

1 **Validity and internal consistency of EQ-5D-3L quality of life tool among pre-dialysis patients**
2 **with chronic kidney disease in Sri Lanka, a lower middle-income country**

3

4 **Short title:** *Validity of EQ-5D-3L among CKD patients*

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20

21 **Abstract**

22

23 **Objective**

24 EQ-5D-3L is a generic QOL tool used mainly in economic evaluations. Burden of Chronic Kidney
25 Disease (CKD) is rising in Sri Lanka. Assessing the validity of generic QOL tools creates new
26 opportunities of their utilization among patients with CKD.

27

28 **Methods**

29 A cross-sectional study was conducted among 1036 CKD patients, selected using the simple
30 random sampling technique. The validity was tested with six a-priori hypotheses. These included
31 construct validity assessments, evaluating convergent validity and performing known group
32 comparisons. EQ-5D-3L, Short Form-36 (SF-36), Center for Epidemiological Studies Depression
33 Scale (CES-D-20) and General Health Questionnaire-12 (GHQ-12) were used to assess QOL,
34 presence of depression and psychological distress respectively. Internal consistency of the whole
35 tool and when each item is removed was assessed by Cronbach alpha.

36

37 **Results**

38 The response rate was 99.2%. Majority of participants were males (n=646,62.4%) in the age
39 category of 41-60 (n=530; 51.2%). Most were in either stage 4 or 5 of CKD (n=646,75.1%). The
40 summary measures of SF-36, positively and significantly correlated with the EQ-5D-3L index and
41 VAS scores (p<0.001). EQ-5D-3L QOL scores were significantly different between the group with
42 depression and without as measured by CES-D-20 (p<0.001). Assessed using GHQ-12, similar

43 significance was detected between the group with psychological distress and without ($p < 0.001$).

44 The Cronbach alpha was 0.834 and when each item was removed, ranged from 0.782 to 0.832.

45

46 **Conclusion**

47 EQ-5D-3L is a valid generic QOL tool with satisfactory internal consistency to be used among

48 CKD patients in the pre-dialysis stage.

49

50 **Key words:** Chronic Kidney Diseases, Quality of life, EQ-5D-3L, Validity

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52

53 **Introduction**

54 Chronic Kidney Disease (CKD) has become a major global burden of disease accounting for a
55 significant mortality and disability adjusted life years (1). In the Global Burden of Disease Study-
56 2015, it was ranked as the “12th most common cause of death” with an increased overall mortality
57 over 30% in the previous decade (2). This rise has been “alarming” in the low- and middle-income
58 settings (3). Additional emphasis on CKD has been recommended in relation to these settings
59 owing to the existing deficiencies in health policies and practices (2).

60
61 Sri Lanka which is an agricultural lower-middle-income country, is affected by the rising trend of
62 chronic non-communicable diseases (NCDs) due to demographic and epidemiological transitions
63 (4,5). CKD has become a major burden of the healthcare system in Sri Lanka (6). With the
64 contribution of occurrence of unexpected types of it like CKD of unknown etiology as well as due
65 to the concomitant increase of incidence of other NCDs, its burden is expected to rise further (6,7).
66 In addition, CKD impose numerous social and economic threats in Sri Lanka(8).

67
68 Quality of life (QOL) reflects a person’s subjective evaluation of his or her position of life in the
69 living contexts (4). The QOL related to impact of health conditions is referred to as health-related
70 QOL (9). Measurement of QOL become utmost important among patients with CKD, due to the
71 problems they are forced to face by the disease condition. They face a diverse range of symptoms,
72 distresses and even depression (1,10). Furthermore, the condition would make them suffer from
73 social and financial inabilities as well. They need to be in a potential waiting period for getting the
74 dialysis done, even when they enter that stage.

75

76 Health-related QOL can be measured by using generic as well as disease specific tools (11). SF-
77 36 and EQ-5D-3L are such generic QOL tools (12). Assessment of validity of QOL tools, for
78 specific disease conditions would create many opportunities for utilization within specific settings
79 (13). This is particularly beneficial for generic QOL tools, as this allows QOL comparisons
80 between different conditions (14). Validity measures to what extent the tool measures what it is
81 expected to measure (15,16). Reliability reflects the reproducibility of the same concept when
82 repeated measures are observed. It can be assessed by methods including internal consistency and
83 test-retest method (17).

84
85 In the absence of gold standard tests for measurements like QOL, the validity assessments could
86 be done for construct validity with methods such as “convergent/divergent validity assessments”
87 and “known group comparisons” (13,15,18). The EQ-5D-3L health states have been valued using
88 preference of general population in Sri Lanka(19). Furthermore using it, health related QOL has
89 been assessed in relation to several main chronic NCDs in Sri Lanka (4, 20). Yet the validity of it,
90 in relation to CKD has not been assessed.

91
92 The purpose of this study is to assess the validity and the internal consistency of EQ-5D-3L among
93 patients with kidney diseases who are in their pre-dialysis stage.

94 95 **Materials and Methods**

96 **Selection of the sample**

97 A descriptive cross-sectional study was conducted in Anuradhapura district of Sri Lanka. This
98 district, located in the North Central Province, is experiencing a rising trend of CKD. Patients

99 with CKD confirmed by a medical specialist based on the recommended guidelines (ie. Glomerular
100 Filtration Rate (GFR) being less than 60ml/min per 1.73m² body surface area in two measurements
101 made three months apart) comprised the study population. All patients above 18 years were
102 included. Patients who had renal transplantations were excluded.

103
104 The sample size (n) for the estimation of the construct validity was based on the publication of
105 Cohen (1992) for the “product-moment correlation coefficient”(21). Cohen (1992) recommends a
106 sample size of 783 for a small effect size (21). With an assumed response rate of 75%, minimal
107 sample size was calculated as 1044. Patients with CKD in the district of Anuradhapura are
108 registered in a population-based CKD register according to the geographic health units in which
109 they reside. The district comprise 19 health units and the required number of study units were
110 allocated to the 19 health units in proportionate to the number of registered patients in each health
111 unit. Using the population based register as the frame, simple random sampling technique was
112 used to select the study units from each the 19 health units within the district.

113

114 **Assessment of validity and internal consistency**

115 The construct validity of the EQ-5D-3L was assessed using the following six a-priori hypotheses.

- 116 1. The EQ-5D-3L index scores would significantly correlate with SF-36 summary scores in
117 the positive direction with acceptable strength
- 118 2. The EQ-5D-3L VAS scores would significantly correlate with SF-36 summary scores in
119 the positive direction with acceptable strength
- 120 3. The EQ-5D-3L index scores would be significantly different between the groups with
121 depression and without depression

- 122 4. The EQ-5D-3L VAS scores would be significantly different between the groups with and
123 without depression
- 124 5. The EQ-5D-3L index scores would be significantly different between the groups with
125 depression and without depression
- 126 6. The EQ-5D-3L VAS scores would be significantly different between the groups with and
127 without psychological distress

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129

130 The internal consistency was assessed using Cronbach alpha measurement for all the items as well
131 as when each item is removed.

132

133 EQ-5D-3L developed by the EuroQol group consist of a descriptive system and a Visual Analogue
134 Scale (VAS). The descriptive system comprises of five questions (on mobility, self-care, daily
135 activities, pain and mood) with each carrying three levels of possible responses. Each level reflects
136 a level of impairment as “with no problem”, “with some problems” and “with severe problems”.
137 An index score can be obtained from these questions which is expressed as a negative or positive
138 fraction. VAS may range from 0 to 100 and reflects the general health as perceived by the
139 participant (22). EQ-5D-3L has been previously translated to Sinhalese language and population
140 norms has been developed in 2014 (19). Other tools used comprised interviewer administered
141 forms of SF-36, CES-D-20 and GHQ-12, in addition to the tool to assess socio-demographic and
142 medical details.

143 SF-36 was used in the assessment of a-priori hypothesis 1 and 2. It includes 36 items out of which
144 35 are used to calculate eight QOL domain scores. Four each of these domains give rise to the

145 “physical-component” and “mental-component” summary measures. SF-36 focuses on the period
146 of previous 28 days in getting the responses (23). Its validity has been ensured in Sri Lankan setting
147 for several conditions (24,25). Furthermore it has been used in this setting to explore QOL of
148 several conditions (4,20).

149
150 The presence of depression was screened by the CES-D. It has 20 questions and a maximum score
151 of 60 is allocated. A score above 15 is indicative of depression. Its sensitivity is over 80% and the
152 specificity is over 90% in relation to the local setting (26). In screening for psychological distress,
153 GHQ-12 questionnaire was used. It gives a maximum score of 12. A cut-off value of two or more
154 has been recommended to the local setting with a sensitivity and specificity more than 70% (27).

155

156 **Data analysis**

157 Since the normality assessment showed non-normal distributions non-parametric techniques were
158 used in the analysis. For the a-priori hypothesis 1 and 2, Spearman correlation coefficient was
159 used(28). For the a-priori hypotheses No. 3 to 6, Mann Whitney U test was used(29). The
160 significance level was considered as 5%, but when lower p values were observed, relevant
161 significant levels were reported.

162

163 Ethics approval was obtained from the Ethics Review Committee of the Faculty of Medicine,
164 University of Colombo prior to the data collection (EC-15-081). Informed written consent was
165 taken from participants.

166

167

168 **Results**

169 The response rate was 99.2%. The median (IQR) age of the participants was 59 (52 to 66) years.

170 More than half (51.2%) the population were between 41-60 years old. The majority were males

171 (62.4%) and were unemployed (64.7%). Nearly four fifth were in stages of 4 or 5 in the CKD

172 staging. Of the population 64.2% were screening positive for depression while 74.4% were

173 positive for psychological distress (Table 1).

174

175 **Table 1: Characteristics of the participants**

Characteristic (N=1036)	Frequency	Percentage (%)
Age (Years)		
18 - 40	39	3.8
41 - 60	530	51.2
61- 80	467	45.1
Gender		
Male	646	62.4
Female	390	37.6
Highest education level		
No formal education	73	7.0
Up to Grade 5	398	38.4
From Grade 6 to 11	361	34.8
Passed GCE (O/L)	173	16.7
GCE (A/L) and above	31	3.0
Employment status		
Not employed	670	64.7
Employed	366	35.3
Presence of co-morbidities		
Comorbidities present	735	70.9

No comorbidities	301	29.1
CKD stage		
Early stage	258	24.9
Stage 4	626	60.4
Stage 5	152	14.7
Depression status		
Depressed	665	64.2
Not depressed	371	35.8
Psychological distress status		
Distressed	772	74.5
Not distressed	264	25.5

176

177

178 The descriptive system of the EQ-5D-3L comprises of five questions (on mobility, self-care, daily
179 activities, pain and mood) with each carrying three levels of possible responses. Except in the
180 self-care domain, in all other four domains, the majority had stated level 2 or 3 responses (i.e.
181 either having some or major problems). For the pain and the mood domains, responses with some-
182 or-severe problems were reported by more than three fourth. In addition, in more than half of the
183 participants, the mobility and the usual activities have been affected to a greater or lesser degree
184 (Table 2).

185

186

187 **Table 2: Distribution of responses for the descriptive question of the EQ-5D-3L**

Item	Response		
	No problem N (%)	Some problem N (%)	Severe problem N (%)
Mobility	500 (48.3)	519 (50.1)	17 (1.6)
Self-care	623 (60.1)	388 (37.5)	25 (2.4)
Usual activities	462 (44.6)	544 (52.5)	30 (2.9)
Pain	175 (16.9)	714 (68.9)	147 (14.2)
Mood	253 (24.4)	652 (62.9)	131 (12.6)

188

189 Role-limitation-emotional domain had recorded lowest scores out of the eight domains of the SF-
190 36. The mental-component summary score has recorded a slightly higher score than that of the
191 physical-component. Mean EQ-5D-3L index score was 0.52 (SD 0.33). Median scores of all the
192 eight domains of both physical health and mental health summary components had the scores
193 below 50.0. The highest mean score was for the Vitality domain (45.29; SD 11.53) while the lowest
194 was for the Role-limitation-emotional (23.94; SD 33.25) (Table 3).

195

196

197 **Table 3: QOL scores for domains of SF-36 and EQ-5D-3L**

Domain	Mean (SD)	Median (IQR)
SF-36 General Health	38.17 (19.33)	30.00 (25.00- 50.00)
SF-36 Physical functioning	42.02 (23.58)	40.00 (25.00- 60.00)
SF-36 Pain	36.86 (16.58)	42.50 (22.50- 45.00)
SF-36 Role-limitation-physical	27.26 (34.12)	0.00 (0.00- 50.00)
SF-36 Role-limitation-emotional	23.94 (33.25)	0.00 (0.00- 33.33)
SF-36 Vitality	45.29 (11.53)	50.00 (40.00- 53.75)
SF-36 Social functioning	42.78 (22.03)	50.00 (25.00- 62.50)
SF-38 Emotional well being	48.38 (9.33)	48.00 (44.00- 52.00)
SF-36 Physical summary score	36.08 (14.70)	35.00 (26.25 – 42.50)
SF-36 Mental summary score	40.10 (12.10)	39.10 (34.83 -43.09)
EQ-5D-3L index score	0.52 (0.33)	0.58 (0.34 – 0.75)
EQ-5D-3L VAS score	51.35 (16.88)	50.00 (40.00- 60.00)

198
 199 The Spearman correlation coefficients between SF-36 summary measures versus the EQ5D-3L
 200 index and VAS scores were statistically significant ($p < 0.001$) as well as positive in direction, even
 201 though being lower in strength (Table 4). The index values showed relatively stronger associations
 202 than the VAS scores.

203
 204 **Table 4: Correlation of SF-36 summary scores with EQ-5D-3L scores**

	EQ-5D-3L index score Spearman rho (p)	EQ-5D-3L VAS score Spearman rho (p)
SF-36 Physical summary score	0.28 (<0.001)	0.21 (<0.001)
SF-36 Mental summary score	0.34 (<0.001)	0.18 (<0.001)

205
 206

207 The comparison of the EQ-5D-3L and SF-36 scores between the depressed and non-depressed
 208 groups were carried out to test the 5th a-priori hypotheses (Table 5). It shows that statistically
 209 significant differences are observed between the QOL measures between the two groups as
 210 detected by both the tools (p<0.001).

211
 212 **Table 5: Known group comparison among participant with or without depression with SF-**
 213 **36 summary scores and EQ-5D-3L scores**

	With depression Mean (SD) Median (IQR)	Without depression Mean (SD) Median (IQR)	Significance of difference
EQ-5D-3L index score	0.41 (0.34) 0.34 (0.34- 0.66)	0.73 (0.22) 0.75 (0.60- 0.81)	P<0.001
EQ-5D-3L VAS score	46.83 (14.95) 40.00 (40.00- 50.00)	59.46 (17.12) 60.00 (40.00- 70.00)	P<0.001
SF-36 physical summary score	33.64 (13.82) 33.75 (24.38- 40.63)	40.44 (15.24) 36.25 (30.00- 48.13)	P<0.001
SF-36 Mental summary score	37.68 (11.29) 38.13 (31.83- 41.60)	44.45 (12.28) 40.50 (37.13- 46.00)	P<0.001

214
 215 Similar statistically significant differences are shown between the groups with and without
 216 psychological distress (p<0.001) (Table 6).

217

218 **Table 6: Known group comparison among participant with or without psychological**
 219 **distress with SF-36 summary scores and EQ-5D-3L scores**

	With distress Mean (SD) Median (IQR)	Without distress Mean (SD) Median (IQR)	Significance of difference
EQ-5D-3L index score	0.45 (0.34) 0.46 (0.34- 0.75)	0.72 (0.22) 0.75 (0.58- 0.81)	P<0.001
EQ-5D-3L VAS score	49.16 (15.90) 50.00 (40.00- 60.00)	57.77 (18.02) 60.00 (40.00- 70.00)	P<0.001
SF-36 physical summary score	33.01 (12.96) 33.75 (24.53- 40.00)	45.03 (15.80) 41.25 (32.50- 57.50)	P<0.001
SF-36 Mental summary score	37.79 (10.63) 38.29 (32.86- 41.33)	46.85 (13.54) 41.13 (37.78- 53.22)	P<0.001

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221

222 The internal consistency reflected by the Cronbach alpha was 0.834. It is higher than all the alpha
 223 values obtained when each question is removed (Table 7).

224

225 **Table 7: Internal consistency of the EQ-5D-3L**

Instance	Cronbach alpha
When all items are present	0.834
When 1 st question is removed	0.782
When 2 nd question is removed	0.815
When 3 rd question is removed	0.784
When 4 th question is removed	0.788
When 5 th question is removed	0.832

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227

228

229 **Discussion**

230 This is the first study documenting the validity of the EQ-5D-3L among pre-dialysis patients with
231 CKD. All the six a-priori hypotheses were found to be true in relation to this generic QOL tool.
232 Hence this study paved the way towards opportunities of using EQ-5D-3L on patients with CKD,
233 which is becoming a rising burden in this lower-middle income setting.

234
235 Higher proportion (i.e. more than 75%) of participants has responded as having some-or-severe
236 problems in relation to the pain and mood domains. This is compatible with the other documented
237 literature depicting that mental well-being of CKD affected participants must be given more
238 emphasis(10). Additionally, it is in par with the findings of the present study with 75% being
239 psychologically distressed and nearly 65% being depressed.

240
241 All the individual summary scores had means and medians less than 50. The figures are in general
242 lower than the post-myocardial infarction and post-stroke QOL measurements in Sri Lanka (4,20).
243 Comparatively the VAS values of the EQ-5D-3L too has remained around the value of 50, further
244 proving the negative impact, CKD imposes on the lifestyles of the affected patients.

245
246 Swank and Mullen (2017) state that in interpreting convergent validity by this method, must
247 consider three factors; significance, direction and the effect size(28). The Spearman correlation
248 coefficients showed a significant association between the SF-36 summary scores versus EQ-5D-
249 3L index and VAS scores in the positive direction. This shows that the parameters of EQ-5D-3L
250 have measured the relevant constructs in the similar manner as that of SF-36 proving its construct
251 validity. However, the effect sizes of the associations were approximately in the range of 0.2 to

252 0.4. This range can be classified as “acceptable and of medium strength”(28,30). The relatively
253 weak strengths of associations are acceptable due to the high number of other factors affecting the
254 variability of these outcome parameters. Furthermore, due to the complexities of constructs, the
255 interpretation of findings in this regard is recommended to be not exactly similar to interpreting
256 other bivariate correlations (31).

257

258 The index values showed relatively stronger associations compared to VAS figures. This may be
259 explained by the fact that the index scores include more domains whereas the VAS score is a single
260 general estimation of the participant. Since the SF-36 summary scores too include multiple
261 domains in them, they can be assumed to be more strongly correlated with the EQ-5D-3L index
262 score.

263

264 Both the depressed and psychologically distressed groups had relatively lower EQ-5D-3L scores
265 compared to their counterparts. This proves that the EQ-5D-3L is valid in differentiating two
266 groups which are known or assumed to be different in relation to QOL. The depressed and
267 distressed people would perceive the position of their life at a lower level than those who are not.
268 Hence the QOL of depressed and distressed groups can be assumed to be lower. In the present
269 study EQ-5D-3L has been able to detect this difference. The SF-36 values too were mentioned to
270 prove that actually there was a difference of QOL between the two groups compared.

271

272 The highest internal consistency was seen when all the items are present in the tool as reflected by
273 the Cronbach alpha values. This proves that even when all the five questions are included in the

274 tool, homogeneity of the responses is preserved. The alpha value being more than 0.7, reflects a
275 satisfactory internal consistency as categorized conventionally (32).

276

277 There were several limitations of the study. Firstly the reliability of the EQ-5D-3L was only tested
278 using the internal consistency in the study. To measure the reliability by test-retest method, a
279 clinically stable period is needed (33,34). If inter-rater methods are used, a minimum time period
280 which would eliminate the answers given to the previous responder is needed in between the data
281 collections (35). Since EQ-5D-3L captures the QOL at the “time of completion” (22), the
282 administration of other methods becomes debatable. On the other hand internal-consistency,
283 though not being the sole representation, could be assumed to reflect the reliability characteristics
284 of tools (36). However, to prevent any over-generalizability of the findings, in the title of the
285 current study, the word “internal consistency” was used instead of the word “reliability”.

286

287 Secondly the QOL scores were not adjusted to the morbidities those were present among the
288 participants. Majority of the participants were suffering from different comorbid conditions (nearly
289 71%) with different severities. Hence it was not feasible to adjust for these. However as shown in
290 literature, concomitant non-communicable medical conditions are common among the patients
291 with CKD (6,7) and the sample of this study too represent more or less similar characteristics.

292

293

294 **Conclusions**

295 EQ-5D-3L is a valid generic QOL tool with satisfactory internal consistency to be used among
296 CKD patients in the pre-dialysis stage

297

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432 **Supporting information**

433 S1 Appendix : Data used in the analysis