Article:
Taarnhøj, GA, Kennedy, FR orcid.org/0000-0002-4910-2505, Absolom, KL orcid.org/0000-0002-5477-6643 et al. (5 more authors) (2018) Comparison of EORTC QLQ-C30 and PRO-CTCAE™ questionnaires on six symptom items. Journal of Pain and Symptom Management, 56 (3). pp. 421-429. ISSN 0885-3924

https://doi.org/10.1016/j.jpainsymman.2018.05.017

Comparison of EORTC QLQ-C30 and PRO-CTCAE™ questionnaires on six symptom items

Gry Assam Taarnhøj[1], Fiona Kennedy[2], Kate Absolom [2], Christina Bæksted[3], Ivan Vogelius[1], Christoffer Johansen[1], Galina Velikova[2*] and Helle Pappot[1*].

1. Department of Oncology, Rigshospitalet, Copenhagen, Denmark
2. Leeds Institute of Cancer and Pathology, School of Medicine, University of Leeds, Leeds, United Kingdom
3. Documentation & Quality, Danish Cancer Society, Copenhagen, Denmark
*Joint Senior Authors

Corresponding author: Gry Assam Taarnhøj MD, Dpt. Of Oncology, Rigshospitalet, Blegdamsvej 9, Section 3994, 2100 Copenhagen Ø, Denmark, Tel.:+45 35450737 / +45 51943003, e-mail: gry.assam.taarnhoej@regionh.dk

Field Code Changed

Key words: Quality of life, questionnaires, correlations, consistency, reliability, patient-reported outcomes.

Running head: Comparison of validated questionnaires on six symptom items.

Abstract word count: 250.

Text word count: 2645.

Number of tables: 4.

Number of figures: 3.

Abstract

Context: Clinical studies have over the past decade paid increasing attention to health-related quality of life(HRQOL) data. Multiple questionnaires are often administered resulting in overlapping questions increasing patient burden.

Objective: To examine the correlations between the commonly used European Organization for Research and Treatment of Cancer(EORTC) Quality of Life questionnaire(QLQ-C30) and the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events(PRO-CTCAE™) on six coinciding items in order to determine consistency between overlapping items.

Methods: Data was prospectively collected from patients attending two cancer centres in the United Kingdom. Participants completed the QLQ-C30 every 4 weeks and the PRO-CTCAE at least once a week for 12 weeks. Data was collected by the internet or interactive voice response. For the six coinciding items in QLQ-C30 and PRO-CTCAE: pain, nausea, vomiting, constipation, diarrhoea and fatigue, comparisons were made between all possible related responses by aligning the four responses in the QLQ-C30 with two condensed versions of the five responses in the PRO-CTCAE. Consistency and reliability was determined with the Intraclass Correlation Coefficient and Cronbach's α.

Results:247 patients completed 785 QLQ-C30 and 2501 PRO-CTCAE questionnaires. Moderate(ICC > 0.5) to good(ICC > 0.75) reliability and Cronbach's α>0.7 was found on all coinciding questions except for questions concerning the severity of nausea and vomiting as a result of relatively few patients responding to these questions. Items on frequency showed better correlations than the severity and interference items.

Conclusions: The good reliability and consistency between the QLQ-C30 and PRO-CTCAE supports future attempts to minimise patient burden by shortening HRQOL questionnaires.

Introduction

Within the last decade health-related quality of life (HRQOL) has become an integral part of clinical studies, usually as a secondary endpoint, or as a primary endpoint evaluation of palliative treatments (1-6). The choice of HRQOL instrument is an important part of study design to ensure it suitably captures the clinical status of the patient population in order to appropriately assist future clinical decisions. The preferred design of this data collection is self-reporting by the patient using electronic or paper questionnaires thus avoiding the clinician's interpretation (3;7;8). Often several questionnaires are combined to maximize coverage of HRQOL issues. This leads to overlapping items resulting in increased patient burden, poorly completed questionnaires or both (9;10).

Of all the existing cancer specific HRQOL instruments, the European Organization for Research and Treatment of Cancer Quality of Life Questionnnaire-C30 (QLQ-C30) is among the most commonly known and used in Europe while the Functional Assessment of Cancer Therapy (FACT) and Functional Assessment of Chronic Illness Therapy (FACIT) are more widespread in the United States (10-13). The QLQ-C30 was first developed in 1987 (as QLQ-C36), and was subsequently developed in 1997 into the version used today (version 3.0). It comprises nine multi-item scales: five functional scales, three symptom scales and a global health scale (14). It has been translated and validated into more than 100 languages and used in thousands of clinical studies(15). While patients complete the QLQ-C30 questionnaire, clinicians register side-effects during oncological treatment using the Common Terminology Criteria for Adverse Events (CTCAE). However, clinician reporting has been shown to underestimate the severity of patients' symptoms and not always representative of the patients underlying health status (7). Standard clinician-based reporting of CTCAE focuses on 'treatment safety', and traditionally clinical trials primarily report the severe toxicities (Grade 3 and 4). This approach does not provide sufficient information on the mild or moderate adverse events, which when persistent may still significantly affect patients' lives and influence their adherence to the treatment. This concept of 'treatment tolerability' has become increasingly important with the use of oral targeted treatments. To address this growing need the National Cancer Institute (NCI) developed the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE™) in 2014 (7). The PRO-CTCAE has since been used in several clinical studies and has has garnered increasing

interest from the US Food and Drug Administration (FDA) as a complement to CTCAE grading to capture symptomatic toxicities in clinical trials of new cancer therapies (16;17).

While the QLQ-C30 comprises 30 questions, the PRO-CTCAE library comprises 124 items representing 78 symptomatic toxicities from which the relevant items are chosen depending on the study population. The two questionnaires were developed for different reasons, the PRO-CTCAE™ being foremost an instrument for monitoring symptomatic toxicities during cancer treatment, whereas QLQ-C30 covers multi-dimensional aspects of HRQOL. Thus, direct competition between the two instruments as a whole is not possible. Nevertheless, six symptoms are included in both the QLQ-C30 and the PRO-CTCAE™ questionnaires: nausea, vomiting, constipation, diarrhea, tiredness/fatigue and pain. We aimed to assess the equivalence of responses to these six symptom questions in QLQ-C30 and PRO-CTCAE™ in order to determine if the number of questions for the patients can be reduced in clinical studies using both measures.

Methods

Data was collected in a proof of principle study evaluating feasibility, patient uptake and compliance with using an Internet or Interactive Voice Response (1) system for collecting both patient-reported adverse events and HRQOL questionnaire data. The study design was based on the standard scenario in clinical trials where adverse events data is collected in real time for safety purpose, and HRQOL data is collected at pre-defined less frequent time points usually to assess the impact of treatment as a secondary outcome.

Participants in the study were patients receiving oncological or surgical treatment for a range of cancers at the Leeds Cancer Centre, St James's University Hospital, Leeds, or University Hospitals Bristol NHS Foundation Trust, Bristol, United Kingdom. Patients were eligible if they had either early or metastatic disease with Eastern Cooperative Oncology Group (ECOG) performance status (PS) 0-2, and were receiving one of the five main cancer treatment modalities: chemotherapy, targeted agents, hormonotherapy, radiotherapy or surgery. The sample size was estimated as recommended for pilot studies, 42 patients per treatment group (30 patients allowing for 30% attrition rate), total sample of 252 patients (18).

Patients were asked to complete the PRO-CTCAE™ items at least once per week (plus any other time they experienced the adverse events or symptoms). In addition, patients were presented with EORTC QLQ-C30 questionnaire once every four weeks over a 12 week study period, thus giving the possibility of 988 completed QLQ-C30 and 3211 completed PRO-CTCAE™ questionnaires, both questionnaires being presented to the patients at baseline and with the regular intervals onwards. Consequently, a maximum of 988 replies of both the QLQ-C30 and the PRO-CTCAE™ on the same date could be included in analysis. Only questionnaires completed on the same date were included. Patients had a choice between internet or IVR completion.

Analysis

For each of the six symptoms, we made a comparison between the distribution of responses in the four categories in QLQ-C30 and the distribution of responses in the five categories in the PRO-CTCAE™. In PRO-CTCAE™, there are one, two or three items for each symptom: pain (frequency, severity, interference with daily activities), nausea (frequency, severity), vomiting (frequency, severity), constipation (frequency, severity), diarrhea (frequency), tiredness/fatigue (severity, interference with daily activities). Comparison with the QLQ-C30 was made for each of the items. For the PRO-CTCAE™ there are different response options depending on whether the questions concern frequency, severity or interference with daily activities, whereas the response options in the QLQ-C30 are the same for all questions. See table 1 for a linear display of possible corresponding questions in the QLQ-C30 and PRO-CTCAE™ questionnaires. The PRO-CTCAE™ questionnaire used in the present study was an earlier version of the current PRO-CTCAE™ published by the National Cancer Institute in 2014 (7;17). There is one difference in items concerning constipation: we used two items (frequency and severity) while the current version has only one (severity).

We initially created a heat map (See Figure 1) of the frequency of responses to examine visually if there was a consistent pattern in the patient responses to the middle category on PRO-CTCAE (Occasionally/Moderate/Somewhat) corresponding QLQ-C30 “A little” or “Quite a bit”. We then investigated two possible consistency patterns (Figure 2), allocating the middle category responses to either

"Quite a bit (Pattern A) or to "A little" (Pattern B), thus transforming the 5-level scale of the PROCTCAE™ to a 4-level scale.

For analysis we included all aligned replies on the same date, thereby allowing multiple responses from each patient. This could potentially influence the level of consistency between the two questionnaires because of the influence of e.g. clinical characteristics. However, the study group also performed the following analysis on only one set of questionnaires per patient and found no differences, thus analysis continued with all aligned responses.

Correlation tests were performed for both possible correspondence patterns according to Figure 1A+B. Intraclass Correlation Coefficient and Cronbach's α were computed in SPSS statistical package version 22.0 using a two-sided ANOVA mixed-effects method, to determine consistency and reliability (19;20). Conceptually, the ICC is a measure of the variance in a sample. ICC values less than 0.5 were indicative of poor reliability, values between 0.5 and 0.75 indicated moderate reliability, values between 0.75 and 0.9 indicate good reliability and values above 0.9 indicated excellent reliability (21). Cronbach's α is a measure of consistency, in this case between the two questionnaires. Cronbach's α ≥0.7 was deemed acceptable (22).

Results

The baseline demographic and clinical data for the participants are displayed in table 2 and show an even distribution of men and women. The majority of the participants were aged 51-75 years. Almost a quarter (22.1%) of the patients were treated for breast cancer. As planned, there was an even spread across the treatment modalities. A total of 247 patients completed 785 QLQ-C30 and 2501 PRO-CTCAE™ questionnaires, giving a completeness of data of 79 % and 78 %, respectively. Depending on the QLQ-C30 symptom and corresponding PRO-CTCAE™, between 72 and 704 aligned comparable replies on the same date were found. Of the 785 completed QLQ-C30 questionnaires, 72 were not accompanied by a completed PRO-CTCAE™ on the same date and were for this reason excluded from the analysis.

The six symptoms were scored very differently in frequency with a large amount of patients never experiencing nausea (59.8%), vomiting (88.8%), diarrhea (59.3%) or constipation (61.5%) whereas pain and fatigue showed a more mixed picture but nonetheless appear correlated in the heat map of figure 1. Figure 1

suggests differences in correlations between the QLQ-C30 and PRO-CTCAE™ depending on the type of question (frequency or severity). For questions on frequency there is a pattern of better correlation between the PRO-CTCAE™ reply 'Occasionally' with the QLQ-C30 reply 'A little'. The picture for questions on severity is more mixed and the 'Moderate' response in PRO-CTCAE™ seems evenly correlated to the answers 'A little' and 'Quite a bit' in the QLQ-C30. These findings are also observed in the correlation and reliability tests in table 3 that show higher values for correlation pattern B for frequency items than the mixed picture for the severity items in pattern A. The highest ICC of 0.901 was found for QLQ-C30 q15 (question 15, vomiting) vs. PRO-CTCAE™ frequency of vomiting with a Cronbach's α of 0.948 in correlation pattern B. As very few patients experienced nausea or vomiting the following questions on the severity thereof were naturally only answered by relatively few patients resulting in 261 and 72 completed questionnaires, respectively. As a result thereof QLQ-C30 q14 (nausea) vs. PRO-CTCAE™ severity of nausea and QLQ-C30 q15 (vomiting) vs. PRO-CTCAE™ severity of vomiting did not reach an ICC above 0.5 (0.452 and 0.405, respectively, in correlation pattern B). The results are shown in figure 1 and table 3.The graphic heat maps in figure 1 correspond well to the overall high ICCs and Cronbach's α in table 3 regardless of which correspondence pattern was applied.

More discrepancies between replies were found when applying correlation pattern A (33% disagreement) than pattern B (27% disagreement) (seen graphically in figure 3A+B), and again consistent with the higher values of the ICCs and Cronbach's α for pattern B (table 3). Overall figure 3 displays a high level of agreement between the QLQ-C30 and the PRO-CTCAE™.

Discussion

This study has demonstrated that internal consistency between QLQ-C30 and PRO-CTCAE™ with Cronbach's α is high on almost all the coinciding items from the two instruments when comparison is made with equal 4-level scales.

The frequency of the symptoms in our population corresponds well to what we know about symptoms in the population of cancer patients undergoing oncological treatment (23-25). The correlation tests in table 3 show us that PRO-CTCAE™ items on frequency are better correlated with QLQ-C30 items than PRO-CTCAE™

items on severity. The reason for this may be explained by several factors: 1) the evident nature of the items in the QLQ-C30 being foremost understood as questions on frequency and therefore carrying the strong correlation, 2) frequency being a more quantitative measure easier to grade compared to severity and finally 3) the varying response options in the PRO-CTCAE™ questionnaire potentially making the patients shift between options because of the wording and not so much because of the rankings, which is more apparent in the QLQ-C30 as this questionnaire has the same reply format to all questions perhaps facilitating comprehension. Also, the psychometrics of the PRO-CTCAE™ has to the authors' knowledge not been tested through Rasch analysis. This may question the scale and perception of the PRO-CTCAE™ and could also explain the findings above (26).

The findings of varying internal consistency and reliability depending on the chosen correlation pattern (Figures 1A+B and 3A+B) may be a result of the linguistic differences between the two questionnaires but may have disturbed the overall conclusions with its complexity. Good consistency exists between PRO-CTCAE™ and QLQ-C30 on almost all corresponding items, regardless of which correlation pattern used, thus enhancing the need for thorough choice between the two when planning studies. The two severity items not reaching the acceptable values are estimated to not have done so because of the relative few patients reporting the symptoms, an element that Intraclass Correlation Coefficient and Cronbach's α are known to be sensitive to (21;22).

A recent study by Dueck et al. used the EORTC QLQ-C30 to verify the validity, reliability and responsiveness of PRO-CTCAE™ in a large cancer population. This study found consistent large correlations between analogous items in QLQ-C30 and PRO-CTCAE™. The study also demonstrated convergent validity between the two questionnaires meaning that the PRO-CTCAE™ single items were associated in the expected direction of the QLQ-C30 HRQOL or subscale summary score. However, this study was designed to validate the use of PRO-CTCAE™ and does not discuss the implications of these findings in daily clinical use in terms of patient burden (27). Another study by Stiel et al. looked at the correlation between a number of different quality of life questionnaires (FACIT-G, QLQ-C30, SEIQoL (28) and MIDOS (29;30)). This study demonstrated a number of items (well-being, physical and functional domains) with high correlation thus

favouring shortened questionnaires for the benefit of the patients (31). Our study echoes the findings by Dueck et al. and strengthens the evidence to attempt to minimize patient burden by shortening questionnaires.

However, the few comparisons of questionnaire items performed to date have not rendered an overall agreement on how to handle multiple and burdensome questionnaire items, although one study by Chochinov et al. (1997) interestingly replaced diagnostic questionnaires with a single item "Are you depressed?" and thereby correctly identified the eventual diagnostic outcome of all patients (32).

With the results of the present study in mind, one could argue to minimize the number of questions by applying the questionnaires relevant to the aim and population while ensuring no overlapping questions are presented to the patient. For a clinical study in which the capture of quality of life domain scores is a paramount issue one could, with our results in mind, warrant the use of a complete EORTC QLQ-C30 with PRO-CTCAE™ questions as a supplement. For clinical trials testing new therapeutics the use of an abbreviated version of QLQ-C30 as a supplement to a larger sum of PRO-CTCAE™ may also be feasible to ensure capture of symptom toxicities. Abbreviated versions of the QLQ-C30 have in certain populations been demonstrated reliable, internal consistency and validity which therefore enables more freedom of choice when planning which patient reported outcomes to use in clinical studies (10;33;34). The EORTC has also, with the individual patient in mind, initiated the development of a Computer Adaptive Testing for the QLQ-C30 dimensions which, when validated, adds interesting possibilities to the choice of PROs in clinical studies (35).

The present study was conducted in a diverse cancer population therefore the correspondence between PRO-CTCAE™ and QLQ-C30 might be dependent on the population, in the sense that different cancer and treatments groups experience a range of symptoms at different levels of frequency, severity and interference in daily life. Our results from a population of very mixed cancer types might therefore not apply to more disease specific settings.

This study adds to the dawning of evidence describing correlations between the EORTC QLQ-C30 with PRO-CTCAE™, in our case on the six coinciding items. However, our findings need a platform of agreement on how to minimize the load on patients. For this purpose patient involvement may be the next step.

The overall conclusion is that there is a good correspondence between PRO-CTCAE™ and QLQ-C30 for the six overlapping symptoms when applying equal level scales and that for some symptoms; use of questions from one questionnaire can be sufficient, thus diminishing the patient burden.

Acknowledgments

The data reported here was collected as part of the Cancer Research UK funded REPORT-UK study. We would like to thank the participating patients and the support provided by the research nurses and study steering group. We would also particularly like to thank Beverly Clayton for her contribution to participant recruitment and study management. We are grateful to Dr. Sandra Mitchell (Research Scientist, Outcomes Research Branch, National Cancer Institute, Bethesda, MD) for reviewing and providing helpful comments on the last version of the manuscript. Dr. Gry Assam Taarnhøj was funded by the Danish Cancer Society, grant number R150-A10114.

References

1. Basch E, Deal AM, Kris MG et al. Symptom Monitoring With Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial. J.Clin.Oncol. 2016;34:557-65.

2. Berry DL, Hong F, Halpenny B et al. Electronic self-report assessment for cancer and self-care support: results of a multicenter randomized trial. J.Clin.Oncol. 2014;32:199-205.

3. Di MM, Gallo C, Leighl NB et al. Symptomatic toxicities experienced during anticancer treatment: agreement between patient and physician reporting in three randomized trials. J.Clin.Oncol. 2015;33:910-5.

4. Velikova G, Booth L, Smith AB et al. Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial. J.Clin.Oncol. 2004;22:714-24.

5. Quinten C, Coens C, Ghislain I et al. The effects of age on health-related quality of life in cancer populations: A pooled analysis of randomized controlled trials using the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 involving 6024 cancer patients. Eur.J.Cancer 2015;51:2808-19.

6. Juul T, Petersen MA, Holzner B, Laurberg S, Christensen P, Gronvold M. Danish population-based reference data for the EORTC QLQ-C30: associations with gender, age and morbidity. Qual.Life Res. 2014;23:2183-93.

7. Basch E, Reeve BB, Mitchell SA et al. Development of the National Cancer Institute's patient-reported outcomes version of the common terminology criteria for adverse events (PRO-CTCAE). J.Natl.Cancer Inst. 2014;106.

8. Mooney KH, Beck SL, Wong B et al. Automated home monitoring and management of patient-reported symptoms during chemotherapy: results of the symptom care at home RCT. Cancer Med. 2017;6:537-46.

9. Basch E, Abernethy AP, Mullins CD et al. Recommendations for incorporating patient-reported outcomes into clinical comparative effectiveness research in adult oncology. J.Clin.Oncol. 2012;30:4249-55.

10. Chiu L, Chiu N, Chow E et al. Comparison of three shortened questionnaires for assessment of quality of life in advanced cancer. J.Palliat.Med. 2014;17:918-23.

11. Danna BJ, Metcalfe MJ, Wood EL, Shah JB. Assessing Symptom Burden in Bladder Cancer: An Overview of Bladder Cancer Specific Health-Related Quality of Life Instruments. Bladder.Cancer 2016;2:329-40.

12. Cella DF, Tulsky DS, Gray G et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. J.Clin.Oncol. 1993;11:570-9.

13. Webster K, Cella D, Yost K. The Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System: properties, applications, and interpretation. Health Qual.Life Outcomes. 2003;1:79.

14. 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;85:365-76.

15. EORTC Developement of QLQ-C30; http://groups.eortc.be/qol/qlq-c30-development.

Ref Type: Generic

16. Trotti A, Colevas AD, Setser A, Basch E. Patient-reported outcomes and the evolution of adverse event reporting in oncology. J.Clin.Oncol. 2007;25:5121-7.

17. Kluetz PG, Chingos DT, Basch EM, Mitchell SA. Patient-Reported Outcomes in Cancer Clinical Trials: Measuring Symptomatic Adverse Events With the National Cancer Institute's Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE). Am.Soc.Clin.Oncol.Educ.Book. 2016;35:67-73.

18. Lancaster GA, Dodd S, Williamson PR. Design and analysis of pilot studies: recommendations for good practice. J.Eval.Clin.Pract. 2004;10:307-12.

19. de Vet HCW, Terwee CB, Mokkink LB, Knol DL. Measurement in Medicine 2011.

20. Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. Psychol.Bull. 1979;86:420-8.

21. Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. J Chiropr Med 2016;15:155-63.

22. Tavakol M, Dennick R. Making sense of Cronbach's alpha. Int.J Med Educ. 2011;2:53-5.

23. Butt Z, Rosenbloom SK, Abernethy AP et al. Fatigue is the most important symptom for advanced cancer patients who have had chemotherapy. J.Natl.Compr.Canc.Netw. 2008;6:448-55.

24. Reilly CM, Bruner DW, Mitchell SA et al. A literature synthesis of symptom prevalence and severity in persons receiving active cancer treatment. Support.Care Cancer 2013;21:1525-50.

25. Henry DH, Viswanathan HN, Elkin EP, Traina S, Wade S, Cella D. Symptoms and treatment burden associated with cancer treatment: results from a cross-sectional national survey in the U.S. Support.Care Cancer 2008;16:791-801.

26. Boone WJ. Rasch Analysis for Instrument Development: Why, When, and How? CBE.Life Sci.Educ. 2016;15.

27. Dueck AC, Mendoza TR, Mitchell SA et al. Validity and Reliability of the US National Cancer Institute's Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE). JAMA Oncol. 2015;1:1051-9.

28. Joyce CR, Hickey A, McGee HM, O'Boyle CA. A theory-based method for the evaluation of individual quality of life: the SEIQoL. Qual.Life Res. 2003;12:275-80.

29. Radbruch L, Sabatowski R, Loick G et al. Cognitive impairment and its influence on pain and symptom assessment in a palliative care unit: development of a Minimal Documentation System. Palliat.Med. 2000;14:266-76.

30. Radbruch L, Sabatowski R, Loick G, Jonen-Thielemann I, Elsner F, Hormann E. [MIDOS--validation of a minimal documentation system for palliative medicine]. Schmerz. 2000;14:231-9.

31. Stiel S, Psych D, Kues K, Krumm N, Radbruch L, Elsner F. Assessment of quality of life in patients receiving palliative care: comparison of measurement tools and single item on subjective well-being. J.Palliat.Med. 2011;14:599-606.

32. Chochinov HM, Wilson KG, Enns M, Lander S. "Are you depressed?" Screening for depression in the terminally ill. Am.J.Psychiatry 1997;154:674-6.

33. Groenvold M, Petersen MA, Aaronson NK et al. The development of the EORTC QLQ-C15-PAL: a shortened questionnaire for cancer patients in palliative care. Eur.J.Cancer 2006;42:55-64.

34. Lien K, Zeng L, Nguyen J et al. Comparison of the EORTC QLQ-C15-PAL and the FACIT-Pal for assessment of quality of life in patients with advanced cancer. Expert.Rev.Pharmacoecon.Outcomes.Res. 2011;11:541-7.

35. Petersen MA, Groenvold M, Aaronson NK et al. Development of computerised adaptive testing (CAT) for the EORTC QLQ-C30 dimensions - general approach and initial results for physical functioning. Eur.J.Cancer 2010;46:1352-8.