# A Patient-Based Utility Measure of Health for Clinical Trials of Cancer Therapy Based on the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire

A. Simon Pickard, PhD,[1,2] James W. Shaw, PhD, PharmD, MPH,[1] Hsiang-Wen Lin, MS, PhD,[1]
Peter C. Trask, PhD, MPH,[3] Neil Aaronson, PhD,[4] Todd A. Lee, PharmD, PhD,[1,2] David Cella, PhD[5,6]

[1]Center for Pharmacoeconomic Research, College of Pharmacy, University of Illinois at Chicago, Chicago, IL, USA; [2]Center for Management of Complex Chronic Care, Edward Hines Jr. VA Hospital, Hines, IL, USA; [3]Pfizer, Inc., New London, CT, USA; [4]The Netherlands Cancer Institute, Amsterdam, The Netherlands; [5]Feinberg School of Medicine, Northwestern University, Chicago, IL, USA; [6]Center for Outcomes Research and Education, Evanston Healthcare, Evanston, IL, USA

## ABSTRACT

**Background:** The European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (QLQ-C30) is a widely used quality-of-life measure in oncology. The ability to translate QLQ-C30 responses into utility scores would further expand its use in medical decision-making. The aims of this study were to: 1) map QLQ-C30 responses onto patient time trade-off utility scores; and 2) compare a multiattribute approach to a global evaluation approach to modeling utility scores.

**Methods:** Two distinct approaches were applied to data from 1432 cancer patients. The multiattribute approach used psychometric analysis and expert input to select a subset of functioning and symptom scale items for modeling. The second approach focused on global health and quality-of-life items based on a conceptual model. Model selection criteria included parsimony, statistical significance and logical consistency of parameter estimates, predictive accuracy, number of states described, and scale range.

**Results:** The optimal multiattribute model included nine variables for five items from different scales, described 144 unique states, predicted values ranging from 0.63 to 1.00, but it had poor predictive accuracy (cross-validation pseudo-$R^2$ = 0.056). The best-fitting global approach-based model described 24 unique states using eight indicators for two items from one scale (plus a constant) and predicted values ranging from 0.17 to 1.00 (cross-validation pseudo-$R^2$ = 0.127).

**Conclusions:** Multiattribute models produced a greater number of unique predicted values, while global models exhibited more desirable statistical properties and a wider range of values. The recommended models will enable users to predict cancer patients' utilities from existing and future QLQ-C30 data sets.

*Keywords:* cancer, EORTC QLQ-C30, preferences, quality of life, utility.

## Introduction

One of the most widely used measures of health in clinical trials specific to cancer is the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) [1]. The QLQ-C30 is a multidimensional measure with scales grouped into functioning, symptoms, and global quality-of-life (QOL) categories. While the psychometric properties of the QLQ-C30 are well established, it was developed as a profile measure and was not designed to combine scale scores to form a single summary score.

In contrast, the utility-based approach to health assessment represents health as a single score, where dead is typically assigned a value of 0 and best health is assigned a value of 1. Utilities can be generated using a variety of elicitation methods and perspectives: 1) elicited directly or generated indirectly with utility measures; 2) from the perspective of patients or community/general population (whether direct or indirect); and 3) elicited indirectly with a generic or cancer-specific measure

(whether from the perspective of patients or community). Direct methods for utility elicitation include the standard gamble or the time trade-off (TTO) [2]. Alternatively, utilities can be generated in an indirect manner using measures such as the Health Utilities Index Mark 3 [3] and the EQ-5D [4–6]. Indirect utility measures involve self-completion of a health state classifier system and the subsequent application of a set of preference weights to obtain an index-based single summary score. The algorithms derived for most indirect measures are based on stated preferences for hypothetical health states described by the health state classifier obtained from the community and/or general population. This approach facilitates the calculation of quality-adjusted life-years (QALYs), which are useful to compare the incremental benefit of cancer treatments and preventives in cost-effectiveness analyses [7–13]. Several studies have developed utility-based algorithms for QLQ-C30, typically mapping responses/scores from QLQ-C30 onto EQ-5D scores [14–16].

A third approach is to obtain preferences for own health from patients who have experienced cancer, and use statistical techniques to map those preferences onto responses to a cancer-specific profile measure. Disease-specific measures may be more sensitive to change than generic preference-based measures because condition-specific measures are intended to capture disease and treatment effects deemed important to patients [17,18]. Dobrez et al. identified several factors that support the usefulness of a cancer-specific, patient-based utility measure

*Address correspondence to:* A. Simon Pickard, Center for Pharmacoeconomic Research and Departments of Pharmacy Practice and Administration, College of Pharmacy, University of Illinois at Chicago, 833 South Wood St., Rm 164, M/C886, Chicago, IL 60612-7230, USA. E-mail: pickard1@uic.edu

[16,19]. The ability to calculate QALYs from cancer patients' responses to a disease-specific measure of functioning and QOL may complement indirect utility measures that incorporate societal health preferences when examining the outcomes of clinical trials, particularly when applied to privatized health-care systems where most products and services are not funded by the general population. In addition, understanding patient utilities for health outcomes associated with different treatment options could facilitate shared decision-making between clinicians and cancer patients. Thus, the ability to generate a patient preference-based score from the QLQ-C30 descriptive system could expand its use in priority setting for both clinical and policy purposes.

## Objectives

The aims of this study were to: 1) estimate a utility-based algorithm by mapping QLQ-C30 responses onto patient utilities for own health; and 2) compare a multiattribute approach to a global evaluation approach to modeling utilities for own health.

## Methods

### Data Source

Data were drawn from a previously collected sample of patients who participated in a prospective study at one of five academic medical centers: Rush–Presbyterian–St. Luke's Medical Center, Robert H. Lurie Cancer Center of Northwestern University, Fox Chase Cancer Center, Johns Hopkins Oncology Center, and Medical College of Ohio [19]. Original selection criteria included the ability to read and speak English, and a diagnosis of cancer or human immunodeficiency virus/acquired immunodeficiency syndrome. In the current study, we focused on cancer patients and excluded respondents who either failed to comprehend the TTO, as judged by the interviewer, or did not complete the utility assessment exercise and/or QLQ-C30 questionnaire.

### Measures

In addition to providing demographic and clinical information, the respondents were asked to complete several health status questionnaires, including the QLQ-C30 version 2. QLQ-C30 version 2 is a 30-item, self-completed questionnaire with scales measuring physical functioning (PF, five items), emotional functioning (EF, four items), cognitive functioning (CF, two items), role functioning (RF, two items), and social functioning (SF, two items) [20]. A sixth-scale QOL includes two items that evaluate overall QOL and health. The remaining items are divided among multiitem symptom scales measuring nausea and vomiting (NV, two items), pain (PA, two items), and fatigue (FA, three items), and single-item scales that pertain to financial concerns and other somatic complaints. The two items on the QOL scale utilize a 7-point response scale ranging from "very poor" to "excellent." On QLQ-C30 version 2, PF items have dichotomized responses (i.e., "yes" or "no"), and the other scales have four response options ranging from "not at all" to "very much." QLQ-C30 version 3 restructured the PF scale into items with four response options.

Patient utility for their current health was elicited by an interviewer using the TTO method [21]. A visual aid was used to help patients understand the exercise. Initially, the patient was asked whether his or her current health state was better than, worse than, or equal to being dead. If the patient responded that his or her current health state was worse than being dead, then the utility for own current health was assigned a value of −1. If the patient equated his or her own current health with being dead, then the utility of own current health was assigned a value of 0. Otherwise, the patient was asked to participate in an exercise where he or she was offered a choice between living 1 year in his or her current health state, defined as health over the preceding 2 weeks, or a specified amount of time less than 1 year in perfect health. The amount of time in perfect health was incrementally lowered until the patient became indifferent to living a year in his or her current health state and the specified amount of time in perfect health.

### Analytic Approach

Multiattribute and global approaches were employed to develop models for predicting own health utilities from subsets of QLQ-C30 items. The two approaches are described in detail in the next sections.

*Multiattribute approach.* Initially, we sought to develop utility mapping algorithms using a multiattribute approach. This approach was applied in many utility mapping studies [16,19,22–24]. The multiattribute approach is based on the notion that an individual's preference for a given health state is determined by his or her perceived status in multiple domains of health (e.g., physical, emotional, social). The approach follows from multiattribute utility theory [25] and von Neumann–Morgenstern expected utility theory [26]. Nevertheless, as operationalized in most research contexts, including utility mapping studies, it is not fully consistent with MAUT, with the primary inconsistency being a reversal in the parameters that are presumed to be known (or measured) and unknown (or estimated). Because of this, the multiattribute approach has been labeled as an empirical or "statistical inference" model [27]. That the approach operates as MAUT in reverse does not invalidate its use. On the contrary, it has been shown that models developed to predict utilities using the multiattribute approach outperform those that are more fully consistent with MAUT [27].

*Global approach.* The second approach to deriving preference-based algorithms using QLQ-C30 items was based on a theory of global health preference formation (GHPF) [28], where utility mapping models were generated from the two items that comprised the QLQ-C30's QOL scale. The conceptual basis of the GHPF draws in part from reasoning coauthor JSW used to explain findings in the US valuation of the EQ-5D health states related to the relationship between respondent characteristics and preferences for hypothetical health states [4]. Consistent with the reasoning of Nord [29], the theory distinguishes between the concepts of QOL and utility. The theory states that the preference or utility (i.e., desirability) of a health state to an individual is a function of the perceived QOL (i.e., satisfaction and overall positive feelings) that the state imparts or would impart, if presented in a hypothetical scenario. When asked to value a health state, the individual evaluates multiple components of health, or health in general, against his or her reference standards. To the extent that the aggregate of these evaluations is positive, the individual perceives the health state to be associated with a higher level of (health-related) QOL. This perception alone then determines the desirability of the health state. The preceding evaluations are assumed to be uncorrelated with the preference after accounting for perceived (health-related) QOL. While the GHPF theory is a simple extension of the work of other judgment theorists [30], it provides an alternative to the traditional view of preferences being formed directly as a consequence of concurrent evaluations of multiple dimensions of health. Further, the concept of rational decision-making based on a