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Mapping FACT-Melanoma Quality-of-Life Scores to EQ-5D Health Utility Weights

Robert L. Askew, MPH[1], Richard J. Swartz, PhD[2], Yan Xing, MD, PhD, MS[1], Scott B. Cantor, PhD[1], Merrick I. Ross, MD[1], Jeffrey E. Gershenwald, MD[1], J. Lynn Palmer, PhD[1], Jeffrey E. Lee, MD[1], Janice N. Cormier, MD, MPH[1,]*

[1]*The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA;* [2]*Rice University, Houston, TX, USA*

A B S T R A C T

Objectives: We sought to develop a mapping function from functional assessment of cancer therapy-melanoma (FACT-M) quality of life scores to the EuroQol-5D (EQ-5D) utility scores. **Methods:** FACT-M and EQ-5D scores were collected during a prospective study of melanoma-related quality of life at a tertiary cancer care center in the United States. The study sample was divided into development and validation datasets with equal distributions by cancer stage and treatment status. Censored Least Absolute Deviation (CLAD) and Ordinary Least Squares (OLS) regression analyses were performed using the developmental dataset to derive mapping functions, and model performance was examined through comparisons of residuals and measures of fit in the validation dataset. Exploratory analyses examined the predictive ability of clinical factors and individual subscales. **Results:** Of 273 patients, 75 were undergoing treatment with 198 in follow-up surveillance. Relatively even distributions were observed by melanoma stage: I/II (n = 102), III (n = 100), and IV (n = 71). OLS regression resulted in a mapping function of EQ-5D = 0.0037*FACT-M+0.2238 with an R^2 0.499. CLAD regression resulted in a mapping function of EQ-5D = 0.0042*FACT-M+0.1648 with pseudo R^2 0.328. When applied to the validation dataset, correlations between observed and predicted values resulted in identical coefficients (r = 0.824, $P < 0.001$). Though the mapping functions were similar, residuals were smaller at the 20th, 40th, and 60th percentiles using the OLS model. The CLAD derived mapping function resulted in smaller residuals only for patients whose EQ-5D = 1. **Conclusions:** The OLS mapping function demonstrated better predictive ability and will facilitate the derivation of utilities when direct population preference measures are not available.

Keywords: EQ-5D, functional assessment of cancer therapy, health-state utility, melanoma, quality of life, questionnaires.

Introduction

Health-Related Quality of Life (HRQOL) has been shown to be an independent predictor of patient survival [1–4] functional status [5], and response to therapy [6]. Many HRQOL instruments are available for assessing patient status in the context of chronic disease, including the functional assessment of chronic illness therapy (FACIT) measurement system [7]. The cancer-specific subset of instruments within this system share the functional assessment of cancer therapy-general (FACT-G) as a common core component; the items comprising this common component facilitate comparisons of patient status across cancer populations [8] Disease-specific modules have been developed and validated for inclusion with the FACT-G to address the unique concerns of patients with specific types of cancer [7] The melanoma-specific version of the FACT questionnaire, known as the FACT-melanoma (FACT-M), was developed at The University of Texas M. D. Anderson Cancer Center and has been validated for use in patients with all stages of melanoma [9,10]. Like many other HRQOL instruments, the primary outcomes of the FACT questionnaires are subscale scores that are derived by summing individual item responses along with a separate, combined score of the instrument representing overall HRQOL.

Health utilities are related but distinct from HRQOL, as they are measures of preference for distinct health states [11]. Specifically, utilities assess the value assigned by populations to specific health states using standardized methods such as time-tradeoff or standard gamble evaluation techniques [12]. Health utilities such as the EuroQol-5D (EQ-5D) provide preference weights from the general population that can be used to calculate quality-adjusted life years (QALYs) for cost-effectiveness analyses and can inform discussions of health-related resource allocation [13,14]. The EQ-5D has been endorsed as a health utility standard by the National Institute for Clinical Excellence (NICE) in Europe [15] and in the United States by its inclusion in the US Agency for Healthcare Research and Quality (AHRQ) Medical Expenditure Panel Survey [14,16].

HRQOL is most commonly assessed in the context of clinical trials using disease-specific instruments because of the known advantages of responsiveness and sensitivity to change, however cost-effectiveness analyses may be precluded by such a choice. Several methodologies for mapping HRQOL to health utility scores have been developed and evaluated, of which regression analysis is the most common due to its simplicity and efficiency in terms of

* *Address correspondence to:* Janice N. Cormier, Department of Surgical Oncology, Unit 1484, The University of Texas MD Anderson Cancer Center, 1400 Hermann Pressler Drive, P.O. Box 301402, Houston, TX 77030-1402 USA.

E-mail: jcormier@mdanderson.org.

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data requirements [17]. Mapping functions have been developed for multiple disease-specific HRQOL instruments, including those for inflammatory bowel disease [18] Parkinson's disease [19], oral health [20], sleep disorders [21], and other cancer-specific instruments [22–24]. Negatively skewed data is commonly observed in studies of health-related quality of life, and the results of studies deriving mapping analyses have varied. In order to improve the accuracy of mapping formulas, multiple approaches have been employed including omitting poorly correlated domains [23] and evaluating items individually to determine inclusion in a mapping model [24]. Likewise, these studies often contrast multiple regression methods with the more accurate model recommended for use in cost-benefit analyses. The objective of this analysis was to explore whether a reliable mapping function could be developed to impute EQ-5D health utility values from FACT-M quality of life scores to facilitate future cost-effectiveness analysis in the absence of direct preference measures.

Methods

Instruments

The common core component of the FACT questionnaires (FACT-G) is composed of four subscales assessing physical well-being (7 items), functional well-being (7 items), social/family well-being (7 items), and emotional well-being (6 items) [7,8]. The melanoma specific module of the FACT-M adds 16 items related to the unique concerns of melanoma patients along with an additional 8 items related to the concerns of melanoma patients undergoing surgery [9]. Numerical values from zero to four are assigned to Likert scale responses representing degrees of frequency or difficulty with each item related to patient quality of life (ranging from "not at all" to "very much"). The individual scale scores are summed, and the combined score of the FACT-M represents overall HRQOL for patients with melanoma. HRQOL scores for the FACT-M range from 0 to 204.

The EQ-5D is a five-item health state utility that was developed to provide a summary index measure of health status for use in the economic evaluation of health care and has been shown to be a valid and reliable instrument in a variety of contexts [25–28]. This instrument was selected for utility mapping due to its wide-spread adoption in the United States and abroad. The EQ-5D contains one item for each of five dimensions of HRQOL (i.e., mobility, self-care, usual activities, pain or discomfort, and anxiety or depression) [25,29]. For each item, there are three response options available indicating no problems, moderate problems, or extreme problems. Patient responses to the five items reflect a specific health state that corresponds to a population preference weight for that state on a continuous scale of 0 (death) to 1 (perfect health). For both the FACT-M and the EQ-5D, higher scores represent better health states.

FACT-M and EQ-5D scores were collected at the time of patient enrollment into an IRB-approved prospective cohort study designed to validate the FACT-M questionnaire [10]. Enrollment was conducted at the outpatient Melanoma and Skin Center at a tertiary cancer care center in Houston, Texas. Individual items of the FACT-M were converted to subscale and summary scores using standardized FACIT scoring conventions [30]. Patient responses to the five-item EQ-5D were transformed to health state preference values using the United States valuation scoring algorithms [31]. Full and subscale HRQOL scores were examined through stratification according to clinically important covariates and HRQOL percentile groups.

Statistical analysis

The cohort was divided into two distinct datasets for independent development and validation procedures through stratified random assignment by disease stage and treatment status to ensure comparable distributions. Using the developmental dataset, ordinary least squares (OLS) regression was employed to derive a preliminary mapping function for the FACT-M, Because OLS regression is known to be sensitive to ceiling and floor effects and to non-normal data [32], censored least absolute deviation (CLAD) regression was selected as a viable alternative to OLS, as it is a form of median regression that minimizes the sum of absolute residuals, and as such is not as sensitive to deviations from normality and homoscedasticity [33]. The OLS and CLAD derived mapping functions were then tested in the validation dataset to compare performance with respect to regression residuals, strength of correlation between predicted and observed values, and measures of fit. T-tests were conducted for patients groups defined by disease stage, treatment status, and EQ-5D score percentile. Wilcoxon rank-sum tests were applied to median comparisons. Subsequent exploratory analyses examined the effect of using individual subscales in model building, and because important differences in HRQOL have been noted in this population [10,34], expanded models incorporating clinical covariates were also compared. All statistical transformations and analyses were conducted using STATA/SE 9.2 (StataCorp LP, College Station, TX).

Results

The majority of patients in this study were white (98%), married (80%), and male (58%), and the median age was 52 (range: 20–79) (Table 1). Relatively even distributions of patients were observed with respect to melanoma stage I/II (n = 102), stage III (n = 100), and stage IV (n = 71); 273 patients were surveyed, 75 were in active treatment and 198 were in follow-up surveillance. The mean FACT-M scores for the development and validation datasets were similar at 176.1 (SD 24.1) and 174.9 (SD 23.5), respectively. The mean EQ-5D scores for the development and validation datasets were identical at 0.88 (SD 0.13). Negatively skewed FACT-M and EQ-5D scores with ceiling effects were observed for the entire patient cohort (Fig. 1A,B). A substantial gap in EQ-5D scores from 0.86 to 1.00 was also observed, reflecting a function of the US scoring algorithm. In general, EQ-5D and FACT-M total and subscale scores decreased in the expected direction with regard to disease stage and treatment status (Table 2). When stratified by score percentile groups, mean EQ-5D scores ranged from 0.70 to 1.0 (30% of scale), whereas the mean FACT-M total scores for the same EQ-5D percentile groups ranged from 147.2 to 192.1 (22.0%). When further stratified by FACT-M subscales, greater discrimination was observed in the physical (27.9%) and functional (28.6%) subscales than for the social/family (13.2%) and emotional (16.7%) subscales. When the same patients were independently stratified by FACT-M percentile groups, a greater range of means scores was observed in both the total and subscale scores, with likewise the greatest range observed in the physical (34.6%) and functional (41.8%) domains. For the full FACT-M, the mapping function derived from the OLS regression was $EQ\text{-}5D = a\ [FACT\text{-}M] + y\text{-}intercept$ with $a = 0.0037$ and $y\text{-}intercept = 0.2238$. For the OLS regression, R^2 was equal to 0.499 ($P < 0.001$). CLAD regression resulted in a mapping function with $a = 0.0042$ and a $y\text{-}intercept$ of 0.01648 with a pseudo R^2 of 0.328. Additional mapping was separately carried out from the four core FACT-G subscales in the functional form of $EQ\text{-}5D = a\ [FACT\text{-}G] + y\text{-}intercept$. The OLS function estimated a at 0.0056 and the y-intercept at 0.3554 with an R^2 value of 0.393 ($P < 0.001$). The CLAD function estimated a at 0.0069 and the y-intercept at 0.2531 with a pseudo R^2 of 0.235.

Mapping from the more limited FACT-G data led to correlations between observed and predicted values of 0.63 ($P < 0.001$) in the

Table 1 – Demographic and clinical profile of patients stratified by dataset.

	Combined		Development		Validation	
	n = 273	%	n = 138	%	n = 135	%
Race/ethnicity						
Caucasian	268	98.1	135	97.9	133	98.5
Hispanic	3	1.1	1	0.7	2	1.5
African American	1	0.4	1	0.7	—	—
Other	1	0.4	1	0.7	—	—
Gender						
Male	159	58.2	79	57.2	80	59.3
Female	114	41.8	59	42.8	55	40.7
Marital status						
Married	218	79.8	111	80.4	107	79.2
Never married	27	9.9	16	11.6	11	8.2
Separated or divorced	21	7.7	18	5.8	13	9.6
Widowed	7	2.6	3	2.2	4	3.0
AJCC melanoma stage						
I/II	102	37.4	51	37.0	51	37.8
III	100	36.6	51	37.0	49	36.3
IV	71	26.0	36	26.0	35	25.9
Treatment						
Active treatment	75	27.5	38	27.5	37	27.4
Follow-Up	198	72.5	100	72.5	98	72.6
FACT-M scores						
Mean (SD)	176	(23.8)	176	(24.1)	175	(23.5)
Median (range)	182	(75–204)	183	(89–203)	179	(75–204)
EQ-5D scores						
Mean (SD)	0.88	(0.13)	0.88	(0.13)	0.88	(0.13)
Median (range)	0.85	(0.27–1.00)	0.84	(0.40–1.00)	0.85	(0.27–1.00)

AJCC, American Joint Committee on Cancer; EQ-5D, EuroQol-5D; FACT-M, functional assessment of cancer therapy-melanoma.

validation dataset. The OLS model resulted in slightly smaller residuals for stage III patients, but for patients with stage I/II and IV disease, the OLS model resulted in larger residuals (Table 3). The CLAD model was more accurate at the extreme ends of the score range, and the OLS algorithm resulted in smaller residuals in between. When both the OLS and CLAD mapping functions derived from the FACT-M were applied to the validation dataset, correlations between observed and predicted values greatly improved with identical coefficients ($r = 0.82$, $P < 0.001$). Comparisons of the models in terms of absolute deviations of the predicted scores from the observed scores revealed that the mapping functions were similar in terms of their predictive ability (mean absolute value of residuals: OLS = 0.06, CLAD = 0.05). Mean raw residuals from the OLS model, however, were less than half the size of those from the CLAD model (OLS = 0.009; CLAD = 0.020). The CLAD model resulted in slightly smaller residuals for stage III patients; for patients with stage I/II and IV disease, the OLS model resulted in smaller residuals. While the residuals from both models appeared to be normally distributed (Fig. 2A,B), the OLS model was more accurate across the range of scores, resulting in smaller mean residuals at the 20th, 40th, and 60th percentiles of the EQ-5D. The CLAD derived mapping function resulted in smaller residuals only for patients whose EQ-5D score was equal to 1. Because of the skewed distribution of HRQOL scores, median residual values were also compared by percentile group (Fig. 3). When compared with the residuals from the CLAD model, median residuals from the OLS model were smaller for each percentile group ($P < 0.001$) with the sole exception again for when the EQ-5D reflected perfect health. It is also important to note that the OLS model produced the lowest mean residual values when EQ-5D scores were greater than 0.7 and less than 1.

Subsequent exploratory analyses examined the predictive ability of each of the FACT-M subscales separately. When considered in isolation, no single factor explained more variance than the total FACT-M score (Table 4). The same was true when multiple scale factors were present in the model (data not shown). Of note, the melanoma module appeared to have equivalent predictive ability, and slight differences were observed (OLS $R^2 = 0.52$; CLAD $R^2 = 0.38$) when all subscales were separately included in the same model. The results of the likelihood ratio test comparing these models (total score vs. all individual subscale scores), however, suggested that they were not statistically different. Likewise, alternative models incorporating disease stage and treatment status produced slightly modified mapping functions, but no significant differences were observed between the competing models when examining measures of fit. Given the nonsignificant results of the post-hoc analysis, the rule of parsimony was observed for the selected models, and the OLS model using the FACT-M total score was selected.

Conclusions

In this analysis, several methodological techniques were evaluated for mapping FACT-M scores to the EQ-5D health utility index. The FACT-M mapping function derived from Censored Least Absolute Deviation (CLAD) regression was determined to be a more accurate predictor of EQ-5D scores only when its value was 1.0. When health utility was less than 1.0, regression analyses using OLS demonstrated better predictive ability. Although the FACT-M and the EQ-5D both assess related HRQOL domains, the mechanisms for deriving and interpreting scores from each instrument are fundamentally different. The FACT-M is a descriptive measure that employs a series of Likert scales, whereas the summary scores are treated as continuous variables for analysis. The EQ-5D employs ordinal scales that are transformed onto a continuous

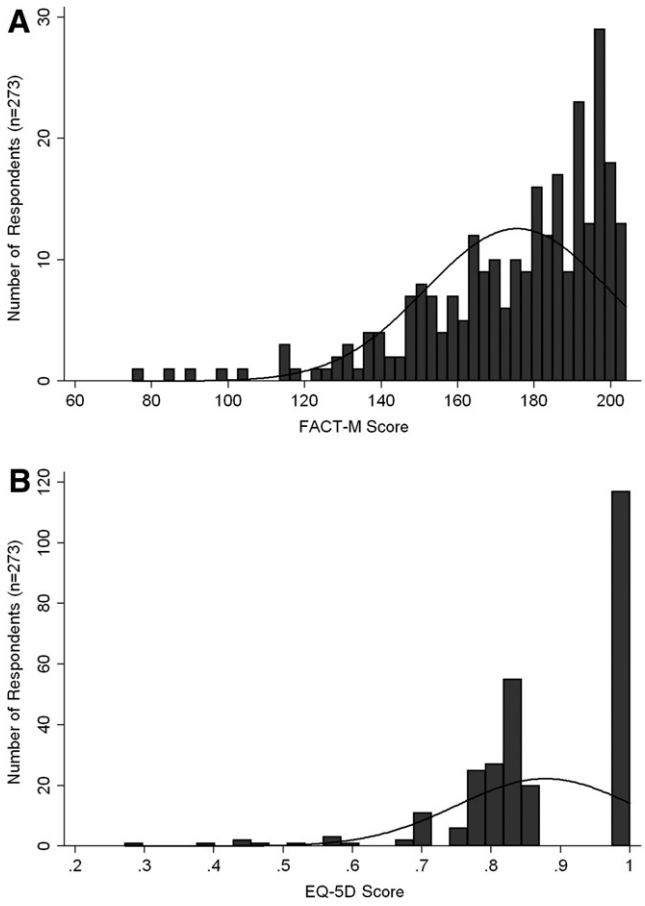

Fig. 1 – Distributions of the (A) functional assessment of cancer therapy-melanoma (FACT-M) and (B) EuroQol-5D (EQ-5D) scores of the combined cohort.

scale representing societal preferences for specific health states. Although there has been some debate concerning the validity of transformation from ordinal HRQOL measures to continuous health utility scales [35,36], the results of this analysis lend support that despite these differences, scores can be transformed using statistically derived mapping equations. It is clear from this analysis, however, that the performance of the mapping function derived from each technique across the HRQOL score range warrants further discussion.

For melanoma patients, distress and other major concerns related to surgical scarring, disfigurement, and mortality differentially affect HRQOL at various time-points from diagnosis through post-treatment surveillance [37,38]. Therefore it is not surprising that the OLS model performance was enhanced when additional melanoma-specific items were included in the analysis. To ensure that the FACT-M scores reflected these differences for patients with localized and advanced disease states, recruitment for this cohort targeted an equal distribution of patients according to disease stage [9]. Nevertheless, the HRQOL data in this sample remained clustered towards the positive end of the scales with the greatest unexplained variance remaining at the lower end of the scale. Caution is warranted, therefore, when applying this algorithm to cohorts of patients predominately located at the lower end of these HRQOL scales. Substantial ceiling effects were also observed in this cohort of patients with a significant gap in EQ-5D scores from 0.86 to 1.00; this bimodal distribution is in part due to the instruments scoring mechanism with perfect health corresponding to a value of 1.00 and the next lowest health state value possible for the US valuation at 0.86 [13]. The ceiling effect was not observed to the same degree for the FACT-M administered to the same cohort of patients. This finding along with the expanded range of FACT-M scores may lend further support for the use of disease-specific instruments when responsiveness to change and sensitivity are critical aspects of assessment. It may also indicate that important HRQOL information is captured in the FACT-M that is not covered in the five-item EQ-5D. Furthermore, the observed differences in model performance when comparing the results of the FACT-G and the FACT-M mapping functions may also be attributed to the added information captured by the melanoma and melanoma-surgery specific items. Nevertheless, as clustered patient data is often observed on the positive end of scales in HRQOL research [39] this model is expected to adequately approximate group level health utilities for exploratory cost-effectiveness comparisons.

In the preliminary mapping analysis using the smaller FACT-G scale, performance of the OLS and CLAD algorithms were similar, but the additional items of the FACT-M improved OLS model performance with higher correlation coefficients between observed and predicted values and greater variance explained by the model. Others have similarly reported that OLS regression provides better predictive ability for health utility index scores than more traditionally robust regression procedures [40,41]. In a cohort of prostate cancer patients, Wu et al. [22] found that OLS regression outperformed median regression, resulting in an R^2 of 0.58 and a mean absolute residual of 0.146. Likewise, Dobrez et al. [24] using a more complex item selection method found that OLS functioned adequately (mean residual = 0.03) to predict directly derived health utility values in patients with breast, prostate, colon, lung, lymphoma, and other malignancies. While OLS has generally outperformed CLAD regression, this finding has not been universal because Cheung et al. [23] found that CLAD models provided marginally better predictive ability in a cohort of English or Chinese speaking cancer patients. Nevertheless, the predictive ability of the mapping function from the present study was better with OLS resulting in lower mean absolute residuals of 0.06 versus 0.08 reported by Cheung et al. [23]. Furthermore, the performance of the OLS model using total scores (without clinical covariates) performed as well if not better than the alternative models considered, resulting in an R^2 value of 0.5. As detailed in a recent review of HRQOL mapping techniques [42], this value is high for studies mapping disease-specific to generic HRQOL measures that generally range from 0.2 to 0.5. Given the known limitations of R^2 values in model comparisons, however, additional accuracy measures are reported here along the HRQOL scale continuum to allow investigators to decide whether regression mapping and the reported mapping function are appropriate for their population of interest. While no single OLS regression model examined out-performed all other models, the model using the total FACT-M score was selected based on both performance measures and on its ease of use.

It is important to note that the majority of patients in this sample were white and in post-treatment surveillance, which reflects the melanoma population in general. While caution is warranted when applying the mapping algorithm to large non-white cohorts, of the over 68,000 newly diagnosed melanoma cases in the US annually [43] over 90% of patients are white [44]. Although the original preference weights for the EQ-5D were derived from general populations, it is recognized that patients with melanoma or other conditions may report differing values for the same health states [45]; additional variance is also possible when examined along the continuum of HRQOL scores. However, among the competing techniques for transforming descriptive measures of HRQOL to health utility indices, the method chosen has been judged to be less important to the predictive ability than the sensitivity and range of associated instrument scores [17]. The level of

Table 2 – Mean (SD) HRQOL subscale scores stratified by disease stage, treatment status, and percentile groups.

	FACT–M subscales (range)						FACT-M total score range: 0–204	EQ-5D range: 0.0–1.0
	Physical range: 0–28	Functional range: 0–28	Social/family range: 0–28	Emotional range: 0–24	Melanoma range: 0–64	Melanoma surgical range: 0–32		
Stage								
I/II: n = 102	26.2 (2.9)	24.8 (4.2)	25.2 (3.6)	20.8 (3.5)	58.1 (6.6)	29.0 (4.4)	184.1 (20.1)	0.91 (0.14)
III: n = 100	23.9 (5.1)	22.9 (4.9)	24.6 (3.6)	19.7 (3.7)	54.8 (8.5)	23.8 (6.4)	169.7 (25.8)	0.85 (0.13)
IV: n = 71	23.2 (4.8)	21.7 (5.7)	25.0 (3.0)	18.6 (4.2)	54.9 (7.1)	28.1 (5.3)	171.5 (22.4)	0.86 (0.11)
Treatment status								
Active: n = 75	21.7 (5.6)	20.5 (5.6)	23.9 (3.7)	18.5 (4.3)	52.0 (7.9)	26.5 (6.2)	163.2 (24.3)	0.83 (0.11)
Surveillance: n = 198	25.6 (3.5)	24.3 (4.4)	25.3 (3.3)	20.3 (3.6)	57.6 (6.9)	27.0 (5.8)	180.2 (21.9)	0.89 (0.13)
EQ-5D percentiles								
20%: n = 54	19.4 (6.0)	18.4 (6.1)	22.5 (4.7)	17.5 (4.6)	47.5 (9.2)	22.3 (7.9)	147.2 (27.8)	0.70 (0.12)
40%: n = 49	24.1 (3.0)	22.7 (4.0)	24.6 (2.8)	19.6 (3.5)	53.8 (6.3)	24.7 (5.9)	169.4 (17.3)	0.82 (0.01)
60%: n = 53	24.5 (3.7)	22.1 (4.6)	24.9 (3.0)	18.8 (3.7)	56.0 (4.9)	27.0 (4.7)	173.3 (15.1)	0.85 (0.01)
80/100%: n = 117	27.2 (1.5)	26.4 (2.2)	26.2 (2.5)	21.5 (2.9)	61.0 (2.9)	29.8 (2.9)	192.1 (9.4)	1.0 (0.00)
Range difference: max – min	7.8	8.0	3.7	4.0	13.5	7.5	44.9	0.3
[Standardized range difference]	[27.9%]	[28.6%]	[13.2%]	[16.7%]	[21.1%]	[23.4%]	[22.0%]	[30.0%]
FACT-M percentiles								
20%: n = 52	18.0 (5.2)	15.9 (4.6)	21.4 (4.5)	15.6 (3.7)	44.2 (6.8)	21.4 (7.9)	136.5 (19.1)	0.73 (0.13)
40%: n = 55	23.1 (3.0)	21.6 (3.5)	24.3 (2.7)	18.7 (3.3)	53.3 (4.0)	25.0 (5.4)	166.0 (4.9)	0.84 (0.08)
60%: n = 52	26.4 (1.7)	24.3 (2.5)	25.0 (2.9)	19.8 (3.5)	58.6 (2.5)	27.1 (4.5)	181.2 (3.0)	0.88 (0.09)
80%: n = 54	27.1 (1.1)	26.4 (1.7)	26.1 (2.0)	21.3 (2.4)	61.0 (2.0)	29.3 (2.9)	191.3 (2.8)	0.95 (0.82)
100%: n = 60	27.7 (0.6)	27.6 (0.7)	27.5 (1.3)	23.2 (1.3)	62.3 (1.8)	31.0 (1.6)	199.1 (2.4)	0.97 (0.82)
Range difference: max–min	9.7	11.7	6.1	7.6	18.1	9.6	62.6	0.24
[Standardized range difference]	[34.6%]	[41.8%]	[21.8%]	[31.7%]	[28.3%]	[30.0%]	[30.7%]	[24.0%]

EQ-5D, EuroQol-5D; FACT-M, functional assessment of cancer therapy-melanoma; HRQOL, health-related quality of life.

Table 3 – Mean residuals* from the OLS and CLAD prediction models in the validation dataset stratified by disease stage, treatment status, and EQ-5D percentile groups.

	FACT-M			FACT-G		
	OLS		CLAD	OLS		CLAD
Stage						
I/II (n = 51)	0.0119	<	0.0200†	0.0197	>	0.0017†
III (n = 49)	0.0127	>	0.0122†	0.0033	<	0.0184†
IV (n = 35)	0.0023	<	0.0307†	0.0139	>	0.0003†
Treatment status						
Undergoing treatment (n = 37)	0.0036	<	0.0240†	0.0058	>	0.0033†
Follow-up surveillance (n = 98)	0.0104	<	0.0198†	0.0114	>	0.0087†
EQ-5D (overall)	0.0085	<	0.0199†	0.0099	>	0.0072†
Percentiles						
20th (n = 28)	0.0607	<	0.0752†	0.0804	>	0.0784†
40th (n = 25)	0.0265	<	0.0510†	0.0369	<	0.0499†
60th (n = 23)	0.0156	<	0.0434†	0.0073	<	0.0217†
80/100th [EQ-5D = 1] (n = 59)	0.0656	>	0.0286†	0.0792	>	0.0502†

CLAD, censored least absolute deviation; EQ-5D, EuroQol-5D; OLS, ordinary least squares.
* Absolute values of mean residuals presented; † indicates significant difference ($P < 0.05$).

precision observed for this mapping function when predicting EQ-5D index scores from the FACT-M supports its use for exploratory comparisons among cohorts with moderate to high HRQOL. Residual variance from the mapping function was below or near previously established clinically meaningful difference thresholds (i.e. minimal important differences [MID]) in group comparisons, indicating that the differences between predicted and observed residual values were not clinically meaningful at this level. Specifically, the difference between mean observed and mean predicted values of EQ-5D scores (0.005) are below established minimal important differences (MID) for the EQ-5D (0.06) [46]. It is important to note, however, that negative residual values at the lower end of the HRQOL continuum were countered by positive residual values at the higher end, thus artificially reducing the mean value somewhat for the residuals. Nevertheless, the mean absolute value of the OLS residuals were identical to the MID, so given this proximity, transformation of FACT-M scores into EQ-5D utility weights is recommended only for group-level analysis and not for individual clinical decisions. This mapping function was derived to provide point estimates for decision-analytic models to facilitate comparative effectiveness and cost-effectiveness comparisons when direct measures of health utility are not available. Additional study is warranted to examine the predictive ability in minority and international populations as well as in patients with a broader range of low HRQOL scores.

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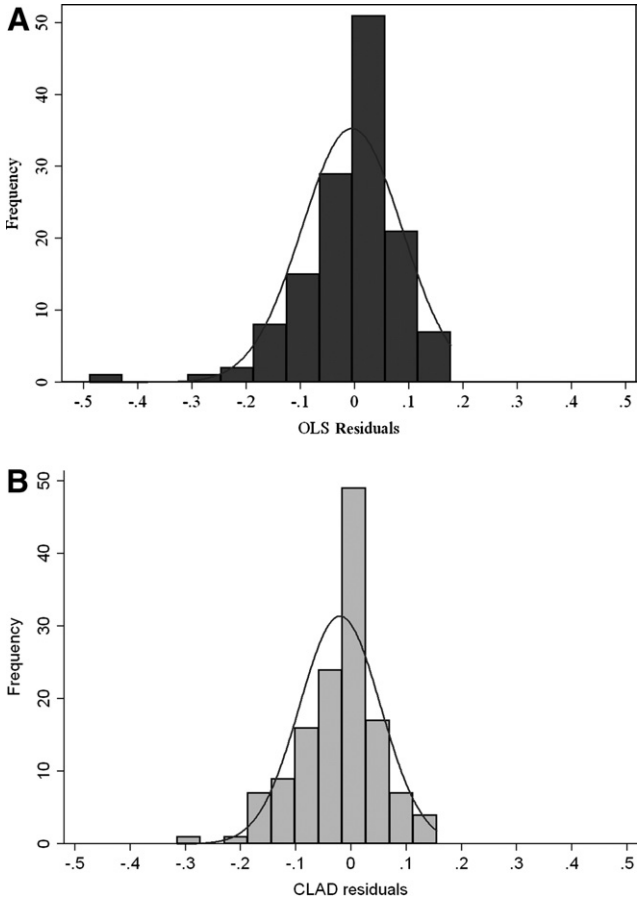

Fig. 2 – Distributions of residuals from (A) ordinary least squares (OLS) and (B) censored least absolute deviation (CLAD) derived mapping functions.

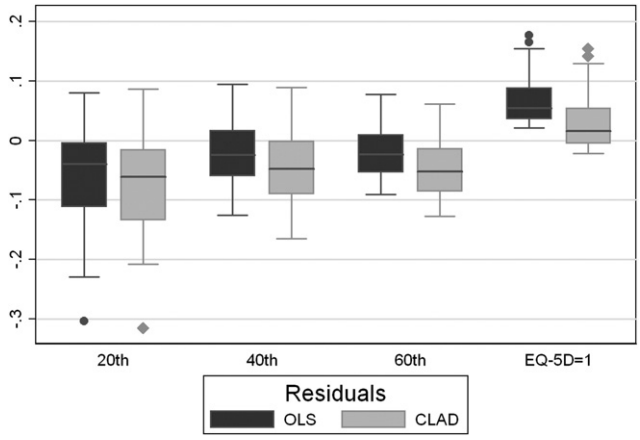

Fig. 3 – Box plot of ordinary least squares (OLS) and censored least absolute deviation (CLAD) residuals (median, 25/75th percentile, upper/lower adjacent values, and outliers) stratified by EuroQol-5D (EQ-5D) percentile groups.

Table 4 – Regression coefficients, y-intercepts, and R^2 values for HRQOL domains of the FACT-M predicting EQ-5D index scores.

Domain scales	Coefficients	y-intercept	R^2
Physical	0.0154*	0.5001*	0.358*
Functional	0.0141*	0.5463*	0.355*
Social/family	0.0124*	0.5667*	0.110*
Emotional	0.0137*	0.5990*	0.179*
FACT-general (physical + functional + social/family + emotional)	0.0056*	0.3554*	0.393*
Melanoma	0.0109*	0.2640*	0.435*
Melanoma surgery	0.0111*	0.5827*	0.269*
Melanoma module (melanoma + melanoma surgery)	0.0078*	0.2329*	0.499*
Total FACT-M (FACT-general + melanoma module)	0.0037*	0.2238*	0.499*

FACT-M, functional assessment of cancer therapy-melanoma.
* Denotes statistical significance ($P < 0.001$).

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