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## The effects of direct and indirect burden of care on the quality of life of end-stage renal disease (ESRD) patients and their caregivers: A mixed-method study protocol

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**ABSTRACT**

**Introduction:** The number of patients in Malaysia requiring dialysis is expected to rise substantially in the future due to aging population and rising prevalence of diabetes mellitus and hypertension. Hence, more individuals will be expected to adopt the caregiver role in the future. The upward trends of end-stage renal disease (ESRD) and caregiving for dialysis patients have imposed detrimental consequences on both the patients and their caregivers in terms of their psychological well-being and quality of life. Despite the current circumstances, there remains a dearth of study in Malaysia exploring the psychosocial factors specifically on the economic impacts of ESRD management.

**Methods and analysis:** This two-phase sequential explanatory mixed method design, incorporating a quantitative design in Phase 1 and a qualitative study in Phase 2, will be conducted in four governmental hospitals along with 10 other non-governmental organisations or private dialysis centres within the Klang Valley vicinity. Phase 1 consists of a cross-sectional survey in three main sections: demographic details, economic assessment, and psychological assessment will be conducted among 236 pairs of patient-caregiver dyad. 30 participants will be recruited in Phase 2 to undergo a focus group discussion. Participants will be recruited through referral from nephrologists or nurses in the nephrology unit. Descriptive statistics, Pearson correlation, one-way ANOVA and multiple regression analyses will be utilised for data analysis in Phase 1. Thematic analysis with open and axial coding will be employed in Phase 2 to determine the codes and themes elicited from the focus group discussion.

**Ethics and dissemination:** The National Medical Research and Ethics Committee (MREC) and the research ethics committee of Tuanku Muhriz UKM Chancellor's Hospital (HTCM) and University of Malaya Medical Centre (UMMC) have approved the proposed study. Findings will be published in peer-reviewed scientific journals and presented in national or international conferences with minimal anonymised data.

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3 51 **ARTICLE SUMMARY**  
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6 52 **Strengths and limitations of this study**  
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- 8  
9 53 ● This study will be the first in Malaysia to utilise the sequential mixed method approach for  
10 54 examining the psychosocial factors and quality of life of both haemodialysis and peritoneal  
11 55 dialysis patients and their caregivers.  
12  
13 56 ● The inclusion of both patients and caregivers in the study will serve to provide more  
14 57 comprehensive and holistic perspectives, regarding the management of ESRD in Malaysia.  
15 58 ● This research will scrutinise the financial and economic burden, as well as the  
16 59 complications involved in the management of ESRD, to provide a comprehensive finding  
17 60 on their impact on the quality of life of the participants.  
18  
19 61 ● The study is restricted to within the Klang Valley vicinity; hence, the findings obtained  
20 62 may not apply to ESRD patients and caregivers located in other Malaysian states.  
21  
22 63 ● The restricted dissemination of paper-and-pen or web-based questionnaires to within a  
23 64 population of participants who are able to communicate or read in the Malay language,  
24 65 may lead to the omission of unique perspectives from the non-Malay literate population.  
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29 67 *Keywords:* Burden of care, quality of life, end-stage renal disease (ERSD), patient, caregiver  
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## 68 INTRODUCTION

69 According to the Global Burden of Disease, chronic kidney disease (CKD) is ranked  
70 among the top 20 causes of death, and is currently a significant public health concern.[1] CKD  
71 is regarded as a high-stress illness due to the chronicity of the disease, as well as the long-term  
72 treatment required,[1] where end-stage renal disease (ESRD) is considered the last stages of  
73 CKD.[2] In Malaysia, the incidence and prevalence of patients with ESRD have been on an  
74 upward trend for the past 20 years.[3] The number of Malaysians with CKD is projected to  
75 significantly increase in the future, due to the ageing population and the increasing prevalence  
76 of diabetes mellitus (DM) and hypertension. It has been established that CKD is profoundly  
77 associated to DM and hypertension.[2] In 2018, the 24th Report of the Malaysia Dialysis and  
78 Transplant Registry revealed that over the preceding 10 years, the acceptance rates for both  
79 haemodialysis (HD) and peritoneal dialysis (PD) have nearly doubled, while the prevalence  
80 rate has increased by more than two-fold. A total of 39,711 patients received dialysis treatment  
81 in 2016, with 35,781 and 3930 patients on HD and PD respectively. Meanwhile, the prevalence  
82 rate of HD and PD stood at 1159 per million population, and 127 per million population  
83 respectively.[4] If the present trend remains unchecked, it can be anticipated that by 2040, there  
84 will be more than 106,000 Malaysian ESRD patients requiring dialysis. With this projected  
85 prevalence, the cost, with regards to the health care system, is estimated to be RM 3.21  
86 billion.[3]

87 It is to be expected that with the rising number of renal failure patients,[5] more  
88 individuals will adopt the caregiver role in the future. The caregiver of a patient refers to those  
89 who are actively involved in helping patients cope and manage their chronic illness during the  
90 course of their treatment.[6] The incidence and prevalence of ESRD give rise to negative  
91 effects on the psychological well-being of both ESRD patients and their caregivers,[7-11] as  
92 well as their quality of life.[12,13] In comparison to their caregivers, ESRD patients are more

## Direct and Indirect Burden of Care of ESRD Patients and Caregivers

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2  
3 93 prone to depression, and a lower quality of physical and psychological well-being.[10]  
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5 94 According to Goh and Griva,[9] the prevalence of depression among ESRD patients was  
6  
7 95 estimated to be around 20% to 30%, whereas their anxiety ranged between 12% and 52%. The  
8  
9  
10 96 contributing factors toward the lower quality of life among dialysis patients have been  
11  
12 97 identified as the increasing prevalence of depression, anxiety, and suicidal ideation.[14] On the  
13  
14 98 other hand, caregivers for patients (especially those under dialysis treatment) are subjected to  
15  
16 99 a great workload, as they shoulder most of the responsibilities.[7] Caring for ESRD patients  
17  
18 100 often involve great physical, emotional, and economic demands.[15] It has been established  
19  
20 101 that compared to individuals who are not caregivers, caregivers of chronic patients are four  
21  
22 102 times more likely to be diagnosed with depression, and three times more likely to seek help for  
23  
24 103 anxiety issues.[16] Also, caregivers for dialysis patients are reported to have a lower quality of  
25  
26 104 life, compared to caregivers for non-dialysis patients.[13]

31 105 Despite the current situation, there remains a dearth of research on the psychosocial  
32  
33 106 factors and the economic impact of ESRD on the patients and caregivers in Malaysia. Studies  
34  
35 107 focusing on the well-being of Malaysia's ESRD patients are sorely lacking, and in the case of  
36  
37 108 caregivers, almost non-existent. Therefore, there is a need for further investigations in this area,  
38  
39 109 particularly with regards to the patients' and caregivers' quality of life, the care burden, as well  
40  
41 110 as issues related to depression, anxiety, the coping mechanism, and social support. Another  
42  
43 111 neglected area has to do with the financial and economic sustainability required by ESRD  
44  
45 112 patients and caregivers, with regards to the management of the disease. To the best of our  
46  
47 113 knowledge, thus far, no studies have been conducted in the Southeast Asian region on the  
48  
49 114 economic costs incurred by ESRD patients and their caregivers. In view of this situation, this  
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51 115 study delves into the impact of the psychosocial factors and burden of care on the quality of  
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53 116 life of ESRD patients and their caregivers.  
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## 118 **Study Objectives**

119 Phase 1 of this study focuses on the following objectives:

- 120 1. To investigate the relationship between psychosocial factors (depression, anxiety,  
121 coping strategies, social support, care burden, economic burden) and quality of life,  
122 with regards to caregivers and patients with ESRD.
- 123 2. To compare the psychosocial factors and quality of life between haemodialysis patients  
124 and their caregivers with peritoneal dialysis patients and their caregivers.
- 125 3. To determine the predictors (demographic, psychosocial and socioeconomic factors),  
126 that can lead to quality-of-life improvement among caregivers and patients with ESRD.

127 Phase 2 of this study focuses on the following objective:

- 128 1. To explore the perceptions of ESRD patients and their caregivers, with regards to the  
129 impact of the economic burden they have to endure, on their quality of life.

## 130 **METHODS AND ANALYSIS**

### 131 **Design and methods**

132 Phase 1 of this undertaking involves the use of a sequential explanatory mixed methods  
133 design with quantitative data collection, while Phase 2 involves a qualitative study.[17] In  
134 Phase 1, the researchers will conduct a cross-sectional survey study among ESRD patients and  
135 their caregivers. A cross-sectional approach is preferred, as this approach is time-saving, in  
136 terms of questionnaire distribution and information collection from a sizeable number of  
137 participants.[18] Meanwhile in Phase 2, a qualitative study involving focus group discussions  
138 will be conducted among the ESRD patients and their caregivers. The focus group discussion  
139 approach can give rise to a fruitful and in-depth understanding of an individual's experiences  
140 and perceptions towards a certain phenomenon.[19] Furthermore, in comparison to individual  
141 interviews with participants, focus groups have the tendency to provide more ideas and



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3 142 information.[20] Focus group discussions allow participants to consider and share their  
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5 143 perspectives regarding the economic burden they take on when it comes to ESRD management,  
6  
7 144 as well as the impact of this illness on their quality of life. For this undertaking, a sequential  
8  
9 145 explanatory design is used to substantiate the findings from the quantitative study by providing  
10  
11 146 supporting evidence from the qualitative study findings.[21] The data findings from the  
12  
13 147 quantitative and qualitative studies will be integrated to provide a holistic insight into the  
14  
15 148 psychosocial factors and quality of life experienced by ESRD patients and their caregivers  
16  
17 149 undergoing different treatment modalities.

### 150 **Study setting**

151 The investigation will be conducted in the nephrology unit of the Tuanku Muhriz UKM  
152 Chancellor's Hospital (HTCM), Selayang Hospital (HSEL), Kuala Lumpur Hospital (HKL),  
153 and the University of Malaya Medical Centre (UMMC), along with ten other non-governmental  
154 organisation (NGO) or private dialysis centres in the Klang Valley.

### 155 **Patient and public involvement**

156 One patient, one caregiver, one health psychologist, and two formal care providers  
157 (namely a nephrologist and a dialysis nurse) will be recruited to form the advisory committee.  
158 This committee will be tasked with reviewing the protocol, as well as structuring the interview  
159 schedule and questionnaire to provide the design for the study. During the course of this  
160 undertaking, the advisory committee will also be referred to for advice and feedback, whenever  
161 necessary.

### 162 **Participants and recruitment**

163 Participating ESRD patients will be recruited through referrals from nephrologists, or  
164 nurses in the nephrology units, while the caregivers will be recruited through referrals from the  
165 ESRD patients themselves. This sampling method will ensure that data accumulation from the

166 participants is effective, efficient, and cost-effective.[22] ESRD-diagnosed patients, eligible  
167 for participation in this study, need to be above 18 years of age, and currently receiving  
168 treatment in a hospital, an NGO establishment, or a private dialysis centre in the Klang Valley.  
169 It is also essential that the participants are able to communicate and read in Bahasa Malaysia,  
170 the national language of Malaysia. Patients exhibiting severe mental illness, or those who have  
171 undergone a kidney transplant, will be excluded from the study. As for the recruitment of  
172 caregivers, it is essential that they be above 18 years of age, and are verified as the family  
173 caregiver of an ESRD patient currently undergoing dialysis treatment in a hospital, an NGO  
174 establishment, or a private dialysis centre in the Klang Valley. It is also required that the  
175 caregiver has undergone the experience of accompanying the ESRD patient for dialysis  
176 treatment at least once, and is able to read as well as communicate in Bahasa Malaysia. Formal  
177 caregivers, caregivers of patients who have undergone a kidney transplant, or caregivers of  
178 patients exhibiting severe mental illness symptoms, will be excluded from the study.

### 179 **Sample size**

#### 180 *Phase 1: Quantitative study*

181 The calculation for the proposed quantitative study sample size is based on the multiple  
182 linear regression formula by Tabachnick and Fidell,[23] which is expressed as  $N > 50 + 8m$ ,  
183 where  $m$  is the number of predictors. Based on this formula, the recommended number of  
184 participants is 98 pairs of patients and caregivers. Taking into consideration the drop-out rate,  
185 unresponsive surveys, and incomplete submission of data by participants, the sample size for  
186 this undertaking will be increased by 20%.[24,25] Consequently, 118 pairs of haemodialysis  
187 patients-caregivers and 118 pairs of peritoneal dialysis patients-caregivers ( $N=236$  pairs) will  
188 be recruited for the quantitative study.

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3 190 *Phase 2: Qualitative study*  
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5 191 For the qualitative study, the researchers will conduct six focus group discussions, with  
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7  
8 192 each group comprising five participants.[26-28] Hence, 30 participants (15 patients and 15  
9  
10 193 caregivers) will be involved in the focus group discussion, or until data saturation is deemed  
11  
12 194 achieved. This process is typical for qualitative studies, whereby the emphasis is on the arrival  
13  
14 195 at saturation point. The saturation point is arrived at when no new information, ideas or themes  
15  
16 196 are forthcoming from the participants.[29]  
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20 197 **Instruments**  
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23 198 *Phase 1: Quantitative study*  
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25 199 The web-based or paper-based questionnaire to be distributed to the participants  
26  
27 200 consists of three sections: demographic sheet, economic assessment and psychological  
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29 201 assessment. The demographic information of ESRD patients and caregivers, which will be  
30  
31 202 collected through the questionnaire, covering age, gender, race, religion, marital status,  
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33 203 education level, occupation, monthly household income, relationship with patient/caregiver,  
34  
35 204 CKD staging, method of dialysis, duration of dialysis, frequency of dialysis, frequency of  
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37 205 hospital follow-up, frequency of hospitalisation, and duration of care extended by caregivers.  
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39 206 Economic assessment, the second section of the questionnaire, covers the participants' source  
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41 207 of funding, direct monthly cost, indirect weekly cost (time), and perceived economic/ financial  
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43 208 burden.  
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48 209 Psychological assessment, the final section of the questionnaire, consists of six scales.  
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50 210 However, the coping strategy scale and the burden of care scale differs between patients and  
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52 211 caregivers. The coping behaviour among the ESRD patients will be evaluated by the Malay  
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54 212 version of Brief Coping Orientation to Problems Experienced (Brief-COPE) inventory. The  
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56 213 inventory comprises 28 items with 14 dimensions: self-distraction, active coping, denial,  
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58 214 substance use, use of emotional support, use of instrumental support, behavioural  
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3 215 disengagement, venting, positive reframing, planning, humour, acceptance, religion, and self-  
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5 216 blame.[30] The Malay version of Brief-COPE, validated through Malaysian breast cancer  
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7 217 women patients, is reported to have good internal consistency ( $\alpha=.51$  to  $.99$ ).[31] Meanwhile,  
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9 218 the Caregiver Cope (Cg Cope) questionnaire, developed by Ibrahim and colleagues [32] will  
10  
11 219 be used to assess the coping strategies employed by caregivers of ESRD patients. This  
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13 220 questionnaire consists of 19 items with six domains of coping strategies. Namely, these  
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15 221 domains are distraction, caring for patient, venting, religion, recreation, and social support.  
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17 222 Participants will rate based on the 5-point Likert scale (1 = I have never done this, 5 = I do this  
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19 223 very frequently). The validation study conducted among caregivers of schizophrenia patients  
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21 224 in Malaysia yielded Cronbach's alpha values ranging between  $.54$  and  $.82$ .[32]

22 225 In order to assess their perception of the care burden on their caregivers, the Self-  
23  
24 226 Perceived Burden Scale (SPBS) will be distributed to the ESRD.[33] The SPBS, which consists  
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26 227 of 10-items, is rated by way of a 5-point Likert scale (1 = Not at all, 5 = All of the time). The  
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28 228 Malay translated 10-item SPBS utilised in Ting et al.'s study[34] revealed this scale to be valid  
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30 229 and reliable for urology cancer patients ( $\alpha=.99$ ). As for the caregiver burden, this will be  
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32 230 examined by the 22-item Zarit Burden Interview (ZBI).[35] Participants will rate their burden  
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34 231 on a 5-point Likert scale (0 = Rarely, 4 = Nearly always). In Malaysia, the Malay version of  
35  
36 232 ZBI (MZBI) was validated through family caregivers to cancer patients, with the scale  
37  
38 233 delivering a high internal consistency ( $\alpha=.89$ ).[36]

39 234 The 19-item Medical Outcome Study (MOS) Social Support Survey developed by  
40  
41 235 Sherbourne and Stewart[37] will be used to examine the participants' perception of social  
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43 236 support. This brief, multidimensional, self-administered scale, rated with the use of a 5-point  
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45 237 Likert scale (1 = None at all, 5 = Available at all times), measures four categories of social  
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47 238 support: informational, instrumental, positive social interactions, and affectionate support. In  
48  
49 239 Malaysia, the Malay version of the MOS Social Support survey was validated through a sample  
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240 of HIV patients. This Malay version of the survey portrayed good psychometric properties,  
241 with high Cronbach's alpha for all the subscales ( $\alpha > .87$ ) and for the overall scale ( $\alpha = .96$ ).[38]

242 The General Anxiety Disorder-7 (GAD-7), a screening tool and severity indicator  
243 developed by Spitzer et al,[39] will be used to assess the generalised anxiety disorder among  
244 the participants. The scale contains 7 items, and is rated with the use of the 4-point Likert scale  
245 (0 = Not at all, 3 = Nearly every day). The Malay version of GAD-7, validated through female  
246 patients in a government-funded primary care clinic, delivered good internal consistency  
247 reliability ( $\alpha = .74$ ).[40] The participants' severity of depression will be assessed through the  
248 Patient Health Questionnaire-9 (PHQ-9).[41] The PHQ-9 consists of 9 items and is rated using  
249 the 4-point Likert scale (0 = Not at all, 3 = Nearly every day). In Malaysia, the questionnaire  
250 was validated through female patients in a primary care clinic, and the Malay version of PHQ-9  
251 showed good internal reliability ( $\alpha = .70$ ).[42]

252 The 36-item Short Form Survey (SF-36) will be utilised to assess the health-related  
253 quality of life of the participants. The SF-36 consists of eight subscales, measuring different  
254 domains of health-related quality of life. Namely, these subscales are physical functioning (PF),  
255 role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning  
256 (SF), role-emotional (RE), and mental health (MH). Also, two component scores are derived  
257 from the eight subscales. These are the physical component summary (PCS), which consists of  
258 PF, RP, BP, and GH, as well as the mental component summary (MCS), which consists of VT,  
259 SF, RE, and MH.[43] The Malay version of SF-36, validated through post-coronary artery  
260 bypass grafting surgery (CABG) patients, delivered good internal consistency reliability, with  
261 Cronbach's alpha values ranging from .73 to .90 for the subscales.[44]

## 262 *Phase 2: Qualitative study*

263 A focus group discussion schedule will be developed, based on a literature review and  
264 expert input by nephrologists in the research team. The questions for the focus group discussion

265 will be tailored to elicit responses from ESRD patients and caregivers regarding the economic  
266 burden they shoulder and its effect on their quality of life. The focus group discussion will be  
267 divided into six sections: demographic details, source of ESRD treatment funding, direct costs  
268 of ESRD management, indirect costs of ESRD management, economic burden experienced by  
269 them, and lastly, their perception of quality of life.

## 270 **Data collection**

### 271 *Phase I: Quantitative study*

272 Conventional paper-and-pencil/web-based questionnaires will be utilised. Potential  
273 participants, identified through referrals from nephrologists or nurses in the nephrology units,  
274 will be approached for recruitment during their dialysis treatments in the respective  
275 hospital/dialysis centre. Potential caregiver participants can be approached while they are  
276 waiting for their patients' treatment to be completed. For the caregivers who are not present  
277 during the patients' treatment, the researchers will call them up, or meet up with them during  
278 the patients' next treatment in the respective hospitals/dialysis centres. The recruitment process  
279 progresses with the researcher briefing the caregiver and patient on the aims and procedures of  
280 the study. Potential participants who respond in the affirmative, with regards to whether he/she  
281 has been previously diagnosed with severe mental illness, will be excluded from the study.  
282 Potential participants will be given ample time to consider their involvement in the study. Upon  
283 receiving their consent, the participants will be provided with a questionnaire, which can be  
284 filled out in approximately 30 minutes. The researchers will entertain any questions the  
285 participants may have regarding the questionnaire. The completed questionnaires will be kept  
286 securely for the data analysis process. Subject withdrawal criteria include a whereby the  
287 participant voluntarily withdraws his/her consent to participate in the study, or when the  
288 principal investigator, for any reason, ends the participation. Participants are free to withdraw  
289 from the study at any time by stating their intention during the course of the survey, or by

290 emailing the principal investigator, whose email address and telephone number are included in  
291 the informed consent form. As the sample size calculation takes into consideration the  
292 participant drop-out rate, participants who withdraw from the study will not be replaced.

### 293 *Phase 2: Qualitative study*

294 Potential participants will be approached either during their hospital/dialysis centre  
295 visitation or at an appointed time most convenient to them. The researchers will provide the  
296 caregivers and patients a briefing on the aims and procedures of the study. Potential participants  
297 who respond in the affirmative with regards to whether he/she has been previously diagnosed  
298 with severe mental illness will be excluded from the study. Participants will be given sufficient  
299 time to consider their participation in the focus group discussion. The discussion will be held  
300 at a designated date, time, and venue decided by the researchers and the discussion is  
301 anticipated to go on for an hour. The discussions will be recorded and data will be transcribed  
302 verbatim, after which the recording will be deleted, in keeping with established ethical  
303 standards. Subject withdrawal criteria include a situation whereby the participant voluntarily  
304 withdraws his/her consent to participate in this study, or when the principal investigator, for  
305 any reason, ends the participation. Participants are free to withdraw from the study at any time  
306 by stating their intention during the course of the survey or by emailing the principal  
307 investigator, whose email address and telephone number are included in the informed consent  
308 form. The arrival at data saturation point is not affected by the withdrawal of a participant(s)  
309 who will not be replaced.

### 310 **Data analysis**

#### 311 *Phase 1: Quantitative study*

312 IBM Statistical Package for the Social Sciences (SPSS) software for Windows, version  
313 23 [45] will be used to process the data. Descriptive statistics, Pearson correlation, ANOVA

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3 314 and multiple regression analysis will be utilised for data analysis. Statistical significance will  
4  
5 315 be set at .05. Descriptive statistics will be used to analyse and summarise the respondents' data  
6  
7 316 while Pearson correlations will be used to investigate the relationship between psychosocial  
8  
9 317 factors (depression, anxiety, coping strategies, social support, care burden, and economic  
10  
11 318 burden) and quality of life of the participants. ANOVA will be conducted to compare the  
12  
13 319 psychosocial factors and quality of life between haemodialysis patients and their caregivers  
14  
15 320 and peritoneal dialysis patients and their caregivers. And lastly, multiple linear regression  
16  
17 321 analysis will be utilised to examine the predictors (demographic, psychosocial factors and  
18  
19 322 socioeconomic) which can lead to an improvement in the participants' quality of life.  
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### 24 323 *Phase 2: Qualitative study*

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27 324 Thematic analysis will be conducted with the use of NVivo software for Windows  
28  
29 325 version 11 (update 4).[46] Open and axial coding will be utilised in the thematic analysis, to  
30  
31 326 determine the codes and themes from the focus group discussion. This will serve to facilitate  
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33 327 an in-depth examination of the perception of the economic burden faced by the participants in  
34  
35 328 the management of ESRD and its impact on their quality of life.  
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## 39 329 **ETHICS AND DISSEMINATION**

### 40 41 42 330 **Ethical considerations**

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45 331 The researchers will adhere to the principles of the Declaration of Helsinki [47] and the  
46  
47 332 Malaysian Good Clinical Practice Guidelines.[48] During the data collection process, the  
48  
49 333 privacy of the participants is protected through the separation of the informed consent forms  
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51 334 from the questionnaire responses. All documents will be deposited in a secured cabinet and all  
52  
53 335 data will be stored in a password protected computer to which only the researchers have access.  
54  
55 336 All documents and data will be stored for a period of seven years, after which they will be  
56  
57 337 shredded and deleted. No participant identifiers (name, identity card number, address, phone  
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3 338 number, etc) will be traceable and a unique study ID will be assigned. No medical records will  
4  
5 339 be accessible. Participants will have no access to any personal information, and to ensure the  
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7 340 element of anonymity, they will not be informed of the study findings.  
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#### 10 341 **Dissemination**

11  
12 342 The findings from this study will be published in peer-review scientific journals and at  
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14 343 national or international conferences. Minimal anonymised data uploaded as supplementary  
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16 344 material for review purposes in scientific journal publications or conferences will adhere  
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18 345 strictly to the ethical principles stipulated. Only group data will be published and no personal  
19  
20 346 identifier will be collected or made public. Relevant permissions from all parties involved will  
21  
22 347 be obtained prior to any publication. The findings from this study can serve as a guide for  
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24 348 Malaysian policymakers, health care providers and society during their efforts to improve the  
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26 349 quality of life of caregivers and ESRD patients through the engagement of effective and holistic  
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28 350 interventions.  
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#### 33 351 **Author contributions**

34 352 All authors were involved in writing the study protocol. SYC and NI drafted the manuscript.  
35  
36 353 CSS, NA, RI and AHAG provided critical revision and feedback of the manuscript. All authors  
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38 354 have read and approved the final manuscript.  
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48 358 and analysis, decision to publish, or preparation of the manuscript.  
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#### 53 359 **Competing interest**

54 360 The authors declared that there is no conflict of interest.  
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3 362 **Ethics approval**  
4

5 363 The work has been approved by the Medical Research and Ethics Committee (MREC)  
6 [NMRR-21-1012-59714] and the research ethics committee of Tuanku Muhriz UKM  
7 364 Chancellor's Hospital (HTCM) [UKM PPI/111/8/JEP-2021-078] and the University of Malaya  
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10 367 (HKL) have been obtained.  
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25 371 **Data sharing statement**  
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27 372 Not required as this study is a study protocol.  
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For peer review only



# BMJ Open

## The effects of direct and indirect burden of care on the quality of life of patients with end-stage renal disease and their caregivers in the Klang Valley, Malaysia: Protocol for a mixed-methods study

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11 4 with end-stage renal disease and their caregivers in the Klang Valley, Malaysia:  
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13 5 Protocol for a mixed-methods study  
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18 7 Norhayati Ibrahim<sup>1,2</sup>, Sin Yee Chu<sup>1\*</sup>, Ching Sin Siau<sup>3</sup>, Noh Amit<sup>3</sup>, Rozmi Ismail<sup>4</sup>, Abdul Halim  
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**ABSTRACT**

**Introduction:** The number of patients in Malaysia requiring dialysis is expected to rise substantially in the future due to the ageing population and increasing prevalence of diabetes mellitus and hypertension. Hence, more individuals will be expected to adopt the caregiver role in the future. The upward trends of end-stage renal disease (ESRD) and caregiving for dialysis patients have detrimental consequences on both the patients and their caregivers regarding their psychological well-being and quality of life. Despite the current circumstances, there remains a dearth of study in Malaysia exploring the psychosocial factors, specifically on the economic impacts of ESRD management.

**Methods and analysis:** This two-phase sequential explanatory mixed-methods design, incorporating a quantitative design in Phase 1 and a qualitative study in Phase 2, will be conducted in four governmental hospitals along with ten other non-governmental organisations or private dialysis centres within the Klang Valley vicinity. Phase 1 consists of cross-sectional survey that will be conducted among 236 pairs of the patient-caregiver dyad. 30 participants will be recruited in Phase 2 to undergo focus group discussion. Participants will be recruited purposively through inclusion and exclusion criteria. Descriptive statistics, Pearson correlation, ANOVA, and regression analyses will be utilised for data analysis in Phase 1, whereas thematic analysis with open and axial coding will be employed in Phase 2.

**Ethics and dissemination:** The National Medical Research and Ethics Committee (MREC) [NMRR-21-1012-59714] and the research ethics committee of Tuanku Muhriz UKM Chancellor's Hospital (HTCM) [UKM PPI/111/8/JEP-2021-078] and University of Malaya Medical Centre (UMMC) [MREC ID NO: 202178-10346] have approved the proposed study. Participants informed consent in both studies will be obtained beforehand, and no personal identifiers will be obtained from the participants to protect their anonymity. Findings will be

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3 50 published in peer-reviewed scientific journals and presented in national or international  
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5 51 conferences with minimal anonymised data.  
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9 52 **ARTICLE SUMMARY**

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12 53 **Strengths and limitations of this study**

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14 54 ● This study will be the first in Malaysia to utilise the sequential mixed-methods approach  
15 55 to examine the psychosocial factors and quality of life of patients undergoing  
16 56 haemodialysis and peritoneal dialysis treatments and their caregivers.  
17 57 ● The inclusion of both patients and caregivers in the study will provide more comprehensive  
18 58 and holistic perspectives regarding ESRD management in Malaysia.  
19 59 ● This research will scrutinise the psychological well-being, financial burden, and  
20 60 complications involved in ESRD management to provide a comprehensive finding on their  
21 61 impact on the participant's quality of life.  
22 62 ● The study is restricted to the Klang Valley vicinity; hence, the findings may not apply to  
23 63 patients with ESRD and their caregivers in other Malaysian states.  
24 64 ● The restricted dissemination of paper-and-pen or web-based questionnaires to within a  
25 65 population of participants who can communicate or read in the Malay language may lead  
26 66 to the omission of unique perspectives from the non-Malay literate population.  
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32 67  
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34 68 *Keywords:* Burden of care, quality of life, end-stage renal disease (ESRD), patient, caregiver  
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## 69 INTRODUCTION

70 According to the Global Burden of Disease, chronic kidney disease (CKD) is ranked  
71 among the top 20 causes of death and is currently a significant public health concern.[1] CKD  
72 is regarded as a high-stress illness due to the chronicity of the disease and the long-term  
73 treatment required,[1] where end-stage renal disease (ESRD) is considered the last stage of  
74 CKD.[2] In Malaysia, the incidence and prevalence of patients with ESRD have been an  
75 upward trend for the past 20 years.[3] The number of Malaysians with CKD is projected to  
76 significantly increase in the future due to the ageing population and the increasing prevalence  
77 of diabetes mellitus (DM) and hypertension. It has been established that CKD is profoundly  
78 associated with DM and hypertension.[2] In 2018, the 24th Report of the Malaysia Dialysis  
79 and Transplant Registry revealed that over the preceding ten years, the acceptance rates for  
80 both haemodialysis (HD) and peritoneal dialysis (PD) have nearly doubled, while the  
81 prevalence rate has increased by more than two-fold. A total of 39,711 patients received  
82 dialysis treatment in 2016, with 35,781 and 3930 patients on HD and PD, respectively.  
83 Meanwhile, the prevalence rate of HD and PD stood at 1159 per million population and 127  
84 per million population, respectively.[4] If the present trend remains unchecked, it can be  
85 anticipated that by 2040, there will be more than 106,000 Malaysian patients with ESRD  
86 requiring dialysis. With this projected prevalence, the cost of the health care system is  
87 estimated to be RM 3.21 billion.[3]

88 It is to be expected that with the rising number of renal failure patients,[5] more  
89 individuals will adopt the caregiver role in the future. The caregiver of a patient refers to those  
90 actively involved in helping patients cope and manage their chronic illness during their  
91 treatment.[6] The chronicity of kidney failure and various treatment complications posed  
92 significant changes in patients' lifestyles, leading to caregivers experiencing a high care  
93 burden.[7] Care burden is common among caregivers and typically refers to the kind of distress

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3 94 comprising of physical, psychological, social, and financial aspects faced by caregivers as the  
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5 95 result of caregiving.[8,9] Care burden can also be in the direct and indirect burden of care,  
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8 96 whereby the direct burden of care refers to the monetary costs of treatment. In contrast, the  
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10 97 indirect burden refers to the caregivers' psychological well-being and quality of life.

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13 98 On the other hand, ESRD is highly burdensome in patients 'daily lives and time-  
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15 99 consuming, especially among elderly HD patients, resulting in patients experiencing frustration  
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17 100 and causing patients to perceive that they are a burden to their family members.[10] Thus, self-  
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19 101 perceived burden arises when care recipients possess feelings of dependence, frustration, and  
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21 102 anxiety, leading to guilt for the caregiver's hardship.[11] The incidence and prevalence of  
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23 103 ESRD give rise to adverse effects on the psychological well-being of both patients with ESRD  
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25 104 and their caregivers,[12-16] and their quality of life.[9,17] Compared to their caregivers,  
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27 105 patients with ESRD are more prone to depression and a lower quality of physical and  
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29 106 psychological well-being.[15] According to Goh and Griva,[14] the prevalence of depression  
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31 107 among patients with ESRD is estimated to be around 20% to 30%, whereas their anxiety ranged  
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33 108 between 12% and 52%. The contributing factors toward the lower quality of life among dialysis  
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35 109 patients have been identified as the increasing prevalence of depression, anxiety, and suicidal  
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37 110 ideation.[18] In contrast, perceived social support served as a protective factor against the low  
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39 111 quality of life among patients.[19,20] High perceived social support could reduce the risk of  
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41 112 hospitalisation among haemodialysis patients by 15%, along with improving their quality of  
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43 113 life.[21] On top of that, a conducive environment helps haemodialysis patients to take a more  
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45 114 positive attitude towards their disease, including improving their coping strategies.[22]

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48 115 Caregivers for patients (especially those under dialysis treatment) are subjected to a  
49  
50 116 significant workload, as they shoulder most of the responsibilities.[12] Caring for patients with  
51  
52 117 ESRD often involve tremendous physical, emotional, and economic demands.[23] Care burden  
53  
54 118 among caregivers is often inter-related with socio-demographics (age, gender, ethnicity,

## Direct and Indirect Burden of Care of Patients with ESRD and Caregivers

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2  
3 119 marital status, education, employment, income and religion/spirituality) of caregivers and  
4  
5 120 patients, disease-related factors (treatment modality, frequency of weekly dialysis sessions,  
6  
7 121 duration and frequency of dialysis, duration of illness, comorbidity, level of patient's  
8  
9 122 dependency), situational and relational factors (relationship to the patient, the duration of  
10  
11 123 caregiving), environmental factors including social support and psychological factors including  
12  
13 124 depression and anxiety.[24] Past literature showed evidence that caregivers who seek social  
14  
15 125 support from family and friends experienced a lesser burden of care than caregivers without  
16  
17 126 solid support networks[25]. Due to the reason that social support can diminish the impact of  
18  
19 127 emotional care burden and stress by providing a solution to the problem, a distraction from the  
20  
21 128 issue, or facilitating healthy behaviours needed.[26,27] Similarly, Nagarathnam, Sivakumar,  
22  
23 129 and Latheef,[28] stated that seeking social support was the dominant coping mechanism in  
24  
25 130 caregivers of renal replacement therapy. Also, it has been established that caregivers of chronic  
26  
27 131 patients are four times more likely to be diagnosed with depression and three times more likely  
28  
29 132 to seek help for anxiety issues than individuals who are not caregivers.[29] Notably, caregivers  
30  
31 133 for dialysis patients are reported to have a lower quality of life than caregivers for non-dialysis  
32  
33 134 patients.[17] In addition, the quality of life of caregivers with patients undergoing  
34  
35 135 haemodialysis was reported to be lower in all aspects compared to the general healthy  
36  
37 136 population; however, the quality of life of these caregivers was higher than the patients under  
38  
39 137 their care. [9]

40  
41 138 Despite the current situation, a dearth of research still exists, particularly on the  
42  
43 139 psychosocial factors and the economic impact of ESRD among patients and caregivers in  
44  
45 140 Malaysia. Studies focusing on the well-being of Malaysian patients with ESRD are sorely  
46  
47 141 lacking, and in the case of caregivers, almost non-existent. Therefore, there is a need for further  
48  
49 142 investigations in this area, particularly regarding the patients' and caregivers' quality of life,  
50  
51 143 care burden, depression, anxiety, coping mechanisms, and social support. Another neglected  
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3 144 area has to do with the financial and economic sustainability faced by patients with ESRD and  
4  
5 145 their caregivers regarding the management of this disease. To the best of our knowledge, thus  
6  
7 146 far, no studies have been conducted in the Southeast Asian region on the economic costs  
8  
9 147 incurred by patients with ESRD and their caregivers. Given this situation, this study delves into  
10  
11 148 examining the relationships between the psychosocial factors and quality of life of patients  
12  
13 149 with ESRD and their caregivers. Apart from that, this study will examine the comparison  
14  
15 150 between patients undergoing haemodialysis treatment and their caregivers with patients  
16  
17 151 undergoing peritoneal dialysis treatment and their caregivers to assess the impact of differences  
18  
19 152 in treatment modalities on their psychosocial factors and quality of life. Besides that, the  
20  
21 153 associations between demographic, psychosocial factors, socioeconomic factors and quality-  
22  
23 154 of-life among caregivers and patients with ESRD will be examined. Lastly, the impact of  
24  
25 155 psychological well-being and economic burden faced by the patients and caregivers towards  
26  
27 156 their quality of life will be explored in-depth within this study.  
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### 34 157 **Study Objectives**

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37 158 Phase 1 of this study focuses on the following objectives:  
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- 39 159 1. To investigate the relationships between psychosocial factors (depression, anxiety,  
40  
41 160 coping strategies, social support, care burden, economic burden) and quality of life  
42  
43 161 among caregivers and patients with ESRD.  
44  
45
- 46 162 2. To compare the psychosocial factors and quality of life between patients undergoing  
47  
48 163 haemodialysis and their caregivers with patients undergoing peritoneal dialysis and  
49  
50 164 their caregivers.  
51  
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- 53 165 3. To determine the variables (demographic, psychosocial and socioeconomic factors)  
54  
55 166 associated with quality-of-life among caregivers and patients with ESRD.  
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3 169 Phase 2 of this study focuses on the following objective:  
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- 5 170 1. To explore the perceptions of patients with ESRD and their caregivers regarding their  
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7  
8 171 psychological well-being and their economic burden in the management of ESRD and  
9  
10 172 its impact on their quality of life  
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## 13 173 **METHODS AND ANALYSIS**

### 14 15 16 174 **Design and methods**

17  
18 175 This study involves the usage of a sequential explanatory mixed methods design and  
19  
20 176 methodological triangulation with Phase 1 involving quantitative data collection, while Phase  
21  
22 177 2 involves a qualitative study.[30] Generally, the explanatory design is used when researchers  
23  
24 178 need qualitative data to expand on or explain initial quantitative findings[31] or when  
25  
26 179 quantitative results are required to direct the selection of participants for a qualitative study.[32]  
27  
28 180 Thus, the qualitative data collection emerges from and is linked to the quantitative results.[33]  
29  
30 181 Therefore, a sequential explanatory mixed-methods study design is imperative in this study due  
31  
32 182 to the rigidity of the questionnaire in Phase 1 in eliciting more in-depth information  
33  
34 183 specifically on the psychological well-being and financial factors faced by the participants.  
35  
36 184 Thus, Phase 2 will be conducted to elicit more in-depth information from the participants and  
37  
38 185 better understand the study phenomena overall. Doyle, Brady, and Byrne stated that sequential  
39  
40 186 explanatory mixed-methods design is used to substantiate the findings from the quantitative  
41  
42 187 study by providing supporting evidence from the qualitative study findings.[34] On the other  
43  
44 188 hand, methodological triangulation involving mixed-methods design increases the credibility  
45  
46 189 and validity of research findings.[35] In Phase 1, the researchers will conduct a cross-sectional  
47  
48 190 survey study among the patients with ESRD and their caregivers. A cross-sectional approach  
49  
50 191 is preferred, as this approach is time-saving in terms of questionnaire distribution and  
51  
52 192 information collection from a sizeable number of participants.[36] Meanwhile, in Phase 2, a  
53  
54 193 qualitative study involving focus group discussions will be conducted among the patients with  
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3 194 ESRD and their caregivers. The focus group discussion approach can give a fruitful and in-  
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6 195 depth understanding of an individual's experiences and perceptions towards a specific  
7  
8 196 phenomenon.[37] Furthermore, compared to individual interviews with participants, focus  
9  
10 197 groups tend to provide more ideas and information.[38] Focus group discussions allow  
11  
12 198 participants to consider and share their perspectives regarding the psychological well-being  
13  
14 199 and economic burden they take on when it comes to ESRD management and the impact of  
15  
16 200 these on their quality of life. The data findings from Phase 1 and Phase 2 of the study will be  
17  
18 201 integrated to provide a more holistic and comprehensive insight into the psychosocial factors  
19  
20 202 and quality of life experienced by patients with ESRD and their caregivers undergoing different  
21  
22 203 treatment modalities through the process of triangulation. This mixed-method integration  
23  
24 204 technique will be able to answer the study's objectives.[30] Also, it is beneficial in confirming  
25  
26 205 findings, more comprehensive data, increased validity, and enhanced understanding of studied  
27  
28 206 phenomena through the role of triangulation in the mixed-methods study.[39]  
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### 34 207 **Study setting**

35  
36 208 The investigation will be conducted in the nephrology unit of the Tuanku Muhriz UKM  
37  
38 209 Chancellor's Hospital (HTCM), Selayang Hospital (HSEL), Kuala Lumpur Hospital (HKL),  
39  
40 210 and the University of Malaya Medical Centre (UMMC), along with ten other non-governmental  
41  
42 211 organisation (NGO) or private dialysis centres in the Klang Valley. The hospitals were chosen  
43  
44 212 purposively based on their location in the Klang Valley and are specialist hospitals, non-  
45  
46 213 governmental organisations (NGO), and private centres offering dialysis treatment for patients  
47  
48 214 with ESRD.  
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### 53 215 **Milestones and timelines**

54  
55 216 The literature review for this study has been completed. The current status of this  
56  
57 217 research is in the pilot testing stage. The pilot study is expected to be completed in two months  
58  
59 218 to test the instruments' validity and reliability for quantitative data collection in the main study.  
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3 219 Quantitative data collection will take approximately three months to be completed, and  
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5 220 qualitative data collection will commence once the quantitative data collection is finalised for  
6  
7 221 a duration of two months. The expected timeline for this study will take approximately seven  
8  
9 222 months to complete, with the final manuscript is expected to be completed in October 2022.

### 12 223 **Patient and public involvement**

14 224 One patient, caregiver, health psychologist, and two formal care providers (namely, a  
15 225 nephrologist and a dialysis nurse) will be recruited to form the advisory committee. This  
16 226 committee will be tasked with reviewing the protocol and structuring the interview schedule  
17 227 and questionnaire to provide the design for the study. The advisory committee will also be  
18 228 referred to for advice and feedback whenever necessary throughout this study.

### 27 229 **Participants and recruitment**

29 230 Patients with ESRD and their caregivers will be recruited in dyads in both phases of  
30 231 studies. Specifically, potential patients in Phase 1 will be recruited purposively through  
31 232 referrals from nephrologists or nurses in the nephrology units. In contrast, the caregivers in  
32 233 Phase 1 will be recruited purposively through referrals from the patients themselves. This  
33 234 sampling method will ensure that data accumulation from the participants is effective, efficient,  
34 235 and cost-effective.[40] Whereas, for Phase 2, participants will be a subset of Phase 1  
35 236 participants. Participants in Phase 1 will be selected purposively to share their views on their  
36 237 psychological well-being, financial burden, and quality of their life in focus group discussions  
37 238 to ensure that different perspectives are represented. The demographic variables to be  
38 239 considered are age groups (young adults, middle-aged adults, and older adults) and sex (male  
39 240 and female). The inclusion and exclusion criteria will be utilised within the overall eligible  
40 241 population to ensure that the samples fulfil our study aims. Inclusion and exclusion criteria for  
41 242 both phases are similar. Patients have to fulfil these criteria; ESRD-diagnosed patients, eligible  
42 243 for participation in this study, need to be above 18 years of age, and currently receiving

1  
2  
3 244 treatment in a hospital, an NGO establishment, or a private dialysis centre in the Klang Valley  
4  
5 245 to be eligible to participate in the study. It is also essential that the participants can  
6  
7 246 communicate and read in Bahasa Malaysia, the national language of Malaysia. All patients  
8  
9 247 diagnosed with ESRD and their caregivers are welcome to participate in this study. There is no  
10  
11 248 restriction on the initiation of patients' dialysis to recruit a wide range of study participants.  
12  
13 249 However, patients exhibiting severe mental illness, or those who have undergone a kidney  
14  
15 250 transplant, will be excluded from the study. As for the recruitment of caregivers, they must be  
16  
17 251 above 18 years of age and are verified as the family caregiver of an ESRD patient currently  
18  
19 252 undergoing dialysis treatment in a hospital, an NGO establishment, or a private dialysis centre  
20  
21 253 in the Klang Valley. It is also required that the caregiver has undergone the experience of  
22  
23 254 accompanying the ESRD patient for dialysis treatment at least once and can read and  
24  
25 255 communicate in Bahasa Malaysia. Formal caregivers, caregivers of patients who have  
26  
27 256 undergone a kidney transplant, or caregivers exhibiting severe mental illness symptoms, will  
28  
29 257 be excluded from the study.  
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### 36 258 **Sample size**

#### 39 259 Phase 1: Quantitative study

41 260 The proposed quantitative study sample size calculation is based on the multiple linear  
42  
43 261 regression formula by Tabachnick and Fidell[41], which is expressed as  $N > 50 + 8m$ , where  $m$   
44  
45 262 is the number of predictors. This study will include six predictors (depression, anxiety, coping  
46  
47 263 strategies, social support, care burden, economic burden) and based on the sample size  
48  
49 264 calculated by Tabachnick and Fidell, it is estimated to be 98 participants. However, due to  
50  
51 265 dyads of participants being recruited, thus, 98 pairs of patients and caregivers is assumed. On  
52  
53 266 the other hand, sample size estimation is also calculated via power analysis using G\* Power  
54  
55 267 programme for F test (multiple linear regression: fixed model, R<sup>2</sup> deviation from zero) with an  
56  
57 268 effect size of 0.15 (medium),  $\alpha$  at 0.05, power at 0.80 and six predictors. Similarly, the power

269 analysis estimated a minimum sample size of 98, which corresponds to the sample size  
270 estimation by Tabachnick and Fidell [41]. For this study, considering the drop-out rate,  
271 unresponsive surveys, and incomplete submission of data by participants, the sample size for  
272 this study will be increased by 20%.[42,43] Hence, 118 pairs of haemodialysis patients-  
273 caregivers and 118 pairs of peritoneal dialysis patients-caregivers (N=236 pairs) will be  
274 recruited for the quantitative study, which is equivalent to a total of 472 participants.

## 275 Phase 2: Qualitative study

276 Qualitative study typically emphasises data saturation, where the saturation point is  
277 achieved when no new information, ideas or themes are forthcoming from the participants. [44]  
278 Data saturation can be identified within five[45] or three to six focus group discussions[46]  
279 with a minimum of four to a maximum of twelve participants in a group.[47] This process is  
280 typical for qualitative studies, whereby the emphasis is on arrival at saturation point. Therefore,  
281 based on past literature, the researchers will conduct six focus group discussions, with each  
282 group comprising five participants at least for this qualitative study. Hence, a minimum of 30  
283 participants (15 patients and 15 caregivers) will be involved in the focus group discussion.

## 284 Instruments

### 285 Phase 1: Quantitative study

286 The web-based or paper-based questionnaire to be distributed to the participants  
287 consists of three sections: demographic sheet, economic assessment, and psychological  
288 assessment (Table 1).

289

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293

**Table 1**  
**Summary of instruments for patient and caregiver**

	Patient	Caregiver
Demographic information	Age, gender, race, religion, marital status, education level, occupation, monthly household income, relationship with patient/caregiver, method of dialysis, duration of dialysis, frequency of dialysis, and duration of care extended by caregivers.	
Economic assessment	Source of funding, direct monthly cost, indirect weekly cost (time), and perceived economic/ financial burden.	
Psychological assessment		
Coping behaviour	Brief Coping Orientation to Problems Experienced Inventory (Brief-COPE)	Caregiver Cope (CgCope™)
Perceived burden	Self-Perceived Burden Scale (SPBS)	Zarit Burden Interview (ZBI)
Social support	Medical Outcome Study Social Support Survey (MOS-SSS)	
Anxiety	General Anxiety Disorder-7 (GAD-7)	
Depression	Patient Health Questionnaire-9 (PHQ-9)	
Quality of life	Short Form Survey (SF-36)	

294

### 295 *Demographics information*

296 The demographic information of the patients and their caregivers, which will be  
 297 collected through the questionnaire, covering age, gender, race, religion, marital status,  
 298 education level, occupation, monthly household income, relationship with patient/caregiver,  
 299 method of dialysis, duration of dialysis, frequency of dialysis, and duration of care extended  
 300 by caregivers.

### 301 *Economic assessment*

302 The second section of the questionnaire, the economic assessment, covers the  
 303 participants' source of funding, direct monthly cost, indirect weekly cost (time), and perceived  
 304 economic/ financial burden.

### 305 *Psychological assessment*

1  
2  
3 306 The final section of the questionnaire consists of six scales regarding psychological  
4  
5  
6 307 assessment. However, the coping strategy scale and the burden of care scale differs between  
7  
8 308 patients and caregivers. The coping behaviour among the patients will be evaluated by the  
9  
10 309 Malay version of the Brief Coping Orientation to Problems Experienced Inventory (Brief-  
11  
12 310 COPE). The inventory comprises 28 items with 14 dimensions: self-distraction, active coping,  
13  
14 311 denial, substance use, use of emotional support, use of instrumental support, behavioural  
15  
16 312 disengagement, venting, positive reframing, planning, humour, acceptance, religion, and self-  
17  
18 313 blame.[48] The Malay version of Brief-COPE, validated through Malaysian breast cancer  
19  
20 314 women patients, has good internal consistency ( $\alpha=.51$  to  $.99$ ).[49] Meanwhile, the Caregiver  
21  
22 315 Cope (CgCope™) questionnaire, developed by Ibrahim and colleagues [50], will be used to  
23  
24 316 assess the coping strategies employed by the caregivers. This questionnaire consists of 19 items  
25  
26 317 with six domains of coping strategies. Namely, these domains are distraction, caring for patient,  
27  
28 318 venting, religion, recreation, and social support. Participants will rate based on the 5-point  
29  
30 319 Likert scale (1 = I have never done this, 5 = I do this very frequently). The validation study  
31  
32 320 conducted among caregivers of schizophrenia patients in Malaysia yielded Cronbach's alpha  
33  
34 321 values ranging between  $.54$  and  $.82$ .[50]

39  
40 322 To assess their perception of the care burden on their caregivers, the Self-Perceived  
41  
42 323 Burden Scale (SPBS) will be distributed to the ESRD.[11] The SPBS, which consists of 10-  
43  
44 324 items, is rated by a 5-point Likert scale (1 = Not at all, 5 = All of the time). The Malay translated  
45  
46 325 10-item SPBS utilised in Ting et al.'s study[51] revealed this scale to be valid and reliable for  
47  
48 326 urology cancer patients ( $\alpha=.99$ ). As for the caregiver burden, it will be examined by the 22-  
49  
50 327 item of Zarit Burden Interview (ZBI).[52] Participants will rate their burden on a 5-point Likert  
51  
52 328 scale (0 = Rarely, 4 = Nearly always). In Malaysia, the Malay version of ZBI (MZBI) was  
53  
54 329 validated through family caregivers to cancer patients, with the scale delivering a high internal  
55  
56 330 consistency ( $\alpha=.89$ ).[53]

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2  
3 331 The 19-item Medical Outcome Study Social Support Survey (MOS-SSS) developed by  
4  
5 332 Sherbourne and Stewart[54] will be used to examine the participants' perception of social  
6  
7 333 support. This brief, multidimensional, self-administered scale, rated using a 5-point Likert scale  
8  
9 334 (1 = None at all, 5 = Available at all times), measures four categories of social support:  
10  
11 335 informational, instrumental, positive social interactions, and affectionate support. In Malaysia,  
12  
13 336 the Malay version of the MOS-SSS was validated through a sample of HIV patients. This  
14  
15 337 Malay version of the survey portrayed good psychometric properties, with high Cronbach's  
16  
17 338 alpha for all the subscales ( $\alpha > .87$ ) and the overall scale ( $\alpha = .96$ ).[55]

18  
19 339 The General Anxiety Disorder-7 (GAD-7), a screening tool and severity indicator  
20  
21 340 developed by Spitzer et al.,[56] will be used to assess the generalised anxiety disorder among  
22  
23 341 the participants. The scale contains 7 items and is rated using the 4-point Likert scale (0 = Not  
24  
25 342 at all, 3 = Nearly every day). The Malay version of GAD-7, validated through female patients  
26  
27 343 in a government-funded primary care clinic, delivered good internal consistency reliability ( $\alpha$   
28  
29 344 = .74).[57]

30  
31 345 The participants' severity of depression will be assessed through the Patient Health  
32  
33 346 Questionnaire-9 (PHQ-9).[58] The PHQ-9 consists of 9 items and is rated using the 4-point  
34  
35 347 Likert scale (0 = Not at all, 3 = Nearly every day). In Malaysia, the questionnaire was validated  
36  
37 348 through female patients in a primary care clinic, and the Malay version of PHQ-9 showed good  
38  
39 349 internal reliability ( $\alpha = .70$ ).[59]

40  
41 350 The 36-item Short Form Survey (SF-36) will be utilised to assess the health-related  
42  
43 351 quality of life of the participants. The SF-36 consists of eight subscales, measuring different  
44  
45 352 domains of health-related quality of life. Namely, these subscales are physical functioning (PF),  
46  
47 353 role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning  
48  
49 354 (SF), role-emotional (RE), and mental health (MH). Also, two-component scores are derived  
50  
51 355 from the eight subscales. These are the physical component summary (PCS), which consists of  
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## Direct and Indirect Burden of Care of Patients with ESRD and Caregivers

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3 356 PF, RP, BP, and GH, and the mental component summary (MCS), which consists of VT, SF,  
4  
5 357 RE, and MH.[60] The Malay version of SF-36, validated through post-coronary artery bypass  
6  
7 358 grafting surgery (CABG) patients, delivered good internal consistency reliability, with  
8  
9 359 Cronbach's alpha values ranging from .73 to .90 for the subscales.[61]  
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11  
12

## 13 360 Phase 2: Qualitative study

14  
15 361 A focus group discussion schedule will be developed, based on a literature review and  
16  
17 362 expert input by nephrologists in the research team. The questions for the focus group discussion  
18  
19 363 will be tailored to elicit responses from the patients with ESRD and their caregivers regarding  
20  
21 364 their psychological well-being and economic burden they faced, and its impact on their quality  
22  
23 365 of life. The focus group discussion schedule will be piloted among caregivers and patients to  
24  
25 366 examine the clarity and feasibility of the questions. The focus group discussion will be divided  
26  
27 367 into five sections: demographic details, source of ESRD treatment funding, direct and indirect  
28  
29 368 costs of ESRD management, the impact of their psychological well-being towards their quality  
30  
31 369 of life, and lastly, the impact of economic burden experienced by them towards their quality of  
32  
33 370 life.  
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39 371 **Data collection**40  
41  
42 372 Phase 1: Quantitative study

43  
44 373 Conventional paper-and-pencil/web-based questionnaires will be utilised. The response  
45  
46 374 rate of participants who responded positively out of those potentially eligible participants who  
47  
48 375 are invited to be involved in the study will be recorded. Potential participants (patients),  
49  
50 376 identified through referrals from nephrologists or nurses in the nephrology units, will be  
51  
52 377 recruited during their dialysis treatments in the respective hospital/dialysis centre. In contrast,  
53  
54 378 potential participants (caregivers) will be approached whilst waiting for their patient's  
55  
56 379 treatment to be completed. For the caregivers who are not present during the patients' treatment,  
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3 380 the researchers will call them up or meet up with them during the patients' subsequent treatment  
4  
5 381 in the respective hospitals/dialysis centres. The recruitment process progresses with the  
6  
7 382 researcher briefing the caregiver and patient on the aims and procedures of the study. Potential  
8  
9 383 participants who respond in the affirmative regarding whether they have been previously  
10  
11 384 diagnosed with severe mental illness will be excluded from the study. Potential participants  
12  
13 385 will be given ample time to consider their involvement in the study. Upon receiving their  
14  
15 386 consent, the participants will be provided with a questionnaire, which can be filled out in  
16  
17 387 approximately 30 minutes. The researchers will entertain any questions the participants may  
18  
19 388 have regarding the questionnaire. The completed questionnaires will be kept securely for the  
20  
21 389 data analysis process. Subject withdrawal criteria include a situation whereby the participants  
22  
23 390 voluntarily withdraws their consent to participate in the study or when the principal investigator,  
24  
25 391 for any reason, ends the participation. Participants are free to withdraw from the study at any  
26  
27 392 time by stating their intention during the course of the survey or by emailing the principal  
28  
29 393 investigator, whose email address and telephone number are included in the informed consent  
30  
31 394 form. As the sample size calculation considers the participant drop-out rate, participants who  
32  
33 395 withdraw from the study will not be replaced.

#### 396 Phase 2: Qualitative study

397 The response rate of participants who responded positively out of those potentially  
398 eligible participants who are invited to be involved in the study will be recorded. Potential  
399 participants from Phase 1 will be recruited purposively based on the inclusion and exclusion  
400 criteria. The researchers will provide the caregivers and patients with a briefing on the aims  
401 and procedures of the study. Participants will be given sufficient time to consider their  
402 participation in the focus group discussion. The discussion will be held at a designated date,  
403 time, and venue decided by the researchers and is anticipated to last for an hour. The  
404 discussions will be recorded, and data will be transcribed verbatim, after which the recording

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3 405 will be deleted, in keeping with established ethical standards. Subject withdrawal criteria  
4  
5 406 include a situation whereby the participants voluntarily withdraws their consent to participate  
6  
7 407 in this study or when the principal investigator, for any reason, ends the participation.  
8  
9 408 Participants are free to withdraw from the study at any time by stating their intention during  
10  
11 409 the course of the discussion or by emailing the principal investigator, whose email address and  
12  
13 410 telephone number are included in the informed consent form. The arrival at the data saturation  
14  
15 411 point is not affected by the withdrawal of a participant(s) who will not be replaced.  
16  
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## 20 412 **Data analysis**

### 23 413 Phase 1: Quantitative study

24  
25 414 IBM Statistical Package for the Social Sciences (SPSS) software for Windows, version 23[62]  
26  
27 415 will be utilised to process the data. Descriptive statistics, Pearson correlation, ANOVA and  
28  
29 416 multiple regression analysis will be utilised for data analysis. Statistical significance will be set  
30  
31 417 at .05. Descriptive statistics will be used to compute frequencies, percentages, means, and  
32  
33 418 standard deviation, summarising the respondents' data. Pearson correlations will be conducted  
34  
35 419 to examine the relationships between psychosocial factors (depression, anxiety, coping  
36  
37 420 strategies, social support, care burden, and economic burden) and participants' quality of life.  
38  
39 421 To examine the impact of differences in treatment modalities towards the participants'  
40  
41 422 psychosocial factors and quality of life, ANOVA will be conducted between haemodialysis  
42  
43 423 patients and their caregivers and peritoneal dialysis patients and their caregivers. A multiple  
44  
45 424 regression model will be fitted to examine the association between psychosocial factors,  
46  
47 425 socioeconomic factors and quality of life, whilst adjusting for potential confounding factors  
48  
49 426 such as demographic factors (occupation, monthly household income, relationship with  
50  
51 427 patient/caregiver, and method of dialysis).  
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### 57 428 Phase 2: Qualitative study

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3 429 Thematic analysis will be conducted using NVivo software for Windows version 11  
4  
5 430 (update 4).[63] The researchers will conduct thematic analysis to determine the codes and  
6  
7 431 themes from the focus group discussion. Main ideas will be derived through open coding, and  
8  
9 432 the themes will be generated through axial coding based on the focus group discussion  
10  
11 433 undergone by the participants. This qualitative study will facilitate an in-depth examination of  
12  
13 434 the participants' perception of their psychological well-being and economic burden in the  
14  
15 435 management of ESRD and its impact on their quality of life. Triangulation will be utilised in  
16  
17 436 this research using multiple data sources from participants to develop a comprehensive  
18  
19 437 understanding of the study phenomena. Triangulation has been viewed as a qualitative research  
20  
21 438 strategy to test validity by converging information from different sources.[64] The data  
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23 439 findings from the qualitative study will be integrated with quantitative study findings to answer  
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25 440 the study's objectives and have holistic insight into the study phenomena.  
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### 31 441 **IMPLICATIONS OF THE STUDY**

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34 442 To our best knowledge, there is a lack of study focusing on the ESRD population in  
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36 443 Malaysia. Therefore, this study will be a pioneering study to include mixed methods of  
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38 444 quantitative and qualitative study designs to evaluate the psychosocial factors and quality of  
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40 445 life of patients with ESRD and their caregivers. Apart from that, this study incorporated both  
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42 446 the perspectives of patients and caregivers, hence providing a more in-depth understanding and  
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44 447 overview of the psychological well-being and financial burden they have to face in terms of  
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46 448 illness management and the impact of these on their quality of life. Through this study, future  
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48 449 researchers might have an enhanced understanding of this study phenomena and may navigate  
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50 450 them to develop an intervention programme focusing on the well-being of the patients and their  
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52 451 caregivers. Also, the current study will examine the comparison of psychosocial factors and  
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54 452 the quality of life between patients undergoing HD treatment and their caregivers with patients  
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56 453 undergoing CAPD treatment and their caregivers. With this comparison being made, this study  
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3 454 will provide society and policymakers with a better understanding of the treatment modalities  
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5 455 that have a better impact on the psychological well-being and quality of life of both the patients  
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7 456 and caregivers. Also, this study can provide an in-depth insight into the financial burden the  
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9 457 patients and caregivers have to face in the management of this illness. Thus, it might contribute  
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11 458 crucial knowledge to the Malaysian government and non-governmental organisations in  
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13 459 providing aid to those who are financially burdened.  
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## 18 460 **ETHICS AND DISSEMINATION**

### 21 461 **Ethics approval**

23 462 The work has been approved by the Medical Research and Ethics Committee (MREC)  
24  
25 463 [NMRR-21-1012-59714] and the research ethics committee of Tuanku Muhriz UKM  
26  
27 464 Chancellor's Hospital (HTCM) [UKM PPI/111/8/JEP-2021-078] and the University of Malaya  
28  
29 465 Medical Centre (UMMC) [MREC ID NO: 202178-10346]. Also, relevant permissions and  
30  
31 466 approvals from the hospital directors of Selayang Hospital (HSEL) and Kuala Lumpur Hospital  
32  
33 467 (HKL) have been obtained.  
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### 38 468 **Ethical considerations**

40 469 The researchers will adhere to the principles of the Declaration of Helsinki[65] and the  
41  
42 470 Malaysian Good Clinical Practice Guidelines.[66] The participants' privacy is protected during  
43  
44 471 the data collection process by separating the informed consent forms from the paper-based  
45  
46 472 questionnaire responses. All documents will be deposited in a secured cabinet, and all data will  
47  
48 473 be stored in a password-protected computer to which only the researchers have access. All  
49  
50 474 documents and data will be stored for seven years, after which they will be shredded and  
51  
52 475 deleted. No participant identifiers (name, identity card number, address, phone number) will  
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54 476 be traceable, and a unique study ID will be assigned. No medical records will be accessible.  
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3 477 Participants will have no access to any personal information, and to ensure the element of  
4  
5 478 anonymity, they will not be informed of the study findings.

#### 8 479 **Dissemination**

9  
10 480 The findings from this study will be published in peer-review scientific journals and at  
11  
12 481 national or international conferences. Minimal anonymised data uploaded as supplementary  
13  
14 482 material for review purposes in scientific journal publications or conferences will adhere  
15  
16 483 strictly to the ethical principles stipulated. Only group data will be published, and no personal  
17  
18 484 identifier will be collected or made public. Relevant permissions from all parties involved will  
19  
20 485 be obtained before any publication. The findings from this study can serve as a guide for  
21  
22 486 Malaysian policymakers, health care providers, and society to improve the quality of life of  
23  
24 487 patients with ESRD and their caregivers through the engagement of constructive and holistic  
25  
26 488 interventions.

#### 31 489 **Author contributions**

32  
33 490 All authors were involved in writing the study protocol. SYC and NI drafted the manuscript.  
34  
35 491 CSS, NA, RI and AHAG provided critical revision and feedback of the manuscript. All authors  
36  
37 492 have read and approved the final manuscript.

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44  
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46  
47 496 and analysis, decision to publish, or preparation of the manuscript.

#### 51 497 **Competing interest**

52  
53 498 The authors declared that there is no conflict of interest.

#### 56 499 **Provenance and peer-review**

57  
58 500 Not commissioned, externally peer-reviewed.  
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3 501 **Data sharing statement**  
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5 502 Not required as this study is not a clinical trial study protocol.  
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# BMJ Open

## The effects of psychosocial and economic factors on the quality of life of patients with end-stage renal disease and their caregivers in the Klang Valley, Malaysia: Protocol for a mixed-methods study

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Manuscript ID	bmjopen-2021-059305.R2
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Keywords:	MENTAL HEALTH, Dialysis < NEPHROLOGY, End stage renal failure < NEPHROLOGY, Chronic renal failure < NEPHROLOGY, Adult nephrology < NEPHROLOGY

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Manuscripts

Psychosocial and Economic Factors on the Quality of Life of Patients with ESRD and  
Caregivers

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The effects of psychosocial and economic factors on the quality of life of  
patients with end-stage renal disease and their caregivers in the Klang Valley,  
Malaysia: Protocol for a mixed-methods study

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Psychosocial and Economic Factors on the Quality of Life of Patients with ESRD and Caregivers

2

26 **ABSTRACT**

27 **Introduction:** The number of patients in Malaysia requiring dialysis is expected to rise  
28 substantially in the future due to the ageing population and increasing prevalence of diabetes  
29 mellitus and hypertension. Hence, more individuals will be expected to adopt the role of  
30 caregivers in the future. The upward trend of end-stage renal disease (ESRD) and caregiving  
31 for dialysis patients has detrimental consequences for both patients and caregivers in terms of  
32 their psychological well-being and quality of life. Despite the current circumstances, there are  
33 very few studies in Malaysia that have explored the psychosocial factors, specifically on the  
34 economic impact of the management of ESRD.

35 **Methods and Analysis:** This two-phase sequential explanatory mixed-methods design,  
36 incorporating a quantitative design (Phase 1) and a qualitative study (Phase 2), is to be  
37 conducted in four government hospitals and ten other non-governmental organisations or  
38 private dialysis centres within the Klang Valley, Malaysia. A cross-sectional survey (Phase 1)  
39 involving 236 pairs of the patient-caregiver dyad, while focus group discussions (Phase 2)  
40 involving 30 participants. The participants for both phases will be recruited purposively using  
41 inclusion and exclusion criteria. Descriptive statistics, independent sample *t*-tests, multiple  
42 regression and thematic analysis will be utilised for the data analysis in Phase 1 and Phase 2,  
43 respectively.

44 **Ethics and Dissemination:** Approval for the proposed study has been obtained from the  
45 National Medical Research and Ethics Committee (MREC) [NMRR-21-1012-59714] and the  
46 Research Ethics Committee of Hospital Canselor Tuanku Muhriz UKM (HCTM) [UKM  
47 PPI/111/8/JEP-2021-078] and University of Malaya Medical Centre (UMMC) [MREC ID NO:  
48 202178-10346]. The informed consent of the participants for both studies will be obtained  
49 beforehand, and no personal identifiers will be obtained from the participants to protect their

50 anonymity. The findings will be published in peer-reviewed scientific journals and presented  
51 in national or international conferences with minimal anonymised data.

## 52 **ARTICLE SUMMARY**

### 53 **Strengths and limitations of this study**

- 54 ● This study will be the first in Malaysia to utilise the sequential mixed-methods approach  
55 to examine the psychosocial factors, economic factors, and quality of life of patients  
56 undergoing haemodialysis and peritoneal dialysis treatments and their caregivers.
- 57 ● The inclusion of both patients and caregivers in the study will provide more a  
58 comprehensive and holistic perspective of the management of ESRD in Malaysia.
- 59 ● This research will scrutinise the psychosocial well-being, economic burden, and  
60 complications involved in ESRD management to provide a comprehensive finding on their  
61 impact on the quality of life of the participants.
- 62 ● The study will be restricted to the vicinity of the Klang Valley, so the findings may not be  
63 applicable in other Malaysian states; restricted dissemination of the paper-and-pen or web-  
64 based questionnaires to a population of participants who are able to communicate or read  
65 in the Malay language may lead to the omission of unique perspectives from the non-  
66 Malay literate population.
- 67 ● Purposive sampling will be used to recruit the participants for the survey, and the  
68 recruitment method is not intended to ensure a representative sample. As such, the findings  
69 from the quantitative survey will have limited generalisability.

71 *Keywords:* Burden of care, quality of life, end-stage renal disease (ESRD), patient, caregiver

## 72 INTRODUCTION

73 According to the Global Burden of Disease, chronic kidney disease (CKD) is ranked  
74 among the top 20 causes of death, and is currently a significant public health concern.[1] CKD  
75 is regarded as a high-stress illness due to the chronicity of the disease and the long-term  
76 treatment required,[2] where end-stage renal disease (ESRD) is considered as the last stage of  
77 CKD.[3] In Malaysia, the incidence and prevalence of patients with ESRD have been showing  
78 an upward trend for the past 20 years.[4] The number of Malaysians with CKD is projected to  
79 significantly increase in the future due to the ageing population and the increasing prevalence  
80 of diabetes mellitus (DM) and hypertension. It has been established that CKD is profoundly  
81 associated with DM and hypertension.[3] In 2018, the 24th Report of the Malaysian Dialysis  
82 and Transplant Registry revealed that over the preceding ten years, the acceptance rate for both  
83 haemodialysis (HD) and peritoneal dialysis (PD) has nearly doubled, while the prevalence rate  
84 has increased by more than two-fold. A total of 39,711 patients received dialysis treatment in  
85 2016, with 35,781 and 3930 patients being on HD and PD, respectively. Meanwhile, the  
86 prevalence rate of HD and PD stood at 1,159 per million population and 127 per million  
87 population, respectively.[5] If the present trend remains unchecked, it is anticipated that by  
88 2040, there will be more than 106,000 Malaysian patients with ESRD requiring dialysis. With  
89 this projected prevalence, the cost to the healthcare system is estimated to be RM 3.21 billion.[4]  
90 It is to be expected that with the rising number of renal failure patients,[1] more individuals  
91 will be adopting the caregiver role in the future. Caregivers refers to those who are actively  
92 involved in helping patients to cope with and manage their chronic illness during their  
93 treatment.[6] The chronicity of kidney failure and various treatment complications bring about  
94 significant changes in the lifestyles of patients, leading to caregivers having to shoulder a high  
95 burden of care.[7] This burden of care is common among caregivers, and it typically refers to

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96 the kind of distress, comprised of physical, psychological, social, and financial aspects, faced  
97 by them as a result of caregiving.[8-9]

98 ESRD is highly burdensome in the daily lives of patients and is also time-consuming,  
99 especially among elderly HD patients, resulting in patients experiencing frustration and causing  
100 them to perceive that they are a burden to their family members.[10] This self-perceived burden  
101 arises when the recipients of care possess feelings of dependence, frustration, and anxiety,  
102 leading to guilt about the hardship being imposed on the caregiver.[11] The incidence and  
103 prevalence of ESRD have adverse effects on the psychological well-being of both patients and  
104 their caregivers,[12-16] and their quality of life.[9, 17] Compared to their caregivers, patients  
105 with ESRD are more prone to depression and a lower quality of physical and psychological  
106 well-being.[15] According to Goh and Griva,[14] the prevalence of depression among patients  
107 with ESRD is estimated to be around 20% to 30%, whereas their level of anxiety ranges  
108 between 12% and 52%. Depression and anxiety symptoms occur more frequently among  
109 patients undergoing dialysis than patients who have undergone kidney transplantation.[18]  
110 Patients under peritoneal dialysis have also been reported to have significantly higher levels of  
111 depression symptoms than those on haemodialysis.[19] Conversely, a qualitative study  
112 conducted by Avdal et al.[20] showed evidence that both haemodialysis and peritoneal dialysis  
113 patients frequently experience depression along with other psychological problems, such as  
114 decreased social support, burnout, despair, and anxiety. Apart from these, patients and their  
115 caregivers have to face high treatment costs, out-of-pocket costs, and other comorbidities that  
116 arise, which can be overwhelming and cause those in low or middle-income families to bear a  
117 financial burden.[21] In Malaysia, the cost of haemodialysis and peritoneal dialysis per patient  
118 per year stands at RM 39,791 and RM 37,576, respectively.[22] Based on past literature in  
119 other countries, the high treatment costs have led to numerous caregivers having to suffer a  
120 financial burden and to willingly mortgage their valuable items to cover those costs.[23-24] In

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121 contrast to these studies, Mohd Fadzli, Mohd Rasani and Keng[21] stated that Malaysian  
122 patients and caregivers who are reportedly being fully-funded for their treatment may not face  
123 a financial burden, but those belonging to low-income families experience a tremendous  
124 financial burden. Mixed findings have been reported when comparing the quality of life of  
125 haemodialysis and peritoneal dialysis patients. Al Wakeel et al.[25] and Hsu et al.[26] found  
126 that peritoneal dialysis patients have a better quality of life than those on haemodialysis.  
127 Alternatively, Gonçalves et al.[27] concluded that haemodialysis has a better significant  
128 influence on the quality of life of patients compared to peritoneal dialysis as the physical  
129 functioning and emotional functioning aspects have been reported to be higher among  
130 haemodialysis patients. Meanwhile, De Abreu et al.,[28] Griva et al.,[19] and Iyasere et al.[29]  
131 suggested evidence that there is no significant difference between the levels of quality of life  
132 between the two different dialysis modalities. Generally, the factors contributing to a lower  
133 quality of life among dialysis patients have been identified as the increasing prevalence of  
134 depression, anxiety, and suicidal ideation.[30] In contrast, perceived social support serves as a  
135 protective factor against a low quality of life among patients.[31-32] A high perception of  
136 social support can reduce the risk of hospitalisation among haemodialysis patients by 15%,  
137 along with improving their quality of life.[33] On top of that, a conducive environment helps  
138 haemodialysis patients to take a more positive attitude towards their disease, including  
139 improving their coping strategies.[34]

140 Caregivers for patients (especially those under dialysis treatment) are subjected to a  
141 significant workload, as they shoulder most of the responsibilities.[12] Caring for patients with  
142 ESRD often involves tremendous physical, emotional, and economic demands.[35] The burden  
143 of care among caregivers is often inter-related with the socio-demographics (age, gender,  
144 ethnicity, marital status, education, employment, income and religion/spirituality) of the  
145 caregivers and patients, disease-related factors (treatment modality, frequency of weekly

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146 dialysis sessions, duration and frequency of dialysis, duration of illness, comorbidity, level of  
147 patient's dependency), situational and relational factors (relationship to the patient, the duration  
148 of caregiving), environmental factors, including social support, and psychological factors  
149 including depression and anxiety.[36] Past literature has shown evidence that caregivers who  
150 seek social support from family and friends experience a lesser burden of care than caregivers  
151 without solid support networks.[37] This is because social support can diminish the impact of  
152 the emotional burden and stress of care by providing solutions to problems, distractions from  
153 issues, or facilitating the required healthy behaviours.[38-39] Similarly, Nagarathnam,  
154 Sivakumar, and Latheef[40] stated that seeking social support is the dominant coping  
155 mechanism in caregivers of patients undergoing renal replacement therapy. Also, it has been  
156 established that caregivers of chronic patients are four times more likely to be diagnosed with  
157 depression and three times more likely to seek help for anxiety issues than individuals who are  
158 not caregivers.[41]

159 There is a high correlation between the psychological well-being of caregivers and  
160 patients. Gerogianni et al.[13] stated that caregivers have higher levels of anxiety and  
161 depression when dialysis patients under their care are having high levels of anxiety and  
162 depression. In line with this study, Bardak et al.[42] reported that depressive symptoms are  
163 higher among caregivers of haemodialysis patients than among caregivers of peritoneal dialysis  
164 or kidney transplant patients. Monárrez-Espino, Delgado-Valles and Ramírez-García[43]  
165 reported a similar result, whereby caregivers of peritoneal dialysis patients have better  
166 psychological well-being in terms of anxiety and depression compared to caregivers of  
167 haemodialysis patients. Due to the reason that patients under haemodialysis treatment were  
168 perceived to be more difficult to care for compared to patients under treatment for other  
169 modalities.[15] In contrast, Cantekin, Kavurmacı, and Tan[44] suggested evidence that a higher  
170 burden of care was observed among caregivers of peritoneal dialysis patients than caregivers

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171 of patients undergoing haemodialysis treatment. This study was in line with the study  
172 conducted by Al Wakeel and Bayoumi[45], whereby the burden of care among the peritoneal  
173 dialysis group of caregivers was significantly higher than those in the haemodialysis group.  
174 The educational level, age, health, and capability of the patient with regard to self-care serve  
175 as the determinants of the burden of care among caregivers.[44-45] Notably, caregivers of  
176 dialysis patients reportedly have a lower quality of life than caregivers of non-dialysis  
177 patients.[17] The quality of life of caregivers with patients undergoing haemodialysis was  
178 reported to be lower in all aspects compared to the general healthy population; however, the  
179 quality of life of these caregivers was higher than the patients under their care.[9] Since  
180 caregivers of haemodialysis patients experience a high burden of care, this will have a negative  
181 effect on their quality of life.[46] Conversely, Monárrez-Espino, Delgado-Valles and Ramírez-  
182 García[43] concluded that there is no significant difference in terms of quality of life between  
183 caregivers of haemodialysis and peritoneal dialysis patients.

184 Despite the current situation, there is still a dearth of research, particularly with regard  
185 to the psychosocial factors and the economic impact of ESRD among patients and caregivers  
186 in Malaysia. Studies focusing on the well-being of Malaysian patients with ESRD are sorely  
187 lacking, and almost non-existent in the case of caregivers. Therefore, there is a need for further  
188 investigations to be carried out in this area, particularly with regard to the quality of life, burden  
189 of care, depression, anxiety, coping mechanisms, and social support of patients and their  
190 caregivers. Another neglected area has to do with the economic burden faced by patients with  
191 ESRD and their caregivers with regard to the management of this disease. As far as is known,  
192 thus far, no studies have been conducted in the Southeast Asian region on the economic costs  
193 incurred by patients with ESRD and their caregivers. Given this situation, this study will delve  
194 into a comparison of the psychosocial factors, economic factors, and quality of life of patients  
195 with ESRD and their caregivers. Apart from that, the associations between demographic factors,

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196 psychosocial factors, economic factors and quality-of-life among caregivers and patients with  
197 ESRD will be examined. Lastly, the perception of psychosocial well-being and economic  
198 burden along with their quality of life will be explored in-depth in this study.

### 199 **Study Objectives**

200 Phase 1 of this study focuses on the following objectives:

- 201 1. To compare the psychosocial factors, economic factors, and quality of life between  
202 caregivers of patients undergoing haemodialysis and caregivers of patients undergoing  
203 peritoneal dialysis.
- 204 2. To compare the psychosocial factors, economic factors, and quality of life between  
205 patients undergoing haemodialysis and patients undergoing peritoneal dialysis.
- 206 3. To determine the variables (demographic, psychosocial and economic factors)  
207 associated with quality of life among caregivers of patients with ESRD.
- 208 4. To determine the variables (demographic, psychosocial and economic factors)  
209 associated with quality of life among patients with ESRD.

210 Phase 2 of this study focuses on the following objective:

- 211 1. To explore the perceptions of patients with ESRD and their caregivers regarding their  
212 psychosocial well-being and economic burden in the management of ESRD and its  
213 impact on their quality of life

## 214 **METHODS AND ANALYSIS**

### 215 **Design and Methods**

216 This study involves the use of a sequential explanatory mixed methods design  
217 incorporating methodological and investigator triangulation. Phase 1 of the study involves the  
218 collection of quantitative data, while Phase 2 has to do with a qualitative study.[47] Generally,  
219 an explanatory design is used when researchers need qualitative data to expand on or explain  
220 their initial quantitative findings[48] or when quantitative results are required to direct the



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221 selection of participants for a qualitative study.[49] Thus, the collection of qualitative data  
222 emerges from and is linked to the quantitative results.[50] Therefore, due to the rigidity of  
223 the questionnaire in Phase 1, a sequential explanatory mixed methods study design is  
224 imperative in this study to elicit more in-depth information, specifically on the psychosocial  
225 well-being and economic factors faced by the participants. Thus, Phase 2 will be conducted to  
226 elicit more in-depth information from the participants and to gain a better overall understanding  
227 of the phenomena being studied. Doyle, Brady, and Byrne[51] stated that a sequential  
228 explanatory mixed methods design is used to substantiate the findings from a quantitative study  
229 by providing supporting evidence from the findings of a qualitative study. However,  
230 triangulation involving a mixed methods design increases the credibility and validity of the  
231 research findings.[52] In Phase 1, a cross-sectional survey will be conducted among patients  
232 with ESRD and their caregivers. A cross-sectional approach is preferred as it saves time in  
233 terms of the distribution of questionnaires and the collection of information from a sizeable  
234 number of participants.[53] Meanwhile, in Phase 2, a qualitative study will be conducted  
235 involving focus group discussions among patients with ESRD and their caregivers. A focus  
236 group discussion approach can give a fruitful and in-depth understanding of an individual's  
237 experiences and perceptions of a specific phenomenon.[54] Furthermore, compared to  
238 individual interviews with participants, focus groups tend to provide more ideas and  
239 information.[55] The focus group discussions will enable the participants to consider and share  
240 their perspectives regarding the psychosocial well-being and economic burden they have to  
241 undertake when it comes to the management of ESRD and the impact of these on their quality  
242 of life. The data findings from Phase 1 and Phase 2 of the study will be integrated through the  
243 triangulation process to provide a more holistic and comprehensive insight into the  
244 psychosocial factors, economic factors and quality of life experienced by caregivers and their  
245 ESRD patients undergoing different treatment modalities. This mixed methods integration

246 technique will be able to answer the objectives of this study.[47] Also, the role of triangulation  
247 in the mixed methods study will be beneficial in confirming the findings, providing more  
248 comprehensive data, increasing the validity, and enhancing the understanding of the  
249 phenomena being studied.[56]

### 250 **Study Setting**

251 The investigation will be conducted in the nephrology units of Hospital Canselor  
252 Tuanku Muhriz UKM (HCTM), Hospital Selayang (HSEL), Hospital Kuala Lumpur (HKL),  
253 and the University of Malaya Medical Centre (UMMC), along with ten other non-governmental  
254 organisations (NGOs) or private dialysis centres in the Klang Valley, Malaysia. The hospitals  
255 were chosen purposively based on their location in the Klang Valley, and are specialist  
256 hospitals, non-governmental organisations (NGO), and private centres offering dialysis  
257 treatment for patients with ESRD.

### 258 **Milestones and Timelines**

259 The literature review for this study has been completed, and currently, this research is  
260 in the pilot testing stage. The pilot study to test the validity and reliability of the instruments  
261 for the quantitative data collection in the main study is expected to be completed in two months.  
262 The quantitative data collection will take approximately three months to be completed, and the  
263 qualitative data collection, which will last for two months, will commence once the quantitative  
264 data collection is finalised. The expected timeline for the completion of this study is  
265 approximately seven months, with the final manuscript expected to be completed in October  
266 2022.

### 267 **Patient and Public Involvement**

268 One patient, caregiver, health psychologist, and two formal care providers (namely, a  
269 nephrologist and a dialysis nurse) will be recruited to form the Advisory Committee. This  
270 committee will be tasked with reviewing the protocol and structuring the interview schedule

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271 and questionnaire to provide the design for the study. The Advisory Committee will also be  
272 referred to for advice and feedback, whenever necessary, throughout this study.

### 273 **Participants and Recruitment**

274 Patients with ESRD and their caregivers will be recruited in dyads in both phases of the  
275 study. Specifically, potential patients in Phase 1 will be recruited purposively through referrals  
276 from nephrologists or nurses in the nephrology units. In contrast, the caregivers in Phase 1 will  
277 be recruited purposively through referrals from the patients themselves. This sampling method  
278 will ensure that the data accumulated from the participants will be effective, efficient, and cost-  
279 effective.[57] However, the participants in Phase 2 will be a subset of the participants in Phase  
280 1. The participants in Phase 2 will be selected purposively to share their views on their  
281 psychosocial well-being, economic burden, and quality of life in focus group discussions to  
282 ensure that different perspectives are represented. The demographic variables to be considered  
283 are age group (young adults, middle-aged adults, and older adults), and gender (male and  
284 female). A set of inclusion and exclusion criteria will be utilised within the overall eligible  
285 population to ensure that the samples fulfil the aims of this study. The inclusion and exclusion  
286 criteria for both phases are similar. Patients have to fulfil these criteria: ESRD diagnosis, above  
287 18 years old, Malaysian nationality, and currently receiving treatment at a hospital, an NGO  
288 establishment, or a private dialysis centre in the Klang Valley. It is also essential that the  
289 potential participants are able to communicate in and read Bahasa Malaysia, the national  
290 language of Malaysia. All patients diagnosed with ESRD and their caregivers are welcome to  
291 participate in this study. There is no restriction on the duration of the patients' initiation to  
292 dialysis in order to recruit a wide range of study participants. However, patients exhibiting  
293 severe mental illness or those who have undergone a kidney transplant will be excluded from  
294 the study. As for the recruitment of caregivers, they must be above 18 years of age and verified  
295 as the family caregiver of an ESRD patient currently undergoing dialysis treatment at a hospital,

296 an NGO establishment, or a private dialysis centre in the Klang Valley. The caregiver is also  
297 required to have undergone the experience of accompanying the patient for dialysis treatment  
298 at least once, and must be able to read and communicate in Bahasa Malaysia. Formal caregivers,  
299 caregivers of patients who have undergone a kidney transplant, or caregivers exhibiting  
300 symptoms of severe mental illness will be excluded from the study.

### 301 **Sample Size**

#### 302 Phase 1: Quantitative Study

303 The proposed quantitative study sample size calculation is based on the multiple linear  
304 regression formula by Tabachnick and Fidell,[41] which is expressed as  $N > 50 + 8m$ , where  
305  $m$  is the number of predictors. This study will include six predictors (depression, anxiety,  
306 coping strategies, social support, burden of care, and economic burden), and the sample size,  
307 based on the calculation by Tabachnick and Fidell,[58] is estimated to be 98 participants.  
308 However, as the participants are to be recruited in dyads, it is assumed that there will be 98  
309 pairs of patients and caregivers. Besides that, the estimated sample size is also calculated via a  
310 power analysis using the G\* Power programme for the F test (multiple linear regression: fixed  
311 model,  $R^2$  deviation from zero) with an effect size of 0.15 (medium),  $\alpha$  at 0.05, power at 0.80  
312 and six predictors. Similarly, the power analysis estimated a minimum sample size of 98, which  
313 corresponded with the estimated sample size by Tabachnick and Fidell.[58] For this study,  
314 taking into consideration the drop-out rate, non-response rate, and incomplete submission of  
315 data by participants, the sample size for this study has been increased by 20%.[59-60] Hence,  
316 118 pairs of haemodialysis patients-caregivers and 118 pairs of peritoneal dialysis patients-  
317 caregivers ( $N = 236$  pairs), which is equivalent to a sample size of 472 participants, will be  
318 recruited for the quantitative study.

#### 319 Phase 2: Qualitative Study

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320 A qualitative study typically emphasises data saturation, where the saturation point is  
 321 achieved when no new information, ideas or themes are forthcoming from the participants.[61]  
 322 Data saturation can be identified within five[62] or three to six focus group discussions[63]  
 323 with a minimum of four and a maximum of twelve participants in a group.[64] This process is  
 324 typical for qualitative studies, whereby the emphasis is on arriving at the saturation point.  
 325 Therefore, based on past literature, six focus group discussions will be conducted in this  
 326 research, with each group being comprised of at least five participants for this qualitative study.  
 327 Hence, a minimum of 30 participants (15 patients and 15 caregivers) will be involved in the  
 328 focus group discussions.

### 329 Instruments

#### 330 Phase 1: Quantitative Study

331 The web-based or paper-based questionnaire to be distributed to the participants  
 332 consists of three sections: demographic sheet, economic assessment, and psychosocial  
 333 assessment (Table 1).

**Table 1**  
**Summary of instruments for patient and caregiver**

	Patient	Caregiver
Demographic information	Age, gender, race, religion, marital status, education level, occupation, monthly household income, relationship with patient/caregiver, method of dialysis, duration of dialysis, frequency of dialysis, and duration of care extended by caregivers.	
Economic assessment	Source of funding, monthly cost, weekly cost (time), and perceived economic burden.	
Psychosocial assessment		
Coping behaviour	Brief Coping Orientation to Problems Experienced Inventory (Brief-COPE)	Caregiver Cope (CgCope™)
Perceived burden	Self-Perceived Burden Scale (SPBS)	Zarit Burden Interview (ZBI)
Social support	Medical Outcome Study Social Support Survey (MOS-SSS)	

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Anxiety	General Anxiety Disorder-7 (GAD-7)
Depression	Patient Health Questionnaire-9 (PHQ-9)
Quality of life	Short Form Survey (SF-36)

334

335 *Demographic information*

336 The demographic information of the patients and their caregivers, which will be  
 337 collected through the questionnaire, covers age, gender, race, religion, marital status, education  
 338 level, occupation, monthly household income, relationship with patient/caregiver, method of  
 339 dialysis, duration of dialysis, frequency of dialysis, and duration of care extended by caregivers.

340 *Economic assessment*

341 The second section of the questionnaire, the economic assessment, covers the source of  
 342 funding, monthly cost, weekly cost (time), and perceived economic burden of the participants.

343 *Psychosocial assessment*

344 The final section of the questionnaire consists of six scales for the psychosocial  
 345 assessment. However, the coping strategy and burden of care scales differ between patients and  
 346 caregivers. The coping behaviour among the patients will be evaluated by the Malay version  
 347 of the Brief Coping Orientation to Problems Experienced Inventory (Brief-COPE), which is  
 348 comprised of 28 items with 14 dimensions: self-distraction, active coping, denial, substance  
 349 use, use of emotional support, use of instrumental support, behavioural disengagement, venting,  
 350 positive reframing, planning, humour, acceptance, religion, and self-blame.[65] The Malay  
 351 version of the Brief-COPE, which has been validated by Malaysian breast cancer women  
 352 patients, has good internal consistency ( $\alpha=.51$  to  $.99$ ).[66] Meanwhile, the Caregiver Cope  
 353 (CgCope™) questionnaire, developed by Ibrahim and colleagues,[67] will be used to assess  
 354 the coping strategies employed by the caregivers. This questionnaire consists of 19 items, with  
 355 six domains of coping strategies, namely, distraction, caring for the patient, venting, religion,  
 356 recreation, and social support. The participants will be rated based on a 5-point Likert scale (1

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357 = I have never done this; 5 = I do this very frequently). The validation study conducted among  
358 caregivers of schizophrenia patients in Malaysia yielded Cronbach's alpha values ranging  
359 between .54 and .82.[67]

360 To assess the self-perceived burden among patients with ESRD, the Self-Perceived  
361 Burden Scale (SPBS) will be distributed to the patients.[11] The SPBS, which consists of 10  
362 items, is rated by a 5-point Likert scale (1 = Not at all; 5 = All the time). The Malay version of  
363 the 10-item SPBS utilised in the study by Ting et al.[68] revealed that this is a valid and reliable  
364 scale for urological cancer patients ( $\alpha = .99$ ). Meanwhile, the care burden on caregivers will be  
365 examined by 22 items in the Zarit Burden Interview (ZBI).[69] The participants will rate their  
366 burden on a 5-point Likert scale (0 = Rarely, 4 = Nearly always). In Malaysia, the Malay  
367 version of the ZBI (MZBI) has been validated by family caregivers of cancer patients, with the  
368 scale delivering a high internal consistency ( $\alpha = .89$ ).[70]

369 The 19-item Medical Outcome Study Social Support Survey (MOS-SSS) developed by  
370 Sherbourne and Stewart[71] will be used to examine the participants' perception of social  
371 support. This brief, multidimensional, self-administered scale, rated using a 5-point Likert scale  
372 (1 = None at all; 5 = Available at all times), measures four categories of social support:  
373 informational, instrumental, positive social interactions, and affectionate support. In Malaysia,  
374 the Malay version of the MOS-SSS has been validated through a sample of HIV patients. This  
375 Malay version of the survey portrayed good psychometric properties, with high Cronbach's  
376 alpha values for all the subscales ( $\alpha > .87$ ) and the overall scale ( $\alpha = .96$ ).[72]

377 The General Anxiety Disorder-7 (GAD-7), a screening tool and severity indicator  
378 developed by Spitzer et al.[73], will be used to assess the generalised anxiety disorder among  
379 the participants. The scale contains 7 items and is rated using a 4-point Likert scale (0 = Not at  
380 all; 3 = Nearly every day). The Malay version of the GAD-7, which has been validated through

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381 female patients in a government-funded primary care clinic, delivers a good internal  
382 consistency reliability ( $\alpha = .74$ ).[74]

383 The participants' severity of depression will be assessed through the Patient Health  
384 Questionnaire-9 (PHQ-9).[75] The PHQ-9 consists of 9 items and is rated using a 4-point Likert  
385 scale (0 = Not at all; 3 = Nearly every day). In Malaysia, the questionnaire has been validated  
386 through female patients in a primary care clinic, and the Malay version of the PHQ-9 shows a  
387 good internal reliability ( $\alpha = .70$ ).[76]

388 The 36-item Short Form Survey (SF-36) will be utilised to assess the health-related  
389 quality of life of the participants. The SF-36 consists of eight subscales for measuring different  
390 domains of health-related quality of life, namely, physical functioning (PF), role-physical (RP),  
391 bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional  
392 (RE), and mental health (MH). Also, two main component scores are derived from the eight  
393 subscales. These are the physical component summary (PCS), which consists of the PF, RP,  
394 BP, and GH, and the mental component summary (MCS), which consists of the VT, SF, RE,  
395 and MH.[77] The Malay version of the SF-36, which has been validated by post-coronary  
396 artery bypass grafting surgery (CABG) patients, delivers good internal consistency reliability,  
397 with Cronbach's alpha values ranging from .73 to .90 for the subscales.[78]

### 398 Phase 2: Qualitative Study

399 A focus group discussion schedule will be developed, based on a literature review and  
400 expert input by nephrologists in the research team. The questions for the focus group  
401 discussions will be tailored to elicit responses from the patients with ESRD and their caregivers  
402 regarding their psychosocial well-being and the economic burden being faced by them, and its  
403 impact on their quality of life. The focus group discussion schedule will be piloted among the  
404 caregivers and patients to examine the clarity and feasibility of the questions. The focus group  
405 discussions will be divided into five sections: demographic details, source of ESRD treatment



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406 funding, costs of ESRD management, the impact of their psychosocial well-being on their  
407 quality of life, and lastly, the impact of the economic burden experienced by them on their  
408 quality of life.

### 409 **Data Collection**

#### 410 Phase 1: Quantitative Study

411 Conventional paper-and-pencil/web-based questionnaires will be utilised. The response  
412 rate of the participants who respond positively out of those potentially eligible participants who  
413 are invited to be involved in the study will be recorded. Potential participants (patients),  
414 identified through referrals from nephrologists or nurses in the nephrology units, will be  
415 recruited during their dialysis treatments in the respective hospitals/dialysis centres. In contrast,  
416 potential participants (caregivers) will be approached whilst waiting for their patients'  
417 treatment to be completed. For the caregivers who are not present during the patients' treatment,  
418 the researchers will call them up or meet with them during the patients' subsequent treatment  
419 at the respective hospitals/dialysis centres. The recruitment process will progress with the  
420 researcher briefing the caregivers and patients on the aims and procedures of the study.  
421 Potential participants who respond in the affirmative as to whether they have been previously  
422 diagnosed with severe mental illness will be excluded from the study. Potential participants  
423 will be given ample time to consider their involvement in the study. Upon receiving their  
424 consent, the participants will be provided with a questionnaire, which can be completed in  
425 approximately 30 minutes. The researchers will entertain any questions the participants may  
426 have regarding the questionnaire. The completed questionnaires will be kept securely for the  
427 data analysis process. The criteria for the withdrawal of a subject include a situation whereby  
428 the participant voluntarily withdraws his/her consent to participate in the study or when the  
429 principal investigator, for any reason, ends the participation. Participants are free to withdraw  
430 from the study at any time by stating their intention to do so during the course of the survey or

431 by emailing the principal investigator, whose email address and telephone number are included  
432 in the informed consent form. As the calculation of the sample size takes into account the drop-  
433 out rate for participants, those who withdraw from the study will not be replaced.

#### 434 Phase 2: Qualitative Study

435 The response rate of participants who respond positively out of those potentially  
436 eligible participants who are invited to be involved in the study will be recorded. Potential  
437 participants from Phase 1 will be recruited purposively based on the inclusion and exclusion  
438 criteria for Phase 2 study. The researchers will brief the caregivers and patients on the aims and  
439 procedures of the study. Participants will be given sufficient time to consider their participation  
440 in the focus group discussions. The discussion will be held at a designated date, time, and venue  
441 to be decided by the researchers, and is anticipated to last for an hour. The discussions will be  
442 recorded, and the data will be transcribed verbatim, after which, the recording will be deleted,  
443 in keeping with established ethical standards. The subject withdrawal criteria include a  
444 situation where the participant voluntarily withdraws his/her consent to participate in this study  
445 or when the principal investigator, for any reason, ends the participation. Participants are free  
446 to withdraw from the study at any time by stating their intention to do so during the course of  
447 the discussion or by emailing the principal investigator, whose email address and telephone  
448 number are included in the informed consent form. The arrival at the data saturation point will  
449 not be affected by the withdrawal of a participant(s), who will not be replaced.

#### 450 Data Analysis

##### 451 Phase 1: Quantitative Study

452 The IBM Statistical Package for the Social Sciences (SPSS) software for Windows  
453 (version 27)[79] will be utilised for the data processing, while descriptive statistics,  
454 independent sample *t*-tests and multiple regression analyses will be utilised for the data analysis.  
455 The statistical significance will be set at .05, and descriptive statistics will be used to compute

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456 the frequencies, percentages, means, and standard deviation, and to summarise the data from  
457 the respondents. To answer Objectives 1 and 2, which are to examine the differences in the  
458 treatment modalities on the participants' psychosocial factors, economic factors and quality of  
459 life, independent sample *t*-tests will be conducted between caregivers of haemodialysis and  
460 peritoneal dialysis patients (Objective 1) and between haemodialysis and peritoneal dialysis  
461 patients (Objective 2).

462 To answer Objectives 3 and 4, two multiple linear regression models will be fitted to  
463 examine the association between the psychosocial factors (depression, anxiety, coping  
464 strategies, social support, burden of care, and self-perceived burden), economic factors and the  
465 quality of life of caregivers (Objective 3) and patients with ESRD (Objective 4), whilst  
466 adjusting for potential demographic and clinical confounding factors (age, gender, race,  
467 religion, marital status, education level, occupation, monthly household income, relationship  
468 with patient/caregiver, method of dialysis, duration of dialysis, frequency of dialysis, and  
469 duration of care extended by caregivers) (Figure 1).

### 470 Phase 2: Qualitative Study

471 This qualitative study will facilitate an in-depth examination of the participants'  
472 perception of their psychosocial well-being and economic burden in the management of ESRD  
473 and its impact on their quality of life. A thematic analysis approach will be employed to analyse  
474 the data from the focus groups.[80-81] The data from the focus groups will be audio recorded  
475 and then transcribed accordingly. A copy of the transcripts will be given to the participants  
476 involved in the focus groups for feedback and approval before the analysis is carried out. For  
477 storage purposes, the data will be kept in a safety cabinet with a passcode, and only the research  
478 team will have access to the stored data. An initial reading of the focus group transcripts will  
479 be carried out. The transcripts will be re-read and coded individually to identify the key  
480 components of the psychosocial well-being, economic burden, and quality of life of

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481 participants. The data will be analysed by a team of researchers using NVivo software for  
482 Windows (version 11) (update 4).[82] The coding process begins with open coding by coding  
483 lines, statements and/or paragraphs. The data analysis will be considered to have reached  
484 saturation point when no new categories emerge. Each transcript will be coded and recoded  
485 several times.[81]

486 Next, a cross-validation to check the coding and transcripts will be undertaken by an  
487 independent rater, who will be provided with six interview transcripts. The independent rater's  
488 task will have to conduct a thematic analysis and check the appropriateness of that analysis.  
489 The independent rater's feedback will be compared with the identified themes. Any  
490 disagreements that may emerge in terms of sub-themes and themes will be discussed with the  
491 independent rater, and will be resolved through discussions with the independent rater and  
492 feedback from the research team.

### 493 Triangulation

494 Triangulation will be used in this research to gain a more accurate understanding of the  
495 phenomena being studied, i.e., the psychosocial well-being, economic burden and the impact  
496 of these on the quality of life of caregivers and patients. These phenomena will be examined  
497 from different methodological angles using quantitative and qualitative methods.[83] This  
498 approach will provide the means to verify and/or interrogate the data, thereby increasing the  
499 confidence in the results. Therefore, two types of triangulations will be involved. The first type  
500 is data triangulation using different approaches (quantitative and qualitative designs) in which  
501 information will be gathered from different sources, namely the participants (caregivers and  
502 patients), discussions and feedback from the research team, and with the participation of an  
503 independent rater or checker for the analysis. The second type is investigator triangulation, in  
504 which different investigators (i.e., student researchers, supervisors) will be involved in the data  
505 collection and an independent rater will participate in the data analysis. The use of two or more

investigators independently can lead to more valid and reliable data,[84] and checking for divergences between researchers will result in minimal divergence, i.e., reliability.

## IMPLICATIONS OF THE STUDY

As far as is known, there is a lack of studies focusing on the ESRD population in Malaysia. Therefore, this will be a pioneer study that includes mixed methods of quantitative and qualitative study designs to evaluate the psychosocial factors, economic factors, and quality of life of patients with ESRD and their caregivers. Apart from that, this study incorporates the perspectives of both the patients and caregivers, hence providing a more in-depth understanding and overview of the psychosocial well-being and economic burden being faced by them in terms of illness management and the impact of these on their quality of life. Garnering the perspectives of both the caregivers and patients and examining the factors associated with their quality of life will further the understanding that caregivers and their patients function as an interdependent unit rather than as separate entities. Therefore, intervention programmes addressing the psychosocial and economic well-being of ESRD patients and their caregivers should be carried out together. Additionally, study variables of populations within different treatment modalities, namely haemodialysis and peritoneal dialysis, can be examined, thus, providing a wider range of perspectives. Individuals who are choosing or are advised to take up haemodialysis or peritoneal dialysis will be able to understand the psychosocial and economic burdens of each treatment modality, and its impact on their quality of life. This will better prepare them to face these difficulties. Through this study, future researchers will have an enhanced understanding of these phenomena and may be able to navigate them to develop intervention programmes that focus on the well-being of the patients and their caregivers. From the perspective of hospitals, patient education programmes can be shaped based on the information obtained to prepare and support individuals who plan to or are undergoing the two treatment modalities. By making a comparison between

531 haemodialysis and peritoneal dialysis, this study will provide society and policymakers with a  
532 better understanding of the treatment modalities so as to have a better impact on the  
533 psychosocial well-being and quality of life of both the patients and caregivers. Also, this study  
534 can provide an in-depth insight into the psychosocial and economic burden faced by the  
535 patients and caregivers in the management of this illness. Thus, it might contribute crucial  
536 knowledge to the Malaysian government and non-governmental organisations in providing aid  
537 and resources on a macro level to those who are financially burdened and improvise the quality  
538 of life of both patients with ESRD and their caregivers.

## 539 **ETHICS AND DISSEMINATION**

### 540 **Ethics Approval**

541 The work has been approved by the Medical Research and Ethics Committee (MREC)  
542 [NMRR-21-1012-59714] and the research ethics committees of Hospital Canselor Tuanku  
543 Muhriz UKM (HCTM) [UKM PPI/111/8/JEP-2021-078] and the University of Malaya  
544 Medical Centre (UMMC) [MREC ID NO: 202178-10346]. Also, the relevant permission and  
545 approvals have been obtained from the directors of Hospital Selayang (HSEL) and Hospital  
546 Kuala Lumpur (HKL).

### 547 **Ethical Considerations**

548 The researchers will adhere to the principles of the Declaration of Helsinki[85] and the  
549 Malaysian Good Clinical Practice Guidelines.[86] The privacy of the participants will be  
550 protected during the data collection process by separating the informed consent forms from the  
551 paper-based questionnaire responses. All the documents will be deposited in a secure cabinet,  
552 and all the data will be stored in a password-protected computer to which only the researchers  
553 will have access. All the documents and data will be stored for seven years, after which they  
554 will be shredded and deleted. No participant identifiers (name, identity card number, address,  
555 phone number) will be traceable, and a unique study ID will be assigned. No medical records

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556 will be accessible. Participants will have no access to any personal information, and to ensure  
557 the element of anonymity, they will not be informed of the study findings.

558 **Dissemination**

559 The findings from this study will be published in peer-review scientific journals and at  
560 national or international conferences. Minimal anonymised data will be uploaded as  
561 supplementary material for review purposes in scientific journal publications or conferences,  
562 and these will adhere strictly to the ethical principles stipulated. Only group data will be  
563 published, and no personal identifier will be collected or made public. The relevant permission  
564 will be obtained from all the parties involved before any publication. The findings from this  
565 study can serve as a guide for Malaysian policymakers, healthcare providers, and society to  
566 improve the quality of life of patients with ESRD and their caregivers through the engagement  
567 of constructive and holistic interventions.

568 **Contributors**

569 All authors were involved in writing the study protocol. SYC and NI drafted the manuscript.  
570 CSS, NA, RI and AHAG provided critical revision and feedback of the manuscript. All authors  
571 have read and approved the final manuscript.

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576 **Competing interests**

577 The authors declared that there is no conflict of interest.

578 **Provenance and peer-review**

579 Not commissioned, externally peer-reviewed.

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## Psychosocial and Economic Factors on the Quality of Life of Patients with ESRD and Caregivers

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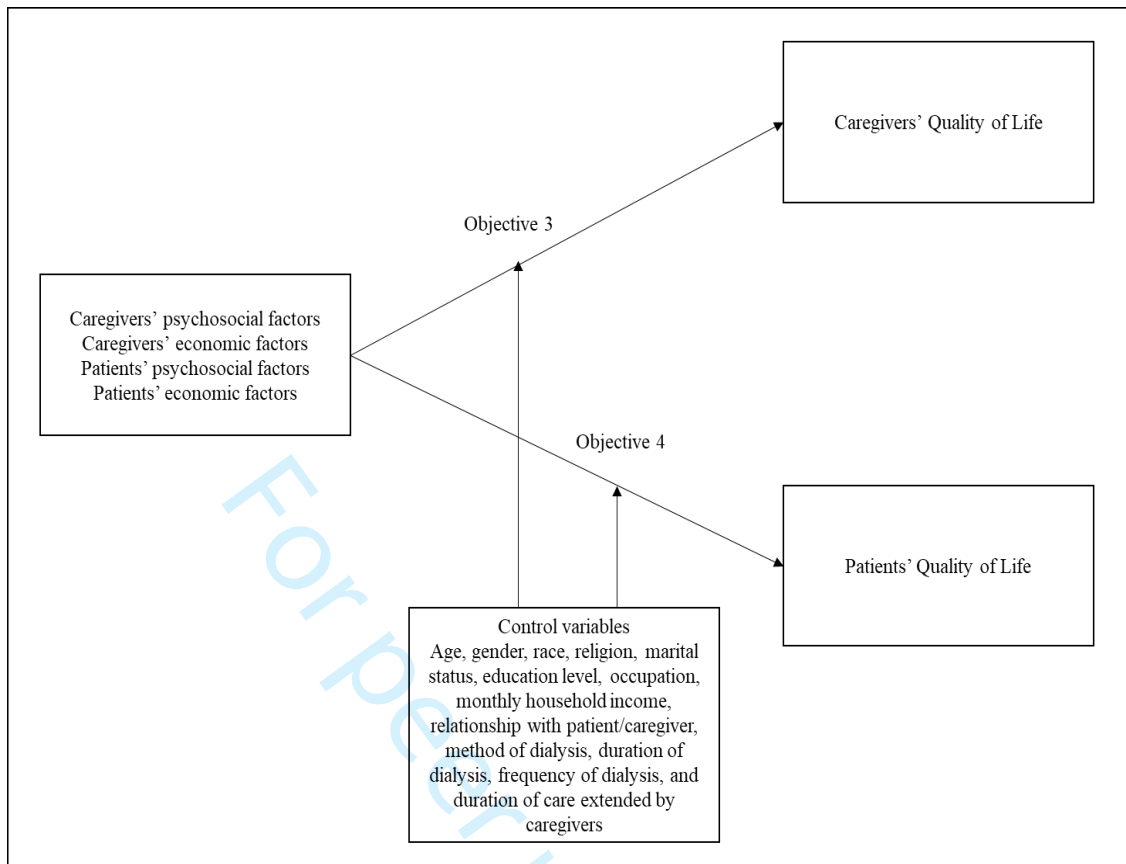
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798 **Figure – legend**

799 Figure 1. Analytic plan for Objective 3 and Objective 4 of the study. Two multiple linear  
800 regression models will be fitted to examine the association between the psychosocial factors  
801 (depression, anxiety, coping strategies, social support, burden of care, and self-perceived  
802 burden), economic factors and the quality of life of caregivers (Objective 3) and patients with  
803 ESRD (Objective 4), whilst adjusting for potential demographic and clinical confounding  
804 factors (age, gender, race, religion, marital status, education level, occupation, monthly  
805 household income, relationship with patient/caregiver, method of dialysis, duration of dialysis,  
806 frequency of dialysis, and duration of care extended by caregivers).



**Figure 1. Analytic plan for Objective 3 and Objective 4 of the study**

# BMJ Open

## The effects of psychosocial and economic factors on the quality of life of patients with end-stage renal disease and their caregivers in the Klang Valley, Malaysia: protocol for a mixed-methods study

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Keywords:	MENTAL HEALTH, Dialysis < NEPHROLOGY, End stage renal failure < NEPHROLOGY, Chronic renal failure < NEPHROLOGY, Adult nephrology < NEPHROLOGY

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10 3 **The effects of psychosocial and economic factors on the quality of life of**  
11 4 **patients with end-stage renal disease and their caregivers in the Klang**  
12 5 **Valley, Malaysia: protocol for a mixed-methods study**  
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18 7 Norhayati Ibrahim<sup>1,2</sup>, Sin Yee Chu<sup>1\*</sup>, Ching Sin Siau<sup>3</sup>, Noh Amit<sup>3</sup>, Rozmi Ismail<sup>4</sup>, Abdul Halim  
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57 24 Word count: 5639 words  
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3 26 **ABSTRACT**  
4

5 27 **Introduction:** The number of patients in Malaysia requiring dialysis is expected to rise  
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8 28 substantially in the future due to the ageing population and increasing prevalence of diabetes  
9  
10 29 mellitus and hypertension. Hence, more individuals will be expected to adopt the role of  
11  
12 30 caregivers in the future. The upward trend of end-stage renal disease (ESRD) and caregiving  
13  
14 31 for dialysis patients has detrimental consequences for both patients and caregivers in terms of  
15  
16 32 their psychological well-being and quality of life. Despite the current circumstances, there are  
17  
18 33 very few studies in Malaysia that have explored the psychosocial factors, specifically on the  
19  
20 34 economic impact of the management of ESRD.  
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24 35 **Methods and analysis:** This two-phase sequential explanatory mixed-methods design,  
25  
26 36 incorporating a quantitative design (Phase 1) and a qualitative study (Phase 2), is to be  
27  
28 37 conducted in four government hospitals and ten other non-governmental organisations or  
29  
30 38 private dialysis centres within the Klang Valley, Malaysia. A cross-sectional survey (Phase 1)  
31  
32 39 will include 236 patient-caregiver dyads, while focus group discussions (Phase 2) will include  
33  
34 40 30 participants. The participants for both phases will be recruited purposively. Descriptive  
35  
36 41 statistics, independent sample t-tests, and multiple regression analysis will be used for analyses  
37  
38 42 in Phase 1, and thematic analysis will be used in Phase 2.  
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42 43 **Ethics and dissemination:** Approval for the study has been obtained from the National  
43  
44 44 Medical Research and Ethics Committee (MREC) [NMRR-21-1012-59714] and the Research  
45  
46 45 Ethics Committee of Hospital Canselor Tuanku Muhriz UKM (HCTM) [UKM PPI/111/8/JEP-  
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48 46 2021-078] and University of Malaya Medical Centre (UMMC) [MREC ID NO: 202178-  
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50 47 10346]. The informed consent of the participants will be obtained beforehand, and no personal  
51  
52 48 identifiers will be obtained from the participants to protect their anonymity. The findings will  
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54 49 be published in peer-reviewed scientific journals and presented in national or international  
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56 50 conferences with minimal anonymised data.  
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3 51 **ARTICLE SUMMARY**  
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5 52 **Strengths and limitations of this study**  
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- 8 53 ● This study will, to our knowledge, be the first in Malaysia to utilise the sequential mixed-  
9 54 methods approach to examine the psychosocial factors, economic factors, and quality of  
10 55 life of patients undergoing haemodialysis and peritoneal dialysis treatments and their  
11 56 caregivers.  
12  
13 57 ● The inclusion of both patients and caregivers in the study will provide more a  
14 58 comprehensive and holistic perspective of the management of ESRD in Malaysia.  
15  
16 59 ● This research will scrutinise the psychosocial well-being, economic burden, and  
17 60 complications involved in ESRD management to provide a comprehensive finding on their  
18 61 impact on the quality of life of the participants.  
19  
20 62 ● The study will be restricted to the vicinity of the Klang Valley, so the findings may not be  
21 63 applicable in other Malaysian states; restricted dissemination of the paper-and-pen or web-  
22 64 based questionnaires to a population of participants who are able to communicate or read  
23 65 in the Malay language may lead to the omission of unique perspectives from the non-  
24 66 Malay literate population.  
25  
26 67 ● Purposive sampling will be used to recruit the participants for the survey, and the  
27 68 recruitment method is not intended to ensure a representative sample—as such, the  
28 69 findings from the quantitative survey will have limited generalisability.  
30 70

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33 71 **Keywords:** Burden of care, quality of life, end-stage renal disease (ESRD), patient, caregiver  
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## 72 INTRODUCTION

73 According to the Global Burden of Disease, chronic kidney disease (CKD) is ranked among  
74 the top 20 causes of death, and is currently a significant public health concern.[1] CKD is  
75 regarded as a high-stress illness due to the chronicity of the disease and the long-term treatment  
76 required,[2] where end-stage renal disease (ESRD) is considered as the last stage of CKD.[3]  
77 In Malaysia, the incidence and prevalence of patients with ESRD have been showing an upward  
78 trend for the past 20 years. [4] due to the ageing population and the increasing prevalence of  
79 diabetes mellitus (DM) and hypertension [3]. In 2018, the 24th Report of the Malaysian  
80 Dialysis and Transplant Registry revealed that over the preceding ten years, the acceptance rate  
81 for both haemodialysis (HD) and peritoneal dialysis (PD) has nearly doubled, while the  
82 prevalence rate has increased by more than two-fold. A total of 39,711 patients received  
83 dialysis treatment in 2016, with 35,781 and 3930 patients being on HD and PD, respectively.If  
84 the present trend remains unchecked, it is anticipated that by 2040, there will be more than  
85 106,000 Malaysian patients with ESRD requiring dialysis. With this projected prevalence, the  
86 cost to the healthcare system is estimated to be RM 3.21 billion.[4] It is to be expected that  
87 more individuals will be adopting the caregiver role in the future due to the rising number of  
88 renal failure patients.[1]

89 Caregivers refers to those who are actively involved in helping patients to cope with  
90 and manage their chronic illness during their treatment.[5] The chronicity of kidney failure and  
91 various treatment complications bring about significant changes in the lifestyles of patients,  
92 leading to caregivers having to shoulder a high burden of care.[6] This burden of care is  
93 common among caregivers, and it typically refers to the kind of distress, comprised of physical,  
94 psychological, social, and financial aspects, faced by them as a result of caregiving.[7-8] The  
95 care burden among caregivers is often inter-related with the socio-demographics (age, gender,  
96 ethnicity, marital status, education, employment, income and religion/spirituality) of the

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3 97 caregivers and patients, disease-related factors (treatment modality, frequency of weekly  
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5 98 dialysis sessions, duration and frequency of dialysis, duration of illness, comorbidity, level of  
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7 99 patient's dependency), situational and relational factors (relationship to the patient, the duration  
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9  
10 100 of caregiving), environmental factors, including social support, and psychological factors  
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12 101 including depression and anxiety.[9] Past literature has shown evidence that caregivers who  
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14 102 seek social support from family and friends experience a lesser burden of care than caregivers  
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16 103 without solid support networks.[10] This is because social support can diminish the impact of  
17  
18 104 the emotional burden and stress of care by providing solutions to problems, distractions from  
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20 105 issues, or facilitating the required healthy behaviours.[11-12] Similarly, Nagarathnam,  
21  
22 106 Sivakumar, and Latheef[13] stated that seeking social support is the dominant coping  
23  
24 107 mechanism in caregivers of patients undergoing renal replacement therapy. Also, it has been  
25  
26 108 established that caregivers of chronic patients are four times more likely to be diagnosed with  
27  
28 109 depression and three times more likely to seek help for anxiety issues than individuals who are  
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30 110 not caregivers.[14]

35 111 There is a high correlation between the psychological well-being of caregivers and  
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37 112 patients. Gerogianni et al.[15] stated that caregivers have higher levels of anxiety and  
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39 113 depression when dialysis patients under their care are having high levels of anxiety and  
40  
41 114 depression. In line with this study, past studies also reported that caregivers of haemodialysis  
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43 115 have deteriorated psychological well-being compared to caregivers of peritoneal dialysis or  
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45 116 kidney transplant patients.[16-17] Due to the reason that patients under haemodialysis  
46  
47 117 treatment were perceived to be more difficult to care for compared to patients under treatment  
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49 118 for other modalities.[18] In contrast, Al Wakeel and Bayoumi[19] and Cantekin, Kavurmacı,  
50  
51 119 and Tan[20] suggested evidence that a higher burden of care was observed among caregivers  
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53 120 of peritoneal dialysis patients than caregivers of patients undergoing haemodialysis treatment.  
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55 121 The educational level, age, health, and capability of the patient with regard to self-care serve  
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3 122 as the determinants of the burden of care among caregivers.[19-20] Notably, caregivers of  
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5 123 dialysis patients reportedly have a lower quality of life than caregivers of non-dialysis  
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7 124 patients.[21] The quality of life of caregivers with patients undergoing haemodialysis was  
8  
9 125 reported to be lower in all aspects compared to the general healthy population due to the high  
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11 126 burden of care[22]; however, the quality of life of these caregivers was higher than the patients  
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13 127 under their care. [8] Conversely, Monárrez-Espino, Delgado-Valles and Ramírez-García[17]  
14  
15 128 concluded that there is no significant difference in terms of quality of life between caregivers  
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17 129 of haemodialysis and peritoneal dialysis patients.

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21 130 Generally, ESRD is highly burdensome in the daily lives of patients and is also time-  
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23 131 consuming, especially among elderly HD patients, resulting in patients experiencing frustration  
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25 132 and causing them to perceive that they are a burden to their family members.[23] This self-  
26  
27 133 perceived burden arises when the recipients of care possess feelings of dependence, frustration,  
28  
29 134 and anxiety, leading to guilt about the hardship being imposed on the caregiver.[24] The  
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31 135 incidence and prevalence of ESRD have adverse effects on the psychological well-being of  
32  
33 136 both patients and their caregivers,[15, 18, 25-27] and their quality of life.[8, 21] Compared to  
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35 137 their caregivers, patients with ESRD are more prone to depression and a lower quality of  
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37 138 physical and psychological well-being.[18] The prevalence of depression among patients with  
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39 139 ESRD is estimated to be around 20% to 30%, whereas their level of anxiety ranges between 12%  
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41 140 and 52%.[26] Depression and anxiety symptoms occur more frequently among patients  
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43 141 undergoing dialysis than patients who have undergone kidney transplantation.[28] Also,  
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45 142 patients under peritoneal dialysis have also been reported to have significantly higher levels of  
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47 143 depression symptoms than those on haemodialysis.[29] Conversely, a qualitative study showed  
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49 144 evidence that both haemodialysis and peritoneal dialysis patients frequently experience  
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51 145 depression along with other psychological problems, such as decreased social support, burnout,  
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53 146 despair, and anxiety.[30] Apart from these, patients and their caregivers have to face high  
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3 147 treatment costs, out-of-pocket costs, and other comorbidities that arise, which can be  
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5 148 overwhelming and cause those in low or middle-income families to bear a financial burden.[31]  
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7 149 Based on past literature in other countries, the high treatment costs have led to numerous  
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9 150 caregivers having to suffer a financial burden and to willingly mortgage their valuable items to  
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11 151 cover those costs.[32-33] In contrast to these studies, Mohd Fadzli, Mohd Rasani and Keng[31]  
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13 152 stated that Malaysian patients and caregivers who are reportedly being fully-funded for their  
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15 153 treatment may not face a financial burden, but those belonging to low-income families  
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17 154 experience a tremendous financial burden. Mixed findings have been reported when comparing  
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19 155 the quality of life of haemodialysis and peritoneal dialysis patients. Al Wakeel et al.[34] and  
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21 156 Hsu et al.[35] found that peritoneal dialysis patients have a better quality of life than those on  
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23 157 haemodialysis. Alternatively, Gonçalves et al.[36] concluded that haemodialysis has a better  
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25 158 significant influence on the quality of life of patients compared to peritoneal dialysis as the  
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27 159 physical functioning and emotional functioning aspects have been reported to be higher among  
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29 160 haemodialysis patients. Meanwhile, several past literatures have suggested evidence that there  
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31 161 is no significant difference between the levels of quality of life between the two different  
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33 162 dialysis modalities [29, 37-38]. The factors contributing to a lower quality of life among  
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35 163 dialysis patients have been identified as the increasing prevalence of depression, anxiety, and  
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37 164 suicidal ideation.[39] Conversely, perceived social support serves as a protective factor against  
38  
39 165 a low quality of life among patients.[40-41] A high perception of social support can reduce the  
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41 166 risk of hospitalisation among haemodialysis patients by 15%, along with improving their  
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43 167 quality of life.[42] Also, a conducive environment helps haemodialysis patients to take a more  
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45 168 positive attitude towards their disease, including improving their coping strategies.[43]  
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54 169 Despite the mixed findings, there is still a dearth of research, particularly with regard  
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56 170 to the psychosocial factors and the economic impact of ESRD among patients and caregivers  
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58 171 in Malaysia. Studies focusing on the well-being of Malaysian patients with ESRD are sorely  
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3 172 lacking, and almost non-existent in the case of caregivers. Therefore, there is a need for further  
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5 173 investigations to be carried out in this area, particularly with regard to the quality of life, burden  
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8 174 of care, depression, anxiety, coping mechanisms, and social support of patients and their  
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10 175 caregivers. Another neglected area has to do with the economic burden faced by patients with  
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12 176 ESRD and their caregivers with regard to the management of this disease. As far as is known,  
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15 177 thus far, no studies have been conducted in the Southeast Asian region on the economic costs  
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17 178 incurred by patients with ESRD and their caregivers. Given this situation, this study will  
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19 179 compare the psychosocial factors, economic factors, and quality of life of patients with ESRD  
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21 180 undergoing HD and PD treatment modalities and their caregivers. Apart from that, the  
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24 181 associations between demographic factors, psychosocial factors, economic factors and quality  
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26 182 of life among caregivers and patients with ESRD will be examined. Lastly, the perception of  
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28 183 psychosocial well-being and economic burden in the management of the illness and its impact  
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30 184 on the quality of life of patients with ESRD and their caregivers will be explored in-depth.

### 33 185 **Study objectives**

35 186 Phase 1 of this study focuses on the following objectives:

- 37 187 1. To compare the psychosocial factors, economic factors, and quality of life between  
38 188 caregivers of patients undergoing haemodialysis and caregivers of patients undergoing  
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40 189 peritoneal dialysis.
- 42 190 2. To compare the psychosocial factors, economic factors, and quality of life between  
43  
44 191 patients undergoing haemodialysis and patients undergoing peritoneal dialysis.
- 46 192 3. To determine the variables (demographic, psychosocial and economic factors)  
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48 193 associated with quality of life among caregivers of patients with ESRD.
- 50 194 4. To determine the variables (demographic, psychosocial and economic factors)  
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52 195 associated with quality of life among patients with ESRD.

54 196 Phase 2 of this study focuses on the following objective:

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3 197 1. To explore the perceptions of patients with ESRD and their caregivers regarding their  
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5 198 psychosocial well-being and economic burden in the management of ESRD and its  
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8 199 impact on their quality of life  
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## 10 200 **METHODS AND ANALYSIS**

### 11 12 201 **Design and methods**

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14 202 This study involves the use of a sequential explanatory mixed methods design incorporating  
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16 203 methodological and investigator triangulation. Phase 1 of the study involves the collection of  
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18 204 quantitative data, while Phase 2 has to do with a qualitative study.[44] Generally, an  
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20 205 explanatory design is used when researchers need qualitative data to expand on or explain their  
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22 206 initial quantitative findings[45] or when quantitative results are required to direct the selection  
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24 207 of participants for a qualitative study.[46] Thus, the collection of qualitative data emerges from  
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26 208 and is linked to the quantitative results.[47] Therefore, due to the rigidity of the questionnaire  
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28 209 in Phase 1, a sequential explanatory mixed methods study design is imperative in this study to  
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30 210 elicit more in-depth information, specifically on the psychosocial well-being and economic  
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32 211 factors faced by the participants. Thus, Phase 2 will be conducted to elicit more in-depth  
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34 212 information from the participants and to gain a better overall understanding of the phenomena  
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36 213 being studied. Doyle, Brady, and Byrne[48] stated that a sequential explanatory mixed methods  
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38 214 design is used to substantiate the findings from a quantitative study by providing supporting  
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40 215 evidence from the findings of a qualitative study. However, triangulation involving a mixed  
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42 216 methods design increases the credibility and validity of the research findings.[49] In Phase 1,  
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44 217 a cross-sectional survey will be conducted among patients with ESRD and their caregivers. A  
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46 218 cross-sectional approach is preferred as it saves time in terms of the distribution of  
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48 219 questionnaires and the collection of information from a sizeable number of participants.[50]  
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50 220 Meanwhile, in Phase 2, a qualitative study will be conducted involving focus group discussions  
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52 221 among patients with ESRD and their caregivers. A focus group discussion approach can give  
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3 222 a fruitful and in-depth understanding of an individual's experiences and perceptions of a  
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5 223 specific phenomenon.[51] Furthermore, compared to individual interviews with participants,  
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7 224 focus groups tend to provide more ideas and information.[52] The focus group discussions will  
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9 225 enable the participants to consider and share their perspectives regarding the psychosocial well-  
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11 226 being and economic burden they have to undertake when it comes to the management of ESRD  
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13 227 and the impact of these on their quality of life. The data findings from Phase 1 and Phase 2 of  
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15 228 the study will be integrated through the triangulation process to provide a more holistic and  
16  
17 229 comprehensive insight into the psychosocial factors, economic factors and quality of life  
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19 230 experienced by caregivers and their ESRD patients undergoing different treatment modalities.  
20  
21 231 This mixed methods integration technique will be able to answer the objectives of this study.[44]  
22  
23 232 Also, the role of triangulation in the mixed methods study will be beneficial in confirming the  
24  
25 233 findings, providing more comprehensive data, increasing the validity, and enhancing the  
26  
27 234 understanding of the phenomena being studied.[53]

### 235 **Study setting**

236 The investigation will be conducted in the nephrology units of Hospital Canselor Tuanku  
237 Muhriz UKM (HCTM), Hospital Selayang (HSEL), Hospital Kuala Lumpur (HKL), and the  
238 University of Malaya Medical Centre (UMMC), along with ten other non-governmental  
239 organisations (NGOs) or private dialysis centres in the Klang Valley, Malaysia. The hospitals  
240 were chosen purposively based on their location in the Klang Valley, and are specialist  
241 hospitals, non-governmental organisations (NGO), and private centres offering dialysis  
242 treatment for patients with ESRD.

### 243 **Milestones and timelines**

244 The literature review for this study has been completed, and currently, this research is in the  
245 pilot testing stage. The pilot study to test the validity and reliability of the instruments for the  
246 quantitative data collection in the main study is expected to be completed in two months. The

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3 247 quantitative data collection will take approximately three months to be completed, and the  
4  
5 248 qualitative data collection, which will last for two months, will commence once the quantitative  
6  
7  
8 249 data collection is finalised. The expected timeline for the completion of this study is  
9  
10 250 approximately seven months, with the final manuscript expected to be completed in October  
11  
12 251 2022.

### 14 252 **Patient and public involvement**

16  
17 253 One patient, caregiver, health psychologist, and two formal care providers (namely, a  
18  
19 254 nephrologist and a dialysis nurse) will be recruited to form the Advisory Committee. This  
20  
21 255 committee will be tasked with reviewing the protocol and structuring the interview schedule  
22  
23 256 and questionnaire to provide the design for the study. The Advisory Committee will also be  
24  
25  
26 257 referred to for advice and feedback, whenever necessary, throughout this study.

### 28 258 **Participants and recruitment**

30 259 Patients with ESRD and their caregivers will be recruited in dyads in both phases of the study.  
31  
32 260 Specifically, potential patients in Phase 1 will be recruited purposively through referrals from  
33  
34 261 nephrologists or nurses in the nephrology units. In contrast, the caregivers in Phase 1 will be  
35  
36 262 recruited purposively through referrals from the patients themselves. This sampling method  
37  
38 263 will ensure that the data accumulated from the participants will be effective, efficient, and cost-  
39  
40 264 effective.[54] However, the participants in Phase 2 will be a subset of the participants in Phase  
41  
42 265 1. The participants in Phase 2 will be selected purposively to share their views on their  
43  
44 266 psychosocial well-being, economic burden, and quality of life in focus group discussions to  
45  
46 267 ensure that different perspectives are represented. The demographic variables to be considered  
47  
48 268 are age group (young adults, middle-aged adults, and older adults), and gender (male and  
49  
50 269 female). A set of inclusion and exclusion criteria will be utilised within the overall eligible  
51  
52 270 population to ensure that the samples fulfil the aims of this study. The inclusion and exclusion  
53  
54 271 criteria for both phases are similar. Patients have to fulfil these criteria: ESRD diagnosis, above  
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2  
3 272 18 years old, Malaysian nationality, and currently receiving treatment at a hospital, an NGO  
4  
5 273 establishment, or a private dialysis centre in the Klang Valley. It is also essential that the  
6  
7 274 potential participants are able to communicate in and read Bahasa Malaysia, the national  
8  
9 275 language of Malaysia. All patients diagnosed with ESRD and their caregivers are welcome to  
10  
11 276 participate in this study. There is no restriction on the duration of the patients' initiation to  
12  
13 277 dialysis in order to recruit a wide range of study participants. However, patients exhibiting  
14  
15 278 severe mental illness or those who have undergone a kidney transplant will be excluded from  
16  
17 279 the study. As for the recruitment of caregivers, they must be above 18 years of age and verified  
18  
19 280 as the family caregiver of an ESRD patient currently undergoing dialysis treatment at a hospital,  
20  
21 281 an NGO establishment, or a private dialysis centre in the Klang Valley. The caregiver is also  
22  
23 282 required to have undergone the experience of accompanying the patient for dialysis treatment  
24  
25 283 at least once, and must be able to read and communicate in Bahasa Malaysia. Formal caregivers,  
26  
27 284 caregivers of patients who have undergone a kidney transplant, or caregivers exhibiting  
28  
29 285 symptoms of severe mental illness will be excluded from the study.  
30  
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34

### 35 286 **Sample size**

#### 36 37 287 Phase 1: Quantitative study

38  
39 288 The proposed quantitative study sample size calculation is based on the multiple linear  
40  
41 289 regression formula by Tabachnick and Fidell,[55] which is expressed as  $N > 50 + 8m$ , where  
42  
43 290  $m$  is the number of predictors. This study will include six predictors (depression, anxiety,  
44  
45 291 coping strategies, social support, burden of care, and economic burden), and the sample size,  
46  
47 292 based on the calculation by Tabachnick and Fidell,[55] is estimated to be 98 participants.  
48  
49 293 However, as the participants are to be recruited in dyads, it is assumed that there will be 98  
50  
51 294 pairs of patients and caregivers. Besides that, the estimated sample size is also calculated via a  
52  
53 295 power analysis using the G\* Power programme for the F test (multiple linear regression: fixed  
54  
55 296 model,  $R^2$  deviation from zero) with an effect size of 0.15 (medium),  $\alpha$  at 0.05, power at 0.80  
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1  
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3 297 and six predictors. Similarly, the power analysis estimated a minimum sample size of 98, which  
4  
5 298 corresponded with the estimated sample size by Tabachnick and Fidell.[55] For this study,  
6  
7 299 taking into consideration the drop-out rate, non-response rate, and incomplete submission of  
8  
9 300 data by participants, the sample size for this study has been increased by 20%.[56-57] Hence,  
10  
11 301 118 pairs of haemodialysis patients-caregivers and 118 pairs of peritoneal dialysis patients-  
12  
13 302 caregivers (N = 236 pairs), which is equivalent to a sample size of 472 participants, will be  
14  
15 303 recruited for the quantitative study.  
16  
17  
18

#### 19 304 Phase 2: Qualitative study

20  
21 305 A qualitative study typically emphasises data saturation, where the saturation point is achieved  
22  
23 306 when no new information, ideas or themes are forthcoming from the participants.[58] Data  
24  
25 307 saturation can be identified within five[59] or three to six focus group discussions[60] with a  
26  
27 308 minimum of four and a maximum of twelve participants in a group.[61] This process is typical  
28  
29 309 for qualitative studies, whereby the emphasis is on arriving at the saturation point. Therefore,  
30  
31 310 based on past literature, six focus group discussions will be conducted in this research, with  
32  
33 311 each group being comprised of at least five participants for this qualitative study. Hence, a  
34  
35 312 minimum of 30 participants (15 patients and 15 caregivers) will be involved in the focus group  
36  
37 313 discussions.  
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40

#### 41 314 **Instruments**

##### 42 315 Phase 1: Quantitative study

43  
44 316 The web-based or paper-based questionnaire to be distributed to the participants consists of  
45  
46 317 three sections: demographic sheet, economic assessment, and psychosocial assessment (Table  
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48 318 1).  
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**Table 1. Summary of instruments for patient and caregiver participants**

	Patient	Caregiver
Demographic information	Age, gender, race, religion, marital status, education level, occupation, monthly household income, relationship with patient/caregiver, method of dialysis, duration of dialysis, frequency of dialysis, and duration of care extended by caregivers.	
Economic assessment	Source of funding, monthly cost, weekly cost (time), and perceived economic burden.	
Psychosocial assessment		
Coping behaviour	Brief Coping Orientation to Problems Experienced Inventory (Brief-COPE)	Caregiver Cope (CgCope™)
Perceived burden	Self-Perceived Burden Scale (SPBS)	Zarit Burden Interview (ZBI)
Social support	Medical Outcome Study Social Support Survey (MOS-SSS)	
Anxiety	General Anxiety Disorder-7 (GAD-7)	
Depression	Patient Health Questionnaire-9 (PHQ-9)	
Quality of life	Short Form Survey (SF-36)	

319

320 *Demographic information*

321 The demographic information of the patients and their caregivers, which will be collected  
 322 through the questionnaire, covers age, gender, race, religion, marital status, education level,  
 323 occupation, monthly household income, relationship with patient/caregiver, method of dialysis,  
 324 duration of dialysis, frequency of dialysis, and duration of care extended by caregivers.

325 *Economic assessment*

326 The second section of the questionnaire, the economic assessment, covers the source of funding,  
 327 monthly cost, weekly cost (time), and perceived economic burden of the participants.

328 *Psychosocial assessment*

329 The final section of the questionnaire consists of six scales for the psychosocial assessment.

330 However, the coping strategy and burden of care scales differ between patients and caregivers.

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2  
3 331 The coping behaviour among the patients will be evaluated by the Malay version of the Brief  
4  
5 332 Coping Orientation to Problems Experienced Inventory (Brief-COPE), which is comprised of  
6  
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8 333 28 items with 14 dimensions: self-distraction, active coping, denial, substance use, use of  
9  
10 334 emotional support, use of instrumental support, behavioural disengagement, venting, positive  
11  
12 335 reframing, planning, humour, acceptance, religion, and self-blame.[62] The Malay version of  
13  
14 336 the Brief-COPE, which has been validated by Malaysian breast cancer women patients, has  
15  
16 337 good internal consistency ( $\alpha=.51$  to  $.99$ ).[63] Meanwhile, the Caregiver Cope (CgCope™)  
17  
18 338 questionnaire, developed by Ibrahim and colleagues,[64] will be used to assess the coping  
19  
20 339 strategies employed by the caregivers. This questionnaire consists of 19 items, with six  
21  
22 340 domains of coping strategies, namely, distraction, caring for the patient, venting, religion,  
23  
24 341 recreation, and social support. The participants will be rated based on a 5-point Likert scale (1  
25  
26 342 = I have never done this; 5 = I do this very frequently). The validation study conducted among  
27  
28 343 caregivers of schizophrenia patients in Malaysia yielded Cronbach's alpha values ranging  
29  
30 344 between  $.54$  and  $.82$ .[64]

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34  
35 345 To assess the self-perceived burden among patients with ESRD, the Self-Perceived  
36  
37 346 Burden Scale (SPBS) will be distributed to the patients.[24] The SPBS, which consists of 10  
38  
39 347 items, is rated by a 5-point Likert scale (1 = Not at all; 5 = All the time). The Malay version of  
40  
41 348 the 10-item SPBS utilised in the study by Ting et al.[65] revealed that this is a valid and reliable  
42  
43 349 scale for urological cancer patients ( $\alpha = .99$ ). Meanwhile, the care burden on caregivers will be  
44  
45 350 examined by 22 items in the Zarit Burden Interview (ZBI).[66] The participants will rate their  
46  
47 351 burden on a 5-point Likert scale (0 = Rarely, 4 = Nearly always). In Malaysia, the Malay  
48  
49 352 version of the ZBI (MZBI) has been validated by family caregivers of cancer patients, with the  
50  
51 353 scale delivering a high internal consistency ( $\alpha = .89$ ).[67]

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55  
56 354 The 19-item Medical Outcome Study Social Support Survey (MOS-SSS) developed by  
57  
58 355 Sherbourne and Stewart[68] will be used to examine the participants' perception of social  
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2  
3 356 support. This brief, multidimensional, self-administered scale, rated using a 5-point Likert scale  
4  
5 357 (1 = None at all; 5 = Available at all times), measures four categories of social support:  
6  
7 358 informational, instrumental, positive social interactions, and affectionate support. In Malaysia,  
8  
9 359 the Malay version of the MOS-SSS has been validated through a sample of HIV patients. This  
10  
11 360 Malay version of the survey portrayed good psychometric properties, with high Cronbach's  
12  
13 361 alpha values for all the subscales ( $\alpha > .87$ ) and the overall scale ( $\alpha = .96$ ).[69]  
14  
15

16  
17 362 The General Anxiety Disorder-7 (GAD-7), a screening tool and severity indicator  
18  
19 363 developed by Spitzer et al.[70], will be used to assess the generalised anxiety disorder among  
20  
21 364 the participants. The scale contains 7 items and is rated using a 4-point Likert scale (0 = Not at  
22  
23 365 all; 3 = Nearly every day). The Malay version of the GAD-7, which has been validated through  
24  
25 366 female patients in a government-funded primary care clinic, delivers a good internal  
26  
27 367 consistency reliability ( $\alpha = .74$ ).[71]  
28  
29

30  
31 368 The participants' severity of depression will be assessed through the Patient Health  
32  
33 369 Questionnaire-9 (PHQ-9).[72] The PHQ-9 consists of 9 items and is rated using a 4-point Likert  
34  
35 370 scale (0 = Not at all; 3 = Nearly every day). In Malaysia, the questionnaire has been validated  
36  
37 371 through female patients in a primary care clinic, and the Malay version of the PHQ-9 shows a  
38  
39 372 good internal reliability ( $\alpha = .70$ ).[73]  
40  
41

42 373 The 36-item Short Form Survey (SF-36) will be utilised to assess the health-related  
43  
44 374 quality of life of the participants. The SF-36 consists of eight subscales for measuring different  
45  
46 375 domains of health-related quality of life, namely, physical functioning (PF), role-physical (RP),  
47  
48 376 bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional  
49  
50 377 (RE), and mental health (MH). Also, two main component scores are derived from the eight  
51  
52 378 subscales. These are the physical component summary (PCS), which consists of the PF, RP,  
53  
54 379 BP, and GH, and the mental component summary (MCS), which consists of the VT, SF, RE,  
55  
56 380 and MH.[74] The Malay version of the SF-36, which has been validated by post-coronary  
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3 381 artery bypass grafting surgery (CABG) patients, delivers good internal consistency reliability,  
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5 382 with Cronbach's alpha values ranging from .73 to .90 for the subscales.[75]  
6

7  
8 383 Phase 2: Qualitative study  
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10 384 A focus group discussion schedule will be developed, based on a literature review and expert  
11  
12 385 input by nephrologists in the research team. The questions for the focus group discussions will  
13  
14 386 be tailored to elicit responses from the patients with ESRD and their caregivers regarding their  
15  
16 387 psychosocial well-being and the economic burden being faced by them, and its impact on their  
17  
18 388 quality of life. The focus group discussion schedule will be piloted among the caregivers and  
19  
20 389 patients to examine the clarity and feasibility of the questions. The focus group discussions  
21  
22 390 will be divided into five sections: demographic details, source of ESRD treatment funding,  
23  
24 391 costs of ESRD management, the impact of their psychosocial well-being on their quality of  
25  
26 392 life, and lastly, the impact of the economic burden experienced by them on their quality of life.  
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30  
31 393 **Data collection**  
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33 394 Phase 1: Quantitative study  
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35 395 Conventional paper-and-pencil/web-based questionnaires will be utilised. The response rate of  
36  
37 396 the participants who respond positively out of those potentially eligible participants who are  
38  
39 397 invited to be involved in the study will be recorded. Potential participants (patients), identified  
40  
41 398 through referrals from nephrologists or nurses in the nephrology units, will be recruited during  
42  
43 399 their dialysis treatments in the respective hospitals/dialysis centres. In contrast, potential  
44  
45 400 participants (caregivers) will be approached whilst waiting for their patients' treatment to be  
46  
47 401 completed. For the caregivers who are not present during the patients' treatment, the  
48  
49 402 researchers will call them up or meet with them during the patients' subsequent treatment at  
50  
51 403 the respective hospitals/dialysis centres. The recruitment process will progress with the  
52  
53 404 researcher briefing the caregivers and patients on the aims and procedures of the study.  
54  
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56 405 Potential participants who respond in the affirmative as to whether they have been previously  
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2  
3 406 diagnosed with severe mental illness will be excluded from the study. Potential participants  
4  
5  
6 407 will be given ample time to consider their involvement in the study. Upon receiving their  
7  
8 408 consent, the participants will be provided with a questionnaire, which can be completed in  
9  
10 409 approximately 30 minutes. The researchers will entertain any questions the participants may  
11  
12 410 have regarding the questionnaire. The completed questionnaires will be kept securely for the  
13  
14 411 data analysis process. The criteria for the withdrawal of a subject include a situation whereby  
15  
16 412 the participant voluntarily withdraws his/her consent to participate in the study or when the  
17  
18 413 principal investigator, for any reason, ends the participation. Participants are free to withdraw  
19  
20 414 from the study at any time by stating their intention to do so during the course of the survey or  
21  
22 415 by emailing the principal investigator, whose email address and telephone number are included  
23  
24 416 in the informed consent form. As the calculation of the sample size takes into account the drop-  
25  
26 417 out rate for participants, those who withdraw from the study will not be replaced.

## 30 418 Phase 2: Qualitative study

31  
32  
33 419 The response rate of participants who respond positively out of those potentially eligible  
34  
35 420 participants who are invited to be involved in the study will be recorded. Potential participants  
36  
37 421 from Phase 1 will be recruited purposively based on the inclusion and exclusion criteria for  
38  
39 422 Phase 2 study. The researchers will brief the caregivers and patients on the aims and procedures  
40  
41 423 of the study. Participants will be given sufficient time to consider their participation in the focus  
42  
43 424 group discussions. The discussion will be held at a designated date, time, and venue to be  
44  
45 425 decided by the researchers, and is anticipated to last for an hour. The discussions will be  
46  
47 426 recorded, and the data will be transcribed verbatim, after which, the recording will be deleted,  
48  
49 427 in keeping with established ethical standards. The subject withdrawal criteria include a  
50  
51 428 situation where the participant voluntarily withdraws his/her consent to participate in this study  
52  
53 429 or when the principal investigator, for any reason, ends the participation. Participants are free  
54  
55 430 to withdraw from the study at any time by stating their intention to do so during the course of  
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2  
3 431 the discussion or by emailing the principal investigator, whose email address and telephone  
4  
5 432 number are included in the informed consent form. The arrival at the data saturation point will  
6  
7  
8 433 not be affected by the withdrawal of a participant(s), who will not be replaced.  
9

#### 10 434 **Data analysis**

##### 11 12 435 Phase 1: Quantitative study

13  
14 436 The IBM Statistical Package for the Social Sciences (SPSS) software for Windows (version  
15  
16 437 27)[76] will be utilised for the data processing, while descriptive statistics, independent sample  
17  
18 438 *t*-tests and multiple regression analyses will be utilised for the data analysis. The statistical  
19  
20 439 significance will be set at .05, and descriptive statistics will be used to compute the frequencies,  
21  
22 440 percentages, means, and standard deviation, and to summarise the data from the respondents.  
23  
24 441 To answer Objectives 1 and 2, which are to examine the differences in the treatment modalities  
25  
26 442 on the participants' psychosocial factors, economic factors and quality of life, independent  
27  
28 443 sample *t*-tests will be conducted between caregivers of haemodialysis and peritoneal dialysis  
29  
30 444 patients (Objective 1) and between haemodialysis and peritoneal dialysis patients (Objective  
31  
32 445 2).  
33  
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36

37 446 To answer Objectives 3 and 4, two multiple linear regression models will be fitted to  
38  
39 447 examine the association between the psychosocial factors (depression, anxiety, coping  
40  
41 448 strategies, social support, burden of care, and self-perceived burden), economic factors and the  
42  
43 449 quality of life of caregivers (Objective 3) and patients with ESRD (Objective 4), whilst  
44  
45 450 adjusting for potential demographic and clinical confounding factors (age, gender, race,  
46  
47 451 religion, marital status, education level, occupation, monthly household income, relationship  
48  
49 452 with patient/caregiver, method of dialysis, duration of dialysis, frequency of dialysis, and  
50  
51 453 duration of care extended by caregivers) (Figure 1).  
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##### 55 56 454 Phase 2: Qualitative study

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3 455 This qualitative study will facilitate an in-depth examination of the participants' perception of  
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5 456 their psychosocial well-being and economic burden in the management of ESRD and its impact  
6  
7 457 on their quality of life. A thematic analysis approach will be employed to analyse the data from  
8  
9 458 the focus groups.[77-78] The data from the focus groups will be audio recorded and then  
10  
11 459 transcribed accordingly. A copy of the transcripts will be given to the participants involved in  
12  
13 460 the focus groups for feedback and approval before the analysis is carried out. For storage  
14  
15 461 purposes, the data will be kept in a safety cabinet with a passcode, and only the research team  
16  
17 462 will have access to the stored data. An initial reading of the focus group transcripts will be  
18  
19 463 carried out. The transcripts will be re-read and coded individually to identify the key  
20  
21 464 components of the psychosocial well-being, economic burden, and quality of life of  
22  
23 465 participants. The data will be analysed by a team of researchers using NVivo software for  
24  
25 466 Windows (version 11) (update 4).[79] The coding process begins with open coding by coding  
26  
27 467 lines, statements and/or paragraphs. The data analysis will be considered to have reached  
28  
29 468 saturation point when no new categories emerge. Each transcript will be coded and recoded  
30  
31 469 several times.[78]

32  
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36  
37 470 Next, a cross-validation to check the coding and transcripts will be undertaken by an  
38  
39 471 independent rater, who will be provided with six interview transcripts. The independent rater's  
40  
41 472 task will have to conduct a thematic analysis and check the appropriateness of that analysis.  
42  
43 473 The independent rater's feedback will be compared with the identified themes. Any  
44  
45 474 disagreements that may emerge in terms of sub-themes and themes will be discussed with the  
46  
47 475 independent rater, and will be resolved through discussions with the independent rater and  
48  
49 476 feedback from the research team.

#### 477 Triangulation

478 Triangulation will be used in this research to gain a more accurate understanding of the  
49  
50 479 phenomena being studied, i.e., the psychosocial well-being, economic burden and the impact  
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3 480 of these on the quality of life of caregivers and patients. These phenomena will be examined  
4  
5 481 from different methodological angles using quantitative and qualitative methods.[80]This  
6  
7 482 approach will provide the means to verify and/or interrogate the data, thereby increasing the  
8  
9 483 confidence in the results. Therefore, two types of triangulations will be involved. The first type  
10  
11 484 is data triangulation using different approaches (quantitative and qualitative designs) in which  
12  
13 485 information will be gathered from different sources, namely the participants (caregivers and  
14  
15 486 patients), discussions and feedback from the research team, and with the participation of an  
16  
17 487 independent rater or checker for the analysis. The second type is investigator triangulation, in  
18  
19 488 which different investigators (i.e., student researchers, supervisors) will be involved in the data  
20  
21 489 collection and an independent rater will participate in the data analysis. The use of two or more  
22  
23 490 investigators independently can lead to more valid and reliable data,[81] and checking for  
24  
25 491 divergences between researchers will result in minimal divergence, i.e., reliability.  
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## 33 **ETHICS AND DISSEMINATION**

### 34 **Ethics Approval**

35  
36 494 The work has been approved by the Medical Research and Ethics Committee (MREC)  
37  
38 495 [NMRR-21-1012-59714] and the research ethics committees of Hospital Canselor Tuanku  
39  
40 496 Muhriz UKM (HCTM) [UKM PPI/111/8/JEP-2021-078] and the University of Malaya  
41  
42 497 Medical Centre (UMMC) [MREC ID NO: 202178-10346]. Also, the relevant permission and  
43  
44 498 approvals have been obtained from the directors of Hospital Selayang (HSEL) and Hospital  
45  
46 499 Kuala Lumpur (HKL).  
47  
48  
49

### 50 **Ethical considerations**

51  
52 501 The researchers will adhere to the principles of the Declaration of Helsinki[82] and the  
53  
54 502 Malaysian Good Clinical Practice Guidelines.[83] Participants will be required to provide  
55  
56 503 informed consent. The privacy of the participants will be protected during the data collection  
57  
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3 505 process by separating the informed consent forms from the paper-based questionnaire  
4  
5 506 responses. All the documents will be deposited in a secure cabinet, and all the data will be  
6  
7 507 stored in a password-protected computer to which only the researchers will have access. All  
8  
9 508 the documents and data will be stored for seven years, after which they will be shredded and  
10  
11 509 deleted. No participant identifiers (name, identity card number, address, phone number) will  
12  
13 510 be traceable, and a unique study ID will be assigned. No medical records will be accessible.  
14  
15 511 Participants will have no access to any personal information, and to ensure the element of  
16  
17 512 anonymity, they will not be informed of the study findings.  
18  
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### 21 513 **Dissemination**

22  
23 514 The findings from this study will be published in peer-review scientific journals and at national  
24  
25 515 or international conferences. Minimal anonymised data will be uploaded as supplementary  
26  
27 516 material for review purposes in scientific journal publications or conferences, and these will  
28  
29 517 adhere strictly to the ethical principles stipulated. Only group data will be published, and no  
30  
31 518 personal identifier will be collected or made public. The relevant permission will be obtained  
32  
33 519 from all the parties involved before any publication. The findings from this study can serve as  
34  
35 520 a guide for Malaysian policymakers, healthcare providers, and society to improve the quality  
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37 521 of life of patients with ESRD and their caregivers through the engagement of constructive and  
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39 522 holistic interventions.  
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### 49 526 **Contributors**

50  
51 527 All authors were involved in writing the study protocol. SYC and NI drafted the manuscript.  
52  
53 528 CSS, NA, RI and AHAG provided critical revision and feedback of the manuscript. All authors  
54  
55 529 have read and approved the final manuscript.  
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4

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6  
7  
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9  
10 533 and analysis, decision to publish, or preparation of the manuscript.

11  
12 **534 Competing interests**  
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14 535 The authors declared that there is no conflict of interest.

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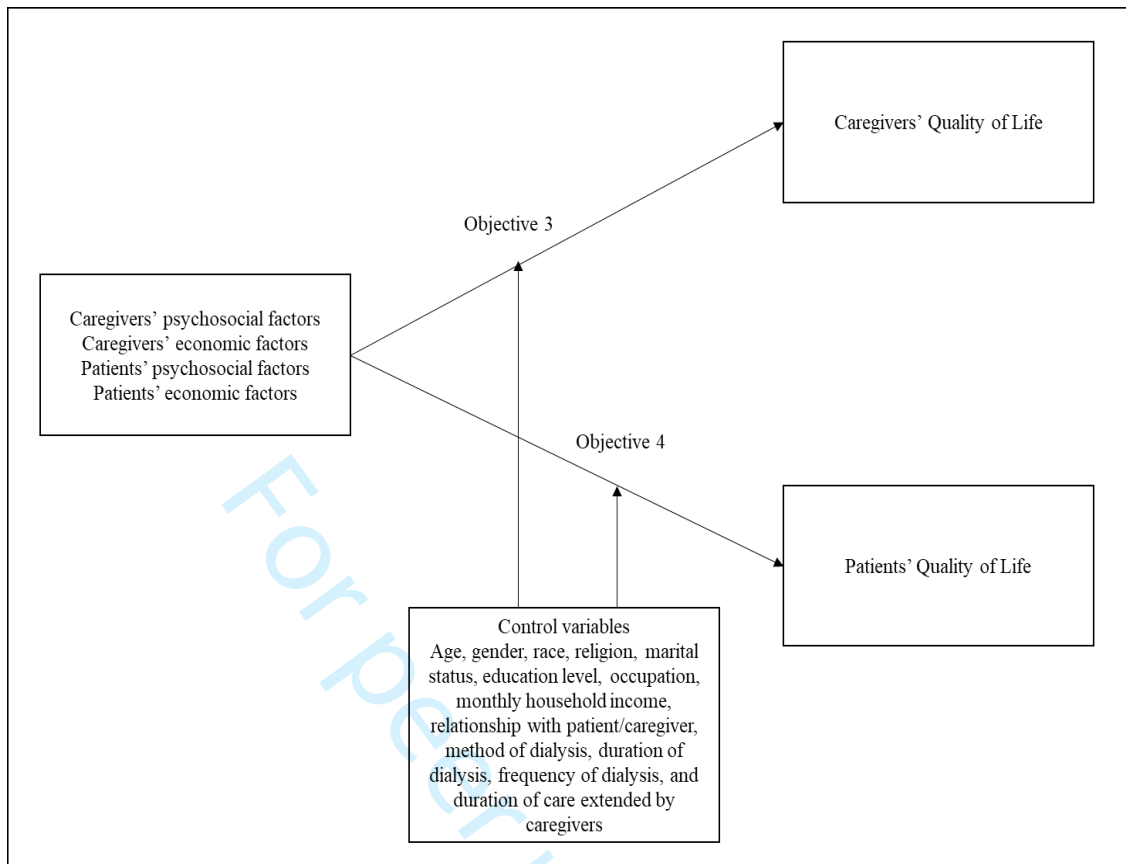
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3 **748 Figure – legend**  
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5 **749 Figure 1. Analytic plan for Objective 3 and Objective 4 of the study**  
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8 750 Two multiple linear regression models will be fitted to examine the association between the  
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10 751 psychosocial factors (depression, anxiety, coping strategies, social support, burden of care, and  
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12 752 self-perceived burden), economic factors and the quality of life of caregivers (Objective 3) and  
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14 753 patients with ESRD (Objective 4), whilst adjusting for potential demographic and clinical  
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16 754 confounding factors (age, gender, race, religion, marital status, education level, occupation,  
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18 755 monthly household income, relationship with patient/caregiver, method of dialysis, duration of  
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20 756 dialysis, frequency of dialysis, and duration of care extended by caregivers).  
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**Figure 1. Analytic plan for Objective 3 and Objective 4 of the study**