QOL/PRO研究会　第16回研究セミナー

# 選好に基づく尺度の世界: 健康の価値を測定するとは

## 15D©

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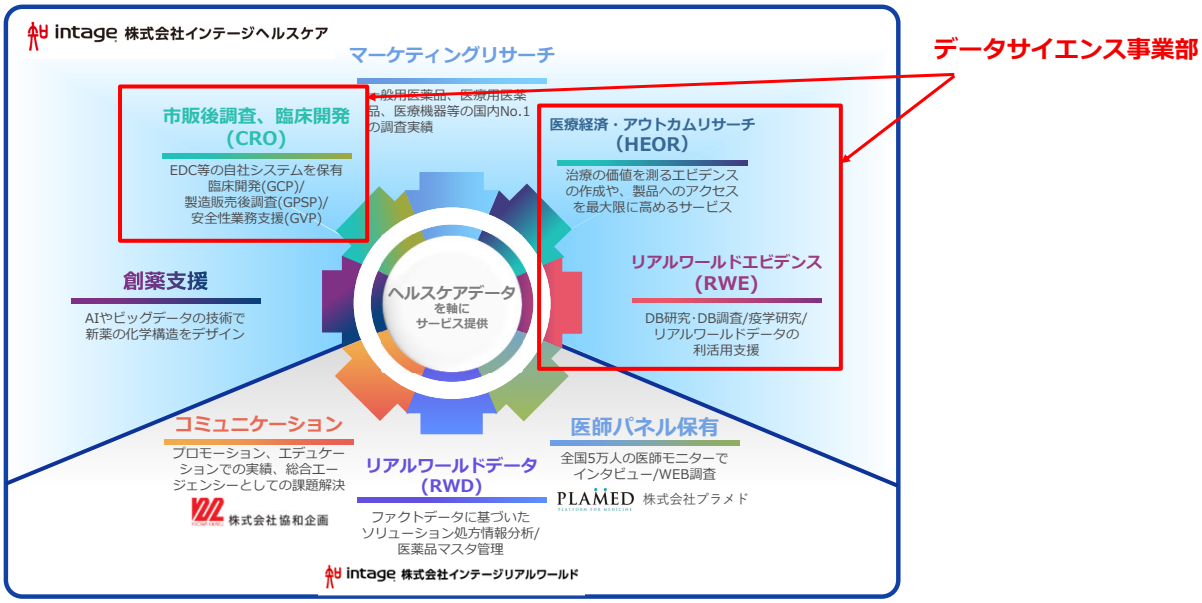
2022年3月12日 (V1.3)

intage 株式会社インテージヘルスケア



## INTAGE Group Healthcare Companies



## Dislcaimer

- 示される意見はわたし個人のものであり、所属する組織を代表するものではない
- 15Dの尺度の開発と販売と直接関わっていない。今の所。しかし、感動が良い尺度として興味深い。





## 15Dとは

- 健康関連QOLを測定するために開発された包括的な評価尺度
- 自己記入式。「現在の健康状態」について回答する。紙とオンライン形式が可能。
- 1992年にヘルシンキ大学の研究者（Sintonen et al.)に開発された
  - 1981年：12項目の尺度の作成
  - 1986年：12項目→15項目の尺度の作成
  - 1992年：15項目の尺度の完成
- プロファイル型とインデックス型の尺度として使用できる

開発したきっかけについて

*From “Accounts from developers of generic health state utility instruments explain why they produce different QALYs: A qualitative study” (Pickles et al 2019)*

“…a mission of developing the best instrument on the market, claiming that **existing [instruments] were of poor quality**.”

“…could not be sure that existing generic measures would capture the issues of importance to their target population.”

## 15Dの特徴

- **15項目**があって、**各項目が5段階**である（簡便で、**５分程度**かかる。）
- 32の言語バージョンが存在する。新しい翻訳（言語的妥当性）も可能
- **日本語版**は、2013年に研究者（Okamoto et al.)によって開発されている
- 日本語版の**信頼性は確認済み**（internal consistency & test-retest reliability）ですが、**日本の換算式(表)がない**。今のところ。フィンランドとデンマーク、またノルウエーの換算式(表)が存在する。
- 回答結果をもとに「完全な健康＝1」「死亡＝0」と基準化された健康状態のスコアが算出可能。臨床的に重要な変化の最小量(MCID)は+/-0.015だと言われている。





## 15Dの特徴

| | |
|---|---|
| **質問紙の日本語版** | あり（Okamoto et al. 2013） |
| **対象集団** | 成人<br>※しかし、海外では「16D」（12-18歳）と「17D」(8-11歳）いう小児版もあるし、プロキシーの利用も可能 |
| **質問項目** | 質問紙は15問、classification systemは①移動の程度、②視力、③聴力、④呼吸、⑤睡眠、⑥食事、⑦話し、⑧排泄、⑨日常活動、⑩精神機能、⑪不快と症状、⑫うつ、⑬悩み、⑭活力、⑮性活動　・・・の15領域。 |
| **各質問の水準数** | 5 |
| **価値づけ(valuation)方法** | • Rating scale method (VAS) with magnitude estimation (マグニチュード推定法)。<br>計３つのタスク（ノルウエーでよりシンプルなアプローチを利用した）。<br>【フィンランド】https://doi.org/10.1016/0160-7995(81)90019-8<br>【デンマーク】 https://www.sdu.dk/-/media/files/om_sdu/centre/cohere/working+papers/20087.pdf<br>【ノルウエー】 ① https://doi.org/10.1016/j.jval.2017.09.018 (n=2256)<br>②【simple版】https://doi.org/10.1007/s11136-018-2043-9 (=120)<br>• Additive model $V_H = \sum_j I_j(x_j) w_j(x_j)$ where Ij(xj) = the average relative importance people attach to various levels of dimension j (j = 1, 2,..,15), and wj(xj) = the average value people place on various levels of dimension j. |
| **使用許諾** | Prof. Harri Sintonen, University of Helsinki, Finland<br>http://www.15d-instrument.net/contact/ |
| **使用料** | 有料（学術研究から無料） |

## 15Dの質問表

### 英語版

http://www.15d-instrument.net/site/assets/files/1002/15d_english.pdf

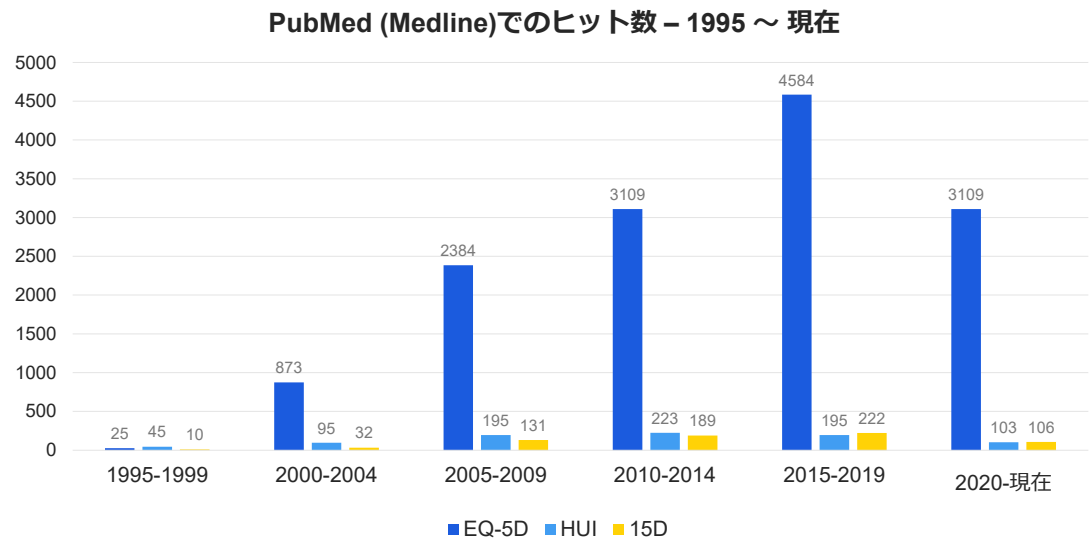
### 日本語版

https://doi.org/10.1371/journal.pone.0061721.s001



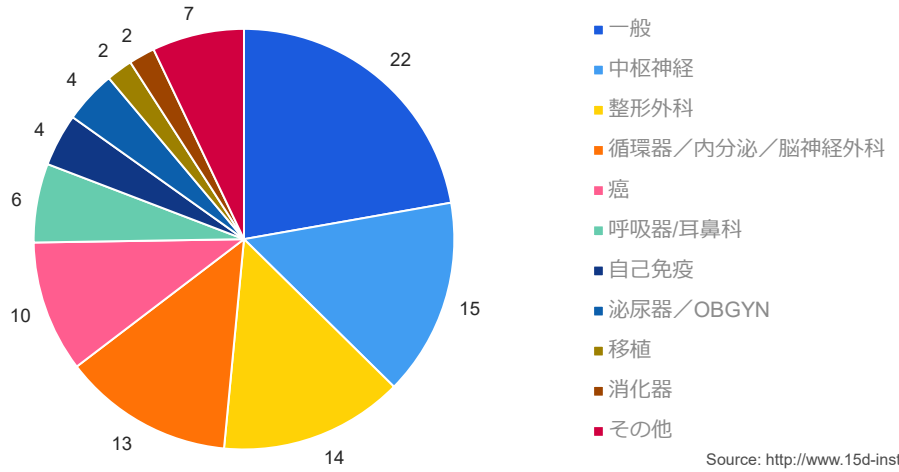


## 文献のヒット数



## 15Dの論文の治療分野

### 論文の治療分野（%）（n=603)




Source: http://www.15d-instrument.net/publications/
(rough coding based on titles as of March 12, 2022)





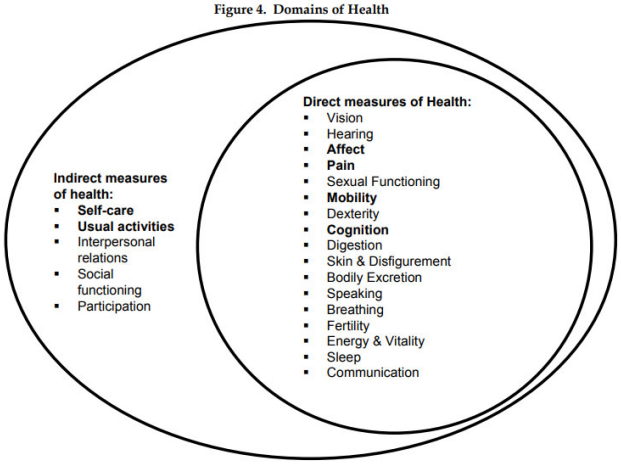
## 15Dの項目

| | 項目 | 日本語 | EQ-5D | HUI3 |
|---|---|---|---|---|
| (1) | Mobility (move) | 移動の程度 | ✓（移動） | ✓（歩行、器用さ） |
| (2) | Vision (see) | 視力 | | ✓（視力） |
| (3) | Hearing (hear) | 聴力 | | ✓（聴力） |
| (4) | Breathing (breath) | 呼吸 | ✓（ふだんの活動） | |
| (5) | Sleeping (sleep) | 睡眠 | | |
| (6) | Eating (eat) | 食事 | ✓（身の回りの管理） | |
| (7) | Speech (speech) | 話し | | ✓（会話） |
| (8) | Excretion (excret) | 排泄 | ✓（身の回りの管理） | |
| (9) | Usual activities (uact) | 日常活動 | ✓（ふだんの活動） | |
| (10) | Mental function (mental) | 精神機能 | | ✓（認知） |
| (11) | Discomfort and symptoms (disco) | 不快と症状 | ✓（痛み／不快感） | ✓（痛み） |
| (12) | Depression (depr) | うつ | ✓（不安／ふさぎ込み） | |
| (13) | Distress (distr) | 悩み | ✓（不安／ふさぎ込み） | |
| (14) | Vitality (vital) | 活力 | | |
| (15) | Sexual activity (sex) | 性活動 | | |

# WHO-ICF

## WHO International Classification of Functioning, Disability and Health (ICF)

Figure 4. Domains of Health




Chatterji S et al. The conceptual basis for measuring and reporting on health. Global Programme on Evidence for Health Policy Discussion Paper No 45, WHO 2002.

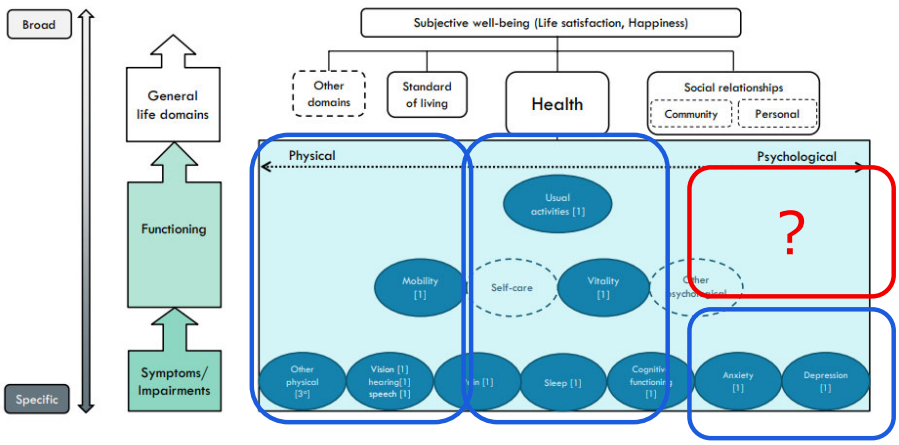




# 15Dのconceptual map (retrospective)

From “A conceptual map of health-related quality of life dimensions: key lessons for a new instrument” (Olsen et al. 2019)

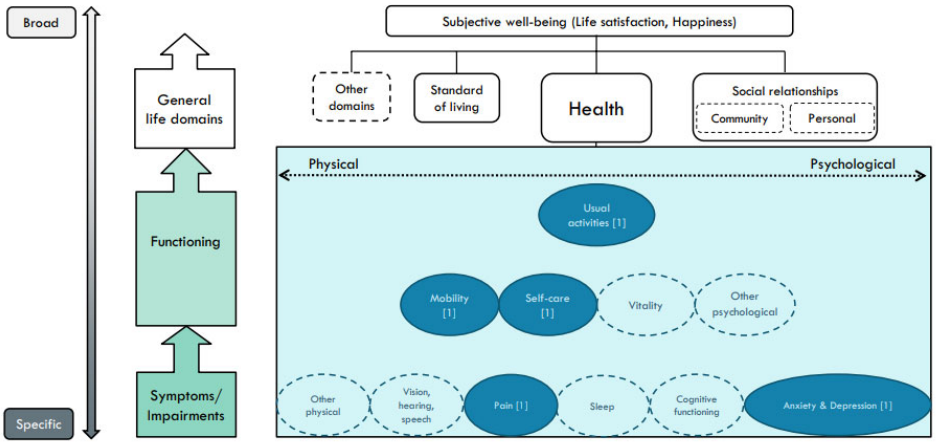
15D



# EQ-5Dのconceptual map (retrospective)

From “A conceptual map of health-related quality of life dimensions: key lessons for a new instrument” (Olsen et al. 2019)

EQ-5D



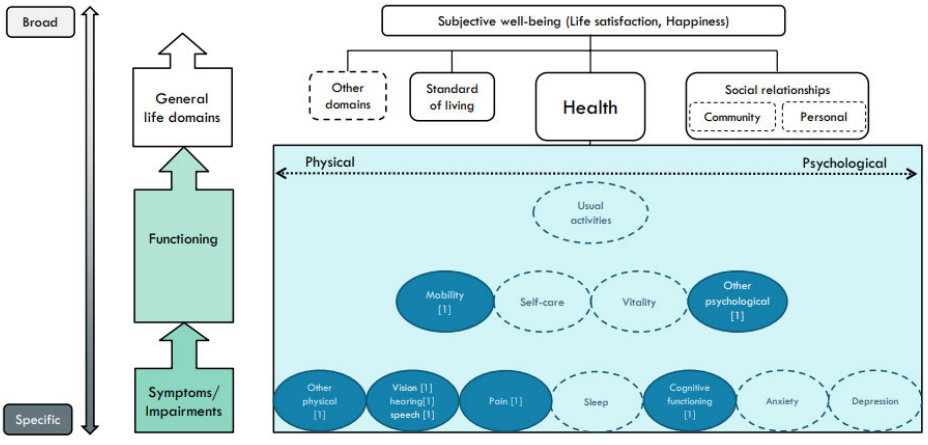





# HUI3のconceptual map (retrospective)

From “A conceptual map of health-related quality of life dimensions: key lessons for a new instrument” (Olsen et al. 2019)

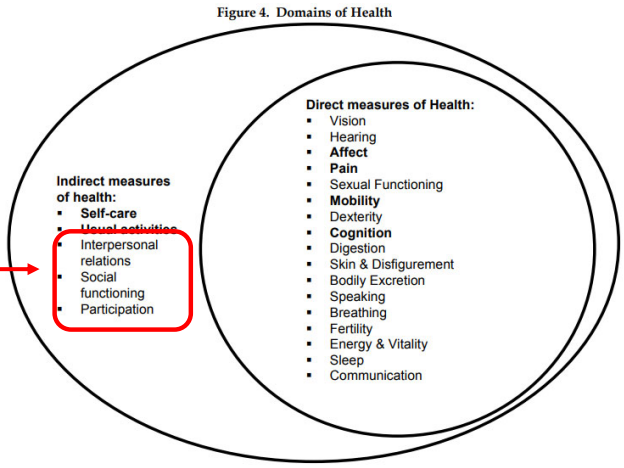
HUI3



# WHO-ICF

## WHO International Classification of Functioning, Disability and Health (ICF)

人間関係とか
社会の参加を考
慮するべき？




Chatterji S et al. The conceptual basis for measuring and reporting on health. Global Programme on Evidence for Health Policy Discussion Paper No 45, WHO 2002.



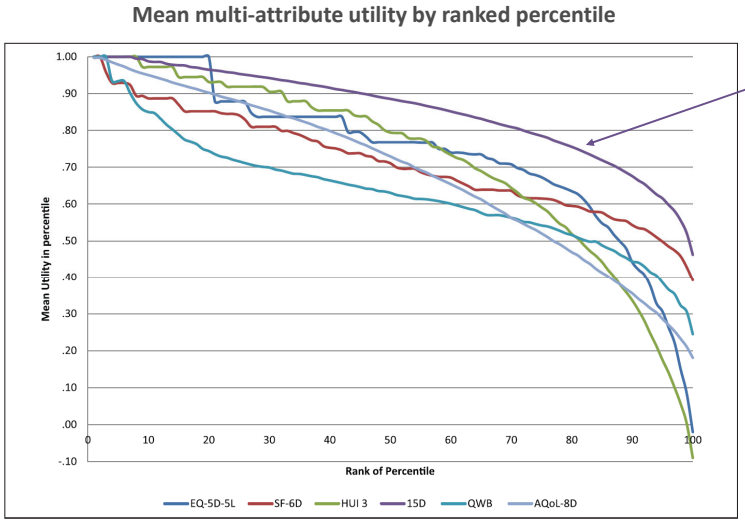


# 15D Health States

| | Published | Attribute/ Domain | Health states | |
|---|---|---|---|---|
| HUI2 | 1992 | 7 | 24,000 | |
| HUI3 | 1995 | 8 | 972,000 | |
| EQ-5D-3L | 1990 | 5 | 243 | |
| EQ-5D-5L | 2011 | 5 | 3,125 | (5 levels $^{5\ dimensions}$) |
| SF-6D | 1998 | 6 | 18,000 | |
| 15D | 1990 | 15 | 3,052,000,000 | (5 levels $^{15\ dimensions}$) |

引用：能登 真一基先生。PBM（Preference-Based Measure）活用の可能性。第7回QOL/PRO研究会学術集会（2019.12.14）

# 15Dの傾向①




- 効用値が高めに出る傾向がある。
- 効用値が「compress」(圧縮)されている（＝標準偏差が低い）し、effect sizeが大きいと言われている

Source: Richard et al. 2016. Measuring the Sensitivity and Construct Validity of 6 Utility Instruments in 7 Disease Areas





# 15Dの傾向②

## 15Dはより感動がある？　特に健康状態が悪化する場合（改善でなく）？？

**Comparison of two utility instruments, the EQ-5D and the 15D, in the critical care setting; Vainiola et al 2010**

"The distribution of the 15D scores (all positive values) was one-peaked and continuous and, importantly, only 6% of the patients evaluated their health state as perfect at 6 months after critical illness, indicating **better discriminatory power of the 15D in minor health problems**…. In conclusion, the **15D may be more sensitive than the EQ-5D in terms of discriminatory power and responsiveness to clinically important change**."

**Comparison of EQ-5D and 15D instruments for assessing the health-related quality of life in cardiac surgery patients; Heiskanen et al 2016**

"**15D seems to be more sensitive to change** and indicates improvement in health utility more often than the EQ-5D does."

**Validation of EQ-5D and 15D in the assessment of health-related quality of life in chronic pain; Vartiainen 2017**

"**EQ-5D appeared less sensitive than 15D** especially in those patients with chronic pain who had a better health status."

# 15Dの傾向②

## でも、欠点もあるようです。また、EQ5Dより長い。

**Comparison of preference-based utilities of the 15D, EQ-5D and SF-6D in patients with HIV/AIDS; Stavem et al 2005**

"When comparing the 15D and the SF-6D, the 15D had a larger proportion of patients scoring in the upper tenth of the scale, which **may reduce the potential to detect improvements** in quality of life, but **increase the potential to detect deterioration**."

**Validation and comparison of 15-D and EQ-5D-5L instruments in a Spanish Parkinson's disease population sample; Garcia-Gordillo et al 2014**

"**15D has better efficiency and greater sensitivity to detect clinical changes in Parkinson's disease severity** of the symptoms. Meanwhile the **EQ-5D-5L is better to detect clinical HRQoL changes**. Additionally, the **EQ-5D-5L questionnaire requires less time than 15-D** to be administered...."





# 15Dの傾向②

**Responsiveness and minimal important score differences in quality-of-life questionnaires: a comparison of the EORTC QLQ-C30 cancer-specific questionnaire to the generic utility questionnaires EQ-5D and 15D in patients with multiple myeloma; Kvam et al 2011.**

"**15D was less responsive than the EQ-5D in patients who deteriorated**. Our results are supported by the findings in a study by Linde et al. comparing EQ-5D and 15D in patients with rheumatoid arthritis. They found that the **EQ-5D was more responsive than the 15D in both improved and deteriorated patients**. However, the 15D has showed higher responsiveness statistics than the EQ-5D in patients with chronic obstructive pulmonary disease (COPD), in rehabilitation of musculoskeletal, cardiovascular and psychosomatic disorders and in the critical care setting."

**Can EQ-5D and 15D be used interchangeably in economic evaluations? Assessing quality of life in post-stroke patients; Lunde 2021**

"The results show that **EQ-5D and 15D should not be used interchangeably** in economic evaluations. EQ-5D is likely to give a more favourable cost utility ratio than 15D. The utility scores generated from the two instruments differ significantly different from each other, even though they correlate well. The instruments also rank individuals in terms of health status differently."

# 15DのValue Setの作成（３つのタスク）

**Task #1 (“top task”)**

- 15項目のうち、各項目のために最も良い（高い）水準を相対的にVASの定規上に置く（評価する）→ つまり、回答者は、 VASを使用して、異なる15項目ために最大な選択肢を「最も重要」から「最も重要でない」という観点から評価する

**Task #2 (“bottom task”)**

- Task #1と同様に15項目のうち、各項目のために最も良くない（低い）水準を相対的にVASの定規上に置く（評価する）→ つまり、回答者は、 VASを使用して、異なる15項目ために最悪な選択肢を「最も重要でない」から「最も重要でない」という観点から項目を評価する

**Task #3 (“within-dimension task”)**

- それぞれの項目のために全ての水準をVASの定規の上に置く（評価する）。また、死んだ状態を評価する。

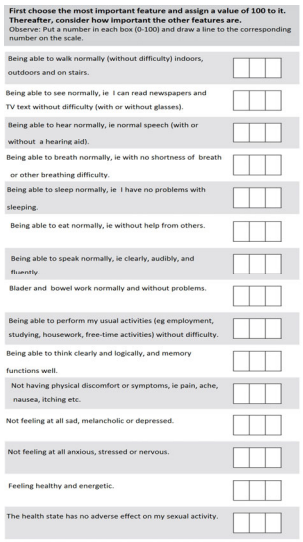
【フィンランド】https://doi.org/10.1016/0160-7995(81)90019-8
【デンマーク】 https://www.sdu.dk/-/media/files/om_sdu/centre/cohere/working+papers/20087.pdf
【ノルウエー】 ① https://doi.org/10.1016/j.jval.2017.09.018 ②【simple版】https://doi.org/10.1007/s11136-018-2043-9

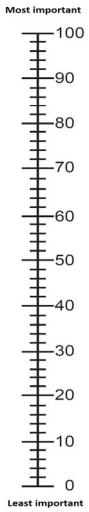




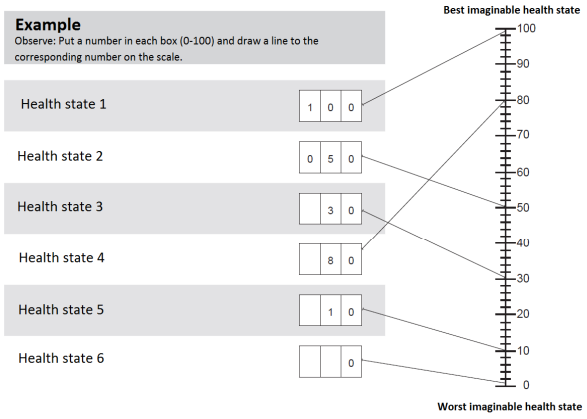
# 15DのValue Setの作成（３つのタスク）

**Task #1 (“top task”)**



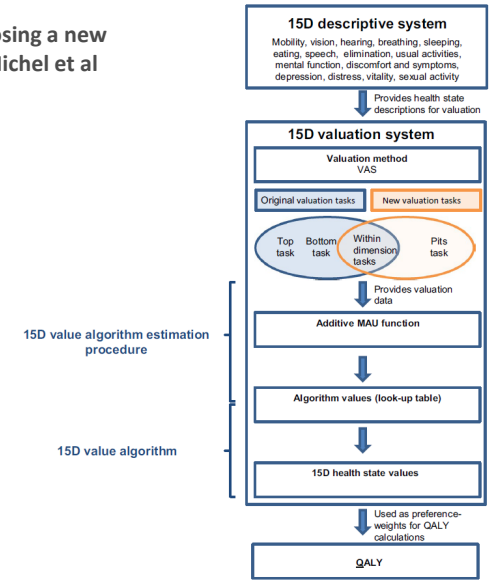

**Task #3 (“within-dimension task”)**




**ノルウエーで開発したシンプル版は上記の”within-dimension task”にpits taskを加えて実施する**

# 15DのValue Setの作成（３つのタスク）

From “A Norwegian 15D value algorithm: proposing a new procedure to estimate 15D value algorithms” Michel et al 2019








# ご参考まで

15D Instrument Website

お勧めのサイト。
英語ですが、15Dについての情報、かつQOL尺度の作成、検証(validation)に関する情報が豊富である。

http://www.15d-instrument.net/15d/

# ご清聴ありがとうございました！

Healthier Decisions

我々は情報に命を与え、医療を享受する人、医療を提供する人、
健康を願うすべての人々が納得の選択をするための力となります

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株式会社インテージヘルスケア
部署名　医療経済・アウトカムリサーチ室
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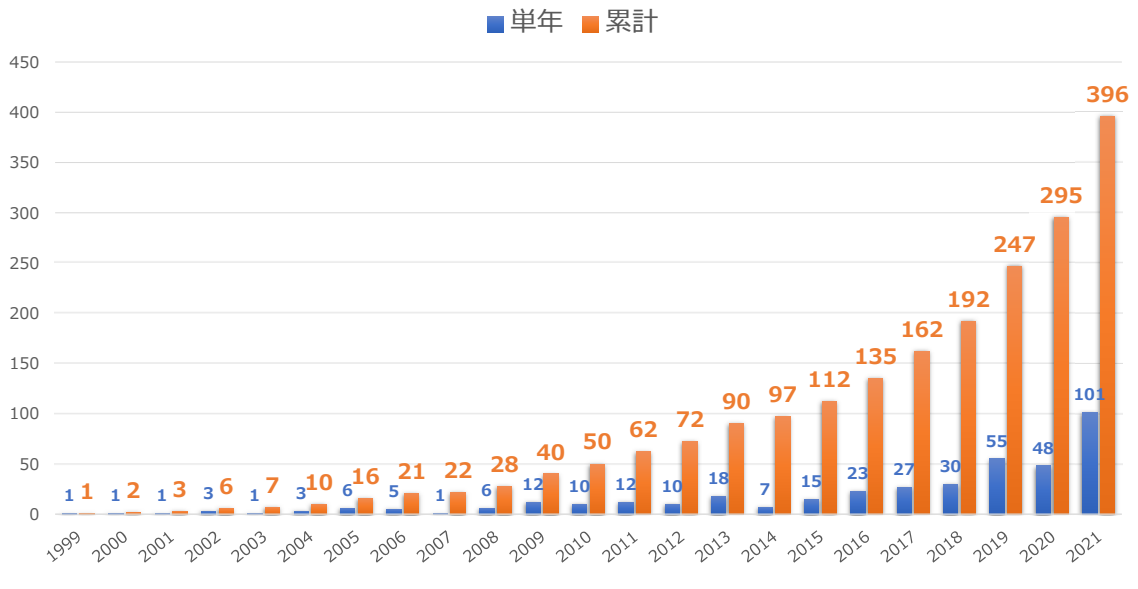
Email: m.lopresti@intage.com

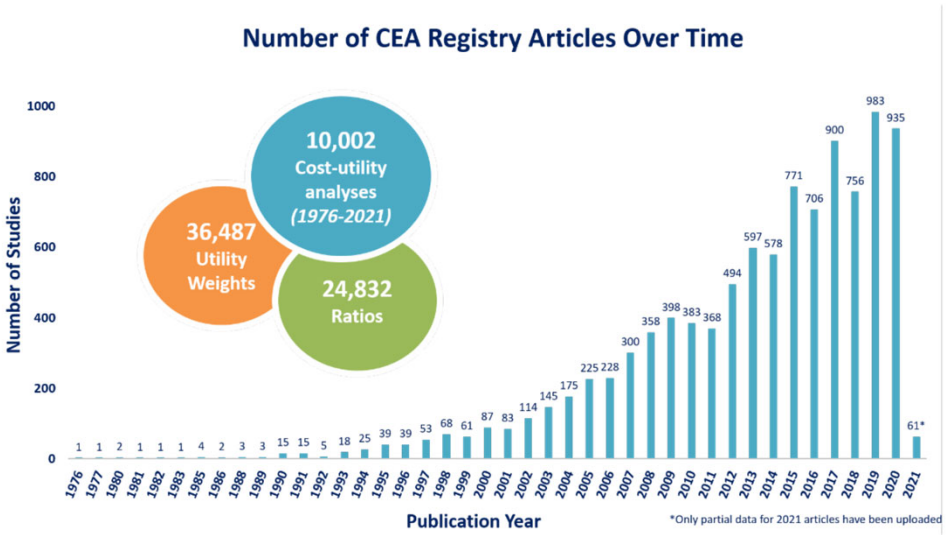
# PBMを用いた日本の研究の現状

新潟医療福祉大学
医療経済・QOL研究センター
能登　真一

# 国内におけるQOL値報告の推移

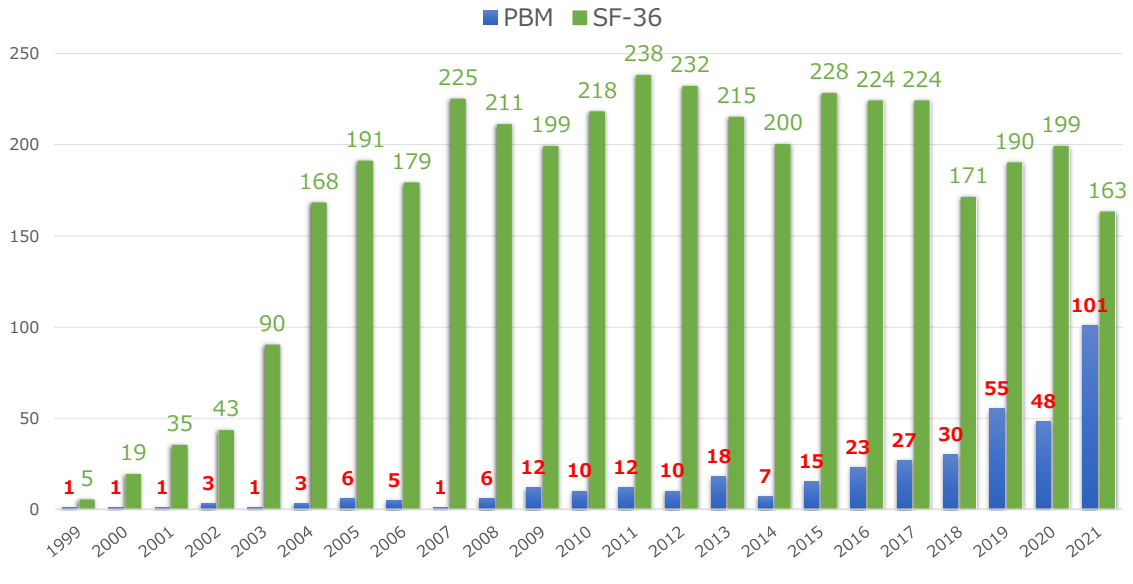


# CEA Registry

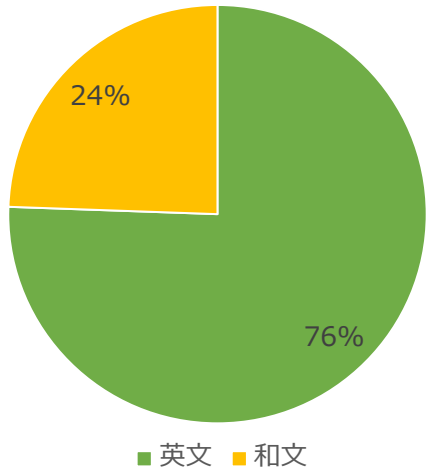


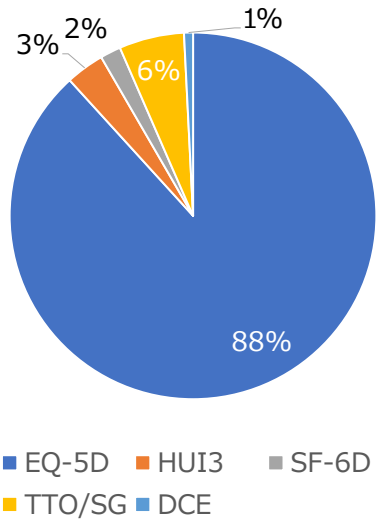

The CEA Registry has been updated to include analyses published through **2020 adding** 996 studies, 2,370 ratios, and **3,125 utility weights** to the database.

# 国内におけるQOL値報告の推移

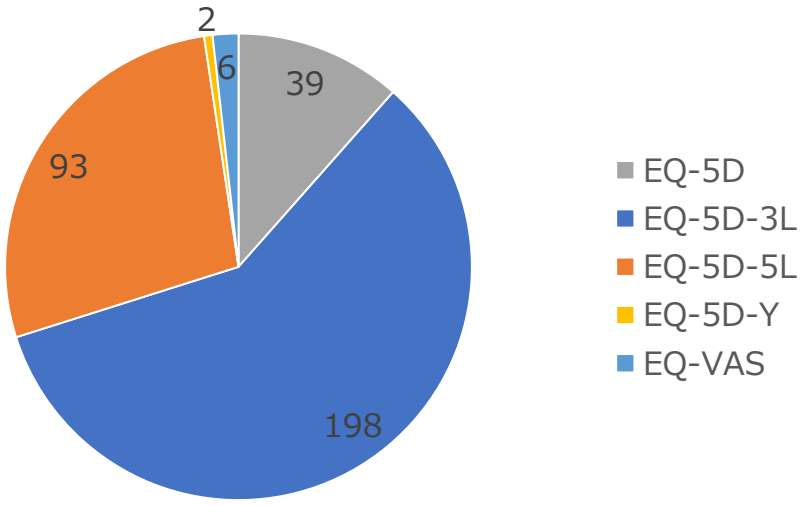


# 日本人を対象にQOL値を報告した論文の内訳

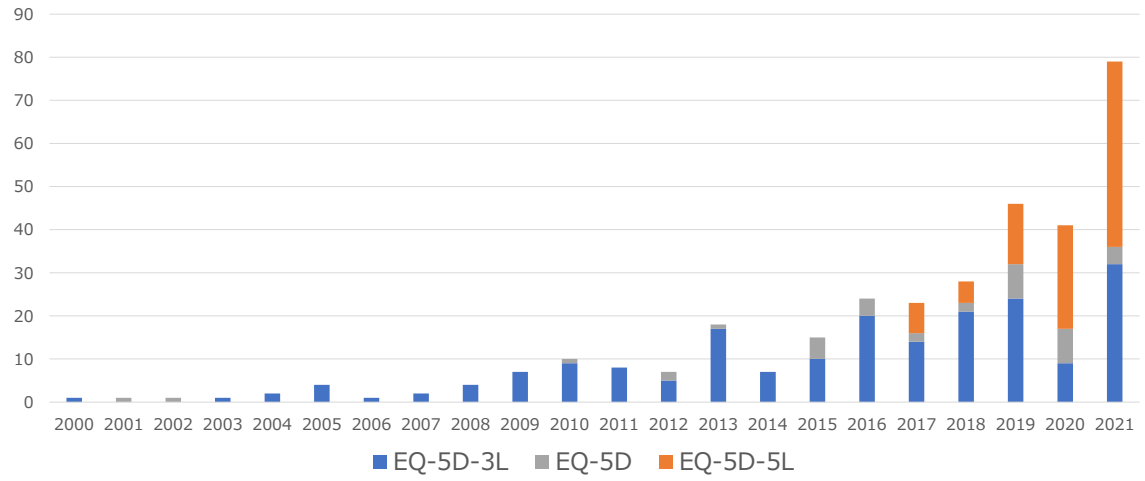


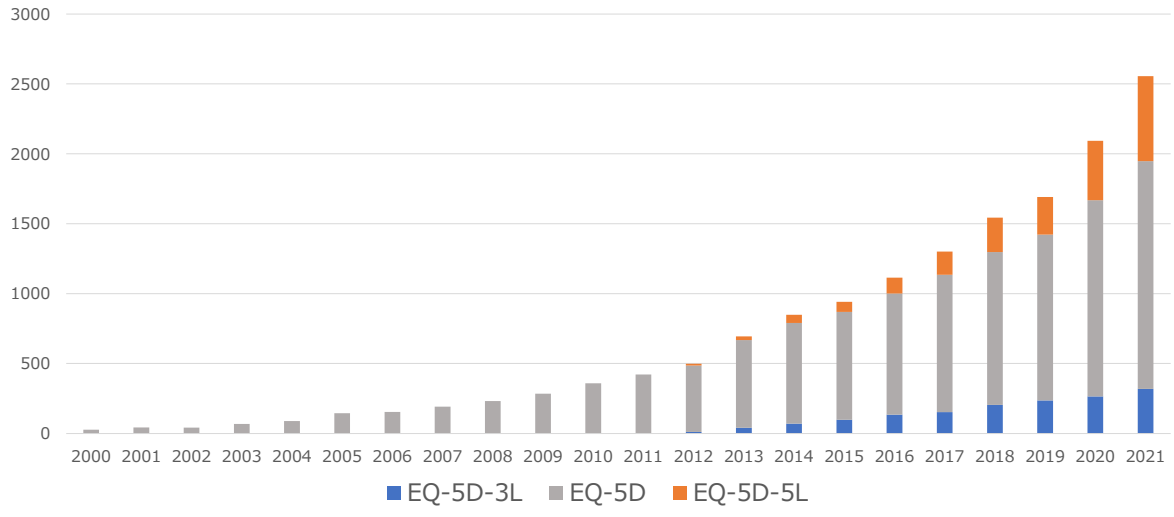

# EQ-5Dの内訳



# EQ-5D-3Lから5Lへ



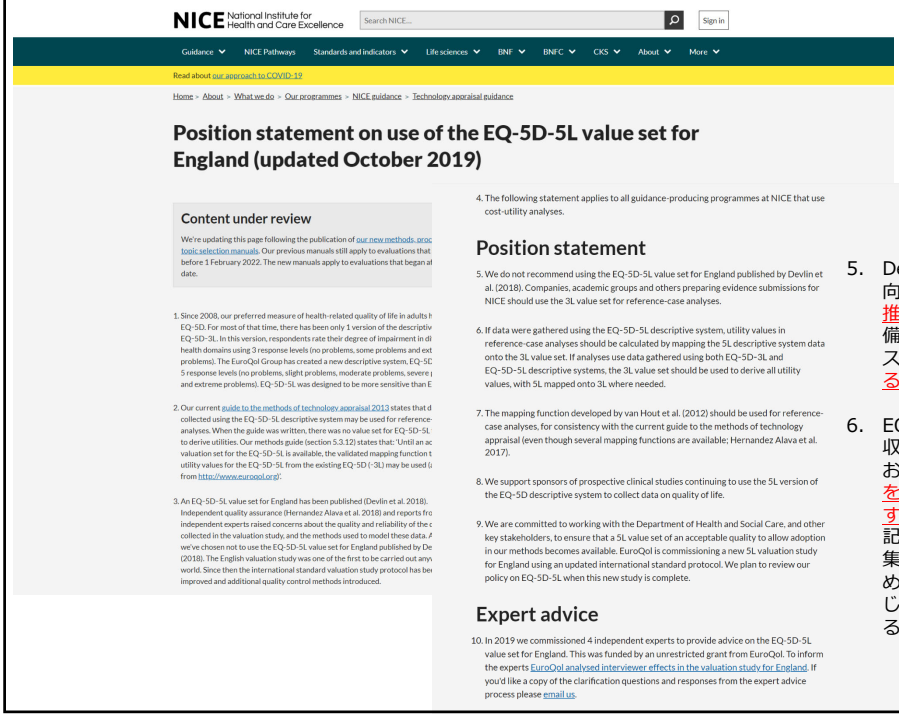

# EQ-5D-3Lから5Lへ 世界では



# 英国NICEにとってのEQ-5D

- EQ-5D（EQ-5D-3L）の使用を推奨
- 一方で，EQ-5Dがすべての症状に適しているとは限らないことを認めている　⇒　e.g., 聴覚障害はHUI3を使用

- 希少疾患の場合：EQ-5Dが不適切であるという強い証拠がない限り，ほとんどの状況でEQ-5Dを使用することを維持する
- 臨床試験や文献でEQ-5Dが使用できない場合のガイドラインはない



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Read about our approach to COVID-19

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**Position statement on use of the EQ-5D-5L value set for England (updated October 2019)**

**Content under review**

We're updating this page following the publication of our new methods, proc topic selection manuals. Our previous manuals still apply to evaluations that before 1 February 2022. The new manuals apply to evaluations that began a date.

1. Since 2008, our preferred measure of health-related quality of life in adults h EQ-5D. For most of that time, there has been only 1 version of the descriptiv EQ-5D-3L. In this version, respondents rate their degree of impairment in di health domains using 3 response levels (no problems, some problems and ext problems). The EuroQol Group has created a new descriptive system, EQ-5D 5 response levels (no problems, slight problems, moderate problems, severe and extreme problems). EQ-5D-5L was designed to be more sensitive than E

2. Our current guide to the methods of technology appraisal 2013 states that d collected using the EQ-5D-5L descriptive system may be used for reference- analyses. When the guide was written, there was no value set for EQ-5D-5L to derive utilities. Our methods guide (section 5.3.12) states that: 'Until an ac valuation set for the EQ-5D-5L is available, the validated mapping function t utility values for the EQ-5D-5L from the existing EQ-5D (-3L) may be used ( from http://www.euroqol.org/'.

3. An EQ-5D-5L value set for England has been published (Devlin et al. 2018). Independent quality assurance (Hernandez Alava et al. 2018) and reports fro independent experts raised concerns about the quality and reliability of the c collected in the valuation study, and the methods used to model these data. A we've chosen not to use the EQ-5D-5L value set for England published by De (2018). The English valuation study was one of the first to be carried out anyw world. Since then the international standard valuation study protocol has bee improved and additional quality control methods introduced.

4. The following statement applies to all guidance-producing programmes at NICE that use cost-utility analyses.

**Position statement**

5. We do not recommend using the EQ-5D-5L value set for England published by Devlin et al. (2018). Companies, academic groups and others preparing evidence submissions for NICE should use the 3L value set for reference-case analyses.

6. If data were gathered using the EQ-5D-5L descriptive system, utility values in reference-case analyses should be calculated by mapping the 5L descriptive system data onto the 3L value set. If analyses use data gathered using both EQ-5D-3L and EQ-5D-5L descriptive systems, the 3L value set should be used to derive all utility values, with 5L mapped onto 3L where needed.

7. The mapping function developed by van Hout et al. (2012) should be used for reference-case analyses, for consistency with the current guide to the methods of technology appraisal (even though several mapping functions are available; Hernandez Alava et al. 2017).

8. We support sponsors of prospective clinical studies continuing to use the 5L version of the EQ-5D descriptive system to collect data on quality of life.

9. We are committed to working with the Department of Health and Social Care, and other key stakeholders, to ensure that a 5L value set of an acceptable quality to allow adoption in our methods becomes available. EuroQol is commissioning a new 5L valuation study for England using an updated international standard protocol. We plan to review our policy on EQ-5D-5L when this new study is complete.

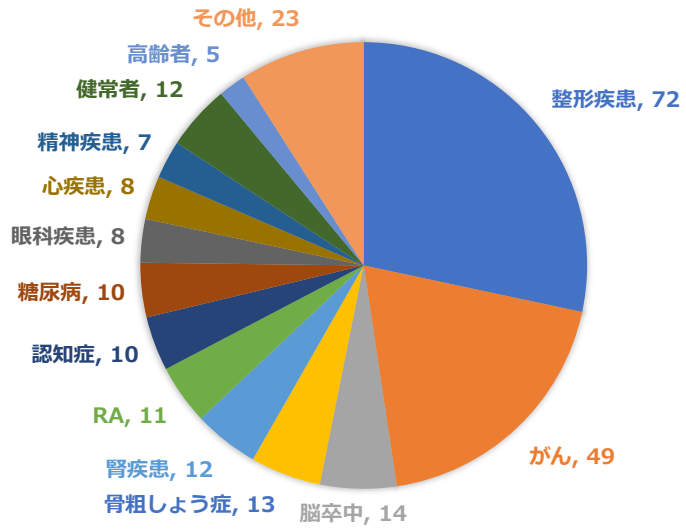
**Expert advice**

10. In 2019 we commissioned 4 independent experts to provide advice on the EQ-5D-5L value set for England. This was funded by an unrestricted grant from EuroQol. To inform the experts EuroQol analysed interviewer effects in the valuation study for England. If you'd like a copy of the clarification questions and responses from the expert advice process please email us.

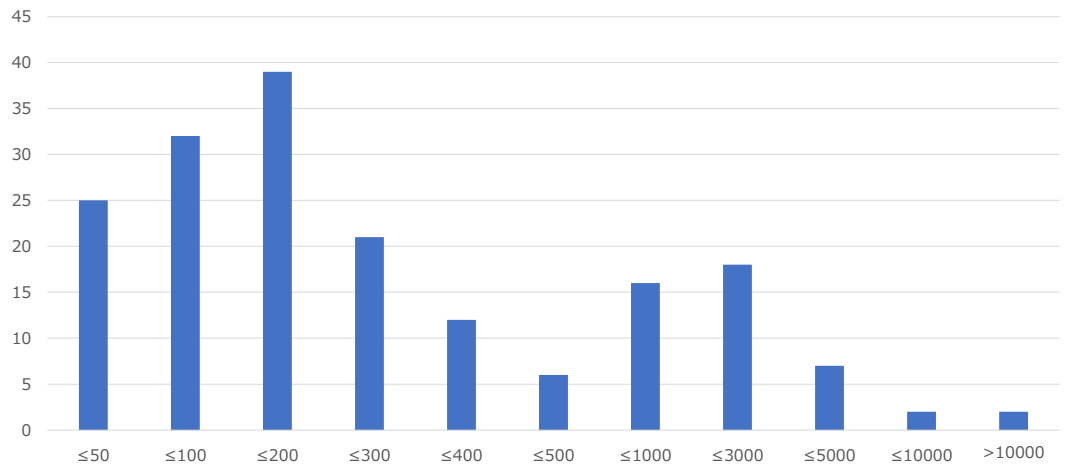
5. Devlinら（2018）が発表したイングランド向けのEQ-5D-5Lバリューセットの使用は推奨しない．NICEへのエビデンス提出を準備する企業，学術団体などは，リファレンスケース分析に3Lバリューセットを使用する必要がある．

6. EQ-5D-5L記述システムを用いてデータを収集した場合，レファレンスケース分析における効用値は，5L記述システムのデータを3Lバリューセットにマッピングして計算する必要がある．EQ-5D-3L と EQ-5D-5L 記述システムの両方を使用してデータを収集した場合，すべての効用値を導出するために 3Lバリューセットを使用し，必要に応じて 5L を 3L にマッピングする必要がある．

# 日本人を対象にQOL値を報告した論文の内訳




# 症例数による論文の比較



L.B. Mokkink et al. / Journal of Clinical Epidemiology 63 (2010) 737–745


# 妥当性と反応性を検討するために（COSMIN）

**Table 8. Generic hypotheses to evaluate construct validity and responsiveness**

| Generic hypotheses*: | |
|---|---|
| 1. | Correlations with (changes in) instruments measuring similar constructs should be ≥0.50. |
| 2. | Correlations with (changes in) instruments measuring related, but dissimilar constructs should be lower, i.e. 0.30-0.50. |
| 3. | Correlations with (changes in) instruments measuring unrelated constructs should be <0.30. |
| 4. | Correlations defined under 1, 2, and 3 should differ by a minimum of 0.10. |
| 5. | Meaningful changes between relevant (sub)groups (e.g. patients with expected high vs low levels of the construct of interest) |
| 6. | For responsiveness, AUC should be ≥ 0.70 |

| | サンプルサイズ |
|---|---|
| Excellent | ≥100 |
| Good | 50-99 |
| Fair | 30-49 |
| Poor | ＜30 |

# 解釈可能性を検討するために（COSMIN）

**Appendix 5. Information to extract on interpretability of PROMs**

The content of this table is based on the Box Interpretability from the original COSMIN Checklist [1]

| PROM (ref) | Distribution of scores in the study population | Percentage of missing items and percentage of missing total scores | Floor and ceiling effects | Scores and change scores available for relevant (sub)groups | Minimal important change (MIC) or minimal important difference (MID) | Information on response shift |
|---|---|---|---|---|---|---|
| PROM A (ref 1) | | | | | | |
| PROM A (ref 2) | | | | | | |
| PROM A (ref 3) | | | | | | |
| PROM B (ref 1) | | | | | | |
| … | | | | | | |

PharmacoEconomics (2020) 38:159–170
https://doi.org/10.1007/s40273-019-00854-w

SYSTEMATIC REVIEW

## Measurement Properties of Commonly Used Generic Preference-Based Measures in East and South-East Asia: A Systematic Review

Xinyu Qian[1] · Rachel Lee-Yin Tan[1] · Ling-Hsiang Chuang[2] · Nan Luo[1]

Table 1 Included papers and studies, by category

| | No. of papers/studies |
|---|---|
| Measurement property | |
| Construct validity | 73/1363 |
| Test-retest reliability | 25/61 |
| Responsiveness | 16/80 |
| PBM | |
| EQ-5D-3L | 46/498 |
| EQ-5D-5L | 28/311 |
| EQ-VAS | 37/405 |
| SF-6D | 20/197 |
| HUI2 | 2/16 |
| HUI3 | 6/55 |
| QWB | 2/22 |
| Country/district | |
| China | 19/376 |
| Hong Kong | 10/177 |
| Japan | 5/38 |
| Malaysia | 4/21 |
| Singapore | 19/374 |
| South Korea | 7/159 |
| Taiwan | 6/184 |
| Thailand | 6/146 |
| Vietnam | 1/12 |
| Indonesia | 2/17 |
| Disease groups | |
| Cancer | 10/225 |
| Developmental disease | 1/14 |
| Diabetes | 5/56 |
| Eye disease | 3/32 |
| Gastric disease | 1/6 |
| General population | 17/302 |
| Genitourinary disease | 1/24 |
| Heart disease | 2/47 |
| Hepatitis | 2/31 |
| HIV | 3/39 |
| Injury | 1/60 |
| Kidney disease | 2/15 |
| Mental disorders | 3/65 |
| Multiple conditions | 3/130 |
| Musculoskeletal disease | 6/113 |
| Neurological disease | 3/78 |
| Respiratory disease | 3/32 |
| Rheumatic disease | 9/150 |
| Skin disease | 1/2 |
| Stroke | 3/71 |
| Thyroid disease | 1/12 |

**Table 2** Grading results for EQ-5D in different countries/districts and different disease groups

| | Quality of PBM, quality of evidence, and references | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Construct validity | | | Test-retest reliability | | | Responsiveness | | |
| China | + | H | [21, 27, 28, 41–43, 45, 57, 72, 75, 76, 82, 83, 85, 87, 89, 90] | ± | H | [27, 41, 75] | | | |
| Hong Kong | + | H | [17, 18, 20, 70, 79] | ± | *L*[b] | [20, 70, 79] | + | *V*[b,c] | [19] |
| Japan | ± | M[a] | [56, 66, 67] | | | | + | *H* | [56] |
| Malaysia | + | H | [53, 65, 71] | – | *V*[b,c] | [53] | | | |
| Singapore | + | H | [12–14, 38, 40, 47, 50, 68, 74, 77, 84, 86] | ± | L[b] | [12, 37, 38, 47] | ± | H | [12–14, 38, 51, 68] |
| South Korea | + | H | [29–32, 34, 39] | ± | L[b] | [29–32, 34] | + | H | [29, 33] |
| Taiwan | ± | H | [15, 16, 26, 36, 44, 88] | ± | *M*[a] | [15, 36] | + | M[a] | [16, 26, 44] |
| Thailand | + | H | [35, 58, 60–63] | ± | *L*[b] | [58, 63] | + | M[a] | [60, 63] |
| Vietnam | ± | H | [69] | | | | | | |
| Indonesia | ± | *H* | [59] | – | *L*[b] | [59] | | | |
| Cancer | + | H | [30, 32, 34, 36, 38, 42, 67] | ± | L[b] | [30, 32, 34, 36–38] | ± | M[c] | [38] |
| Diabetes | + | H | [39, 57, 58, 74] | ± | *L*[b] | [58] | | | |
| Eye disease | + | H | [13, 14] | | | | ± | H | [13, 24] |
| Gastric disease | + | H | [53] | – | *V*[b,c] | [53] | | | |
| General population | + | H | [15, 28, 31, 35, 41, 45, 59, 65, 66, 71, 75, 83, 85, 88, 89] | ± | M[a] | [15, 31, 41, 59, 75] | | | |
| Genitourinary disease | ± | H | [90] | | | | | | |
| Heart disease | + | H | [60, 82] | | | | + | *M*[c] | [60] |
| Hepatitis | + | *L*[b] | [27] | + | H | [27] | | | |
| HIV | + | H | [62, 69, 72] | | | | | | |
| Injury | + | H | [26] | | | | + | L[b] | [26] |
| Kidney disease | + | H | [86] | | | | | | |
| Mental disorders | ± | H | [12, 68] | ± | L[b] | [12] | ± | M[a] | [12, 68] |
| Multiple conditions | + | H | [61, 63, 77] | + | *L*[b] | [63] | + | *L*[b] | [63] |
| Musculoskeletal disease | + | H | [18, 20, 21, 87] | + | *L*[b] | [20] | + | *V*[b,c] | [19] |
| Neurological disease | + | H | [50] | | | | + | *L*[d] | [51] |
| Respiratory disease | + | M[a] | [17, 56] | | | | + | *H* | [56] |
| Rheumatic disease | + | H | [29, 40, 47, 70, 76, 84] | ± | *L*[b] | [29, 47, 70] | + | *M*[c] | [29] |
| Skin disease | + | *H* | [43] | | | | | | |
| Stroke | ± | H | [16, 44] | | | | + | H | [16, 33, 44] |
| Thyroid disease | + | H | [79] | – | *L*[b] | [79] | | | |

Quality of PBM: + indicates sufficient results; ± indicates inconsistent results; – indicates insufficient results

Italicised font indicates that grading is based on no more than three studies

Quality of evidence: H indicates high; M indicates moderate; L indicates low; V indicates very low

*Quality of Life Research* **12**: 555–563, 2003.




## A comparison of the responsiveness of different generic health status measures in patients with asthma

Toru Oga[1], Koichi Nishimura[1], Mitsuhiro Tsukino[2], Susumu Sato[2], Takashi Hajiro[3] & Michiaki Mishima[2]
[1]*Respiratory Division, Kyoto-Katsura Hospital (E-mail: ogat@df7.so-net.ne.jp);* [2]*Department of Respiratory Medicine, Graduate School of Medicine, Kyoto University, Kyoto;* [3]*Department of Pulmonary Medicine, Kobe Nishi City Hospital, Kobe, Japan*

**Table 3.** Treatment steps, $FEV_1$ and health status scores during the first 6 months in the 54 patients with asthma

| | Baseline | 3 months | 6 months | *p*-Value[a] |
|---|---|---|---|---|
| Treatment steps (1–5) | 1.8 ± 1.3 | 3.2 ± 0.5* | 3.1 ± 0.6* | <0.001 |
| $FEV_1$ (%predicted) | 74.4 ± 20.3 | 86.7 ± 18.4** | 85.6 ± 19.9** | 0.002 |
| AQLQ (1–7) | | | | |
| Symptoms | 4.34 ± 1.40 | 5.98 ± 1.05* | 6.04 ± 0.97* | <0.001 |
| Activities | 4.60 ± 1.30 | 5.84 ± 1.06* | 6.01 ± 1.07* | <0.001 |
| Emotions | 4.54 ± 1.47 | 5.71 ± 1.24* | 6.00 ± 1.04* | <0.001 |
| Environment | 5.34 ± 1.30 | 6.13 ± 1.02* | 6.16 ± 1.06* | <0.001 |
| Total | 4.59 ± 1.21 | 5.91 ± 0.98* | 6.04 ± 0.94* | <0.001 |
| SF-36 (0–100) | | | | |
| PF | 78.2 ± 21.3 | 84.7 ± 17.9 | 88.5 ± 13.9** | 0.01 |
| SF | 72.5 ± 27.2 | 84.8 ± 21.7** | 84.8 ± 21.0** | 0.008 |
| RP | 57.4 ± 43.3 | 81.9 ± 33.1* | 81.9 ± 36.2* | <0.001 |
| RE | 63.0 ± 44.3 | 81.5 ± 34.1*** | 77.8 ± 40.4 | 0.04 |
| VT | 50.8 ± 20.6 | 60.4 ± 20.2*** | 63.0 ± 20.5** | 0.006 |
| MH | 60.7 ± 19.4 | 67.4 ± 19.2 | 70.1 ± 20.0*** | 0.04 |
| BP | 63.9 ± 26.4 | 78.9 ± 23.8** | 74.8 ± 26.8*** | 0.008 |
| GH | 41.4 ± 16.4 | 53.1 ± 17.5* | 57.1 ± 18.5* | <0.001 |
| NHP (0–100) | | | | |
| Energy | 50.3 ± 31.1 | 35.8 ± 31.6*** | 30.9 ± 31.6** | 0.005 |
| Pain | 24.8 ± 28.8 | 16.9 ± 26.5 | 18.5 ± 29.4 | 0.32 |
| Emotional reactions | 27.9 ± 27.2 | 14.0 ± 19.9** | 16.9 ± 24.0*** | 0.008 |
| Sleep | 30.6 ± 29.5 | 18.9 ± 25.0 | 21.9 ± 29.1 | 0.08 |
| Social isolation | 32.1 ± 30.2 | 16.3 ± 24.3** | 18.1 ± 28.4*** | 0.007 |
| Physical mobility | 13.4 ± 17.8 | 8.3 ± 15.0 | 7.9 ± 15.0 | 0.14 |
| EQ5D | | | | |
| Utility (−0.111–1) | 0.808 ± 0.187 | 0.887 ± 0.145*** | 0.879 ± 0.146*** | 0.02 |

**Table 5.** Responsiveness from baseline to 3 and 6 months in the 54 patients with asthma

| | 0–3 months | | 0–6 months | |
|---|---|---|---|---|
| | Effect size | Standardized response mean | Effect size | Standardized response mean |
| $FEV_1$ (%predicted) | 0.61 | 0.67 | 0.55 | 0.58 |
| AQLQ | | | | |
| Symptoms | 1.16 | 1.04 | 1.21 | 1.08 |
| Activities | 0.95 | 0.99 | 1.08 | 0.99 |
| Emotions | 0.80 | 0.84 | 0.99 | 1.07 |
| Environment | 0.61 | 0.62 | 0.63 | 0.57 |
| Total | 1.10 | 1.07 | 1.21 | 1.11 |
| SF-36 | | | | |
| PF | 0.31 | 0.36 | 0.48 | 0.57 |
| SF | 0.45 | 0.45 | 0.45 | 0.42 |
| RP | 0.57 | 0.52 | 0.57 | 0.53 |
| RE | 0.42 | 0.34 | 0.33 | 0.28 |
| VT | 0.46 | 0.48 | 0.59 | 0.53 |
| MH | 0.35 | 0.35 | 0.48 | 0.47 |
| BP | 0.57 | 0.58 | 0.41 | 0.41 |
| GH | 0.71 | 0.66 | 0.95 | 0.81 |
| NHP | | | | |
| Energy | 0.44 | 0.43 | 0.61 | 0.52 |
| Pain | 0.26 | 0.32 | 0.20 | 0.26 |
| Emotional reactions | 0.50 | 0.55 | 0.39 | 0.44 |
| Sleep | 0.42 | 0.51 | 0.31 | 0.38 |
| Social isolation | 0.51 | 0.51 | 0.45 | 0.44 |
| Physical mobility | 0.28 | 0.36 | 0.30 | 0.39 |
| EQ5D | | | | |
| Utility | 0.41 | 0.36 | 0.37 | 0.32 |

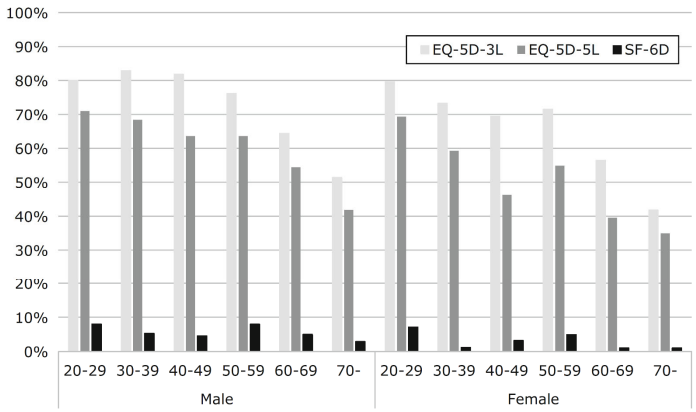
Qual Life Res (2016) 25:707–719
DOI 10.1007/s11136-015-1108-2

CrossMark

## Japanese population norms for preference-based measures: EQ-5D-3L, EQ-5D-5L, and SF-6D

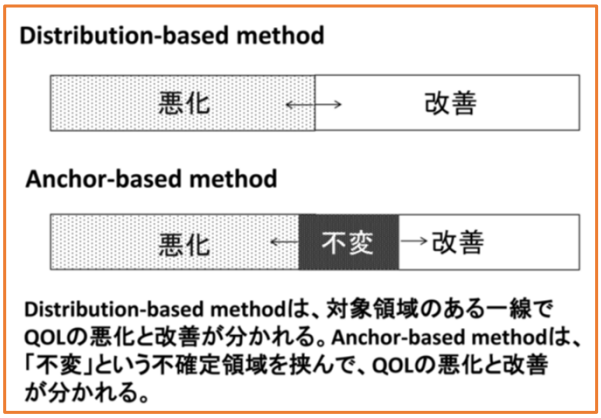
Takeru Shiroiwa[1] · Takashi Fukuda[1] · Shunya Ikeda[2] · Ataru Igarashi[3] · Shinichi Noto[4] · Shinya Saito[5] · Kojiro Shimozuma[6]

**Fig. 3** Percentage of respondents reporting full health




# Minimally important difference: MID

●特定領域におけるQOLスコアの最小の差（値）




宮崎　貴久子．行動医学研究　Vol.21, No. 1, 8–11, 2015

Qual Life Res (2016) 25:707–719
DOI 10.1007/s11136-015-1108-2

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**Japanese population norms for preference-based measures: EQ-5D-3L, EQ-5D-5L, and SF-6D**

Takeru Shiroiwa[1] · Takashi Fukuda[1] · Shunya Ikeda[2] · Ataru Igarashi[3] · Shinichi Noto[4] · Shinya Saito[5] · Kojiro Shimozuma[6]

- The differences in the QOL scores between respondents with and those without any **diseases** were 0.064 for measurements based on the EQ-5D-3L, 0.061 for measurements based on the EQ-5D-5L, and 0.073 for measurements based on the SF-6D, which is regarded as the between-group MID in the general population.
- If **symptoms** were used in the same analysis, the differences were 0.093 for both the EQ-5D-3L and EQ-5D-5L and 0.112 for the SF-6D.
- Considering our results, the between group MID can be estimated to range between 0.05 and 0.1 for all three measures.

VALUE IN HEALTH 20 (2017) 644–650

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**Instrument-Defined Estimates of the Minimally Important Difference for EQ-5D-5L Index Scores**

Nathan S. McClure, MSc[1], Fatima Al Sayah, PhD[1], Feng Xie, BSc(Pharm), MSc, PhD[2,3], Nan Luo, PhD[4], Jeffrey A. Johnson, PhD[1,*]

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| | Health state | Index score | Absolute difference in index score | Average |
|---|---|---|---|---|
| Possible single-level transitions to a *better* state | 33332 | 0.615 | 0.039 | 0.037* |
| | 33323 | 0.622 | 0.046 | |
| | 33233 | 0.596 | 0.020 | |
| | 32333 | 0.621 | 0.044 | |
| | 23333 | 0.614 | 0.038 | |
| **Baseline Health State** | **33333** | **0.577** | ------- | 0.086 |
| Possible single-level transitions to a *worse* state | 43333 | 0.487 | 0.090 | |
| | 34333 | 0.472 | 0.104 | |
| | 33433 | 0.447 | 0.130 | |
| | 33343 | 0.391 | 0.185 | |
| | 33334 | 0.411 | 0.165 | |

(D) Japan

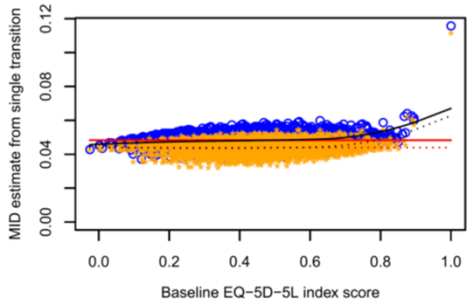


**Table 2 – Summary statistics of instrument-defined MID estimates for EQ-5D-5L country-specific scoring algorithms.**

| Country | Mean ± SD | Median | Q1 | Q3 |
|---|---|---|---|---|
| Canada | 0.056 ± 0.011 | 0.056 | 0.049 | 0.063 |
| Canada* | 0.037 ± 0.001 | 0.037 | 0.037 | 0.038 |
| China | 0.069 ± 0.007 | 0.069 | 0.064 | 0.074 |
| China* | 0.058 ± 0.005 | 0.058 | 0.054 | 0.061 |
| Spain | 0.061 ± 0.008 | 0.060 | 0.055 | 0.066 |
| Spain* | 0.045 ± 0.009 | 0.046 | 0.039 | 0.051 |
| Japan | 0.048 ± 0.004 | 0.048 | 0.046 | 0.051 |
| Japan* | 0.044 ± 0.004 | 0.044 | 0.041 | 0.047 |
| England | 0.063 ± 0.013 | 0.064 | 0.055 | 0.073 |
| England* | 0.037 ± 0.008 | 0.037 | 0.031 | 0.042 |
| Uruguay | 0.063 ± 0.019 | 0.062 | 0.050 | 0.076 |
| Uruguay* | 0.040 ± 0.010 | 0.039 | 0.033 | 0.046 |

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Preference-Based Assessments

## Japanese Population Norms of EQ-5D-5L and Health Utilities Index Mark 3: Disutility Catalog by Disease and Symptom in Community Settings

Takeru Shiroiwa, MPH, PhD, Shinichi Noto, PhD, Takashi Fukuda, PhD

ICC = 0.53

**Figure 1.** Comparison of population norms between the EQ-5D-5L and HUI3.

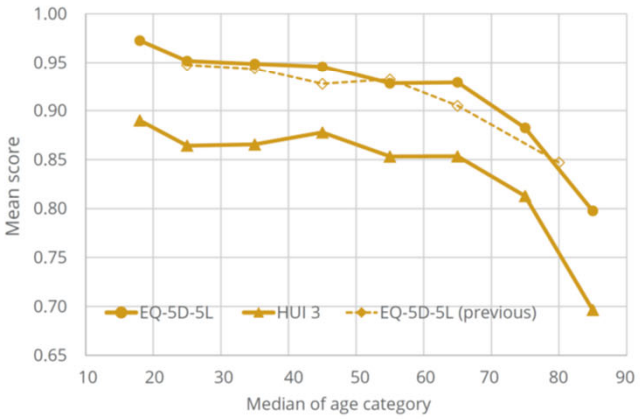



**Table 4.** Disutility associated with disease.

| Variable | N | EQ-5D-5L | | HUI3 | |
|---|---|---|---|---|---|
| | | Coefficient | *P*-value | Coefficient | *P*-value |
| Diabetes | 341 | −0.046 | <.001 | −0.055 | <.001 |
| Obesity | 8 | −0.034 | .417 | 0.019 | .780 |
| Hyperlipidemia | 135 | −0.002 | .816 | −0.004 | .782 |
| Thyroid disease | 45 | −0.006 | .722 | −0.046 | .097 |
| Depression | 140 | −0.184 | <.001 | −0.282 | <.001 |
| Dementia | 27 | −0.222 | <.001 | −0.426 | <.001 |
| Parkinson disease | 15 | −0.352 | <.001 | −0.421 | <.001 |
| Other neuropathic diseases | 49 | −0.211 | <.001 | −0.232 | <.001 |
| Eye diseases | 158 | −0.049 | <.001 | −0.101 | <.001 |
| Ear diseases | 33 | −0.033 | .114 | −0.108 | .001 |
| Hypertension | 838 | −0.005 | .275 | −0.006 | .388 |
| Stroke | 92 | −0.265 | <.001 | −0.293 | <.001 |
| Angina or myocardial infarction | 131 | −0.073 | <.001 | −0.081 | <.001 |
| Other cardiovascular diseases | 142 | −0.054 | <.001 | −0.068 | <.001 |
| Cold | 18 | −0.083 | .004 | −0.040 | .368 |
| Allergic rhinitis | 68 | −0.027 | .069 | −0.049 | .029 |
| COPD | 11 | −0.114 | .002 | −0.075 | .161 |
| Asthma | 85 | −0.025 | .0603 | −0.035 | .086 |
| Other respiratory diseases | 72 | −0.121 | <.001 | −0.116 | <.001 |
| Gastroduodenal diseases | 90 | −0.053 | <.001 | −0.040 | .040 |
| Liver or gallbladder diseases | 53 | −0.067 | <.001 | −0.072 | .004 |
| Other gastrointestinal diseases | 87 | −0.087 | <.001 | −0.085 | <.001 |
| Tooth diseases | 214 | −0.013 | .129 | −0.021 | .091 |
| Atopic dermatitis | 78 | −0.031 | .025 | −0.049 | .014 |
| Other dermatologic diseases | 91 | −0.043 | .001 | −0.037 | .050 |
| Gout | 37 | −0.012 | .556 | −0.022 | .460 |
| Rheumatoid arthritis | 63 | −0.103 | <.001 | −0.096 | <.001 |
| Arthrosis | 194 | −0.157 | <.001 | −0.101 | <.001 |
| Shoulder pain | 108 | −0.051 | <.001 | −0.043 | .014 |
| Back pain | 323 | −0.117 | <.001 | −0.100 | <.001 |
| Osteoporosis | 58 | −0.034 | .034 | −0.054 | .025 |
| Kidney diseases | 83 | −0.079 | <.001 | −0.122 | <.001 |
| Benign prostatic hyperplasia | 89 | −0.029 | .024 | −0.054 | .008 |
| Menopausal problem | 7 | −0.048 | .286 | −0.007 | .925 |
| Bone fracture | 45 | −0.124 | <.001 | −0.125 | <.001 |
| Injury without bone fracture and burn injury | 38 | −0.134 | <.001 | −0.075 | .009 |
| Anemia or blood diseases | 24 | −0.079 | .001 | −0.121 | .001 |
| Malignant neoplasm | 101 | −0.084 | <.001 | −0.103 | <.001 |
| Pregnant or postpartum disorders | 13 | −0.058 | .082 | 0.019 | .695 |
| Infertility | 8 | −0.077 | .071 | −0.118 | .059 |
| Other | 273 | −0.080 | <.001 | −0.101 | <.001 |

Table 5. Disutility associated with symptoms.

| Variable | N | EQ-5D-5L | | HUI3 | |
|---|---|---|---|---|---|
| | | Coefficient | *P*-value | Coefficient | *P*-value |
| Intercept | | 0.996 | <.001 | 0.908 | <.001 |
| Age, y | | | | | |
| 16-19 | 743 | — | — | — | — |
| 20-29 | 1279 | −0.015 | .005 | −0.019 | .020 |
| 30-39 | 1265 | −0.011 | .040 | −0.011 | .183 |
| 40-49 | 1292 | −0.010 | .064 | 0.005 | .495 |
| 50-59 | 1302 | −0.023 | <.001 | −0.015 | .056 |
| 60-69 | 1370 | −0.022 | <.001 | −0.016 | .040 |
| 70-79 | 1433 | −0.059 | <.001 | −0.049 | <.001 |
| 80-89 | 1499 | −0.130 | <.001 | −0.147 | <.001 |
| Sex | | | | | |
| Male | 5057 | — | — | — | — |
| Female | 5126 | −0.009 | <.001 | 0.012 | <.001 |
| Main symptom | | | | | |
| No symptoms | 6310 | — | — | — | — |
| Fever | 31 | −0.078 | .002 | −0.122 | <.001 |
| Sluggishness | 109 | −0.155 | <.001 | −0.192 | <.001 |
| Sleeplessness | 74 | −0.165 | <.001 | −0.206 | <.001 |
| Irritability | 58 | −0.140 | <.001 | −0.259 | <.001 |
| Forgetfulness | 42 | −0.147 | <.001 | −0.301 | <.001 |
| Headache | 147 | −0.093 | <.001 | −0.125 | <.001 |
| Dizziness | 53 | −0.098 | <.001 | −0.075 | .003 |
| Blurred vision | 55 | −0.056 | .004 | −0.116 | <.001 |
| Visual impairment | 59 | −0.113 | <.001 | −0.238 | <.001 |
| Buzzing | 73 | −0.052 | .001 | −0.085 | <.001 |
| Hearing impairment | 45 | −0.093 | <.001 | −0.268 | <.001 |
| Palpitation | 50 | −0.094 | <.001 | −0.127 | <.001 |
| Breathlessness | 53 | −0.159 | <.001 | −0.160 | <.001 |
| Chest pain | 33 | −0.212 | <.001 | −0.223 | <.001 |
| Cough and/or sputum | 162 | −0.066 | <.001 | −0.070 | <.001 |
| Nasal congestion or mucus | 139 | −0.032 | .001 | −0.065 | <.001 |
| Wheezing | 27 | −0.101 | <.001 | −0.142 | <.001 |
| Indigestion or heartburn | 84 | −0.071 | <.001 | −0.102 | <.001 |
| Diarrhea | 55 | −0.066 | <.001 | −0.118 | <.001 |
| Constipation | 89 | −0.071 | <.001 | −0.077 | <.001 |
| Lack of appetite | 10 | −0.136 | <.001 | −0.087 | .129 |
| Abdominal pain or stomachache | 52 | −0.110 | <.0001 | −0.143 | <.001 |
| Pain due to hemorrhoids | 20 | −0.060 | .0120 | −0.063 | .104 |
| Dental pain | 52 | −0.055 | <.001 | −0.137 | <.001 |
| Swelling or bleeding from the gums | 37 | −0.038 | .049 | −0.067 | .025 |
| Trouble biting | 21 | −0.081 | .001 | −0.106 | .005 |
| Rash (eg, urticaria, blotch) | 52 | −0.052 | .001 | −0.065 | .008 |
| Itching (eg, eczema, tinea pedis) | 91 | −0.067 | <.001 | −0.087 | <.001 |
| Stiff shoulders | 388 | −0.050 | <.001 | −0.058 | <.001 |
| Back pain | 637 | −0.112 | <.001 | −0.101 | <.001 |
| Arthritic pain | 291 | −0.154 | <.001 | −0.130 | <.001 |
| Limb motion problems | 104 | −0.300 | <.001 | −0.328 | <.001 |
| Numbness of limbs | 109 | −0.185 | <.001 | −0.174 | <.001 |
| Coldness of limbs | 53 | −0.093 | <.001 | −0.093 | <.001 |
| Swelling or heaviness of legs | 36 | −0.171 | <.001 | −0.144 | <.001 |
| Difficulty in urinating | 33 | −0.096 | <.001 | −0.177 | <.001 |
| Frequent urination | 124 | −0.055 | <.001 | −0.104 | <.001 |
| Acraturesis | 30 | −0.211 | <.001 | −0.154 | <.001 |
| Menstrual disorder | 39 | −0.049 | .008 | −0.118 | <.001 |
| Bone fracture, sprain, or abarticulation | 71 | −0.120 | <.001 | −0.161 | <.001 |
| Incisura or burn | 20 | −0.083 | .001 | −0.141 | <.001 |
| Other | 165 | −0.134 | <.001 | −0.096 | <.001 |

## ゾルゲンスマの費用対効果評価に係る取扱いについて

中医協　総－３
４．１．２８

<ゾルゲンスマの費用対効果評価の経緯>

○　2020年５月13日に、中医協総会において費用対効果評価の対象品目としてH３（著しく保険償還価格が高いもの）指定された（※）。

※　適応である脊髄性筋萎縮症は指定難病であるが、著しく保険償還価格が高いものとして、中医協総会において指定された。

○　2021年10月の費用対効果評価専門組織で、製造販売業者から提出された分析データ等及び公的分析結果については、一定の科学的妥当性はあるものの、薬事承認時等のデータでは、費用対効果評価における長期有効性に関するデータが不足していることから、必要なデータ収集を行うこととし、分析を中断とする決定案が策定された（※）。

※　費用対効果評価において日本のゾルゲンスマの臨床実態を反映したデータが必要であるが、薬事承認時等のデータは、日本での臨床実態を反映した長期有効性に関するデータが不足しており、追加データが必要。

○　2021年12月の費用対効果評価専門組織で、追加データの収集計画案が策定された（※）。

※　分析再開には、既存の海外臨床試験と同程度以上の日本人長期データ、症例数の集積が必要と考える。したがって、年間10-20例、５年間のデータを収集するとして、2026年５月までデータ収集を計画。

<方針>

○　ゾルゲンスマの費用対効果評価について、費用対効果評価専門組織での結果を踏まえ、追加のデータを収集するために、分析を一旦中断とする。

○　2026年５月まで必要なデータ収集を行い、年１回、費用対効果評価専門組織で進捗状況について報告を行う（その間に必要なデータが集まった場合には、早期に分析を再開する）。

○　必要なデータが集まった時点で速やかに分析を行い、その結果を、中医協総会に報告する。

1

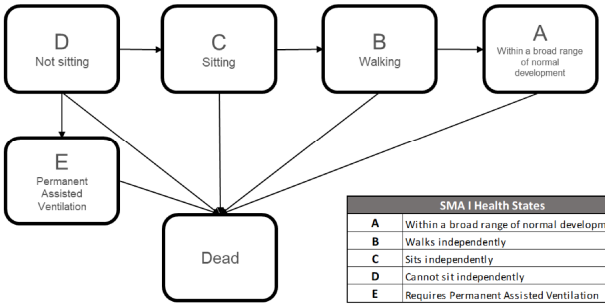
Onasemnogene abeparvovec for treating spinal muscular atrophy

HST REPORT

This report was commissioned by the National Institute for Health Research Systematic Reviews Programme as project number 128205

BMJ Technology Assessment Group

Figure 10.Model schematic (adapted from Figure 34 in the supplementary appendix to the CS)




| SMA I Health States | |
|---|---|
| A | Within a broad range of normal development |
| B | Walks independently |
| C | Sits independently |
| D | Cannot sit independently |
| E | Requires Permanent Assisted Ventilation |

Table 35. HSUVs used in the base case cost-effectiveness analysis

| Health state | Description | Utility value | Reference |
|---|---|---|---|
| E | PAV | 0 | Assumption based on the ERG interim report |
| D | Not sitting - BSC | 0.19 | Thompson *et al.* 2017[70] |
| | Not sitting - onasemnogene | 0.29 | Thompson et al. 2017[70] and on treatment utility of 0.1 as per US ICER report[69] |
| C | Sits unassisted - BSC | 0.60 | Tappenden *et al.* 2018[85] |
| | Sits unassisted - onasemnogene | 0.65 | Tappenden *et al.* 2018[85] and on treatment utility of 0.05 as per US ICER report[69] |
| B | Walks unassisted | General population | Ara and Brazier 2010[86] |
| A | Broad range of normal development | | |

Abbreviations: HSUV, health state utility value; PAV, permanent assisted ventilation

Table 81. Summary of alernative HRQoL sources identified in the SLR (adapted from Table 42 of the Supplementary Appendix)

| Health state† | CHERISH: PedsQL mapped to EQ-5D-Y (Thompson et al. 2017[70]) | | Lloyd: Clinician-proxy Case Vignette EQ-5D-Y (Lloyd et al. 2017[89]) | | European study: Parent-proxy EQ-5D-3L, UK reports only (Thompson et al. 2017[70]) | |
|---|---|---|---|---|---|---|
| | Health state | Utility value | Health state | Utility value | Health state | Utility value |
| E | SMA type 2: Worsened (from baseline) | 0.730 | SMA type 1: Requires ventilation | -0.33 | SMA type 1 | 0.190 |
| D | SMA type 2: Stabilisation of baseline function | 0.756 | SMA type 1: Baseline | -0.12 | SMA type 1 | 0.190 |
| C | SMA type 2: Moderate improvement | 0.764 | SMA type 1: Reclassified as SMA type 2† | -0.04 | SMA type 2 | 0.100 |
| B | SMA type 2: Walks unaided | 0.878 | SMA type 1: Reclassified as SMA type 3‡ | 0.71 | SMA type 3 | 0.540 |
| A | Identified studies did not included an A state. The A state (within broad range of normal development) is assumed to have HRQoL equivalent to the UK general population | | | | | |
| Justification for exclusion from the base case | The mapping described by Kahn et al 2014 has several methodological limitations: for example, it was conducted in a population that differed considerably (school children aged of 11 to 15 years) to SMA type 1 babies. In addition, the values seem implausibly high; for example, it seems unlikely that for an individual who requires PAV would be considered as being three quarters of that of an individual in perfect health | | The study uses clinician-proxy assessment, which is less preferred to parent-proxy assessments, as per the NICE reference case. In addition, the study reported a negative utility (a health state worse than death) for 'reclassified SMA type 2'. A negative utility value for the C state (sits unassisted) lacks face validity and was deemed implausible by UK clinical experts (UK advisory board, May 2019)[88] | | Whilst this study uses parent-proxy assessment, which is preferred to clinician-proxy assessments, the results for the SMA type 2 group (used as proxy for the C state [sit unassisted]) lack face validity, as they are lower than the utility value reported for SMA type 1 patients who fail to achieve any milestones. Due to this lack of face validity, a scenario using values reported for SMA type 2 and 3 groups from this study is also not formally modelled | |

CADTH Drug Reimbursement Review

# Pharmacoeconomic Report

ONASEMNOGENE ABEPARVOVEC (ZOLGENSMA)

(Novartis Pharmaceuticals Canada Inc.)

**Table 5: CADTH Revisions to the Submitted Economic Evaluation**

| Stepped analysis | Sponsor's value or assumption | CADTH value or assumption |
|---|---|---|
| Changes to derive the CADTH estimate | | |
| 1. Comparative efficacy of onasemnogene abeparvovec with nusinersen (motor function milestone achievement) | Based on the sponsor-submitted indirect treatment comparison; onasemnogene is generally more effective than nusinersen with respect to motor milestone achievement.<br>All patients standing at age 5 on onasemnogene abeparvovec are considered to be "within a broad range of normal development."<br>Note: In the early phase of the model, the highest state obtained was maintained for patients on either onasemnogene abeparvovec and nusinersen. The only difference between the 2 comparators was the discontinuation rate applied to nusinersen, which could subsequently lead to regression. | Assumed equal efficacy for nusinersen and onasemnogene abeparvovec, with transition probabilities for the first 8 cycles for onasemnogene abeparvovec applied to nusinersen.<br>No patients on onasemnogene could reach "within a broad range of normal development" at age 5.<br>Note: Extrapolation phase of the model and its assumptions were not altered. |
| 2. Survival on nusinersen compared with onasemnogene abeparvovec | On-trial survival (mortality and requirement of permanent ventilation from the unable to sit state) was used for the early phase of the model (approximately 30 months), leading to different survival rates for patients on nusinersen in comparison to onasemnogene abeparvovec. | Assumed equal survival for patients on nusinersen and onasemnogene abeparvovec, with the survival with onasemnogene abeparvovec for the entire time horizon applied to patients on nusinersen. |
| 3. Utility increment while in the "unable to sit assisted" and "sitting unassisted" health states for interim milestone achievement. | "Unable to sit unassisted": All patients receive 0.1 increase in health state utility value.<br>"Sitting unassisted": All patients receive 0.05 increase in health state utility value while on treatment. | No increment applied to either health state. |
| 4. Utility value for patients on permanent ventilation | 0.0 (equivalent to death). | 0.190, the same value as that for patients in the "unable to sit unassisted" health state. |
| 5. Utility value for patients "walking unassisted" | Age-adjusted general population utility was 0.954 at age 25 to 0.685 at age ≥ 75 | 0.760 from Love et al. (2019), for patients with SMA type 3.[19] |

Neuromuscular Disorders

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ABSTRACT ONLY | VOLUME 29, SUPPLEMENT 1, S130, OCTOBER 01, 2019

# P.218Utility based health related quality of life in children and adolescents with spinal muscular atrophy

D. Love • R. Hicks • Y. Wei • E. Zapata Aldana • S. Almobarak • C. Campbell

DOI: https://doi.org/10.1016/j.nmd.2019.06.332

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Spinal muscular atrophy (SMA) is a degenerative motor neuron disease and while rare, is the most common genetic cause of infant mortality, and a significant cause of morbidity. The treatment landscape for SMA has shifted, with recent approval of a first disease modifying therapy, and others in late stage clinical trials. These high cost novel therapies require data on health-related quality of life (HRQOL) to properly understand their economic impact. Children with all types of SMA 0-18 years of age, and caregivers, were identified by The Canadian Neuromuscular Disease Registry and distributed questionnaires with the Health Utilities Index® (HUI®) Mark 2 and Mark 3, which are utility based HRQOL measures. Scores range from 0 to 1.0 for death to perfect health. All parents and youth aged 13 – 18 years old completed HUI measures. Additional measures included Quality of My Life, PedsQL Core, PedsQL Neuromuscular. Phone facilitators were available to help subjects complete the questionnaire. Forty-six parents and 14 youth completed the HUI HRQOL measures. The overall HRQOL HUI2 and HUI3 scores, respectively for the parent reported group was 0.54 (SD=0.18) and 0.31 (SD=0.27), and for the youth self-report 0.53, (SD=0.18) and 0.33 (SD=0.28). The parent reported scores for the HUI2 and HUI3, respectively, for SMA Type I is 0.42 (SD=0.12) and 0.14 (SD=0.19)(n=10), Type II 0.49 (SD=0.07) and 0.24 (SD=0.12)(n=27), Type III 0.76 (SD=0.20) and 0.62 (SD=0.27)(n=7). Youth self- report scores for Type I's are 0.55 (SD=0.18) and 0.29 (SD=0.36) (n=4), Type II 0.45 (SD=0.12) and 0.23 (SD=0.16)(n=7), Type III 0.57 (SD=0.01) and 0.41 (SD=0.02)(n=2). Additional HRQOL values and categories will be presented. Patient and parent reported utility based HRQOL in SMA are reported overall and by SMA type. The availability of utility based HRQOL data for patients with SMA is essential for various stakeholders for understanding the health economics of new therapies for SMA.



## Article Info

### Identification

DOI: https://doi.org/10.1016/j.nmd.2019.06.332

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PharmacoEconomics
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SYSTEMATIC REVIEW

# Systematic Literature Review to Identify Utility Values in Patients with Spinal Muscular Atrophy (SMA) and Their Caregivers

C. Simone Sutherland[1] · Pollyanna Hudson[2] · Stephen Mitchell[2] · Noman Paracha

**Table 4** Summary of published proxy-derived mean HSUVs for patients with SMA by type (standard deviation) [standard error] [95% confidence interval]

| Health state | Proxy-derived HSUVs | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Reference | NICE TA588 ERG-preferred values[a] [65] | NICE TA588 ACM1 [65] | NICE TA588 ACM2 [65] | NICE TA588 ACM3 [65] | Lloyd et al. [46] | Lo et al. [56] | López-Bastida et al. [47] | Love et al. [58] | Malone et al. [48] | Sampson and Garau [49] | Thompson et al. [50] |
| Publication description | NICE report | NICE report | NICE report | NICE report | Full-text publication | Abstract and associated poster | Full-text publication | Abstract | Full-text publication | Full-text publication | Abstract and associated poster |
| PBM used | EQ-5D-Y vignette [46, 70] | PedsQL mapped to EQ-5D | EQ-5D-Y vignette [46, 70] | Clinical experts | Clinical experts assessed Types 1 and 2 SMA case studies using EQ-5D-Y and PedsQL–NMM (baseline states only) | DCE survey of UK general population | EQ-5D-3L (caregivers as proxies) | HUI3[b] | PedsQL data from CHERISH mapped to EQ-5D-Y using a published algorithm [36] | EQ-5D-3L | Three options: 1. Parent proxy using EQ-5D-3L 2. Case vignette study of physician-rated EQ-5D-5L and PedsQL (motor function health) 3. CHERISH mapped to EQ-5D using a published algorithm (unspecified) |
| Overall Types 1–3 SMA | – | – | – | – | – | – | 0.158 (0.44) | 0.31 (0.27) | – | 0.22[c] | UK[d] 0.167 |
| Type 1 SMA (early onset) | | | | | | | | | | | |
| Baseline/overall Type 1 SMA | – | – | – | – | − 0.12 (0.19) | – | – | 0.14 (0.19) | – | – | – |
| Worsening | – | – | – | – | − 0.24 (0.14) | – | – | – | – | – | – |
| Improvement | – | – | – | – | − 0.17 (0.17) | – | – | – | – | – | – |
| None | − 0.240 | 0.733 | − 0.240 | − 0.020 | – | – | – | – | – | – | – |
| Mild | − 0.120 | 0.752 | − 0.120 | 0.100 | – | – | – | – | – | – | – |
| Moderate | − 0.170 | 0.752 | − 0.170 | 0.200 | – | – | – | – | – | – | – |
| Permanent ventilation | – | – | – | – | – | – | – | – | 0.730 | – | – |
| Non-sitting | – | – | – | – | – | – | – | – | 0.756 | – | – |

Canadian Journal of Health Technologies
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September 2021 Volume 1 Issue 9

CADTH Reimbursement Review

# Semaglutide (Rybelsus)

**Sponsor:** Novo Nordisk Canada Inc.
**Therapeutic area:** Diabetes mellitus, type 2

**Table 84: Summary of outcome measures and their measurement properties**

| Outcome Measure | Type | Conclusions about Measurement Properties | MID |
|---|---|---|---|
| SF-36v2 | Generic questionnaire measuring multidimensional health concepts and to capture a full-range of health states. | **Validity and Reliability:** Evidence of validity and reliability in general populations, with evidence supporting adequate validity among patients with T1D and T2D. However, validity and reliability in some dimensions among diabetes patients were not optimal, suggesting revalidation of the questionnaire among this patient population. | **General (non-disease specific) MID:** • 2-points in PCS; • 3-points in MCS; • 2 to 4 points for individual dimensions. **Patients with T2D:** A benchmark based on 1-point change was suggested.[95] However, the validity of this benchmark is unclear. |
| CoEQ | Questionnaire aimed at weight loss clinical trials assessing intensity and type of food cravings, and subjective sensations of appetite and mood, and the individual's perceived level of control against a craved food item. | **Validity and Reliability:** Validity and reliability were assessed in patients in weight loss trials. Evidence suggested the questionnaire may be useful for assessing impact of eating and weight and quality of life. No literature was identified that assessed validity and reliability in diabetes patients. | No literature pertaining to MIDs was retrieved. |
| DTR-QOL | Japanese specific questionnaire assessing the influence of diabetes treatment on a patient's HRQoL. | **Validity and Reliability:** Validity and reliability were assessed and considered adequate in Japanese patients in with diabetes. | No literature pertaining to MIDs was retrieved. |
| IWQoL-Lite-CT | Questionnaire originally developed for assessment of HRQoL in obesity trials and expanded to apply to diabetes trials per FDA guidance. | **Validity and Reliability:** Validity and reliability were assessed in patients in weight loss trials and diabetes trials. Evidence suggested higher validity and reliability among weight loss trials compared to diabetes trials. However, validity and reliability were adequate for use among diabetes patients with further examination of the questionnaire in future diabetes trials. | No literature pertaining to MIDs was retrieved |
| DTSQs | Diabetes-specific questionnaire assessing patient satisfaction to treatment. | **Validity and Reliability:** Validity and reliability were not assessed in diabetes patients. | No literature pertaining to MIDs was retrieved. |

新薬と臨牀 2017；66：1493-1509

原 著

# Wearing-off現象を発現したパーキンソン病患者に対するゾニサミド50mgの安全性および有効性の検討

長期使用に関する特定使用成績調査の中間報告

石橋 千秋[1]
丸山 秀徳[2]
野元 正弘[3]

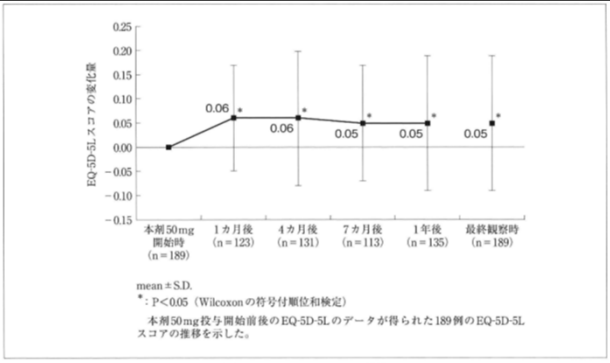


**図3** EQ-5D-5Lスコアの推移

**表5** 患者背景要因別EQ-5D-5Lスコア変化量

| | 全体 | 25mg増量群 | 50mg新規群 | ジスキネジア | | 幻覚 | |
|---|---|---|---|---|---|---|---|
| | | | | なし | あり | なし | あり |
| 症例数 | 189 | 138 | 51 | 117 | 72 | 137 | 52 |
| 50mg投与開始時 | 0.57±0.19 | 0.58±0.20 | 0.54±0.19 | 0.58±0.20 | 0.56±0.18 | 0.60±0.19 | 0.50±0.19 |
| 最終観察時 | 0.62±0.20 | 0.62±0.20 | 0.61±0.18 | 0.63±0.20 | 0.61±0.19 | 0.64±0.20 | 0.56±0.18 |
| 変化量* | 0.05±0.14 | 0.04±0.13 | 0.07±0.14 | 0.05±0.13 | 0.05±0.15 | 0.04±0.13 | 0.07±0.16 |
| Wilcoxonの符号付順位和検定 | P<0.001 | P<0.001 | P<0.001 | P<0.001 | P=0.002 | P<0.001 | P<0.001 |

日本臨床作業療法研究　No.8：31－36，2021　　ISSN：2188-8418
原　著　　Open Access

# 回復期リハビリテーション病棟における健康関連QOLの変化と代理人回答の一致度について―脳卒中患者へのEQ-5D-5Lによる評価―

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2）新潟医療福祉大学リハビリテーション学部作業療法学科

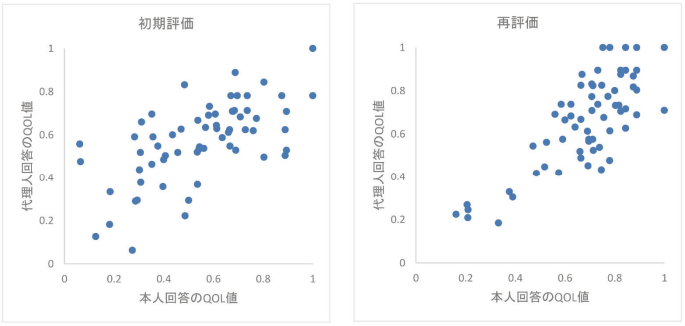


図1　本人回答と代理人回答のQOL値の散布図

表3　本人および作業療法士による代理人回答の一致度

| | 初期評価 | | | | 再評価 | | | |
|---|---|---|---|---|---|---|---|---|
| | 係数 | 95%信頼区間 | F値 | p値 | 係数 | 95%信頼区間 | F値 | p値 |
| QOL値 | 0.62 | 0.44; 0.75 | 4.22 | <0.01 | 0.78 | 0.66; 0.86 | 8.25 | <0.01 |
| | 初期評価 | | | | 再評価 | | | |
| | 係数 | 95%信頼区間 | Z値 | p値 | 係数 | 95%信頼区間 | Z値 | p値 |
| 移動の程度 | 0.65 | 0.51; 0.78 | 5.35 | <0.01 | 0.64 | 0.47; 0.81 | 5.45 | <0.01 |
| 身の回りの管理 | 0.70 | 0.57; 0.82 | 5.70 | <0.01 | 0.73 | 0.58; 0.88 | 5.88 | <0.01 |
| ふだんの生活 | 0.47 | 0.31; 0.64 | 3.96 | <0.01 | 0.62 | 0.46; 0.78 | 5.24 | <0.01 |
| 痛み／不快感 | 0.47 | 0.28; 0.67 | 3.92 | <0.01 | 0.44 | 0.22; 0.66 | 3.59 | <0.01 |
| 不安／ふさぎ込み | 0.30 | 0.05; 0.56 | 2.46 | 0.01 | 0.51 | 0.26; 0.76 | 4.09 | <0.01 |

# Preference-Based EQ-5D Index Scores for Chronic Conditions in the United States

*Patrick W. Sullivan, PhD, Vahram Ghushchyan, PhD*

***Key words:*** *health-related quality of life; cost-utility analysis; cost-effectiveness analysis; utility; chronic disease; ICD-9; econometric methods.* ***(Med Decis Making 2006; 26:410–420)***

**Table 3** EQ-5D Index Scores, Age, and Comorbidity Burden by ICD-9 in the 2000–2002 MEPS

| ICD-9 Classification | *n* | Mean Age | NCC[b] 25% | NCC[b] 50% | NCC[b] 75% | Unadjusted Mean EQ-5D | Unadjusted EQ-5D 25% | Unadjusted EQ-5D 50% | Unadjusted EQ-5D 75% | Regression Results[a] Disutility of Condition[a] | Regression Results[a] Condition[a] Standard Error | Regression Results[a] Statistical Significance (Condition) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ICD-9 173 Other Malig Neopl Skin | 453 | 67 | 3 | 4 | 6 | 0.812 | 0.768 | 0.816 | 1.000 | −0.0137 | 0.0001 | * |
| ICD-9 174 Malig Neo Female Breast | 201 | 64 | 3 | 4 | 6 | 0.803 | 0.708 | 0.816 | 1.000 | −0.0156 | 0.0002 | * |
| ICD-9 185 Malign Neopl Prostate | 160 | 70 | 3 | 4 | 6 | 0.772 | 0.708 | 0.810 | 0.860 | −0.0153 | 0.0002 | * |
| ICD-9 216 Benign Neoplasm of Skin | 443 | 49 | 2 | 3 | 5 | 0.861 | 0.800 | 0.827 | 1.000 | −0.0002 | 0.0001 | |
| ICD-9 239 Unspecified Neoplasm | 389 | 58 | 2 | 4 | 6 | 0.795 | 0.778 | 0.827 | 1.000 | −0.0174 | 0.0001 | * |
| ICD-9 242 Thyrotoxicosis | 188 | 54 | 2 | 4 | 6 | 0.800 | 0.761 | 0.827 | 1.000 | −0.0131 | 0.0002 | * |
| ICD-9 244 Acquired Hypothyroidism | 789 | 57 | 3 | 4 | 6 | 0.821 | 0.778 | 0.827 | 1.000 | −0.0005 | 0.0001 | * |
| ICD-9 246 Oth Disorders of Thyroid | 1035 | 61 | 2 | 4 | 6 | 0.783 | 0.748 | 0.810 | 0.844 | −0.0224 | 0.0001 | * |
| ICD-9 250 Diabetes Mellitus | 2778 | 60 | 3 | 4 | 6 | 0.751 | 0.708 | 0.800 | 0.844 | −0.0351 | 0.0001 | * |
| ICD-9 259 Oth Endocrine Disorders | 552 | 55 | 2 | 4 | 6 | 0.806 | 0.778 | 0.827 | 1.000 | −0.0168 | 0.0001 | * |
| ICD-9 272 Dis of Lipoid Metabolism | 3433 | 61 | 3 | 4 | 6 | 0.810 | 0.778 | 0.827 | 1.000 | −0.0049 | 0.0001 | * |
| ICD-9 274 Gout | 412 | 62 | 2 | 4 | 6 | 0.771 | 0.708 | 0.810 | 0.844 | −0.0221 | 0.0001 | * |
| ICD-9 278 Obesity/Hyperaliment | 131 | 47 | 2 | 4 | 6 | 0.744 | 0.708 | 0.800 | 0.844 | −0.0500 | 0.0002 | * |
| ICD-9 285 Anemia Nec/Nos | 407 | 55 | 3 | 5 | 7 | 0.753 | 0.708 | 0.800 | 0.844 | −0.0209 | 0.0001 | * |
| ICD-9 289 Other Blood Disease | 130 | 64 | 3 | 4 | 6 | 0.749 | 0.708 | 0.800 | 0.827 | −0.0359 | 0.0002 | * |
| ICD-9 296 Affective Psychoses | 247 | 42 | 2 | 3 | 6 | 0.693 | 0.506 | 0.778 | 0.844 | −0.0897 | 0.0002 | * |
| ICD-9 300 Neurotic Disorders | 1896 | 49 | 2 | 4 | 6 | 0.739 | 0.708 | 0.800 | 0.844 | −0.0494 | 0.0001 | * |
| ICD-9 309 Adjustment Reaction | 189 | 48 | 2 | 4 | 6 | 0.739 | 0.597 | 0.800 | 0.844 | −0.0337 | 0.0002 | * |
| ICD-9 311 Depressive Disorder Nec | 3086 | 48 | 2 | 3 | 5 | 0.732 | 0.708 | 0.800 | 0.844 | −0.0625 | 0.0001 | * |
| ICD-9 345 Epilepsy | 120 | 45 | 2 | 3 | 5 | 0.766 | 0.708 | 0.827 | 1.000 | −0.0078 | 0.0002 | * |
| ICD-9 346 Migraine | 980 | 41 | 2 | 3 | 5 | 0.806 | 0.778 | 0.827 | 1.000 | −0.0297 | 0.0001 | * |
| ICD-9 354 Mononeuritis Upper Limb | 351 | 50 | 2 | 3 | 6 | 0.771 | 0.766 | 0.816 | 0.827 | −0.0379 | 0.0001 | * |
| ICD-9 355 Mononeuritis Leg | 401 | 53 | 2 | 4 | 6 | 0.751 | 0.708 | 0.800 | 0.827 | −0.0344 | 0.0001 | * |
| ICD-9 360 Disorders of the Globe | 282 | 51 | 2 | 3 | 5 | 0.828 | 0.778 | 0.827 | 1.000 | −0.0064 | 0.0001 | * |
| ICD-9 362 Retinal Disorders Nec | 223 | 72 | 3 | 5 | 7 | 0.792 | 0.708 | 0.816 | 0.844 | −0.0156 | 0.0002 | * |
| ICD-9 365 Glaucoma | 634 | 69 | 3 | 5 | 7 | 0.782 | 0.708 | 0.810 | 0.860 | −0.0130 | 0.0001 | * |
| ICD-9 366 Cataract | 766 | 73 | 3 | 5 | 7 | 0.770 | 0.708 | 0.810 | 0.844 | −0.0171 | 0.0001 | * |
| ICD-9 368 Visual Disturbances | 175 | 53 | 2 | 4 | 6 | 0.810 | 0.778 | 0.827 | 1.000 | −0.0046 | 0.0002 | * |
| ICD-9 369 Blindness and Low Vision | 159 | 61 | 3 | 5 | 7 | 0.694 | 0.543 | 0.778 | 0.827 | −0.0498 | 0.0002 | * |
| ICD-9 375 Lacrimal System Disorder | 127 | 63 | 3 | 5 | 7 | 0.808 | 0.778 | 0.827 | 1.000 | −0.0002 | 0.0002 | |
| ICD-9 379 Eye Disorders Nec | 393 | 57 | 2 | 4 | 6 | 0.805 | 0.768 | 0.827 | 1.000 | −0.0081 | 0.0001 | * |
| ICD-9 389 Hearing Loss | 320 | 69 | 4 | 5 | 7 | 0.776 | 0.708 | 0.800 | 0.860 | −0.0060 | 0.0001 | * |
| ICD-9 401 Essential Hypertension | 7085 | 61 | 2 | 4 | 5 | 0.789 | 0.761 | 0.816 | 1.000 | −0.0250 | 0.0000 | * |
| ICD-9 410 Acute Myocardial Infarct | 244 | 62 | 3 | 5 | 7 | 0.704 | 0.575 | 0.778 | 0.843 | −0.0409 | 0.0002 | * |
| ICD-9 413 Angina Pectoris | 228 | 69 | 4 | 6 | 9 | 0.695 | 0.517 | 0.768 | 0.827 | −0.0412 | 0.0002 | * |
| ICD-9 414 Oth Chr Ischemic Hrt Dis | 183 | 66 | 4 | 6 | 8 | 0.738 | 0.708 | 0.794 | 0.827 | −0.0336 | 0.0002 | * |
| ICD-9 424 Oth Endocardial Disease | 214 | 56 | 2 | 4 | 6 | 0.789 | 0.708 | 0.816 | 1.000 | −0.0059 | 0.0002 | * |
| ICD-9 427 Cardiac Dysrhythmias | 649 | 67 | 3 | 5 | 7 | 0.774 | 0.708 | 0.810 | 0.843 | −0.0190 | 0.0001 | * |
| ICD-9 428 Heart Failure | 284 | 71 | 5 | 6 | 9 | 0.636 | 0.437 | 0.708 | 0.810 | −0.0635 | 0.0002 | * |
| ICD-9 429 Ill-Defined Heart Dis | 1204 | 69 | 3 | 5 | 7 | 0.716 | 0.619 | 0.778 | 0.827 | −0.0492 | 0.0001 | * |
| ICD-9 436 CVA | 340 | 68 | 3 | 5 | 7 | 0.650 | 0.463 | 0.768 | 0.816 | −0.0524 | 0.0001 | * |

*(continued)*

**Table 3** (continued)

| ICD-9 Classification | *n* | Mean Age | NCC[b] 25% | NCC[b] 50% | NCC[b] 75% | Unadjusted Mean EQ-5D | Unadjusted EQ-5D 25% | Unadjusted EQ-5D 50% | Unadjusted EQ-5D 75% | Regression Results[a] Disutility of Condition[a] | Regression Results[a] Condition[a] Standard Error | Regression Results[a] Statistical Significance (Condition) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ICD-9 436 CVA | 340 | 68 | 3 | 5 | 7 | 0.650 | 0.463 | 0.768 | 0.816 | −0.0524 | 0.0001 | * |
| ICD-9 444 Arterial Embolism | 201 | 66 | 3 | 5 | 7 | 0.734 | 0.708 | 0.778 | 0.827 | −0.0198 | 0.0002 | * |
| ICD-9 453 Oth Venous Thrombosis | 109 | 65 | 3 | 5 | 7 | 0.727 | 0.597 | 0.778 | 0.827 | −0.0380 | 0.0002 | * |
| ICD-9 455 Hemorrhoids | 246 | 51 | 2 | 3 | 6 | 0.826 | 0.800 | 0.827 | 1.000 | −0.0008 | 0.0002 | * |
| ICD-9 459 Oth Circulatory Disease | 367 | 64 | 3 | 5 | 7 | 0.732 | 0.708 | 0.778 | 0.827 | −0.0376 | 0.0001 | * |
| ICD-9 473 Chronic Sinusitis | 2047 | 45 | 2 | 3 | 5 | 0.853 | 0.800 | 0.827 | 1.000 | −0.0022 | 0.0001 | * |
| ICD-9 477 Allergic Rhinitis | 3326 | 46 | 2 | 3 | 5 | 0.853 | 0.800 | 0.827 | 1.000 | −0.0009 | 0.0001 | * |
| ICD-9 492 Emphysema | 296 | 68 | 3 | 5 | 7 | 0.663 | 0.508 | 0.708 | 0.810 | −0.0667 | 0.0001 | * |
| ICD-9 493 Asthma | 1604 | 46 | 2 | 3 | 5 | 0.797 | 0.761 | 0.827 | 1.000 | −0.0213 | 0.0001 | * |
| ICD-9 518 Other Lung Diseases | 167 | 59 | 3 | 5 | 7 | 0.714 | 0.597 | 0.778 | 0.827 | −0.0428 | 0.0002 | * |
| ICD-9 519 Oth Resp System Diseases | 294 | 52 | 2 | 3 | 5 | 0.816 | 0.768 | 0.827 | 1.000 | −0.0277 | 0.0001 | * |
| ICD-9 525 Other Dental Disorder | 567 | 43 | 1 | 2 | 4 | 0.853 | 0.800 | 0.833 | 1.000 | −0.0030 | 0.0001 | * |
| ICD-9 530 Diseases of Esophagus | 1500 | 55 | 3 | 4 | 6 | 0.785 | 0.761 | 0.816 | 0.844 | −0.0216 | 0.0001 | * |
| ICD-9 531 Gastric Ulcer | 344 | 57 | 3 | 5 | 7 | 0.727 | 0.597 | 0.800 | 0.827 | −0.0269 | 0.0002 | * |
| ICD-9 535 Gastritis and Duodenitis | 224 | 49 | 2 | 4 | 7 | 0.765 | 0.708 | 0.800 | 0.844 | −0.0116 | 0.0002 | * |
| ICD-9 536 Stomach Function Disord | 1211 | 53 | 2 | 4 | 6 | 0.773 | 0.708 | 0.810 | 1.000 | −0.0228 | 0.0001 | * |
| ICD-9 537 Oth Gastroduodenal Dis | 392 | 56 | 2 | 4 | 6 | 0.750 | 0.708 | 0.800 | 0.843 | −0.0311 | 0.0001 | * |
| ICD-9 553 Other Abdominal Hernia | 480 | 57 | 2 | 4 | 6 | 0.770 | 0.708 | 0.810 | 0.827 | −0.0326 | 0.0001 | * |
| ICD-9 558 Oth Noninf Gastroenterit | 117 | 53 | 2 | 4 | 6 | 0.777 | 0.768 | 0.827 | 0.844 | −0.0429 | 0.0002 | * |
| ICD-9 562 Diverticula of Intestine | 195 | 64 | 4 | 5 | 7 | 0.735 | 0.708 | 0.778 | 0.827 | −0.0302 | 0.0002 | * |
| ICD-9 564 Funct Digestive Dis Nec | 396 | 56 | 3 | 5 | 7 | 0.728 | 0.708 | 0.800 | 0.833 | −0.0346 | 0.0001 | * |
| ICD-9 569 Oth Intestinal Disorders | 254 | 57 | 2 | 4 | 6 | 0.794 | 0.761 | 0.816 | 1.000 | −0.0193 | 0.0002 | * |
| ICD-9 573 Oth Liver Disorders | 113 | 52 | 2 | 4 | 6 | 0.729 | 0.597 | 0.778 | 0.827 | −0.0567 | 0.0002 | * |
| ICD-9 574 Cholelithiasis | 148 | 52 | 3 | 4 | 6 | 0.782 | 0.708 | 0.816 | 1.000 | −0.0288 | 0.0002 | * |
| ICD-9 575 Oth Gallbladder Disorder | 218 | 51 | 2 | 4 | 6 | 0.793 | 0.761 | 0.827 | 1.000 | −0.0083 | 0.0002 | * |
| ICD-9 586 Renal Failure Nos | 102 | 58 | 4 | 6 | 8 | 0.651 | 0.506 | 0.708 | 0.816 | −0.0603 | 0.0002 | * |
| ICD-9 592 Renal/Ureteral Calculus | 299 | 49 | 2 | 3 | 5 | 0.832 | 0.800 | 0.827 | 1.000 | −0.0159 | 0.0001 | * |
| ICD-9 593 Oth Renal & Ureteral Dis | 229 | 60 | 3 | 5 | 8 | 0.712 | 0.708 | 0.778 | 0.827 | −0.0527 | 0.0002 | * |
| ICD-9 596 Other Bladder Disorders | 259 | 62 | 4 | 6 | 7 | 0.706 | 0.597 | 0.778 | 0.827 | −0.0430 | 0.0002 | * |
| ICD-9 599 Oth Urinary Tract Disor | 761 | 49 | 2 | 3 | 5 | 0.826 | 0.800 | 0.827 | 1.000 | −0.0093 | 0.0001 | * |
| ICD-9 602 Oth Prostatic Disorders | 315 | 60 | 3 | 4 | 6 | 0.788 | 0.759 | 0.810 | 1.000 | −0.0163 | 0.0001 | * |
| ICD-9 610 Benign Mammary Dysplasia | 143 | 51 | 2 | 3 | 5 | 0.852 | 0.810 | 0.827 | 1.000 | −0.0107 | 0.0002 | * |
| ICD-9 611 Other Breast Disorders | 407 | 49 | 2 | 3 | 5 | 0.838 | 0.800 | 0.827 | 1.000 | −0.0008 | 0.0001 | * |
| ICD-9 620 Noninflam Dis Ovar/Aduex | 204 | 35 | 1 | 2 | 4 | 0.859 | 0.800 | 0.827 | 1.000 | −0.0044 | 0.0002 | * |
| ICD-9 623 Noninflamm Dis Vagina | 116 | 49 | 2 | 4 | 6 | 0.822 | 0.778 | 0.827 | 0.860 | −0.0285 | 0.0002 | * |
| ICD-9 626 Disorder of Menstruation | 317 | 37 | 2 | 3 | 4 | 0.872 | 0.800 | 0.844 | 1.000 | −0.0092 | 0.0001 | * |
| ICD-9 627 Menopausal Disorders | 1003 | 56 | 2 | 4 | 6 | 0.817 | 0.778 | 0.827 | 1.000 | −0.0081 | 0.0001 | * |
| ICD-9 696 Psoriasis/Like Disorders | 176 | 51 | 2 | 3 | 5 | 0.834 | 0.778 | 0.827 | 1.000 | −0.0150 | 0.0002 | * |
| ICD-9 698 Pruritus & Like Cond | 106 | 60 | 3 | 6 | 7 | 0.730 | 0.527 | 0.800 | 0.844 | −0.0304 | 0.0002 | * |
| ICD-9 700 Corns and Callosities | 153 | 64 | 3 | 4 | 7 | 0.789 | 0.761 | 0.800 | 0.844 | −0.0214 | 0.0002 | * |

# まとめ

◆国内におけるPBMを用いたエビデンスを整理した

◆近年は増加傾向にあり，その多くがEQ-5Dを用いた研究である

◆測定特性（妥当性，信頼性，反応性，解釈可能性）に関する研究が少なく，今後，取り組むべき課題である

◆HTAに用いるためには，疾患の特性にあわせたPBMの選択と評価方法の検討が必要である

2022年3月12日 QOL-PRO研究会 研究セミナー
選好に基づく尺度の世界: 健康の価値を測定するとは

# 直接法を用いた取り組みについて

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## 背景

- 医療経済評価に用いられる患者のQOLを表す（utilityやQOL値と呼ばれる）スコアは、多くの場合EQ5Dのようなgeneric preference-based measures（GPBM）によって測定されたスコアに基づいている。
- 一方で、これらの標準的なアプローチが難しかったり適切でない場合がある。
- そんなときの対策として一般の人々に健康状態等を想起させ、それをタイムトレードオフ法等によってスコア化する直接法と呼ばれる方法が存在する。
- 近年ではこの直接法をvignette-based methods（VBM）と呼んでいる。
- しかし、意外にもこれまでこの方法に関するガイダンスや方法論的レビューはなかった。

2

# 本日ご紹介する論文

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## Vignette-Based Utilities: Usefulness, Limitations, and Methodological Recommendations

Louis S. Matza, PhD, Katie D. Stewart, MA, Andrew J. Lloyd, DPhil, Donna Rowen, PhD, John E. Brazier, PhD

ABSTRACT

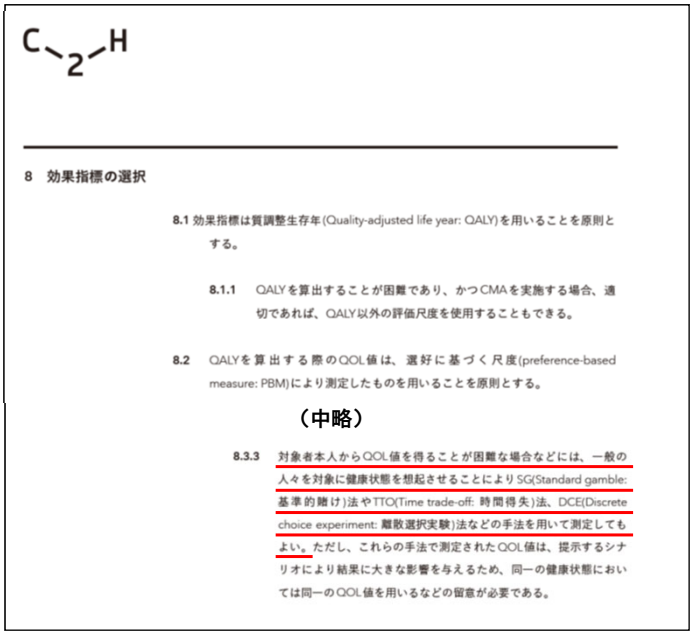
Health technology assessment agencies often prefer that utilities used to calculate quality-adjusted life years in cost-utility analyses (CUAs) are derived using standardized methods, such as generic preference-based measures completed by patients in clinical trials. However, there are situations when no standardized approach is feasible or appropriate for a specific medical condition or treatment that must be represented in a CUA. When this occurs, vignette-based methods are often used to estimate utilities. A vignette (sometimes called a "scenario," "health state description," "health state vignette," or "health state") is a description of a health state that is valued in a preference elicitation task to obtain a utility estimate. This method is sometimes the only feasible way to estimate utilities representing a concept that is important for a CUA. Consequently, vignette-based studies continue to be conducted and published, with the resulting utilities used in economic models to inform decision making about healthcare resource allocation. Despite the potential impact of vignette-based utilities on medical decision making, there is no published guidance or review of this methodology. This article provides recommendations for researchers, health technology assessment reviewers, and policymakers who may be deciding whether to use vignette-based methods, designing a vignette study, using vignette-based utilities in a CUA, or evaluating a CUA that includes vignette-based utilities. Recommendations are provided on: (A) when to use vignette-based utilities, (B) methods for developing vignettes, (C) valuing vignettes, (D) use of vignette-based utilities in models, and (E) limitations of vignette methods.

*Keywords:* cost-utility analysis, health state utilities, health state vignettes, time trade-off, utility assessment, vignette-based methods

VALUE HEALTH. 2021; ■(■):■–■

3

# 【参考】シン・分析ガイドラインにおける直接法



$C_2H$

8 効果指標の選択

8.1 効果指標は質調整生存年(Quality-adjusted life year: QALY)を用いることを原則とする。

8.1.1 QALYを算出することが困難であり、かつCMAを実施する場合、適切であれば、QALY以外の評価尺度を使用することもできる。

8.2 QALYを算出する際のQOL値は、選好に基づく尺度(preference-based measure: PBM)により測定したものを用いることを原則とする。

（中略）

8.3.3 対象者本人からQOL値を得ることが困難な場合などには、一般の人々を対象に健康状態を想起させることによりSG(Standard gamble: 基準的賭け)法やTTO(Time trade-off: 時間得失)法、DCE(Discrete choice experiment: 離散選択実験)法などの手法を用いて測定してもよい。ただし、これらの手法で測定されたQOL値は、提示するシナリオにより結果に大きな影響を与えるため、同一の健康状態においては同一のQOL値を用いるなどの留意が必要である。

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# VBMが活用される場面

- EQ5DのようなGPBMではなく、VBMによるアプローチが必要になる場面には下記のようなものがある：
  - 希少疾病など、研究の対象となる患者で十分なサンプルサイズが確保できない場合
  - QOLを構成する要素のうち特定の要素のみを変動させたときのスコアへの影響について定量化が必要な場合
  - 治療プロセスの違いによるスコアへの影響(process utility)について定量化が必要な場合
  - 頻度の低い急性期イベントのスコアが必要な場合
  - GPBMで測定可能な頻度より早く健康状態が変動してしまう場合

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# 【参考】EQ-5DやHUIの想起インターバルとレベル表現

| | EQ5D | HUI |
|---|---|---|
| 想起インターバル | 各項目において、あなたの今日の健康状態を最もよく表しているものを、それぞれ1つずつお答えください。 | あなたができること、できないことの普段の程度について、最もあてはまるものをひとつ選んでください。 |
| レベル表現 | 歩き回るのに問題はない | 歩行器具なしに難なく近所を歩き回る事ができる |

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## Vignetteの作成方法

- Vignette(スコア化したい健康状態を説明した記述)として記述する各項目は、それぞれ文献や実際の患者に対するインタビューの結果等でサポートされていなければならない。また、Vignetteを作成する際は下記の要件を満たすように検討する:
  - 回答者が研究したい健康状態について十分に理解できるように、長くなりすぎず、理解しやすい記述にする。
  - Vignetteで患者のすべての経験を表現することはできないため、典型的な患者の経験を記述する(その結果推定されるスコアはその中間的な健康状態に関するものとなる)。
  - VBMによる研究は、ある健康状態間のスコアの差について推定することを目的としていることが多いため、それらの健康状態間の違いについて比較しやすいようにデザインする。

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## Vignetteの作成方法(続き)

- Vignetteに対する回答者の認知を高めるため、イメージ図やビデオ等の補足資料を用意することも有用である。
- 「治療が必要かもしれない」のように、回答者によって解釈が変動してしまう不確実性のある表現を避ける。記述から連想する条件が変わってしまえば、その結果、推定されるスコアも変動してしまう。
- 研究したい健康状態の具体名(病名)を表示するかについては慎重に検討する。病名の表示は記述の明確さを高めたり、バイアスの原因になったり等、利点と欠点がある。
- 箇条書きや色分け等は回答者の理解を向上させるために有用である。

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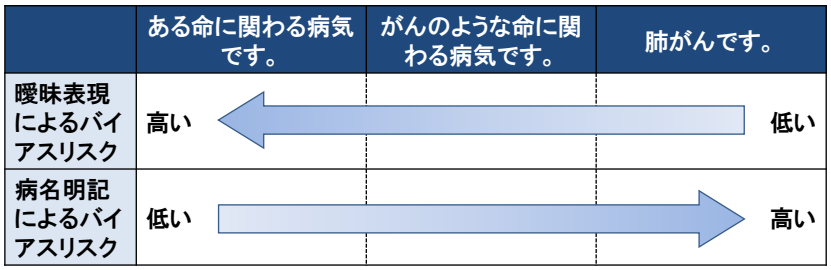
## 【参考】曖昧表現と病名明記によるバイアスのトレードオフ




- 疾患領域別にそれぞれのバイアスリスクのバランスも異なるはずのため慎重な検討が必要
- 別途、先入観や誤解を取り除く丁寧な事前説明も有用

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## Vignetteの作成方法（続き）

- 上記の要件を満たす案の作成後、医師や患者の意見を参考に修正を行う。
- また、パイロット調査を行い、実際の回答者からのフィードバックに基づき修正を検討する必要がある。

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## Vignetteのスコアリング

- 作成したVignetteのスコアリングには、一般の人々を対象にタイムトレードオフ法やスタンダードギャンブル法が使われることが多い。
- スコアリング方法の詳細は、各国のHTA評価機関が利用しているGPBMとの比較可能性を考慮するとよい。

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## 【参考】なぜか触れられていないDCE

- Vignetteのスコアリングには離散選択実験法と呼ばれる方法もある。
- 近年開発が進められているPBMのほとんどがDCEでスコアリングされている。

DCE法のイメージ

| 属性 | 健康状態A | 健康状態B |
|---|---|---|
| 症状について | 痛みがあります。 | 痛みはほとんどありません。 |
| 日常生活について | 症状のせいで普段通りに日常生活ができません。 | 症状のせいで日常生活が妨げられることがあります。 |
| 生存期間 | 10年生きて、その後死亡します。 | 5年生きて、その後死亡します。 |

- どちらが好ましいですか？と尋ねる
- 各属性の内容を色々と組み替えて1回答者当たり複数セットについて回答していただき多変量解析でスコアを求める。

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# VBMによって作成したスコアの活用方法

- 医療経済評価に利用する場合、GPBMによって推定したベースラインスコアからの差分についてVBMで推定したスコアを利用することも行われる。
- このとき、ダブルカウントを避けるため、GPBMによって推定したスコアに影響し得るような要素がVignetteに含まれていないか確認することが重要である。

**VBMのよくある使い方**

| パラメータ | 値 | ソース |
|---|---|---|
| 増悪前の乳がん患者のQOL値 | 0.8 | 臨床試験データ |
| 有害事象(吐き気など)発生時の減少QOL値 | -0.05 | VBMデータ |

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# VBMの限界点

- 推定したスコアの妥当性はVignetteがどの程度正しく説明されいてるかに依存する。
- Vignetteは実際の患者が経験したすべての側面を含めることは難しい。
- また、Vignetteがある特定の側面にだけ焦点を当てていて、その他の側面について説明がない場合、その特定の側面に対する影響を過大評価してしまうかもしれない。

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# 結論

- 各国のHTA評価機関は患者から直接取得したGPBMを好んで利用するかもしれないが、既存の尺度では測定することのできない新しいアウトカムをもたらす治療や、新しい治療プロセス、新しい有害事象は常に存在しうる。
- もし患者から直接取得するPBMの利用が難しかったり、適切でない場合は、VBMによるアプローチは唯一の選択肢になる。
- 医療経済評価に利用されるその他パラメータと同様に、VBMによって定量化されるスコアは最終的な医療資源配分に関する意思決定に多大な影響を及ぼす可能性があるため、その方法論や報告は慎重に検討されなければならない。

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