Igarashi A¹⁾, Finch AP²⁾, Yang Z³⁾, Sakata Y⁴⁾, Azuma-Kasai M⁴⁾, Tomita K⁴⁾, Ishii M⁴⁾, Ikeda M⁵⁾ 1) The University of Tokyo, 2) EuroQol Research Foundation, 3) Jinan University, 4) Eisai Co., Ltd., 5) Osaka University Graduate School of Medicine

BACKGROUNDS

- The need for adding a new dimension or multiple dimensions to EQ-5D has been discussed to better capture specific health conditions in the generic EQ-5D classification system. Among various conditions, a cognition bolt-on for EQ-5D and its 5-level response version (EQ-5D-5L) has been shown to improve their ability to evaluate health states^{1,2)}.
- Developing a new value set incorporating a bolt-on dimension using the standard EuroQol valuation technology (EQ-VT) protocol, however, raises some challenges. The standard approach requires a full-scale valuation study with a large general population sample. Additionally, generated value sets may become inconsistent with existing ones, and rank order after bolt-on may change due to sampling errors or interviewer effects. To overcome these challenges, a study recently proposed an approach for developing bolt-on value sets based on existing EQ-5D value sets³⁾. This approach uses a modified main-effects model (hereafter, a scaling factor model).
- We applied this approach and a conventional approach to previously published cognition dimensions using existing Japanese value sets^{4,5)}.

OBJECTIVES

• To experimentally evaluate the valuation methods of the EQ-5D-5L bolt-ons with the scaling factor model and conventional approach using three cognition dimensions, the cognition bolt-on version of the Japanese EQ-5D-5L (hereafter, EQ-5D-5L+C)^{2,6)} and additional two previously experimentally developed cognition dimensions⁷⁾, added to the EQ-5D-5L.

Original cognition dimension

I have no problems with cognition

Japanese cognition dimension

認知機能に問題はない

認知機能に少し問題がある

認知機能にかなり問題がある

認知機能に極度の問題がある

Original English wording

I have no problems with remembering things

I am unable to remember things

I have slight problems with remembering things

I have moderate problems with remembering things

I have severe problems with remembering things

Japanese translation prepared for this study

物事を思い出したり、覚えておくのに問題はない

物事を思い出したり、覚えておくことができない

物事を思い出したり、覚えておくのに少し問題がある

物事を思い出したり、覚えておくのにかなり問題がある

物事を思い出したり、覚えておくのに中程度の問題がある

COGNITION

認知機能

認知機能に中程度の問題がある

I have slight problems with cognition

I have severe problems with cognition

I have extreme problems with cognition

I have moderate problems with cognition

COGNITION (memory, comprehension, concentration, thinking)

認知機能 (例:記憶力[もの忘れ]、理解力、集中力、思考力)

please register your study by using the online EQ registration page: www.eurogol.org.

Arm 2: Remembering things

METHODS

- The use of EQ-5D-5L cognition bolt-on version was granted by the EuroQol group.
- This study was part of the research "Efficiency and Optimization of Care in Nursing Homes" from the Perspectives of QOL and Medical Economics", which was approved by the ethics committee of the Graduate School of Pharmaceutical Sciences, The University of Tokyo.

1. Study population

- Adults (≥18 years) living in Tokyo, Osaka, and Kumamoto who were capable of providing consent and comprehended Japanese were recruited from the Japanese general population using snowball sampling.
- With a target sample size of 810 individuals, the study planned to randomize participants into three arms of 270 individuals each (90 per city). Allocation was guided by the population composition by sex and age in Japan⁸⁾

2. Study procedure

- For EQ-5D-5L+C, the linguistically and psychometrically validated Japanese version⁶⁾ was used. For Remembering things⁷⁾ and Thinking clearly⁷⁾, the Japanese versions were unavailable. Their translations were prepared according to the following three-step process: forward and back translations and finalization (Figure 1).
- Preferences were collected through face-to-face, one-on-one interviews conducted by 9 trained interviewers using the composite time trade-off (cTTO) valuation method^{9,10)} (EQ-VT version 2.7.2). The interviews were conducted from June 27 to August 7, 2023.
- After giving consent, participants were randomized to three arms (Arm 1: EQ-5D-5L+C, Arm2: EQ-5D-5L+Remembering things, and Arm 3: EQ-5D-5L+Thinking clearly). Each participant valued a randomly selected block of 10 health states and the worst possible health state (555555).
- Using an orthogonal design³⁾, we selected 31 health states on the basis of a 6*5 orthogonal array, i.e., 30 health states and the worst possible health state.

3. Data analysis

- The "1-cTTO" values were modeled for each arm independently using the scaling factor model, with EQ-5D-5L disutility weights estimated from the existing Japanese value sets^{4,5)}. We also fitted the "1-cTTO" values into the 24-parameter conventional main-effects model. Both models used a Tobit model and maximum likelihood estimation.
- Model prediction accuracy was assessed using indices of fit, including mean absolute errors (MAEs) and Pearson's correlation coefficient. Lower MAE values indicate higher prediction accuracy.

RESULTS

1. Study population

- In total, 864 Japanese participated in this study. The distribution of sex and age were similar across the three arms (Table 1).
- For statistical analysis, one participant was excluded due to data inaccuracy, and data of 863 participants were analyzed.

Table 1. Participant demographic characteristics

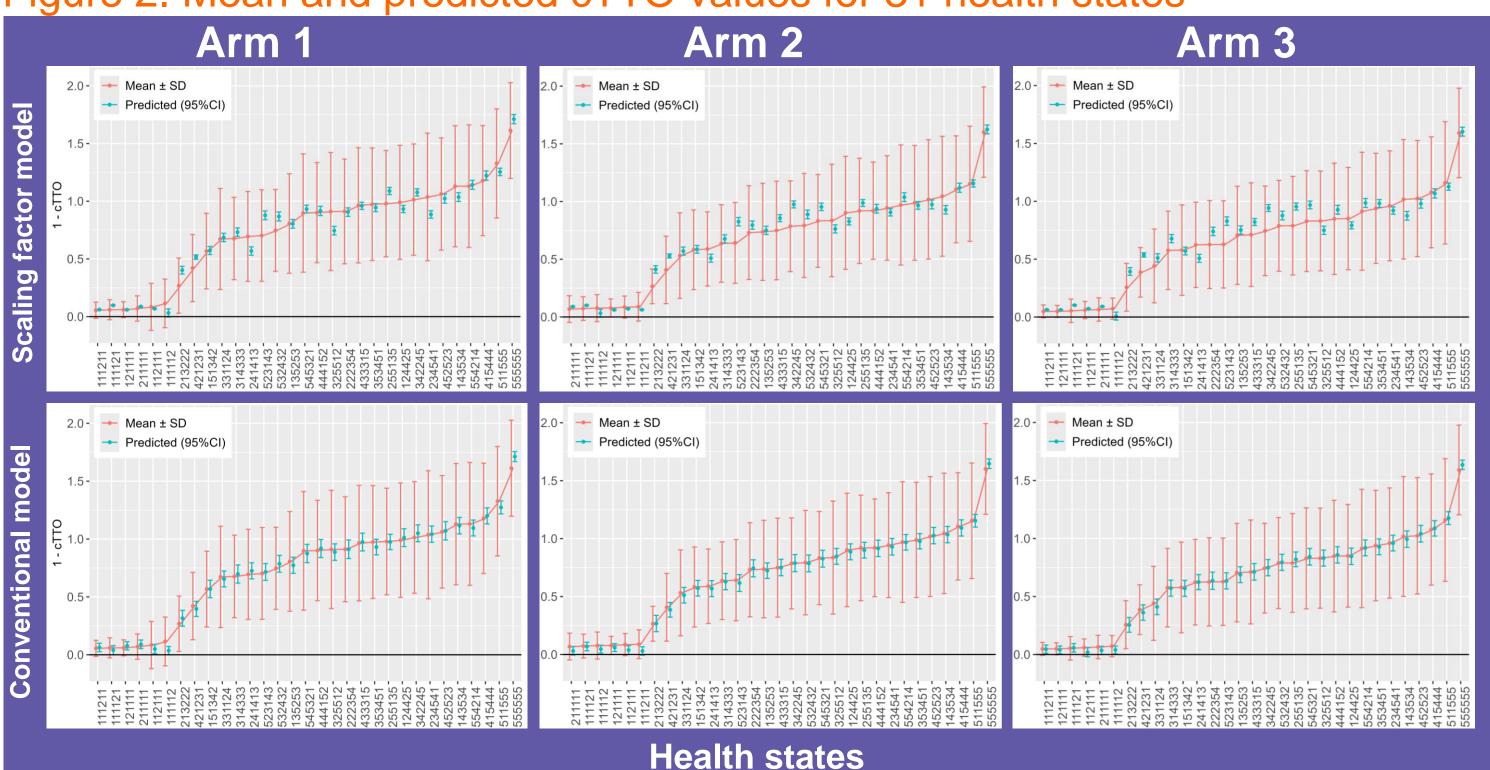
| | | Arm 1 | | Arı | Arm 2 | | Arm 3 | |
|---|---|-------|--------|-----|--------|-----|--------|--|
| Characteristics | | n | (%) | n | (%) | n | (%) | |
| Total | | 287 | | 289 | | 288 | | |
| Sex | Male | 144 | (50.2) | 143 | (49.5) | 144 | (50.0) | |
| | Female | 143 | (49.8) | | (50.5) | 144 | · · | |
| Age, years | 18 – 24 | 25 | (8.7) | 28 | (9.7) | 27 | (9.4) | |
| | 25 – 34 | | , | 49 | (17.0) | 49 | (17.0) | |
| | 35 – 44 | 57 | (19.9) | 59 | (20.4) | 56 | (19.4) | |
| | 45 – 54 | 63 | (22.0) | 56 | (19.4) | 66 | (22.9) | |
| | 55 – 64 | 58 | , | 64 | (22.1) | 54 | (18.8) | |
| | 65 – 74 | | • | 29 | (10.0) | 35 | (12.2) | |
| | ≥75 | 2 | (0.7) | 4 | (1.4) | 1 | (0.3) | |
| Employment | | 151 | (52.6) | 159 | (55.0) | 149 | (51.7) | |
| type | Working full-time (nonregular) | 11 | (3.8) | 11 | (3.8) | 2 | (0.7) | |
| | Working part-time | 46 | (16.0) | 46 | (15.9) | 58 | (20.1) | |
| | Self-employed | | ` , | | (9.0) | | • | |
| | Unemployed (stay-at- home mother/father) | | (10.5) | | (10.4) | 31 | (10.8) | |
| | Unemployed (retired) | 7 | (2.4) | 6 | (2.1) | 15 | (5.2) | |
| | Student | 16 | (5.6) | 11 | (3.8) | 9 | (3.1) | |
| | Others | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | |
| Educational | Junior high school | 3 | (1.0) | 5 | (1.7) | 1 | (0.3) | |
| attainment | High school | 90 | (31.4) | 88 | (30.4) | 97 | (33.7) | |
| | Vocational school | 39 | (13.6) | 37 | (12.8) | 47 | (16.3) | |
| | Junior college | 32 | (11.1) | 37 | (12.8) | 25 | (8.7) | |
| | University | | (41.1) | 118 | (40.8) | 110 | (38.2) | |
| | Graduate school | 5 | (1.7) | 3 | (1.0) | | ` ' | |
| -Lilaraw, at aas | Others | 0 | (0.0) | 1 | (0.3) | 0 | (0.0) | |
| History of serious sickness/disease, Yes | | 39 | (13.6) | 40 | (13.8) | 44 | (15.3) | |
| History of serious sickness/disease in the family, Yes | | 127 | (44.3) | 124 | (42.9) | 130 | (45.1) | |
| Experience of caregiving to non- family members, Yes | | 21 | (7.3) | 30 | (10.4) | 20 | (6.9) | |

Note: Percentages may not sum to 100% due to rounding.

3. cTTO values

• The mean and predicted "1-cTTO" values are presented in Figure 2. These values were slightly discrepant, but no large discrepancies were observed in all three arms.

Figure 2. Mean and predicted cTTO values for 31 health states



Note: Health states are presented in ranked order.

collection. All the contributions were funded by Eisai Co., Ltd.

Acknowledgement We appreciate Dr. Kim Rand from Maths in Health for his support in data analysis and Clinical Study

medical writing. We also thank INTAGE Healthcare Inc. and interviewers for their contribution in data

Abbreviations Support, Inc. for their support in project planning, administration, data collection, statistical analysis, and

cTTO, composite time trade-off; EQ-5D-5L+C, the cognition bolt-on version of the Japanese EQ-5D-5L; mo, mobility; sc, self-care; ua, usual activities; pd, pain/discomfort; ad, anxiety/depression; co, cognition; SD, standard deviation; CI. confidence interval.

2. Scaling factor model and conventional linear mixed model

• After adding each cognition dimension to the existing EQ-5D-5L, the estimated coefficients for the scaling factor model expanded in all arms, and the rank order of two core dimensions in the conventional linear mixed model changed for Arm 1 (Table 2).

Figure 1. Three patterns of descriptions for cognition bolt-on dimensions

© EuroQol Research Foundation. EQ-5D™ is a trade mark of the EuroQol Research Foundation. Reproduced by permission of EuroQol Research

Foundation. This is a modified EQ-5D. Reproduction of this version is not allowed. For reproduction, use or modification of the EQ-5D (any version),

Arm 3: Thinking clearly

Original English wording

I am unable to think clearly

考えをまとめるのに問題はない

考えをまとめることができない

考えをまとめるのに少し問題がある

考えをまとめるのにかなり問題がある

考えをまとめるのに中程度の問題がある

I have no problems in thinking clearly

I have slight problems in thinking clearly

I have severe problems in thinking clearly

I have moderate problems in thinking clearly

Japanese translation prepared for this study

COGNITION

認知機能

Arm 1: EQ-5D-5L+C

Table 2. Coefficients of scaling factor model and conventional linear mixed model

| | Arm 1 | | Arm | | Arm 3 | | |
|---------|----------------------|-----------------------|----------------------|---|----------------------|-----------------------|--|
| Model | Scaling factor model | Linear mixed model | Scaling factor model | Linear mixed model | Scaling factor model | Linear mixed model | |
| 1+Scale | 1.3667 | _ | 1.3991 | _ | 1.4201 | _ | |
| mo2 | 0.0639 | 0.0901 | | 0.0312 | Values identical to | 0.0355 | |
| mo3 | 0.1126 | 0.1400 | | 0.0999 | | 0.0744 | |
| mo4 | 0.1790 | 0.2081 | | 0.1833 | | 0.1887 | |
| mo5 | 0.2429 | 0.2452 | | 0.2196 | | 0.2497 | |
| sc2 | 0.0436 | 0.0773 | | 0.0595 | | 0.0401 | |
| sc3 | 0.0767 | 0.1388 | | 0.1040 | | 0.0913 | |
| sc4 | 0.1243 | 0.2294 | | 0.1909 | | 0.1917 | |
| sc5 | 0.1597 | 0.2210 | | 0.2525 | | 0.2338 | |
| ua2 | 0.0504 | 0.0501 | | 0.0380 | | 0.0195 | |
| ua3 | 0.0911 | 0.0865 | Values identical to | 0.0910 | | 0.0765 | |
| ua4 | 0.1479 | 0.2293 | _ | "Scaling factor model" for Arm 1 0.2275 "Scaling factor model" for Arm 1 0.2395 | | 0.2029 | |
| ua5 | 0.1748 | 0.2183 | moder for All I | | 0.2254 | | |
| pd2 | 0.0445 | 0.0632 | | 0.0300 | | 0.0459 | |
| pd3 | 0.0682 | 0.1427 | | 0.1078 | | 0.1180 | |
| pd4 | 0.1314 | 0.2681 | | 0.2655 | | 0.3075 | |
| pd5 | 0.1912 | 0.4152 | | 0.4017 | | 0.4519 | |
| ad2 | 0.0718 | 0.0392 | | 0.0690 | | 0.0579 | |
| ad3 | 0.1105 | 0.0477 | | 0.1124 | | 0.0872 | |
| ad4 | 0.1682 | 0.1689 | | 0.1652 | | 0.1789 | |
| ad5 | 0.1960 | 0.2150 | | 0.2685 | | 0.2360 | |
| co2 | 0.0316 | 0.0362 | 0.0322 | 0.0463 | 0.0079 | 0.0396 | |
| co3 | 0.1318 | 0.1379 | 0.0620 | 0.0814 | 0.0534 | 0.0894 | |
| co4 | 0.3291 | 0.3368 | 0.2053 | 0.2387 | 0.1403 | 0.1870 | |
| co5 | 0.3930 | 0.3980 | 0.2753 | 0.2646 | 0.2320 | 0.2382 | |

Note: For all three arms, the italicized coefficients of the five core dimensions for the scaling factor model were extracted from Ikeda et al. 2015⁴⁾., and they were rounded to the fourth decimal place for this poster to enhance readability.

4. Prediction accuracy

 The MAEs of the scaling factor model and conventional model were 0.0720 and 0.1305, 0.0748 and 0.0885, and 0.0985 and 0.0685 in Arms 1, 2, and 3, respectively (Table 3).

Table 3 Model prediction accuracy

| Table of Model | prediction accura | lOy | | |
|-----------------------------------|----------------------|----------------------|------------------------------|----------------------------|
| Index for precision | Model | Arm 1: EQ-5D-5L+C | Arm 2: Remembering things | Arm 3: Thinking clearly |
| MAE | Scaling factor model | 0.0720 | 0.0748 | 0.0985 |
| | Linear mixed model | 0.1305 | 0.0885 | 0.0685 |
| Pearson's correlation coefficient | Scaling factor model | 0.9726 | 0.9706 | 0.9574 |
| Coemcient | Linear mixed model | 0.9122 | 0.9539 | 0.9722 |

CONCLUSION

- This experimental study examined the valuation methods for creating a tariff for the Japanese population.
- The results suggest that a scaling factor model may offer a comparable method to the conventional model, and the scaling factor model could be used to calculate "bolt-on" QOL scores.
- Further experimental studies on valuation using the recently proposed approach and cognition dimensions are warranted.

- Krabbe et al. The effect of adding a cognitive dimension to the EuroQol multiattribute
- health-status classification system. J Clin Epidemiol. 1999;52:293-301 Janssen, et al. The cognition dimension revisited: A detailed study on its added value and interactions with EQ-5D core dimensions. The 30th Scientific Plenary Meeting of
- Yang et al. Effect of health state sampling methods on model predictions of EQ-5D-5L values: Small designs can suffice. Value Health. 2019;22:38-44. Ikeda et al. Developing a Japanese version of the EQ-5D-5L value set. J Natl Inst

the EuroQol Group. Montréal, September 12–14, 2013.

Shiroiwa et al. Comparison of value set based on DCE and/or TTO data: Scoring for EQ-5D-5L health states in Japan. Value Health. 2016;19:648-54. 6) Igarashi et al. Linguistic and psychometric validation of the cognition bolt-on version of

the Japanese EQ-5D-5L for the elderly. JAD. 2023;91:1447-1458.

7) Finch et al. Selecting bolt-on dimensions for the EQ-5D: Testing the impact of hearing, sleep, cognition, energy, and relationships on preferences using pairwise choices. Med Decis Making. 2021;41:89-99. 8) Statistics Bureau of Japan. 2020 Population Census Basic Tabulation: Table 1-1, Male and female, age (each age), total number of nationalities, average age and median

age - nationwide, prefectures, 21 metropolitan areas, special districts, cities with a

population of 500,000 or more. 2021. https://www.e-stat.go.jp/stat-search/filedownload?statInfId=000032144434&fileKind=0. Last updated November 30, 2021 Accessed on February 13, 2023. (in Japanese)

EQ-5D-5L valuation protocol. Value Health. 2014;17:445-53.

9) Janssen et al. Introducing the composite time trade-off: A test of feasibility and face validity. Eur J Health Econ. 2013;14 Suppl 1:S5-13. 10) Oppe et al. A program of methodological research to arrive at the new international

Sources of funding This study was funded by Eisai Co., Ltd. and Biogen Inc.