

A systematic review of the patient reported outcome (PRO) instruments used in clinical trials in head and neck surgery.

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Abstract

Introduction

There is a growing number of clinical trials in patients with head and neck cancer. Although not often the primary outcome, patient reported outcomes (PROs) are now an important component. The aim of this structured review was to identify and report the characteristics of the questionnaires used and summarise the findings in the literature.

Materials and methods

A search of several online databases was devised using the following key terms: head and neck oncology, head and neck surgery, reconstruction, clinical trials patient-reported outcomes, questionnaires, Quality of Life (QoL), validated instruments, and patient satisfaction. Information was collected relating to the topic of the paper, sample size, selection criteria, the main advantages and disadvantages of the PRO used, and if the tool was used in conjunction with any other.

Results

1342 papers were screened, of which 54 articles eligible; across these papers, 22 questionnaires were identified. The primary reason for utilising a tool was its relevance to the focus of the paper; including features such as xerostomia, pain, swallowing to name a few.

Discussion

We recommend that outcome measures for clinical trials should be chosen in relation to the following criteria: appropriateness, reliability, validity, responsiveness, precision, interpretability, acceptability and feasibility; to allow the patient experience to be the focus of the primary outcome. Clinical trials use validated questionnaires but the PRO measures

tended not to be the focus of the trial. There is merit in future clinical trials having PRO measures as the primary outcome and designed around an explicit hypothesis.

Introduction

Measurement of patient QoL is imperative as UK head and neck cancer incidence is increasing.¹ The associated debilitating physiological and psychological morbidities may thus become more prevalent². Side effects of treatment and functional difficulties can exacerbate emotional distress, depression, and self-esteem issues. The scope of randomised controlled trials in head and neck cancer is treatment; many compare toxicity of different treatment regimens or provide ideal interventions for side effects such as xerostomia. However, there is no universal instrument that is sufficiently robust to compare QoL and morbidity in patients followed up after initial surgical resection, chemotherapy and radiotherapy³.

Clinicians find it difficult to determine precisely what physical and emotional trauma affects each patient after initial head and neck cancer management, and to what severity. However, it is these very effects that affect adherence, compliance, morbidity and mortality⁴. It is here that patient-related outcomes become paramount. This review aims to summarise the literature in respect to the PROM used, the focus of the research and the key clinical findings.

Materials and methods

A search strategy was devised using the following key terms: head and neck oncology, head and neck surgery, reconstruction, clinical trials, patient-reported outcomes, questionnaires, QoL, validated instruments, and patient satisfaction. The following databases were examined: Handle-on-qol, Medline, Ebase (Excerpta Medica), HAPI (Health and Psychosocial Instruments), Science Citation Index/Social Sciences Citation Index, Ovid Evidence-Based Medicine databases and PsychINFO.

Only manuscripts written in English were included. All instruments included in the review were identified as PROMs measuring head and neck-related QoL and/or satisfaction that had undergone development and validation with head and neck cancer patients. For the appraisal of the psychometric and operational performance of the instruments we looked for evidence of criteria as in Table 1. PRISMA guidance was considered in the search and presentation of the results⁵. A total of 2072 papers were identified describing QoL (QOL) measures. From an evaluation of the abstracts and available full text, 54 relevant papers were closely examined (Figure 1).

Results

From 54 papers⁶⁻⁵⁹, the authors found 22 QoL measures, which satisfied our inclusion criteria (Figure 1). In many studies the authors used more than one instrument. The most common tool used in the search was the EORTC QLQ C30, with its use in 18 of the 54 papers. The second most common was the EORTC QLQ-H&N35 tool which was used in 14 papers. The above two instruments are intended to be utilised together, which was the case in 11 papers.

The primary reason for utilisation of a tool was for its ability to be general or specific when measuring QoL (Table 2). Papers favoured tools that were well-validated, easy to use, and those that had a focus on functional and psychological aspects of QoL. Conversely, disadvantages were deemed to be a lack of relevance to the focus of the paper, low levels of completion, and those that required large numbers for statistical significance. Table 3 summarises the main foci of the clinical trials.

Discussion

In the included papers, PROMs are generally utilised as a secondary outcome to quantify the effect of a treatment modality, rather than as a primary outcome in relation to the patient experience. In undertaking this review, the authors are aware of its limitations: by including papers only written in English, there is exclusion of a potentially large number of studies that could give further insight into how PROMs are utilised. In addition, there were restrictions in obtaining further papers by an inability to access the full text in our searches. The authors recommend that outcome measures for clinical trials should be chosen in relation to the criteria stated in Table 1. Analysis of the papers allows us to determine the key focus of the trial and why each PRO instrument was utilised.

General Instruments

EQ-5D assesses mobility, self-care, usual activities, pain and anxiety. The instrument was developed for clinical and economic evaluation of healthcare and was designed for use alongside condition-specific instruments⁵⁹. The instrument was used by one study¹⁹, assessing PET-CT surveillance versus neck dissection in advanced head and neck cancer. EQ-5D was used along with EORTC QLQ-C30, H&N35 and MD Anderson Dysphagia Index (Table 4). Mehanna et al¹⁹ commented on the utilisation of EQ-5D in deriving quality adjusted life years to assess economic viability between the treatment groups.

COOP-WONCA Functional status charts assess general functional status aimed at primary care; the domains include: physical fitness, feelings, daily activities, social activities, change in health and overall health. COOP-WONCA charts were used by Van Bokhorst et al²² in their trial assessing perioperative enteral nutrition and QoL of severely malnourished patients. The COOP-WONCA charts are not specific for cancer and so were used along with EORTC

QLQ-C30. Van Bokhorst concluded that the COOP-WONCA charts were not sensitive enough to pick up significant changes in QoL²².

Cancer-specific Instruments

EORTC QLQ C30 consists of a general QoL questionnaire composed of functional scales, symptom scales, a global health status and QoL status. The questionnaire was acceptable to patients with 60% completing it in less than 30 minutes⁶¹. Eighteen randomised control trials used the EORTC QLQ C30, more than any other measure (Table 4). Eleven studies used EORTC QLQ C30 with the QLQ-H&N35 as is intended. The focus of most papers which utilised EORTC QLQ C30 was different chemotherapy medications and their effectiveness.

The Spitzer QoL index covers 5 domains: activity, daily living, health, support and outlook. The instrument was used by two studies in the review, Robert et al⁴⁹ were assessing a novel chemotherapy regime and Elliot et al⁵⁰ were measuring the effectiveness of a medication in preventing radiation mucositis. It was commented that if one question in the index is not answered the results cannot be interpreted which could be an issue in smaller studies; in addition, the index may be subject to patient and reviewer bias⁵⁰.

The Rotterdam Symptom checklist consists of four main scales: physical symptom distress, psychological distress, activity level, and overall valuation of life. Griffiths et al⁵¹ were the only trial to use this instrument. The paper assessed QoL in patients on the continuous hyper-fractionated accelerated radiotherapy randomised trial, which showed there was no clear difference in QoL compared to conventional radiotherapy. The authors modified the checklist by adding four domains: cough, coughing up blood, hoarseness and restlessness. Griffiths⁵¹ used the RSCL alongside the Hospital Anxiety and Depression Scale.

Head and Neck Cancer-specific Instruments

The EORTC Head and Neck cancer module (QLQ-H&N35) is a module which is designed to be used in conjunction with the EORTC QLQ C30. This consists of scales including pain, swallowing, senses, speech, social eating, social contact and sexuality. 11 papers used the EORTC QLQ C30 in conjunction with QLQ-H&N35, 7 used EORTC QLQ C30 without the Head and neck module and 3 used the QLQ-H&N35 without the EORTC QLQ C30 (Table 4). The focus the papers was in the comparison of different treatment regimes, particularly chemotherapeutic agents which was the case for 7 of the 11 papers.

The QoL Radiation Therapy Instrument (QoL-RTI) is designed specifically for radiation therapy. The instrument was used by one study in our search which was assessing the effect of a novel radiotherapy regime. The regime showed QoL returned to baseline after 1 month of treatment and it had acceptable toxicity. The instrument was acceptable to patients with 90% completing both pre-treatment and end of treatment questionnaires, but compliance reduced between month 3 and month 12 post treatment⁵⁸.

The University of Washington QoL questionnaire is a head and neck-specific instrument. 9 papers used the UoWQoL (Table 4), two of which used it in conjunction with the Neck Dissection Impairment Index and the University of Michigan Xerostomia Questionnaire. The purpose of most the papers was to assess the effectiveness of different radioprotective regimes during radiotherapy; however, most papers saw that there was still a decrease in QoL despite intervention. The authors of these papers praised the UoWQoL as a general health measure but commented that it was insensitive to changes regarding xerostomia. Owen et al³⁴ found a lack of compliance to completion.

The ROTG modified University of Washington Head and Neck Symptom Questionnaire is essentially the same as the UoWQoL but focuses more on the effects of radiation in the head and neck³⁸. It is used by three studies assessing the symptoms of patients undergoing radiotherapy who found that there is a negative change in QoL scores following treatment, particularly in relation to mucositis and xerostomia^{38,39,40} (Table 4).

The University of Michigan Xerostomia-related QoL scale is specific to mouth and throat dryness. Four of the papers included used this instrument, all of which measured QoL in different radiotherapy techniques; those with parotid-sparing had an increase in QoL compared to other regimes (Table 4).

The Neck Dissection impairment index (NDII) is designed to assess function, particularly related to the shoulder, following neck dissection. This instrument was used in two studies to assess the effects of different treatments, including exercises and TENS, on QoL. There was found to be no statistical significance between treatments in either study. Both studies used the index along with more general head and neck indices for an overall view of QoL. The NDII was praised for its simplicity and specificity to neck dissection related QoL (Table 4).

The Performance Status Scale for Head and Neck Cancer is a clinician-rated instrument. The three domains are understandable speech, normalcy of diet and eating in public. Three separate studies used the PSS-HN, one in conjunction with H&N35 and EORTC QLQ-C30 and one in conjunction with the MD Anderson Dysphagia inventory (Table 4). The studies showed that chemoradiotherapy causes a deterioration in QoL but that there is no difference between different chemoradiotherapy regimes.

Functional Assessment of Cancer Therapy-Head and Neck is a self-reported instrument; the domains are physical, social, emotional, and functional well-being. Five studies in this review used FACT-HN, reporting it useful for functional assessment; the papers evaluated the difference in efficacy and QoL between different chemoradiotherapy regimes. There was found to be no difference in QoL between treatment and control groups in all the studies. Simon et al³⁸ reported low completion rates (60%) in their study comparing Gefitinib with methotrexate. Most studies reported the FACT-HN's utility in measuring functional performance for patients with head and neck cancer. (Table 4)

The FHNSI-10 is aimed at patients with refractory, recurrent or advanced disease. It is a subset of the FACT H&N and was designed to capture physical symptoms of disease. Two studies used the FHNSI-10; Stewart et al⁴³ utilised it in conjunction with the Functional Assessment of Cancer Therapy H&N instrument, as they reported that FHNSI-10 is ineffective for assessing general QoL. Again, the studies were assessing different chemotherapy regimens; no mention was made of patient acceptability⁷⁰.

The MD Anderson Dysphagia Inventory (MDADI) is a self-administered instrument for assessing dysphagia; it includes items grouped into domains of dysphagia; global, emotional, functional and physical. The inventory was used by two studies in our review both of which praised it for its specific use with swallowing, but also used a more general measure alongside (Table 4). Hutcheson et al⁴⁵ used the study to assess QoL following chemoradiotherapy which was found to decrease.

The Head and Neck Radiotherapy Questionnaire is directed towards physical symptoms of skin, throat, stomatitis, digestion, energy and psychosocial for head and neck radiotherapy patients. All four of the studies that used this instrument were related to the prevention of xerostomia in patients undergoing radiotherapy; most radioprotective agents did not have a significant effect on QoL. Ringash et al complimented the disease specificity and ease of completion, however they also comment that data from healthy individuals is not available and while the score can remain the same the patients may have swapped pre-treatment problems with post-treatment problems⁷³.

HNQoL is a validated QoL instrument divided into four domains: eating and swallowing, communication, head and neck pain and emotional wellbeing. The only study to utilise this instrument identified QoL between patients who underwent chemoradiotherapy plus a neck dissection versus chemotherapy alone; no difference in QoL was found. Donatelli-Lassig et al⁵⁹ determined that the disease specificity of the HNQoL was a useful feature.

Head and Neck Cancer inventory (HNCI) is a reliable validated health status instrument. Lazarus et al⁵⁵ utilised this study in assessing swallowing and tongue strength exercises in patients who underwent primary chemotherapy with or without adjuvant chemotherapy. Those who underwent exercises had an increase in QoL.

Miscellaneous Instruments

The Hospital Anxiety and Depression Scale is an instrument with two domains (anxiety and depression)⁷⁵. Four studies in the sample used the HADS which focussed on whether implantation of coping strategies improved QoL, which was found to be the case. All the

studies commented that it was a useful psychological test, but Scheifke et al⁹ commented the need to use another instrument for a more rounded assessment.

The Dermatology life quality index is a dermatology-specific QoL instrument⁷⁶. It was utilised by one trial in the search which was based on skin symptoms associated with etuximab. The trial also used the EORTC QLQ-C30 (Table 4).

The Hearing Handicap Inventory for the Elderly is a specific instrument for assessing QoL issues due to hearing loss. The instrument is valid, reliable and easy to use⁷⁷. Schultz et al⁵⁷ were the only study to use this instrument, utilising it for hearing loss associated with head and neck cancer, showing that patients undergoing radiotherapy are more likely to have hearing related problems.

The Modified WHO performance status scale is a five-point scale based on ability to work and is not a true QoL instrument⁷⁸; it was utilised by Correy et al⁵⁶ in the assessment of PEG vs NG tubes, where there was found to be no significant difference in QoL.

Conclusion

There have been a variety of questionnaires used in clinical trials following H&N cancer; these have tended to be secondary outcomes. It is important when focusing on patient reported outcomes to include a validated questionnaire that is optimal to the hypothesis being tested between arms of the trial. It is worthwhile considering more than one questionnaire and to be as specific as possible in selection; in addition, anchoring a PROM with an objective measurement will be beneficial in ensuring the patient experience as the primary outcome. Although underlying issues have been widely discussed, three of our criteria:

appropriateness, precision and interpretability, are not always included in lists of desirable properties of instruments. The remaining five criteria are widely cited and identified in the same or similar terminology as in this review (Table 1).

In this review, the main areas where PROs were used in clinical trials were for evaluating the differences between different chemotherapy medications, the differences in techniques for preventing xerostomia, and between different radiotherapy regimes, amongst others. For the main, there was little difference in QoL between different treatment regimens; those papers that focussed on specific patient experience measures such as implementation of coping strategies, found an increase in QoL. In the future, trials can be broadened to include PROs as the primary outcome with an explicit hypothesis.

Conflict of interest: The authors have no conflict of interest to declare.

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Validity
Reliability
Responsiveness
Appropriateness
Precision
Interpretability
Acceptability
Feasibility

Table 1. Criteria required to be evidenced by the instruments

Type of PRO instrument	Number of instruments	Names of instruments
General	2	EQ-5D; COOP-WONCA
Cancer Specific	3	EORTC QLQ C30; Spitzer QoL; Rotterdam Symptom Checklist
Head & Neck Cancer Specific	13	EORTC QLQ-H&N35; University of Washington QoL; ROTG Modified University of Washington QoL; University of Michigan Xerostomia Questionnaire; QoL-RTI; NDII; PSS H&N; MD Anderson Dysphagia Inventory; FACT H&N, FHNSI-10; H&N QoL; HNCI; H&N Radiotherapy Questionnaire

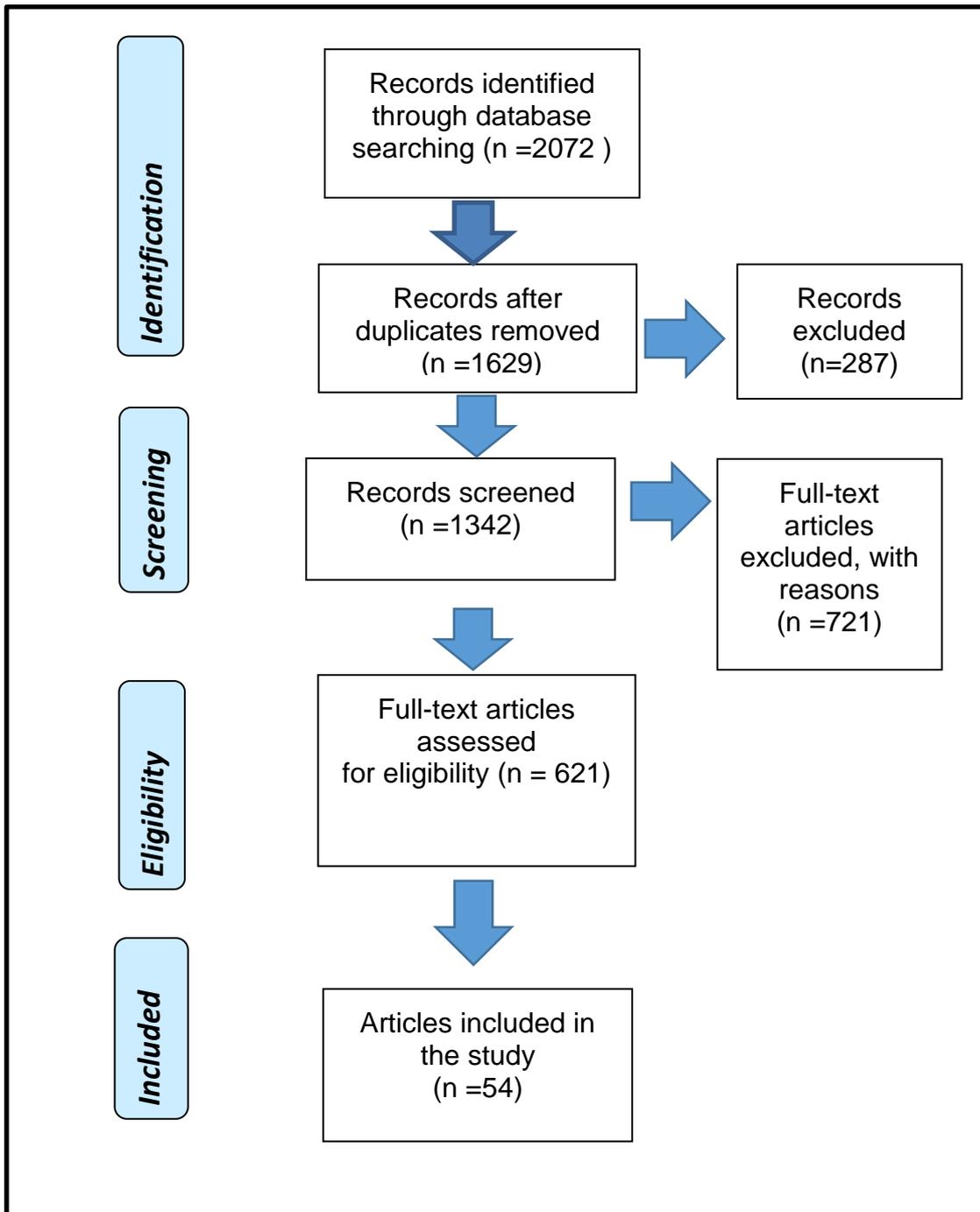
Miscellaneous	4	Hospital Anxiety & Depression Scale; Hearing Handicap Inventory; Dermatology Life Questionnaire; Modified WHO PS
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Table 2. Types of Patient Reported Outcome (PRO) instrument used

Focus of the Trial	Number of Trials with this Focus
Chemotherapy/ Chemoradiotherapy regimens	13
Xerostomia/ Mucositis	12
Radiotherapy regimens	11
Dietary intake	3
Psychosocial interventions	2
Pain medications	2
QoL	2
Coping strategies	2
PET CT vs SND for monitoring	1
Hyperbaric oxygen therapy	1
Utilising EMG studies	1
Shoulder exercises	1
Dermatitis	1
Hearing Loss	1
Swallowing	1

Table 3. Focus of clinical trials

Figure 1 Search results included in the review



Questionnaire	First Author/ Year	Focus of the RCT	Number of patients	Inclusion & Exclusion Criteria	Main Advantages	Main Disadvantages	Other Instruments
EORTC QLQ-C30	Duncan et al 2005 ⁶	Xerostomia/Mucositis	138	Non-metastatic; had RT	Broad view of QoL Brief Validated	Not specific to oral cavity as needed Not H&N specific	
	Rivera et al 2009 ⁷	Chemotherapy in metastatic disease	442	Recurrent or metastatic cancer	Cancer-specific Self-administered Multi-dimensional		HN35
	Machiels et al 2015 ⁸	Chemotherapy in metastatic disease	483	Recurrent or metastatic cancer	Cancer-specific Validated		HN35
	Potthoff et al 2014 ⁹	Medication for pain intensity	34	Cetuximab chemoradiotherapy rhagades	Cancer-specific Broad view of health Pt recorded		Dermatological Life Quality Index
	Bottomley et al 2013 ¹⁰	Chemotherapy vs chemoradiotherapy	450	Neck nodes but no metastases	Broad view of health		H&N35
	Van Herpen et al 2010 ¹¹	Symptom control	358	Unresectable, advanced SCC	Robust Validated Frequently used in RCTs Functional & symptomatic scales	Not H&N specific	H&N35
	Machiels et al 2014 ¹²	Chemotherapy in metastatic disease	474	Recurrent SCC not amenable to salvage	Good scale for measuring pain		H&N35
	Mesia et al 2010 ¹³	Chemotherapy medication	442	Previously untreated advanced SCC	Cancer-specific Broad view of health	Lack of compliance to completion	H&N35
	Schiefke et al 2008 ¹⁴	QoL after SND	49	Sentinel node bx or SND	Validated Reliable	May need large numbers for statistical significance	H&N35 Hospital Anxiety and Depression Scale

	Ackerstaff et al 2008 ¹⁵	Chemotherapy medication	207	Ineligible for salvage surgery	Validated		H&N35
	Vilela et al 2005 ¹⁶	Coping strategy therapy	101	Completed cancer treatment	Validated		Hospital Anxiety and Depression Scale
	Heukelom et al 2013 ¹⁷	Chemoradiotherapy	268	T3/4 tumour new diagnosis	Validated		H&N35
	Uster et al 2013 ¹⁸	Dietary intake post H&N cancer	58	Those who would benefit from nutritional support	Cancer-specific	Not specific to nutrition	
	Mehanna et al 2016 ¹⁹	PET-CT in advanced SCC	564	N2 or N3 metastases	Validated Frequently used	Not H&N specific	EQ-5D Hi 35 MD Anderson dysphagia
	Teguh et al 2009 ²⁰	Hyperbaric oxygen	19	RT treatment tongue SCC	Validated		Performance Status Scale for Head and Neck Cancer H&N35
	Fang et al 2008 ²¹	Different RT rxs	203	Requiring radical RT	Validated		H&N35
	Van bokhorst et al 2000 ²²	Enteral nutrition	49	Malnourished	Cancer-specific Validated		COOP-WONCA
	Myers et al 1999 ²³	Psychosocial intervention	47	H&N SCC, no previous mental health issue	Cancer-specific		Hospital Anxiety and Depression Scale
EORTC QLQ-H&N35	Rivera et al 2009 ⁷	Chemotherapy in metastatic disease	442	Recurrent or metastatic cancer	H&N cancer-specific	Low completion May not be relevant for general QoL factors	EORTC QLQ-C30
	Machiels et al 2015 ⁸	Chemotherapy in metastatic disease	483	Recurrent or metastatic cancer	Validated		EORTC QLQ-C30
	Bottomley et al 2013 ¹⁰	Chemotherapy vs chemoradiotherapy	450	Neck nodes but no metastases	Designed for surgery, radiotherapy and chemoradiotherapy		EORTC QLQ-C30
	Van Herpen et al 2010 ¹¹	Symptom control	358	Unresectable, advanced SCC	Specific to H&N i.e. xerostomia etc, Good previous use in cancer clinical trials		EORTC QLQ-C30

	Machiels et al 2014 ¹²	Chemotherapy in metastatic disease	474	Recurrent SCC not amenable to salvage	H&N specific		EORTC QLQ-C30
	Mesia et al 2010 ¹³	Chemotherapy medication	442	Previously untreated advanced SCC	H&N specific		EORTC QLQ-C30
	Van Rij et al 2008 ²⁴	Xerostomia related to RT	192	For curative RT	Good for xerostomia		
	Bower et al 2009 ²⁵	Effects of treatment modalities for H&N	231	Any form of curative Rx	Validated H&N specific		
	Schiefke et al 2008 ¹⁴	QoL after SND	49	Sentinel node bx or SND	Validated Reliable H&N specific	May need large numbers for statistical significance	EORTC QLQ-C30 Hospital Anxiety and Depression Scale
	Ackerstaff et al 2008 ¹⁵	Chemotherapy medications	207	Ineligible for salvage surgery	Validated		EORTC QLQ-C30
	Heukelom et al 2013 ¹⁷	Chemoradiotherapy	268	T3/4 tumour new diagnosis	Validated		EORTC QLQ-C30
	Mehanna et al 2016 ¹⁹	PET-CT in advanced SCC	564	N2 or N3 metastases	H&N specific		MD Anderson Dysphagia Inventory
	Teguh et al 2009 ²⁰	Hyperbaric oxygen	19	RT treatment tongue SCC	H&N specific i.e swallowing		Performance Status Scale for Head and Neck Cancer EORTC QLQ-C30
	Fang et al 2008 ²¹	Different RT regimes	203	Requiring radical RT	Validated H&N specific		EORTC QLQ-C30
University of Michigan Xerostomia Questionnaire	Chang et al 2009 ²⁶	Xerostomia	15	Disease free 1yr post-surgery; had RT	Simple Validated	Not suitable for less invasive RT treatments w/ lower doses	
	Scrimger et al 2007 ²⁷	Saliva Production	188	Bilateral RT to parotids	Specific to clinical question		UoWQoL
	Warde et al 2000 ²⁸	Xerostomia	28	RT; no anticholinergic medications	Simple		

	Lin et al 2003 ²⁹	Xerostomia	36	Post-parotid sparing RT	H&N specific Validated Specific to xerostomia	May not be as useful when sample size small	
University of Washington QoL	Scrimger et al 2007 ²⁷	Saliva Production	188	Bilateral RT to parotids	Well-rounded general health view	Insensitivity when related to question of xerostomia	University of Michigan Xerostomia Questionnaire
	Parikh et al 2011 ³⁰	Electromyographic studies	38	Selective neck dissection	Good for functional measures		Neck Dissection Impairment Index
	Lydiatt et al 2008 ³¹	Depression medication	23	No pre-existing mental health condition	Self-administered Focuses on aspects of daily life		
	Brennan et al 2009 ³²	Staged vs elective neck treatment	25	T1-2 N0 SCC new diagnosis	General health view		
	Oton-Leite et al 2011 ³³	Laser therapy with RT	60	Undergoing RT salivary glands	Simple Brief Validated Easy to complete and interpret H&N cancer-specific		
	Owen et al 2011 ³⁴	Radio frequency ablation	21	Unresectable SCC or previously failed Rx	H&N specific	Lack of compliance to completion	
	Jha et al 2000 ³⁵	RT induced xerostomia	16	Eligible for RT	General health view	Not specific to xerostomia or RT	
	Johnson et al 2002 ³⁶	Radioprotection of mucosa	33	Resection + RT	Good for functional measures	heavily weighted on patient symptoms	
	Jha et al 2003 ³⁷	Xerostomia	76	Requiring RT	Good for functional measures		
RTOG-modified University of Washington QoL H&N Symptom	Hoffman et al 2014 ³⁸	GM-CSF effect of RT symptoms	114	No previous chemoradiotherapy	Self-administered Validated Specific to RT	Lack of compliance to completion	

	Heron et al 2009 ³⁹	Stereotactic body radiotherapy	25	Recurrent SCC	General health but with specific RT aspect		
	Fisher et al 2003 ⁴⁰	Xerostomia post RT	249	RT	Function specific Good for RT		
Neck Dissection Impairment Index	Parikh et al 2011 ³⁰	Electromyographic studies	38	Selective neck dissection	Simple		University of Washington QoL
	McNeely et al 2008 ⁴¹	Exercise for shoulder pain	52	Neck dissection, shoulder dysfunction	Specific for neck dissection issues		Functional Assessment of Cancer Therapy H&N
FHNSI-10	Kushwaha et al 2015 ⁴²	Palliative chemotherapy medications	117	Pt ineligible for salvage surgery/RT/chemo	Specific for advanced/recurrent cancer Brevity		
	Stewart et al 2009 ⁴³	Methotrexate recurrent SCC	486	Recurrent SCC with RT not amenable to salvage	Good for symptomatic measures	Not useful for general health	Functional Assessment of Cancer Therapy H&N
Performance Status Scale for Head and Neck Cancer	Mittal et al 2015 ⁴⁴	Swallowing/ Saliva Production	13	Chemoradiotherapy	H&N cancer-specific		
	Hutcheson et al 2014 ⁴⁵	Chemotherapy in relation to swallowing	47	Untreated stage IV SCC	Disease specific, Involves another person i.e. the clinician	Involves another person i.e. the clinician	MD Anderson Dysphagia Inventory
	Teguh et al 2009 ²⁰	Hyperbaric oxygen	19	RT treatment tongue SCC	Good for functional activities such as swallowing		H&N35 EORTC QLQ-C30
Functional Assessment of Cancer Therapy H&N	Rischin et al 2010 ⁴⁶	Chemoradiotherapy effectiveness	850	Previously untreated advanced SCC	H&N cancer-specific Good for chemo/radiotherapy Rx options		
	Simon et al 2009 ⁴³	Methotrexate recurrent SCC	486	Recurrent SCC with RT not amenable to salvage	H&N cancer-specific	Low completion	FHNSI-10

	Cohen et al 2006 ⁴⁷	Chemoradiotherapy	53	Stage II or III SCC	Good focus on chemo and radiotherapy options		
	McNeely et al 2008 ⁴¹	Exercise for shoulder pain	52	Neck dissection, shoulder dysfunction	Good for function & exercise		Neck Dissection Impairment Index
	Ringash et al 2008 ⁴⁸	RT	171	Locally advanced SCC III/IV	Good for function Good for RT		
MD Anderson Dysphagia Inventory	Hutcheson et al 2014 ⁴⁵	Chemotherapy in relation to swallowing	47	Untreated stage IV SCC	Specific to swallowing	Needs to be used in conjunction with another questionnaire for more rounded assessment	Performance Status Scale for Head and Neck Cancer
	Mehanna et al 2016 ¹⁹	PET-CT in advanced SCC	564	N2 or N3 metastases	Another more specific dimension related to H&N		H&N35
Spitzer QoL Index	Robert et al 1997 ⁴⁹	Chemotherapy medications	26	Recurrent or metastatic cancer	Related to basic living tasks	Not H&N cancer specific	
	Elliot et al 2006 ⁵⁰	Prevention of radiation dermatitis	547	Stage III or IV SCC requiring RT	Validated Self-assessment	May be subject to reviewer or pt bias	Head and Neck Radiotherapy Questionnaire
Hospital Anxiety and Depression Scale	Griffiths et al 1999 ⁵¹	Physical & Psychological symptoms	615	SCC treatment	Psychologically specific	Data needs to be analysed in several ways to ensure consistency	Rotterdam Symptom Checklist
	Schiefke et al 2008 ¹⁴	QoL after SND	49	Sentinel node bx or SND	Psychologically specific	Needs to be used in conjunction with another questionnaire for more rounded assessment	EORTC QLQ-C30
	Vilela et al 2005 ¹⁶	Coping strategy therapy	101	Completed cancer treatment	Psychologically specific		EORTC QLQ-C30
	Myers et al 1999 ²³	Psychosocial intervention	47	H&N SCC, no previous mental health issue	Psychologically specific		EORTC QLQ-C30
Head and Neck Radiotherapy Questionnaire	Elliot et al 2006 ⁵⁰	Prevention of radiation dermatitis	547	Stage III or IV SCC requiring RT	H&N cancer-specific RT specific	May be subject to reviewer or pt bias	Spitzer QoL Index

	Ringash et al 2005 ⁵²	Post-RT xerostomia	130	RT to parotids	Validated Cancer-specific RT specific Multi-dimensional Easy to complete	Questionnaire disease specific Uses summary scores so may not be adequate for xerostomia assessment Does not assess patient weighting of problem	
	Wong et al 2003 ⁵³	TENS post RT	37	Xerostomia post radial RT	Easy to complete		
	Warde et al 2002 ⁵⁴	Oral pilocarpine for RT	130	RT with inclusion of parotids	RT specific		
EQ-5D	Mehanna et al 2016 ¹⁹	PET-CT in advanced SCC	564	N2 or N3 metastases	Good for cost effectiveness assessment		EORTC QLQ-C30 H&N35 MD Anderson dysphagia
Head and Neck Cancer Inventory	Lazarus et al 2013 ⁵⁵	Swallowing/ Tongue strength	23	Post-op SCC resection; no pre-existing dysphagia	Good for functional scores		
Modified WHO Performance Status Scale	Corry et al 2008 ⁵⁶	PEG vs NG	33	RT and needing enteral feeding	Specific to NG tubes Simple	Not related to cancer	
Dermatological Life Quality Index	Potthoff et al 2014 ⁹	Medication for pain intensity	34	Cetuximab chemoradiotherapy rhagades	Specific to dermatology	Not related to H&N cancer	EORTC QLQ-C30
Rotterdam Symptom Checklist	Griffiths et al 1999 ⁵¹	Physical & Psychological symptoms	615	SCC treatment	Cancer specific General view of health Pt recorded		Hospital Anxiety and Depression Scale
Hearing Handicap Inventory for the Elderly	Schultz et al 2010 ⁵⁷	Hearing loss of H&N cancer patients	141	Had RT	Specific to hearing loss	Not relevant for any other features of H&N cancer	
QoL-RTI	Maguire et al 2011 ⁵⁸	RT therapy in advanced SCC	30	Stage III or IV SCC requiring RT	Radiation and RT specific Good for swallowing measurements	Not related to other aspects of H&N cancer	

COOP-WONCA	Van bokhorst et al 2000 ¹²	Enteral nutrition	49	Malnourished	Generic Practical Easy	Not specific to cancer or H&N	EORTC QLQ-C30
HNQoL	Donatelli-Lassig et al 2008 ⁵⁹	QoL post chemoradiotherapy	65	Inclusive of SND	Cancer-specific H&N specific		

Table 4. Patient Reported Outcome Measures used in papers relevant to Head & Neck Cancer.