

1 **Full title**

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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:**

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

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38 **Abstract**

39

40 **OBJECTIVES**

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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 24th 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

| 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 |

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 31st 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 31st 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: $p = 1 - \exp(-r \cdot t)$
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 ^b | Value (Mean) | Range | Parameter distribution ^c |
|-------------------------|---|------------------|---------------------------|-------------------------------------|
| 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 | 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 | 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 | |

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

| 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 |

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

287 b=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 ^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 | |

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

| 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* |

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 24th 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.

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463

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480

481

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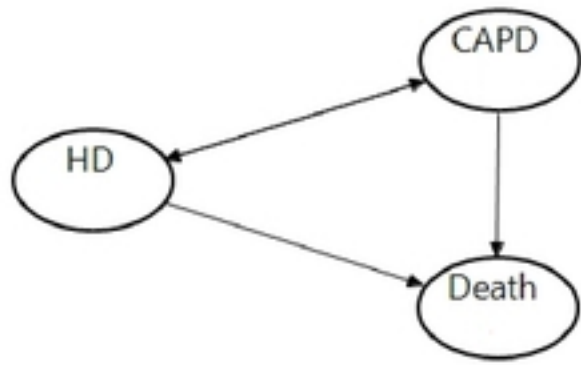
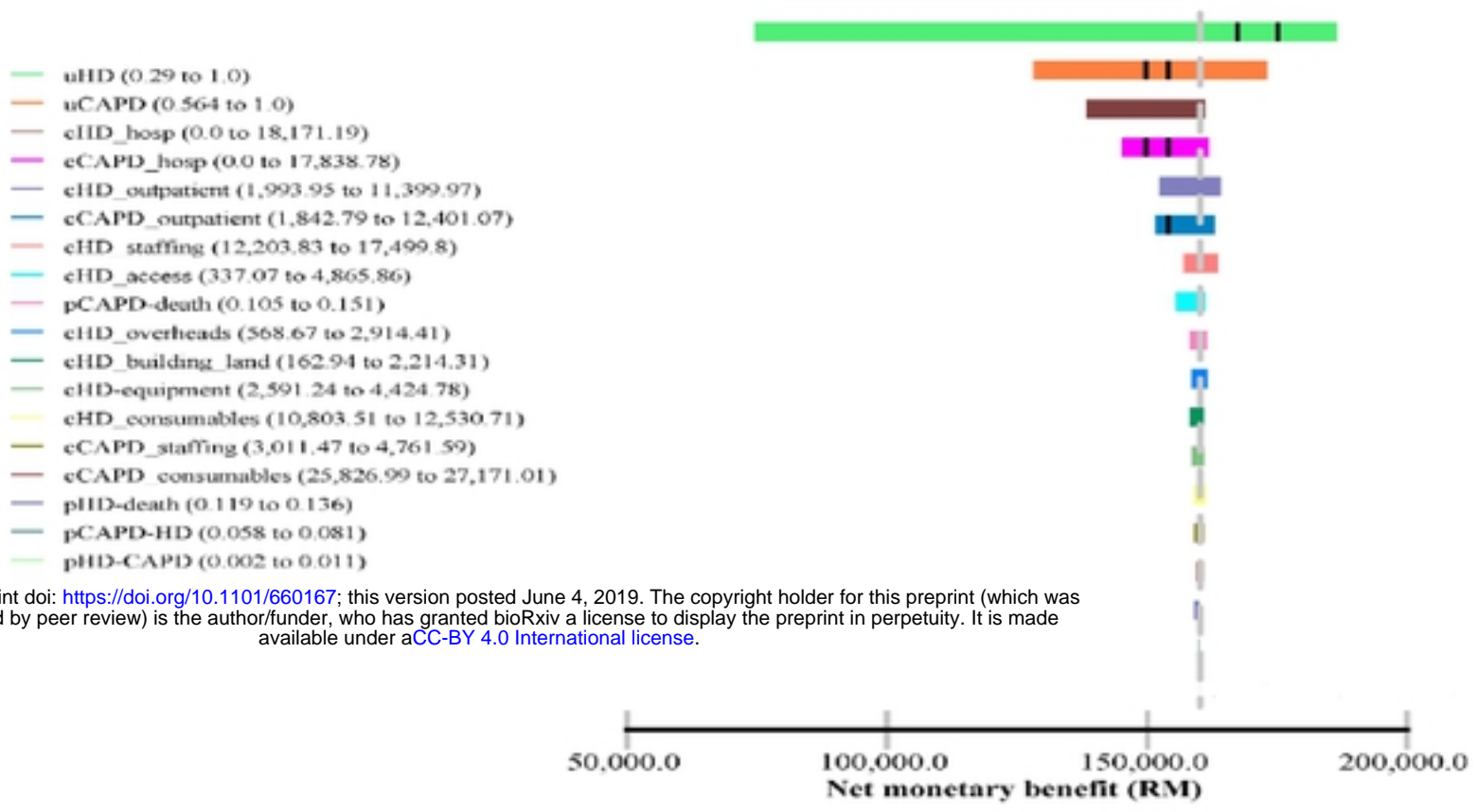


Figure 1: Markov model transition diagram



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

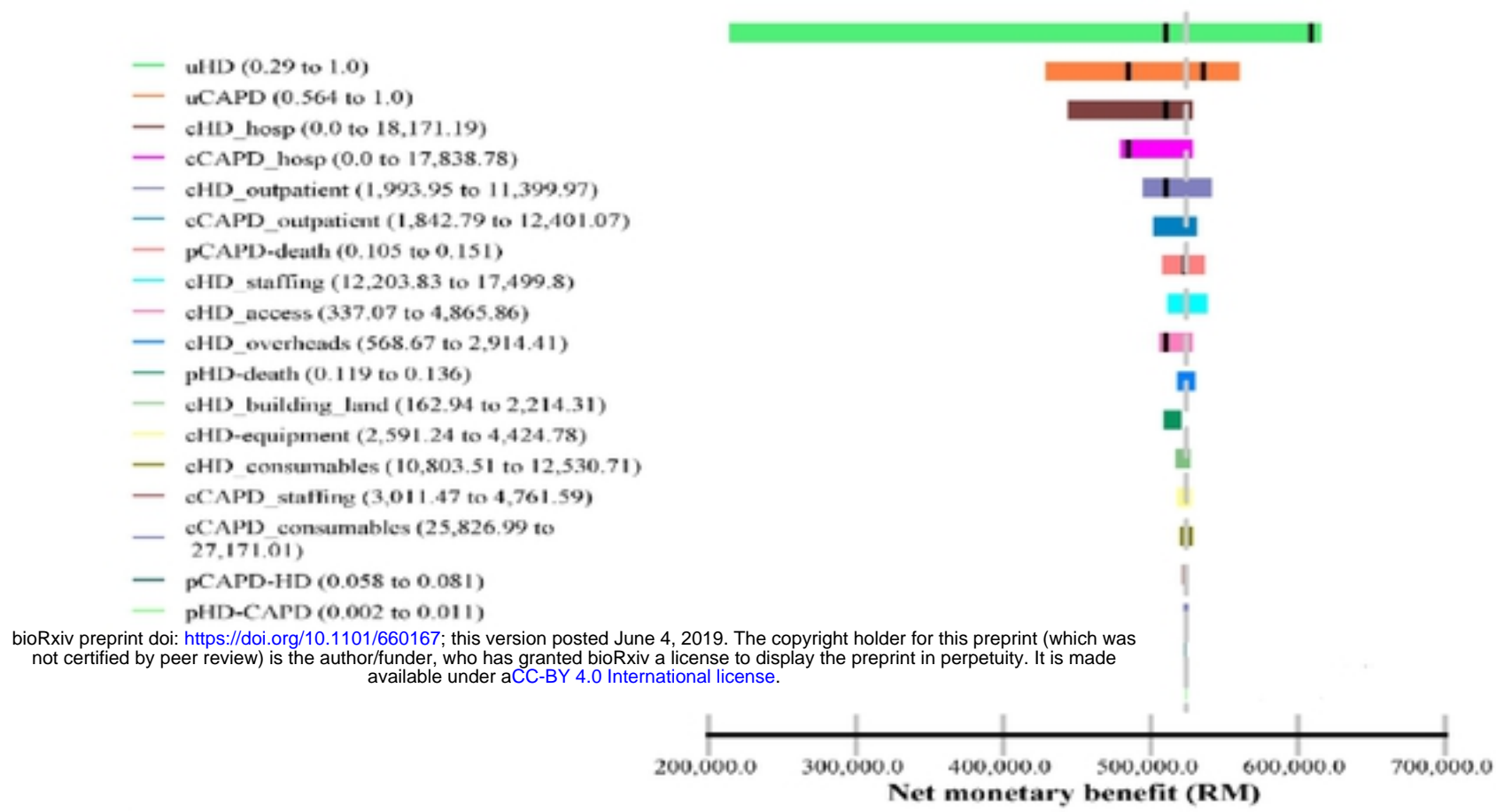


Figure 3: Tornado diagram (undiscounted)

*Cost effectiveness threshold=RM120,000

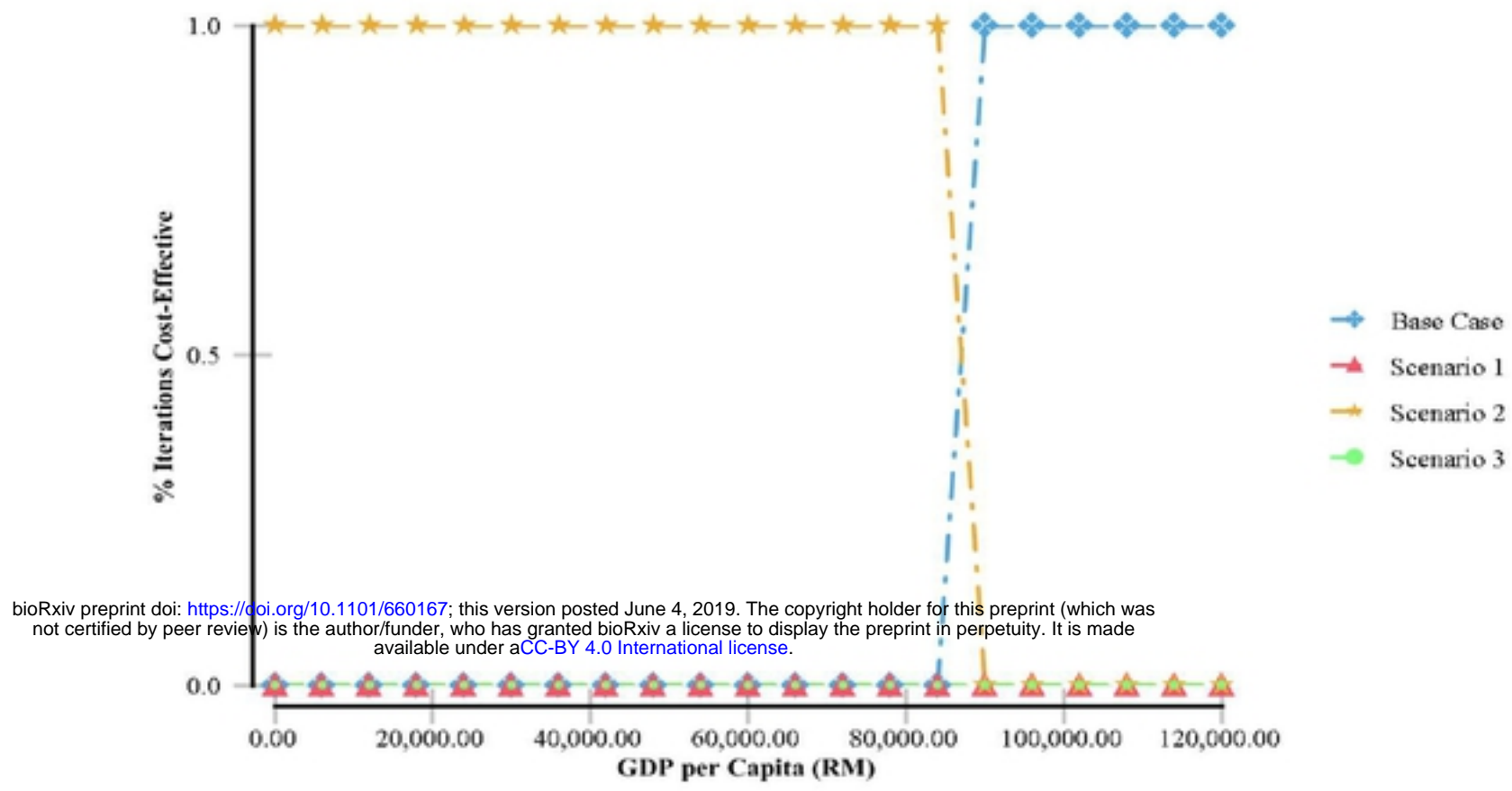


Figure 4: Cost effectiveness acceptability curve (discounted and undiscounted)