



MEDIZINISCHE
UNIVERSITÄT
INNSBRUCK

Development of thresholds for clinical importance for the EORTC measures

Johannes M. Giesinger

**Department of Psychiatry, Psychotherapy
and Psychosomatics**

Innsbruck Medical University

Symptom monitoring and screening in daily oncological practice

- It is well-known that many cancer symptoms and treatment side-effects are undetected and therefore undertreated
(e.g. Weingart 2005 JGIM, Pakhomov 2008 AJMC)
- Often limited time for patient-clinician communication (i.p. in outpatient units)
- This makes systematic symptom monitoring important for adequate symptom management
- The QLQ-C30 and the EORTC CAT measures appear to be suitable for symptom monitoring as they cover important functioning domains and key cancer symptoms

Symptom monitoring and screening in daily oncological practice

- To date, much research has been done on minimal important differences/changes for the QLQ-C30, but only very few studies on interpretation of absolute scores, i.e. thresholds for clinical importance
- Interpretability of absolute scores (in the context of screening) relies on the availability of cut-off scores, i.e. thresholds that allow a clinician to tell whether the severity of a symptom is “normal” or not
- Thresholds for clinical importance will also allow to calculate prevalence rates for symptoms / problems from EORTC measures
- **Cut-off scores should not reflect if a problem is a “disorder” but help to identify clinically important problems**

Recent studies on developing cut-off scores

Content-based approaches:

(determine cut-off scores according to response categories)

Johnsen et al (2009): symptom prevalences for haematological patients based on QLQ-C30: “not at all” – no symptom; “a little” – symptom present; “quite a bit” or “very much” – severe symptom;

Distribution-based approaches:

(relate PRO scales to score distributions in reference populations)

Velikova et al. (2004): symptom screening using general population mean as cut-off score

Gulbrandsen et al. (2004): age- and sex-adjusted general population means

Recent studies on developing cut-off scores

Anchor-based approaches:

(relate PRO scales to external criteria)

Snyder et al. (2009; 2010): anchoring QLQ-C30 scales to the Supportive Care Needs Survey (external criterion); patients with unmet needs considered as positive cases

Snyder et al. (2011): asked for the two most bothersome issues to classify positive cases

Johnsen et al. (2012): supplemented the QLQ-C30 with questions on problem intensity, problem burden, and felt need, i.e. the Three-Levels-of-Needs Questionnaire (3LNQ)

EORTC QLQ project: Objectives

Development of cut-off scores for symptom screening in daily clinical practice, at the individual patient level, for 14 of the 15 domains included in the QLQ-C30 and their corresponding EORTC CAT measures:

- A) Evaluation of what makes a symptom relevant** for patient-clinician consultation based on qualitative interviews with patients and health professionals
- B) Definition of anchor items** as external criteria for determining thresholds by an expert board based on the information collected in aim A
- C) Determination of cut-off scores** for the QLQ-C30 and the CAT measures using the anchor items determined in aim B

Funded by a grant from the EORTC Quality of Life Group

EORTC QLQ project: Collaborators

- Fabio Efficace (Rome)
- Juan I Arraras (Pamplona)
- John Ramage (Basingstoke)
- Teresa Young (London)
- Morten Petersen, Mogens Groenvold (Denmark)
- Krzysztof Tomaszewski (Cracow)
- Bernhard Holzner, Fanny Loth (Innsbruck)

Aim A: Methods

Aim

Evaluation of what makes a symptom clinically important,
i.e. relevant for patient-clinician consultation

Sample

Cancer patients (N=83) and health care professionals (n=67) from Austria, Italy, the Netherlands, Poland, Spain and the UK

Assessment

- Qualitative interview to identify aspects for clinical importance
- Importance ratings for six predefined anchors

Aim A: Sample characteristics

Patient sample (N = 83)

| | | |
|-------------------------|----------------------|-------------|
| Age | mean (SD) | 60.1 (12.3) |
| Sex | Women | 41 (50.6) |
| | Men | 40 (49.4) |
| Diagnosis | Breast cancer | 20 (24.7) |
| | Colorectal cancer | 16 (19.8) |
| | Lung cancer | 9 (11.1) |
| | Stomach cancer | 8 (9.9) |
| UICC stage | I | 5 (7.4) |
| | II | 21 (30.9) |
| | III | 19 (27.9) |
| | IV | 23 (33.8) |
| Treatment status | On treatment | 62 (80.1) |
| | No current treatment | 16 (20.0) |

Health care professional sample (N = 67)

| | | |
|------------------------------|------------------|------------|
| Age | mean (SD) | 44.2 (9.8) |
| Sex | | N(%) |
| | Women | 44 (65.7) |
| | Men | 23 (34.3) |
| Profession | Nurse | 21 (31.3) |
| | Oncologist | 20 (29.9) |
| | Psychooncologist | 11 (16.4) |
| | Surgeon | 7 (10.4) |
| | Other | 8 (11.9) |
| Profession experience | In general | 18.1 (9.5) |
| | Cancer specific | 14.4 (8.7) |

Aim A - Results

The results from the quantitative part in aim A suggest to include the following anchors:

- limitations in everyday life
- need for help
- worries by partner or family

The results from the qualitative part highlight the importance of the:

- emotional impact of a symptom/problem
- limitations in everyday life
- need for help
- specific relationships between individual problems/symptoms
- duration and frequency


Received: 24 February 2017 | Revised: 28 July 2017 | Accepted: 24 August 2017

DOI: 10.1002/pon.4548

WILEY

PAPER

A cross-cultural convergent parallel mixed methods study of what makes a cancer-related symptom or functional health problem clinically important

Johannes M. Giesinger¹  | Neil K. Aaronson² | Juan I. Arraras³ | Fabio Efficace⁴ | Mogens Groenvold⁵ | Jacobien M. Kieffer² | Fanny L. Loth¹ | Morten Aa. Petersen⁵ | John Ramage⁶ | Krzysztof A. Tomaszewski⁷ | Teresa Young⁸ | Bernhard Holzner¹ |
on behalf of the EORTC Quality of Life Group

¹Department of Psychiatry, Psychotherapy and Psychosomatics, Medical University of Innsbruck, Innsbruck, Austria

²Division of Psychosocial Research and Epidemiology, The Netherlands Cancer Institute, Amsterdam, The Netherlands

³Medical Oncology Department, Hospital of Navarre, Pamplona, Spain

⁴Health Outcomes Research Unit, Italian Group for Adult Hematologic Diseases (GIMEMA) Data Center, Rome, Italy

Abstract

Objective: In this study, we investigated what makes a symptom or functional impairment clinically important, that is, relevant for a patient to discuss with a health care professional (HCP). This is the first part of a European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group project focusing on the development of thresholds for clinical importance for the EORTC QLQ-C30 questionnaire and its corresponding computer-adaptive version.

Methods: We conducted interviews with cancer patients and HCPs in 6 European countries.

Psycho-oncology 2017

Aim B - Definition of anchor items

Consensus Discussion of the findings of aim A at the EORTC Quality of Life Group Meeting in Oslo (Spring 2016) and via e-mail to define anchor items for aim C

Content of anchor items:

- Limitations of everyday life
- Need for help or care
- Worries by patient or his/her family/partner

Standard EORTC response format:

Not at all – A little – Quite a bit – Very much

Classification rule:

Selecting a “red” category for any of the anchor items makes a symptom/problem clinically important

Aim B - Examples for anchor items

The following questions ask about the impact of symptoms or problems you may experience on your daily life and on you or your family/partner. In addition, we would like to know if you needed any help or care because of symptoms or problems.

| Domain | Anchor | English anchor item |
|-----------------------------|---------------|---|
| Physical functioning | limitations | Has your physical condition limited your daily life? |
| | need for help | Have you needed any help or care because of your physical condition? |
| | worries | Has your physical condition caused you or your family/partner to worry? |
| Fatigue | limitations | Has fatigue limited your daily life? |
| | need for help | Have you needed any help or care because of fatigue? |
| | worries | Have you had fatigue causing you or your family/partner to worry? |
| Pain | limitations | SKIPPED FOR THIS DOMAIN (C30 assesses interference with daily life) |
| | need for help | Have you needed any help or care because of pain? |
| | worries | Have you had pain causing you or your family/partner to worry? |

Aim C - Objective and Methods

Objective

Determination of cut-off scores for the QLQ-C30 and the CAT measures (104 items in total) using the anchor items determined in aim B

Sample

Recruitment of 500 cancer patients in Austria, Italy, the Netherlands, Poland, Spain, and the UK:

- Any diagnosis, any treatment
- Equal sample sizes for treatment status (on / off treatment) and treatment intention (curative / palliative)
- Not more than 20% per diagnostic group

Total number of items

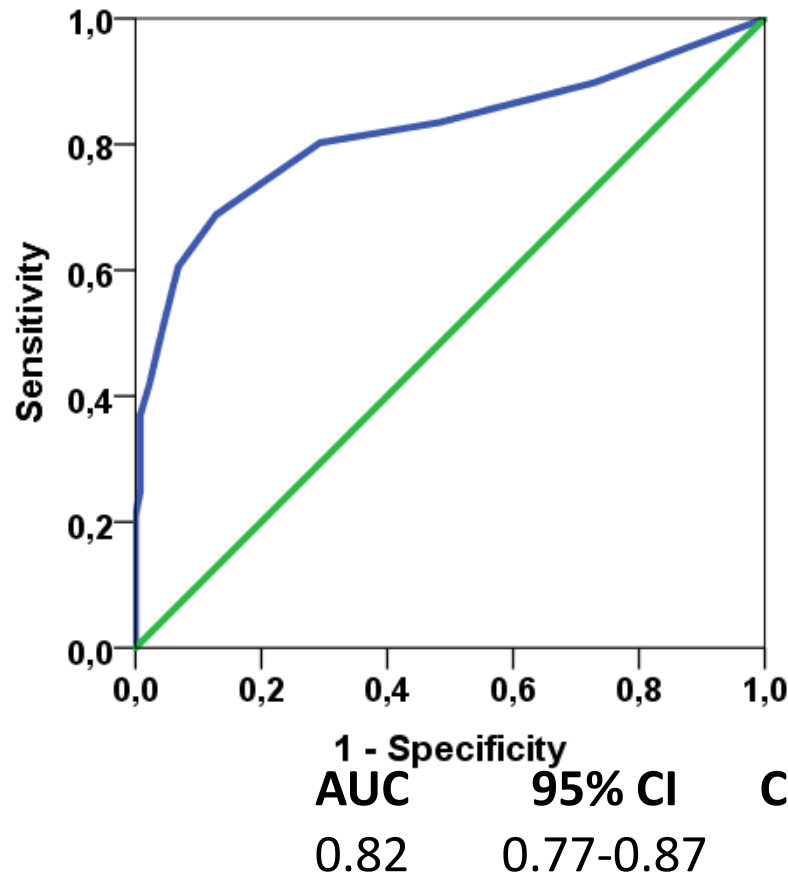
30 items – QLQ-C30 • 35 items – EORTC CAT short-forms • 39 anchor items

| Scale | Additional items | Total # items | Max Information for 0-100 scores of about | Approx. score transformed to IRT metric* (score range) |
|--------------|------------------|---------------|---|--|
| PF | +2 | 7 | 83 | 0.4 (-2.7;1.0) |
| SF | +2 | 4 | 80 | 0.3 (-1.9;0.8) |
| RF | +2 | 4 | 80 | 0.3 (-1.9;0.8) |
| EF | +3 | 7 | 70 | 0.1 (-2.5;1.2) |
| CF | +2 | 4 | 80 | 0.2 (-2.4;0.9) |
| FA | +2 | 5 | 39 | 0.1 (-1.2;2.2) |
| NV | +2 | 4 | 10 | -1.5 (-1.8;1.7) |
| PA | +2 | 4 | 25 | -1.0 (-1.9;1.8) |
| DY | +3 | 4 | 20 | -0.2 (-0.7;1.6) |
| SL | +3 | 4 | 30 | 0.0 (-0.8;1.8) |
| AP | +3 | 4 | 10 | -0.3 (-0.5;2.0) |
| CO | +3 | 4 | 10 | -0.3 (-0.6;2.3) |
| DI | +3 | 4 | 10 | -0.5 (-0.7;1.6) |
| FI | +3 | 4 | 10 | -0.4 (-0.6;1.8) |
| QL | --- | 2 | --- | --- |
| Total | +35 | 65 | | |

Aim C - Patient characteristics (N=302)

| | | Mean (SD) |
|---------------------|----------------------|-------------|
| Age | | 61.3 (12.6) |
| | | N (%) |
| Sex | Women | 164 (54.8) |
| | Men | 135 (45.2) |
| Diagnosis | Breast cancer | 84 (27.8) |
| | Prostate cancer | 43 (14.2) |
| | Lung cancer | 26 (8.6) |
| | Head and neck cancer | 28 (9.3) |
| | Other | 121 (40.1) |
| UICC stage | I | 55 (18.8) |
| | II | 87 (29.8) |
| | III | 72 (24.7) |
| | IV | 78 (26.7) |
| Treatment status | on treatment | 212 (70.4) |
| | off treatment | 89 (29.6) |
| Treatment intention | curative | 191 (65.9) |
| | palliative | 99 (34.1) |

Physical Functioning

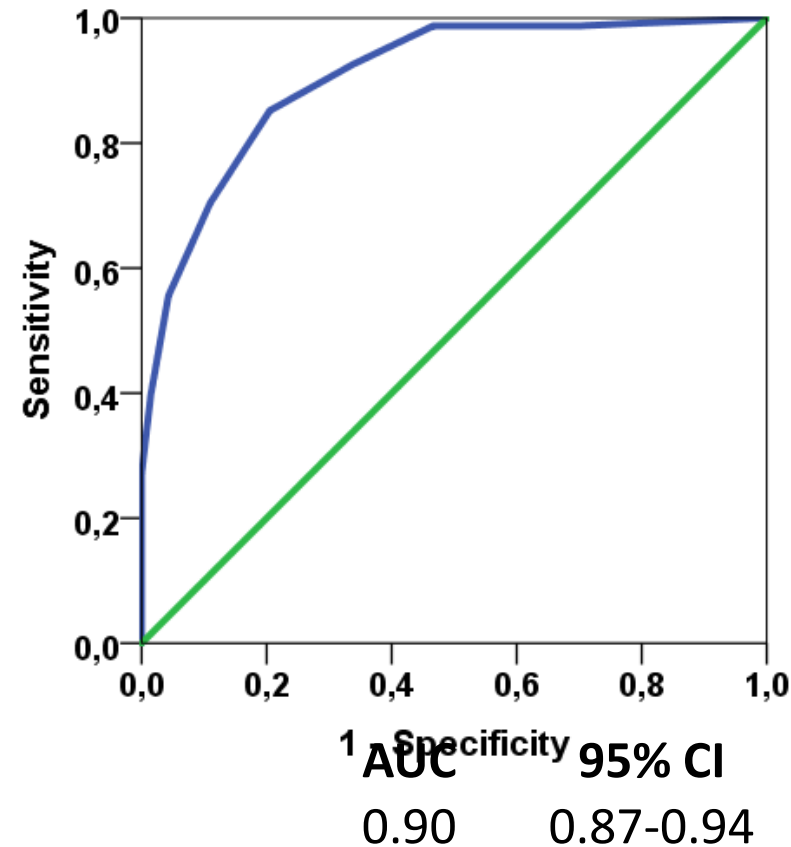


Results from the ROC analysis

| AUC | 95% CI | |
|-----------|-------------|-------------|
| 0.82 | 0.77-0.87 | |
| Cut-offs | Sensitivity | Specificity |
| 70 | 0.60 | 0.94 |
| 76 | 0.68 | 0.88 |
| 83 | 0.80 | 0.72 |

| AUC | 95% CI | Cut-offs | Sensitivity | Specificity |
|------|-----------|----------|-------------|-------------|
| 0.82 | 0.77-0.87 | 83 | 0.80 | 0.72 |

Emotional Functioning

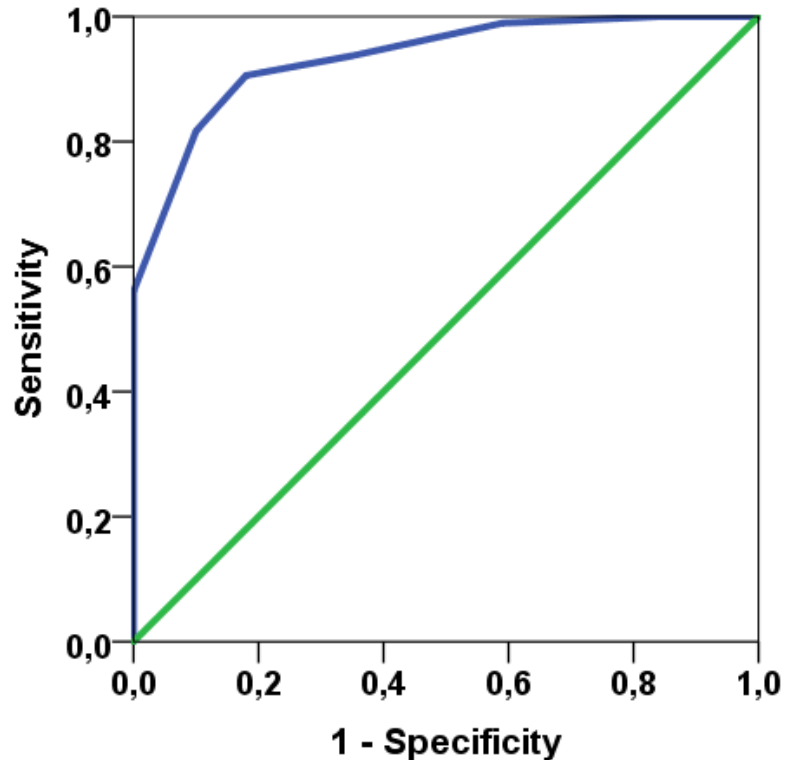


Results from the ROC analysis

| AUC | 95% CI | |
|-----------|-------------|-------------|
| 0.90 | 0.87-0.94 | |
| Cut-off | Sensitivity | Specificity |
| 63 | 0.71 | 0.89 |
| 71 | 0.85 | 0.79 |
| 79 | 0.93 | 0.66 |

| AUC | 95% CI | Cut-off | Sensitivity | Specificity |
|------|-----------|---------|-------------|-------------|
| 0.90 | 0.87-0.94 | 71 | 0.85 | 0.79 |

Fatigue



Results from the ROC analysis

AUC

0.93

95% CI

0.90-0.96

Cut-off

28

39

50

Sensitivity

0.99

0.89

0.80

Specificity

0.57

0.83

0.91

AUC

0.93

95% CI

0.90-0.96

Cut-offs

39

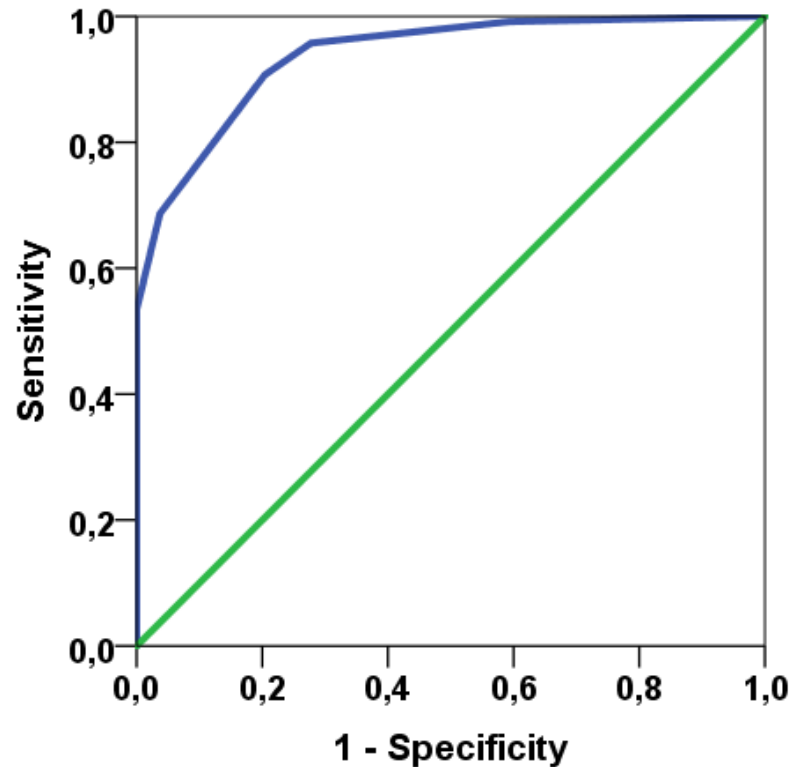
Sensitivity

0.89

Specificity

0.83

Pain



Results from the ROC analysis

| AUC | 95% CI |
|------|-----------|
| 0.94 | 0.91-0.97 |

| Cut-off | Sensitivity | Specificity |
|-----------|-------------|-------------|
| 25 | 0.96 | 0.70 |
| 42 | 0.78 | 0.91 |
| 58 | 0.71 | 0.96 |

| AUC | 95% CI | Cut-offs | Sensitivity | Specificity |
|------|-----------|----------|-------------|-------------|
| 0.94 | 0.91-0.97 | 42 | 0.78 | 0.91 |

Overview of the remaining EORTC QLQ-C30 scales

| | AUC | 95% CI | Cut-off | Sensitivity | Specificity | pos. cases |
|------------------------|------|-----------|---------|-------------|-------------|------------|
| Cognitive functioning | 0.88 | 0.83-0.93 | 75 | 0.88 | 0.73 | 10.7% |
| Role functioning | 0.90 | 0.87-0.94 | 58 | 0.88 | 0.80 | 21.3% |
| Social functioning | 0.86 | 0.81-0.91 | 75 | 0.93 | 0.56 | 19.6% |
| Diarrhea | 0.94 | 0.91-0.97 | 17 | 1.00 | 0.83 | 6.7% |
| Constipation | 0.91 | 0.84-0.98 | 50 | 0.79 | 0.94 | 9.3% |
| Dyspnoea | 0.90 | 0.86-0.94 | 50 | 0.59 | 0.95 | 19.3% |
| Sleep disturbances | 0.86 | 0.81-0.92 | 50 | 0.77 | 0.86 | 20.4% |
| Appetite loss | 0.90 | 0.86-0.95 | 50 | 0.81 | 0.88 | 10.3% |
| Financial difficulties | 0.90 | 0.84-0.96 | 17 | 0.91 | 0.82 | 11.3% |

Prevalence of clinically important problems

| | On-treatment | | On-treatment |
|------------------------------|--------------|-------------------------------|--------------|
| Physical Functioning | 52.6 % | Fatigue | 42.1 % |
| Social Functioning | 55.0 % | Dyspnoea | 13.8 % |
| Role Functioning | 35.5 % | Appetite loss | 16.1 % |
| Emotional Functioning | 39.3 % | Sleep disturbances | 30.0 % |
| Cognitive Functioning | 34.3 % | Pain | 20.4 % |
| | | Nausea / Vomiting | 11.8 % |
| | | Diarrhea | 25.2 % |
| | | Constipation | 12.4 % |
| | | Financial difficulties | 27.4 % |

Next steps

- Finish recruitment (currently ~350/500)
- Final ROC analyses (and sensitivity analyses) to obtain thresholds for the EORTC QLQ-C30 and the EORTC CAT measures
- Publication of results
- Implementation in daily clinical practice to improve symptom identification

Many thanks for your attention!

johannes.giesinger@i-med.ac.at

