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A comprehensive assessment protocol including patient reported outcomes, physical tests, and biological sampling in newly diagnosed patients with head and neck cancer: is it feasible?

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Abstract

Purpose Large cohort studies are needed taking into account cancer-related, personal, biological, psychobehavioral, and lifestyle-related factors, to guide future research to improve treatment and supportive care. We aimed to evaluate the feasibility of a comprehensive baseline assessment of a cohort study evaluating the course of quality of life (QoL).

Methods Newly diagnosed head and neck cancer (HNC) patients were asked to participate. Assessments consisted of questionnaires (635 items), a home visit (including a psychiatric interview, physical tests, and blood and saliva collection), and tissue collection. Representativeness of the study sample was evaluated by comparing demographics, clinical factors, depression, anxiety, and QoL between responders and non-responders. Feasibility was evaluated covering the number of questions, time investment, intimacy, and physical burden.

Results During the inclusion period (4 months), 15 out of 26 (60 %) patients agreed to participate. Less women participated, 13 % in responders group versus 63 % in non-responders group ($p=0.008$). No other differences were found between responders and non-responders. Responders completed more than 95 % of the questionnaires' items and rated the number of questions, time investment and intimacy as feasible, and the physical and psychological burden as low. It took on average 3 h to complete the questionnaires and 1.5 h for the home visit.

Conclusions This study reveals that a comprehensive assessment including various questionnaires, physical measurements, and biological assessments is feasible according to patients with newly diagnosed HNC. A large prospective cohort study has started aiming to include 739 HNC patients and their informal caregivers in the Netherlands.

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Introduction

Worldwide, each year, head and neck cancer (HNC) accounts for more than 633,000 new cases and over 355,000 deaths [1]. In the Netherlands, the incidence of HNC increased from 2,474 in 2001 to 2,970 in 2011 [http://www.cijfersoverkanker.nl/. 2013. Ref Type: Online Source], mainly due to aging, increased tobacco consumption by females in the 1980s, and an increasing number of human papilloma virus-related oropharyngeal carcinomas [http://data.euro.who.int/hfadb. 2014. Ref Type: Online Source, 2,

3]. Current 5-year survival rate of patients with advanced HNC in the Netherlands is approximately 60 % [http://www.cijfersoverkanker.nl/. 2013. Ref Type: Online Source]. For certain subsites, e.g., oropharyngeal carcinoma, survival is improving [4]. Due to the increasing incidence and improved survival rates, more patients with HNC have to cope with various physical and psychosocial problems associated with the cancer diagnosis and treatment, such as decreased general and mental health, oral dysfunction, swallowing and speech problems, and emotional distress, severely compromising health-related quality of life (HRQoL) [5–12]. Compared to other types of cancer, including breast, colon, and prostate cancers, HNC patients report high levels of distress [13]. At the same time, an increasing number of studies suggest that HRQoL has prognostic value for survival [14–20]. However, most previous studies on HRQoL and survival in HNC patients had some limitations related to relatively small sample sizes, the focus on specific subsites of HNC, adjustment for only a few confounders (e.g., lifestyle, demographic, and clinical characteristics), or inclusion of only a few aspects of HRQoL (16–25). Furthermore, little is known about the course of HRQoL of patients with HNC and its determinants across the cancer trajectory. Previous studies showed that several domains of HRQoL, including general health, mental health, physical function, appearance, employment, and social functioning declined during and immediately after treatment and improved after 6 months [5, 6, 10–12, 21–24]. Studies including long-term follow-up showed that HRQoL stabilized 1 year after treatment and was not significantly different from baseline levels at 5-year follow-up [5–7, 23, 24]. However, Mehanna et al. [12] reported 10 years after diagnosis, significantly lower HRQoL scores than before treatment, which was recently confirmed by Oskam et al. [25].

A recent review among patients with HNC [26] showed that the majority of studies examining the course of HRQoL over time were limited by their retrospective study design, their focus on only a few aspects of HRQoL instead of all domains [27], the use of patient-reported outcomes (PROs) only, the small sample size, and lack of pre-treatment measurements of HRQoL [28]. In addition, studies examining the association between HRQoL and survival lacked to adjust for all relevant confounders and different study designs were used [29]. Therefore, there is need for a large multi-institutional prospective cohort study evaluating the course of HRQoL in patients with HNC and its relation with survival integrating all relevant cancer-related, personal, genetic, biological, psychobehavioral, physical, lifestyle-related, and social factors. Comprehensive insight in all these factors assessed in a standardized manner is necessary to unravel these complex associations. A study of this magnitude has never been carried out among patients with HNC, and it is unclear whether it is feasible to conduct such an extensive objective assessment of physical and cognitive function, lifestyle, a psychiatric

interview, and collection of blood, saliva, and tumor tissue, in addition to a large number of PROs. Thus, the aim of the present study is to assess the feasibility of a comprehensive baseline assessment among patients with HNC.

Materials and methods

Sample and setting

As part of clinical routine in our institution, all newly diagnosed HNC patients are asked to fill out questionnaires on HRQoL and emotional distress during their first visit via OncoQuest [30]. OncoQuest is a touch screen computer system to monitor HRQoL in clinical practice and includes three questionnaires: the European Organization for Research and Treatment of Cancer (EORTC), Quality of Life Questionnaire core module (QLQ-C30), [31, 32], EORTC Head and Neck Module (HN35) [33], and Hospital Anxiety and Depression Scale (HADS) [34].

The 30-item EORTC QLQ-C30 includes a global quality of life scale, five function scales regarding physical, role, emotional, cognitive, and social functioning, three symptom scales (nausea and vomiting, fatigue, and pain), and six single items related to dyspnea, insomnia, loss of appetite, constipation, diarrhea, and financial difficulties [31, 35]. The 35-item EORTC QLQ-HN35 is a tumor-specific module addressing symptoms specifically associated with HNC, including pain, swallowing, senses, speech, social eating, social contact, and sexuality, as well as ten single items covering problems with teeth, dry mouth, sticky saliva, cough, opening the mouth wide, weight loss, weight gain, use of nutritional supplements, feeding tubes, and painkillers [32]. The HADS is a 14-item scale for measuring emotional distress and includes a total scale and an anxiety (HADS-A) and depression (HADS-D) subscale [34]. A total score of >15 is used as an indicator of a high psychological distress. For the subscales, cutoff points of ≥8 are indicators of high levels of anxiety or depression.

From January to mid-April 2012, every new patient with HNC was screened for eligibility for the current feasibility study. Patients presenting with oral, oropharyngeal, hypopharyngeal, and laryngeal cancers and patients with neck metastasis of unknown primary tumor with proven squamous cell histology (aged 18 years or older, treated with curative intent), who were able to write, read, and speak Dutch were eligible. Patients suffering from severe psychiatric comorbidities (e.g., schizophrenia, Korsakov's syndrome, and severe dementia) were excluded. Eligible patients were asked to participate in this feasibility study by the treating surgeon, and subsequently, the research physician provided more detailed information about the study and handed out written information. Non-participants were asked for their reason for not participating. All patients signed an informed consent

statement prior to participation. The Institutional Review Board of the VU University Medical Center approved the study.

Procedures and assessments

After all eligible patients filled out the three questionnaires (EORTC QLQ C30, EORTC HN35, HADS) as clinical procedure, study participants filled out the comprehensive baseline assessment, consisting of 36 questionnaires and in total 762 items, which took place before the start of treatment. The questionnaires consisted variable subdomains, including general and disease-specific QoL, cancer-related, personal, psychobehavioral, physical, lifestyle-related, social factors, and health care costs (Table 1). According to patient's preference, the PROs were sent by postal mail, or a link was e-mailed to fill out the PROs via internet. Subsequently, the research physician visited the patients at their homes or in the hospital according to preference of the patients, to conduct a psychiatric interview, physical tests, and collection of blood. At the end of the visit, patients were instructed to collect five saliva samples during the same evening and next morning and to wear an accelerometer (Actitrainer, Actigraph, Fort Walton Beach, Florida) for the next 7 days. Three to 5 days after the home visit, a telephone interview was conducted to assess diet using a 24-h recall. Tumor tissue was gathered during the participants' panendoscopic procedure, which is performed as a part of the diagnostic workup. This procedure aims to determine the field of surgery and to investigate the presence of other tumors. During this panendoscopy, a supplemental biopsy was taken for the current study besides the diagnostic tissue collection for the pathology department. An overview of all outcome measures included in the baseline assessment protocol is presented in Table 1. The assessment protocol was developed in collaboration with the coordinator of the Netherlands Study of Depression and Anxiety (NESDA) study [33]. NESDA is a large prospective cohort study which aims to describe the long-term course and consequences of depressive and anxiety disorders.

Outcome measures

The primary outcome of this study was the feasibility of the baseline assessment protocol, as evaluated by representativeness of the study population, achievability of baseline assessments, and accuracy of the protocol.

Representativeness was assessed by the following questions:

– What percentage of eligible patients is willing to participate?
– What are the main reasons for not participating?

– Are there differences between participants and non-participants regarding age, gender, diagnosis, comorbidity, stage, treatment, HRQoL, and emotional distress?

Achievability was evaluated by the following items:

– A study-specific questionnaire consisting of four-point Likert scales (not feasible, a bit feasible, quit feasible, very much feasible) covering the number of items, time investment, intimacy and burden of the PROs, and the home visit.
– The number of items successfully completed was registered as well as the time needed to complete the PROs, as estimated by patients and the home visits as measured by a research physician.

Accuracy of the assessment protocol was evaluated using the following questions:

– Is the protocol clear to other assessors (i.e., two experienced fieldworkers and a coordinator from the NESDA study)?
– Is the assessment protocol complete, clear, and accurate according to the research physician (A.N.)?

Statistical analysis

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) 20.0 (SPSS Inc., Chicago, IL). Descriptive statistics (mean/standard deviation (SD)/proportions) were generated for demographic and clinical characteristics, emotional distress, and HRQoL and questions on representativeness and achievability.

Differences in age, gender, diagnosis, comorbidity, stage, treatment, emotional distress, and HRQoL between participants and non-participants were tested with Mann-Whitney U test or χ^2 test. For the comparison of emotional distress and HRQoL, we used results from the OncoQuest database.

Results

Representativeness

During a time period of 14 weeks, 26 eligible patients were asked, of whom 15 (58 %) were willing to participate (Fig. 1). The main reason for not participating was the high burden of recently being diagnosed with cancer, leaving no room for additional inconvenience ($n=8$; 30 %). However, all of these patients indicated that they would have been interested in participation at another point in time. Other reasons for non-

Table 1 Overview of all outcome measures included in the assessment protocol: patient-reported outcome, (home) visit (physical tests and interviews), and biological and clinical factors

Outcomes	Measurement instrument	Number of items
Patient-reported outcome		
Quality of life		
Generic	EuroQuol-5D (EQ-5D)	6
Disease-specific	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-core 30 (EORTC QLQ-C30)	30
Tumor-specific	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire module, Head and Neck 35 (EORTC QLQ-HN35)	35
Speech	Speech Handicap Index (SHI)	31
Swallowing	Swallowing QoL Questionnaire (SwalQoL)	47
Shoulder	Shoulder Disability Questionnaire (SDQ)	16
Hearing	Caron questionnaire on hearing	19
Malnutrition	Short Nutritional Assessment Questionnaire (SNAQ)	4
Cancer-related factors		
Comorbidity	Adult comorbidity evaluation (ACE-27)	2
Personal factors		
Personality	Neuroticism-Extroversion-Openness-Five factor inventory (*NEO-FFI*)	60
Locus of control	Pearlin and Schooler mastery scale (PSMS)	5
Coping	Mental Adjustment to Cancer scale (MAC)	39
Self-efficacy	Generalized self-efficacy scale (GES)	10
Well-being	Posttraumatic Growth Inventory (PTGI)	21
Physical appearance	Body Image Scale (BIS)	10
Life events	Brugha Questionnaire	13
Coping	Utrechtse Coping List (UCL)	46
Psychobehavioral factors		
Severity anxiety/depression	Hospital Anxiety and Depression Scale (HADS)	14
Fatigue	Multidimensional Fatigue Inventory (MFI)	20
Fatigue	Fatigue Quality List (FQL)	1
Sleep quality	Pittsburgh Sleep Quality Index (PSQI)	15
Fear of recurrence	Cancer Worry Scale (CWS)	8
Cognition	Cognitive Failure Questionnaire (CFQ)	25
Physical factors		
Sexual function		
Males	International index of Erectile Function (IIEF)	19
Females	Female Sexual Function Index (FSFI)	15
Females	Study-specific questionnaire on fertility	16
Lifestyle-related factors		
Alcohol intake	Study-specific questions	13
Alcohol dependence	Study-specific questions	7
Drug use	Study-specific questions	7
Smoking	Study-specific questions	8
Nicotine dependence	Study-specific questions	5
Physical activity	Physical Activity Scale for the Elderly (PASE)	31
Leisure	Study-specific questions	15
Social factors		
Social support	Social Support List Interactions (SSL-I12)	12
Participation	Impact on Participation and Autonomy (IPA)	43
Health care use/costs		
Need and use care	Study-specific questionnaire	28

Table 1 (continued)

Outcomes	Measurement instrument	Number of items
Costs	Trimbos and iMTA questionnaire on Costs associated with Psychiatric illness (TiC-P): Adapted version for HNC	30
(Home) visit		
Personal factors		
Demographic	Standard questions	23
Socioeconomic status/literacy	Standard questions	27
Psychobehavioral factors		
Presence MDD	Composite international diagnostic interview (CIDI)—Major Depressive Disorder (MDD)	Variable
Anxiety disorder	Composite international diagnostic interview (CIDI)—Anxiety disorders (GAD, SOC, PAN, AG)	Variable
Pain	Brief Pain Inventory (BPI)	13
Physical factors		
Speech quality	Speech recording (perceptual and objective analyses)	n.a.
Pulmonary function	Peak flow	n.a.
Strength—upper extremity	JAMAR handgrip dynamometer	n.a.
Strength—lower extremity	30s chair stand test	n.a.
Cardiorespiratory fitness	Chester Step test	n.a.
Body composition	Height, weight, body mass index, waist+hip circumference, thickness of four skin folds	n.a.
Blood pressure	Systolic and diastolic blood pressure	n.a.
Visual motor processing speed	Trail making test part A	n.a.
Executive functioning	Trail making test part B	n.a.
Activity monitoring	Accelerometer	n.a.
Food	24-h recall	n.a.
Social factors		
Loneliness	De Jong-Gierveld Loneliness Scale	11
Health care use/costs		
Work productivity	Productivity and disease questionnaire (PRODISQ)	14
Biological and clinical factors		
Cancer-related factors		
Cancer location/stage	Standard questions, from medical record	n.a.
Treatment modality	Standard questions, from medical record	n.a.
Biological factors		
Tumor markers	Tumor tissue	n.a.
Biomarkers	Blood	n.a.
General laboratory	Blood	n.a.
DNA	Blood	n.a.
Proteomics	Blood	n.a.
Gene expression (RNA)	Blood	n.a.

MDD major depressive disorder, *n.a.* not applicable, *AD* generalized anxiety disorder, *SOC* social phobia, *PAN* panic disorder, *AG* agoraphobia

participation were not willing to participate in any research project (*n*=2; 8 %) or not willing to participate in this specific study protocol (*n*=1; 4 %).

Except for gender, no differences in demographic and clinical characteristics, emotional distress, and HRQoL were found between participants and non-participants. The proportion of women among non-participants (64 %) was higher than among participants (13 %), *p*=0.008 (Table 2).
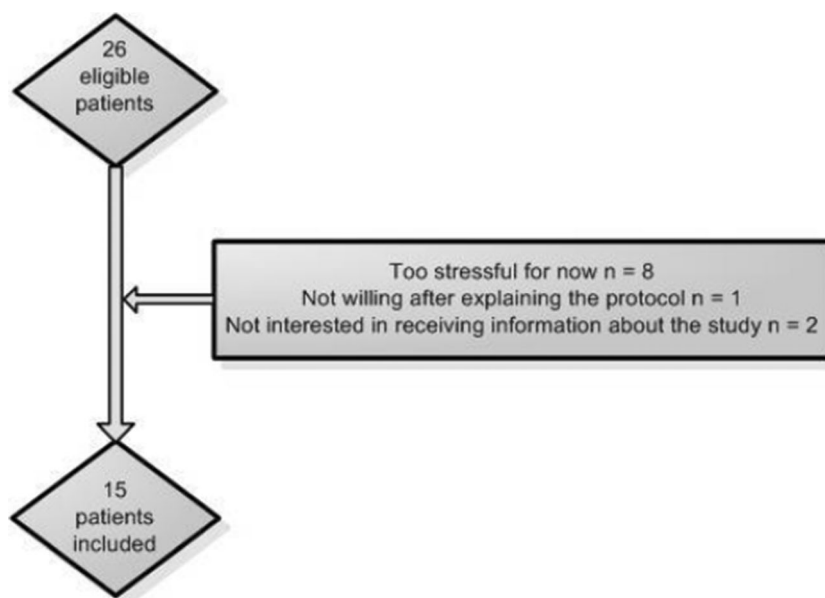
One participant (7 %) and two non-participants (18 %) did not fill out OncoQuest, and consequently, their data on HRQoL and psychological distress were missing.

Achievability

All participating patients filled out the questionnaires with 95–99 % (*n*=8) to 100 % (*n*=7) of the items completed. Two

Fig. 1 Flowchart of all eligible patients and the reasons for non-participation

patients did not fill out the questionnaire on sexuality because they were not sexually active. No problems were detected with other questionnaires. The majority of the patients (80 %) preferred the pen-and-paper version over the internet-based method. Completing the PROs took on average 167 min (range 100–270). All patients filled out the PROs within 1 week. One patient needed 270 min to complete the PROs due to concentration problems. Compared to the other patients, this was exceptionally long (range without this particular patient 100–210 min).

Most patients (*n*=12) preferred the research physician to conduct the interview, physical tests, and blood collection during a home visit. Assessments of the other three patients were conducted during a hospital visit. The visits took on average 100 min (range 60–145).

Some of the physical tests and biological sample collections could not be performed (Table 3). The Chester step test was not conducted in three patients due to physical impairments such as an amputated leg, cardiac history, or severe mobility problems. Accelerometer data of six patients were missing due to the following: surgery within a few days after the baseline measurement (*n*=1), a percutaneous endoscopic gastrostomy (PEG) tube placement within a few days after baseline assessment (*n*=2), wheelchair dependence (*n*=1), crutches dependence in daily life (*n*=1), and losing the accelerometer (*n*=1). All other physical tests were completed by all patients. The cognitive test and the psychiatric interview were conducted in all patients without experiencing any problems. Dietary telephonic interview at the end of the assessments were taken in 11 (73 %) patients. Four interviews were missed because treatment already started. Blood and saliva samples were collected in 13 patients (87 %) patients; two patients refused to give blood samples, and two patients did not return their saliva samples. Tumor tissue from eight participants

(53 %) was collected during panendoscopy at the VU University Medical Center. Reasons for not collecting supplemental biopsies were as follows: unknown primary tumor (*n*=2), no extra biopsies during panendoscopy because of immediate surgery (*n*=3), biopsy already taken in outpatient clinic (*n*=1), and unknown (*n*=1).

Patients evaluated the number of items, the time investment and personal or intimate character of the PROs, and the physical tests as feasible to very much feasible (Table 4). Regarding intimacy of questions, one patient found a questionnaire on sexuality too intimate and therefore rated the item intimacy as "a bit feasible" for intimacy. One patient found the time investment of the home visit too long. Due to the presence of a child, this home visit took much longer compared to the other patients (145 min).

Protocols

Generally, the research physician reported the home visits to be very pleasant. Concentration problems were present in two patients according to the research physician. Another patient was somewhat long-winded and expanding to various topics during the (psychiatric) interview and had to be redirected to the questions continuously. No adverse events occurred during the visits. Furthermore, the protocols were independently judged as clear by the research physician, two other experienced fieldworkers, and a research coordinator.

Discussion

This pilot study showed that it is feasible to conduct a comprehensive baseline assessment comprising a large number of PROs, interviews, physical tests, and biological sample

Table 2 Differences in demographic and clinical characteristics, psychological distress, and health-related quality of life between participants and non-participants

Characteristics	Participants (*n*=15)	Non-participants (*n*=11)	Difference (*p* value)
Gender, *n* (%) male	13 (87)	4 (36)	0.008
Age, mean±SD (range) (years)	63±12 (40–80)	62±8 (52–78)	0.926
Tumor location, *n* (%)			0.986
Oral cavity	4 (27)	3 (27)	–
Oropharynx	5 (33)	3 (27)	–
Hypopharynx	0 (0)	0 (0)	–
Larynx	5 (33)	4 (36)	–
Unknown primary	1 (7)	1 (9)	–
Disease stage, *n* (%)			0.749
I	2 (13)	2 (18)	–
II	1 (7)	1 (9)	–
III	5 (33)	3 (27)	–
IV	7 (46)	5 (45)	–
Type of treatment, *n* (%)			0.486
CHRT	8 (53)	4 (36)	–
RT	4 (27)	2 (18)	–
SURG	1 (7)	3 (27)	–
TOE+SN	2 (13)	2 (18)	–
Comorbidity, *n* (%)			
None	4 (27)	3 (27)	0.683
Mild	3 (20)	3 (27)	–
Moderate	7 (47)	3 (27)	–
Severe	1 (7)	2 (18)	–
	Participant (*n*=14)	Non-participant (*n*=9)	
HADS			
Total score, mean±SD	10±8	11±5	0.587
Depression score ≥8, *n* (%)	3 (21 %)	1 (11 %)	0.546
Anxiety score ≥8, *n* (%)	3 (21 %)	4 (44 %)	0.262
Total score >15, *n* (%)	3 (21 %)	2 (22 %)	0.966
EORTC QLQ-C30, mean±SD			
Global quality of life	78±15	64±29	0.145
Physical function	87±15	81±23	0.480
Role function	88±24	74±30	0.229
Emotional function	60±22	69±20	0.296
Cognitive function	88±21	94±8	0.402
Social function	92±18	85±28	0.508

SD standard deviation, *CHRT* chemoradiation therapy, *EORTC QLQ C30* European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30, *HADS* Hospital Anxiety and Depression Scale, *RT* radiotherapy, *SURG* surgery, *TOE+SN* transoral excision and sentinel node procedure

collection among newly diagnosed HNC patients. We found the study sample to be a representative reflection of patients with HNC, and the achievability of the assessment protocol was high.

Representativeness

The present study showed that 58 % of newly diagnosed HNC patients were willing to participate in a comprehensive

assessment. Our response rate was somewhat lower compared to 76–97 % reported in the other prospective cohort studies on HRQoL in HNC patients [5, 7, 10, 36, 37]. Differences in response rate may be related to the large number of questionnaires included, since only one to three questionnaires were included in the previously mentioned studies. Taking into account our comprehensive assessments, we consider our response rate to be acceptable. Of all eligible patients, 30 %

Table 3 Achievability of physical tests and biological sample collection

Physical assessments	Percentage performed	Reasons for not performing physical assessments
Grip strength	100	–
30-s chair stand test	93	Amputated leg ($n=1$)
Step test	80	Amputated leg ($n=1$) Cardiac history ($n=1$) Severe immobility ($n=1$)
Accelerometer	53	Amputated leg ($n=1$) Severe immobility ($n=1$) PEG tube placement ($n=2$) Lost accelerometer ($n=2$) Surgery, within a few days after visit ($n=1$)
Biological sample collection	Percentage performed	Reasons for not performing biological assessment
Blood collection	87	Unwillingness ($n=2$)
Saliva collection	87	Not returned ($n=2$)
Tissue collection	53	Biopsy already taken ($n=1$) No extra biopsies, direct surgery ($n=3$) No extra biopsies, unknown primary tumor ($n=2$) Reason not registered ($n=1$)

PEG percutaneous endoscopic gastrostomy

would like to participate in the study but not at this specific moment. The most important argument for not participating was that the protocol seems too burdensome. For a future study, we can now better inform eligible patients on the time investments and feasibility of the protocol. The remaining 12 % of eligible patients were not willing to participate in any study, and it is likely that this proportion will also be missed in a forthcoming cohort study.

In our study, females were found to be less likely to participate, which is in contrast to the pilot study of Hammerlid et al. [38] who found all non-participants to be men. Another prospective study on long-term HRQoL in patients with HNC found no significant differences between participants and non-participants in demographic and clinical characteristics [7]. Therefore, our under-representativeness of women may be coincidental. On the other hand, it may be related to the higher, but non-significant anxiety levels we found among non-participants, since, in patients with HNC, women are more likely to report higher levels of anxiety than men [39]. However, due to the small sample size, the non-significant differences in anxiety between participants and non-participants should be interpreted with caution. Studies among newly diagnosed cancer patients are at risk for selection bias underestimating problems related to emotional distress and HRQoL. Therefore, we will closely monitor differences in main characteristics between responders and non-responders in a future cohort study.

Achievability

Despite the considerable time investment (average of 270 min in total), our results showed that almost all patients found the study to be feasible to very much feasible. However, some patients experienced some problems with the questionnaires on sexuality, particularly those who were not sexually active. To avoid unnecessary confrontation with intimate questions in a future cohort study, we will therefore add a remark at the start of this questionnaire that patients can skip this questionnaire if not applicable. Regarding the (home) visits, we noticed that a quiet environment is important to prevent unnecessary delay in conducting the interviews and physical tests.

The home visits were almost fully completed. Blood and saliva was collected in 87 % of the patients which we considered to be acceptable. A relatively large proportion (40 %) of patients did not wear the accelerometer due to various reasons, of which some were largely unavoidable such as amputated leg and crutches dependence, whereas others may be prevented or (rapidly) solved. In this study, we did not give an accelerometer to patients undergoing a PEG tube placement which potentially hampers physical activities for a certain period of time. However, it seems that the patients may be

Table 4 Feasibility of the questionnaires and home visit

	Not feasible	A bit feasible	Feasible	Very much feasible
Questionnaires, *n* (%)				
Number of items	–	–	12 (86)	2 (14)
Time investment	–	–	6 (40)	8 (57)
Personal or intimate character of questions	–	1 (7)	7 (50)	6 (43)
Home visits, *n* (%)				
Number of questions	–	–	3 (21)	11 (79)
Time investment	1 (7)	–	4 (29)	9 (64)
Personal or intimate character of questions	–	–	2 (14)	12 (86)
Burden of physical assessments	–	–	2 (14)	12 (86)

able to wear an accelerometer. Furthermore, a new device may quickly be sent to patients who lost their device. Tissue collection was successful in 53 % of the participants. In most cases, supplemental tumor biopsies for this study were not taken due to logistical reasons including immediate surgical treatment of tumor, biopsies already taken in outpatient clinic, or because of an unknown primary tumor. In this pilot study, we did not collect tumor tissue samples from the surgical specimen from the pathology department, but we are planning to do so in a future study if tumor tissue is available.

Strengths and limitations

To our knowledge, this pilot study is the first to evaluate a comprehensive assessment protocol of this extent in newly diagnosed HNC patients before treatment. In addition, the inclusion of objective physical tests and biological sample collection in addition to PROs is a strength of this study. Another strength of this study was the ability to compare data on HRQoL and psychological distress between participants and non-participants, providing a thorough investigation of the representativeness of the included study sample. This study was limited by its focus on baseline assessment only, and we did not collect data on the feasibility of follow-up measurements. However, other longitudinal studies on HRQoL in patients with HNC reported acceptable dropout rates varying between 6 and 14 % [7, 36]. Whether dropout rates will be similar in the forthcoming cohort study remains unclear. Furthermore, while almost all single questionnaires were validated, it is unclear whether assessment of multiple single valid questionnaires impacts the validity. A previous study examining the influence of the structure of questionnaires on response outcomes showed that changes in order of questionnaires did not substantially affect the outcomes [40]. In the present study, assessments were conducted in a hierarchical order, starting with the main outcome measure health-related quality of life, following by questionnaires assessing covariates.

In conclusion, this study showed that it is feasible to conduct a comprehensive assessment protocol including PROs, interviews, physical tests, and collection of biological samples in newly diagnosed HNC patients before the start of treatment. Therefore, we will set up a large multicenter cohort study in patients with HNC evaluating the course of HRQoL over time starting at diagnosis and the relationship between HRQoL and survival, taking into account cancer-related, personal, genetic, biological, psychobehavioral, physical, lifestyle-related, and social factors, the Netherlands Quality of life and Biomedical Cohort studies in cancer, Head and Neck (NET-QUBIC_HNC).

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