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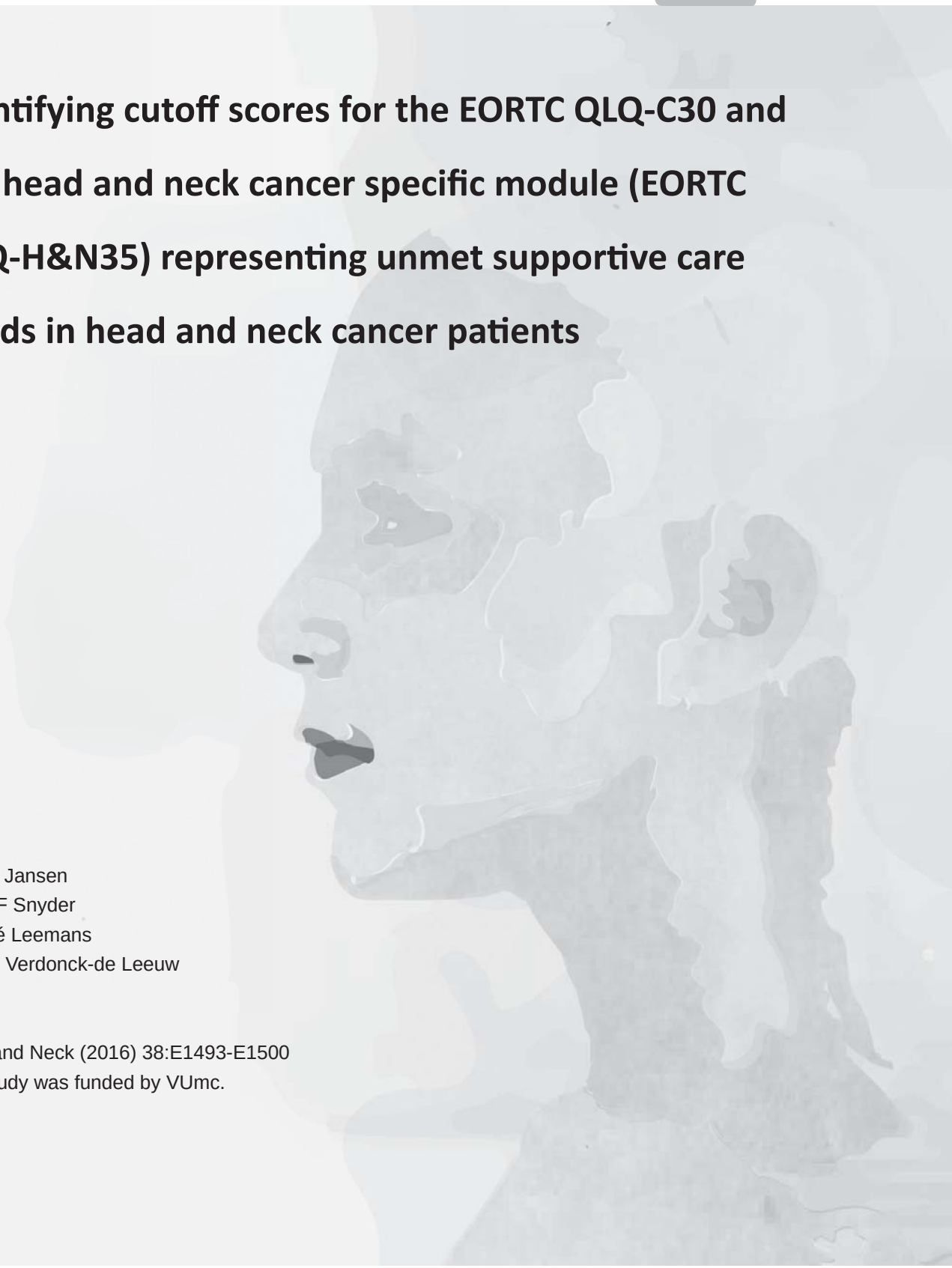
Identifying cutoff scores for the EORTC QLQ-C30 and the head and neck cancer specific module (EORTC QLQ-H&N35) representing unmet supportive care needs in head and neck cancer patients



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ABSTRACT

Background. For use of the European Organization for Research and Treatment of Cancer generic health-related quality of life module (EORTC QLQ-C30) and head and neck cancer (HNC)-specific module (QLQ-H&N35) in clinical practice, guidance on interpretation of individual patients' scores is needed.

Purpose. This study investigates cutoff scores for the EORTC QLQ-C30 and QLQ-H&N35 to identify HNC patients who may require clinical attention.

Methods. Ninety-six HNC patients completed the EORTC QLQ-C30, QLQ-H&N35 and questions on supportive care needs. For all EORTC domains with the ability to discriminate between patients with and without unmet needs (area under the receiver operating characteristic curve (AUC) ≥ 0.70), the accuracy (e.g., sensitivity and specificity) of potential cutoff scores were calculated.

Results. Cutoff scores (sensitivity ≥ 0.80 and specificity ≥ 0.60) of 90 (functioning domains) and 5 - 10 (symptom domains) were found on seven of 28 continuous EORTC QLQ-C30 and QLQ-H&N35 domains. Borderline cutoff scores (sensitivity ≥ 0.70 and specificity ≥ 0.60 or sensitivity ≥ 0.80 and specificity ≥ 0.50) were found on five other domains.

Conclusion. This study provided cutoff scores on the EORTC QLQ-C30 and QLQ-H&N35 based on patients' perceptions of their needs for supportive care. Future research is needed on the replicability of these cutoff scores.

INTRODUCTION

Head and neck cancer (HNC) patients are often confronted with general cancer or HNC-specific problems caused by the tumor or its treatment, such as fatigue[1], anxiety[2], depression[3], swallowing problems[4], restrictions in speech[5] and nutrition[6]. These problems can significantly impair patients' health-related quality of life (HRQOL)[1,6,7].

Several patient-reported outcome measures (PROMs) have been developed for research purposes to gain insight into patients' functioning and problems influencing their HRQOL. The European Organization for Research and Treatment of Cancer (EORTC) generic (EORTC QLQ-C30)[8,9] and HNC-specific (EORTC QLQ-H&N35)[10] module are frequently used PROMs measuring HRQOL in research targeting HNC patients. Nowadays, PROMs – including the EORTC measures – are also being used in clinical practice for individual patient management (i.e., screen for problems and monitor progress)[11-16]. Usage of PROMs in clinical practice may improve patient-clinician communication and may improve patient outcomes[17].

For use of the EORTC measures in clinical practice, guidance on interpretation of individual patients' scores is needed. In other words, information on scores representing a problem for an individual patient that requires attention is needed[18]. One approach is to compare patients' scores with normative data from other patient populations or the general population. While normative data for the EORTC QLQ-C30 and QLQ-H&N35 in the general Dutch population have been reported[19,20], these normative data do not necessarily represent the score that discriminates between individual cancer patients with and without a perceived unmet need for supportive care. Therefore, Snyder et al.[21-23] identified cutoff scores on the EORTC QLQ-C30 that can discriminate between patients with and without perceived unmet needs as measured using the Supportive Care Needs Survey Short-Form 34 (SCNS-SF34)[24].

However, the previous studies of Snyder et al.[21-23] did not include HNC patients and did not include disease-specific modules, such as the EORTC QLQ-H&N35. The aim of the present study was to investigate whether the earlier defined cutoff scores on the EORTC QLQ-C30 from other cancer populations are replicable in HNC patients and to identify cutoff scores on the EORTC QLQ-H&N35 that discriminate between HNC patients with and without unmet needs as perceived by the patients themselves.

MATERIALS AND METHODS

Design and study measures

Patients in the post-treatment phase using OncoQuest at the Department of Otolaryngology – Head and Neck Surgery of VU University Medical Center (VUmc) in Amsterdam, the Netherlands from April to September 2013 were asked to participate in this cross-sectional study. OncoQuest is a touch-screen computer-assisted system aiming to monitor HRQOL in clinical outpatient practice[12,13]. Patients participating in OncoQuest are asked to complete several PROMs (including the EORTC QLQ-C30 and QLQ-H&N35) at their first visit to the outpatient clinic and at follow-up visits after treatment. Patients were included in this study when they were treated for cancer of the oral cavity, pharynx, larynx, nasal cavity or major salivary glands with curative intent, were in the post-treatment phase, and were older than 18 years. Patients were excluded when they had cognitive impairments or did not understand the Dutch language. According to the Dutch Medical Research Involving Human Subjects Act, ethical approval was not necessary, because patients were not subjected to procedures or required to follow rules of behavior.

Patients participating in OncoQuest were asked to participate in this study after they completed OncoQuest[12,13]. Patients willing to participate were asked to complete a questionnaire at home and return it in a pre-addressed and pre-stamped envelope. The questionnaire included items on HNC patients' need for supportive care.

The SCNS-SF34 was used to measure supportive care needs from the patient's perspective in the last month on 34 items representing physical & daily living, psychological, sexuality, patient care & support and health system & information needs[24,25]. Evidence supporting the validity of the SCNS-SF34 has been reported among English[25,26], French[27], German[28], Chinese[29,30] and Japanese[31] cancer populations. For usage in Dutch studies (including this study), the SCNS-SF34 has been translated into Dutch according to the EORTC translation guideline[32].

In addition to the SCNS-SF34, we used the SCNS-HNC, a PROM on the need for supportive care concerning eleven HNC-specific issues (e.g., problems with chewing and/or swallowing or problems with speech), developed by a multidisciplinary team consisting of a psychologist, speech pathologist, linguist, physician and health scientist. The SCNS-HNC has not yet been validated, whereas the SCNS-SF34 has been validated as previously reported, however, not among Dutch HNC patients. Only separate SCNS items were used

and no combination of items (i.e., SCNS domains) to define cutoff scores on the EORTC QLQ-C30 and QLQ-H&N35. The usage of SCNS items instead of domains, corresponds to previous studies by Snyder et al. in which SCNS items were shown to have better discriminative ability than SCNS domains[21-23].

On both the SCNS-SF34 and the SCNS-HNC, patients were asked to report their need for supportive care on a 5-point, two-level response scale[24]. The first level consists of two broad categories of need, i.e., 'no need' and 'some need'. The 'no need' scale is further subdivided into '1 = not applicable' for issues that were no problem to the patient and '2 = satisfied' for issues on which a patient needed support but the support was satisfactory. The 'some need' level has three categories indicating the level of need for additional care: 3 = low, 4 = moderate and 5 = high. Thus scores ≤ 2 indicate no unmet need and scores > 2 indicate some level of unmet need.

In addition, all patients included in this study completed the EORTC QLQ-C30 and QLQ-H&N35[8-10] using OncoQuest[12,13]. The 30-item EORTC QLQ-C30 (version 3.0) includes 15 different domains, namely a global HRQOL domain (2 items), five functioning domains: physical functioning (5 items), role functioning (2 items), emotional functioning (4 items), cognitive functioning (2 items) and social functioning (2 items), three symptom domains: nausea/vomiting (2 items), fatigue (3 items) and pain (2 items) and six single items relating to dyspnea, insomnia, loss of appetite, constipation, diarrhea and financial difficulties[8,9]. The EORTC QLQ-H&N35 module covers specific issues on HNC and comprises 18 different domains, namely seven symptom domains: oral pain (4 items), swallowing (5 items), senses (2 items), speech (3 items), social eating (4 items), social contact (5 items) and sexuality (2 items) and 11 single items covering problems with teeth, dry mouth, sticky saliva, cough, opening the mouth wide, feeling ill, weight loss or weight gain, use of nutritional supplements, feeding tubes, and painkillers[10]. For functioning domains and the global HRQOL domain, a higher score indicates a better level of functioning, while for the symptom domains, a higher score represents higher levels of symptoms or problems[8-10]. The EORTC QLQ-C30 and QLQ-H&N35 have both shown good psychometric properties (i.e., validity, reliability and responsiveness) in cancer patients[9,10].

Finally, socio-demographic characteristics (i.e., age and gender) were patient-reported and clinical characteristics (i.e., tumor site and disease stage) were retrieved from patients' medical records.

Table 1. Overview of hypothesized relationships between the EORTC QLQ-C30 and QLQ-H&N35 domains and SCNS-SF34 and SCNS-HNC items, and the resulting area under the ROC curve

EORTC QLQ-C30	Item of the SCNS-SF34 or SCNS-HNC and the corresponding area under the ROC curve
Hypothesized AUC < 0.70[1]	
Global quality of life	Item 'Feeling unwell a lot of the time (AUC = 0.812)'
Physical functioning	Items 'Pain (AUC=0.652)', 'Lack of energy/tiredness (AUC = 0.779)', 'Feeling unwell a lot of the time (AUC = 0.614)', 'Work around the home (AUC = 0.819)', 'Not being able to do the things you used to do (AUC = 0.730)' or 'Problems with mobility of head, neck and shoulders (AUC = 0.705)'
Role functioning	Items 'Work around the home (AUC = 0.788)' and 'Not being able to do the things you used to do (AUC = 0.724)'
Emotional functioning	Items 'Anxiety (AUC = 0.861)', 'Feeling down or depressed (AUC = 0.850)', 'Feelings of sadness (AUC = 0.853)', 'Fears about the cancer spreading (AUC = 0.792)', 'Worry that the results of treatment are beyond your control (AUC = 0.804)', 'Uncertainty about the future (AUC = 0.750)', 'Learning to feel in control of your situation (AUC = 0.846)', 'Keeping a positive outlook (AUC = 0.759)', 'Feelings about death and dying (AUC = 0.769)' or 'Concerns about the worries of those close to you (AUC = 0.728)'
Fatigue	Item 'Lack of energy/tiredness (AUC = 0.847)'
Pain	Item 'Pain (AUC = 0.666)'
Hypothesized AUC < 0.70[1]	
Cognitive functioning	Item 'Not being able to do the things you used to do (AUC = 0.646)'
Social functioning	Item 'Not being able to do the things you used to do (AUC = 0.875)'
Nausea/vomiting	Items 'Feeling unwell a lot of the time (AUC = 0.710)' and 'Being given information about aspects of managing your illness and side-effects at home (AUC = 0.617)'
Dyspnea	Items 'Feeling unwell a lot of the time (AUC = 0.626)' and 'Being given information about aspects of managing your illness and side-effects at home (AUC = 0.633)'
Insomnia	Items 'Lack of energy/tiredness (AUC = 0.569)', 'Feeling unwell a lot of the time (AUC = 0.647)' and 'Being given information about aspects of managing your illness and side-effects at home (AUC = 0.663)'
Loss of appetite	Items 'Feeling unwell a lot of the time (AUC = 0.629)', 'Being given information about aspects of managing your illness and side-effects at home (AUC = 0.642)' or 'Being informed about nutrition (AUC = 0.572)'
Constipation	Items 'Feeling unwell a lot of the time (AUC = 0.448)' and 'Being given information about aspects of managing your illness and side-effects at home (AUC = 0.524)'
Diarrhea	Items 'Feeling unwell a lot of the time (AUC = 0.612)' and 'Being given information about aspects of managing your illness and side-effects at home (AUC = 0.563)'
Financial problem	None

Table 1. Continued

EORTC QLQ-H&N35	Item of the SCNS-SF34 or SCNS-HNC
Hypothesized AUC ≥ 0.70[1]	
Oral pain	Item 'Pain (AUC = 0.739)'
Swallowing	Item 'Problems with chewing and/or swallowing (AUC = 0.814)'
Speech	Item 'Problems with speech (AUC = 0.840)'
Sexuality	Items 'Changes in sexual feelings (AUC = 0.822)', 'Changes in sexual relationships (AUC = 0.805)' or 'To be given information about sexual relationships (AUC = 0.567)'
Dry mouth	Item 'Problems with a dry mouth and/or sticky saliva (AUC = 0.754)'
Sticky saliva	Item 'Problems with a dry mouth and/or sticky saliva (AUC = 0.791)'
Hypothesized AUC < 0.70[1]	
Senses	Item 'Being informed about nutrition (AUC = 0.625)'
Social eating	Item 'Problems with chewing and/or swallowing (AUC = 0.741)'
Social contact	Items 'Problems with speech (AUC=0.639)' or 'Problems with hearing (AUC = 0.637)'
Teeth	Item 'Oral hygiene (AUC = 0.555)'
Opening mouth	Item 'Problems with chewing and/or swallowing (AUC = 0.649)'
Coughing	Item 'Being given information about aspects of managing your illness and side-effects at home (AUC = 0.629)'
Feeling ill	Item 'Feeling unwell a lot of the time (AUC = 0.717)'
Pain killers	None
Nutrition supplement	None
Feeding tube	None
Weight loss	None
Weight gain	None

Abbreviations: EORTC QLQ-C30, European Organization for Research and Treatment of Cancer generic health-related quality of life module; EORTC QLQ-H&N35, EORTC head and neck cancer-specific health-related quality of life module; SCNS-SF34, Supportive Care Needs Survey Short-Form 34; SCNS-HNC, Supportive Care Needs Survey Head and Neck Cancer Module; ROC, receiver operating characteristic; AUC, area under the ROC curve.
Underlined items are the items of the SCNS-SF34 or SCNS-HNC with best discriminative ability, which were used in further analyses.
[1] An AUC ≥ 0.70 is considered to indicate acceptable to excellent discriminative ability[33].

Statistical analyses

All analyses were performed using the IBM Statistical Package for the Social Science (SPSS) version 20 (IBM Corp., Armonk, NY USA). Socio-demographic and clinical characteristics of the study population were summarized using descriptive statistics (e.g., frequencies and percentages).

Based on previous studies on cutoff scores for the EORTC QLQ-C30 and researchers' expectations, we formulated *a priori* hypotheses on the EORTC QLQ-C30 and QLQ-H&N35 domains' ability to discriminate between patients with and without unmet needs based on items of the SCNS-SF34 and SCNS-HNC (i.e., item score > 2 versus score ≤ 2) (Table 1). For EORTC domains with content similar to items on the SCNS-SF34 or SCNS-HNC (e.g., the EORTC fatigue domain and the SCNS-SF34 item on lack of energy/tiredness) a better discriminative ability was hypothesized than for domains with less similar content (e.g., EORTC teeth domain and the SCNS-HNC item on oral hygiene). The ability of the EORTC domains to discriminate between HNC patients with and without unmet needs was investigated by calculating the area under the receiver operating characteristic curve (AUC). Although there are no firm cutoffs for AUC values that represent good discriminative ability, a score ≥ 0.70 is suggested to indicate acceptable to excellent discriminative ability[33].

In total, 37 hypotheses were formulated on 14 EORTC QLQ-C30 domains: 21 relationships on six EORTC QLQ-C30 domains were expected to demonstrate acceptable discriminative ability (i.e., an AUC ≥ 0.70), whereas 16 relationships on eight other EORTC QLQ-C30 domains were expected to show poor discriminative ability (i.e., an AUC < 0.70). In addition, 16 hypotheses were formulated on 13 EORTC QLQ-H&N35 domains: eight relationships on six EORTC QLQ-H&N35 domains were expected to demonstrate acceptable discriminative ability, whereas eight relationships on seven other EORTC QLQ-H&N35 domains were expected to demonstrate poor discriminative ability. Some SCNS-SF34 and SCNS-HNC items were hypothesized to be related to several different EORTC domains (e.g., the SCNS-SF34 item on 'Work around the home' was hypothesized to be related to physical functioning and role functioning), therefore, only 19 of the 34 SCNS-SF34 items and seven of the 11 SCNS-HNC items were used in this study.

For all EORTC domains with AUCs ≥ 0.70, the sensitivity, specificity, positive and negative predictive value of potential cutoff scores were calculated using descriptive statistics. For this study, potential cutoff scores were defined as candidate cutoff scores when sensitivity

≥ 0.80 and specificity ≥ 0.60 or as borderline candidate cutoff scores when sensitivity ≥ 0.70 and specificity ≥ 0.60 or sensitivity ≥ 0.80 and specificity ≥ 0.50. In addition, Pearson's correlation coefficient of the EORTC domain and the SCNS item was presented.

RESULTS

From April to September 2013, 139 patients who used the OncoQuest system for routine PROM assessment (including the EORTC QLQ-C30 and QLQ-H&N35) as part of standard clinical care during follow-up consultations were asked to participate in this study. In total 107 of 139 (77%) patients completed the questionnaire on their supportive care needs; these responders were comparable to non-responders regarding age, gender and clinical characteristics. For this particular study, 96 of 107 patients were included; 11 patients were excluded since they had a tumor other than HNC (n = 5), had lymph node metastasis of an unknown primary (n = 3), had a benign tumor (n = 1), received palliative treatment (n = 1) or EORTC data was not available (n = 1). Median time between completion of EORTC measures using OncoQuest and the questionnaire on their supportive care needs was 6 days (inter quartile range = 1 - 20). Most of the patients were male (61%) and were younger than 65 years (58%) (Table 2). The majority of patients had a tumor of the pharynx (35%), followed by the oral cavity (26%), larynx (25%), nasal cavity (7%) and major salivary glands (6%). More than half of all patients had stage III or IV disease (52%).

In total, 45 of the 53 (85%) *a priori* formulated hypotheses on the ability to discriminate between patients with and without unmet needs based on the SCNS-SF34 and SCNS-HNC were supported by the findings of this study. Of the six EORTC QLQ-C30 domains hypothesized to have acceptable discriminative ability to identify unmet needs based on the SCNS-SF34 or SCNS-HNC items (i.e., AUC ≥ 0.70), five domains (global quality of life, physical functioning, role functioning, emotional functioning, fatigue) showed acceptable discriminative ability (0.79 ≤ AUC ≤ 0.86). On the sixth domain, pain, a borderline AUC of 0.67 was found. Acceptable discriminative ability was (unexpectedly) also found on the EORTC QLQ-C30 social functioning (AUC = 0.88) and nausea/vomiting domains (AUC = 0.71). On the EORTC QLQ-H&N35, six domains were hypothesized to demonstrate acceptable discriminative ability (oral pain, swallowing, speech, sexuality, dry mouth and sticky saliva), all of which were supported by our findings (0.74 ≤ AUC ≤ 0.84). Acceptable discriminative ability was (unexpectedly) also found on social eating (AUC = 0.74) and feeling ill (AUC = 0.72).

Table 2. Patient characteristics

Characteristics (n = 96)	No. of patients (%)
Age	
- < 65 years	56 (58%)
- ≥ 65 years	40 (42%)
Sex	
- Male	59 (61%)
- Female	37 (39%)
Living arrangements	
- Living alone	18 (19%)
- Living with a partner	57 (59%)
- Living with (a partner and) children	19 (20%)
- Living in an institution	1 (1%)
- Other arrangements (e.g., living with parents)	1 (1%)
Education level	
- Elementary and lower education	43 (45%)
- Secondary education	31 (32%)
- Higher education	22 (23%)
Tumor site	
- Oral cavity	25 (26%)
- Pharynx	34 (35%)
- Larynx	24 (25%)
- Nasal cavity	7 (7%)
- Major salivary glands	6 (6%)
Disease stage (UICC)	
- Stage I	21 (22%)
- Stage II	21 (22%)
- Stage III	18 (19%)
- Stage IV	34 (33%)
- Unknown	2 (2%)
Type of treatment	
- Surgery	24 (25%)
- Radiotherapy	23 (24%)
- Surgery and (chemo)radiation	29 (30%)
- Chemoradiation	20 (21%)
Time since last cancer treatment	
- < 6 months	19 (20%)
- 6 - 18 months	18 (10%)
- 18 - 30 months	11 (11%)
- > 30 months	48 (50%)

Abbreviations: UICC, International Union Against Cancer.

For all 15 EORTC QLQ-C30 and QLQ-H&N35 domains with acceptable discriminative ability and the pain domain with a borderline acceptable discriminative ability, the sensitivity, specificity and positive and negative predictive value of various cutoff scores were calculated. On the EORTC domains on which multiple SCNS-SF34 or SCNS-HNC items showed an AUC ≥ 0.70, the SCNS-SF34 or SCNS-HNC item with the highest AUC was used in further analyses. Since the SCNS-SF34 items found to have the strongest association with the EORTC QLQ-C30 emotional functioning domain in this study (i.e., 'anxiety') was different from the item ('feelings of sadness') in two previous studies[21,22], the sensitivity, specificity and positive and negative predictive value of various cutoff scores on the EORTC QLQ-C30 emotional functioning domain was calculated using both items.

In Table 3, candidate cutoff scores (sensitivity ≥ 0.80 and specificity ≥ 0.60) and borderline candidate cutoff scores (sensitivity ≥ 0.70 and specificity ≥ 0.60 or sensitivity ≥ 0.80 and specificity ≥ 0.50) on all domains with acceptable discriminative ability are presented. On four of the eight EORTC QLQ-C30 domains with acceptable discriminative ability (physical functioning, role functioning, emotional functioning and social functioning), we were able to identify candidate cutoff scores with sensitivity ≥ 0.80 and specificity ≥ 0.67. On the global quality of life and fatigue domain, borderline candidate cutoff scores were found (with sensitivity = 0.70 and specificity = 0.78 and sensitivity = 0.90 and specificity = 0.58, respectively). On the pain and nausea/vomiting domains no (borderline) candidate cutoff scores were identified, since the highest reachable sensitivity scores were respectively 0.62 and 0.50.

Of the eight EORTC QLQ-H&N35 domains with acceptable discriminative ability, for three domains (swallowing, sexuality and sticky saliva) candidate cutoff scores were identified with sensitivity ≥ 0.85 and specificity ≥ 0.62. On the EORTC QLQ-H&N35 domain on oral pain, speech and social eating borderline candidate cutoff scores were identified (all of which had sensitivity ≥ 0.72 and specificity ≥ 0.61 or sensitivity = 0.90 and specificity = 0.56). On the domains dry mouth and feeling ill no candidate cutoff scores were identified.

Table 3: Sensitivity, specificity and positive and negative predictive value of different cutoff scores on various EORTC domains

EORTC domain	SCNS-SF34 or SCNS-HNC item	Correlation	Cut-off[1]	Sensitivity	Specificity	PPV	NPV
EORTC QLQ-C30							
Global quality of life[2]	Feeling unwell a lot of the time[3]	-0.501	60	0.50	0.97	0.63	0.94
			70	0.60	0.87	0.35	0.95
			80	0.70	0.78	0.27	0.96
			90	0.90	0.47	0.16	0.98
Physical functioning[2]	Work around the home[3]	-0.435	80	0.45	0.91	0.56	0.86
			85	0.60	0.87	0.55	0.89
			90	0.85	0.67	0.41	0.94
			100	0.95	0.49	0.33	0.97
Role functioning[2]	Work around the home[3]	-0.443	60	0.30	0.88	0.40	0.83
			80	0.65	0.82	0.48	0.90
			90	0.85	0.71	0.44	0.95
Emotional functioning[2]	Anxiety	-0.618	70	0.53	0.90	0.53	0.90
			80	0.65	0.81	0.42	0.91
			90	0.82	0.71	0.38	0.95
			100	1.00	0.53	0.32	1.00
	Feelings of sadness[3]	-0.610	70	0.59	0.91	0.59	0.91
			80	0.71	0.82	0.46	0.93
			90	0.82	0.71	0.38	0.95
			100	0.94	0.52	0.30	0.98
Fatigue[2]	Lack of energy/tiredness[3]	0.737	**20**	0.90	0.58	0.49	0.93
			30	0.63	0.83	0.63	0.83
			40	0.50	0.97	0.88	0.81
Pain[2,4]	Pain[3]	0.376	10	0.62	0.69	0.24	0.92
			20	0.39	0.82	0.25	0.90
Social functioning	Not being able to do the things you used to do	-0.706	80	0.52	0.99	0.93	0.85
			90	0.80	0.92	0.77	0.93
Nausea/ vomiting	Feeling unwell a lot of the time	0.434	10	0.50	0.91	0.39	0.94
			20	0.30	0.98	0.60	0.92

Table 3: Continued

EORTC domain	SCNS-SF34 or SCNS-HNC item	Correlation	Cut-off[1]	Sensitivity	Specificity	PPV	NPV
EORTC QLQ-H&N35							
Oral pain	Pain	0.302	5	0.85	0.45	0.19	0.95
			10	0.77	0.61	0.24	0.94
			20	0.62	0.80	0.32	0.93
			30	0.46	0.87	0.35	0.91
Swallowing	Problems with chewing and/or swallowing	0.580	**5**	0.88	0.62	0.45	0.94
			10	0.72	0.75	0.50	0.88
			20	0.52	0.86	0.57	0.84
Speech	Problems with speech	0.619	**10**	0.90	0.56	0.33	0.96
			20	0.74	0.77	0.44	0.92
			30	0.74	0.87	0.58	0.93
			40	0.37	0.97	0.78	0.86
Sexuality	Changes in sexual feelings	0.440	**10**	0.88	0.71	0.28	0.98
			20	0.75	0.74	0.27	0.96
			40	0.63	0.89	0.42	0.95
			60	0.38	0.92	0.38	0.92
Dry mouth	Problems with a dry mouth and/or sticky saliva	0.474	10	0.94	0.31	0.43	0.91
			40	0.62	0.81	0.64	0.79
			70	0.18	0.97	0.75	0.68
Sticky saliva	Problems with a dry mouth and/or sticky saliva	0.535	**10**	0.85	0.65	0.57	0.89
			40	0.47	0.89	0.70	0.75
Social eating	Problems with chewing and/or swallowing	0.420	**5**	0.72	0.63	0.41	0.87
			10	0.64	0.82	0.55	0.87
			20	0.36	0.93	0.64	0.81
Feeling ill	Feeling unwell a lot of the time	0.464	10	0.50	0.92	0.42	0.94
			40	0.20	1.00	1.00	0.92

Abbreviations: EORTC, European Organization for Research and Treatment of Cancer; SCNS-SF34, Supportive Care Needs Survey Short-Form 34; SCNS-HNC, Supportive Care Needs Survey Head and Neck Cancer Module; QLQ-C30, generic health-related quality of life module; QLQ-H&N35, head and neck cancer-specific health-related quality of life module; PPV, positive predictive value; NPV, Negative predictive value.

[1] Cutoff scores are underlined and in bold when sensitivity ≥ 0.80 and specificity ≥ 0.60 (candidate) and in bold when sensitivity ≥ 0.70 and specificity ≥ 0.60 or sensitivity ≥ 0.80 and specificity ≥ 0.50 (borderline candidate). When applicable, potential cutoff scores surrounding the candidate cutoff scores were also presented.

[2] Cutoff scores on these domains based on the SCNS-SF34 have been reported in previous studies on breast, prostate, colorectal and lung cancer patients[21-23].

[3] Same SCNS-SF34 or SCNS-HNC item as used in previous studies[21-23].

[4] Although discriminative ability was borderline (AUC = 0.67) the sensitivity, specificity and positive and negative predictive values of cutoff scores were reported, since previous studies reported an acceptable discriminative ability (0.74 ≤ AUC ≤ 0.78) on this domain[21-23].

DISCUSSION

This study aimed to investigate whether the earlier defined cutoff scores on the EORTC QLQ-C30 in breast, prostate, colorectal, and lung cancer patients are replicable in HNC patients and to identify cutoff scores on the EORTC QLQ-H&N35. Cutoff scores on the EORTC QLQ-C30 and QLQ-H&N35 are helpful in clinical practice for identifying HNC patients who require more attention[18].

Results showed that the cutoff scores on the EORTC QLQ-C30 domains that represent in our opinion the most optimal trade-off between sensitivity and specificity in the present study (i.e., sensitivity ≥ 0.80 and specificity ≥ 0.60 or sensitivity ≥ 0.70 and specificity ≥ 0.60 (borderline) or sensitivity ≥ 0.80 and specificity ≥ 0.50 (borderline)) were partly similar to previously defined cutoff scores[21-23]. We found cutoff scores of 90 on physical functioning, role functioning and emotional functioning and additional borderline cutoff scores on global quality of life (80) and fatigue (20), which were similar to the cutoff scores in previous studies[21-23]. On the pain domain, no cutoff scores were identified with acceptable sensitivity and specificity in our study, while cutoff scores of 10 and 20 were proposed in previous studies[21-23]. Besides the defined cutoff scores on these five domains, we also identified a cutoff score of 90 on the domain on social functioning for use in HNC patients. In previous studies no cutoff scores were identified for this domain, since the discriminative ability on social functioning was borderline unacceptable (i.e., AUC = 0.64 - 0.68)[21-23]. In addition to cutoff scores on the EORTC QLQ-C30, we also identified cutoff of scores of 5 or 10 on the swallowing, sexuality and sticky saliva domain of the EORTC QLQ-H&N35 and borderline cutoff scores ranging from 5 - 30 on the domains on oral pain, speech and social eating. For external validation purposes, future studies are recommended to investigate whether these newly defined cutoff scores on the EORTC QLQ-H&N35 are replicable in other Dutch and non-Dutch HNC patients. Also, future studies are recommended on the replicability of the newly defined cutoff score on the EORTC QLQ-C30 social functioning domain in HNC populations and whether it results in an acceptable trade-off between sensitivity and specificity in other cancer populations as well. Besides, it should be investigated whether use of the defined cutoff scores on the EORTC QLQ-C30 and QLQ-H&N35 also identify patients with problems, who do not identify the corresponding unmet needs themselves. These patients may not identify their need for supportive care, perhaps since they are not aware of potential care available for their problem (e.g., regarding fatigue or insomnia), or are focused on other issues; however, they may still benefit from supportive care.

In the present study, the defined cutoff scores on the EORTC QLQ-H&N35 domain of oral pain was higher compared to mean scores in a reference group of the Dutch general population[20]. At least one of the defined cutoff scores on all other EORTC QLQ-C30 and QLQ-H&N35 domains were comparable to normative data[19,20]. When using our defined (higher) cutoff score on the domain of oral pain, patient scores will be less often identified as potentially concerning compared to using the normative data[20]. This may be appropriate, since this study aimed to target patients with unmet needs for supportive care and did not aim to target patients who experience problems but do not have a need for additional supportive care.

On seven of the 28 continuous EORTC QLQ-C30 and QLQ-H&N35 domains (physical functioning, role functioning, emotional functioning, social functioning, swallowing, sexuality and sticky saliva), we were able to identify cutoff scores with sensitivity ≥ 0.80 and specificity ≥ 0.60. In addition, five other domains (global quality of life, fatigue, oral pain, speech and social eating) had at least one cutoff score with sensitivity ≥ 0.70 and specificity ≥ 0.60 or sensitivity ≥ 0.80 and specificity ≥ 0.50, which we regarded as borderline. This was largely in line with expectations, since we had hypothesized acceptable discriminative ability on only 12 domains; for two of these domains (pain and dry mouth) no (candidate) cutoff scores were identified. Future studies should focus on identifying cutoff scores on these two domains, as well as the other domains on which, as hypothesized, no cutoff scores were found.

The appropriateness of a cutoff score involves a trade-off between sensitivity and specificity and depends on the action taken in response to scores highlighted as potentially concerning. When the PROM only signals a need for further evaluation of the potential problem, followed by additional supportive care if required, sensitivity may be favored over specificity. In contrast, specificity may be favored over sensitivity if a deviating score is directly followed by an action (e.g., prescription of medication or other treatment decisions) without further evaluation by a clinician or nurse specialist. Since PROMs measuring HRQOL mostly have a signaling function, it may be acceptable to favor sensitivity over specificity.

Besides making a trade-off between sensitivity and specificity, the appropriateness of cutoff scores can be evaluated based on positive and negative predictive values. In this study, negative predictive values of both candidate and borderline cutoff scores were high (ranging from 0.88 to 1.00), indicating that 88 to 100% of patients were correctly identified as having no problem. The positive predictive value of most cutoff scores was

quite low (most positive predictive values were ≤ 0.45; range: 0.24 to 0.77), indicating that for several cutoff scores > 55% of patients were signaled with a deviating score while not perceiving an unmet need. We believe that this low positive predictive value may not be especially concerning, since a deviant score is expected to be followed by non-intensive further evaluation (e.g., asking the patient about the potential concerning problem). However, as previously reported[21], it is important to minimize alert fatigue caused when a high proportion of signaled patients do not need additional care.

A potential limitation of this study is that cutoff scores on the EORTC QLQ-C30 and QLQ-H&N35 are defined using the SCNS-SF34 and SCNS-HNC as the anchor. Although the SCNS-SF34 is validated in other non-Dutch studies[25-31], this PROM has not yet been validated among Dutch HNC patients. The SCNS-HNC is newly developed and has not yet been validated. Further research to validate the SCNS-SF34 in Dutch HNC patients and the SCNS-HNC generally is needed to confirm the findings reported here.

Another limitation is the discrepancy in recall period, since patients did not complete the EORTC questionnaires and SCNS-SF34 and SCNS-HNC at the same time (median difference was 6 days), and the EORTC and SCNS questionnaires have different recall periods (1-week compared to 1-month). However, since patients completed the SCNS-SF34 and SCNS-HNC after completion of the EORTC measures, the different recall periods of the questionnaires may partly counteract the discrepancy due to differences in when the questionnaires were completed. In addition, patients were recruited after primary treatment for HNC via OncoQuest[12,13], which may have resulted in selection bias, and the sample size of this study was small. Future studies should therefore be performed to confirm the results of this study regarding cutoff scores on especially the EORTC QLQ-H&N35 in larger HNC populations including patients at time of diagnosis, during treatment, and in the palliative or end-of-life phase of the disease.

In summary, we were able to replicate previously defined cutoff scores on four of the functioning domains (80 - 100) and fatigue domain (20) of the EORTC QLQ-C30 and to identify new cutoff scores on the EORTC QLQ-C30 social functioning domain (90) and several EORTC QLQ-H&N35 domains (5 - 30) in HNC patients. These cutoff scores may assist in interpretation of individual patient's scores in clinical practice. Future research is needed to investigate whether the newly defined cutoff scores on the EORTC QLQ-C30 and QLQ-H&N35 can be replicated in other patient cohorts, and the usefulness of the cutoff scores in clinical practice.

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