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Using the PCI in the identification of fatigue following treatment for head and neck cancer

Rogers SN, Semple C, Humphris GM, Lowe D and Kanatas A

Professor Simon N Rogers Faculty of Health and Social Care, Edge Hill University, Ormskirk, L39 4QP and Liverpool Head and Neck Centre, Liverpool University Hospital Aintree, Liverpool, UK
simonn.rogers@aintree.nhs.uk ORCID: 0000-0002-5989-6142

Dr Cherith J Semple Institute of Nursing and Health Research, Ulster University, Shore Road, Newtownabbey, Co. Antrim, BT37 0QB and South Eastern Health & Social Care Upper Newtownards Road, Belfast, BT16 1RH. cherith.semple@setrust.hscni.net
ORCID: 0000-0002-4560-7637

Professor Gerald M Humphris School of Medicine, Medical & Biological Sciences, North Haugh, St Andrews, UK gmh4@st-andrews.ac.uk

Mr Derek Lowe Medical Statistician, Director, Astraglobe Ltd, Congleton, Cheshire.
astraglobeltd@btconnect.com

Professor Anastasios Kanatas, Leeds Teaching Hospitals and St James Institute of Oncology, Leeds Dental Institute and Leeds General Infirmary, Leeds, UK anastasios.kanatas@nhs.net

Corresponding author
Professor Simon N Rogers FRCS FRCS (maxfac) MD, Liverpool Head and Neck Centre, Liverpool University Hospital Aintree, Liverpool, UK
simonn.rogers@aintree.nhs.uk / snrogers.aintree@gmail.com Tel : 0151 529 5287

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Abstract

Fatigue has a profound impact on the physical, social and emotional aspects of health-related quality of life (HRQOL) for head and neck cancer (HNC) patients. The aim of this study is to describe the clinical characteristics and HRQOL for those HNC patients who raise the issue of fatigue on a prompt tool as something they wish to discuss in their review consultation. The prompt tool used was the Patient Concerns Inventory (PCI). The data is from a cluster-controlled trial conducted at two UK HNC centres (Leeds and Liverpool). Eight consultants were randomised to use the PCI. In addition, PCI patients completed the UW-QOLv4, Distress thermometer and EQ-5D-5L. There were 140 patients who attended clinics at a median (IQR) of 108 (70-165) days after the end of treatment. The PCI item 'fatigue' was the 6th most commonly selected, by 29% (40). Those with advanced tumours were more likely (36% 30/83 Vs 18% 10/56, $p=0.02$) to have selected the fatigue item, as were those having received radiotherapy +/- chemotherapy as treatment (39% 34/87 Vs 11% 6/53, $p<0.001$). The PCI fatigue group reported significantly worse overall QOL, social-emotional and physical function composite scores, distress thermometer score, and EQ-5D scores. PCI-fatigue was common in those with sleeping, nausea, mood, depression, mobility, breathing and energy level concerns. In conclusion, given the frequency of fatigue as an issue that patients want to discuss in review consultations and the detrimental consequence of the symptom, it is appropriate to screen and seek interventions that might help patient fatigue.

Introduction

Head and neck cancer (HNC) survivors commonly experience cancer-related fatigue (CRF) and this relates to disease, treatment and individual patient characteristics [1]. Moderate and severe fatigue was reported in one fifth of HNC survivors [2]. Cancer-related fatigue compromises survival rates and negatively impacts on activities of daily living (ADLs) [3]. Fatigue is a barrier to getting back to work [4]. Although the precise mechanism for CRF experienced by HNC survivors is unclear and is probably multi-factorial, radiation to the central nervous system has been implicated, particularly the treatment dose to the brainstem and medulla [5]. Neuroinflammation can also contribute to chronic systemic symptoms such as fatigue, sleep disturbance, chronic widespread pain, mood disorders, neuropsychiatric symptoms, and temperature dysregulation [6]. Patients receiving intensity-modulated radiation therapy (IMRT) seem to have high rates of fatigue, and further research on how inflammation contributes to fatigue is needed [7]. Depression and fatigue symptoms are interlinked and correlate to poor health-related quality of life outcomes (HRQOL) [8]. Evaluation throughout the treatment is important [9] and fatigue is at its worse around the 6th week of radiation treatment, and slowly improves thereafter [10]. Various clinical characteristics associated with worse fatigue have been suggested for example, younger age, previous radiation, depression, and other symptoms such as poor sleep, reduced social activity and cognitive dysfunction [11,12]. In a study which utilised the Modified Brief Fatigue Inventory (MBFI), comorbidity and cancer stage were also implicated [13]. It has been suggested that both fatigue and depression should be periodically assessed as both are late effects [14]. It is already appreciated that fatigue is an issue that patients wish to talk about in their consultations but little is known about the patient characteristic. Previous reports using the Patient Concerns Inventory (PCI) following HNC treatment has placed fatigue as the 5th most frequent item of the 56 items, being common in early and late stage disease across all sites (oral, oropharyngeal, laryngeal and other) [15].

The aim of this study is to describe the clinical characteristics and HRQOL for those HNC patients who raise the issue of fatigue as something they wish to discuss in their review consultation. Understanding the complexity of CRF as it relates to clinical characteristics and using this knowledge to guide the development of targeted, individualised interventions is critical for reducing the burden of this symptom for HNC survivors.

Method

The methods have been described previously [16]. Briefly, the data is from a pragmatic cluster-controlled trial conducted at two UK Cancer Centres, namely Aintree and Leeds. Fifteen consultants (the clustering factor) were randomised, eight to 'using' and seven to 'not using' an intervention incorporating the PCI prompt list at all their trial clinics. Eligible patients were treated curatively for primary or secondary HNC, and included all sites, stages of disease and treatments. Patients treated palliatively or with recurrence, history of cognitive impairment, psychoses or dementia were excluded. The focus of this paper is to report results from the first 'baseline' post-treatment consultation of only the PCI intervention group patients. The PCI prompt list consists of 56 clinical items [17] which patients selected from, at clinic, before seeing their consultant. The patient generated list guides the outpatient consultation and it covers a range of symptoms and potential problems patients may face after treatment. The item relating to fatigue is described as "fatigue/tiredness" on the prompt list , and which in this paper we will simply refer to as "fatigue". Patients were also asked to select from a list of 18 types of health professional, who they would 'like to see or be referred to'. Previous work [18] grouped PCI items into four domains: Physical and Functional well-being (29 items), Treatment-related (4 items), Social care/Social well-being (9 items)' Psychological and Emotional well-being/Spiritual (14 items).

Clinical and demographic data were collected by a baseline questionnaire or by extraction from electronic records. HRQOL and PCI data were completed electronically (desktop, tablet, iPAD). HRQOL data included UW-QOLv4 [19], Distress thermometer [20] and EQ-5D-5L [21]. The UW-QOLv4 questionnaire consists of 12 single question domains, with between 3 and 5 response options scaled evenly from 0 (worst) to 100 (best) according to response hierarchy (Rogers 2002). It also contains a question about overall QOL in which patients are asked to consider not only physical and mental health, but also many other factors, such as family, friends, spirituality or personal leisure activities that were important to their enjoyment of life. Subsequent analysis has led to the development of subscale composite scores [22] and domain algorithms to screen for significant problems/dysfunction [23].

The statistical analysis focussed on variables associated with selection of the fatigue item from the PCI prompt list. We considered patient and clinical casemix variables and also a wide range of HRQOL measures. Fishers Exact test was used to compare patient groups regarding selection of the fatigue item. Spearman's correlation coefficient (r_s) was used to assess association between the UWQOL activities domain response options and those of the EQ5D-5L usual activities domain. The PCI trial has ethical approval from North West - Liverpool Central Research Ethics Committee REC reference: IRAS 16/NW/0465, Project ID: 189554. It also has approval from the Health Research Authority (HRA). The Research and Development Department at Aintree University Hospital NHS Trust (AUH) is coordinating the trial and AUH is the sponsor for the trial.

Results

Patients recruited to the trial and having baseline data were first discussed at multidisciplinary team (MDT) meetings between January 2017 and December 2018, with first trial clinics between April 2017 and October 2019. Of 288 patients in the trial, 140 were in the PCI intervention group. Clinics were a median (IQR) of 189 (120-255) days after diagnosis and 108 (70-165) after the end of treatment. Characteristics of the 140 PCI group patients can be determined from Table 1.

The mean number of items selected by the 140 PCI patients for discussion in their consultation was 6.60, median (IQR) 5 (2-9), range 0 to 28 with 15 or more items selected by 9% (13). The PCI item ‘fatigue’ was the 6th most commonly selected, by 29% (40), coming after ‘dry mouth’ (49%, 68), ‘fear of cancer coming back’ (34%, 48), ‘dental health/teeth’ (34%, 48), ‘chewing/eating’ (33%, 46) and ‘salivation’ (33%’ 46). The longer the consultation the more likely the fatigue item had been selected for discussion (Table 1). Those with advanced tumours were more likely (36% 30/83 Vs 18% 10/56, p=0.02) to have selected the fatigue item, as were those having received radiotherapy +/- chemotherapy (39% 34/87 Vs 11% 6/53, p<0.001).

Selection of the ‘fatigue’ item was associated with most of the measured HRQOL variables (Table 2). In particular, there was a clear gradient of selection with overall QOL, ranging from 11% selecting fatigue in patients reporting very good or outstanding QOL to 55% if reporting very poor or poor overall QOL. Clear gradients were seen also regarding the distress thermometer score, the EQ-5D visual analogue scale and EQ-5D TTO crosswalk values. Regarding the UWQOL, this was also evident for both the social-emotional and physical function composite scores. Strong associations were seen with the UWQOL activity domain, the EQ-5D usual activities domain and also with UWQOL recreation, mood, anxiety, saliva and taste domains.

The UWQOL activities domain has five response options, namely, (1) I am usually in bed or chair and don't leave home, (2) I don't go out because I don't have the strength, (3) I am often tired and have slowed down my activities although I still get out (4) There are times when I can't keep up my old pace, but not often and (5) I am as active as I have ever been. Seven patients responded to option 1 or option 2 and 86% (6/7) of these selected fatigue for discussion in their consultation, as did 52% (27/52) for option 3, 11% (4/35) for option 4 and 7% (3/46) for option 5. The EQ5D usual activities domain also has five response options (1) I have no problems doing my usual activities, (2) I have slight problems doing my usual activities, (3) I have moderate problems doing my usual activities, (4) I have severe problems doing my usual activities and (5) I am unable to do my usual activities. Six patients selected option 4 or option 5 and 83% (5/6) selected fatigue, as did 52% (12/23) for option 3, 31% (11/35) for option 2 and 16% (12/76) for option 1. Spearman correlation between the two 5-point measures was $R_s=-0.55$, $p<0.001$.

Quite clearly the greater the number of PCI items selected the more likely was this number to include fatigue (Table 3), and the same could be said for each of the four PCI domains, and also if health professionals were also selected. Only 2 of the 56 PCI items were not selected by these patients and 4 had very small denominators of under 5 patients; for 48 of the other 50 items the selection of fatigue was higher when that item was selected than when that item was not selected. When sleeping was selected fatigue was also selected in 81% (13/16); higher fatigue selection rates of around 50% and higher were also seen for many variables (Table 3) including nausea (83%, 5/6), mood (83%, 5/6), depression (75%, 6/8), mobility (70%, 7/10), breathing (67%, 6/9) and energy levels (60%, 15/25).

Discussion

CRF following the diagnosis of HNC tends to be under-reported, potentially persistent and of substantial significance to patients, impacting on HRQOL and survival. There are many different aspects including physical, pain, psychological and social factors which contribute to patients' perceived levels of CRF [2]. The PCI is a well reported prompt list [15,16,18] and as well as allowing a wide range of factors to be considered it is also an holistic approach to delivering patient-centred care. It can be integrated into routine clinics [24,25]. The specific issue of fatigue reported by the PCI has not previously been assessed in detail, and this novel data has been taken from a cluster randomisation trial involving eight different consultants. The variety of consultants across two centres, set within the context of routine follow-up consultations means that the findings of this study are pertinent to current practice. The sample comprises of the range of HNC sites managed by head and neck oncology surgeons. The focus of the assessment is around three to six months following completion of treatment. Nautiyal et al [1] reported a dramatic improvement in fatigue levels across the first 3 months post-treatment, followed by a slow improvement over the remainder of the first year, but with higher fatigue levels than those of healthy individuals. Although a fatigue specific questionnaire such as the Modified Brief Fatigue Inventory (MBFI) was not used, the degree of fatigue experienced by the patient will be reflected by the activity and recreation domains of the UW-QOL [26,27]. There are other factors that might contribute to fatigue such as HPV status as this and inflammation were found to be independent predictors of fatigue over time [28]. As the PCI can be used at consultations, the prompt of fatigue affords an opportunity for further exploration, plus provision of informal advice and support for both patients and their caregivers. Other unmet needs self-report measures [29] or Vanderbilt Head and Neck Symptom survey [30] might fulfil a similar purpose.

Over a quarter of the patients wished to talk about fatigue at their consultations. Fatigue was more common when primary treatment related to radiotherapy +/- chemotherapy rather than surgery alone, and expressed by patients with advanced stage. In this sample there was little obvious difference in the frequency that patients wished to talk about fatigue by age, gender, comorbidity and socio-economic group. Those selecting fatigue reported significantly worse QOL, lower scores in the UW-QOL domains apart from appearance, chewing, shoulder and speech. In addition, patients reported worse intimacy, fear of recurrence, distress, and were more likely to report moderate to extreme problems in usual activities (EQ-5D). Fatigue on the PCI was combined with other issues such as appetite, energy levels, sleeping, depression and mood and this reflects the complex nature of inter-related symptoms.

In those patients with CRF, anaemia or hypothyroidism, if present should be corrected and pain control attended to. It is possible to consider additional interventions. Even though patients might feel too tired to exercise and the symptom persists, there is evidence that if appropriately graded they can complete an exercise programme, with notable benefits. HNC patients can find it a challenge to exercise [27] and prescription should be individually tailored to patient characteristics [31]. A clinic-supported, 12-week progressive strength-training exercise intervention for HNC patients was associated with significant improvements in physical functioning outcomes and improved management of tiredness and fatigue [32]. Physical exercise interventions demonstrated improvements in physical function, muscular endurance, range of motion, overall quality of life, and showed reductions in pain, and fatigue [33]. Progressive resistance training in cachectic HNC patients during radiotherapy seems to be safe and feasible and may have beneficial effects of general fatigue and quality of life [34]. A home-based personalized behavioural physical activity intervention with fitness graded motion exergames (PAfitME) has been shown to be feasible and acceptable with improvement in CRF, ADL dependence, cardiorespiratory fitness, balance, muscle strength, and shoulder forward flexion [3]. Another aspect that might make a positive impact is optimisation of nutrition. HNC patients can be malnourished at the time of diagnosis and the side-effects of treatment can exacerbate this through detrimental effects on loss of taste, mucositis, xerostomia, anorexia, nausea and vomiting. Nutritional advice and use of supplements should be used to increase dietary intake and to prevent therapy-associated weight loss [35]. In nasopharyngeal carcinoma patients, nutrition counselling combined with head and neck rehabilitation exercises greatly reduced fatigue three months after intensity-modulated radiotherapy (IMRT) [36]. Poor sleep quality is another factor that is related to fatigue and if obstructive sleep apnoea is a contributing factor to sleep disturbance this needs to be addressed [37]. Interventions aimed at the interaction between the emotional aspects of fatigue and HNC outcomes are appropriate and can have long-term beneficial effects [38]. In a study of fatigability, depression, and self-esteem among HNC patients, Joseph et al reported that over two thirds of patients had fatigue and a larger proportion suffered from depression [14]. The role of social support is vital as it improves emotional adaptation and reduces depressive symptoms. Also, an appreciation of the difficulties involved in social activities exacerbated by a sense of fatigue can result in further social isolation [8]. As the issue of CRF tends to be multi-factorial further research is needed using complex intervention methodology.

In conclusion, a significant proportion of HNC patients following treatment wish to discuss the issue of fatigue during their out-patient consultation. Fatigue is associated with poor outcomes. As fatigue can be a patient concern over an extended period of time, the PCI prompt list approach could facilitate the discussion during follow-up and allow for further investigation and targeted onward referral based on the aetiology of the fatigue.

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Declaration of Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Table 1 : Selection of the PCI ‘fatigue’ item, by casemix

		%	PCI FATIGUE SELECTED Patients	P value**
	Total patients	29	40/140	
Hospital	Aintree	27	22/82	0.70
	Leeds	31	18/58	
Days from diagnosis to first clinic (TERTILES)	≤144	19	9/48	0.16
	125-227	36	16/45	
	≥228	32	15/47	
Days from end of treatment to first clinic (TERTILES)	≤79	29	14/49	0.84
	80-138	26	12/46	
	≥139	31	14/45	
Duration of consultation (minutes) TERTILES	≤8 mins	11	4/37	0.005
	9-12 mins	29	14/49	
	≥13 mins	42	21/50	
Gender	Female	37	18/49	0.12
	Male	24	22/91	
Age	<55	38	11/29	0.48
	55-64	26	16/52	
	65-74	31	10/32	
	≥75	18	3/17	
Tumour site:	Oral cavity	18	10/55	0.10
	Oropharynx	36	15/42	
	Larynx	30	9/30	
	Other	46	6/13	
Overall clinical stage	Advanced 3-4	36	30/84	0.02
	Early 1-2	18	10/56	
Primary treatment*:	S only	13	6/46	0.004
	S only & FF	-	0/7	
	RT or RT/CT only	39	15/38	
	S & (RT or RT/CT)	45	14/31	
	S & (RT or RT/CT) & FF	28	5/18	
WHO comorbidity	0	32	28/88	0.55
	1	25	7/28	
	2-4	21	5/24	
ACE27 comorbidity	None	32	23/71	0.25
	Mild	24	10/41	
	Moderate	20	5/25	
	Severe	67	2/3	
Living situation	Alone in house/flat	17	5/29	0.17
	With others in house/flat	32	35/111	
Working	Yes	29	14/48	>0.99
	No	29	25/86	
Financial benefits	Yes	31	15/49	0.69
	No	27	21/78	
Smoking habit	Current	19	3/16	0.48
	Former	27	22/81	
	Never	34	13/38	
Alcohol habit	Current	24	24/100	0.10
	Former	37	11/30	
	Never	60	3/5	
IMD 2019 quintile	1=least deprived	50	8/16	0.32
	2	28	8/29	
	3	18	4/22	
	4	24	4/17	
	5=most deprived	29	16/56	

* Surgery (S), RadioTherapy (RT), ChemoTherapy (CT), Free Flap transfer (FF)

** Fishers Exact test

Table 2: Selection of the PCI ‘fatigue’ item, by QOL measures

		PCI FATIGUE SELECTED		P value**
		%	Patients	
	All patients	29	40/140	
UWQOL Overall Quality of life	Outstanding/ Very good	11	5/47	0.002
	Good	31	15/48	
	Fair	41	14/34	
	Very Poor / Poor	55	6/11	
Distress thermometer (DT)	Zero	11	4/36	0.02
	1-3	26	10/38	
	4-5	39	13/33	
	6-10	39	13/33	
UWQOL social-emotional subscale	<60	52	13/25	<0.001
	60-79	40	21/53	
	80-100	10	6/62	
UWQOL physical function subscale	<60	39	16/41	0.001
	60-79	36	20/55	
	80-100	9	4/44	
UWQOL items				
Social-emotional subscale				
• Pain	Best possible response	17	9/53	0.05
	Somewhere in-between	33	16/48	
	Dysfunction	38	15/39	
• Activity	Best possible response	7	3/46	<0.001
	Somewhere in-between	36	29/80	
	Dysfunction	57	8/14	
• Recreation	Best possible response	11	7/61	<0.001
	Somewhere in-between	39	28/71	
	Dysfunction	63	5/8	
• Shoulder	Best possible response	26	22/85	0.64
	Somewhere in-between	34	14/41	
	Dysfunction	29	4/14	
• Mood	Best possible response	8	4/48	<0.001
	Somewhere in-between	41	31/75	
	Dysfunction	29	5/17	
• Anxiety	Best possible response	15	7/47	0.003
	Somewhere in-between	29	20/69	
	Dysfunction	54	13/24	
Physical function subscale				
• Appearance	Best possible response	21	9/43	0.41
	Somewhere in-between	31	27/86	
	Dysfunction	36	4/11	
• Swallowing	Best possible response	14	7/50	0.01
	Somewhere in-between	36	26/73	
	Dysfunction	41	7/17	
• Chewing	Best possible response	19	11/57	0.11
	Somewhere in-between	36	23/64	
	Dysfunction	32	6/19	
• Speech	Best possible response	28	18/64	0.68
	Somewhere in-between	27	18/66	
	Dysfunction	40	4/10	
• Taste	Best possible response	12	5/41	0.008
	Somewhere in-between	32	23/72	
	Dysfunction	44	12/27	
• Saliva	Best possible response	12	5/41	0.001
	Somewhere in-between	23	11/47	
	Dysfunction	46	24/52	
Other items:				
• Intimacy	Best possible response	25	27/110	0.04
	Somewhere in-between	50	12/24	
	Dysfunction	17	1/6	

• Fear of recurrence*	0 or 25	50	8/16	0.01
	50	40	17/43	
	75	21	13/62	
	100	11	2/19	
EQ-5D				
Mobility (walking about)	No problems	25	24/96	0.36
	Slight problems	37	7/19	
	Moderate/severe/unable	36	9/25	
Self-care (washing or dressing myself)	No problems	24	27/113	0.03
	Slight problems	55	6/11	
	Moderate/severe/unable	44	7/16	
Usual activities	No problems	16	12/76	<0.001
	Slight problems	31	11/35	
	Moderate/severe/unable	59	17/29	
Pain (or discomfort)	No pain or discomfort	15	8/54	0.01
	Slight pain or discomfort	33	14/42	
	Moderate/severe/extreme	41	18/44	
Anxiety/depression	Not anxious or depressed	21	14/67	0.01
	Slightly anxious or depressed	29	17/58	
	Moderate/severe/extreme	60	9/15	
EQ-5D-5L TTO crosswalk values (TERTILES)	≤.6950	45	17/38	0.001
	.6951-.8370	31	19/61	
	≥.8371	10	4/41	
EQ5D Visual analogue scale (VAS) TERTILES	≤69	46	21/46	<0.001
	70-81	32	14/44	
	≥82	10	5/50	

*(0) I am fearful all the time that my cancer might return and I struggle with this n=2, (25) I get a lot of fears of recurrence and these can really preoccupy my thoughts n=14, (50) I am sometimes having fearful thoughts but I can usually manage these (75) I have a little fear with occasional thoughts but they don't really bother me (100) I have no fear of recurrence

** Fishers Exact test

Table 3: Selection of the PCI 'fatigue' item and other PCI data

		PCI FATIGUE SELECTED		P value
		%	Patients	
	Patients	29	40/140	
No of PCI selected: overall	<5	2	1/57	<0.001
	5-9	30	15/50	
	10-14	65	13/20	
	≥15	85	11/13	
PCI items selected by domain:				
Physical function	<5	8	6/75	<0.001
	5-9	37	16/43	
	≥10	82	18/22	
Cancer treatment	None	24	24/98	0.11
	≥1	38	16/42	
Social care & social wellbeing	None	23	25/109	0.01
	≥1	48	15/31	
Psychological, emotional wellbeing/spiritual	None	11	7/65	<0.001
	1	27	12/44	
	≥2	68	21/31	
No. of Health professionals selected	None	23	17/75	0.05
	≥1	35	23/65	
Other PCI items selected by at least 20% of patients overall	Dry mouth	40	27/68	0.005
	Fear of cancer coming back	48	23/48	<0.001
	Dental health/Teeth	44	21/48	0.006
	Chewing/eating	43	20/46	0.009
	Salivation	48	22/46	0.001
	Swallowing	51	20/39	<0.001
	Taste	42	16/38	0.04
	Sore mouth	45	15/33	0.03
	Mucus	48	16/33	0.007
	Shoulder	45	14/31	0.03
	Pain in the head and neck	57	17/30	<0.001
	Cancer treatment	39	11/28	0.17
Other PCI items*	Activity	50	3/6	0.35
	Appetite	52	14/27	0.004
	Bowel habit	50	6/12	0.10
	Breathing	67	6/9	0.02
	Energy levels	60	15/25	<0.001
	Indigestion	50	3/6	0.35
	Mobility	70	7/10	0.006
	Nausea	83	5/6	0.007
	Pain elsewhere	54	7/13	0.05
	Sleeping	81	13/16	<0.001
	Vomiting	80	4/5	0.02
	Financial benefits	67	4/6	0.06
	Speech/voice/being understood	60	9/15	0.01
	Anxiety	56	9/16	0.02
	Depression	75	6/8	0.007
	Memory	60	6/10	0.03
	Mood	83	5/6	0.007
	Self-esteem	67	4/6	0.06
	Personality & temperament	60	3/5	0.14
Other Health professionals*				
	Oral rehab team	57	4/7	0.10
	Physiotherapy	63	5/8	0.04
	Audiologist	50	4/8	0.23

*when these items were selected then Fatigue was selected in at least 50% of the patients. Denominators under 5 were omitted