Article

MDMP&P Policy & Practice

MDM Policy & Practice
1–11
© The Author(s) 2019
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/2381468319842532
journals.sagepub.com/home/mdm
SAGE

The EORTC QLU-C10D: The Canadian Valuation Study and Algorithm to Derive Cancer-Specific Utilities From the EORTC QLQ-C30

Helen McTaggart-Cowan, Madeleine T. King, Richard Norman, Daniel S. J. Costa, A. Simon Pickard, Dean A. Regier, Rosalie Viney, and Stuart J. Peacock on behalf of the Canadian MAUCa Team

Abstract

Objective. The EORTC QLQ-C30 is widely used for assessing quality of life in cancer. However, QLQ-C30 responses cannot be incorporated in cost-utility analysis because they are not based on general population's preferences, or utilities. To overcome this limitation, the QLU-C10D, a cancer-specific utility algorithm, was derived from the QLQ-C30. The aim of this study was to obtain Canadian population utility weights for the QLU-C10D. **Methods.** Respondents from a Canadian research panel expressed their preferences for 16 choice sets in an online discrete choice experiment. Each choice set consisted of two health states described by the 10 QLU-C10D domains plus an attribute representing duration of survival. Using a conditional logit model, responses were converted into utility decrements by evaluating the marginal rate of substitution between each QLU-C10D domain level with respect to duration. **Results.** A total of 3,363 individuals were recruited. A total of 2,345 completed at least one choice set and 2,271 completed all choice sets. The largest utility decrements were associated with the worse levels of Physical Functioning (−0.24), Pain (−0.18), Role Functioning (−0.15), Emotional Functioning (−0.12), and Nausea (−0.12). The remaining domains and levels had decrements of −0.05 to −0.09. The utility of the worst possible health state was −0.15. **Conclusion.** Respondents from the general population were most concerned with generic health domains, but Nausea and Bowel Problems also had an impact on the individual's utility. It is unclear as to whether cancer-specific domains will affect cost-utility analysis when evaluating cancer treatments; this will be tested in the next phase of the study.

Keywords

cancer, discrete choice experiment, QLQ-C30, quality of life, utility

Date received: May 4, 2018; accepted: February 18, 2019

Introduction

The pan-Canadian Oncology Drug Review within the Canadian Agency for Drugs and Technology in Health promotes rigorous and objective cancer drug reviews through the use of clinical and economic evaluations, as well as patient perspectives and experiences. For the economic evaluation component of this process, cost-utility analysis (CUA) is recommended to guide the prioritization of new therapies, including cancer drugs, within a constrained budget.[1,2] In CUA, outcomes are expressed

Corresponding Author

Helen McTaggart-Cowan, BC Cancer, 675 West 10th Avenue, Vancouver, British Columbia V5Z 1L3, Canada; Telephone: (604) 675 8000 ext. 7065 (hcowan@bccrc.ca).

This Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (http://www.creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).

using quality-adjusted life years (QALYs). QALYs are derived by adjusting life years by the quality of the survival time in a given health. This adjustment, referred to as a utility index, represents a typical individual's preference for each health state, bounded at one (full health) and zero (dead); negative values are possible indicating states worse than dead. To facilitate comparability across health states and conditions, conventionally, responses to generic multi-attribute utility instruments (MAUIs) afford utilities to be incorporated into CUA. These instruments, such as the Health Utilities Index Mark 3[3] and EQ-5D,[4] cover broad health dimensions pertaining to, for example, mobility and self-care. Despite their wide applicability, generic MAUIs may not be sensitive to changes specific to issues that concern cancer patients.[5] Instead, many researchers collect patient-reported outcomes using disease-specific instruments. In the context of cancer, the use of cancer-specific quality of life instruments, such as the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire–Core 30 (QLQ-C30)[6] is widespread; in 2012, more than 9,000 QLQ-C30 user agreements were signed for clinical trials and academic studies.[7] However, the QLQ-C30 was not originally designed to produce utilities, which has limited its usefulness for priority setting and resource allocation decisions.

Recently, the Multi-Attribute Utility in Cancer (MAUCa) Consortium, comprising international researchers with expertise in psychometrics, health economics, and oncology, facilitated the development of an algorithm to derive cancer-specific utilities based on the QLQ-C30 instrument. This was achieved through extensive analysis of QLQ-C30 data, applying psychometric criteria and patient input to reduce the instrument's original 30 items to form the 10 domains of the QLU-C10D's health state classification system,[8] and then developing a valuation method based on discrete choice experiment (DCE) methods.[9] The MAUCa Consortium's goal is to provide a set of country-specific utility scoring algorithms that can be applied to data from the QLQ-C30 to generate utilities; the use of identical valuation methods across countries creates a unique opportunity to explore predictors of health outcome values (e.g., country, age, sex, education, and health status) in the future. While Australia was the first to produce country-specific utility weights for the QLU-C10D,[10] there is a need to inform cancer priority setting and resource allocation decisions in other countries, including Canada, with country-specific utility weights for the QLU-C10D. The aim of this article is to produce QLU-C10D utility weights for the Canadian general population using the standard MAUCa DCE methods.

Methods

QLU-C10D Health State Classification System

The derivation of the QLU-C10D health state classification system is described elsewhere.[8] In brief, adapting previously used methods,[11] the MAUCa Consortium identified core QLQ-C30 domains, confirmatory factor analysis confirmed the QLQ-C30 measurement model, and results from Rasch and psychometric analyses, as well as patient preferences, guided item selection. The QLU-C10D consists of 10 domains, which directly map to 13 items of the QLQ-C30 (Table 1); all domains are assessed during the past week. Nine of these domains are described by the same four levels as for QLQ-C30 items: not at all, a little, quite a bit, and very much. The remaining domain—Physical Functioning—has more complex levels (see Table 1). The name, QLU-C10D, has been endorsed by the EORTC Quality of Life Group Executive Committee: "QLU" indicates it is a utility measure; "C" indicates its origin in the EORTC's core questionnaire; and "10D" indicates its 10 domains.[8]

Discrete Choice Experiment

The QLU-C10D health state classification system was valued in the Canadian setting using the DCE methodology developed for the Australian valuation. Details of the experimental design and piloting of the valuation survey methodology have been reported previously.[9,10] In summary, respondents were presented with choice sets in

Faculty of Health Sciences, Simon Fraser University, Burnaby, British Columbia, Canada (HMC, SJP); Canadian Centre for Applied Research in Cancer Control, Vancouver, British Columbia, Canada (HMC, DAR, SJP); Cancer Control Research, BC Cancer, Vancouver, British Columbia, Canada (HMC, DAR, SJP); Faculties of Science and Medicine, University of Sydney, Sydney, New South Wales, Australia (MTK); School of Public Health, Curtin University, Perth, Western Australia, Australia (RN); Sydney Medical School, University of Sydney, Sydney, New South Wales, Australia (DSJC); Pain Management Research Institute, Royal North Shore Hospital, Sydney, New South Wales, Australia (DSJC); Department of Pharmacy Systems, Outcomes, and Policy, University of Illinois at Chicago, Illinois, USA (ASP); School of Population and Public Health, University of British Columbia, Vancouver, British Columbia, Canada (DAR); Centre for Health Economics Research and Evaluation, University of Technology, Sydney, New South Wales, Australia (RV).
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. Financial support for this study was provided entirely by grants from Canadian Cancer Society Research Institute (703548, 2015-703549). The funding agreement ensured the authors' independence in designing the study, interpreting the data, writing, and publishing the report.

Table 1 The QLU-C10D Health State Classification System

Dimension	Level	Stem	Descriptor	QLQ-C30 Item Scores
Physical Functioning[a,b]	1	You have . . .	No trouble taking a long walk outside of the house	Item 2 (long walk) = 1
	2		No trouble taking a short walk outside of the house, but at least a little trouble taking a long walk	Item 3 (short walk) = 1 AND Item 2 $\geq$ 2
	3		A little trouble taking a short walk outside of the house, and at least a little trouble taking a long walk	Item 3 = 2 AND Item 2 $\geq$ 2
	4		Quite a bit or very much trouble taking a short walk outside the house	Item 3 $\geq$ 3 AND Item 2 $\geq$ 2
Role Functioning	1	You are limited in pursuing	Not at all	Item 6 = 1
	2	your work or other daily	A little	Item 6 = 2
	3	activities . . .	Quite a bit	Item 6 = 3
	4		Very much	Item 6 = 4
Social Functioning[a,c]	1	Your physical condition or	Not at all	Items 26 AND 27 = 1
	2	medical treatment interferes	A little	Items 26 OR 27 = 2[c]
	3	with your social or family	Quite a bit	Items 26 OR 27 = 3[c]
	4	life . . .	Very much	Items 26 OR 27 = 4[c]
Emotional Functioning	1	You feel depressed . . .	Not at all	Item 24 = 1
	2		A little	Item 24 = 2
	3		Quite a bit	Item 24 = 3
	4		Very much	Item 24 = 4
Pain	1	You have pain . . .	Not at all	Item 9 = 1
	2		A little	Item 9 = 2
	3		Quite a bit	Item 9 = 3
	4		Very much	Item 9 = 4
Fatigue	1	You feel tired . . .	Not at all	Item 18 = 1
	2		A little	Item 18 = 2
	3		Quite a bit	Item 18 = 3
	4		Very much	Item 18 = 4
Sleep	1	You have trouble sleeping . . .	Not at all	Item 11 = 1
	2		A little	Item 11 = 2
	3		Quite a bit	Item 11 = 3
	4		Very much	Item 11 = 4
Appetite	1	You lack appetite . . .	Not at all	Item 13 = 1
	2		A little	Item 13 = 2
	3		Quite a bit	Item 13 = 3
	4		Very much	Item 13 = 4
Nausea	1	You feel nauseated . . .	Not at all	Item 14 = 1
	2		A little	Item 14 = 2
	3		Quite a bit	Item 14 = 3
	4		Very much	Item 14 = 4
Bowel problems[a,c]	1	You . . .	Do not have constipation or diarrhea at all	Items 16 AND 17 = 1
	2		Have a little constipation or diarrhea	Items 16 OR 17 = 2[c]
	3		Have constipation or diarrhea quite a bit	Items 16 OR 17 = 3[c]
	4		Have constipation or diarrhea very much	Items 16 OR 17 = 4[c]
Duration	1	You will live in this health	1 year, and then die	Not applicable
	2	state for . . .	2 years, and then die	Not applicable
	3		5 years, and then die	Not applicable
	4		10 years, and then die	Not applicable

[a]Three dimensions of the QLU-C10D each involve two QLQ-C30 items.
[b]The Physical Functioning dimension includes "long walk" and "short walk" from the QLQ-C30; for the DCE, the levels are determined together, but were presented in the DCE survey separately, as shown in Figure 1.
[c]For Social Functioning and Bowel Problems, the QLU-C10D level is determined by the maximum value of the two component items.

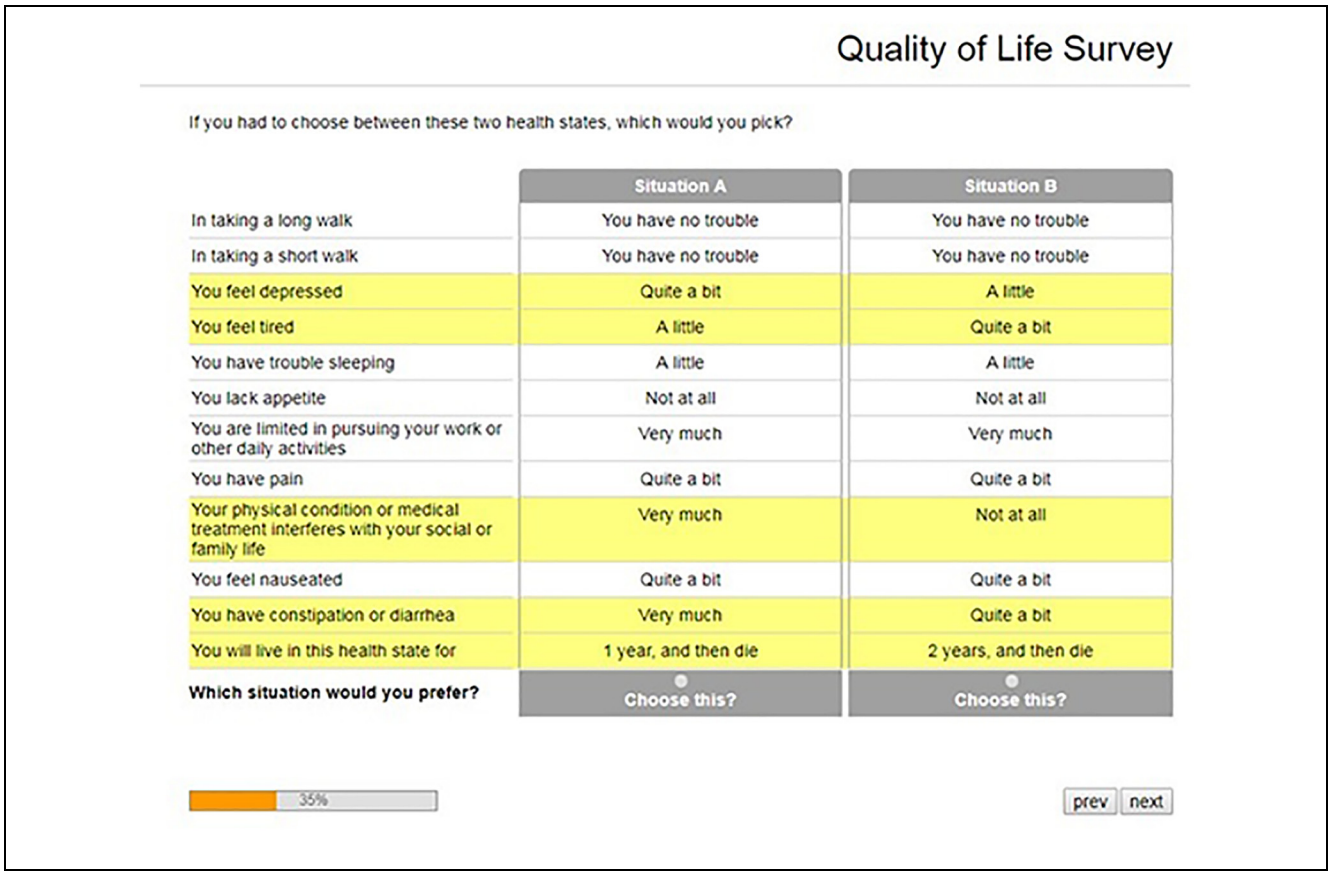

Figure 1 Example choice set from the discrete choice experiment valuation task.

which they had to choose between two health states, each with a specified duration of life years. The experimental design underpinning the DCE contained 11 attributes: the 10 QLU-C10D domains and duration of survival. However, to facilitate respondent comprehension of the complex levels of the Physical Functioning domain, the two component items, "long walk" and "short walk," were presented separated in the valuation survey (Figure 1). Because the QLU-C10D contains a large number of domains, the DCE experimental design was specified such that only four of its domains differed in each choice sets, and these were highlighted in yellow to reduce the cognitive complexity of the choice task; this presentation format was pilot-tested and found to be feasible.[9]

The QLU-C10D health state classification system has 4^{10} possible health states: 960 choice sets were selected to maximize statistical efficiency, and to estimate main effects and all two-factor interactions involving duration. A balanced incomplete block design constrained the number of QLU-C10D domains that differed between health states in any given choice set to four.[9] Each respondent randomly received 16/960 choice sets without replacement; which option seen as Situation A or Situation B was randomized within each choice set. The order of the QLU-C10D domains was also randomized for each respondent but the order was kept the same for the respondent when completing the 16 choice sets.

Data Collection

Sampling and survey administration for all country-specific valuations in the MAUCa Consortium were undertaken by SurveyEngine, a company that specializes in choice experiments.[12] For this study, respondents over 18 years of age from the Canadian general population were recruited from an online panel. Quota sampling ensured age, sex, and province/territory of residence aligned with the Canadian Census.[13] While the determination of appropriate sample sizes in choice experiments is difficult,[14] the sample size was selected to exceed the suggested 20 responses per choice set to estimate reliable models.[15]

Respondents completed the following survey components, in order: 1) self-reported health, assessed by the General Health Question of the SF-36[16] and the QLQ-C30[6]; 2) DCE valuation task; 3) DCE feedback (i.e., perceived difficulty and clarity of, as well as the choice strategy used in, the valuation task); 4) sociodemographic characteristics; and 5) additional self-reported health, assessed by the Kessler-10[17] and the EQ-5D-5L.[4] The length of time the respondent transitions between survey pages were recorded. The study protocol was approved by the Research Ethics Board at BC Cancer and the University of British Columbia (H15-03293).

Data Analysis

Sample Representation. The sample was characterized in the terms of age, sex, province/territory of residence, highest level of education, marital status, and self-reported General Health Question. Chi-squared tests assessed the study sample representation in comparison to the Canadian general population.[13] The mean time spent on the whole survey and on the choice sets were recorded. The aggregate mean responses to the QLU-C10D, EQ-5D-5L, and Kessler-10, as well as the correlation between QLU-C10D and EQ-5D-5L, were reported. Choice inconsistencies were assessed by the frequencies of respondents selecting one option among all choice sets (e.g., all Situation A).

Utility Estimation. DCE responses were analyzed using a functional form in which the QLU-C10D attribute levels interacted with the duration variable[18]:

$$U_{isj} = \alpha TIME_{isj} + \beta X'_{isj} TIME_{isj} + \varepsilon_{isj}, \qquad (1)$$

where X'_{isj} was a set of dummy variables relating to the levels of the QLU-C10D health state presented in option j and ε_{isj} was a random error term distributed independently and identically normal. This approach has previously been used to estimate utilities from DCE data to ensure consistency with standard QALY model restrictions[14,18,19]: 1) all health states converges as survival duration tends to zero and 2) the relationship between utility and time is constrained to be linear (i.e., constant proportional time tradeoff).

The modelling approach followed that was used in the Australian valuation study.[10] First, a conditional logit model was used to analyze the DCE responses (Model 1). A clustered sandwich estimator using the vce (cluster) option in STATA adjusted the standard errors to allow for intro-individual correlation as each respondent was asked to consider 16 DCE choice sets. The impact of moving away from one level of each domain is investigated through two-factor interaction terms with the continuous duration term rather than through the main effect (e.g., the effect of moving from level 1 to level 2 in the Pain domain is determined by using a Pain level 2* Duration interaction term). If non-monotonic ordering was present between domain levels in the conditional logit model, another conditional logit model was run after collapsing non-monotonic domain levels (Model 2). A log-likelihood ratio test assessed the model fit between Model 1 and Model 2.

Results

Sample Characteristics and Representation

Respondents from the Canadian general population entered the study (n = 3,956); of which, 3,421 consented to participate in the study. From the pool of consented respondents, n = 2,459 were considered eligible because they were using the appropriately sized electronic device (n = 329 excluded) and their personal characteristics were not already aligned with the quota sampling recruitment strategy (n = 633 excluded). The final analysis set included 2,345 respondents: 74 completed at least one choice set and 2,271 completed all choice sets. Post hoc analysis showed that there were no statistically significant differences between the eligible respondents (n = 2,459) and the final analysis set (n = 2,345) in terms of sex, age, province/territory of residence, and language for which the survey was completed. Of the 2,271 respondents who completed the entire survey, the median (interquartile range) to complete all choice sets and demographics was 21 minutes 11 seconds (16 minutes 32 seconds). The completion of the 16 choice sets was 5 minutes 13 seconds (6 minutes 17 seconds).

The study sample differed statistically from the general population in all measured characteristics except for age, sex, and province/territory of residence (Table 2). Compared with the general population, the sample consisted of statistically more participants whose primary language is English, completed college education, and reported poorer health based on the General Health Question. Table 3 presents the aggregate scores (mean ± standard deviation [SD]) for the QLU-C10D (0.753 ± 0.212), EQ-5D-5L (0.833 ± 0.156), and the Kessler-10 (17.91 ± 7.68). The QLU-C10D and EQ-5D-5L are highly correlated at 0.773.

Utility Estimates

The conditional model revealed that respondents preferred additional life years (Table 4). All movements

Table 2 Self-Reported Health and Sociodemographic Characteristics of the Sample Compared With Those of the Canadian General Population

Question	Level	Number	Proportion	Population Value[a]	χ^2 Statistic	*P* Value
Gender	Male	1,120	0.48	0.48	0.17	0.92
	Female	1,217	0.52	0.52		
	Other	8	0.03	Not reported		
Age (years)	18–29	454	0.19	0.20	6.89	0.33
	30–39	409	0.17	0.17		
	40–49	468	0.20	0.21		
	50–59	421	0.18	0.18		
	60–69	303	0.13	0.11		
	70 or older	290	0.12	0.13		
Province or territory of residence	Alberta	249	0.11	0.12	9.10	0.77
	British Columbia	302	0.13	0.13		
	Manitoba	86	0.04	0.04		
	New Brunswick	53	0.02	0.02		
	Newfoundland and Labrador	35	0.02	0.02		
	Nova Scotia	62	0.03	0.03		
	Northwest Territory	1	0.00	0.00		
	Nunavut Territory	0	0.00	0.00		
	Ontario	911	0.39	0.39		
	Quebec	561	0.24	0.23		
	Prince Edward Island	13	0.01	0.00		
	Saskatchewan	69	0.03	0.03		
	Yukon Territory	3	0.00	0.00		
Primary language spoken at home	English	1,736	0.74	0.58	445.5	<0.01
	French	541	0.23	0.22		
	Other	68	0.03	0.20		
Marital status	Single	728	0.32	0.28	65.2	<0.01
	Legally married	924	0.41	0.48		
	In a common-law relationship	316	0.14	0.11		
	Separated, but still legally married	59	0.03	0.03		
	Divorced	174	0.08	0.06		
	Widowed	79	0.04	0.06		
Education level	No certificate, diploma, or degree	99	0.04	0.15	237.4	<0.01
	High school certificate or equivalent	549	0.24	0.24		
	Apprenticeship or trade certificate or diploma	174	0.08	0.12		
	College, CEGEP, or other non-university certificate or diploma	666	0.29	0.20		
	University certificate or diploma below the bachelor's level	226	0.10	0.05		
	University certificate, diploma, or degree at bachelor's level or above	566	0.25	0.23		
General health question	Excellent	257	0.11	0.22	284.9	< 0.01
	Very good	800	0.34	0.38		
	Good	877	0.37	0.29		
	Fair	334	0.14	0.11		
	Poor	77	0.03			

[a]Rounding of proportions to two decimal places.

Table 3 Instrument Scores

	Mean	SD	Min	Max
QLU-C10D	0.753	0.212	−0.122	1.000
EQ-5D-5L	0.833	0.156	−0.039	0.949
Kessler-10	17.91	7.68	10	50

away from "no problems" (level 1) in each of the domains were valued negatively. With two exceptions, incremental moves to the next worst domain level were associated with an absolutely larger coefficient. The two non-monotonicities were the worst two levels of the Fatigue and Sleep domains. The model was reestimated constraining the respective levels to be the same to remove these non-monotonicities. The log-likelihood ratio test indicated that there was no improvement in fit between the unconstrained and constrained models ($\chi^2 = 1.29$, $P = 0.52$). As per the Australian QLU-C10D valuation study,[10] the estimates from the parsimonious Model 2 (constrained) defined the Canadian value set for the QLU-C10D.

Model 2 revealed that the Physical Functioning and Pain domains most greatly affected the individual's utility function (Table 5); this was followed by Role Functioning, Nausea, and Emotional Functioning. Sizeable decrements were observed for Social Functioning and Bowel Problems; smaller decrements for Fatigue and Sleep.

Three post hoc analyses were conducted. First, left-right bias appears to be present even though the order which the respondents view the scenarios was randomized. However, the left-right bias did not have an impact on the resulting Canadian value set for the QLU-C10D. Second, the inconsistencies in the choice sets were tested by exploring the frequencies of which a respondent would select Situation As and Situation Bs among all 16 choice sets. We observed that approximately 1% of respondents "clicked through," selecting the majority of Situation As or Situation Bs. These respondents were not deleted from analysis as this may result in the removal of valid preferences, induce sample selection bias, and reduce the statistical efficiency and power of the estimated choice models.[20] Third, the sample was reweighted to better reflect the demographic characteristics of the Canadian general population. We observed no differences in the utility decrements for the QLU-C10D domains. Details from the post hoc analyses are available from the authors.

QLU-C10D Utility Calculation

As per the conditions set by the EORTC Quality of Life Group, the QLU-C10D cannot be used as a standalone instrument. The Canadian value set must therefore be applied to select items of the completed QLQ-C30 to obtain QLU-C10D utility scores. A utility index of one is assigned to individuals whose QLQ-C30 responses indicate they are at level 1 of all 10 domains of the QLU-C10D (1111111111); an index of −0.15 is assigned to the worst possible state (4444444444). For all other health states, the utility score for individual i is calculated as follows:

$$QLU{-}C10D_i = 1 - \sum_{d=1}^{10} w_{dl} | QLU{-}C10D_{dli}, \qquad (2)$$

where w is the utility weight for each level l of domain d of the QLU-C10D. STATA and SPSS codes for the Canadian QLU-C10D value set are available as electronic supplemental material.

Discussion

This study determined the Canadian value set for the QLU-C10D, a cancer-specific algorithm for calculating utilities from quality of life data collected using the QLQ-C30. By applying the Checklist for REporting VAluaTion StudiEs (CREATE),[21] the presented approach is considered theoretically and empirically stronger than using approaches that map QLQ-C30 responses to other generic MAUIs.[22] The results revealed that the main contributors of an individual's utility were Physical Functioning, Role Functioning, and Emotional Functioning, as well as Pain; the cancer-sensitive domains, Nausea and Bowel Problems, also had a sizeable impact on the individual's utility. The utility decrements for the cancer-sensitive domains were generally smaller than those of the generic domains, with the exception of Nausea, which is a common symptom of cancer and its treatments. However, this does not necessarily limit the impact of cancer-sensitive domains in a particular economic evaluation, as this will also be affected by how prevalent the cancer-specific symptoms are and the difference in symptom prevalence between trial arms or other comparator groups. The extent to which inclusion of cancer-specific domains, such as Nausea and Bowel Problems, provides a more relevant and sensitive measure of utility for cancer interventions than generic MAUIs will depend on the clinical context, and may be most beneficial for therapies alleviating such symptoms or causing less symptoms due to reduced toxicity. Future head-to-head comparisons between the QLU-C10D and generic MAUIs are needed to determine the circumstances in which cancer-specific domains make a difference to decision making.

Table 4 Conditional Logit: Model 1 (Unconstrained) and Model 2 (Montonicity Imposed)

Mean		Model 1—Coefficient[a] (Robust SE)	Model 2—Coefficient[a] (Robust SE)
Duration	Linear	0.488 (0.021)***	0.486 (0.021)***
Physical Functioning × Duration[a]	2	−0.026 (0.007)***	−0.026 (0.007)***
	3	−0.070 (0.008)***	−0.070 (0.008)***
	4	−0.118 (0.007)***	−0.117 (0.007)***
Role Functioning × Duration[a]	2	−0.013 (0.006)**	−0.013 (0.006)**
	3	−0.050 (0.006)***	−0.049 (0.006)***
	4	−0.071 (0.006)***	−0.070 (0.006)***
Social Functioning × Duration[a]	2	−0.004 (0.006)	−0.004 (0.006)
	3	−0.028 (0.006)***	−0.027 (0.006)***
	4	−0.044 (0.005)***	−0.044 (0.005)***
Emotional Functioning × Duration[a]	2	−0.021 (0.006)***	−0.022 (0.006)
	3	−0.037 (0.006)***	−0.037 (0.006)***
	4	−0.060 (0.006)***	−0.060 (0.006)***
Pain × Duration[a]	2	−0.014 (0.006)**	−0.014 (0.006)**
	3	−0.060 (0.006)***	−0.059 (0.006)***
	4	−0.087 (0.006)***	−0.087 (0.006)***
Fatigue × Duration[a]	2	−0.016 (0.005)***	−0.015 (0.005)***
	3	−0.027 (0.006)***	−0.026 (0.005)***
	4	−0.025 (0.005)***	−0.026 (0.005)***
Sleep × Duration[a]	2	−0.030 (0.005)***	−0.029 (0.005)***
	3	−0.037 (0.006)***	−0.034 (0.005)***
	4	−0.032 (0.005)***	−0.034 (0.005)***
Appetite × Duration[a]	2	−0.015 (0.005)***	−0.015 (0.005)***
	3	−0.021 (0.006)***	−0.021 (0.006)***
	4	−0.025 (0.005)***	−0.025 (0.005)***
Nausea × Duration[a]	2	−0.036 (0.005)***	−0.036 (0.005)***
	3	−0.045 (0.006)***	−0.045 (0.006)***
	4	−0.069 (0.005)***	−0.059 (0.005)***
Bowel problems × Duration[a]	2	−0.016 (0.005)***	−0.016 (0.005)***
	3	−0.028 (0.006)***	−0.028 (0.006)***
	4	−0.037 (0.005)***	−0.037 (0.005)***
Log-likelihood		−22376.9	−22377.55
Parameters		31	29
AIC		44815.8	44813.1
BIC		45080.5	45101.6

AIC, Akaike information criterion; BIC, Bayesian information criterion.
[a]The coefficient for each level of each dimension was estimated as the interaction of that level with duration.
Levels of statistical significance: ***1%; **5%.

Initial models for both Canada and Australia revealed some inconsistent orderings of utility decrements across domain levels; however, the non-monotonicities differed across countries. Canada had inconsistencies in the highest levels of Fatigue and Sleep; Australia had inconsistencies in the lowest levels of Social Functioning and in the highest levels of Sleep and Appetite Loss. Consistent with the Australian study and others, constraints were imposed to remove non-monotonicities[23–27]; model fit was not compromised. For both countries, Physical Functioning had the largest utility decrements for each level. It is possible that the presentation of two aspects in that domain (i.e., long walk and short walk), covering a large range of mobility, may have amplified the impact on the individual's utility. The worse possible state for both countries were negative and similar in magnitude: Canada, −0.15; and Australia, −0.10. The conditional logit was selected over the mixed logit results because economic evaluation is mostly concerned with the mean response; preference heterogeneity is a secondary concern. The choice of a monotonic main-effects model for calculating utility is readily accessible for a range of end users, clinically interpretable and consistent with the EORTC quality of life conceptual model.[10]

The QLU-C10D health state classification system was valued using a DCE. This approach was selected over the conventional standard gamble and time tradeoff due to its strong theoretical measurement framework, its well

Table 5 Utility Decrements Used in the QLU-C10D Utility Algorithm[a]

Dimension	Level	Utility, w_{dl} (95% CI)
Physical Functioning	1	0
	2	−0.053 (−0.828 to −0.024)
	3	−0.143 (−0.175 to −0.112)
	4	−0.241 (−0.271 to −0.212)
Role Functioning	1	0
	2	−0.027 (−0.051 to −0.004)
	3	−0.101 (−0.127 to −0.076)
	4	−0.144 (−0.168 to −0.121)
Social Functioning	1	0
	2	−0.009 (−0.031 to 0.013)
	3	−0.056 (−0.081 to −0.032)
	4	−0.090 (−0.112 to −0.068)
Emotional Functioning	1	0
	2	−0.045 (−0.068 to −0.022)
	3	−0.076 (−0.100 to −0.052)
	4	−0.124 (−0.145 to −0.101)
Pain	1	0
	2	−0.029 (−0.051 to −0.005)
	3	−0.121 (−0.146 to −0.096)
	4	−0.179 (−0.201 to −0.155)
Fatigue	1	0
	2	−0.032 (−0.052 to −0.010)
	3	−0.053 (−0.072 to −0.033)
	4	−0.053 (−0.072 to −0.033)
Sleep	1	0
	2	−0.059 (−0.080 to −0.038)
	3	−0.070 (−0.090 to −0.050)
	4	−0.070 (−0.090 to −0.050)
Appetite	1	0
	2	−0.031 (−0.051 to −0.010)
	3	−0.043 (−0.066 t0 −0.020)
	4	−0.051 (−0.072 to −0.030)
Nausea	1	0
	2	−0.074 (−0.095 to −0.052)
	3	−0.093 (−0.116 to −0.070)
	4	−0.122 (−0.144 to −0.101)
Bowel problems	1	0
	2	−0.033 (−0.054 to −0.011)
	3	−0.057 (−0.079 to −0.032)
	4	−0.077 (−0.097 to −0.055)

[a]From Model 2, conditional logit, monotonicity imposed.

established statistically robust experimental design and modelling methods, and its feasibility with online recruitment and data collection.[14,18,19] In this study, respondents appraised choice sets containing 12 attributes. While the relatively larger number of attributes raised concerns regarding the cognitive burden of the respondents, innovative work was conducted to have only four domains differ in each choice set; the differing levels were identified by the respondents' preferred format of yellow highlighting.[9] Allowing only some domains to differ across choice sets will require respondents, who employ heuristics such as considering a single attribute, to tradeoff between other attributes.

There are limitations associated with this study. First, the valuation survey sample consisted of a large number of respondents, with quota sampling achieving population representativeness for age, sex, and province/territory of residence. However, when the other sociodemographic variables were compared (e.g., education level, self-reported health), the study respondents' characteristics significantly differed to that of the general population. This impact, in terms of bias to the utility estimates, in this study is unknown, as the degree to which each demographic variable influences respondent preferences has not yet been determined. This question will be assessed by the MAUCa Consortium in a future analysis of pooled data from international valuations of the QLU-C10D. Second, the QLU-C10D has a relatively large number of domains, each one adding further utility decrements. This may result in a wider range of utility scores than utilities generated from generic MAUIs, which may lead to different funding decisions when incorporated in CUAs; this will be explored in the future. Third, we did not test potential interactions between pairs of QLU-C10D domains although we acknowledge that they have existed; the influence of potential interactions will be explored in the future both quantitatively and qualitatively. Instead, we took a more parsimonious approach for three reasons: 1) testing all possible interactions would require an unfeasibly large sample size; 2) there is no conceptual framework to guide the choice of a manageable subset among the many possible interactions; and 3) the inclusion of complex interactions may render the model incomprehensible to end-users. We feel the parsimonious model presented in this article is clinically interpretable and likely captures much of the signal in aggregate presences. Finally, while the construction of the QLU-C10D health state classification system involved pooled international data sets, the developmental work for the DCE was conducted primarily in Australia[8,9] raising concerns that the methods may not be applicable to the Canadian setting. However, the robust results and consistent estimates, aligned with our expectations, alleviated our concerns.

To this end, the Canadian value set is quite similar to the Australian value set for the QLU-C10D,[10] implying that Canadians and Australians may not be different in the way they value health states. This raises the fundamental question of whether there is a need to generate distinct sets of national weights. Previous work has

indicated that most of the observed differences between national value sets stem from differences in analytical methods rather than valuing different study populations.[28] However to guide societal decisions, the Canadian Agency for Drugs and Technologies in Health recommends that preferences of the Canadian general population should be the reference case.[1] The Canadian QLU-C10D value set facilitates the use of EORTC QLQ-C30 responses to afford cancer-specific utility weights that may be more sensitive to differences resulting from cancer care than a generic MAUI; this may be more informative in guiding cancer priority setting and resource allocation decisions in Canada. The widespread use of the QLQ-C30 to measure quality of life outcomes of cancer patients will enable utilities not only to be estimated prospectively but also from a large number of retrospective studies. We intend to conduct head-to-head comparisons of the QLU-C10D versus generic MAUIs assess its performance. The availability of more QALY estimates and CUAs will enable decision makers to be more informed when allocating resources in Canada's publicly funded health care system.

Authors' Note

Earlier versions of this article were presented at the Canadian Centre for Applied Research in Cancer Control meeting, May 2017, Toronto, and the International Society for Quality of Life Research, October 2017, Philadelphia.

Acknowledgments

The Canadian MAUCa Team, in addition to those named as authors, consists of the following members, all of whom made some contribution to the research reported in this article: Kelvin Chan, Jeffery Hoch, Natasha Leighl, and Nicole Mittmann.

Supplemental Material

Supplementary material for this article is available on the *Medical Decision Making Policy & Practice* website at https://journals.sagepub.com/home/mpp.

ORCID iD

Madeleine T. King https://orcid.org/0000-0001-7192-2887

References

1. Canadian Agency for Drugs and Technologies in Health. Guidelines for the Economic Evaluation of Health Technologies: Canada 2017—4th edition [cited March 7, 2018]. Available from: https://cadth.ca/dv/guidelines-economic-evaluation-health-technologies-canada-4th-edition
2. National Institute for Health and Clinical Excellence. *Guide to the Methods of Technology Appraisal*. London: NICE; 2013.
3. Feeny D, Furlong W, Torrance GW, et al. Multiattribute and single-attribute utility functions for the health utilities index mark 3 system. *Med Care*. 2002;40(2):113–28.
4. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20(10):1727–36.
5. Pickard AS, Wilke CT, Lin HW, Lloyd A. Health utilities using the EQ-5D in studies of cancer. *Pharmacoeconomics*. 2007;25(5):365–84.
6. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*. 1993;85(5):365–76.
7. Velikova G, Coens C, Efficace F, et al. Health-related quality of life in EORTC clinical trial—30 years of progress from methodological developments to making a real impact on oncology practice. *Eur J Cancer*. 2012;1(Suppl. 10):141–8.
8. King MT, Costa DS, Aaronson NK, et al. QLU-C10D: a health state classification system for a multi-attribute utility measure based on the EORTC QLQ-C30. *Qual Life Res*. 2016;25(3):625–36.
9. Norman R, Viney R, Aaronson NK, et al. Using a discrete choice experiment to value the QLU-C10D: feasibility and sensitivity to presentation format. *Qual Life Res*. 2016;25(3):637–49.
10. King MT, Viney R, Pickard AS, et al. Australian utility weights for the EORTC QLU-C10D, a multi-attribute utility instrument derived from the cancer-specific quality of life questionnaire, EORTC QLQ-C30. *Pharmacoeconomics*. 2018;36(2):225–38.
11. Young T, Yang Y, Brazier JE, Tsuchiya A, Coyne K. The first stage of developing preference-based measures: constructing a health-state classification using Rasch analysis. *Qual Life Res*. 2009;18(2):253–65.
12. SurvryEngine GmbH. SurveyEngine decision modelling technology [cited October 31, 2017]. Available from: https://surveyengine.com/index.html
13. Statistics Canada. 2006 census of population [cited July 6, 2017]. Available from: http://www12.statcan.gc.ca/census-recensement/2006/index-eng.cfm
14. Norman R, Viney R, Brazier J, et al. Valuing SF-6D health states using a discrete choice experiment. *Med Decis Making*. 2014;34(6):773–86.
15. Lancsar E, Louviere J. Conducting discrete choice experiments to inform healthcare decision making: a user's guide. *Pharmacoeconomics*. 2008;26(8):661–77.
16. Ware JE Jr, Sherbourne CD. The MOS 36-item Short-Form Health Survey (SF-36). I. Conceptual framework and item selection. *Med Care*. 1992;30:473–83.
17. Kessler RC, Andrews G, Colpe LJ, et al. Short screening scales to monitor population prevalences and trends in

non-specific psychological distress. *Psychol Med.* 2002; 32(6):959–76.
18. Bansback N, Tsuchiya A, Brazier J, Anis A. Canadian valuation of EQ-5D health states: preliminary value set and considerations for future valuation studies. *PLoS One*. 2012;7(2):e31115.
19. Viney R, Norman R, Brazier JE, et al. An Australian discrete choice experiment to value EQ-5D health states. *Health Econ*. 2014;23(6):729–42.
20. Lancsar E, Louviere J. Deleting "irrational" responses from discrete choice experiments: a case of investigating or imposing preferences? *Health Econ*. 2006;15(8):797–811.
21. Xie F, Pickard AS, Krabbe PF, et al. A Checklist for Reporting Valuation Studies of Multi-Attribute Utility-Based Instruments (CREATE). *Pharmacoeconomics*. 2015; 33(8):867–77.
22. McTaggart-Cowan H, Teckle P, Peacock S. Mapping utilities from cancer-specific health-related quality of life instruments: a review of the literature. *Expert Rev Pharmacoecon Outcomes Res*. 2013;13(6):753–65.
23. Brazier JE, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. *J Health Econ*. 2002;21(2):271–92.
24. Rowen D, Brazier J, Young T, et al. Deriving a preference-based measure for cancer using the EORTC QLQ-C30. *Value Health*. 2011;14(5):721–31.
25. Mukuria C, Rowen D, Brazier JE, Young TA, Nafees B. Deriving a preference-based measure for myelofibrosis from the EORTC QLQ-C30 and the MF-SAF. *Value Health*. 2015;18(6):846–55.
26. Mulhern B, Rowen D, Jacoby A, et al. The development of a QALY measure for epilepsy: NEWQOL-6D. *Epilepsy Behav*. 2012;24(1):36–43.
27. Siu LL, Shapiro JD, Jonker DJ, et al. Phase III randomized, placebo-controlled study of cetuximab plus brivanib alaninate versus cetuximab plus placebo in patients with metastatic, chemotherapy-refractory, wild-type K-RAS colorectal carcinoma: the NCIC Clinical Trials Group and AGITG CO.20 Trial. *J Clin Oncol*. 2013;31(19):2477–84.
28. Augestad LA, Rand-Hendriksen K, Kristiansen IS, Stavem K. Impact of transformation of negative values and regression models on differences between the UK and US EQ-5D time trade-off value sets. *Pharmacoeconomics*. 2012;30(12):1203–14.