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The experience of recurrent oropharyngeal cancer and its impact on function and quality of life outcomes

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A thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy



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Statement of originality

I declare that this thesis is my own work except where otherwise stated.

Grainne Brady

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Abstract

Background:

Recurrent oropharyngeal cancer (rOPC) presents some of the most challenging decision-making in head and neck cancer (HNC) practice. Persistent toxicities from previous treatments, including long-term and late swallowing dysfunction, coupled with the potential function and quality of life (QoL) morbidity of further treatment(s) can influence decision-making. National guidelines emphasise that patients must be counselled on the function and QoL morbidity of treatments. However, little is known about the functional morbidity of treatments and essential patient experience data is lacking.

Aim:

To address gaps in the current evidence base with a focus on function, QoL, patient priorities, and patient and carer experience.

Method:

A systematic review was undertaken to investigate if and how function, QoL and patient experience data are collected and reported for patients undergoing curative and non-curative treatments for rOPC. This informed the development and undertaking of a multi-centre mixed methods study to investigate function and QoL outcomes, patient priorities and the patient and carer experience of rOPC which was underpinned by patient and public involvement and engagement (PPI/E) from concept to completion.

Results:

Function and QoL will change with treatment for rOPC. Treatment-related priorities do not and remain focused on cure or survival, with patients acknowledging lower success rates and the possibility of poorer function/ QoL. Patient and carer experiences vary in terms of the opportunity for shared decision-making (SDM), pre-treatment counselling and ongoing support during and following treatment, highlighting an inequity of care.

Conclusion:

Clinical practice needs to focus on the provision of personalised care and SDM where patient concerns, values and priorities define the care, treatment and support provided. This

needs to be informed by future research seeking to define core outcomes required to inform this SDM process and to capture the unique and changing needs of patients and their caregivers throughout the treatment pathway.

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Thesis outputs

Publications:

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Publications (protocols):

Swallowing, voice and speech and quality of life outcomes in patients receiving surgical and non-surgical treatment for residual, recurrent and new primary oropharyngeal cancer in a previously irradiated field: a systematic review PROSPERO CRD42021236540]

Publications in press:

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Publications (conference abstracts):

Brady, G., Roe, J., Paleri, V., Lagergren, P., & Wells, M. Advances in Communication and Swallowing. 'That was a bigger blow than getting the cancer in the first place… to be diagnosed with recurrence' The patient and carer experience of recurrent oropharyngeal cancer (OPC) and changes to swallowing and quality of life - a qualitative study. UK Swallowing Research Group 2022 Conference, 09 Feb 2024. Advances in Communication and Swallowing. (*in press*)

Brady, G., Roe, J., Paleri, V., Lagergren, P., & Wells, M. Swallowing, voice and speech and quality of life outcomes in patients receiving surgical and non-surgical treatment for residual, recurrent and new primary oropharyngeal cancer in a previously irradiated field: a systematic

review. UK Swallowing Research Group 2022 Conference, 05 Feb 2022.Advanced in Communication and Swallowing, vol. 26, no. s1, pp. S1-S14, 2023.

Conference presentations:

Event/ location	Date	Title	Format
British Association of Head and Neck Oncologists - London	17th May 2024	Recurrent oropharyngeal cancer- functional status, patient priorities and patient experience at point of diagnosis.	Poster
International Centre for Recurrent head and Neck Cancer (IReC) Inaugural Study Day- London	16th May 2024	PICO framework for trial development- re-irradiation for recurrence	Invited panel member
Irish Head and Neck Society Annual Meeting	19th April 2024	Early patient-reported functional and quality of life (QoL) outcomes in patients having curative and non-curative treatment for recurrent oropharyngeal cancer (OPC)	Poster
Royal Marsden Applied Health Research Away Day- London	13th October 2023	Patient experience, functional and quality of life outcomes in patients receiving surgical and non-surgical treatment for recurrent oropharyngeal cancer	Invited speaker
RMH annual SLT conference- London	19th September 2023	Recurrent HNC - the role of the SLT	Invited speaker
Imperial College Academic Training Office (CATO) North-West London Research	27th September 2023	Recruitment challenges in clinical research involving research participants with a diagnosis of recurrent head and neck cancer; a single study experience in the real world	Poster

symposium- London			
Imperial College Academic Training Office (CATO) North-West London Research symposium- London	22nd September 2021	Patient involvement in the design of a study to investigate functional and quality of life outcomes for patients undergoing treatments for recurrent oropharyngeal cancer	Poster
British Association of Head and Neck Oncologists - London	14th May 2021	Preparing the patient for salvage surgery in the setting of recurrent/ residual head and neck cancer (R/R HNC); maximising functional outcomes.	Oral
British Association of Head and Neck Oncologists - London	14th May 2021	Trismus following transoral robotic surgery for residual/ recurrent oropharyngeal cancer - a case series	Poster
British Association of Head and Neck Oncologists - London	14th May 2021	Functional outcomes following open and transoral robotic surgery for residual/ recurrent head and neck cancer (R/RECURRENT HNC): a case series	Poster

Collaborations:

Hardman, J. C., Holsinger, F. C., **Brady, G. C**., Beharry, A., Bonifer, A. T., D'Andréa, G., ... & Paleri, V. (2022). Transoral robotic surgery for recurrent tumors of the upper aerodigestive tract (RECUT): an international cohort study. *Journal of the National Cancer Institute*, *114*(10), 1400-1409.

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Draft collaborative articles:

Williamson, A., **Brady, G**., Harris, N., Abdul Haris, P., Bisase, B, Chiu, K.…… &. Paleri, V. Multi-disciplinary evidence-based consensus statements on the management of patients with recurrent head and neck cancer treated by salvage surgical procedures: The International Centre for Recurrent Head and Neck Cancer (IReC) (*under review*)

Abbreviations

BRACS - Boston Residue and Clearance Scale

CPS- Chicago Priority Scale

DIGEST- Dynamic Imaging Grade of Swallowing Toxicity

DoIMRT- Dysphagia Optimised Intensity Modulated Radiotherapy

DOSS- Dysphagia Outcome Severity Scale

EORTC- European Organisation for Research and Treatment of Cancer

FA- Framework Analysis

FEES- Flexible Endoscopic Evaluation of Swallowing

FOIS- Functional Oral Intake Scale

G-tube- Gastrostomy

HNC- Head and neck cancer

HPV- Human papilloma virus

ICF- International Classification of Functioning Disability and Health

IDDSI- International Dysphagia Diet Standardisation Initiative

IMRT- Intensity Modulated Radiotherapy

IQR- Interquartile range

IReC- International Centre for Recurrent Head and Neck Cancer

MDADI- MD Anderson Dysphagia Inventory

MDT- Multidisciplinary team

NA- Not applicable

NHS- National Health Service

NIHR- National Institute of Health Research

OPC- Oropharyngeal cancer

PAS- Penetration Aspiration Scale

PIC- Participant identification centre

PPI/E- Patient and Public Involvement/ Engagement

PSS-HN- Performance status scale for head and neck cancer

PSS-HN EiP Performance Status Scale for Head and Neck Cancer Eating in Public

PSS-HN NoD Performance Status Scale for Head and Neck Cancer Normalcy of Diet

PSS-HN UoS Performance Status Scale for Head and Neck Cancer Understandability of Speech

QoL- Quality of life

RCSLT- Royal College of Speech and Language Therapists

RM- Royal Marsden

rOPC- recurrent oropharyngeal cancer

RTOG- Radiation Therapy Oncology Group

SDM- Shared decision-making

SHI- Speech Handicap Index

SLT- Speech and language therapist/ therapy

TORS- Transoral robotic surgery

UKSRG- UK Swallow Research Group

UWQoL- University of Washington Quality of Life Questionnaire

WHO- World Health Organisation

Chapter 1 Background

1.1 Introduction

This thesis aimed to identify and address gaps in the current evidence base for recurrent oropharyngeal cancer (rOPC) with a focus on functional and quality of life (QoL) outcomes, treatment-related priorities and patient and carer experience.

It has been highlighted in national guidelines that patients with recurrent cancer should be counselled on the likely functional (speech and swallowing) and QoL impact of further treatments (Homer and Winter, 2024). However, my clinical experience working as a speech and language therapist (SLT) at the Royal Marsden NHS Foundation Trust's International Centre for Recurrent Head and Neck Cancer Centre (IReC) revealed that there is little evidence to support this counselling or indeed the ongoing rehabilitation of these patients.

In the initial stages of the funding application for this research and early literature searches to develop my research ideas, it became apparent that data on functional , QoL and experience of patients with rOPC is very limited. This led to the development of a number of research questions. However, before introducing these research questions, the first part of this introductory chapter describes why a focus on function and QoL is important. The structures and functions of the oropharynx are introduced and altered function including impaired swallowing and communication discussed. Secondly, this chapter outlines the clinical features of primary oropharyngeal cancer (OPC), treatments, functional and QoL implications. The remainder of the chapter will introduce rOPC, examining the existing literature relating to treatments, decision-making and potential functional and QoL implications.

1.1.1 Anatomy and structures

The pharynx is the medical term referring to the back of the throat. It is divided into three parts, the nasopharynx, oropharynx, and laryngopharynx. The oropharynx anatomically sits just behind the mouth and includes the posterior third of the tongue, the soft palate, and the back wall of the throat, also known as the posterior pharyngeal wall (Ellis and Mahadevan, 2018). The oropharynx plays a key part in swallowing foods and fluids and is a conduit through which we inhale and exhale air and produce speech. With any changes in the anatomy or physiology of the back of the tongue or throat there is the potential for a person to have difficulties swallowing (dysphagia). The ability to produce clear voice/ speech may also be impaired.

1.1.2 Swallowing and the impact of dysphagia

Dysphagia is the medical term to describe difficulties with eating, drinking and swallowing (RCSLT, 2023). Dysphagia can cause changes to swallowing efficiency and safety (Hutcheson et al., 2017). When swallowing safety is impaired, particles of food and fluids can enter the lungs rather than the stomach (aspiration) (Logemann, 1995). When swallowing efficiency is reduced, food and fluids are insufficiently cleared from the throat (Hutcheson et al., 2017). Eating and drinking can take a long time and be very effortful or uncomfortable. Changes to swallowing efficiency or safety can result in serious health complications including malnutrition, dehydration, and aspiration related pneumonia (RCSLT, 2023). Some patients with dysphagia may require the use of a permanent feeding tube placed into their stomach which is called a gastrostomy (RCSLT, 2023). As eating and drinking are hugely linked to pleasure and social activities, the presence of dysphagia can have a huge impact on a person’s quality of life (QoL) (RCSLT, 2023).

1.1.3 Communication and the impact of changes to speech and voice

Speech is produced by air moving from the lungs through the voice box (larynx), causing the vocal cords to vibrate to produce sound (Mathieson, 2013). This sound then moves and resonates through the pharynx/ throat and into the oral cavity where it is shaped into speech sounds using the articulators including the lips, tongue and soft palate (Mathieson, 2013). Any changes in anatomy to the throat, palate and mouth can cause changes to the biomechanics of speech production. How a person's speech and voice sound is hugely linked to their identity and sense of self. Any changes to a person's communication can have a significant psychosocial impact (RCSLT, 2023).

1.2 Oropharyngeal cancer (OPC)

1.2.1 Incidence of OPC

In the UK, approximately 3,000 patients are diagnosed with OPC annually (Homer and Winter, 2024). The number of cases continues to rise with a doubling of incidence between 2000 and 2016 (Homer and Winter, 2024). In comparison to other types of head and neck cancer (HNC), OPC has the highest incidence of advanced stage at time of diagnosis (Creaney et al., 2022). This means that there can be a higher rate of treatment failure with disease relapse/ recurrence.

1.2.2 Causes

Traditionally the main risk factors for all HNC subsites including the oropharynx have been a history of tobacco and alcohol use (Schache et al., 2016). More recently, human papilloma virus (HPV) has been recognised as a risk factor for the development of OPC (Schache et al., 2016). The discovery of a virally-induced aetiological category has led to the development of a UK-wide HPV vaccination programme available for both boys and girls aged 12-13 years (Jopson and Callender, 2022). Prior to 2018, the vaccination was only available for girls due to the known link between HPV disease and the development of

cervical cancer. However, despite the current UK-wide vaccination programme, rates of OPC disease in the UK are likely to continue to increase (Schache et al., 2016). This is in part due to the late adoption of the vaccination programme for boys, the latency period from HPV infection to OPC development (Madathil et al., 2020) and also more recently the reduction in the number of children vaccinated due to the COVID-19 pandemic (GOV.UK, 2023). Also, whilst HPV-related disease appears to result in a rising incidence of OPC in many developed countries, in the UK a previous multicentre cross-sectional retrospective study involving 1600 patients with OPC found that all aetiological categories are increasing, including both HPV-related and non-HPV-related disease (Schache et al., 2016).

HPV positivity in OPC is considered a positive prognostic marker despite often presenting at a later stage of disease in comparison to HPV-negative OPC (Mehanna et al., 2016a). HPV-positive OPC patients are generally younger, with minimal or absent smoking history, and HPV-positive disease generally responds more favourably to treatment even when diagnosed at an advanced stage (Zanoni et al., 2019). HPV-positive disease has shown a 58% reduction in the risk of death when compared to HPV-negative OPC (Ang et al., 2010). However, HPV-related disease is almost exclusively a Western issue, with very low rates in other parts of the world (Noronha et al., 2024).

1.2.3 Presentation

Patients with OPC often present with a lump in the neck as their primary and often sole symptom at presentation, however pain on swallowing (odynophagia), earache (otalgia) and subtle changes to speech quality known as ‘hot potato speech’ may also be present (Mehanna et al., 2016a). As HPV-positive disease often presents with a small and/or undetectable primary tumour in the oropharynx, with metastases (spread) to the neck, this results in a higher staging at presentation (Ang et al., 2010).

1.2.4 Staging

The relative severity or extent of OPC is expressed using the 8th edition of the American Joint Committee on Cancer/ Union for International Cancer Control (AJCC/UICC) TNM staging system (Zanoni et al., 2019). This system stages oropharyngeal disease depending on the extent/ size of the tumour itself (T-stage), the presence or absence of spread to the regional lymph nodes in the neck (N-stage) and the presence or absence of disease spread/ metastases to other organs of the body (M-stage) (Roland et al., 2016).

1.2.5 Prognosis

Disease staging and HPV status will impact overall prognosis (Mehanna et al., 2016a). A previous randomised controlled trial with over 700 patients with OPC, although powered to examine overall survival between two radiation treatment regimens, also reported survival rates with respect to HPV status (Ang et al., 2010). In the HPV-positive group compared to the HPV-negative group, 3-year survival rates were significantly better at 82.4%, vs. 57.1%, $p<0.001$ (Ang et al., 2010). In addition to tumour stage, this study also highlighted smoking history, tumour staging and nodal spread as prognostic indicators for risk of death with oropharyngeal disease.

1.2.6 Evolution of treatment for OPC

Surgery, radiation (the delivery of high dose x-rays) and chemotherapy are used in the treatment of OPC (Mehanna et al., 2016a). Over the past quarter of a century the landscape of treatment for OPC has changed significantly (Howard et al., 2016).

Historically, open surgery was the mainstay of treatment for primary OPC. The aim of surgery in the management of HNC is complete removal of the tumour with an appropriate excision margin surrounding the tumour (Homer and Fardy, 2016). Open surgery for OPC generally involves access procedures including a pharyngotomy (surgical incision into the

pharynx/ throat via the neck) or mandibulotomy (jaw-splitting procedure), with or without a tracheostomy (surgically created stoma through the windpipe) (Mehanna et al., 2016a). Depending on the size of the tumour excised, reconstruction using a flap of muscle and/or skin from elsewhere in the body (for example the arm or the leg) is often required (Mehanna et al., 2016a). Post-surgical changes to the anatomy of the oropharynx can cause significant changes to a person's ability to be able to eat and drink comfortably and safely. Their speech clarity may also be impacted.

Although surgery was believed to be the most effective treatment option for many years, a seminal review paper was published in 2002 by Parsons and colleagues in the United States (Parsons et al., 2002) which investigated the treatment of primary OPC with surgery or organ sparing radiation treatment. In the absence of a randomised controlled trial investigating superiority of radiotherapy treatment (organ-sparing) or surgery in the treatment of OPC, they conducted a non-randomised retrospective pooled data analysis on survival and complications. The study included data for over 6000 patients treated for OPC with either radiotherapy treatment with or without neck dissection surgery (removal of the lymph nodes of the neck), or surgery with or without post-operative radiotherapy over a 30-year period at academic institutions in the US and Canada (Parsons et al., 2002). This review concluded very similar rates in overall survival between primary radiation or primary surgery (5-year overall survival 47% versus 43% respectively, $p= 0.2$) however, there was a marked increase in severe complications with surgery (23% versus 6% $p<.0001$) (Parsons et al., 2002). Due to the high risk of severe complications demonstrated in this review, primary radiation treatment began to gradually take the place of open surgery. Further developments in the non-surgical treatment of primary OPC came with the addition of chemotherapy to radiation schedules. A more recent large meta-analysis including more than 16,000 patients with HNC showed an 8.1% absolute survival benefit for patients with OPC treated with concurrent chemoradiation versus radiation alone (Blanchard et al., 2016). Due to the previously noted high risk of complications with open surgery, and the demonstrated

enhanced survival with the addition of chemotherapy to radiotherapy regimes, combined chemoradiation thus became the mainstay of treatment for OPC.

However, over time, long term and late toxicity with swallowing decline in patients previously treated with chemoradiation became a concern. Machtay and colleagues (Machtay et al., 2008) completed a secondary analysis of Radiation Therapy Oncology Group (RTOG) trials of chemoradiation for locally advanced squamous cell carcinoma of the head and neck (RTOG 91-11, 97-03, and 99-14) (Machtay et al., 2008). In a sample of 230 patients, with a medium follow up of just under 3 years, severe late toxicity was noted in 43%, including severe dysfunction of the larynx or pharynx (dysphagia), feeding tube dependence, and non-cancer related death which was recorded as pneumonia (Machtay et al., 2008).

The cumulative impact of previous research highlighting the high surgical complications rates and late toxicities from non-surgical treatments has driven more recent research in primary OPC management to focus on the development of smarter, kinder treatments to minimise the potential treatment burden on function and overall QoL. Such advances have included the development, and now standard of care use, of intensity modulated radiation therapy (IMRT) for all HNC patients having radiation treatment in the UK (Nutting, 2016). IMRT allows for more accurate delivery of radiation treatment to the target tumour and where possible reduces the dose to the surrounding tissues (Nutting, 2016). For example, a common side effect of radiation treatment is xerostomia (dry mouth). A previous UK randomised controlled trial compared the rate of xerostomia in patients treated with IMRT and non-conformal traditional radiation treatment in 94 patients with OPC or hypopharyngeal SCC . This study demonstrated that by using IMRT to reduce the radiation dose to the parotid glands (salivary secreting), there was a significant reduction in xerostomia at 1-2 years post-treatment (Nutting et al., 2011). More recently a multicentre UK-based phase III randomised controlled trial involving 122 patients with OPC and hypopharyngeal SCC investigated a dysphagia-optimised intensity modulated radiation treatment (DoIMRT) to

standard IMRT (Nutting et al., 2023). Provisional findings from this study did not show a clinically significant difference in patient reported swallowing QoL scores at one-year post-treatment. However, confidence in the superiority of DoIMRT is supported by improvements across secondary clinician rated measures and secondary patient reported outcomes (Nutting et al., 2023).

Surgical advances have included the use of minimally invasive surgical techniques such as transoral laser microsurgery (TLM) or transoral robotic surgery (TORS). In comparison to open surgery, TORS has been found to have less morbidity and presumed superior functional outcomes (Mehanna et al., 2016a). However, there have been very few studies comparing functional outcomes for TORS versus open surgery (Park et al., 2020). A recent systematic review and meta-analysis comparing TORS and open surgery found superior disease-free survival rates for TORS however, was unable to find any evidence to suggest that functional outcomes would be superior (Park et al., 2020). This was at least in part due to the high degree of heterogeneity (I^2= 78%) between studies in terms of method and timing of functional outcome measurement (Park et al., 2020).

As highlighted in the literature, one of the other potential benefits of minimally invasive surgery is to achieve accurate pathological staging of the disease specimen (Hamilton and Paleri, 2017). This could potentially allow de-escalation of non-surgical follow-up (adjuvant) radiation treatment to reduce any potential long-term toxicity. This however remains under investigation with an ongoing large multicentre randomised control trial looking specifically at patients with HPV-positive OPC (Owadally et al., 2015).

There has been a clear paradigm shift in the focus of current research in primary OPC treatment to not only focus on survival outcomes, but to place equal importance on optimising functional and QoL outcomes. In many of the trials mentioned above (Owadally et al., 2015, Petkar et al., 2016, Nutting et al., 2023) the primary outcome measure is

patient-reported swallowing-related quality of life using the MD Anderson Dysphagia Inventory (MDADI) (Chen et al., 2001). In addition to the primary outcome measures in these trials, a range of multidimensional swallowing and QoL secondary outcomes are included. This is in line with previous consensus guidelines on the conduct of phase III organ preservation trials where radiation treatment is compared with surgical management (Lefebvre et al., 2009).

Changes in research protocols in the management of primary disease have also been reflected in clinical practice, with guidelines defining the role of the SLT who has a key role in supporting patients before, during and following treatments to optimise both function and subsequent QoL (Schache et al., 2021). A minimum standard for multidimensional functional outcome measurement in clinical practice in primary HNC at baseline and following treatment has also been recommended to facilitate the early initiation of SLT functional rehabilitation (Schache et al., 2021).

1.2.7 Current treatment of primary OPC in the United Kingdom

Early-stage disease, classified as tumour staging T1-T2 with no nodal spread (N0), is single modality treatment; either minimally invasive surgery (transoral robotic surgery or transoral laser surgery) or radiation treatment (Homer and Winter, 2024). Open surgery for early-stage disease is not recommended given the potential functional morbidity in terms of speech and swallowing outcomes (Homer and Winter, 2024).

National guidelines highlight that there are no high-quality trials comparing survival with minimally invasive surgery (TORS or laser) and radiation treatment modalities however, retrospective case series demonstrate equipoise in survival outcomes (Homer and Winter, 2024). In a recent multicentre randomised controlled trial where swallowing-related QoL was the primary endpoint, patients treated with radiation were found to have superior swallowing-

related QoL however, the result did not reveal a clinically significant difference between the two treatment groups (Nichols et al., 2019).

For advanced staged disease with tumour stage T3-T4 and/or any nodal involvement, combined modality treatment (more than one form of treatment) is recommended including radiation treatment with chemotherapy or surgery with adjuvant (chemo)radiation (Homer and Winter, 2024).

1.2.8 Treatment decision making

It is internationally mandated that treatment decision-making must be undertaken within the context of a HNC multidisciplinary team (MDT) (Licitra et al., 2016). All patients undergoing treatment for primary or recurrent HNC must be discussed at a MDT meeting and an agreed treatment plan must be clearly documented (Schache et al., 2021). Given the potential impact of HNC on a range of bodily functions (respiration, swallowing, speech and voice) and the multi-modal treatments available, it is recommended that a range of experienced clinicians are included within these MDTs (Licitra et al., 2016). Decision-making regarding treatment options is quite often based on the operability or non-operability of the tumour based on the size and location, the potential functional deficit in addition to patient and clinician preferences (Mehanna et al., 2016a).

1.2.9 Impact on function and quality of life (QoL)

Even with treatment advances in radiation treatment and minimally invasive surgery for OPC, there still remains a potential impact on both function and QoL.

A previous prospective study described patient reported swallowing outcomes in 65 patients who underwent parotid sparing IMRT (Roe et al., 2014). The MDADI (Chen et al., 2001) was used as the primary outcome measure. The MDADI is a patient reported outcome measure

with a composite score calculated from 20-100, where a higher score indicates a better swallowing-related QoL (Chen et al., 2001). Guidance has been published on the classification of MDADI composite scores as optimal (≥80), adequate (≥60-<80) and poor (<60) (Goepfert et al., 2017). Roe and colleagues (Roe et al., 2014) identified a clinically significant difference in swallowing-related QoL from baseline prior to treatment initiation (mean 86.9) to 12 months post-treatment (71.3). More recently in a phase III randomised control trial comparing dysphagia optimised IMRT versus standard IMRT, swallowing-related QoL using the MDADI was also shown to be impaired at 1 year post-treatment in both treatment groups (standard IMRT: 70.3, dysphagia optimised IMRT: 77.7) (Nutting et al., 2023). Likewise, impaired swallowing-related QoL was noted using the MDADI in an open-label, phase 2, randomised trial comparing primary TORS versus primary radiation in 68 patients (Nichols et al., 2019). One-year outcomes demonstrate a degree of swallowing-related QoL impairment with MDADI scores noted at mean 86·9 (SD 11·4) in the radiotherapy group versus 80·1 (13·0) in the TORS plus neck dissection group however, this is difficult to interpret as baseline scores are not reported and many of the patients in the TORS group required adjuvant radiation. All three of these studies demonstrate that despite the most recent advances in radiation techniques and/or minimally invasive surgery, patients continue to report a degree of swallowing-related QoL impairment at 12 months post-treatment.

A previous systematic review investigated QoL outcomes for patients undergoing radiation treatment with/ without chemotherapy for HNC (Klein et al., 2014). Similarly, QoL outcomes were also investigated for patients undergoing primary surgery for HNC with/ without post-operative radiation treatment in another study (Rathod et al., 2015). A number of sources of potential bias were highlighted in the included studies in both reviews, including but not limited to stating a priori hypothesis, unclear/ absent statistical planning for missing data and unreported assessment interval. Both studies reported an initial deterioration in overall QoL which gradually returns to baseline post-treatment despite ongoing persisting symptoms

including eating, drinking and swallowing-related difficulties, and changes to appearance (Rathod et al., 2015, Klein et al., 2014). A possible explanation offered for the return of overall QoL scores in the presence of ongoing potentially high symptom burden is response shift over time (Rathod et al., 2015). However, caution is advised with interpretation of the finding of QoL return to baseline without recognising that for many patients in these studies, QoL is significantly impacted at baseline (Rathod et al., 2015) thus patients continue to have potential unmet needs at 12 months post-treatment.

A seminal paper reporting on a retrospective cohort study involving 104 patients with HNC compared overall QoL, anxiety and depression in HNC patients with no/ minimal dysphagia (n=31) and those with a known dysphagia (n=73) (Nguyen et al., 2005). This study identified that those patients with a moderate-severe dysphagia on instrumental evaluation of swallowing, had a statistically significant lower overall QoL (p=0.005), and increased depression (p=0.005) and anxiety scores (p=0.005) (Nguyen et al., 2005). Given the known impact of primary OPC treatment, the importance of considering function and QoL in treatment decision-making is clear.

1.3 Recurrent oropharyngeal cancer (rOPC)

1.3.1 Incidence

Despite ongoing advances in treatment techniques used for OPC, the incidence of disease recurrence remains high, in particular for HPV-negative disease. A recent systematic review including 9 studies and 2,974 patients, reported an incidence rate of locoregional rOPC at 9% for HPV-positive disease and 26% for HPV- negative disease (Asheer et al., 2020).

Disease which recurs within 12 months of previous radiation treatment is referred to as residual disease, between 12 months and five years as recurrent disease and more than five years can be referred to as second primary disease (Hardman et al., 2020). Frequently,

patients will have had previous radiation as part of their initial treatment for HNC (Hardman et al., 2020). In this setting, residual, recurrent and new primary disease categories can be considered as a homogenous group, due to the technical difficulties involved in re-challenging treatments (complex surgery/ re-irradiation) and potential baseline functional difficulties and/or persisting or late toxicities due to previous radiation exposure (Brady et al., 2020). For the purposes of this thesis, I have grouped these three categories of patients together under the umbrella term of rOPC.

1.3.2 Prognosis

Historically, due to the poor prognosis and potential morbidity of curative treatment options including surgery and re-irradiation, the majority of patients were treated palliatively (Mehanna et al., 2016b). However, a recent systematic review with meta-analysis including 22 studies and 1,105 patients, investigated the survival rates over time for patients treated for rOPC with curative intent (Jayaram et al., 2016). It was found that prior to the year 2000, the 5-year survival rate was just 18% whilst in the last two decades (from 2000 onwards), the survival rate increased to 51% ($p < .0001$) for patients treated with surgery. This study also compared survival rates between curative treatment modalities. The authors concluded superior 5-year survival for surgery in comparison to re-irradiation treatment (26% vs 16%, respectively; $p < .001$) (Jayaram et al., 2016). The evidence base for improved survival has signalled a paradigm shift in the management of rOPC, with more patients being considered for potentially curative treatment options (Mehanna et al., 2016b). The area of rOPC continues to be an evolving landscape of new treatments and techniques with more patients now living with and beyond a diagnosis of rOPC. The treatment options for rOPC are now considered.

1.3.3 Treatment and oncological outcomes

Surgery

The current UK standard of care for the curative management of rOPC is open surgery which involves surgical lip and/or jaw-split (mandibulotomy) and/or surgical opening of the throat (pharyngotomy) for access, with likely free tissue transfer reconstruction of the surgical defect (Mehanna et al., 2016b). Open surgery for rOPC has been associated with high morbidity rates (Zafereo et al., 2010). More recently transoral robotic surgery (TORS) has emerged as a potentially less morbid surgical treatment option (Paleri et al., 2020). A multi-centre case control study investigated the outcomes for 128 patients undergoing surgical management of rOPC (White et al., 2013). Treatment options included open surgery (n=64) and TORS (n=64). Patients who had TORS were found to have a lower incidence of tracheostomy use (n=14 vs n=50; p<.001), significantly shorter operation times (111 minutes versus 350 minutes; p<.001), less blood loss (49ml vs 331ml; p< .001) and reduced feeding tube use (n=23 vs n=48; p< .001). The 2-year recurrence-free survival rate was significantly higher in the TORS group than in the open surgery treatment arm (74% and 43%, respectively) (p = .01) (White et al., 2013). In a more recent systematic review and metanalysis investigating survival outcomes for the use of TORS in recurrent HNC (including OPC), 8 studies involving 161 patients were included, with a similar 2-year recurrence free survival rate at 74% (Hardman et al., 2020).

Re-irradiation

Historically using conventional radiation techniques, overall survival rates for patients treated with re-irradiation were poor, with almost a quarter of patients experiencing severe toxicity related complications (Spencer et al., 2001). In an era of advanced radiation techniques there may be opportunities for re-irradiation and it would appear that overall survival is enhanced in the adjuvant setting following salvage surgery rather than as a single modality treatment (Mehanna et al., 2016b). A recent retrospective single site cohort study

investigated disease control rates and late toxicities for 137 patients treated with re-irradiation for recurrent HNC (Bots et al., 2017). Five-year loco-regional control rates were superior for re-irradiation delivered in the post-operative setting (after surgery for recurrence) rather than as a single modality treatment (46% versus 20%; p= .05), however 16 instances of toxicity grade 4 or above[1] were noted (Bots et al., 2017). A more recent study looked at overall survival at two-years and toxicity grading for 65 patients undergoing re-irradiation as a single modality treatment (n=40) versus systemic non curative treatment (n=25). Re-irradiation improved 2-year overall survival, (32 % versus 11 %), compared to systemic therapy alone ($p < 0.05$). Grade 3+ toxicity was significantly higher in the re-irradiation group compared to those treated by systemic therapy (53 % vs. 28 %, $p < 0.001$), including three treatment-related deaths in the re-irradiation group (Chen et al., 2024).

Non-curative treatments

In patients with rOPC where surgery/ re-irradiation is not possible due to the site and extent of the disease or the individual's performance status, palliative systemic treatments may be offered (Mehanna et al., 2016b). A recent multicentre retrospective review was conducted across Europe, Asia, and Latin/ North America investigating the survival outcomes for the various palliative systemic treatment options available (Grünwald et al., 2020). The study included 733 patients with recurrent HNC, including 30% who had rOPC, across 71 sites. The most popular treatments included platinum-based combination chemotherapy treatments. Overall survival was 8 months (95% CI: 7.0–8.0), and one-year survival was 30.9% (95% CI: 27.5–34.3) (Grünwald et al., 2020). More recently with the emergence of immunotherapy treatments, a phase III randomized controlled trial was undertaken to determine whether pembrolizumab as monotherapy or in combination with chemotherapy improved overall survival compared with cetuximab plus chemotherapy as a first line

[1] Grade 3 toxicity Severe or medically significant but not immediately life-threatening; hospitalisation or prolongation of hospitalisation indicated; disabling; limiting self-care and activities of daily living (ADL). Grade 4 toxicity indicates that the problem is life threatening requiring urgent intervention. Grade 5 is death. SHAH, S. 2022. Common terminology criteria for adverse events. National Cancer Institute: USA, 784, 785.

treatment for recurrent HNC (Burtness et al., 2019). This study, which included 882 participants, showed that a carefully selected group of patients with specific tumour markers (programmed death ligand 1 (PD-L1) and a combined pathological score (CPS) of 1 or greater), had enhanced overall survival with pembrolizumab administered as a single modality treatment, when compared to cetuximab plus chemotherapy alone (12·3 months vs 10·3 months, 0·78 [0·64–0·96], p=0·0086) (Burtness et al., 2019). The more recently published follow up data (up to four years) demonstrates that for selected patients there is a potential long term response to these drugs (Harrington et al., 2023)

1.3.4 Function and quality of life (QoL) outcomes

Surgery

Tube feeding and tracheostomy dependence are often used as a surrogate marker for functional outcomes in the treatment of rOPC with curative intent. When comparing the TORS versus open surgery approach, White and colleagues reported greater tube feeding dependence rates at 1-year post-surgery in the open surgery group (20%) vs the TORS group (3%) (p=.002) (White et al., 2013). However, the number of feeding tubes present at baseline (following previous treatment), or the number placed prophylactically in the open surgery group is unknown. In a more recent international multicentre cohort study reporting functional outcomes following TORS for disease recurrence, tracheostomy dependence at one year was 10.8% (n=21/195) and tube feeding dependence was 33.8% (n=66/195) (Hardman et al., 2022).

Re-irradiation

Bots et al (2017) reported on both survival and late toxicity following re-irradiation (Bots et al., 2017). The European Organization for Research and Treatment of Cancer (EORTC) Radiation Therapy Oncology Group (RTOG) late radiation toxicity scoring criteria (Cox, 1995) was used in this study and severe toxicities of grade 4 or more persisting at 6 months

post re-irradiation were recorded in addition to feeding tube dependence (Bots et al., 2017) Unfortunately, the EORTC/ RTOG late radiation toxicity, unlike the EORTC/ RTOG acute toxicity rating scale, does not allow for the reporting of toxicity to the pharynx/ oesophagus, which includes swallowing difficulty/ dysphagia (Cox, 1995). Feeding tube dependence is also reported in this study, with just 2/137 patients requiring tube feeding at 6 months post re-irradiation, which appears quite low given the known risk of ongoing swallowing difficulties following primary radiation treatment (Roe et al., 2014). However, given the potential late impact of radiation on swallowing up to six years post-treatment (Patterson et al., 2018), perhaps the follow up interval for this surrogate marker of function was too short. Also, for a large proportion of these patients the site of disease at primary diagnosis (53%) or recurrence (29%) was the larynx (Bots et al., 2017). Definitive treatment or treatment for recurrence most likely involved surgical removal of the larynx (laryngectomy) for the majority of these patients. This may negate the need for a feeding tube as following laryngectomy surgery, the risk of aspiration and aspiration-related complications is no longer anatomically possible. However, without the use of standardised swallowing measures, the true impact on swallowing function in the setting of re-irradiation for HNC recurrence remains unknown.

Non-curative treatments

The KEYNOTE-040 (n= 495) and 048 (n=882) trials (Cohen et al., 2019, Burtness et al., 2019) compared pembrolizumab alone with standard of care, or with chemotherapy versus cetuximab with chemotherapy respectively for patients with confirmed recurrent and/or metastatic HNC disease. A secondary and exploratory analysis was also completed describing QoL outcome data for both trials (Rischin et al., 2022, Harrington et al., 2021). The European Organisation for Research and Treatment of Cancer 30-question quality of life (EORTC QLQ-C30), the EORTC 35-question quality-of-life head and neck cancer–specific module (EORTC QLQ-H&N35), were used to measure QoL outcomes. Endpoints included mean change from baseline in EORTC QLQ-C30 global health status/quality of life (GHS/QoL) and time to deterioration (TTD) in EORTC QLQ-C30 GHS/QoL and EORTC

QLQ-H&N35 pain and swallowing. The secondary analysis of QoL outcomes within the KEYNOTE-040 showed stable QoL at 15 weeks for those treated with immunotherapy, whilst a deterioration was noted for those treated with standard of care. Similarly, in the KEYNOTE-048 trial there was no clinically significant difference between or within treatment groups from baseline pre-treatment to week 15 post-treatment initiation using the EORTC QLQ-C30 GHS/ QoL, functioning or symptom scores (Rischin et al., 2022). What is notable in this study is the degree of baseline QoL impairment across all treatment groups- the EORTC QLQ-C30 GHS/QoL score is scored between 0-100 where a higher score depicts a higher QoL. In KEYNOTE-040 baseline EORTC QLQ-C30 GHS/ QoL was reported between 55.81 and 56.02 and in the KEYNOTE- 048 between 59.7 and 62.19 (Rischin et al., 2022, Harrington et al., 2021).

1.3.5 Treatment decision making

As noted previously, all patients presenting with HNC must be discussed at a HNC MDT meeting so that treatment options can be discussed and documented (Schache et al., 2021). Treatment decision-making can be complex in HNC, in particular for patients with disease recurrence (Brady et al., 2020). These decisions often involve a trade-off between potential cure and function including changes to respiration, swallowing and communication (Mehanna et al., 2016b). Whilst the goal of MDT decision-making in cancer care is to devise an individualised optimal treatment plan (Licitra et al., 2016), the barriers to patient involvement in that process have been highlighted in the literature (Hamilton et al., 2016). A recent UK based ethnographic study explored patient engagement in decisions regarding HNC in both the primary and recurrent setting (Hamilton et al., 2022). This study involved the observation of 35 MDT meetings, 37 MDT clinics and interviews with both patients and staff. Purposive sampling was used to include patients where more than one treatment option was available. This study concluded that MDT discussion will result in a ‘firm’ recommendation which is presented to and generally accepted by the patient within a medical model of care, with little opportunity to incorporate patient values or priorities into treatment decision-making

(Hamilton et al., 2022). National guidelines recommend that the baseline level of function and toxicity from previous treatments, in addition to the potential functional morbidity of any further treatments, should be considered in treatment decision-making for disease recurrence (Mehanna et al., 2016b). However, as highlighted in this chapter, there is a paucity of literature in relation to the potential functional impact of various treatment options. Theoretically, and in the absence of strong evidence, MDTs may be either under or over-estimating the impact of potential treatment options on function while determining the MDT recommendation and indeed the patients' own values and priorities may not be known or considered at this time. In addition, the patient's ability to engage in discussions and decision-making is diminished by the manner in which the 'best' treatment option is presented to them by the surgeon or oncologist following MDT discussion (Hamilton et al., 2022) and further hampered by a feeling of 'disempowerment' at a highly stressful time when faced with a diagnosis and complex decisions (Hamilton et al., 2022).

1.4 Summary

This chapter has demonstrated how OPC is increasing (Schache et al., 2016) in the UK and that despite ongoing developments in the surgical and radiation treatments used to treat primary OPC, recurrence rates remain high (Mandapathil et al., 2014). Historically, rOPC was considered to have a very poor prognosis and the majority of patients received palliation or best supportive care (Mehanna et al., 2016b). However, recent evidence has changed the landscape of how patients with rOPC are treated with enhanced survival with surgical techniques (Jayaram et al., 2016). Huge advances have also occurred with the adoption of immunotherapy as a first line treatment for inoperable disease recurrence. As a result, more patients are now being actively treated for rOPC and are living longer. However, the complexity of decision-making for patients and multidisciplinary teams in the treatment of rOPC has been highlighted in the literature (Mehanna et al., 2016b). The assumption is that curative treatments may be functionally morbid and that life-prolonging treatments may be somewhat 'kinder'. At present there is a lack of literature to support this. Also, the process of

MDT decision-making may not emphasise the importance of including patient priorities/ values at the time of treatment decision-making.

The apparent paradigm shift in the management of rOPC poses a new challenge to MDTs caring for these patients. HNC MDTs across the UK must equip themselves with the knowledge and skills to not only provide the most advanced and potentially curative or life prolonging treatments but also to continue to try and improve function and QoL outcomes whilst embedding individual patient priorities and values in the provision of personalised care and patient-centred treatment decisions.

National guidelines highlight the need to counsel patients on potential functional, QoL and survival outcomes for the various treatment options for rOPC so that patients can make an informed decision balancing the potential for reduced function and subsequent poorer QoL versus longer survival (Mehanna et al., 2016b). SLTs are core members of the HNC MDT and responsible for the comprehensive assessment of people being considered for treatment and for counselling them on likely swallowing and communication outcomes (Schache et al., 2021). In a recent qualitative study investigating the factors influencing decision-making in HNC recurrence, symptom burden and quality of life were highlighted as important factors influencing decision-making (Rhoten et al., 2021). However, the literature to date regarding rOPC has focused mainly on survival. If patients are to make informed treatment decisions regarding the range of treatment options available based on potential functional and/or QoL changes, robust functional and QoL outcome data and patient experience data must be available for all treatment options for rOPC. This information will also support the development of clinical care protocols to support these patients before, during and after these treatments.

This thesis aims to identify and address gaps in the current evidence base of rOPC with focus on function and quality of life (QoL) outcomes, patient priorities and patient and carer experience of rOPC for those undergoing curative and non-curative treatments.

This information will inform clinical practice for SLT and MDT members providing support and care to patients with rOPC who are making decisions about their treatment options and throughout their treatment pathway. This thesis will also inform further research in rOPC defining effective methods for the measurement of changes to function and QoL in rOPC.

In the next chapter the aims and objectives of this study will be explained in detail.

Chapter 2 Thesis overview

2.1 Publications and outputs

Brady, G., Lagergren, P., Paleri, V., Roe, J, & Wells, M. (2021) Patient involvement in the design of a study to investigate functional and quality of life outcomes for patients undergoing treatments for rOPC. Poster presentation. The North West London Research Symposium, London September 23rd, 2021.

This chapter will provide a summary of the research questions devised to address the two main objectives of this thesis, the methods used and the patient and public involvement/ engagement and participation (PPI/E) which has been key in the design and delivery of this research. The subsequent Chapter 3 will focus on the first study within this thesis, which was a systematic review. Chapter 4 will describe the methodology for the mixed methods study. In the subsequent Chapters 5 and 6 the results of the qualitative and quantitative workstreams will be presented separately, followed by Chapter 7 which will include the integrated findings. Chapter 8, the final chapter, will detail the strengths and limitations of this work in the context of the wider literature and will present a summary of the combined implications of this thesis for clinical practice and future research.

2.2 Patient and Public Involvement and Engagement (PPI/E)

The National Institute of Health Research (NIHR) describes patient and public involvement/ engagement (PPI/E) as research which is carried out 'with' or 'by' members of the public rather than 'to', 'about' or 'for' them (NIHR, 2021). PPI/E is partnership working between patients, caregivers and members of the public with researchers to inform and shape research priorities, design and methods (Price et al., 2022). The benefits of PPI/E in healthcare research have been highlighted including quality and relevance (NIHR, 2021), as well as financial in terms of reducing costs of under-recruitment with thorough trial design and consultation (Levitan et al., 2018).

Partnership working with patients has been key to the development of this thesis, from deciding on the overarching aim of this thesis, to shaping the methods, protocol development and subsequent amendments, through to results interpretation and dissemination. Throughout this chapter, where each study is described in relation to the overarching research goal and specific objectives for this thesis, a description of the influence of PPI/E will also be included.

2.3 Thesis aim

The literature reviewed in chapter one, in addition to patient and public involvement/ engagement (PPI/E), led to the development of a number of research priorities in relation to function and quality of life (QoL) outcomes. These included treatment-related priorities and patient and carer experience of rOPC including diagnosis, undergoing active treatments, and living with and beyond the diagnosis and treatment of rOPC. For the purposes of this thesis, active treatment is defined as either potentially curative treatments (surgery or re-irradiation) or non-curative and potentially life-prolonging treatments (chemotherapy, immunotherapy and/or clinical trials of investigational agents). This does not include patients who opt for best supportive care. While these treatments have been shown to potentially enhance the overall survival for patients with rOPC, there is a paucity of literature in relation to function and QoL outcomes. This includes patient treatment-related priorities and patient and carer experience of rOPC.

The PPI/E group for this piece of research was initially set up in 2018. Patients with rOPC and their family members/ caregivers were offered the opportunity to join a PPI/E group to set research priorities and be involved in planning and delivering a research project in the area. Initial meetings, which took place between 2018 and 2019, were very influential in the funding application development for this thesis. This initial PPI/E work was funded by a successful application for PPI/E funding support which was provided by the NIHR Research Design Service (RDS). Although the membership of the PPI/E group has changed over the

years due to patient deaths and changing circumstances, some members of the founding PPI/E research steering group have continued to work on this research from funding to dissemination. Over the years they have been joined by others working within the International Centre for Recurrent Head and Neck Cancer (IReC) PPI/E group.

In the initial planning meetings to inform the funding application for this research, the patient and carer experts by experience highlighted the need for people diagnosed with rOPC in future to be more aware of the potential impact of treatments on function/ QoL so that they could make informed choices regarding their treatment options.

'I would have found information on speech and swallowing very helpful in my decision-making...I didn't have that information and that was what I was worried about'.

Many of the patients had received different opinions as to how their recurrent disease should be managed, based on the potential morbidity of treatments. One gentleman reported how he had been offered palliative care at one centre as surgery *'could not be considered'*. However, when he went for a second opinion, surgery was '*offered as a potential curative treatment option*', and he accepted.

The PPI/E group raised concern that patients might not be offered treatment choices based on the opinions of healthcare professionals regarding potential morbidity of procedures/ treatments rather than the patients themselves being given the information required to empower them to make their own decision.

'The decision is entirely personal, but information is required to make the decision'.

This thesis aimed to identify and address gaps in the current evidence base of rOPC with focus on function and quality of life (QoL) outcomes, patient priorities and patient and carer

experience of rOPC for those undergoing curative and non-curative treatments. This aim was shaped by the PPI/E input ensuring its relevance to patients with recurrence from its inception.

2.4 Thesis objectives

The objectives of this thesis are to:

1. Identify and evaluate the existing literature for communication, swallowing and QoL outcomes, and patient experience, to define knowledge gaps.
2. Investigate the communication, swallowing, QoL outcomes, and treatment-related priorities for patients with rOPC and how these may change over time.
3. Explore the patient and carer experience of rOPC including diagnosis, treatment decision-making and living with the consequences of treatment.

2.5 Methodology

To meet these three objectives, two studies including three workstreams have been completed, including a systematic review of existing literature, an observational repeated-measures quantitative workstream and a longitudinal qualitative workstream, which were concurrently conducted as part of an overall mixed methods study.

2.6 Study 1: Systematic review:

To address the first objective of this PhD, a systematic review investigated the measurement and reporting of function and QoL outcomes and patient/carer experience in patients receiving surgery, re-irradiation, chemotherapy, immunotherapy and/or clinical trials of investigational agents for rOPC. The PPI/E group clearly highlighted that patients require further information on potential communication and swallowing outcomes of the various treatment options, and thus a systematic review of the current literature on this was planned and executed. The systematic review identified function and/or QoL outcome data for

patients with rOPC treated by surgery alone, but no data for patients treated with systemic anti-cancer therapies or radiotherapy. No patient or carer experience data was identified. The systematic review study will be described in detail in Chapter 3 including how these findings influenced the protocol development for the mixed methods study.

2.7 Study 2: Mixed methods study

This mixed methods study addressed research objective two. The mixed methods methodology will be described in detail in Chapter 4. The design of this study was directly influenced by the PPI/E group and the findings from the systematic review. The PPI/E group emphasised the importance of including not only quantitative data, but qualitative data so that the functional outcomes could be contextualised in how patients actually experienced change in function and QoL. The PPI/E group were also very clear that this experience has the potential to change over time so that a longitudinal element needed to be included. Thus, patients with locally rOPC treated with surgery, re-irradiation, chemotherapy, immunotherapy and/or clinical trials of investigational agents, were invited to take part in a repeated-measures, prospective observational workstream measuring function and QoL outcomes before, during and after treatment for rOPC. Uniquely, a concurrent longitudinal qualitative workstream using interviews with patients and caregivers was conducted to investigate patient and carer experience of function and QoL change over time. The primary research site for this thesis was a tertiary cancer referral centre in London where referrals for treatment options for recurrent disease are received from all over the United Kingdom. As a result, patients undergoing active, life prolonging treatments either curative or non-curative were included. Patients opting for best supportive care as a first line treatment were excluded as such patients were not routinely referred to the research centre for treatment. At the initial stages of planning this thesis, an audit of referrals to the research site, identified on average 75 referrals meeting this criteria per year.

2.7.1 Workstream 1: Observational study

The observational quantitative workstream aimed to identify the communication, swallowing and QoL outcomes and treatment-related priorities for patients undergoing active treatment(s) (as described above) for loco-regionally rOPC. The methodology involved using validated outcome tools at pre-defined timepoints, the need for which was highlighted by the systematic review. The primary endpoint was change in swallowing-related QoL, from diagnosis to six months following treatment initiation, measured using the MD Anderson Dysphagia Inventory (MDADI) (Chen et al., 2001), a patient-reported outcome measure. Secondary outcomes included objective measures of speech and swallow function, and patient priorities at baseline and predefined timepoints thereafter using a range of patient-reported and clinician-rated outcome tools. The data collection methods and tools were reviewed and approved by the PPI/E group. Although the research team had initially wanted to include a measure of decision regret, the PPI/E group felt that this would be 'unacceptable'. They explained that whatever their treatment choices were, they were now 'committed to' and that was now 'their reality'. The PPI/E group advised that if the research team wanted to explore this that it would be much more appropriate to gently tease out this information in an interview setting.

2.7.2 Workstream 2: Qualitative study

The objective of the qualitative workstream was to explore the patient and carer experience of function and QoL changes for patients with loco-regionally rOPC undergoing surgery, re-irradiation, chemotherapy, immunotherapy and clinical trials of investigational agents using semi structured interviews. The PPI/E group were very clear that caregivers should be included in the interview study. *'Caregivers should be included as interviewees, as key functional concerns and QoL concerns will impact caregivers too'.* The group explained that communication and eating and drinking *'is social'* involving *'more than just the patient'.* The PPI/E group explained that *'the diagnosis, treatment and aftermath have such an impact on the family'.*

Although originally planned to include participants prospectively, a decision to include a retrospective cohort was informed by discussions with the PPI/E group. The PPI/E group described a period of 'adjustment' and 're-evaluation' after treatment and felt that in the prospective cohort with baseline and six month follow up interviews, this might not be captured. The PPI/E group described how changes in function and QoL can change for a prolonged period following treatment and thus advised that patients/ caregivers who are at least 12 months following diagnosis were included. Unfortunately, it was not possible to do this prospectively within the time constraints of this PhD therefore, the qualitative workstream included two cohorts:

a) a prospective longitudinal cohort involving patients recruited to the observational workstream (and their caregivers) taking part in interviews before treatment commences and at six months following treatment initiation and
b) a retrospective cohort which includes patients and caregivers who are at least 12 months after treatment initiation.

The topic guide for the interviews was also co-designed with the PPI/E group.

Partnership working with the project PPI/E group resulted in important modifications to the research question, methods, design and data collection tools used in this study. This is summarised in Figure 2-1.

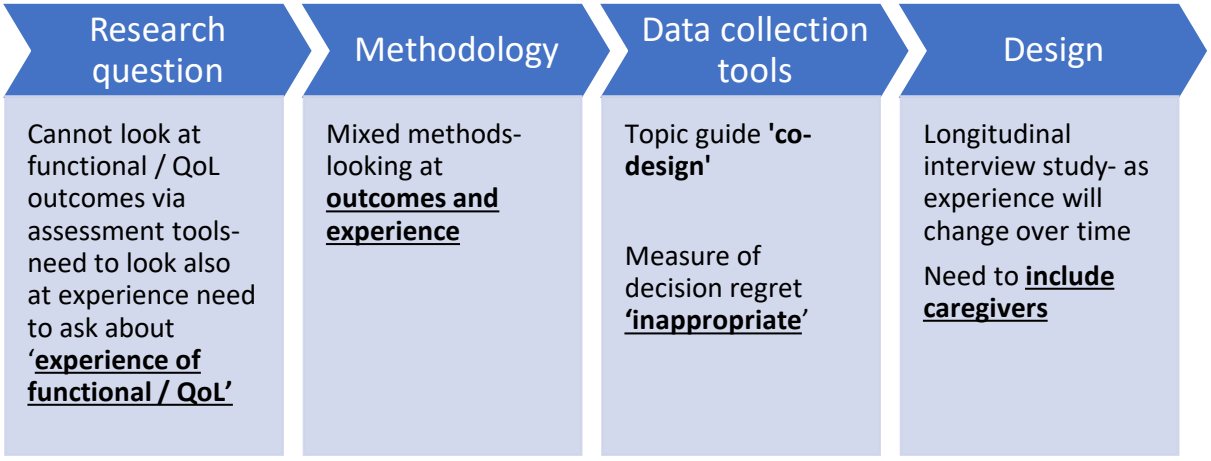


Figure 2-1: Influence of Patient and Public Involvement, Engagement and Participation (PPI/E) on research question, methodology, data collection tools and overall design

The findings of the quantitative and qualitative workstreams and the integration of these results were also discussed and reviewed by the PPI/E group.

2.8 Summary

In this chapter, the overall research aim, three key objectives and three workstreams of this thesis have been introduced. The integral PPI/E work which informed the overall thesis, in addition to how each individual workstream was shaped and influenced was described. The main aim of this research has been summarised including reviewing the existing literature to identify if and how function, QoL and patient experience data is reported and what are the findings, and to prospectively investigate function, QoL and patient treatment-related priorities and to explore patient and carer experience of rOPC over time. To address these aims a mixed methods design has been introduced including a mixed methods narrative systematic review, a prospective repeated measures observational workstream and a longitudinal qualitative workstream using in depth interviews with patients and caregivers at different timepoints along the care pathway. A mixed methods design has been adopted to best meet the aims of the research and also fit with the pragmatic epistemological standpoint of the research, and the research priorities as highlighted by the PPI/E group.

Chapters 3 will describe the systematic review in detail including a detailed account of method, analysis, results, and conclusions. Chapter 4 will give a detailed description of the mixed methods methodology, followed by the quantitative findings in Chapter 5 and qualitative findings in Chapter 6. The integration and interpretation of the combined qualitative and quantitative findings are presented in Chapter 7. Chapter 8, the final chapter, will include an overview of the strengths and limitations of this work, implications for practice and future research based on the combined findings of this thesis.

Chapter 3 A systematic review of patient experience, function and quality of life outcomes in patients receiving surgical and non-surgical treatment for rOPC.

3.1 Publications and outputs

This systematic review was published in Advances in Communication and Swallowing in December 2023 (Brady et al 2023) and was presented as a poster at the UK Swallow Research Group (UKSRG) meeting in January 2022. The poster presentation was awarded joint second prize at this international conference. The published article is attached in Appendix 1.

3.2 Introduction and objectives

The first chapter of this thesis provided an overview of the literature in relation to primary OPC and functional outcomes, and rOPC, prognosis, treatment options and functional outcomes. The overview highlighted a lack of function, QoL and patient experience data in relation to patients with rOPC. Systematic reviews completed in the area of recurrent HNC (Williamson et al., 2023) or more specifically transoral robotic surgery (TORS) management of recurrent disease (Hardman et al., 2020) focused primarily on survival outcomes, reporting crude measures of functional outcomes including gastrostomy and/or tracheostomy dependence.

As explained in Chapter 2 the first objective of this thesis was to identify and evaluate the existing literature for communication, swallowing outcomes and patient experience and define knowledge gaps.

To evaluate the existing literature and define gaps in knowledge, a systematic review was undertaken with a focus on patients with residual, recurrent and new primary oropharyngeal disease in a previously irradiated area. The aim of this systematic review was to identify if function and QoL outcomes and patient experience data are reported, how they are

measured and what are the function and QoL outcomes and patient experience in patients with rOPC. As with previous and upcoming chapters, the umbrella term of rOPC will be used throughout this chapter to refer to this group of patients who have residual disease (within 12 months of previous treatment), recurrent disease (between one and five years following previous treatment) or new primary disease in a previously irradiated field (greater than five years following previous treatment). The methods, results, discussion and recommendations for future research will be discussed in this chapter.

3.3 Method

This systematic review used a population, intervention, comparison, outcome (PICO) framework (Schardt et al., 2007) which is summarised in Table 3-1.

Table 3-1 Population, Intervention, Comparator, Outcome (PICO) breakdown of systematic review question

Population	Patients undergoing curative and non-curative treatment for residual, recurrent or new primary oropharyngeal disease in a previously irradiated field.
Intervention	Surgery open or transoral robotic, re-irradiation, immunotherapy, chemotherapy, clinical trial of investigational agent.
Comparator	Not required.
Outcome	Speech, voice, swallowing, QoL, patient experience outcomes.

This framework was divided as follows to report on the following: for patients with rOPC (**P**opulation), undergoing curative or non-curative treatment (**I**ntervention), are functional, QoL and patient experience measures reported, and if so, how are they reported and what are the findings (**O**utcomes). A comparator was not a requirement for this review.

The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines were used to carry out the systematic review (Moher et al., 2010). The protocol was registered on PROSPERO, an international prospective register of systematic reviews (CRD42021236540).

The main objectives of the systematic review were to:

1. report on the function and QoL outcomes and patient experience data for patients with rOPC
2. describe how function and QoL outcomes and patient experience data are measured for patients with rOPC

3.3.1 Data synthesis

It was anticipated from similar reviews in the primary disease setting (Roe et al., 2010) that the number of studies identified may be low and the heterogeneity between studies found high and so statistical analysis for comparison of outcomes across modalities (meta-analysis) was not planned, instead a narrative synthesis to describes trends in the existing quantitative and qualitative literature in relation to the objectives of the review was instead planned.

3.3.2 Eligibility criteria

Study characteristics

All observational studies, including qualitative and experimental designs, both prospective and retrospective, were included. Only peer-reviewed articles published in English were included. Given the hypothesised lack of literature in the field, no limitation was placed on year of publication. Abstracts and conference proceedings were excluded. Studies were excluded if cohorts of primary and rOPC were mixed unless a subgroup analysis of rOPC outcomes was available. Likewise, studies were excluded if they investigated head and neck

disease recurrence rather than rOPC specifically, unless a subgroup analysis of findings for rOPC was available. The inclusion criteria are listed in Table 3.2.

Table 3-2 Inclusion criteria

1	Adults aged 18 years or older with a diagnosis of recurrent, residual or new primary (recurrent) OPC in a previously irradiated area
2	Participants undergoing treatment for rOPC including surgery (open or transoral robotic), re-irradiation, immunotherapy, and/or chemotherapy, and/or clinical trials of investigational agents
3	Function and/or QoL outcomes and/or patient experience data reported (validated or unvalidated tools/ methods including long-term feeding tube and tracheostomy usage/ qualitative findings)
4	English language
5	Full text available

3.3.3 Primary and secondary outcome measures

The primary outcome measures included the reporting of either function, QoL or patient experience outcomes. For this review functional outcome data were defined as any data presented in relation to swallowing and communication (including speech and voice) outcomes using previously validated or unvalidated measures. QoL outcomes included data measured using validated health related QoL patient-reported outcome measures. Patient and carer experience were defined as any data that were collected with the intention to provide information about patients' and caregivers' experiences with rOPC 'including the impact of the disease or condition or related therapy or clinical investigation, and patient preferences with respect to treatment of the disease or condition' (FDA, 2016).

Primary outcome measures

1. functional outcomes including swallowing, speech and QoL outcomes.
2. patient experience outcomes

Secondary outcome measures

1. gastrostomy dependence at > 6 months post-treatment
2. tracheostomy dependence at >6 months post-treatment

3.3.4 Identification of studies

A systematic computer-based search was performed using the following electronic health databases: MEDLINE, CINAHL, and Embase. Additional searches were carried out on Web of Science and the meta-registries of Trials Databases (ClinicalTrials.gov and ISRCTN). The WHO International Clinical Trials Registry Platform (ICTRP) and the Australian New Zealand Clinical Trials Register (ANZCTR) were also included in the search.

3.3.5 Search strategy

The search terms detailed below were identified by the author alongside discussion with the supervisory team with the advice of a medical librarian.

Search terms included “OPC” AND “recurrent” OR “residual disease” OR “second primary’ OR “radiation induced” AND “swallow” OR “dysphagia” OR “speech” OR “voice” OR “quality of life” OR “patient experience” OR “functional outcomes” AND “salvage surgery” OR “salvage therapy” OR “re-irradiation”. All search terms were exploded where possible and any subject headings relevant to each database were included.

The search strategy was confirmed following several iterations. It was originally piloted in Embase to refine and check between June and July 2021, with a repeat and refined search carried out in November 2022 following a break in studies and detailed feedback from a declined peer-review journal submission. The final search strategy was refined with the inclusion of patient experience and also additional citation searches were completed for the included articles.

3.3.6 Study selection

Results from the searches were collated into Endnote (Endnote[x9]), a reference management software programme. The references were then transferred into Covidence systematic

review software (Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org). Following removal of 256 duplicates, the remaining 796 article titles and abstracts were screened for inclusion by authors GB, MW and PL[2] using the inclusion criteria for screening listed in Table 3.3. Articles were included for full-text review where it was not possible to use the abstract to fully assess eligibility.

Table 3-3 Inclusion criteria for article screening

1	Study involved human participants who were at least 18 years of age
2	English language
3	Diagnosis of rOPC
4	Undergoing active treatments including surgery, re-irradiation, immunotherapy, chemotherapy or clinical trials of investigational agents
5	Functional and/or QoL outcomes and/or patient experience referred to in the text
6	Full text article available

Following the initial stage of abstract screening the full texts of 47 articles were retrieved and assessed using the same inclusion criteria detailed in Table 3-3. The reference lists of included articles were hand searched, and a citation search was completed to ensure as many relevant papers were included.

During both the abstract and full text review stages of the review, any ambiguities or uncertainties as to whether an article should be included were presented to the supervisory team and resolved via discussion.

3.3.7 Data extraction

A data extraction table was devised using Excel for Mac (version 16.77.1). Data inputted included study characteristics including location, patient characteristics, treatment modality, primary and secondary outcomes used, timepoints for data collection and the outcome

[2] GB= Grainne Brady, MW= Mary Wells and PL= Pernilla Lagergren.

measures used. The main findings in relation to swallowing, speech and QoL outcomes, gastrostomy and tracheostomy dependence rates and any patient experience data reported were also included as seen in Table 3-4.

3.3.8 Risk of Bias Assessment

The aim of any systematic review is to collate and synthesise all studies that meet prespecified eligibility criteria. To enable a reviewer to reach reliable conclusions, the potential limitations or biases of the included studies must be recognised and reported (Cumpston et al., 2020). A risk of bias assessment can facilitate this (Boutron et al., 2019). Several assessment tools are available and were considered for this systematic review. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) (Guyatt et al., 2011) is a Cochrane standard however was out ruled for this study as it is designed specifically for assessment of bias for systematic reviews of randomised controlled trials (RCTs) rather than risk of bias for individual studies. As it was hypothesised that the type of studies included in this review would be non-RCTs, the Risk of Bias in Non-Randomised Studies (RoBiNS) (Sterne et al., 2016) was also considered but deemed unsuitable as this tool was designed for longitudinal cohort design studies only. It was anticipated at the time of the systematic review protocol development was that the majority of included studies would be observational. The Risk Of Bias Assessment Tool for Nonrandomized Studies (RoBANS) (Kim et al., 2013) was also considered as it is suitable for observational studies including case series. However, the final decision for using the Methodological Index for Non-Randomised Studies (MINORS) (Slim et al., 2003) was made when the article search was completed. This tool was decided upon as it is appropriate for observational studies including case series and is designed specifically for surgical studies. The inclusion criteria for this review resulted in the inclusion of studies investigating surgical outcomes only. A quality assessment threshold was not used for the systematic review as again it was anticipated that the included papers would be observational studies and were likely to be of poor quality. Also, the exclusion of papers on the basis of a quality threshold was not in

keeping with the overall aim of the review, which was to examine the current literature to identify if function and QoL outcomes and patient experience data are reported, how they are measured and what are the function and QoL outcomes and patient experience data reported for patients with rOPC.

The risk of bias assessment was carried out by author GB, with one member of the supervisory team (MW) repeating the assessment for a proportion of the identified articles. Although not encountered, it was planned that any discrepancies would be resolved by consultation with another author (JR)[3].

3.4 Results

3.4.1 Study selection

The literature search findings are summarised in Figure 3-1 PRISMA flow diagram. Following the removal of duplicate records, 796 studies were identified and 47 included for full text review with 17 studies included for data extraction. The primary reason for exclusion was that only survival outcomes were reported (n=16); these included studies focusing on surgery (n=10), chemotherapy (n=3), re-irradiation (n=2) and immunotherapy (n=1). Other reasons for exclusion included the study using a general HNC cohort, where functional/ QoL or general toxicity outcomes were reported but with no subgroup analysis for patients with recurrent (n=10) or mixed primary/ rOPC cohorts (n=1). One qualitative study was identified; however, it was excluded as it was not specific to rOPC but a more general recurrent HNC caseload.

[3] JR= Justin Roe

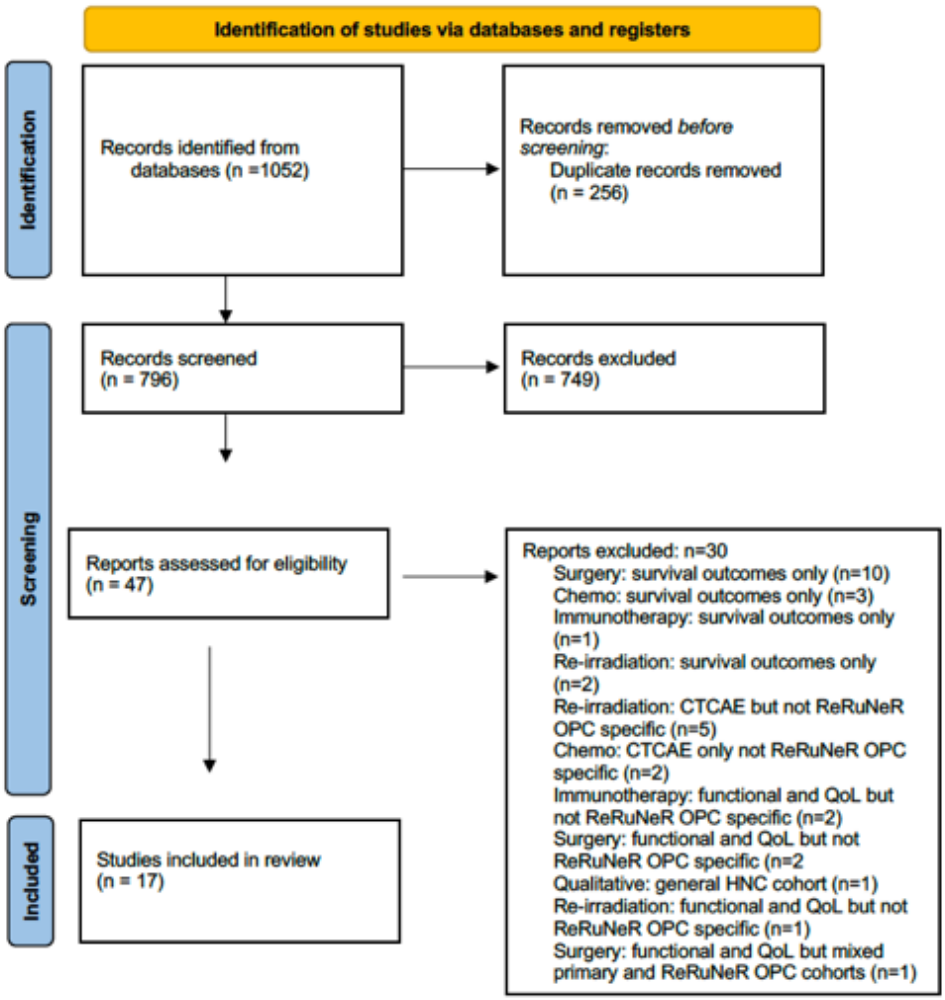


Figure 3-1: PRISMA Diagram

3.4.2 Study characteristics

Study characteristics are summarised in Table 3-4. The geographic distribution of studies is as follows: US (n=8), France (n=4), UK (n=2), Japan (n=1), Australia (n=1) and multicentre (n=1). All studies were published between 2009 and 2022. Two studies included a prospective design, and the majority were single centre case series (n=12). No qualitative/ patient experience studies were identified.

Table 3-4 Study characteristics, timepoints for outcome measurement, outcome measures used and main findings.

Author	**Year**	**Location**	**Study design**	**Intervention**	**Function/ Quality of Life outcomes primary or secondary, validated (V) or unvalidated (UV):**	**No of participants**	**Timepoints**	**Outcome measures used**	**Main findings**
(Charters et al., 2022)	2022	Australia	Case series	TORS[a]	Primary V	3	Baseline 3 months 12 months	**All timepoints:** FOIS [b], PSS-HN-NoD[c], PSS-HN-UoS[d], Gastrostomy (G-tube) **12 month data only:** MDADI [e] SHI[f] PAS[g], BRCS[h], PSS-HN-EiP[i]	<u>Case 2:</u> **FOIS[b]** Baseline: 5, 3 months: 3 12 months: 4 **PSS- HN-NoD[c]** Baseline 50, 3 months 20, 12 months: 30 **PSS-HN- UoS[d]** Baseline 100, 3 months 50, 12 months: 75 **PEG removal**: 10 months PAS 12 months: 7 <u>Case 4:</u> **FOIS[b]** Baseline: 4, 3 months: 2, 12 months: 2 **PSS- HN-NoD[c]** Baseline 30, 3 months 20, 12 months: 20 **PSS-HN- UoS[d]** Baseline 100, 3 months 75, 12 months: 75 PEG removal: not removed. PAS 12 months: 8

									Case 6: **FOIS[b]** Baseline: 4, 3 months: 2 12 months: 2 **PSS- HN-NoD[c]** Baseline 50, 3 months 20, 12 months: 40 **PSS-HN- UoS[d]** Baseline 100, 3 months 75, 12 months: 100 PEG removal: not removed. **PAS[g]** 12 months: 8 **SHI[f]**: no baseline data. Mean score of 25 (1-120) at 12 months. **MDADI[e]**: no baseline data. Mean score of 41 at 12 months **PSS-HN-EiP[i]:** no baseline data. Median score of 25 at 12 months.
(Culié et al., 2015)	2015	France	Case series	Open and TORS[a]	Secondary V	34	Baseline 6 months	Speech intelligibility (unvalidated) DOSS[j]	**DOSS[i]** Baseline DOSS 6-7: 47% 6 months DOSS 6-7: 26%. Baseline DOSS 3-5: 24% 6 month DOSS 3-5: 45% Baseline DOSS 1-2: 29% (non-oral feeding) 6 month DOSS 1-2: 29% **Speech intelligibility** Speech intelligibility baseline: No baseline data

									Speech intelligibility 6 months: 6% normal speech, 32% slightly altered (repetition NOT required), 45% slightly altered (repetition required) and 16% unintelligible.
(D'Andréa et al., 2022)	2022	France	Case series	Open and TORS[a]	Primary V	53	Baseline, 3 months 1 year 2 years 3 years 4 years 5 years	MDADI EORTC-QLQ-C30[k] EORTC-QLQ-H&N35[l] Gastrostomy (G-Tube) Tracheostomy	**MDADI[e]:** Baseline MDADI: 61.2 1 year MDADI: 64.3 2 year MDADI: 57.5 **EROTC-QLQ-C30[k]:** Baseline QLQ-C30: 61.2 1 year QLQ-C30: 59.5 1 year QLQ-C30: 80.6 **G-Tube**: 1 year: 33% 2 years: 23.1% **Tracheostomy**: Decannulation: 97.1%/
(Dean et al., 2010)	2010	United States	Case control study	Open and TORS[a]	Secondary UV	21	No baseline 6 months	G-Tube Tracheostomy	G-tube dependency: Open salvage surgery: 43% TORS[a]: 0% Tracheostomy dependency: Open salvage surgery: 7% TORS[a]: 0%
(Hardman et al., 2022)	2022	Global	Case series	TORS[a]	Secondary UV	199	No baseline 1 year	G-Tube Tracheostomy	Tracheostomy dependency at 1 year: 7% G-tube dependency at 1 year: 35%

(Kano et al., 2013)	2013	Japan	Case series	Open and TORS[a]	Secondary UV	11	Baseline Undefined follow up	G-Tube Oral feeding (unvalidated)	**G-tube rate:** Baseline: 18% Post operatively (undefined timepoint): 45% **Oral feeding:** Baseline: oral feeding alone: 82%, oral feeding with tube feeding: 18%, NBM: 0 Post operatively (undefined timepoint): oral feeding alone: 55%, oral feeding with tube feeding: 27%, NBM: 18
(Kostrzewa et al., 2010)	2010	United Kingdom	Case series	Open surgery	Primary UV	36	No baseline Undefined follow up	G-Tube Oral feeding (unvalidated)	G-Tube rate: No baseline data Post-surgery (undefined timepoint): 52% Diet type (unvalidated): No baseline data Post-surgery (undefined timepoint): regular: 11%, liquid:17% puree: 14%
(Mazerolle et al., 2022)	2022	France	Case series	Open surgery	Secondary UV	42	No baseline Undefined follow up	Respiratory status Nutritional status	Nutritional status: No baseline data Post-surgery (undefined timepoint): Oral intake only: 12%, enteral intake only: 71%, mixed oral/ enteral feeing: 17%
(Patel et al., 2016)	2015	United States	Case series	Open and TORS[a]	Secondary UV	34	No baseline Undefined follow up	G-Tube Tracheostomy rate	G-tube dependence: No baseline data. Post-surgery (undefined timepoint): G-tube dependence: 64.7% Tracheostomy:

									No baseline data: Post-surgery (undefined timepoint): G-tube dependence: 14.7%
(Philouze et al., 2017)	2017	France	Case series	Open and TORS[a]	Secondary UV	52	No baseline Undefined follow up	G-Tube	G-tube dependence: No baseline data. Post-surgery (undefined timepoint): G-tube dependence: 34.6%
(Pipkorn et al., 2019)	2018	United States	Case series	TORS[a]	Secondary UV	18	No baseline Undefined follow up	G-Tube	G-tube dependence: Baseline: 11% Post-surgery (undefined timepoint): 28%
(Sharma et al., 2022)	2022	United States	Case series	Open surgery	Secondary UV	30	No baseline Within 90 days of surgery	G-Tube	No baseline data G-tube (within 90 days of surgery): 38.1% (with an additional 61.9% requiring NGT) Tracheostomy (within 90 days of surgery): 56.7%
(Sweeny et al., 2016)	2016	United States	Case series	Open and TORS[a]	Secondary UV	69	Baseline 1 year	G-Tube	G-tube 25% at baseline Post-surgery: 64%
(Tassone et al., 2022)	2022	United States	Case series	Open surgery	Primary UV	89	No baseline 1 year	G-Tube Tracheostomy	G-tube: Baseline: 30% (n=89) 12 months: 43% (n=51) Tracheostomy: Baseline: 6% (n=89) 12 months: 29% (n=51- includes altered airway)

(White et al., 2013)	2013	United States	Case control study	Open and TORS[a]	Secondary UV	128	No baseline 1 year	G-Tube	G-tube: No baseline data 12 months: 3 % for TORS and 31% for open
(Williamson et al., 2021)	2021	United Kingdom	Case series	TORS[a]	Primary V	3	Baseline Undefined follow up	UWQoL[m] MDADI	**MDADI[e]:** Baseline: 66.7 Post-surgery: 66.7 (timeframe not specified) **UWQoL[m]:** Pre and post-surgery surgery mean scores (timeframe not specified): Pain: 75- 66.7 Appearance: 75- 58.3 Activity: 50- 58.3 Recreation: 75- 73.3 Swallowing: 70- 63.3 Chewing: 50- 56.7 Speech: 100- 63.3 Speech: 100- 63.3 Shoulder: 100- 80 Taste: 85- 70 Saliva: 70-56.7 Mood: 62.5- 60 Anxiety: 47.5- 70
(Zafereo et al., 2009)	2009	United States	Case control study	Other	Secondary UV	41	Undefined follow up	Oral intake (unvalidated) Speech mode (unvalidated)	Unvalidated oral intake: Baseline: Non-oral 5%, partial oral 17%, liquid only 7% and soft/ regular 71%.

								Speech intelligibility (unvalidated) Tracheostomy rate	Post-surgery: non-oral 32%, partial oral 32%, liquid only 5% and soft/ regular 32%.

[a] Transoral robotic surgery
[b] Functional Oral Intake Scale
[c] Performance Status Scale for Head and Neck Cancer Normalcy of Diet
[d] Performance Status Scale for Head and Neck Cancer Understandability of Speech
[e] MD Anderson Dysphagia Inventory
[f] Speech Handicap Index
[g] Penetration Aspiration Scale
[h] Boston Residue and Clearance Scale
[I] Performance Status Scale for Head and Neck Cancer Eating in Public
[j] Dysphagia Outcome Severity Scale
[k] European Organisation for Research and Treatment (EORTC) Quality of Life for Cancer Patients
[l] European Organisation for Research and Treatment (EORTC) Quality of Life for Cancer Patients - Head and Neck
[m] University of Washington Quality of Life Questionnaire

3.4.3 Participant characteristics:

In total, the studies included 863 patients with rOPC (Range 3-199). All studies investigated outcomes for surgical procedures, either open surgery or transoral robotic surgery. No oncological (non-surgical) studies were identified reporting on function or QoL outcomes for rOPC specifically.

3.4.4 Risk of bias

MINORS risk of bias assessment findings are summarised in Table 3-5. Only one of the included studies had a comparator group. For the non-comparative studies, the median MINORS score was 8 (out of a possible 12) with a range of 7-10. The one study which included a comparator group was rated with a MINORS score of 14 (out of a possible 24). Each item is scored from 0-2 where 0 indicates that the item was not reported, 1 indicates that it was reported but inadequately and 2 indicates that it was adequately reported within the article.

Table 3-5: Risk of bias assessment using Methodological Index for Non-Randomised Studies (MINORS) (Slim et al., 2003)

Study	Charters et al	Culié et al	D'Andrea et al	Dean et al	Hardman et al	Kano et al	Kostrzewa et al	Mazerolle et al	Patel et al	Philouze et al	Pipkorn et al	Sharma et al[2]	Sweeney et al	Tassone et al	White et al	Williamson et al	Zafereo et al
A clearly stated aim	1	2	1	2	2	0	2	2	2	2	2	2	2	2	2	2	2
Inclusion of consecutive data	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Prospective collection of data	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Endpoints appropriate to the aim of the study	1	1	2	2	2	1	1	2	2	1	1	1	1	1	1	2	1
Unbiased assessment of the study endpoint	0	0	0	0	0	0	0	0	0	0	0	1	1	2	0	0	0
Assessment tests appropriate with the aim	2	1	2	1	1	1	1	1	1	1	1	1	1	2	1	2	1
Loss of samples <5%	2	0	0	2	1	0	0	2	2	2	2	2	0	0	0	0	1

Prospective calculation of the study size	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
An adequate control group*															2		
Contemporary groups*															2		
Baseline equivalence of groups*															2		
Adequate statistical analysis*															2		
Total score:	**8**	**6**	**9**	**9**	**8**	**4**	**6**	**9**	**9**	**8**	**8**	**9**	**7**	**9**	**14**	**10**	**7**

MINORS Scoring (Slim et al., 2003)
0: not reported
1: reported but inadequately
2: adequately reported
* for use with studies where there is a comparator group

3.4.5 Are function, QoL and patient experience outcomes reported?

Out of the 796 articles reporting outcomes for treatments for rOPC, specific functional or QoL data were available for patients with rOPC in 2% (n=17). Within the 17 articles included, functional/QoL measures were reported as a primary outcome in 29% (n=5), survival was reported as the primary measure in 71% (n=12). No patient/carer experience data were identified.

3.4.6 How are outcomes measured and what are the findings?

Swallowing

Validated swallowing outcome measures were used in 23% of studies (n=5). These measures included the MD Anderson Dysphagia Inventory (MDADI) (Chen et al., 2001) (n=3), the Functional Oral Intake Scale (FOIS) (Crary et al., 2005) (n=1), the Performance Status Scale for Head and Neck Cancer (PSS-HN) (List et al., 1990) Normalcy of Diet (NOD) and Eating in Public (EIP) subscales (n=1). Two studies reported on validated swallowing outcome measures obtained using an instrumental evaluation of swallowing. One study described the use of Flexible Endoscopic Evaluation of Swallowing (FEES) and the Penetration-Aspiration Scale (PAS) (Rosenbek et al., 1996) and Boston Residue And Clearance Scale (BRACS) (Kaneoka et al., 2013). Another study described the use of videofluoroscopy and the Dysphagia Outcome and Severity Scale (DOSS) (O'Neil et al., 1999).

Charters et al (2022) reported on swallowing outcomes for 3 patients who underwent TORS for rOPC (Charters et al., 2022). Baseline and 12-month outcomes were reported for the FOIS, and PSS-HN NoD scores. Here the FOIS score indicated a change from baseline where patients were managing a total oral diet with some diet modification (FOIS: 5) to being tube dependent with limited oral intake (FOIS: 3). PSS-HN NoD data showed a deterioration from soft chewable diet (PSS-HN NoD: 50) to pureed diet (PSS-HN NoD: 30). A number of

12-month swallowing outcomes were reported including the MDADI, PSS-HN EiP, PAS and the BRACS. No baseline data on these measures were included, however 12-month findings show impaired swallowing-related QoL with an average MDADI composite score of 43 (a score of 100 indicates no swallowing difficulties) and median PSS-HN EiP score of 25 (ordinal scale descriptor: eats only alone). On the PAS and BRACS it was found that all 3 participants had unsafe swallowing with confirmed aspiration and inefficient swallowing, with confirmed post-swallow residue on instrumental evaluation of swallowing using FEES.

D'Andréa et al (2022) also reported on the MDADI at 12 months for patients undergoing TORS and open salvage surgery (D'Andréa et al., 2022). Overall, although a deterioration in mean composite MDADI scores from 71.4 at baseline to 64.3 at 1 year was noted, this change was not statistically significant (p=0.13), nor did it reach the criterion for clinical significance (10-point change in MDADI composite score). The authors further clarify with individual patient data analysis that only 7 patients (30.4%) reported a 1-year clinically meaningful decrease of the MDADI score of more than ten points, while two patients (8.7%) reported a clinically meaningful increase in the MDADI composite score.

The Williamson et al (2021) report on 3 patients who underwent TORS with robotic assisted flap reconstruction documented stable MDADI scores pre- and post-surgery with a composite score at baseline and follow up of 66.7. Here, the timepoint for post-surgical review was not defined (Williamson et al., 2021).

Culié et al (2015) reported on a case series of patients undergoing TORS and open salvage surgical procedures. Baseline and six-month DOSS scores were reported and demonstrated a deterioration in swallowing function with increased aspiration of food/ fluids. At baseline 47% of participants were on full oral intake (DOSS score of 6-7), which reduced to 26% six months post-surgery. There was an increased number of patients requiring diet modification

(DOSS score 3-5). However, between baseline and six months, the number of patients requiring non-oral feeding remained stable at 29%.

Speech

Validated speech intelligibility measures, namely the Speech Handicap Index (SHI) and the PSS-HN Understandability of Speech (UoS) subscale (List et al., 1990) were both used in one single study. Other non-validated measures of speech intelligibility included a non-standardised/ validated rating of intelligibility or a comment on speech mode (n=2). Following TORS, speech outcomes were reported by Charters et al (2022) using the PSS-HN UoS and the SHI. No baseline data were reported but 12-month data demonstrated reduced speech intelligibility with a median score of 75 on the PSS-HN UoS subscale (understandable most of the time but occasional repetition necessary) and 25 on the SHI (score from 0-120 with a higher score indicative of higher level of speech difficulties). Speech outcomes following both open surgery and TORS were reported by Culié et al (2015) using an unvalidated measure rating speech intelligibility from 0-3 (0 was severely altered/ unintelligible and 3 was normal/ near normal). No baseline data were reported, and six-month data were available for 31/34 participants- here only two patients presented with normal/ near normal speech at six months post-surgery.

Zafereo et al (2009) also reported unvalidated measures of speech intelligibility and in 41 patients reported that speech was > 80% intelligible. Again, baseline speech data were not available.

QoL

Validated QoL measures were used in two studies including the University of Washington QoL Questionnaire version 4 (UWQoLv4) (Rogers et al., 2002) (n=1) and European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire

– Core 30 for cancer patients in general (QLQ-C30) and Quality of Life for Head and Neck Cancer (QLQ-H&N35) together (n=1).

D'Andréa et al (2022) reported EORTC QLQ-C30 scores at baseline and 1 year showed non-significant change in global health status with preoperative mean score of 61and 59 at 1 year (p=0.96). The EORTC QLQ-H&N35 demonstrated some increased difficulties with sticky saliva, difficulty with social contact, eating and speech. Williamson et al (2021) used the UWQoLv4 following TORS with free flap reconstruction. Mean scores for each symptom subscale at baseline and at an undefined timepoint post-surgery were reported. Increased mean scores indicating some levels of improvement were noted in the following domains: pain, activity, chewing and anxiety. Reduction in mean scores, indicating deterioration, were reported in the remaining domains of appearance, recreation, swallowing, speech, shoulder, taste, saliva, and mood.

Gastrostomy tube dependence:

Where non-validated measures of swallowing function were reported, gastrostomy tube use was the most popular outcome reported in 88% of studies (n=15). Some studies (n=3) also specified oral versus non-oral feeding. Other studies (n=2) focused on method of nutritional intake using three categories, gastrostomy with oral feeding, gastrostomy alone or oral feeding alone.

Long-term feeding tube rate (at least six months) was reported in 7/17 studies. A further 9 studies did not specify the timepoint or included data within 30 days of the surgery. Pooled data (n=128) demonstrate a long-term gastrostomy dependence rate of 23.42% (95% CI 10.2 to 36.6).

Long-term tracheostomy tube rate:

Tracheostomy tube rate was reported in 47% of studies (n=8). Long-term tracheostomy dependence (at least six months) was reported in 3/17 studies. A further two studies reported tracheostomy use post-surgery but did not define the timeframe. Pooled data (n=309) demonstrate a long-term tracheostomy rate of 9.3% (95% CI 8.48 to 10.1).

3.5 Discussion

This systematic review aimed to assess if function, QoL and patient experience are measured in patients undergoing treatment for rOPC. To the authors knowledge this is the first systematic review investigating function, QoL and patient experience, specifically for patients with rOPC and across curative and non-curative treatment modalities.

The review identified 17 articles reporting functional/QoL outcomes for patients undergoing treatments for rOPC, with just five articles reporting functional/QoL as a primary measure. This demonstrates that survival as the primary outcome remains the focus in the current literature in rOPC, with only a minority of articles reporting function/QoL outcomes. All of the 17 articles included in this review focused on surgical trials. No specific functional or QoL data for patients with rOPC undergoing non-surgical treatments were identified in this systematic review. Also, no patient experience data were identified. Collectively, these findings demonstrate significant gaps in the current literature base focusing on function and QoL outcomes, and essential patient experience data for patients with rOPC.

Such gaps in the literature are not congruent with the current clinical guidelines for the management of HNC patients. The routine use of validated specific functional outcome measures to guide rehabilitation for communication and swallowing in HNC is specified in national guidelines (Schache et al., 2021). Also, in relation to research, the findings are somewhat of a divergence from the focus of research in primary OPC. As mentioned in Chapter 1 of this thesis, there has been a shift in the focus of current research in primary

OPC treatment to place equal importance on optimising function and QoL outcomes, alongside survival. In many recent and ongoing trials, the primary outcome measure is a patient-reported measure of swallowing function or QoL. In line with long standing previous consensus guidelines on research in primary HNC, the ongoing trials in primary OPC often include a range of multidimensional swallowing and QoL secondary outcomes (Lefebvre et al., 2009).

A large number of articles in this review were excluded as they reported survival outcomes solely. Aside from reporting survival data only, many articles were excluded from this review due to the inclusion of mixed cohorts of HNC patients, with either general recurrent HNC cohorts or mixed primary and recurrent disease groups, with no subgroup analysis for rOPC. This thesis is focusing on a single subtype of recurrent HNC, namely rOPC. The rationale for this is that in comparison to other subtypes of HNC, the OPC subgroup are considered quite unique, in particular those with human papilloma virus (HPV) related disease, who are often younger (less than 60 years) with low co-morbidity, and absent or low smoking history (Ang et al., 2010). In the UK, the majority of these patients will have undergone organ-sparing treatment regimens with radiation therapy +/- chemotherapy. As a result, these patients will most likely present with significant treatment side-effects in the form of changes to swallowing function, voice, speech and overall QoL (Roe et al., 2014, Patterson et al., 2018). In addition, there can be a high level of psychological distress and emotional burden following previous treatment (Ringash et al., 2018). Further treatment for disease recurrence may cause additional impairments or compound a unique set of baseline physical and psychological burden found in a potentially unique set of younger patients with OPC. With a growing number of patients with rOPC in the UK, specific function and QoL data in relation to this unique cohort are required. This information is needed so that patients can be accurately counselled on the likely impact of the available treatments on function and QoL as part of the informed consent process and to support shared decision making.

It is known from previous literature in primary oropharyngeal disease that to accurately demonstrate the impact of treatment on function and QoL, multidimensional assessment at pre-defined timepoints is required (Roe et al., 2010). In this review, seven of the included studies did not report on baseline data and, a further eight studies reported post-surgical function and/or QoL data however did not define the follow up time point(s). Pre-treatment baseline level of function has been cited as the key predictor for longer term swallowing outcomes for patients with HNC (Frowen et al., 2010) . Given the risk of baseline functional difficulties in patients with recurrent disease (Hardman et al 2020), accurate baseline and longitudinal data measurements with pre-defined follow-up timepoints are imperative to accurately measure any potential change.

This systematic review identified just three studies reporting speech outcomes. The standard of care for curative management of rOPC is at present open surgery. National guidelines highlight the potential functional morbidity including speech (Homer and Winter, 2024), however, based on this review, speech outcomes do not appear to be reported routinely. In the studies reporting speech outcomes, only one study used a previously validated speech outcome measure however, all studies did demonstrate altered speech in the post operative phase.

The majority of studies (n=14) included data on gastrostomy use post-surgery. Gastrostomy tube dependence in HNC is widely reported in the literature. However, its limitations as a gross proxy for swallowing outcomes have also been highlighted (Roe et al., 2014). As a unidimensional measure, the presence of a gastrostomy does not give an accurate/holistic measure of swallowing status. Many HNC patients may be having a combination of both oral intake and gastrostomy feeding (Patterson et al., 2018), particularly in the setting of disease recurrence when patients have had previous radiation treatment (Hardman et al., 2020). Also, it is imperative to provide baseline data on gastrostomy use prior to the initiation of further treatment for disease recurrence. Without the provision of baseline data, it is

impossible to ascertain if gastrostomy tube presence is a consequence of primary disease management or because of the treatment of recurrent disease. Therefore, for future research when reporting on gastrostomy tube usage, accurate baseline data is required, and the terms gastrostomy dependence should be clearly defined. To accurately report on swallowing function, this should be reported in the presence of other dimensions of function, not least using a validated tool of swallowing outcome measurement. In this review eleven studies included gastrostomy tube dependence with or without tracheostomy tube dependence as the only measures of function post-surgery. Pooled data (n=128) demonstrate a long-term gastrostomy feeding rate of almost a quarter (23.42%, 95% CI 10.2 to 36.6). In comparison to a previous systematic review reporting outcomes for TORS for recurrent HNC where long-term gastrostomy rate was recorded as 5% (Paleri et al., 2020), this estimate does seem to be high. This may be explained by the previous review including all HNC cohorts (not specific to rOPC) or only one treatment method (TORS rather than all surgery). Also, it is noted by the authors that the definition of long-term use is not clear in the included studies. The current review defined long-term gastrostomy use as at least six months post-surgery.

This review has demonstrated some variation in outcomes in relation to the studies using patient- and clinician-reported measures of swallowing function. It is known from the literature in relation to primary disease that clinician- and patient-reported measures of toxicity are not always congruent (Falchook et al., 2016). Both within and across surgery types (TORS and open), mixed findings are reported using the MDADI. One study reports stable post-TORS findings (Williamson et al., 2021) and another reports a deterioration (Charters et al., 2022), although both of these studies included only three patients each. A further study, with a much larger cohort (n= 53) (D'Andréa et al., 2022) reports outcomes for both open and TORS surgery and details an overall mean deterioration in MDADI composite scores but that deterioration did not meet statistical or clinical significance. The clinically significant difference in MDADI composite score has been defined in a previous study as a

10-point difference using a combination of criterion standards including aspiration scores, feeding tube status and diet scores (Hutcheson et al., 2016). The methodology for this study however excluded patients with recurrent disease therefore one must consider in future research if the critical 10-point clinically significant difference is suitable in the recurrent setting. This is particularly relevant as we know that most of these patients will have baseline swallowing difficulties with lower diet scores, higher rates of gastrostomy tube usage and increased aspiration from their previous treatments +/- tumour related complications (Paleri et al., 2020).

With regards to QoL measurement, only two trials were identified where validated health-related QoL tools were used, namely the UWQoLv4 questionnaire and the EORTC QLQ-C30 used in combination with the EORTC QLQ-H&N35. In an area of HNC practice where many treatment decisions are based on the potential impact of further treatments on QoL, one would expect a much greater focus within the literature. Although stable outcomes were reported by Williamson and colleagues (Williamson et al., 2021) it would appear that some aggregate data are missing in the publication. Scoring of the UWQoLv4 tool typically involves presenting the questionnaire data from two subscale scores, one for 'Physical Function' and another for 'Social-Emotional Function.' The Physical Function subscale score is computed as the simple average of six domain scores – those of chewing, swallowing, speech, taste, saliva and appearance. The Social-Emotional subscale score is also computed as the simple average of six domain scores - those of anxiety, mood, pain, activity, recreation and shoulder function. Such scores are not provided in this publication, thus making results difficult to interpret. Also, a small sample size is noted in this study with just three patients. In a larger study by D'Andréa et al (2022) non-significant changes in EORTC QLQ-C30 scores at baseline and 1 year were reported. However, the EORTC QLQ-H&N35 demonstrated some increased difficulties with sticky saliva, difficulty with social contact, eating and speech. This echoes findings by Williamson and colleagues who, when reporting symptoms using the UWQoLv4 tool, noted increased symptoms in relation to

swallowing, speech, taste, saliva, in addition to shoulder, appearance, recreation and mood (Williamson et al., 2021). However, as shown in previous literature, the content validity of EORTC QLQ-C30 and QLQ-H&N35 (Degboe et al., 2018) has not been widely documented in relation to patients with disease recurrence. Similarly, much of the literature in relation to the development of the UWQoLv4 questionnaire has focused on patients treated for primary disease, who are now cancer free (Rogers et al., 2010a).

3.6 Critique

This systematic review is not without its limitations. As noted, in preparing the protocol for this review it was hypothesised that literature regarding function and QoL data was in its infancy in the area of rOPC. For this reason, meta-analysis was neither planned nor subsequently undertaken and instead, a narrative review of the evidence was completed. The data presented focuses solely on (potentially curative) surgical outcome data. A high level of bias was noted using the risk of bias assessment for included studies, which must be considered in the interpretation of the findings of this review. The majority of the studies were observational and retrospective in nature. Only two of the included studies were prospective, only one had a comparator group, and neither reported a sample size calculation.

Given the limited evidence on function and QoL data in the recurrent HNC population, it may have been sensible to include all recurrent HNC studies rather than those specifically pertaining to rOPC. For example, two large randomised controlled trials (Burtness et al., 2019, Cohen et al., 2019) reporting standardised QoL outcome measures for patients with recurrent and metastatic HNC including rOPC were excluded, as a subgroup analysis for rOPC disease was not presented in the published data. However, swallowing outcomes were not reported, even in these larger studies. This, in addition to the findings of this systematic review, strengthens the argument for the routine recording of swallowing function

not only in surgical trials but also in non-surgical intervention studies including patients with rOPC and indeed recurrent HNC in general.

3.7 Conclusion and implications

The overarching aim of the systematic review was to identify gaps in the current literature. The significant gaps identified in this review have highlighted numerous areas for future research.

1. The absence of any studies reporting function/QoL outcomes for patients having non-surgical management of rOPC highlights the need for further research in this area.
2. Patient experience data were also not identified across treatment modalities, which highlights a further gap in knowledge in the field in relation to patient experience of function and QoL change with treatment.
3. When outcomes are reported in rOPC, this review has identified that the studies are at high risk of bias. High quality research is required in this area.
4. Previous consensus guidelines have been published on the conduct of trials in primary HNC to include swallowing and communication standardised outcome tools focusing on a range of clinician-reported, instrumental evaluation and patient-reported outcome measures (Lefebvre et al., 2009). It is clear from this systematic review that similar standards should be applied in trials looking at rOPC. This highlights a number of potential aims for outputs from future research in the area.
5. This systematic review also identified a number of outcome tools which are in use in surgical trials for rOPC, however the clinically meaningful difference testing or indeed the initial validation of these tools did not include patients with recurrent disease. This review has emphasised that further research is required to identify, develop and validate outcome measures for use in the recurrent setting to guide the development of similar recommendations for the conduct of trials focusing on rOPC.

Unfortunately, not all the questions raised by this systematic review could be addressed within the timeframe and remit of study of this thesis.

One such question which was raised and addressed but not completed within the timeframe of this thesis was the secondary analysis of a large data set of QoL outcomes for patients with rOPC who underwent non-curative treatment within the KEYNOTE-040 (Cohen et al., 2019) and 048 trials (Burtness et al., 2019). Secondary analyses of QoL outcomes for both trials were completed and published (Rischin et al., 2022, Harrington et al., 2021). However, due to the inclusion criteria of the systematic review, these two large trials were excluded. Although validated QoL outcomes tools were used, namely the EORTC-QLQ-C30 and EORTC-QLQ-H&N35, a subgroup analysis for patients with rOPC was not completed. From the data provided within the publications, it was assumed that a large number of participants with rOPC were included due to the reporting of HPV status. As a result, I contacted one of the lead authors in these trials and dedicated over 12 months of time negotiating with the pharmaceutical company trials sponsor to get a data sharing agreement in place so that I could access and analyse the data. Although the negotiation process was successful and an international data sharing agreement is currently in place, this did not come in time to complete and report on within the remit of this thesis. Plans to continue with this analysis in the future will be outlined in Chapter 8.

As described in the previous chapter, PPI/E input has been hugely influential at all stages of this research process. Once the systematic review was complete, the findings were presented to the PPI/E study group. The PPI/E study group felt that the priority for research following the systematic review was to be able to accurately describe how rOPC and the available treatments impact on QoL and function, and to do this they emphasised that there must be further research incorporating patient experience data to highlight areas of concern for patients and family members. Once the priorities and concerns of patients are established, this may then lead to further research which could lead to a consensus on

which tools, or combination of tools should be validated and used at which timepoints, to accurately provide a holistic and multidimensional profile of function and QoL for patients with rOPC.

As a result, a mixed methods study investigating function and QoL change over time and patient and carer experience of rOPC from diagnosis to treatment and beyond in all patients undergoing all modalities of treatment for rOPC was designed. The remainder of this thesis will describe this study focusing initially on the methodology in Chapter 4.

Chapter 4 Mixed methods study methodology

4.1 Publications and outputs

Brady, G., Roe, J., Lagergren, P., Paleri, V., & Wells, M. (2023) *Recruitment challenges in clinical research involving research participants with a diagnosis of recurrent head and neck cancer; a single study experience in the real world.* Poster presentation. The North West London Research Symposium, London September 27th, 2023.

4.2 Introduction

The previous Chapter 3 documented the findings of the systematic review, which identified significant gaps in the current literature, identifying and highlighting numerous areas for future research. Working in collaboration with the study PPI/E group, priorities for further research were identified including the exploration of the communication, swallowing, quality of life (QoL) outcomes, concerns, priorities and experiences of patients with recurrent oropharyngeal disease and their caregivers over time. This objective was achieved using a mixed methods study. To the authors knowledge this is the first mixed methods study aiming to investigate function and QoL and patient/ carer experience in this patient group. A convergent design mixed methods study included both a longitudinal qualitative interview workstream investigating patient and carer experience of function and QoL change over time, and an observational repeated measures quantitative workstream measuring change in swallowing, communication, QoL outcomes and patient priorities over time. This chapter will describe the study methodology including the background, aims and objectives. Data collection methods and the rationale for their choice, qualitative and quantitative data analysis and their integration will also be described. The qualitative workstream results will then be presented in Chapter 5, followed by the quantitative workstream results in Chapter 6 and their integration in Chapter 7.

4.3 Background

Mixed methods research is a methodology which involves collecting, analysing and integrating qualitative and quantitative data in a single study (Creswell and Clark, 2017). A key facet of mixed methods research is that the knowledge generated by the combined quantitative and qualitative data is greater than the sum of its parts (Bazeley, 2012). It has been described as quite an intuitive approach by which to make sense of a phenomenon or new knowledge (Creswell and Clark, 2017) and one that lends itself well for use in clinical research. As an experienced SLT, when diagnosing and managing swallowing and communication problems in patients, I often combine quantitative and qualitative information. For example, when assessing a patient's swallowing function, I may often use an instrumental evaluation or clinician-rated outcome measure however I will never look at these findings in isolation. In clinical practice I combine this quantitative objective information with the qualitative subjective information gained through careful case history taking, incorporating the patient's own description and experience. These data are then integrated to make a diagnosis and form a plan of treatment or rehabilitation. This method of generating new information in clinical practice befits the use of mixed methods research.

One of the main advantages of mixed methods methodology highlighted in the literature is that it can harness the strengths of both qualitative and quantitative research methods to offset the potential pitfalls of each approach (Creswell and Clark, 2017). It can be argued that quantitative research can lack the individual participant voice or view and can potentially miss important contextual information. Qualitative research can also have its own disadvantages, with the potential for researcher bias and the potential lack of generalisability of findings (Creswell and Clark, 2017).

This mixed methods study, forming the second study within this PhD, involved two workstreams, one quantitative and one qualitative, where the findings were integrated. The quantitative workstream measured change in function (swallowing and communication) and

quality of life (QoL) over time using a range of clinician-reported, patient-rated and instrumental evaluation methods. To provide a further in-depth knowledge of how patients and caregivers experience these changes over time, within the qualitative workstream, concurrent longitudinal qualitative data were also collected using in-depth interviews conducted at pre-specified timepoints. To the authors knowledge, this is the first time such long-term patient and carer experience qualitative data has been collected in this patient population. The overarching aim of the mixed methods study was to gain an in-depth understanding of change in function, QoL, patient concerns and priorities over time, contextualised with qualitative data focusing on patient and carer experience of rOPC from diagnosis to treatment and beyond. The remainder of this chapter will discuss how this was achieved.

4.4 Epistemological assumptions

The planning and development of any research proposal begins with an acknowledgement of the philosophical assumptions regarding how knowledge is gained by the researcher (Crotty, 1998). This epistemological standpoint later informs a theoretical view, which will shape and influence the methodology and subsequent methods for collecting and analysing data. For example, quantitative research is often associated with a positivist worldview where knowledge is gained from cause and effect thinking (Creswell and Clark, 2017). Experimentation is completed via reductionist methods to investigate how selected variables interact, using detailed measurements and observations (Creswell and Clark, 2017). Post-positivist researchers agree with the positivist paradigm but believe that environmental and individual differences can influence the reality of actions. Conversely, in a constructivist paradigm, meaning is formed through a participant's view of a phenomenon. Qualitative research is associated with a post-positivism or constructivist paradigm. My worldview as a clinician is that knowledge can and must be gained from multiple sources and the key to quality patient care is to integrate these various sources of information. My standpoint as a researcher stems from this clinical background and rejects the perceived dichotomy between

two opposing paradigms - positivism and constructivism - as false. My belief is that there is a continuum of how knowledge is gained, from positivism to post-positivism to constructivism, and that these types of knowledge can co-exist and complement each other. Pragmatism centres on the idea that knowledge does exist in the external world, and thus can be measured by quantitative means, however knowledge is experienced by individuals and this must be measured qualitatively (Creswell and Clark, 2017). Pragmatism is most frequently described in the context of mixed methods research (Hampson and McKinley, 2023). A pragmatist paradigm focuses on employing a number of methods to gain knowledge that will best fit the research question, valuing both subjective and objective data sources (Tashakkori and Teddlie, 2003). However, this view has been criticised in the literature as being somewhat non-committal or convenient. It has been argued that researchers may become distracted with the technicalities of the methods in mixed methods research to the detriment of the background methodology (Hampson and McKinley, 2023). In keeping with a pragmatist paradigm, I have committed to respecting both views on data collection, treating both the quantitative and qualitative data as equal, and planning methods for each workstream in keeping with the background methodology to ensure the data are as robust as possible. I have also acknowledged and planned for the critical stage of data integration in keeping with mixed methods research methodology. This will be expanded on further within this chapter.

4.5 Research aim

The aim of this mixed methods study was to identify and explore function (swallowing and communication) and QoL outcomes, patient priorities and patient and carer experiences of rOPC over time including diagnosis, treatment decision-making and living with the consequences of treatment.

The use of mixed methods is particularly important in the setting of rOPC. Treatment decision-making in rOPC can be influenced by the presumed potential function and QoL

morbidity of curative treatments. However, we have found that quantitative function and QoL data in this population are of poor quality and patient experience data are absent from the literature (Brady et al., 2023). Given that patients with rOPC have previous/ current experience of function and QoL change due to their previous treatment(s) for primary disease, it is important not only to quantify further change during and after salvage or palliative treatment(s). It is also imperative to contextualise such changes with how patients and caregivers experience and prioritise them. Acknowledging the importance of past and present experience (measured qualitatively) and how it influences our current and future actions (measured quantitatively), is the crux of the pragmatist paradigm and underpins the mixed methods research approach.

4.6 Research design

In keeping with the overall aim of this thesis, a convergent mixed methods design was used. This is an appropriate design when the researcher wants to compare and contrast qualitative and quantitative data to gain a complete understanding of the research problem using methods such as corroboration, validation or illustration (Creswell and Clark, 2017). This mixed methods study was based on the convergent design model summarised in Figure 1 (Creswell and Clark, 2017). A convergent design was utilised as it is very much in keeping with a pragmatist worldview. The design essentially merges the knowledge gained from two approaches into a larger understanding of the research problem. Both data sources are treated as equal in terms of importance in relation to the overall research objective. Within the convergent design, which is also described as a parallel design, qualitative and quantitative data collected and analysed concurrently, with the data integration/ merging phase occurring after both sets of data have been collected and analysed (Shorten and Smith, 2017).

Although the concept of the convergent design model appears relatively straightforward, the process of merging or integration is potentially the most complex step and requires pre-

planning from the protocol development stages right through to the data analysis stages. Creswell & Clark's model, as shown in Figure 4-1, suggests that there is no cross over between the data sources. However, in reality for this research, as early as the planning and design stages, much thought was devoted to both methods of data collection so that they could be integrated at a later time (Fetters et al., 2013).

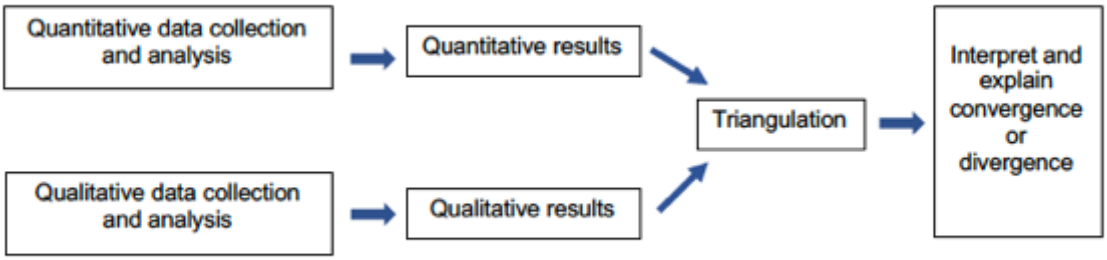


Figure 4-1: Mixed methods convergent design (Creswell and Clark, 2017)

Creswell and Clark (2017) describe four main stages in implementing a convergent mixed methods design. The researcher designs and collects the qualitative and quantitative data concurrently. Creswell and Clark specify that the two types of data do not need to be collected in any particular sequence as they are not inter-dependent but both types of data have equal weighting within the study. The two sets of data are then analysed separately, using quantitative and qualitative analysis techniques which are appropriate to the research question. Once the two datasets have been obtained and analysed, the researcher moves towards merging the two sets of results. A further aspect not truly reflected in the convergent diagram representation seen in Figure 4-1 was some cross over between methods, which occurred due to logistical reasons. In this study the qualitative data were mostly collected after the quantitative data using the same sample of participants. The researcher was subsequently aware of the function and QoL status of the participant at the time of interviewing. This may have influenced the researcher's line of questioning or probing on particular aspects of function or concern in the interview, or this prior knowledge may have

influenced the qualitative analysis. Also, the participant's involvement in an assessment of swallowing and measurement of QoL as part of the quantitative data collection, may have heightened the participant's awareness of changes or potential changes to function /QoL prior to their interview. This has been referred to in the literature as an interactive approach, where data collection and analysis can drive changes in the data collection procedures in an iterative way (Fetters et al., 2013). Such real-world influences of various information sources for both the participant and researcher align with the pragmatist standpoint, which must be contrasted to the much more discrete and orderly model presented by Creswell and Clark. With this in mind, specific considerations in mixed methods research, such as sampling, will be considered before describing these four main stages of the convergent model design. The importance of reflexivity will also be described later in this chapter.

Within the context of a mixed methods convergent design there were many design decisions to undertake, including but not limited to sampling (Creswell and Clark, 2017):

1. Will the qualitative and quantitative samples include the same or different individuals?
2. Will the sample size for both workstreams be the same or different?
3. Is there the potential to design parallel data collection questions?
4. Is there a particular order to data collection and how will the two sources be collected?

At all decision points, the researcher worked with the study PPI/E group, and ensured the decisions were in keeping with the overall pragmatist paradigm and congruent with mixed methods methodology. The remainder of this chapter will provide some further details on sampling, quantitative and qualitative data collection and analysis methods followed by a description of the integration method including the carefully considered issues inherent in the mixed methods design introduced above. The influence of PPI/E will be discussed throughout.

4.7 Sampling

Traditionally quantitative and qualitative research use very different philosophies and techniques for sampling and for determining the desired sample size. Quantitative research often uses probability based random sampling aiming to achieve a representative sample of the population, whereas qualitative research uses non-probability based purposive sampling aiming to recruit participants from specific groups (Bryman, 2016). Quantitative research has well established and robust statistical formulae to calculate how many participants are required in experimental or hypothesis driven research. In qualitative research the sample size can vary based on the qualitative analysis plan which is being used. An example of this is phenomenological research which requires only a small number of participants (10 or less) whereas grounded theory may require a larger sample which is not pre-specified but achieved when data saturation is reached and generally has a larger sample (20-30 participants) (Onwuegbuzie and Collins, 2007). Mixed methods research is slightly more complex in terms of sampling as there must be a sampling design which is both robust and justified for both the quantitative and qualitative workstreams and must be in line with the overall research question and objectives. As mentioned, when describing the epistemological assumptions of this research, it was essential to pay close attention to the methodology in addition to the technicalities (methods) of carrying out a mixed methods study.

When deciding on a sampling design in mixed methods research, one of the first considerations must be the time orientation and the relationship of the two data sets (Shorten, 2017). In line with convergent or parallel design mixed methods methodology, recruitment to each workstream in this study was concurrent. However, for the quantitative workstream prospective participants were recruited only, whilst for the qualitative workstream participants were recruited both prospectively and retrospectively and the qualitative workstream involved caregivers also. For the prospective cohort, participants

were recruited from the same pool of patients for both the quantitative and qualitative data collection, however participation in either arm was optional and so sample sizes were not equal. The qualitative workstream was pre-planned as being smaller in desired sample than the quantitative study. This was in part so that the volume of qualitative data within the longitudinal study would be manageable within this time bound research study. The design of the sampling method for the prospective participants was nested, which means that the participants enrolled in the longitudinal qualitative workstream were part of the larger pool of patients enrolled in the longitudinal quantitative workstream (Shorten and Smith, 2017).

However, as previously mentioned, the overall qualitative workstream also included caregivers and a separate sample of retrospective participants who were not included in the prospective quantitative workstream. Thus the overall sampling design for the longitudinal mixed methods study was multi-level (Onwuegbuzie and Collins, 2007). For the qualitative workstream, purposive sampling was utilised to ensure a deep insight into the experience of rOPC was gained across curative and non-curative pathways. For the quantitative workstream a probability-based sample size calculation was undertaken for the primary outcome measure to demonstrate generalisability to the population of patients with rOPC. Again, the methodology of mixed methods was adhered to with this sampling method, with due attention paid to the sampling in both the quantitative and qualitative workstreams. Instead of adhering to traditional dichotomies of quantitative and qualitative random and non-random sampling, the sampling method chosen for this study for each method was based on the type of generalisability of interest for the overall research objective (Onwuegbuzie & Collins, 2007). For the quantitative workstream the aim was to look at changes in function and QoL over time and to try to make some form of generalisation from the sample about the overall population with rOPC. For the qualitative workstream, the aim of generalisation was to gain an in-depth and rich understanding of the patient and carer experience rOPC over time, from diagnosis to treatment and beyond.

The background, design, data collection and analysis will now be discussed for the quantitative workstream firstly, and then the qualitative workstream. The integration method will then be explained thereafter.

4.8 Quantitative methods

4.8.1 Quantitative workstream design

A prospective non-randomised, non-interventional descriptive observational cohort study was undertaken. A prospective design was chosen because the systematic review, previously discussed in Chapter 3, had identified a lack of prospective data in the research literature.

4.8.2 Quantitative workstream objectives

The primary objective of this workstream was to measure change in swallowing function over time for patients receiving treatment for rOPC. Swallowing function was evaluated using a patient-reported outcome (PRO) measure, namely the MD Anderson Dysphagia Inventory (MDADI) (Chen et al., 2001). This outcome measure was used to measure change in swallowing-related QoL from baseline to 6 months.

Secondary objectives for the study were to:

1. Investigate potential changes in swallowing-related QoL for up to 6 months using the MDADI (Appendix 2)
2. Investigate potential changes in function for up to 6 months using
    (i) The Performance Status Scale for Head and Neck Cancer (PSS- HN) scale (normalcy of diet, eating in public and understandability of speech scales) (List et al., 1990). (Appendix 3)
    (ii) the 100 mL Water Swallow Test (WST) (Patterson et al., 2011) (Appendix 4)

(iii) the International Dysphagia Diet Standardisation Initiative (IDDSI) Functional Diet Scale (FDS) (Steele et al., 2018) (Appendix 5)

(iv) the Dynamic Imaging Grade of Swallowing Toxicity for Flexible Endoscopic Evaluation of Swallowing (DIGEST-FEES) grade (Starmer et al., 2021) (Appendix 6)

3. Assess patient-reported QoL and priority concerns using the University of Washington Quality of Life (UWQoL) Questionnaire (v.04) (Rogers et al., 2002) (Appendix 7)
4. Assess patient-reported priority concerns at baseline and 6 months using the Chicago Priority Scale (CPS) (Sharp et al., 1999) (Appendix 8)
5. Report on gastrostomy tube usage up to 3 and 6 months

4.8.3 Inclusion/ exclusion criteria

Patients with biopsy proven loco-regionally residual, recurrent, or new primary OPC in a previously irradiated field who were undergoing surgery (open or transoral robotic), re-irradiation, immunotherapy, chemotherapy or a clinical trial of an investigational agent were included in the study. Inclusion/ exclusion criteria are listed in Table 4-1. For the remainder of this chapter, as with all other chapters in this thesis, the population will be referred to as patients with rOPC.

Table 4-1: Inclusion/ exclusion criteria for quantitative workstream.

Inclusion criteria	Exclusion criteria
• Adult (aged 18 years or over) competent to provide consent • Have a diagnosis of rOPC	• Any previous medical condition, other than HNC, which has a known impact on communication/ swallowing (Parkinson's Disease,

• Have adequate linguistic and cognitive function to participate to complete questionnaires. • English speaking	Multiple Sclerosis, cerebral vascular accident (CVA)

4.8.4 Sample size

As previously mentioned, the goal of the quantitative workstream was to make some generalisation regarding function and QoL change over time in the sample in relation to the overall population of patients with rOPC undergoing curative or non-curative treatments. A probability-based sample size calculation was undertaken. The sample size calculation was based on the primary endpoint, change in MDADI scores from baseline to six months following treatment initiation for rOPC. Previous data have shown that a 10-point between-group difference in MDADI score is clinically significant (Hutcheson et al., 2016). However, it must be noted that in the study used to identify this clinically significant difference, patients with recurrent disease were excluded.

Data collected within a pilot study by the research team as part of a service evaluation which was approved by the Committee for Clinical Research at the Royal Marsden NHS Foundation Trust (Royal Marsden SE REHAB1249) were utilised to calculate the sample size. Pilot data including 10 patients treated surgically for recurrent HNC demonstrated a mean composite MDADI score of 66.50 at baseline and 52.60 at six months with a standard deviation of the difference of 23.68. Using a two-sided alpha of 5% and 80% power, a total of 25 participants were required to complete the paired questionnaires at baseline and six months post-treatment (power function, STATA). An additional three patients were included in the desired sample to cover for 10% drop out, bringing the total sample to 28 patients. From reviewing previous numbers of patients referred for management of recurrent HNC to the Royal Marsden Hospital per year with the majority of patients having rOPC, combined with the ongoing development of the International Centre for Recurrent Head and Neck

Cancer (IReC) at that time, and with a planned data collection period of 18-months, the sample appeared feasible to recruit.

4.8.5 Endpoint selection

As demonstrated by the systematic review findings described in Chapter 3, there is a lack of consistency in what functional outcome measures are used in patients with rOPC and at what timepoints. The outcome measures selected for this study, as recommended in the primary disease literature, encompass multidimensional measures of swallowing function including patient-reported, clinician-rated and instrumentally evaluated outcomes (Lefebvre et al., 2009). The primary outcome measure (MDADI) is a patient-reported measure of swallowing-related QoL. This is in line with many recent and ongoing interventional studies in primary HNC (Nutting et al., 2023, Owadally et al., 2015, Nichols et al., 2019). The primary endpoint measure, in combination with the secondary endpoints, and the interview data collectively encompass the different dimensions of the International Classification of Functioning and Disability (ICF) (WHO, 2002) as summarised in Table 4-2. The ICF utilizes domains of body functions and structures, activities and participation, as well as environmental and personal factors to fully encapsulate the concepts of health and disability. The ICF provides a rich and holistic framework for understanding of functioning. The ICF has been recommended as a framework to guide functional outcome measurement in primary HNC (Roe et al., 2014, Nund et al., 2019) and is particularly valuable in the setting of rOPC. The framework provides a holistic view of impairment of body structure (for example impairment in strength of the muscles at the back of the tongue) or function (ability to propel food through the throat/pharynx), activity limitations (ability to eat food/ drink fluids) or participation restrictions (enjoying a family meal). The framework also considers the social and environmental factors that construct an individual's everyday reality.

Patients with rOPC have been treated for primary HNC previously. They may have impaired function at baseline, and they may or may not enjoy or prioritise eating/ drinking. These

factors need to be considered to obtain a holistic view of what health or disability feels like for these individuals. As mentioned previously, decisions are often made about treatments for rOPC based on the potential morbidity of treatments, however little is known about the true functional morbidity or indeed how patients prioritise these functions in relation to their overall QoL. The combination of primary and secondary outcome measures for this research were carefully chosen with this in mind, to encompass all levels of the ICF and to measure patient priorities. The ICF as a multidimensional framework for conceptualising health and disability, is in keeping with the philosophical underpinnings for this research, a pragmatist paradigm where knowledge includes multiple sources to address the underlying research question. With a convergent mixed methods design, consideration at the planning phase was undertaken to facilitate the later integration of qualitative and quantitative findings. It was agreed amongst the research team that a patient-reported outcome measuring swallowing-related quality of life, which includes ICF domains of activity and participation would potentially be comparable with the qualitative findings reporting patient experience of changes in function and QoL over time. Given that the domain of participation is included, it was felt that there may also be the potential for integration of carer experience, as eating is often a social experience with families cooking for each other and/ or eating together.

Table 4-2: Endpoints, administration and ICF domain(s) assessed.

Target	Outcome measure	Administration	ICF domain
Swallowing	MD Anderson Dysphagia Inventory	Patient reported	• Activity • Participation
Swallowing	Performance Status Scale for Head and Neck Cancer (PSS-HN) Normalcy of diet	Clinician rated	• Activity
Swallowing	PSS-HN Eating in Public	Clinician rated	• Participation
Speech	PSS-HN Understandability of Speech	Clinician rated	• Activity • Participation
Swallowing	100 mL Water Swallow Test	Clinician rated	• Body structures and function
Swallowing	International Dysphagia Diet Standardisation Initiative Functional Diet Scale score	Clinician rated	• Activity
Swallowing	Dynamic Imaging Grade of Swallowing Toxicity - Flexible Endoscopic Evaluation of Swallowing (DIGEST-FEES)	Instrumentally evaluated	• Body structures and function
Quality of life	University of Washington QoL Questionnaire version 4	Patient reported	• Body structures and function • Activity • Participation • Environmental
Patient priorities	Chicago Priority Scale	Patient reported	• Body structures and function • Activity • Participation
Patient and carer experience	Interview data	Patient and carer reported	• Environmental and personal factors

4.8.6 Study flow and timepoints

Sequential patients who were referred to the Royal Marsden NHS Foundation Trust for management of newly diagnosed loco-regionally rOPC were identified via the weekly head

and neck MDT meeting. At their next scheduled appointment with the clinical team, potential participants were provided with a participant information sheet (PIS). If participants were willing to participate, written consent was obtained. The initial set of outcome measures were collected at this stage. All outcome measures were completed prior to treatment commencement (baseline) and at three- and six-months following treatment initiation, apart from the Chicago Priority Scale which was collected at baseline and six months only. The rationale for this was based on the advice from the PPI/E group who felt that it would be too frequent to reassess patient priorities at each timepoint.

Table 4-3 details the outcome measures and timepoints for data collection. Given that the research ethics application was initiated during the COVID-19 pandemic, a remote consenting and data collection method were also included in the original ethics approval application. The study protocol was reviewed and approved by the Royal Marsden NHS Foundation Trust Committee for Clinical Research (CCR5242) and the Health Research Authority (HRA) (IRAS: 297893) and the study opened for recruitment on 01/01/2022. Due to lower than anticipated recruitment rates at the research centre, a substantial amendment was submitted in April 2023 to open up two participant identification sites to the prospective arm of the study (SA02). This was approved in May 2023 (AM2304/07) with subsequent PIC site opening at Newcastle on 19th September 2023.

Reasons for lower than predicted recruitment to the observational study were several. This included an unexpectedly long period between funding application and research initiation, and a corresponding change in clinical landscape with the publication of some key pieces of research. This included the RECUT (Hardman et al., 2022) paper which investigated survival outcomes for patients undergoing transoral robotic surgery (TORS) for recurrent disease and the KEYNOTE series (Burtness et al., 2019, Cohen et al., 2019), which investigated the use of immunotherapy in the treatment of recurrent disease. The latter series resulted in the approval of immunotherapy as a first line treatment for patients with unresectable rOPC. At

the point of planning for this research, patients would have opted to go to the main research site to receive TORS or immunotherapy as part of a clinical trial. Whereas following these key pieces of research, TORS for recurrent disease became available much more widely across the country and immunotherapy became standard of care. This meant that there were much fewer patients being referred to the research centre for TORS or immunotherapy, which was not standard of care.

Table 4-3: observational study data acquisition and time points

Timepoint	Measure	Domain	Endpoint	Mode	
Baseline, 3 & 6 months	MD Anderson Dysphagia Inventory	Swallowing-related QoL	Composite score	Remote/ in person	Primary outcome measure
Baseline, 3 & 6 months	University of Washington Quality of Life questionnaire version 4	Health related QoL	Composite scores of physical and social-emotional functioning are derived from 12 domains. Patients can also highlight up to 3 priority concerns from the previous 7 days	Remote/ in person	Secondary outcome measures
Baseline, 3 & 6 months	Performance Status Scale for Head and Neck Cancer (PSS-HN)	Normalcy of Diet, Eating in public and speech intelligibility	Score for each subset	Remote/ in person	
Baseline, 3 & 6 months	100 mL WST	Swallowing function	Swallowing capacity score (mL/second)	Remote/ in person	

Baseline, 3 & 6 months	International Dysphagia Diet Standardisation Initiative Functional Diet Scale	Diet modification	Diet score (1-8)	Remote/ in person	
Baseline, 3 & 6 months	Dynamic Imaging Grade of Swallowing Toxicity - Flexible Endoscopic Evaluation of Swallowing (DIGEST-FEES)	Swallowing toxicity rating	Summary score (0-4)	**In person only**	
Baseline and 6 months	Chicago Priority Scale	Patient priority rating of treatment outcomes	Ranked 1-12 priorities	Remote/ in person	

4.8.7 Statistical analysis

IBM SPSS Statistics Version 29.0.1.0 (171) was used in the quantitative data analysis. Baseline patient characteristics (age, gender, ethnicity and previous HNC treatment history) were summarised in addition to the diagnostic (site and time of recurrence) and treatment details (type of treatment, in the case of surgery use of reconstruction and tracheostomy, feeding tube presence and type) using descriptive statistics. The study protocol had specified that the primary endpoint data would be analysed to compare mean MDADI composite score from baseline to six months following treatment initiation. Following tests for normality, using a two-sided paired t-test in the presence of normally distributed data or a Wilcoxin test in the presence of non-normally distributed data was pre-planned. A statistical plan was made for missing data in line with the scoring manual for the primary outcome

measure (Chen et al 2001). If 50% or more of the questions in a subscale were not answered, the subscale was considered as missing. If more than 50% were answered, we calculated the mean score of the questions answered for each subscale. However, the desired sample size was not maintained at the second timepoint due to sample attrition and so statistical testing was not undertaken. Descriptive statistics were used to describe the change in MDADI scores. Of note the data were not normally distributed so median and inter quartile range (IQR) were used to describe the data.

Secondary endpoints (PSS,100 mL WST, IDDSI-FDS score, DIGEST-FEES and UWQoLv4, and CPS scores) were summarised using summary statistics. Again, medians with IQR were used as a skewed distribution was observed.

4.9 Qualitative methods

The qualitative workstream of this mixed methods study included a longitudinal prospective and retrospective interview study with both patients with rOPC and their caregivers. The study PPI/E group were in full agreement with the research team that patient experience data were essential to provide context to the quantitative data. The PPI/E group were also very clear that caregivers should be involved, as any changes to function including communication and/or swallowing would not only impact the patient, but their family and loved ones.

4.9.1 Qualitative workstream design

This workstream originally involved a prospective longitudinal interview study using a nested subgroup of participants from the quantitative workstream. Caregivers of these participants were also invited to take part as suggested by the PPI/E group. The prospective participants were invited to interview at two timepoints; at baseline prior to commencing treatment and at six months following treatment initiation. The study protocol was reviewed and approved by

the Royal Marsden NHS Foundation Trust Committee for Clinical Research (CCR5242) and the Health Research Authority (HRA) (IRAS: 297893) and opened for recruitment in November 2022. Following a meeting with the study PPI/E group, where recruitment rates (lower than expected at six months post-treatment initiation) and provisional findings were discussed, a retrospective cohort was added via a substantial amendment AM2302-06, which was approved in March 2023. The rationale as described by the PPI/E group for the inclusion of a retrospective cohort, were that changes in function and QoL can occur much later than six months following treatment initiation. The study PPI/E group advised that the inclusion of a retrospective group of participants who were at least 12 months following treatment initiation would give greater insight into the longitudinal experience of rOPC. Study documents for all workstreams including participant information sheets and consent forms are included in Appendix 9.

4.9.2 Qualitative workstream objective

To investigate patient and carer experience of function and QoL change over time before, during and after treatment for rOPC.

4.9.3 Inclusion/ exclusion criteria

Both patients and caregivers were invited to participate in this workstream as advised by the study PPI/E group. The addition of caregivers introduced a new cohort of individuals to the study, which thus required consideration of qualitative data analysis and eventual quantitative and qualitative integration. A considerable amount of discussion and reflection with the study PPI/E group was undertaken regarding the eventual integration of a cohort of caregivers to the study and how that data might be considered at the integration phase. In this study, caregivers and patients were offered interviews undertaken alone (individual) or together (joint patient and carer). All caregivers who agreed to take part in this study, took part in joint interviews as agreed with the patient participant. It was thus discussed and

agreed with the PPI/E group that the joint patient and carer interviews would be analysed in the context of how changes in function and QoL over time are experienced by the dyad (patient and carer together) rather than looking at patient and caregivers in isolation, unless there was clear evidence of divergence in opinion or experience. This method of analysis has been completed in dyads in other areas of cancer care where the functional sequelae of treatment are thought to have a significant impact on the patient and carer dynamic, for example in prostate and breast cancer (Cincidda et al., 2023). Speaking and eating are social endeavours and will not only impact the patient individually but their partners and family members. The inclusion criteria for patients and caregivers are summarised in tables 4-4 and 4-5.

Table 4-4: Inclusion/ exclusion criteria patient participants

Inclusion criteria	**Exclusion criteria**
• Adult (aged 18 years or over) competent to provide consent • Diagnosis of rOPC • Adequate linguistic and cognitive function to participate in interview • English speaking	• Any previous medical condition, other than HNC, which has a known impact on communication/ swallowing (Parkinson's Disease, Multiple Sclerosis, cerebral vascular accident (CVA)

Table 4-5: Inclusion/ exclusion criteria (carer participants)

Inclusion criteria	**Exclusion criteria**
• Caregivers of patients 18 years or over who have been diagnosed with rOPC • Adequate linguistic and cognitive function to participate in interview • English speaking	• Not fulfilling all of the inclusion criteria

4.9.4 Sampling

As mentioned earlier, the sampling scheme for the prospective qualitative study was nested within the quantitative exploratory prospective workstream. However, within this nested

strategy, purposive sampling was used to ensure that patients from curative and non-curative treatment options were recruited, males and females and where possible from a diverse ethnic background. The rationale for this was to ensure a rich insight into the patient and carer experience across treatment pathways for a range of individuals. Overall, the sampling method for the mixed methods study was multi-level, as a separate group of participants and caregivers were recruited for the retrospective interviews. Again, purposive sampling was used here to ensure that participants were recruited across treatment pathways. Expected recruitment rates included approximately 20-30 patients (10-15 prospective patients and 10-15 retrospective patients) and 10-20 caregivers (5-10 caregivers of retrospective patients and 5-10 caregivers of prospective patients). However, it was planned that recruitment would cease when no new themes were emerging from the data, a phenomenon known as data saturation (Bryman, 2016). This was facilitated by the concurrent data collection and analysis which is in line with the chosen analysis approach, namely Framework Approach (Ritchie and Spencer, 1994)

4.9.5 Data collection

Options for data collection methods in the qualitative workstream in this thesis included the use of focus groups or individual interviews. Both methods are widely used in qualitative research and there are pros and cons for both data collection methods. Focus groups typically involve a number of participants (at least four) in addition to the moderator, and the focus of the group interview is to elicit the participants' views on a particular subject (Bryman, 2016). The group dynamics can be utilised to elicit differing opinions and how the participants may react to similar/ differing viewpoints. An individual interview however typically involves the interviewer and the interviewee (Bryman, 2016). The two potential data collection methods were discussed with the PPI/E group. Given the nature of HNC and rOPC, the PPI/E group, some of whom were unable to speak, were concerned that if a participant had communication difficulties, they might not be able to, or may find it difficult to participate in a group discussion. To facilitate the inclusion of all patients regardless of their

communication ability and method, the decision was made to use individual rather than group interviews. In qualitative interviewing, the interviews can be unstructured involving a very broad aide memoire for the interviewer, or semi-structured where the research has a list of topics to be discussed in the form of a topic schedule. As a relatively novice qualitative researcher, on liaison with my supervisory team, it was decided to proceed with semi-structured interviews with the use of a topic guide (Appendix 10). The topic guide was developed in consultation with the study PPI/E group and the research supervisory team. Interviews were undertaken almost exclusively remotely (unless the use of non-verbal communication precluded the use of video calls) in an effort to make the appointment as convenient and comfortable for patients and their family members. Video calls were utilised rather than audio calls, as it felt a more natural way to communicate, with the added contextual cues provided by verbal expression or body language (Williams et al., 2013). Quite often these interviews were conducted out of office hours, and the researcher was also based at home in an effort to create a more equitable power balance. The potential influence of the researcher being an experienced clinician in HNC and the impact of this on the perception of power balance will be expanded on in further detail when reflexivity is explored in the next section of this chapter. The decision to conduct interviews remotely with all parties outside of the hospital environment was made jointly with the PPI/E project group. When an in-person interview was required, in particular for those participants who were unable to speak, interviews took place in the hospital environment in a quiet confidential space. When participants were unable to speak, adaptations were made to the interview to suit their individual communication needs. For example, one gentleman used a text to speech app to communicate, supplemented by some mouthing and writing. Another gentleman used writing; here the interview was recorded but the interviewer read aloud what the interviewee had written. The interviews were both video and audio recorded and detailed notes were made regarding any non-verbal communication methods used. The audio from the video recordings and/or the audio recordings were anonymised and securely transferred to a professional transcription service who transcribed the recordings verbatim. The written

transcription was then checked by myself, and annotated with anything further of note contained in the field notes or observed when watching back/ listening to the recording.

4.9.6 Analysis

In this study, qualitative data were collected via in depth interviews. This allowed the research participants to communicate their individual experiences of rOPC and the impact on function and overall QoL. It is not the purpose of qualitative analysis to group the participants' responses into pre-defined categories, but to identify the units of meaning and group them into categories which potentially relate to each other in relation to the research question (Ritchie and Spencer, 1994). Some time was spent exploring and considering a range of different factors and approaches to qualitative data analysis. As the research aimed to explore patient and carer experiences of function and QoL over time, methods which focus on the analysis of patient experience were considered. Phenomenology is the study of subjective experience, however, is typically used with smaller sample sizes (Rodriguez and Smith, 2018). Grounded theory was excluded as this study was not aiming to generate a theory, but to explore patient/ carer experience. Another facet within the decision-making was the underlying pragmatism paradigm of the research, where knowledge is gained from a range of methods, and these methods are chosen based on the research question. Framework approach (FA) as described by Ritchie & Spencer (1994) was chosen for this research as both a qualitative data management and analysis approach. This approach sits under the general umbrella of thematic analysis, however it allows for both inductive and deductive theme development based on the themes which are derived from the data and also themes relating to the objectives of the research (Gale et al., 2013). FA was derived from social researchers in the UK in the 1980s. It has become increasingly popular in healthcare research. The approach facilitates an audit trail from the primary data to the themes generated and can work very well within a research team setting in particular when a more junior researcher is being guided by more experienced qualitative researchers, as was the case with this research (Ward et al., 2013). The primary data were the interview

transcripts, however during the interview data collection phase, field notes were also recorded at the end of each interview. In this study as outlined in the guidelines for fieldnotes by Phillippi and Lauderdale (2017) field notes were completed shortly after each interview was completed. These field notes included the time, date and participant identification number. Demographic information was also noted including the participant age, treatment pathway and then interview details including the setting, number of participants (individual or dyadic) (Phillippi and Lauderdale, 2017). Notes and observations made during the interview were recorded, including any adjustments made due to the communication needs of the participant and any observations of displays of emotion, or of the balance between contributors in dyadic interviews. These also included any deviations to the topic schedule and the rationale for this. Field notes were closely maintained along with the researcher's reflexive log which noted any observations/ reflections on how the researcher may have biased the interview. Reflexivity and the use of a reflective log for this study will be expanded upon in a later section of this chapter.

NVivo software for Mac (version 20) was used to assist with data management during the analysis. The computer software programme was used as a tool to aid efficiency in data management and to document a clear audit trail from the raw data to interpretation. FA includes 5 key stages as summarised in Figure 4.2. These stages will now be discussed in further detail. Please note that although the stages are presented here as 5 discrete steps. In reality, the process of analysis was not linear and often moved between the 5 different stages to verify interpretative themes.

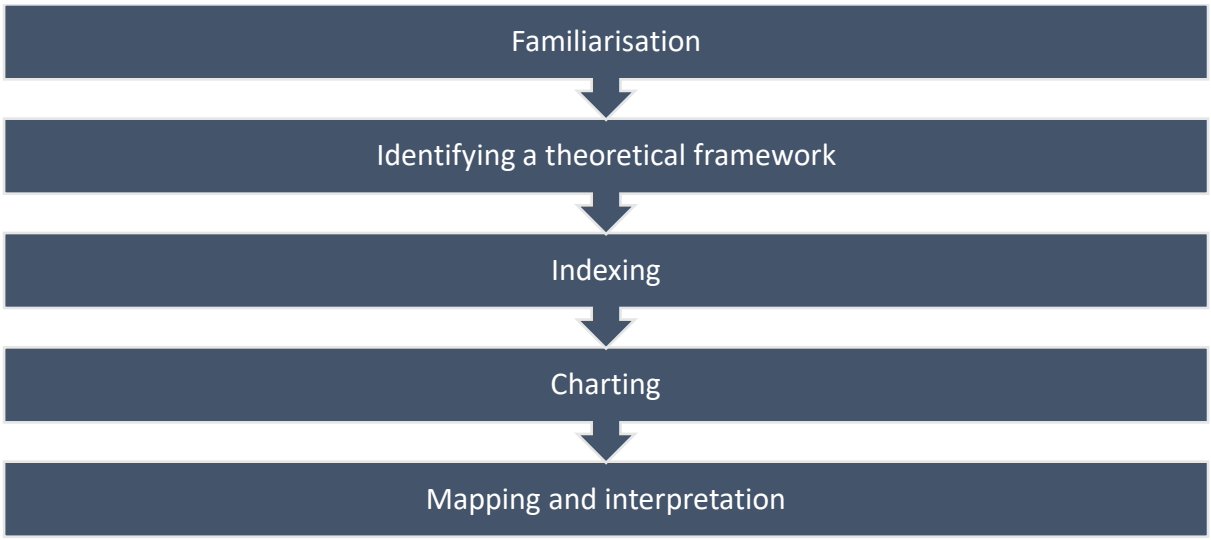


Figure 4-2: Framework analysis

FA stage 1: Familiarisation phase

During the familiarisation phase the interview transcripts were read and re-read by researcher GB. This was done whilst listening to the audio recordings, and simultaneously reviewing any field notes taken during the interviews. For those participants who were non-verbal, video recordings of the interviews were also viewed whilst reading and re-reading the transcripts. If a patient was non-verbal, researcher GB would either read aloud the written information when a patient used writing or repeat what the patient said via their text to speak app. This was because often the output from such communication devices is not picked up sufficiently on audio recordings. Phrases within the transcript were then coded using open coding. This is a process by which a label is assigned to a piece of text. This initial coding was completed within Excel and resulted in an initial 196 codes. An example of this initial attempt at open coding is included in Table 4-6. With the assistance of an experienced qualitative researcher within the team (MW) this initial attempt at coding was further refined not only to take quotations from the transcript as a code, but to label pieces of text from the interview. The initial codes presented in Table 4-6 were combined into the 'diagnosis of recurrent disease' code and that the excerpts in figure 4-3 illustrate how sections of text were coded to this and inputted into NVivo.

Table 4-6: Initial draft of open coding

Interview participant identifier	Code number	Open coding
1	1	'no residual activity'
	2	'supposed to be cancer free'
	3	'eating difficult'
	4	'Pain'
	5	'recurrent cancer'
	6	'Scan'
	7	'shock'
	8	'jolt'

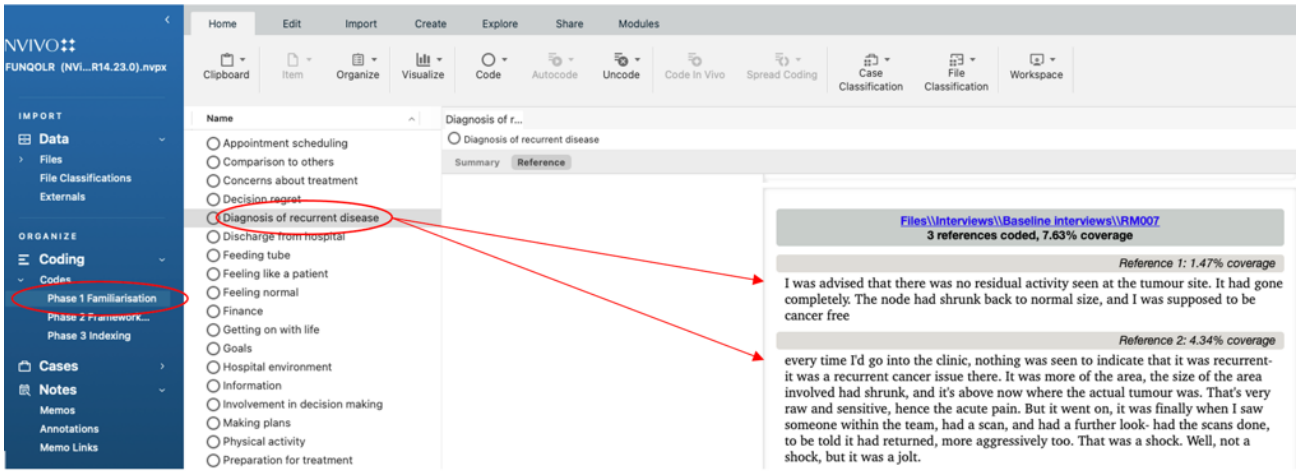


Figure 4-3: Familiarisation phase, open code 'diagnosis of recurrence' and corresponding interview data

Within the FA literature, there are times where this process of open coding may only be completed for a proportion of the total transcripts. However, as I was new to this analysis method, this was completed with every transcript. Whilst this was being done, the open coding was entered into the NVivo software package and the researcher also began to build the NVivo database including the characteristics of the participants (age, sex, ethnicity, treatment pathway) in addition to interview timepoint (pre-treatment, 6 months post-

treatment initiation, >12 months post-treatment initiation) and nature (individual or joint). Open coding of all interviews resulted in approximately 150 code names.

FA stage 2: Developing a theoretical framework

The researcher moved between reviewing the open coding in NVivo and to the excerpts from the transcripts or the entire transcript if needed and then back to the open coding again. This was not a linear process and much more cyclical. Based on the open coding, the researcher made any required notes/ annotation, identifying more abstract themes, under which others could be categorised. The goal of this second phase, to develop a theoretical framework, was to try and build a series of higher-level codes (or themes) with sub themes from the open codes identified in phase one familiarisation. The researcher defined each theme within NVivo so that it was clear what the original intention and meaning for the theme or subtheme was. An example of this is included in figure 4-4. Here there are five main themes with a number of subthemes. For each theme and subtheme, a definition was outlined. Within NVivo, an analytical framework was built, which linked directly back to the source data.

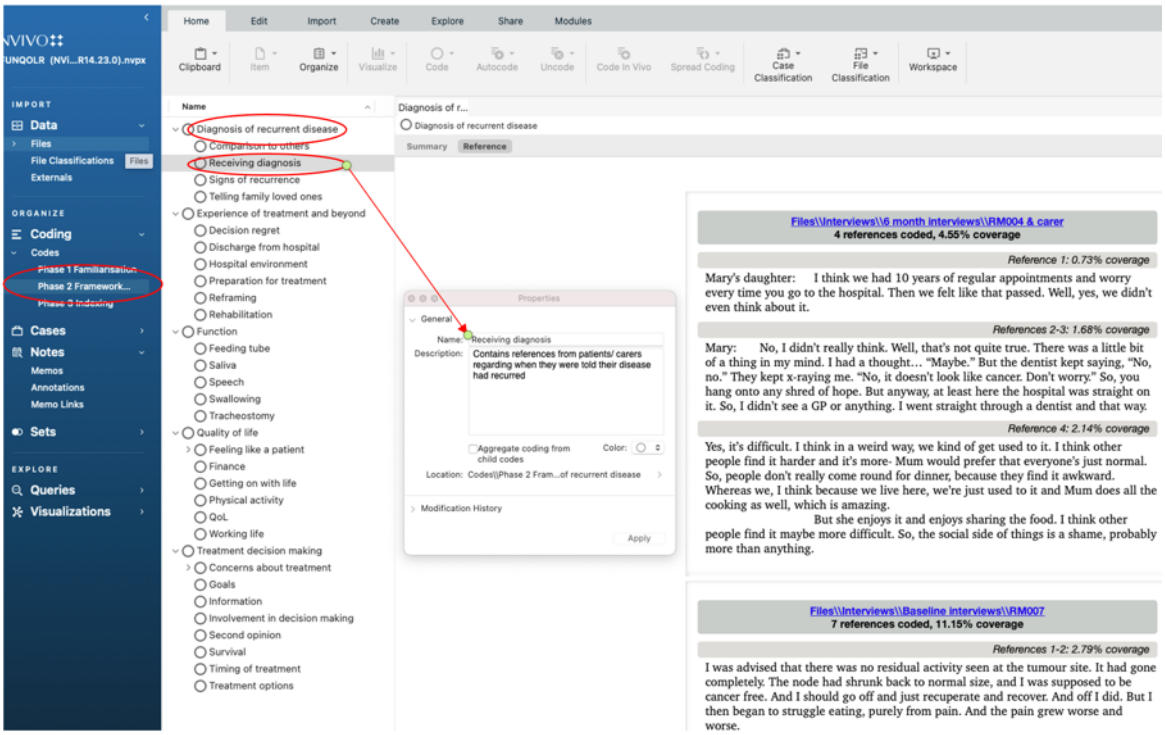


Figure 4-4: Example of stage 2 of analysis, developing an analytical framework with theme, subtheme (and definition) linking to direct quotations from transcripts

This process enabled cross-checking and cross-referencing between the original definition and excerpts from different participants. This cross-referencing between the definitions and the transcripts was a lengthy process, with constant refining of the theme and subtheme names and definitions. The aim of defining the themes and subthemes was so that the labels were as meaningful as possible. With ongoing coding and refining, themes and subthemes began to emerge from the data and were constructed into an analytical framework. The analytical framework was a scheme for coding data which could be used across all interview transcripts. In line with FA, concurrent data collection and analysis was ongoing. This meant that with each new transcript, the analytical framework was revisited with further refinement as required. This emerging framework, which was a hierarchy of themes and subthemes, was discussed with the research team and all members were asked to apply this framework to a proportion of the transcripts. Some modifications were made to the framework to reflect how the themes and definitions related to the original aims and questions of the research.

The framework decided on with the research team included five main themes namely, diagnosis of recurrent disease, function, quality of life, treatment decision-making and experience of treatment and beyond. The final theme was specific to the interview data collected at the second timepoint for the prospective interviews and the retrospective interviews. Each main theme included multiple subthemes. Figure 4-5 demonstrates this and shows as with all the themes there was a direct link between theme, subtheme and the interview data.

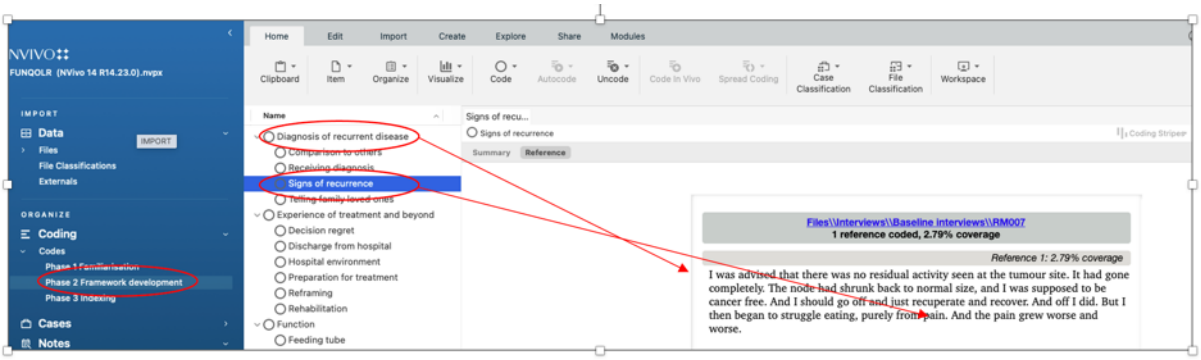


Figure 4-5: Stage 2 development of an analytical framework; code: diagnosis of recurrence; subcode- signs of recurrence

FA stage 3: Indexing

The familiarisation, coding and framework development described in stages 1-2 involved breaking down the data into meaningful themes and subthemes. Indexing, the next stage, involved reconstructing the data looking more in depth at these themes to explore any divergent or convergent views. The aim of this indexing phase was to offer a deeper understanding of the theme or subtheme in relation to the research question. An example of the evolving analysis of the theme 'diagnosis of recurrence' and the corresponding subtheme 'signs of recurrence' will be presented to illustrate this. Indexing for the subtheme 'signs of recurrence' involved further refinement to include a category for those participants who exhibited signs of recurrence, those who did not and those who had symptoms but were unsure if these symptoms were signs of disease recurrence. A further example of indexing was under the category of 'treatment decision making' including those participants who

described their experience of being given a choice of treatments, those who were not given a choice when deciding on a treatment plan, and those who felt it was not their decision.

FA stage 4: Charting

Charting is the phase of analysis which is the defining feature of FA in comparison to other variations of thematic analysis. Here summary statements were developed under each main theme for each interview participant. A summary matrix chart was developed where each column corresponded to a main theme, and each row corresponded to an interview participant. Unfortunately, it was not possible to build the matrix in the NVivo version used for this research, so the framework was built using Excel for Mac (version 16.77.1). The matrix provided an overall summary of the data however the detail corresponding to each individual participant was not lost. An example of this is included in Figure 4-6. Here three interview participants are included, with summary statements in relation to each main theme. Where possible, the details from the indexing phase were included to show convergence/ divergence across interview participants.

	Diagnosis of recurrence	Treatment decision making	Function	QoL	Treatment and beyond
Framework analysis: overview FUNQOLR	**Signs & symptoms, receiving diagnosis, telling others, comparison to others**	**Treatment options, involvement, information, concerns, second opinion**	**Swallowing, speech, feeding tube, tracheostomy, saliva**	**Physical activity, working life, finance, getting on with life, feeling like a patient**	**Preparedness, treamtnet environment, discharge, rehab, reframing, decision regret**
RM007. Baseline interview. Individual. Male 62. Mixed/ multiple ethnic group. Immunotherapy.	Increasing pain on swallowing. Total shock at diagnosis, 'jolt'. Unable to tell others until there was a clear plan/ schedule of treatment.	Surgery offered but 'life changing' with no guarentees. Lack of clear information. Concerned about treatment schedule rather than side effects. Main concern regarding efficacy of treatment. No second opinion.	No concerns regarding speech. Main concern regarding swallowing as impacting nutrition and needs nutrition to 'fight' the cancer. Main focus pre treatment was swallowing.	Concerned that surgery would result in permanent changes to quality of life.	NA
RM008 & carer. Basline interview. Dyadic. Male 62. White British. Immunotherapy clinical trial.	Total shock at diagnosis having been given a very favourable prognosis for primary disease (90%). Feels much better off than others. Carer concerned about relaying bad news to others.	At second diagnosis offered chemotherapy. Surgery not an option as too morbid and no guarentee. GP friend advised second opinion. Different treatment pathway with clinical trial- unaware that he was being referred for trials.	Some mild swallowing difficulties at baseline however no major concerns.	Hopeful that immunotherapy would be a kinder treatmnet and main concern is that patient remains as well as possible for as long as possible.	Developing some swallowing changes. Overall surprised at how well he has felt during treatment.
RM009. Baseline interview. Individual. Male 60. White British. Immunotherapy.	Increasing pain on swallowing. Total shock at diagnosis. Considers himself lucky in comparison to others and lucky to be in the UK where treatments are available. Concerned about others worrying about him due to his diagnosis.	Treatment options not discussed, no discussion just a fate compli. Patients not involved in MDTs. Lack of information. List of side effects very scary. Concerns about becoming bed bound and being a burden.	Concners regarding swallowing and nutrition and ability to gain and maintain strength.	Concens about being bed bound and being a burden. Just wants to be able to live his life without being sick.	NA

Figure 4-6: Example of framework matrix for three interview participants; summary statements across 5 main themes.

FA stage 5: Mapping and interpreting

The final stage in the FA is mapping and interpreting. Again, the stages of FA do not occur in a linear fashion and in reality, the mapping and interpreting begins as soon as the researcher commences the familiarisation phase. As a researcher I think there is an automatic tendency to attempt to start interpreting the data, or trying to work out explanations for or concepts which explain convergence or divergence between participants and/or themes immediately. This phase of analysis again involved reducing the five identified themes (diagnosis of recurrence, treatment decision making, function, QoL, and treatment and beyond) further into an overall conceptual model which would encompass the complex relationships within and between five main themes across the three interview timepoints. Initially this was done by hand, and three overarching conceptual themes emerged which were temporally related namely 'the journey to diagnosis', the journey to treatment' and the journey to treatment and beyond' as can be seen in Figure 4-7. Descriptions were developed for each of the overarching themes to include a summary of its contents. This included a summary diagram with illustrative quotations from the interviews reflecting the convergence/ divergence and providing a possible explanation for such observations. This process was lengthy, with multiple iterations, and consultations with the research team and PPI/E group.

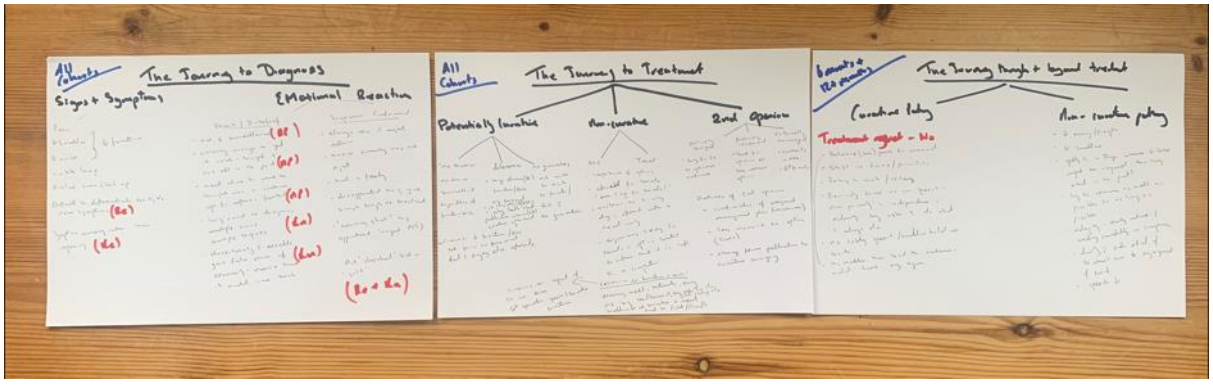


Figure 4-7: Early mapping and interpretation

These paper diagrams were converted into a digital PowerPoint presentation and were discussed with the study PPI/E group and research supervisors. Ongoing discussion and refinement occurred. One key change at this time including re-labelling the three overarching themes which included the five previously identified subthemes. The previous label 'The journey to diagnosis' became 'Here we go again' and included details on the signs and symptoms of disease, and emotional reactions. 'The journey to treatment' became 'Do I have a choice?' and included experience in relation to treatment choices, access to second opinions and involvement in decision making. 'The journey to treatment and beyond' was re-labelled 'A personal trade off' to include patient/ carer accounts of the experience of changes in function, reflections on preparedness for treatment, and finding ongoing balance. The study supervisory team (MW) in conjunction with the PPI/E group felt that the revised labels were more patient-focused, reflecting the patient experience rather than a pathway of care. This re-labelling was congruent with the underlying philosophical standpoint of mixed methods research within a pragmatic paradigm, which highlights the centrality of patient experience to knowledge.

4.10 Mixed methods study flow and timepoints

A convergent design mixed methods study schema, including the timepoints for recruitment and qualitative and quantitative data collection, is summarised in Figure 4-8.

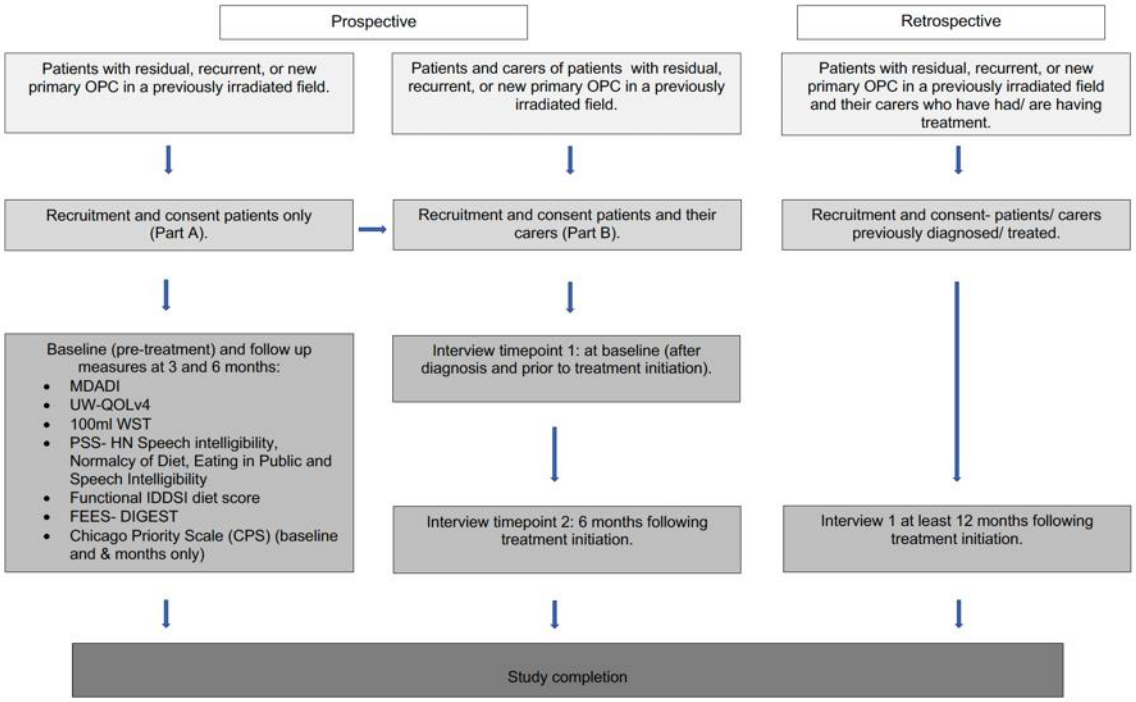


Figure 4-8: Study schema

Interview timepoints at baseline were concurrent with the quantitative data collection, however, did not happen on the same day. The reasons for this were two-fold. Quite often patients would have a long day at the hospital at timepoint one for baseline quantitative collection as they would be attending for several other appointments in their work up to commencing treatment. To add an additional appointment/ time to interview was considered potentially too burdensome for patients and their caregivers. Interviews were undertaken almost exclusively remotely (unless the use of non-verbal communication precluded the use of video calls) to make the appointment as convenient and comfortable for patients and their family members. Quite often these interviews were conducted out of office hours, and the researcher was also based at home in an effort to create a more equitable power balance. The potential influence of the researcher being an experienced clinician in HNC and the impact of this on the perception of power balance will be expanded on in further detail when reflexivity is explored in the next section of this chapter. The decision to conduct interviews

remotely with all parties outside of the hospital environment was made jointly with the PPI/E project steering group.

4.11 Reflexivity

Reflexivity is a key concept in qualitative research although many different definitions exist. As a junior researcher it can be a difficult concept to understand and then in turn practice throughout the research process. Olmos-Vega and colleagues (2023) aimed to produce a comprehensive definition of reflexivity to guide researchers on how to practise it (Olmos-Vega et al., 2023). Although they did not conduct a systematic review, a search of the literature focused on reflexivity produced definitions, which were inductively analysed to identify key themes. Following this, Olmos-Vega and colleagues (2023) defined reflexivity as a continuous multifaceted process, where researchers critically appraise how their subjectivity can influence the research process (Olmos-Vega et al., 2023). Reflexivity can have various purposes, and this will link to the epistemological standpoint of the researcher. In the early qualitative literature the term 'bracketing' was often used, particularly within anthropology or phenomenology (Ashworth, 1999), this involved the researcher aiming to neutralise any potential bias from their subjectivity by setting aside any personal or contextual attributes which may impact the research. However, more recently it has been argued that such attempts at neutralisation are futile and may in fact generate an unintended power imbalance between the researcher and subject by setting the researcher as somewhat distant from the subjects as an impartial observer (Holmes, 2020). A further purpose of reflexivity may be acknowledgement of the likely bias/ impact of the researcher on the research process. However, this approach does not lend itself to exploring the impact of the acknowledged subjectivity on the research (Olmos-Vega et al., 2023). Explanatory reflexivity aims to further explore the impact/ potential bias of the researcher on the research. Historically, highlighting this potential bias is inherent with subjectivity as a potential negative bias. More contemporary qualitative research now attempts to capitalise on this subjectivity and how it can have a positive influence on all aspects of the research

planning, data collection and analysis (Olmos-Vega et al., 2023). Typologies for reflexivity have been described previously in the literature to highlight how the subjectivity of the researcher can influence many aspects of the research from design to interpretation (Walsh, 2003). The typology described by Walsh which encompasses four dimensions of reflexivity, personal, interpersonal, methodological and contextual, has been used as a framework for the reflexivity log used during this study (Walsh, 2003). An excerpt of this reflexive log which attempted to cover these four dimensions is included in Appendix 11. Framing reflexivity as an integral part of qualitative research aligns with the pragmatist epistemological standpoint, where knowledge can be gained and understood from various sources depending on the research question. The researcher's background as an experienced head and neck SLT who has worked almost exclusively with patients with recurrent disease for many years has undoubtably influenced the design, data capture and analysis of the data in this research study and the reflexive log used for this study attempted to capture, acknowledge and explain this influence on the research.

4.12 Integration

Within the mixed methods convergent design, the qualitative and quantitative data sets are collected concurrently and each set of data is analysed separately before merging (Creswell and Clark, 2017). The intent of integration within this design is to gain a greater understanding of the phenomenon which is under investigation. The merging of the databases and interpretations should be comprehensive and offer validation, confirmation or expansion of each other. As previously mentioned, at the design stage, the nature of the topic guide and the type of quantitative methods being used were carefully considered so that they would be conducive to later merging via integration (Fetters et al., 2013). This section will describe how integration at the interpretation and reporting level was achieved for this study.

The main approaches to integration at the interpretation and reporting stages are described in the literature as follows; integration via narration, via data transformation or with the use of joint/visual displays (Fetters et al., 2013), in addition to triangulation (O'Cathain et al., 2010).

Integration through narrative is achieved through narrative description of the qualitative and quantitative findings. There are three ways to achieve this narrative; the weaving approach, the contiguous approach and the staged approach (Fetters et al., 2013). The weaving approach involves writing both qualitative and quantitative findings together on a theme-by-theme basis. The contiguous approach to integration involves the presentation of qualitative and quantitative findings in a single report but in different sections. The staged approach, often used in multi-stage research designs, reports findings contemporaneously, publishing these separately as separate steps. The narrative approach through weaving was considered for this research as this subtype of narrative approach appeared to fit with the underlying philosophy of the mixed methods design, with the merged dataset being presented together. The other two subtypes of integration through narrative were ruled out for this study, as they appeared to treat the two datasets as separate, reflecting a multiple method design rather than a true mixed methods methodology. An area of critique in the literature on mixed methods research is the extent to which researchers genuinely merge/ integrate their findings at the interpretation and reporting phases rather than just providing a summary of the findings of each method (Bryman, 2007).

Creswell & Clark (2017) describe data integration at the interpretation and reporting phase via data transformation. Data transformation involves transforming the results from one data set into the form of the other data set and performing further analysis. For example, qualitative themes may be transformed into dichotomous data (i.e., swallowing is/ is not a priority) and transformed into a binary form- this could then in turn be merged with the existing dataset of quantitative data and if suitable, further statistical analysis undertaken. Given the mixed methods research question of this study, to identify function and QoL

concerns, priorities and outcomes, the option to use data transformation techniques was ruled out. The primary rationale for this decision was that transforming the rich qualitative data would be reductionist, and also would discount any potential integration of the carer perspective, which was collected qualitatively only. Conversely, there was also the option to transform the quantitative data into narrative summaries and perform further analysis using an appropriate qualitative method, however again this did not appear congruent with the original qualitative analysis using FA, where there is a clear audit trail on interpretive findings to the raw data. It was thus decided not to use data transformation but to use primary data analysis integration, using the research question of the mixed methods study to guide in the integration of findings from both data sets to identify convergence, divergence or expansion (Creswell and Clark, 2017).

Joint display tables are also described in the literature as a method to bring together the data through visual representation, using for example a table, graph or matrix (Fetters et al., 2013). The joint display tables were compiled so that the qualitative and quantitative findings were presented side by side and results compared to identify the relative 'fit' of the data in terms of confirmation, expansion or any divergence. This idea of data 'fit' is also very closely related to the triangulation protocol described by O'Cathain and colleagues (O'Cathain et al., 2010). Integration via the triangulation protocol requires the researcher to list the findings from each component of a study on the same page and consider where findings demonstrate agreement, partial agreement, dissonance or indeed silence (O'Cathain et al., 2010). The concept of silence within this protocol appeared particularly pertinent to the aims of this study as it includes findings which arise from one dataset but not from another. The background and rationale for this study highlighted the importance of looking not only at function and QoL outcomes but incorporating patient/ carer experience also. In the planning stages this suggested that the patient/ carer experience data would provide further information/ knowledge not captured by the existing quantitative measures for investing function and QoL outcomes. Therefore, the integration plan needed to include a space

where such additional findings could be included in the interpretation. In addition to this, as carer experience data were also collected within this study, space within the triangulation protocol was required for this too.

This combined use of joint display tables with a triangulation protocol appeared to fit with the research question of the study, and also ensured equity across the two data sets in keeping with the mixed methods methodology. In addition to the visual display of integration, via joint tables, and a triangulation protocol to identify agreement, partial agreement, discordance and silence it was also felt that narrative integration would also be required, where the quantitative and qualitative findings are described thematically in relation to the research questions for this study. The combination of joint tables and narrative description has been reported in the literature in particular with previous convergent mixed methods studies (Fetters et al., 2013). The inclusion of a triangulation protocol for these approaches appears to be rather unique to this study. What is also quite unique to this study is some matched, individual patient, quantitative and qualitative data. To incorporate this a decision was made to include the individual patient data sets for each domain within a joint table. Thus, the summary qualitative and quantitative findings for the sample are presented via the joint tables in addition to some individual patient data. This appears to fit well with the FA to data analysis used in the quantitative workstream, as using the summary matrix, the overall results for the sample are presented, but the individual patient data and stories are maintained. This combined integration method is also consistent with the theoretical ICF framework (WHO, 2002). The inclusion of summary and matched individual patient data ensures that the personal and environmental factors are included in addition to body structures and function, activity limitations and participation restrictions.

It was felt that combining all three approaches, joint display tables (with summary sample data and individual data sets), with a triangulation protocol and a weaving narrative description, would facilitate further meta-inferencing; to reach an overall

conclusion, explanation, conceptual understanding (Tashakkori and Teddlie, 2003) of this unique merged dataset. The steps to using all three approaches in combination within this study will be explained next. A worked example of a mixed methods study completed in the field of physiotherapy, was used as a framework to plan the steps taken for integration in this study at the interpretation and reporting phase (Skamagki et al., 2024).

The first stage in integration for this study was to create a joint display table for each domain included in the overall research question of this study. There were four main domains in total including function; swallowing and speech, QoL and treatment-related priorities, and these domains were explored at two timepoints: before treatment initiation and following treatment initiation. All prospective and retrospective qualitative data were thus included. Carer perspectives were also integrated. A template for the integration of data for each domain and each timepoint was devised (Figure 4.7). In the first column of the joint display the domain was named, the subsequent two columns included a summary of the quantitative and qualitative findings, followed by three individual matched patient data sets. The bottom row of each table then included a summary of the triangulation protocol findings: agreement, partial agreement, discordance or silence. Each joint table was then explained using a weaving narrative where the qualitative and quantitative findings were described firstly, and then the triangulation protocol explained in terms of agreement, partial agreement discordance or silence.

Table 4-7: Example joint display table

Domain	**Qualitative findings**	**Quantitative findings**
Swallowing	Summary of qualitative findings	Summary of quantitative findings
Individual patient data 1		
Individual patient data 2		
Individual patient data 3		
Triangulation		
Weaving narrative		

The integration and combining of inferences to form these main findings will be discussed in detail in Chapter 7. Firstly, an in-depth description of the qualitative findings will be provided in Chapter 5, followed by the quantitative findings in Chapter 6.

4.13 Summary

The second objective of this PhD was to identify and explore the patient communication, swallowing, QoL outcomes, and treatment-related priorities and the patient and carer experience of rOPC over time. This research objective arose from the findings of the systematic review presented in Chapter 3, in collaboration with the study PPI/E group. This objective was achieved using a mixed methods study combining both qualitative and quantitative methods of data collection.

A convergent mixed methods study design was chosen, where qualitative and quantitative data collection were undertaken concurrently with separate analysis of each type of data prior to integration. Qualitative methods aimed to explore patient and carer experience of rOPC with a focus on changes to function (swallowing and speech) and QoL over time using

a longitudinal interview design. FA was used to analyse the qualitative data. Patient and carer qualitative data were conceptualised as a dyad of experience and thus analysis reflected this conceptualisation.

Quantitative methods aimed to measure change in swallowing function over time using a patient-reported outcome measure of swallowing-related QoL as the primary endpoint and a range of multidimensional secondary endpoints looking at both communication, swallowing and overall QoL.

Careful consideration was undertaken by the researcher to practise reflexivity, acknowledging her influence on the research design, data collection, analysis and interpretation given their personal and professional experience of working with patients with recurrent disease for many years.

In line with mixed methods methodology, integration was achieved using primary data integration techniques using a combination of joint display tables, a triangulation approach and a weaving type of narrative description.

Chapter 5 will now look at the results of the qualitative workstream followed by Chapter 6 which will document the findings of the quantitative workstream using the methods outlined for each workstream in this chapter. Chapter 7 will then look at the findings of the integration of qualitative and quantitative findings also outlined earlier in this chapter.

Chapter 5 Qualitative results

5.1 Publication and outputs:

Brady, G., Roe, J., Paleri. V., Lagergren, P & Wells, M. *Patient and carer experience of diagnosis, treatment and living with rOPC- a qualitative study (in press).*

Brady, G., Roe, J., Paleri. V., Lagergren, P & Wells, M. *That was a bigger blow than getting the cancer in the first place… to be diagnosed with recurrence' The patient and carer experience of rOPC (OPC) and changes to swallowing and quality of life - a qualitative study. Oral presentation.* UK Swallow Research Group, Birmingham, 8th February 2024.

5.2 Introduction

The previous chapter detailed the methodology of the mixed methods study including FA for qualitative analysis. This chapter will provide a detailed description of the results of the qualitative workstream.

This aim of this longitudinal qualitative workstream was to investigate patients' and caregivers' experiences of being diagnosed with rOPC, the treatment decision-making process and living with the consequences of those decisions. Patients recruited to the mixed methods study were invited to take part in qualitative interviews at baseline and six months, mirroring the quantitative data collection at these time points. An additional sample of patients was recruited at 12 months following treatment initiation for rOPC and were also included.

Thus, there were three timepoints for qualitative data collection in this study, including the prospective cohort who were interviewed at baseline before treatment initiation, and again six months later, and a retrospective cohort who were interviewed at least 12 months

following treatment initiation. The remainder of this chapter will focus on the results of this longitudinal qualitative workstream.

5.3 Participants

All participants, who provided consent to take part in the prospective observational study, were also invited to take part in a prospective longitudinal qualitative study, along with their caregivers, using in-depth semi structured interviews. In total ten participants and three caregivers took part in the prospective interviews and a further twelve participants and four caregivers took part in retrospective interviews. This totalled 22 patient participants and seven caregivers and a total 26 interviews undertaken across the three timepoints. When caregivers were involved, joint interviews were undertaken, which was the request of the patient participant. Demographic details and interview timepoints are summarised in Table 5-1.

Table 5-1: Participant demographics, and interview timepoints

Total participants: n=29 (patients: 22; caregivers: 7) **Total interviews (n=26)**		**Longitudinal sample: (n=10)**		**Retrospective sample: (n=12)**
		Baseline: 9	**6 months: 5**	**One year or more: 12**
Sex	Male	8		11
	Female	2		1
Age	Median	62		64
	Range	47-77		59-70
Ethnicity	White	9		11
	Mixed	1		0
	Asian/ Asian British	0		1
Treatment	Curative	4		7
	Non-curative	6		5
Interview type	Individual	10		9
	Joint	4		3

5.4 Setting

The interviews took place between December 2022 and November 2023. The majority of interviews were conducted via video call where both the interviewer and interviewee(s) were at home. The interviews often took place out of office hours so that the participants could fit the interview in around their working day or hospital appointments. No effort was made to conceal the fact that the interviewer was in their home environment, however the interview was undertaken in a quiet confidential space. Two participants who had no verbal speech took part in a face-to-face interview in a clinic room at the hospital. For these patients, one of whom was accompanied by his wife, alternative and augmentative communication methods were used, including mouthing, writing and the use of text-to-speech digital applications. As an experienced SLT, the interviewer was skilled in communicating with individuals who do not use verbal speech. All interviews ranged in timing from 22 to 40 minutes.

5.5 Interviews in context

Interview participants included a mix of those diagnosed with residual disease (disease diagnosed within twelve months of treatment for primary disease), recurrent disease (disease diagnosed between twelve months and five years of treatment for primary disease) and new primary disease in a previously irradiated field (disease diagnosed five years or more since treatment for primary disease). For ease, all participants in the analysis are referred to as having disease recurrence as per the other chapters of this thesis. If the timepoint for their disease recurrence appeared pertinent to their experience, this was reported in the findings. Participants in the prospective baseline interviews had received their diagnosis over the past two- three weeks and had been enlisted into a treatment pathway, either curative or non-curative, and were fully informed of this. Many of these patients were awaiting a date for treatment initiation. Some of these participants also had follow up interviews at six months following curative or non-curative treatment initiation. All of the participants who were recruited prospectively consented to interviews at baseline and six

months. However, due to treatment start dates, or indeed participants becoming unwell, not all participants were interviewed at both timepoints. One female patient was interviewed at six months only, as it was not possible to find a suitable time for interview prior to her surgical date. Of the nine interviews conducted prospectively at timepoint one, only four of these participants were able, willing or available to take part in interviews at timepoint two. Prior to timepoint two, four of these patients were receiving end of life care or had died, and one did not wish to take part in a follow up interview.

Those participants who were recruited for retrospective interview were all at least twelve months following treatment initiation for disease recurrence and were also on a curative or non-curative treatment pathway. Those who were on a curative pathway had undergone surgical treatment at least twelve months prior, and those on a non-curative pathway had commenced palliative immunotherapy/ chemotherapy or a clinical trial of an investigational agent at least twelve months prior. One patient, Walter, who had been recruited retrospectively, had been initially treated with curative surgery for disease recurrence, however, was then found to have metastatic disease spread and so was on a non-curative treatment pathway at the time of interview. He has been described as curative to non-curative throughout the findings. Another patient, Toby, had curative surgery initially, however by the time of his follow up interview had been diagnosed with residual disease and was being worked up for laryngectomy surgery. He was referred to as curative throughout as, at the time of both of his interviews, curative remained his pathway of care.

Patient and carer participants in both the prospective and retrospective groups appeared to be very open to sharing their experiences, however at times, recollecting their journey or reflecting on their ongoing experience resulted in patients and caregivers becoming emotional. This was common across interviews at all time points. As an experienced SLT working in cancer and palliative care for a number of years, I was proficient in supporting individuals through difficult conversations however, conducting an interview for research is

very different than my usual clinical role. If a participant became upset during the interview process, I firstly ensured the participant wanted to continue and offered follow up in the form of a review with their clinical nurse specialist and/or referral to psychological support services. I also kept field notes to document any emotions the participants were displaying and in my reflexive log I would document any emotions or reactions I felt that may have influenced the interview or my later analysis. The importance of reflexivity in qualitative research was discussed previously discussed in Chapter four, and excerpts from the reflexive log are included in Appendix 11.

Regardless of interview timepoint, a common area of dialogue which emerged early in almost all the interviews included participants' experience of primary disease. Although not included in the topic guide specifically, participants shared their experience of primary disease diagnosis, treatment and side effects. Participants' experience of disease recurrence was thus framed within the context of their experience of primary disease. After the discussion of primary disease, participants usually went on to describe how their recurrence was diagnosed. This generally happened with little prompting from the interviewer via the topic guide. This description included any particular symptoms, investigations and communication of results and the emotional reactions experienced by the participants. For the participants in the prospective cohort, the interviews at the initial timepoint focused on the participants' knowledge, expectations and concerns regarding upcoming treatments. For the second timepoint prospective and retrospective interviews, the remainder of the interview generally focused on the participants' experience of treatment, in comparison to their preconceptions and their ongoing life, QoL and function thereafter.

Although not asked directly by the interviewer, almost all the retrospective participants who were treated with curative intent reflected on whether they had made the right decision about their treatment. This was not referred to by those undergoing treatment with non-curative intent.

As an interview appeared to be nearing its end, I always asked if the participants had any questions. Overwhelmingly, participants commented that they hoped their participation would help others in the future. It was not uncommon for the participants and caregivers to express their gratitude to the interviewer for taking the time to hear their story, with some reporting how they felt that the interview was quite therapeutic. One carer in particular followed up with an email to thank the researcher for what she referred to as the 'couples therapy session'.

5.6 Main findings

The rich patient and carer experience data which emerged from the prospective and retrospective interviews will be presented in three main themes, with two-three subthemes included for each main theme.

The first theme entitled 'Here we go again' refers to the participants' experience of recurrent disease diagnosis in the context of having previously been diagnosed and treated for primary disease. Participants set the scene with their description of their previous experience of primary disease diagnosis and their experience of primary treatment and its aftermath. They usually described any signs and symptoms of recurrence, included under the subtheme 'Something not quite right'. Emotional reactions to the diagnosis of recurrence are presented under the subtheme of 'Was I shocked?', and the realisation that life must continue following the diagnosis, falls under the subtheme of 'What now?'.

The second theme entitled 'Do I have a choice' describes participants' experiences of how they ended up on a particular treatment pathway, including access to second opinions under the subtheme 'Second opinions why, how and where?'. A further subtheme included under this theme addresses participants' involvement in decision-making; 'Who's decision is it anyway?'

The first two main themes ‘Here we go again’ and ‘Do I have a choice?’ relate to all interview timepoints however, the third theme ‘A personal trade off’ is specific to the second timepoint (six months following treatment initiation) for the prospective interviews and the retrospective interviews. This theme relates to living with and beyond the diagnosis and treatment of disease recurrence and finding balance between survival, overall QoL and functional status in both the curative and non-curative treatment pathways. Subthemes included within this overall theme include ‘Are we ever ready?’ which describes participants’ experience of preparedness for treatment. A further subtheme ‘Would I do it all again?’ captures participants’ reflections on the decisions they made earlier in their journey. This subtheme particularly relates to the patients who had experienced curative treatment in the form of surgery only. A final subtheme, which relates to both curative and non-curative pathways, ‘How I look at things now’, provides a description of participants’ experiences of reframing priorities and perspectives on overall QoL. This theme makes use of the longitudinal nature of this study, enabling the main concerns and priorities of participants who had completed treatment to be compared and contrasted with those of participants, who at the time of interviewing, were still waiting to commence treatment. The three main themes and subthemes are summarised in Figure 5-1.

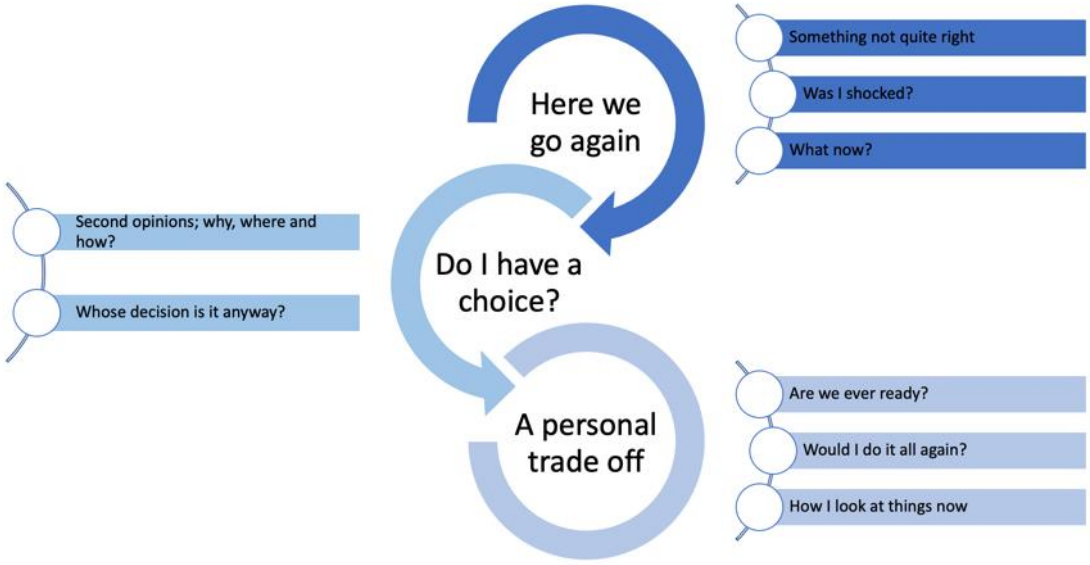


Figure 5-1: Main themes and subthemes

These three themes will be explored in further detail. Descriptions from the themes are supported with quotations from the transcripts. Participants have been provided with pseudonyms. Caregivers will be identified using a '(c)' following their pseudonym. The participants' age, patient treatment pathway and interview timepoint (prospective timepoint one T1, or two T2, and retrospective T3) will be included in the description. Where relevant, a brief description of their functional and disease status will be described to provide context. Pseudonyms, timing of disease, treatment pathway and interview timepoint are summarised in Tables 5-2 and 5-3.

Table 5-2: Prospective participants, pseudonyms, interview timepoint, disease category and treatment pathway

Pseudonyms: (prospective participants)	Timepoint 1 (T1) interview (Yes/ No)	Timepoint 2 (T2) interview (Yes/ No)	Disease category	Treatment pathway
Andy	Yes	No	Residual	Non-curative
Gerard and wife Sophie	Yes	Yes	Recurrent	Non-curative
Ken	Yes	No	Recurrent	Non-curative
Kim	Yes	Yes	Recurrent	Curative
Matt	Yes	Yes	Recurrent	Curative
Barry	Yes	No	New primary	Non-curative
Rob	Yes	No	Recurrent	Non-curative
Toby and partner Kate	Yes	Yes (Toby only)	New primary	Curative
Paul	Yes	No	Residual	Non-curative
Deirdre and daughter Tara	No	Yes	New primary	Curative

Table 5-3: Retrospective participants; pseudonyms, disease category and treatment pathway

Pseudonyms: (Retrospective participants)	Timepoint 3 (T3) interview (Yes/ No)	Disease category	Treatment pathway
Dan and wife Poppy	Yes	New primary	Curative
Michael	Yes	Recurrent	Curative
Stuart	Yes	Recurrent	Curative
Tim	Yes	Residual	Non-curative
Walter and wife Sally	Yes	Recurrent	Curative initially then non-curative
Richard	Yes	Recurrent	Non-curative
Jack	Yes	Residual	Curative
Satish	Yes	Recurrent	Curative
Peter and wife Holly	Yes	Recurrent	Non-curative
Dave	Yes	Recurrent	Non-curative
Tom and wife Shiela	Yes	New primary	Non-curative
Judy	Yes	Recurrent	Curative

5.6.1 Theme 1: 'Here we go again'

Jack (61, curative, T3), encapsulated the feelings of many participants when recalling his experience of receiving the diagnosis that his cancer had returned.
'That was a bigger blow than getting the cancer in the first place, recurrence really'.

The way by which the recurrent disease presented and the reaction to the diagnosis was often compared and contrasted to the participants' experience of primary disease diagnosis.

Participants often discussed the process of moving from suspicious symptoms to receiving the diagnosis from their care team, with reference to their previous experience of primary disease diagnosis and treatment.

This overall theme of 'Here we go again' includes three subthemes. The first 'Something not quite right' describes the participants' experience of symptom presentation which led to their diagnosis and the second 'Was I shocked' includes a description of the emotions experienced at receiving the diagnosis. A third interrelated sub-theme, 'What next?' relates to the participants' experience of what they did next after hearing the news of their diagnosis.

'Something not quite right':

Some participants had some new and suspicious symptoms, others struggled to decipher new symptoms from persisting toxicities from previous treatment. Others had no new symptoms, and their recurrence was picked up on routine surveillance.

When participants recalled experiencing symptoms, this primarily related to a perceived change in function. Andy (67, T1, non-curative) reported difficulties eating due to pain.
'I began to struggle eating, purely from pain. And the pain grew worse and worse'.
Others experienced changes to voice. Paul (77, T1, non-curative) described gradual changes to his voice which echoed his previous presentation at point of primary disease

diagnosis. He also suspected something was not quite right as he described a feeling of gradual worsening of symptoms rather than improvement over time following radiotherapy. '*My voice was having a downturn again, just generally, certain amount of pain down the right side of my face and neck, nothing serious it just, instead of improving it was getting worse'.*

Others like Satish (67, T3, curative) reported their difficulties in differentiating new symptoms, which might be suggestive of disease recurrence, from persisting toxicities related to treatment; *'it had been so bad inside (the mouth) that I didn't have the sensation to be able to judge if there was anything there. Obviously, what happens is that with all the radiotherapy, the saliva glands and all are different so you don't have enough sensation to know if something's there or not'.*

Participants described how since their treatment they had multiple persisting symptoms which were not quite right but could be reasonably explained as a side effect of their previous treatment. Some of these symptoms included pain, saliva changes and swallowing difficulties. This meant that patients were not always completely surprised by their diagnosis. The emotional reactions described by patients and their caregivers will be explored next.

'Was I shocked?'

Because participants in this study had been through a diagnosis of HNC previously, many were suspicious that their symptoms meant the disease might be back.

Paul (77, T1, non-curative) reported how the diagnosis really just *'confirmed his suspicions'*. Whereas Jack (61, T3, curative), described how he was somewhat prepared for receiving the diagnosis by some '*signs'* he received along the pathway of care. Jack had initiated an earlier review with his consultant as he was concerned regarding new onset ear pain. Jack had experienced this before his original diagnosis of primary disease, and he could also feel a lump on his tongue. He saw his consultant, who initially explained to Jack that she was not

overly concerned, however advised a routine MRI. Jack had this and then received an unexpected telephone call from an administration team informing him that he had been booked for an *'urgent'* PET scan. This, coupled with the fact that his consultant was surrounded by several other staff members when he arrived at his appointment for results, pre-warned him of the diagnosis; *'When I went in the room you know it's not good news when there are four or five people in there rather than just the one person you are expecting.'*

Others were much more shocked by the diagnosis. Some participants described a lengthy process to diagnosis with multiple investigations which were often inconclusive. Sally(c) wife of Walter (57, T3, curative to non-curative), reported how her husband had multiple biopsies, all of which were clear. She described that the process of repeated biopsies was very tough on her and her husband, and that with each clear biopsy, she felt progressively reassured that there was nothing there. That was until the fifth consecutive biopsy.
'they thought it was scar tissue, but, in fact…, there were four biopsies where they kept cutting deeper and all four were showing up as non-cancerous', 'we felt quite reassured and because the biopsies 'I mean, it was gruelling because it was stressful waiting all the time, but because they kept coming back as negative, I think we just expected them to be negative… then the last one wasn't'.

Another group of participants who appeared to be particularly shocked by their diagnosis, when interviewed at any timepoint, were those who were diagnosed with new primary disease in a previously irradiated area. These participants had an interval of at least five years following their primary treatment before their diagnosis of further HNC disease. These participants had completed their five-year routine surveillance and their pathway to diagnosis was somewhat different. They required re-referral back into the system by their GP or dentist when symptoms arose. Quite often these participants were not re-referred to their previous cancer treating centre and instead went through the Ear Nose and Throat (ENT) team at

their local district general hospital prior to re-referral back to their original cancer treatment centre for a specialist opinion on management.

Toby (67, T1, curative), who was diagnosed following 17 disease-free years, described how he had not even thought that the disease could potentially be back. Toby was under the impression that he was being treated for acid reflux. He went to his follow up appointment alone, for what he thought was unresolving acid reflux and fainted when he was given his diagnosis; *'I went on my own because I thought I'd got acid reflux. And he told me that I'd got cancer… And I'll be honest, it put me on the deck'.* Kate(c), Toby's partner, described her shock at his diagnosis and also her guilt for not being there for him at that appointment when he was told; *'Obviously, I felt awful that I wasn't there when he was told initially. Because he phoned me to go down to the hospital, so I could tell in his voice that there was something wrong, and I thought, well… I was hoping that maybe they were just taking him in straight away, you know, admit him for the acid reflux, that he'd maybe badly burned his throat. I was trying to be positive'.*

Another gentleman, Barry (60, T1, non-curative) had his initial laryngectomy surgery 20 years prior to his diagnosis of recurrent disease. Barry echoed this disbelief at the diagnosis; *'You thought that after 20 years the cancer is gone and it hits you like a tonne of bricks. You think that once they've told you, after the first 5 years have gone, you've said, goodbye to cancer'.*

Family members of those out of surveillance appeared to have the same sense of disbelief. Tara(c), daughter of Deirdre (69, T2, curative) who had 18 disease free years prior to curative surgery explained; '*I think we had 10 years of regular appointments and worry every time you go to the hospital. Then we felt like that had all passed. Well, yes, we didn't even think about it.'*

Whilst others, who remained under surveillance including Michael (63, T3, curative) described a deep feeling of disappointment rather than shock; *'shock is not the right word. I don't know, just disappointed'.*

Some reported a feeling of injustice. Gerard (62, T1, non-curative) explained how unlucky he felt that his case just did not reflect with the statistics for his primary disease; *'The doctor said, "It's an 85% or 90% chance of complete cure." So, you're, sort of, riding on that sort of way of thinking, "Oh yes, yes, I've got a good chance." Then, when they said, "It's recurred." and then going into the clinic and saying, "Can you guarantee me three years?" and he said, "No." it was a bit of a blow really'.*

Others reported ongoing side effects from their previous treatment and worried about what might happen with further treatment. Kim (62, T1, curative) explained that she felt she had not yet recovered from her primary disease treatment and was concerned regarding further treatment. She spoke about her inability to play with her granddaughter before any further treatment; *'I already can't do things with her. Like we used to go to the park and run round the park with her and stuff like that, and I can't do that now and I don't want that to be any worse than it is now'.*

Following initial shock and/ or disappointment of the diagnosis, there appeared to be a shift in thinking and like Kim, beginning to think about what will happen next.

'What now?'

Some participants reported reacting in a very similar way to how they had when they were first diagnosed with their primary disease. Judy (60, T3, curative) recalled that she had been terrified and had left all fact-finding on treatment and outcomes to her family members.

'I do remember being absolutely terrified. I didn't research very much. I did as I did before, I let my husband and daughter do it, and they would tell me as much as they felt I could deal with'.

Likewise, Jack (61, T3, curative) reverted to what he had done when he was diagnosed with his primary disease. *'I did a bit of research about where I would be after radiotherapy. I knew I would have a dry mouth, quite possibly blisters inside the mouth, difficulty eating. I knew my taste would totally change. But I also knew over time that would largely recover. It's quite possible there would be permanent effects but the bulk of the effects would recover'.* However, Jack voiced his frustrations following his diagnosis of recurrence. The facts were not available to him for his recurrent disease as they had been for his primary disease. *'I found it very difficult to find details about success rates. I got the impression from talking about it it's much of a muchness. You know, that's obviously a big thing you want to think about. If it's only a 20% success rate with one and 80% with another it's a no-brainer, isn't it? But I wasn't getting stats like that'.* With the little data he could find on outcomes, Jack appeared to have a realisation that in light of his newly diagnosed recurrence any functional gains that he had made since his last treatment would most likely be lost again; '*This is the annoying thing. I just started to get back into some semblance of normal eating when this recurrence happened'.*

Others, however, were more concerned with everyday life, which needed to continue due to their roles as spouse, parent, employee/employer etc. Sophie (c), wife of Gerard (62 T1, non-curative), described the surreal feeling of receiving the diagnosis and then immediately after the appointment having to think about what they would cook that evening for the family. *'We ended up in Sainsbury's, which was hilarious, deciding what to have for dinner that night. We just laughed and just said, "What are we doing?" We were wandering up and down an aisle in Sainsbury's thinking, "What are we having for dinner?" because you've still got to*

do those things. You've still got to do those everyday things but you've just had that kind of news that is definitely not what you were hoping for'

Regardless of initial reaction to the diagnosis, a common dialogue with both patient and carer participants was an anxiety for treatment to take place as soon as possible. The bigger the delay between diagnosis and treatment, the greater the impact this may have on the overall outcome be it cure or survival. However, patients experienced the pathway to treatment very differently, including their involvement in the treatment decision-making process. This will be explored next.

5.6.2 Theme 2: 'Do I have a choice?'

Participants shared their experience of their journey to a particular treatment pathway. One of the key differences noted between participants was in whether they felt they had any choice about treatment once they were diagnosed with recurrence.

Some participants shared their experience of not having a choice with regards to their treatment and being offered one single option. Some participants were offered an explanation as to why there was only one treatment option, but others were not given any specific explanation or rationale.

Paul (77, T1, non-curative) explained that he was told that further radiation was not possible, and that other options quickly became more limited due to medical complications.
'Basically, more radiotherapy wasn't on and that the choice was between immunotherapy and chemotherapy. There was the weekly team meeting the following Wednesday. Since they had already decided that my kidneys were not really up to chemotherapy, it seemed fairly clear to me that the decision was going to be made to go for immunotherapy'.

Dave (70, T3, non-curative) simply stated that he was told his treatment would be *'palliative and that was it*'.

A single management option was also discussed at times for some patients undergoing curative treatment. Judy (60, T3, curative) explained this; *'The only one (option), really, was robotic surgery. And the Professor explained what would have happened previously, which sounded absolutely horrendous, and what would happen now, which also sounded horrendous. And so, very quickly, I was back in the machine, and I was having pre-surgery checks and so on, and then I was in for surgery'.*

Kim (62, T1, curative) explained further how she would have liked to have been offered further choices if they were available; *'I would have like to have had a discussion like…we think this is the best for you, but you can try this, this or this if you want to, but if you try them and leave it too long, then this option won't be open to you or whatever, you know?'* Kim reported that she felt *'railroaded'* into surgery.

Other participants were offered a choice between curative and non-curative treatment options. Some participants explained that although presented with this dichotomy, their experience was that this was not really a choice, as survival was their key concern. Walter (56, T3, curative to non-curative) explains this; '*There was a lot of discussion about whether to have the surgery or to go down a treatment trial plan. So, we discussed it with Professor A and Professor B and tried to weigh up the benefits. The surgical route was the only potential cure and given my age, that I was relatively fit, it became a bit of a no-brainer not to go down the route of surgery'.*

Likewise, Toby (67, T1, curative) also explained that *'Although it wasn't dwelt on, it was a slight suggestion that I could've probably pulled out completely and said, let's just let it take*

its course, and if it spreads, it spreads, and if it stops where it is, I can live with it. That was never an option for me, like, but it was mentioned'.

Others described much more of a dilemma when faced with the choice of a potentially curative option, which would have the potential for life changing impact on function and QoL, or non-curative life prolonging options.

Poppy (c) wife of Dan (65, T3, curative) explained how there was a lot of discussion regarding treatment pathway; *'The Professor went away and did all that testing. Then he came back and said, "Your numbers are good." He* [the Professor] *seemed really excited about it. But then at the same time, initially the first time that he saw the surgeon he said, "I don't think I can get it out." Then he changed his mind having spoken to the radiologist and said, "Actually I think we can get it out but it's going to be difficult." Then they had quite a big dilemma because obviously we knew that it would have a massive effect on his voice and his swallowing, and they said that really clearly'.* Dan, reported however, that he felt '*They* [the MDT] *were pushing me towards the op and said it was the only chance of a cure'.* Dan and his wife opted for the surgery and although Dan is now cancer free, he can no longer speak and is tracheostomy and gastrostomy dependent.

Unlike Dan, for others, such as Andy (62, T1, non-curative) the risk was not worth taking in terms of survival in the context of changes to function and quality of life; *'with surgery, it would be extensive, and that some of the surgery involved would leave you with permanent- would permanently affect the quality of living life afterwards. But it was the usual route to excise the cancer. But then there was again no guarantee that it would not return after that, and that would mean we would then fall back to the other options, which you could have taken at the outset, instead of the surgery'.*

Likewise, Gerard (62, T1, non-curative) echoed Andy's concern regarding a potentially lengthy recovery period with lack of guarantee in terms of outcome with surgery; *'if we go down the surgery side, there's a chance I'll be laid up in hospital for two or three weeks. Within a few months, it might sprout out somewhere else'.*

Both Andy and Gerard opted for non-curative treatments. Gerard had this as part of a clinical trial, whereas Andy had it as standard of care first line treatment.

Overall, there was a common theme of uncertainty around treatment choices and decision-making and for some a second opinion was sought either by the individual or by their medical team.

Second opinions why, where and how?

Second opinions were accessed by many participants. Some participants were encouraged by friends/ family who work in healthcare to seek a second opinion, others actively sought an opinion from different institutions in an effort to maximise their outcomes in terms of survival and function. Some also passively received a referral for second opinion with some not really understanding why they were being referred.

One gentleman, Michael (63, T3, curative), described his experience of receiving two dichotomous opinions in one day. The first explaining that only palliation was possible, the second offering a potential cure. Michael explains; '*it was like I was on an emotional rollercoaster because at 10:30 in the morning, in effect, I was being told, well no dates or times, but there's nothing we can do… prepare for death, and then a few hours later, there was another man telling me, you can have it all cut out'*. Michael acknowledged the support of friends who work within the NHS in a related field who advised him to pursue a second opinion which ultimately resulted in him being disease free several years following curative surgery; *'I was just very fortunate that I happened to be friends with these people… without*

that connection and without her persistence, I wonder whether we'd be having this conversation now'.

Satish (67, T3, curative) described how he was originally offered an extensive open surgery involving the removal of his voice box and tongue for his disease recurrence. However due to his connections in healthcare he sought a second opinion in an effort to maximise his functional outcome; *'Because my wife is a consultant herself and we had friends that were consultants, that we were able to access other ways of looking at it rather than the singular option that I was offered'.* Ultimately, by seeking a second opinion, Satish's management plan changed from an extensive surgical procedure to a less invasive option which enabled him to retain his voice box.

Other participants sought a second opinion not on the advice of others but on a completely self-driven basis. Matt (47, T1, curative) was the youngest participant in the interview study and the only participant in this cohort who was treated surgically previously with no history of radiation. His consultant had explained to him that his case had been discussed at the MDT meeting and radiation treatment had been advised. Matt questioned his consultant regarding the MDT decision; '*was* [the MDT decision] *unanimous?*'. When Matt was informed that the decision was not unanimous, he asked his consultant whom he would recommend for a second opinion; *'I said to him, not doubting you and your expertise, is there maybe someone else we can get referred to or have a conversation with?'.* Matt explained that he had done some research and was aware of the potential impact of radiation on swallowing and wanted to maximise his functional outcome. Matt explained that his motivation for seeking multiple opinions, which he self-funded as a private patient, was to maximise his QoL afterwards; '*A huge amount of my life is based around eating and enjoying food, and just everything that goes around that… When we go on holiday, we regularly pick places that have got really good restaurants, or there's a food scene there, that kind of thing. So, food is really important to both of us. And so, trying to keep as much of what goes around that as*

possible'. Matt did lots of self-driven research into standard of care intensity modulated radiation treatment (IMRT) versus proton beam therapy (PBT). He was aware that survival outcomes were comparable, and so wanted the option which would offer the optimal functional outcome. Matt decided on standard of care IMRT as the evidence is still awaited for PBT, and following multiple second opinions was happy with the Consultant, whom he considered the best in his field who offered IMRT.

Other participants found themselves being referred for second opinions but not really knowing why or where to go. Kim (62, T1, curative) discussed her experience of this. '*No-one discussed with me about what my options were or different treatments I could have, not that I remember, and then I just got a phone call. I got a phone call saying... asking if it was okay to refer me to the London for an opinion regarding surgery and that was like the first thing I knew about the surgery or anything really. So, it all came a bit out of the blue'.*

Gerard (62, T1, non-curative) reflected how he was not fully aware that the point of his second opinion was to consider trials; *'The oncologist at (my local hospital) wrote a letter referring me and said I was up for trials. I said, "Well no I'm not," (Laughter) "I didn't say that… but I didn't say I was up for a trial." You know, they said they had something that could be of interest to me but it really wasn't explained to me'.*

Regardless of the route by which a second opinion was accessed, a common experience appeared to be that the process caused some additional anxiety to the patient in terms of elapsed time at an already very anxious time.

Sophie (c) wife of Gerard (62, T1, non-curative) explained that she questioned this whilst they were waiting to hear about the appointment for his second opinion.

'[the second opinion] made us realise that he did have a choice'… but we did worry… had going for a second opinion…?" Was that the right option? It seemed slow and it was important to get the treatment started quicker, whatever the treatment was?'

Whilst Kim (62, T1, curative) also became quite anxious while waiting to hear further news about her appointment; '*So I think about three weeks went by and I hadn't heard anything so I phoned up because I was concerned because I don't know how these things grow and if I should be having some treatment whilst waiting so I phoned up and the secretary said, "Well, I can't see anything on the system." I hate it when you have to phone people, and I said, "Well, he phoned me himself," and she said, "Well, it's not recorded." It was like, "You're lying." Anyway, she said that "I'll go and make phone calls." Eventually, she came back to me and said, yes, she couldn't see that I'd been referred or anything. Anyway, she said someone will call me back. Someone did call me back then and I don't know if I'd been forgotten about and, oh, all of a sudden, "Let's get this sorted," or I just happened to phone at the right time. I don't know'.*

The pathway to a second opinion appeared both inequitable in terms of access but also appeared to add to the feeling of uncertainty at an already very anxious time. Those participants who actively sought a second opinion, inherently positioned themselves central to their treatment decision-making. However, for others who may not have had a second opinion or the rationale for it left unexplained, had a very different experience of involvement in treatment decision making.

'Whose decision is it anyway?'

For some, treatment decision-making involved complete partnership working, between the patient, their family and the MDT. Poppy (c) wife of Dan (56, T3, curative) explains this.
'we obviously made the decision for surgery after long discussions with both [professors of oncology and surgery] *and we actually had a meeting with both of them. It was quite good*

because they counteracted each other's… they discussed it very openly between the two of them, so we had a complete view of both of their opinions'

Others experienced being somewhat involved in decision making, but felt they were being led by the preference at the hospital with regards to the treatment pathway- many were aware that their case had been discussed at an MDT meeting but didn't know the exact details. Sally(c) wife of Walter (65, T3, curative to non-curative) describes her experience of this; *'they had a big meeting before with I think the whole team and they went through all of the details…probably much more detail than we saw in our meeting. That was their steer as a hospital'*

Others felt much less involved or informed about any discussions regarding treatment such as Ken (60, T1, non-curative); *'They have these multi-disciplinary team meetings, I'm a big believer that the patient should be part of that. I think a lot of patients- I mean not all patients would want to do that but I think it would make you feel less powerless if you realised what rationale was going on and why'… 'it was never put to me. It's just that it's been given to me as a fait accompli, this therapy'*.

Kim (63, T1, curative) explained how she felt that there could have been further discussion and involvement, or at least an opportunity to ask questions before confirming the treatment plan; *'I have felt like I am on a conveyor belt- in out next and I know everyone is busy but I don't know but some discussion and making me understand what's going on, and I would have liked to have known if I had any other option, so I could make… to me, my only option is this surgery as far as I know'.*

Richard (67, T3, non-curative) explained that although often given the opportunity to ask questions, this felt more tokenistic; '*I suppose they always say, "Have you got any questions?" and this and that but you quite often don't get the feeling that the consultants*

particularly have enough time to just sit there and have a quiet elongated chat about something. You always feel that they're under such time pressure that you don't want to hold them up and really try and talk through it'. You never quite get to the bottom or how long have I got to live, what is a tumour actually going to do and that sort of thing'.

In contrast some participants did not feel that it was their role to be involved in decision-making such as Rob (62, T1, non-curative); *'I just go with what the doctor says… he's the man with the plan'.*

Others described their experience of being involved in the decision-making to become part of a clinical trial. Peter (67, T3, non-curative) discussed agreeing to the tests for a clinical trial; *'I felt like I went through a series of tests like an astronaut, to be honest with you. It almost felt like a test getting to the trial'*. Peter then explained feeling that he did not actually have any say in the ultimate decision regarding the actual treatment received.
'And of course, then the team are explaining to you that a bloody computer is going to select you, to take the human element out of it. As the recipient listening to this you're thinking, "Crikey."

The longitudinal design of this qualitative workstream investigated not only the experience of diagnosis and the journey to treatment, but also the experience of living with and beyond a diagnosis of rOPC. Interview timepoints two (T2) and three (T3) allow us to look at the experience of rOPC and any function and QoL changes that have or are continuing when a patient and their carer are now established on a treatment pathway. The underlying uncertainty running through the first two themes 'Here we go again' and 'Do I have a choice' has now resolved somewhat, however it does appear to be replaced by an ongoing desire to find balance when living with the consequences of the treatment choices. This will be explored further in the final theme 'A personal trade off'.

5.6.3 Theme 3 'A personal trade off'

Participants' accounts provided a sense of how circumstances had changed between diagnosis, treatment, rehabilitation and living with a beyond a diagnosis of rOPC. This theme provides an overview of how participants appeared to find balance between survival and living with the consequences of disease and/or treatment. The first of three subthemes; 'Are we ever ready?'; includes participants' reflections on how prepared they felt they were for their treatment in comparison to their actual experience of treatment. The second subtheme 'Would I do it all again?' refers to how patients and caregivers now feel about their treatment choices. The third subtheme entitled 'How I look at things now?' focuses on reframing perceptions of quality of life, in the setting of changed or changing function and circumstances regardless of treatment modality and pathway.

'Are we ever ready?'

The prospective baseline interviews provided a real-time account of how patients were preparing for their treatment, as these individuals had an upcoming or awaited treatment start date. The longitudinal design of this study and the inclusion of a retrospective cohort also provided an opportunity for individuals to reflect on their experience of treatment compared to how they were counselled in advance. This provided the opportunity to identify convergence/ divergence between pre-treatment counselling/ preparation and their actual reality of having treatment and how this may have impacted their ability to deal with any function or QoL change.

With regards to preparation for curative surgery, prospective patients reported that the pre-operative preparation phase was overwhelming.

Kim (62, T1, curative) explained that when she came to meet with the surgeon, she was given a treatment plan and had her pre-operative anaesthetic assessment all on the same day; *'It was all a bit overwhelming for me. Yes. I came for an appointment, and I ended up*

having a pre-op and all that. So, I ended up being there a lot longer than I thought I was going to be'. As we heard already, Kim described a feeling of being *'railroaded'* and that she didn't want to seem '*ungrateful*' by '*asking too many questions*. However, Kim did seem to be aware that the surgery may result in functional changes and she was mindful of that when weighing up her options to proceed with the surgery; *'I don't want to have surgery and put myself through a lot and my family through a lot and my outcome is no better and I carry on being not able to do things and stuff... I feel I just might as well let cancer take its course'*

At her follow up interview at timepoint two, Kim reflected that she felt ill-prepared for the surgery and despite being six months beyond the surgery, didn't really feel that she understands why or what happened; *'When I got to the point of having the operation, because I only came down the night before. I still didn't really know what was going to happen and I still don't really know now what happened, how they did the operation or anything…Hopefully if they had explained to me what they were going to do, how they were going to do it, it might have eased me a bit. But because I don't know, I don't know, do you know what I mean, whether it would have eased me or not?'* Kim also reflected on the process of a second opinion, she felt that if there was more knowledge locally about the second opinion process and rationale that might have help with her anxiety; *'I don't know, because it wasn't just new to me. I don't know if the people who I was dealing with here, I don't know that they knew the process really, to be able to explain to me'.*

Others felt that although they met many professionals and were given lots of time for discussion, they were never quite fully informed as to what was going to happen. Toby (67, T1, curative) explained in his first interview how he felt he was never getting the entire picture. He had several meetings with different members of the team however, felt that with each meeting something new was introduced. He recalls being told about the planned tracheostomy, something he was not aware of. *'I know that things keep getting added on… like the tracheostomy… which came out the blue'.* His partner Kate (c) described that she

had been disappointed not to have been present for all the pre-surgery conversations as Toby had been an inpatient for his RIG and many of the conversations took place at the bedside rather than at a scheduled appointment, which she could have made herself available for. *I unfortunately, I wasn't at that meeting. I would've liked to have been at it, but I can appreciate it's difficult getting everybody that was involved in it. I came down at 10 o'clock, when Toby was under the impression that was when it was. But I think I was there for about two and a half hours in the end. And then, because we still didn't know what time it was going to be, I left to get some lunch'.* Prior to surgery, Toby explained that he was quite optimistic about his recovery, as based on his assessments before his operation his baseline level of function was quite good; '*I'll be honest, as simple as it was, Thursday put me at ease slightly with the fact that how well I did, apparently, on the* [swallow] *test. And I can appreciate that if I'm pretty good now, and then the operation will take some of that away, that to get back to where I was, yeah, on Thursday, is going to be quite a bit easier than if I'd have been rubbish on Thursday for the test. That's the impression I got. First hurdle is down, you know?'*. However, in his follow up interview, Toby reflected that he was not prepared for how big an operation it would be, how long the recovery would be and the gravity of changes to function which he would experience; *'Well, obviously it was a big operation. The actual surgery I seemed to cope with quite well. The recovery time was a lot longer than I thought it would be, as opposed to the hospital three weeks… Post leaving the hospital has been quite difficult. I think it might have been six weeks into post-operation that I was given the news that I wouldn't be able eat and drink. It was probably as difficult to take on board as being told in April that I'd actually got cancer'.*

The patients and caregivers who were interviewed retrospectively reflected on how ill-prepared they were for treatment in comparison to their now reality of living with the function and QoL changes following curative surgery. Participants sometimes felt that discussions about the potential functional outcomes of treatment had been too optimistic or misdirected as explained by Poppy (c) wife of Dan, (65, T3, curative);*'There was never a discussion*

about that it might lead to a complete loss of voice' and Walter, (56, T3, curative to non-curative).

'I seem to remember being more focused on loss of speech as a potential outcome than the swallowing aspect, which is what has become a much bigger problem. I don't really recall that being discussed to the level that it is currently at and has been'.

Others reported that the information was either sufficient or perhaps too much, as the participants' themselves were confident that they would be able to deal with whatever might happen once the disease had been eradicated.

Jack, (61, T3, curative), describes how he had been counselled on how difficult his recovery was going to be in terms of swallowing, however he was not daunted by this; '*I had no illusions about how tough it would be. But also, I was pretty confident I would do everything. I knew there was a whole team there to support me, help me through it and to assess me and advise me and do what I can.'*

Others were more focused on the goal of survival, therefore the focus on function pre-treatment was superfluous to their information needs. Michael (63, T3, curative) explained this. *'The warnings and advice leading up to the operation were quite heavy and I realise now why. It was preparation for afterwards, "You won't be able to speak properly. You won't be able to eat properly or the same." For me, it wasn't quite so necessary. That was a secondary issue for me… 'I didn't feel I had a choice. It was have it done or die. So, there was no question for me. Just get on with it'*

The importance of getting the correct balance in terms of information for the individual was highlighted by Satish (67, T3, curative); *'I think the problem is if you try and prepare people too much as to what to expect, they might either be disappointed or think that's going to be a real struggle, I might never be able to do it. I don't know what the right… Maybe ignorance is*

bliss and you just cope the best you can. I'm not sure but I think it depends very much on the individual'.

There were few or no concerns regarding potential functional changes in the non-curative setting despite some of these patients presenting with changes to their swallowing/ voice at point of diagnosis. Participants appeared to be more aware of the potential medical side effects of treatments. Some patients were very anxious when reading the information leaflets, whereas others didn't read them and only wanted to think about the side effects if and when they arose.

The contrasting views of Ken (60, T1, non-curative) and Sophie (c) wife of Gerard (62, T1, non-curative) both about to commence the same treatment, illustrate this.
Ken explained*; 'One of the nurses went through, with me, and gave me the printed sheet, which is really scary. I know it's been compiled by people that are suffering from… It goes bang, bang, bang, bang, bang, and it's like all the bad things. These are all the bad things that can happen to you. I think it's important that they say, "None of it might happen to you, one of these might happen to you." I think it needs to be a bit more balanced, it was a bit shocking to read that sheet'.* Sophie (c) wife of Gerard explained; *'We're not those people that read every negative thing. We like to take our medicine and then if we don't feel great, or something feels a bit weird, then we might look and think, "Should I be feeling dizzy or whatever it is?" Rather than look and go, "Oh, I'm going to be dizzy, I'm going to be sick, I'm going to be tired, I'm going to be…".* In the follow up interview at timepoint two, both Gerard and his wife reflect on how well he has been over the past six months of treatment with little or no side effects. Gerard explained '*I've not had any ill-effects regarding the treatment'.* He describes how he continues to deal with things if and when any symptoms crop up. Gerard provided an example to illustrate this- he recently experienced some ulcers in his mouth, and he has been referred to a surgeon to review them. Gerard explained how he was discussing this with his GP friend; *'I have a friend who is a GP, and I spoke to him the other day, I said,*

"I've got to go up to see a surgeon." "Why?" I said, "I don't know, they just want me to see a surgeon about the ulcers in my mouth." So that's it. If you sit and analyse everything, you'll end up going down a dark hole and start worrying about it, and I don't want to do that'.

When participants reflected on their preparedness for treatment, although not included in the topic schedule, a common theme of dialogue for those who were treated curatively with surgery related to whether they would make the same decision again regardless of their functional outcome. This will now be explored further under the sub theme 'Would I do it all again?

'Would I do it all again?'

Deirdre, (69, T2, curative) was interviewed six months after her curative surgery, at which point she remained unable to eat and drink, with complete reliance on her gastrostomy. Prior to her surgery she was eating and drinking without any known difficulty and enjoyed cooking for and eating with her family and friends. Disease free at six months, Deirdre reported that she would have the operation again, as it was the only option for cure; *'Whatever happens, however bad the outcome, I would still have had it done. I would definitely have had the operation because there wasn't a choice'.*

Likewise, Poppy (c), wife of Dan (65, T3, curative) who is now tracheostomy and gastrostomy reliant and uses mouthing or a text to speech application to communicate explained; *'I believe Dan would say he wouldn't have made a different decision anyway, even if they said, you might lose your voice completely'*. Dan provided non-verbal agreement (head nodding), emphasising that his focus would still be '*survival',* which he communicated using his mobile phone.

Conversely, Walter (56, T3, curative to non-curative) did have curative surgery, but his circumstances have now changed and is no longer disease free. He is now undergoing

palliative treatment for metastatic disease and explains he is not sure if he made the correct decision, given the life-changing impact of his surgery; *'I ask myself the question, if I know what I know now, sorry, would I still go through with it? I don't know. There's a part of me that thinks I might have been better off taking my chances with the trial which I'm now on. My wife seems to think that that wouldn't have worked because the surgery removed… although it came back, the surgery removed it and it's very, very unlikely that the chemo and the immunotherapy would have got rid of it. It's hypothetical. My life, our life has changed, massively, and my life has changed forever in terms of what I have to do in order to eat orally, because I had a feeding tube for about 15 months and that was, like, a massive focus for me, to get rid of that. I've managed to do that, but everything has changed, really, you know, our social life, my own working situation. So, going back to the question, I don't know. It's very difficult'.*

Irrespective of how prepared patients and their caregivers felt for their treatment, almost all participants, either curative or non-curative, whether sampled prospectively or retrospectively, appeared to have re-framed their priorities in relation to their overall QoL. This reframing appeared to apply to whatever functional impairment was most significant for the participants including swallowing, speech, energy and physical activity. This process of reframing will be explored in the next section.

'How I look at things now'

The descriptions of the trajectory of change in function for those treated curatively and non-curatively were different. Following curative treatment, participants described a sudden deterioration post-treatment, which persisted at six months. Eventually, a slow and gradual improvement was described by the retrospective sample, requiring considerable motivation and drive.

Judy (60, T3, curative) describes how: *'nothing seemed to work at all, and it was just part of my body just, sort of, breaking down, I suppose. And then it was up to me to try and build it back up again'.* Although Judy made progress with her swallowing and had her gastrostomy removed and can eat almost anything now; *'if it's something I enjoy, I'll eat it',* her speech didn't recover fully and felt that she could no longer work; *'I stopped my job, because I felt that when I was speaking to clients on the phone, they weren't always able to understand… And it was that realisation, I think, that every time I shook someone's hand and introduced myself, there was that flicker of, "Oh, what's wrong with her?" And in the end, it just became too much. So, I don't work'.*

Stuart (70, T3, curative) describes his experience of recovery and apparent recalibration of in the context of his increasing age; *'I am 70 now, so I'm not a 40-year-old, 50-year-old man who can go all over the place and do whatever I want to do. There are times when I get weary. It's not unknown for me to have an afternoon siesta, whereas a few years ago I wouldn't have thought about it'.* Stuart reflects that prior to his surgery, he was very focused on his voice/ speech outcome. However, following his surgery, and having experienced a deterioration in speech, he feels that his concerns in relation to function have changed. '*If I was diagnosed with it today, I think my priority today would be long-term health and mobility. I think that would be my priority today. Maybe not the voice because, again, I've learnt to live with the voice. But if it happened today, yes, I think long-term health and mobility, and if I've got to sacrifice speech to have that, then I would sacrifice speech'.* Unlike Judy, Stuart reported that he did return and stay at work as working was a huge part of his QoL. He makes ongoing adaptations in his daily life so that his speech does not impact on his ability to work and his overall QoL. '*I'm still working overseas where English is not the first language for clients. Sometimes it's difficult, but I have a team out there and they understand me. The family, the grandchildren, they all understand me, but if I go into a restaurant and order a meal, quite often, waiters don't understand me, so the family steps in or I have to indicate on a menu what I'm ordering'.*

Dan (56, T3, curative) who can no longer speak and eat or drink reports that he now focuses on times in his day where he feels '*normal*' despite these functional changes, *'There are times you feel exactly the same as before. In the theatre... Watching TV'.* Dan spoke of his love of travel, and how he focuses on any *'enjoyment of life'.*

For some patients swallowing after treatment is just not their main priority as it has been very difficult since their original treatment. Kim (63, T2, curative) explains this; *'When people were trying to get me to eat after the surgery. I had to keep explaining to people that I couldn't eat before the surgery so why do you think I'm going to eat after the surgery?'.* However, other aspects of QoL are very important including activity and energy, although improving, Kim continues to make adaptations; *'I used to be able to stand there all day and iron till I got rid of it. I can't do that anymore. I had to do a little bit and have a rest and just try not to look at it, and then go back and do a bit more another day or something. I'm just slowly but surely doing a bit more. I've just started a beginner's Pilates class which I'm enjoying, to try and help me get a bit of strength and stuff back'.* Kim also reflects on how she is now pain free. '*Pain is a funny thing because when you've not got it anymore you forget about it quite easily*'.

For patients undergoing non-curative treatments, there appeared to be an experience of a more gradual decline in function and other aspects of QoL.

Tim (63, T3, non-curative) describes his swallowing; "I am a little more careful of eating… I don't look forward to eating socially. I can eat, but I must be very careful, but that's the biggest one on the quality of life".

Sophie (c) wife of Gerard (62, T2, non-curative) describes the impact Gerard's decline in swallowing has had on the entire family; *'Food has been hard… and food is so important,*

isn't it, when families get together and socially with friends? So, I think maybe that was something that, at times, can bring you down a little bit. We want to eat as a family, we don't want to be eating all different meals. You know, we want to do it- because that's what we've always done'.

With regards to overall QoL, Sheila (c), wife of Tom (70, T3, non-curative) reports how she has noticed a physical decline in her husband and overall, he can no longer take part in many activities which he used to do; *'He liked walking, being outside, playing with the dog, gardening, all of those things, so this isn't an option that's open to him at the moment'.*

Regardless of the trajectory, an ongoing process for both patients and caregivers to find balance was evident with an apparent reframing of priorities. Prior to treatment at the point of diagnosis and treatment decision, patients and caregivers are focused on cure or survival. However, once patients have had their treatment or are established on a line of treatment, there appears to be a shift in focus towards function and overall QoL.

In the curative setting, this appeared to involve participants coming to terms with what has been lost in return for cure, whether that be their speech, their job, their ability to eat and drink or all of the above. This shift from retrograde focus on what once was, is now centred in the present and how life can be enjoyed despite what was lost with treatment.

Walter (56, T3, curative to non-curative) reflected on his recovery post-surgery, prior to his diagnosis of metastatic disease: *'There's a balance between what your able to put up with in return for just living…You always, obviously, look to be positive and what you're able to… but it's a trade-off with what you're losing'.*

For those in the non-curative setting, there is a similar refocus as to what can be enjoyed and appreciated in the present. Although Gerard (62, T2, non-curative) has experienced

some changes in his swallowing, overall, he has felt quite well. His wife Sophie (c) explains how they have managed to enjoy a good QoL despite ongoing treatment; '*once* [the treatment] *started, if friends invited us out or things, we could more confidently say we'd love to go. We've done a couple of weekends away, we went to a concert down in Worthing, stayed over. So, you kind of know that, even though you're at work, Gerard has not been so tired. Nothing like the radiotherapy, not that kind of tiredness. So, we know we can do that and then still come back and go back to work the next day and get through the week. It has been quite nice, hasn't it?'.*

However, there is a trend to look towards the future to potential junctures when patients may once again need to decide between ongoing survival and function/ QoL. Tim's (63, T3, non-curative) description captures this *'If it gets to the point where you can't look forward to eating something, let's say with a feeding tube… … you start to struggle with the point of it to be honest'.*

5.7 Discussion

This aim of this longitudinal qualitative study was to investigate patients' and caregivers' experiences of being diagnosed with rOPC, the treatment decision-making process and living with the consequences of those decisions.

The participants' experience of diagnosis, treatment and living with and beyond recurrent disease was frequently described in the context of their previous experience of primary HNC diagnosis, treatment and aftermath.

Many participants were not overly shocked by their diagnosis as given their experience of previous HNC, many recognised the signs and symptoms. However, it appeared that the longer the interval between primary treatment and disease recurrence diagnosis, the greater the shock. Regardless of the time interval between primary disease and recurrence, the

overwhelming emotion was disappointment, and for some this was followed by fear of what further treatment might mean.

Patients with rOPC have first-hand experience of how arduous HNC treatment can be and how destructive it can be for function and QoL. Despite this, patients with rOPC and their family members prioritise survival over the potential side effects of treatment at diagnosis, which is consistent with previous qualitative studies in both the primary disease (Windon et al., 2019) and in the recurrence setting (Rhoten et al., 2021). If there is a chance of cure, patients and family members want that. In the case of inoperable disease where only non-curative options are possible, patients and their caregivers want to choose the treatment option which will give them the best survival options. For both groups there is an urgency to commence treatment as early as possible to optimise their cure or survival outcome as much as possible. This appears to highlight a disconnect between what healthcare teams believe patients are most concerned about i.e., function / QoL and what patients are actually most worried about i.e., survival. This has been recognised previously in the literature (Hamilton et al., 2022).

Data from this study demonstrate a shift in patient focus following treatment initiation, with greater priority given to function and QoL once patients have had their treatment or are on an established treatment pathway. In the salvage surgery setting, patients in this study appear to experience a sharp decline in function with treatment, which is concurrent with previous studies measuring functional outcomes post-surgery (Charters et al., 2022, Culié et al., 2015, Kano et al., 2013, Pipkorn et al., 2019, Sweeny et al., 2016, White et al., 2013). Previous studies have measured this quantitatively only, what this study adds is a greater understanding of the impact of those changes on the patient and their caregivers. Some participants in this study found the sharp decline in their function very distressing, and others less so. For those participants with a good baseline level of swallowing function pre-treatment, this decline appeared to have a dramatic impact on their overall QoL, and

swallowing becomes their focus. For those with a less favorable baseline level of functioning, patients remain less concerned about swallowing and are more focused on other facets of QoL such as activity. This may be because prior to their treatment swallowing was no longer an enjoyable experience to them given persistent toxicity from their previous treatment. The importance of baseline level of functioning in predicting functional outcomes is well documented in the context of primary HNC (Frowen and Perry, 2006). From this study it can be inferred that in the recurrent setting professionals may be able to extrapolate some information regarding patient values and priorities for treatment based on their history of functional recovery following primary treatment. However, unlike the primary disease setting, given the paucity of current literature on functional outcomes following treatment for disease recurrence, we cannot determine whether baseline level of function is predictive of functional recovery (Brady et al., 2023). However, this study signals that a patient's experience or reaction to functional changes may differ according to their baseline level of function.

Those participants who are treated with non-curative intent also experience a shift in focus as they begin to experience much more subtle changes in their swallowing. Although changes may appear to be less dramatic than in the salvage surgical setting, these changes can have a significant impact on the individual's QoL and their family. To the authors knowledge, the impact of recurrent HNC on caregivers and family members has not been investigated previously, but our findings are in keeping with the impact of swallowing difficulties on caregivers in the primary disease setting (Nund et al., 2014).

The longitudinal nature of this study provided further insight into the apparent recalibration of what QoL is for patients over time who have been treated or are being treated for rOPC. Patients who are treated curatively appear to achieve acceptance regarding their compromised level of function caused by their treatment. This appears to what has been described in the literature as a "response shift" where adaptation occurs as a result of changes in circumstances and has led to a recalibration of focus (Ilie et al., 2019).

Participants treated curatively in this study were aware of what they have lost in terms of function, however, they also identify this loss as essentially the cost of cure. This study demonstrates several examples of this including a lady [Kim] who is disease free at six months post-surgery but is now gastrostomy dependent since her surgery. She however recognises that she has made gains in other areas of her QoL including her levels of activity. She now has enough energy again to start doing more housework and some physical exercise. Another gentleman who can no longer speak, or swallow and is both tracheostomy and gastrostomy dependent now focuses on what he can do to enjoy his life, namely independent travel and spend time with his wife and daughter. Response shift appears to be required to deal with the prospect of one's future life with the limitations imposed by the curative treatment(s) received (Echteld et al., 2005), including changes to speech and swallowing.

One might not expect to see such a response shift in the non-curative setting, as the prognostic outlook for the future is very different. However, this study demonstrates that there does appear to be recalibration for those participants in the non-curative group. The qualitative data provide some further insights and possible explanation for this, and this may to relate to the fact that participants are experienced when it comes to HNC and its treatment. One prospective participant and his wife describe their 'relief' that the participant remains 'so well' and is able to: participate in social events albeit with adaptations; continue to work; and fit in trips away with his family between treatment appointments. The World Health Organisation define QoL as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (World Health Organization. Division of Mental and Prevention of Substance, 1997). This gentleman's overall goal was to remain alive, but perhaps he envisioned the cost for that survival much greater in terms of how unwell treatment might make him. It seemed that this, coupled with presumed effective symptom

control measures, had resulted in perceived improvements or at least acceptance in all aspects of his QoL.

5.8 Critique

Participants were recruited at a single site and lacked ethnic diversity. Levels of deprivation were unrecorded. The lead author GB was involved in the care of some of the participants who were interviewed retrospectively, which may have influenced the participants' accounts. Results may not be generalisable to patients treated at a non-specialist cancer centre. Sample attrition resulted in only a small number of participants in the prospective sample were available to take part in the follow up interview at timepoint one. For those patients who had died or indeed had become very unwell because of their disease may have provided a very different viewpoint.

5.9 Conclusion and implications

Patients and caregivers want and need to be fully informed of all of the available treatment options for their disease with accurate survival information, and function and QoL data. This has implications not only for clinical practice but for future research in the area so that pre-treatment counselling is based on robust and relevant data to help patients to make decisions about their treatment and care.

Treatment decision-making is complex in the setting of rOPC. Decisions are often based on what is perceived by professionals to be functionally "too morbid" with salvage surgery or "kinder" with life-prolonging non-curative treatments. Patients and their caregivers want to survive and when the option is to choose between cure and function / QoL, cure appears to be favoured. When cure is not an option, patients still appear to want to live as long as possible. However, as the prognosis gets shorter priorities shift, with QoL/ function taking precedence over survival.

5.10 Summary

This chapter has detailed the findings from the longitudinal qualitative workstream using the methodology described in Chapter 4. This qualitative workstream forms part of a larger mixed methods workstream. The quantitative findings will be described in the next Chapter 6, which will give us further information on the functional and QoL outcomes across curative and non-curative treatment pathways. This information will then be integrated with the qualitative findings presented here forming the overall findings of this thesis in Chapter 7.

Chapter 6 Quantitative Results

Having reported the findings of the qualitative workstream of the mixed methods study in Chapter 5, this chapter will provide a summary of the results of the quantitative workstream. The quantitative workstream included a prospective repeated measures observational study. The aim of this workstream was to measure change in function (swallowing and speech) and quality of life (QoL) over time and patient priorities and concerns while undergoing treatment for rOPC. This included both curative (surgery and radiotherapy) and non-curative treatment options (immunotherapy, chemotherapy, and clinical trials of investigational agents). As previously described in Chapter 4, this was achieved by prospectively recruiting participants and measuring their functional and QoL outcomes using a range of patient-reported and clinician-rated outcome measures at pre-defined timepoints, namely at point of diagnosis prior to treatment initiation, and three- and six-months following treatment initiation. Priority concerns were also measured over time using a patient-reported measure.

The enrolment and data flow process will be described firstly, followed by a description of the participants. The purpose of this study was exploratory, and although a sample size calculation was completed in advance, the study was underpowered, therefore the analysis is descriptive. Patient characteristics (age, gender, timing of recurrence, ethnicity, treatment pathway) are summarised using descriptive statistics. On testing, the data collected was not normally distributed, so medians and interquartile ranges (IQRs) with boxplots are used primarily to describe the findings. Medians and IQRs are also presented in tabular form for some of the outcome measures. The analysis of each outcome measure will be described pre- and post-treatment initiation. The analysis will include findings in relation to the entire sample but will also group the data as per treatment pathway, curative or non-curative, for the summary scores for the outcome tools used.

This chapter will conclude with a summary of the main quantitative findings, which will be considered with the findings of the systematic review presented in Chapter 3. The quantitative findings will be integrated with the Chapter 5 qualitative findings in Chapter 7.

6.1 Enrolment

A total of 39 participants were identified as eligible for recruitment to this workstream. Eight declined, four were referred for MDT discussion only and never attended the recruitment site for treatment/ evaluation, and two commenced treatments locally prior to their appointment at the recruitment site. One participant was identified at a participant identification centre (PIC). A total of 25 participants across two recruitment sites were enrolled into the study. Figure 6.1. shows the enrolment and analysis flow for this study.

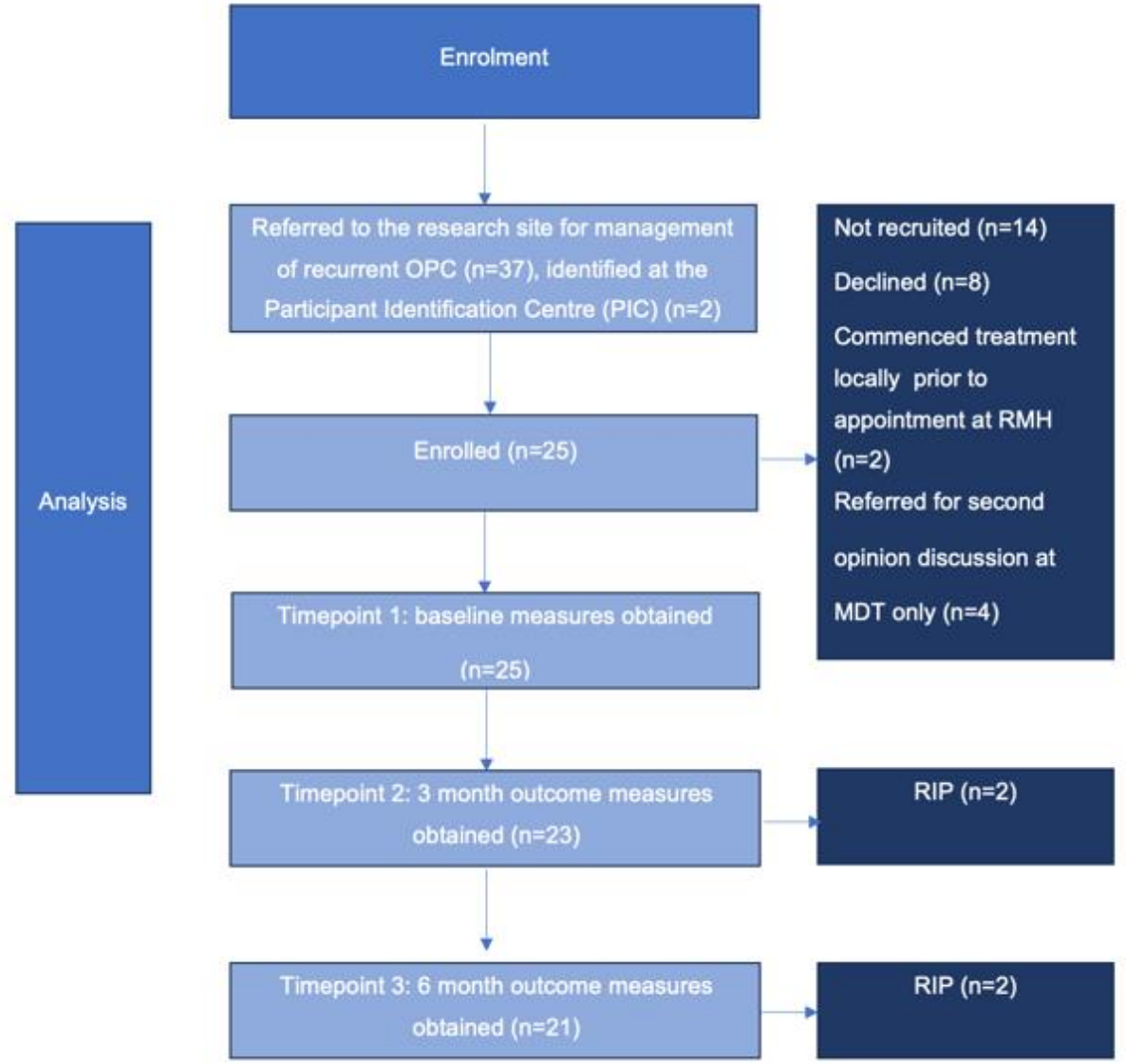


Figure 6-1: Enrolment and participant flow from consent through to data collection.

Ethical issues and data collection

The study protocol was reviewed and approved by the Royal Marsden NHS Foundation Trust Committee for Clinical Research (CCR5242) and the Health Research Authority (HRA) (IRAS: 297893) and the study opened for recruitment on 01/01/2022. In the post COVID-19 era, provisions were made so that the protocol included the option for patients to be recruited remotely with the option for remote follow up outcome measure collection also.

As the research was conducted at a tertiary referral centre, many of the participants had to travel to attend appointments and opted for remote follow up unless attending the centre for another appointment. Also due to lower than expected recruitment rates, an amendment was submitted to open Participant Identification Centres (PICs) (CCR5242 AM2304-07 approved 16/05/23). Although two sites volunteered as potential PICs, only one site managed to open due to reduced capacity in the local research & development teams. Due to geographical distances, it was agreed that recruitment of participants from a PIC would be completed remotely only. The Research Ethics Committee specified that the use of Flexible Endoscopic Evaluation of Swallowing (FEES) was an optional measure for this study, and this was clearly stated in the participant information leaflet. As a result, the data set for FEES for this study is incomplete. Also, although a remote protocol was in place for 100 mL water swallow testing, for those participants who took part in telephone consultations only, this measure was not collected also and thus the dataset was also incomplete. Table 6.1 gives a breakdown of each participant, with any missing outcomes, including the reason.

Table 6-1: Breakdown of each time point for each participant, including reasons for delays and for missing outcomes (red indicates outcomes were not completed, green indicates that they were

Participant ID	Visit	MD Anderson Dysphagia Inventory (MDADI)	University of Washington Quality of Life Questionnaire.	Performance Status Scale for Head and Neck Cancer	IDDSI Functional Diet Scale Score	100 mL Water Swallow Test	Flexible Endoscopic Evaluation of Swallowing (optional)	Chicago Priority Scale
001	1	Yes	Yes	Yes	Yes	Yes	No- patient choice	Yes
	2	RIP	RIP	RIP	RIP	RIP	RIP	RIP
	3	RIP	RIP	RIP	RIP	RIP	RIP	RIP
002	1	Yes	Yes	Yes	Yes	Yes	No-remote review	Yes
	2	Yes	Yes	Yes	Yes	Yes	No-remote review	NA
	3	Yes	Yes	Yes	Yes	Yes	No-remote review	Yes
003	1	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	2	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	NA
	3	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	Yes

004	1	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	2	Declined	Declined	Yes	Yes	No- safety concern	No- remote review	NA
	3	Yes	Yes	Yes	Yes	No- safety concern	Yes	Yes
005	1	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	Yes
	2	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	NA
	3	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	Yes
006	1	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	2	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	NA
	3	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	Yes
007	1	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	2	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	NA
	3	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	Yes
008	1	Yes	Yes	Yes	Yes	Yes	Yes	Yes

	2	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	NA
	3	Yes	Yes	Yes	Yes	Yes	Yes	Yes
009	1	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	Yes
	2	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	NA
	3	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	Yes
010	1	Yes	Yes	Yes	Yes	Yes	No- patient choice	Yes
	2	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	NA
	3	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	Yes
011	1	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	2	Yes	Yes	Yes	Yes	No- safety concern	No- remote review	NA
	3	Yes	Yes	Yes	Yes	No- safety concern	Yes	Yes
012	1	Yes	Yes	Yes	Yes	Yes	No- remote review	Yes

	2	Yes	Yes	Yes	Yes	Yes	No- remote review	NA
	3	Yes	Yes	Yes	Yes	Yes	No- remote review	Yes
013	1	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	No- patient declined
	2	Yes	Yes	Yes	Yes	No- safety concern	Yes	NA
	3	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	No- patient declined
014	1	Yes	Yes	Yes	Yes	Laryngectomy	Laryngectomy	Yes
	2	Yes	Yes	Yes	Yes	Laryngectomy	Laryngectomy	NA
	3	RIP	RIP	RIP	RIP	RIP	RIP	RIP
015	1	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	2	RIP	RIP	RIP	RIP	RIP	RIP	RIP
	3	RIP	RIP	RIP	RIP	RIP	RIP	RIP
016	1	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	2	Yes	Yes	Yes	Yes	No-safety concern	Yes	NA
	3	Yes	Yes	Yes	Yes	No-safety concern	Yes	Yes
017	1	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	Yes

	2	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	NA
	3	RIP	RIP	RIP	RIP	RIP	RIP	RIP
018	1	Yes	Yes	Yes	Yes	Yes	No- patient choice	Yes
	2	Yes	Yes	Yes	Yes	Yes	No- remote review	NA
	3	Yes	Yes	Yes	Yes	Yes	No- remote review	Yes
019	1	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	2	Yes	Yes	Yes	Yes	No- safety concern	Yes	NA
	3	Yes	Yes	Yes	Yes	No- safety concern	Yes	Yes
020	1	Yes	Yes	Yes	Yes	No- Safety concern	Yes	Yes
	2	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	NA
	3	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	Yes
021	1	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	2	Yes	Yes	Yes	Yes	No- safety concern	No- remote review	NA

	3	Yes	Yes	Yes	Yes	No- safety concern	No- remote review	Yes
022	1	Yes	Yes	Yes	Yes	No- safety concern	Yes	Yes
	2	Yes	Yes	Yes	Yes	No- safety concern	Yes	NA
	3	Yes	Yes	Yes	Yes	No- safety concern	Yes	Yes
023	1	Yes	Yes	Yes	Yes	No- safety concern	Yes	Yes
	2	Yes	Yes	Yes	Yes	Laryngectomy	Laryngectomy	NA
	3	Yes	Yes	Yes	Yes	Laryngectomy	Laryngectomy	Yes
024	1	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	Yes
	2	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	NA
	3	Yes	Yes	Yes	Yes	No- safety concern	No- patient choice	Yes
025	1	Yes	Yes	Yes	Yes	No- remote telephone review only	No- remote review	Yes

	2	Yes	Yes	Yes	Yes	No- remote telephone review only	No- remote review	NA
	3	Yes	Yes	Yes	Yes	No- remote telephone review only	No- remote review	Yes

6.2 Participants

The sample included 20 males and five females. 24 were recruited at a tertiary referral cancer centre in London, and one at a tertiary referral centre in the Northeast. There were slightly more participants undergoing curative treatments (n=14). The majority of participants (n=22) were White British across curative and non-curative pathways. Median age in the non-curative group at 61 years was slightly younger than the curative group at 66 years. Timing of recurrence was grouped into three categories; residual where the disease was diagnosed within 12 months of primary treatment completion, recurrent where the disease was diagnosed 12 months – five years following primary treatment and new primary disease in those participants diagnosed at least five years following their treatment for primary disease. There were more participants in the curative group with new primary disease (n=8) compared to the non-curative group (n=1) and more participants with residual disease (n=4) in the non-curative group in comparison to the curative group (n=1). In keeping with this, the median time in months since primary treatment was longer in the curative group at 60 months compared to the non-curative group at 14 months. Demographic details for the sample are summarised in Table 6.2.

Table 6-2: Participant demographic and disease data including sex, age, ethnicity, recurrent disease timing, treatment pathway and treatment type.

n=25		Total	Curative (n=14)	Non curative (n=11)
Sex	Male	20	11	9
	Female	5	3	2
Ethnicity	White British	22	13	9
	Mixed- White & Black African	1	0	1
	Asian	2	1	1
Age	Mean(SD)	64 (11)	66 (15)	61 (5)
	Median(IQR))	64 (55-70)	68 (54- 82)	61 (58-64)
	Range	41-88	41-88	52-70
Recurrent disease classification	Residual disease	5	1	4
	Recurrent disease	12	6	6
	New primary disease	8	7	1
Previous radiation treatment		24	13	11
Time since primary disease	Median (months)	15.5	60	14
	Range (months)	4-240	8-211	4-240
Treatment type			Surgery (n=13) Radiation (n=1)	Clinical trial (n=7), Immunotherapy (n=2), Chemotherapy (n=2).

6.3 Primary endpoint

Patient-reported swallowing-related quality of life (QoL) was the primary outcome for this study and was measured using the MD Anderson Dysphagia Inventory (MDADI). All participants (n=25) completed the MDADI at baseline, 22 at three months and 21 at six months following treatment initiation.

Of the total 69 MDADI questionnaires included in this analysis, six were incomplete. In two of the six incomplete questionnaires 10% (two questionnaire items) were not answered. In the remaining, 5% (one questionnaire item) was not answered by participants. All six items which were left unanswered across the three timepoints were different. Table 6.3 summarises completion rates and a missing data analysis for the MDADI across timepoints.

Table 6-3 MD Anderson Dysphagia Inventory data completeness and missing data analysis

Timepoint	Subscale	Item	N	Missing
Baseline	Emotional	Embarrassed	25	0
		Self- conscious	25	0
		Upset	24	1
		Do not go out	25	0
		Others irritated	25	0
		Low self-esteem	25	0
	Functional	Difficult cooking	24	1
		Lose income	25	0
		Limit social/ personal	24	1
		Go out	25	0
		Excluded	25	0
	Physical	More difficult	25	0
		Great effort	25	0
		Takes longer	25	0
		People ask	25	0
		Cough with liquids	25	0
		Limit intake	24	1
		Weight	25	0
		Huge amount	25	0
3 months	Emotional	Embarrassed	23	0
		Self- conscious	22	1
		Upset	23	0
		Do not go out	23	0
		Others irritated	23	0
		Low self-esteem	23	0

	Functional	Difficult cooking	23	0
		Lose income	23	0
		Limit social/ personal	23	0
		Go out	23	0
		Excluded	23	0
	Physical	More difficult	23	0
		Great effort	23	0
		Takes longer	22	1
		People ask	22	1
		Cough with liquids	23	0
		Limit intake	23	0
		Weight	23	0
		Huge amount	23	0
6 months	Emotional	Embarrassed	21	0
		Self- conscious	21	0
		Upset	21	0
		Do not go out	21	0
		Others irritated	21	0
		Low self-esteem	21	0
	Functional	Difficult cooking	21	0
		Lose income	21	0
		Limit social/ personal	21	0
		Go out	21	0
		Excluded	21	0
	Physical	More difficult	21	0
		Great effort	21	0
		Takes longer	20	1
		People ask	21	0
		Cough with liquids	21	0
		Limit intake	21	0
		Weight	21	0
		Huge amount	21	0

6.3.1 MDADI composite Score

Data for the MDADI composite score (total score) are presented. The scoring for the composite score ranges from 20-100 where 20 is the worst possible score indicating very poor swallowing-related QoL, and 100 is the highest possible score indicating very good swallowing-related QoL.

The baseline MDADI composite score for the sample was 60 (IQR: 52.15-81.75), at three months this deteriorated to 56.50 (IQR 49.75- 72.0) returning to 60 (IQR 54.75- 75.75) at six months (Figure 6.2). Of note there are two outliers with excellent functioning at the second timepoint and a wide IQR at all timepoints.

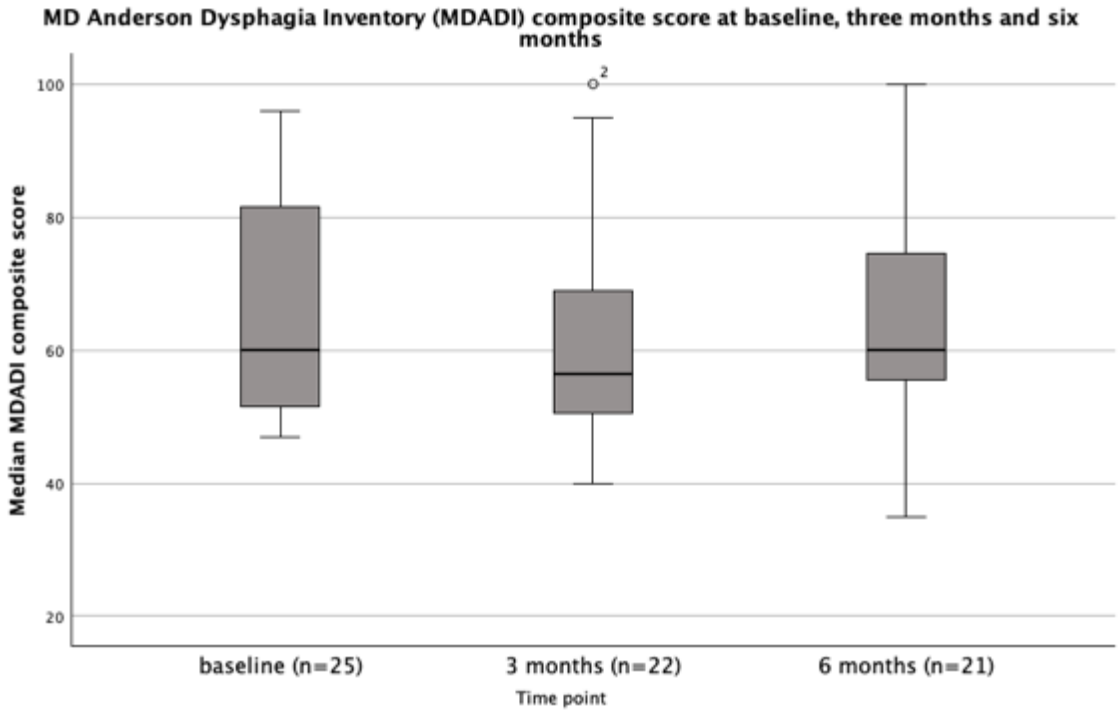


Figure 6-2: MD Anderson Dysphagia Inventory (MDADI) composite scores at baseline prior to treatment initiation, and three and six months following treatment initiation. Scores range from 20-100 where 20 is the worst possible score. Scores of ≥80 are considered optimal, ≥60-<80 adequate ,<60 poor. At each timepoint the horizontal line represents the median, the box represents the interquartile range and the whiskers demonstrate the minimum and maximum values. Outliers are marked with a o.

The MDADI median composite scores for the participants who underwent curative and non-curative treatment are presented in Table 6.4. At baseline and three months, composite scores are comparable. At six months, median score is slightly higher in the non-curative group however a wide range of scores are note at all time points across treatment pathways.

Table 6-4: MDADI composite score across all time points for participants undergoing curative and non-curative treatment.

		Baseline	Three months	Six months
Curative	Number of participants (n)	14	12	12
	Median MDADI Composite score	60	57	59
	IQR	45- 76	42-72	48-71
Non-curative	Number of participants (n)	11	10	9
	Median MDADI Composite score	61	56	65
	IQR	47-75	46-67	56- 74

The MDADI composite score is comprised of three subscales: the functional, emotional and physical scales. The composite scores of each of the three subscales will now be presented.

6.3.2 MDADI functional scale

Figure 6-3 demonstrates a median baseline functional score of 64 (IQR 44.5- 83.5), which deteriorated to 60 (IQR 45-85) at three months and improved to 68 (IQR 50.5- 85.5) for the sample.

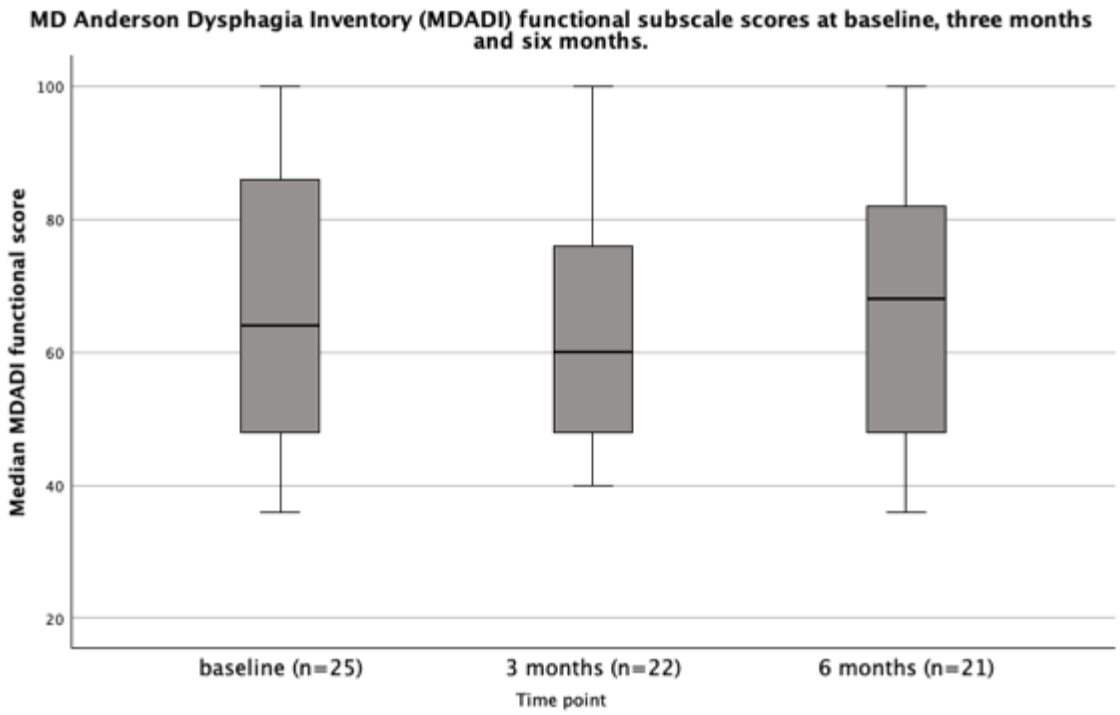


Figure 6-3: MD Anderson Dysphagia Inventory (MDADI) functional subscale scores at baseline prior to treatment initiation, and three and six months following treatment initiation. Scores range from 20-100 where 20 is the worst possible score. At each timepoint the horizontal line represents the median, the box represents the interquartile range and the whiskers demonstrate the minimum and maximum values.

MDADI emotional scale

Figure 6-4 summarises the MDADI emotional subscale score for the sample across timepoints. Here an increase in median emotional subscale is noted by six months, following an initial deterioration at three months.

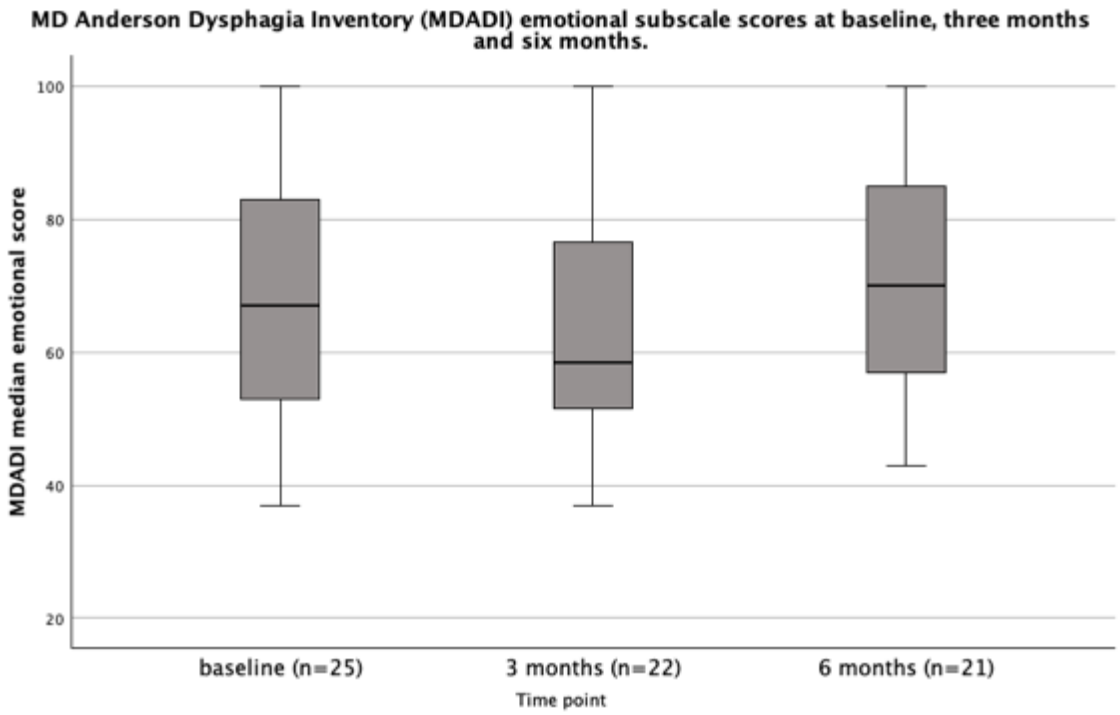


Figure 6-4: MD Anderson Dysphagia Inventory emotional subscale scores at baseline prior to treatment initiation, and three and six months following treatment initiation. Scores range from 20-100 where 20 is the worst possible score. At each timepoint the horizontal line represents the median, the box represents the interquartile range and the whiskers demonstrate the minimum and maximum values.

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6.3.3 MDADI physical scale

Figure 6-5 summarises the MDADI median physical composite scores.

At baseline, median physical score was 58 (IQR: 43-73), which deteriorated to 53 (IQR: 49-67) at three months and improved to 60 (IQR: 51-69) at six months. A number of outliers are noted at the six months, with three participants having demonstrated very high scores and one a very low score. A wide IQR was noted at all timepoints.

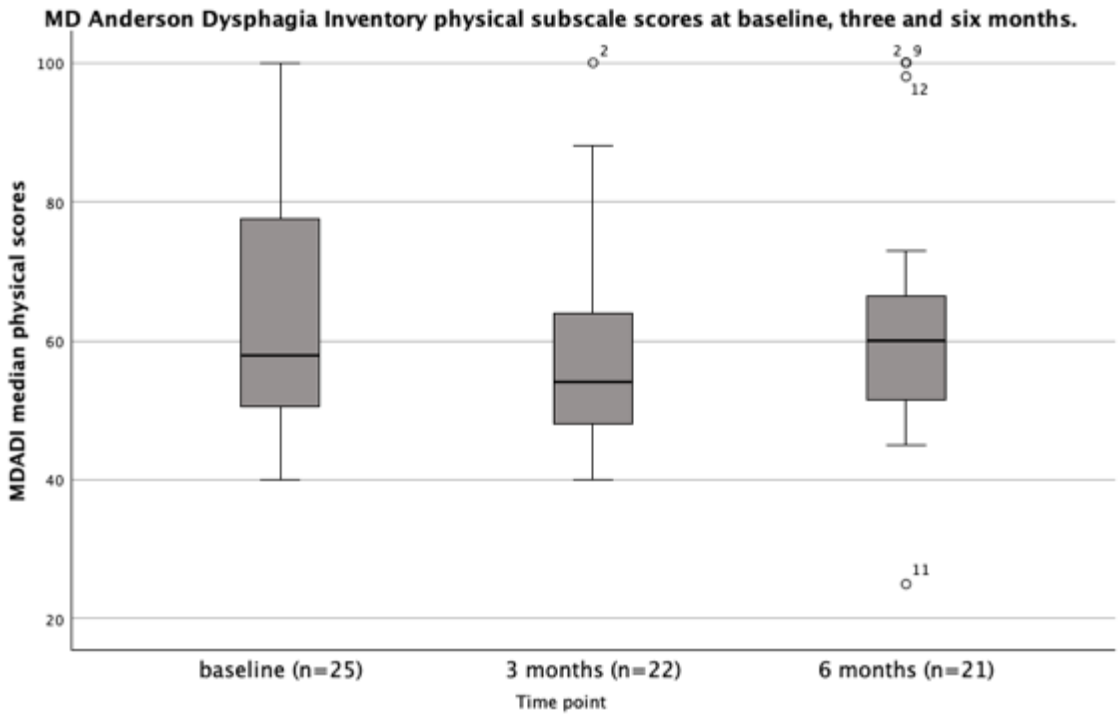


Figure 6-5 MD Anderson Dysphagia Inventory physical subscale scores at baseline prior to treatment initiation, and three and six months following treatment initiation. Scores range from 20-100 where 20 is the worst possible score. At each timepoint the horizontal line represents the median, the box represents the interquartile range and the whiskers demonstrate the minimum and maximum values. Outliers are marked with a o.

6.4 Secondary endpoints

6.4.1 University of Washington Quality of Life Questionnaire (UWQoLv4)

Twenty-five participants completed the UWQoLv4 questionnaire at baseline, 22 at three months and 21 at six months. Composite scores for the physical and social-emotional subscales were generated. Here 0 represents the worst possible score and 100 represents the best possible score. Symptom domain significance and patient prioritisation are reported in addition to a global QoL rating score across all three timepoints.

Physical composite scores

As per Figure 6-6 the median physical score was 68 (IQR: 58- 88) at baseline, 64 (IQR 41-80) at three months, and 63 (IQR 46- 78) at six months. A normative reference point is included in red. A mild deterioration in physical composite score is noted between baseline

and three months, and three months and six months. The median and IQR are summarised by treatment pathway for each timepoint in Table 6-5.

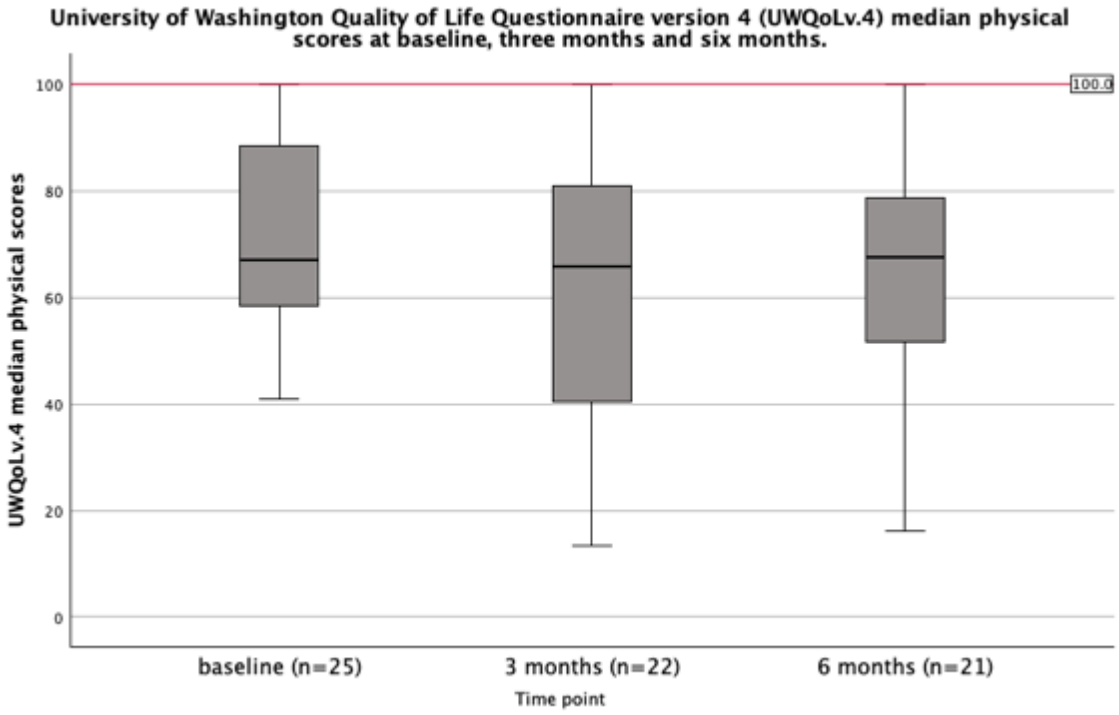


Figure 6-6: University of Washington quality of life questionnaire v.4 physical composite scores at baseline before treatment initiation, and three and six months following treatment initiation. The scale ranges from 0-100 where '0' is the worst possible functioning. At each timepoint the horizontal line represents the median, the box represents the interquartile range and the whiskers demonstrate the minimum and maximum values.

Table 6-5: University of Washington Quality of Life Questionnaire v.4 physical composite score by treatment pathway

		Baseline	Three months	Six months
Curative	Number of participants (n)	14	12	12
	Median physical composite score	70	64	68
	IQR	56- 84	42- 86	50-86
Non-curative	Number of participants (n)	11	10	9
	Median physical composite score	63	71	67
	IQR	49-77	56-86	57-77

Social-emotional composite scores

As per Figure 6-7 the median social-emotional score was 70 (IQR: 50-82) at baseline and remained stable at 70 (IQR 54.5-85) at three months and improved to 74 (IQR 58- 85) at six months. Normative reference is included in this figure in red. Social-emotional scores remain stable between three and six months with a mild increase at six months. The median and IQR are summarised by treatment pathway for each timepoint in Table 6-6. At all timepoints the social-emotional score was lower in the non-curative treatment group, however, had improved for both groups at six months.

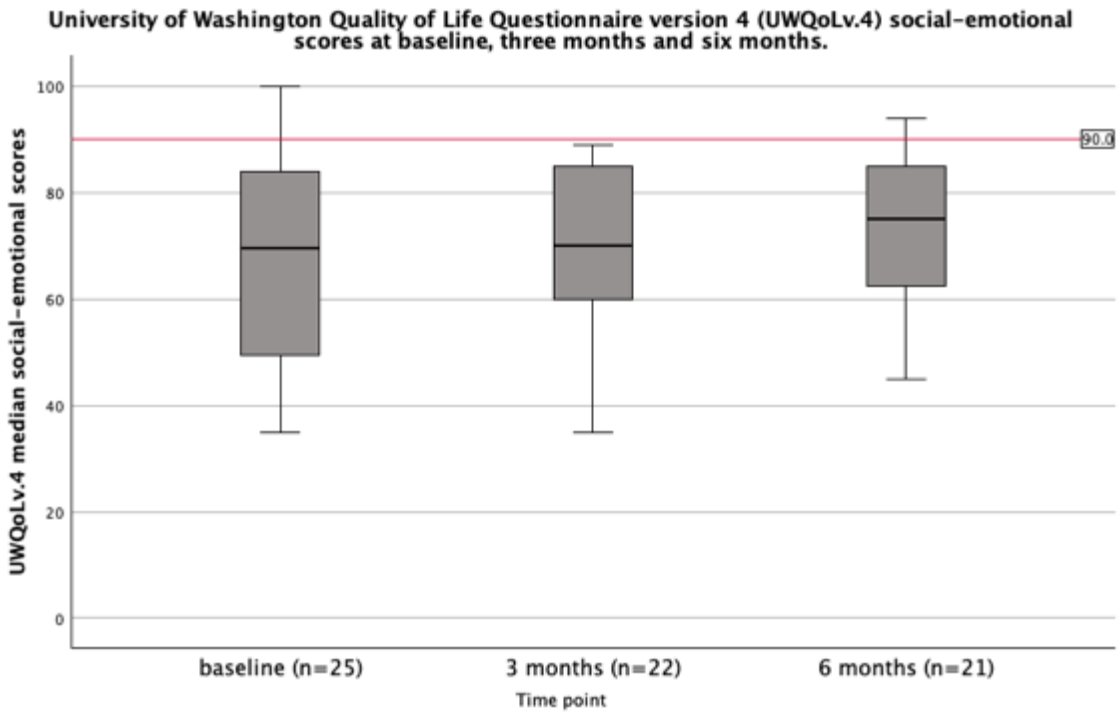


Figure 6-7: University of Washington Quality of Life Questionnaire v.4 physical composite scores at baseline before treatment initiation, and three and six months following treatment initiation. The scale ranges from 0-100 where '0' is the worst possible functioning. At each timepoint the horizontal line represents the median, the box represents the interquartile range and the whiskers demonstrate the minimum and maximum values.

Table 6-6: University of Washington Quality of Life Questionnaire v4 social-emotional composite score by treatment pathway

		Baseline	Three months	Six months
Curative	Number of participants (n)	14	12	12
	Median social-emotional composite score	80	77	83
	IQR	68- 92	67-87	75-91
Non-curative	Number of participants (n)	11	10	9
	Median social-emotional score	50	58	63
	IQR	34-66	44-72	49- 77

Symptom domain significance

The UWQoLv4 questionnaire includes a number of symptom domains, and the scoring guidance provides an algorithm to identify which symptoms are categorised as significant. The symptoms in relation to swallowing and communication (swallowing, chewing, saliva, taste, and speech) are presented in Table 6-7 in terms of the proportion of participants presenting with significant issues in these areas at baseline, three and six months. Swallowing, chewing, and saliva all increase in symptom significance over the three time points. Taste remains unchanged. Speech symptoms reach their peak at three months and then improve but do not return to baseline.

Table 6-7: University of Washington Quality of Life Questionnaire version 4 (UWQoLv4) functional symptom scale domain significance at baseline, three and six months.

UWQoLv4 domain	Time point	Number of participants (n)	Significant problem n (%)
Swallowing	Baseline	25	5 (20%)
	Three months	22	10 (45%)
	Six months	21	9 (43%)
Chewing	Baseline	25	3 (12%)
	Three months	22	5 (23%)
	Six months	21	5 (24%)
Saliva	Baseline	25	4 (16%)
	Three months	22	4 (18%) * x2 reported too much saliva
	Six months	21	5 (24%) * x1 reported too much saliva
Taste	Baseline	25	0
	Three months	22	1 (5%)
	Six months	21	0
Speech	Baseline	25	2 (8%)
	Three months	22	4 (18%)
	Six months	21	2(10%)

Prioritisation of patient selected physical and social functions.

Patients were offered the opportunity to report on the most important concerns for them in the preceding seven days. They were able to select three functions from 12 areas including swallowing and areas that impact eating and drinking such as chewing ability, presence of saliva and taste. Speech was also included. The most frequently reported concerns are summarised for the entire sample at all timepoints in Figures 6-8 - 6.10. At baseline prior to treatment initiation, pain, swallowing and mood were the three most frequently reported priority concerns. At three- and six-months following treatment initiation, swallowing, saliva, pain and speech are the most frequently reported concerns.

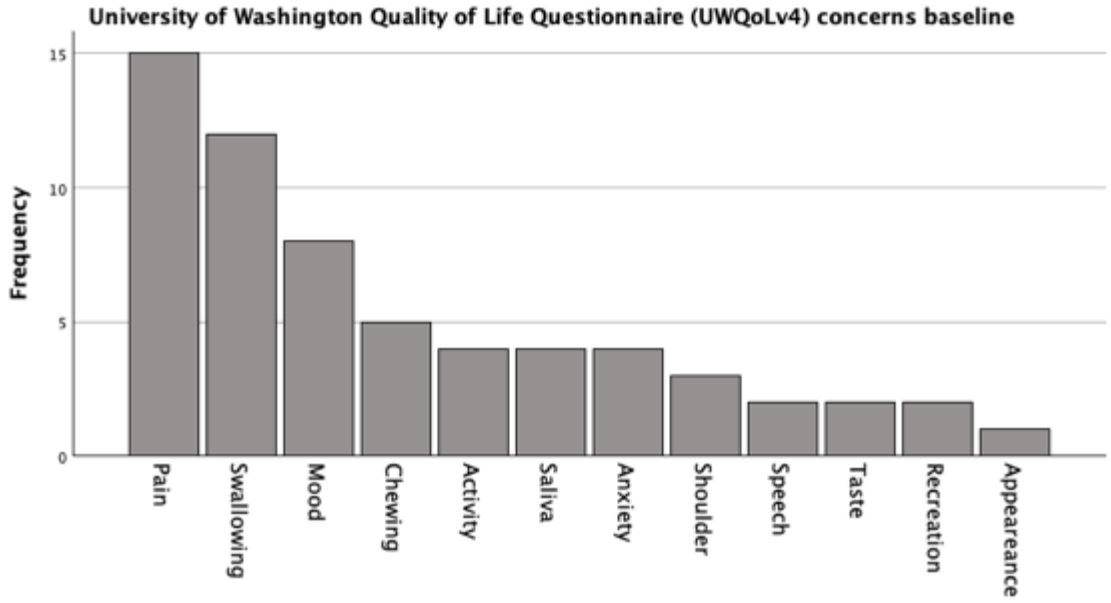


Figure 6-8: University of Washington Quality of Life Questionnaire version 4 (UWQoLv4) patient priority concerns at baseline

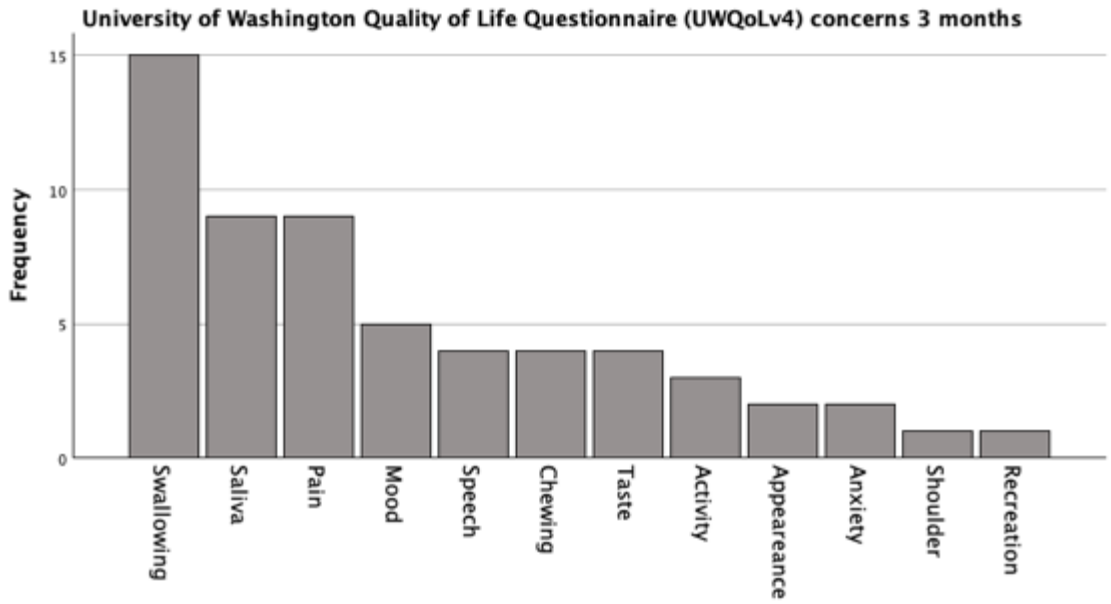


Figure 6-9: University of Washington Quality of Life Questionnaire version 4 (UWQoLv4)patient priority concerns at three months following treatment initiation.

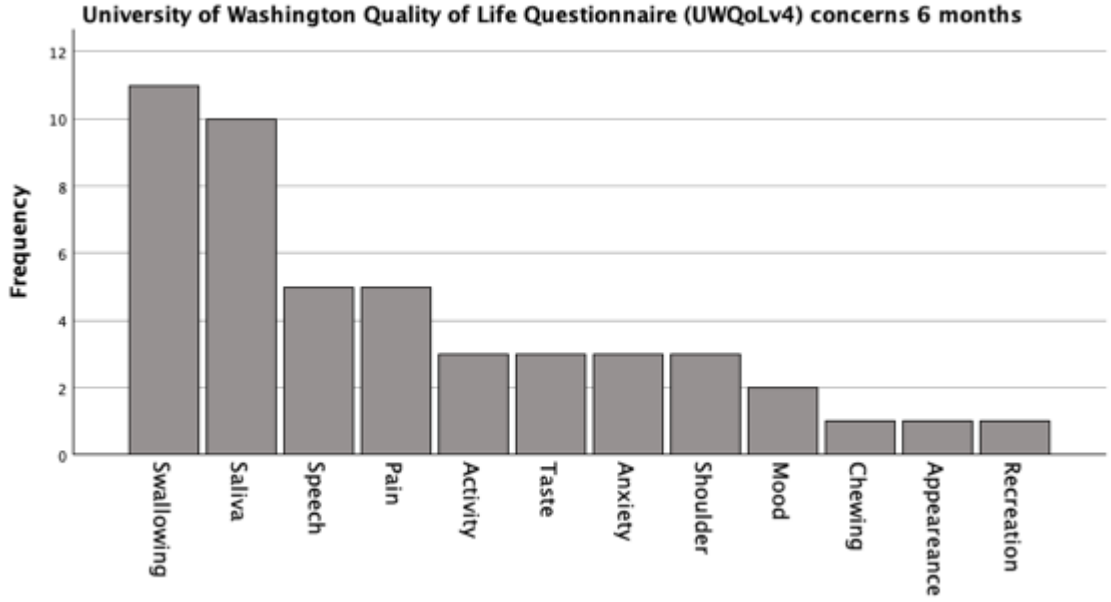


Figure 6-10: University of Washington Quality of Life Questionnaire version 4 (UWQoLv4) patient priority concerns at six months following treatment initiation.

Although numbers were small, differences were observed in priority concerns between curative and non-curative treatment groups as seen in Figures 6-11-6.13. In both groups the most frequently reported concern at baseline was pain. Second to this was swallowing for the curative group which was not rated by the non-curative group as a priority at this time point. At three- and six-months following treatment initiation, pain remained the top priority concern, however swallowing was the second most frequently reported priority concern in the non-curative group. Swallowing remained the top priority concern in the curative group, followed by pain at three and six months. A broader range of concerns is noted in the curative group at baseline and three months but by six months this appears to be more balanced across treatment groups.

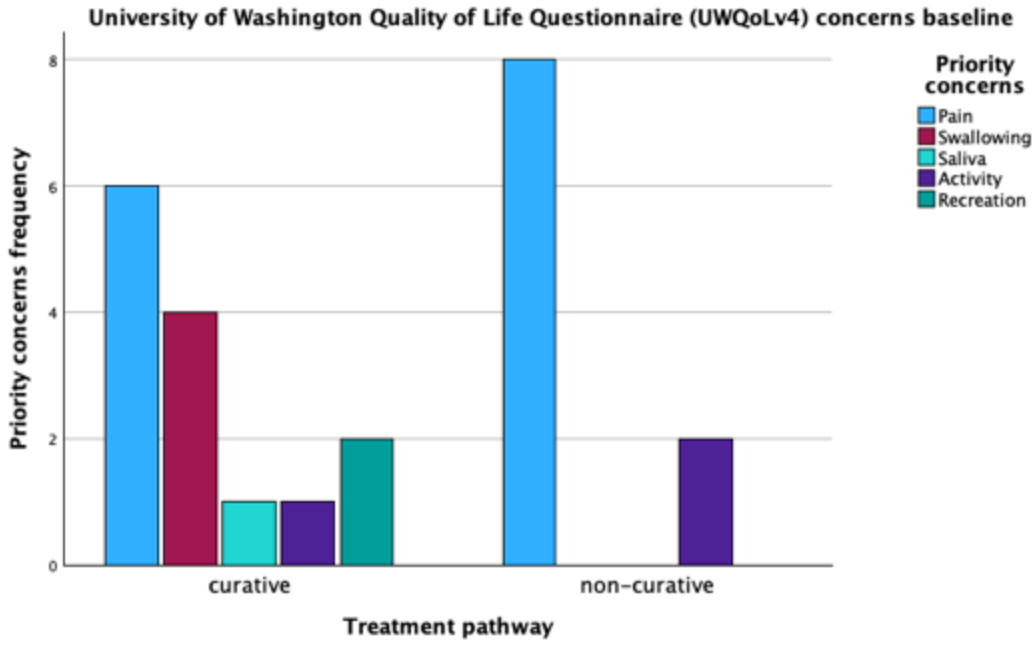


Figure 6-11: University of Washington Quality of Life Questionnaire version 4 (UWQoLv4) patient priority concerns at baseline for participants undergoing curative and non-curative treatment.

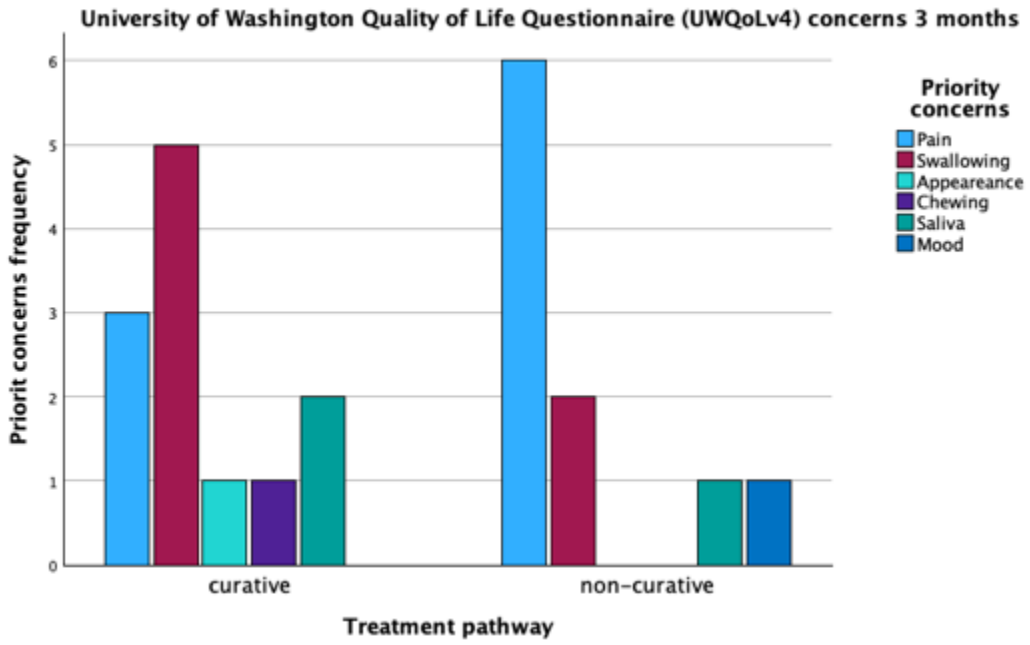


Figure 6-12: University of Washington Quality of Life Questionnaire version 4 (UWQoLv4)patient priority concerns at baseline for participants undergoing curative and non-curative treatment.

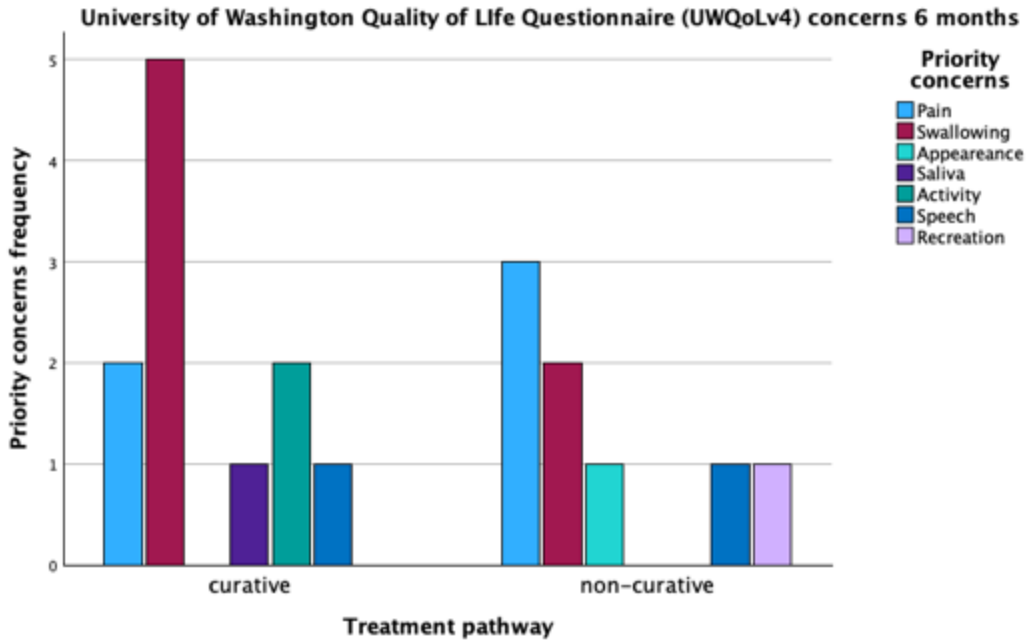


Figure 6-13: University of Washington Quality of Life Questionnaire version 4 (UWQoLv4)patient priority concerns at six months following treatment initiation for participants undergoing curative and non-curative treatment.

Health-related and global quality of life

Participants were given the opportunity to rate their overall health-related QoL in the preceding seven days. The score can range from 0 to 100 where 0 is the worst possible score and 100 is the best possible score.

Figure 6-14 summarises the QoL scores for the entire sample. At baseline a score of 60 (IQR 40-60) was noted, which deteriorated to 40 (IQR 20-60) at three months, returning to 60 (IQR 40-60) at six months.

Although small numbers, when the scores are presented by treatment pathway (curative and non-curative) stable QoL is noted across all three time points for the curative group (Table 6-8). In the non-curative group, there is a drop in QoL at 3 months returning to baseline at six months. Of note a wide range of scores is noted at the six-month mark for both treatment groups.

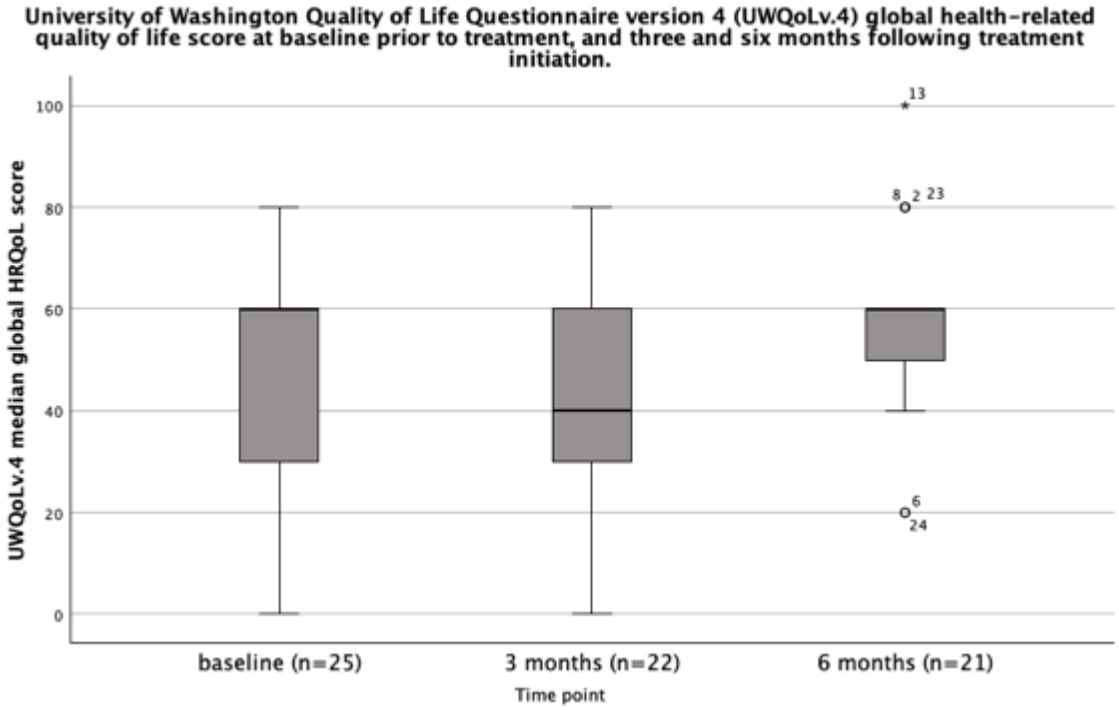


Figure 6-14: University of Washington Quality of Life Questionnaire Global Health Related QoL scoring for the entire sample across all three timepoints; at baseline prior to treatment, and three and six months post-treatment. At each timepoint the horizontal line represents the median, the box represents the interquartile range and the whiskers demonstrate the minimum and maximum values. Outliers are marked with a o.

Table 6-8: University of Washington Quality of Life- health-related QoL scoring by treatment pathway across all three timepoints.

		Baseline	Three months	Six months
Curative	Number of participants (n)	14	12	12
	Median global health related QoL score	60	60	60
	IQR	35-85	50-70	52-68
Non-curative	Number of participants (n)	11	10	9
	Median global health related QoL score	60	40	60
	IQR	40-80	20-60	40-80

6.4.2 Performance Status Scale for Head and Neck Cancer (PSS-HN).

Data for the three PSS-HN subscales, namely normalcy of diet, eating in public and understandability of speech are presented. In keeping with the original publication on the validation of the PSS-HN, the distribution of patient scores, as well as median scores for the three subscales will be presented in Tables 6-9 to 6-11.

PSS-HN Normalcy of Diet (NoD)

Normalcy of Diet (NoD) scores are summarised in Table 6-9 for the sample and by treatment group. At baseline there were three participants who were unable to eat/drink prior to commencing treatment, this increased to six at three months and reduced to five at six months following treatment initiation. Increased diet modification was noted across treatment groups, with an increase in participants requiring pureed/ non-chew diet from two at baseline to seven at six months. Of note although five participants in the curative group were managing a regular diet at six months, there were no participants in the non-curative group managing a regular diet at six months post-treatment. However, this is not a consistent cohort as there was sample attrition across the timepoints.

Table 6-9: Performance Status Scale for Head and Neck Cancer (PSS-HN) Normalcy of Diet (NoD) frequency and median scores at baseline, three months and six months.

Timepoint		**Baseline**			**3 months**			**6 months**		
Score	Description	Curative (n= 14)	Non-curative (n=11)	**Total (n= 25)**	Curative (n=13)	Non curative (n=10)	**Total (n=23)**	Curative (n=13)	Non-curative (n=8)	**Total (n=21)**
100	Full diet (no restrictions)	1	0	**1**	1	0	**2**	1	1	**2**
90	Full diet (liquid assist)	4	3	**7**	2	1	**3**	4	0	**4**
80	All meats	1	0	**1**			**0**			**0**
70	Carrots, celery			**0**			**0**			**0**
60	Dry bread and crackers	1	1	**2**			**0**			**0**
50	Soft chewable foods	4	4	**8**	3	4	**7**	0	1	**1**
40	Soft foods requiring no chewing			**1**	1	0	**1**	2	3	**5**
30	Pureed foods	1	1	**1**	1	1	**2**	1	1	**2**
20	Warm liquids	1		**1**	1	0	**1**			**0**
10	Cold liquids			**0**	2	0	**2**	2	0	**2**
0	Non-oral feeding only	1	2	**3**	2	4	**6**	3	2	**5**
Median		**50**			**40**			**40**		

PSS-HN Eating in Public (EiP)

The majority (two-thirds) of participants had some level of restriction in eating in public at baseline. The degree of restriction heightened in both curative and non-curative groups, with more participants eating alone by six months. This eating in public findings for the entire sample at all time points and by treatment pathway are summarised in Table 6-10.

Table 6-10: Performance Status Scale for Head and Neck Cancer (PSS-HN) Eating in Public (EiP) frequency and median scores at baseline, three and six months.

Timepoint		**Baseline (n=25)**			**3 months (n=23)**			**6 months (n=21)**		
Score	Description	Curative (n= 14)	Non-curative (n=11)	**Total**	Curative (n= 13)	Non-curative (n=10)	**Total (n)**	Curative (n= 13)	Non-curative (n=8)	**Total**
100	No restriction of place, food or companion	1	2	**3**	3	0	**3**	4	1	**5**
75	No restriction in place but restricts diet when in public	5	2	**7**	2	2	**4**	3	2	**5**
50	Eats only in the presence of selected persons in selected places	2	1	**3**	3	1	**4**	1	0	**1**
25	Eats only at home in the presence of familiar persons	2	4	**6**	2	4	**6**	1	2	**3**
0	Always eats alone	1	2	**3**	3	3	**6**	4	3	**7**
Median		**75**			**50**			**25**		

PSS-HN Understandability of Speech (UoS)

Understandability of Speech decreased over time. At baseline 24/25 of the entire sample were fully intelligible and this decreased to 16/23 and 21/21 at three months and six months respectively. Similar reduction in UoS was noted in both curative and non-curative groups. UoS scores are summarised for the entire sample and by treatment pathway in Table 6-11.

Table 6-11: Performance Status Scale for Head and Neck Cancer (PSS-HN) Understandability of Speech (UoS) frequency and median at baseline, three and six months

Timepoint		**Baseline**			**3 months**			**6 months**		
Score	Description	Curative (n= 14)	Non-curative (n=11)	**Total**	Curative (n= 13)	Non-curative (n=10)	**Total (n)**	Curative (n= 13)	Non-curative (n=8)	**Total**
100	Always understandable	23	1	**24**	9	7	**16**	7	5	**12**
75	Understandable most of the time occasional repetition necessary	0	0	**0**	0	2	**2**	3	1	**4**
50	Usually understandable; face-to-face contact necessary	0	0	**0**	2	3	**0**	2	1	**3**
25	Difficult to understand	0	0	**0**	0			1	1	**2**
0	Never understandable; may use written communication	0	1	**0**	1	1	**2**	0	0	**0**
Median		**100**			**100**			**100**		

6.4.3 International Dysphagia Diet Standardisation Initiative Functional Diet Scale (IDDSI-FDS)

The IDDSI Functional Diet Scale (FDS) aims to classifies dysphagia severity according to the degree of diet limitation. The scale ranges from 0-8 where 0 corresponds to nil by mouth and 8 corresponds to regular diet and fluids. Lower numbered scores on the IDDSI-FDS reflect greater diet texture restriction. At baseline the median IDDSI-FDS was 7 (Range 0-8) which reduced to 6 (range 0-8) at three and six months. IDDSI-FDS scores for the sample and by treatment pathway are summarised in Table 6-12.

Table 6-12: International Dysphagia Diet Standardisation Initiative Functional Diet Scale (IDDSI-FDS)

Timepoint	**Baseline**			**3 months**			**6 months**		
Score	Curative (n= 14)	Non-curative (n=11)	**Total (n= 25)**	Curative (n=13)	Non curative (n=10)	**Total (n= 23)**	Curative (n=13)	Non-curative (n=8)	**Total (n=21)**
0	0	2	**2**	3	2	**5**	3	1	**4**
1	1	2	**3**	1	2	**3**	1	2	**3**
2									
3	1	0	**1**	1	0	**1**	1	0	**1**
4									
5	1	0	**1**	2	1	**3**	1	0	**1**
6	2	2	**4**	3	2	**5**	2	2	**4**
7	0	2	**2**	0	2	**2**	0	2	**2**
8	5	1	**6**	3	1	**4**	5	1	**6**
Median	**7**			**6**			**6**		

6.4.4 Gastrostomy tube usage

Gastrostomy tube usage is summarised in Figure 6-15. Gastrostomy tube usage was observed to increase for the entire sample at three months, remain stable at six months for the non-curative group but decrease for the curative group.

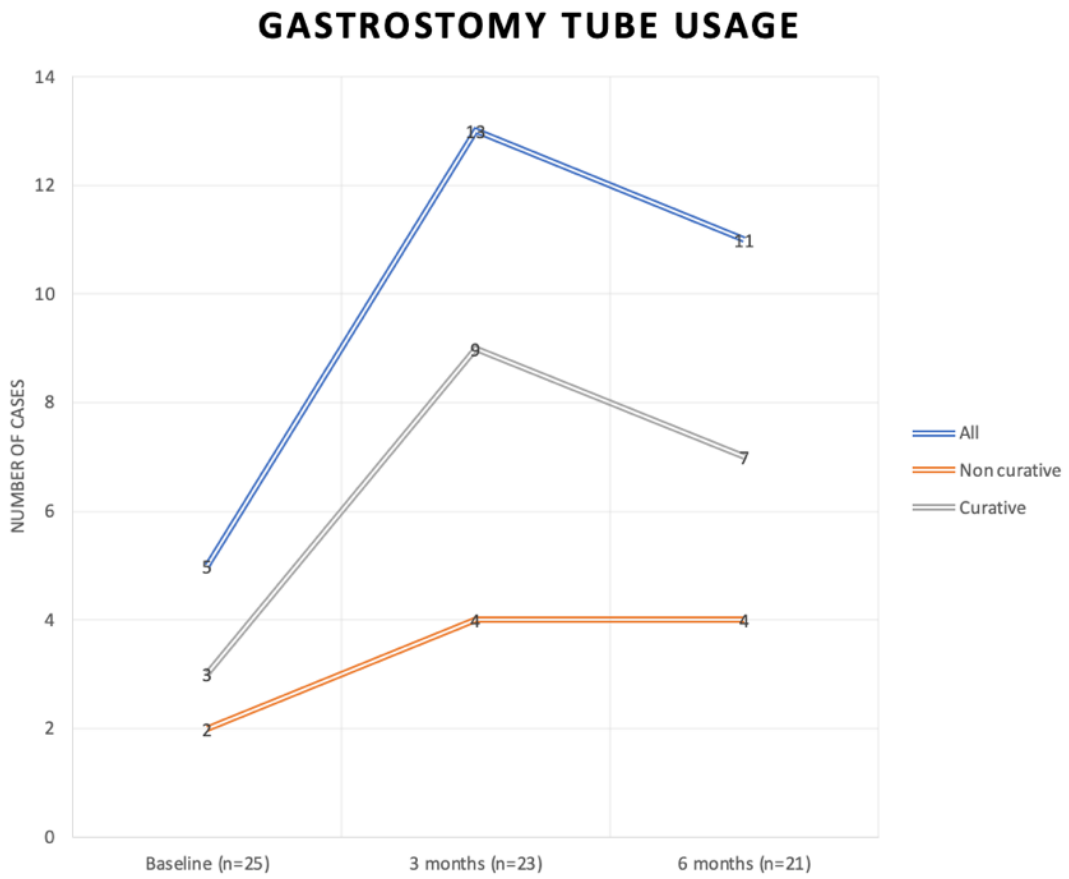


Figure 6-15: Gastrostomy tube usage at baseline, three and six months. The blue line represents the sample, and the grey and orange line represent the curative and non-curative treatment group participants.

6.4.5 100 mL Water Swallow Test (100 mL WST)

Patients were asked to drink 100 mL of water as quickly as is comfortably possible as described in appendix 4. Swallowing performance was measured using swallow capacity, which is the number of millilitres swallowed divided by the time taken to swallow it. The test was not performed if the patient reported or was observed coughing/ choking on fluids, in which case it was scored as zero for swallow capacity. If the participant presented as nil by mouth at baseline, the test was not completed.

At baseline, it was deemed safe and possible to carry out the 100 mL water swallow test in 17/25 participants (n= 6 clinically unsafe, n=1 laryngectomy, n=1 telephone review only). At three months, it was deemed safe and possible to carry out the 100 mL water swallow test in 5/23 participants (n= 14 clinically unsafe, n=2 laryngectomy, n=1 telephone review only). At six months it was deemed safe and possible to carry out the 100 mL water swallow test in 5/21 participants (n= 14 clinically unsafe, n=1 laryngectomy, n=1 telephone review only). The median swallowing capacity at baseline was 9.75ml/seconds (IQR 6.2-16.3), 16.6 (IQR 13.25- 33.15) at three months, and 17.92 (IQR 12-33.15) at six months. As seen in Figure 6-16, the median swallow capacity findings are above the reference line for healthy females at 12.3 and healthy males at 18.7 within similar age groups.

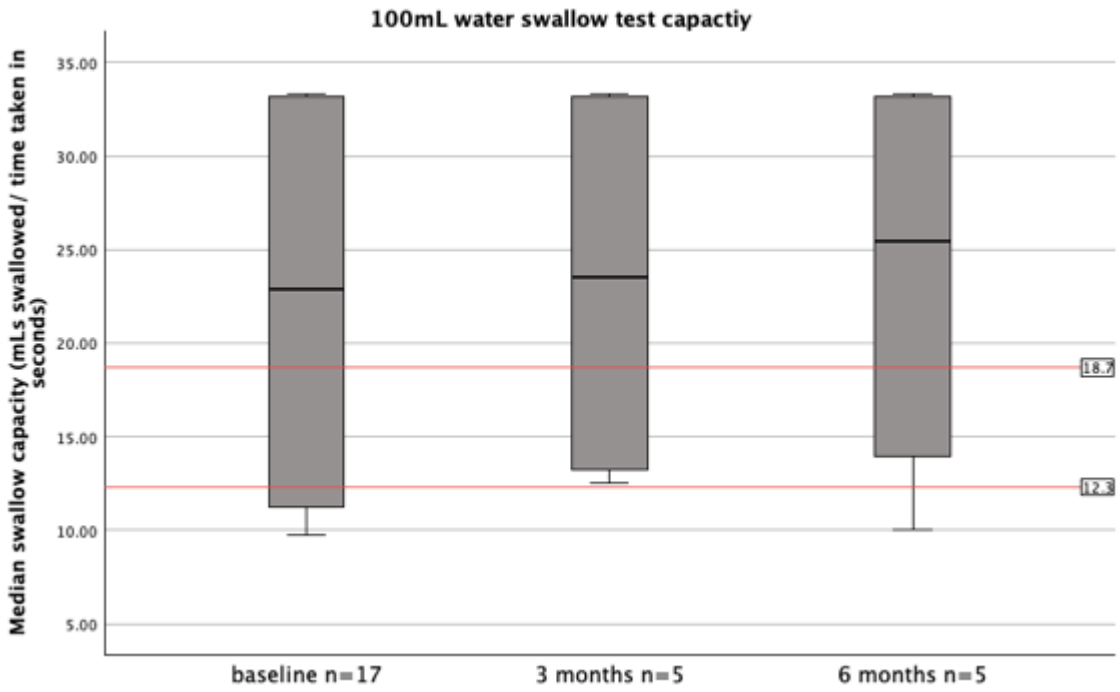


Figure 6-16: 100 mL Water Swallow Test capacity at baseline prior to treatment initiation, three- and six-months post-treatment initiation. Red lines indicate the female normative reference at 12.3 and the male normative reference at 18.7. At each timepoint the horizontal line represents the median, the box represents the interquartile range and the whiskers demonstrate the minimum and maximum values.

6.4.6 Flexible Endoscopic Evaluation of Swallowing (FEES)

Instrumental evaluation of swallowing was carried out using Flexible Endoscopic Evaluation of Swallowing (FEES) see appendix 6. The Dynamic Imaging Grade of Swallowing Toxicity (DIGEST) was used as the outcome measure to quantify the FEES findings. The DIGEST summary score is rated from 0- 4 where 0= no dysphagia, 1= mild dysphagia, 2 =moderate dysphagia, 3= severe dysphagia and 4= life threatening dysphagia (Starmer et al., 2021). Given that FEES was an optional requirement in this study, and remote follow up also optional/ essential for PIC sites, the FEES data for this study is incomplete. At baseline, FEES data was collected in 11/25 patients, at three months 4/22 at 3 months, and 6/21 at six months.

Of those participants who underwent FEES at baseline, 5/14 presented with severe dysphagia (DIGEST: 4), 2/14 presented with moderate dysphagia (DIGEST: 3), 2/14 had

mild dysphagia (DIGEST 2) and 2/14 had no dysphagia (DIGEST: 0). Of those participants who underwent FEES at three months (n=4), 2 had profound/ life threatening dysphagia (DIGEST: 4) and 2 had severe dysphagia (DIGEST: 3). At six months of the six participants who underwent FEES, 4/6 had severe dysphagia (DIGEST: 3), one had profound/ life threatening dysphagia (DIGEST: 4), and one had moderate dysphagia (DIGEST: 2).

6.4.7 Chicago Priority Scale (CPS)

The Chicago Priority Scale (CPS) (Sharp et al., 1999) rates patient treatment-related priorities from a rating of 1 (most important) to 12 (least important). The CPS was completed by 24/25 participants at baseline and 20/21 at six months. One participant declined to fill out this questionnaire at both timepoints. Priority ratings at baseline and six months for the sample are summarised in Figure 6-17 and by treatment group in figure 6-18. Being cured of cancer, living as long as possible and pain were the top three priorities at baseline and six months both within and across treatment pathways.

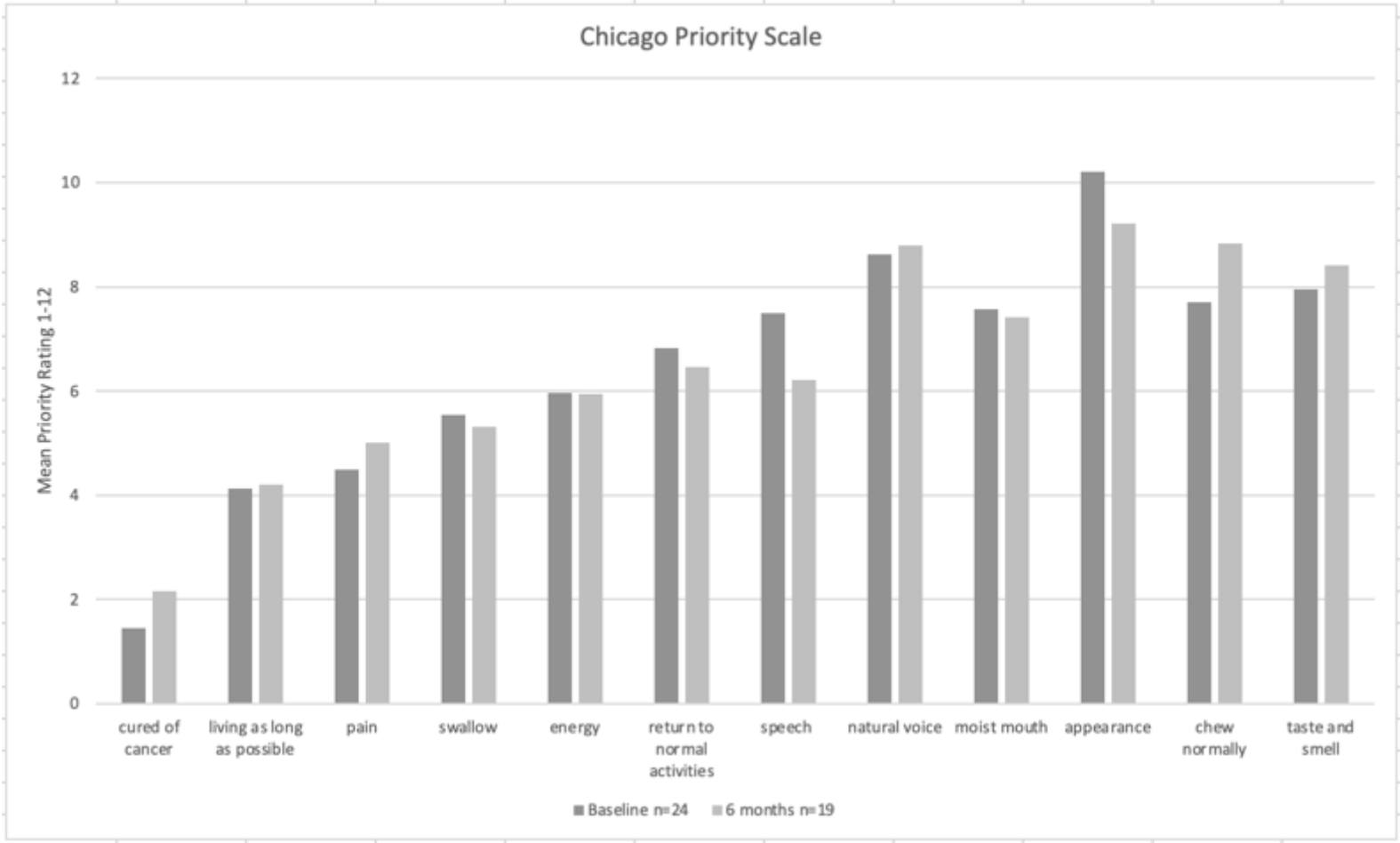


Figure 6-17: Chicago Priority Scale (CPS) priority ratings at baseline and six months. Participants rated priorities from 1-12 where 1 was the most important and 12 was the least important.

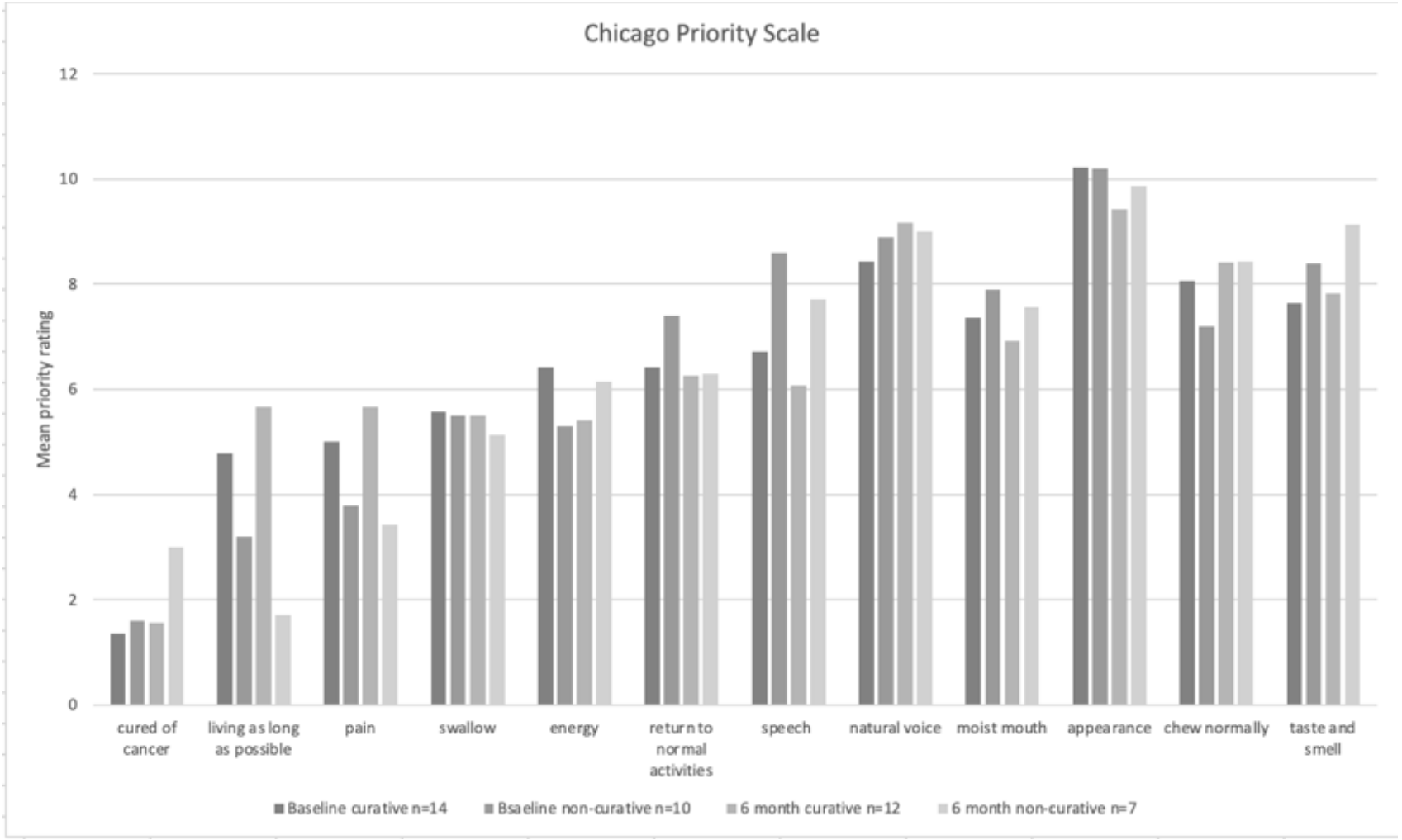


Figure 6-18: Chicago Priority Scale (CPS) priority ratings at baseline and six months by treatment pathway. Participants rated priorities from 1-12 where 1 was the most important and 12 was the least important.

6.5 Discussion

The aim of the quantitative workstream of this mixed methods research was to answer the following research question 'what are the functional (speech and swallow) and QoL outcomes, and concerns and priorities, for patients undergoing treatment for rOPC?'. The aim was to describe the swallowing, communication and QoL profile and patient priorities for adults with rOPC undergoing treatment both before and after treatment initiation, and to compare these time points.

Twenty-five patients participated in this study. There was some attrition of participants due to the disease process, and there were some incomplete data sets which were detailed in Table 6.1.

The key findings from this study were that swallowing was less than optimal, and QoL was impaired at baseline prior to treatment initiation for the participants in this study. Clinician-rated measures of swallowing and speech function show a deterioration over time; however, this is not reflected in the findings from the patient-reported swallowing-related QoL tool used in this study. Concerns regarding function -related symptoms do change over time, with swallowing becoming more of a priority from baseline to three and six months. Overall, QoL for the participants in this study did not change greatly from baseline prior to treatment initiation, to six months following treatment initiation. Being cured of their cancer and living as long as possible were the main priorities for participants in this study at all timepoints.

6.5.1 Swallowing outcomes

The MDADI was the primary endpoint for this workstream. The purpose of the MDADI, as per the original developers of this tool, is to assess how dysphagia affects the QoL of patients with HNC (Chen et al., 2001). The tool includes three constructs including swallowing (or difficulty swallowing/ dysphagia), eating, and the impact on various aspects of life caused by swallowing or eating difficulties. The three constructs are included in the

overall composite score, which is calculated from 19 separate items and includes three subscales: emotional, functional and physical. Guidance has been published on the classification of MDADI composite scores as optimal (≥80), adequate (≥60-<80) and poor (<60) (Goepfert et al., 2017). For the participants in this study, swallowing-related QoL was found to be just within the adequate bracket prior to treatment initiation, based on the median composite scores recorded. The median composite score deteriorated to a level of swallowing function categorised as poor at three months, with subsequent recovery thereafter back to the baseline level of swallowing function at six months following treatment initiation. The deterioration at three months did not meet the criteria for a clinically significant change using the previously published reference of 10-point change (Hutcheson et al., 2016). However, the study used to identify this 10-point clinically significant difference excluded patients with recurrent HNC.

The MDADI subscales, namely the emotional, physical and functional also show little overall change in the sample from baseline to six months. At all three time points the functional subscale demonstrated adequate functioning for the sample and remained unchanged from baseline to six months with a non-clinically significant deterioration at three months. The emotional score demonstrated adequate functioning at baseline, with a clinically significant decrease in functioning at three months to a poor level of functioning, with a return to baseline functioning at six months following treatment initiation. The physical subscale demonstrated poor swallowing at baseline. A clinically significant increase from baseline to three months (10-point increase) was noted, with a return to baseline by six months (poor functioning). Of note the physical subscale contains all 4 items in the questionnaire which relate to the swallowing construct.

When these data are compared to MDADI data reported in the systematic review in Chapter 3, although only surgical studies were identified, the results are similar. Where baseline levels of swallowing function were reported using the MDADI, adequate functioning

(composite score ≥60-<80) was reported at baseline (Williamson et al., 2021, D'Andréa et al., 2022). No clinically significant differences in pre- and post- surgery MDADI composite scores were noted in the two surgical trials reporting longitudinal data (Williamson et al., 2021, D'Andréa et al., 2022). Little guidance in the literature is provided on how to interpret the MDADI subscale scores. Although the MDADI is widely used in HNC trials as either a primary or secondary endpoint in the primary disease literature, the composite score is the most frequently reported measure (Toft et al., 2024).

Swallowing outcomes were also assessed using clinician-reported measures of swallowing function, namely the PSS- HN and the International IDDSI-FDS. Some discordance was noted between the MDADI patient reported scores and the PSS-HN clinician-rated scores. The PSS-HN normalcy of diet subscale and the IDDSI-FDS demonstrated a deterioration in diet scores with a greater proportion of participants requiring diet modification or nil by mouth status following treatment initiation, with a peak in deterioration at three months. However, by six months, there does appear to be a change in functional status again, with more participants managing a regular diet (with or without a liquid assist) at six months in comparison to three months, signalling some recovery of function but not a complete return to baseline level of functioning. The PSS-HN EiP scores show greater restriction in eating in public over time with a peak in restriction at three months, although restrictions persist at three months, there does appear to be some improvement by six months, but not returning back to baseline level of functioning. In relation to the systematic review findings reported in Chapter 3, the review contained only one small study (n=3) where PSS-HN NOD and EiP outcomes were reported (Charters et al., 2022). Here an increase in diet modification and restrictions in eating in public were also reported.

Gastrostomy tube usage findings appeared to follow a similar pattern to the PSS-HN NOD data and IDDSI-FDS findings, with a peak in usage at three months, followed by a reduction in use at six months, but not back to baseline level of gastrostomy use. The systematic review findings in Chapter 3 reported long term gastrostomy dependence (six months or

more post-treatment initiation) of approximately a quarter of patients (n=128). In this study, gastrostomy feeding tube use at six months was just over double this at just over 50%. Although participant numbers are small, this may be explained by the inclusion of patients who had non-curative treatment. Although there was a reduction in G-tube usage for the curative treatment group from three to six months, this reduction in use was not mirrored by the non-curative treatment group in this workstream.

A possible explanation for the discrepancy between the patient reported MDADI findings and the clinician rated PSS data, IDDSI-FDS data and gastrostomy data, may be that in recent literature the content validity for the MDADI has been questioned, in particular for specific subgroups of HNC who have more severe dysphagia and are nil by mouth and dependent on tube feeding due to their dysphagia (Toft et al., 2024). We know from the gastrostomy data that by six months half of the sample had a gastrostomy and coupled with the PSS data we know that > 20% of the overall sample were nil by mouth at three and six months. The topic of dysphagia severity is also very relevant to the findings in relation to the 100 mL water swallow test. Unfortunately, the follow up data for the 100 mL water swallow test is greatly lacking as the majority of study participants did not fulfil the criteria for this assessment based on safety concerns regarding coughing/ choking. Interestingly those who did meet the criteria demonstrated median scores greater than the published normative data. In the setting of more severe dysphagia, perhaps this test in its current form may not be the most suitable for this patient group.

6.5.2 Communication outcomes

Communication outcomes were measured using the PSS- HN understandability of speech (UoS) subscale. Information on speech outcomes was also obtained using the UWQoLv4 symptom domain prioritisation. The PSS-HN UoS, suggest that the majority of the cohort are fully intelligible at baseline prior to treatment initiation. The proportion of participants who are fully intelligible decreases over time and this was observed in both patients undergoing

curative and non-curative treatment. The UWQoLv4 symptom domain profile also suggests that for some participants, speech does become more of a significant issue over time, in particular at three months. The findings of the systematic review discussed in Chapter 3 in relation to communication outcomes are very limited, with just one paper reporting the PSS-HN UoS outcomes. This study included just three surgical patients and no baseline data are provided, but it does report ongoing impairments of speech at 12 months post-surgery. What is surprising in the data from this workstream is that understandability of speech appears to reduce in both curative and non-curative treatment groups, and this cannot be attributed to anatomical changes with surgery alone.

6.5.3 Patient reported quality of life (QoL)

Changes in QoL for participants were recorded in this workstream using the University of Washington quality of life questionnaire version 4 (Rogers et al., 2010a). Guidance in relation to reporting the UWQoLv4 findings advises that the composite scores of the two included subscales should be reported, namely the physical subscale and the social-emotional subscale. The scales range from 0-100 where 0 represents the worst possible score and 100 represents the best possible score. The scoring guidelines categorise changes in scores over time as a 'small' difference (4 subscale units), a 'moderate' difference (10 subscale units) and a 'large' difference (16 subscale units) (Rogers et al., 2010a). Composite scores for both subscales were below normative reference points, signalling impaired QoL at all timepoints for the sample.

In relation to the physical subscale, a mild deterioration in QoL was noted from baseline to three months and again a further mild deterioration from three months to six months. Although similar physical composite scores were noted across treatment pathways for the curative and non-curative treatment groups, the trajectory of change was different. Whereas the curative treatment group experienced a mild deterioration from baseline to three months, the non-curative treatment group experienced a mild improvement. The curative treatment

group then experienced a mild improvement by six months, and a mild deterioration was noted for the non-curative treatment group.

With the social-emotional subscale, stable scores were noted from baseline to three months with a mild improvement noted at six months for the sample. Overall, the social-emotional score was lower at all timepoints for the patients undergoing non-curative treatment pathway. Again, the trajectory for change for both treatment groups was different, with an initial deterioration for the curative group followed by an improvement, whereas the non-curative group experienced a gradual improvement over the three time points.

In relation to the systematic review reported in Chapter 3, the results are comparable with overall stable QoL. However, one caveat with this is that the one study which used the UWQoLv4 questionnaire had a very small sample (n=3). In a larger study by Andre et al using a different measure of QoL, non-significant changes in QoL are reported from baseline to 1 year following surgical management. As previously noted, the systematic review did not identify any studies reporting quality of life outcomes specific to rOPC.

6.5.4 Patient concerns and priorities

To assess patient treatment related priorities and any potential change over time, participants were asked to complete the CPS at baseline prior to treatment initiation and again at six months following treatment initiation. Here participants were asked to rate the relative importance of 12 treatment goals on an ordinal scale from one to twelve, where one was the most important and twelve the least. There was no change in ranking between baseline prior to treatment initiation and six months after treatment initiation. “Being cured of cancer”, “living as long as possible” being “pain free” remained the key priorities for patients with rOPC. Priorities were similar for patients treated curatively and non-curatively.

Participant concerns regarding symptoms were also collected using the UWQoLv4. These findings demonstrated that unlike treatment-related priorities, concerns regarding symptoms did change over time for the participants in this study. For the entire sample, at baseline prior to treatment initiation pain was the top priority concern for participants, followed by swallowing and mood. At three- and six-months following treatment initiation, swallowing became the top priority concern followed by, saliva, pain and speech. A possible explanation over time for the change in concern may be symptoms only become a concern if and when they are experienced. The PSS-HN data show that swallowing and speech do change over time for this patient group, with speech and swallowing becoming more troublesome following treatment initiation. However, instead of having anticipatory concerns regarding symptoms, concerns about specific symptoms only arise as these symptoms present.

6.6 Critique

This workstream used a prospective design which minimised recall bias and allowed the research to be planned according to the needs of the clinical population and in order to answer the key research questions. Although the data analysis was descriptive it was predefined, and a sample size was calculated prior to recruitment. This workstream was developed in partnership with a patient and public involvement/ engagement (PPI/E) group.

6.6.1 Power

Prior to recruitment and data collection a sample size calculation was carried out. The sample size calculation was based on the primary endpoint for the observational quantitative workstream i.e., change in patient-reported swallowing-related QoL, using the MDADI, from baseline to 6 months following treatment initiation. Using pilot data collected previously at the research site, with a two-sided alpha of 5% and 80% power a total of 25 participants were required to complete the paired questionnaires at baseline and 6 months + 10% to cover drop out. Although 25 participants were recruited and enrolled with baseline data

collection, the planned additional 10% was not recruited, due to attrition, the study was underpowered to allow for statistical analysis. This limited the findings to be descriptive only. The heterogeneity of the outcomes recorded across the outcome measures used, demonstrated that further work is required with a larger sample to be able to make clearer judgements about which tools are the most appropriate for this population of patients and to allow for statistical analysis using the appropriate tools. However, patients with rOPC are an underrepresented population in the current literature base, in particular in relation to function and QoL outcome measurement. This study has started to explore in more detail key patient-centred issues around function, and patient priorities and concerns.

6.6.2 Multi-centre

Although every effort was made to open up PICs for this study, during the time constraints of the study, only one other site opened. The lack of participants across multiple sites in this study is a limitation. Further studies would benefit from being multi-centre and international in order to capture a wider range of presentations. No patients undergoing re-irradiation were recruited.

6.6.3 Incomplete data and sample attrition

The fact that the use of FEES was optional and remote follow up consultation was optional for participants in this study was a limitation in this study as this resulted in poor follow up data in terms of instrumental evaluation of swallowing outcomes. Inter-rater reliability testing for FEES was also not included.

The 100mL WST data was also limited. Participants who scored zero were excluded from the analysis, which might have reduced its clinical utility in this study – future studies should include this, as well as conducting the test on people with a laryngectomy.

Overall, there was attrition of the sample due to the course of the disease.

6.7 Conclusion and implications

The aim of this workstream was to investigate function, QoL and patient priorities over time for patients with a diagnosis of rOPC. To measure changes to function a range of patient-reported and clinician-rated measures were used.

Patient-reported swallowing-related QoL measured using the MDADI demonstrated impaired swallowing at baseline prior to treatment initiation, and no clinically significant changes in swallowing from baseline prior to treatment initiation to six months following treatment initiation. Clinician-rated measures did show a deterioration in swallowing function with increased need for diet modification, gastrostomy tubes and increased restrictions in eating/ drinking in public. This change was noted irrespective of treatment pathway.

Only mild changes in patient-reported QoL were observed over time. A mild deterioration was noted in physical component scores and a mild improvement overall was noted in the social-emotional aspect of QoL between baseline and six months post-treatment. Symptoms and their significance in relation to speech and swallowing function did increase over time for participants. Further investigation and triangulation with qualitative data is required to see if there is any evidence of response shift or recalibration regarding QoL over time.

In relation to treatment-related priorities, these did not change over time. Being cured of cancer and living as long as possible were the key priorities for participants at baseline and six months following treatment initiation. Level of concern regarding specific functional symptoms did change over time, which appeared to be in keeping with the onset/ deterioration in such functions.

6.8 Summary

This chapter has outlined the findings from the quantitative workstream of the mixed methods study. Chapter 7 will integrate the quantitative findings presented in this chapter

with the qualitative findings presented in Chapter 5. Integrated findings will form the key results from this research.

Chapter 7 Integration

The aim of this mixed methods study was to identify and explore function (swallowing and communication) and QoL outcomes, patient priorities and patient and carer experiences of rOPC over time, including diagnosis, treatment decision-making and living with the consequences of treatment.

A convergent, mixed methods study design was undertaken, which included both a longitudinal qualitative interview workstream investigating patient and carer experience, and an observational repeated measures quantitative workstream measuring change in swallowing, communication, and QoL outcomes and patient priorities over time. Chapter 5 included an in-depth description of the findings from the qualitative workstream and Chapter 6 focused on the findings of the quantitative workstream. As a mixed methods study, integration of the quantitative and qualitative aspects is planned at the stages of design, methods and interpretation to enhance the results gained and maximise the advantages of both quantitative and qualitative data (Fetters et al., 2013). The ultimate goal of mixed methods research is that the combined findings of the quantitative and qualitative data will yield results which are greater than the sum of the two individual parts (Creswell and Clark, 2017). This chapter will focus on the overall findings of the mixed methods study including the integration of the qualitative and quantitative.

The objective of this mixed methods study was to identify function (swallowing and communication) and QoL outcomes, concerns and priorities and patient and carer experience of diagnosis, treatment decision-making and living with the consequences of treatment. The combined findings of the qualitative and quantitative workstreams will be presented to address this objective, by integrating data collected for two timepoints- at baseline prior to treatment initiation, and six months and beyond after treatment initiation. The integration across these two time points will include both the findings from the

participants recruited prospectively (quantitative and qualitative data) and retrospectively (qualitative data only). The qualitative findings include both patient and carer experience data.

The integration involved a review of the inferences made from the qualitative findings and the quantitative findings at timepoints one and two, and a merging of these inferences together to develop meta inferences (Younas et al 2023) in relation to the overall aims of the study. The integration, inference and meta inference development will be described.

Firstly, this chapter will begin with a review of function (swallowing and speech), QoL and treatment-related priorities at time point one (before treatment initiation). The data will be described in terms of the quantitative findings including the patient-reported MDADI (Chen et al., 2001) and a number of clinician-rated swallowing measures including PSS-HN NoD and UoS subscales (List et al., 1990), and baseline gastrostomy tube data. QoL and patient concerns regarding symptoms will be presented using the UWQoLv4 (Rogers et al., 2002), and patient priorities using the CPS (Sharp et al 1999). These data will be integrated with patient and carer experience data from the three main qualitative themes ‘Here we go again’, ‘Do I have a choice’ and ‘A personal trade off’. This process will be repeated for timepoint two (six months and beyond post-treatment initiation).

Merging of the data sets was achieved at both time points using a combination of integration techniques. As described in Chapter 4, a visual display of integration, via joint tables, was completed. The qualitative and quantitative data are presented alongside each other in relation to the research questions of the study (Fetters et al 2013). This included four joint tables focusing on (1) swallowing, (2) speech, (3) QoL and (4) treatment-related priorities. To further explore this side-by-side comparison a triangulation protocol (O’Cathain et al 2010) was used to identify agreement, partial agreement, discordance and silence between the two data sources. The rationale and potential explanation for the outcome of the

triangulation protocol was elaborated using a weaving narrative. Here, the quantitative and qualitative findings are described thematically in relation to the research questions for this study (Fetters et al 2013). For each joint display table summary information was presented alongside matched qualitative and quantitative data sources from three individuals. This was to ensure that outliers in terms of quantitative findings and the individual voices of participants are acknowledged in addition to the collective findings of the sample.

This chapter concludes with a summary of integrated qualitative and quantitative inferences (meta inferences) (Younas et al., 2023) which form the main findings of this thesis. This includes a further consideration of the domains of function (speech & swallowing), QoL, and treatment-related priorities which relate directly to the research aims of this thesis. This also more broadly contemplates the patient experience and the additional information gained from this study via the synergistic impact of combining both the quantitative and qualitative data. The influence of the knowledge-based inferences gained via the background literature review in Chapter 1, systematic review in Chapter 3 and my own experiential based inferences developed over several years of experience in the field of rOPC are acknowledged and incorporated also. This is in line with the methodology defined by Younas and colleagues (Younas et al., 2023) and as described in Chapter 4. The final chapter (Chapter 8) of this thesis will focus on the clinical and research implications of the study's main findings.

7.1 Quantitative and qualitative data driven inferences.

The participants' accounts of swallowing, speech, QoL, and treatment-related priorities collected qualitatively (combined retrospective and prospective data) and the quantitative outcomes in these domains are now considered at baseline prior to treatment initiation and at six months and beyond post-treatment initiation. For each of these domains, a joint display table has been developed, including overall summary data for the sample and matched quantitative and qualitative data obtained for three participants. For each joint

display table triangulation is defined and further explanation provided through a weaving narrative.

The same three cases will be used throughout the integration analysis as these three individuals took part in interviews at timepoint one (before treatment) and timepoint two (six months post-treatment initiation) and have three difference treatment pathways as detailed below. One participant was also interviewed on both occasions with his wife so that the carer perspective is included, which is also in line with the aims of the thesis.

1. Gerard is a 62-year-old gentleman who was diagnosed with recurrent disease and commenced non-curative treatment using immunotherapy as part of a clinical trial. He was previously treated at another centre with chemoradiation and was referred to the research site for second opinion and subsequent treatment as outlined above. He was interviewed jointly with his wife Sophie. He lives at home with his wife and their two adult children. He continues to work full time as does his wife. He likes running, eating out with friends and family holidays.
2. Toby is a 67-year-old gentleman who was diagnosed with new primary disease and was initially offered radical open surgery (lip split, mandibulotomy, base of tongue resection, laryngectomy and free flap reconstruction) at his local hospital. He was referred to the research site for minimally invasive surgery and subsequently underwent robotic assisted open surgery. Toby lives at home with his long-term partner and their two adult children. He is recently retired. He loves socialising with friends, going to music concerts and going to the gym.
3. Kim is a 62-year-old lady. She was diagnosed with recurrent disease having previously been treated with proton beam therapy. She lives at home with her husband. She continues to work full time and is the main breadwinner of the household. Her daughter and granddaughter live close by. She loves spending time with her granddaughter and socialising with her girlfriends.

7.2 Timepoint one prior to treatment initiation.

7.2.1 Swallowing

Table 7-1: Joint display table for qualitative and quantitative findings regarding swallowing at timepoint one prior to treatment initiation

Main theme	**Qualitative findings**	**Quantitative findings[1]**
Here we go again- Something not quite right	Participants were aware of their baseline swallowing difficulties. Quite often further deterioration in swallowing or discomfort on swallowing was the presenting symptom of their disease recurrence. For those participants who were diagnosed with residual/ early recurrent disease, ongoing toxicity from their previous treatment made it difficult for some participants to decipher between persisting toxicities and emerging symptoms indicative of new disease. When participants voiced their concern regarding swallowing it didn't necessarily relate to the enjoyment of food, they were concerned for example that they would not be strong enough to fight the disease, or in the setting of a prophylactic gastrostomy pre- surgery, to have to live with a gastrostomy long term.	MDADI (Chen et al., 2001) composite score: 60 (IQR: 52.15-81.75) Median PDD-HN NoD (List et al., 1990) score: 50 Gastrostomy tube: 20% UWQoLv4 (Rogers et al., 2002): swallowing included in top 3 concerns: yes CPS (Sharp et al., 1999): swallowing ranked 4/12 in order of priority
Gerard and his wife Sophie	Gerard: *'[Swallowing]…It's fine. I mean I just had dinner tonight, that was a bit of a struggle eating the broccoli and that. Sometimes it's fine and then, other days, you feel like it's sort of sticking at the back of your throat'.*	MDADI composite score: 84 PSS-HN NoD: 90 Gastrostomy: no Swallowing in top three concerns on UWQoLv4: No

		CPS: swallowing ranked 5/12
Toby	*'The biggest reason I'd like to get rid of the RIG, and I know I need to be able to eat and drink before I do, is it doesn't seem normal. It makes me feel like there is something wrong with me, which I know there is at the moment, but it would be nice to jump out of bed every morning and not see it, like, you know? And then consequently, if the RIG wasn't there, I'd get back to doing things that I think the RIG might impose on like at the gym. But I'm big enough to admit that if I can't drink and I can't swallow, the RIG is going to keep me alive'.*	MDADI composite: 60 (adequate) PSS-HN NoD: 50 (soft food) Gastrostomy: yes (prophylactic) Swallowing in top three concerns on UWQoLv4: Yes CPS: swallowing ranked 4/12
Kim	*'My swallowing is a pain in the bum because [before my first treatment] I did enjoy my food and it was like a social thing… but not anymore…'*	MDADI composite: 50 (poor) PSS-HN NoD: 20 (hot and cold liquids) Gastrostomy: yes Swallowing in top three concerns on UWQoLv4: No CPS: swallowing ranked 3/12
Triangulation: partial agreement, participants had baseline swallowing difficulties, and it was one of the top symptoms concerns however, was not one of the top three treatment-related priorities for most.		

[1]*Quantitative findings:*

- *MD Anderson Dysphagia Inventory (MDADI) composite scores range from 20-100 where 20 is the worst possible score. Scores of ≥80 are considered optimal, ≥60-<80 adequate ,<60 poor.*
- *Performance Status Scale for Head and Neck Cancer (PSS-HN) Normalcy of Diet (NoD): scores range from 0 to 100, with higher scores indicating better performance. 100= normal diet (no restrictions), 90 (normal diet liquid assist), 80 (all meats), 70 (carrots and celery), 60 (dry bread, crackers), 50 (soft chewable foods), 40 (soft foods requiring no chewing), 30 (pureed foods), 20 (warm liquids), 10 (cold liquids), and 0 (nil by mouth).*
- *Chicago Priority Scale (CPS): participants rank priorities 1-12 where 1 is the most important and 12 is the least.*

Participants in this study presented with impaired swallowing function at baseline and for many it was one of their top three symptom concerns however, for the sample was not ranked in the top three treatment-related priorities.

Patients were aware of their swallowing difficulties, and this was reflected in the MDADI data. As noted in Chapter 6, guidance has been published on the classification of MDADI composite scores as optimal (≥80), adequate (≥60-<80) and poor (<60) (Goepfert et al., 2017). For the participants in this study, swallowing-related QoL was found to be within the adequate bracket prior to treatment initiation based on the median composite scores recorded. Clinician rated measures of swallowing function also highlighted impaired level of function at baseline. The PSS-HN NoD (List et al., 1990) demonstrated a median score of 50 at baseline. The PSS-HN NoD subscale assesses the degree to which a patient is able to tolerate a regular diet by assigning a ranking of ten food categories where 0 is the worst score (non-oral feeding) and 100 is the best score (regular diet with no restrictions) (List et al., 1990). At baseline a minority of patients (20%) were reliant on or requiring supplementary feeding using gastrostomy.

The UWQoLv4 symptom profile data show that patients were concerned about their swallowing at baseline. The qualitative data revealed that quite often further deterioration in swallowing or discomfort on swallowing was the presenting symptom of their disease recurrence. For those participants who were diagnosed with residua or early recurrent disease, ongoing toxicity from their previous treatment made it difficult for some participants to decipher between persisting toxicities and emerging symptoms indicative of new disease.

Both qualitative and quantitative measures demonstrate that swallowing impairment was present and of concern for the participants in this study prior to treatment initiation. Not only is there agreement between qualitative and quantitative data, but within the quantitative data

there is concordance between the patient reported and clinician rated measures. Swallowing however, is not one of the top three treatment related priorities.

Gerard describes how although he manages with his oral intake, at times, certain consistencies can be tricky. Toby had a gastrostomy fitted prior to his salvage surgery in anticipation of compromised function following surgery. Adequate swallowing function is noted at baseline (MDADI: 60), however Toby is hugely motivated to have his gastrostomy removed after his treatment. Some might assume that he actually wants to be able to eat and drink, however Toby reports that his main motivation for having the gastrostomy removed is not his swallowing ability/ but is from an aesthetic and practical perspective as he is a very active person and feels that the gastrostomy gets in his way while exercising. Whilst Kim reports that since her original treatment, her swallowing has never recovered and although she doesn't require a gastrostomy, she can only manage drinks and is reliant on nutritional supplements. For Kim, swallowing is one of her top three treatment-related priorities.

7.2.2 Speech

Table 7-2: Joint display table for qualitative and quantitative findings regarding speech at timepoint one prior to treatment initiation.

Main themes/ subthemes	**Qualitative findings**	**Quantitative findings[1]**
Here we go again- something not quite right	Some participants noted ongoing residual changes in their voice following their previous treatment. Others described a downturn in their voice quality which was a sign of their disease recurrence. However, overall patients were not concerned regarding their voice/ speech/ communication prior to treatment.	PSS-HN UoS (List et al., 1990): 24/25 participants were fully intelligible prior to treatment initiation. UWQoLv4: (Rogers et al., 2002) priority concerns: speech ranked 5th most frequently reported concern.
Gerard and his wife Sophie	*[My voice]… can vary from a sort of husky gruff, which is when I pitch it at the level that I would normally speak. But if I go and do a much lower register it is less impacted, but that is a bit of an effort too. Yes, I don't think I'll be joining the choir any time soon.*	PSS-HN UoS: 100
Toby	*'If there's any difference in my speech but I can still talk and people can still understand me, I can live with that. I'm not going to get despondent about not being able to speak in the tone that I'm speaking now. I would be more concerned if I couldn't speak at all'*	PSS-HN UoS: 100

Kim	*I just can't talk for long, without having a drink. Unfortunately, my work involved a lot of telephone work, but it's me and one other lady who's like the same age as me. We get on really well, but she covers for me for most of the phone calls. So, I've managed to carry on with my job. So, my speech doesn't worry me now. I can live with it, but I am concerned about what it might be like afterwards.*	PSS-HN UoS: 100
Triangulation: partial agreement, silence		

[1]*Quantitative findings:*

- *Performance Status Scale for Head and Neck Cancer (PSS-HN) Understandability of Speech (UoS) scores range from 0 to 100, with higher scores indicating better performance.*
  100 (full intelligible), 75 (Understandable most of the time; occasional repetition necessary), 50 (usually understandable; face-to-face contact necessary) 25 (difficult to understand), 0(never understandable; may use written).

For the participants in this study, prior to treatment initiation, speech was generally intact for the majority. One gentleman who had a laryngectomy as his primary disease treatment many years ago was unable to produce voice/ speech. One participant noted changes in his voice which had made him suspicious regarding his diagnosis of recurrent disease, whilst another noted that her voice had changed since her previous treatment and found it hard to talk for long periods of time. However, overall, participants reported that they were not concerned regarding their speech prior to treatment. Partial agreement was noted between quantitative and qualitative data as the majority of participants were fully intelligible at baseline however, some did notice changes in their communication (voice) at baseline and this was not reflected in the PSS-HN understandability of speech subscale data. Although speech and voice are separated as constructs of overall communication by clinicians, when asked about speech, participants did not differentiate speech and voice and instead spoke about their communication in general. The PSS-HN data did not reflect any changes in voice, and there was no measure as to how change in communication was impacting overall QoL or ability to work, or the effort involved in prolonged speaking. In terms of patient

concerns regarding speech, it was ranked as the 5th most frequently noted concern using the UWQoLv4 questionnaire.

Within the individual patient data, although he has reported some changes in his voice, Gerard is not hugely concerned over this, but does mention the increased effort. He does not talk about any impact his upcoming non-surgical treatment may have on his voice. Although Toby has no baseline difficulties with communication, Kim already struggles, and they are both equally as concerned regarding how their communication may change with surgery. Kim noted her difficulties with her voice at baseline, in particular for work. Toby is fully confident that he will be able to speak again, but that it just might sound different.

7.2.3 Quality of life

Table 7-3 Joint display table for qualitative and quantitative findings regarding quality of life at timepoint one prior to treatment initiation.

Main themes/subthemes	**Qualitative findings**	**Quantitative findings[1]**
Here we go again. Something not quite right Was I shocked? What now?	Participants described that their QoL had not returned to baseline since their previous treatment. Some participants continued to experience ongoing toxicity in terms of fatigue, lack of physical activity whilst others voiced their frustration at just beginning to feel somewhat 'normal' and then they were diagnosed with recurrence. Given that these patients are experienced HNC patients, they knew that whatever the treatment there would be some compromise with QoL. The diagnosis had a significant psychological impact on participants and their caregivers. For many their greatest fear- the fear of recurrence had become a reality.	UWQoLv4 (Rogers et al., 2002) Physical composite score: 68 (IQR: 58- 88) Social- emotional score: 70 (IQR: 50-82) UWQoLv4 top 3 concerns at baseline: pain, swallowing and mood
Gerard and his wife Sophie	*Sophie: 'with the immunotherapy, we got the impression that he would be well for longer, whereas the chemo just seems to- I know you had it with radiotherapy, which really does knock you out. I think we felt that chemo seems to have more negative effects on people, so we were hoping that perhaps the immunotherapy would be something that he could feel well for longer'*	UWQoLv4: Physical score: 83 Social Emotional score: 79 Top concerns reported: activity and pain.
Toby	*I had the camera up my nose. And then, they spotted this cancer on my throat. Initially, I went on my own because I thought I'd got acid reflux. And he told me*	UWQoLv4 (Rogers et al., 2002): Physical score: 95 Social Emotional score: 85

	that I'd got cancer, and obviously I was on the back foot then. So, we were talking about taking my voice box out, and taking a piece out of my jaw, and taking a piece out of my hip. And I'll be honest, it put me on the deck, like. Then, eventually, I came round, and bearing in mind I've never done that, in 67 years, eventually I came round'	Swallowing, mood and anxiety reported as concerns.
Kim	*'To tell you the honest truth, I had the first treatment, and I don't know if it's because my cancer has started again, but I don't feel any different from when it ended, which must be getting on for 18 months ago now, to now. I don't feel I've got any more energy. I don't feel like I've got over it yet'.* *'When I was diagnosed again, I sort of knew what my options were, but I'd sort of blocked it out'*	UWQoLv4: Physical score: 43 Social-Emotional score: 45 Saliva, mood and anxiety reported as concerns.
Triangulation: partial agreement, partial silence		

[1]Quantitative findings: University of Washington Quality of Life Questionnaire version 4 (UWQoLv4) physical and social-emotional scores range from 0-100 where '0' is the worst possible functioning.

QoL was already impaired for many of the participants in this study at baseline. The UWQoLv4 questionnaire includes two overall scales measuring QoL, namely the physical subscale and the social-emotional scale. Here a score of 0 represents the worse possible score, and 100 the best. Normative reference for the physical score is 100, and for the social- emotional score is 95. Although participants report in the qualitative data that there may have been some improvement following primary treatment there is agreement between the qualitative and quantitative data that QoL did not appear to return to normative reference levels following primary disease treatment. QoL may also have been impacted by the

presence of their disease recurrence. Many participants reported that they were in pain, or no longer able to do what they used to do in terms of daily activities or physical exercise.

From the qualitative interviews, it was clear that from the participant's previous experience of HNC treatment as a patient or carer, they did have concerns about what impact upcoming treatment might have on their overall health status. As one can see from Sophie, the wife of patient Gerard, many of the participants just wanted to ensure that they could continue to feel as well as possible for as long as possible. Sophie compared her previous experience of Gerard's treatment when he experienced the side effects of chemoradiation. They were hopeful that with immunotherapy the impact would be much less on Gerard's overall wellbeing and QoL. It is also very clear from the qualitative analysis, and in particular the individual patient data, that the diagnosis has a real impact on mood and overall psychological status. Although a list of concerns regarding mood/ anxiety may be captured using some quantitative measures, to get a sense of what it feels like to be given this diagnosis can only be obtained via qualitative means. Toby reflects on his experience, saying describing how he attended his appointment alone when was given the diagnosis of recurrence and the option of open surgery as the only potential curative measure - he fainted and remembers little else of the appointment. Although when asked to report any concerns using the UWQoLv4, which does include mood/ anxiety, he chose not to report any concerns and his individual symptom domain scores did not reach the criteria for significance. This is different for Kim, who reported that she had tried to avoid thinking about her disease, however mood and anxiety were reported as two of her top three concerns. Kim reflected on how she felt that she had not recovered from her previous treatment when she was diagnosed with recurrence.

7.2.4 Treatment-related priorities

Table 7-4 Joint display table for qualitative and quantitative findings regarding treatment-related priorities at timepoint one prior to treatment initiation

Main themes/ sub themes	**Qualitative findings**	**Quantitative findings**
'Do I have a choice?' Second opinions why, when and where? Whose decision is it anyway	Participants and their caregivers overwhelmingly reported that their goal was to be cured and if cure was not available to live as long as possible. Changes to function or QoL came secondary to the overall goal of cure/ survival. However, there are very mixed qualitative findings on if and how participants could voice their treatment-related priorities to influence any potential treatment decisions. For some there was no decision, because only a single treatment option given, some received or actively sought a second opinion to ensure their goals for treatment were met (cure/survival), and others felt it was the doctor's decision to make.	CPS (Sharp et al., 1999) top 5 treatment-related priorities: 1. Being cured of cancer 2. Living as long as possible 3. Pain 4. Swallow 5. Energy
Gerard and his wife Sophie	Gerard: "Can you guarantee me three years?" and he said, "No." which was a huge blow' *'purely by chance [I got a second opinion] because I've got a friend who is a GP'* *Sophie: '[the second opinion] made us realise that he did have a choice'… but we did worry…going for a second opinion…?" Was that the right option?* *Yes, was it the right option? Because it seemed to be putting off the treatment and was it important to get the treatment*	CPS top 5 treatment-related priorities: 1. Being cured 2. Living as long as possible 3. Energy 4. Moist mouth 5. Swallow

	started quicker, whatever the treatment was?'	
Toby	*'Although it wasn't dwelt on, it was a slight suggestion that I could've probably pulled out completely and said, "Let's just let it take its course, and if it spreads, it spreads, and if it stops where it is, I can live with it."* *That was never an option for me, like, but it was mentioned'.*	CPS top 5 treatment-related priorities: 1. Being cured 2. Living as long as possible 3. Pain 4. Swallow 5. Activities
Kim	*'If I haven't got quality of life, I don't see the point in putting myself and my family through all this'.* *'Yes, I would have like to discuss some options you know, "We think this is the best for you, but you can try this, this or this if you want to, but if you try them and leave it too long, then this option won't be open to you," or whatever, you know?* *'I knew it was going to be surgery, but I didn't know any detail, but then the next minute, I'm in London and I'm being booked in…. it was like railroading'*	CPS top 5 treatment-related priorities: 1. Being cured 2. Living as long as possible 3. Swallow 4. Pain 5. Energy
Triangulation: Agreement noted overall between summary qualitative data and summary quantitative data where participants' main priority was cure or survival. However, in the individual data for both Kim and Gerard other aspects of QoL were also priorities including pain and energy.		

Regardless of whether the treatment pathway was curative or non-curative, being cured of cancer, and living as long as possible were the main treatment-related priorities for the participants in this study as evidenced in both the quantitative and qualitative data. In the quantitative analysis there were more patients on a curative pathway than on a non-curative pathway so this may account for the sample findings. However, if we look at the individual patient data, although Kim and Toby were on curative pathways, Gerard was on a non-

curative pathway and his priority remained focused on being cured. This may reflect his hopes that something might change in the future, particularly as he was being treated within a clinical trial or perhaps his diagnosis of incurable disease had not fully been absorbed at this early stage following diagnosis.

Delays in commencing treatment, as described by Sophie, wife of Gerard, whilst they were waiting for second opinion was perceived as a potential threat to the efficacy of treatment. This caused increased anxiety at an already hugely anxious time. Gerard was encouraged by his GP friend to seek a second opinion after initially being provided with one potential treatment option at his local hospital. His wife described that when they received a second opinion, they felt they had been given the option to make a choice between treatments. They felt that only for the advice of their GP friend they might not have requested a second opinion.

Although Kim was offered a second opinion, she felt that regardless of her goals for treatment and indeed her concerns regarding QoL, she was not given any potential choices/ alternatives to surgery.

Toby describes that cure was his goal. The idea of palliation was mentioned but that was not an option for him as he wanted to live. However, he also prioritised how life might be like afterwards. He was offered laryngectomy surgery at his local hospital, however, he opted for the minimally invasive technique offered at the research site. At the time he couldn't imagine not being able to speak or indeed having a permanent stoma/ opening in his neck through which he would breathe. So, although two curative options were offered, he opted for the minimally invasive treatment, with the hope of not only achieving cure, but to also maintain his QoL.

7.3 Timepoint two six months and beyond following treatment initiation.

7.3.1 Swallowing

Table 7-5 Joint display table for qualitative and quantitative findings regarding swallowing at timepoint two six months or more following treatment initiation.

Main theme	Qualitative findings	Quantitative findings[1]
A personal trade off How I look at things now Would I do it all again	A deterioration in swallowing is described by all participants, whether prospective, retrospective, curative or non-curative. The trajectory for change depending on treatment pathway is different, with the curative group describing a sudden deterioration following surgery, with either no improvement or a gradual improvement over time. In the non-curative group more gradual, subtle changes are reported prospectively at the six month mark but then on slowly progressing by the retrospective group. As swallowing difficulties occur, participants describe being much more concerned regarding their swallowing and how it is impacting their QoL, in particular for those with adequate swallowing function before treatment. With time the curative group appear to be able to rationalise this trade off. However, for the non-curative treatment group, as survival becomes less attainable, the declining QoL experienced through eating/drinking appears to become more important.	MDADI (Chen et al., 2001) composite score: 60 (IQR 54.75- 75.75) *(in comparison to 60 (IQR: 52.15-81.75) at baseline).* Median PSS-HN NoD (List et al., 1990): 40 *(in comparison to 50 at baseline).* Gastrostomy tube usage: 52% (*in comparison to 20% at baseline)* UWQoLv4 (Rogers et al., 2002): swallowing is now the most frequently reported priority concern at six months following treatment initiation (*previously ranked 2nd at baseline)* CPS (Sharp et al 1999). Swallowing ranked 4/12 *(same as baseline)*
Gerard and his wife Sophie	Sophie: '*Food has been hard… and food is so important, isn't it, when families get together and socially with friends? So, I think maybe that was something that, at*	MDADI composite score: 68 (adequate) *(84 at baseline)*

	times, can bring you down a little bit. We want to eat as a family, we don't want to be eating all different meals. You know, we want to do it- because that's what we've always done'	PSS-HN NoD: 50 *(90 at baseline)* Gastrostomy: No Swallowing in top three concerns on UWQoLv4: yes *(no at baseline)* CPS: swallowing ranked 3/12 (*5/12 at baseline)*
Toby	*Not being able to eat and drink…. I went into quite a dark place…. I started talking about not being able to enjoy my kids' weddings because I couldn't drink and I couldn't eat, and going out for meals, which is a big part of our family. Sitting around the table and we're all talking about what they did at work all day, again, massive part of our family*	MDADI composite score: 54 (poor) *(60 at baseline)* PSS Normalcy of diet: 0 *(50 at baseline)* Gastrostomy: Yes Swallowing in top three concerns on UWQoLv4: yes (yes *at baseline)* CPS: swallowing ranked 3/12 (4*/12 at baseline)*
Kim	'*I had to keep explaining to people that I couldn't eat before the surgery, so, "Why do you think I'm going to eat after the surgery?'* *'[Swallowing] I don't feel like it is any different from when I came out. I don't feel that changing, getting any easier.*	MDADI composite score: 35 (poor) *(50 at baseline)* PSS-HN NoD: 10 (20 at baseline) Gastrostomy: Yes

	'I don't know what I would do without [the feeding tube] because I couldn't take enough in'.	Swallowing in top three concerns on UWQoLv4: no (no *at baseline)* CPS: swallowing ranked 7/12 (3*/12 at baseline)*
Triangulation: Discordance between summary sample patient-reported swallowing outcome and qualitative data. MDADI shows stable swallowing, whilst PSS and gastrostomy data demonstrated a deterioration. Swallowing is now more of a concern to participants as see in the UWQoLv4 concerns data. Agreement between clinician-rated measures and qualitative findings for the sample and by matched data cases. Silence: impact on family life		

[1]*Quantitative findings:*

- *MD Anderson Dysphagia Inventory (MDADI) composite scores range from 20-100 where 20 is the worst possible score. Scores of ≥80 are considered optimal, ≥60-<80 adequate ,<60 poor.*
- *Performance Status Scale for Head and Neck Cancer (PSS-HN) Normalcy of Diet (NoD): scores range from 0 to 100, with higher scores indicating better performance. 100= normal diet (no restrictions), 90 (normal diet liquid assist), 80 (all meats), 70 (carrots and celery), 60 (dry bread, crackers), 50 (soft chewable foods), 40 (soft foods requiring no chewing), 30 (pureed foods), 20 (warm liquids), 10 (cold liquids), and 0 (nil by mouth).*
- *Chicago Priority Scale: participants rank priorities 1-12 where 1 is the most important and 12 is the least.*

The summary quantitative findings showed stable MDADI composite scores from baseline, however clinician-rated measures show a deterioration. There is a clear discordance between patient-rated swallowing using the MDADI and qualitative findings, which reflect that swallowing has now become much more troublesome for some participants and is having much more of an impact on overall QoL. Clinician-rated measures of swallowing function either direct (PSS-HN) or by proxy measure (gastrostomy tube use) show a deterioration in swallowing function, which is much more in keeping with that described qualitatively. This is also reflected in the longitudinal individual patient data presented. Here for all three participants, a clinically significant deterioration in MDADI composite score is noted (clinically significant > 10 points) with corresponding deterioration in PSS scores. Toby discusses his ongoing struggles with being nil by mouth, troublesome secretions and

reliance on a gastrostomy feeding tube at six months post-treatment. Kim, although not troubled by secretions, remains reliant on her feeding tube but can manage liquids. Perhaps because of her already poor baseline functioning prior to surgery, she is not as concerned about this as Toby is, and she does not rate swallowing as a priority concern.
Sophie, wife of Gerard, describes a more subtle change in his swallowing, however, highlighting the impact on family life. This impact is not reflected in the quantitative data, despite there being a social eating domain within the PSS. This is an example of where following the triangulation protocol reveals silence. Here although Gerard continues to eat with others, the fact that he has had to change his diet and struggles more with certain consistencies is noted by the family. They have had to change the family meal menu options.

Whilst Toby and Kim remain in the relative short-term period following their surgery, many of the retrospective participants in the curative group describe gradual improvements following treatment with eating/drinking but not a return to baseline. Whilst others who are no longer eating/ drinking due to the severity of their swallowing impairment, reported a level of ‘acceptance’ in terms of functional outcome which they consider a trade-off in return for their ultimate goal of cure/ survival. Participants in the non-curative (prospective and retrospective) treatment group describe a more subtle and gradual deterioration in swallowing function. As and when this decline occurs, these retrospective participants appear also to negotiate acceptability in terms of functional decline and ongoing survival. However, as the prognosis for survival shortens, and swallowing continues to deteriorate, there appears to be a point where it becomes much more challenging to justify the trade-off for ongoing survival.

7.3.2 Speech

Table 7-6 Joint display table for qualitative and quantitative findings regarding speech at timepoint two six months or more following treatment initiation.

Main theme/ sub theme	**Qualitative findings**	**Quantitative findings[1]**
A personal trade off- are we ever ready?	There were mixed accounts of how speech had been impacted by the treatment. Some participants reported that they had been surprised by the severity of their speech changes, some not being unable to speak, others who felt too self-conscious to continue with their job, whilst others had made significant adaptations to continue with their working and social life as before despite changes to their speech. Mixed reports were noted in terms of pre-treatment counselling with some participants reporting that they were ill prepared for their outcome, whilst others felt they had too much counselling regarding speech when their outcome was better than anticipated.	PSS-HN UoS (List et al., 1990): 12/21 participants fully intelligible at 6 months UWQoLv4 (Rogers et al., 2002): priority concerns speech 3rd most frequently reported concern.
Gerard and his wife Sophie	*'My voice has got slightly gravellier. But again, that's about it really'*	PSS-HN UoS: 100
Toby	*'The mucous is horrendous, I went out with a load of my old football mates and then I was talking and spitting up saliva every couple of minutes… I can only talk for a couple of minutes before having to clear the saliva;*	PSS-HN UoS: 100
Kim	*'I would like to be able to talk a bit better than I am doing at the moment. There are certain words that, I don't know, pronunciation, don't know how you describe it really, I do struggle with'*	PSS-HN UoS: 100

Triangulation: partial agreement: quantitative data and qualitative summary data demonstrate a deterioration in speech for some participants however this is not reflected in the individual data. The individual qualitative patient data demonstrates a change in all three participants which is not captured by the PSS rating.
Silence: the impact of deterioration in speech is evident through qualitative data with one participant unable to return to work. This is not captured in the quantitative data.

[1]*Quantitative findings:*

- *Performance Status Scale for Head and Neck Cancer (PSS-HN) Understandability of Speech (UoS) scores range from 0 to 100, with higher scores indicating better performance.*
  100 (full intelligible), 75 (Understandable most of the time; occasional repetition necessary), 50 (usually understandable; face-to-face contact necessary) 25 (difficult to understand), 0(never understandable; may use written).

Quantitative data demonstrate a deterioration in understandability of speech overall at six months in comparison to time point one. Quantitative data also demonstrate that speech is now a greater priority for participants than at baseline. However, there are mixed accounts of how speech is impacted, with some reporting no speech difficulties at this timepoint. Retrospectively participants describe how this has impacted their professional roles. There are mixed reports regarding how prepared participants felt about their speech outcome. Some participants reflect how they have learned to live with their new speech. However, what is missing from the quantitative data, but is included in the qualitative data, is the impact of reduced speech clarity, or for some absent speech, on daily functioning within their own environment. Here, triangulation highlights silence once more. Some participants manage to return to work, whilst others cannot maintain their professional role following treatment. For caregivers it can have a huge impact on the dynamics of a relationship when the spontaneity and intimacy of speech is lost or suddenly different. This is not captured in the quantitative data.

When individual patient data sources are examined, the three matched datasets describe a deterioration in speech that is not reflected quantitatively. This could be because voice per se is not measured, or as noted previously because speech and communication are much

more than just understandability, there must be comfort, ease and confidence with one's own communication. The PSS-HN UoS data does not capture these constructs.

7.3.3 Quality of life

Table 7-7 Joint display table for qualitative and quantitative findings regarding quality of life at timepoint two six months or more following treatment initiation.

Main theme	**Qualitative findings**	**Quantitative findings[1]**
A personal trade off- How I look at things now Would I do it all again?	Patients describe how overall QoL changes with time. Like with swallowing, the trajectory is different for patients on a curative and non-curative treatment pathway. For those undergoing curative treatment there is a sudden decline in mainly the physical aspects of QoL post-surgery (mobility/ activity). From the prospective longitudinal and retrospective data there appears to be a gradual improvement over time if the treatment has been successful. In the non-curative group, there appears to be a gradual decline in the physical components of QoL over time. A cross over is seen here when a patient on a curative pathway enters into a non-curative pathway- the trajectory changes from a gradual improvement to a gradual decline, however post-surgery, the starting point at which this gradual decline begins is much lower. What is common to both groups, however, is a recalibration of what QoL is at various junctures- after surgery, after confirmation of cure or otherwise, and at progress points or otherwise with non-curative treatment.	UWQoLv4 (Rogers et al., 2002): Physical score: 63 (IQR 46-78) *(in comparison to 68 (IQR: 58-88) at baseline)* Emotional-social score 74 (IQR 58- 85) *(in comparison to 70 (IQR: 50-82) at baseline)* UWQoLv4 top 3 concerns at six months: swallowing, saliva, and speech/ pain *(in comparison to pain, swallowing and mood at baseline).*

Gerard and his wife Sophie	*Sophie: 'I think we thought… You've been so well, so driving to the appointments, going to work the next day, having enough energy at the weekend to do gardening, go out, I think we probably hadn't expected it to be quite like that. I think we probably thought you'd be perhaps more tired, like you were with the chemo and the radiotherapy'.* *'But yes, so I think that has been a pleasant surprise. Because he has been really well. And when we've seen friends, they've said how well you look. So yes, it's just… Yes, I think that's definitely…* *I mean, we've done some long walks and… Energy. You've done a couple of runs. So yes, you've felt really good'.*	UWQoLv4: Physical score: 80 *(in comparison to 83 at baseline)* Social-Emotional score: 85 *(in comparison to 79 at baseline)* UWQoLv4 top concerns reported: swallowing and saliva. *(in comparison to activity and pain at baseline)*
Toby	*'I went into quite a dark place. I started doing things at home that were totally out of character for me, like disappearing out of the house without telling anybody and leaving my phone here. Obviously, as soon as they saw my phone still here, they assumed the worst. It took me a good month to get out of that, but they were brilliant with me, they understood. Well, they used to come looking for me. But yeah, and it was a massive change in my life'*	UWQoLv.4: Physical score: 37 *(in comparison to 95 at baseline)* Social-Emotional score: 80 *(in comparison to 85 at baseline)* Top concerns reported: swallowing, saliva, anxiety. *(in comparison to swallowing, mood and anxiety at baseline).*

Kim	*'Every month I feel better than the previous month, like stamina and strength-wise'.* *'I used to be able to stand there all day and iron till I got rid of it. I can't do that anymore. I had to do a little bit and have a rest and just try not to look at it, and then go back and do a bit more another day or something. I'm just slowly but surely doing a bit more. I've just started a beginner's Pilates class which I'm enjoying, to try and help me get a bit of strength and stuff back, yes'.* *'I am looking after my granddaughter again sometimes… I take her to the park and things when it is nice, and I used to run around with her. I can't do that at the moment. It is just getting a bit of a level of fitness back to be able to do little things like that again, yes'*	UWQoLv.4: Physical score: 43 *(same as baseline)* Social-Emotional score: 80 *(in comparison to 45 at baseline)* Top concerns reported: activity, saliva, anxiety. *(in comparison to saliva, mood and anxiety at baseline)*
Triangulation: partial agreement		

[1]Quantitative findings: University of Washington Quality of Life Questionnaire version 4 (UWQoLv4) physical and social-emotional scores range from 0-100 where '0' is the worst possible functioning.

Quantitative findings demonstrate a deterioration in physical functioning which is reflected in the qualitative data with participants describing reduced activity or increased fatigue. Social-emotional scores however demonstrate a mild increase in functioning from baseline to six months. This is also mirrored overall in the qualitative data with an apparent reframing/ recalibrating what QoL actually is, with some participants explaining how they now focus on what activities they can enjoy rather than what is no longer possible (speaking or eating/ drinking).

However, from the individual patient data it is clear that some patients are really struggling like Toby. For Toby there does appear to be a discordance between the qualitative data and

the quantitative social-emotional score, which remains quite high. If we look at the individual patient data in some further detail, both Gerard and Kim show increased social-emotional QoL. Gerard's wife explains that they are both pleasantly surprised at how well he has been. Based on their experience of previous HNC treatment, their perception was that Gerard would be feeling much worse during his treatment. However, he is much better than they expected and is able to work, socialise, remain active etc. Likewise, Kim reports that in comparison to how she felt before, she is gradually improving and now pain free.

Toby's situation is somewhat different. He has had a marked deterioration in his physical score, and a small deterioration in his social-emotional score. However, this is in contrast to Toby's description of how he was feeling. Toby describes that he was in a really dark place psychologically because of his inability to eat/ drink. However, there is an indication that his description was in the past and he has now come out of this, and this might explain his social-emotional score. A lot has changed for Toby since he had his salvage surgery, not only did his surgery fail to have the desired functional outcome, but by the time of his second interview, Toby had been told that he had persistent disease. At the time of the second interview, Toby was awaiting laryngectomy surgery. The contrast between his UWQoLv4 social emotional score and his description may be explained simply by improvements which have happened over the course of time as his description is in the past tense. Or it may relate to a reframing due to a change in circumstances including his diagnosis of persistent disease and his then awaited further salvage surgery. Although in the setting of persistent disease it might be assumed that a social emotional score may change however, further analysis and consideration of his treatment related priorities may explain this in the next section.

7.3.4 Treatment-related priorities

Table 7-8 Joint display table for qualitative and quantitative findings regarding treatment-related priorities at timepoint two six months or more following treatment initiation

Main theme/ sub themes	Qualitative findings	Quantitative findings
A personal trade off would do it all again? How I look at things now	Being cured of cancer and surviving as long as possible to be able to be there for family members and significant others remained a key treatment-related priority for patients. However, if there was an 'easier' way to achieve this with equipoise in survival outcomes, patients would choose the least invasive option in the case of surgery, or the perceived kinder option in the case of non-surgical treatment.	CPS (Sharp et al., 1999) top five treatment-related priorities: 1. Being cured of cancer 2. Living as long as possible 3. Pain 4. Swallow 5. Energy
Gerard and his wife Sophie	'I'd like to see my son graduate from university, which is another two years down the line. I mean, the doctor at my original hospital, when I asked him whether he could guarantee me the three years, he said no, which was a bit of a shock. So, fingers crossed, I'll make that milestone and maybe a bit more'	CPS top five treatment-related priorities: 1. Living as long as possible 2. Being cured of my cancer 3. Swallow 4. Energy 5. Moist mouth
Toby	'I was given, in my opinion, two options. One was to take the immunotherapy, not get rid of it and always there was a chance that there was a timeline for me actually not being here in the future….The fact that it doesn't get rid of it, and it doesn't guarantee that it won't spread'. The decision [to have laryngectomy surgery] although it's quite extreme… I get this positivity out of the negativity of having it done, you know? I'd love to have	CPS top five treatment-related priorities: 1. Being cured of my cancer 2. Living as long as possible 3. Swallow 4. Pain 5. Moist mouth

	a drink or have a bowl of soup, and hopefully get rid of this bloody mucus, even though I've got to learn how to talk and all this sort of stuff, you know?	
Kim	No, I've no regrets, I don't. No, my pain has gone. Pain is a funny thing because when you've not got it anymore you forget about it quite easily. My pain has gone. I suppose right at this moment I am not in any life-threatening danger. I've got a good prognosis at the moment.	CPS top five treatment-related priorities: 1. Being cured of my cancer 2. Energy 3. Swallow 4. Pain 5. Moist mouth
Triangulation: partial agreement		

The quantitative data demonstrate that participants continue to rate cure and survival as the top two treatment-related priorities - with no change from timepoint one to time point two. The qualitative data offers agreement in part with this. For those patients treated curatively, who are now disease free, cure continues to be prioritised over everything. This is true even for those participants with the most adverse functional outcomes (gastrostomy dependent/ tracheostomy dependent/ poor or no speech). However, for those who are on a non-curative pathway or indeed for the minority of participants who, due to the course of the disease, progressed from a curative to a non-curative pathway, they appear to be showing signs of a different focus, particularly within the setting of declining function. Here it is more about finding balance, and as survival becomes less attainable with time, and QoL is declining/ impacted by treatment side effects, the priority appears to shift more towards QoL. This is not reflected in the quantitative data.

If we look at the three cases of matched data, Kim is now cured, she is very happy with her progress with physical activity and energy, and despite not being back to her baseline level of swallowing and being gastrostomy dependent, she has no regrets. Toby who has also had

surgery, although in a very different situation as he has not been cured of his disease and requires further treatment, also remains focused on cure. At the time of interview, he was contemplating radical laryngectomy surgery to achieve this. Although he opted for the less invasive option when first diagnosed, as this is no longer available, he will do whatever it takes to be cancer free. Also, given his poor functional status, he can see the potential benefits of laryngectomy surgery as he is currently unable to swallow. Gerard, who remains very well, continues to work, socialise and keep active. His treatment priority however has changed, it was cure at timepoint one and now this has changed to staying alive for as long as possible. He remains very focused on being alive so that he is there for his family for as long as possible. This change in priority may reflect some acceptance on Gerard's behalf regarding his overall diagnosis and prognosis.

7.4 Meta inferences

Meta inference development involved several sources of information. The quantitative and qualitative data-driven inferences were merged the knowledge-based inferences (from the literature review in Chapter 1, and the systematic review in Chapter 3). My own experiential-based inferences following several years of working in rOPC were acknowledged, as these were also influential in the meta inference development. The meta inferences which emerged addressed the main objectives of this research and, by combining the quantitative and qualitative data via integration, resulted in findings which could never have been reached by using either qualitative or quantitative research methods alone. Four main findings (meta inferences) of the study emerged, including: patient and carer experience, treatment-related priorities, function and QoL, and concerns regarding symptoms. One can argue that the first meta inference is the overarching finding as it should and must be inherent in all aspects of care. For each subsequent meta inference, namely treatment-related priorities, function and QoL, and symptom concerns, the centrality of patient/ carer experience is also emphasised. To confirm the validity of each of these meta inferences, each statement was examined individually before reviewing and linking with the study data

(Chapters 5 and 6), and the systematic review and literature review (Chapters 1 and 3), whilst acknowledging any experience-based inferences. The validity of the inferences and meta inferences was also discussed with the research team and the study PPI/E group, with refinements as required.

7.4.1 Meta inference 1: Patient and carer experience

When patients are diagnosed with disease recurrence, one of their greatest fears, the fear of recurrence, becomes a reality. The overarching findings of this mixed methods research are that although there may be a common treatment, common outcomes and common goal of cure/ survival, each patient and/or carer experiences this differently. For each individual patient and their carer, every effort must be made to enhance that individual's experience of the care they are receiving. At the point of diagnosis and treatment decision making, and at every juncture in care thereafter, there must at least be the option for SDM.

The majority of participants in this study wanted to be involved in SDM but some wanted their doctors to make the decision or wanted their family members to receive the information required to decide or be prepared for treatment. Patients must be made aware of their treatment choices in an accessible and appropriate manner individual to them. Patients must feel that they are fully involved in decision-making, even if that decision is to all to doctors to determine what is best. However, patient concerns and priorities must be listened to and addressed. Patient and caregivers, if they wish to, must be aware at all times of what will happen next in terms of their pathway of care. In some regards shared decision-making may in fact be easier in the recurrent setting in comparison to the primary disease setting. One of the difficult things in the primary setting is how do you possibly prepare people for HNC side effects when it is so hard to imagine what these will really be like. From this study we can see that in the recurrent setting, patients have some genuine knowledge of what HNC treatment is like and how the side effects can impact daily life and overall QoL and so perhaps they can be more fully prepared for treatment for recurrence.

Michael, 63, who underwent curative surgery, felt very strongly that there should be equity of care for all patients. He pushed for a second opinion because he was aware that he could have one and he knew how to get one through friends who work in healthcare. Michael was not willing to accept that palliation was the only option for him. He feels that there is a lot more work to do so that healthcare teams and patients are fully aware of the treatment options and second opinion referral routes and that patients are empowered with information to decide.

'It was like I was on an emotional rollercoaster because at 10:30 in the morning, in effect, I was being told, well no dates or times, but "There's nothing we can do. Prepare for death," and then a few hours later, there was another man telling me, "You can have it all cut out."… I say this with no blame attached or irreverence, but I think we all treat doctors as gods and if they say it's X, you tend to accept it. I've seen people being given diagnoses and they accept what they're being told. What I've learned is that there is often a second opinion and there is another way'… I'm sure in 10 years' time, it'll be very different. There will be a proper methodology for recurrent head and neck cancers, and that's what we want. I would like people in the future not to have to go through that worry.
(Michael, 63, interviewed retrospectively underwent curative surgery)

7.4.2 Meta inference 2: Treatment-related priorities

Patients and their caregivers want to survive and when the option is to choose between cure and function/ QoL, cure is favoured. When cure is not an option, patients still appear to want to live as long as possible, prioritising survival over function/ QoL. If a less invasive option is available for patients to have that will not compromise their overall survival, they will choose this. Patient's treatment-related priorities do not appear to change over time if their disease remains stable. Cure/ survival remain key whatever the cost in terms of function/ QoL. However there does appear to be some more consideration for QoL, if and when a patient's

circumstances change. This was seen in the non-curative setting over time at junctures between treatment options, or when curative treatment was not successful. It seems that when the prognostic outlook begins to shorten, more consideration is given to function and QoL.

Jack, 62 who underwent successful curative treatment articulates his clear goal before treatment; '*Obviously the number one priority is to save my life. That's what you have to bear in mind. But I pretty much knew it was going to leave me with maybe life-changing effects. Not necessarily life-limiting but certainly life-changing. But I knew I would end up with difficultly talking and difficulty eating'.*
(Jack 62 interviewed retrospectively who underwent curative open surgery)

Whereas Tim 63, T3, who continues to undergo non-curative but has recently experienced a deterioration in his swallowing. His description captures this greater focus on QoL in the setting of ongoing decision-making regarding the next line of non-curative treatment.
'If it gets to the point where you can't look forward to eating something, let's say with a feeding tube… … you start to struggle with the point of it to be honest'.
(Tim, 63, interviewed retrospectively who was on a non-curative treatment pathway).

This demonstrates the need to explore patients' own priorities for treatment and to return to these throughout the treatment trajectory, supporting these wherever possible as part of shared decision making.

7.4.3 Meta inference 3: Function and QoL

Function and QoL are impaired prior to treatment initiation and are likely to change after treatment for rOPC. Swallowing function and aspects of quality of life are at risk of deterioration. Some aspects of quality of life may improve with treatment for rOPC. To find balance between the sacrifices made to achieve cure or prolonged survival, when

deterioration in function and QoL occurs, patients and their caregivers appear to be able to recalibrate what QoL is and means to them. Healthcare professionals need to be able to provide appropriate support to patients to facilitate this recalibration process.

Stuart, 70 who had curative surgery for two separate disease recurrences explains how his outlook has changed over time.

If I was diagnosed with it today, I think my priority today would be long-term health and mobility. I think that would be my priority today. Maybe not the voice because, again, I've learnt to live with the voice. But if it happened today, yes, I think long-term health and mobility, and if I've got to sacrifice speech to have that, then I would sacrifice speech. (Stuart, 70, who underwent curative transoral robotic surgery on two occasions)

7.4.4 Meta inference 4: Patient and carer symptom concerns

Symptom concerns can change over time in response to symptom presentation. In contrast to the focus on survival outcomes prior to treatment, patients and their caregivers do not seem to experience anticipatory concerns regarding swallowing/ QoL outcomes. This may be due to their past experiences, and how patients and caregivers have knowledge about these already. However, if and when symptoms arise, these symptoms may become a significant concern which require addressing. Patients and caregivers are not always prepared for the severity or persistence of physical symptoms following treatment. When patients are ill prepared, symptoms appear to cause higher levels of concern and distress. Appropriate and accurate pre-treatment counselling is required however this is a very difficult balance to achieve due to individual patient and carer preferences. Satish, 67 who underwent curative surgery illustrates this:

'I think the problem is if you try and prepare people too much as to what to expect, they might either be disappointed or think that's going to be a real struggle, I might never be able to do it. I don't know what the right… Maybe ignorance is bliss, and you just cope the best you can. I'm not sure but I think it depends very much on the individual'.

(Satish, 67 who underwent curative open surgery)

7.5 Discussion

The aim of this mixed methods study was to measure function and QoL outcomes, concerns, priorities and patient and carer experiences of rOPC. This aim was addressed using a mixed methods convergent design including a repeated measures observational quantitative workstream and a longitudinal qualitative workstream involving interviews with both patients and their caregivers. To the authors knowledge this is the first mixed methods study of its kind to be undertaken with this patient population.

The primary outcome in the quantitative workstream, a patient reported outcome measure of swallowing-related QoL, the MDADI, demonstrated no change in swallowing from before treatment to six months following treatment initiation. This particular outcome measure, the MDADI, is widely used in the HNC research as a primary or secondary outcome measure in many large international trials (Nutting et al., 2023, Owadally et al., 2015). In line with best practice guidance for the conduct of HNC research (Lefebvre et al., 2009), multi-faceted measures of swallowing were also used in the quantitative workstream, including a number of secondary outcome measures. The secondary outcome measures focusing on function (swallowing and speech) were clinician-rated measures and either objective or subjective. In this study there was discordance between the primary and secondary outcome measures in relation to swallowing function. Secondary endpoints suggested a deterioration in swallowing function. A discordance in patient and clinician rated outcomes has been highlighted previously in primary HNC research. However, in the primary setting, it has been found that clinicians can underestimate the level of impairment (Falchook et al., 2016). Consequently, there is an emphasis in both clinical practice and research to utilise patient reported-outcome measures (Nguyen et al., 2020). In this study however, if we looked at the primary outcome measure of the quantitative workstream in isolation, one might disregard the secondary outcome findings and interpret no change in swallowing as demonstrated by the

MDADI. However, as per the aim of the mixed methods study, we have a deeper understanding of swallowing from the qualitative data. In this study, the qualitative workstream data demonstrates disagreement with the patient-reported swallowing outcome but is more concordant with the clinician-rated outcomes showing a decline in swallowing. Such dissonance brings into question the validity of the MDADI for use in this patient population. In fact, the validity of this tool has already been questioned in relation to patients with severe dysphagia/ gastrostomy tube reliance (Toft et al., 2024).

This study not only investigated swallowing outcomes but also speech. The quantitative workstream included one measure of speech, which demonstrated a decline in speech intelligibility after patients were treated for rOPC. The qualitative data demonstrated agreement with this, illustrating patient and carer reports of deterioration in speech. However, the qualitative data also offered further insight and expansion highlighting the impact of speech deterioration on the individual, relationships and working life. Returning to work, although a more recent focus within the literature on primary disease (Yu et al., 2022), has not been explored in the disease recurrence context. The ability to return to work was, however, a strong theme throughout the qualitative interviews. The impetuous to return to work was not only for financial reasons, but also for self-efficacy and as an aspect of QoL. Return to work has not been considered in the literature to date in the recurrent setting. Changes to voice were reported by participants either as a persisting toxicity from their previous treatment or as a presenting symptom for disease recurrence. These changes were not captured quantitatively at timepoint one or two, as a validated measure of voice was not included in the study protocol, which is a limitation.

With regards to QoL, the quantitative data has shown that some elements of QoL, namely the physical domains, decline over time, in particular for those undergoing curative treatment. Agreement was noted with the qualitative data, with many participants describing that they had experienced changes in their physical status and ability to participate in

activities of daily living. Those who underwent curative treatment described a marked and sudden deterioration in their physical functioning followed by a degree of improvement which did not reach their baseline level of functioning. For some this may be an improvement in strength, energy levels or mobility. For others this may be gradual improvement in speech or swallowing. Regardless of the domain of recovery, participants who had experienced any improvement appeared to focus on this positive. One example of this is a gentleman who can no longer speak or swallow since his curative treatment. However, he focused on the gains he had made with his physical fitness and return to strength training.

The trajectory of change in QoL was not the same for participants on a non-curative treatment pathway. Overall, from baseline prior to treatment initiation to six months following treatment initiation, a mild improvement in physical functioning was noted. This is in part explained via the qualitative findings, where participants report some symptomatic relief with treatment commencement or when symptoms such as pain were addressed.

An area of common QoL improvement noted quantitatively from baseline to six months in the entire sample and across treatment pathways was in the social-emotional QoL scale. One might not expect this in either the curative or non-curative setting given the perceived potential functional/ QoL morbidity with curative treatment, or the palliative diagnosis associated with non-curative treatment. The qualitative data in this study provides further explanation as to why participants may experience improvements in some aspects of social-emotional domains of QoL. Patients, particularly in the curative group, appear to experience a phenomenon known as ‘response shift’ where patients experience better outcomes over time, not because the patient is physically doing better (as we can see from the deterioration in physical QoL related score) but because the patient has adapted to their new circumstances (Sprangers & Schwartz, 1999).

The qualitative data in this study demonstrates several examples of this including a lady who at six months post curative treatment remains gastrostomy-dependent but is delighted to have sufficient energy to look after her granddaughter again. Another gentleman who can no longer speak or swallow now focuses on what he can do to enjoy his life, namely independent travel and spending time with his wife and daughter. Response shift appears to be required to deal with the outlook of one's future life with the limitations imposed by the curative treatment(s) received including reduced or absent speech clarity or swallowing ability (Echteld et al., 2005).

One might not expect to see such a response shift in the non-curative setting, as the outlook for the future is very different prognostically. However, overall outlook does appear to change for those participants in the non-curative group. The qualitative data provide some further insights and possible explanation for this. One prospective participant and his wife describe their 'relief' that the participant remains 'so well' and is able to: participate in social events albeit with adaptations, continue to work, and fit in trips away with his family between treatment appointments. The WHO defines QoL as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (World Health Organization. Division of Mental and Prevention of Substance, 1997). This gentleman's overall goal is to remain alive, however as an experienced HNC patient, he expected to feel much worse in pursuit of this goal through anti-cancer treatment. Perhaps this, coupled with appropriate symptom control measures, has resulted in an improvement in all aspects of his QoL.

The quantitative and qualitative data in this study demonstrate that patient symptom-related concerns can change over time. From the UWQoLv4 data we see a shift in concerns regarding symptoms from pre-treatment to six months following treatment initiation. Pain, swallowing and mood were the main symptom concerns pre-treatment and at six months, swallowing, saliva and speech/ pain were the main symptoms of concern. Concern in

relation to symptoms appears to be reactive rather than anticipatory. We know from the quantitative data that symptoms change over time, with swallowing and speech deteriorating. Pain, as noted by one of the participants 'is funny… you don't notice how bad it is until it is gone'. In this instance this lady reported how her pain was eliminated with curative surgery for rOPC. Others commended the efficient and effective relief of pain through symptom control measures whist receiving non-curative treatment. However, we also know from the quantitative data in this study that swallowing, and speech can deteriorate with curative and non-curative treatments.

With increased swallowing difficulties can come increased difficulties with saliva control and management, resulting in the experience of excess volumes of mucous, which can be very troublesome for patients. As evident in the qualitative interviews, participants did not always feel adequately prepared for the severity and persistence of symptoms experienced with treatments and noted, in particular, that when they felt ill-prepared, symptoms were of significant concern. One lady who remains nil by mouth at six months post curative treatment questioned why she had to wait for her gastrostomy to be placed post operatively. She felt that her team had been over optimistic about her outcome and that further with preparation, both informational (being warned of severity of outcome) and practical (pre-operative placement of gastrostomy), her discharge and recovery following surgery would have been smoother.

Unlike symptom concerns, treatment-related priorities did not change over time for the participants in this study. Almost all participants in this study articulated very clearly that cure was their ultimate goal and if cure was not achievable then they wanted to live for as long as possible so that they could be there for their loved ones. Potential function or QoL decline was not prioritised in decision-making at the point of diagnosis. Although decisional regret was not a focus of this study, almost all participants who underwent curative treatment reported that they would make the same decision again regarding their treatment, regardless

of the functional outcome, because their treatment had been successful and achieved cure. For those participants who had progressed from a curative pathway to a non-curative pathway, there was some evidence of decisional regret however it was difficult to know if they experienced regret that they had the surgery, or that the surgery didn't achieve cure or perhaps a combination of both.

Within the non-curative setting, the topic of decisional regret was neither addressed nor volunteered by participants. The retrospective group of patients undergoing non-curative treatments did, however, explain that as symptoms and indeed disease progresses, QoL and function may become more significant in decision-making again. In this setting, cure is most definitely not an option and survival is becoming less sustainable with time.

7.6 Conclusion and implications

The overarching finding of this mixed methods research is the importance of patient and carer experience. It is not possible to separate treatment-related priorities, function and quality of life and symptom concerns, from patient and carer experience. When we talk about treatment-related priorities we need to think about the patient experience. Rather than asking do we know what the patient wants, we need to ensure that the patient/ carer feels that they have been given adequate and appropriate information to understand their options. Do they feel like they have had the opportunity to make their priorities heard and be involved in decision making? When we think about function and QoL changes rather than verifying if a patient has been informed about potential changes, we need to think about what their experience of function and QoL is like before, during and after treatment. Are patients and caregivers aware that this is likely to change and in what direction and at what timepoint? This is the same for patient and carer concerns regarding symptoms, if and when they arise. For each individual patient and their carer, every effort must be made to enhance that individual's experience of the care they are receiving. This study has offered the most detailed account, to our knowledge, of information in relation to patient and carer experience

of OPC recurrence diagnosis, treatment decision making, treatment and living with and beyond treatment. Being diagnosed with rOPC is a significant life event, however this does not preclude a positive patient and carer experience. In this study we have heard accounts where patients were given their diagnosis alone. Although second opinions were accessed by some patients, the pathway to accessing a second opinion was not always explicit or understood by both patients and healthcare professionals. There were very mixed reports regarding patient involvement in decision-making with some experiencing a lack of involvement or a feeling of being pushed towards a particular or sole treatment route. The experience of pre-treatment counselling also varied greatly, with some reporting how ill-prepared they felt before their treatment, whilst others, many of whom admitted they felt overwhelmed at the time, could see the benefits of the preparations following the event.

Judy, 60 who underwent curative surgery explains this.

'You know, the stark reality is that cancer treatment isn't kind. But then, it has to be that way in order to be successful, however kindness from others can go a long way in making a horrible situation a lot better'.

(Judy, 60 who underwent curative transoral robotic surgery)

7.7 Summary

This chapter has described the main findings of the mixed methods study including the integration of the qualitative and quantitative findings. The next chapter will summarise the findings of the thesis in relation to the overall research aim and objectives. This will include the findings of the systematic review and mixed methods study. A critique of all workstreams will be included and the clinical and research implications discussed.

Chapter 8 Discussion, critique and implications

The aim of the final chapter of this thesis is to provide a comment on how the results presented in Chapters 3, 5, 6 and 7 answer the important research questions posed in this thesis, and how these findings relate to the wider context of published literature. The limitations of this thesis will be discussed and the central implications of this study for clinical practice and future research outlined.

8.1 Review of research aims objectives and questions.

8.1.1 Research aim

The overall aim of this thesis was to identify and address gaps in the current evidence base for rOPC with focus on function and quality of life (QoL) outcomes, patient priorities and patient and carer experience of rOPC for those undergoing curative and non-curative treatments.

8.1.2 Thesis objectives

The objectives of this thesis were to:

1. Identify and evaluate the existing literature for communication, swallowing and QoL outcomes, and patient experience, to define knowledge gaps.
2. Investigate the communication, swallowing, QoL outcomes, and treatment-related priorities for patients with rOPC and how these may change over time.
3. Explore the patient and carer experience of rOPC including diagnosis, treatment decision-making and living with the consequences of treatment.

To address research objective one, a systematic review was undertaken to investigate if and how function and QoL outcomes and patient experience are reported in this population and to determine what is known about these outcomes. To the authors knowledge this was the first systematic review aiming to report on function, QoL and patient experience for patients

undergoing both curative and non-curative treatments for rOPC. The systematic review identified a paucity of studies reporting on function and QoL outcomes specifically for patients undergoing curative surgical treatment for rOPC. No studies investigating function and QoL outcomes for patients undergoing non-surgical treatments were identified. When outcomes were reported, the studies were generally of poor quality. Heterogeneity across studies, including the use of different or unvalidated function and QoL outcome tools, at different or undefined timelines for follow up outcome measurement, negated the possibility of completing any data synthesis. In the studies reporting swallowing outcomes, there are mixed findings from clinician versus patient-reported outcomes (using the MDADI). Clinician-rated measures demonstrated consistent deterioration after treatment whilst the MDADI showed stable or a non-clinically significant deterioration. Speech outcomes were rarely reported and when they were, a deterioration was noted. QoL outcomes were reported as stable. The review did not identify any patient experience data. Significant gaps in the literature were identified in relation to function and QoL outcomes and patient and carer experience data in the field of rOPC. These findings indicated a number of research questions which ultimately led to the development of a mixed methods study investigating both function and QoL outcomes with curative and non-curative treatment for rOPC, and patient and carer experience of rOPC.

To address research objectives two and three, a longitudinal mixed methods study was undertaken to identify function and QoL outcomes, patient concerns and treatment-related priorities and patient and carer experience or rOPC. To the authors knowledge this was the first mixed methods longitudinal study of its kind in the area of rOPC. The study involved the prospective measurement of function and QoL outcomes, patient priorities and concerns in a sample of patients with rOPC undergoing curative or non-curative treatments. A range of patient-reported swallowing and QoL outcome tools, clinician-rated swallowing/ speech and instrumentally evaluated swallowing before and after treatment initiation for rOPC were used. Concurrent qualitative data collection was undertaken to explore patient and carer

experience of rOPC over time including diagnosis, treatment decision-making and living with the consequences of treatment. The protocol for the mixed methods study was designed in partnership with the study PPI/E group, a group of patients who have undergone treatment for recurrent HNC.

8.2 Main findings

Function and QoL will change with treatment for rOPC. Treatment-related priorities do not and remain focused on cure or survival, with patients acknowledging lower success rates and the possibility of poorer function /QoL. If this goal is achieved, patients can adapt and experience stable if not improved QoL regardless of their functional status. If not, maintaining QoL becomes increasingly difficult when function has deteriorated.

Although treatment-related priorities, function and QoL outcomes can all be measured quantitatively, and inferences can be made about 'response shift', this thesis has provided a new and deeper understanding of this process with the concurrent collection of qualitative data.

In clinical practice, MDTs often make decisions about the treatment of rOPC based on their perceived functional or QoL morbidity. However, the systematic review within this thesis, has demonstrated that such recommendations are based on poor or absent function and QoL outcome data. The mixed methods study has demonstrated that the intention of such recommendations may be disparate to the patient and carer treatment-related goals. This thesis has also demonstrated that for some patients, while some elements of their QoL reduce some areas may improve with curative and non-curative treatment within the first six months of treatment initiation. The new knowledge generated from this thesis has emphasised the importance of person-centred and personalised care and should inspire MDTs to review their approach to treatment decision-making and ongoing care for patients with rOPC.

This thesis has also demonstrated that patients' and their respective caregivers' experiences vary hugely in terms of their diagnosis, opportunity for SDM, pre-treatment counselling and ongoing support during and following treatment, highlighting an inequity of care. This thesis has highlighted that the care pathway for all patients with rOPC needs to be improved.

The main findings of this thesis have several implications for both clinical practice and future research which will be addressed later in this chapter. Prior to this, the main findings will be discussed within the context of the existing HNC literature. This work will propose an argument for the conceptualisation of rOPC as a distinct entity from primary OPC. This will also be considered in the context of primary endpoints and outcome measurement for future research.

8.2.1 Main findings in the context of existing literature

Primary versus recurrent disease

Often it appears that the knowledge generated from research in primary OPC is applied to the management of rOPC. Examples of this include interventions where we use the same treatment doses considered curative in the primary setting in re-irradiation trials (Chen et al., 2024). Likewise in surgical trials surgical margins are a much debated issue when the same definition for what is considered 'clear margins' in treatment naive tissue is often imposed on re-irradiated tissue (Hardman et al., 2022). Similarly, assumptions about function and QoL are often made in the recurrent setting based on what we know or do clinically in the primary setting. Such assumptions include the influence of baseline functional status, tube feeding protocols, emotional and psychological status and how we measure functional outcomes. However, this thesis has demonstrated that the functional status of patients with rOPC before and after treatment can be very different to those patients with primary disease. This, coupled with their level of experience of HNC treatment and recovery, can be influential how

patients and their caregivers react to their diagnosis. Their decision-making or thoughts on the use of non-oral feeding in rOPC versus primary disease can be fundamentally different. The data generated from this thesis will now be discussed to consider rOPC as a distinct entity from primary OPC.

Baseline level of functioning

We know from the literature on primary disease that treatment for OPC can have a devastating impact on function and QoL with acute, long term and late effects of treatment (Roe et al., 2014, Patterson et al., 2018). We also know that one of the key factors in predicting functional outcomes following primary treatment is baseline level of functioning (Frowen et al., 2010). From this thesis, it is clear that patients with rOPC are likely to already have some level of functional deficit at the time of diagnosis of recurrent disease. The starting point for embarking on treatment in the recurrent setting in this study (median MDADI composite score of 60 in this study) was very different from that reported in the literature on commencement of primary disease management (mean MDADI composite score of 86.9 at baseline as per Roe and colleagues (Roe et al., 2014). This thesis has revealed some insights into how that impaired level of function at baseline may impact patients and their caregivers as they go through treatment for rOPC. We cannot simply assume that a poor baseline level of functioning is going to result in a poor swallowing-related or overall QoL following treatment as the literature would suggest in the primary disease setting. The mixed methods study within this thesis demonstrates that for some, swallowing may no longer be a priority or an expected source of enjoyment in life given their previous treatment. Therefore, if the prognosis for swallowing recovery is poor following treatment, this may not be a major consideration for all patients in terms of impact on overall QoL. However, what this study also shows is that in the case of severe dysphagia post-treatment, regardless of the starting position, secretion management can be very troublesome for patients following treatment. The impact of difficulties with secretions has been highlighted in the literature previously in the relapsed and metastatic HNC disease

population. While investigating the content validity of the commonly used QoL measures, namely the EORTC QLQ-C30 and QLQ-H&N35, for patients with relapsed/ metastatic HNC disease, Degboe and colleagues highlighted how patients interviewed in their study suggested that excessive mucous may be a worthwhile addition to these tools (Degboe et al., 2018). Indeed, in this study, the UWQoLv4 questionnaire was used and here symptom item 10 is focused on saliva. Using this item, patients are asked to rate their saliva production from the following four options (1) my saliva is of normal consistency (2) I have less saliva than normal, but it is enough (3) I have too little saliva and (4) I have no saliva. Like the EORTC QLQ-C30 and QLQ-H&N35, the UWQoLv4, one might assume that this question has been developed in primary HNC patients in mind. It does not have an option for patients to report having too much saliva, or indeed an item to report any symptoms in relation to excessive mucous production. When answering this question, it was common for patients in this study to leave this item unrated or include comments such as 'too much saliva', 'loads of saliva' on the written questionnaire. Although dry mouth is a common sequala of radiation to the head and neck region (Nutting et al., 2011) and a significant issue for patients following primary treatment for OPC (Roe et al., 2014), the trajectory for change in saliva may be somewhat different for patients in the recurrent setting. Patient-reported outcome measures aiming to capture this would need to be sufficiently broad to allow reporting of issues with saliva from both ends of the spectrum, from having zero saliva as can be the case following primary treatment, to having excessive amounts, which can be the case with severe dysphagia in the recurrent setting, as demonstrated through the qualitative data in this thesis. Baseline level of functioning in the primary disease setting is often used in the decision-making regarding the use of non-oral or enteral feeding. This will now be considered further using the data generated from this thesis highlighting the differences between primary and rOPC.

Non-oral feeding decision making

In the primary HNC setting, practice regarding the indications, timing and type of enteral feeding in patients undergoing chemo(radiation) varies. Whilst some centres use a prophylactic gastrostomy, placed pre-treatment in the absence of a baseline dysphagia, others take a more reactive approach (Paleri et al., 2018). Indeed, previous research has shown that for some patients who receive appropriate on-treatment MDT support, feeding tubes may be avoided (Roe et al., 2016). The relationship between method and timing of enteral feeding is not well understood in the current literature base for primary HNC disease (Patterson et al., 2016). However, it has been hypothesised that the presence of a gastrostomy tube may reduce oral intake earlier, leading to a potentially greater period of nil by mouth increasing the potential for atrophy of the swallowing musculature (Patterson et al., 2016). Therefore, a reactive tube feeding protocol may promote enhanced swallowing outcomes post-treatment in the primary disease setting.

In this thesis, the baseline gastrostomy rate was 20% pre-treatment, which increased to 52% at six months across curative and non-curative treatment pathways. The qualitative workstream provided some insights into the experience of needing and having a gastrostomy. For the patients treated curatively both in the prospective and retrospective groups, it appeared that many patients had their feeding tubes fitted prophylactically, whilst others had their tubes fitted reactively after their surgery. However, the qualitative data did not reveal any evidence of a clear decision-making pathway for prophylactic versus reactive tube feeding in the surgical. The variation in practice may be explained by the lack of high-quality outcome data in the curative setting in the systematic review. Due to a lack of evidence to inform practice, some patients may have been predicted to have a better swallowing outcome. Or perhaps due to the potential application of practice in primary OPC which is avoidance of tube feeding to enhance swallowing outcomes. The qualitative data in this thesis however has demonstrated that patients who have a reactive gastrostomy in the acute recovery phase following surgery, can find this extremely traumatic. A common area of

dialogue in the qualitative interviews was the discomfort/ prolonged length of hospital stay caused by having a gastrostomy placed reactively. One patient described the pain caused when coughing when his gastrostomy was fitted after his surgery. He explained how he was coughing more as he was unable to swallow his secretions.

For many in the non-curative setting, the gastrostomy appeared to have been placed reactively in the setting of deteriorating swallowing and compromised nutritional status. As reported in the findings of the systematic review this thesis, swallowing outcomes are not reported for non-curative treatments and so perhaps a lack of awareness of the potential for swallowing deterioration contributes to this reactive tube feeding practice. However, this thesis has confirmed that swallowing can deteriorate in the non-curative setting and that patients are concerned regarding their nutrition. Participants in the qualitative workstream of the mixed methods study highlighted their anxiety regarding their nutrition, as they felt they needed to be well nourished so that they could 'fight the cancer'. We also have some evidence to suggest that poor pre-treatment nutritional status is associated with negative post-immunotherapy outcomes (Guller et al., 2021). Given the evidence generated from the mixed methods study in this thesis, and in the context of the existing literature highlighting the importance of optimised nutrition, there may be an argument for a prophylactic approach to gastrostomy in the recurrence setting contrary to practice in the primary disease setting.

Reaction to diagnosis

When considering the emotional reaction to a diagnosis of rOPC, when a person receives their diagnosis, their status changes immediately. Prior to the diagnosis of cancer recurrence, patients were considered cancer-free and now they no longer are. In the general cancer population, fear of recurrence (FOR) can occur in up to 72% of cancer survivors (Simard et al., 2013). In longitudinal studies of FOR in the general cancer population, up to a quarter of patients can have high levels of FOR at up to 2.5 years following treatment.

FOR in the HNC population has been highlighted as a frequently reported unmet need (Rogers et al., 2010b), and has been linked with high levels of anxiety (Fenech et al., 2024). One must then hypothesise about what happens to that person when that fear becomes a reality. How does that impact on psychological status?

Much of the literature on FOR focuses on the first 12 months post-treatment in the HNC population. We know from the literature that the majority of HNC patients have low declining FOR after diagnosis, but approximately one in five patients, who are typically younger and female, experience persistent high levels of FOR for up to six months (Deuning-Smit et al., 2022). Does this FOR persist after six and 12 months and if so, does it in some way prepare patients for the diagnosis?

In this thesis, the data showed that those patients who were diagnosed closer to their original treatment (residual or recurrent disease) appeared to be less shocked in comparison to those who were diagnosed many years after their original treatment (new primary disease). However, the literature also highlights that patients who have a previous diagnosis of recurrence, are at greater risk for high levels of FOR and anxiety following treatment for their recurrent disease (Deuning-Smit et al., 2022). Although this is something that is appreciated in the primary disease setting and often patients are routinely asked about this following primary disease treatment using tools such as the Patient Concerns Inventory for Head and Neck Cancer (PCI-HN) (Rogers et al., 2009), this is not seem to be the case in the recurrence setting. This particular tool, the PCI-HN was developed for use in the primary setting and has led to the development of intervention packages to try and address FOR (Humphris and Ozakinci, 2008). However, such assessment tools or intervention protocols are not available in the recurrent setting. We need to consider how we assess and address the support needs of patients specifically when they have previously experienced FOR and now have recurrence.

In the wider cancer recurrence setting a previous review study investigated the psychological responses to cancer recurrence in the breast cancer population. This study identified that stress and anxiety increase at the point of diagnosis, as one might expect, however the stress was contained and did not result in diffuse emotional distress or QoL disruption (Andersen et al., 2005). In a later published review of recurrence using meta-ethnography to synthesis qualitative data across tumour types (breast, ovarian and oral cancer), a similar pattern was noted and a recommendation for the implementation of stress and anxiety management at the point of diagnosis of recurrence was recommended (Wanat et al., 2016).

Previous literature related to the HNC recurrence population, specifically those diagnosed with oral cancer, has investigated psychosocial responses to the diagnosis in an effort to develop a theoretical understanding of the recurrent oral cancer at the point of diagnosis (Griffiths et al., 2008). Similar reactions were noted by Griffiths and colleagues regarding the reaction of patients including shock and disappointment. Griffiths and colleagues also identified a level of acceptance, that the diagnosis of recurrence would cause death (Griffiths et al., 2008). This is contrary to the findings in this thesis as the patients, even on a non-curative pathway, remained hopeful that something could be done to keep them alive for as long as possible. This may reflect the changing landscape of recurrent HNC management over the past five to ten years. The qualitative study completed by Griffiths and colleagues was published 16 years ago at a time where the majority of patients were treated palliatively (Griffiths et al., 2008). The participants recruited for the workstreams within this thesis were very knowledgeable about the new and emerging treatments for recurrent disease. Many were actively seeking second opinions or signing up for clinical trials in the hope that perhaps a new treatment would be found. The data generated from this thesis has demonstrated that patients who are diagnosed with rOPC certainly experience stress and anxiety at the point of diagnosis, but the unique longitudinal nature of this study gives further insight into how the support needs of patients may change over time. Previously this was not

a consideration in the literature as historically patients with disease recurrence were considered to have a very short prognosis.

This thesis has demonstrated that at the point of diagnosis interventions to target stress and anxiety may be welcomed by patients and family members, however during and after treatment other types of support may be required specific to the individual symptoms and concerns that the patient and their family may have. This strengthens the need for the MDT to routinely assess and reassess the individual support needs and concerns of patients and family members throughout the course of the disease from point of diagnosis to treatment and beyond and for some to end of life care.

Collectively, the above observations show us that patients with rOPC are fundamentally different from patients with primary disease, in terms of level of experience of HNC disease, baseline functional and emotional status, symptom severity and in terms of the tools and resources that are available. Consequently, it can be argued that rOPC and its impact should be viewed, treated, and measured as a completely different entity to primary HNC. The data generated in this thesis will be used to explore these areas further.

Primary and secondary endpoints

The primary outcome measure used in this thesis was the MDADI. This is the most widely used outcome measure in HNC clinical practice and research and is frequently used as the primary endpoint or secondary outcome measure in many large international trials in primary HNC management (Nutting et al., 2023, Nichols et al., 2019). I chose this tool as the primary endpoint for many reasons. As a clinician I have used it for many years in my clinical practice, and because of its widespread use in HNC research. It also had included patients with recurrent disease in its initial validation (Chen et al., 2001). However, on further examination, the initial validation was undertaken with 100 patients, and only 8% of these patients had oropharyngeal disease. Since this initial validation in 2001 not only have

treatments changed, but the demographic of HNC patients has also changed, with greater numbers of patients with oropharyngeal disease, which in the UK, includes both HPV related and non-HPV related disease (Schache et al., 2016). Patients with oropharyngeal disease, in particular those with HPV related disease, have been highlighted in the existing literature as a unique cohort of patients, who are younger, healthier and fitter (Goldsmith and Roe, 2015). The majority of patients included in the initial validation of the MDADI had laryngeal disease. This clearly raises the question whether the needs of a patient treated for recurrent larynx cancer in 2001, match the needs of a patient undergoing treatment for rOPC in 2024?

The 10-point clinically significant difference previously established for patients using the MDADI (Hutcheson et al., 2016) has recently come under scrutiny, with the suggestion that a smaller change may be clinically important to a highly functioning patient with OPC (McDowell et al., 2024). It would be reasonable to hypothesise that in the setting of impaired and vulnerable swallowing at baseline, a patient with rOPC who perhaps has consciously or unconsciously compensated well for their pre-existing dysphagia over a number of years is also more sensitive to even the smallest change in swallowing function. Therefore, a less than 10-point change in the MDADI may be clinically significant here also. As previously mentioned in Chapter 6, the content validity of the MDADI has more recently come under scrutiny, in particular for those patients with severe dysphagia or those who are gastrostomy dependent (Toft et al., 2024). Given the severity of dysphagia observed at baseline or developed over time in the sample of participants in this thesis, one might question the appropriacy of the MDADI as the primary end point in this study.

Survival versus functional outcomes

There has been a clear paradigm shift in the focus of recent and current research in primary OPC treatment to not only focus on survival outcomes, but to place equal if not greater importance on function and QoL outcomes. This is clear from a number of recent intervention studies where in comparison of treatment options, the primary outcome

measure was a patient-reported swallowing-related QoL measure, namely the MDADI. This includes a trial investigating dysphagia optimised IMRT versus standard of care IMRT (Nutting et al., 2023), the initial phase II trial of a phase II/III trial investigating de-escalation of adjuvant treatment for patients with human papilloma virus (HPV)- related OPC (Owadally et al., 2015), and a further two intervention trials investigating radiation treatment versus minimally invasive surgery for primary OPC (Simon et al., 2018, Nichols et al., 2019).

Based on my systematic review completed as part of this thesis, the focus of the literature in the recurrence setting remains on survival as the primary outcome. This may be a result of the change in the overall management of OPC recurrence. As mentioned in the introductory chapters of this thesis, historically rOPC had a very poor prognosis and the majority of patients were treated palliatively. However, in more recent years this is changing with more and more patients being considered for potentially curative treatments. Essentially treatments for rOPC are evolving as we continue to learn more about the disease from basic science investigations to intervention trials to function and QoL and patient experience data. In primary OPC, the treatment options available such as TORS or radiation for early disease or IMRT versus PBT, offer comparable survival outcomes, and so naturally the focus of research is on function and QoL outcome optimisation. Treatment of rOPC is an evolving landscape and the treatment options that are on offer to patients currently do not offer equipoise in survival, for example when a patient is offered surgery (curative) versus immunotherapy (non-curative). If, and when, a curative option is presented to a patient and their carer, this thesis has demonstrated that the majority of patients will opt for potential cure in line with their key treatment-related priority. Therefore, patients need accurate survival statistics on the various treatment options available. In addition, accurate function and QoL data must also be provided. One of the key findings of this thesis is that patients appear to adapt to the functional and QoL implications if their treatment-related goal is achieved. However, if it is not, achieving this balance and finding QoL is much more difficult. Survival data on all available treatment options is required but insufficient alone. Function

and QoL data on all available treatment options is also required and also insufficient alone. Therefore, future research must aim to deliver both with equal robustness. The new knowledge gained through this thesis demonstrating the optimal conditions to achieve recalibration of QoL must also be presented to patients to provide context to the survival, function and QoL data. This will help patients to be more informed about what life might be like in all possible scenarios prior to making an informed decision regarding treatment.

Finding an appropriate balance in intervention trials regarding primary and secondary endpoints is extremely difficult however, using methods such as developing a core outcome set in partnership working with patients, caregivers and healthcare professionals may help to achieve this balance.

8.3 Critique

8.3.1 Strengths of this thesis

Patient and public involvement/ engagement (PPI/E)

The PPI/E at each stage of the research cycle for this thesis including the funding application, proposal design and development, data interpretation and now results dissemination, has been a strength of this thesis. From the study inception, the aims of the study have been in line with the questions that patients with recurrent HNC have. The systematic review questions and subsequent findings were discussed with the PPI/E group. As discussed in Chapter 3, although numerous gaps and priorities for research were identified with the systematic review, the PPI/E group helped prioritise the research questions which would be addressed in the subsequent mixed methods study. Indeed, the concept of a mixed methods study was driven by the PPI/E group. Initially the research team had planned a prospective study investigating function and QoL outcomes measured quantitatively. However, the study PPI/E group insisted that it was imperative that patient experience is also measured as swallowing/ speaking is more than just a score on an

assessment tool. The PPI/E group also insisted that the impact on caregivers/ family members must also be measured. Recurrent HNC is never experienced by a patient in isolation, with the day to day lives of their family members and caregivers are also impacted. Caregivers were subsequently also included in the qualitative workstream.

As part of this mixed methods study, recruitment was slower than expected, with reduced take up from prospective participants for the follow up interviews at timepoint two (six months following treatment initiation). This was discussed with the study PPI/E group in an effort to problem solve. At this point the study PPI/E group advised that a retrospective cohort should be included in the study, who are at least 12 months following treatment initiation, to obtain a true understanding of the patient and carer experience and how this may change over time.

The PPI/E group were also consulted again for their insights at the point of qualitative data analysis and integration with the quantitative data. The PPI/E group felt that the findings of the study were in line with their own personal experience. In particular, the PPI/E group were consulted regarding how to integrate the carer data. They advised that the carer data should be viewed jointly with the patient data again reiterating that rOPC is 'felt' just as much by the family/ loved ones as the patient themselves. They also felt that the retrospective data gave a true representation of the recovery following treatment. The PPI/E group commented in particular that after six months patients would still be experiencing a lot of functional side effects after surgery and that in fact the recovery process was much lengthier. Likewise in the non-curative setting, if a patient is doing well treatment can continue for up to two years (one PPI/E member was on pembrolizumab) and so it is important to get a longer-term picture of what function and QoL look like over time.

Study rigour

Each study has been reported according to published tools, and the protocols were prespecified, allowing transparency and rigour of the research methods. An experienced qualitative and mixed methods researcher supported and reviewed the qualitative research and integration with the quantitative findings. Likewise, an experienced quantitative researcher supported and reviewed the quantitative research. All members of the research team participated in reviewing aspects of the research, for example abstract screening and the risk of bias assessment for the systematic review, and the framework analysis of the qualitative findings. This allowed me to be in charge of the whole research package, however as a novice researcher, minimised any potential mistakes or bias that could have occurred if working independently.

Methodological approach

Another strength of this research is the methodology used. Measuring function and QoL in HNC, although under-researched in the recurrent HNC setting, is not a new concept in HNC research itself. However, combining prospective longitudinal repeated-measures research with prospective and retrospective longitudinal qualitative research via mixed methods is novel. The integration method used, combined joint display tables, triangulation protocol and a weaving narrative, is also quite innovative.

8.3.2 Limitations of this thesis

The limitations of the systematic review will be considered firstly followed by the mixed methods study.

Systematic review limitations

Inclusion criteria

Although there are merits to having a very focused research question and subsequent inclusion criteria for a systematic review, it is possible that the inclusion criteria may have been too narrow. Given the limited evidence on function and QoL data in the recurrent HNC population, it may have been sensible to include all recurrent HNC and make some inferences based on the number of patients with rOPC included.

Analysis

In preparing the systematic review protocol, it was hypothesised that literature regarding function and QoL data for rOPC was in its infancy. For this reason, meta-analysis was neither planned nor subsequently undertaken and instead, a narrative review of the evidence was completed. The data presented focuses solely on (potentially curative) surgical outcome data. A quality assessment cut off criteria was not utilised in order to identify the maximum number of articles. As a result, when the risk of bias assessment was completed a high level of bias was noted, with the majority of the studies observational and retrospective in design.

Mixed methods study limitations

Sample size

To the author's knowledge, this is the first study to attempt to complete a sample size calculation to prospectively measure change in swallowing-related QoL in patients undergoing a range of curative and non-curative treatments for rOPC. However, the desired sample size was not met. Using a two-sided alpha of 5% with 80% power, 25 participants (+10% to cover drop out) were required for the primary endpoint, which was change in MDADI from baseline to six months. Although 25 participants were recruited, the additional 10% were not. Due to sample attrition, the study ultimately was underpowered. As a result,

descriptive statistics only could be used to measure change in MDADI composite score from baseline to six months. However, as noted, concerns regarding the content validity of the primary outcome measure have been published in the literature since protocol development. The data in this thesis also add to such concerns with the observed dissonance between MDADI findings and clinician-rated and patient experience data.

Incomplete data and sample attrition

The data collection was incomplete in the mixed methods study in both the quantitative and qualitative workstreams. In the quantitative workstream, the fact that the use of FEES was optional and remote follow up consultation was often favoured for participants in this study was a limitation and resulted in poor follow up data in terms of instrumental evaluation of swallowing outcomes. In the qualitative study, there was also a lack of uptake for participation in interviews at both timepoint one, prior to treatment initiation, and the second interview timepoint, at six months following treatment initiation. Although 25 participants were recruited prospectively, only 10 took part in interviews before commencing treatment, and a further five at timepoint two. This was due to a plethora of reasons including patient and researcher availability in particular for timepoint one when there was a short window between diagnosis and treatment commencement. At timepoint two, many participants declined to take part in a follow up interview as they were/ became unwell or had other treatment-related priorities. There was also sample attrition due to the nature of the disease, with four patients dying between baseline and six months.

Sample representativeness

Although multi-site, the majority of the recruitment for this study took place at a tertiary referral centre in London for the prospective workstream and exclusively for the retrospective qualitative participants. This, coupled with the fact that the majority of the participants were male and White British, limits the generalisability of findings to different geographical

locations, including underserved populations and those from different ethnic and cultural backgrounds.

Bias and reflexivity

As an experienced clinician working in the field of recurrent HNC for many years, there was certainly potential for my experience to bias the findings of this study. Also, the prospective group of participants had their quantitative measures collected prior to their qualitative interviews. Although blinded to their outcome measures at this point, it is possible that completing the questionnaires made some patients more attuned to function and QoL changes and may have influenced what they reported or highlighted during their interviews. I was not blinded to their outcome measures and so it is possible that my knowledge of their function / QoL status may have influenced the way in which I interviewed the participants. In addition, in the retrospective cohort, approximately 50% of this sample were known to me as a clinician. I had been involved in their pre-treatment clinical care, and during and post-treatment rehabilitation. This certainly may have biased what these participants reported in their interviews or indeed what I interpreted from their interviews given that their background and previous history was known to me.

To try to mitigate such sources of bias, I maintained a reflexive log throughout the data collection and analysis to monitor and manage the personal thoughts and reactions I had to the data and the analysis process. For the participants who were known to me, I did specify to them prior to interview that I was trying to gain a deep understanding of their experience and explained that this may include both negative and positive experiences of their pre-treatment or post-treatment rehabilitation and it was important to hear both. In a further effort to mitigate bias a sample of the retrospective patients also had the opportunity to review my findings to ensure I had interpreted their interviews correctly.

Despite these limitations, this study, has resulted in some important implications for clinical practice and future research. These implications will now be explored.

8.4 Implications for clinical practice

This thesis has several implications for clinical pathways of care, SDM and pre-treatment counselling.

8.4.1 Care pathways

Prior to this work, clinical experience demonstrated that functional outcomes were affected by surgery, whether open or transoral robotic, and with or without reconstruction. My clinical experience was as the SLT involved in the assessment of these patients prior to their treatment. This pre-treatment evaluation usually included a range of patient-reported and clinician-rated measures of function / QoL and instrumental evaluation of swallowing (Paleri et al., 2020). However, patients with rOPC undergoing non-curative treatment at the research centre were not routinely seen for baseline pre-treatment evaluation or counselling. There are a number of potential reasons for this. Firstly, it was perhaps assumed that function did not change as dramatically for these patients as it would for a patient undergoing curative treatment. Secondly, historically, patients undergoing non-curative treatment had a very short prognosis, and perhaps it was felt that from a functional recovery or maintenance perspective intervention if available may not have had an impact. Thirdly, the landscape of non-curative treatments for recurrent HNC has changed dramatically over the past five to ten years and as a result, the potential impact on function is not well understood for these new treatments. This thesis has, however, shown that for patients undergoing non-curative treatment, function and QoL can change over time and changes to swallowing can have a significant impact on QoL. These changes not only impact the patient but their caregivers and loved ones also. National guidelines state that all patients undergoing treatment for HNC, where there are potential changes to function, should be

referred to SLT pre-treatment for baseline evaluation and counselling (Homer and Winter, 2024). Therefore, this thesis has demonstrated that all patients with rOPC, who are being considered for both curative and non-curative treatments must be referred to SLT for pre-treatment evaluation and counselling. It has been suggested in a previous review paper that seeing non-curative patients pro-actively, has the potential to identify patients who are at risk of aspiration and aspiration-related complications, which could cause treatment breaks/ cessation if a patient becomes too unwell (Brady et al., 2020). The aim would not only be to mitigate these risks as much as is possible, but also to maximise the individual's functional independence and related QoL (Brady et al., 2020).

National guidelines also advocate the provision of prehabilitation for patients preparing for HNC treatment. Prehabilitation outlines a set of principles to empower people with cancer to prepare for their treatment, through promoting healthy behaviours and individualised exercise advice and programmes, nutrition and psychological interventions, which can be applied to both acute and ongoing cancer treatment (Bloom, 2017). At my centre this is routinely undertaken for patients being admitted for HNC surgery, in either the primary or recurrent setting, but not for patients undergoing non-curative treatments for rOPC. The quantitative and qualitative findings of this thesis have demonstrated that patients undergoing non-curative treatment are at risk of nutritional compromise. They experience changes to their ability to engage in physical exercise and daily tasks and would most likely benefit from interventions addressing these areas before, during and after treatment. Again, to ensure adherence to national guidance, and to ensure equity in service provision, all patients with rOPC regardless of their treatment pathway should be offered prehabilitation.

In clinical practice, the pre-treatment functional evaluation can quite often feed into the MDT recommendation for treatment in the case of a patient with rOPC that is technically operable. This will now be considered further within the context of SDM and personalised care.

8.4.2 Personalised care and shared decision making

As discussed, national guidelines state that patients with suspected or confirmed HNC recurrence or second primary disease must be presented at a HNC centre MDT. At this meeting the agreed diagnosis, staging, discussions and treatment plan are documented in addition to a named individual who will confirm the outcome of the meeting to the patient (Homer and Winter, 2024). While the goal of multidisciplinary (MDT) decision-making in cancer care is to devise an individualised optimal treatment plan (Licitra et al., 2016), the barriers to patient involvement in that process have been highlighted (Hamilton et al., 2022). A recent UK-based ethnographic study exploring patient engagement in decisions regarding HNC in both the primary and recurrent setting concluded that MDT discussion often results in a 'firm' recommendation which is presented to, and generally accepted by, the patient within a medical model of care, with little opportunity to incorporate patient values or priorities into treatment decision-making (Hamilton et al., 2022)

In clinical practice, when a patient is being considered for curative surgery, the baseline evaluation of function is often considered within this decision-making process. The information gained from a pre-treatment assessment is often relayed back to the MDT and an attempt is made to make predictions about the likely functional outcomes from the proposed surgical treatment plan based on the baseline level of functioning. As outlined previously, the assumption that the baseline level of functioning will predict the functional outcome is based on research in the primary disease setting. When this knowledge is applied in the recurrence setting, the MDT assumes that if the patient had a 'good' level of function at baseline they are potentially a 'good' candidate for curative surgery as they would potentially have a more favourable functional outcome. Conversely, those patients who had a 'poor' level of function at baseline, would have a worse functional prognosis and thus a curative treatment option would be considered by the MDT to be functionally too morbid. The 'firm' recommendation from such discussions is then relayed to the patient in clinical practice as described by Hamilton and colleagues (Hamilton et al., 2022). In my experience of clinical

practice, this discussion takes place without the patient, in the absence of routine assessment/ documentation of patient values, goals or beliefs. This thesis suggests that this needs to change.

The NHS Long Term Plan sets out recommendations for personalised care for patients (which is also referred to as person-centred care) including SDM (NHS, 2019). SDM is a process in which healthcare professionals and patients work together to select treatments, management or support packages, based on evidence and the individual's informed preferences. Inherent in this process is the patient's understanding of the care, treatment and support options that are available, including the benefits and risks of the available options. Regardless of what the MDT might perceive the 'best' option for a patient, all available options must be discussed with patients including survival outcomes and implications for function and QoL. This thesis has demonstrated that SDM does not always happen with all patients with rOPC and is a priority area for change in clinical practice. The literature to date on SDM in patient care, the oncology setting and more specifically HNC has highlighted the challenges in implementing SDM (Jovanovic et al., 2022, Warner et al., 2023, Shickh et al., 2023). One of the key challenges reported is the doctor's ability to convey and the patient's ability to grasp a potential scenario with one treatment option versus another. What this thesis has demonstrated is that patients with rOPC potentially have greater capacity to grasp a potential scenario given their prior experience of treatment and accompanying functional decline.

8.4.3 Pre-treatment counselling

In line with the recommendation for a greater focus on personalised care and SDM in clinical practice, pre-treatment counselling must also be reviewed. Findings from this body work have highlighted that patients and their caregivers did not always feel prepared for the side effects/ changes to function and QoL, which occurred over time. In addition, patients have individual preferences when it comes to information provision and resources. Clinicians must

work with patients to identify the best way to provide accurate information which is understandable to patients and their caregivers. Given the treatment-related priorities observed in this thesis, patients and their caregivers want to know the survival statistics for the available treatment options and accurate function and QoL information including swallowing, communication, secretion management, activity, energy and pain.

In this thesis, I have demonstrated that clinicians need to invest time in counselling patients before treatment. The first stage should be to assess patients individually to see how best they can process the information. For example, they may prefer written or verbal information, and they may want to meet someone who has been or is being treated, to understand their experience. The presumption that arranging consultations with clinicians and, for example, pre-operative anaesthetic assessment on one day as the patient has travelled, it may be best to offer the patient the option of staggered pre-treatment visits if more time is required to process information. The team must elucidate if the patient wants all of the information directly or if it needs to be filtered via a family member. Also, the need for a second opinion and the most efficient and effective pathway to achieve this must be established. Although MDT navigators are in place to ensure the transition of information from one centre to another, there appears to be a lack of navigation when it comes to the patient experience as they traverse between centres for opinions until care has formally been transferred. Previous research has highlighted how vulnerable and anxious patients can feel at the time of diagnosis (Griffiths et al., 2008) and this thesis has demonstrated that a lack of clear pathway to a second opinion appears to heighten such anxiety. Although a number of changes in clinical practice have been suggested via the findings of this thesis, much of this practice will be based on the facts and figures provided by further research. Recommendations for changes in clinical practice are made in the context of an understanding of an already pressured NHS. The next section of this chapter will consider the implications the data from this thesis has on future research.

8.5 Implications for future research

The unifying outcome which was identified in the quantitative and qualitative and overall combined findings from this thesis is that the treatment-related goal for patients and their caregivers is for cure if possible, and if cure is not possible, then they want to be able to survive as long as is possible so that they can be there for their family and loved ones. If this goal is achieved, patients can adapt and experience stable if not improved QoL regardless of their functional status. If not, maintaining QoL becomes increasingly difficult when function has deteriorated. These findings have several implications for future research.

8.5.1 Areas for further research

This thesis has demonstrated that the key treatment-related priorities for patients and caregivers are cure and survival. Therefore, patients need accurate information on survival for the various treatment options available. However, in addition to this, accurate function and QoL data must also be provided. One of the key findings of this thesis is that patients appear to adapt to the function and QoL implications if their treatment-related goal is achieved. However, if it is not, achieving this balance and finding QoL is much more difficult. This is critically important information which patients must understand in addition to the survival, functional and QoL data. Patients require more than just the statistics. The information needs to be presented in such a way that regardless of their experience, patients can make an informed decision. The assimilation of such complex and multifaceted information is in itself an area for future research. Similar work has been done in the palliative care field making use of illness trajectories to inform advance care planning (Murray et al., 2005). Illness trajectories are used to describe the course of a disease as experienced by a patient over time. In this original conceptualisation, the cancer trajectory was typically short and progressive with a gradual decline towards death (Murray et al., 2005). This concept has recently been updated to incorporate the illness trajectory of patients undergoing newer more novel treatments to reflect a temporary improvement in response to therapy, a long term response to therapy, and a rapid response due to an

adverse event (Geijteman et al., 2024). Since their original development, the trajectories now includes other dimensions of wellbeing including physical, social, psychological and spiritual changes (Murray et al., 2017). However, an area for possible research in the future might be to co-design such trajectories for the various treatment pathways and to investigate their potential impact on SDM. This would be a novel way to use illness trajectories as not all patients with rOPC die from their disease. If this was to be focused on in future studies, the first step would be to gather the data required to build such trajectories. This will be explored in the next section.

Endpoints for future research

There are many complexities involved in the selection of outcome measurement in research. For example, when looking at survival data, there can be several different endpoints including overall survival, disease free survival, progression free survival and the survival endpoint can impact the length of the study. It is not the purpose of this thesis to critique the survival data for this population, but given my findings, there must be a balance between reporting of survival and function and QoL outcome data for this population. Based on the findings of the systematic review reported in Chapter 3, function and QoL outcomes are already being measured in a number of ways using different tools and at different timepoints. The validity of some of these endpoints has been questioned in the wider HNC literature, and this thesis has added to such concerns specifically in relation to the use of the MDADI for patients with rOPC. This thesis has also highlighted is that rOPC appears to be a different entity from primary OPC, requiring careful consideration of how to measure outcomes in the future and not simply adopt the methodological considerations from primary disease research when it comes to outcomes selection. The findings from this thesis strengthen the fact that if are to meet the informational needs of our patients and help them in the process of SDM between treatments, we need to have comparable end points in future research.

PPI/E

This thesis has also demonstrated the crucial role of PPI/E in the development, review and interpretation of research findings. Collectively, these points signal the need for healthcare workers and patients to work together to design and develop future research in this area, starting with a set of core outcome measures including survival and function and QoL that are relevant, important and meaningful to both patients and healthcare professionals.

Core outcome set

A core outcome set requires development specific to the needs of patients with rOPC. With a core set of outcomes, we need to determine what the meaningful clinically significant difference is for the rOPC population. This thesis has highlighted that this needs to be specifically determined for the rOPC population rather than adopting this information from the primary disease literature. The optimal timepoints for data collection across treatment modalities must also be determined. This thesis has provided some provisional data on this, with the PPI/E group highlighting the need for longitudinal qualitative data collection at a timepoint of more than 12 months following diagnosis, and the rich patient experience data collected at this timepoint on this recommendation. Longitudinal data collection should be mirrored by the acquisition of quantitative data. Once the core outcome set has been defined, future research then needs to determine appropriate sample size calculations across treatment groups. This work could commence with data obtained for the initial validation of any new tools. Accurate sample size calculations will ensure future studies are suitably powered to allow a more in-depth statistical analysis.

This thesis has also highlighted the importance of patient and carer experience data to provide rich and meaningful contextual information to allow interpretation of the quantitative data. The PPI/E group explained in their input in the integration phase of the mixed methods study, that it was the qualitative data that allowed the quantitative data to be explained in terms of an individual's experience rather than a flow process via a patient care pathway.

The PPI/E group explained that it is this essential patient and carer experience data that will enable future patients to better understand the context of the survival, function and QoL outcome statistics that are presented. Future studies must continue to incorporate PPI/E at all stages of the research from concept to analysis and interpretation to dissemination.

8.6 Summary and conclusion

The overall aim of this thesis was to identify and address gaps in the current evidence base for rOPC with a focus on function and quality of life (QoL) outcomes, patient priorities and patient and carer experience of rOPC for those undergoing curative and non-curative treatments.

The systematic review which formed part of this thesis identified a very limited number of studies reporting on function and QoL outcomes, specifically for patients undergoing curative surgical treatment for rOPC. When outcomes were reported, the studies were generally of poor quality. Heterogeneity across studies was noted including the use of different or unvalidated function and QoL outcome tools, at different or undefined timelines for follow up outcome measurement. The review did not identify any studies reporting on function and QoL outcomes for patients undergoing non-curative management for rOPC specifically. Essential patient and carer experience data was absent in the existing literature on all treatments for rOPC.

The subsequent mixed methods study sought to address some of these gaps with a longitudinal study design investigating function and QoL outcomes, treatment-related priorities and patient and carer experience of rOPC. The new data generated from this mixed methods study has shown that function and QoL change with treatment for rOPC. However, treatment-related priorities do not and remain focused on cure and survival. If the treatment-related goal is achieved, the qualitative data demonstrated how patients can adapt and experience stable if not improved QoL regardless of their functional status. If the overall

treatment goal is not achieved or maintained, preserving QoL becomes increasingly difficult as function deteriorates. This thesis has provided new knowledge on how patients' and their respective caregivers' experiences vary hugely in terms of their diagnosis, opportunity for SDM, pre-treatment counselling and ongoing support during and following treatment highlighting inequities of care.

Collectively the data generated from this thesis provides significant contributions to the theoretical framework by which rOPC should be conceptualised and which should influence subsequent clinical management and future research in the area.

Theoretically, using the integrated findings of the mixed methods study, this thesis proposes a re-conceptualisation of rOPC as a distinct entity from primary OPC. This thesis has shown that patients with rOPC are fundamentally different from patients with primary OPC. They have knowledge and personal experience of HNC treatment and its aftermath and are at a different starting point from a function and QoL perspective. Based on this theory, we cannot simply extrapolate knowledge from the primary OPC population to the rOPC setting. There is a need to provide clinical care and design future research including the use of suitable outcome measures that meet the specific needs of patients with rOPC.

Clinically, this thesis has provided new knowledge that has the potential to influence how treatment decisions are made not ***for*** but ***with*** this patient population. It is imperative that healthcare professionals identify the key treatment-related goal for the patient and their caregivers, and this must be acknowledged when discussing all other relevant clinical information in treatment planning. Given the patients' and caregivers' level of experience with HNC treatment and its aftermath, this experience must be harnessed so that patients can truly envision the potential scenarios with various treatment options in keeping with true shared decision making. This will ultimately influence the informed consent process and pre-

treatment counselling for all patients with rOPC. However, the potential scenarios must be based on further research using appropriate endpoints collected at meaningful timepoints.

Methodologically, this thesis provides a robust framework for future studies in rOPC. Firstly, the thesis has provided a worked example for PPI/E throughout all stages of research from funding application, protocol development and amendment, through to data analysis and interpretation. This ensures that the research is aligned with the research questions posed and prioritised by patients and is relevant. This thesis has also shown that outcome measures which are routinely used in primary HNC research and clinical practice may not be the most appropriate way to measure change in function and QoL in the setting of rOPC research. These data signal the need for a core outcome set unique to the needs of patients with rOPC and relevant to the healthcare professionals working in partnership. The core outcome set, once agreed, will allow for the collection of comparable robust data so that patients can be accurately counselled on survival, function and QoL data for all available curative and non-curative treatments. The unique longitudinal design of this study has also provided important information on the optimal timepoints for data collection. The retrospective group of patients described changes and adaptations in function and QoL extending beyond 12 months after treatment in this thesis, and thus longer-term data collection should be considered in future trial development. This work has also highlighted not only the crucial role that patient and carer experience data has in providing context and meaning to quantitative data, but a methodological framework to do so via mixed methods data integration.

8.7 Future collaborations and research plans

This programme of research has highlighted multiple areas for further research. Throughout the course of this research the groundwork for ongoing research collaborations have been established.

One area of ongoing work is the secondary analysis of the previously unpublished rOPC data from the KEYNOTE trials. A considerable amount of work and negotiation has taken place between the industry pharmaceutical sponsor and the researchers from these trials to clarify the rationale to revisit the QoL data to look at change in overall QoL and symptom profile using the data from these trials. This will immediately provide some further data on the QoL profile for patients with rOPC. It may also give us some further details on the utility of the EORTC QLQ-C30 and EORTC HN35 in the recurrence population when compared with the findings of this thesis. This information, along with the insights learned from this thesis on outcome measurement of function and QoL in the recurrence population will help to build towards the development of a core outcome set (COS) for this population. Once a COS is established it can be used to compare the different treatment modalities available using endpoints relevant to both patients and clinicians. It may also potentially inform the development of illness trajectories which were mentioned earlier in this chapter.

Following a discussion of the preliminary findings of this thesis in the context of future trial development at the national study day hosted by International Centre for Recurrence Cancer (IReC) earlier this year, initial plans have been made with the support of the IReC collaborative to commence work on the development of a COS. Working on a COS is one of my key priority areas for future research following this thesis and will involve continuing the patient partnerships which have not been both established and embedded in my future research plans.

An ongoing research funding application with embedded co-design methodology has also resulted from the evidence generated from this thesis is to develop a Patient Decision Aid (PDA) and a Patient Concerns Inventory (PCI) for people diagnosed with recurrent HNC.

8.8 Final remarks

I set out on this research with the hope to highlight the function and QoL implications of all treatment options for patients with rOPC and to drive service development so that appropriate and equitable services can be in place to support all patients before, during and following treatment for rOPC. However, over the course of this research I have identified my professional bias in focusing solely on function and QoL outcomes. As a core member of the head and neck MDT, with the knowledge gained through this thesis, I now see my role as an advocate for my patients to receive the highest quality personalised care and to be equipped with the information they need to be able to engage in true SDM about their treatment. As a clinical academic, I recognise my responsibility to guide the development of future studies to try and answer the many remaining unanswered questions to facilitate this in clinical practice.

I hope this thesis acts as a motion to improve the provision of personalised care to all patients with a diagnosis of recurrent HNC, where their concerns, values and priorities define the care, treatment and support they and their caregivers receive throughout their diagnostic and treatment pathway.

References

ANDERSEN, B. L., SHAPIRO, C. L., FARRAR, W. B., CRESPIN, T. & WELLS-DIGREGORIO, S. 2005. Psychological responses to cancer recurrence. *Cancer,* 104**,** 1540-7.

ANG, K. K., HARRIS, J., WHEELER, R., WEBER, R., ROSENTHAL, D. I., NGUYEN-TÂN, P. F., WESTRA, W. H., CHUNG, C. H., JORDAN, R. C., LU, C., KIM, H., AXELROD, R., SILVERMAN, C. C., REDMOND, K. P. & GILLISON, M. L. 2010. Human Papillomavirus and Survival of Patients with Oropharyngeal Cancer. *The New England journal of medicine,* 363**,** 24-35.

ASHEER, J., JENSEN, J. S., GRØNHØJ, C., JAKOBSEN, K. K. & BUCHWALD, C. V. 2020. Rate of locoregional recurrence among patients with oropharyngeal squamous cell carcinoma with known HPV status: a systematic review. *Acta Oncologica,* 59**,** 1131-1136.

ASHWORTH, P. 1999. " Bracketing" in phenomenology: Renouncing assumptions in hearing about student cheating. *International Journal of Qualitative Studies in Education,* 12**,** 707-721.

BAZELEY, P. 2012. Integrative analysis strategies for mixed data sources. *American Behavioral Scientist,* 56**,** 814-828.

BLANCHARD, P., VOLK, R. J., RINGASH, J., PETERSON, S. K., HUTCHESON, K. A. & FRANK, S. J. 2016. Assessing head and neck cancer patient preferences and expectations: a systematic review. *Oral oncology,* 62**,** 44-53.

BLOOM, E. 2017. Prehabilitation evidence and insight review. *MacmillanCancer Support*.

BOTS, W. T., VAN DEN BOSCH, S., ZWIJNENBURG, E. M., DIJKEMA, T., VAN DEN BROEK, G. B., WEIJS, W. L., VERHOEF, L. C. & KAANDERS, J. H. 2017. Reirradiation of head and neck cancer: long-term disease control and toxicity. *Head & neck,* 39**,** 1122-1130.

BOUTRON, I., PAGE, M. J., HIGGINS, J. P., ALTMAN, D. G., LUNDH, A., HRÓBJARTSSON, A. & GROUP, C. B. M. 2019. Considering bias and conflicts of interest among the included studies. *Cochrane handbook for systematic reviews of interventions***,** 177-204.

BRADY, G., ROE, J., PALERI, V., LAGERGREN, P. & WELLS, M. 2023. Patient experience, functional and quality of life outcomes in patients receiving surgical and non-surgical treatment for residual, recurrent, or new oropharyngeal cancer in a previously irradiated field: A systematic review. *Advances in Communication and Swallowing,* 26**,** 109-123.

BRADY, G. C., HARDMAN, J. C., PALERI, V., HARRINGTON, K. J. & ROE, J. W. G. 2020. Changing paradigms in the treatment of residual/recurrent head and neck cancer: implications for dysphagia management. *Curr Opin Otolaryngol Head Neck Surg,* 28**,** 165-171.

BRYMAN, A. 2016. *Social research methods*, Oxford university press.

BURTNESS, B., HARRINGTON, K. J., GREIL, R., SOULIÈRES, D., TAHARA, M., DE CASTRO, G., PSYRRI, A., BASTÉ, N., NEUPANE, P. & BRATLAND, Å. 2019. Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. *The Lancet,* 394**,** 1915-1928.

CHARTERS, E., BOGAARDT, H., FREEMAN-SANDERSON, A., BALLARD, K., DAVIES, S., OATES, J. & CLARK, J. 2022. Swallowing and communication outcomes following primary transoral robotic surgery for advanced or recurrent oropharyngeal cancer: Case series. *International journal of speech-language pathology,* 24**,** 407-416.

CHEN, A. M., HARRIS, J. P., NABAR, R., TJOA, T., HAIDAR, Y. & ARMSTRONG, W. B. 2024. Re-irradiation versus systemic therapy for the management of local-regionally recurrent head and neck cancer. *Radiotherapy and Oncology,* 196.

CHEN, A. Y., FRANKOWSKI, R., BISHOP-LEONE, J., HEBERT, T., LEYK, S., LEWIN, J. & GOEPFERT, H. 2001. The development and validation of a dysphagia-specific quality-of-life questionnaire for patients with head and neck cancer: the MD Anderson dysphagia inventory. *Archives of Otolaryngology–Head & Neck Surgery,* 127**,** 870-876.

CINCIDDA, C., PIZZOLI, S. F. M., ONGARO, G., OLIVERI, S. & PRAVETTONI, G. 2023. Caregiving and Shared Decision Making in Breast and Prostate Cancer Patients: A Systematic Review. *Current Oncology,* 30**,** 803-823.

COHEN, E. E., SOULIÈRES, D., LE TOURNEAU, C., DINIS, J., LICITRA, L., AHN, M.-J., SORIA, A., MACHIELS, J.-P., MACH, N. & MEHRA, R. 2019. Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised, open-label, phase 3 study. *The Lancet,* 393**,** 156-167.

COX, J. D. 1995. Toxicity criteria of the radiation therapy oncology group (RTOG) and the European organization for research and treatment of cancer (EORTC). *Int. J. Radiat. Oncol. Biol. Phys.,* 31**,** 1341-1346.

CRARY, M. A., MANN, G. D. C. & GROHER, M. E. 2005. Initial psychometric assessment of a functional oral intake scale for dysphagia in stroke patients. *Archives of physical medicine and rehabilitation,* 86**,** 1516-1520.

CREANEY, G., MCMAHON, A. D., ROSS, A. J., BHATTI, L. A., PATERSON, C. & CONWAY, D. I. 2022. Head and neck cancer in the UK: what was the stage before COVID-19? UK cancer registries analysis (2011-2018). *British Dental Journal,* 233**,** 787-793.

CRESWELL, J. W. & CLARK, V. L. P. 2017. *Designing and conducting mixed methods research*, Sage publications.

CROTTY, M. J. 1998. The foundations of social research: Meaning and perspective in the research process. *The foundations of social research***,** 1-256.

CULIÉ, D., BENEZERY, K., CHAMOREY, E., ETTAICHE, M., FERNANDEZ, J., POISSONNET, G., RISS, J.-C., HANNOUN-LÉVI, J.-M., CHAND, M.-E. & LEYSALLE, A. 2015. Salvage surgery for recurrent oropharyngeal cancer: post-operative oncologic and functional outcomes. *Acta oto-laryngologica,* 135**,** 1323-1329.

CUMPSTON, M., CHANDLER, J., THOMAS, J., HIGGINS, J. P., DEEKS, J. J. & CLARKE, M. J. 2020. Chapter I: Introduction. *Cochrane Handbook for Systematic Reviews of Interventions,* 6.

D'ANDRÉA, G., BORDENAVE, L., NGUYEN, F., TAO, Y., PALERI, V., TEMAM, S., MOYA-PLANA, A. & GORPHE, P. 2022. A prospective longitudinal study of quality of life in robotic-assisted salvage surgery for oropharyngeal cancer. *European Journal of Surgical Oncology*.

DEAN, N. R., ROSENTHAL, E. L., CARROLL, W. R., KOSTRZEWA, J. P., JONES, V. L., RENEE'A, D., CLEMONS, L. & MAGNUSON, J. S. 2010. Robotic-assisted surgery for primary or recurrent oropharyngeal carcinoma. *Archives of Otolaryngology–Head & Neck Surgery,* 136**,** 380-384.

DEGBOE, A., KNIGHT, S. L., HALLING, K., TRIGG, A., AL-ZUBEIDI, T., ALDHOUSE, N., KITCHEN, H., WIRTH, L. & ROGERS, S. N. 2018. Patients' experience of recurrent/metastatic head and neck squamous cell carcinoma and their perspective on the EORTC QLQ-C30 and QLQ-H&N35 questionnaires: a qualitative study. *Journal of patient-reported outcomes,* 2**,** 1-13.

DEUNING-SMIT, E., CUSTERS, J. A. E., MIROŠEVIČ, Š., TAKES, R. P., JANSEN, F., LANGENDIJK, J. A., TERHAARD, C. H. J., BAATENBURG DE JONG, R. J., LEEMANS, C. R., SMIT, J. H., KWAKKENBOS, L., VERDONCK-DE LEEUW, I. M. & PRINS, J. B. 2022. Prospective longitudinal study on fear of cancer recurrence in patients newly diagnosed with head and neck cancer: Course, trajectories, and associated factors. *Head & Neck,* 44**,** 914-925.

ECHTELD, M. A., DELIENS, L., OOMS, M. E., RIBBE, M. W. & VAN DER WAL, G. 2005. Quality of life change and response shift in patients admitted to palliative care units: a pilot study. *Palliative Medicine,* 19**,** 381-388.
ELLIS, H. & MAHADEVAN, V. 2018. *Clinical anatomy: applied anatomy for students and junior doctors*, John Wiley & Sons.
FALCHOOK, A. D., GREEN, R., KNOWLES, M. E., AMDUR, R. J., MENDENHALL, W., HAYES, D. N., GRILLEY-OLSON, J. E., WEISS, J., REEVE, B. B., MITCHELL, S. A., BASCH, E. M. & CHERA, B. S. 2016. Comparison of Patient- and Practitioner-Reported Toxic Effects Associated With Chemoradiotherapy for Head and Neck Cancer. *JAMA Otolaryngology–Head & Neck Surgery,* 142**,** 517-523.
FDA. 2016. *Assessment of the Use of Patient Experience Data in Regulatory Decision-Making* [Online]. Available: https://www.fda.gov/drugs/development-approval-process-drugs/assessment-use-patient-experience-data-regulatory-decision-making [Accessed January 18th 2023].
FENECH, A. L., HUMPHRIS, G. M., LAURENCEAU, J.-P., SIEGEL, S. D., ROGERS, S. N., OZAKINCI, G., CRAWFORD, J. & PRING, M. 2024. Anxiety, Depression, and Fear of Cancer Recurrence in Head and Neck Cancer. *Health Psychology*.
FETTERS, M. D., CURRY, L. A. & CRESWELL, J. W. 2013. Achieving integration in mixed methods designs-principles and practices. *Health Serv Res,* 48**,** 2134-56.
FROWEN, J., COTTON, S., CORRY, J. & PERRY, A. 2010. Impact of demographics, tumor characteristics, and treatment factors on swallowing after (chemo) radiotherapy for head and neck cancer. *Head & Neck: Journal for the Sciences and Specialties of the Head and Neck,* 32**,** 513-528.
FROWEN, J. J. & PERRY, A. R. 2006. Swallowing outcomes after radiotherapy for head and neck cancer: A systematic review. *Head & Neck,* 28**,** 932-944.
GALE, N. K., HEATH, G., CAMERON, E., RASHID, S. & REDWOOD, S. 2013. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. *BMC medical research methodology,* 13**,** 1-8.
GEIJTEMAN, E. C. T., KUIP, E. J. M., OSKAM, J., LEES, D. & BRUERA, E. 2024. Illness trajectories of incurable solid cancers. *BMJ,* 384**,** e076625.
GOEPFERT, R. P., FULLER, C. D., GUNN, G. B., HANNA, E. Y., LEWIN, J. S., ZAVERI, J. S., HUBBARD, R. M., BARROW, M. P. & HUTCHESON, K. A. 2017. Symptom burden as a driver of decisional regret in long-term oropharyngeal carcinoma survivors. *Head Neck,* 39**,** 2151-2158.
GOLDSMITH, T. A. & ROE, J. W. 2015. Human papilloma virus-related oropharyngeal cancer: opportunities and challenges in dysphagia management. *Curr Opin Otolaryngol Head Neck Surg,* 23**,** 185-90.
GOV.UK. 2023. *Concern over drop in HPV vaccine coverage among secondary school pupils* [Online]. Available: https://www.gov.uk/government/news/concern-over-drop-in-hpv-vaccine-coverage-among-secondary-school-pupils [Accessed June 6th 2023].
GRIFFITHS, M. J., HUMPHRIS, G. M., SKIRROW, P. M. & ROGERS, S. N. 2008. A qualitative evaluation of patient experiences when diagnosed with oral cancer recurrence. *Cancer Nurs,* 31**,** E11-7.
GRÜNWALD, V., CHIROVSKY, D., CHEUNG, W. Y., BERTOLINI, F., AHN, M.-J., YANG, M.-H., CASTRO, G., BERROCAL, A., SJOQUIST, K. & KUYAS, H. 2020. Global treatment patterns and outcomes among patients with recurrent and/or metastatic head and neck squamous cell carcinoma: Results of the GLANCE H&N study. *Oral oncology,* 102**,** 104526.
GULLER, M., HERBERG, M., AMIN, N., ALKHATIB, H., MAROUN, C., WU, E., ALLEN, H., ZHENG, Y., GOURIN, C., VOSLER, P., TAN, M., KOCH, W., EISELE, D., SEIWERT, T., FAKHRY, C., PARDOLL, D., ZHU, G. & MANDAL, R. 2021. Nutritional Status as a Predictive Biomarker for Immunotherapy Outcomes in Advanced Head and Neck Cancer. *Cancers,* 13**,** 5772.
GUYATT, G., OXMAN, A. D., AKL, E. A., KUNZ, R., VIST, G., BROZEK, J., NORRIS, S., FALCK-YTTER, Y., GLASZIOU, P. & DEBEER, H. 2011. GRADE guidelines: 1.

Introduction—GRADE evidence profiles and summary of findings tables. *Journal of clinical epidemiology,* 64**,** 383-394.
HAMILTON, D., BENJAMIN, H., RICHARD, T., JANET, W. & CATHERINE, E. 2022. How do patients make decisions in the context of a multidisciplinary team: an ethnographic study of four head and neck cancer centres in the north of England. *BMJ Open,* 12**,** e061654.
HAMILTON, D. & PALERI, V. 2017. Role of transoral robotic surgery in current head & neck practice. *The Surgeon,* 15**,** 147-154.
HAMILTON, D. W., HEAVEN, B., THOMSON, R. G., WILSON, J. A. & EXLEY, C. 2016. Multidisciplinary team decision-making in cancer and the absent patient: a qualitative study. *BMJ Open,* 6**,** e012559.
HAMPSON, T. & MCKINLEY, J. 2023. Problems posing as solutions: Criticising pragmatism as a paradigm for mixed research. *Research in Education,* 116**,** 124-138.
HARDMAN, J., LIU, Z., BRADY, G., ROE, J., KERAWALA, C., RIVA, F., CLARKE, P., KIM, D., BHIDE, S., NUTTING, C., HARRINGTON, K. & PALERI, V. 2020. Transoral robotic surgery for recurrent cancers of the upper aerodigestive tract-Systematic review and meta-analysis. *Head Neck,* 42**,** 1089-1104.
HARDMAN, J. C., HOLSINGER, F. C., BRADY, G. C., BEHARRY, A., BONIFER, A. T., D'ANDRÉA, G., DABAS, S. K., DE ALMEIDA, J. R., DUVVURI, U. & FLOROS, P. 2022. Transoral Robotic Surgery for Recurrent Tumors of the Upper Aerodigestive Tract (RECUT): An International Cohort Study. *Journal of the National Cancer Institute,* 114**,** 1400-1409.
HARRINGTON, K. J., BURTNESS, B., GREIL, R., SOULIÈRES, D., TAHARA, M., JR, G. D. C., PSYRRI, A., BRANA, I., BASTÉ, N., NEUPANE, P., BRATLAND, Å., FUEREDER, T., HUGHES, B. G. M., MESIA, R., NGAMPHAIBOON, N., RORDORF, T., ISHAK, W. Z. W., LIN, J., GUMUSCU, B., SWABY, R. F. & RISCHIN, D. 2023. Pembrolizumab With or Without Chemotherapy in Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma: Updated Results of the Phase III KEYNOTE-048 Study. *Journal of Clinical Oncology,* 41**,** 790-802.
HARRINGTON, K. J., SOULIÈRES, D., LE TOURNEAU, C., DINIS, J., LICITRA, L. F., AHN, M.-J., SORIA, A., MACHIELS, J.-P. H., MACH, N. & MEHRA, R. 2021. Quality of life with pembrolizumab for recurrent and/or metastatic head and neck squamous cell carcinoma: KEYNOTE-040. *JNCI: Journal of the National Cancer Institute,* 113**,** 171-181.
HOLMES, A. G. D. 2020. Researcher Positionality--A Consideration of Its Influence and Place in Qualitative Research--A New Researcher Guide. *Shanlax International Journal of Education,* 8**,** 1-10.
HOMER, J. J. & FARDY, M. J. 2016. Surgery in head and neck cancer: United Kingdom National Multidisciplinary Guidelines. *J Laryngol Otol,* 130**,** S68-s70.
HOMER, J. J. & WINTER, S. C. 2024. Head and Neck Cancer: United Kingdom National Multidisciplinary Guidelines. *The Journal of Laryngology & Otology,* 138**,** S1-S224.
HOWARD, J., MASTERSON, L., DWIVEDI, R. C., RIFFAT, F., BENSON, R., JEFFERIES, S., JANI, P., TYSOME, J. R. & NUTTING, C. 2016. Minimally invasive surgery versus radiotherapy/chemoradiotherapy for small-volume primary oropharyngeal carcinoma. *Cochrane Database Syst Rev,* 12**,** Cd010963.
HUMPHRIS, G. & OZAKINCI, G. 2008. The AFTER intervention: a structured psychological approach to reduce fears of recurrence in patients with head and neck cancer. *British journal of health psychology,* 13**,** 223-230.
HUTCHESON, K. A., BARROW, M. P., BARRINGER, D. A., KNOTT, J. K., LIN, H. Y., WEBER, R. S., FULLER, C. D., LAI, S. Y., ALVAREZ, C. P., RAUT, J., LAZARUS, C. L., MAY, A., PATTERSON, J., ROE, J. W., STARMER, H. M. & LEWIN, J. S. 2017. Dynamic Imaging Grade of Swallowing Toxicity (DIGEST): Scale development and validation. *Cancer,* 123**,** 62-70.

HUTCHESON, K. A., BARROW, M. P., LISEC, A., BARRINGER, D. A., GRIES, K. & LEWIN, J. S. 2016. What is a clinically relevant difference in MDADI scores between groups of head and neck cancer patients? *The Laryngoscope,* 126**,** 1108-1113.
ILIE, G., BRADFIELD, J., MOODIE, L., LAWEN, T., ILIE, A., LAWEN, Z., BLACKMAN, C., GAINER, R. & RUTLEDGE, R. D. H. 2019. The Role of Response-Shift in Studies Assessing Quality of Life Outcomes Among Cancer Patients: A Systematic Review. *Front Oncol,* 9**,** 783.
JAYARAM, S. C., MUZAFFAR, S. J., AHMED, I., DHANDA, J., PALERI, V. & MEHANNA, H. 2016. Efficacy, outcomes, and complication rates of different surgical and nonsurgical treatment modalities for recurrent/residual oropharyngeal carcinoma: a systematic review and meta-analysis. *Head & neck,* 38**,** 1855-1861.
JOPSON, R. & CALLENDER, J. 2022. Are UK healthcare professionals equipped to provide information and support on Human Papillomavirus to patients diagnosed with cancer of the head and neck? *Journal of Radiotherapy in Practice,* 21**,** 165-170.
JOVANOVIC, N., DOYLE, P. C. & THEURER, J. A. 2022. Supporting Patient Autonomy in Shared Decision Making for Individuals With Head and Neck Cancer. *Am J Speech Lang Pathol,* 31**,** 1588-1600.
KANEOKA, A. S., LANGMORE, S. E., KRISCIUNAS, G. P., FIELD, K., SCHEEL, R., MCNALLY, E., WALSH, M. J., O'DEA, M. B. & CABRAL, H. 2013. The Boston residue and clearance scale: preliminary reliability and validity testing. *Folia Phoniatrica et Logopaedica,* 65**,** 312-317.
KANO, S., HOMMA, A., HAYASHI, R., KAWABATA, K., YOSHINO, K., IWAE, S., HASEGAWA, Y., NIBU, K., KATO, T. & SHIGA, K. 2013. Salvage surgery for recurrent oropharyngeal cancer after chemoradiotherapy. *International journal of clinical oncology,* 18**,** 817-823.
KIM, S. Y., PARK, J. E., LEE, Y. J., SEO, H.-J., SHEEN, S.-S., HAHN, S., JANG, B.-H. & SON, H.-J. 2013. Testing a tool for assessing the risk of bias for nonrandomized studies showed moderate reliability and promising validity. *Journal of clinical epidemiology,* 66**,** 408-414.
KLEIN, J., LIVERGANT, J. & RINGASH, J. 2014. Health related quality of life in head and neck cancer treated with radiation therapy with or without chemotherapy: a systematic review. *Oral Oncol,* 50**,** 254-62.
KOSTRZEWA, J. P., LANCASTER, W. P., ISELI, T. A., DESMOND, R. A., CARROLL, W. R. & ROSENTHAL, E. L. 2010. Outcomes of salvage surgery with free flap reconstruction for recurrent oral and oropharyngeal cancer. *The Laryngoscope,* 120**,** 267-272.
LEFEBVRE, J.-L., ANG, K. K. & PANEL, L. P. C. 2009. Larynx preservation clinical trial design: key issues and recommendations—a consensus panel summary. *International Journal of Radiation Oncology* Biology* Physics,* 73**,** 1293-1303.
LEVITAN, B., GETZ, K., EISENSTEIN, E. L., GOLDBERG, M., HARKER, M., HESTERLEE, S., PATRICK-LAKE, B., ROBERTS, J. N. & DIMASI, J. 2018. Assessing the financial value of patient engagement: a quantitative approach from CTTI's patient groups and clinical trials project. *Therapeutic innovation & regulatory science,* 52**,** 220-229.
LICITRA, L., KEILHOLZ, U., TAHARA, M., LIN, J.-C., CHOMETTE, P., CERUSE, P., HARRINGTON, K. & MESIA, R. 2016. Evaluation of the benefit and use of multidisciplinary teams in the treatment of head and neck cancer. *Oral Oncology,* 59**,** 73-79.
LIST, M. A., RITTER-STERR, C. & LANSKY, S. B. 1990. A performance status scale for head and neck cancer patients. *Cancer,* 66**,** 564-569.
LOGEMANN, J. A. 1995. Dysphagia: evaluation and treatment. *Folia Phoniatr Logop,* 47**,** 140-64.
MACHTAY, M., MOUGHAN, J., TROTTI, A., GARDEN, A. S., WEBER, R. S., COOPER, J. S., FORASTIERE, A. & ANG, K. K. 2008. Factors associated with severe late toxicity after concurrent chemoradiation for locally advanced head and neck cancer: an RTOG analysis. *Journal of Clinical Oncology,* 26**,** 3582.

MADATHIL, S., ROUSSEAU, M.-C., JOSEPH, L., COUTLÉE, F., SCHLECHT, N. F., FRANCO, E. & NICOLAU, B. 2020. Latency of tobacco smoking for head and neck cancer among HPV-positive and HPV-negative individuals. *International Journal of Cancer,* 147**,** 56-64.
MANDAPATHIL, M., ROESSLER, M., WERNER, J. A., SILVER, C. E., RINALDO, A. & FERLITO, A. 2014. Salvage surgery for head and neck squamous cell carcinoma. *European Archives of Oto-Rhino-Laryngology,* 271**,** 1845-1850.
MATHIESON, L. 2013. *Greene and Mathieson's the Voice and its Disorders*, Wiley.
MAZEROLLE, P., FUCHSMANN, C., SCHULTZ, P., BENMOUSSA, N., MALARD, O., BOZEC, A., DENEUVE, S., FOLIA, M., PERRÉARD, M. & LASNE-CARDON, A. 2022. Salvage total glossectomy and total glosso-laryngectomy: Are they worth it? A GETTEC French multicenter study. *Oral Oncology,* 130**,** 105896.
MCDOWELL, L., KING, M. T., HUTCHESON, K. A., RINGASH, J., YOM, S. S., CORRY, J., HENSON, C., MEHANNA, H. & RISCHIN, D. 2024. A Hard Truth to Swallow: Critically Evaluating the MD Anderson Dysphagia Inventory (MDADI) as an Endpoint in Human Papillomavirus-associated Oropharyngeal Cancer Trials. *Int J Radiat Oncol Biol Phys*.
MEHANNA, H., EVANS, M., BEASLEY, M., CHATTERJEE, S., DILKES, M., HOMER, J., O'HARA, J., ROBINSON, M., SHAW, R. & SLOAN, P. 2016a. Oropharyngeal cancer: United Kingdom National Multidisciplinary Guidelines. *J Laryngol Otol,* 130**,** S90-s96.
MEHANNA, H., KONG, A. & AHMED, S. 2016b. Recurrent head and neck cancer: United Kingdom national multidisciplinary guidelines. *The Journal of Laryngology & Otology,* 130**,** S181-S190.
MOHER, D., LIBERATI, A., TETZLAFF, J. & ALTMAN, D. G. 2010. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg,* 8**,** 336-341.
MURRAY, S. A., KENDALL, M., BOYD, K. & SHEIKH, A. 2005. Illness trajectories and palliative care. *Bmj,* 330**,** 1007-11.
MURRAY, S. A., KENDALL, M., MITCHELL, G., MOINE, S., AMBLÀS-NOVELLAS, J. & BOYD, K. 2017. Palliative care from diagnosis to death. *Bmj,* 356**,** j878.
NGUYEN, H., BUTOW, P., DHILLON, H., MORRIS, L., BROWN, A., WEST, K. & SUNDARESAN, P. 2020. Using patient-reported outcomes (PROs) and patient-reported outcome measures (PROMs) in routine head and neck cancer care: What do health professionals perceive as barriers and facilitators? *Journal of Medical Imaging and Radiation Oncology,* 64**,** 704-710.
NGUYEN, N. P., FRANK, C., MOLTZ, C. C., VOS, P., SMITH, H. J., KARLSSON, U., DUTTA, S., MIDYETT, A., BARLOON, J. & SALLAH, S. 2005. Impact of dysphagia on quality of life after treatment of head-and-neck cancer. *International Journal of Radiation Oncology* Biology* Physics,* 61**,** 772-778.
NHS. 2019. *Shared decision-making: summary guide* [Online]. Available: https://www.england.nhs.uk/publication/shared-decision-making-summary-guide/ [Accessed August 15th 2024].
NICHOLS, A. C., THEURER, J., PRISMAN, E., READ, N., BERTHELET, E., TRAN, E., FUNG, K., DE ALMEIDA, J. R., BAYLEY, A., GOLDSTEIN, D. P., HIER, M., SULTANEM, K., RICHARDSON, K., MLYNAREK, A., KRISHNAN, S., LE, H., YOO, J., MACNEIL, S. D., WINQUIST, E., HAMMOND, J. A., VENKATESAN, V., KURUVILLA, S., WARNER, A., MITCHELL, S., CHEN, J., CORSTEN, M., JOHNSON-OBASEKI, S., EAPEN, L., ODELL, M., PARKER, C., WEHRLI, B., KWAN, K. & PALMA, D. A. 2019. Radiotherapy versus transoral robotic surgery and neck dissection for oropharyngeal squamous cell carcinoma (ORATOR): an open-label, phase 2, randomised trial. *The Lancet Oncology,* 20**,** 1349-1359.
NIHR. 2021. *Briefing notes for researchers* [Online]. Available: https://www.nihr.ac.uk/documents/briefing-notes-for-researchers-public-involvement-in-nhs-health-and-social-care-research/27371#how-to-cite-this-guidance [Accessed December 5th 2023].

NORONHA, V., PRABHASH, K., BABU, K. G., CHATURVEDI, P., KURIAKOSE, M., BIRUR, P., ANAND, A. K., KAUSHAL, A., MAHAJAN, A., SYIEMLIEH, J., SINGHAL, M., GAIROLA, M., RAMACHANDRA, P., GOYAL, S., JOHN, S., NAYYAR, R., PATIL, V. M., RAO, V., ROSHAN, V. & RATH, G. K. 2024. Indian clinical practice consensus guidelines for the management of oropharyngeal cancer: Update 2022. *Cancer Research, Statistics, and Treatment,* 7**,** S12-S16.

NUND, R. L., BROWN, B., WARD, E. C., MACLEAN, J., ROE, J., PATTERSON, J. M. & MARTINO, R. 2019. What Are We Really Measuring? A Content Comparison of Swallowing Outcome Measures for Head and Neck Cancer Based on the International Classification of Functioning, Disability and Health (ICF). *Dysphagia,* 34**,** 575-591.

NUND, R. L., WARD, E. C., SCARINCI, N. A., CARTMILL, B., KUIPERS, P. & PORCEDDU, S. V. 2014. Carers' experiences of dysphagia in people treated for head and neck cancer: a qualitative study. *Dysphagia,* 29**,** 450-8.

NUTTING, C. 2016. Radiotherapy in head and neck cancer management: United Kingdom National Multidisciplinary Guidelines. *Journal of laryngology and otology,* 130**,** S66-S67.

NUTTING, C., FINNERAN, L., ROE, J., SYDENHAM, M. A., BEASLEY, M., BHIDE, S., BOON, C., COOK, A., DE WINTON, E. & EMSON, M. 2023. Dysphagia-optimised intensity-modulated radiotherapy versus standard intensity-modulated radiotherapy in patients with head and neck cancer (DARS): a phase 3, multicentre, randomised, controlled trial. *The Lancet Oncology,* 24**,** 868-880.

NUTTING, C. M., MORDEN, J. P., HARRINGTON, K. J., URBANO, T. G., BHIDE, S. A., CLARK, C., MILES, E. A., MIAH, A. B., NEWBOLD, K., TANAY, M., ADAB, F., JEFFERIES, S. J., SCRASE, C., YAP, B. K., A'HERN, R. P., SYDENHAM, M. A., EMSON, M. & HALL, E. 2011. Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial. *Lancet Oncol,* 12**,** 127-36.

O'NEIL, K. H., PURDY, M., FALK, J. & GALLO, L. 1999. The dysphagia outcome and severity scale. *Dysphagia,* 14**,** 139-145.

O'CATHAIN, A., MURPHY, E. & NICHOLL, J. 2010. Three techniques for integrating data in mixed methods studies. *BMJ,* 341**,** c4587.

OLMOS-VEGA, F. M., STALMEIJER, R. E., VARPIO, L. & KAHLKE, R. 2023. A practical guide to reflexivity in qualitative research: AMEE Guide No. 149. *Medical teacher,* 45**,** 241-251.

ONWUEGBUZIE, A. J. & COLLINS, K. M. 2007. A Typology of Mixed Methods Sampling Designs in Social Science Research. *The Qualitative Report,* 12**,** 281-316.

OWADALLY, W., HURT, C., TIMMINS, H., PARSONS, E., TOWNSEND, S., PATTERSON, J., HUTCHESON, K., POWELL, N., BEASLEY, M. & PALANIAPPAN, N. 2015. PATHOS: a phase II/III trial of risk-stratified, reduced intensity adjuvant treatment in patients undergoing transoral surgery for Human papillomavirus (HPV) positive oropharyngeal cancer. *BMC cancer,* 15**,** 1-10.

PALERI, V., HARDMAN, J., BRADY, G., GEORGE, A. & KERAWALA, C. 2020. Transoral Robotic Surgery for Residual and Recurrent Oropharyngeal Cancers. *Otolaryngologic Clinics of North America,* 53**,** 1091-1108.

PALERI, V., PATTERSON, J., ROUSSEAU, N., MOLONEY, E., CRAIG, D., TZELIS, D., WILKINSON, N., FRANKS, J., HYNES, A. M. & HEAVEN, B. 2018. Gastrostomy versus nasogastric tube feeding for chemoradiation patients with head and neck cancer: the TUBE pilot RCT.

PARK, D. A., LEE, M. J., KIM, S.-H. & LEE, S. H. 2020. Comparative safety and effectiveness of transoral robotic surgery versus open surgery for oropharyngeal cancer: A systematic review and meta-analysis. *European Journal of Surgical Oncology,* 46**,** 644-649.

PARSONS, J. T., MENDENHALL, W. M., STRINGER, S. P., AMDUR, R. J., HINERMAN, R. W., VILLARET, D. B., MOORE-HIGGS, G. J., GREENE, B. D., SPEER, T. W. &

CASSISI, N. J. 2002. Squamous cell carcinoma of the oropharynx: surgery, radiation therapy, or both. *Cancer: Interdisciplinary International Journal of the American Cancer Society,* 94**,** 2967-2980.
PATEL, S. N., COHEN, M. A., GIVI, B., DIXON, B. J., GILBERT, R. W., GULLANE, P. J., BROWN, D. H., IRISH, J. C., DE ALMEIDA, J. R. & HIGGINS, K. M. 2016. Salvage surgery for locally recurrent oropharyngeal cancer. *Head & neck,* 38**,** E658-E664.
PATTERSON, J., MCCOLL, E., CARDING, P. & WILSON, J. 2018. Swallowing beyond six years post (chemo) radiotherapy for head and neck cancer; a cohort study. *Oral oncology,* 83**,** 53-58.
PATTERSON, J. M., BRADY, G. C. & ROE, J. W. 2016. Research into the prevention and rehabilitation of dysphagia in head and neck cancer: a UK perspective. *Current opinion in otolaryngology & head and neck surgery,* 24**,** 208-214.
PATTERSON, J. M., HILDRETH, A., MCCOLL, E., CARDING, P. N., HAMILTON, D. & WILSON, J. A. 2011. The clinical application of the 100 mL water swallow test in head and neck cancer. *Oral oncology,* 47**,** 180-184.
PETKAR, I., ROONEY, K., ROE, J. W., PATTERSON, J. M., BERNSTEIN, D., TYLER, J. M., EMSON, M. A., MORDEN, J. P., MERTENS, K. & MILES, E. 2016. DARS: a phase III randomised multicentre study of dysphagia-optimised intensity-modulated radiotherapy (Do-IMRT) versus standard intensity-modulated radiotherapy (S-IMRT) in head and neck cancer. *BMC cancer,* 16**,** 1-10.
PHILLIPPI, J. & LAUDERDALE, J. 2017. A Guide to Field Notes for Qualitative Research: Context and Conversation. *Qualitative Health Research,* 28**,** 381-388.
PHILOUZE, P., PÉRON, J., POUPART, M., PUJO, K., BUIRET, G. & CÉRUSE, P. 2017. Salvage surgery for oropharyngeal squamous cell carcinomas: A retrospective study from 2005 to 2013. *Head & neck,* 39**,** 1744-1750.
PIPKORN, P., SINHA, P., KALLOGJERI, D., ADKINS, D., THORSTAD, W. T., RICH, J. T. & JACKSON, R. S. 2019. Outcomes of relapsed human papillomavirus-related oropharyngeal squamous cell carcinoma treated with curative intent. *Head & Neck,* 41**,** 1312-1319.
PRICE, A., CLARKE, M., STANISZEWSKA, S., CHU, L., TEMBO, D., KIRKPATRICK, M. & NELKEN, Y. 2022. Patient and Public Involvement in research: A journey to co-production. *Patient Educ Couns,* 105**,** 1041-1047.
RATHOD, S., LIVERGANT, J., KLEIN, J., WITTERICK, I. & RINGASH, J. 2015. A systematic review of quality of life in head and neck cancer treated with surgery with or without adjuvant treatment. *Oral Oncology,* 51**,** 888-900.
RCSLT. 2023. *Dysphagia and eating, drinking and swallowing needs* [Online]. Available: https://www.rcslt.org/members/clinical-guidance/dysphagia/ [Accessed June 6th 2023].
RHOTEN, B. A., SELLERS, J. I., BARAFF, B., HOLLER, K. H. & RIDNER, S. H. 2021. A qualitative examination of patient priorities and preferences during treatment decision-making for recurrent head and neck cancer. *Supportive Care in Cancer,* 29**,** 377-385.
RINGASH, J., BERNSTEIN, L. J., DEVINS, G., DUNPHY, C., GIULIANI, M., MARTINO, R. & MCEWEN, S. Head and neck cancer survivorship: learning the needs, meeting the needs. Seminars in radiation oncology, 2018. Elsevier, 64-74.
RISCHIN, D., HARRINGTON, K. J., GREIL, R., SOULIÈRES, D., TAHARA, M., DE CASTRO, G., JR., PSYRRI, A., BRAÑA, I., NEUPANE, P., BRATLAND, Å., FUEREDER, T., HUGHES, B. G. M., MESÍA, R., NGAMPHAIBOON, N., RORDORF, T., ISHAK, W. Z. W., HONG, R. L., MENDOZA, R. G., JIA, L., CHIROVSKY, D., NORQUIST, J., JIN, F. & BURTNESS, B. 2022. Pembrolizumab alone or with chemotherapy for recurrent or metastatic head and neck squamous cell carcinoma: Health-related quality-of-life results from KEYNOTE-048. *Oral Oncol,* 128**,** 105815.
RITCHIE, J. & SPENCER, L. 1994. Bryman A, Burgess RD. Qualitative data analysis for applied policy research. *Analyzing qualitative data***,** 173-194.

RODRIGUEZ, A. & SMITH, J. 2018. Phenomenology as a healthcare research method. *Evidence Based Nursing,* 21**,** 96-98.
ROE, J. W., CARDING, P. N., DWIVEDI, R. C., KAZI, R. A., RHYS-EVANS, P. H., HARRINGTON, K. J. & NUTTING, C. M. 2010. Swallowing outcomes following Intensity Modulated Radiation Therapy (IMRT) for head & neck cancer - a systematic review. *Oral Oncol,* 46**,** 727-33.
ROE, J. W., DRINNAN, M. J., CARDING, P. N., HARRINGTON, K. J. & NUTTING, C. M. 2014. Patient-reported outcomes following parotid-sparing intensity-modulated radiotherapy for head and neck cancer. How important is dysphagia? *Oral oncology,* 50**,** 1182-1187.
ROE, J. W. G., CARDING, P. N., DRINNAN, M. J., HARRINGTON, K. J. & NUTTING, C. M. 2016. Swallowing performance and tube feeding status in patients treated with parotid-sparing intensity-modulated radiotherapy for head and neck cancer. *HEAD AND NECK-JOURNAL FOR THE SCIENCES AND SPECIALTIES OF THE HEAD AND NECK,* 38**,** 1436-1444.
ROGERS, S., EL-SHEIKHA, J. & LOWE, D. 2009. The development of a Patients Concerns Inventory (PCI) to help reveal patients concerns in the head and neck clinic. *Oral oncology,* 45**,** 555-561.
ROGERS, S. N., GWANNE, S., LOWE, D., HUMPHRIS, G., YUEH, B. & WEYMULLER JR, E. A. 2002. The addition of mood and anxiety domains to the University of Washington quality of life scale. *Head & Neck: Journal for the Sciences and Specialties of the Head and Neck,* 24**,** 521-529.
ROGERS, S. N., LOWE, D., YUEH, B. & WEYMULLER JR, E. A. 2010a. The physical function and social-emotional function subscales of the University of Washington Quality of Life Questionnaire. *Archives of Otolaryngology–Head & Neck Surgery,* 136**,** 352-357.
ROGERS, S. N., SCOTT, B., LOWE, D., OZAKINCI, G. & HUMPHRIS, G. M. 2010b. Fear of recurrence following head and neck cancer in the outpatient clinic. *European Archives of Oto-Rhino-Laryngology,* 267**,** 1943-1949.
ROLAND, N., PORTER, G., FISH, B. & MAKURA, Z. 2016. Tumour assessment and staging: United Kingdom National Multidisciplinary Guidelines. *J Laryngol Otol,* 130**,** S53-s58.
ROSENBEK, J. C., ROBBINS, J. A., ROECKER, E. B., COYLE, J. L. & WOOD, J. L. 1996. A penetration-aspiration scale. *Dysphagia,* 11**,** 93-98.
SCHACHE, A., KERAWALA, C., AHMED, O., BRENNAN, P. A., COOK, F., GARRETT, M., HOMER, J., HUGHES, C., MAYLAND, C. & MIHAI, R. 2021. British Association of Head and Neck Oncologists (BAHNO) standards 2020. *Journal of oral pathology & medicine: official publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology,* 50**,** 262-273.
SCHACHE, A. G., POWELL, N. G., CUSCHIERI, K. S., ROBINSON, M., LEARY, S., MEHANNA, H., RAPOZO, D., LONG, A., CUBIE, H. & JUNOR, E. 2016. HPV-related oropharynx cancer in the United Kingdom: an evolution in the understanding of disease etiology. *Cancer research,* 76**,** 6598-6606.
SCHARDT, C., ADAMS, M. B., OWENS, T., KEITZ, S. & FONTELO, P. 2007. Utilization of the PICO framework to improve searching PubMed for clinical questions. *BMC medical informatics and decision making,* 7**,** 1-6.
SHAH, S. 2022. Common terminology criteria for adverse events. *National Cancer Institute: USA,* 784**,** 785.
SHARMA, B. K., CONTRERA, K. J., JIA, X., FLEMING, C., LORENZ, R. R., KOYFMAN, S. A., MAHOMVA, C., ARIANPOUR, K., BURKEY, B. B. & FRITZ, M. 2022. Outcomes After Oral Cavity and Oropharyngeal Salvage Surgery. *The Laryngoscope*.
SHARP, H. M., LIST, M., MACCRACKEN, E., STENSON, K., STOCKING, C. & SIEGLER, M. 1999. Patients' priorities among treatment effects in head and neck cancer: Evaluation of a new assessment tool. *Head & Neck: Journal for the Sciences and Specialties of the Head and Neck,* 21**,** 538-546.

SHICKH, S., LEVENTAKOS, K., LEWIS, M. A., BOMBARD, Y. & MONTORI, V. M. 2023. Shared Decision Making in the Care of Patients With Cancer. *American Society of Clinical Oncology Educational Book*, e389516.
SHORTEN, A. & SMITH, J. 2017. Mixed methods research: expanding the evidence base. Royal College of Nursing.
SIMARD, S., THEWES, B., HUMPHRIS, G., DIXON, M., HAYDEN, C., MIRESKANDARI, S. & OZAKINCI, G. 2013. Fear of cancer recurrence in adult cancer survivors: a systematic review of quantitative studies. *Journal of Cancer Survivorship,* 7**,** 300-322.
SIMON, C., CABALLERO, C. A., FORTPIED, C., EVANS, M., KOIVUNEN, P., STELMES, J.-J., URBANOWICZ, M., BOURHIS, J., ZIMMERMANN, F., KLUSSMANN, J. P., DIETZ, A., SPRIANO, G., LEEMANS, C. R., SINGER, S., TINHOFER, I., PATTERSON, J., QUAGLINI, S., HUNTER, K. & GREGOIRE, V. 2018. BEST OF: A phase III study assessing the best of radiotherapy (Intensity Modulated RadioTherapy, IMRT) compared to the best of surgery (Trans-Oral Surgery, TOS) in patients with T1-T2, N0 oropharyngeal squamous cell carcinoma (OPSCC). *Journal of Clinical Oncology,* 36**,** TPS6098-TPS6098.
SKAMAGKI, G., KING, A., CARPENTER, C. & WÅHLIN, C. 2024. The concept of integration in mixed methods research: a step-by-step guide using an example study in physiotherapy. *Physiotherapy Theory and Practice,* 40**,** 197-204.
SLIM, K., NINI, E., FORESTIER, D., KWIATKOWSKI, F., PANIS, Y. & CHIPPONI, J. 2003. Methodological index for non-randomized studies (minors). *Development and validation of a new instrument,* 2003**,** 73.
SPENCER, S. A., HARRIS, J., WHEELER, R. H., MACHTAY, M., SCHULTZ, C., SPANOS, W., ROTMAN, M. & MEREDITH, R. 2001. RTOG 96-10: reirradiation with concurrent hydroxyurea and 5-fluorouracil in patients with squamous cell cancer of the head and neck. *Int J Radiat Oncol Biol Phys,* 51**,** 1299-304.
STARMER, H. M., ARRESE, L., LANGMORE, S., MA, Y., MURRAY, J., PATTERSON, J., PISEGNA, J., ROE, J., TABOR-GRAY, L. & HUTCHESON, K. 2021. Adaptation and Validation of the Dynamic Imaging Grade of Swallowing Toxicity for Flexible Endoscopic Evaluation of Swallowing: DIGEST-FEES. *Journal of Speech, Language, and Hearing Research*, 1-9.
STEELE, C. M., NAMASIVAYAM-MACDONALD, A. M., GUIDA, B. T., CICHERO, J. A., DUIVESTEIN, J., HANSON, B., LAM, P. & RIQUELME, L. F. 2018. Creation and initial validation of the international dysphagia diet standardisation initiative functional diet scale. *Archives of physical medicine and rehabilitation,* 99**,** 934-944.
STERNE, J. A., HERNÁN, M. A., REEVES, B. C., SAVOVIĆ, J., BERKMAN, N. D., VISWANATHAN, M., HENRY, D., ALTMAN, D. G., ANSARI, M. T. & BOUTRON, I. 2016. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *bmj,* 355.
SWEENY, L., ROSENTHAL, E. L., CLEMONS, L., STEVENS, T. M., MCINTOSH, E. R. C. & CARROLL, W. R. 2016. Outcomes after surgical salvage for recurrent oropharyngeal squamous cell carcinoma. *Oral Oncology,* 60**,** 118-124.
TASHAKKORI, A. & TEDDLIE, C. 2003. Issues and dilemmas in teaching research methods courses in social and behavioural sciences: US perspective. *International journal of social research methodology,* 6**,** 61-77.
TASSONE, P., WIESER, M., GIVENS, A., ELLIOTT, Z., PHILIPS, R., CURRY, J., BARRETTE, L. X., CANNADY, S., MAHOMVA, C. & LAMARRE, E. 2022. Factors Leading to Gastrostomy Tube and Tracheostomy Requirements in Patients Treated Initially With Radiotherapy and Salvaged With Surgery and Free Flap Reconstruction. *The Laryngoscope*.
TOFT, K., BEST, C. & DONALDSON, J. 2024. Assessment of patients with head and neck cancer using the MD Anderson Dysphagia Inventory: Results of a study into its comprehensiveness, comprehensibility and relevance to clinical practice. *International Journal of Language & Communication Disorders,* n/a.
WALSH, R. 2003. The methods of reflexivity. *The Humanistic Psychologist,* 31**,** 51-66.

WANAT, M., BOULTON, M. & WATSON, E. 2016. Patients' experience with cancer recurrence: a meta-ethnography. *Psychooncology,* 25**,** 242-52.
WARD, D. J., FURBER, C., TIERNEY, S. & SWALLOW, V. 2013. Using F ramework A nalysis in nursing research: a worked example. *Journal of advanced nursing,* 69**,** 2423-2431.
WARNER, B. E., LOUND, A., GRAILEY, K., VINDROLA-PADROS, C., WELLS, M. & BRETT, S. J. 2023. Perspectives of healthcare professionals and older patients on shared decision-making for treatment escalation planning in the acute hospital setting: a systematic review and qualitative thematic synthesis. *EClinicalMedicine,* 62**,** 102144.
WHITE, H., FORD, S., BUSH, B., HOLSINGER, F. C., MOORE, E., GHANEM, T., CARROLL, W., ROSENTHAL, E., SWEENY, L. & MAGNUSON, J. S. 2013. Salvage surgery for recurrent cancers of the oropharynx: comparing TORS with standard open surgical approaches. *JAMA Otolaryngology–Head & Neck Surgery,* 139**,** 773-777.
WHO. 2002. *International Classification of Functioning, Disability and Health ICF Checklist* [Online]. Available: https://www.who.int/publications/m/item/icf-beginner-s-guide-towards-a-common-language-for-functioning-disability-and-health [Accessed December 3rd 2021].
WILLIAMS, K., HERMAN, R. & BONTEMPO, D. 2013. Comparing audio and video data for rating communication. *West J Nurs Res,* 35**,** 1060-73.
WILLIAMSON, A., HAYWOOD, M. & AWAD, Z. 2021. Feasibility of free flap reconstruction following salvage robotic-assisted resection of recurrent and residual oropharyngeal cancer in 3 patients. *Ear, Nose & Throat Journal,* 100**,** 1113S-1118S.
WILLIAMSON, A., JASHEK-AHMED, F., HARDMAN, J. & PALERI, V. 2023. Functional and quality-of-life outcomes following salvage surgery for recurrent squamous cell carcinoma of the head and neck: a systematic review and meta-analysis. *Eur Arch Otorhinolaryngol,* 280**,** 4597-4618.
WINDON, M. J., D'SOUZA, G., FARAJI, F., TROY, T., KOCH, W. M., GOURIN, C. G., KIESS, A. P., PITMAN, K. T., EISELE, D. W. & FAKHRY, C. 2019. Priorities, concerns, and regret among patients with head and neck cancer. *Cancer,* 125**,** 1281-1289.
WORLD HEALTH ORGANIZATION. DIVISION OF MENTAL, H. & PREVENTION OF SUBSTANCE, A. 1997. WHOQoL : measuring quality of life. Geneva: World Health Organization.
YOUNAS, A., FÀBREGUES, S. & CRESWELL, J. W. 2023. Generating metainferences in mixed methods research: A worked example in convergent mixed methods designs. *Methodological Innovations,* 16**,** 276-291.
YU, J., SMITH, J., MARWAH, R. & EDKINS, O. 2022. Return to work in patients with head and neck cancer: Systematic review and meta-analysis. *Head Neck,* 44**,** 2904-2924.
ZAFEREO, M. E., HANASONO, M. M., ROSENTHAL, D. I., STURGIS, E. M., LEWIN, J. S., ROBERTS, D. B. & WEBER, R. S. 2009. The role of salvage surgery in patients with recurrent squamous cell carcinoma of the oropharynx. *Cancer: Interdisciplinary International Journal of the American Cancer Society,* 115**,** 5723-5733.
ZAFEREO, M. E., WEBER, R. S., LEWIN, J. S., ROBERTS, D. B. & HANASONO, M. M. 2010. Complications and functional outcomes following complex oropharyngeal reconstruction. *Head Neck,* 32**,** 1003-11.
ZANONI, D. K., PATEL, S. G. & SHAH, J. P. 2019. Changes in the 8th edition of the American Joint Committee on Cancer (AJCC) staging of head and neck cancer: rationale and implications. *Current oncology reports,* 21**,** 1-7.

Appendices

Appendix 1: Systematic review publication

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Review Article

Patient experience, functional and quality of life outcomes in patients receiving surgical and non-surgical treatment for residual, recurrent, or new oropharyngeal cancer in a previously irradiated field: A systematic review

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Abstract.
BACKGROUND: National guidance recommends counselling on functional (swallowing/ speech/ voice) and quality of life outcomes (QoL) for patients with recurrent, residual or new primary head and neck cancer (HNC) in a previously irradiated field (ReRuNeR).
AIM: To investigate the measurement and reporting of function and QoL outcomes and patient/carer experience for ReRuNeR, focussing exclusively on oropharyngeal cancer (OPC).
METHODS: Systematic narrative review of quantitative/qualitative studies.
RESULTS: Seventeen articles reporting functional/ QoL outcomes following surgery were included. Gastrostomy dependence was the primary method of reporting function. Previously validated outcome measures (OMs) were used for reporting swallowing in four, speech in one and QoL in two trials. Qualitative data or non-surgical studies reporting function/QoL outcomes specific to ReRuNeR OPC were not identified. Methodological issues and heterogeneity noted across studies including absent baseline data, varying/ undefined timepoints for outcome measurement and the use of unvalidated tools. Patient-reported swallowing outcomes were mixed. Whereas instrumental assessment of swallowing showed a deterioration in safety/ efficiency. A post-surgical decline in speech was noted. Stable overall HR-QoL was reported but an increase in specific symptoms including speech, saliva and swallowing were noted. Pooled long term gastrostomy feeding rate was 23.42% (95% CI 10.2 to 36.6) ($n = 108$).

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CONCLUSION: A core dataset of patient and clinician-rated OMs is required to provide a comprehensive understanding of functional and QoL complications with ReRuNeR OPC. In combination with patient/carer experience data, these data can be used to inform pre-treatment counselling, rehabilitation and future clinical trial design.

Keywords: Head and neck cancer, recurrent disease, quality of life, functional outcomes

PROSPERO study ID: CRD42021236540

1. Introduction

Head and neck cancer (HNC) is the sixth most common cancer in the world and is increasing in incidence (Hardman et al., 2020). Squamous cell carcinomas (SCC) account for the majority of these tumours, with an increasing number of oropharyngeal cancers associated with the human papilloma virus (HPV). Treatments for primary disease include (chemo)radiation and/or surgery, with many patients undergoing multi-modality treatment. The impact of such treatments on function, including swallowing, speech, voice and overall quality of life (QoL), in the primary disease setting have been well documented (Patterson, McColl, Carding, & Wilson, 2018; Roe, Drinnan, Carding, Harrington, & Nutting, 2014).

Despite ongoing advancements in the treatment of primary oropharyngeal disease, rates of residual (diagnosed within 12 months of previous treatment), recurrent (diagnosed between 12 months and 5 years of previous treatment) and second primary disease (diagnosed > 5 years following previous treatment) remain high at approximately 20–30% (Hardman et al., 2020; Leeman et al., 2017; Mandapathil et al., 2014; Warnakulasuriya, 2009).

Residual, recurrent or new primary (ReRuNeR) oropharyngeal cancer (OPC) present some of the greatest challenges in HNC practice (Brady, Hardman, Paleri, Harrington, & Roe, 2020). Not only do these patients often present with functional issues such as difficulties with swallowing, speech and/or voice due to long-term/ late-onset effects from their prior treatment (Patterson et al., 2018), but the newly diagnosed disease and/ or the proposed treatment plan may further cause or compound such difficulties. In addition to disease and treatment-related issues, patients who have undergone treatments for HNC are also known to have a high level of psychological stressors, which can further add to symptom burden and overall QoL (Ringash et al., 2018).

The UK standard of care for ReRuNeR OPC is open surgery, an intervention associated with high morbidity (Mehanna, Kong, & Ahmed, 2016). Transoral robotic surgery (TORS) is now being considered as a minimally invasive option with encouraging oncological control (Paleri, Hardman, Brady, George, & Kerawala, 2020). There may be opportunities for re-irradiation; however, this has the potential for severe treatment toxicity. Non-curative options include palliative systemic treatments or best supportive care. More recently, immunotherapy is being utilised. In the UK, pembrolizumab, with or without platinum-based chemotherapy, is now used for untreatable metastatic or unresectable recurrent head and neck squamous cell carcinoma in patients whose tumours express a specific biomarker (PD-L1 with a combined positive score of 1 or more) (NICE, 2020).

Historically, patients with ReRuNeR OPC were considered to have a very poor prognosis with the majority of patients offered palliative treatments or best supportive care. However, over the past 20 years, there has been a paradigm shift in the treatment of recurrent HNC, with evidence to support increased survival rates for patients treated curatively using surgery, in particular for patients with ReRuNeR OPC (Jayaram et al., 2016). For those patients who are not suitable for surgical resection, the focus in recent literature has been on enhanced life-prolonging treatments such as the use of immunotherapy.

National guidelines suggest that patients diagnosed with ReRuNeR disease should be fully counselled on the likely functional and QoL impact of the available treatments (Mehanna et al., 2016).However, although there has been an apparent paradigm shift in studies investigating enhanced survival for patients with ReRuNeR OPC, there appears to be a lack of literature examining functional, QoL and patient experience outcomes for all treatment modalities in ReRuNeR OPC.

The aim of this systematic review is to identify if functional and QoL outcomes and patient experience data are reported, how they are measured and what are the functional and QoL outcomes and patient experience data reported for patients with ReRuNeR OPC. Working definitions for functional outcomes, QoL and patient experience as used in this review will be provided under methods.

2. Methods

This systematic review used a population, intervention, comparison, outcome (PICO) framework (Schardt, Adams, Owens, Keitz, & Fontelo, 2007). This framework was divided as follows to report on the following: for patients with ReRuNeR OPC (Population), undergoing curative or non-curative treatment (Intervention), are functional, QoL and patient experience measures reported, and if so, how are they reported and what are the findings (Outcomes). A comparator was not a requirement for this review.

The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines were used to carry out the systematic review (Moher, Liberati, Tetzlaff, & Altman, 2010). The protocol was registered on PROSPERO an international prospective register of systematic reviews (CRD42021236540).

The main objectives of the systematic review were:

1. To report on the functional and QoL outcomes and patient experience data for patients with ReRuNeR OPC
2. To describe how functional, QoL outcomes and patient experience data are measured for patients with ReRuNeR OPC

2.1. Eligibility criteria

2.1.1. Study characteristics

All observational studies, including qualitative and experimental designs, both prospective and retrospective, were included. Only peer- reviewed articles published in English were included. No limitation was placed on year of publication. Abstracts and conference proceedings were excluded. Studies were excluded if cohorts of primary and ReRuNeR OPC were mixed unless a subgroup analysis of ReRuNeR OPC outcomes was available. Likewise, studies were excluded if they investigated head and neck disease recurrence rather than ReRuNeR OPC specifically, unless a subgroup analysis of findings for ReRuNeR OPC was available.

2.2. Inclusion criteria

1. Adults aged 18 years or older with a diagnosis of recurrent, residual or new primary oropharyngeal disease in a previously radiated area
2. Participants undergoing treatment for ReRuNeR OPC including surgery (open or transoral robotic), re-irradiation, chemotherapy, and/or immunotherapy
3. Functional and/or QoL outcomes and/or patient experience data reported (validated or unvalidated tools/ methods including long-term feeding tube and tracheostomy usage/ qualitative findings)
4. English language
5. Full text available

2.3. Primary and secondary outcome measures

The primary outcome measures included the reporting of either functional or QoL or patient experience outcomes. For the purposes of this systematic review functional outcome data includes any data presented in relation to swallowing and communication (including speech and voice) outcomes using previously validated or unvalidated measures. QoL outcomes include data measured using validated health related QoL patient-reported outcome measures. Patient and carer experience data includes any data that is collected with the intention to provide information about patients' experiences with ReRuNeR OPC 'including the impact of the disease or condition or related therapy or clinical investigation, and patient preferences with respect to treatment of the disease or condition' (FDA, 2016).

2.4. Primary outcome measures

1. Functional outcomes including swallowing, speech and HR-QoL outcomes
2. Patient experience outcomes

2.5. Secondary outcome measures

3. Gastrostomy dependence at >6 months post treatment
4. Tracheostomy dependence at >6 months post treatment

2.5. Identification of studies

A systematic computer-based search was performed using the following electronic health databases: MEDLINE, CINAHL, and Embase. Additional searches were carried out on Web of Science and the meta-registries of Trials Databases (ClinicalTrials.gov and ISRCTN). The WHO International

Clinical Trials Registry Platform (ICTRP) and the Australian New Zealand Clinical Trials Register (ANZCTR) were also included in the search.

Additional citation searches were completed for selected articles.

2.6. Search strategy

Search terms included "oropharyngeal cancer" AND "recurrent" OR "residual disease" OR "second primary' OR "radiation induced" AND "swallow" OR "dysphagia" OR "speech" OR "voice" OR "quality of life" OR "patient experience" OR "functional outcomes" AND "salvage surgery" OR "salvage therapy" OR "re-irradiation". All search terms were exploded when possible and any subject headings relevant to each database were included.

2.7. Selection of studies

The initial database searches were combined and 1,052 articles were imported into Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org). Following removal of 256 duplicates, the remaining 796 article titles and abstracts were screened for inclusion and exclusion criteria by authors GB, MW and PL.

These criteria were applied to the titles and abstracts, and articles that did not meet the inclusion criteria were excluded. Articles were included for full-text review where it was not possible to use the abstract to fully assess eligibility. The full texts of 47 articles were retrieved and assessed using the inclusion criteria. Senior author MW reviewed 10% of these articles also to ensure agreement with assessment of eligibility. Any ambiguities or discrepancies were resolved by discussion with author JR.

2.8. Data extraction

A data extraction table was devised using Microsoft Excel. Data inputted included study location, patient characteristics, treatment modality, primary and secondary outcomes used, timepoints data collection, swallowing and QoL results, and feeding tube and tracheostomy use.

2.9. Risk of Bias

A study-level risk of bias assessment was performed for all included studies by authors GB and MW. All included studies were observational in design so the Methodological Index for Non-Randomised Studies (MINORS) tool was utilised (Kim et al., 2013).

2.10. Data synthesis

Quantitative data: It was anticipated from similar reviews in the primary disease setting (Roe et al., 2010) that the number of studies identified may be low and the heterogeneity between studies found high and so statistical analysis for comparing outcomes across modalities (meta-analysis) was not planned.

2.11. Qualitative data

The intended method to synthesise any qualitative data findings was meta ethnography, a method of qualitative data synthesis which is gaining increasing focus on health care research (Atkins et al., 2008). This method aims to complete a secondary analysis to compare and contrast concepts across qualitative studies, to gain a deeper insight into the topic (Sattar, Lawton, Panagioti, & Johnson, 2021).

3. Results

3.1. Study selection

The literature search findings are summarised in Fig. 1 PRISMA flow diagram. Following the removal of duplicate records, 796 studies were identified and 47 included for full text review with 17 studies included for data extraction. The primary reason for exclusion was that only survival outcomes only reported ($n = 16$); this included studies focusing on surgery ($n = 10$), chemotherapy ($n = 3$), re-irradiation ($n = 2$) and immunotherapy ($n = 1$). Other reasons for exclusion included general HNC cohort where functional/ QoL or general toxicity outcomes were reported but with no subgroup analysis for patients with ReRuNeR ($n = 10$) or mixed primary/ ReRuNeR OPC cohorts ($n = 1$). One qualitative study was identified; however, it was excluded as it was not specific to ReRuNeR OPC but a more general recurrent HNC caseload.

3.2. Study characteristics

Study characteristics are summarised in Table 1. The geographic distribution of studies is as follows:

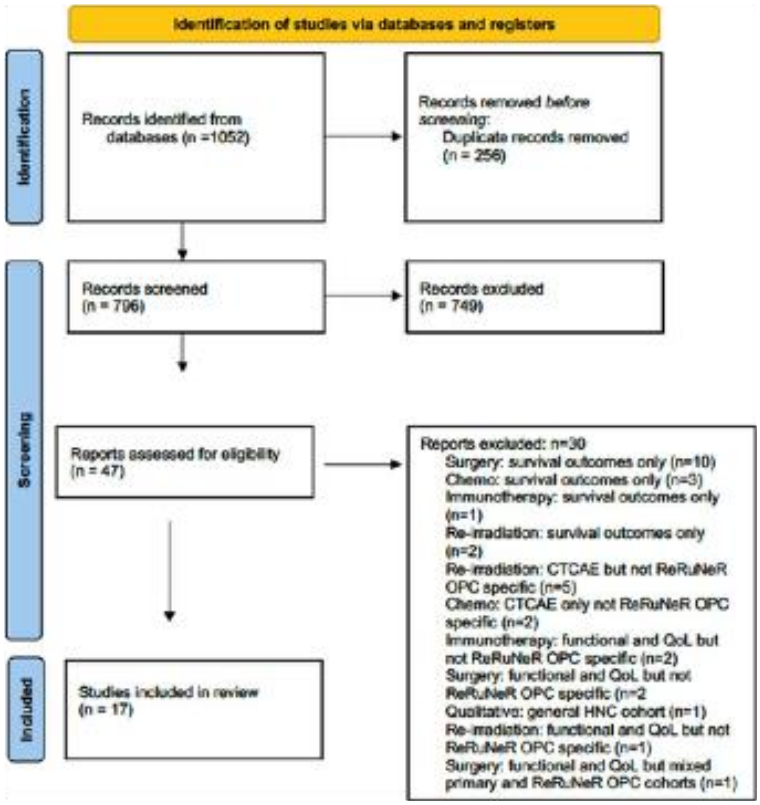


Fig. 1. PRISMA diagram.

US ($n = 8$), France ($n = 4$), UK ($n = 2$), Japan ($n = 1$), Australia ($n = 1$) and multicentre ($n = 1$). All studies were published between 2009 and 2022. Two studies included a prospective design, and the majority were single centre case series ($n = 12$). No qualitative/patient experience studies were identified.

3.3. Patient characteristics

In total the studies included 863 patients with ReRuNeR OPC (Range 3–199). All studies investigated outcomes for surgical procedures, either open surgery or transoral robotic surgery. No oncological studies were identified reporting on functional or QoL outcomes for ReRuNeR OPC specifically. The authorship team of two large immunotherapy trials and one re-irradiation trial, who reported function and QoL data for a more general HNC cohort were contacted to see if a subgroup analysis was available for patients with ReRuNeR OPC; however, the data were not available for review at the time of writing.

3.4. Risk of bias

MINORS risk of bias assessment findings are summarised in Table 2. All but one of the included studies did not involve a comparator group. For the non-comparative studies, the median MINORS score was 8 (out of a possible 12) with a range of 7–10. The one study which included a comparator group was rated with a MINORS score of 14 (out of a possible 24). Each item is scored from 0–2 where 0 indicates that the item was not reported, 1 indicates that it was reported but inadequately and 2 indicates that it was adequately reported within the article.

Table 1
Study characteristics

Author	Year	Location	Study design	Intervention	Function/ Quality of Life outcomes primary or secondary, validated (V) or unvalidated (UV):	No of participants	Timepoints	Outcome measures used
(Charters et al., 2022)	2022	Australia	Case series	TORS[a]	Primary V	3	Baseline 3 months 12 months	FOIS [b] MDADI [c] SHI[d] PASe, BRCS[f], PSS-HN- NOD[g], PSS-HN-EIP[h], PSS-HN-UoS[i], Gastrostomy rate
(Culié et al., 2015)	2015	France	Case series	Open and TORS	Secondary V	34	Baseline 6 months	Speech intelligibility (unvalidated) DOSS[j]
(D'Andréa et al., 2022)	2022	France	Case series	Open and TORS	Primary V	53	Baseline, 3 months 1 year 2 years 3 years 4 years 5 years	MDADI EORTC-QLQC30[k] EORTC-QLQH&N35[l] Gastrostomy rate Tracheostomy rate
(Dean et al., 2010)	2010	United States	Case control study	Open and TORS	Secondary UV	21	No baseline 6 months	Gastrostomy rate Tracheostomy rate
(Hardman et al., 2022)	2022	Global	Case series	TORS	Secondary UV	199	No baseline 1 year	Gastrostomy rate Tracheostomy rate
(Kano et al., 2013)	2013	Japan	Case series	Open and TORS	Secondary UV	11	Baseline Undefined follow up	Gastrostomy rate Oral feeding (unvalidated)
(Kostrzewa et al., 2010)	2010	United Kingdom	Case series	Open surgery	Primary UV	36	No baseline Undefined follow up	Gastrostomy rate Oral feeding (unvalidated)

(Mazerolle et al., 2022)	2022	France	Case series	Open surgery	Secondary UV	42	No baseline Undefined follow up	Respiratory status Nutritional status
(Patel et al., 2016)	2015	United States	Case series	Open and TORS	Secondary UV	34	No baseline Undefined follow up	Gastrostomy rate Tracheostomy rate
(Philouze et al., 2017)	2017	France	Case series	Open and TORS	Secondary UV	52	No baseline Undefined follow up	Gastrostomy rate
(Pipkorn et al., 2019)	2018	United States	Case series	TORS	Secondary UV	18	No baseline Undefined follow up	Gastrostomy rate
(Sharma et al., 2022)	2022	United States	Case series	Open surgery	Secondary UV	30	No baseline Within 30 days of surgery	Gastrostomy rate
(Sweeny et al., 2016)	2016	United States	Case series	Open and TORS	Secondary UV	69	No baseline 1 year	Gastrostomy rate
(Tassone et al., 2022)	2022	United States	Case series	Open surgery	Primary UV	89	No baseline 1 year	Gastrostomy rate Tracheostomy rate
(White et al., 2013)	2013	United States	Case control study	Open and TORS	Secondary UV	128	No baseline 1 year	Gastrostomy rate Tracheostomy rate
(Williamson, Haywood, & Awad, 2021)	2021	United Kingdom	Case series	TORS	Primary V	3	Baseline Undefined follow up	UW-QOL[m] MDADI
(Zafereo et al., 2009)	2009	United States	Case control study	Other	Secondary UV	41	Undefined follow up	Oral intake (unvalidated) Speech mode (unvalidated) Speech intelligibility (unvalidated) Tracheostomy rate

[a]Tranoral robotic surgery; [b]Functional Oral Intake Scale; [c]MD Anderson Dysphagia Inventory; [d]Speech Handicap Index; [e]Penetration Aspiration Scale; [f]Boston Residue and Clearance Scale; [g]Performance Status Scale for Head and Neck Cancer - Normalcy of Diet; [h]Performance Status Scale for Head and Neck Cancer - Eating in Public; [i]Performance Status Scale for Head and Neck Cancer - Understandability of Speech; [j]Dysphagia Outcome Severity Scale; [k]European Organisation for Research and Treatment (EORTC) Quality of Life for Cancer Patients; [l]European Organisation for Research and Treatment (EORTC) Quality of Life for Cancer Patients - Head and Neck; [m]University of Washington Quality of Life Questionnaire.

Table 2
Risk of bias assessment using MINORS (Kim et al. 2013)

Study	Charters et al.	Culle et al.	D' Andrea et al.	Dean et al.	Hardman et al.	Kano et al.	Kostrzewa et al.	Mazerolle et al.	Patel et al.	Philouze et al.	Pipkorn et al.	Sharma et al.	Sweeney et al.	Tassone et al.	White et al.	Williamson et al.	Zafereo et al.
A clearly stated aim	1	2	1	2	2	0	2	2	2	2	2	2	2	2	2	2	2
Inclusion of consecutive data	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Prospective collection of data	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Endpoints appropriate to the aim of the study	1	1	2	2	2	1	1	2	2	1	1	1	1	1	1	2	1
Unbiased assessment of the study endpoint	0	0	0	0	0	0	0	0	0	0	0	1	1	2	0	0	0
Assessment tests appropriate with the aim	2	1	2	1	1	1	1	1	1	1	1	1	1	2	1	2	1
Loss of samples < 5%	2	0	0	2	1	0	0	2	2	2	2	2	0	0	0	0	1
Prospective calculation of the study size	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
An adequate control group															2		
Contemporary groups															2		
Baseline equivalence of groups															2		
Adequate statistical analysis															2		
Total score:	**8**	**6**	**9**	**9**	**8**	**4**	**6**	**9**	**9**	**8**	**8**	**9**	**7**	**9**	**14**	**10**	**7**

MINORS Scoring (Kim et al. 2013): 0: not reported; 1: reported but inadequately; 2: adequately reported.

3.5. Results

Out of the 796 articles reporting outcomes for treatments for ReRuNeR OPC, specific functional and/or QoL data were available for patients with ReRuNeR OPC in 2% ($n = 17$). Within the 17 articles included, functional and/or QoL measures were reported as a primary outcome in 29% ($n = 5$), survival was reported as the primary measure in 71% ($n = 12$).

3.5.1. Swallowing outcomes

Validated swallowing outcome measures were used in 23% of studies ($n = 5$). These measures included the MD Anderson Dysphagia Inventory (MDADI) (Chen et al., 2001) ($n = 3$), the Functional Oral Intake Scale (FOIS) (Crary, Mann, & Groher, 2005) ($n = 1$), the Performance Status Scale for Head and Neck Cancer (PSS-HN)(List, Ritter-Sterr, & Lansky, 1990) normalcy of diet (NOD) and eating in public (EIP) subscales ($n = 1$). Two studies reported on validated swallowing outcome measures obtained using an instrumental evaluation of swallowing. One study described the use of Flexible Endoscopic Evaluation of Swallowing (FEES) and the Penetration-Aspiration Scale (PAS)(Rosenbek, Robbins, Roecker, Coyle, & Wood, 1996) and Boston Residue and Clearance Scale (BRCS) (Kaneoka et al., 2013). Another study described the use of videofluoroscopy and the Dysphagia Outcome and Severity Scale (DOSS) (O'Neil, Purdy, Falk, & Gallo, 1999).

Charters et al. (2022) reported on swallowing outcomes for 3 patients who underwent TORS for ReRuNeR OPC. Baseline and 12-month outcomes were reported for the FOIS, and PSS NOD scores. Here the FOIS score indicated a change from baseline where patients were managing a total oral diet with some diet modification (FOIS: 5) to being tube dependent with limited oral intake (FOIS: 3). PSS-NOD data showed a deterioration from soft chewable diet (PSS NOD: 50) to pureed diet (PSS NOD: 30). A number of 12 month swallowing outcomes were reported including the MDADI, PSS-EIP, Penetration-Aspiration Scale (PAS) score and the Boston Residue and Clearance Scale. No baseline data on these measures were included, however 12-month findings show impaired swallowing related QoL with an average MDADI composite score of 43 (a score of 100 indicates no swallowing difficulties) and median PSS EIP score of 25 (ordinal scale descriptor: eats only alone). PAS scores and Boston Residue and Clearance scales report that all 3 participants had unsafe swallowing with confirmed aspiration and inefficient swallowing, with confirmed post-swallow residue on instrumental evaluation of swallowing using FEES.

D'Andréa et al. (2022) also reported on the MDADI at 12 months for patients undergoing TORS and open salvage surgery. Overall, although a deterioration in mean composite MDADI scores from 71.4 at baseline to 64.3 at 1 year was noted, this change was not statistically significant ($p = 0.13$) nor did it reach the criterion for clinical significance (10-point change in MDADI composite score). The authors further clarify with individual patient data analysis that only 7 patients (30.4%) reported a 1-year clinically meaningful decrease of the MDADI score of more than ten points, while two patients (8.7%) reported a clinically meaningful increase in the MDADI composite score.

Williamson et al. (2021) report on 3 patients who underwent TORS with robotic assisted flap reconstruction and documented stable MDADI scores pre- and post-surgery with a composite score at baseline and follow up of 66.7. Here, the timepoint for post-surgical review was not defined.

Culié et al. (2015) reported on a case series of patients undergoing TORS and open salvage surgical procedures. Baseline and 6-month DOSS scores were reported and demonstrated a deterioration in swallowing function with increased aspiration of food/ fluids. At baseline 47% of participants were on full oral intake (DOSS score of 6-7), which reduced to 26% 6 months post-surgery. There was an increased number of patients requiring diet modification (DOSS score 3–5). However, between baseline and 6 months, the number of patients requiring non-oral feeding remained stable at 29%.

3.5.2. Speech outcomes

Validated speech intelligibility measures, namely the Speech Handicap Index (SHI) (Rinkel et al., 2008) and the PSS Understandability of Speech (PSS-UoS) subscale (List et al., 1990) were both used in one single study. Other non-validated measures of speech intelligibility included a non-standardised/ validated rating of intelligibility or a comment on speech mode ($n = 2$).

Following TORS, speech outcomes were reported by Charters et al. (2022) using the PSS UoS and the SHI. No baseline data were reported but 12-month data demonstrated reduced speech intelligibility with a median score of 75 on the PSS UoS subscale (understandable most of the time but occasional repetition

necessary) and 25 on the SHI (score from 0–120 with a higher score indicative of higher level of speech difficulties).

Speech outcomes following both open surgery and TORS were reported by Culie et al. (2015)_ using an unvalidated measure rating speech intelligibility from 0–3 (0 was severely altered/ unintelligible and 3 was normal/ near normal). No baseline data were reported, and 6-month data were available for 31/34 participants- here only 2 patients presented with normal/ near normal speech at 6 months post-surgery.

Zafereo et al. (2009) also reported unvalidated measures of speech intelligibility and in 41 patients reported that speech was > 80% intelligible. Again, baseline speech data were not available.

3.5.3. HRQoL outcomes

Validated health-related QoL measures were used in two studies including the University of Washington QoL (UW-QoL) questionnaire (Rogers et al., 2002) ($n = 1$) and European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life for Cancer Patients (QLQ-30) and Quality of Life for Head and Neck Cancer (QLQ-H&N35) together ($n = 1$).

D'Andréa et al. (2022) reported EORTC-QLQ-C30 scores at baseline and 1 year showed non-significant change in global health status with preoperative mean score of 61.18 and 59.38 at 1 year ($p = 0.96$). The EORTC QLQ-H&N35 demonstrated some increased difficulties with sticky saliva, difficulty with social contact, eating and speech. Williamson et al. (2021) used the UW-QoL following TORS with free flap reconstruction. Mean scores for each symptom subscale at baseline and at an undefined timepoint post-surgery were reported. Increased mean scores indicating some level of improvement were noted in the following domains: pain, activity, chewing and anxiety. Reduction in mean scores, indicating deterioration, were reported in the remaining domains of appearance, recreation, swallowing, speech, shoulder, taste, saliva, and mood.

3.5.4. Patient experience outcomes

No patient experience data were identified.

3.5.5. Gastrostomy tube dependence

Where non-validated measures of swallowing function were reported, gastrostomy tube use was the most popular outcome reported in 88% of studies ($n = 15$). Some studies ($n = 3$) also specified oral versus non-oral feeding. Other studies ($n = 2$) focused on method of nutritional intake using three categories, gastrostomy with oral feeding, gastrostomy alone or oral feeding alone.

Long-term feeding tube rate (at least 6 months) was reported in 7/17 studies. A further 9 studies did not specify the timepoint or included data within 30 days of the surgery. Pooled data ($n = 128$) demonstrates a long-term gastrostomy dependence rate of 23.42% (95% CI 10.2 to 36.6).

3.5.6. Long-term tracheostomy tube rate

Tracheostomy tube rate was reported in 47% of studies ($n = 8$). Long-term tracheostomy dependence (at least 6 months) was reported in 3/17 studies. A further 2 studies reported tracheostomy use post-surgery but did not define the timeframe. Pooled data ($n = 309$) demonstrates a long-term tracheostomy rate of 9.3% (95% CI 8.48 to 10.1).

4. Discussion

This systematic review aimed to assess if function, QoL and patient experience are measured in patients undergoing treatment for ReRuNeR OPC. Only 17 articles were identified reporting functional and/or QoL outcomes for patients undergoing treatments for ReRuNeR OPC, five reporting functional/QoL as a primary measure. All 17 articles focused on surgical trials. No specific functional, QoL, patient experience of qualitative data for patients with ReRuNeR OPC undergoing non-surgical treatments were identified in this systematic review.

The measurement of HR-QoL in HNC has been recommended in both clinical practice and research over the past number of years (Rogers, Semple, Babb, & Humphris, 2016). The routine use of validated specific functional outcome measures to guide rehabilitation for communication and swallowing in HNC continues to emerge and has only recently been added as a recommendation in national guidelines (Schache et al., 2021). As a result, this review included previously validated measures of HR-QoL and all measures (validated and unvalidated) of communication and swallowing function were included.

Aside from reporting survival data only, many articles were excluded from this review due to the inclusion of mixed cohorts of HNC patients, with either general recurrent HNC cohorts or mixed primary and recurrent disease groups, with no subgroup analysis for ReRuNeR OPC. In comparison to other

subtypes of head and neck cancer, the OPC subgroup are considered quite unique, in particular those with HPV related disease, who are often younger (less than 60 years) with low co-morbidity, absent or low smoking history (Ang et al., 2010). The incidence of OPC disease is increasing in the UK (Schache et al., 2016). This may be in part due to the emergence of new aetiological categories such as human papilloma virus (HPV), however, non-HPV-related disease which is associated with traditional causative factors including alcohol and tobacco consumption is also increasing (Schache et al., 2016). In the UK, many of these patients will have undergone organ-sparing treatment regimes with radiation therapy +/- chemotherapy. As a result, these patients will most likely be presenting with treatment side-effects in the form of changes to swallowing function, voice/speech and overall QoL (Patterson, McColl, Carding, & Wilson, 2018; Roe, Drinnan, Carding, Harrington, & Nutting, 2014). In addition, there can be a high level of psychological distress and emotional burden following previous treatment (Ringash et al., 2018). Further treatment for disease recurrence may cause further impairments or compound a unique set of baseline physical and psychological burden found in a potentially unique set of younger patients with OPC. With a growing number of patients with ReRuNeR OPC in the UK, specific functional and QoL data in relation to this unique cohort is required.

It is known from previous literature in the primary oropharyngeal disease that to accurately demonstrate the impact of treatment on function/ QoL, multidimensional assessment at pre-defined timepoints is required (Roe et al., 2010). In this review, 7 of the included studies did not report on baseline data and, a further 8 studies reported post-surgical functional and/or QoL data however did not define the follow up period. Pre-treatment baseline level of function has been cited as the key predictor for longer term swallowing outcomes for patients with HNC (Frowen, Cotton, Corry, & Perry, 2010). Given the risk of baseline functional difficulties in patients with ReRuNeR disease (Hardman et al. 2020), accurate baseline and longitudinal data measurements with pre-defined follow-up timepoints are imperative to accurately measure any potential change. Such methodological issues, in addition to the use of different outcome tools, make interpretation of the collective data difficult and any form of meta-analysis impossible.

This systematic review identified just three studies reporting speech outcomes. The standard of care for curative management of ReRuNeR OPC is at present open surgery. National guidelines highlight the potential functional morbidity including speech (Mehanna et al., 2016), however, based on this review, speech outcomes do not appear to be reported routinely. In the studies reporting speech outcomes, only one study used a previously validated speech outcome measure however, all studies did demonstrate altered speech in the post operative phase.

The majority of studies ($n = 14$) included data on gastrostomy use post-surgery. Eleven of these studies included gastrostomy tube dependence with or without tracheostomy tube dependence as the only measures of function post-surgery. In our review, pooled data ($n = 128$) demonstrates a long-term gastrostomy feeding rate of almost a quarter (23.42, 95% CI 10.2 to 36.6). In comparison to a previous systematic reviews reporting outcomes for TORS for recurrent HNC where long-term gastrostomy rate was recorded as 5% (Paleri et al., 2020), this estimate does seem to be higher. This may be due to the previous review including all HNC cohorts (not specific to ReRuNeR OPC) or only one treatment method (TORS rather than all surgery). Also, it is noted by the authors here that the definition of long-term use is not clear in the included studies. The current review defined long-term gastrostomy use as at least 6 months post-surgery. Given such ambiguities, the case for future studies to look at specific subgroups of HNC for more accurate/ clearly defined functional outcomes is strengthened. Gastrostomy tube use is widely used in the literature as a proxy for swallowing outcomes. As a unidimensional measure, it does not give an accurate/holistic measure of swallowing status. Many HNC patients may be having a combination of both oral intake and gastrostomy feeding. Also, without the provision of baseline data it is impossible to ascertain if gastrostomy tube presence is a consequence of primary disease management or because of the treatment of ReRuNeR disease.

There appears to be some variation in outcomes in relation to the studies using patient- and clinician-reported measures of swallowing function. It is known from the literature in relation to primary disease that clinician and patient-reported measures of toxicity are not always congruent (Falchook et al., 2016). Both within and across surgery types (TORS and open), mixed findings are reported using the MDADI. One study reports stable post-TORS findings (Williamson et al., 2021) and another reported a deterioration (Charters et al., 2022), although both of these studies included only 3 patients each. A

further study, with a much larger cohort ($n = 53$) (D'Andréa et al., 2022) reports outcomes for both open and TORS surgery and details an overall mean deterioration in MDADI composite scores but that deterioration did not meet statistical or clinical significance. A previous study investigated the clinically meaningful difference in MDADI scores for patients with HNC using a combination of criterion standards including aspiration scores, feeding tube status and diet scores (Hutcheson et al., 2016). The methodology for this study however excluded patients with recurrent disease. It might thus be questioned if the MDADI and the critical 10-point clinically significant difference is suitable in the recurrent setting when we know that most of these patients will have baseline swallowing difficulties with lower diet scores, higher rates of gastrostomy tube usage and increased aspiration from their previous treatments +/- tumour related complications (Paleri et al., 2020).

With regards to QoL measurement, only 2 trials were identified where validated health-related quality of life tools were used, namely the UW-QoL questionnaire and the EORTC QLQ-C30 used in combination with the EORTC QLQ-H&N35. In an area of HNC practice where many treatment decisions are based on the potential impact of further treatments on QoL, one would expect a much greater focus within the literature. Although stable outcomes were reported by Williamson and colleagues (Williamson et al., 2021) it would appear that some aggregate data is missing in the publication. Scoring of the UW-QoL tool typically involves presenting the questionnaire data from two subscale scores, one for 'Physical Function' and another for 'Social-Emotional Function.' The Physical subscale score is computed as the simple average of 6 domain scores – those of chewing, swallowing, speech, taste, saliva and appearance. The Social-Emotional subscale score is also computed as the simple average of 6 domain scores - those of anxiety, mood, pain, activity, recreation and shoulder function. Such scores are not provided in this publication thus difficult to interpret. Also, a small sample size is noted in this study with just three patients. In a larger study by D'Andréa et al. (2022) non-significant changes in EORTC-QLQ-C30 scores at baseline and 1 year were reported. However, the EORTC QLQ-H&N35 demonstrated some increased difficulties with sticky saliva, difficulty with social contact, eating and speech. This echoes findings by Williamson and colleagues who, when reporting symptoms using the UW-QoL tool, noted increased symptoms in relation to swallowing, speech, taste, saliva, in addition to shoulder, appearance, recreation and mood. However, as noted in previous literature, the content validity of EORTC QLQ-C30 and QLQ-H&N35 (Degboe et al., 2018) has not been widely documented in relation to patients with disease recurrence. Similarly, much of the literature in relation to the development of the UW-QoL questionnaire has focused on patients treated for primary disease, who are now cancer free (Rogers, Lowe, Yueh, & Weymuller Jr, 2010).

This systematic review is not without its limitations. As noted, in preparing the protocol for this review it was hypothesised that literature regarding function and QoL data was in its infancy in the area of ReRuNeR. For this reason, meta-analysis was neither planned nor subsequently undertaken and instead, a narrative review of the evidence is presented. The data presented focuses solely on (potentially curative) surgical outcome data. A high level of bias was noted using the risk of bias assessment for included studies, which must be considered in the interpretation of the findings of this review. The majority of the studies were observational and retrospective in nature. Only two of the included studies were prospective, only one had a comparator group, and neither reported a sample size calculation.

Given the limited evidence on functional and QoL data in the recurrent HNC population, it may have been sensible to include all recurrent HNC studies rather than those specifically pertaining to OPC. For example, two large randomised controlled trials (Burtness et al., 2019; Cohen et al., 2019) reporting standardised QoL outcome measures for patients with recurrent and metastatic HNC including ReRuNeR OPC were excluded, as a subgroup analysis for ReRuNeR OPC disease was not presented in the published data. Although attempts were made to obtain the OPC data from the authors, this was not possible at the time of writing.

Previous consensus guidelines have been published on the conduct of trials in primary disease management to include swallowing and communication standardised outcome tools focusing on a range of clinician-reported, instrumental evaluation and patient-reported outcome measures (Lefebvre, Ang, & Panel, 2009). It is clear from this systematic review that similar standards are neither available nor applied in trials looking at ReRuNeR disease. Further research is required to identify, develop and validate outcome measures for use in the recurrent setting to guide the development of similar recommendations for the conduct of trials focusing on ReRuNeR OPC.

5. Conclusion

This review has highlighted that only a small proportion of studies in ReRuNeR OPC report functional and QoL outcomes. These studies focus on surgical treatments, and functional and QoL outcomes for ReRuNeR OPC are not reported specifically in non-surgical trials. Patient experience or qualitative data have not been reported for patients with ReRuNeR OPC.

Where functional and QoL outcomes are reported in surgical trials, there does not appear to be consensus on the outcome tools which should be used, or the timepoints where data should be collected. Consequently, little or no comparison in data is possible across surgical trials. The reviewed literature does show that changes to function and QoL are likely to occur at least transiently. To accurately describe how ReRuNeR OPC and the available treatments impact on QoL and function, there needs to be further research driven by patient experience data highlighting areas of concern. Further research must focus on findings which could lead to a consensus on which tools, or combination of tools should be validated and used at which timepoints, to accurately provide a holistic and multidimensional profile of function and QoL for patients with ReRuNeR OPC.

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Conflict of interest

Professor Vinidh Paleri is a proctor for Intuitive Medical Inc. The other authors have no conflicts of interest to disclose.

References

Ang, K.K., Harris, J., Wheeler, R., Weber, R., Rosenthal, D.I., Nguyen-Tân, P.F.,... & Gillison, M.L. (2010). Human Papillomavirus and Survival of Patients with Oropharyngeal Cancer. *The New England Journal of Medicine*, *363*(1), 24-35. doi:10.1056/NEJMoa0912217

Atkins, S., Lewin, S., Smith, H., Engel, M., Fretheim, A., & Volmink, J. (2008). Conducting a meta-ethnography of qualitative literature: Lessons learnt. *BMC Medical Research Methodology*, *8*(1), 21. doi:10.1186/1471-2288-8-21

Brady, G.C., Hardman, J.C., Paleri, V., Harrington, K.J., & Roe, J.W. (2020). Changing paradigms in the treatment of residual/recurrent head and neck cancer: implications for dysphagia management. *Current Opinion in Otolaryngology & Head and Neck Surgery*, *28*(3), 165-171.

Burtness, B., Harrington, K.J., Greil, R., Soulières, D., Tahara, M., de Castro, G.,... & Bratland, Å. (2019). Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. *The Lancet*, *394*(10212), 1915-1928.

Charters, E., Bogaardt, H., Freeman-Sanderson, A., Ballard, K., Davies, S., Oates, J., & Clark, J. (2022). Swallowing and communication outcomes following primary transoral robotic surgery for advanced or recurrent oropharyngeal cancer: Case series. *International Journal of Speech-Language Pathology*, *24*(4), 407-416.

Chen, A.Y., Frankowski, R., Bishop-Leone, J., Hebert, T., Leyk, S., Lewin, J., & Goepfert, H. (2001). The development and validation of a dysphagia-specific quality-of-life questionnaire for patients with head and neck cancer: the MD Anderson dysphagia inventory. *Archives of Otolaryngology--Head & Neck Surgery*, *127*(7), 870-876.

Cohen, E.E., Soulières, D., Le Tourneau, C., Dinis, J., Licitra, L., Ahn, M.-J.,... & Mehra, R. (2019). Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised, open-label, phase 3 study. *The Lancet*, *393*(10167), 156-167.

Crary, M.A., Mann, G.D.C., & Groher, M.E. (2005). Initial psychometric assessment of a functional oral intake scale for dysphagia in stroke patients. *Archives of Physical Medicine and Rehabilitation*, *86*(8), 1516-1520.

Culié, D., Benezery, K., Chamorey, E., Ettaiche, M., Fernandez, J., Poissonnet, G.,... & Leysalle, A. (2015). Salvage surgery for recurrent oropharyngeal cancer: post-operative oncologic and functional outcomes. *Acta oto-Laryngologica*, *135*(12), 1323-1329.

D'Andréa, G., Bordenave, L., Nguyen, F., Tao, Y., Paleri, V., Ternam, S.,... & Gorphe, P. (2022). A prospective longitudinal study of quality of life in robotic-assisted salvage surgery for oropharyngeal cancer. *European Journal of Surgical Oncology*.

Dean, N.R., Rosenthal, E.L., Carroll, W.R., Kostrzewa, J.P., Jones, V.L., Renee' A.D.,... & Magnuson, J.S. (2010). Robotic-assisted surgery for primary or recurrent oropharyngeal carcinoma. *Archives of Otolaryngology--Head & Neck Surgery*, *136*(4), 380-384.

Degboe, A., Knight, S.L., Halling, K., Trigg, A., Al-Zubeidi, T., Aldhouse, N.,... & Rogers, S. N. (2018). Patients' experience

of recurrent/metastatic head and neck squamous cell carcinoma and their perspective on the EORTC QLQ-C30 and QLQ-H&N35 questionnaires: a qualitative study. *Journal of Patient-Reported Outcomes*, *2*(1), 1-13.

Falchook, A.D., Green, R., Knowles, M.E., Amdur, R.J., Mendenhall, W., Hayes, D.N.,... & Chera, B.S. (2016). Comparison of Patient- and Practitioner-Reported Toxic Effects Associated With Chemoradiotherapy for Head and Neck Cancer. *JAMA Otolaryngology–Head & Neck Surgery*, *142*(6), 517-523. doi:10.1001/jamaoto.2016.0656

FDA. (2016). *Assessment of the Use of Patient Experience Data in Regulatory Decision-Making*. https://www.fda.gov/drugs/development-approval-process-drugs/assessment-use-patient-experience-data-regulatory-decision-making

Frowen, J., Cotton, S., Corry, J., & Perry, A. (2010). Impact of demographics, tumor characteristics, and treatment factors on swallowing after (chemo) radiotherapy for head and neck cancer. *Head & Neck: Journal for the Sciences and Specialties of the Head and Neck*, *32*(4), 513-528.

Hardman, J.C., Holsinger, F.C., Brady, G.C., Beharry, A., Bonifer, A.T., D'Andréa, G.,... & Floros, P. (2022). Transoral Robotic Surgery for Recurrent Tumors of the Upper Aerodigestive Tract (RECUT): An International Cohort Study. *Journal of the National Cancer Institute*, *114*(10), 1400-1409.

Hutcheson, K.A., Barrow, M.P., Lisec, A., Barringer, D.A., Gries, K., & Lewin, J.S. (2016). What is a clinically relevant difference in MDADI scores between groups of head and neck cancer patients? *The Laryngoscope*, *126*(5), 1108-1113.

Jayaram, S.C., Muzaffar, S.J., Ahmed, I., Dhanda, J., Paleri, V., & Mehanna, H. (2016). Efficacy, outcomes, and complication rates of different surgical and nonsurgical treatment modalities for recurrent/residual oropharyngeal carcinoma: a systematic review and meta-analysis. *Head & Neck*, *38*(12), 1855-1861.

Kaneoka, A.S., Langmore, S.E., Krisciunas, G.P., Field, K., Scheel, R., McNally, E.,... & Cabral, H. (2013). The Boston residue and clearance scale: preliminary reliability and validity testing. *Folia Phoniatrica et Logopaedica*, *65*(6), 312-317.

Kano, S., Homma, A., Hayashi, R., Kawabata, K., Yoshino, K., Iwae, S.,... & Shiga, K. (2013). Salvage surgery for recurrent oropharyngeal cancer after chemoradiotherapy. *International Journal of Clinical Oncology*, *18*(5), 817-823.

Kim, S.Y., Park, J.E., Lee, Y.J., Seo, H.-J., Sheen, S.-S., Hahn, S.,... & Son, H.-J. (2013). Testing a tool for assessing the risk of bias for nonrandomized studies showed moderate reliability and promising validity. *Journal of Clinical Epidemiology*, *66*(4), 408-414.

Kostrzewa, J.P., Lancaster, W.P., Iseli, T.A., Desmond, R.A., Carroll, W.R., & Rosenthal, E.L. (2010). Outcomes of salvage surgery with free flap reconstruction for recurrent oral and oropharyngeal cancer. *The Laryngoscope*, *120*(2), 267-272.

Lefebvre, J.-L., Ang, K.K., & Panel, L.P.C. (2009). Larynx preservation clinical trial design: key issues and recommendations—a consensus panel summary. *International Journal of Radiation Oncology* Biology* Physics*, *73*(5), 1293-1303.

List, M.A., Ritter-Sterr, C., & Lansky, S.B. (1990). A performance status scale for head and neck cancer patients. *Cancer*, *66*(3), 564-569.

Mazerolle, P., Fuchsmann, C., Schultz, P., Benmoussa, N., Malard, O., Bozec, A.,... & Lasne-Cardon, A. (2022). Salvage total glossectomy and total glosso-laryngectomy: Are they worth it? A GETTEC French multicenter study. *Oral Oncology*, *130*, 105896.

Mehanna, H., Kong, A., & Ahmed, S.K. (2016). Recurrent head and neck cancer: United Kingdom National Multidisciplinary Guidelines. *Journal of Laryngology & Otology*, *130*, S181-S190. doi:10.1017/S002221511600061X

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D.G. (2010). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg*, *8*(5), 336-341.

NICE. (2020). *Pembrolizumab for untreated metastatic or unresectable recurrent head and neck squamous cell carcinoma*. Retrieved from https://www.nice.org.uk/guidance/ta661/chapter/1-Recommendations

O'Neil, K.H., Purdy, M., Falk, J., & Gallo, L. (1999). The dysphagia outcome and severity scale. *Dysphagia*, *14*(3), 139-145.

Paleri, V., Hardman, J., Brady, G., George, A., & Kerawala, C. (2020). Transoral Robotic Surgery for Residual and Recurrent Oropharyngeal Cancers. *Otolaryngologic Clinics of North America*, *53*(6), 1091-1108. doi:10.1016/j.otc.2020.07.016

Patel, S.N., Cohen, M.A., Givi, B., Dixon, B.J., Gilbert, R.W., Gullane, P.J.,... & Higgins, K.M. (2016). Salvage surgery for locally recurrent oropharyngeal cancer. *Head & Neck*, *38*(S1), E658-E664.

Patterson, J., McColl, E., Carding, P., & Wilson, J. (2018). Swallowing beyond six years post (chemo) radiotherapy for head and neck cancer; a cohort study. *Oral Oncology*, *83*, 53-58.

Philouze, P., Péron, J., Poupart, M., Pujo, K., Buiret, G., & Céruse, P. (2017). Salvage surgery for oropharyngeal squamous cell carcinomas: A retrospective study from 2005 to 2013. *Head & Neck*, *39*(9), 1744-1750.

Pipkorn, P., Sinha, P., Kallogjeri, D., Adkins, D., Thorstad, W.T., Rich, J.T., & Jackson, R.S. (2019). Outcomes of relapsed human papillomavirus-related oropharyngeal squamous cell carcinoma treated with curative intent. *Head & Neck*, *41*(5), 1312-1319.

Ringash, J., Bernstein, L.J., Devins, G., Dunphy, C., Giuliani, M., Martino, R., & McEwen, S. (2018). *Head and neck cancer survivorship: learning the needs, meeting the needs*. Paper presented at the Seminars in radiation oncology.

Rinkel, R.N., Verdonck-de Leeuw, I.M., van Reij, E.J., Aaronson, N.K., & Leemans, C.R. (2008). Speech Handicap Index in patients with oral and pharyngeal cancer: better understanding of patients' complaints. *Head Neck*, *30*(7), 868-874. doi: 10.1002/hed.20795. PMID: 18302270.

Roe, J.W., Carding, P.N., Dwivedi, R.C., Kazi, R.A., Rhys-Evans, P.H., Harrington, K.J., & Nutting, C.M. (2010). Swallowing outcomes following Intensity Modulated Radiation Therapy (IMRT) for head & neck cancer - a systematic review. *Oral Oncol*, *46*(10), 727-733. doi:10.1016/j.oraloncology.2010.07.012

Roe, J.W., Drinnan, M.J., Carding, P.N., Harrington, K.J., & Nutting, C.M. (2014). Patient-reported outcomes following parotid-sparing intensity-modulated radiotherapy for head and neck cancer. How important is dysphagia? *Oral Oncology*, *50*(12), 1182-1187.

Rogers, S.N., Gwanne, S., Lowe, D., Humphris, G., Yueh, B., & Weymuller Jr, E.A. (2002). The addition of mood and anxiety domains to the University of Washington quality of life scale. *Head & Neck: Journal for the Sciences and Specialties of the Head and Neck*, *24*(6), 521-529.

Rogers, S.N., Lowe, D., Yueh, B., & Weymuller Jr, E.A. (2010). The physical function and social-emotional function subscales of the University of Washington Quality of Life Questionnaire. *Archives of Otolaryngology–Head & Neck Surgery*, *136*(4), 352-357.

Rogers, S.N., Semple, C., Babb, M., & Humphris, G. (2016). Quality of life considerations in head and neck cancer: United Kingdom National Multidisciplinary Guidelines. *J Laryngol Otol*, *130*(S2), S49-s52. doi:10.1017/s0022215116000438

Rosenbek, J.C., Robbins, J.A., Roecker, E.B., Coyle, J.L., & Wood, J.L. (1996). A penetration-aspiration scale. *Dysphagia*, *11*(2), 93-98.

Sattar, R., Lawton, R., Panagioti, M., & Johnson, J. (2021). Meta-ethnography in healthcare research: a guide to using a meta-ethnographic approach for literature synthesis. *BMC Health Services Research*, *21*(1), 50. doi:10.1186/s12913-020-06049-w

Schache, A., Kerawala, C., Ahmed, O., Brennan, P.A., Cook, F., Garrett, M.,... & Mihai, R. (2021). British Association of Head and Neck Oncologists (BAHNO) standards 2020. *Journal of oral pathology & medicine: official publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology*, *50*(3), 262-273.

Schache, A.G., Powell, N.G., Cuschieri, K.S., Robinson, M., Leary, S., Mehanna, H.,... & Junor, E. (2016). HPV-related oropharynx cancer in the United Kingdom: an evolution in the understanding of disease etiology. *Cancer Research*, *76*(22), 6598-6606.

Schardt, C., Adams, M.B., Owens, T., Keitz, S., & Fontelo, P. (2007). Utilization of the PICO framework to improve searching PubMed for clinical questions. *BMC Medical Informatics and Decision Making*, *7*(1), 1-6.

Sharma, B.K., Contrera, K.J., Jia, X., Fleming, C., Lorenz, R.R., Koyfman, S.A.,... & Fritz, M. (2022). Outcomes After Oral Cavity and Oropharyngeal Salvage Surgery. *The Laryngoscope*.

Sweeny, L., Rosenthal, E.L., Clemons, L., Stevens, T.M., McIntosh, E.R.C., & Carroll, W.R. (2016). Outcomes after surgical salvage for recurrent oropharyngeal squamous cell carcinoma. *Oral Oncology*, *60*, 118-124.

Tassone, P., Wieser, M., Givens, A., Elliott, Z., Phillips, R., Curry, J.,... & Lamarre, E. (2022). Factors Leading to Gastrostomy Tube and Tracheostomy Requirements in Patients Treated Initially With Radiotherapy and Salvaged With Surgery and Free Flap Reconstruction. *The Laryngoscope*.

White, H., Ford, S., Bush, B., Holsinger, F.C., Moore, E., Ghanem, T.,... & Magnuson, J.S. (2013). Salvage surgery for recurrent cancers of the oropharynx: comparing TORS with standard open surgical approaches. *JAMA Otolaryngology–Head & Neck Surgery*, *139*(8), 773-777.

Williamson, A., Haywood, M., & Awad, Z. (2021). Feasibility of free flap reconstruction following salvage robotic-assisted resection of recurrent and residual oropharyngeal cancer in 3 patients. *Ear, Nose & Throat Journal*, *100*(10_suppl), 1113S-1118S.

Zafereo, M.E., Hanasono, M.M., Rosenthal, D.I., Sturgis, E.M., Lewin, J.S., Roberts, D.B., & Weber, R.S. (2009). The role of salvage surgery in patients with recurrent squamous cell carcinoma of the oropharynx. *Cancer: Interdisciplinary International Journal of the American Cancer Society*, *115*(24), 5723-5733.

Appendix 2: MD Anderson Dysphagia Inventory

M D Anderson Dysphagia Inventory (MDADI) (Chen et al., 2001)

This questionnaire asks for your views about your swallowing ability. This information will help us understand how you feel about swallowing.

The following statements have been made by people who have problems with their swallowing. Some of these statements may apply to you.

Please read each statement and circle the response which best reflects your experience in the past week.

G1. **My swallowing ability limits my day to day activities.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

E2. **I am embarrassed by my eating habits.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

F1. **People have difficulty cooking for me.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

P2. **Swallowing is more difficult at the end of the day.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

E7. **I do not feel self-conscious when I eat.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

E4. **I am upset by my swallowing problem.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

P6. **Swallowing takes great effort.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

E5. **I do not go out because of my swallowing problem**.

Strongly Agree Agree No opinion Disagree Disagree Strongly

F5. **My swallowing difficulty has caused me to lose income.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

P7. **It takes me longer to eat because of my swallowing problem**.

Strongly Agree Agree No opinion Disagree Disagree Strongly

P3. **People ask me, "Why can't you eat that?"**

Strongly Agree Agree No opinion Disagree Disagree Strongly

E3. **Other people are irritated by my eating problem.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

P8. **I cough when I try to drink liquids.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

F3. **My swallowing problems limit my social and personal life.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

F2. **I feel free to go out to eat with my friends, neighbors, and relatives.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

P5. **I limit my food intake because of my swallowing difficulty.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

P1. **I cannot maintain my weight because of my swallowing problem.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

E6. **I have low self-esteem because of my swallowing problem.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

P4. **I feel that I am swallowing a huge amount of food.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

F4. **I feel excluded because of my eating habits.**

Strongly Agree Agree No opinion Disagree Disagree Strongly

Appendix 3: Performance Status Scale in Head and Neck (PSS-HN) cancer standard operating procedure (SOP)

Purpose: To describe the procedures employed when evaluating the Normalcy of Diet, Place of Eating and Understandability of Speech scores using the Performance Status Scale for Head and Neck Cancer (PSS-HN) (List et al., 1990).

Scope: This SOP outlines the procedure to be carried out by researcher GB or trained Speech and Language Therapists (SLTs), performing the PSS-HN for CCR5242 FUNQoLR.

Procedure:

Timing: The PSS-HN assessment is to be carried out at the time points as specified in the protocol: at baseline, and at 3, 6 months following treatment initiation.

Assessor: The PSS-HN assessment should only be performed by appropriately trained staff researcher GB or trained SLT

Assessment: It is anticipated that the PSS-HN assessment will take approx. 5 minutes to complete. Scores for the PSS-HN assessment are determined following an unstructured interview. The scores range from 0 to 100, with higher scores indicating better performance. There are separate scores for each of the 3 subscales. The subscales with the various food items and options can be found in the associated guidance document.

Interviewer instructions for the three subscales are outlined below.

Normalcy of diet subscale:

- It is recommended that the assessor begins by asking the patient what kinds of food they have been eating, and what foods have been difficult to eat. Based on the patient's response, an item should be chosen at the low end of the scale.
- The assessor should move up the scale giving examples of foods in each category, asking the patient whether they are eating these foods. Even if a patient state they eat everything, enquiries should be made about specific items beginning with score 50 (soft chewable foods) and move upwards.
- The assessor should stop at an item at, and above, which the patient cannot eat. The patient receives the score below this item.
- If the patient eats a full diet, an enquiry should be made if the patient needs to drink more liquids than usual with meals. Eating a full diet with intake of extra fluids is scored 90.

- If the patient can take foods orally, but is also using a feeding tube, the score should be based on solid foods and indicate that a feeding tube is used.

Public eating subscale:

The patient should be asked:

- where they eat – in a restaurant, at home, at friends/relatives' homes, etc.
- with whom they eat – always alone, with family/friends, etc.
- if they choose different foods when eating with others – softer, less messy, etc.
- when was the last time they ate in a restaurant, MacDonald's, picnic, family reunion.
- The score beside the description that best fits the patient should be chosen.

A patient on a restricted diet (e.g., tube feeding, pureed foods) who does not eat in public but will join others in a public eating setting should be scored 75.

Inpatients should receive a score of 999.

Understandability of speech subscale:

This score is based on the interviewer's ability to understand the patient during conversation (in this case, based on conversation about normalcy of diet and public eating).

The score beside the description that best fits the patient should be chosen.

The assessor should assess the clarity of speech when not directly facing the patient, or whether face-to-face contact is required to understand them.

Normalcy of Diet	Eating in public	Speech intelligibility
100 Full diet with no restrictions 90 Full diet with liquid assistance 80 All meats 70 Carrots, celery (crunchy) 60 Dry bread & crackers 50 Soft, chewable foods (pasta, canned soft fruits, fish) 40 Soft foods requiring no chewing e.g., mashed potato, apple sauce 30 Puree 20 Warm liquids 10 Cold liquids 0 Non oral	100 No restriction of place, food or companion (eats out at any opportunity) 75 No restriction of place, but restricts diet when in public (eats anywhere, but may limit intake to less "messy" foods (e.g., liquids) 50 Eats only in presence of selected persons in selected places 25 Eats only at home in presence of selected persons 0 Always eats alone.	100 Always understandable 75 Understandable most of the time; occasional repetition necessary 50 Usually understandable; face-to-face 25 Never understandable; may use written. 0 No communication

Appendix 4:100 mL Water Swallow Test (100 mL WST) standard operating procedure (SOP)

Purpose: To describe the procedures employed when evaluating swallowing using the 100 mL WST (Patterson et al., 2011).

Scope: This SOP outlines the procedure to be carried out by researcher GB or trained Speech and Language Therapists (SLTs), performing the100 mL WST for CCR5242 FUNQoLR.

Procedure:
The 100 mL WST is to be carried out at the time points as specified in the protocol: at baseline and at 3, 6 months following treatment initiation.
Assessor: The 100 mL WST should only be performed by researcher GB or trained SLT
Equipment: Stopwatch, disposable cup, syringe or measuring cup and tap water

Assessment

- It is anticipated that the 100 mL WST assessment will take approx. 2 minutes to complete.
- Patient should be alert, in an upright, comfortable position. If possible, the patient should be allowed to rest for a few minutes after arrival to gain composure.
- If a patient is already using a head posture on fluids to eliminate aspiration/ penetration the WST should still be performed. This does not mean an immediate failure.
- It should also be re-emphasised that patients can take as much time as they need, and they may stop the test at any time if they feel uncomfortable.
- The assessor measures 100 mL of water (neither warm, nor chilled) in a plastic cup using the syringe or measuring cup.
- The patient is asked to drink all the water “as quickly as possible, without making themselves uncomfortable”, and without trying to talk during the assessment.
- The assessor simultaneously places their fingers gently on the patient’s thyroid cartilage to measure the number of swallows. Timing starts when the water touches the patient’s bottom lip and stops on the last swallow (including any breaks that might be required between swallows), including any final clearance swallow.

- The WST should not be performed if individuals have been recommended by their managing clinician to remain nil by mouth. If there are overt signs of significant aspiration (explosive coughing, prolonged coughing) or the patient is becoming distressed, the assessment and timing is stopped immediately.
- It is acceptable if patients cannot finish the test – inability to complete the test is an important result and should be recorded It is recommended that patients who are unable to complete the WST should be highlighted to SLTs for further review as per standard care.

Recording and Reporting

The assessor records:

- The number of swallows taken
- The time taken to complete the task (in seconds; round to nearest second)
- The amount of water the patient swallowed.
- The presence/absence of any signs of aspiration/ penetration (throat clear/ cough/ wet voice) during or after the task.

Appendix 5: IDDSI Functional Diet Scale Score (FDS) standard operating procedure (SOP)

Purpose: To describe the procedures employed when calculating the IDDSI-FDS score

Scope: This SOP outlines the procedure to be carried out by the researcher GB or trained SLT when assigning the IDDSI-FDS-score for CCR5242 FUNQoLR.

Procedure:

Timing: The IDDSI-FDS is to be carried out at the time points as specified in the protocol: at baseline, and at 3-, and 6-months following treatment initiation.

Assessor: The IDDSI-FDS assessment should only be performed by appropriately trained staff co-investigator GB or trained SLT

Assessment: It is anticipated that the IDDSI-FDS assessment will take approx. 2 minutes to complete. The IDDSI-FDS score is determined following an unstructured interview regarding the food and drinks currently being managed by the patient. The scores range from 0 to 8 with higher scores indicating better function. The IDDSI-FDS score corresponds to the number in the intersecting cell of the column showing the food level and the row showing the drink level recommended for the patient. An IDDSI Functional Diet Scale score of 0 applies for recommendations of nothing by mouth (NBM), with exclusive nonoral feeding (Steele et al., 2018).



FOOD LEVELS						
7	6	5	4	3	N/A (no food)	
3	2	1	N/A	N/A	0	N/A (no drinks)
4	3	2	1	N/A	N/A	4
5	4	3	2	1	N/A	3
6	5	4	3	2	1	2
7	6	5	4	3	2	1
8	7	6	5	4	3	0

DRINK LEVELS

Appendix 6: Dynamic Imaging Grade of Swallowing Toxicity for Flexible Endoscopic Evaluation of Swallowing (DIGEST-FEES) standard operating procedure

Purpose: To describe the procedures employed when evaluating swallowing toxicity using the DIGEST-FEES grading system.

Scope: This SOP outlines the procedure to be carried out by the researcher GB or trained Speech and Language Therapists (SLTs) when assigning a DIGEST-FEES grading for CCR5242 FUNQoLR.

Procedure:
Timing: The DIGEST-FEES is to be carried out at the time points as specified in the protocol: at baseline, and 3- and 6-months following treatment initiation

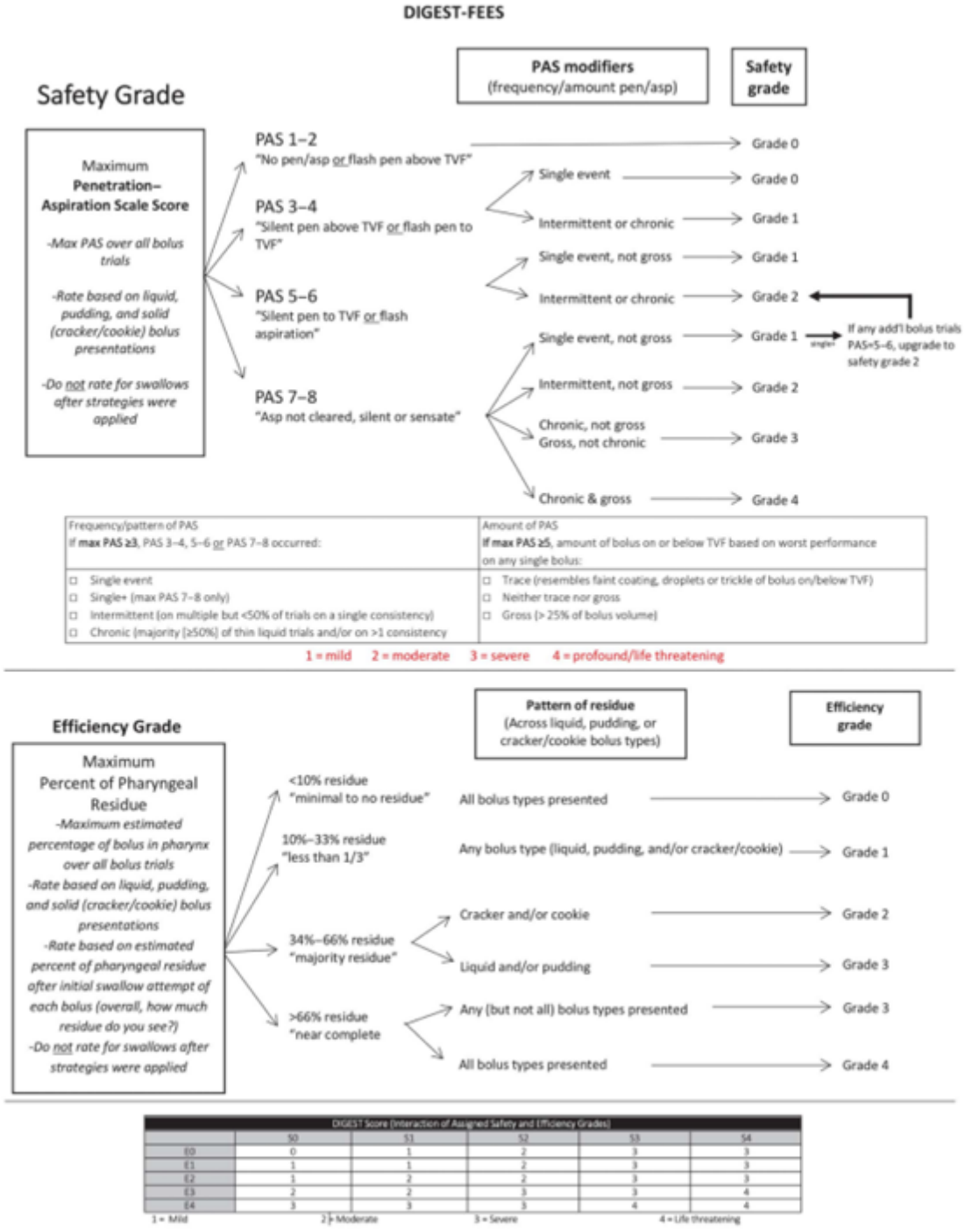
Assessor: the DIGEST-FEES rating should only be performed by co-investigator GB or appropriately trained SLT

Assessment: It is anticipated that the FEES procedure will take approx. 20 minutes to complete with DIGEST grading occurring immediately after. The Flexible Endoscopic Evaluation of Swallowing is carried out as per the guidelines in the Royal Marsden Flexible Endoscopic Evaluation of Swallowing (FEES) policy 1762. Based on the volume of residue and presence or absence of penetration/ aspiration, a DIGEST-FEES grading is assigned per the figure below (Starmer et al., 2021).

Bolus protocol:

	Volume	**Consistency**
1	5ml	Thin fluids
2	5ml	Thin fluids
3	10ml	Thin fluids
4	10ml	Thin fluids
5	Cup drinking	Thin fluids
6	5ml	Puree (custard)
7	5ml	Puree (custard)
8	Small bite	Soft easy chew (banana)
9	Small bite	Soft easy chew (banana)

10	Small bite	Regular diet (biscuit)
11	Small bite	Regular diet (biscuit)
12	Cup drinking	Thin fluids



Appendix 7: University of Washington Quality of Life Questionnaire v.4

University of Washington Quality of Life Questionnaire (UWQoLv4)

(Rogers et al 2002)

This questionnaire asks about your health and quality of life **over the past seven days**. Please answer all of the questions by checking one box for each question.

Check one box for each question 1-12:

1. **Pain**.

I have no pain.

There is mild pain not needing medication.

I have moderate pain - requires regular medication (codeine or nonnarcotic).

I have severe pain controlled only by narcotics.

I have severe pain, not controlled by medication.

2. **Appearance**. (Check one box:)

There is no change in my appearance.

The change in my appearance is minor.

My appearance bothers me but I remain active.

I feel significantly disfigured and limit my activities due to my appearance.

I cannot be with people due to my appearance.

3. **Activity**. (Check one box:)

I am as active as I have ever been.

There are times when I can't keep up my old pace, but not often.

I am often tired and have slowed down my activities although I still get out.

I don't go out because I don't have the strength.

I am usually in bed or chair and don't leave home.

4. **Recreation**. (Check one box:)

There are no limitations to recreation at home or away from home.

There are a few things I can't do but I still get out and enjoy life.

There are many times when I wish I could get out more, but I'm not up to it.

There are severe limitations to what I can do, mostly I stay at home and watch TV.

I can't do anything enjoyable.

5. **Swallowing**. (Check one box:)

I can swallow as well as ever.

I cannot swallow certain solid foods.

I can only swallow liquid food.

I cannot swallow because it "goes down the wrong way" and chokes me.

6. **Chewing**. (Check one box:)

I can chew as well as ever.

I can eat soft solids but cannot chew some foods.

I cannot even chew soft solids.

7. **Speech**. (Check one box:)

My speech is the same as always.

I have difficulty saying some words but I can be understood over the phone.

Only my family and friends can understand me.

I cannot be understood.

8. **Shoulder**. (Check one box:)

I have no problem with my shoulder.

My shoulder is stiff but it has not affected my activity or strength.

Pain or weakness in my shoulder has caused me to change my work.

I cannot work due to problems with my shoulder.

9. **Taste**. (Check one box:)

I can taste food normally.

I can taste most foods normally.

I can taste some foods.

I cannot taste any foods.

10. **Saliva**. (Check one box:)

My saliva is of normal consistency.

I have less saliva than normal, but it is enough.

I have too little saliva.

I have no saliva.

11. **Mood**. (Check one box:)

My mood is excellent and unaffected by my cancer.

My mood is generally good and only occasionally affected by my cancer.

I am neither in a good mood nor depressed about my cancer.

I am somewhat depressed about my cancer.

I am extremely depressed about my cancer.

12. **Anxiety**. (Check one box:)

I am not anxious about my cancer.

I am a little anxious about my cancer.

I am anxious about my cancer.

I am very anxious about my cancer.

Which issues have been the most important to you during the past 7 days?

Check up to 3 boxes.

Pain	Chewing	Mood
Appearance	Speech	Anxiety
Activity	Shoulder	
Recreation	Taste	
Swallowing	Saliva	

GENERAL QUESTIONS:

Compared to the month before you developed cancer, how would you rate your health-related quality of life? check one box:

Much better

Somewhat better

About the same

Somewhat worse

Much worse

In general, would you say your **health-related quality of life** during the past 7 days has been: check one box:

Outstanding

Very good

Good

Fair

Poor

Very poor

Overall quality of life includes not only physical and mental health, but also many other factors, such as family, friends, spirituality, or personal leisure activities that are important to your enjoyment of life. Considering everything in your life that contributes to your personal well-being, rate your **overall qualityoflife**duringthepast7days. Check one box:

Outstanding

Very good

Good

Fair

Poor

Very poor

Please describe any other issues (medical or nonmedical) that are important to your quality of life and have not been adequately addressed by our questions (you may attach additional sheets if needed).

Appendix 8: Chicago Priority Scale

Chicago Priority Scale

(Sharp et al., 1999)

Please rate the following list of statements and asked to rate in order of priority from 1 (most important) to 12 (least important):

	Priority rating 1-12
Being cured of my cancer	
Living as long as possible	
Having no pain	
Being able to swallow all foods and drinks	
Having a normal amount of energy for me	
Returning to my activities as soon as possible	
Having my speech understood easily	
Keeping my natural voice	
Having a comfortably moist mouth	
Keeping my appearance unchanged	
Being able to chew normally	
Keeping my sense of taste and smell	

Appendix 9: Study documents

The ROYAL MARSDEN
NHS Foundation Trust

Participant Information Sheet - Patients

FUNQOLR

Changes to function and quality of life and patient experience for patients undergoing treatments for recurrent oropharyngeal cancer.

CCR 5242

Study Sponsor: The Royal Marsden NHS Foundation Trust.

Contents

1. Invitation to participate in the above study
2. What is the purpose of this research?
3. Why have I been invited?
4. Do I have to take part?
5. Who is organising the research?
6. What does the research involve?
7. What are the alternatives to participation?
8. What are the possible disadvantages and risks of taking part?
9. What are the possible benefits of taking part?
10. How will we use information about you?
11. What are your choices about how your information is used?
12. More information about General Data Protection Regulations (GDPR)
13. Who has reviewed this study?
14. What if something goes wrong?
15. How will I find out the results of the study?
16. Contact for further information

1. Invitation to participate in the above study:

You have been invited to take part in the research study named above. This Participant Information Sheet will help you decide if you would like to take part. It sets out why we are doing the study, what your participation would involve, the benefits, the risks and what will happen after the study ends. We will go through this information with you and answer any questions you may have.

You can decide to take part in the research today or if you need a little more time to decide please do and we will contact you by telephone over the coming days to confirm if you would like to participate in the study. We would encourage you to speak about your participation with a family

friend/ relative. If you do not have anyone with you today we can arrange a video call so that you can discuss with a family friend/ relative.

In this research study we will use information from you and your medical records. We will only use information that we need for the research study. We will let very few people know your name or contact details, and only if they really need it for this study. Everyone involved in this study will keep your data safe and secure. We will also follow all privacy rules. At the end of the study we will save some of the data in case we need to check it. We will make sure no-one can work out who you are from the reports we write.

The information sheet tells you more about this.

2. What is the purpose of this research?

The purpose of this research project is to measure changes in communication, swallowing and quality of life in patients with a diagnosis of recurrent head and neck cancer, and to investigate patient and family friend/ relative experience of recurrent cancer of the head and neck (cancer which has returned after previous treatment).

3. Why have I been invited?

You have been invited to take part in this study as you are currently under the care of the Royal Marsden NHS Foundation Trust and are receiving treatment for recurrent head and neck cancer.

4. Do I have to take part?

No, taking part in this research is voluntary. If you decide to take part, you will be given this information sheet to keep and be asked to sign a consent form

If you do not want to take part, you do not need to. If you wish to withdraw from the research at any time during the study, you can do. If you do not wish to take part or wish to withdraw from the study at any time you do not have to give a reason and your treatment will not be affected in any way.

5. Who is organising the research?

The research is being carried out by the Head and Neck Unit at the Royal Marsden Hospital with Professor Vinidh Paleri (Consultant head and neck surgeon) and a research team including Grainne Brady (Speech & Language Therapist) and Dr Justin Roe (Consultant Speech & Language Therapist).

Grainne Brady is completing this research as part of her PhD training. This research is funded by the National Institute of Health Research (NIHR).

6. What does the research involve?

During the COVID19 pandemic, national guidelines have advised to minimise face-to-face contact with patients and recommended remote consultations. As such some of your study visits may be face-to-face or via telephone / video consultation.

If you are eligible and decide to take part in this study you will be required to provide written informed consent. If the consultation is being conducted face-to-face then consent will be obtained in-person with wet ink signature on the consent form. For remote telephone / video consultations, verbal consent will be sought and clearly documented in your medical notes. You will also be asked to sign a consent form which should be returned to the study team via:

- Post
- Email (please bring the original wet ink signed copy to your next hospital appointment)
- In person at your next face-to-face hospital appointment

The research involves (1) interviews with patients and family friends/ relatives and (2) assessment of communication and swallowing before, during and after any further treatments which you may be having.

(1) Interview:
You will be invited to take part in an interview with Grainne Brady which will take place before you start any treatment and again in six months-time. The interview will take place via video call so that you do not have to attend the hospital. The interview will take approximately 45 minutes where you will be asked about your experience of being diagnosed and treated for recurrent disease and your experience of any difficulties with eating, drinking, speech or voice and your overall quality of life. The interviews will be audio recorded and then transcribed anonymously. Once the interview has been transcribed the audio recording will be permanently deleted.

(2) Assessment of swallowing and communication:
You will meet with a member of the Speech & Language Therapy team before you start your treatment and again 3, 6 and 12 months following your treatment so that your speech, voice and swallowing can be assessed.
The assessment will take approximately 45 minutes and will include the following:

1. Two questionnaires asking questions about your eating/ drinking and your overall quality of life.
2. A meeting with a speech & language therapist (SLT) who will ask you some questions regarding what sort of foods/ fluids you can manage to eat. Your speech and voice quality will also be observed by the SLT.
3. You will complete a timed water swallow test- the SLT will see how quickly you can swallow 100mls of water (approximately ½ a small glass of water).

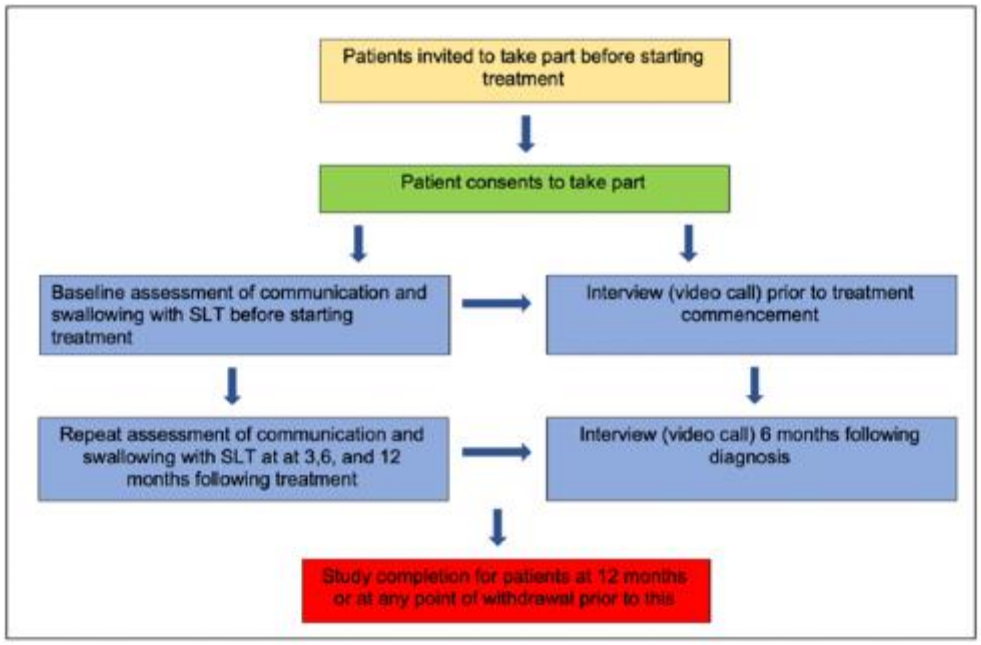
4. You will also be asked to rate a list of priorities/ concerns which are commonly associated with head and neck cancer, ranking this list from 1-12 depending on how important they are to you.
5. A camera test where a small camera (nasendoscope) will be inserted through your nose and into your throat- the SLT will then give you some food/ fluids so that your swallowing safety/ efficiency can be assessed. This assessment is called a Flexible Endoscopic Evaluation of Swallowing. Please see diagram 1. (This part of the assessment is optional and if you do not feel comfortable with the test it can be omitted).

Diagram 1: Flexible Endoscopic Evaluation of Swallowing



Please note that all local infection prevention and control measures will be strictly adhered to ensure that all examinations/ assessments are COVID secure. If you prefer all assessments number 1-5 can be undertaken via video consultation as an alternative to face-to-face appointments. Your research involvement is summarised in diagram 1.

Diagram 2: Research involvement



7. What are the alternatives to participation?

If you do not wish to take part in the study but you have concerns about swallowing, communication and/or quality of life, you will still see a SLT for assessment of swallowing, communication and related quality of life as per the normal care pathway. This assessment can take place at the Royal Marsden however, if more convenient a referral to your local SLT service can be made so that you can be seen closer to your home.

8. What are the possible disadvantages and risks of taking part?

There is the possibility that discussion of some of the issues raised during the interviews and questionnaires may cause some emotion. In the event that you do become upset by any of the issues raised, the interview can be discontinued at any time and support will be available from your Clinical Nurse Specialist. With regards to the examination of swallowing the procedures are safe and generally well tolerated by patients. Some patients find the camera somewhat uncomfortable going through the nose- if you do not wish to have the camera test you do not have to or if you consent to the camera test but find that it is too uncomfortable the examination can be discontinued. If you are found to have swallowing/ communication difficulties you will be referred to the SLT team at the Royal Marsden or locally depending on your preference.

9. What are the possible benefits of taking part?

Although taking part may not help you personally, you will be helping us understand your experience of recurrent head and cancer and the potential functional and quality of life changes, so we can develop our rehabilitation and support services for patients in the future.

10. How will we use information about you?

We will need to use information from you and from your medical records for this research project. This information will include your hospital number. People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study. Any data about you will be handled, processed, stored and destroyed in compliance with the Data Protection Act 2018.

11. What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

12. More information about General Data Protection Regulations (GDPR)

We need to provide you with information about how your data are processed for transparency purposes under the new General Data Protection Regulation, or GDPR as it is more commonly known. The Royal Marsden NHS Foundation Trust is the sponsor for this study. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. As previously detailed, The Royal Marsden NHS Foundation Trust will keep identifiable information about you for 5 years after the study has finished, in line with local policies and legal requirements.

The Royal Marsden NHS Foundation Trust will use your name, hospital number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from the Royal Marsden NHS Foundation Trust and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The only people in the Royal Marsden NHS Foundation Trust who will have access to information that identifies you will be people who need to contact you to contribute to your clinical care, facilitate study participation or audit the data

collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name or contact details.

You can find out more about how RM uses your information by contacting the Data Protection Officer at RM: dpo@rmh.nhs.uk

13. Who has reviewed this study?

This study has been reviewed and approved locally by the Royal Marsden Committee for Clinical Research (CCR).

All research in the NHS is reviewed by an independent group of people, called a Research Ethics Committee (REC) to protect your interests. This study has been reviewed and given a favourable opinion by the South Central-Hampshire B Research Ethics.

14. What if something goes wrong?

This is a non-invasive observational study, so it is unlikely to cause you harm. However, the Royal Marsden hospital has a duty of care to participants. NHS Litigation Authority will cover standard clinical negligence by employees, staff and health professionals employed by the Royal Marsden NHS Foundation Trust.

If you are unhappy about any aspect of this research, please contact the Patient Advice and Liaison Service (PALS) for further advice (0800 783 7176).

15. How will I find out the results of the study?

You will receive a letter detailing the main findings of the study once it has been completed.

16. Contact for further information

If you have any questions about the research or have questions about taking part and what that involves, please contact the speech & language therapy department on rmhslt.chelsea@nhs.net or by telephone on 02078082815.

Thank you very much for taking time to read this information sheet.

Grainne Brady BSc (Hons) MRes MRSCLT
HEE/ NIHR Clinical Doctoral Research Fellow
Department of Speech, Voice and Swallowing, The Royal Marsden NHS Foundation Trust
Department of Surgery and Cancer Imperial College London

The ROYAL MARSDEN
NHS Foundation Trust

Participant Information Sheet – Family / Friend / Relative

FUNQOLR

Changes to function and quality of life and patient experience for patients undergoing treatments for recurrent oropharyngeal cancer.

CCR 5242

Study Sponsor: The Royal Marsden NHS Foundation Trust.

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8. What are the possible benefits of taking part?
9. What are your choices about how your information is used?
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11. Who has reviewed this study?
12. What if something goes wrong?
13. How will I find out the results of the study?
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1. Invitation to participate in the above study

You have been invited to take part in the research study named above. This Participant Information Sheet will help you decide if you would like to take part. It sets out why we are doing the study, what your participation would involve, the benefits, the risks and what will happen after the study ends. We will go through this information with you and answer any questions you may have. You can decide to take part in the research today or if you need a little more time to decide please do and we will contact you by telephone over the coming days to confirm if you would like to participate in the study.

In this research study we will use information from you. We will only use information that we need for the research study. We will let very few people know your name or contact details, and only if they really need it for this study. Everyone involved in this study will keep your data safe and secure.

We will also follow all privacy rules. At the end of the study, we will save some of the data in case we need to check it. We will make sure no-one can work out who you are from the reports we write.

The information sheet tells you more about this.

2. What is the purpose of this research?

The purpose of this research project is to measure changes in communication, swallowing and quality of life in patients with a diagnosis of recurrent head and neck cancer (cancer which has returned after previous treatment) and what to find out what it is like for patients and their family friend/ relatives to experience these changes over time.

3. Why have I been invited?

You have been invited to take part in this study as your family friend/ relative is currently under the care of the Royal Marsden NHS Foundation Trust and are receiving treatment for recurrent head and neck cancer.

4. Do I have to take part?

No, taking part in this research is voluntary. If you decide to take part, you will be given this information sheet to keep and be asked to sign a consent form.

If you do not want to take part, you do not need to. If you wish to withdraw from the research at any time during the study, you can do so. If you do not wish to take part or withdraw from the study at any time you do not have to give a reason and your family friend's/ relative's treatment will not be affected in any way.

5. Who is organising the research?

The research is being carried out by the Head and Neck Unit at the Royal Marsden Hospital with Professor Vinidh Paleri (Consultant head and neck surgeon) and a research team including Grainne Brady (Speech & Language Therapist) and Dr Justin Roe (Consultant Speech & Language Therapist). Grainne Brady is completing this research as part of her PhD studies which she is completing at the Royal Marsden and Imperial College London, funded by the National Institute of Health Research (NIHR).

6. What does the research involve?

If you are eligible and decide to take part in this study, you will be required to provide written informed consent. If the consent consultation is being conducted face-to-face then consent will be obtained in-person with wet ink signature on the consent form. For remote telephone / video consultations, verbal

consent will be sought and clearly documented. You will also be asked to sign a consent form which should be returned to the study team via:

- Post
- Email (please bring the original wet ink signed copy to your next hospital appointment)
- In person at your next face-to-face hospital appointment

For patients the research involves two interviews and a series of assessments of communication and swallowing undertaken by the Speech and Language Therapy team.

For family friends/ relatives, the research involves two interviews, one completed when your friend/ relative is diagnosed and again at 6 months following their diagnosis.

During the interview you will be asked some questions in relation to your priorities and concerns about your family friend/ relative's swallowing, communication and overall quality of life. You can be interviewed either separately or together with your friend/relative who is having treatment. The interview will take approximately 45-60mins and will take place via video/ telephone call at a time that is convenient to you. Once the interview has taken place, the recording will be anonymised and transcribed using a professional transcription service. Once the interview has been transcribed anonymously the recording will be deleted immediately. The contents of the interview will then be analysed by a member of the research team to identify key themes.

7. What are the possible disadvantages and risks of taking part?

There is the possibility that discussion some of the issues raised during the interviews may cause some emotion. In the event that you do become upset by any of the issues raised, the interview can be discontinued immediately, and support will be available for your friend's/ family member's Clinical Nurse Specialist.

8. What are the possible benefits of taking part?

Although taking part may not help you personally, you will be helping us to understand your experience of recurrent head and neck cancer as a family friend/ relative so that we can develop our rehabilitation and support services for patients and their friends/ family members in the future.

How will we use information about you?

We will need to use information from you for this research project. This information will include:

- name
- telephone number
- email

People will use this information to do the research. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure. Once we have finished the study, we will keep

some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

9. What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

10. More information about General Data Protection Guidelines (GDPR)

We need to provide you with information about how your data are processed for transparency purposes under the new General Data Protection Regulation, or GDPR as it is more commonly known. The Royal Marsden NHS Foundation Trust is the sponsor for this study. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. As previously detailed, The Royal Marsden NHS Foundation Trust will keep identifiable information about you for 5 years after the study has finished, in line with local policies and legal requirements.

The Royal Marsden NHS Foundation Trust will use your name and contact details to contact you about the research study, and make sure that relevant information about the study is recorded to oversee the quality of the study. Individuals from the Royal Marsden NHS Foundation Trust and regulatory organisations may look at your research records to check the accuracy of the research study. The only people in the Royal Marsden NHS Foundation Trust who will have access to information that identifies you will be people who need to contact you to facilitate study participation or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name or contact details.

You can find out more about how RM uses your information by contacting the Data Protection Officer at RM: dpo@rmh.nhs.uk

11. Who has reviewed this study?

This study has been reviewed and approved locally by the Royal Marsden Committee for Clinical Research (CCR).

All research in the NHS is reviewed by an independent group of people, called a Research Ethics Committee (REC) to protect your interests. This study has been reviewed and given a favourable opinion by the South Central-Hampshire B Research Ethics.

some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

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The ROYAL MARSDEN
NHS Foundation Trust

Participant Information Sheet – Retrospective Patient (Part B)

FUNQOLR

Changes to function and quality of life and patient experience for patients undergoing treatments for recurrent oropharyngeal cancer.

CCR 5242

Study Sponsor: The Royal Marsden NHS Foundation Trust.

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7. What are the possible disadvantages and risks of taking part?
8. What are the possible benefits of taking part?
9. What are your choices about how your information is used?
10. More information about General Data Protection Regulations (GDPR)
11. Who has reviewed this study?
12. What if something goes wrong?
13. How will I find out the results of the study?
14. Contact for further information

1. Invitation to participate in the above study

You have been invited to take part in the research study named above. This Participant Information Sheet will help you decide if you would like to take part. It sets out why we are doing the study, what your participation would involve, the benefits, the risks and what will happen after the study ends. We will go through this information with you and answer any questions you may have. You can decide to take part in the research today or if you need a little more time to decide please do and we will contact you by telephone over the coming days to confirm if you would like to participate in the study.

In this research study we will use information from you. We will only use information that we need for the research study. We will let very few people know your name or contact details, and only if they really need it for this study. Everyone involved in this study will keep your data safe and secure. We will also follow all privacy rules. At the end of the study, we will save some of the data in case we need to check it. We will make sure no-one can work out who you are from the reports we write.

The information sheet tells you more about this.

2. What is the purpose of this research?

The purpose of this research project is to measure changes in communication, swallowing and quality of life in patients with a diagnosis of recurrent head and neck cancer (cancer which has returned after previous treatment) and what to find out what it is like for patients and their family friend/ relatives to experience these changes over time.

3. Why have I been invited?

You have been invited to take part in this study as you are under the care of the Royal Marsden NHS Foundation Trust and have undergone surgery for your recurrent head and neck cancer at least 12 months ago or you have started palliative treatments within the last 12 months have received/are receiving treatment for recurrent head and neck cancer.

4. Do I have to take part?

No, taking part in this research is voluntary. If you decide to take part, you will be given this information sheet to keep and be asked to sign a consent form.

If you do not want to take part, you do not need to. If you wish to withdraw from the research at any time during the study, you can do so. If you do not wish to take part or withdraw from the study at any time you do not have to give a reason and your treatment will not be affected in any way.

5. Who is organising the research?

The research is being carried out by the Head and Neck Unit at the Royal Marsden Hospital with Professor Vinidh Paleri (Consultant head and neck surgeon) and a research team including Grainne Brady (Speech & Language Therapist) and Dr Justin Roe (Consultant Speech & Language Therapist). Grainne Brady is completing this research as part of her PhD studies which she is completing at the Royal Marsden and Imperial College London, funded by the National Institute of Health Research (NIHR).

6. What does the research involve?

If you are eligible and decide to take part in this study, you will be required to provide written informed consent. If the consent consultation is being conducted face-to-face then consent will be obtained in-person with wet ink signature on the consent form. For remote telephone / video consultations, verbal consent will be sought and clearly documented. You will also be asked to sign a consent form which should be returned to the study team via:

- Post
- Email (please bring the original wet ink signed copy to your next hospital appointment)
- In person at your next face-to-face hospital appointment

Your participation will include taking part in an interview with a member of the research team. The interview will take place at least 12 months after your surgery / within 12 months of commencing your palliative treatment(s) for your head and neck cancer.

During the interview you will be asked some questions in relation to your priorities and concerns about your swallowing, communication and overall quality of life.. The interview will take approximately 45-60mins and will take place via video/ telephone call at a time that is convenient to you. The interview will be audio recorded and transcribed anonymously using a professional transcription service. Once the interview has been transcribed anonymously the recording will be deleted immediately. The contents of the interview will then be analysed by a member of the research team to identify key themes.

7. What are the possible disadvantages and risks of taking part?

There is the possibility that discussion some of the issues raised during the interviews may cause some emotion. In the event that you do become upset by any of the issues raised, the interview can be discontinued immediately, and support will be available for you.

8. What are the possible benefits of taking part?

Although taking part may not help you personally, you will be helping us to understand your experience of recurrent head and neck cancer so that we can develop our rehabilitation and support services for patients and their friends/ family members in the future.

How will we use information about you?

We will need to use information from you for this research project. This information will include:

- name
- telephone number
- email

People will use this information to do the research. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

9. What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

10. More information about General Data Protection Guidelines (GDPR)

We need to provide you with information about how your data are processed for transparency purposes under the new General Data Protection Regulation, or GDPR as it is more commonly known. The Royal Marsden NHS Foundation Trust is the sponsor for this study. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. As previously detailed, The Royal Marsden NHS Foundation Trust will keep identifiable information about you for 5 years after the study has finished, in line with local policies and legal requirements.

The Royal Marsden NHS Foundation Trust will use your name and contact details to contact you about the research study, and make sure that relevant information about the study is recorded to oversee the quality of the study. Individuals from the Royal Marsden NHS Foundation Trust and regulatory organisations may look at your research records to check the accuracy of the research study. The only people in the Royal Marsden NHS Foundation Trust who will have access to information that identifies you will be people who need to contact you to facilitate study participation or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name or contact details.

You can find out more about how RM uses your information by contacting the Data Protection Officer at RM: dpo@rmh.nhs.uk

11. Who has reviewed this study?

This study has been reviewed and approved locally by the Royal Marsden Committee for Clinical Research (CCR).

All research in the NHS is reviewed by an independent group of people, called a Research Ethics Committee (REC) to protect your interests. This study has been reviewed and given a favourable opinion by the South Central-Hampshire B Research Ethics.

12. What if something goes wrong?

This is a non-invasive observational study, so it is unlikely to cause you harm. However, the Royal Marsden hospital has a duty of care to participants. NHS Litigation Authority will cover standard clinical negligence by employees, staff and health professionals employed by the Royal Marsden NHS Foundation Trust.

If you are unhappy about any aspect of this research, please contact the Patient Advice and Liaison Service (PALS) for further advice (0800 783 7176).

13. How will I find out the results of the study?

You will receive a letter detailing the main findings of the study once it has been completed.

14. Contact for further information

If you have any questions about the research or have questions about taking part and what that involves, please contact the speech & language therapy department on rmhslt.chelsea@nhs.net or by telephone on 02078082815.

Thank you very much for taking time to read this information sheet.

Grainne Brady BSc (Hons) MRes MRSCLT
HEE/ NIHR Clinical Doctoral Research Fellow
Department of Speech, Voice and Swallowing, The Royal Marsden NHS Foundation Trust
Department of Surgery and Cancer Imperial College London

The ROYAL MARSDEN
NHS Foundation Trust

Informed consent form (patients)

Study Title: Changes to function and quality of life and patient experience for patients undergoing treatments for recurrent oropharyngeal cancer 'FUNQOLR'

Study Site: The Royal Marsden NHS Foundation Trust

Principal Investigator: Professor Vinidh Paleri

Participant Trial ID: .....

Please initial each box

1. I confirm that I have read and understand the information sheet dated _____ version_____ for the above study and have had the opportunity to consider the information, ask questions and have these answered satisfactorily.	
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	
3. I agree to take part in Part A (assessment of swallowing/ communication over time) of the above study.	
4. I agree to take part in Part B (interviews) of the above study.	
5. I agree to my GP being informed of my participation.	

Name of Participant	Date	Signature
Researcher	Date	Signature

Where consent has been obtained remotely, countersignature required:

_____	_____	_____
Name of Person taking consent	Date	Signature

Distribution list:1 copy for participant, 1 copy for research study file, 1 copy (original) for participant's medical notes

The ROYAL MARSDEN
NHS Foundation Trust

Informed consent form (family members / significant others)

Study Title: Changes to function and quality of life and patient experience for patients undergoing treatments for recurrent oropharyngeal cancer 'FUNQOLR'

Study Site: The Royal Marsden NHS Foundation Trust

Principal Investigator: Professor Vinidh Paleri

Participant Trial ID: .....

Please initial each box

1. I confirm that I have read and understand the information sheet dated _____ version_____ for the above study and have had the opportunity to consider the information, ask questions and have these answered satisfactorily.	
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	
3. I agree to take part in Part B of the above study (interviews).	

Name of Participant	Date	Signature
Researcher	Date	Signature

Where consent has been obtained remotely, countersignature required:

_____	_____	_____
Name of Person taking consent	Date	Signature

Distribution list: 1 copy for participant, 1 copy for research study file

The ROYAL MARSDEN
NHS Foundation Trust

Informed consent form – Retrospective Patients (Part B)

Study Title: Changes to function and quality of life and patient experience for patients undergoing treatments for recurrent oropharyngeal cancer 'FUNQOLR'

Study Site: The Royal Marsden NHS Foundation Trust

Principal Investigator: Professor Vinidh Paleri

Participant Trial ID: .....

Please initial each box

1.	I confirm that I have read and understand the information sheet dated _____ version_____ for the above study and have had the opportunity to consider the information, ask questions and have these answered satisfactorily.	
2.	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	
3.	I agree to take part in Part B (interviews) of the above study as outlined in the information sheet dated _____ version_____	

Name of Participant	Date	Signature
Researcher	Date	Signature

Where consent has been obtained remotely, countersignature required:

_____	_____	_____
Name of Person taking consent	Date	Signature

Distribution list:1 copy for participant, 1 copy for research study file, 1 copy (original) for participant's medical notes

Appendix 10: Interview topic schedule

- Tell me about your experience of being diagnosed/ your partner/ family member being diagnosed with recurrent head and neck cancer?
- Tell me about the treatment options discussed and any decisions you may have made?
- Tell me about any potential side effects of treatment which you are/were aware of?
- What are/were your concerns regarding further treatment?
- What are your priorities at present?
- Tell me about your/ your partner's/ family member's speech and swallowing?
- Is there anything else that you think I should know to help me understand your situation?
- Is there anything you would like to ask me?

Appendix 11: Reflexive log

As discussed in Chapter 4 when reviewing the methodology of this study, I emphasised the importance of reflexivity throughout the research process. I wanted to both acknowledge and appreciate my role in the collection, analysis and interpretation of data during this research process. To do this I maintained a reflexive log to document any potential personal, interpersonal, methodological and contextual biases which may have been present.

The reflexive log kept by myself throughout this research firstly set out my own position as a clinician and researcher which I could refer to as I reflected on data collection, analysis and integration. Below is the position statement I devised at the outset of my research, and some excerpts from my reflective log which I kept throughout the research.

Personal and professional background:
I am a Speech & Language Therapist with over 16 years' experience working in the field of head and neck cancer. For the past seven years, much of my work has been with patients with recurrent head and neck cancer, predominately treated with salvage surgery. I have worked in the National Health Service for 12 years now, working solely at the Royal Marsden NHS Foundation Trust. I have always been very focused on evidence based practice and patient experience. I have some experience in quantitative research from my master's and limited experience in analysing interview data for some service evaluation projects. However, I am a novice when it comes to qualitative research and relied heavily on the expertise of my research team and supervisors. Although a novice researcher, my experience in working with patients, made interviewing very enjoyable. I was not apprehensive about engaging with participants for interviews, it was the analysis of the data which I was much more apprehensive about. I felt a huge responsibility with the qualitative data to ensure that the analysis was as robust as possible given the generosity that the patient and caregivers demonstrated in sharing their very personal experiences.
Below are some excerpts from the reflective diary- these have been transcribed from the paper journal I maintained throughout the research.

20th December 2022 (prospective participant- interview at timepoint one- individual interview)
First interview of two today with ___. He is due to start his immunotherapy next week. I have never met this gentleman before but he recalled meeting my SLT colleagues during his previous radiation treatment. At times it was quite difficult to keep this gent on track he asked a number of times why I had chosen to do research in rOPC and how I felt it was going to

change things. He mentioned a number of times at the end of the interview how grateful he was for the care he has received and also for having the opportunity to take part in the interview. I immediately felt guilty that a patient would have to feel grateful for receiving care.

20th December 2022 (retrospective participant and carer – joint interview with patient and wife)
Interview with ___ and his wife today. We did it at the hospital as he was coming for another appointment and he said he finds video calls very difficult as they rarely pick up the output from his text to speech app and doesn't like doing long conversations using the chat function on video calls. I recall meeting this gentleman once before, I was providing cover for one of the other therapists and saw him jointly with the surgeon. He said he didn't recall me but I know he knows the SLT team very well. I was aware of his case as he has been discussed at our case discussions, and some other members of the team have asked my advice on his management. I was very impressed during the interview how much time his wife gave for him to respond- she never interjected until she was sure he was finished or only when I pointed a question/ comment towards her. She became quite emotional at times recalling their joint experiences including that of their daughter. I was very impressed how he has focuses on what he can do to enjoy life and appears not to dwell on what he has lost (tracheostomy and gastrostomy dependent- uses a text to speech app to communicate).

9th Feb 2023 *(prospective participant- interview at timepoint one- individual)*
Interview with ___ one day before her salvage TORS surgery. The signal was actually quite bad so I did take lots of field notes and will need to go through the transcription with these. This lady became very upset on a number of occasions during the interview. It was very difficult for me not to slip into clinician role and provide advice/ reassurance as she clearly felt very informed about her upcoming procedure. At the end of the interview, I made sure she had the contact details for her CNS and sought her permission to contact her so that they could have some further discussions. She seemed happy with this at the end of the conversation.

15th November 2023 *(prospective participant- interview at timepoint two- patient and his wife)*
It was lovely to see ___ with his wife for their second follow up interview today. He is now six months into immunotherapy as part of a clinical trial. I collected his quantitative measures when he was in the hospital for an appointment earlier this week. He referred to my assessment throughout the interview when I asked questions about eating/drinking. As per his baseline interview this was done in the evening when he and his wife were finished work. They had just had their dinner. I didn't conceal the fact that I was at home too and before the

interview started, we joked about having online shopping deliveries due to arrive. In comparison to when I saw him in the clinic room earlier this week- he seemed more relaxed. This may have been because I was clearly at home also and our conversation seemed more like a catch up than an interview.