

**EORTC Quality of Life Utility-Core 10  
Dimensions (QLU-C10D)  
- User Manual**

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## Aim of user manual and target audience

This user manual addresses researchers and industry members who want to collect cancer-specific health-related quality of life (HRQoL) data and use that data for the calculation of preference-based scores and quality-adjusted life years (QALYs). It provides information and guidance on the proper legal and scientific use of the EORTC Quality of Life Utility – Core 10 Dimensions (QLU-C10D) including modes of administration, scoring, presentation of results, and translations.

The QLU-C10D is the EORTC's health utility instrument which enables calculation of utility scores from the parent HRQoL instrument, EORTC QLQ-C30, based on 10 of the 15 dimensions covered by the QLQ-C30. These 10 dimensions were carefully selected based on comprehensive psychometric analysis of a vast international data set including a variety of cancer diagnoses as well as HRQoL expert discussion.

Acknowledging the various professional backgrounds of potential users, Part 1 of the EORTC QLU-C10D manual provides some theoretical background on preference-based and non-preference based HRQoL instruments and research and an overview of different fields of application. Part 2 provides guidance on the practical administration of the EORTC QLU-C10D. The manual may be used in conjunction with other EORTC manuals and the EORTC QLG website (<https://qol.eortc.org/manuals>) which contains information on most current developments. Weblinks to respective resources are provided. For further information and assistance regarding the QLU-C10D, such as licencing, translations and ongoing investigations, you can also contact the EORTC Quality of Life Department (QLD) directly (<https://qol.eortc.org/quality-of-life-department/>).

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# PART 1 - BACKGROUND INFORMATION

## Key message box

- Involved research groups and institutions: EORTC Quality of Life Group and Quality of Life Department, MAUCa Consortium
- Health-related quality of life (HROQL):
  - a multidimensional concept that encompasses a patient's subjective perception of the effect of disease and treatment on physical, psychological and social aspects of daily life
  - assessed using patient-reported outcome (PRO) measures
- There are two large groups of PROs:
  1. HRQoL profile measures:
    - result in individual scores for different HRQoL dimensions (e.g. separately for physical functioning, psychosocial, pain, fatigue, etc.)
    - scores represent the extent of the patient's well-being or the severity of symptoms
    - designed for use in clinical studies and clinical routine
  2. Preference-based measures (PBMs)
    - results in one single 'index' score that represents the 'value' of a reported 'health state', which incorporates all HRQoL dimensions included in the health state
    - values are derived from health preferences that have been provided by a target group (usually the general population)
    - designed for use in economic evaluations, often to calculate quality-adjusted life years (QALYs)

## 1. RESEARCH GROUPS AND INSTITUTIONS

### 1.1 The EORTC Quality of Life Group (QLG)

The European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group (QLG) is a multi-disciplinary, international group of researchers and clinicians dealing with cancer. It formed in 1980 and has dedicated its activities to health-related quality of life (HRQoL) in oncology ever since. This encompasses advocating HRQoL measurement in clinical studies and practice by providing a refined HRQoL measurement system, driving forward methodological research in the field, and, in cooperation with the EORTC Quality of Life Department (QLD), supporting EORTC disease-specific groups in the incorporation of HRQoL outcomes in EORTC clinical trials. It is open to researchers and clinicians all over the world who have an interest in HRQoL research in oncology. The EORTC is a registered not-for-profit organization, which means that all income is used for research, education and user support.

The EORTC QLG website (<https://qol.eortc.org/>) provides detailed information and updates on the EORTC HRQoL measurement system, including user manuals, available language versions, key references, licencing information, upcoming events and ongoing research projects.

## **1.2 The EORTC Quality of Life Department (QLD)**

The Quality of Life Department (QLD) is a division of the EORTC Data Center dedicated to a coherent policy and providing a standard approach in conducting HRQoL research in cancer clinical trials. The principal tasks of the QLD are to support the incorporation of HRQoL data collection into clinical trial protocols, to establish an adequate infrastructure for the data management of studies which include HRQoL endpoints, and to guide analysis of HRQoL data in EORTC clinical trials. It also manages the translation and licencing of EORTC HRQoL measures.

## **1.3 The MAUCa Consortium**

The Multi-attribute Utility in Cancer (MAUCa) Consortium is an international group of HRQoL researchers who developed the EORTC QLU-C10D health state classification system and valuation methodology.

## 2. THEORETICAL BACKGROUND AND TERMINOLOGY

### 2.1 Measuring and valuing health – HRQoL profiles versus preference-based measurement

HRQoL is a multidimensional concept and encompasses a patient's subjective perception of the effect of their disease and treatment on physical, psychological and social aspects of daily life (Bottomley et al. 2016). Several patient-reported outcome (PRO) instruments exist that can be used to measure a patient's HRQoL. PRO instruments can broadly be divided into two groups, namely the HRQoL profile measures and preference-based measures (PBMs) (Drummond 2005). The two types of instruments represent two different approaches to HRQoL assessment (measuring versus valuing health) and their results serve different research purposes (clinical research versus health economics research).

#### 211 *HRQoL profile measures*

HRQoL profile measures are questionnaires with scoring algorithms that produce a series, or 'profile' of individual domain scores. In general, domains include aspects of functioning (e.g. physical functioning) and, depending on their target group, generic symptoms (e.g. pain) or disease-specific symptoms. HRQoL profile measures are used predominantly in clinical research, e.g. as measures of secondary outcomes in trials or in observational studies and registries to investigate HRQoL trajectories and to evaluate the impact of disease and treatment on different aspects of functioning and well-being. HRQoL profile measures are increasingly being used in clinical practice where they may serve as HRQoL screening tools to enable early detection of symptoms and improve clinical care. Commonly used HRQoL profile measures in the field of cancer include the EORTC Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) and the Functional Assessment of Cancer Therapy – General (Fact-G).

#### 212 *Preference-based measures (PBMs)*

PBMs are designed to take into account the preference towards a particular health profile or outcome (Drummond 2005), i.e. to "value" health. They consist of two parts:

- 1) a so-called "health state classification system", i.e. a set of health/HRQoL aspects (domains), which may take on different severity levels, yielding a number of unique "health states", each defined by a unique combination of domains and levels;
- 2) a preference-based scoring algorithm, which uses a series of preference weights (determined in a "valuation study") to combine the various domains into a single 'index' score.

So PBMs are similar to HRQoL profile measures in that they include a number of questions on different HRQoL aspects/domains, each with a number of response options, but their scoring algorithm is very different because it uses preference weights to yield a single "index" score, also called a "utility" score. PBMs are therefore also called "utility instruments".

The outcome of a PBM for a particular patient at a particular time is therefore a single number, expressed on a special scale known as a “utility” that expresses the “value” assigned to that patient’s health state (as described by their self-reported response to the questionnaire) and weighted by the preferences of the target population included in the valuation study that yielded the preference weights.

The utility scale has special characteristics: it is anchored at 0 (representing being dead, or a state equivalent to it) and has a maximum of 1 (representing optimal/best imaginable health). Depending on the preference weights for the most severe levels in the scoring algorithm, scores below 0 (i.e. health states worse than death) are possible. The preference weights that contribute to the final values assigned to the health states described by the PBM have to be elicited previously in the target population (most often the general population of a country) in a “valuation study” and then form a so-called “value set”. As these utility scores are designed for use in health economic decisions, which are generally made in the context of health budgets within a country or health service, country-specific value sets are ideal, but this requires a separate valuation study for each country, and this is not always feasible.

Historically, PBM were generic, i.e. relevant across a wide range of health conditions. But in recent years, a number of disease-specific PBMs have been developed. With regard to disease-specific PBMs, systematic differences in health valuations may arise depending on who is included in the valuation study; a general population yields “societal values” and a patient population yields “patient values”. However, the extent of potential systematic differences needs further research. The vast majority of value sets for PBMs represent societal values as this to date is the preferred perspective in economic studies. However, an important argument to investigate patient preferences is that respondents from the general population usually can relate to generic HRQoL issues, such as pain, but may have more difficulty imaging and hence valuing the impact of severe fatigue, as experienced by cancer patients, for example. The EORTC QLQ is currently investigating utility differences between societal and patient in a single country to provide a basis for further discussion on how to proceed in future.

PBMs are usually used in cost-utility analyses (CUAs). CUA is a method in of economic evaluation that compares different health interventions with regard to their costs, HRQoL consequences and survival. A CUA’s final outcome is the incremental cost-effectiveness ratio (ICER), also more precisely often called incremental cost-utility ratio (ICUR), which is the difference in costs between two interventions divided by their difference in effect. The treatment effect is typically expressed in quality-adjusted life years (QALYs), which is the survival time adjusted for quality of life, i.e. for the utility, which can be assessed by a PBM (Drummond 2005). Figure 1 on the next page shows a brief overview of the characteristics of HRQoL profile measures and PBMs.



HRQoL PROFILE MEASURE	PREFERENCE-BASED MEASURE
Psychometric approach	Utility approach
A respondent describes his/her own HRQoL	Scores represent the <u>value</u> of health states
Domains of HRQoL are kept separate, a series of domain scores describe a HRQoL <i>profile</i>	Domains of HRQoL are combined into a single <i>index</i>
Each domain score is typically derived from several items (questions)	Typically one item (question) per domain
Typically items (questions) are unweighted, typically average or sum of items	Domains are weighted, weights are derived using a preference-based method
Ordinal scales, no anchors. Minimum and maximum values are a function of scoring algorithm. Often linearly transformed to 0 – 100 range.	Interval scale, anchored at 0 (dead) and 1 (fullhealth), values worse than death are possible. The maximum value is always 1 and minimum values are a function of weights and scoring algorithm

Figure 1: Overview characteristics of HRQoL profile measures versus preference-based measures

## 2.2 Generic and disease-specific preference-based measures

Two types of PBMs can be distinguished: generic and disease-specific.

Generic PBMs are currently predominantly used for the assessment of utilities for CUAs. They use general, fundamental HRQoL dimensions, which make them applicable for most medical conditions, thereby allowing comparability between different diseases and treatments (Dolan 1997, Drummond 2005, Rowen, Zouraq, et al. 2017). The most prominent generic utility measures are the EQ-5D-3L (The EuroQol Group 1990), the EQ-5D-5L (Herdman et al. 2011), the Short-Form Six-Dimensions (SF- 6D) (Brazier et al. 2002), the Health Utility Index Mark 2 (HUI2) (Horsman et al. 2003), the Health Utility Index Mark 3 (HIU3) (Grootendorst et al. 2000), and the 15D (Sintonen 2001).

Even though generic PBMs are the preferred choice for performing CUAs in a health economic setting, various aspects have been criticised, especially regarding their appropriateness in certain settings, such as in oncology. Their measurement properties vary across conditions as some might lack sensitivity in specific health states (Bharmal et al. 2006, Rowen, Brazier, et al. 2017, Rowen et al. 2012, Rowen et al. 2012). This could be a result of the usually lower number of dimensions included in a generic PBM or due to fewer/more coarse response options.

Alternatively, it may be that the included dimensions do not measure the issues most relevant to the target patient population. Independent of the potential explanations, inappropriate scale coverage in specific conditions, mostly this refers to ceiling effects, are an issue in generic PBMs (Brazier et al. 2004, Conner-Spady et al. 2015, Janssen et al. 2013, Sullivan et al. 2005). This means that some of these instruments report full health

(i.e. a utility of 1) for the patient even though s/he has an impaired quality of life or a reduction in health status (Pickard et al. 2012, van Dongen- Leunis et al. 2016).

Therefore, there is an ongoing debate on the potential added value of disease-specific PBMs which might be able to overcome many of these limitations.

Disease-specific PBMs may overcome many of the limitations of generic PBMs. Some show a better validity, sensitivity and responsiveness in the disease under investigation (Krahn et al. 2007, Wiebe et al. 2003, Rowen, Brazier, et al. 2017). However, it has been claimed that disease-specific PBMs might exaggerate health problems due to a focusing effect, i.e. a proposed tendency to perceive the condition-specific aspect more important when presented to a person even though generic aspects may be potentially equally important, which in turn might translate into a lower sensitivity for comorbid conditions (Brazier et al. 2010, Versteegh et al. 2012). However, so far this proposal has not been tested. A further concern regarding disease-specific PBMs is that they need to be developed and evaluated for each specific disease, which would be time- and cost-intensive. In addition, comparability of scores across studies and diseases, as desired by many stakeholders in health economics, becomes more complicated. However, it is well known that even generic PBMs result in different utility scores (Färkkilä et al. 2014, Li et al. 2022), and therefore do not yield comparable scores. This raises questions about whether disease-specific instruments need to be comparable to results from generic instruments, and whether health economics evaluations might benefit from a broader range of quality of life information even though becoming even more complex.

These considerations all suggest the need to evaluate the potential gain in accuracy and appropriateness by developing and comparing novel disease-specific PBMs with traditional generic ones. How a variety of PBM measures can be used in regulatory practice also needs to be clarified.

### **2.3 The EORTC QLQ measurement system**

A core activity of the EORTC QLQ is the continuous extension and refinement of the EORTC HRQoL measurement system. This consists of a range of HRQoL profile measures and one PBM (the QLU-C10D). The following provides a brief overview — for details please refer to <https://qol.eortc.org/quality-of-life-group/#>.

A main body of the EORTC measurement system is the *Quality of Life Questionnaire-Core 30* (QLQ-C30) as the core instrument (and its computer-adaptive version, the *EORTC CAT*) which can be complemented with site- and treatment-specific modules, all covering functional and symptomatic aspects of the (specific) disease and/or treatment. In addition stand-alone measures are available for specific purposes, such as for the assessment of patient satisfaction or communication.

Furthermore, the EORTC provides two kinds of item collections which allow the construction of custom-built question sets, an item response theory (IRT-) calibrated item bank, which comprises all items from the EORTC CAT (i.e. covering the content of the domains of the QLQ-C30) and an item library, a repository of all questions used in EORTC instruments. For details on the use of the item bank and item library please refer to the EORTC QLD (<https://qol.eortc.org/quality-of-life-department/>).

These EORTC instruments produce HRQoL profiles and were designed for use as outcome measures in cancer clinical studies and HRQoL screening in clinical practice. The development of the Quality of Life Utility-10 Dimensions (QLU-C10D) allows data collected with the EORTC QLQ-C30 to now also be used in health economics research by providing a preference-based scoring algorithm for the calculation of cancer-specific health utilities.

## **2.4 What shall I use – an EORTC HRQoL profile measure or the EORTC QLU-C10D?**

Use an EORTC HRQoL profile measure (QLQ-C30 +/- site- and treatment-specific modules), when an array of scores representing individual dimensions/domains of HRQoL is of interest, e.g. when a differential measurement of effects of a disease/health condition or health intervention is required on specific single domains or various HRQoL domains. This may be the case in clinical studies and where interventions target a specific aspect of HRQoL (most commonly when HRQoL is a secondary endpoint in a clinical trial), or in clinical practice where tracking a set of symptoms and functioning aspects supports disease management, or in disease registries where the aim may be to learn about trajectories covering various aspects of HRQoL. The QLQ-C30 also provides the possibility of calculating a summary score across different HRQoL domains for research objectives including a more general HRQoL endpoint (Giesinger et al. 2016).

Apply the EORTC QLU-C10D scoring algorithm to QLQ-C30 data when an economic evaluation is required, including calculation of QALYs for CUA. In this case, data from the QLQ-C30 provide the respondent's health state descriptions, and then you must decide which country-specific algorithm to use, as this will determine the preference-weights that are applied to calculate the utility scores and hence the QALYs.

Both of these purposes (profile and preference-based scoring) can be achieved by using the QLQ-C30 and scoring it as per its standard scoring algorithm and also applying the QLU-C10D preference-based scoring algorithm.

# PART 2: EORTC QLU-C10D – GUIDELINES FOR USERS

## Terminology overview

### Preference-based measure (PBM):

- a HRQoL instrument that results in a single index value expressing the “value” on a “utility” scale of a certain health state to be used in health economics research
- synonyms: utility instrument, multi-attribute utility instrument (MAUI)

### Utility:

the “value” assigned to a health state by a target population (mostly the general population of a country) by providing preferences for health states

- anchored at 0 (representing death) and 1 (representing best imaginable health)
- synonyms: health state utility value (HSUV), utility value

**Value set/tariff:** the utility values for the health states described by a PBM provided by a specific population (usually the general population of a country)

**Quality-adjusted life year (QALY):** survival time adjusted for quality of life, using utility scores as the adjustment factor)

## 3. The EORTC QLU-C10D

### 3.1 The development of the QLU-C10D from the QLQ-C30

The EORTC Quality of Life Utility-Core 10 Dimensions (QLU-C10D) is a preference-based measure based on the profile HRQoL instrument of the EORTC, the QLQ-C30 (Aaronson et al 1993). Its health state classification system was developed by the Multi-Attribute Utility Cancer (MAUCa) Consortium and included a thorough mixed methods approach to select domains and items from the QLQ-C30, including a range of classical psychometric analyses plus item-response theory analyses of a large international QLQ-C30 data set and qualitative interviews with cancer patients, health care experts, and HRQoL researchers (King et al. 2016).

The rationale for its development was the increasing knowledge on measurement issues of generic PBMs in certain populations and for specific purposes and the lack of cancer-specific PBMs which may better capture cancer-specific HRQoL aspects. Also generic PBMs are predominantly used in health economics investigations. In contrast to cancer-specific HRQoL measures, generic PBMs are not routinely included in cancer clinical trials, as they do not provide much if any additional information to the cancer-specific profile measures typically used in cancer clinical trials. Further, although the individual domains of a PBM can be reported like a HRQoL profile, they are usually based on single items which come with a larger measurement error than scales based on several items.

### 3.2 What is a QLU-C10D health state?

The QLU-C10D incorporates a health classification system consisting of 13 items of the parent instrument QLQ-C30. The items form 10 domains (physical functioning (PF), role functioning (RF), social functioning (SF), emotional functioning (EF), pain (PA), fatigue (FA), sleep (SL), appetite (AP), nausea (NA), and bowel problems (BO)) (see Figure 2: QLU-C10D Health State).

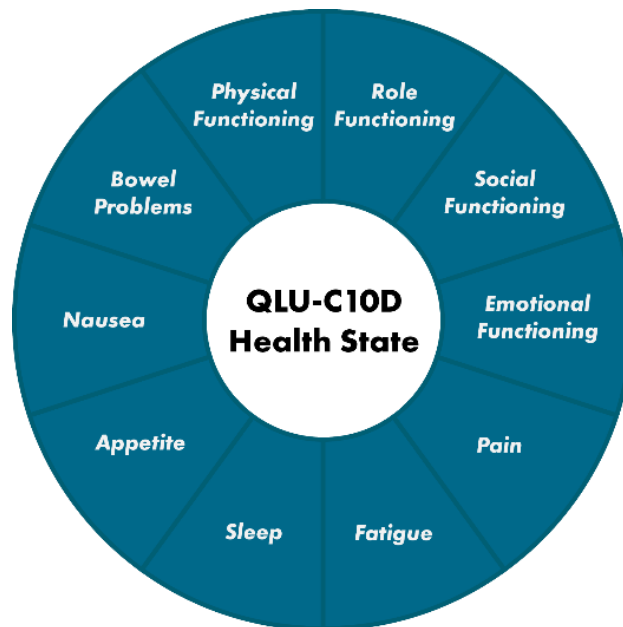


Figure 2: QLU-C10D Health State

Each domain can take on four levels which describe levels of impairment:

- Level 1:** no problems
- Level 2:** some problems
- Level 3:** quite a bit problems
- Level 4:** severe problems

A QLU-C10D health state is described by a 10-digit code providing the level of impairment per domain, i.e. a total of  $4^{10} = 1048576$  health states can be described, with the best state being 1111111111 (no problems in any domains) and the worst state being 4444444444 (severe problems in all domains).

Table 1 shows the QLU-C10D health state classification system including translation from QLQ-C30 response levels to QLU-C10D domain levels. The recall period is the same as for the QLQ-C30 items.



## EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials:

Your birthdate (Day, Month, Year):

Today's date (Day, Month, Year):

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	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a <u>long</u> walk?	1	2	3	4
3. Do you have any trouble taking a <u>short</u> walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

### During the past week:

	Not at All	A Little	Quite a Bit	Very Much
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4

[Please go on to the next page](#)

### During the past week:

	Not at All	A Little	Quite a Bit	Very Much
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your <u>family</u> life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your <u>social</u> activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

### For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past week?

1 2 3 4 5 6 7

Very poor

Excellent

30. How would you rate your overall quality of life during the past week?

1 2 3 4 5 6 7

Very poor

Excellent

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Figure 3: QLQ-C30

Table 1: QLU-C10D health state classification system and translation of QLQ-C30 responses to QLU-C10D domain levels

QLU-C10D			
Domain	Level	Health state descriptions	Translation of QLQ-C30 response levels to QLU-C10D domain levels
Physical Functioning (PF) *	1 2 3 4	No trouble taking a long walk outside of the house No trouble taking a short walk outside of the house, but at least a little trouble taking a long walk At least a little trouble taking a short walk outside of the house, and at least a little trouble taking a long walk Quite a bit or very much trouble taking a short walk outside the house	Item 2 (long walk) = 1 Item 3 (short walk) = 1 AND Item 2 $\geq$ 2 Item 3 = 2 AND Item 2 $\geq$ 2  Item 3 $\geq$ 3 AND Item 2 $\geq$ 2
Role Functioning (RF)	1 2 3 4	Not at all limited in pursuing work or other daily activities A little limited in pursuing work or other daily activities Quite a bit limited in pursuing work or other daily activities Very much limited in pursuing work or other daily activities	Item 6 = 1 Item 6 = 2 Item 6 = 3 Item 6 = 4
Social Functioning (SF)	1 2 3 4	Physical condition or medical treatment interferes <b>not at all</b> with social or family life Physical condition or medical treatment interferes <b>a little</b> with social or family life Physical condition or medical treatment interferes <b>quite a bit</b> with social or family life Physical condition or medical treatment interferes <b>very much</b> with social or family life	Items 26 AND 27 = 1 Items 26 OR 27 = 2 Items 26 OR 27 = 3 Items 26 OR 27 = 4
Emotional Functioning (EF)	1 2 3 4	feeling <b>not at all</b> feeling depressed feeling <b>a little</b> depressed feeling <b>quite a bit</b> depressed feeling <b>very much</b> depressed	Item 24 = 1 Item 24 = 2 Item 24 = 3 Item 24 = 4
Pain (PA)	1 2 3 4	<b>no</b> pain <b>a little</b> pain <b>quite a bit</b> pain <b>very much</b> pain	Item 9 = 1 Item 9 = 2 Item 9 = 3 Item 9 = 4
Fatigue (FA)	1 2 3 4	<b>not at all</b> tired <b>a little</b> pain <b>quite a bit</b> pain <b>very much</b> pain	Item 18 = 1 Item 18 = 2 Item 18 = 3 Item 18 = 4
Sleep disturbance (SL)	1 2 3 4	<b>no</b> trouble sleeping <b>a little</b> trouble sleeping <b>quite a bit</b> trouble sleeping <b>very much</b> trouble sleeping	Item 11 = 1 Item 11 = 2 Item 11 = 3 Item 11 = 4
Appetite loss (AP)	1 2 3 4	<b>not at all</b> lacking appetite <b>a little</b> lacking appetite <b>quite a bit</b> lacking appetite <b>very much</b> lacking appetite	Item 13 = 1 Item 13 = 2 Item 13 = 3 Item 13 = 4
Nausea (NA)	1 2 3 4	<b>not at all</b> feeling nauseated <b>a little</b> feeling nauseated <b>quite a bit</b> feeling nauseated <b>very much</b> feeling nauseated	Item 14 = 1 Item 14 = 2 Item 14 = 3 Item 14 = 4
Bowel problems (BO)	1 2 3 4	<b>no</b> constipation or diarrhoea <b>a little</b> constipation or diarrhoea <b>quite a bit</b> constipation or diarrhoea <b>very much</b> constipation or diarrhoea	Items 16 AND 17 = 1 Items 16 OR 17 = 2 Items 16 OR 17 = 3 Items 16 OR 17 = 4
* In the rare case of responses on PF that do not follow the logical order (e.g. more severe impairment on “short walk” than on “long walk”) use the more severe health state (e.g. more severe impairment on “short walk”).			



### 3.3 EORTC QLU-C10D valuations

#### *Eliciting health preferences using a discrete choice experiment (DCE)*

EORTC QLU-C10D valuations are performed using a standardised and well-validated methodology developed by the MAUCa Consortium (Norman, Viney, et al. 2016). Health preferences are elicited using a discrete-choice experiment (DCE). In the DCE each respondent is presented with 16 different choice sets which comprise two hypothetical health scenarios each consisting of a health state defined by the ten domains of the QLU-C10D and a survival time in that respective health state (1, 2, 5 or 10 years). An example choice set is shown in Figure 4: Example choice set. Respondents are asked to select which of the two health scenarios they prefer in each choice set. This is a forced choice, meaning they cannot progress without providing an answer. The selection of 16 choice sets each respondent is asked to complete is selected randomly out of a total of 960 which are determined by methods of optimal design theory.

Since a total of 11 attributes (10 HRQoL domains + survival time) represents quite a complex health scenario and choice task, in each choice set only five attributes are allowed to differ between the described health states in order to keep the cognitive burden at a manageable level. The order of the ten HRQoL domains is randomised for each respondent but kept constant within each individual respondent's DCE. The DCE has been thoroughly tested with regard to impact of order of attributes (Norman, Kemmler, et al. 2016), graphical presentation (Norman, Viney, et al. 2016), and test-retest reliability (Gamper et al. 2018).

	Situation A	Situation B
In taking a long walk	You have a little trouble	You have a little trouble
In taking a short walk	You have a little trouble	You have a little trouble
You are limiting in pursuing your daily activities	Quite a bit	Quite a bit
Your physical condition interferes with your social or family life	Quite a bit	A little
You feel depressed	Quite a bit	Quite a bit
You have pain	A little	Very much
You feel tired	A little	A little
You have trouble sleeping	Not at all	Not at all
You lack appetite	Quite a bit	Quite a bit
You feel nauseated	A little	Quite a bit
You have constipation or diarrhoea	Not at all	Quite a bit
You will live in this health state for	2 years and then die	5 years and then die
Which situation would you prefer?	<input type="radio"/>	<input type="radio"/>

Figure 4: Example choice set



### ***Standard valuation survey, respondents and sampling***

A standardised valuation procedure has been put in place that is used in all country-specific valuation surveys. Deviations from this procedure need to be approved by the MAUCa-Consortium, the EORTC QLD, and the EORTC HTA working group — please contact the EORTC QLD if you are interested in conducting a new country-specific valuation survey.

To reflect societal health values, preferences are obtained from general population samples and are estimated separately per country. A national valuation sample comprises approximately 1,000 adult respondents (de Bekker-Grob et al. 2015); this number was selected as it exceeded the various rules of thumb around sample size requirements for DCEs, and also the typical range of samples used in existing health DCEs (Soekhai et al. 2019). Recruitment is done using online panels and the valuation survey is performed as a web-based survey, applying quota sampling for age and sex according to national census data. The DCEs are the main body of the valuation survey, which in addition includes sociodemographic and basic clinical information, the EORTC QLQ-C30, four feedback questions on the DCE, self-completion of the EQ-5D-5L (Herdman et al. 2011), and the Kessler K-10 mental health questionnaire (Kessler et al. 2002).

## 4. PROPERTIES AND APPLICATION OF THE QLU-C10D

### 4.1 Psychometric properties

The QLU-C10D showed to be sensitive for differences between known-clinical groups and responsive for changes over time (Shaw et al. 2021, Bulamu et al. 2021, Pilz et al. 2023, Seyringer et al. 2023a, Seyringer et al. 2023b). In addition, it showed beneficial with regard to relative efficiency compared to the EQ-5D-3L in the majority of the performed analyses (Shaw et al. 2021, Pilz et al. 2023, Seyringer et al. 2023a, Seyringer et al. 2023b) which translates into smaller required sample sizes. Ceiling effects of the QLU-C10D utility were negligible (0.7%-8%) and clearly lower than ceiling effects of the EQ-5D-3L in the same samples (Pilz et al. 2023a, Pilz et al. 2023b, Seyringer et al. 2023a, Seyringer et al. 2023b). According to Terwee et al. (2007) ceiling effects of 15% would be considered relevant enough to potentially impact content validity. Ceiling effects of individual domains were pronounced in both instruments (Pilz et al. 2023a, Pilz et al. 2023b, Seyringer et al. 2023a, Seyringer et al. 2023b). This highlights the importance of using the entire QLQ-C30 scales when reporting health profiles as these were designed for this purpose and have higher measurement precision. Additional studies on psychometric properties of the QLU-C10D in different cancer sites and treatment settings are currently ongoing and results will be provided in an updated manual version.

## 4.2 Administration

The items of the EORTC QLU-C10D have to be completed by the patients themselves. It is strongly recommended that the entire parent instrument EORTC QLQ-C30 is administered which includes all QLU-C10D items. This allows the obtaining of the full EORTC QLQ-C30 HRQoL profile as well as the calculation of QLU-C10D utility scores.

Possible modes of administration are paper-pencil based or electronic assessment (for information on electronic data capture please refer to the EORTC QLD). It is also possible to use the EORTC CAT Core measures since they likewise include all items of the QLQ-C30 (Petersen et al. 2018) (see Figure 5). If you plan to do so the EORTC QLD will assist you with the selection of the required domains. For more information on requirements and regulations of CAT administration please refer to the EORTC QLD.

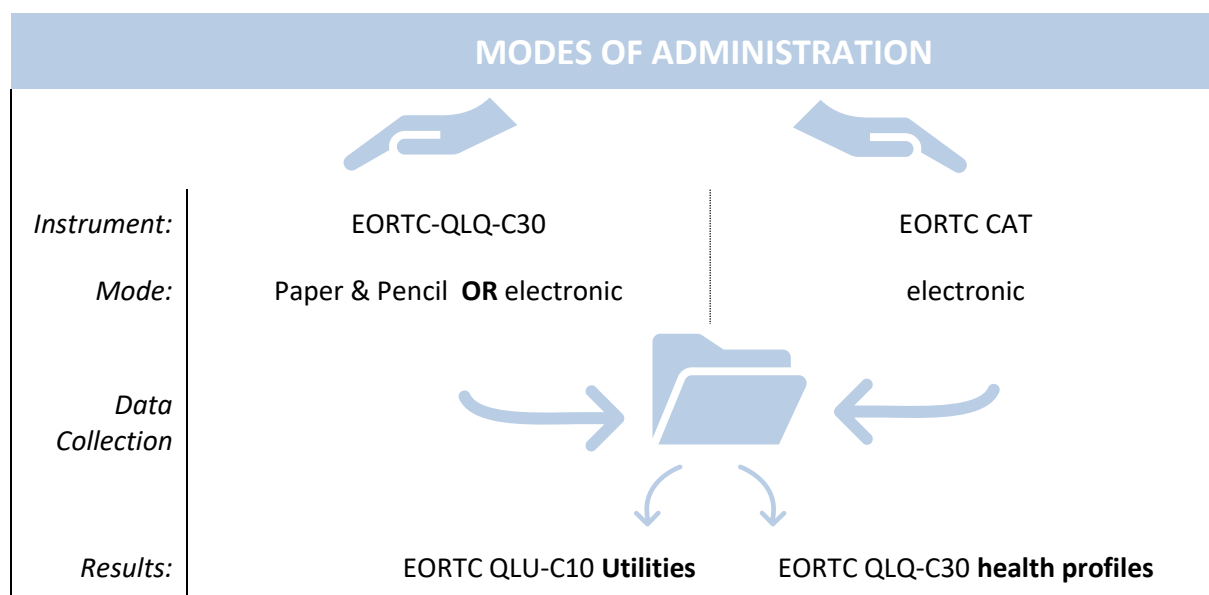


Figure 5: Overview of modes of administration

### 4.3 Scoring and converting health states into an index value

Scoring and converting health states into an index (i.e. utility) value are performed as follows:

1. Describe EORTC QLU-C10D health state using classification system (see Table 1: QLU-C10D health state classification system and translation of QLQ-C30 responses to QLU-C10D domain levels):
  - a. Record responses to QLQ-C30 items: item numbers 2, 3, 6, 9, 11, 13, 14, 16, 17, 18, 24, and 27
  - b. Check validity: only one response per item and no missing item scores.
  - c. Describe EORTC QLU-C10D health state by score responses using Table 1: QLU-C10D health state classification system and translation of QLQ-C30 responses to QLU-C10D domain levels. It is customary to describe a specific health state by listing the single domain scores in the order in which the domains appear in the instrument. For the QLU-C10D the order of domains is as listed in Table 1: QLU-C10D health state classification system and translation of QLQ-C30 responses to QLU-C10D domain levels (PF, RF, SF, EF, PA, FA, SL, AP, NA, BO (see scoring example in section 4.5)).
2. Transform QLU-C10D health state into an index value by attaching the domain scores with the respective weights: the scoring algorithm attaches a weight to each level of each dimensions and subtracts the sum of the weights from 1 (i.e. from “full health”):

$$\text{QLU-C10D utility} = 1 - (\text{response}_{\text{PF}} * \text{weight}_{\text{PF}} + \text{response}_{\text{RF}} * \text{weight}_{\text{RF}} + \text{response}_{\text{SF}} * \text{weight}_{\text{SF}} + \text{response}_{\text{EF}} * \text{weight}_{\text{EF}} + \text{response}_{\text{PA}} * \text{weight}_{\text{PA}} + \text{response}_{\text{FA}} * \text{weight}_{\text{FA}} + \text{response}_{\text{SL}} * \text{weight}_{\text{SL}} + \text{response}_{\text{AP}} * \text{weight}_{\text{AP}} + \text{response}_{\text{NA}} * \text{weight}_{\text{NA}} + \text{response}_{\text{BO}} * \text{weight}_{\text{BO}})$$

Section 4.5 provides a detailed example utility calculation from EORTC QLQ-C30 scores.

Country-specific utility weights need to be inserted and can be obtained from the publication of the respective national value set/tariff (see section 6) or directly from the EORTC QLD. You can also receive respective scoring templates for SPSS, STATA, and SAS from the EORTC QLG (no costs involved).

#### 4.4 Organising QLU-C10D data

We suggest entering QLU-C10D data into a database as follows (see Table 1 for translation of QLQ-C30 levels to QLU-C10D domain levels; NOTE: PF, SF, and BO consist of two items each). To minimise error, where possible we suggest using scoring templates provided in website <https://qol.eortc.org/manuals>.

Pat-ID	COUNTRY	TARIFF	PF	RF	SF	EF	PA	FA	SL	AP	NA	BO
Patient ID		Tariff (Author, year)	-1- no problems -2- a little problems -3- moderate problems -4- severe problems	-1- no problems -2- a little problems -3- moderate problems -4- severe problems	-1- no problems -2- a little problems -3- moderate problems -4- severe problems	-1- no problems -2- a little problems -3- moderate problems -4- severe problems	-1- no problems -2- a little problems -3- moderate problems -4- severe problems	-1- no problems -2- a little problems -3- moderate problems -4- severe problems	-1- no problems -2- a little problems -3- moderate problems -4- severe problems	-1- no problems -2- a little problems -3- moderate problems -4- severe problems	-1- no problems -2- a little problems -3- moderate problems -4- severe problems	-1- no problems -2- a little problems -3- moderate problems -4- severe problems
01	AUS	King et al, 2018	3	1	2	3	2	1	3	4	2	3
02	AUS	King et al, 2018	2	1	2	1	2	1	2	3	1	3
...	...	...	...									

## 4.5 QLU-C10D scoring example for scoring by hand

### 1. Step 1: Record responses to QLQ-C30 items: 2, 3, 6, 9, 11, 13, 14, 16, 17, 18, 24, and 27 score according to Table 1



#### EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials:

Your birthdate (Day, Month, Year):

Today's date (Day, Month, Year):

	Not at All	A Little	Quite a Bit	Very Much	
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4	
2. Do you have any trouble taking a <u>long</u> walk?	1	2	3	4	PF » 3
3. Do you have any trouble taking a <u>short</u> walk outside of the house?	1	2	3	4	
4. Do you need to stay in bed or a chair during the day?	1	2	3	4	
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4	
<b>During the past week:</b>					
	Not at All	A Little	Quite a Bit	Very Much	
6. Were you limited in doing either your work or other daily activities?	1	2	3	4	RF » 1
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4	
8. Were you short of breath?	1	2	3	4	
9. Have you had pain?	1	2	3	4	PA » 2
10. Did you need to rest?	1	2	3	4	
11. Have you had trouble sleeping?	1	2	3	4	SL » 3
12. Have you felt weak?	1	2	3	4	
13. Have you lacked appetite?	1	2	3	4	AP » 4
14. Have you felt nauseated?	1	2	3	4	NA » 2
15. Have you vomited?	1	2	3	4	
16. Have you been constipated?	1	2	3	4	BO » 3

Please go on to the next page

#### During the past week:

	Not at All	A Little	Quite a Bit	Very Much	
17. Have you had diarrhea?	1	2	3	4	BO » 3
18. Were you tired?	1	2	3	4	FA » 1
19. Did pain interfere with your daily activities?	1	2	3	4	
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4	
21. Did you feel tense?	1	2	3	4	
22. Did you worry?	1	2	3	4	
23. Did you feel irritable?	1	2	3	4	
24. Did you feel depressed?	1	2	3	4	EF » 3
25. Have you had difficulty remembering things?	1	2	3	4	
26. Has your physical condition or medical treatment interfered with your <u>family</u> life?	1	2	3	4	SF » 2
27. Has your physical condition or medical treatment interfered with your <u>social</u> activities?	1	2	3	4	
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4	

#### For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall <u>health</u> during the past week?	1	2	3	4	5	6	7
Very poor							Excellent
30. How would you rate your overall <u>quality of life</u> during the past week?	1	2	3	4	5	6	7
Very poor							Excellent

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**2. Step 2: Describe EORTC QLU-C10D health state: domains in order as in Table1 (PF, RF, SF, PA, FA, SL, AP, NA, BO): 3123213423**

**3. Step 3: Transform EORTC QLU-C10D health state into an index value**

Attach weights (the table below illustrates this with the Australian utility weights (King et al. 2018)) to QLU-C10D healthstate = 3123213423

Utility decrements used in the QLU-C10D utility algorithm

Dimension	Level	Utility decrement, $w_{dl}$ (95% CI)
Physical functioning	1	0
	2	-0.081 (-0.051 to -0.110)
	3	-0.151 (-0.120 to -0.182)
	4	-0.250 (-0.220 to -0.280)
Role functioning	1	0
	2	-0.024 (0.001 to -0.049)
	3	-0.090 (-0.066 to -0.114)
	4	-0.139 (-0.117 to -0.161)
Social functioning	1	0
	2	0.000 (0.024 to -0.025)
	3	-0.064 (-0.040 to -0.089)
	4	-0.091 (-0.070 to -0.112)
Emotional functioning	1	0
	2	-0.020 (0.003 to -0.043)
	3	-0.066 (-0.041 to -0.091)
	4	-0.133 (-0.112 to -0.155)
Pain	1	0
	2	-0.053 (-0.029 to -0.078)
	3	-0.129 (-0.105 to -0.153)
	4	-0.155 (-0.133 to -0.177)
Fatigue	1	0
	2	-0.023 (-0.001 to -0.045)
	3	-0.029 (-0.006 to -0.053)
	4	-0.037 (-0.016 to -0.058)
Sleep	1	0
	2	-0.033 (-0.012 to -0.054)
	3	-0.039 (-0.020 to -0.059)
	4	-0.039 (-0.020 to -0.059)
Appetite	1	0
	2	-0.028 (-0.006 to -0.049)
	3	-0.050 (-0.030 to -0.070)
	4	-0.050 (-0.030 to -0.070)
Nausea	1	0
	2	-0.047 (-0.025 to -0.070)
	3	-0.068 (-0.044 to -0.092)
	4	-0.107 (-0.086 to -0.127)
Bowel problems	1	0
	2	-0.047 (-0.025 to -0.068)
	3	-0.078 (-0.054 to -0.102)
	4	-0.094 (-0.073 to -0.115)

From Model 2, conditional logit, monotonicity imposed

**QLU-C10D utility for healthstate**

**3123213423 =**

$$1 - (0.151 + 0 + 0 + 0.066 + 0.053 + 0 + 0.039 + 0.050 + 0.047 + 0.078) = \mathbf{0.516}$$

Table from King et al. 2018 *Pharmacoeconomics* 36, 225–238

#### 4. Example of how to organise QLU-C10D data

Pat-ID	COUNTRY	TARIFF (author, year)	PF	RF	SF	EF	PA	FA	SL	AP	NA	BO	QLU-C10D_utility
01	AUS	King et al., 2018	3	1	2	3	2	1	3	4	2	3	0.516
02	AUS	King et al., 2018	2	1	2	1	2	1	2	3	1	3	0.705
...	...	...											



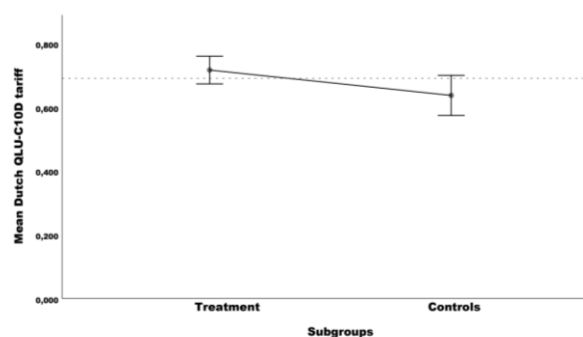
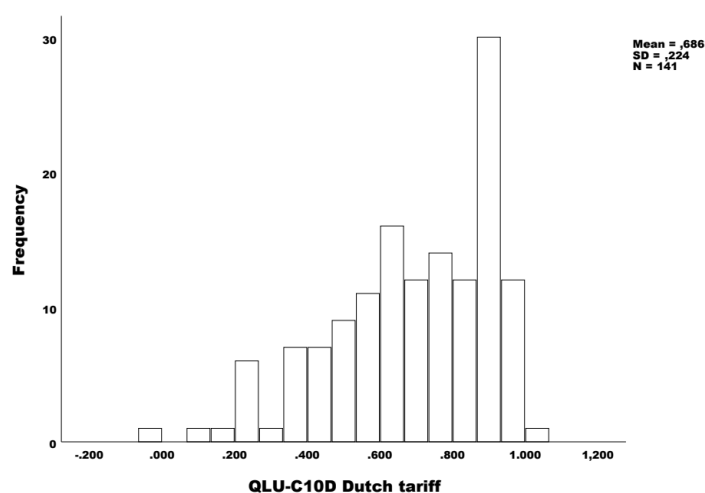
## 5. PRESENTATION OF RESULTS

### 5.1 QLU-C10D index score

The most important target value for health economic analyses evaluation is the QLU-C10D index value (i.e. the utility score). The index can be presented as mean and standard deviation or, in case of skewed data or very small sample sizes, as median and interquartile range. It is recommended that information is provided on the extent of ceiling/floor effects in the specific sample(s). Table 2 and Figure 6 provide an examples for presenting QLU-C10D scores.

*Table 2: Example for presenting index statistics, Dutch tariff*

QLU-C10D Dutch Tariff	Total Sample	Treatment	Controls
	N = 147	n = 89	n = 58
Mean	.69	.72	.64
Standard Error	.02	.02	.03
Standard Deviation	.22	.21	.24
Median	.72	.76	.65
25th	.54	.59	.49
75th	.89	.89	.86



*Figure 6: Examples of graphic representation of QLU-C10D index data in Table 2; Left: Histogram of data distribution; Right: means of both subgroups with 95% CI and dotted line representing the mean of the total sample*

## 5.2 Health profiles

Please note that QLU-C10D domains are not equivalent to the QLQ-C30 domains as they do not contain all items of the respective scale. Therefore, single domain scores are calculated from all QLQ-C30 items and reported as described in the QLQ-C30 scoring manual (Fayers et al. 2001). The QLQ-C30 scoring manual can be downloaded for free from the EORTC QLG website (<https://qol.eortc.org/manuals/>). QLQ-C30 domains are always scaled from 0-100. If not otherwise specified by a hypothesis, preferably all QLQ-C10 scores are reported.

## 6. AVAILABLE VALUE SETS AND FORMATS

QLU-C10D utility scores can be calculated from any available language version of the QLQ-C30 (see QLG website [www.qlg.eortc.be](http://www.qlg.eortc.be)). But recall that country-specific preference weights are also required in the calculation of QLU-C10D utility scores. Be aware that not all countries for which QLQ-C30 translations are available have developed accompanying value sets. Country-specific value sets are continuously being developed. A current overview of completed and ongoing valuations including downloadable scoring codes are available from the website <https://qol.eortc.org/eortc-qlu-c10d/>.

When deciding which country-specific value set is most appropriate, these are the things to think about. For economic evaluations, the most relevant perspective is that of the country in which the respective health care decision will be taken, so the best choice is the value-set of that country. In case no country-specific value set is available for the country to which the associated economic evaluation applies, the analyst has to consider which country with an existing value set is the closest in terms of culture, healthcare setting and language. It is common practice with other PBMs to apply a national value set to data collected in other countries – very often in an international study setting this is also inevitable. However, so far there is no hard evidence with regard to the impact of applying a value set on “non-national” data. There is some indication that potentially as a result of differences in translations and response behaviours across countries/cultures, the respective national value set is the best choice for the data (Kemmler et al. 2019). We recommend that the economic evaluation includes a sensitivity analysis exploring the relationship between choice of valuation algorithm and the results of the economic evaluation.

## 7. QLU-C10D NORMATIVE DATA

Normative data support the applicability and interpretability of PBMs by enabling normative comparisons across specific populations or patient groups (Kendall et al. 1999) and by providing estimates for adjustments for sex and age in health economic evaluations in order to avoid confounding by these variables when comparing groups with different age- and sex-distributions. Normative scores may provide an adequate baseline in economic modelling and a comparator for survivorship studies. Therefore the provision of general population utility norms of PBM is suggested (Norman et al. 2013, van den Berg 2012,

Williams 1999). General population utility norms allow the comparison of utilities between cancer patients and a comparative group reflecting a reality, i.e. a population necessarily containing people with various (chronic) diseases, rather than a hypothetically completely healthy population. This is because in a best-case treatment scenario a cancer patient population will not be returning to a perfect state of health but will still include health impairments with the same prevalence as the general population. Additionally, normative scores can facilitate comparisons across countries, regions and cultures (Clemens et al. 2014), enabling the detection of health inequities in subgroups of the population (Williams 1999). General population utility norms are currently available for commonly applied multi-attribute utility instruments (MAUIs), such as the EQ-5D (Janssen et al. 2014) and the SF-6D (van den Berg 2012, Wong et al. 2018).

To support the interpretability of utilities obtained by the EORTC QLU-C10D, a first set of general population norms has been provided for the countries Canada, France, Germany, Italy Poland, and the UK (Pilz et al. 2022). As further population norms are generated, the QLU-C10D website will be updated.

## **8. CAN I CONVERT UTILITIES OBTAINED WITH ANOTHER INSTRUMENT INTO QLU-C10D UTILITIES?**

Mapping from the QLQ-C30 into the EQ-5D, for example, will not result in the same utility scores as using the QLU-C10D. Such mapping serves a different purpose than measuring QLU-C10D utilities (e.g. in case EQ-5D utilities are required and cannot be obtained directly). Available mapping algorithms for the QLQ-C30 have not been provided or approved by the EORTC QLG and resulting values cannot be considered equivalent to QLU-C10D utilities.

## **9. HOW TO OBTAIN THE QLU-C10D AND TERMS OF USE**

The copyright for the QLU-C10D health state classification system is with the EORTC with all rights reserved. Written prior consent of the EORTC QLD is required for the use and the administration of the QLQ-C30; there is no separate QLU-C10D license. There is no charge for academic users. The QLQ-C30 may be obtained from the EORTC QLG website (<https://qol.eortc.org/questionnaires/>) or by directly contacting the EORTC QLD (<https://qol.eortc.org/quality-of-life-department/>).

Documents containing the scoring algorithms and information on the valuation studies can be obtained from the EORTC QLG website (<https://qol.eortc.org/eortc-qlu-c10d/>).

## 10. HOW TO REFER TO THE QLU-C10D IN PUBLICATIONS

When using the QLU-C10D please provide the reference to the development of the QLU-C10D health state classification system (QLU-C10D: a health state classification system for a multi-attribute utility measure based on the EORTC QLQ-C30. King MT, Costa DS, Aaronson NK, Brazier JE, Cella DF, Fayers PM, Grimison P, Janda M, Kemmler G, Norman R, Pickard AS, Rowen D, Velikova G, Young TA, Viney R. Qual Life Res. 2016 Mar;25(3):625-36. doi: 10.1007/s11136-015-1217-y. Epub 2016 Jan 20. PMID: 26790428) as well as the reference of the respective value set.

## 12. HOW TO DEVELOP ADDITIONAL EORTC QLU-C10D VALUE SETS

The EORTC QLG and the EORTC QLD encourage and support the development of additional national QLU-C10D value sets. With regard to already ongoing valuations please refer to the EORTC QLD. QLU-C10D valuations in additional countries may be performed by researchers/research groups outside the EORTC; in order to create official EORTC values sets they need to comply with the standardised methodology that is in place. The EORTC QLD and the MAUCa-Consortium need to approve the valuation protocol. Please contact the EORTC QLD and/or the MAUCa-Consortium if you are interested in developing EORTC QLU-C10D value sets ([https:// gol.eortc.org/quality-of-life-department/](https://gol.eortc.org/quality-of-life-department/)).

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## APPENDIX A - List of abbreviations

CUA – Cost-Utility Analyses

DCE – Discrete-Choice Experiment

EORTC – European Organisation for Research and Treatment of Cancer

+ EORTC CAT – Computer-Adaptive version of QLQ-C30

+ HTA – EORTC Health Technology Assessment working group

+ QLD – EORTC Quality of Life Department

+ QLG – EORTC Quality of Life Group (multi-professional, international group of researchers and clinicians dealing with cancer)

+ QLQ-C30 – EORTC Quality of Life Questionnaire-Core 30

+ QLU-C10D – EORTC Quality of Life Utility-Core 10 Dimensions

++ 1) PF – Physical Functioning

++ 2) RF – Role Functioning

++ 3) SF – Social Functioning

++ 4) EF – Emotional Functioning

++ 5) PA – Pain

++ 6) FA – Fatigue

++ 7) SL – Sleep

++ 8) AP – Appetite

++ 9) NA – Nausea

++ 10) BO – Bowel Problems

HRQoL – Health-Related Quality of Life

HSUV – Health State Utility Value (short: utility value)

ICER / ICUR – Incremental Cost-Effectiveness Ratio / Incremental Cost-Utility Ratio

MAUCa – Multi-attribute utility in Cancer Consortium (international group of HRQoL researchers who developed the EORTC QLU-C10D health state classification system and valuation methodology)

MAUI – Multi-Attribute Utility Instrument

PBMs – Preference-Based Measures

PRO – Patient-Reported Outcome (instruments); Examples:

+ FaCT-G – Functional Assessment of Cancer Therapy – General

+ EQ-5D – EuroQual of Life Group - 5 Dimensions

+ SF-6D – Short-Form Six-Dimensions

QALYs – Quality-Adjusted Life Years

SPSS – Statistical analysis software