy.* 2014;12:409–420.  
603
- 604 33. Howard K, Salkeld G, White S, McDonald S, Chadban S, Craig JC, et al. The cost-  
605 effectiveness of increasing kidney transplantation and home-based dialysis. *Nephrology*  
606 (Carlton, Vic). 2009;14(1): 123–132.  
607
- 608 34. Haller M, Gutjahr G, Kramar R, Harnoncourt F, Oberbauer, R. Cost-effectiveness analysis  
609 of renal replacement therapy in Austria. *Nephrol Dial Transplant.* 2011;26(9):2988–2995.  
610
- 611 35. Pikea E, Hamidia V, Ringerikea T, Wisloff T, Klempa M. More use of peritoneal dialysis  
612 gives significant savings: a systematic review and health economic decision model. *J Clin*  
613 *Med Res.* 2017;9(2):104-116.  
614
- 615 36. Afiatin Khoe LC, Kristin E, Masytoh LS, Herlinawaty E, Werayingyong P, Nadjib M, et  
616 al. Economic evaluation of policy options for dialysis in end-stage renal disease patients  
617 under the universal health coverage Indonesia. *PLoS ONE.* 2017;12(5), e0177436.  
618
- 619 37. Bavanandan S, Ahmad G, Teo AH, Chen L, Liu FX. Budget impact analysis of peritoneal  
620 dialysis versus conventional in-center hemodialysis in Malaysia. *Value Health Reg Issues.*  
621 2016;9:8-14.  
622
- 623 38. Chaudhary K, Sangha H, Khanna R. Peritoneal dialysis first: rationale. *Clin J Am Soc*  
624 *Nephrol.* 2011;6(2):447-456.  
625
- 626 39. Shafie AA, Lim YW, Chua GN, Hassali MA. Exploring the willingness to pay for a quality-  
627 adjusted life-year in the state of Penang, Malaysia. *Clinicoecon Outcomes Res.* 2014;6:  
628 473–481.  
629

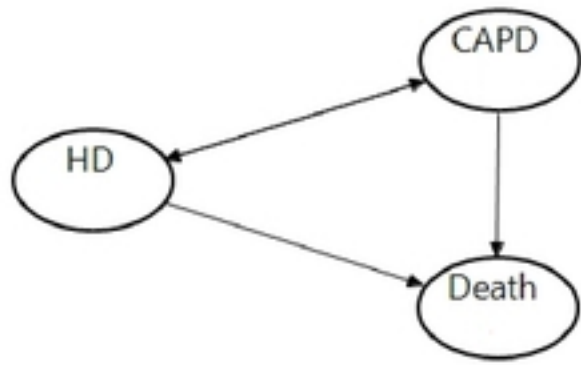
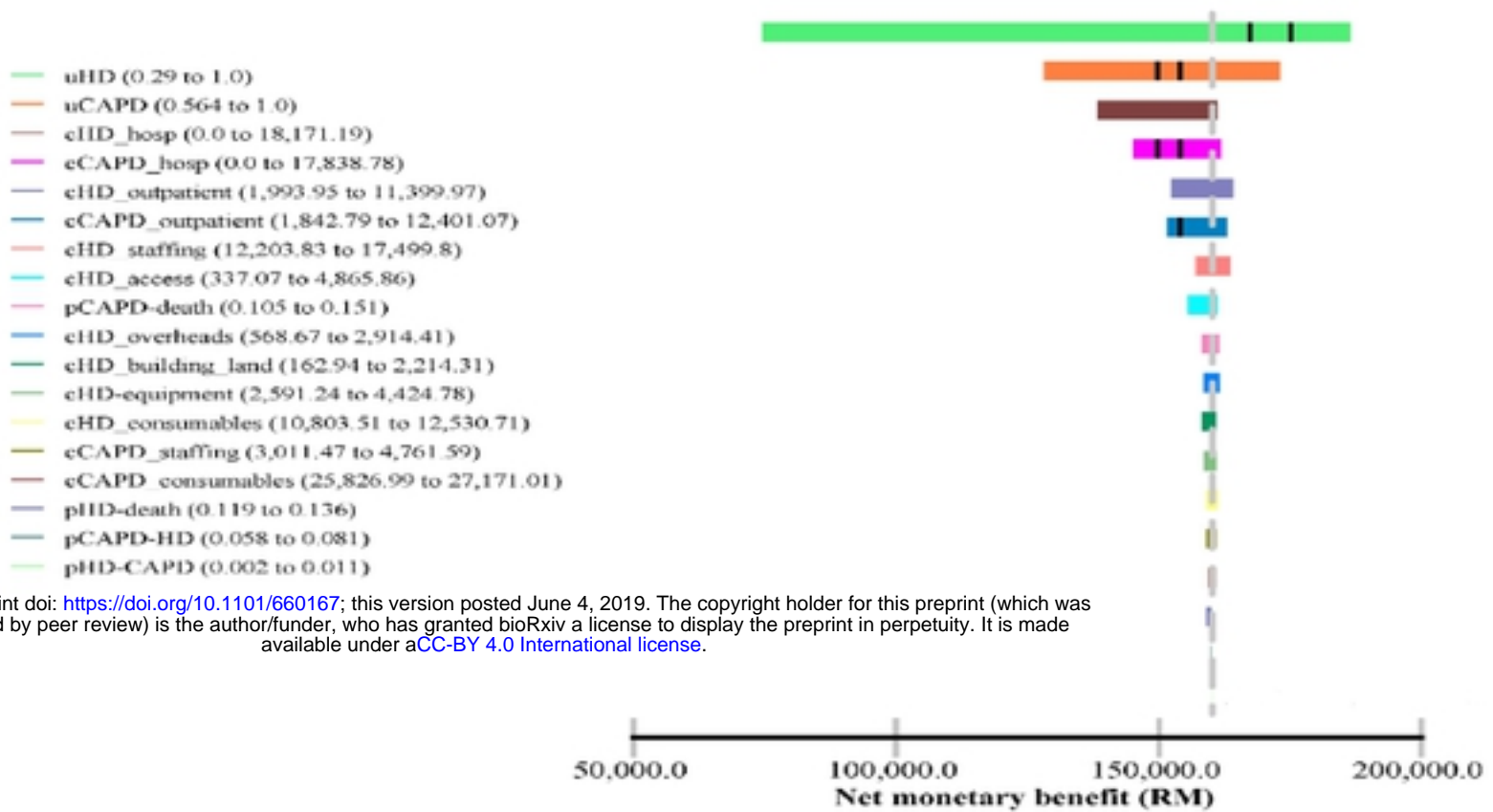


Figure 1: Markov model transition diagram





bioRxiv preprint doi: <https://doi.org/10.1101/660167>; this version posted June 4, 2019. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY 4.0 International license.

Figure 2: Tornado diagram (discounted)  
 \*Cost effectiveness threshold=RM120,000

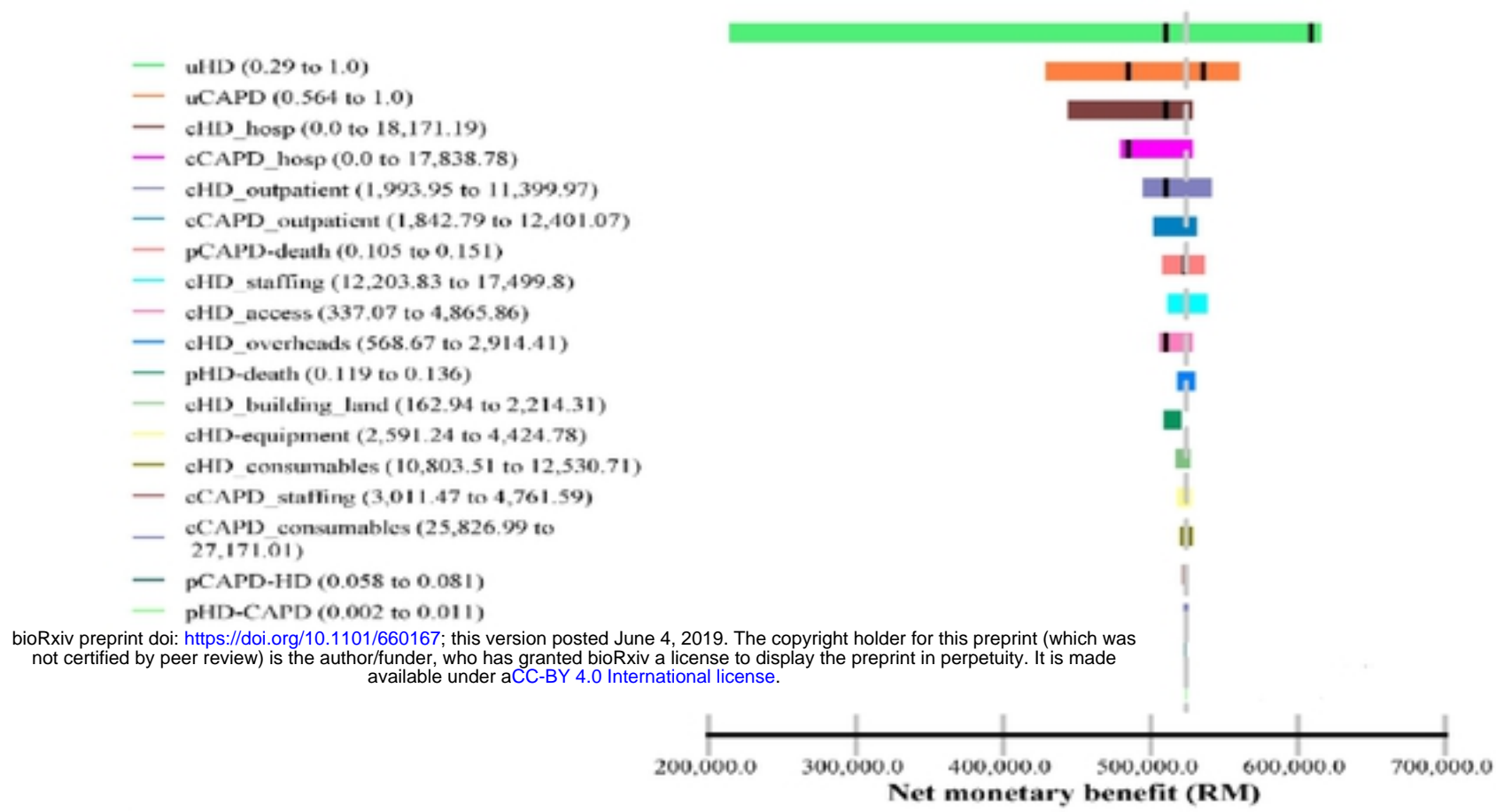


Figure 3: Tornado diagram (undiscounted)

\*Cost effectiveness threshold=RM120,000

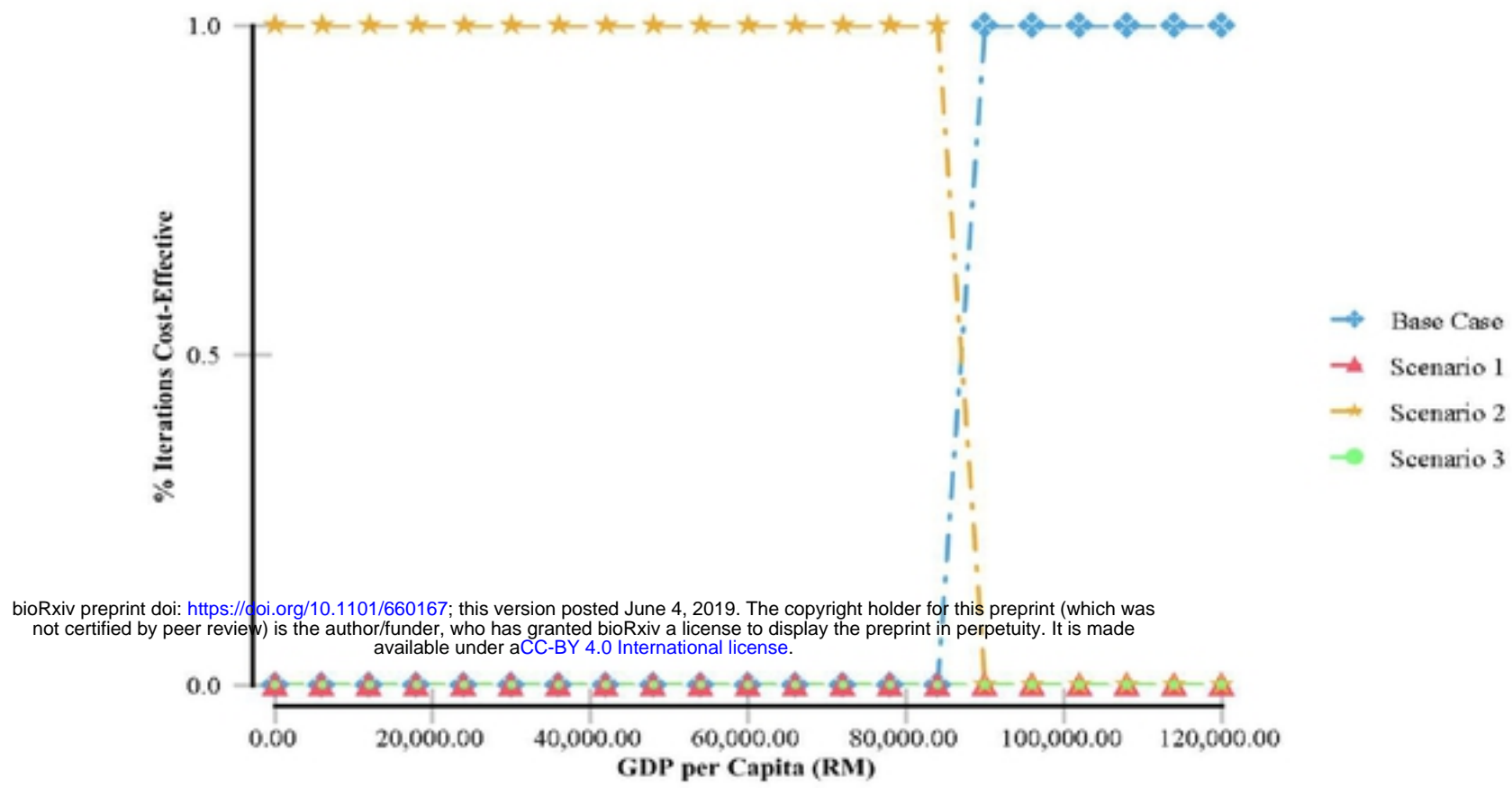


Figure 4: Cost effectiveness acceptability curve (discounted and undiscounted)