Estimating the impact of pill burden on the utility of patients undergoing hemodialysis

Hiroo Shimoda[1], Masatomo Taniguchi[2], Suguru Yamamoto[3], Ataru Igarashi[4], Shin Tokunaga[1], Keigo Hanada[5], Naoki Tashiro[5], Tatsunori Murata[5], Shinji Asada[1]

[1]Kyowa Kirin Co., Ltd., Tokyo, Japan; [2]Fukuoka Renal Clinic, Fukuoka, Japan; [3]Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan; [4]The University of Tokyo, Tokyo, Japan; [5]CRECON Medical Assessment Inc., Tokyo, Japan

Background

Patients with chronic kidney disease (CKD) undergoing hemodialysis (HD) take a high number of prescription medicines due to comorbidities such as hyperphosphatemia. A survey of 700 HD patients showed an average intake of more than 16 oral medications daily, including up to 36 tablets of phosphate binders[1]. The water intake of HD patients is restricted and reducing the pill burden could reduce their psychological burden, while patients' quality of life (QOL) may be improved.

Objectives

We estimated the impact of pill burden on utility scores in HD patients using the vignette-based time trade-off (TTO) method.

Methods: Participants

Participant recruitment: March–August 2024
- Aged ≥20 years, residing in Japan
- Willingness to provide consent
- Ability to understand and follow the study procedures

Pilot study to refine vignette and interview process
- 10 general participants (on-site interview)
- 10 CKD patients undergoing HD (online interview)

Main study
- 100 general participants (on-site interview)

Methods: Statistical analysis

- Characteristics were summarized descriptively and compared with national standard values.
- Utility scores for each health state were summarized descriptively for the total population and subgroups (age, sex, education, and annual household income).
- Utility scores between subgroups were analyzed using unpaired t-test.

Methods: TTO valuation

- Using the finalized vignettes, utility scores were estimated by either the lead-TTO or TTO methods[2].
- 7 hypothetical health states were presented in random order
- Evaluation was continued until the utility score was determined

"I would prefer to…"
1) live 0 years in complete health, then die;
2) live 10 years in the hypothetical health state, then die; or
3) I cannot decide. No difference.

Figure 1. Lead-TTO and TTO methods with ping-pong titration approach
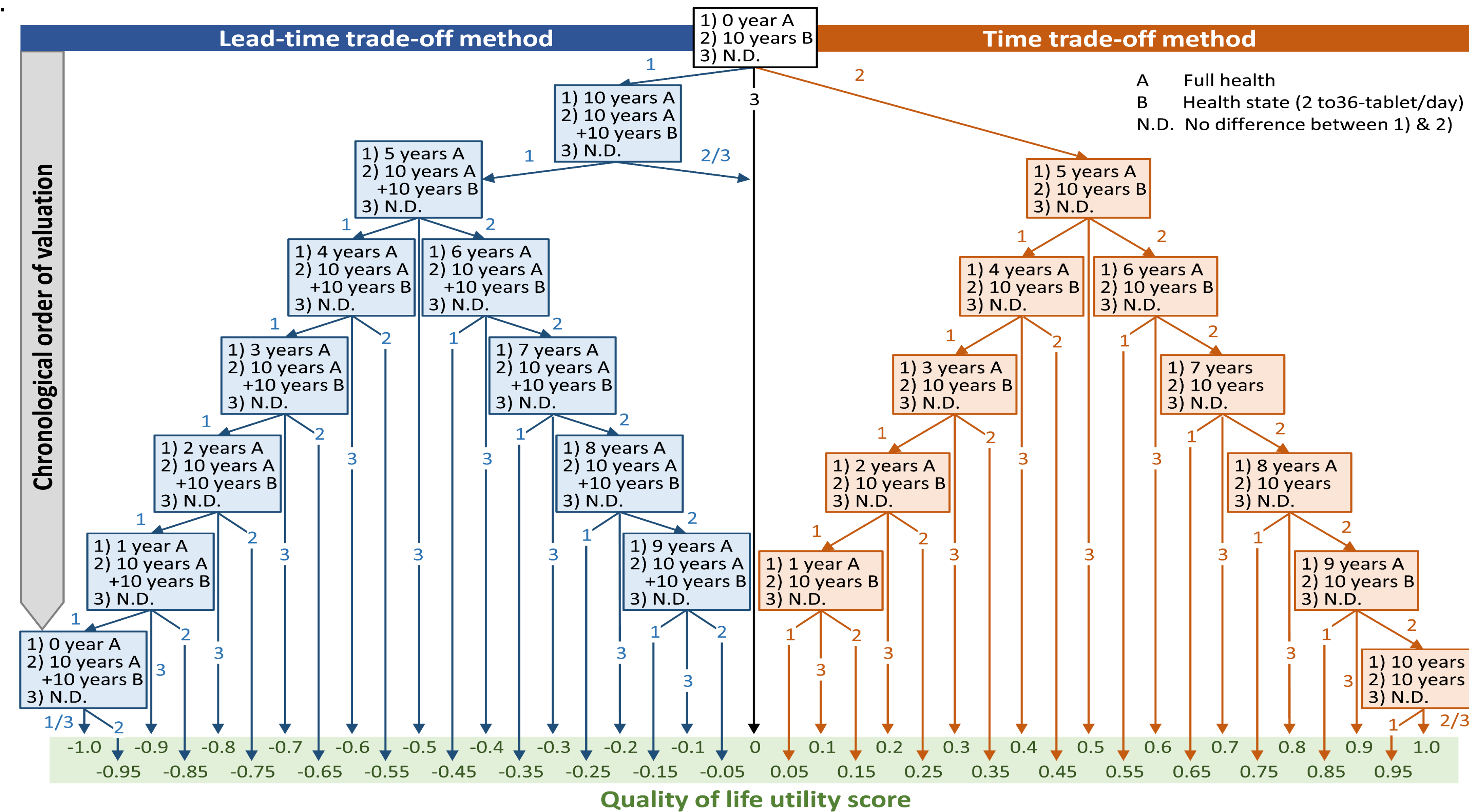
Methods: Vignette development

Vignettes were developed using data from previous studies and input from CKD patients undergoing HD and medical experts.[3–5]

Table 1. Hypothetical health states used in the TTO and lead-TTO methods: common elements across all seven health states

Disease
- I have kidney disease. I cannot remove excess water, excess salt, and wastes from my body. At the same time, I cannot keep essential substances in my body.
- Without appropriate treatment, I may die sooner.
- I have to be treated at a hospital 3 times a week for 3 to 4 hours each visit, without any break.
- I have to take drugs every day to treat comorbidities.

Symptoms
- When the kidney disease advances, I experience symptoms such as swelling, tiredness, and anemia.
- I experience a pounding heart or shortness of breath when exercising.
- I have itchy skin, and it becomes worse when I take a hot bath.

Restrictions in daily life
- The amount of water I can drink is restricted to 900 mL (per 60 kg body weight), including a glass of water (200 mL) each time I take medication, to prevent harmful effects on my heart and blood vessels resulting from excess water retention.
- The amount of nutrients and salts in my food must be strictly controlled to prevent harmful effects on my heart and blood vessels.

Table 2. Seven health states based on the daily number of tablets

2 tablets/day
- I take **1 tablet** at a time, **twice** a day. I use **400 mL** for taking medicine in total.

3 tablets/day
- I take **1 tablet** at a time, **three times** a day. I use **600 mL** for taking medicine in total.

6 tablets/day
- I take **2 tablets** at a time, **three times** a day. I use **600 mL** for taking medicine in total.

9 tablets/day
- I take **3 tablets** at a time, **three times** a day. I use **600 mL** for taking medicine in total.

12 tablets/day
- I take **4 tablets** at a time, **three times** a day. I use **600 mL** for taking medicine in total.

24 tablets/day
- I take **8 tablets** at a time, **three times** a day .I use **600 mL** for taking medicine in total.

36 tablets/day
- I take **12 tablets** at a time, **three times** a day. I use **600 mL** for taking medicine in total.

Results: Demographics

Table 3. Participant demographics

	Participants, n (%)[a]	General population[6-8], %
Total N	107	NA
Age in years, mean (SD)	44.5 (14.32)	47.7 (NA)
Sex, male	54 (50.5)	48.6
Highest level education completed		
School graduate	4 (3.7)	3.0
College/university (bachelor's degree)	71 (66.4)	24.7
College (associate degree)	9 (8.4)	8.0
Technical school	7 (6.5)	12.3
Senior high school	16 (15.0)	38.4
Junior high school	0 (0.0)	11.6
Employment status		
Employed		
Regular staff/employee	50 (46.7)	32.9
Part-time staff/employee	11 (10.3)	9.4
Marginal part-time worker	6 (5.6)	3.9
Temporary worker from a dispatching office	6 (5.6)	1.4
Contract staff	9 (8.4)	2.7
Commissioned worker	3 (2.8)	1.0
Company executive	1 (0.9)	0.9
Self-employed worker (with employees)	0 (0.0)	3.6
Self-employed worker (without employees)	6 (5.6)	0.9
Helping with the family business	0 (0.0)	0.1
Side job	0 (0.0)	0.8
Not working		
Seeking a job	0 (0.0)	2.9
Attending school	4 (3.7)	5.1
Housekeeping	8 (7.5)	16.4
Others (e.g., retired)	3 (2.8)	14.7
Marital status		
Unmarried	47 (43.9)	25.6
Married	53 (49.5)	54.4
Single (widowed)	0 (0.0)	8.2
Single (divorced)	7 (6.5)	5.0
No answer	0 (0.0)	6.8
Annual household income [million yen]		
<2	4 (3.7)	19.7
≥2 to <3	9 (8.4)	14.6
≥3 to <4	14 (13.1)	12.6
≥4 to <5	15 (14.0)	10.3
≥5 to <6	10 (9.3)	8.4
≥6 to <7	10 (9.3)	7.3
≥7 to <8	9 (8.4)	6.2
≥8 to <9	7 (6.5)	4.9
≥9 to <10	4 (3.7)	3.6
≥10	20 (18.7)	12.4

[a]Unless otherwise noted. NA Not available, SD Standard deviation

Results: Utility scores

Figure 2. Mean utility scores by health state
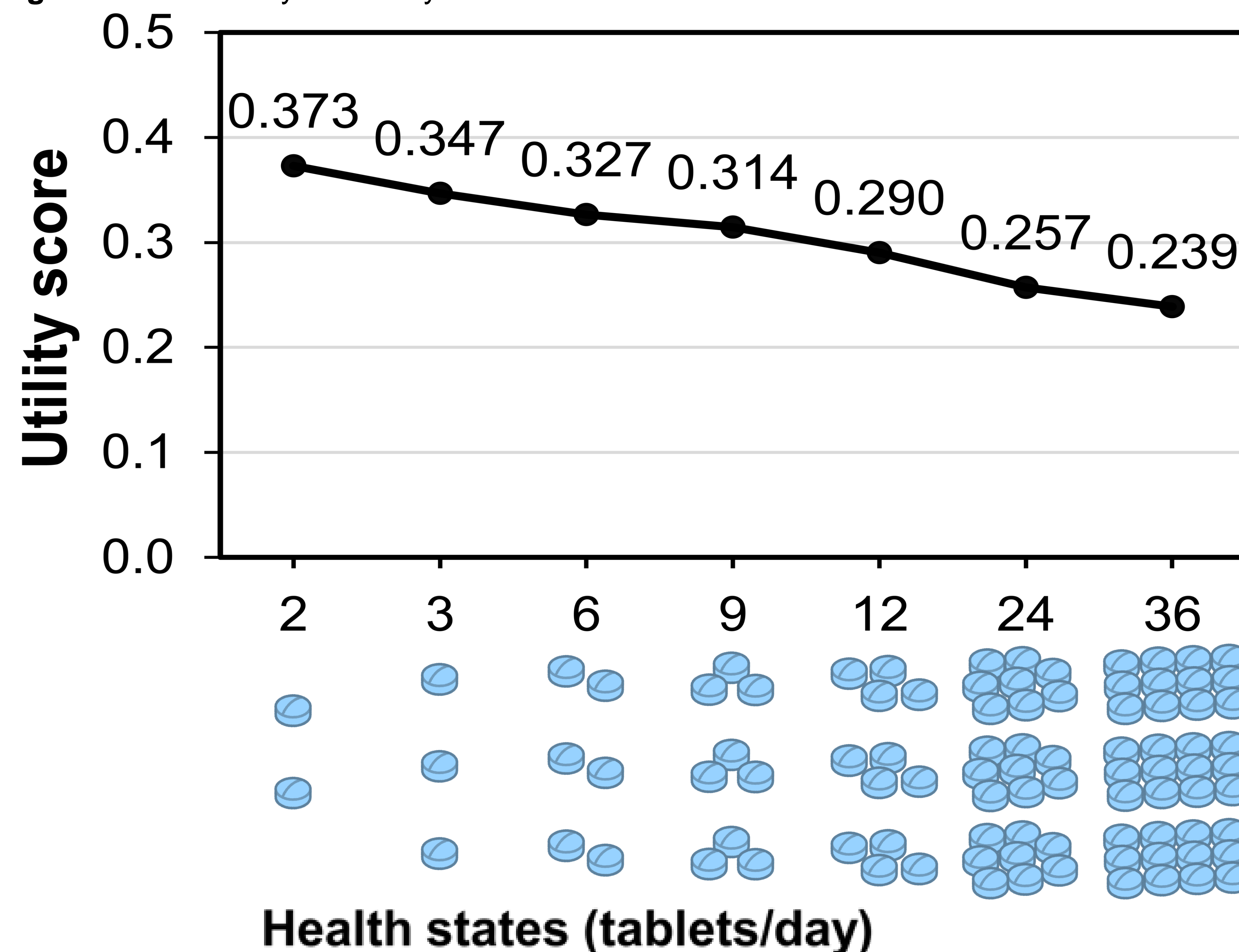
Table 4. Utility scores by health state

Health states	Mean (95% CI)
2 tablets/day	0.373 (0.262–0.484)
3 tablets/day	0.347 (0.233–0.460)
6 tablets/day	0.327 (0.219–0.434)
9 tablets/day	0.314 (0.205–0.424)
12 tablets/day	0.290 (0.180–0.400)
24 tablets/day	0.257 (0.148–0.366)
36 tablets/day	0.239 (0.130–0.348)

Table 5. Comparison of utility scores among different health status groups

Health states	Differences in utility score (vs. reference)						
	2 tablets	3 tablets	6 tablets	9 tablets	12 tablets	24 tablets	36 tablets
2 tablets /day	Reference	0.026 (-0.020, 0.072)	0.046 * (0.004, 0.089)	0.058 ** (0.016, 0.101)	0.083 ** (0.029, 0.136)	0.116 *** (0.065, 0.167)	0.134 *** (0.083, 0.185)
3 tablets /day	-	Reference	0.020 (-0.007, 0.047)	0.032 (-0.002, 0.067)	0.057 * (0.014, 0.099)	0.090 *** (0.047, 0.133)	0.108 *** (0.072, 0.144)
6 tablets /day	-	-	Reference	0.012 (-0.015, 0.039)	0.036 * (0.004, 0.069)	0.070 *** (0.035, 0.104)	0.088 *** (0.052, 0.124)
9 tablets /day	-	-	-	Reference	0.024 (-0.001, 0.050)	0.057 *** (0.031, 0.084)	0.076 *** (0.037, 0.114)
12 tablets /day	-	-	-	-	Reference	0.033 (-0.001, 0.067)	0.051 * (0.010, 0.092)
24 tablets day	-	-	-	-	-	Reference	0.018 (-0.019, 0.055)

Mean (95% confidence interval). * p <0.05, ** p <0.01 and *** p <0.001 by t-test (vs. reference)

Table 6. Subgroup Analysis

Health states	Age			Sex			Education			Annual household income		
	≥44.0 years n = 55	<44.0 years n = 52	p-value	Male n = 54	Female n = 53	p-value	Higher half[a] n = 75	Lower half[b] n = 32	p-value	≥6 million yen n = 55	<6 million yen n = 52	p-value
2 tablets/day	0.307 (0.594)	0.442 (0.560)	0.229	0.394 (0.538)	0.352 (0.623)	0.712	0.393 (0.596)	0.327 (0.544)	0.578	0.298 (0.580)	0.452 (0.573)	0.171
3 tablets/day	0.282 (0.612)	0.415 (0.566)	0.244	0.368 (0.576)	0.325 (0.611)	0.715	0.375 (0.590)	0.280 (0.597)	0.450	0.215 (0.632)	0.487 (0.515)	0.016
6 tablets/day	0.240 (0.579)	0.418 (0.535)	0.101	0.371 (0.533)	0.281 (0.593)	0.410	0.365 (0.555)	0.238 (0.579)	0.297	0.209 (0.590)	0.451 (0.509)	0.025
9 tablets/day	0.263 (0.596)	0.369 (0.543)	0.335	0.345 (0.543)	0.283 (0.601)	0.575	0.345 (0.568)	0.242 (0.577)	0.399	0.209 (0.601)	0.426 (0.518)	0.048
12 tablets/day	0.203 (0.597)	0.383 (0.540)	0.105	0.322 (0.548)	0.258 (0.604)	0.563	0.320 (0.581)	0.220 (0.562)	0.409	0.194 (0.601)	0.392 (0.533)	0.073
24 tablets/day	0.195 (0.566)	0.322 (0.569)	0.251	0.291 (0.528)	0.223 (0.610)	0.539	0.279 (0.575)	0.206 (0.559)	0.545	0.167 (0.577)	0.352 (0.549)	0.093
36 tablets/day	0.175 (0.589)	0.307 (0.542)	0.229	0.262 (0.540)	0.215 (0.599)	0.671	0.251 (0.579)	0.211 (0.547)	0.737	0.123 (0.597)	0.362 (0.513)	0.028

[a]Higher half in education: graduate school or college/university; [b]Lower half in education: college (associate degree), technical school, senior high school, or junior high school. Utility scores between subgroups were analyzed using unpaired t-test.

Conclusions

- The impact of pill burden on utility scores for QOL in CKD patients undergoing HD was estimated using a vignette-based TTO method in the general population.
- Our findings demonstrated that utility scores decreased as the number of tablets increased, and QOL may be improved by reducing the pill burden in HD patients.
- The vignette-based approach may be useful for assessing QOL changes associated with such treatments, supporting their use in cost-utility analyses.

References
1. Intern Med. 2018;57(20):2937–44. 2. J Med Econ. 2023;26(1):565–73.
3. J Med Econ. 2023;26(1):386–93 4. Can J Kidney Health Dis. 2020;7:2054358120914426.
5. Health Qual Life Outcomes. 2015;13:90.
6. e-Stat, The Portal Site of Official Statistics of Japan. 2020 Population census, Tables 1-1, 2-1, 7-2. (https://www.e-stat.go.jp/stat-search/files?page=1&layout=datalist&toukei=00200521&tstat=00000113 6464&cycle=0&tclass1=000001136466&tclass2val=0), partially edited.
7. e-Stat, The Portal Site of Official Statistics of Japan. 2022 Employment Status Survey, Tables 2-1, 11-1, 116. (https://www.e-stat.go.jp/stat-search/files?page=1&layout=datalist&toukei=00200532&tstat=000001163626&cycle=0&tclass1=000001163627&tclass2=000001163628&stat_i) partially edited.
8. Ministry of Health, Labour and Welfare. Summary Report of Comprehensive Survey of Living Conditions 2022. Tables 7&10 in statistics table. (https://www.mhlw.go.jp/toukei/saikin/hw/k-tyosa/k-tyosa22/dl/06.pdf), partially edited.