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Associations Between the EQ-5D-3L and QLU-C10D Descriptive Systems: Use of Correlation Networks to Explore Preference Differences in Solid Tumor Trials

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Introduction

- Health state utilities to inform cost-effectiveness models are commonly derived using the EuroQol 5-dimensional, 3-level (EQ-5D-3L) questionnaire, a generic preference-based measure advocated by the National Institute for Health and Care Excellence[1]
- A potential limitation of generic measures is their lack of condition-targeted content, which may affect their sensitivity to detect important differences in health status for certain conditions[2,3]
- The European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Utility Measure – Core 10 Dimensions (QLU-C10D) questionnaire was developed to derive health state utilities based on dimensions more relevant to patients with cancer.[4] As such, the QLU-C10D is expected to be more sensitive than the EQ-5D-3L in cancer populations
- However, a previous analysis on pooled data from 5 phase 3 trials of nivolumab in solid tumors showed that, on average, the use of the cancer-specific QLU-C10D UK index yielded 2% fewer incremental quality-adjusted life-years (QALYs) between treatments than the EQ-5D-3L UK index[5–7]

Objectives

- We aimed to explore, through dimension-level associations, the drivers of previously reported differences in incremental QALYs in pooled phase 3 nivolumab trial data between the EQ-5D-3L and the QLU-C10D

Methods

- Data were analyzed from 5 randomized phase 3 trials of nivolumab-containing regimens for the treatment of patients with solid tumors, in which the EQ-5D-3L and QLQ-C30 (used to derive the QLU-C10D) were administered (**Table 1**)

Table 1. Phase 3 trials included in this analysis[5]

Trial	Indication	Sample size (all patients randomized)	Treatment groups
CheckMate 037	Advanced (unresectable or metastatic) melanoma patients progressing after anti–CTLA-4 therapy	405	Nivolumab, investigator's choice
CheckMate 066	Previously untreated unresectable or metastatic melanoma	418	Nivolumab, dacarbazine
CheckMate 067	Previously untreated unresectable or metastatic melanoma	945	Nivolumab, nivolumab + ipilimumab, ipilimumab
CheckMate 141	Recurrent or metastatic platinum-refractory squamous cell carcinoma of the head and neck	361	Nivolumab, investigator's choice
CheckMate 238	Completely resected stage IIIB/C or stage IV melanoma with high risk for recurrence	906	Nivolumab, ipilimumab

CTLA-4, cytotoxic T-lymphocyte-associated protein 4.

- The descriptive component of the EQ-5D-3L includes 5 dimensions (**Table 2**)[8]
  - Each EQ-5D-3L dimension is categorized as 1 of 3 levels (level 1, no problems; level 2, some problems; level 3, extreme problems)
- The descriptive component of the QLU-C10D includes 10 dimensions (**Table 2**)[4]
  - Each EORTC QLU-C10D dimension is categorized as 1 of 4 levels (level 1 represents no symptoms or limitations, and level 4 represents the highest level of symptom severity or limitation)
  - QLU-C10D dimensions were derived from the QLQ-C30 as per King et al[4]

Table 2. Dimensions of the EQ-5D-3L and QLU-C10D questionnaires

EQ-5D-3L[8] (no. of items)	QLU-C10D[4] (no. of items)
Mobility (1)	Physical functioning (2)
Self-care (1)	Role functioning (1)
Usual activities (1)	Social functioning (2)
Pain/discomfort (1)	Emotional functioning (1)
Anxiety/depression (1)	Pain (1)
	Fatigue (1)
	Sleep (1)
	Appetite (1)
	Nausea (1)
	Bowel problems (2)

- Associations between levels of each dimension at baseline were assessed through polychoric correlations
- A regularized partial correlation network was estimated to reduce spurious associations occurring due to background correlation between dimensions of the same instrument[9]
- Responses to dimensions on each instrument were cross-tabulated in contingency tables with a chi-square test of association, produced overall and by trial
- Utility decrements associated with the levels of each EQ-5D-3L and QLU-C10D dimension, according to UK value sets,[6,7] were plotted comparatively

Results

- Data were available from 2625 patients at baseline
- Polychoric correlations were highest between the respective QLU-C10D and EQ-5D-3L dimensions shown in **Table 3**
- These associations were consistently significant across trials, as revealed by contingency tables ($P < 0.001$; data not shown)

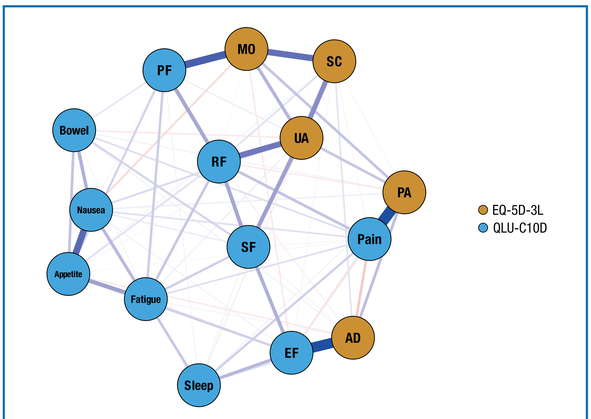
Table 3. Highest polychoric correlations between QLU-C10D and EQ-5D-3L dimensions

Dimensions	Correlation coefficient
Pain and pain/discomfort	$r = 0.865$
Role functioning and usual activities	$r = 0.807$
Physical functioning and mobility	$r = 0.784$
Emotional functioning and anxiety/depression	$r = 0.755$

Correlation network

- The regularized partial correlation network is shown in **Figure 1**

Figure 1. Regularized partial correlation network



Nodes represent dimensions of the EQ-5D-3L and QLU-C10D, where the thickness and color of the edges represents magnitude and positive/negative (dark blue/red) correlations. As part of network estimation, associations that are likely to be spurious are set to zero to improve interpretability.

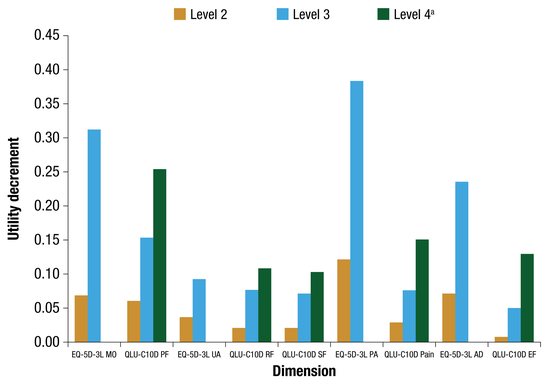
AD, anxiety/depression; EF, emotional functioning; MO, mobility; PA, pain/discomfort; PF, physical functioning; RF, role functioning; SC, self-care; SF, social functioning; UA, usual activities.

- In addition to the dimensions with the highest polychoric correlations described above, the network revealed an independent association between the QLU-C10D social functioning and EQ-5D-3L usual activities dimensions
- QLU-C10D symptom-related dimensions (eg, sleep, bowel problems, appetite loss, nausea, and fatigue) had limited or no independent association with EQ-5D-3L dimensions

Utility decrements among associated dimensions

- The utility decrements for each level of the associated dimensions (using UK value sets[6,7]) are compared in **Figure 2**
- EQ-5D-3L utility decrements are often larger than the QLU-C10D on closely related dimensions, especially for the highest level

Figure 2. Utility decrements for associated dimensions (UK value sets)[6,7]



Utility decrements multiplied by –1 for interpretability, based on the EQ-5D-3L UK value set and the QLU-C10D UK value set.[6,7] All decrements are based on the assumption that other dimensions are fixed at level 1.

The EQ-5D-3L UK value set also incorporates a constant term for any deviations from full health (0.081), and an "N3" term for any level 3 response (0.269).[6]

[a]The EQ-5D-3L comprises 3 levels, so a utility decrement is not available for level 4.

Conclusions

- This analysis of pooled phase 3 nivolumab trial data facilitates a deeper understanding of the potential uses of the cancer-specific QLU-C10D compared with the generic EQ-5D-3L in the evaluation of QALYs
- Treatments with an impact on sleep, bowel function, appetite, nausea, or fatigue will only influence QALYs as derived by the QLU-C10D. However, EQ-5D-3L utility decrements are often larger than the QLU-C10D on closely related dimensions for UK value sets
- Therefore, increased sensitivity achieved through capturing additional dimensions in the cancer-specific measure can be counterbalanced by decreased sensitivity on the dimensions similar to the generic measure
  - This is especially true when the highest level of an EQ-5D-3L dimension is endorsed

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